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Reviewing the articles' conformity to the publishing standards of the Journal, typesetting, reviewing and editing the manuscripts and abstracts in English and publishing process are realized by Galenos.

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Aims and Scope

European Journal of Geriatrics and Gerontology is an international, open access, scientific, peer-reviewed journal in accordance with independent, unbiased, and double-blinded peer-review principles of the Academic Association of Geriatrics. It is a double peer-reviewed journal published quarterly in April, August and December electronically. The publication language of the journal is English.

Our mission is to provide practical, timely, and relevant clinical and basic science information to physicians and researchers practicing the geriatrics and gerontology worldwide. Topics of European Journal of Geriatrics and Gerontology include;

Aging
Aging Biology
Alzheimer's Disease
Biogerontology
Bone health in older people
Cell Biology
Clinical Geriatrics
Clinical Geropsychology
Cognitive Disorders
Demography of Older Populations
Dental and Oral Health
Delirium
Diabetes Mellitus
Dizziness
Disability
Drugs & Aging
Experimental Gerontology
Economics of ageing
Falls
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Geriatric Bioscience
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Geriatric Depression
Geriatric Emergency Medicine
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Geriatric Rheumatology
Geriatric Trauma
Geriatric Urology
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Geriatric Syndromes
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Home and Community-Based Services
Incontinence
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Orthogeriatrics
Polypharmacy
Parkinsons Disease
Parkinsonian syndromes
Pressure Sores
Psychological Gerontology
Sarcopenia
Sleep Disorders
Syncope
Social Gerontology
Stroke Medicine

Special features include rapid communication of important timely issues, surgeon' workshops, interesting case reports, surgical techniques, clinical and basic science review articles, guest editorials, letters to the editor, book reviews, and historical articles in geriatrics and gerontology.

The target audience of the journal includes physicians working in the fields of geriatrics and gerontology and all other health professionals who are interested in these topics.

The evaluation and publication processes of the European Journal of Geriatrics and Gerontology are shaped in acceptance with the guidelines of ICMJE (International Committee of Medical Journal Editors), COPE (Committee of Publication Ethics), EASE (European Association of Science Editors), and WAME (World Association of Medical Editors). The journal also is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

European Journal of Geriatrics and Gerontology is indexed in the TUBITAK/ULAKBIM, EBSCO, Index Copernicus, Gale, ProQuest, J-Gate, CABI, Türk Medline and Turkey Citation Index.

All manuscripts should be submitted through the journal's web page at www.ejgg.org Instructions for authors, technical information, and other necessary forms can be accessed over this web page. Authors are responsible for all content of the manuscripts.

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Submission is considered on the conditions that papers are previously unpublished and are not offered simultaneously elsewhere; that authors have read and approved the content, and all authors have also declared all competing interests; and that the work complies with the Ethical Approval and has been conducted under internationally accepted ethical standards. If ethical misconduct is suspected, the Editorial Board will act in accordance with the relevant international rules of publication ethics (i.e., COPE guidelines).

Editorial policies of the journal are conducted as stated in the rules recommended by the Council of Science Editors and reflected in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (http://www.icmje.org/). Accordingly, authors, reviewers, and editors are expected to adhere to the best practice guidelines on ethical behavior contained in this statement.

Submitted manuscripts are subjected to double-blinded peer-review. The scientific board guiding the selection of the papers to be published in the journal consists of elected specialists of the journal and, if necessary, selected from national and international experts in the relevant field of research. All manuscripts are reviewed by the editor, section associate editors and at least three internal and external expert reviewers. All research articles are interpreted by a statistical editor as well.

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Clinical Geropsychology
Cognitive Disorders
Demography of Older Populations
Dental and Oral Health
Delirium
Diabetes Mellitus
Dizziness
Disability
Drugs & Aging
Experimental Gerontology
Economics of ageing
Falls
Frailty
Geriatrics
Geriatric Bioscience
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Healthy Aging
Home and Community-Based Services
Incontinence
Long-Term Care
Orthogeriatrics
Polypharmacy
Parkinsons Disease
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Psychological Gerontology
Sarcopenia
Sleep Disorders
Syncope
Social Gerontology
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surgeon' workshops, interesting case reports, surgical techniques, clinical and basic science review articles, guest editorials, letters to the editor, book reviews, and historical articles in geriatrics and gerontology.

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The European Journal of Geriatrics and Gerontology accepts invited review articles, research articles, brief reports, case reports, letters to the editor, and images that are relevant to the scope of geriatrics and gerontology, on the condition that they have not been previously published elsewhere. Basic science manuscripts, such as randomized, cohort, cross-sectional, and case control studies, are given preference. All manuscripts are subject to editorial revision to ensure they conform to the style adopted by the journal. There is a double blind kind of reviewing system.

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Manuscripts should be prepared according to ICMJE guidelines (http://www.icmje.org).

Original manuscripts require a structured abstract. Label each section of the structured abstract with the appropriate subheading (Objective, Materials and Methods, Results, and Conclusion). Case reports require short unstructured abstracts. Letters to the editor do not require an abstract. Research or project support should be acknowledged as a footnote on the title page.

Technical and other assistance should be provided on the title page.

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CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA 2001; 285: 1987-91) (http://www.consort-statement.org/);

PRISMA statement of preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org/);

STARD checklist for reporting studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al., for the STARD Group. Towards complete and accurate reporting of diagnostic accuracy studies: the STARD initiative. Ann Intern Med 2003;138:40-4.) (http://www.stard-statement.org/);

STROBE statement, a checklist of items that should be included in reports of observational studies (http://www.strobe-statement.org/);

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

Title Page

Title: The title should provide important information regarding the manuscript's content.

The title page should include the authors' names, degrees, institutional/professional affiliations, a short title, abbreviations, keywords, financial disclosure statement, and conflict of interest statement. If a manuscript includes authors from more than one institution, each author's name should be followed by a superscript number that corresponds to their institution, listed separately. Please provide contact information for the corresponding author, including name, e-mail address, and telephone and fax numbers.

Running Head: The running head should not be more than 40 characters, including spaces, and should be located at the bottom of the title page.

Word Count: A word count for the manuscript, excluding abstract, acknowledgements, figure and table legends, and references, should be provided, not exceeding 3000 words. The word count for an abstract should not exceed 250 words.

Conflict of Interest Statement: This statement must be included in each manuscript to prevent potential conflicts of interest from being overlooked. In case of conflicts of interest, every author should complete the ICMJE general declaration form, which can be obtained at: http://www.icmje.org/coi_disclosure.pdf.

Abstract and Keywords: The second page should include an abstract that does not exceed 250 words. Moreover, as various electronic databases integrate only abstracts into their index, significant findings should be presented in the abstract.

Abstract

Objective: The abstract should state the objective (the purpose of the study and hypothesis) and summarize the rationale for the study.

Materials and Methods: Important methods should be written, respectively.

Results: Important findings and results should be provided here.

Conclusion: The study's new and important findings should be highlighted and interpreted.

Other types of manuscripts, such as case reports, reviews and others, will be published according to uniform requirements. Provide at least 3 keywords below the abstract to assist indexers. Use terms from the Index Medicus Medical Subject Headings List (for randomized studies, a CONSORT abstract should be provided (http://www.consort-statement.org).

Original Articles

Original articles should have the following sections;

Introduction: The introduction should include an overview of the relevant literature presented in summary form (one page), and whatever remains engaging, unique, problematic, relevant, or unknown about the topic must be specified. The introduction should conclude with the rationale for the study, its design, and its objective(s).

Materials and Methods: Clearly describe the selection of observational or experimental participants, such as patients, laboratory animals, and controls, including inclusion and exclusion criteria and a description of the source population. Identify the methods and procedures in sufficient detail to allow other researchers to reproduce your results. Provide references to established methods (including statistical methods), provide references to brief modified methods, and provide the rationale for using them and an evaluation of their limitations. Identify all drugs and chemicals used, including generic names, doses, and routes of administration. The section should include only available information when the plan or protocol for the study was devised on STROBE (http://www.strobe-statement.org).

Statistics: Describe the statistical methods used in enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. Statistically essential data should be given in the text, tables and figures. Provide details about randomization, describe treatment complications, provide the number of observations, and specify all computer programs used.

Results: Present your results in logical sequence in the text, tables, and figures. Do not present all the data provided in the tables and/or figures in the text; emphasize and/or summarize only essential findings, results, and observations in the text. Clinical studies provide the number of samples, cases, and controls included in the study. Discrepancies between the planned number and obtained number of participants should be explained. Comparisons and statistically significant values (i.e. p-value and confidence interval) should be provided.

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Discussion: This section should include a discussion of the data. New and noteworthy findings/results and the conclusions they lead to should be emphasized. Link the conclusions with the study's goals, but avoid unqualified statements and conclusions not completely supported by the data. Do not repeat the findings/results in detail; important findings/results should be compared with those of similar studies in the literature, along with a summarization. In other words, similarities or differences in the obtained findings/results with those previously reported should be discussed.

Study Limitations: Limitations of the study should be detailed. In addition, an evaluation of the implications of the obtained findings/results for future research should be outlined.

Conclusion: The conclusion of the study should be highlighted.

References

Cite references in the text, tables, and figures with numbers in parentheses. Number references consecutively according to the order they first appear in the text. Journal titles should be abbreviated according to the style used in Index Medicus (consult List of Journals Indexed in Index Medicus). Include among the references any paper accepted but not yet published, designating the journal and followed by, in press. Authors are solely responsible for the accuracy of all references.

Examples of References:

1. List All Authors

Bonanni E, Tognoni G, Maestri M, Salvati N, Fabbrini M, Borghetti D, DiCoscio E, Choub A, Sposito R, Pagni C, Iudice A, Murri L. Sleep disturbancesin elderly subjects: an epidemiological survey in an Italian district. Acta Neurol Scand 2010;122:389-397.

2. Organization as Author

American Geriatrics Society 2015 Updated Beers Criteria Expert panel. American geriatrics society 2015 updated Beer criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2015;63: 2227-2246.

3. Complete Book

Ham RJ, Sloane PD, Warshaw GA, Potter JF, Flaherty E. Ham's primary care geriatrics: a case-based approach, 6th ed. Philadelphia, Elsevier/Saunders, 2014.

4. Chapter in Book

BG Katzung. Special Aspects of Geriatric Pharmacology, In:Bertram G. Katzung, Susan B. Masters, Anthony J. Trevor (Eds). Basic and Clinical Pharmacology. 10th edition, Lange, Mc Graw Hill, USA 2007, pp 983-90.

5. Abstract

Reichenbach S, Dieppe P, Nuesch E, Williams S, Villiger PM, Juni P. Association of bone attrition with knee pain, stiffness and disability; a cross-sectional study. Ann Rheum Dis 2011;70:293-8. (abstract).

6. Letter to the Editor

Rovner B. The Role of the Annals of Geriatric Medicine and Research as a Platform for Validating Smart Healthcare Devices for Older Adults. Ann Geriatr. 2017;21:215-216.

7. Supplement

Garfinkel D. The tsunami in 21st century healthcare: The age-related vicious circle of co-morbidity - multiple symptoms - over-diagnosis - over treatment - polypharmacy [abstract]. J Nutr Health Aging 2013;17(Suppl 1):224-227.

Case Reports

Case reports should be structured as follows:

Abstract: An unstructured abstract that summarizes the case.

Introduction: A brief introduction (recommended length: 1-2 paragraphs).

Case Presentation: This section describes the case in detail, including the initial diagnosis and outcome.

Discussion: This section should include a brief review of the relevant literature and how the presented case furthers our understanding of the disease process.

Review Articles

Review articles should not include more than 100 references. Reviews should include a conclusion in which a new hypothesis or study about the subject may be posited. Do not publish methods for literature search or level of evidence. Authors who will prepare review articles should already have published research articles on the relevant subject. There should be a maximum of two authors for review articles.

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Authors can submit for consideration an illustration and photos that are interesting, instructive, and visually attractive, along with a few lines of explanatory text and references. Images in Geriatrics and Gerontology can include no more than 500 words of text, 5 references, and 3 figures or tables. No abstract, discussion or conclusion is required, but please include a brief title.

Letters to the Editor

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ORIGINAL RESEARCH

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Teaching in Geriatrics: The Potential of a Structured Written Feedback for the Improvement of Lectures

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Abstract

Objective: Lectures are worldwide still a widespread concept of knowledge transfer. The module "Medicine of Ageing and of People of Age" (geriatrics) at the Hannover Medical School uses lectures as one means of knowledge transfer.

Materials and Methods: This study aimed to analyze whether a criteria-based written feedback for the lecturers can improve their teaching. In a prospective longitudinal design 17 lectures are rated by a trained student reviewer in two consecutive trimesters according to a questionnaire covering 22 items. The students' perceptions are evaluated using a standardized query with five additional questions.

Results: The overall rating of the lectures (1= not apparent; 5= excellent) improves from 3.8 (T0) to 4.4 points in the second evaluation (T1) (+0.59 points, $p<0.001$). Ratings in all three main categories (content/structure, presentation, visualization) increase significantly in the second series of lectures. A significant amelioration can be seen in six of the 22 items, especially in "content/structure". The perceptions of the students show a trend for a better rating, too.

Conclusion: Lecturers can benefit from an additional feedback to their lectures. The review should follow a standardized procedure and should be communicated transparently. Therefore, an individual criteria-based review by a trained student reviewer is a viable solution.

Keywords: Geriatrics, teaching, evaluation, university, lectures

Introduction

Lectures are the basis of knowledge transfer and should be evaluated according to content and structural criteria. In order to continuously improve the quality of teaching, measurement and evaluation of lectures is crucial (1). The quality of good teaching is based on different criteria examined in the literature. However, there is no unanimous definition of "good teaching", but rather many different points of view, e.g., student satisfaction, outcome of teaching, or the qualification of the teachers. There is also a strong heterogeneity among evaluation questionnaires. This study focuses on an individualized, criteria-based written feedback from a trained student reviewer. Each lecture is evaluated separately with respect to content, organization, and quality.

The module "Medicine of Ageing and of People of Age" (geriatrics) at the Hannover Medical School is taught in the fourth of six years of undergraduate medical education and is divided into a theoretical and a practical part. The optional 20 lectures with 45 minutes each (= one teaching hour) take place within one week. Practical aspects are covered in 10 mandatory teaching units of 90 minutes each, which also include patient contact in the hospital. With a total teaching time of 20 hours, the module is above the national average of 8.3 hours (2). Because of their large proportion and voluntary nature, it is especially important to make the lectures attractive for the students. When it comes to quality assessment, students' evaluations are widely recognized as a feedback tool. However, it is sometimes difficult for the module organizer to decide whether a lecturer

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is teaching successfully since, the central university evaluation forms usually cannot provide feedback for every single lecture. Instead, as a compromise, an overall assessment is recorded that often combines different forms of instruction (seminars, bedside teaching, lectures) as well as different lecturers.

For high-quality lecturing, some features are important. Copeland et al. (1) validated some predictors for successful learning such as clear and organized lectures, a case-based format, encouraging to engage the audience's attention, identifying important points or presenting relevant material with readable slides. According to the Kirkpatrick model, all levels (reaction, learning, behavioral change, organizational performance) should be implemented when delivering feedback to the instructors (3). The study aims to analyze if a criteria-based written feedback for the lecturers can improve the lectures in terms of content, organization and quality. In addition, the study also considered whether the consequence of this feedback was reflected by the general students' evaluations.

Materials and Methods

Study Design: This study is a prospective longitudinal analysis. A total of 14 lecturers are involved in the lectures of the Geriatrics module (October 2017 to March 2018). The lecturers were recruited from different departments of the medical school and among geriatricians from a nearby geriatric hospital. These include the departments of general medicine, cardiology, nephrology, trauma surgery, neurology, history/ethics/philosophy, forensic medicine, clinical pharmacology and psychiatry. The lecturers had no special training before teaching the geriatrics module and there was a wide range of teaching experiences and didactical training. The lecturers were informed in advance, both verbally and in writing, about how the study would be conducted. Of the 14 lecturers, 13 agreed to participate in the study. Subsequently one lecturer withdrew from the study and one lecturer could not be included in the study due to a missing comparison lecture in the second lecture week. As a result, a total sample size of n=11 lecturers (three female and eight male) participated and gave their written consent for the evaluation, thus the willingness to participate was 86%. During the entire module, one lecturer held five lectures, two lecturers held two lectures each, and the remaining lecturers held one lecture (Figure 1).

The study design was reviewed and approved by the Ethics Committee of the Hannover Medical School (no. 3634-2017).

Data Collection

Using a five-point Likert scale (1= not apparent; 5= excellent), the lectures are rated according to a questionnaire that consisted of 22 items in the categories "content/structure", "presentation", and "visualization" (Table 1). The questionnaire

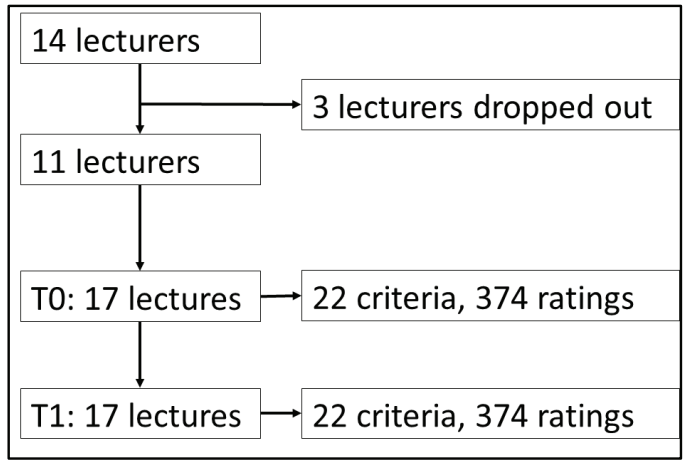

Figure 1. Scheme of the study (T0: first lecture period; T1: second lecture period)

was developed by Ruesseler et al. (4) and based on criteria for effective teaching identified in the literature. As a validated assessment instrument, it was put forth by Newman et al. (5,6). The questionnaire has already been used successfully to evaluate lectures on emergency medicine and surgery (4,6,7). The geriatric lectures at MHH were evaluated over two consecutive trimesters (fall and winter trimester). In total, 17 lectures were evaluated two times employing 22 criteria (n=748 ratings).

The evaluation is carried out by a trained female student from the fifth year who had already completed the module. During a training session prior to the evaluation cycle, a five-member expert (experienced teachers, a MHH alumnus, a trained social scientist of the central evaluation unit) group evaluated a video-taped prototype lecture as an example. The results were presented and discussed in the group, explicitly pointing out possible observation and evaluation errors, such as the halo effect, the primacy effect and the error of central tendency (4,5,7).

Based on the first evaluation in the fall trimester, individual written feedback was emailed to each lecturer for each lecture given. The feedback contains a general summary of strengths and suggestions for improvement, including free comments as well as "closed" items. Furthermore, a comparative rating of the individual aspects compared to the other lecturers is included (Figure 2).

In addition, all students who attended the geriatrics module (T0= 96 students, T1= 76 students) were informed about the study and were invited to participate in the central standard, end-of-trimester student evaluation (Table 2). In the first trimester n=75 students participated and n=60 students in the second trimester (T0 = 78%; T1 = 79%). Among other things, this includes an overall evaluation of the module (scale: 0 points = deficient <> 15 points = very good). In addition to a standardized query, five additional questions were asked that specifically address the teaching objectives, lecture structure, the sequence of the lectures, relevance to routine medical

Table 1. Individual item analysis and test values for the Wilcoxon test (n=17)

Aspect	T0 Mean/ median	T1 Mean/ median	p	Z
Content/structure				
Clear learning objectives	1.41/1	3.82/5	**0.001**	-3.443
Transparent sequencing	1.76/1	4/5	**0.001**	-3.336
Clear organization	3.24/3	4.12/4	**0.003**	-2.950
Connections to prior knowledge	3.94/4	4.35/5	0.112	-1.588
Memorable visualization	4.18/4	4.59/5	0.083	-1.732
Clear instructions	4.29/5	4.47/5	0.454	-0.749
Active inclusion	4.35/5	4.47/5	0.739	-0.333
Appropriate amount of data	4.65/5	4.82/5	0.257	-1.134
Content summaries	2.82/3	4.18/5	**0.002**	-3.108
Adequate time management	3.35/3	4.24/5	0.060	-1.879
Presentation				
Speaking rate	4.41/5	4.53/5	0.480	-0.707
Volume/pronunciation	4.76/5	4.82/5	0.564	-0.577
Enthusiasm for the topic	4.65/5	4.59/5	0.564	-0.577
Respect for listeners	3.71/4	4/4	0.132	-1.508
Inviting questions from listeners	4/4	4.76/5	**0.046**	-1.997
Discussion moderation	4.08/4	4.77/5	0.053	-1.933
Language of the slides	4.24/5	4.53/5	0.131	-1.512
Visualization				
Adequate design	3.88/4	4.18/4	0.132	-1.508
Graphics/diagrams/images	3.76/4	3.82/4	0.903	-0.122
Amount of text on slides	3.76/4	4.06/4	0.166	-1.387
Congruence between image and language	4.18/4	4.65/5	0.097	-1.660
Adequate number of slides	4.18/4	4.94/5	**0.006**	-2.739
Scale 1= not apparent, 5= excellent, bold= significant				

practice, and the students' prior knowledge (scale: 1=agree completely <> 6=disagree completely) (Table 3).

Statistics

Statistical analysis is performed using Microsoft Excel 2018©, version 6.13.1, and SPSS (version 25). A paired-sample t-test is used for the rating differences in the overall evaluation before and after feedback (T0 and T1), a p-value of $p<0.05$ indicates statistical significance. The data for the evaluated items do not show a normal distribution in most cases, which is why the Wilcoxon test for dependent samples is carried out.

The student evaluations, including the additional five questions, are analyzed using the t-test for independent samples after verifying the pre-requisites for this.

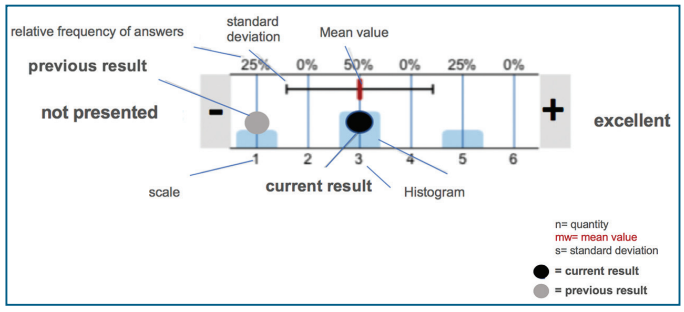

Figure 2. Scheme of visual feedback

Table 2. Some results of the general student evaluation (T0: n=75. T1: n=60)

Question	T0	T1	p	Standard error of the difference
Course content (1= very good <> 6= failure)	1.84	1.62	0.052	0.112
Instructors (standardized academic grade 1- 6)	1.56	1.48	0.469	0.106
Overall evaluation (0 pts.= failure <> 15 pts.= very good)	12.8	13.18	0.198	0.298

Table 3. Results of the additional student survey (T0: n=75. T1: n=60)

Question	T0	T1	p	Standard error
The lecturer has clearly recognizable teaching objectives.	1.757	1.638	0.363	0.131
The content taught in the lecture was well organized.	1.861	1.746	0.332	0.119
The narrative thread of the course was clearly visible.	1.903	1.554	**0.006**	0.125
The relevance of the topics important for future medical practice became clear.	1.608	1.357	**0.022**	0.113
The lecture built upon prior knowledge.	1.676	1.5	0.137	0.117
Scale: 1= agree completely 6= disagree completely, bold= significant				

Results

Reviewing the lectures, a mean rating of 3.8 out of 5 points for all items is calculated at the first evaluation (T0) in the fall trimester and a mean of 4.4 points at the second evaluation (T1) in the winter trimester (±0.59 points, $p<0.001$) (Figure 3). All three main categories (content/structure, presentation, visualization) are rated significantly better in the second series of lectures. A significant improvement can be seen in six of the 22 items (Table 1). The most significant improvement for a single lecture is more than one point, the largest increase can be

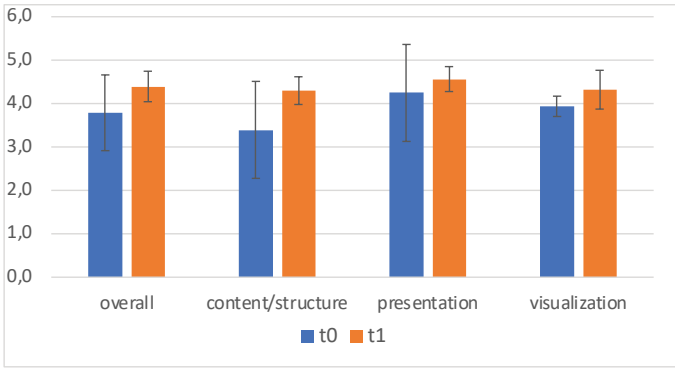

Figure 3. Comparison of the overall review of the lectures and the three major categories at the first (T0) and the second (T1) evaluation (five-point Likert scale; 1=not apparent; 5=excellent)

seen in the category "content/structure".

Similar to the significantly improved results in the reviewer evaluations, there is also a trend of an improvement in the students' general evaluation of the module (Table 2). At first, the geriatrics module is rated with 12.8 out of a possible 15 points. After the intervention this already solid result improves to 13.2 (±0.4) points (n.s.). A positive trend can be seen between the trimesters in the "instructor ratings" starting at 1.56 and moving to 1.48 (n.s.) and as well regarding "course content" moving from 1.84 to 1.62 (p=0.052) (Table 2).

With regard to the additional items that cover the learning outcome and overall satisfaction, the students responded with significantly higher ratings to the question about "being able to recognize the narrative thread (sequencing) running through the lecture series" (p<0.001) and to the question about the "relevance of the topics covered to future medical practice being clear" (p=0.022) (Table 3).

Discussion

Lectures as a means of teaching: Despite the criticism of this format at German medical schools, knowledge is still imparted in over 90% of the time through lectures (8). In the module geriatrics at the Hannover Medical School lectures account for two thirds of the curriculum. This reflects a general tendency in geriatrics-as well as in other small subjects-with their limited teaching resources. Only few different formats for teaching geriatrics in undergraduate medical education are described in the literature (9-11). Most of these studies focus on innovative teaching formats and not on improving the standard lectures themselves. Also, many of these evaluations are based only on student feedback, which gives an overall rating of the module but does usually not rate the single lectures held by individual instructors.

Previous studies have shown that student feedback from the lecture hall does not always appropriately rate the quality of the course content or the materials used (12). Student feedback on instructors can be influenced by other factors that are beyond or only partially within the control of the instructors, for instance the influence of prior knowledge and interest, gender or expectations regarding test scores (13). In contrast to the student feedback, the evaluation by independent reviewers is not influenced by these factors similar to peer reviewing. This has clear advantages compared to a student feedback, as shown by the study of Sterz et al. (7). Furthermore, training of the reviewer prior to the evaluation can minimize the risk of bias (7).

The individual feedback in our study was accepted by the lecturers, because it may have been easier to accept a feedback from a trained student who already passed the module than from the university or a colleague.

In addition, individual feedback on specific lectures is more valuable than a summative feedback on the entire module (14).

A criteria-based feedback is one of the best methods for generating differentiated feedback. It has been shown that a personal written feedback improves the extent and quality of the feedback, especially when it is structured with specific criteria (15).

What did the feedback change? The study shows the biggest improvements in the sub-section "content/structure". This could be due to the fact, that this area offered the most potential for improvement and that the related didactical suggestions could be implemented by the instructors with relative ease. Another explanation could be that lecture content or organization is easier to improve than other aspects since lecturers can reorganize lecture content or structure without changing deeply rooted personal traits or routinely adapted skills.

In contrast, "speaking rate" and "speaking volume" each received the same ratings at both measurement points. Ruesseler et al. (4) saw similar results and pointed out that it is very difficult to change individual characteristics based on a single instance of written feedback.

In addition, there was also a significant improvement in "inviting questions from listeners". In contrast, the category "active inclusion" of students has remained mostly similarly assessed in both periods in our study. Knight and Wood (16) show similar results, although pure interactive classroom activities also have disadvantages. The significant change in "inviting questions" in this study may indicate that instructors were already placing more emphasis on interacting with students because of the feedback given, even though this occurred in the context of traditional lectures. Furthermore, the improvement in the section "content summaries" shows that the feedback encouraged the lecturers to summarize the key facts at the end, which was also directly acknowledged by the students as their

rating in the category "narrative thread of the course" increased significantly in the second lecture week.

Benefit for the lecturers? Breaking down written feedback into identifying strengths and making suggestions for improvement is useful for promoting intrinsic motivation for faculty, as it is a direct recognition of individual performance.

Our survey also found that the lecturers, despite the increased amount of work and the feeling of being observed, viewed the feedback favorably and found added value in it. Moreover, all of the surveyed lecturers were prepared to revise their lectures making it possible to use the feedback as a source of concrete improvements. Reviewing one's own lecture using a criteria-based method and benchmarking it with the other lecturers (Figure 1) May have facilitated acceptance.

The perception of the students: The improved overall rating of the module by the students in the central evaluation suggests that they also saw an improvement not only in the quality of teaching, but also in the quality of their personal learning success. Therefore, the improvement due to the structured feedback was not only noticeable in the evaluation of the instructors, but also in the evaluation of the students.

Study Limitations

Due to the limited number of lectures this study does not make use of a control group, which received no written feedback or an alternative format for feedback. Furthermore, there could be a potential ceiling effect in some categories, because good results have already been achieved in T0. Despite the good prior results, it is still possible to show that written feedback triggered significant improvements in some categories. Another limitation is the conduction of the study with only one reviewer who may have been biased despite the training. Using multiple reviewers could have allowed for a greater reliability. In addition to all of this, a great willingness of the lecturers to participate is necessary for such a study. In total, participation of the lecturers in our study is as high as 86%. Another limiting factor was that learning improvement in students regarding the content taught was not directly tested using an objective competency assessment, but rather by compiling the students' subjective perceptions.

Conclusion

This study shows that a significant improvement in teaching is possible by means of an individualized, criteria-based written feedback for each lecture by an independent as well as trained student reviewer and that students acknowledge the resulting improvements positively.

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Ethics

Ethics Committee Approval: The study design was reviewed and approved by the Ethics Committee of the Hannover Medical School (no: 3634-2017).

Informed Consent: Informed consent was obtained.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: T.P., S.S., Design: T.P., S.S., Data Collection or Processing: T.P., K.H., Analysis or Interpretation: T.P., V.P., S.S., K.H., Literature Search: T.P., V.P., S.S., K.H., Writing: T.P., V.P., S.S., K.H.

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References

1. Copeland HL, Longworth DL, Hewson MG, Stoller JK. Successful lecturing: a prospective study to validate attributes of the effective medical lecture. J Gen Intern Med 2000;15:366-371.
2. Kolb G. Unterricht Q7 (Medizin des Alterns und des alten Menschen) an 36 deutschen medizinischen Faklutäten. In: Kolb G, Leischker, AH, ed. Medizin des alternden Menschen - Lehrbuch zum Gegenstandskatalog der neuen ÄAppO. Wissenschftliche: Verlagsgesellschaft; 2009.
3. Kirkpatrick D. Evaluating training programs: the four levels. vol 46. Evaluation in Education and Human Services. Berrett-Koehler; 1994.
4. Ruesseler M, Kalozoumi-Paizi F, Schill A, Knobe M, Byhahn C, Müller MP, Marzi I, Walcher F. Impact of peer feedback on the performance of lecturers in emergency medicine: a prospective observational study. Scand J Trauma Resusc Emerg Med 2014;22:71.
5. Newman LR, Lown BA, Jones RN, Johansson A, Schwartzstein RM. Developing a peer assessment of lecturing instrument: lessons learned. Acad Med 2009;84:1104-1110.
6. Newman LR, Brodsky DD, Roberts DH, Pelletier SR, Johansson A, Vollmer CM Jr, Atkins KM, Schwartzstein RM. Developing expert-derived rating standards for the peer assessment of lectures. Acad Med. 2012;87:356-363.
7. Sterz J, Hofer SH, Bender B, Janko M, Adili F, Ruesseler M. The effect of written standardized feedback on the structure and quality of surgical lectures: A prospective cohort study. BMC Med Educ 2016;16:292.
8. Singler K, Stuck AE, Masud T, Goeldlin A, Roller RE. [Catalogue of learning goals for pregraduate education in geriatric medicine. A recommendation of the German Geriatric Society (DGG), the German Society of Gerontology and Geriatrics (DGGG), the Austrian Society of Geriatrics and Gerontology (OGGG) and the Swiss Society of Geriatric Medicine (SFGG) on the basis of recommendations of the European Union of Medical Specialists Geriatric Medicine Section (UEMS-GMS) 2013]. Z Gerontol Geriatr 2014;47:570-576.
9. Granero Lucchetti AL, Ezequiel ODS, Oliveira IN, Moreira-Almeida A, Lucchetti G. Using traditional or flipped classrooms to teach "Geriatrics and Gerontology"? Investigating the impact of active learning on medical students' competences. Med Teach 2018;40:1248-1256.
10. Sauer M, Gornig M, Voigt K, Schubel J, Bergmann A. [Interprofessional

multistation practical training in the auditorium : Implementation of the national competence-based catalog of learning objectives for undergraduate medical education in the cross-sectorial area medicine of aging and the aged at the TU Dresden]. Z Gerontol Geriatr 2018;51:903-911.

11. Eckardt R, Nieczaj R, Steinhagen-Thiessen E, Arnold T. [Cross-sectional field Q7"medicine of aging and the elderly" at the Charité - Universitatsmedizin Berlin: Curriculum and evaluation by students]. Z Gerontol Geriatr 2013;46:548-555.
12. Irby DM. Peer review of teaching in medicine. J Med Educ 1983;58:457-461.
13. Hatfield CL, Coyle EA. Factors that influence student completion of course and faculty evaluations. Am J Pharm Educ 2013;77:27.
14. Knol MH, Dolan CV, Mellenbergh GJ, van der Maas HL. Measuring the Quality of University Lectures: Development and Validation of the Instructional Skills Questionnaire (ISQ). PLoS One 2016;11:e0149163.
15. Newton PM, Wallace MJ, McKimm J. Improved quality and quantity of written feedback is associated with a structured feedback proforma. J Educ Eval Health Prof 2012;9:10.
16. Knight JK, Wood WB. Teaching more by lecturing less. Cell Biol Educ 2005;4:298-310.

ORIGINAL RESEARCH

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Evaluation of the Antimicrobial Resistance Rates in Urine Samples of the Elderly

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Abstract

Objective: Urinary tract infections (UTIs) are common in the community. The prevalence of UTIs rises in the elderly as a result of age-related changes and comorbidities. In treating the elderly, it is important to choose antibiotics carefully and avoid unnecessary ones. The goal of this study was to analyze the bacteria isolated from geriatric urine samples and their resistance patterns.

Materials and Methods: Urine culture results in geriatric patients (>65 years old) were analyzed between January 1, 2016 and February 1, 2020. Antibiotic resistance was evaluated in frequently isolated bacteria. In terms of antibiotic resistance, antibiotics that can be used in outpatient therapy and do not require the approval of an infectious disease specialist were investigated.

Results: The records of 37735 urinary samples were screened. In 31.3% (11840/37735) of the urine culture microorganisms were isolated. *Escherichia coli* was the most common microorganism with a rate of 40.1% (4758/11840), followed by *Klebsiella* spp. with 15.5% (1844/11840), *Enterococcus* spp. with 10.3% (1222/11840), and *Pseudomonas aeruginosa* with 3.4% (406/11840). Ceftriaxone resistance of 37.6% was found in *Escherichia coli*; ciprofloxacin resistance was 41.5%, trimethoprim-sulfamethoxazole (TMP-SMX) resistance was 43.4%, and nitrofurantoin resistance was 1%. There was no resistance to fosfomycin. The antibiotic resistance of *Klebsiella* spp. gave a result of 41.6% ceftriaxone resistance, while ciprofloxacin resistance was 32.6%, and TMP-SMX resistance was 39.6%. The antibiotic resistance of *Pseudomonas aeruginosa* was 19.04% ciprofloxacin resistance, and 5.1% amikacin resistance. In *Enterococcus* spp. ampicillin resistance was found to be 42.9%.

Conclusion: Infections in geriatric patients can quickly prove fatal. Antibiotic selection is critical in regard to elderly patients, and knowing regional antimicrobial resistance patterns is important. But balancing efficacy, safety, and tolerability with the development of antimicrobial resistance in this patient population is difficult.

Keywords: Urine sample, antimicrobial resistance, antibiotics, clinical geriatrics, geriatric care management

Introduction

Due to advances in technology and medicine, the population of older adults is steadily increasing. The World Health Organization predicts that the number of people over 60 years will increase from 12% to 22% of the total global population between 2015-2050, and advises countries to adjust their policies accordingly (1). According to the United Nations, Turkey will be among the countries with an elderly community of more than 10% (2). Advances in disease treatment and public health over the last century have resulted in increased life expectancy, a lower birth rate, changes in age pyramids, and a prognostic increase in the proportion of the world's elderly population. Aging causes a progressive and general decline in functional reserve capacity, followed by a loss in all functions. Although aging is not a disease, it does increase the risk of people contracting several diseases, as well as the overall mortality rate (3).

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Urinary tract infections (UTIs) are common in the elderly and have a significant health impact. UTIs are responsible for 15.5% of hospitalizations due to infectious diseases in adults aged over 65, second only to pneumonia. It is responsible for 6.2% of deaths from infectious (4). In UTIs, isolation of the causative agent, determination of antibiotic susceptibility, and appropriate antimicrobial therapy will prevent treatment failure.

Because of the variability of symptoms and laboratory values in elderly patients, empirical treatment is frequently initiated in UTIs. Antibiotic resistance rates rise when antibiotics are misused. Antibiotic resistance is still a major concern all over the world. Knowing and following regional changes in the antibiotic susceptibility of isolated bacteria is critical for treatment efficacy. As a result, the topic is still relevant. Resistance to quinolones, one of the first treatment options for UTIs, has been reported to be as high as 30-42% in studies conducted in our country (5).

The purpose of this study was to determine the distribution of microorganisms and the antibiotic resistance rates isolated from urine samples of geriatric patients.

Materials and Methods

Our study, which was designed as a retrospective cross-sectional descriptive study, examined urine cultures sent to the microbiology laboratory between January 1, 2016, and February 1, 2020. Outpatient and inpatient outcomes with positive urine culture from people over the age of 65 were included. Only one sample of each patient was included. Samples were from the urethral, urinary catheter, nephrostomy, or cystostomy catheter. Detection of 10^5 cfu/mL of one species or two types of microorganisms in cultures, or detection of 104 cfu/mL of one type of microorganism were considered positive. The results were analyzed from laboratory records. Urine samples were evaluated for the presence of *Escherichia coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, and *Enterococcus* spp., as well as the rate of antimicrobial resistance. Other microorganisms that are rarely isolated were not included. In this study, we examined the rates of resistance to antibiotics that can be administered orally or intramuscularly and do not require the approval of an infectious disease specialist. The results were evaluated in terms of antibiotic resistance to such as penicillin, cephalosporin, aminoglycoside, fosfomycin, nitrofurantoin, and trimethoprim-sulfamethoxazole.

Urine samples carried to our hospital's microbiology laboratory are inoculated on 5% sheep blood agar and eosin methylene blue agar using a quantitative method involving a 0.01 mL standard loop. Urine samples are incubated at 35-37 °C for 24-48 hours according to standard procedures. Bacterial identification and antibiotic susceptibility tests are carried out using both conventional and automated systems (Phoenix BD, USA). Antibiogram data are evaluated in accordance with the recommendations of EUCAST (European Committee on Antimicrobial Susceptibility Testing).

Statistics

The data were taken from the hospital information management system and analyzed with the Excel program. Number (n) and % age (%) will be used to define categorical variables.

This study was approved by Başkent University Institutional Review Board (project no: KA21/476).

In organizing the study, Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) rules were followed.

Results

The geriatric patient group was screened, as were the urine culture samples sent during the study period. This group contained 37735 records. In 68.6% (25895/37735) of the urine culture results, there was no growth (Figure 1). The isolated microorganisms were distributed as follows: *Escherichia coli* was isolated in 40.1% (4758/11840), *Klebsiella* spp. in 15.5% (1844/11840), *Enterococcus* spp. in 10.3% (1222/11840), and *Pseudomonas aeruginosa* in 3.4% (406/11840). Other microorganisms (such as *Staphylococci, Candida,* proteus) accounted for 30.4% (3610/11840). The mean age was 77.9±7.9 years, and 59.1% (7004/11840) of the patients were women.

When we evaluated the antibiotic resistance pattern in *Escherichia coli*, ceftriaxone resistance was 37.6%, ciprofloxacin resistance was 41.5%, trimethoprim-sulfamethoxazole (TMP-SMX) resistance was 43.4%, gentamicin resistance was 15.2%, amikacin resistance was 1.7%, and nitrofurantoin resistance was 1%. There was no evidence of resistance to fosfomycin. The antimicrobial resistance rates are shown in Table 1. In the subgroup analysis, antimicrobial resistance in *E. coli* was higher in the male gender in both categories (inpatient and outpatient) (Table 2).

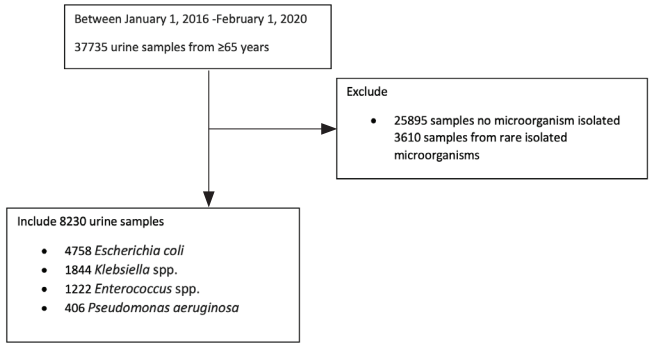

Figure 1. Study flowchart

In *Klebsiella* spp., ceftriaxone resistance was found to be 41.6%, ciprofloxacin resistance was 32.6%, TMP-SMX resistance was 39.6%, gentamicin resistance was 17.2%, and amikacin resistance was 3.5%. In the subgroup analysis, ceftriaxone resistance in *Klebsiella* spp. was over 50% in the inpatient group. TMP-SMX resistance was higher in males, while ciprofloxacin resistance was higher in females (Table 3).

The antibiotic resistance pattern in *Pseudomonas aeruginosa* showed ciprofloxacin resistance to be 19.04%, amikacin resistance was 5.1%, and gentamicin resistance of 8.7%. In the subgroup analysis, in males ciprofloxacin and gentamicin resistance was higher than in females. Antibiotic resistance rates were high in inpatients (Table 4).

In *Enterococcus* spp. ampicillin resistance was found to be 42.9%, and nitrofurantoin resistance was 6.06%. In the subgroup analysis, antimicrobial resistances were higher in females in all categories (Table 5).

Discussion

Atypical infection findings and increasing incidence of asymptomatic bacteriuria (ASB) in the elderly population make it difficult for the clinician to diagnose urinary tract infection.

Table 1. Antibiotic resistance rates of microorganisms

Antibiotic	Microorganisms			
	E. coli	*Klebsiella* spp.	*Enterococcus* spp.	*P. aeruginosa*
Ampicillin	70.5%	71.8%	42.9%	NE
Ceftriaxone	37.6%	41.6%	NE	NE
Ciprofloxacin	41.5%	32.6%	NE	19.04%
Amikacin	1.7%	3.5%	NE	5.1%
Gentamicin	15.2%	17.2%	NE	8.7%
Fosfomycin	0	NE	NE	NE
Nitrofurantoin	1.0%	NE	6.06%	NE
TMP-SMX	43.4%	39.6%	NE	NE

NE: Not effective, TMP-SMX: Trimethoprim-sulfamethoxazole

Table 2. Antibiotic resistance rates of *Escherichia coli*

Antibiotics	Outpatient		Inpatient		All	
	Female	Male	Female	Male	Female	Male
Ampicillin	65.8%	75.7%	74.5%	79.7%	68.6%	76.9%
Ceftriaxone	29.7%	39%	46.6%	53.8%	35.1%	43.6%
Ciprofloxacin	35.6%	46.9%	45.7%	58.1%	38.9%	50.3%
Amikacin	1.4%	1.9%	1.3%	2.1%	1.4%	1.9%
Gentamicin	12.1%	20.5%	16.2%	24.1%	13.4%	21.6%
Fosfomycin	0	0	0	0	0	0
Nitrofurantoin	0.5%	1.5%	1.3%	3.4%	0.8%	2.1%
TMP-SMX	40.2%	49.4%	43.6%	53.8%	41.3%	50.7%

TMP-SMX: Trimethoprim-sulfamethoxazole

Table 3. Antibiotic resistance rates of *Klebsiella* species

Antibiotics	Outpatient		Inpatient		All	
	Female	Male	Female	Male	Female	Male
Ampicillin	65.8%	75.7%	74.5%	79.7%	68.6%	76.9%
Ceftriaxone	32.2%	33.8%	55.9%	58.4%	41.2%	42.6%
Ciprofloxacin	24.3%	22.4%	48.2%	46.1%	33.4%	30.8%
Amikacin	2.1%	3.8%	0.9%	3.8%	1.7%	3.8%
Gentamicin	10.6%	13.5%	27.9%	23.8%	17.1%	17.2%
TMP-SMX	33.5%	37.2%	46.6%	58.4%	38.5%	44.8%

TMP-SMX: Trimethoprim-sulfamethoxazole

Table 4. Antibiotic resistance rates of *Pseudomonas aeruginosa*

Antibiotics	Outpatient		Inpatient		All	
	Female	Male	Female	Female	Female	Male
Ciprofloxacin	11.2%	19.2%	19.7%	25.3%	16.3%	22.5%
Amikacin	0	1.7%	8.7%	7.9%	5.2%	5%
Gentamicin	1.6%	7%	7%	10.9%	7.1%	10.8%

Table 5. Antibiotic resistance rates of *Enteroccoccus species*

Antibiotics	Outpatient		Inpatient		All	
	Female	Male	Female	Male	Female	Male
Ampicillin	45.5%	35.2%	54.9%	32%	50.7%	33.8%
Nitrofurantoin	3.5%	2.4%	12.1%	7.3%	7.7%	3.1%

There is still no consensus for the definition of UTIs in the elderly. UTIs are a common and a serious reason for hospitalization in the older population (6). In our study, we determined the antibiotic resistance in the urinary isolates of patients admitted to our hospital, which is a common factor for admissions. While we found low resistance rates for aminoglycosides (amikacin and gentamicin), and nitrofurantoin, we found no resistance to fosfomycin.

When aminoglycosides are considered among these agents, their Gram-negative activities are good, and urine concentrations reach peak plasma levels within one hour of drug administration (7). However, their use in treating the elderly is avoided due to their nephrotoxic and ototoxic side effects. Chinzowu et al. (8) reported the use of aminoglycosides caused acute kidney injury in the elderly. While it is recommended not to exceed 48 hours in empirical treatment, the duration may be extended in targeted therapy, but caution should be exercised (9). Raveh et al. (10) reported that nephrotoxicity was rare in the use of aminoglycosides for over 11 days in the elderly. Meanwhile their only parenteral use is another challenge. The patient must apply to a healthcare provider for parenteral use. This situation also includes risk factors such as the formation of a regional abscess, hematoma, and thrombophlebitis in intravenous use. However, elderly patients diagnosed with urinary system infections sometimes do not want to be treated in a hospital. On the other hand, aminoglycosides are an appropriate antibacterial agent when patients do not have an oral treatment option or have resistant microorganisms. It is comfortable to use in a single daily dose. Based on these results, it is important to inform the patients and their relatives of its short-term use and closely monitor for side effects.

According to our findings, nitrofurantoin appears to be a viable option with a low rate of resistance. Nitrofurantoin is only approved for the treatment and prevention of lower UTIs (11). It is preferred from a medical perspective when the patient has urinary complaints (dysuria, urgency, frequency) but no systemic findings (fever or hypothermia, anorexia, loss of appetite, regression in cognitive and physical functions). Beers Criteria should be avoided in people with creatinine clearance of less than 30 mL/min or for long-term use, according to the 2015 American Geriatrics Society. The society advises using a safer alternative because there is a risk of pulmonary toxicity, hepatotoxicity, and peripheral neuropathy side effects, particularly with long-term use (12).

In our study, we determined a resistance rate of approximately 40% for ciprofloxacin, ceftriaxone and TMP/SMX. For an appropriate empirical treatment, resistance should be less than 20% (13). Based on our findings, quinolones, third-generation cephalosporins, and TMP/SMX do not appear to be viable options for empirical treatment. On the other hand, nitrofurantoin and TMP/SMX are recommended as first-line empirical treatments of UTIs (14). Quinolones have recently been associated with a higher risk of aortic aneurysm and dissection (15). However, this risk has not been related to age. During quinolone therapy, a high incidence of tendon rupture was noted (16).

In the elderly, metabolic side effects, such as hypoglycemia or hypokalemia, can occur as a result of antibiotic use. Although antibiotic-induced neurotoxicity is uncommon, it is unpredictable. However, different symptoms can be encountered, ranging from delirium to convulsions. Higher risk classes include fluoroquinolones, macrolides, sulfonamides, nitrofurans, and some β-lactams (17).

The Infectious Diseases Society of America lists fosfomycin as a first-line treatment for cystitis because of its ease of administration, but cautions that it may be slightly less effective than other agents (13). Due to its long half-life, studies show that it can be effective in uncomplicated lower UTIs with a single dose or 3 g doses repeated every 48 to 72 hours (18).

Enterococci are microorganisms of the gastrointestinal tract and are common in patients with urinary instrumentation or anatomical anomalies of the urinary tract (19). It is more frequently encountered as a causative agent in catheter-related UTIs and UTIs in those with incontinence or who are diapered.

We reported higher antimicrobial resistance in females than in males, and ampicillin resistance was found to be 42.9%. Vancomycin is avoided in the elderly due to nephrotoxicity, and teicoplanin requires the approval of an infectious disease specialist. Vancomycin-resistant enterococcal (VRE) strains are another threat. In our country, there is an oral form of linezolid available, but it is not approved for use in the treatment of VRE-associated UTIs.

Study Limitations

Our study includes data from a single center, and may not reflect the antimicrobial resistance rate of other regions. More wide-ranging research on this topic is required.

We only screened at the laboratory database. The patients' symptoms, and comorbidities were not investigated, and no differentiation was made between complicated urinary tract infection and asymptomatic bacteriuria (ASB). There was no distinction between agent and colonization. ASB is common in the elderly, although screening or treatment in community and long-term care units is not advised. ASB therapy, according to research, is ineffective in terms of morbidity and mortality in the elderly, and also causes an increase in antimicrobial resistance (20).

Conclusion

It becomes easier for infections to emerge with the decrease of immune responses in old age. Infections in the elderly can quickly prove fatal if the appropriate treatment is not started in time. On the other hand, antibiotics are among the most commonly prescribed new medications in elderly patients. In addition to the difficulty of diagnosing infections, multiple comorbidities, drug side effects, drug-drug or drug-disease interactions, and changes in drug pharmacokinetics and pharmacodynamics further complicate the selection of appropriate antibiotics for elderly patients. Appropriate antibiotic prescription is critical in elderly patients, but balancing efficacy, safety, and tolerability with the development of antimicrobial resistance in this patient population is difficult.

Information: This study was presented at the 3rd International & 13th Academic Geriatrics Congress.

Ethics

Ethics Committee Approval: This study was approved by Başkent University Institutional Review Board (project no: KA21/476) and supported by Başkent University Research Fund.

Informed Consent: The study is retrospective and laboratory-based.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept and Design: T.Y.Y., Ö.K.A., Data Collection or Processing: T.Y.Y., F.S., N.S., Literature Search: T.Y.Y., F.S., Writing: T.Y.Y., F.S., N.S., Supervision: Ö.K.A, H.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. World Health Organization (WHO). 10 facts on ageing and health. WHO; 2017 Available from: https://www.who.int/news-room/fact-sheets/detail/10-facts-on-ageing-and-health. Accessed 22 Nov 2021.
2. Türkbeyler İH, Öztürk ZA, Göl M, Abiyev A, Kaya B, Atakur S, Öz M. What is Geriatrics? Geriatrics or Older Adults Health and Diseases? Eur J Geriatr Gerontol 2019;1:51-55.
3. MA Karan, BO Türkmen. Türkiye'de ve dünyada yaşlılık demografisi, In: Ülger Z, Erdinçler D, Karan MA (eds). Geriatri yaşlı sağlığı ve hastalıkları. First edition, Hipokrat, Ankara, Turkey 2021, pp 3-10.
4. Detweiler K, Mayers D, Fletcher SG. Bacteruria and Urinary Tract Infections in the Elderly. Urol Clin North Am 2015;42:561-568.
5. Çilburunoğlu M, Kirişçi Ö, Yerlikaya H, Uğurlu H, Aral M, Muratdağı G. The Evaluation of The Distribution and Antimicrobial Susceptibility Profile of Strains İsolated From Urine Specimens at A University Hospital. Sakarya Tıp Dergisi 2020;10:677-683.
6. Nicolle LE. Urinary Tract Infections in the Older Adult. Clin Geriatr Med 2016;32:523-538.
7. JE Leggett. Aminoglycosides. In: John E. Bennett, Raphael Dolin, Martin J. Blaser (eds). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Ninth edition, Elsevier, Philadelphia, USA 2020, pp 305-317.
8. Chinzowu T, Roy S, Nishtala PS. Risk of antimicrobial-associated organ injury among the older adults: a systematic review and meta-analysis. BMC Geriatr 2021;21:617.
9. Avent ML, Rogers BA, Cheng AC, Paterson DL. Current use of aminoglycosides: indications, pharmacokinetics and monitoring for toxicity. Intern Med J 2011;41:441-449.
10. Raveh D, Kopyt M, Hite Y, Rudensky B, Sonnenblick M, Yinnon AM. Risk factors for nephrotoxicity in elderly patients receiving once-daily aminoglycosides. QJM 2002;95:291-297.
11. JM Horton. Urinary Tract Agents: Nitrofurantoin, Fosfomycin, and Methenamine. In: John E. Bennett, Raphael Dolin, Martin J. Blaser (eds). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Ninth edition, Elsevier, Philadelphia, USA 2020, pp 461-465.
12. By the American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc 2015;63:2227-2246.
13. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, Moran GJ, Nicolle LE, Raz R, Schaeffer AJ, Soper DE; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011,52:103-120.
14. Nicolle LE. Urinary tract infections in the elderly. Clin Geriatr Med 2009;25:423-436.

15. Pasternak B, Inghammar M, Svanström H. Fluoroquinolone use and risk of aortic aneurysm and dissection: nationwide cohort study. BMJ 2018;360:k678.

16. Daneman N, Lu H, Redelmeier DA. Fluoroquinolones and collagen associated severe adverse events: a longitudinal cohort study. BMJ Open 2015;5:e010077.

17. Falcone M, Paul M, Tiseo G, Yahav D, Prendki V, Friberg LE, Guerri R, Gavazzi G, Mussini C, Tinelli M; ESCMID Study Group for Infections in the Elderly (ESGIE). Considerations for the optimal management of antibiotic therapy in elderly patients. J Glob Antimicrob Resist 2020;22:325-333.

18. Pullukcu H, Tasbakan M, Sipahi OR, Yamazhan T, Aydemir S, Ulusoy S. Fosfomycin in the treatment of extended spectrum beta-lactamase-producing Escherichia coli-related lower urinary tract infections. Int J Antimicrob Agents 2007;29:62-65.

19. WR Miller, CA Arias, BE Murray. Enterococcus Species, Streptococcus gallolyticus Group, and Leuconostoc Species. In: John E. Bennett, Raphael Dolin, Martin J. Blaser (eds). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Ninth edition, Elsevier, Philadelphia, USA 2020, pp 2492-2504.

20. Nicolle LE, Gupta K, Bradley SF, Colgan R, DeMuri GP, Drekonja D, Eckert LO, Geerlings SE, Köves B, Hooton TM, Juthani-Mehta M, Knight SL, Saint S, Schaeffer AJ, Trautner B, Wullt B, Siemieniuk R. Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America. Clin Infect Dis 2019;68:e83-e110.

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What Might be More Associated with Higher or Lower Blood Pressure in Older Adults? Sarcopenia, Obesity, or Sarcopenic Obesity? A Cross-sectional Retrospective Study

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Abstract

Objective: In old age, body composition changes. While the muscle tissue tends to decrease, adipose tissue increases. The term sarcopenic obesity (SO) refers to a combination of sarcopenia and obesity. SO is a geriatric syndrome that has been newly defined and understood the importance. Its relationship to blood pressure is unclear. The study aims to determine which sarcopenia, obesity or SO is more associated with higher or lower blood pressure.

Materials and Methods: Non-hypertensive and not receiving antihypertensive therapy patients who underwent bioelectrical impedance analysis (BIA) and 24-hour ambulatory blood pressure measurements for body composition were included in this retrospective study. Comprehensive geriatric assessment, socio-demographic and laboratory data were recorded. Sarcopenia was diagnosed according to the European Working Group on Sarcopenia in Older People-2 criteria. Fat percentage measured by BIA was used for obesity (38% and 27% for females and males).

Results: Of 167 patients with a mean age of 75.45±8.12 years, 70.6% (n=121) were women. The ratios of sarcopenia, obesity and SO were 14.5% (n=24), 27.8% (n=46) and 42.4% (n=71), respectively. In the sarcopenic group, systolic blood pressure (SBP), daytime mean arterial pressure (MAP), and pulse pressure (PP) were the lowest. The obese group had the highest SBP, MAP, and the lowest daytime pulse rate (PR). SO the group had the lowest MAP at night and the highest daytime PR. After adjusting for confounders, for SO, being female, having high nighttime mean arterial pressure and high daytime PR had a higher odds ratio (respectively, OR 3.271, 0.976, 1.32; p<0.001, 0.046, 0.012).

Conclusion: Obesity might be more related to blood pressure and mean arterial pressure elevation. Sarcopenia and SO might be related to hypotension, low PP, and low mean arterial pressure in older adults.

Keywords: Sarcopenia, sarcopenic obesity, blood pressure, older adults, comprehensive geriatric assessment

Introduction

The older adult population is increasing around the world. As of 2021, already, there are more than 1 billion people aged 60 years or older. This number is expected to double to 1.5 billion by 2050 (1). Body composition in old age changes compared to young people. The muscle ratio decreases while fat ratio increases. Studies show that muscle mass decreases by about 6% per decade. Body fat also increases until the seventh year of life and then decreases (2). Sarcopenia is a geriatric syndrome, referring to low muscle mass, strength, and performance. In the diagnosis of sarcopenia, many different groups have introduced definitions. One of these groups is the European Working Group

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on Sarcopenia in Older People (EWGSOP-2). The definition criteria of sarcopenia were updated by this group in 2018 and cases with low muscle strength were taken as probable sarcopenias. The diagnosis of sarcopenia is confirmed when both muscle strength and mass are low (3). Sarcopenia causes decreased physical performance, increased physical disability, hospitalization, and institutionalization, decreased quality of life, and increased healthcare costs, falls, and mortality in older adults (4,5). Sarcopenia causes metabolic changes that lead to insulin resistance by several different mechanisms in older adults (changes in the neuroendocrine system (insulin resistance, altered anabolic hormone secretion, decreased sex hormones), physical inactivity, decrease in skeletal muscle mass, and decrease in physical activity and energy expenditure) (6-9). In older adults, these conditions can induce disease pathogenicity and cause blood pressure changes.

Obesity and being overweight were associated with higher blood pressure and mortality in the adult group. However, studies examining the effects of overweight and obesity on CVD and mortality in older adults are conflicting. Some studies have even suggested that overweight and obesity, as measured by BMI, are associated with a lower risk of death. This is known as the "obesity paradox" (6).

The term sarcopenic obesity (SO) refers to a combination of sarcopenia and obesity. SO is a geriatric syndrome that is relatively newly defined compared to sarcopenia, and its importance is newly understood. In older adults, sarcopenia, and obesity synergistically increase the effects of each other. The combination of these two epidemic situations causes limitation of functionality in older adults. Both have inflammatory pathways of similar pathogenicity (10). Recent studies have shown that SO is associated with an increased risk of physical disability, cardiovascular morbidity, and mortality compared with sarcopenia or obesity alone (10-13). Previous studies have examined the effects of sarcopenia and obesity on blood pressure (14,15). However, studies examining the effect of the coexistence of these two conditions are limited. Despite increasing research on the association between SO and cardiovascular risk factors, only a limited number of studies to date have evaluated the association between SO and CVD risk in older adults.

The study aims to determine which sarcopenia, obesity or SO is more associated with higher or lower blood pressure.

Materials and Methods

Study design and patient selection

A total of 167 patients who underwent Bioelectrical Impedance Analysis (BIA) and 24-hour ambulatory blood pressure measurements (24 hours-PPM) were included in this cross-sectional retrospective study. The patients included in the study were selected from among the patients whose data were collected between July 2015 and February 2019. The patients were those who had a previous 24-hour blood pressure measurement, did not have a history of hypertension, and did not receive antihypertensive treatment. Sociodemographic findings, comprehensive geriatric assessment tests, and laboratory data of the patients indicated in Table 1 were obtained from their electronic files. Patients whose files were missing (not suitable for BIA, ABPM not complete for 24 hours, laboratory values missing, comprehensive geriatric assessment tests could not be performed or missing) were not included in the study. The patient selection algorithm is summarized in Figure 1. The patients were divided into four groups according to the measurement results. 1. group: Non-sarcopenic, non-obese, normal group, 2. group only sarcopenic, 3. group: Only obesity and 4. group SO. Comparisons were made between the four groups. The STROBE checklist for cross-sectional studies was filled out.

Definition of sarcopenia, obesity, and SO

The diagnosis of sarcopenia was made according to the revised European consensus on the definition and diagnosis from the "EWGSOP-2" (3). These revised diagnostic criteria, which were updated in 2018, mainly use three components: Muscle strength, muscle quantity, and physical performance.

1- Muscle strength: In our study, the handgrip test was used to measure muscle strength. For the evaluation of muscle strength, handgrip strength was measured with an electronic hand dynamometer (GRIP-D, grip strength dynamometer, produced by Takei, Made in Japan). The measurement was made with the arm flexed at 90 degrees from the elbow. The person grasped the force-applied part of the dynamometer with the dominant hand and applied power to the dynamometer with all their might. Measurements were made three times with an interval of one minute. An average of three measurements was taken. The unit of results is kilograms. According to EWGSOP-2 recommendations, local cut-off values were used (grip strengths of <22 kg for females and <32 kg for males) (16).

2- Muscle quantity: Skeletal muscle mass was evaluated by BIA. The measurement was made in the supine position before breakfast after the participant had removed all metal objects. The four electrodes of the device, two each on the right foot and right hand of the person, were attached with the device's adhesive tape. The gender, age, height, and body weight of the individual were entered into the device. Measurements were made at a frequency of 50 kHz. The resistance value in ohms, one of the data items obtained as a result of the analysis, was used to calculate the skeletal muscle mass. The resistance value measured during analysis was used in the following formula to calculate skeletal muscle mass, as suggested by Janssen et al. (17): [(height^2/resistance value in BIA measurement x 0.401) +

Table 1. Demographic and clinical data of groups

	Normal	S only	O only	SO	All	p
N (%)**	26 (15.3)	24 (14.5)	46 (27.8)	71 (42.4)	167	
Age ± SD	75.45±8.12[bcd]	80.94±7.03[ac]	71.75±5.63	80.31±6.36	77.34±7.64	**<0.001***
Gender [n (%)]¶						
Female	8 (5.2)[bcd]	14 (8.9)[a]	35 (21.4)[a]	58 (35.1)[a]	121 (70.6)	**<0.001***
Male	16 (10.1)	9 (5.6)	10 (6.5)	11 (7.3)	46 (29.4)	
Number of drugs used (min-max) (CI 95%)	5.84 (2-9) (5.18-6.51)	5.84 (3-10) (4.91-6.81)	5.57 (3-11) (4.95-6.18)	6.53 (2-14) (5.82-7.24)	6.06 (3-25) (5.68-6.44)	0.201
Body mass index (kg/m^2)# (CI 95%)	23.64±2.65 (22.77-24.52)[bc]	21.28±3.20 (20.20-21.22)[acd]	32.10±3.05 (31.37-32.84)[abd]	24.95±4.55 (24.07-25.83)[bc]	26.21±5.35 (25.54-26.88)	**<0.001**
Fat mass percentage (%) # (CI 95%)	27.56±5.94 (23.78-31.34)[cd]	22.36±4.75 (18.99-25.76)[cd]	38.29±14.87 (32.52-44.06)[abd]	44.56±4.21 (43.61-45.51)[abc]	39.86±10.72 (37.98-41.73)	**<0.001**
Comorbidities¶						
Diabetes mellitus n (%)	11 (6.5)	10 (5.9)	26 (15.5)	27 (16.1)	74 (44)	0.132
Cerebrovascular event n (%)	7 (4.2)	4 (2.3)	5 (2.9)	10 (5.9)	26 (15.5)	**0.115**
Congestive heart failure n (%)	9 (5.6)	12 (7.3)[d]	17 (10.5)	18 (10.9)[b]	57 (34.3)	**0.049**
Depression n (%)	5 (2.9)[d]	3 (1.8)[d]	12 (7.2)d	41 (24.5)[abc]	61 (36.4)	**<0.001**
CGA#						
Katz ADL (CI 95%)	4.93±1.20 (4.48-5.38)	3.95±2.36 (2.95-4.95)[sd]	5.23±1.28 (4.91-5.55)[bd]	4.24±2.14 (3.81-4.67)[bc]	4.52±1.91 (4.27-4.78)	**<0.001**
LB-IADL (CI 95%)	10.5±4.96 (8.64-12.35)[d]	8.83±6.74 (6.98-12.68)[c]	13.71±4.20 (12.41-14.76)[bd]	7.88±5.92 (6.69-9.08)[ac]	10.27±5.95 (9.51-11.03)	**<0.001**
MMSE (CI 95%)	21.36±5.56 (19.28-23.44)[d]	25.04±5.52 (22.70-27.37)[d]	21.82±4.72 (20.64-23.00)[d]	17.77±8.29 (16.10-19.44)[abc]	20.33±7.14 (19.43-21.23)	**<0.001**
MNA-SF (CI 95%)	11.23±1.43 (10.69-11.76)[b]	10.29±1.65 (9.59-10.99)[acd]	11.95±1.49 (11.57-12.32)[b]	11.35±2.00 (10.94-11.75)[b]	11.32±1.80 (11.08-11.56)	**<0.001**
GDS-SF (CI 95%)	3.66±1.82 (2.98-4.37)[d]	5.54±3.87 (3.90-7.17)	5.56±2.85 (4.84-6.27)	5.80±3.21 (5.15-6.45)[a]	5.54±3.10 (5.12-5.95)	**0.029**
Handgrip strength (kg) (CI 95%)	20.68±6.44 (18.62-22.75)[bd]	13.92±7.16 (11.55-16.29)[ac]	21.23±8.82 (19.11-23.35)[bd]	13.66±4.83 (12.73-14.58)[ac]	16.88±7.43 (15.93-17.82)	**<0.001**
Waist circumference (cm) (CI 95%)	90.31±9.97 (87.03-93.59)[c]	83.61±10.08 (80.22-86.99)[c]	108.04±6.7 (106.46-109.62)[abd]	91.33±13.13 (88.75-93.91)[bc]	94.70±13.78 (92.91-96.43)	**<0.001**
Hip circumference (cm) (CI 95%)	97.73±7.72 (95.26-100.20)[c]	92.47±7.04 (89.59-95.34)[c]	117.44±12.8 (114.47-120.42)[abd]	95.26±10.96 (93.06-97.47)[c]	101.41±14.8 (99.56-103.25)	**<0.001**
Mid-arm circumference (cm) (CI 95%)	24.47±2.80 (23.52-25.42)[c]	22.44±4.37 (20.91-23.96)[cd]	29.79±2.90 (29.06-30.52)[abd]	25.07±4.04 (24.18-25.86)[bc]	25.86±4.42 (25.29-26.43)	**<0.001**
Laboratory values#						
Fasting blood glucose (mg/dL) (CI 95%)	111.59±54.32 (93.48-129.70)[c]	112.81±39.32 (98.27-127.35)[c]	134.91±51.97 (121.05-148.77)[abd]	108.08±35.92 (100.38-115.78)[c]	117.10±46.16 (111.04-123.16)	**<0.001**
LDL (mmol/L) (CI 95%)	113.64±47.64 (97.76-129.53)	99.93±32.33 (88.47-111.40)[d]	118.94±33.58 (109.79-128.10)	123.32±27.49 (117.73-128.92)[b]	117.12±34.31 (112.75-121.49)	**0.017**
Calcium (mg/dL) (CI 95%)	9.53±0.69 (9.30-9.76)	9.17±0.87 (8.85-9.49)[d]	9.33±0.65 (9.15-9.51)	9.63±0.54 (9.52-9.74)[b]	9.46±0.66 (9.38-9.54)	**0.003**
Total protein (g)/L (CI 95%)	7.00±0.57 (6.81-7.19)	6.83±0.56 (6.62-7.04)[c]	7.28±0.89 (7.03-7.52)[b]	7.02±0.54 (6.91-7.13)	7.07±0.54 (6.99-7.16)	**0.009**
Albumin (g/L) (CI 95%)	3.91±0.53 (3.73-4.09)[b]	3.49±0.6 (3.28-3.71)[acd]	4.07±0.41 (3.97-4.18)[b]	3.96±0.33 (3.90-4.03)[b]	3.93±0.46 (3.88-3.99)	**<0.001**
Sedimentation rate (CI 95%)	21.16±12.05 (7.17-25.15)[bc]	39.79±28.41 (28.13-48.19)[ad]	32.36±29.04 (21.77-39.06)[ad]	20.01±13.32 (17.24-22.77)[bc]	26.40±22.11 (23.58-29.22)	**<0.001**
Leukocyte (WBC) ($x10^9$/L) (CI 95%)	6.89±2.31 (6.10-7.68)	7.03±2.63 (6.14-7.91)	6.90±1.76 (6.46-7.34)	6.84±1.99 (6.45-7.22)	6.92±2.08 (6.66-7.13)	0.906
CRP (mg/L) (CI 95%)	25.61±63.9 (13.01-58.58)[d]	31.79±32.49 (14.77-36.45)	14.32±33.39 (6.30-22.35)	13.85±20.60 (9.86-17.89)[a]	19.17±36.14 (14.66-23.68)	**0.013**
25-Hydroxy vitamin D (µg/L) (CI 95%)	21.01±18.68 (14.40-27.63)[b]	28.53±14.32 (23.44-33.62)[a]	14.66±20.30 (12.15-17.18)[b]	14.41±8.34 (12.79-16.02)[b]	17.35±13.09 (15.74-18.96)	**<0.001**

**Percentages are given in proportion to the total number of patients, One-Way ANOVA test was used for continuous variables# (mean ± SD), chi-square test was used for ordinal or binary variables¶ (%), bonferroni post-hoc tests were performed. CI: Confidence interval, SD: Standard deviation, Normal: Robust, non-sarcopenic-non-obes group, S: Sarcopenic only group, O: Obes only group, SO: Sarcopenic obesity group, ADL: Activities of daily living, IADL: Instrumental activities of daily living, MMSE: Mini-mental state examination, GDS-SF: Geriatric depression scale short form, MNA-SF: Mini nutritional assessment-short form, LDL: Low density lipoprotein, CRP: C-reactive protein results in bold (p<0.005) are statistically significant, [a]: Significant difference to normal, [b]: Significant difference to SP, [c]: Significant difference to OB, [d]: Significant difference to SO

(gender x 3.825) + (age x -0.071)] + 5.102 (height in meters, resistance in ohms, part 1 for male and 0 for female). The value obtained with this formula was divided by the square meter of the participant's height to obtain the absolute skeletal muscle mass. An absolute skeletal muscle mass value of <7.4 kg/m^2 in women and <9.2 kg/m^2 in men corresponds to decreased skeletal muscle mass (16).

3- Physical performance: Muscle performance was evaluated by walking speed measured on a 4-meter track. The start and endpoints of the track were marked so that the person could see them well. After the walking time was measured with an electronic stopwatch, walking speed was calculated in m/sec with the formula 4 m/walking time (sec). Walking speed <0.8 m/sec was evaluated in favor of decreased muscle performance (3).

Those with low muscle strength were defined as probable sarcopenia. A diagnosis of confirmed sarcopenia was made in those with low skeletal muscle in addition to low muscle strength. In addition, those with low physical performance were diagnosed with severe sarcopenia.

Obesity was defined according to the percentage of fat mass (FM) obtained from the BIA analysis. According to FM, the cut-off scores for obesity are 38% and 27% for women and men, respectively (18). SO was defined as the coexistence of obesity and sarcopenia.

Twenty-four hour ambulatory blood pressure monitoring and examined parameters

Measurements of blood pressure and heart rate were made with a 24-hour ambulatory blood pressure measuring device (Mobil-O-Graph Blood Pressure 24-h monitor). The Mobil-O-Graph 24 h (24-hour monitoring) monitor (I.E.M. GmbH, Stolberg, Germany) is a certified monitor for 24-hour blood pressure monitoring (19). The device was designed to operate every 20 minutes between 07 in the morning and 23 in the evening, and every 30 minutes at night. Before the measurement, the patient's date of birth, height, weight, and smoking status was defined in the software program of the device. Patients were allowed to rest for at least 10 minutes before the measurement. They were informed that they should not drink caffeinated beverages within 30 minutes before the measurement. A cuff suitable for arm circumference measurements was used as a brachial cuff in the measurements. The cuff was attached to the upper arm above the brachial artery mark. The patient's bedtime and wake-up times were noted by the patient and their relatives, and the information on the device was loaded into the software while being read. With this device, the parameters whose comparative results are given in Table 2 could be examined (19).

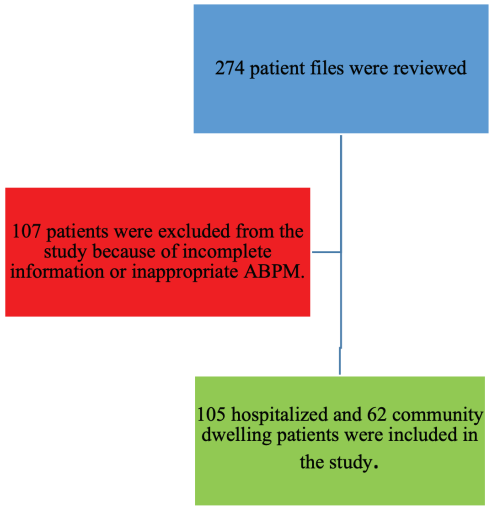

Figure 1. Flow chart of the study participants

Laboratory values

Biochemical parameters were studied using spectrophotometric, C-reactive protein turbidımetric, hormonal tests using ECLIA method and vitamin D levels using HPLC method in Ankara University İbn-i Sina Hospital laboratories. As laboratory values (unit- normal range): Fasting blood glucose (mg/dL 74-100), calculated Glomerular Filtration Rate (hGFR) (mL/min/1.73 m^2>60), calcium (mg/dL 8.8-10.6), total protein (g/L 66-83), albumin (g/L 35-52), leukocyte (WBC) (x10^9/L 4.5-11), hemoglobin (Hb) (g/dL 11.7-16.1), vitamin B12 (pg/mL 126.5-505), TSH (µIU/mL 0.38-5.33), CRP (mg/L 0.0-5.0) and 25-hydroxy vitamin D (µg/L 10-60) values were recorded.

Comprehensive geriatric assessments

Activities of daily living (ADL) were evaluated with the Katz ADL index. This index evaluates dressing, bathing, going to the toilet, getting out of bed, eating, and continence functions over 6 points (20). Instrumental activities of daily living (IADL) were evaluated with the Lawton-Brody IADL scale. On this scale, activities such as using the phone, shopping, preparing meals, housework, laundry, urban transportation, and using drugs properly are evaluated over eight points (21). Cognitive functions were investigated with the mini-mental state examination (MMSE). Low scores on this test, which is evaluated as a total of thirty points, indicate cognitive dysfunction (22). The 15-question short validated form of the geriatric depression score (GDS) was used (23). GDS scores of 5 and above indicate depression. Nutritional status was investigated with a mini-nutritional assessment short-form (MNA). This test, which has proven Turkish validity and reliability, is a test of 14 points. 0-7 points indicate malnutrition, 8-11 points indicate malnutrition risk and 12-14 points indicate normal nutrition (24).

Anthropometric measurements

Body weight, height, body mass index (BMI), waist circumference (WC), hip circumference (HC), and mid-arm circumference (MAC) were measured. A standard measuring device accurate to

0.1 kg and 0.1 cm was used. BMI was calculated as body weight in kilograms divided by the square of height in meters. WC was measured around the smallest abdominal point or midway between the lowest rib and the iliac crest in obese individuals. HC was measured horizontally at the point of greatest lateral extension on the hips or buttocks. MAC measurement was measured between the acromion and the olecranon with the arm raised and internally rotated. All measurements were made by trained personnel.

Statistics

The sample size calculation for this study is based on the following assumptions: According to the results of a previous study (9), the baseline SO rate was 25.8% in older adults. The sample size was calculated as 42 in the calculation made by taking the one-side alpha level of 0.10 and the power of 80%. The suitability of variables to normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov). Descriptive analyses were performed using mean and standard deviation for normally distributed variables, and median and maximum-minimum values for non-normally distributed variables. The frequency of categorical variables was expressed as (%). Chi-square (for categorical variables) and One-Way ANOVA (for continuous variables) tests were used for evaluation between groups in Table 1 and 2. Bonferroni post-hoc tests were performed. Logistic regression analysis was performed to identify conditions that may be associated with sarcopenia and SO risk. Variables that were significant between comparisons were examined as Model 1 and before univariate logistic regression was analyzed. Those that were significant in the univariate analysis were included in the multivariate analysis. After adjusting for confounders, result analysis was performed with Model 3.

Ethics approval and consent to participate: Approval for the study was obtained from the Local Ethics Committee of the Ankara City Hospital with document number E1/1883/2021.

Results

The mean age of the 167 patients included in the study was 75.45±8.12 years. One-hundred twenty-one (70.6%) of them were women. The normal group without sarcopenia consisted of 23 (13.3%), probable sarcopenia 50 (30.1%), confirmed sarcopenia 21 (12.9%), and severe sarcopenia 73 (43.8%). The rates of sarcopenia only, obesity only and SO were 14.5% (n=24), 27.8% (n=46) and 42.4% (n=71), respectively. Demographic and clinical information of the patients is given in Table 1 comparatively. Comprehensive geriatric assessment tests showed a significant difference between the groups. The Katz ADL and MNA scores were the lowest in the sarcopenic group. In the SO group, Lawton-Brody IADL and MMSE scores were the lowest, and the GDS score was the highest. Handgrip strength was also found to be the lowest in the SO group.

The 24-hour ambulatory blood pressure, heart rate, and pulse pressure monitoring results of the groups are shown in Table 2. Daytime and nighttime systolic blood pressure, daytime mean

Table 2. Twenty-four hour blood pressure and pulse rate data of the study groups

# (CI 95%)	Normal	S only	O only	SO	All	p
Daytime SBP (mmHg)	124.21±16.79 (118.68-128.73)	117.63±17.50 (111.71-123.56)[c]	128.23±9.91 (125.85-130.61)[bd]	121.35±13.40 (118.75-123.94)[c]	123.16±14.21 (121.38-124.94)	**0.001**
Night SBP (mmHg)	124.44±17.08 (118.83-130.06)	116.55±17.17 (110.74-122.36)[c]	125.71±13.20 (122.53-128.88)[bd]	117.97±14.04 (115.25-120.68)[c]	120.91±15.29 (119.00-122.81)	**0.001**
Daytime DBP (mmHg)	70.32±10.22 (66.67-73.08)[c]	72.69±11.16 (68.91-76.47)	76.63±7.41 (74.85-78.41)[ad]	72.77±8.08 (71.20-74.33)[c]	73.41±9.00 (72.29-74.54)	**0.002**
Night DBP (mmHg)	68.65±11.08 (65.03-72.28)	70.27±12.34 (66.10-74.45)	72.53±8.72 (70.44-74.63)	69.29±9.09 (67.53-71.05)	70.24±9.87 (69.00-71.47)	0.130
Mean arterial pressure (daytime)	95.18±13.04 (90.89-99.47)	93.00±13.98 (88.26-97.73)[c]	100.21±7.66 (98.37-102.05)[bd]	94.99±9.88 (93.07-96.90)[c]	96.18±10.81 (94.83-97.54)	**0.002**
Mean arterial pressure (night)	94.57±13.56 (90.12-99.03)[d]	91.75±13.68 (87.11-96.38)[d]	97.23±10.57 (94.69-99.77[d]	91.24±10.96 (89.12-93.37)[abc]	93.49±11.93 (92.04-94.98)	**0.008**
Pulse rate (daytime)	72.84±10.37 (69.43-76.25)	76.55±13.60 (71.97-81.16)	72.79±9.59 (70.49-75.10)[d]	77.98±11.58 (75.73-80.22)[c]	75.54±11.45 (74.11-76.97)	**0.010**
Pulse rate (night)	65.21±9.29 (62.15-68.26)	69.86±11.49 (65.97-73.75)	67.36±11.80 (64.52-70.19)	70.76±12.90 (68.26-73.26)	68.83±12.03 (67.33-70.33)	0.058
Pulse pressure (daytime)	50.87±13.07 (46.58-55.17)[b]	41.75±15.25 (36.59-46.91)[a]	48.37±12.62 (45.34-51.41)	47.61±10.33 (45.61-49.82)	47.45±12.55 (45.92-49.03)	**0.012**
Pulse pressure (night)	53.27±14.35 (48.58-57.95)[b]	41.68±16.70 (36.02-47.33)[ac]	50.11±15.24 (46.44-53.77)[b]	47.98±12.12 (45.63-50.32)	48.47±14.49 (46.67-50.26)	**0.004**

One-Way ANOVA test was used for continuous variables# (mean ± SD), Bonferroni post-hoc tests were performed. CI: Confidence interval, SD: Standard deviation, Normal: Robust, non-sarcopenic-non-obes group, S: Sarcopenic only group, O: Obes only group, SO: Sarcopenic obesity group, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

arterial pressure, and daytime and nighttime pulse pressure were lowest in the sarcopenic group. The obese group had the highest daytime and nighttime systolic blood pressure, daytime and nighttime mean arterial pressure, and the lowest daytime pulse rate. In the SO group, mean arterial pressure was the lowest at night and the pulse rate was the highest during the day.

Logistic regression analysis was performed to identify conditions that may be associated with sarcopenia and the risk of SO. Variables that were significant between comparisons in Table 1 and risk factors for blood pressure changes were included in the univariate analysis. Those that were significant in the univariate analysis were included in the multivariate analysis. In the analysis of sarcopenia in Table 3, the values that were significant in previous comparisons were examined as Model 1. After adjusting for age, BMI significant blood pressure values were analyzed in Model 2. Model 3 was established according to Model 1 and Model 2 results. Consequently, age, BMI, daytime SBP, and daytime mean arterial pressure were found to be the most important factors increasing the risk of sarcopenia.

In Table 4, logistic regression analysis was performed in which SO was taken as the dependent variable. In Model 1, clinical and laboratory variables that were significant in previous evaluations were analyzed. In Model 2, after adjusting for gender and other confounders, blood pressure parameters were analyzed. In Model 3, variables that were significant in Model 1 and 2 were analyzed. After adjusting for confounders for SO, being a woman, having a high nighttime mean arterial pressure and a high daytime pulse rate had higher OR. The results are shown in Table 4 and Supplementary Tables 1, 2.

Discussion

We could not find any other study in the literature examining the severity of sarcopenia in older adults and its relationship with 24-hour blood pressure monitoring in separate groups, as only sarcopenia, only obesity, and SO. To our knowledge, this is the first study conducted in this way. In our study, not only muscle mass but also muscle performance was examined in the definition of sarcopenia, and a comprehensive geriatric assessment was made.

The main findings of this study are that obesity may have a greater effect on blood pressure and mean arterial pressure elevation. Sarcopenia and SO may be associated with hypotension, low pulse pressure, low mean arterial pressure in older adults. The rate of CHF, and LDL elevation, which are clinically risk factors for CVD, was more common in the SO group. In the logistic regression analysis for SO, female gender, increased nighttime mean arterial pressure, and increased daytime pulse rate were found to be risk-related factors.

The rates found in our study were 8.9%, 21.4%, and 35.1% for sarcopenia only, obesity only, and SO, respectively, in women. In men it was 5.6%, 6.5% and 7.3%, respectively. In other studies on SO in older adults, the rates range from 0.1% to 85.3% (5,6,13,25-27). Due to the retrospective and cross-sectional design of our study, it is not possible to give the prevalence and therefore the frequency. It can only be used to determine the rate. In addition, the frequency of the female population and inpatients in our study stands out. Prospective studies with homogeneous distribution for gender would be more meaningful to determine complete data and the full efficacy of SO. One of the reasons why SO rates change so much is that a common equation is not used for the definition in the studies. SO definition in this respect is still a big problem. There are calls to create a definition and work with that definition (28,29).

Table 3. Logistic regression analysis for sarcopenia

	ß (odd ratio)	95% CI	p
Model 1			
Age	1.126	(1.073-1.181)	**<0.001***
BMI	0.845	(0.789-0.904)	**<0.001***
Model 2			
Daytime SBP (mmHg)	0.889	(0.809-0.977)	**0.014***
Night SBP (mmHg)	0.992	(0.948-1.039)	0.735
Mean arterial pressure (daytime)	1.122	(1.016-1.239)	**0.024***
Daytime pulse pressure	1.084	(1.002-1.175)	0.055
Night pulse pressure	0.939	(0.876-1.007)	0.079
Model 3			
Age	1.128	(1.074-1.184)	**<0.001***
BMI	0.856	(0.797-0.919)	**<0.001***
Daytime SBP (mmHg)	0.903	(0.839-0.972)	**0.007***
Mean arterial pressure (daytime)	1.112	(1.009-1.225)	**0.033***

CI: Confidence interval, BMI: Body mass index, SBP: Systolic blood pressure

Table 4. Logistic regression analysis for sarcopenic obesity

	ß (odd ratio)	95% CI	p
Model 1			
Gender[a]	3.556	(1.876-6.742)	**<0.001***
Model 2			
Mean arterial pressure (night)	0.0975	(0.953-0.998)	**0.034***
Pulse rate (daytime)	1.038	(1.015-1.063)	**<0.001***
Model 3			
Gender[a]	3.271	(1.695-6.314)	**<0.001***
Mean arterial pressure (night)	0.976	(0.953-1.012)	**0.046***
Pulse rate (daytime)	1.32	(1.007-1.057)	**0.012***

[a]: Be female, CI: Confidence interval

In our study, the highest BMI rate was found in the obese group, and the fat percentage rate was highest in the SO group. One of the most important problems of SO in older adults is the definition of obesity with BMI in the same way as in the general population. However, studies are showing that BMI is insufficient to define the impaired body composition in older adults and it is not an appropriate method, especially in sarcopenic individuals (6,26). In a review that summarizes how the definitions are made, it has been shown that both the definition of sarcopenia and the definition of obesity are made in different ways and that there is no internationally accepted limit value (29).

When the results of comprehensive geriatric assessment tests were examined, we found that Katz ADL and MNA scores were low in sarcopenic patients. In addition, we found that instrumental life activities and cognition were adversely affected in those with SO and may be associated with depression. In the study of Öztürk et al. (5), in which they examined the effects of SO on clinical conditions and quality of life, SO was found to be associated with low cognition and life activity scores, similar to the findings in our study. Scores related to instrumental life activities, cognition, and depression were found to be low in the sarcopenic obese group (5). Many studies since Baumgartner et al. (11), the first descriptor of the term SO, have shown that SO is associated with poor physical performance and reduced life activities compared to sarcopenia and obesity alone (6,25,30). There are also studies showing that SO is associated with malnutrition and cognition disorders (4,30,31). It appears that from clinical repercussions SO is associated with a worse condition than sarcopenia alone and obesity alone.

When laboratory data were examined, fasting blood glucose was lowest in the SO group. The highest was in the obesity group. High fasting blood glucose may be related to insulin resistance. Adding sarcopenia to obesity can shift people to the side of malnutrition. When the general laboratory results are examined, it is seen that nutritional values are low and inflammation values are high in the sarcopenic group. This again suggests that sarcopenia is the most prone to malnutrition and inflammation among the groups we examined. One of the common points of studies on the pathogenesis of sarcopenia and obesity suggests that there may be an underlying mild inflammatory condition, with proinflammatory cytokines secreted from adipose tissue and high lipid influx into muscle fibers. Several endocrine-hormonal, metabolic, and lifestyle aspects play a role in the formation of SO and ultimately influence the pathophysiological aspects that may contribute to the development of cardiovascular diseases and neoplasms (10).

It has been emphasized in some studies that SO can be associated with metabolic syndrome, diabetes mellitus, cardiovascular disease, dyslipidemia, and hypertension (6,13,14,28,32,33). It has been suggested that especially the sarcopenia component of SO may be associated with these diseases with many possible pathological mechanisms that have not yet been explained. Among these, neuronal and hormonal changes are mechanisms, as well as being underweight, malnutrition, low protein intake, physical inactivity, and inflammation (10). However, studies on risk factors for CVD and its effects on blood pressure are very limited. Cross-sectional studies have given inconsistent results (6). Some studies have found SO as a factor that increases the risk of CVD (9,14,15). Some studies have shown that there is no difference between a sarcopenic obese group and other groups (34,35). In the "Cardiovascular Health Study" analysis of Stephen and Janssen (36) which examined the relationship between SO and CVD risk over time, the risk of CVD events was not found to be significantly increased. A recent review showed a consistent association between SO and cardiovascular disease risk. It is also a fact that most of the articles compiled in this study are of cross-sectional design, which cannot evaluate a causal relationship. It is also stated that many studies on this subject have been done on Asian people, so the generalization may be limited (37).

In the results of 24-hour blood pressure monitoring, which was the main purpose of our study, in the sarcopenic group daytime and nighttime systolic blood pressure, daytime means arterial pressure, and daytime and nighttime pulse pressure were the lowest. Daytime and nighttime systolic blood pressure, and daytime and nighttime mean arterial pressure were highest and daytime pulse rate was lowest in the obese group. For the SO group, we found that this group had the lowest mean arterial pressure at night and the highest pulse rate during the day. In logistic regression analysis, high age increased BMI, increased daytime systolic blood pressure, and increased mean daytime arterial pressure was found to be factors that may be associated with sarcopenia. In analyses of SO, female gender increased nighttime mean arterial pressure, and increased daytime pulse rate was found to be risk-related factors. The lowest systolic blood pressure values were significantly found in the sarcopenic group. The relationship between sarcopenia and blood pressure has been a subject of interest before and has been studied. Some studies accept sarcopenia as a cardiovascular risk and find that it is associated with high blood pressure (38,39). In contrast, some studies found sarcopenia to be associated with hypotension and orthostatic hypotension (8,40). In a previous study from our group, we found that sarcopenia may be associated with low blood pressure in older adults who have fallen (41). In this new study, in which we examined the relationship between blood pressure and body composition, the female and hospitalized patient groups had a higher rate. These groups are likely to be frail older adults with poor physical performance, frailty, and prone to dependency. This difference between the patient groups may have affected the results.

It is seen that the obese group has relatively high blood pressure values. In light of this information, we may say that the group associated with low systolic blood pressure is the sarcopenia group, and the group associated with high systolic blood pressure is the obese group. Similar to the results in our study, the New Mexico Aging Process Study also showed that the rate of hypertension was higher in non-sarcopenic obese (42). In the case of sarcopenia, physical inactivity can lead to decreased energy and fat accumulation, especially in the abdominal area. This situation may be reflected in the clinic as a decrease in blood pressure. Conversely, it can be argued that abdominal obesity may lead to hypertension through cytokine activation (6,15).

From the mean arterial pressure measurements that were used as one of the predictors of adverse cardiovascular outcomes, the daytime value was the lowest in the sarcopenic group and the highest in the obese group, while the nighttime value was the lowest in the SO group and highest in the obese group. This result may associate high CVD risk with obesity. In the case of SO, the addition of sarcopenia to obesity appears to reduce the risk relatively. The question to be asked here is does the mean arterial pressure, which is known to be affected by arterial stiffness, really decrease in sarcopenia? What mechanism could this have? The answer to these questions may be the decrease in baroreceptor reflexes in sarcopenic patients and the low physical performance of this patient group as mentioned above. Although the values that increase the CVD risk seem to decrease sarcopenia in the results, it should be considered that these results may have different cut-off values in older adults and sarcopenic patients (41,43).

When the results of the relationship between pulse and pulse pressure are examined, the addition of sarcopenia may be associated with a relative risk reduction for CVD compared to obesity alone. In previous studies, it has been argued that high levels of these values are associated with poor cardiovascular prognosis. In older adults, increased systolic pressure may be due to increased stiffness in the aorta and other large arteries (44). However, there are also studies in which it has been determined that low pulse pressure can be an indicator of poor prognosis and mortality, especially in patients with heart failure. Just as the effects of obesity and being overweight on mortality in older adults are paradoxical, there may be a paradox in these cardiovascular markers. Indicators such as blood pressure, mean arterial pressure, pulse rate, and pulse pressure cannot be used as only a sign of arterial health in older adults since most older adults have malnutrition, neurological disorders, and many comorbidities.

These findings have shown that obesity may have more of an effect on raising blood pressure and mean arterial pressure in older adults. Sarcopenia and SO may be associated with decreased blood and pulse pressure and mean arterial pressure in older adults (45). SO is a relatively new definition. To determine the health problems it is associated with, first of all, a consensus should be reached on its definition and the methods to be used in the definition. Prospective studies involving a large number of participants in the geriatric population, especially including and comparing frail adults and also community-dwelling persons will be interesting and valuable.

Study Limitations

Our study had some limitations. First of all, due to the retrospective cross-sectional design of the study, a causal relationship could not be established between blood pressure values and sarcopenia-SO. Secondly, the results cannot be generalized to all geriatric patients because the rate of inpatients was high in the patient group. Further studies using a sample pool more similar to the general population are needed. Lastly, the BIA method could be affected by the hydration status of individuals. In addition, the accumulation of fat in muscle tissue in obese individuals may lead to a missed diagnosis of sarcopenia. Despite all these disadvantages, the BIA method is accepted as a valid, inexpensive, portable, and reliable method for measuring muscle mass with EWGSOP.

Besides some limitations of the study, there are also quite a few strong aspects. The diagnosis of sarcopenia was made according to the new criteria defined in EWGSOP-2. In the diagnosis of sarcopenia, not only muscle mass but also performance was evaluated. The diagnosis of SO is done with the fat percentage measured by BIA for the definition of obesity. The evaluations and comparisons of the patients were made in a versatile way with sociodemographic data, CGA tests, and, lab data. Blood pressures are not instantaneous data, but a 24-hour measurement. In addition, the participants were divided into four different groups and compared. Thus, the most related component to the investigated factors was determined.

Conclusion

We found that obesity may be more related to blood pressure and mean arterial pressure elevation. Sarcopenia and SO may be associated with hypotension, low pulse pressure, and low mean arterial pressure in older adults. The rate of CHF and LDL elevation, which are clinically risk factors for CVD, were more common in the SO group. In the logistic regression analysis for SO, the female gender increased nighttime mean arterial pressure, and increased daytime pulse rate were found to be risk-related factors. SO is a common and easily overlooked clinical syndrome in older people. Our study showed that these patients may also have cardiovascular risk factors. In the geriatric population, screening should be done by focusing not only on sarcopenia but also on SO.

Ethics

Ethics Committee Approval: Ethics approval and consent to participate: Approval for the study was obtained from the Local

Ethics Committee of the Ankara City Hospital with document number E1/1883/2021.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: V.A., R.B., D.M.S., H.S.Ö., Ç.C., A.Y., M.V., Design: V.A., R.B., D.M.S., T.Ö.T., Data Collection or Processing: H.S.Ö., T.Ö.T., V.A., Analysis or Interpretation: H.S.Ö., R.B., T.Ö.T., Ç.C., S.A., M.V., Literature Search: H.S.Ö., V.A., R.B., Ç.C., Writing: H.S.Ö., R.B.

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References

1. UN Decade of Healthy Ageing 2022 [05/04/2022]. Available from: https://www.who.int/initiatives/decade-of-healthy-ageing
2. Heo M, Faith MS, Pietrobelli A, Heymsfield SB. Percentage of body fat cutoffs by sex, age, and race-ethnicity in the US adult population from NHANES 1999-2004. Am J Clin Nutr 2012;95:594-602.
3. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:601.
4. Beaudart C, Zaaria M, Pasleau F, Reginster JY, Bruyère O. Health Outcomes of Sarcopenia: A Systematic Review and Meta-Analysis. PLoS One 2017;12:e0169548.
5. Öztürk ZA, Türkbeyler İH, Abiyev A, Kul S, Edizer B, Yakaryılmaz FD, Soylu G. Health-related quality of life and fall risk associated with age-related body composition changes; sarcopenia, obesity and sarcopenic obesity. Intern Med J 2018;48:973-981.
6. Atkins JL, Wannamathee SG. Sarcopenic obesity in ageing: cardiovascular outcomes and mortality. Br J Nutr 2020;124:1102-1113.
7. Chen X, Kong C, Yu H, Gong J, Lan L, Zhou L, Gong J, Liu P, Xu L, Deng Q. Association between osteosarcopenic obesity and hypertension among four minority populations in China: a cross-sectional study. BMJ Open 2019;9:e026818.
8. Soysal P, Kocyigit SE, Dokuzlar O, Ates Bulut E, Smith L, Isik AT. Relationship between sarcopenia and orthostatic hypotension. Age Ageing 2020;49:959-965.
9. Chung JY, Kang HT, Lee DC, Lee HR, Lee YJ. Body composition and its association with cardiometabolic risk factors in the elderly: a focus on sarcopenic obesity. Arch Gerontol Geriatr 2013;56:270-278.
10. Silveira EA, da Silva Filho RR, Spexoto MCB, Haghighatdoost F, Sarrafzadegan N, de Oliveira C. The Role of Sarcopenic Obesity in Cancer and Cardiovascular Disease: A Synthesis of the Evidence on Pathophysiological Aspects and Clinical Implications. Int J Mol Sci 2021;22:4339.
11. Baumgartner RN, Wayne SJ, Waters DL, Janssen I, Gallagher D, Morley JE. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. Obes Res 2004;12:1995-2004.
12. Rantanen T, Harris T, Leveille SG, Visser M, Foley D, Masaki K, Guralnik JM. Muscle strength and body mass index as long-term predictors of mortality in initially healthy men. J Gerontol A Biol Sci Med 2000;55:M168-M173.
13. Atmis V, Yalcin A, Silay K, Ulutas S, Bahsi R, Turgut T, Mut Sürmeli D, Selvi Öztorun H, Yaman S, Çoşarderelioğlu Ç, Aras S, Varli M. The relationship between all-cause mortality sarcopenia and sarcopenic obesity among hospitalized older people. Aging Clin Exp Res 2019;31:1563-1572.
14. Khadra D, Itani L, Chebaro Y, Obeid M, Jaber M, Ghanem R, Ayton A, Kreidieh D, E Masri D, Kimura A, Tannir H, El Ghoch M. Association Between Sarcopenic Obesity and Metabolic Syndrome in Adults: A Systematic Review and Meta-Analysis. Curr Cardiol Rev 2020;16:153-162.
15. Park SH, Park JH, Song PS, Kim DK, Kim KH, Seol SH, Kim HK, Jang HJ, Lee JG, Park HY, Park J, Shin KJ, Kim Di, Moon YS. Sarcopenic obesity as an independent risk factor of hypertension. Journal of the American Society of Hypertension. J Am Soc Hypertens 2013;7:420-425.
16. Bahat G, Tufan A, Tufan F, Kilic C, Akpinar TS, Kose M, Erten N, Karan MA, Cruz-Jentoft AJ. Cut-off points to identify sarcopenia according to European Working Group on Sarcopenia in Older People (EWGSOP) definition. Clin Nutr 2016;35:1557-1563.
17. Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. J Appl Physiol (1985) 2000;89:465-471.
18. Levine ME, Crimmins EM. The impact of insulin resistance and inflammation on the association between sarcopenic obesity and physical functioning. Obesity (Silver Spring) 2012;20:2101-2106.
19. Wei W, Tolle M, Zidek W, van der Giet M. Validation of the mobil-O-Graph: 24 h-blood pressure measurement device. Blood Press Monit 2010;15:225-228.
20. Arik G, Varan HD, Yavuz BB, Karabulut E, Kara O, Kilic MK, Kizilarslanoglu MC, Sumer F, Kuyumcu ME, Yesil Y, Halil M, Cankurtaran M. Validation of Katz index of independence in activities of daily living in Turkish older adults. Arch Gerontol Geriatr 2015;61:344-350.
21. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179-186.
22. Thal LJ, Grundman M, Golden R. Alzheimer's disease: a correlational analysis of the Blessed Information-Memory-Concentration Test and the Mini-Mental State Exam. Neurology 1986;36:262-264.
23. Durmaz B, Soysal P, Ellidokuz H, Isik AT. Validity and reliability of geriatric depression scale-15 (short form) in Turkish older adults. North Clin Istanb 2018;5:216-220.
24. Guigoz Y, Vellas B. The Mini Nutritional Assessment (MNA) for grading the nutritional state of elderly patients: presentation of the MNA, history and validation. Nestle Nutr Workshop Ser Clin Perform Programme 1999;1:3-11; discussion 11-2.
25. Roh E, Choi KM. Health Consequences of Sarcopenic Obesity: A Narrative Review. Front Endocrinol (Lausanne) 2020;11:332.
26. Purcell SA, Mackenzie M, Barbosa-Silva TG, Dionne IJ, Ghosh S, Siervo M, Ye M, Prado CM. Prevalence of Sarcopenic Obesity Using Different Definitions and the Relationship With Strength and Physical Performance in the Canadian Longitudinal Study of Aging. Front Physiol 2020;11:583825.
27. Wagenaar CA, Dekker LH, Navis GJ. Prevalence of sarcopenic obesity and sarcopenic overweight in the general population: The lifelines cohort study. Clin Nutr 2021;40:4422-4429.
28. Barazzoni R, Bischoff S, Boirie Y, Busetto L, Cederholm T, Dicker D, Toplak H, Van Gossum A, Yumuk V, Vettor R. Sarcopenic Obesity: Time to Meet the Challenge. Obesity Facts 2018;11:294-305.
29. Baker JF, Harris T, Rapoport A, Ziolkowski SL, Leonard MB, Long J, Zemel B, Weber DR. Validation of a description of sarcopenic obesity defined as excess adiposity and low lean mass relative to adiposity. J Cachexia Sarcopenia Muscle 2020;11:1580-1589.
30. Ciudin A, Simó-Servat A, Palmas F, Barahona MJ. Sarcopenic obesity: a new challenge in the clinical practice. Endocrinol Diabetes Nutr (Engl Ed) 2020;67:672-681.

31. Tolea MI, Chrisphonte S, Galvin JE. Sarcopenic obesity and cognitive performance. Clin Interv Aging 2018;13:1111-1119.
32. Choi KM. Sarcopenia and sarcopenic obesity. Korean J Intern Med 2016;31:1054-1060.
33. Tyrovolas S, Panagiotakos D, Georgousopoulou E, Chrysohoou C, Tousoulis D, Haro JM, Pitsavos C. Skeletal muscle mass in relation to 10 year cardiovascular disease incidence among middle aged and older adults: the ATTICA study. J Epidemiol Community Health 2020;74:26-31.
34. dos Santos EP, Gadelha AB, Safons MP, Nóbrega OT, Oliveira RJ, Lima RM. Sarcopenia and sarcopenic obesity classifications and cardiometabolic risks in older women. Arch Gerontol Geriatr 2014;59:56-61.
35. Chin SO, Rhee SY, Chon S, Hwang YC, Jeong IK, Oh S, Ahn KJ, Chung HY, Woo JT, Kim SW, Kim JW, Kim YS, Ahn HY. Sarcopenia is independently associated with cardiovascular disease in older Korean adults: the Korea National Health and Nutrition Examination Survey (KNHANES) from 2009. PLoS One 2013;8:e60119.
36. Stephen WC, Janssen I. Sarcopenic-obesity and cardiovascular disease risk in the elderly. J Nutr Health Aging 2009;13:460-466.
37. Evans K, Abdelhafiz D, Abdelhafiz AH. Sarcopenic obesity as a determinant of cardiovascular disease risk in older people: a systematic review. Postgrad Med 202;133:831-842.
38. Bai T, Fang F, Li F, Ren Y, Hu J, Cao J. Sarcopenia is associated with hypertension in older adults: a systematic review and meta-analysis. BMC Geriatr 2020;20:279.
39. Han K, Park YM, Kwon HS, Ko SH, Lee SH, Yim HW, Lee WC, Park YG, Kim MK, Park YM. Sarcopenia as a determinant of blood pressure in older Koreans: findings from the Korea National Health and Nutrition Examination Surveys (KNHANES) 2008-2010. PLoS One 2014;9:e86902.
40. Harada H, Ikeda H, Nishiyama Y, Niiyama H, Katoh A, Kai H. Increased arterial velocity pulse index is an independent factor related to skeletal muscle mass reduction and tissue damage in patients with cardiovascular disease. Hypertens Res 2020;43:534-542.
41. Öztorun HS, Bahsi R, Turgut T, Surmeli DM, Cosarderelioğlu C, Atmis V, Yalcin A, Aras S, Varli M. The relationship between sarcopenia and central hemodynamics in older adults with falls: a cross-sectional study. Blood Press Monit 2022;27:87-97.
42. Baumgartner RN, Wayne SJ, Waters DL, Janssen I, Gallagher D, Morley JE. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. Obes Res 2004;12:1995-2004.
43. Wong A, Jaime SJ, Grubbs B, Panton LB, Fischer SM, Figueroa A. Attenuated aortic blood pressure responses to metaboreflex activation in older adults with dynapenia. Exp Gerontol 2020;138:110984.
44. Zhang L, Guo Q, Feng BL, Wang CY, Han PP, Hu J, Sun XD, Zeng WF, Zheng ZX, Li HS, Zhou LB, Luo Q, Jiang LF, Ye HH. A Cross-Sectional Study of the Association between Arterial Stiffness and Sarcopenia in Chinese Community-Dwelling Elderly Using the Asian Working Group for Sarcopenia Criteria. J Nutr Health Aging 2019;23:195-201.
45. Spence JD. Risk from low blood pressure in frail older adults: diastolic pressure and pulse pressure are important. Age Ageing 2021;50:e5-e6.

Supplementary Table 1. Logistic regression analysis for sarcopenia

	ß (odd ratio)	95% CI	p
Model 1			
Age	1.126	(1.073-1.181)	**<0.001***
Gender[a]	1.099	(1.042-1.159)	0.352
Diabetes mellitus	1.009	(0.607-3.184)	0.981
Congestive heart failure	1.390	(0.609-2.675)	0.436
Cerebrovascular event	1.180	(0.427-3.258)	0.479
Depression	0.354	(0.234-2.75)	0.647
Body mass index (kg/m^2)	0.845	(0.789-0.904)	**<0.001***
Fat mass percentage (%)	0.514	(0.165-1.307)	0.752

CI: Confidence interval, [a]: Be female

Supplementary Table 2. Logistic regression analysis for sarcopenic obesity

	ß (odd ratio)	95% CI	p
Model 1			
Age	1.101	(1.044-1.160)	0.647
Gender[a]	3.556	(1.876-6.742)	**<0.001***
Diabetes nellitus	1.137	(0.560-2.311)	0.722
Congestive heart failure	1.016	(0.459-2.250)	0.958
Cerebrovascular event	0.792	(0.302-2.076)	0.635
Body mass index (kg/m^2)	0.769	(0.703-0.840)	0.564
Fat mass percentage (%)	1.073	(1.032-1.117)	0.367

CI: Confidence interval, [a]: Be female

ORIGINAL RESEARCH

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Relationship Between Polypharmacy and Geriatric Syndromes in Older Nursing Home Residents

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Abstract

Objective: Our aim is to determine the prevalence of polypharmacy and the relationship between polypharmacy and geriatric syndromes as well as comorbidity in older nursing home residents (NHR).

Materials and Methods: This observational and cross-sectional study was conducted with 217 adults ≥60 years of age who had Katz index of Independence in activities of daily living score over 4 points and were institutionalized at nursing care home from March to April 2019. Polypharmacy was defined as the daily use of 5 or more medications. Geriatric syndromes include dementia, depression, urinary incontinence (UI), malnutrition, falls, mobility problems, hearing loss, vision impairment.

Results: The prevalence of polypharmacy among NHR was 61.8%. By univariate analysis, polypharmacy was associated with chronic diseases such as heart disease, chronic obstructive pulmonary disease (COPD) and diabetes mellitus, and with geriatric syndromes such as dementia, depression, UI, and mobility problems ($p<0.05$). In the multivariate analyses, depression [odds ratio (OR) =9.57; 95% confidence interval (CI), 2.73-33.60] and mobility problems (OR= 4.88; 95% CI, 1.80-13.25) increased polypharmacy by 9.6 and 4.9-fold respectively.

Conclusion: Comorbidity and geriatric syndromes play an important role in the development of polypharmacy. Monitoring polypharmacy is often necessary as well as giving complex medication regimens for NHR.

Keywords: Activities of daily living, comorbidity, geriatric syndromes, nursing homes, polypharmacy

Introduction

Polypharmacy is becoming increasingly prevalent in older adults each year, particularly in nursing home residents (NHR). Older adults without disabilities can easily access health services to prescribe medications. The lack of assessment of patient's prior medications by each specialist is the main reason for widespread polypharmacy among NHR. Consequently, the risk of polypharmacy increases along with an increased number of hospital admissions and comorbidities.

Polypharmacy does not have a generally accepted definition (1,2). Similarly, it was defined by the World Health Organization as followed: "Polypharmacy is the concurrent use of multiple medications. Although there is no standard definition, polypharmacy is often defined as the routine use of five or more medications. This includes over-the-counter, prescription and/or traditional and complementary medicines used by a patient" (3). The most common definition for polypharmacy is the use of five or more medications (1). According to this definition, the prevalence of polypharmacy ranged from 38.1% to 91.2% in NHR (2,4,5). The prevalence of polypharmacy varied based on numerical definitions of polypharmacy, dependence of NHR, age, and level of care (1).

Polypharmacy increases as the number of comorbidities increases (6). Polypharmacy was found to be associated with heart disease, functional decline, stroke, geriatric syndromes, including cognitive impairment, depression, poor nutrition, and falls (7-9). Polypharmacy in long-term care facilities was associated with comorbid conditions; circulatory diseases, digestive disorders, endocrine and metabolic disorders, genitourinary disorders musculoskeletal disabilities, neurological motor dysfunction,

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pulmonary diseases (5,10). As a result, polypharmacy was associated with the number of hospitalizations, length of stay, emergency department admission and all-cause hospitalization (2). Chang et al. (11) demonstrated an association between polypharmacy and mortality, regardless of chronic conditions.

Understanding the factors associated with polypharmacy is important to reduce negative outcomes of comorbidities. The relationship between polypharmacy and geriatric syndromes has been investigated generally in the community dwelling older outpatients in Turkey (12-17). In addition, research in nursing homes usually focused on the association of polypharmacy with sarcopenia in Turkey (18,19). Based on this background, the aim of this study is to determine the prevalence of polypharmacy and the relationship between polypharmacy and geriatric syndromes as well as comorbidities in older NHR.

Materials and Methods

Study population

This observational and cross-sectional study was conducted with 217 adults, ≥60 years of age who were institutionalized at nursing care home from March to April 2019. The NHRs who had Katz index of independence in activities of daily living (KATZ-ADL) score below 5 points were excluded (20). No sampling was done because it was planned to include all eligible NHRs in this study.

Assessments

Data were collected using a structured questionnaire by researchers through face-to-face interviews with NHRs and the responsible nurses of them. Patients' data about number of chronic diseases and prescribed drugs; falls (in the last year); the presence of urinary incontinence (UI); visual impairment; hearing loss; walking disability (the use of a cane, crutches, walking frame); malnutrition; admission to the hospital in the last six months, were noted. Polypharmacy was defined as the daily use of 5 or more medications (1,21), and NHRs were separated into groups by polypharmacy status as non-polypharmacy and polypharmacy.

Geriatric Syndromes

Functional status

To evaluate functional status, KATZ-ADL scale was used. KATZ-ADL assesses six functions, including dressing, feeding, going to toilet, continence, bathing and transferring. A score of 4 and below indicates functional impairment (20). The NHR who had KATZ-ADL score below 5 points were excluded.

Dementia

The cognitive function of all NHRs is routinely assessed by clinical judgment annually and as needed; NHRs are referred to a neurologist as required. So, participants with a diagnosis of dementia and taking anti-dementia drugs were assessed as having dementia.

Depression

The presence of depression is assessed by the 15 item geriatric depression scale short-form in NHRs every six months; NHRs are referred to a psychiatrist as required. Participants with a diagnosis of depression and taking antidepressant treatment were assessed as having depression.

Falls

A fall was defined as "an unexpected event in which the participant comes to rest on the ground, floor, or lower level" (22). Falls history over the past 12 months has been noted.

UI

UI was defined as the unintentional passing of urine independent of the amount. Participants taking medication for UI were also included.

Visual impairment

Visual impairment was defined as wearing glasses or a decreased ability to see. We assessed visual impairment by clinical judgment.

Hearing loss

Hearing loss was defined as the use hearing aids or the inability to hear as well as an individual with normal hearing.

Mobility problems and using mobility aids

The presence of mobility problems was considered as existent if unsteady walking, difficulty in sitting and standing, difficulty in walking and moving, requiring use of mobility aids or falls were present. The use of a cane, crutches, and walking frame were noted as using mobility aids.

Malnutrition

Malnutrition is assessed by the mini nutritional assessment in NHRs every six months. Participants who received oral nutritional supplements based on a score 7 and lower MNA, were recorded as having malnutrition.

Statistics

Data analyses were performed using SPSS version 25.0 for Windows. Normality was assessed by Kolmogorov-Smirnov's test. Normally distributed quantitative variables were expressed by mean ± standard deviations, and those without normal distribution are expressed by median and minimum-maximum values. Quantitative variables without normal distribution were expressed by mean ± standard deviations in the table if they have statistical significance. Qualitative variables were

expressed as frequency and percentages. Chi-square (X^2) test and Fisher's Exact test were used in the analysis of qualitative variables. The t-test and Mann-Whitney U test were used in the analysis of quantitative variables where available. Multiple logistic regression analysis was performed for multivariate analysis. Logistic Regression model was performed for variables which showed significant relationships with univariate analysis. A value of $p<0.05$ was accepted as statistically significant.

Results

Of the NHRs, 54 (24.9%) were in the 60-69 age group, 85 (39.2%) in the 70-79 age group and 78 (35.9%) in the 80 and over age group. Median (min-max) of age was 76 (61-110). Median (min-max) of medication number of all NHRs was 6 (0-17), 3 (0-4) in non-polypharmacy group, 7 (5-17) in polypharmacy group. Prevalence of polypharmacy was 61.8% in this study. The polypharmacy group had a higher hospital admission rate in last 6 months and a higher comorbidity prevalence than the non-polypharmacy group. There was no relationship between polypharmacy and other socio-demographic characteristics. Descriptive of the groups are shown in Table 1.

Of the NHRs, 38 (17.5%) had at least one chronic disease, 43 (19.8%) had two chronic diseases and 136 (62.7%) had three or more chronic diseases. The most common diseases were hypertension (58.5%), cardiovascular system diseases (27.2%) and benign prostatic hyperplasia (22.6%), followed by chronic obstructive pulmonary disease (COPD) and diabetes mellitus (DM) (19.4%). Falls, malnutrition, hearing loss, and vision impairment were not associated with polypharmacy. Comorbidity status according to polypharmacy is given in Table 2.

Thirteen (6%) participants took one drug, fifty-nine (27.2%) participants took two-four drugs, hundred and five (48.4%) participants took five-nine drugs, and twenty-nine (13.3%) participants ten or more drugs. The most used drugs in both groups were angiotensin-converting enzyme inhibitor&angiotensin-2 receptor blocker, antiplatelet drugs, and diuretics. The most used drugs in NH are given in Table 3.

All chronic diseases, except geriatric syndromes, were significantly associated with polypharmacy in univariate and multivariate analysis. Depression was found to be a better independent predictor of polypharmacy in NHRs compared with other co-morbidities (odds ratio: 9.57; 95% confidence interval: 2.73-33.6; $p<0.001$) (Table 4). However, the depression had wide confidence intervals. In terms of geriatric syndromes, dementia and UI were not associated with polypharmacy in the multivariate analysis (Table 4).

Discussion

In this study, we aimed to determined the relationship between polypharmacy and comorbidities, especially geriatric syndromes, in NHR without functional impairment. Prevalence of polypharmacy was 61.8% and polypharmacy was increased with depression and mobility problems.

There was a significant difference between the polypharmacy group and non-polypharmacy group in scores of Katz ADL. A cross-sectional, observational study conducted by 1002 community-dwelling older women showed that the use of five or more medications resulted in risk of decreasing instrumental ADL (IADL) score (23). A similar outcome was found by combining ADL and IADL (24). Furthermore, studies have found the negative association between ADL score and polypharmacy in chronic diseases (25-27). Also, there were a few studies that have not demonstrated the relationship between polypharmacy and functional decline in NH (28,29). Consequently, health professionals should be aware of the association between polypharmacy and functional decline.

Polypharmacy could be an indicator of an individual's underlying medical condition. There is heterogeneity among

Table 1. Descriptive statistics of study participants

	Non polypharmacy (n=83, 38.2%)	Polypharmacy (n=134, 61.8%)	p
Age (years)	74 (63-110)	77 (61-95)	0.19
Gender			0.21
M (n, %)	49 (59%)	69 (51.5%)	
F (n, %)	34 (41%)	65 (48.5%)	
Education level			0.18
Illiterate (n, %)	4 (4.8%)	15 (11.2%)	
Literate (n, %)	2 (2.4%)	7 (5.2%)	
1 to 11 years (n, %)	42 (50.6%)	63 (47%)	
12 years and above (n, %)	10 (12.1%)	8 (6%)	
Missing	25 (30.1%)	41 (30.6%)	
Marital status (n, %)			0.44
Single	17 (20.7%)	28 (20.7%)	
Married	9 (11%)	6 (4.4%)	
Divorced or widow	56 (67.1%)	97 (72.6%)	
Missing	1 (1.2%)	3 (2.2%)	
Length of stay in institution (n, %)*			0.48
0-6 months	4 (4.8%)	8 (5.97%)	
Above 6 months	79 (95.2%)	125 (93.3%)	
Missing		1 (0.75%)	
Hospital admission in the last 6 months (mean ± SD)	1.22±1.55	2.80±3.13	**<0.001**
Comorbidities (mean ± SD)	1.87±1.23	3.87±1.45	**<0.001**

*Fisher's Exact test, SD: Standard deviation, the bold values indicate the number for statistical significance

Table 2. Comorbidities and geriatric syndromes according to polypharmacy status

Comorbidities	Non polypharmacy (n=83, 38.2%)	Polypharmacy (n=134, 61.8%)	p
KATZ score (median, min-max)	6 (5-6)	6 (5-6)	**0.017**
Diabetes mellitus	8 (9.6%)	34 (25.4%)	**0.004**
Arrhythmia	2 (2.4%)	20 (14.9%)	**0.003**
Cardiovascular disease	9 (10.8%)	50 (37.3%)	**<0.001**
Heart failure	1 (1.2%)	15 (11.2%)	**0.006**
Malignancy*	1 (1.2%)	9 (6.7%)	0.054
COPD	6 (7.2%)	36 (26.9%)	**<0.001**
Hypertension	37 (44.6%)	90 (67.2%)	**0.001**
Benign prostatic hyperplasia	13 (15.7%)	36 (26.9%)	0.055
Thyroid disease	4 (4.8%)	28 (20.9%)	**0.001**
Peripheral vascular disease	1 (1.2%)	14 (10.4%)	**0.01**
Parkinson disease	3 (3.6%)	6 (4.5%)	0.76
Geriatric syndromes			
Dementia	4 (4.8%)	19 (14.2%)	**0.03**
Depression	4 (4.8%)	33 (24.6%)	**<0.001**
Urinary incontinence	5 (6%)	22 (16.4%)	**0.02**
Malnutrition*	0	3 (2.2%)	0.23
Falls*	5 (6%)	7 (5.2%)	0.51
Mobility problems	9 (10.8%)	42 (31.3%)	**0.01**
Using mobility aids	10 (12%)	39 (29.1%)	**0.003**
Hearing loss	12 (14.5%)	25 (18.7%)	0.42
Vision impairment	21 (25.3%)	35 (26.1%)	0.89

COPD: Chronic obstructive pulmonary disease, the bold values indicate the number for statistical significance, *Fisher's Exact test

Table 3. The most commonly used drugs in nursing homes

Drug type	Non polypharmacy (n=83, 38.2%)	Polypharmacy (n=134, 61.8%)	p
PPI	16 (19.3%)	60 (44.8%)	0.00
Antiplatelet drugs	23 (27.7%)	72 (53.7%)	0.00
ACE inhibitor or ARB	22 (26.5%)	71 (53%)	0.00
Diuretic	24 (28.9%)	65 (48.5%)	0.04
Beta blocker	13 (15.7%)	51 (38.1%)	0.00
Calcium channel blocker	10 (12%)	32 (23.9%)	0.032
Vasodilator	6 (7.2%)	33 (24.6%)	0.01
Inhaler beta mimetic	5 (6%)	36 (26.9%)	0.00
SSRI/SNRI	5 (6%)	34 (25.4%)	0.00
Vitamin supplement	5 (6.1%)	38 (28.4%)	0.00
Anticholinergic	6 (7.2%)	33 (24.6%)	0.001
Alpha blocker	10 (12%)	29 (21.6%)	0.074

ACE: Angiotensin-converting enzyme, ARB: Angiotensin II receptor blocker, SNRI: Serotonin and norepinephrine reuptake inhibitors, SSRI: Selective serotonin reuptake inhibitors, PPI: Proton pump inhibitors

studies investigating the relationship between polypharmacy and comorbidities (30). Like our study, Gocer et al. (31) found that the prevalence of polypharmacy was higher in NHR with hypertension, heart disease and COPD. In a systematic review, cognitive impairment, hypertension, and DM were the most prevalent comorbidities in long-term care residents (5). Similarly, prevalence of polypharmacy has increased with an increase in the number of chronic diseases among the community dwelling older adults (32). In a recent cross-sectional retrospective study, polypharmacy was more prevalent in geriatric outpatients with hypertension, DM, and COPD (33). As for the coexistence of heart disease, DM, COPD, the number of medications inevitably increase. Also, the use of anticholinergic drugs strengthens the association between polypharmacy and comorbidities (32). If the medication was continued although the symptoms had resolved, negative outcomes occur (34,35). As a result, medications used by older adults should be evaluated in accordance with international or national guidelines (15,36-39).

The presence of a geriatric syndrome is known to increase the risk of polypharmacy. In our study, by univariate analysis, geriatric syndromes such as dementia, depression, UI, and mobility problems were significantly associated with polypharmacy. In the multivariate analyses, depression and mobility problems were significantly associated with polypharmacy and presences of these diseases increase polypharmacy by 9.6 and 4.8-fold respectively. The Shelter study found that polypharmacy was increased by 2-fold with depression (4). Similarly, depression was independently related to presence of polypharmacy and the use of potentially inappropriate medication in geriatric outpatients (12,14). A multicenter study based on the survey of health and ageing in Europe found that polypharmacy was associated with depression, lack of finance, lower ADL score (26). On the contrary to our findings, Küçükdağlı (14) found that UI in geriatric outpatients was independently related to polypharmacy in univariate and multivariate analysis. As far as dementia is concerned, there was a similar outcome in geriatric outpatients to our study (16). Our study conducted in NHRs with a KATZ score 5 and over. As a result, the study participants were functional and potentially less frail. Polypharmacy could have been related to a broader spectrum of geriatric syndromes, if the study population had been more functionally dependent.

Polypharmacy has a negative impact on conditions affecting mobility, such as falls and functional decline (40-42). We showed that polypharmacy was associated with mobility problems, not falls. A recent cross-sectional study carried out geriatric outpatients found that polypharmacy was independently associated with poor physical performance rather than falls (33). Several studies have shown a relationship between polypharmacy and falls (2). Izza et al. (43) showed that the odds of falling increased by 1.058 times for every additional drug prescribed after adjusting for gender, age, and dementia.

Table 4. Logistic regression analysis where risk of polypharmacy was taken as a dependent variable

Variables	Polypharmacy (>5 drugs)					
	Univariate models			Multivariate model		
	OR	95% CI	p	OR	95% CI	p
CVD	4.89	2.25-10.62	**0.000**	5.71	2.22-14.66	**0.000**
Hypertension	2.54	1.45-4.47	**0.001**	2.63	1.25-5.54	**0.011**
COPD	4.71	1.89-11.76	**0.001**	7.04	2.29-21.60	**0,001**
Depression	6.45	2.19-18.98	**0.001**	9.57	2.73-33.60	**0.000**
Mobility problems	3.75	1.72-8.21	**0.001**	4.88	1.80-13.25	**0.002**
Thyroid disease	5.22	1.76-15.48	**0.003**	6.53	1.83-23.31	**0.004**
Diabetes mellitus	3.19	1.39-7.28	**0.006**	5.58	1.96-15.84	**0.001**
Arrhythmia	7.11	1.61-31.25	**0.009**	7.02	1.31-37.47	**0.023**
UI	3.06	1.11-8.44	**0.03**	2.06	0.58-7.28	0.26
Dementia	3.26	1.07-9.96	**0.04**	3.28	0.82-13.18	0.094

CVD: Cardiovascular disease, UI: Urinary incontinence, COPD: Chronic obstructive pulmonary disease, CI: Confidence interval

A study conducted to community-dwelling adults aged 55 years and over with a fall history indicated that the use of at least five daily prescribed molecules was associated with impaired timed-up and go test after adjusting for the number of comorbidities (44). The presence of the polypharmacy also is a significant risk factor for potentially inappropriate medication use. Thus, it poses a risk of geriatric syndromes (15). Some medications can increase the risk of geriatric syndrome because of their anticholinergic effects, sedative properties or by causing adverse drug reaction (45,46).

In the literature, the most used drugs in NHs were for heart disease medications (31,47). The most prevalent medications taken by all long-term care residents were gastrointestinal agent, diuretic and analgesic/antipyretic drugs in a systematic review (5). In a study conducted by 1843 NHR, they found that rate of use of cardiovascular medications (including antiplatelets, beta blockers, angiotensin-converting enzyme inhibitors, calcium channel blockers, and statins) was decreased following institutionalization over a period of one year (48). Also, in this study, the most common comorbidity was heart disease, as a result, the most frequently used drug group was cardiovascular medications.

Study Limitations

To our knowledge, this is the first study that has recently focused on the relationship between geriatric syndromes and polypharmacy in Turkish NHs. We realized that geriatric syndrome awareness was ensured through regular screening in NH. A relevant limitation of the study was number of NHR. Also, by the reason of conducted in one nursing home, the results cannot be generalized to all the NHR. Additionally, this study does not help to determine cause and effect for certain because of having cross sectional type. NHR were not evaluated with the comprehensive geriatric assessment, previously diagnosed health conditions were noted. Consequently, prevalence of geriatric syndromes can be even higher. Also, visual and hearing loss were assessed subjectively. Therefore, the associations between polypharmacy and visual and hearing loss might not be as well determined.

Conclusion

Comorbidity and geriatric syndromes play a significant role in the prevalence of polypharmacy. Assessment of polypharmacy is necessary during the administration of complex medication regimens for NHR. There was a statistical difference in Katz score between polypharmacy group and non-polypharmacy groups in this study, although it was conducted among individuals who were described independent with Katz ADL. This is the first study evaluating the relationship between polypharmacy and geriatric syndromes in NHRs in Turkey. Given the scarcity of the studies on this subject and difficulty of getting permission for research in Turkish NHs, we believe that this study is valuable. Polypharmacy is common in NHs and is associated with geriatric syndromes. We believe that prevalence of the polypharmacy will increase even further as evaluated through a comprehensive geriatric assessment. With prospective studies, the effect of deprescribing on geriatric syndromes can be investigated. Also, the studies investigating the prescription cascade are needed.

Ethics

Ethics Committee Approval: The study was approved by the Ege University Human Research Ethics Committee (18-11T/16), and taken approval from the Ministry of Family, Labour, and Social Services of The Republic.

Informed Consent: Informed consent was obtained from all participants included in the study. The study was performed in line with the principles of the Declaration of Helsinki.

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Authorship Contributions

Surgical and Medical Practices: F.Ö.K.K., E.T. Concept: F.Ö.K.K., E.T., S.Ş., Design: F.Ö.K.K., E.T., Data Collection or Processing: F.Ö.K.K., E.T., Analysis or Interpretation: F.Ö.K.K., E.T., Literature Search: F.Ö.K.K., E.T., Writing: F.Ö.K.K., E.T.

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References

1. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatrics 2017;17:230.
2. Pazan F, Wehling M. Polypharmacy in older adults: a narrative review of definitions, epidemiology and consequences. Eur J Geriatr Med 2021;12:443-452.
3. World Health Organization (WHO) (2019) Medication Safety in Polypharmacy (WHO/UHC/SDS/2019.11). [Internet]. 2020 [cited 2022 Mar 13]. Available from: https ://apps.who.int/iris/ bitst ream/handl e/10665 /32545 4/WHO-UHC-SDS-2019.11-eng. pdf?ua=
4. Onder G, Liperoti R, Fialova D, Topinkova E, Tosato M, Danese P, Gallo PF, Carpenter I, Finne-Soveri H, Gindin J, Bernabei R, Landi F; SHELTER Project. Polypharmacy in Nursing Home in Europe: Results From the SHELTER Study. J Gerontol A Biol Sci Med Sci 2012;67A:698-704.
5. Jokanovic N, Tan ECK, Dooley MJ, Kirkpatrick CM, Bell JS. Prevalence and Factors Associated With Polypharmacy in Long-Term Care Facilities: A Systematic Review. J Am Med Dir Assoc 2015;16:535.e1-12.
6. Aubert CE, Streit S, Da Costa BR, Collet TH, Cornuz J, Gaspoz JM, Bauer D, Aujesky D, Rodondi N. Polypharmacy and specific comorbidities in university primary care settings. Eur J Intern Med 2016;35:35-42.
7. Tamura BK, Bell CL, Inaba M, Masaki KH. Factors Associated With Polypharmacy in Nursing Home Residents. Clin Geriatr Med 2012;28:199-216.
8. Shah BM, Hajjar ER. Polypharmacy, Adverse Drug Reactions, and Geriatric Syndromes. Clinics in Geriatric Med 2012;28:173-186.
9. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf 2014;13:57-65.
10. Bronskill SE, Gill SS, Paterson JM, Bell CM, Anderson GM, Rochon PA. Exploring Variation in Rates of Polypharmacy Across Long Term Care Homes. J Am Med Dir Assoc 2012;13:309.e15-21.
11. Chang TI, Park H, Kim DW, Jeon EK, Rhee CM, Kalantar-Zadeh K, Kang EW, Kang SW, Han SH. Polypharmacy, hospitalization, and mortality risk: a nationwide cohort study. Sci Rep 2020;10:18964.
12. Yuruyen M, Yavuzer H, Demirdag F, Kara Z, Cengiz M, Yavuzer S, Doventas A, Erdincler DS, Beger T. Is Depression a Predictive Factor for Polypharmacy in Elderly? Bulletin of Clinical Psychopharmacology 2016;26:374-381.
13. Efe M, Saraç ZF, Savaş S, Kılavuz A, Akçiçek SF. Sarcopenia prevalence and the quality of life in older adults: A study from Turkey's east. Ege Journal of Medicine 2021;60(Suppl):52-59.
14. Küçükdağlı P. Polypharmacy and Related Factors in Geriatric Outpatients Eur J Geriatr Gerontol 2019;1:56-60.
15. Kucukdagli P, Bahat G, Bay I, Kilic C, Oren MM, Turkmen BO, Karan MA. The relationship between common geriatric syndromes and potentially inappropriate medication use among older adults. Aging Clin Exp Res 2020;32:681-687.
16. Erbas Sacar D. Association Between Dementia and Common Geriatric Syndromes. Eur J Geriatr Gerontol 2020;2:71-76.
17. Sengul Aycicek G, Arik G, Kizilarslanoglu MC, Sumer F, Pala OO, Can B, et al. Association of polypharmacy with postural instability and impaired balance in community-dwelling older adults in Turkey. Marmara Med J 2021;34:12-17.
18. Tasar PT, Sahin S, Karaman E, Ulusoy MG, Duman S, Berdeli A, Akcicek F. Prevalence and risk factors of sarcopenia in elderly nursing home residents. European Geriatric Medicine 2015;6:214-219.
19. Yalcin A, Aras S, Atmis V, Cengiz OK, Cinar E, Atli T, Varli M. Sarcopenia and mortality in older people living in a nursing home in Turkey. Geriatr Gerontol Int 2017;17:1118-1124.
20. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. J Am Geriatr Soc 1983;31:721-727.
21. Ferner RE, Aronson JK. Communicating information about drug safety. BMJ 2006;333:143-145.
22. Lamb SE, JÃ¸rstad-Stein EC, Hauer K, Becker C; Prevention of Falls Network Europe and Outcomes Consensus Group. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. J Am Geriatr Soc 2005;53:1618-1622.
23. Crentsil V, Ricks MO, Xue QL, Fried LP. A pharmacoepidemiologic study of community-dwelling, disabled older women: Factors associated with medication use. Am J Geriatr Pharmacother 2010;8:215-224.
24. Connolly D, Garvey J, McKee G. Factors associated with ADL/IADL disability in community dwelling older adults in the Irish longitudinal study on ageing (TILDA). Disabil Rehabil 2017;39:809-816.
25. Goyal P, Bryan J, Kneifati-Hayek J, Sterling MR, Banerjee S, Maurer MS, Lachs MS, Safford MM. Association Between Functional Impairment and Medication Burden in Adults with Heart Failure. J Am Geriatr Soc 2019;67:284-291.
26. Mohamed MR, Ramsdale E, Loh KP, Xu H, Patil A, Gilmore N, Obrecht S, Wells M, Nightingale G, Juba KM, Faller B, Onitilo A, Bradley T, Culakova E, Holmes H, Mohile SG. Association of Polypharmacy and Potentially Inappropriate Medications With Physical Functional Impairments in Older Adults With Cancer. J Nat Compr Canc Netw 2021;19:267-274.
27. Bahat G, Tufan F, Bahat Z, Tufan A, Aydin Y, Akpinar TS, Nadir S, Erten N, Karan MA. Comorbidities, polypharmacy, functionality and nutritional status in Turkish community-dwelling female elderly. Aging Clin Exp Res 2014;26:255-259.
28. Wilson NM, Hilmer SN, March LM, Cameron ID, Lord SR, Seibel MJ, Sambrook PN. Associations between drug burden index and physical function in older people in residential aged care facilities. Age Ageing 2010;39:503-507.
29. Vetrano DL, Villani ER, Grande G, Giovannini S, Cipriani MC, Manes-Gravina E, Bernabei R, Onder G. Association of Polypharmacy With 1-Year Trajectories of Cognitive and Physical Function in Nursing Home Residents: Results From a Multicenter European Study. J Am Med Dir Assoc 2018;19:710-713.
30. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health Outcomes Associated with Polypharmacy in Community-Dwelling Older Adults: A Systematic Review. J Am Geriatr Soc 2014;62:2261-2272.
31. Gocer S, Gunay O, Polat T, Ulutabanca R, Sonkaya Z. Polypharmacy and associated factors in people living in a nursing home in Kayseri Turkey. Med Sciences 2017;6:646-652.
32. Masnoon N, Kalisch Ellett L, Shakib S, Caughey GE. Predictors of Mortality in the Older Population: The Role of Polypharmacy and Other Medication and Chronic Disease-Related Factors. Drugs Aging 2020;37:767-776.
33. Ozkok S, Aydin CO, Sacar DE, Catikkas NM, Erdogan T, Kilic C, Karan MA, Bahat G. Associations between polypharmacy and physical performance measures in older adults. Arch Gerontol Geriatr 2022;98:104553.
34. Bahat G, Bay I, Tufan A, Tufan F, Kilic C, Karan MA. Prevalence of potentially inappropriate prescribing among older adults: A comparison of the Beers 2012 and Screening Tool of Older Person's Prescriptions criteria version 2. Geriatr Gerontol Int 2017;17:1245-1251.

35. Krishnaswami A, Steinman MA, Goyal P, Zullo AR, Anderson TS, Birtcher KK, Goodlin SJ, Maurer MS, Alexander KP, Rich MW, Tjia J; Geriatric Cardiology Section Leadership Council, American College of Cardiology. Deprescribing in Older Adults With Cardiovascular Disease. J Am Coll Cardiol 2019;73:2584-2595.

36. Mangin D, Bahat G, Golomb BA, Mallery LH, Moorhouse P, Onder G, Petrovic M, Garfinkel D. International Group for Reducing Inappropriate Medication Use & Polypharmacy (IGRIMUP): Position Statement and 10 Recommendations for Action. Drugs Aging 2018;35:575-587.

37. Bahat G, Ilhan B, Erdogan T, Oren MM, Karan MA, Burkhardt H, Denkinger M, Garfinkel D, Cruz-Jentoft AJ, Morrissey Y, Onder G, Pazan F, Tommelein E, Topinkova E, van der Velde N, Petrovic M. International Validation of the Turkish Inappropriate Medication Use in the Elderly (TIME) Criteria Set: A Delphi Panel Study. Drugs Aging 2021;38:513-521.

38. Bahat G, İlhan B, Erdoğan T, Halil M, Savaş S, Ülger Z, Akyüz F, Bilge AK, Çakır S, Demirkan K, Erelel M, Güler K, Hanağası H, İzgi B, Kadıoğlu A, Karan A, Baral Kulaksızoğlu I, Mert A, Öztürk S, Satman İ, Sever MŞ, Tükek T, Üresin Y, Yalçın Ö, Yeşilot N, Ören MM, Karan MA. Presenting Turkish Inappropriate Medication Use in the Elderly (TIME) Criteria Set in Turkish. Eur J Geriatr Gerontol 2021;3:40-100.

39. Bahat G, Ilhan B, Erdogan T, Halil M, Savas S, Ulger Z, Akyuz F, Bilge AK, Cakir S, Demirkan K, Erelel M, Guler K, Hanagasi H, Izgi B, Kadioglu A, Karan A, Kulaksizoglu IB, Mert A, Ozturk S, Satman I, Sever MS, Tukek T, Uresin Y, Yalcin O, Yesilot N, Oren MM, Karan MA. Turkish inappropriate medication use in the elderly (TIME) criteria to improve prescribing in older adults: TIME-to-STOP/TIME-to-START. Eur Geriatr Med 2020;11:491-498.

40. Peron EP, Gray SL, Hanlon JT. Medication Use and Functional Status Decline in Older Adults: A Narrative Review. Am J Geriatr Pharmacother 2011;9:378-391.

41. Zia A, Kamaruzzaman SB, Tan MP. Polypharmacy and falls in older people: Balancing evidence-based medicine against falls risk. Postgrad Med 2015;127:330-337.

42. Ali MU, Sherifali D, Fitzpatrick-Lewis D, Kenny M, Liu A, Lamarche L, Mangin D, Raina P. Polypharmacy and mobility outcomes. Mech Ageing Dev 2020;192:111356.

43. Izza MAD, Lunt E, Gordon AL, Gladman JRF, Armstrong S, Logan P. Polypharmacy, benzodiazepines, and antidepressants, but not antipsychotics, are associated with increased falls risk in UK care home residents: a prospective multi-centre study. Eur Geriatr Med 2020;11:1043-1050.

44. Langeard A, Pothier K, Morello R, Lelong-Boulouard V, Lescure P, Bocca ML, Marcelli C, Descatoire P, Chavoix C. Polypharmacy Cut-Off for Gait and Cognitive Impairments. Front Pharmacol 2016;7:296.

45. Pana A, Sourtzi P, Kalokairinou A, Velonaki VS. Sarcopenia and polypharmacy among older adults: A scoping review of the literature. Arch Gerontol Geriatr 2022;98:104520.

46. George CJ, Verghese J. Motoric Cognitive Risk Syndrome in Polypharmacy. J Am Geriatr Soc 2020;68:1072-1077.

47. Altiparmak S, Altiparmak O. Drug-using behaviors of the elderly living in nursing homes and community-dwellings in Manisa, Turkey. Arch Gerontol Geriatr 2012;54:e242-e248.

48. Onder G, Vetrano DL, Villani ER, Carfì A, Io Monaco MR, Cipriani MC, Manes Gravina E, Denkinger M, Pagano F, van der Roest HG, Bernabei R. Deprescribing in Nursing Home Residents on Polypharmacy: Incidence and Associated Factors. J Am Med Dir Assoc 2019;20:1116-1120.

ORIGINAL RESEARCH

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Older Age is a Risk Factor for Diastolic Orthostatic Hypotension

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Abstract

Objective: This study aimed to investigate the associations orthostatic hypotension (OH) and the cognitive status of patients.

Materials and Methods: OH diagnosis was achieved by measuring the supine blood pressure (BP), which was taken twice after lying for 5 min and the standing BP, which was taken twice after standing for 3 min. Mini-mental state examination (MMSE) determined the cognitive status of patients. If the score of MMSE was below 24, then the patient was diagnosed with cognitive impairment.

Results: The prevalence of OH, systolic OH (SysOH) and diastolic OH (DiOH) were 31.8% (n=181), 16.7% (n=95), and 24.1% (n=137), respectively. 23.9% of participants had CI. Individuals with older age were at higher risk for OH and DiOH [odds ratio (OR) =1.03, 95% confidence intervals (CI) =1.01-1.05, p=0.012 for OH and OR =1.04, 95% CI =1.01-1.06 p=0.013 for DiOH). In multivariate analysis, OH, SysOH, and DiOH were not related to CI (all p>0.05).

Conclusion: The presence of OH increases with aging, so its evaluation should not be forgotten.

Keywords: Cognition, diastolic hypotension, older adults, orthostatic hypotension, systolic hypotension

Introduction

A slight increase in systolic blood pressure (SBP) is expected when standing up from a lying or sitting position. This increase in SBP is due to the displacement of approximately 500-700 mL of blood from the central circulation to splanic or pulmonary circulation because of standing up. With the effect of gravity, some of the blood accumulates in the lower extremities, and this can cause some degree of cerebral hypoperfusion. The sympathetic nervous system is activated to increase the amount of blood in the central circulation. Factors such as baroreceptor activation, cardiac output, the release of neurotransmitters, and increased vascular tonus try regulating blood pressure (BP). Neurotransmitters such as norepinephrine and dopamine are involved in the regulation of BP due to orthostatic change. The spectrum of the events occurring in the orthostatic response includes sympathetic system activation, parasympathetic system inhibition, and increased systole. With reduced parasympathetic activity, there is an increase in heart rate, sympathetic tone, and vasoconstriction, and then an increase in total peripheral resistance. As a result of all these events, SBP increases due to the change of position (1).

Orthostatic hypotension (OH) is identified as a decline in SBP of at least 20 mmHg and/or a decline of at least 10 mmHg in diastolic BP within 3 min of standing. OH is related to falls, cognitive impairment (CI), dementia, cardiovascular events, syncope, frailty, and mortality (2). OH prevalence in older adults varies from 9% to 50%. These variations in the OH rates are often because of the presence of multimorbidities [diabetes mellitus (DM), dementia, cerebrovascular accident (CVA), Parkinson disease, cardiovascular disease (CVD), hypertension (HT), etc.], older age, measurement technique (active standing test and head-up tilt table), and the status of the participants in the study (community-dwelling, outpatient, hospital, nursing home, etc.) (2,3). The presence of OH, its severity, and chronicity of the decline in orthostatic BP, all affect the perfusion of cerebrum and cognitive decline and may cause CI (2,3). Some researchers found that cognition and OH were associated with each other (4,5), while others found opposing views (6,7). In

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some studies (6,8-10), systolic OH (SysOH) and diastolic OH (DiOH) were considered separately. In these studies (6,10), low SBP was found to be significantly with cognition, but in a few recent studies, it was seen that low DBP also affects cognitive functions as well as SBP and has a role in the development of dementia (8,9). Although it is already known that the presence of SysOH and DiOH enhances the risk of dementia. Up to now, their relationship of OH with CI has not been clearly explained. There are many striking differences among the studies due to the use of different tests to evaluate cognitive functions, small sample sizes, and variable age range sof the samples (3-7).

In this study, we hypothesized that the presence of both DiOH and SysOH is a risk factor for CI. With this research, we aimed to show the relationship between OH, SysOH, DiOH and CI, and to define other states associated with OH.

Materials and Methods

Study design

This study was designed as cross-sectional and included 569 participants, who attended a geriatric outpatient clinic. All over 60 years old patients were included in the study. Patients diagnosed with mild cognitive impairment, dementia, eye/hearing impairment, depression, and delirium were excluded from the study.

All participants gave written informed consent. Written informed consent was obtained from the patient or caregivers in case of cognitive impairment (dementia or delirium). The study was approved by the Local Ethics Committee of Erciyes University (Erciyes University Ethics Committee/decision no: 2019/136).

Data collection

Socio-demographic data (age, gender, and educational level), number of medications, and history of chronic diseases (DM, CVD, HT, CVA, Parkinson's disease) were recorded. The patients were asked whether they had fallen in the last year, the number of falls and whether they were afraid of falling.

The BP of the participants was measured on the brachial artery with an Omron brand oscillometric measurement device. OH diagnosis was achieved by measuring the SBP as taken twice after lying for 5 min and the standing BP taken twice after standing for 3 min. OH was defined as a decline in systolic BP (SBP) of at least 20 mmHg and/or a decline of at least 10 mmHg in diastolic BP (DBP) within 3 min of standing (11). Additionally, OH was evaluated as SysOH and DiOH. Furthermore, in examining OH using this description, SysOH (reduction in SBP >20 mmHg) and DiOH (reduction in DBP >10 mmHg) were investigated independently.

The cognitive status of patients was determined with the mini-mental state examination (MMSE) (12). If the score of MMSE was below 24, the patient was diagnosed with CI.

For each patient, basic and instrumental activities of daily living (ADL) (13,14), (scores range from 0 to 18 points and from 0 to 24 points, respectively), SARC-F questionnaire (15), and FRAIL questionnaire (16) were also recorded. For FRAIL, a total of 0 points is categorized as non-frail, 1 as pre-frail, and 2 and above as frail.

Statistics

Histogram, q-q plots were examined and Shapiro-Wilk's test was applied to assess the data normality. The Levene test was used to test variance homogeneity. To compare the differences between groups, the Pearson chi-square test was applied for categorical variables, and the Mann-Whitney U test was applied for continuous variables. Binary logistic regression analysis models were built to investigate the effect of variables in estimating OH and SysOH and DiOH in geriatric patients. For this reason, each of these variables was dichotomized (OH, SysOH >20 mg/dL and DiOH >10 mg/dL) and separately evaluated. Moreover crude, age and gender-adjusted, and multiple models were fitted separately. Significant variables at $p<0.25$ were included in multiple models and backward elimination was performed to identify independent risk factors. The Wald statistic were used as model selection criteria. Odds ratios (OR) were calculated with 95% confidence intervals. The linearity assumption between the log-odds and the independent variables was checked by visually inspecting the scatter plot between each predictor and the logit values. Multicollinearity assumption of the regression analysis were assessed by checking the Pearson correlation coefficients between the variables and calculating the variance inflation factors (VIF) for each variable. Hosmer-Lemeshow goodness of fit test statistic was calculated to assess the goodness of fit of the final models. All analyses were performed using TURCOSA (Turcosa Analytics Ltd. Co., www.turcosa.com.tr) statistical software. P-values less than 5% were considered statistically significant.

Results

Five hundred and sixty-nine individuals over the age of 60 were included in the study. The mean age of the participants was 72.16+7.38 (range 60-96). Three hundred and ninety-eight (69.9%) of the participants were female. The prevalence of OH, SysOH, and DiOH were 31.8% (n=181), 16.7% (n=95), and 24.1% (n=137), respectively. Table 1 shows the characteristics of the study population based on presence or absent OH, SysOH, and DiOH. Subjects with OH were more likely to be older (71.0 vs 72.0 p=0.029), had more medications (p=0.006), had a lower MMSE score (p=0.003), and all BP measurements were significantly different from non-OH patients. Participants in

the DiOH group were older (71.0 vs 73.0, p=0.001), had more medications (p=0.008), had lower instrumental activity of daily living (IADL) score (p=0.021), had a higher supine SBP and DBP, had lower standing SBP and DBP (for BP p=0.011, <0.001, 0.025 and <0.001 respectively). Individuals with SysOH had a higher supine SBP and DBP, and lower standing SBP (p<0.001 for all). The mean MMSE score was 25.30+4.72. One hundred and thirty-six (23.9%) participants were diagnosed with CI with less than 24 points in the MMSE test.

In the chi-square analysis, CI was significantly related to the presence of OH (p=0.003). When we evaluated the SysOH and DiOH, only DiOH had a significant relationship with CI (p=0.002). As seen in Figure 1, where the distribution of MMSE scores is shown, the mean of MMSE is lower in individuals with OH and DiOH.

After checking the scatter plots between the predictors and the logit values, we did not observe any non-linear relationship. In addition, all correlation coefficients were lower than 0.70 and VIF scores were lower than 5. Thus, we continued the analysis assuming that these assumptions were met. In the built multiple models, there were very few variables were found to be significant. However, the p-values of some variables (KATZ-ADL and MMSE score for SysOH, gender and MMSE score for DiOH) were very close to 0.05. These results show a trend toward statistical significance (17) and we left these variables in the model. The Hosmer-Lemeshow test resulted as X^2=9.179, p=0.327 for OH; X^2=4.745, p=0.784 for SysOH and X^2=14.315, p=0.074 for DiOH. These results revealed the appropriatness of the built multiple binary logistic regression model in order to predict OH, SysOH and DiOH in geriatric patients (Table 2). In the multiple analysis, the OR (95% CI) of age, IADL, MMSE score, gender were 1.03 (1.01-1.05), 1.05 (0.99-1.12), 0.95 (0.91-1.00), 0.66 (0.43-1.00), 1.03 (1.00-1.06) and 0.96 (0.92-1.00) respectively. Low MMSE scores was not associated with OH, SysOH and DiOH in older adults (p=0.084, 0.248, and 0.062, respectively).

Discussion

In the present study, 31.8% of the participants had OH and 23.9% of the participants were diagnosed with CI. The prevalence of SysOH and DiOH was 16.7% and 23.7%, respectively. In this study, OH, SysOH and DiOH was associated with only older age not cognitive impairment.

The prevalence of OH reported in some studies was between 9% and 50%, and increased with older age (3,6,10,18-23). In the present study prevalence of OH was 31.8%. The difference in the prevalence was because of the clinical conditions, ages, comorbidities, and community dwelling-outpatient-inpatient status of the participants. In our study, the prevalence of DiOH of the participants was higher than in the literature (6,8,10,19,23). None of these studies published the demographic data of the DiOH patients. Therefore, we could not compare them with our patients. In some studies (10,19), the participants with OH were younger than those in present study. Additionally, one of the studies had more hypertensive individuals than in the present study (10). Assuming that those with DiOH present in these studies were younger and had more hypertensive participants, we can explain the difference between them and our study.

The relationship between OH and cognition was controversial (3-7,22,24). Some studies found a direct relationship between OH and CI, and OH related to cognitive decline and dementia in follow-up (3,4,19,20,22). Some of the researchers did not show any relationship between OH and CI, due to the retrospective design of the studies, the difference in the methods used in the diagnosis of OH, using different cognitive performance test, or characteristics (community-dwelling, low mean age) of participants (2,3,6). Until now, few articles have examined the relationship between the presence of OH- SysOH- DiOH, and CI (6,10,23). One of these studies found no relationship between these parameters (23). The others discovered that only SysOH was directly related to CI (6,10). In studies to date, a relationship between SBP and cognition has been shown, but in a few studies in recent years, it has been seen that low DBP has an effect on cognitive functions as well as SBP and a role in dementia development (8,9). Multiple mechanisms explain the relationship between OH and CI. In the presence of CI in an area where cardiovascular activities are regulated, OH be may seen together with CI (22). The relationship between OH and cognition is thought to be due to recurring cerebral hypoperfusion (25). In addition, Elmståhl and Rosén (26) showed by EEG that in OH patients, the cerebral blood flow (CBF) decreases, so this may lead to cerebral damage and CI. A 50-60% reduction in CBF in healthy individuals is known to be associated with mild symptoms of cerebral hypoperfusion and the standing position, which is the biggest affect to the CBF, has most decreased CBF (27). Furthermore, CBF may decrease more when the compensatory response is not appropriate due to changes in vascular structures and impaired baroreceptor response in older individuals. Since the blood supply and oxygenation of the brain decreases, cognitive functions may be impaired. Cerebral hypoperfusion secondary to hypotension may induce cortical infarcts, which accelerate the degenerative process of Alzheimer's disease (28). Likewise, cerebral hypoperfusion may cause metabolic changes; this may increase oxidative stress and, cause neurodegeneration and atrophy due to neurotransmitter failure and amyloid deposition (29). In this study, when both SysOH and DiOH were investigated one by one, we did not observe any relationship between CI and both SysOH and DiOH.

Intensive BP control with medications increases the risk of OH in older individuals. It is known in the results of the Systolic

Table 1. Comparison of demographic and clinical variables between OH, systolic OH and diastolic OH groups

Variables	OH		p	Systolic OH		p	Diastolic OH		p
	Non-OH n=388, 68.2%	OH n=181, 31.8%		Non n=474, 83.3%	Systolic OH n=95, 16.7%		Non n=432, 75.9%	Diastolic OH n=137, 24.1%	
Gender Male Female	 109 (63.7) 279 (70.1)	 62 (36.3) 119 (29.9)	0.135	 143 (83.6) 331 (83.2)	 28 (16.4) 67 (16.8)	0.893	 119 (69.6) 313 (78.6)	 52 (30.4) 85 (21.4)	**0.021**
Age (years)	71.0 (66.0-76.0)	72.0 (67.0-79.0)	**0.029**	71.0 (66.0-77.0)	72.0 (72.0-78.0)	0.512	71.0 (66.0-76.0)	73.0 (68.0-80.0)	**0.001**
DM	164 (42.3)	86 (47.5)	0.240	202 (42.6)	48 (50.5)	0.156	185 (42.8)	65 (47.4)	0.342
HT	254 (65.5)	123 (68.0)	0.558	306 (64.6)	71 (74.7)	0.055	285 (66.0)	92 (67.2)	0.799
CVA	25 (6.4)	4 (2.2)	0.032	27 (5.7)	2 (2.1)	0.146	26 (6.0)	3 (2.2)	0.076
CVD	60 (15.5)	37 (20.4)	0.141	74 (15.6)	26 (24.2)	0.042	69 (16.0)	28 (20.4)	0.226
Parkinson disease	25 (6.4)	13 (7.2)	0.742	35 (7.4)	3 (3.2)	0.132	26 (6.0)	12 (8.8)	0.263
Number of comorbidites	3.0 (2.0-4.0)	2.0 (2.0-4.0)	0.855	3.0 (2.0-4.0)	4.5 (3.0-6.0)	0.170	3.0 (2.0-4.0)	2.0 (2.0-3.5)	0.825
Number of medications	4.0 (2.0-5.0)	5.0 (2.2-6.0)	**0.006**	4.5 (3.0-6.0)	4.5 (3.0-6.0)	0.081	3.0 (2.0-4.0)	5.0 (3.0-6.2)	**0.008**
History of falling	128 (33.0)	60 (33.1)	0.970	160 (33.8)	28 (29.5)	0.418	138 (31.9)	50 (36.5)	0.324
Fear of falling	163 (42.0)	90 (49.7)	0.566	208 (44.2)	45 (47.4)	0.566	182 (42.4)	71 (51.8)	0.054
Number of falling	1.0 (1.0-2.5)	2.0 (1.0-3.0)	0.177	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.186	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.492
SARC-F total score	3.0 (1.0-5.0)	3.0 (1.0-5.0)	0.328	3.0 (1.0-5.0)	3.0 (1.0-5.0)	0.899	3.0 (1.0-5.0)	3.0 (2.0-5.0)	0.078
FRAIL total score	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.920	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.788	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.283
KATZ ADL total score	18.0 (18.0-19.0)	18.0 (18.0-18.0)	0.368	18.0 (18.0-18.0)	18.0 (18.0-18.0)	0.734	18.0 (18.0-18.0)	18.0 (17.0-18.0)	0.081
KATZ ADL Dependent Par. dependent Independent	 3 (0.8) 54 (13.9) 331 (85.3)	 1 (0.6) 32 (17.7) 148 (81.8)	0.490	 4 (0.8) 69 (14.6) 401 (84.6)	 0 (0.0) 17 (17.9) 78 (82.1)	0.486	 3 (0.7) 59 (13.7) 370 (85.6)	 1 (0.7) 27 (19.7) 109 (79.6)	0.225
IADL total score	22.0 (18.0-22.0)	21.0 (16.5-22.0)	0.301	21.0 (17.0-22.0)	22.0 (19.0-22.0)	0.326	22.0 (18.0-22.0)	21.0 (16.0-22.0)	**0.021**
IADL Dependent Par. dependent Independent	 14 (3.6) 72 (18.6) 302 (77.8)	 9 (5.0) 36 (19.9) 136 (75.1)	0.670	 20 (4.2) 94 (19.8) 360 (75.9)	 3 (3.2) 14 (14.7) 78(82.1)	0.429	 15 (3.5) 75 (17.4) 342 (79.2)	 8 (5.8) 33 (24.1) 96 (70.1)	0.081
MMSE total score	27.0 (24.0-29.0)	26.0 (22.5-28.0)	**0.003**	27.0 (24.0-29.0)	26.0 (23.0-28.0)	0.246	27.0 (24.0-29.0)	26.0 (22.0-28.0)	**0.001**
MMSE Low Normal	 79 (51.8) 309 (71.4)	 57 (41.9) 124 (28.6)	**0.004**	 112 (82.4) 362 (83.6)	 24 (17.6) 71 (16.4)	0.733	 90 (66.2) 342 (79.0)	 46 (33.8) 91 (21.0)	**0.002**
Supine SBP	130 (120-140)	140 (120-150)	**0.001**	130 (120-140)	140 (130-155)	**<0.001**	130 (120-140)	140 (120-150)	**0.011**
Supine DBP	80.0 (70.0-80.0)	80.0 (70.0-90.0)	**<0.001**	80.0 (70.0-80.0)	80.0 (70.0-90.0)	**<0.001**	80.0 (70.0-80.0)	80.0 (70.0-90.0)	**<0.001**
Standing SBP	130 (120-140)	120 (110-130)	**<0.001**	130 (120-140)	120 (100-130)	**<0.001**	129 (115-140)	120 (110-132.5)	**0.025**
Standing DBP	80.0 (70.0-89.5)	70.0 (60.0-80.0)	**<0.001**	80.0 (70.0-85.0)	70.0 (60.0-80.0)	0.171	80.0 (70.0-88.0)	70.0 (60.0-80.0)	**<0.001**

ADL: Activities of daily living, CVA: Cerebrovascular accident, CVD: Cardiovascular disease, DBP: Diastolic blood pressure, DM: Diabetes mellitus, HT: Hypertension, IADL: Instrumental activities of daily living, MMSE: Mini mental state examination, OH: Orthostatic hypotension, SBP: Systolic blood pressure, data are summarized as n (%), median (1^{st}-3^{rd} quartiles). Significant p-values are shown in bold

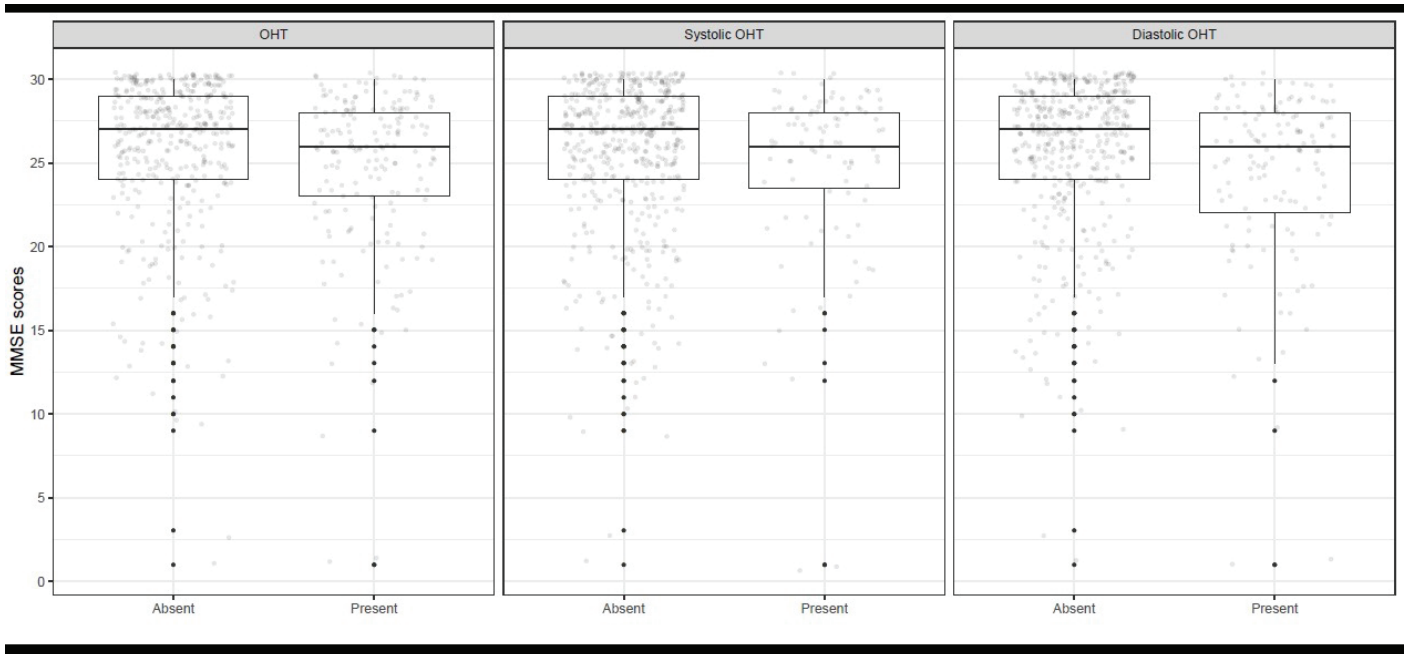

Figure 1. MMSE score distribution of OH, systolic OH and diastolic OH patients. The line in the middle is median, the bottom line is 25 percentiles, the upper line is 75 percentiles

MMSE: Mini mental state examination, OH: Orthostatic hypotension

Table 2. Univariate and multiple binary logistic regression analysis in estimating OH, systolic and diastolic OH in geriatric patients

Variables	Crude model		Adjusted model		Multiple model	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
OH						
Gender (male/female)	1.33 (0.91-1.95)	0.136	-	-	-	-
Age (years)	1.03 (1.01-1.05)	0.012	-	-	1.03 (1.01-1.05)	**0.012**
KATZ-ADL	0.98 (0.88-1.09)	0.693	1.01 (0.91-1.12)	0.887	-	-
IADL	0.99 (0.95-1.03)	0.570	1.01 (0.97-1.05)	0.699	-	-
SARC-F	1.03 (0.96-1.11)	0.382	1.03 (0.96-1.11)	0.439	-	-
Frail	0.98 (0.85-1.12)	0.805	0.97 (0.84-1.11)	0.627	-	-
Number of comorbidites	1.01 (0.88-1.15)	0.896	1.02 (0.89-1.16)	0.809	-	-
MMSE score	0.96 (0.92-0.99)	0.023	0.97 (0.93-1.01)	0.084	-	-
Systolic OH						
Gender (male/female)	0.97 (0.60-1.57)	0.893	-	-	-	-
Age	1.01 (0.98-1.04)	0.406	-	-	-	-
KATZ-ADL	1.05 (0.91-1.21)	0.539	1.06 (0.92-1.24)	0.423	-	-
IADL	1.03 (0.98-1.09)	0.198	1.05 (0.99-1.11)	0.080	1.05 (0.99-1.12)	**0.055**
SARC-F	1.01 (0.92-1.10)	0.818	1.00 (0.91-1.10)	0.989	-	-
Frail	0.95 (0.80-1.13)	0.599	0.94 (0.78-1.12)	0.467	-	-
Number of comorbidites	1.12 (0.95-1.31)	0.181	1.12 (0.95-1.32)	0.181	-	-
MMSE score	0.97 (0.93-1.02)	0.250	0.98 (0.93-1.03)	0.248	0.95 (0.91-1.00)	**0.056**
Diastolic OH						
Gender (male/female)	1.61 (1.07-2.41)	0.021	-	-	0.66 (0.43-1.00)	**0.053**
Age	1.05 (1.02-1.07)	<0.001	-	-	1.03 (1.00-1.06)	**0.017**
KATZ-ADL	0.93 (0.84-1.03)	0.176	0.97 (0.87-1.08)	0.569	-	-
IADL	0.96 (0.92-0.99)	0.041	0.98 (0.94-1.03)	0.451	-	-
SARC-F	1.06 (0.98-1.14)	0.126	1.06 (0.98-1.15)	0.149	-	-
Frail	1.06 (0.91-1.22)	0.456	1.04 (0.89-1.21)	0.645	-	-
Number of comorbidites	0.98 (0.84-1.13)	0.750	0.99 (0.85-1.15)	0.877	-	-
MMSE score	0.95 (0.91-0.99)	0.007	0.96 (0.92-1.00)	0.062	0.96 (0.92-1.00)	0.062

ADL: Activities of daily living, IADL: Instrumental activities of daily living, MMSE: Mini mental state examination, OH: Orthostatic hypotension, OR: Odds ratio, CI: Confidence interval, adjusted models are controlled for age and gender. Significant p-values are shown in bold

Blood Pressure Intervention Trial (SPRINT), that lower BP is not protective from death and morbidities in frail and functionally limited older adults (30,31). Therefore, older people who undergo intensive BP control with medications should be carefully selected and questioned at every clinical visit for the presence and symptoms of OH, because OH may cause clinical situations that may result in morbidity and mortality in older patients.

Study Limitations

This study has some limitations. One of them is the sample size. The sample size may not have been large enough to show the relationship between CI and SysOH and DiOH. Therefore, although the relationship between CI and OH, SysOH and DiOH was significant in the chi-square analysis, this significance was lost in the multivariate analysis. We hope that the relationship between OH and cognitive impairment can be better explained by increasing the sample size in future studies. In this study, MMSE was used to evaluate the cognitive performance of all participants. However, the use of MMSE may be limited for some reasons. The MMSE test is inadequate in evaluating verbal and visual memory, and MMSE is insufficient to detect cognition impairment in people with a high education level. People who have normal cognition with MMSE should be evaluated with other tests (such as Montreal Cognitive Assessment). However, the MMSE is easy to apply in an outpatient clinic and can be done quickly. It is also used in many clinical trials (3,7). We believe that the MMSE is a good tool for cognition screening in outpatients.

Conclusion

Older age was associated with OH-DiOH and DiOH is more common. In older individuals, OH should be screened and treated appropriately. It should be kept in mind that BP targets should be individualized according to frailty, dependency, and cognitive dysfunction in elderly individuals. Prospective studies are needed to reveal the causality between cognitive dysfunction and OH.

Ethics

Ethics Committee Approval: The study was approved by the Local Ethics Committee of Erciyes University (Erciyes University Ethics Committee/decision no: 2019/136).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.Ş.D., S.A., Concept: N.Ş.D., S.A., Design: N.Ş.D., S.A., Data Collection or Processing: N.Ş.D., S.A., G.E.Z., Analysis or Interpretation: N.Ş.D., G.E.Z., S.A., Literature Search: N.Ş.D., S.A., Writing: N.Ş.D., S.A., G.E.Z.

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References

1. Robertson D. The pathophysiology and diagnosis of orthostatic hypotension. Clin Auton Res 2008;18(Suppl 1):2-7.
2. Novak V, Hajjar I. The relationship between blood pressure and cognitive function. Nat Rev Cardiol 2010;7:686-698.
3. Iseli R, Nguyen VTV, Sharmin S, Reijnierse EM, Lim WK, Maier AB. Orthostatic hypotension and cognition in older adults: A systematic review and meta-analysis. Exp Gerontol 2019;120:40-49.
4. Czajkowska J, Ozhog S, Smith E, Perlmuter LC. Cognition and hopelessness in association with subsyndromal orthostatic hypotension. J Gerontol A Biol Sci Med Sci 2010;65:873-879.
5. Matsubayashi K, Okumiya K, Wada T, Osaki Y, Fujisawa M, Doi Y, Ozawa T. Postural dysregulation in systolic blood pressure is associated with worsened scoring on neurobehavioral function tests and leukoaraiosis in the older elderly living in a community. Stroke 1997;28:2169-2173.
6. Yap PL, Niti M, Yap KB, Ng TP. Orthostatic hypotension, hypotension and cognitive status: early comorbid markers of primary dementia? Dement Geriatr Cogn Disord 2008;26:239-246.
7. Maule S, Caserta M, Bertello C, Verhovez A, Naso D, Bisbocci D, Veglio F. Cognitive decline and low blood pressure: the other side of the coin. Clin Exp Hypertens 2008;30:711-719.
8. Peters R, Anstey KJ, Booth A, Beckett N, Warwick J, Antikainen R, Rockwood K, Peters J, Bulpitt CJ. Orthostatic hypotension and symptomatic subclinical orthostatic hypotension increase risk of cognitive impairment: an integrated evidence review and analysis of a large older adult hypertensive cohort. Eur Heart J 2018;39:3135-3143.
9. Qiu C, Winblad B, Fastbom J, Fratiglioni L. Combined effects of APOE genotype, blood pressure, and antihypertensive drug use on incident AD. Neurology 2003;61:655-660.
10. Torres RV, Elias MF, Crichton GE, Dore GA, Davey A. Systolic orthostatic hypotension is related to lowered cognitive function: Findings from the Maine-Syracuse Longitudinal Study. J Clin Hypertens (Greeenwich) 2017;19:1357-1365.
11. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. Neurology 1996;46:1470.
12. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.
13. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. Gerontologist 1970;10:20-30.
14. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179-186.
15. Malmstrom TK, Morley JE. SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. J Am Med Dir Assoc 2013;14:531-532.
16. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012;16:601-608.
17. Rosner B. Fundamentals of biostatistics: Cengage learning; 2015.
18. Curreri C, Giantin V, Veronese N, Trevisan C, Sartori L, Musacchio E, Zambon S, Maggi S, Perissinotto E, Corti MC, Crepaldi G, Manzato E, Sergi G.

Orthostatic Changes in Blood Pressure and Cognitive Status in the Elderly: The Progetto Veneto Anziani Study. Hypertension 2016;68:427-435.

19. Elmståhl S, Widerström E. Orthostatic intolerance predicts mild cognitive impairment: incidence of mild cognitive impairment and dementia from the Swedish general population cohort Good Aging in Skåne. Clin Interv Aging 2014;9:1993-2002.
20. Foster-Dingley JC, Moonen JEF, de Ruijter W, van der Mast RC, van der Grond J. Orthostatic hypotension in older persons is not associated with cognitive functioning, features of cerebral damage or cerebral blood flow. J Hypertens 2018;36:1201-1206.
21. Frewen J, Savva GM, Boyle G, Finucane C, Kenny RA. Cognitive performance in orthostatic hypotension: findings from a nationally representative sample. J Am Geriatr Soc 2014;62:117-122.
22. Mehrabian S, Duron E, Labouree F, Rollot F, Bune A, Traykov L, Hanon O. Relationship between orthostatic hypotension and cognitive impairment in the elderly. J Neurol Sci 2010;299:45-48.
23. Viramo P, Luukinen H, Koski K, Laippala P, Sulkava R, Kivelä SL. Orthostatic hypotension and cognitive decline in older people. J Am Geriatr Soc 1999;47:600-604.
24. Hayakawa T, McGarrigle CA, Coen RF, Soraghan CJ, Foran T, Lawlor BA, Kenny RA. Orthostatic Blood Pressure Behavior in People with Mild Cognitive Impairment Predicts Conversion to Dementia. J Am Geriatr Soc 2015;63:1868-1873.
25. Wolters FJ, Zonneveld HI, Hofman A, van der Lugt A, Koudstaal PJ, Vernooij MW, Ikram MA; Heart-Brain Connection Collaborative Research Group. Cerebral Perfusion and the Risk of Dementia: A Population-Based Study. Circulation 2017;136:719-728.
26. Elmståhl S, Rosén I. Postural hypotension and EEG variables predict cognitive decline: results from a 5-year follow-up of healthy elderly women. Dement Geriatr Cogn Disord 1997;8:180-187.
27. Van Lieshout JJ, Wieling W, Karemaker JM, Secher NH. Syncope, cerebral perfusion, and oxygenation. J Appl Physiol 2003;94:833-848.
28. Suter OC, Sunthorn T, Kraftsik R, Straubel J, Darekar P, Khalili K, Miklossy J. Cerebral hypoperfusion generates cortical watershed microinfarcts in Alzheimer disease. Stroke 2002;33:1986-1992.
29. de la Torre JC. Pathophysiology of neuronal energy crisis in Alzheimer's disease. Neurodegener Dis 2008;5:126-132.
30. Williamson JD, Supiano MA, Applegate WB, Berlowitz DR, Campbell RC, Chertow GM, Fine LJ, Haley WE, Hawfield AT, Ix JH, Kitzman DW, Kostis JB, Krousel-Wood MA, Launer LJ, Oparil S, Rodriguez CJ, Roumie CL, Shorr RI, Sink KM, Wadley VG, Whelton PK, Whittle J, Woolard NF, Wright JT Jr, Pajewski NM; SPRINT Research Group. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged ≥75 Years: A Randomized Clinical Trial. JAMA 2016;315:2673-2682.
31. Bahat G, Ilhan B, Tufan A, Karan MA. Intensive Blood Pressure Treatment in Adults Aged 60 Years or Older. Ann Intern Med 2017;167:288.

ORIGINAL RESEARCH

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The Prevalence and the Effect of COVID-19 Infection in Older Patients with Dementia: A Single-center Experience in the Light of Comprehensive Geriatric Assessment

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Abstract

Objective: Patients diagnosed with dementia are at increased risk for Coronavirus disease-2019 (COVID-19) infection since they are unable to perform hygiene and social distance due to difficulties recalling or their dependency on another person. Also, there is a strong correlation between mortality of COVID-19 and dementia. In this study, we aimed to elucidate the prevalence of COVID-19 in patients with dementia and their cognitive decline during a pandemic.

Materials and Methods: A total of 210 patients diagnosed with dementia and followed up in the outpatient clinics of geriatrics in our university hospital were included in the study. These records were obtained from the hospital information system. Demographic data, comprehensive geriatric assessments, cognitive changes, COVID-19 infection status, and the dates of death were recorded.

Results: Patients were divided into three groups: Mild, moderate, and severe dementia. COVID-19 prevalence was 11.9% in our study population. When we compared patients according to the history of COVID-19 infection status, there were no differences between the type and the stage of dementia between the COVID-19 infection negative and positive groups ($p>0.05$). Age and sex distribution were similar between these two groups ($p>0.05$). The prevalence of geriatric syndromes was similar in COVID-19 infection positive and negative groups. Furthermore, more than half of the patients in every stage of dementia had cognitive decline during the pandemic course. However cognitive decline rates were not different between COVID-19 positive and negative groups ($p>0.05$).

Conclusion: One in every ten patients with dementia had COVID-19 infection to our results. According to our findings, there is no increase in the frequency of COVID-19 between stages of dementia, the restrictions due to the pandemic cause a decline in cognitive functions. During the pandemic, interventions to protect cognitive functions and periodic health control should not be interrupted for patients with dementia.

Keywords: Dementia, COVID-19, SARS-CoV-2, Alzheimer's, cognitive decline

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-COV-2) virus infection has influenced all over the world over the two years, and over 5.6 million deaths have occurred globally as of February 1, 2022, even though the vaccination process (1). Chronic comorbidities were determined as risk factors for Coronavirus disease-2019 (COVID-19) infection, as well as dementia (2). In older patients hospitalized due to COVID-19, the prevalence of dementia is found elevated in recent observational studies (3). A study that looked at dementia and COVID-19 data from different countries discovered a relationship between a load of dementia and COVID-19 events (4). Furthermore, the mortality rate because of COVID-19 has been reported to be higher in dementia patients. On the other hand, there is limited data in the literature about the prevalence of COVID-19 in patients with dementia, one study from Spain reported that the prevalence of COVID-19 in patients with dementia was 15.2% and the mortality rate was 41.9% in patients with COVID-19 (5).

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Patients diagnosed with dementia are at increased risk of COVID-19 infection since patients with dementia are unable to perform hygiene (hand-washing, usage of face mask) and social distance due to not recalling or dependency on basic activities of daily living. Another reason for catching or spreading COVID-19 in people with dementia is that they have to live in-crowd if they need care (2). It is well-known fact that people with dementia are more frail and frailty in older adults increases the risk of infections while decreasing the immune response, putting the specific population at a higher risk (6,7).

Atypical presentation of the COVID-19 infection in older patients makes it difficult to diagnose leading to increased morbidity and mortality of the infected patients with dementia (8). In a study from Turkey, the presence of dementia increased the risk of mortality in both the 60-79 age and >80 age groups (9).

Moreover, another impact of COVID-19 other than direct physical health is the psychological health of older people with dementia, which was affected due to social isolation policies. Increased frailty, reduced quality of life, high level of stress, increased depressive symptoms were observed during the lockdown period of the pandemic course (10).

In this study, we aimed to elucidate the prevalence of COVID-19 in patients with dementia followed up in our outpatient clinic and to show its relation with other geriatric syndromes. The secondary purpose of the study is to provide information about the cognitive decline in dementia patients during the pandemic course and to show the effect of having COVID-19 on cognitive decline.

Materials and Methods

Study design

Patients who were diagnosed with dementia and followed up in the outpatient clinic of geriatrics in our university hospital were included in the study. We performed a retrospective study using the identified electronic records from the hospital information system who were admitted to the hospital between March 11 2020 and March 31, 2021. Two-hundred forty-four patients with dementia were admitted to the outpatient clinic in this period and 210 patients were included after excluding patients with incomplete data, patients diagnosed with delirium, and patients who did not admit to our clinic regularly during the study period. Other conditions that may impair cognitive test performances including acute illness, infection, electrolyte imbalances, etc. were also excluded from the study. Patients were followed up for three-month periods before and during the pandemic course. Their closest MMSE test or the clock drawing test to the date of the pandemic beginning was accepted as before the pandemic score of cognitive examination. For the standard evaluation, 6 months after the first cognitive examination a second MMSE and/or clock drawing test score was recorded a during the pandemic score of cognitive examination. Age, gender, education, marital status, type and stage of dementia, comorbidities, number of medications were collected from the electronic records of the patient's files. Patients were divided into three groups according to their clinical dementia rating scale (11) as mild, moderate, and severe dementia groups.

Comprehensive geriatric assessments of the patients were also recorded from electronic files. Frailty was defined according to the clinical frailty scale (CFS) (12). CFS was defined according to clinical judgment by the physician of the patient between 1 (very fit) to 9 (terminally ill). Patients whose scale was equal to or more than 5 were accepted as patients living with frailty. Incontinence was accepted as either urinary or fecal incontinence or both by expressions of patients or caregivers. Polypharmacy was defined as the usage of 5 or more medications (13). Fall event was recorded if the patient had fallen unintentionally in the previous year. Difficulty in falling asleep, frequent awakening during the night, or awakening early in the morning were categorized as insomnia. Cognitive decline was decided in one of these situations; a) Objective decline in cognitive test scores b) Getting started on NMDA receptor antagonist treatment according to clinical judgment in patients who were previously diagnosed with mild dementia c) The clinical necessity of antipsychotic treatment in moderate to severe dementia.

The risk of malnutrition was evaluated by mini-nutritional assessment-short form (MNA-SF) (14). MNA- SF scores between 8-11 were defined as the risk of malnutrition and, scores lower than 8 were accepted as malnutrition. The presence of depression was assessed by 15-item Yesavage geriatric depression scale (15) and 5 and higher scores were evaluated as depression. Six-item Katz activities of daily living (ADL) score and 8-item Lawton-Brody instrumental activities of daily living (IADL) score were used for assessing the functionality of the patients (16). The cognitive status of patients was evaluated by mini-mental state examination (MMSE) and clock-drawing test (17,18). In MMSE test, six different cognitive domains, orientation, memory registration, attention, delayed recall, language, motor functions, were evaluated. The orientation was assessed through ten questions, year, season, date, day, month, town, county, hospital, floor, and the current president of the Republic of Turkey. Memory registration was tested by memorizing three words, blue, hawk, and tulip. Attention was evaluated by serial 7's backward calculation from 100. One point was given for each correct answer and the maximum score was 5. The delayed recall was questioned via memorized three words earlier on the test. The language was rated by naming two objects and repeating a sentence and being given 3 points. Motor functions were scored over 6 points according to the fulfillment of the given tasks. The maximum MMSE score was 30 points. We had scored the "clock

drawing test" according to an article titled "early diagnosis of dementia via a two-step screening and diagnostic procedure" by Stähelin et al. (19) The patient was asked to draw a clock as a circle and then place the numbers. If the number "12" was at the top, the patient has scored 3 points. If the clock had 12 numbers exactly, the patient was given an additional 1 point. If there were two distinguishable hands, the total score was 5. If the patient showed the time correctly, the maximum score, 6 points, was given.

COVID-19 infection status were obtained from national health system records through the hospital automation program, and e-Nabız, a free service provided by the Ministry of Health. COVID-19 infection was accepted as positive if the SARS-CoV-2 polymerase chain reaction (PCR) test was positive. Those who have been exposed to at least two doses of the COVID-19 vaccine were considered to be fully vaccinated. The date of death was obtained from the death notification system till the date of 30 September 2021 to maintain at least a six-month follow-up time. The causes of death were obtained by examining the epicrisis in e-Nabız or the hospital automatic program.

Ethical approval

The study protocol was adherence with the principles in the Declaration of Helsinki. The Local Ethics Committee of Hacettepe University Hospital approved the study protocol (number: 2022/02-29).

Statistics

The data of three groups according to stage of dementia, and two groups according to COVID-19 infection positivity were analyzed, tests of normality were performed. Categorical variables were stated as number (n) and percentage (%), and continuous variables as median [interquartile range (IQR)] or mean ± standard deviation (SD) values according to the normal distributions or not. To evaluate the relationships between categorical variables, a chi-square test was used. In the comparison of the three variables, Bonferroni correction was wielded. Student's t-test or ANOVA was utilized to compare the normally distributed numerical parameters between two or three independent groups when appropriate, and the Kruskal-Wallis test was used to compare the parameters which were not normally distributed. Wilcoxon analysis was performed for dependent variables, to evaluate the cognitive test results before and during the pandemic course. A value of $p<0.05$ (two-sided) was accepted as statistically significant. The data obtained in the study were analyzed statistically using IBM SPSS Statistics vn. 24.0 software (IBM Co., Armonk, NY, USA).

Results

Between 11 March 2020 and March 2021, a total of 210 patients with a diagnosis of dementia were included in the final analysis. COVID-19 infection was positive in 25 patients, 11.9% of the study population. When three groups as mild, moderate, and severe dementia were compared; the highest mean age was observed in the severe dementia group, whereas the mild dementia group had the lowest mean age and the difference was statistically significant (p-value= 0.006). The female/male ratio was higher in all three groups. The majority of the patients were living at home, whereas only 4 patients were living in long-term care facilities. The most common type of dementia was Alzheimer's disease (AD) in all three groups. Cognitive decline was revealed in 110 patients, 52.3% of all study population. When the stage of dementia progresses, patients living with frailty become more prevalent according to CFS ($p<0.001$). There were no differences between dementia groups regarding the prevalence of comorbidities and geriatric syndromes except urinary incontinence. Urinary incontinence was more commonly seen in severe dementia ($p<0.001$). ADL, IADL, MNA-SF and cognitive test scores (MMSE, 3 words recall, and clock-drawing test) were all worse in severe dementia and the differences were statistically significant ($p<0.001$, p-value= 0.006 and p-value= 0.001, respectively). On the other hand, no difference was observed in cognitive decline in all three different stages of dementia ($p>0.05$). More than half of the patients in every stage have become worse during the pandemic course. The median (IQR) MMSE score during the pandemic was 17 (9.0) whereas it was 21 (10.0) before the pandemic, and the difference was statistically significant, the p-value was calculated lower than 0.001. No significant difference was seen in the COVID-19 rates according to the stage of dementia, whereas severe dementia patients were more commonly hospitalized due to COVID-19 infection (p-value= 0.016). There were similar mortality rates in all three groups during the pandemic course, furthermore, only one patient died from COVID-19 infection in each group. The detailed results are shown in Table 1.

The relationships between COVID-19 disease groups and geriatric syndromes in patients with dementia were summarized in Table 2. No difference was found between COVID-19 PCR positive and negative groups regarding the type and the stage of dementia, age, gender, geriatric syndromes including frailty, falls and polypharmacy. The prevalence of cognitive decline was not different between the two groups ($p>0.05$).

Discussion

In this study, we aimed to investigate the prevalence of the COVID-19 infection in people with dementia and the effect of the pandemics on that vulnerable population. According to our findings, COVID-19 infection is quite common in people with dementia unrelatedly to the stage of the disease. Furthermore all three groups of dementia patients, mild, moderate, and severe, deteriorated during the pandemic era. The most important outcome of this retrospective analysis is that cognitive decline

Table 1. Demographic features of study population according to dementia groups

	Mild (n=80)	Moderate (n=105)	Severe (n=25)	p
Age, mean ± SD	79.44±6.42	81.70±6.93	84.16±7.23	0.006
Age groups, n (%)				
65-74	17 (21.25)	20 (19.1)	3 (12.0)	
75-84	47 (58.75)	47 (44.7)	9 (36.0)	0.027
>85 and older	16 (20.0)[a]	38 (36.2)	13 (52.0)	
Gender, female, n (%)	54 (67.5)	65 (61.9)	20 (80.0)	0.217
Marital status				
Married, n (%)	33 (55.9)	30 (44.1)	7 (50.0)	0.414
Education				
<8 years, n (%)	37 (63.8)	41 (69.5)	10 (76.9)	0.607
Type of dementia, n (%)				
Alzheimer disease	71 (88.8)	91 (86.7)	21 (84.0)	0.862
Others	9 (10.2)	14 (13.3)	4 (16.0)	
Living w/frailty, CFS	21 (15.2)[a]	92 (66.7)	25 (100.0)	<0.001
Comorbidities, n (%)				
Diabetes	23 (28.7)	37 (35.2)	6 (24.0)	0.446
Hypertension	57 (71.3)	69 (65.7)	12 (48.0)	0.102
Coronary artery disease	22 (27.5)	34 (32.7)	4 (16.7)	0.279
Chronic cardiac failure	6 (7.6)	10 (9.6)	1 (4.2)	0.659
Atrial fibrillation	11 (13.9)	19 (18.1)	3 (12.5)	0.664
Hyperlipidemia	15 (19.0)	19 (18.1)	2 (8.4)	0.457
Hypothyroidism	11 (13.9)	9 (8.7)	1 (4.2)	0.296
Asthma	3 (3.8)	4 (3.8)	-	0.622
COPD	6 (7.6)	9 (8.7)	-	0.334
Rheumatological dis.	4 (5.1)	6 (5.8)	1 (4.2)	0.944
Malignancy	10 (12.7)	12 (11.5)	1 (4.2)	0.501
Cerebrovascular disease	5 (6.3)	8 (7.7)	5 (20.0)	0.094
Benign prostate hyperplasia	14 (17.5)	9 (8.7)	3 (12.5)	0.188
Other	17 (21.5)	22 (21.0)	5 (20.8)	0.995
Geriatric syndromes, n (%)				
Incontinence	26 (42.6)[a]	49 (62.8)	21 (100.0)	<0.001
Polypharmacy	54 (74.0)	76 (80.0)	14 (66.7)	0.366
Osteoporosis	34 (54.0)	34 (40.5)	13 (68.4)	0.052
Falls	15 (25.4)	17 (22.1)	9 (47.4)	0.080
Insomnia	18 (30.0)	26 (32.5)	8 (44.4)	0.517
Depression	10 (29.4)	11 (34.4)	2 (66.7)	0.306
Nutritional assessment				
Normal	16 (38.1)	8 (16.7)	-	<0.001
Risk of malnutrition	20 (47.6)	22 (45.8)	3 (21.4)	
Malnourished	6 (14.3)	18 (37.5)	11 (78.6)	
CFS, median (IQR)	4.0 (3.0)	5.0 (3.0)	7.0 (0.0)	<0.001
ADL median (IQR)	4.0 (3.0)	4.0 (3.0)	1.5 (-)	<0.001
IADL, median (IQR)	5.5 (5.25)	0.0 (3.5)	0.5 (-)	<0.001
MNA-SF, median (IQR)	10 (4.5)	10 (5.0)	10.5 (-)	<0.001
YGDS median (IQR)	4.5 (6.25)	4.0 (3.5)	8.0 (-)	0.209
Number of medication, median (IQR)	6 (5.25)	6 (5.0)	6.5 (.)	0.157
MMSE median (IQR)	22 (8.25)	15 (16.0)	0.0 (1.0)	<0.001
Three words, median (IQR)	1.0 (2.0)	0.0 (1.5)	0.0 (0.0)	0.006
Clock-drawing test, median (IQR)	2.0 (6.0)	1.0 (4.0)	0.0 (0.0)	0.001
Cognitive decline, n (%)	50 (62.5)	57 (54.3)	3 (52.0)	0.605
COVID-19 PCR positive	8 (10.0)	14 (13.3)	3 (12.0)	0.786
COVID-19 hospitalization	2 (25.0)	1 (7.1)	2 (66.7)	0.016
COVID-19 vaccines (at least two doses)	29 (36.3)	33 (31.4)	7 (28.0)	0.676
Outcomes				
Exitus	8 (10.0)	22 (21.0)	4 (16.7)	0.474
Causes of death				
COVID-19 related	1 (12.5)	1 (4.6)	1 (25.0)	0.380
Other causes	7 (87.5)	21 (95.4)	3 (75.0)	

COPD: Chronic obstructive pulmonary disease, CFS: Clinical frailty scale, ADL: Activities of daily living, IADL: Instrumental activities of daily living, MNA-SF: Mini-nutritional assessment-short form, YGDS: Yesevage geriatric depression scale, MMSE: Minimental state examination, PCR: Polymerase chain reaction, SD: Standard deviation, COVID-19: Coronavirus disease-2019, [a] After the subgroup analysis, the difference is originated from mild AD, IQR: Interquartile range

Table 2. Geriatric syndromes according to COVID-19 infection PCR positivity

	COVID positive (n=25)	COVID negative (n=186)	p
Age, mean ± SD	82.32±6.34	80.99±7.06	0.374
Gender, female*	17 (68.0)	122 (65.6)	0.812
Type of dementia, AD*	23 (92.0)	161 (86.6)	0.769
Stage, moderate*	13 (54.2)	88 (48.9)	0.821
Living w/frailty, CFS*	18 (75.0)	116 (63.7)	0.277
Incontinence*	9 (50.0)	87 (61.3)	0.358
Polypharmacy*	18 (81.8)	126 (75.4)	0.510
Osteoporosis*	14 (66.7)	67 (46.2)	0.080
Falls*	2 (10.5)	39 (28.7)	0.093
Insomnia*	8 (42.1)	44 (31.7)	0.363
Cognitive decline*	10 (40.0)	110 (59.5)	0.182

*n (%), AD: Alzheimer's disease, CFS: Clinical frailty scale, SD: Standard deviation, COVID-19: Coronavirus disease-2019, PCR: Polymerase chain reaction

was observed in over half of the patients with mild, moderate, and, severe dementia regardless of COVID-19 infection status.

Cognitive decline is an expected outcome in patients with dementia, In a study conducted by Ballard et al. (20) during a 1-year follow-up period, 4-5 points decline was found in MMSE scores in patients with Alzheimer's dementia, lewy body dementia, and vascular dementia. However, this decline becomes more noticeable during the pandemic era. Ismail et al. (21) showed 0.53±0.3 points decline monthly in MMSE scores during the lockdown period in patients with dementia and mild cognitive impairment. Similar to these studies, we also found 4 points of decline in MMSE scores in a 6-month of the period according to our results. Consistent with our findings, in a study from China, it was shown that social isolation correlated with the accelerated decline of cognitive function and neuropsychiatric symptoms both in patients with Alzheimer's dementia and dementia with lewy body (22). Another study conducted in Greece revealed that a significant overall decline in people with mild cognitive impairment and dementia was observed, and the domains most affected were communication, mood, movement, and compliance with the new measures (23).

It is known that clinical conditions of patients with dementia and living with frailty worsen due to the enhancing effect of the pandemics directly increasing the risk of morbidity and mortality from COVID-19 infection, or indirectly diminishing social support and decreasing interaction with the healthcare system. People with dementia are more vulnerable, neglected, and negatively discriminated and they are not capable of caring for themselves. Plenty of studies shows that people with dementia are affected negatively by health decisions in relation to COVID-19 and its long-term effects including neurological damage (24).

There are several factors contributing to the clinical decline in patients with dementia. During social isolation, cognitively intact people could use technology to stay socially connected, on the other hand, people with cognitive impairment who live alone had trouble with using technology. Furthermore, patients with dementia had difficulty in admission to healthcare facilities. A special article by Brown et al. (25) mentioned that follow-ups by telephone or video-conferencing may not be adequate to monitor disease progression.

Dementia is a known risk factor for COVID-19 infection. In a retrospective study from the UK Biobank cohort (23), all-cause dementia was associated with a higher risk of COVID-19 infection. However, age was a confounding factor, since patients with dementia were significantly older than non-dementia patients (23). On the other hand, in our study mean age was not different between COVID-19 PCR positive and negative groups.

Another study executed from electronic health records of the United States revealed that the highest risk of COVID-19 infection belonged to vascular dementia, and they speculated that impaired cerebral blood flow, or damaged endothelium, could be a risk for SARS-CoV 2 entry (26). However, in the current study, we could not find any relationship between the types of dementia and COVID-19 infection since the most common type of dementia in our study was AD.

In a case-control study from Spain, the mortality rate of COVID-19 infection in patients with primary neurodegenerative dementia was 43.4% whereas 21.5% in the control group (27). In another study from Spain, the frequency of COVID-19 in dementia patients was 15.2% and the mortality rate was 41.9% in COVID-19 positive patients (5). In our study, the prevalence of COVID-19 was 11.9%, however, it would not be appropriate to comment on the mortality rate since only 3 patients died from COVID-19 related causes. The mortality rate was significantly higher in patients living in care homes in a previous study (5), however in our study, the number of patients who were living in care homes were too low, therefore this may be the situation explaining the relatively lower mortality rate due to COVID-19 in patients with dementia.

In a review by Azarpazhooh et al. (4), there was a strong correlation between mortality from COVID-19 and dementia. In another review, the presence of dementia increased by 4.2% in the mortality (28). A nationwide study by Esme et al. (9) also found that the presence of dementia increased the risk of mortality by 1.63 times in the 60-79 age group, and 1.47 times in patients older than 80 years of age.

According to our findings, there were no differences in other geriatric syndromes including frailty and malnutrition between COVID-19 PCR positive and negative patients. In an international multi-center study, frailty was increased mortality

risk three times independently of other conditions. Frailty was also associated with increased risk of care requirements (29). Malnutrition is also important for COVID-19 infection. A systematic review stated that the prevalence of malnutrition among older patients with COVID-19 was high and it was associated with negative outcomes including hospital deaths and transfer to intensive care units (30). Analysis of the data from UK Biobank unlike our findings, demonstrated that polypharmacy was associated with COVID-19 (31). Although there are some studies on the relationship between geriatric syndromes and COVID-19 infection, our study was conducted on patients with dementia and included a relatively small sample. When considering the close relationship of dementia with all geriatric syndromes, this could be the reason why there was no difference between COVID-19 positivity and geriatric syndromes. Despite all these limitations, our study is a rare study that combined COVID-19 infection and CGA in patients with dementia.

Study Limitations

This study is an observational study from a university hospital and it has some limitations, first of all, it has a retrospective design with a relatively small population, and there is not a control group of cognitively intact patients to evaluate cognitive decline. Our findings could not be generalized to the whole population, because the number of hospitalized patients with dementia was too low. On the other hand, there are few studies about COVID-19 and dementia. Therefore, although its retrospective design, the study presented the comprehensive geriatric assessment results and their relationship with COVID-19 infection, revealing the study's strength. This study provides "real-world" data giving the frequency of COVID-19 infection in a specialized patient group is another strength of the study.

Conclusion

It is a known fact that patients with dementia are at higher risk of infection, and they have increased morbidity and mortality rates. Since they have trouble with accessing healthcare facilities and need help in daily living activities, they are vulnerable and need protection. Patients with cognitive impairment need additional support to adequately practice infection control procedures during the pandemic era. These procedures are also crucial for caregivers of patients with dementia who may be at risk of COVID-19. Comprehensive geriatric assessments and cognitive evaluations are essential for every dementia patient. To the best of our knowledge, that is the first study to investigate the prevalence of COVID-19 in patients with dementia from Turkey. Although there is no increase in the frequency of COVID-19 between stages of dementia, the restrictions due to the pandemic cause a decline in cognitive functions. During the pandemic, interventions to protect cognitive functions and periodic health control should not be interrupted for patients with dementia.

Ethics

Ethics Committee Approval: The study protocol was adherence with the principles in the Declaration of Helsinki. The Local Ethics Committee of Hacettepe University Hospital approved the study protocol (number: 2022/02-29).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.G.O., Y.Ö., A.O.B., S.C., B.B.D., M.C., M.G.H., Design: M.G.O., Y.Ö., M.G.H., Data Collection or Processing: M.G.O., Y.Ö., A.O.B., S.C., M.G.H., Analysis or Interpretation: M.G.O., Y.Ö., A.O.B., S.C., B.B.D., M.C., M.G.H., Literature Search: M.G.O., A.O.B., S.C., M.G.H., Writing: M.G.O., Y.Ö., S.C., B.B.D., M.C., M.G.H.

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References

1. World Healt Organization WHO Coronavirus-19 Dashboard Available from: https://covid19.who.int/ on 01 November 2021.
2. Mok VCT, Pendlebury S, Wong A, Alladi S, Au L, Bath PM, Biessels GJ, Chen C, Cordonnier C, Dichgans M, Dominguez J, Gorelick PB, Kim S, Kwok T, Greenberg SM, Jia J, Kalaria R, Kivipelto M, Naegandran K, Lam LCW, Lam BYK, Lee ATC, Markus HS, O'Brien J, Pai MC, Pantoni L, Sachdev P, Skoog I, Smith EE, Srikanth V, Suh GH, Wardlaw J, Ko H, Black SE, Scheltens P. Tackling challenges in care of Alzheimer's disease and other dementias amid the COVID-19 pandemic, now and in the future. Alzheimers Dement 2020;16:1571-1581.
3. Atkins JL, Masoli JAH, Delgado J, Pilling LC, Kuo CL, Kuchel GA, Melzer D. Preexisting Comorbidities Predicting COVID-19 and Mortality in the UK Biobank Community Cohort. J Gerontol A Biol Sci Med Sci 2020;75:2224-2230.
4. Azarpazhooh MR, Amiri A, Morovatdar N, Steinwender S, Rezaei Ardani A, Yassi N, Biller J, Stranges S, Tokazebani Belasi M, Neya SK, Khorram B, Sheikh Andalibi MS, Arsang-Jang S, Mokhber N, Di Napoli M. Correlations between COVID-19 and burden of dementia: An ecological study and review of literature. J Neurol Sci 2020;416:117013.
5. Matias-Guiu JA, Pytel V, Matías-Guiu J. Death Rate Due to COVID-19 in Alzheimer's Disease and Frontotemporal Dementia. J Alzheimers Dis 2020;78:537-541.
6. Tsapanou A, Papatriantafyllou JD, Yiannopoulou K, Sali D, Kalligerou F, Ntanasi E, Zoi P, Margioti E, Kamtsadeli V, Hatzopoulou M, Koustimpi M, Zagka A, Papageorgiou SG, Sakka P. The impact of COVID-19 pandemic on people with mild cognitive impairment/dementia and on their caregivers. Int J Geriatr Psychiatry 2021;36:583-587.
7. Waite SJ, Maitland S, Thomas A, Yarnall AJ. Sarcopenia and frailty in individuals with dementia: A systematic review. Arch Gerontol Geriatr 2021;92:104268.

8. Bianchetti A, Rozzini R, Guerini F, Boffelli S, Ranieri P, Minelli G, Bianchetti L, Trabucchi M. Clinical Presentation of COVID19 in Dementia Patients. J Nutr Health Aging 2020;24:560-562.
9. Esme M, Koca M, Dikmeer A, Balci C, Ata N, Dogu BB, Cankurtaran M, Yilmaz M, Celik O, Unal GG, Ulgu MM, Birinci S. Older Adults With Coronavirus Disease 2019: A Nationwide Study in Turkey. J Gerontol A Biol Sci Med Sci 2021;76:e68-e75.
10. Cheung G, Rivera-Rodriguez C, Martinez-Ruiz A, Ma'u E, Ryan B, Burholt V, Bissielo A, Meehan B. Impact of COVID-19 on the health and psychosocial status of vulnerable older adults: study protocol for an observational study. BMC Public Health 2020;20:1814.
11. Hughes CP, Berg L, Danziger W, Coben LA, Martin RL. A new clinical scale for the staging of dementia. Br J Psychiatry 1982;140:566-572.
12. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.
13. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatr 2017;17:230.
14. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition: The Mini Nutritional Assessment. Clin Geriatr Med 2002;18:737-757.
15. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, Leirer VO Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982;17:37-49.
16. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged: the index of ADL: a standardized measure of biological and psychosocial function. JAMA 1963;185:914-919.
17. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.
18. Shulman KI. Clock-drawing: is it the ideal cognitive screening test? Int J Geriatr Psychiatry 2000;15:548-561.
19. Stähelin HB, Monsch AU, Spiegel R. Early Diagnosis of Dementia via a Two-Step Screening and Diagnostic Procedure. Int Psychogeriatr 1997;9(Suppl 1):123-130.
20. Ballard C, O'Brien J, Morris CM, Barber R, Swann A, Neill D, McKeith I. The progression of cognitive impairment in dementia with Lewy bodies, vascular dementia and Alzheimer's disease. Int J Geriatr Psychiatry 2001;16:499-503.
21. Ismail II, Kamel WA, Al-Hashel JY. Association of COVID-19 Pandemic and Rate of Cognitive Decline in Patients with Dementia and Mild Cognitive Impairment: A Cross-sectional Study. Gerontol Geriatr Med 2021;7:23337214211005223.
22. Chen ZC, Liu S, Gan J, Ma L, Du X, Zhu H, Han J, Xu J, Wu H, Fei M, Dou Y, Yang Y, Deng P, Wang XD, Ji Y. The Impact of the COVID-19 Pandemic and Lockdown on Mild Cognitive Impairment, Alzheimer's Disease and Dementia With Lewy Bodies in China: A 1-Year Follow-Up Study. Front Psychiatry 2021;12:711658.
23. Tahira AC, Verjovski-Almeida S, Ferreira ST. Dementia is an age-independent risk factor for severity and death in COVID-19 inpatients. Alzheimers Dement 2021;17:1818-1831.
24. Burns A, Lobo A, Olde Rikkert M, Robert P, Sartorius N, Semrau M, Stoppe G. COVID-19 and dementia: experience from six European countries. Int J Geriatr Psychiatry 2021;36:943-949.
25. Brown EE, Kumar S, Rajji TK, Pollock BG, Mulsant BH. Anticipating and Mitigating the Impact of the COVID-19 Pandemic on Alzheimer's Disease and Related Dementias. Am J Geriatr Psychiatry 2020;28:712-721.
26. Wang Q, Davis PB, Gurney ME, Xu R. COVID-19 and dementia: Analyses of risk, disparity, and outcomes from electronic health records in the US. Alzheimers Dement 2021;17:1297-1306.
27. Reyes-Bueno JA, Mena-Vázquez N, Ojea-Ortega T, Gonzalez-Sotomayor MM, Cabezudo-Garcia P, Ciano-Petersen NL, Pons-Pons G, Castro-Sánchez MV, Serrano-Castro PJ. Case fatality of COVID-19 in patients with neurodegenerative dementia. Neurologia (Engl Ed) 2020;35:639-645.
28. Izcovich A, Ragusa MA, Tortosa F, Lavena Marzio MA, Agnoletti C, Bengolea A, Ceirano A, Espinosa F, Saavedra E, Sanguine V, Tassara A, Cid C, Catalano HN, Agarwal A, Foroutan F, Rada G. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. PLoS One 2020;15:e0241955.
29. Geriatric Medicine Research Collaborative; Covid Collaborative, Welch C. Age and frailty are independently associated with increased COVID-19 mortality and increased care needs in survivors: results of an international multi-centre study. Age Ageing 2021;50:617-630.
30. Damayanthi H, Prabani KIP. Nutritional determinants and COVID-19 outcomes of older patients with COVID-19: A systematic review. Arch Gerontol Geriatr 2021;95:104411.
31. McQueenie R, Foster HME, Jani BD, Katikireddi SV, Sattar N, Pell JP, Ho FK, Niedzwiedz CL, Hastie CE, Anderson J, Mark PB, Sullivan M, O'Donnell CA, Mair FS, Nicholl BI. Multimorbidity, polypharmacy, and COVID-19 infection within the UK Biobank cohort. PLoS One 2020;15:e0238091.

ORIGINAL RESEARCH

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Can PNI and CONUT Scores Predict One-year Survival Both in Older and Younger Hospitalized Patients with COVID-19?

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Abstract

Objective: This study aimed to find out the prognostic effect of the prognostic nutritional index (PNI) and controlling nutritional status (CONUT) score for 1-year mortality prediction in older (≥65 years) and younger (<65 years) hospitalized Coronavirus disease-2019 (COVID-19) patients, separately.

Materials and Methods: This retrospective and the observational study included 368 patients who were admitted to a single tertiary care university hospital due to COVID-19 disease with positive severe acute respiratory syndrome-coronavirus-2 real-time reverse transcriptase-polymerase chain reaction test. Multivariable Cox regression analyses were performed to predict 1-year mortality prediction for the older and younger groups.

Results: Among 368 patients, 112 (30.4%) patients were 65 years and older. There were 45 (12.2%) deaths at the end of the 1-year follow-up. The 1-year mortality rate was higher in the older group (23.2% vs 7.4%). When all patients were analyzed (n=368), PNI [hazard ratio (HR)=0.924, 95% confidence interval (CI)=0.877-0.974, p=0.003] and CONUT (HR=1.423, 95% CI=1.194-1.696, p<0.001) scores were significantly associated with 1-year mortality in multivariable model. When older and younger groups were assessed separately; PNI and CONUT scores failed to estimate 1-year mortality in the older group. On the other hand, the independent estimating capacities of PNI (HR=0.899, 95% CI=0.836-0.966, p=0.004) and CONUT (HR=1.944, 95% CI=1.478-2.557, p<0.001) scores increased when the only younger group was taken into analysis.

Conclusion: PNI and CONUT scores as indicators of nutritional and immune status, predicted 1-year mortality in hospitalized COVID-19 patients. However, their prognostic effects in older patients with COVID-19 may be less prominent. Future, large sample studies are needed to provide data about geriatric COVID-19 patients.

Keywords: Geriatrics, nutritional assessment, COVID-19, PNI, CONUT

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection developed into a global pandemic after first seen in China in 2019. Age, male sex, and the existence of comorbidities are shown to be associated with severe Coronavirus disease-2019 (COVID-19), higher risk of hospitalization, and in-hospital mortality, so far (1-5). Both biological and immune function of humans' decrease gradually with the aging process; this immune aging process is called immunosenescence, contributing to the higher susceptibility to infections, autoimmune diseases, and infections. Immunosenescence causes a low-grade pro-inflammatory state with the increment of inflammatory mediators like IL-6, IL-1RA, TNF-α, IL-1, and C-reactive protein (CRP) called inflammaging. Inflammaging with other features of the immunosenescence may fasten the disease severity of COVID-19 in older adults (6). Regardless of age, the features of COVID-19, including inflammation, hypercatabolism, and increased energy expenditure, may predispose to malnutrition and muscle wasting. On the other hand, preexisting malnutrition and sarcopenia may worsen the disease progression and related complications. The social isolation and quarantine measures due to pandemics may cause changes in dietary habits, difficulties in accessing food, lack of physical activity, and worsening of

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chronic disease. All these issues may contribute to the increment in malnutrition prevalence both before and after the COVID-19 disease (7-9).

The prognostic impact of new nutritional indices based on biochemical and clinical markers in the pandemic world has emerged. Prognostic nutritional index score (PNI) calculated using albumin and lymphocyte; controlling nutritional status score (CONUT) calculated by using albumin, lymphocyte and cholesterol are the major ones (10,11). As they are easy and practical to obtain data about the nutritional status of patients, they are widely used especially in oncology wards.

When the risks and difficulties in managing hospitalized patients with COVID-19 and the effect of nature of the disease on nutritional status itself were considered; we planned to investigate the long-term prognostic effects of PNI and CONUT scores on hospitalized patients with COVID-19, retrospectively. Therefore, we aimed to find out the effect of these indices to predict 1-year mortality both in older and younger patients with COVID-19.

Materials and Methods

Study population and data collection

This retrospective observational study was conducted in a single tertiary care university hospital and included patients with COVID-19 who were admitted to the hospital between June 01 2020 and December 31 2021. All included patients had positive SARS-CoV-2 real-time reverse transcriptase-polymerase chain reaction (RT-PCR) tests (Bioeksen R&D Technologies Ltd, Turkey) taken by a doctor from both combined oropharyngeal and nasopharyngeal samples. The patients who were pregnant and clinically suspected COVID-19 with negative RT-PCR tests were excluded. The data of patients about date of birth, sex, length of stay, comorbidities, medications, and pulmonary computed tomography (CT) findings were obtained from medical records. The laboratory values including white blood cells ($\times 10^3/\mu L$), neutrophils ($\times 10^3/\mu L$), lymphocyte ($\times 10^3/\mu L$), fasting plasma glucose (mg/dL), total cholesterol protein (mg/dL), albumin (g/dL), alanine aminotransferase (U/L), aspartate aminotransferase (U/L), creatinine (mg/dL), CRP (mg/dL), ferritin (µg/L), D-dimer (mg/L) and fibrinogen (mg/dL), taken within 24 hours of admission, were recorded.

Nutritional assessment

The nutritional status of patients was assessed by using PNI and CONUT. PNI score was calculated using the following formula: 10*serum albumin (g/dL) +0.005*total lymphocyte count (per mm^3). Whereas a score of >38 was considered normal nutritional status; scores of 35-38 and <35 were evaluated as moderate and severe malnutrition, respectively (10,12). CONUT score was calculated from serum albumin, total cholesterol, and lymphocyte count. Lymphocyte count was scored as 0, 1, 2, and 3 when it was ≥1.600, 1.200-1.599, 0.800-1.199, and <0.800, respectively. Serum albumin was scored as 0, 2, 4, 6 when it was ≥3.5, 3.0-3.49, 2.5-2.99, <2.5 g/dL, respectively. Serum cholesterol was scored as 0, 1, 2, and 3 when it was ≥180, 140-179, 100-139, and <100 mg/dL, respectively. Finally, the total CONUT score was classified as normal nutritional status, mild, moderate, and severe malnutrition when ıt was 0-1, 2-4, 5-8, and 9-12, respectively (11,12).

Follow-up and outcomes

All the study participants were followed from hospital admission to death or until 31 December 2021. Vital status and the date of death were obtained from the Turkish national death registry. The primary outcome of this study was all-cause mortality.

Ethics approval

The Local Ethics Committee of Hacettepe University approved the study (no: GO 21/818), and conducted according to the guidelines laid down in the Declaration of Helsinki.

Statistics

The variables were controlled by using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test) to determine whether or not they were normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed age. Medians and interquartile range (25-75 percentile) were used for the non-normally distributed and ordinal variables. Categorical variables were summarized in terms of counts and percentages. Whereas normally distributed variables were compared using independent samples t-test, non-normally distributed variables were compared using Mann-Whitney U test between groups. The chi-square test or Fisher's Exact test, where appropriate, was used to compare proportions between groups. The area under curve values were calculated based on the receiver operating characteristic (ROC) curves analysis to estimate predicting capacities of PNI and CONUT regarding mortality in both ≥65 years and <65 years groups and shown as figure. The unadjusted Cox model was used to assess the relationship between 1-year mortality and nutritional indices. Multivariable Cox regression models were also generated by adjusting for age, and gender. As PNI and CONUT scores were calculated by using albumin, cholesterol, and lymphocyte, these laboratory values were not put into models. The results were expressed as hazard ratios (HRs) and corresponding 95% confident intervals (CI). The proportional hazards assumption and model fit were assessed using residual (Schoenfeld and Martingale) analysis. All analyses were considered statistically significant when the p-value was <0.05 and was performed by the Statistical Package of Social Science 23.0 (SPSS Inc., Chicago, IL).

Results

Three-hundred and sixty-eight patients were enrolled in the study. The mean age of the participants at the time of hospital admission was 57.1±15.7 (range, 18-97) with a 46.7% male rate. The median follow-up time was 16.1 months. There were 45 (12.2%) deaths during the 1-year follow-up. The proportions of older patients (57.8%) and male sex (68.9%) were higher in the deceased group, whereas the rate of white blood cells, neutrophils, alanine aminotransferase, serum creatinine, CRP, ferritin, and D-dimer were higher; lymphocyte, total cholesterol, and albumin were lower in the deceased group. Nutritional status, defined by CONUT and PNI, was worst in the deceased group as well (Table 1). One hundred and twelve (30.4%) of the participants were placed in the geriatric (≥65 years) group. Older patients had longer length of stay, higher CRP and D-dimer, and lower albumin and total cholesterol level. Nutritional indices were worse in the geriatric group than younger group. The one-year mortality rate was higher in geriatric group as well (Table 2).

A comparison of the ROC curves is given in Figure 1. The univariable and multivariable (age and sex adjusted) cox models are given in Table 3 and Table 4, in detail. When all patients were analyzed (n=368), PNI (HR=0.924, 95% CI=0.877-0.974, p=0.003) and CONUT (HR=1.423, 95% CI=1.194-1.696, p<0.001) scores were significantly associated with 1-year mortality in a multivariable model. However, when we assessed the older and younger groups, separately in multivariable analysis; PNI and CONUT scores failed to estimate in geriatric group. On the other hand, the independent estimating capacities of PNI (HR=0.899, 95% CI=0.836-0.966, p=0.004) and CONUT (HR=1.944, 95% CI=1.478-2.557, p<0.00) scores for 1-year mortality increased when only younger group were taken into analysis.

Discussion

In the present study, both PNI and CONUT scores were independently associated with 1-year mortality in hospitalized patients with COVID-19. However, when the patients were divided into two groups according to their ages (≥65 years or <65 years of age), we showed that PNI and CONUT scores failed to estimate 1-year mortality risk in geriatric patients. This data was the major finding of our study. To the best of our knowledge, this was the first study investigating the estimating capacities of PNI and CONUT scores to predict 1-year mortality in older and younger hospitalized patients with COVID-19, separately.

PNI score, calculated using albumin and lymphocyte; CONUT score, calculated using albumin, lymphocyte, and cholesterol has gained popularity, especially in oncology and surgery wards as they are easy and practical tools. There are emerging studies supporting their use in clinical practice to predict prognosis, especially in mortality estimation (13-21). Recently, PNI and CONUT have been used in hospitalized patients with COVID-19 (8,22). Bengelloun et al. (23) assessed nutritional status using the CONUT index at hospital admission to predict COVID-19 related health outcomes in 2844 COVID-19 patients (mean age was 67.3±16.5). They found the CONUT index to be an independent indicator of mortality (in-hospital and 30-day mortality) and length of stay similar to us (23). Therefore, we showed that the independent prognostic ability of the CONUT score lasted at least 1-year, when all patients were included in the analysis. However, when older and younger patients were evaluated separately, CONUT score failed to predict 1-year mortality in the older group. Another retrospective observational study from China assessed 295 hospitalized COVID-19 patients and showed PNI and CONUT scores as a prognostic indicators for in-hospital mortality (24). Although this study was consistent with our results, the median age of participants was 58 years. Hu et al. (25) found the independent predictive value of PNI for the severity of COVID-19 and they suggested PNI score as a simple and effective predictor with different sex, age, and BMI for hospitalized patients with COVID-19. Although they presented the independent effect of PNI, the mean age in the study was 44 years [standard deviation (SD)=13.4] (25). Wei et al. (26) published a study in line with this data and showed PNI as an independent predictor of mortality for hospitalized COVID-19 patients. A study from Turkey investigated the estimating capacity of PNI for hospital mortality in COVID-19 patients with cardiovascular risk factors, and found it independently associated with mortality. The mean age of patients in the study was 55.4 years (SD=12.8) (27).

Although there are emerging studies about using PNI and CONUT scores in hospitalized COVID-19 patients, the data about the confounding factors, especially in older patients and comorbidities are missing. The first challenge is immune aging called immunosenescence and inflammaging as a result of cell senescence. The second one is the high prevalence of comorbidities with aging that may cause low-grade inflammation. Thirdly, the data about the frailty status of patients are important when managing hospitalized patients. As, frailty is a dynamic process at all ages, it should be evaluated in all conditions. However, the effect of frailty on hospitalized COVID-19 patients is controversial (28-30). In the light of these data with the enormous effect of virus, the nutritional indices should be interpreted cautiously, especially for COVID-19 patients. Albumin and lymphocyte counts are both used in the calculation of PNI and CONUT scores. Albumin is synthesized in the liver and is an indicator of nutritional status. However, the synthesis of albumin is reduced when systemic inflammation is present and its sensitivity as a nutritional marker decreases as it is a negative acute-phase reactant. Lymphocyte count is an indicator of the immune system and low lymphocyte level

Table 1. Characteristics of patients according to 1-year survival

Parameters	Total	Alive (1-year) (n=323)	Deceased (1-year) (n=45)	p-value
Age	57.1±15.7	55.5±15.1	68.5±15.2	<0.001
≥65 years	112 (30.4)	86 (26.6)	26 (57.8)	<0.001
Sex, male	172 (46.7)	141 (43.7)	31 (68.9)	0.001
Follow-up time, month	16.1 (13.1-17.4)	16.6 (14.9-17.5)	0.8 (0.5-1.7)	<0.001
Length of stay, day	6.0 (4.0-10.0)	6.0 (4.0-9.0)	18.0 (7.5-27.5)	<0.001
Comorbidities				
Diabetes mellitus	83 (25.4)	67 (23.4)	16 (39.0)	0.032
Hypertension	129 (39.4)	106 (37.1)	23 (56.1)	0.020
COPD	19 (5.8)	15 (5.2)	4 (9.8)	0.248
Coronary artery disease	53 (16.2)	40 (14.0)	13 (31.7)	0.004
Cerebrovascular disease	15 (4.6)	11 (3.8)	4 (9.8)	0.091
Malignancy	34 (10.4)	19 (6.6)	15 (36.6)	<0.001
Laboratory indices				
White blood cell, x10^3/uL	4.8 (3.2-6.1)	4.8 (3.2-6.0)	5.6 (3.5-8.2)	0.031
Neutrophils, x10^3/uL	2.9 (1.8-4.3)	2.9 (1.8-4.1)	3.7 (2.2-6.2)	0.009
Lymphocyte, x10^3/uL	1.0 (0.7-1.4)	1.0 (0.7-1.5)	0.8 (0.6-1.2)	0.020
Fasting plasma glucose, mg/dL	105 (90-131)	103 (90-126)	128 (96-167)	0.510
Total cholesterol, mg/dL	188 (146-227)	190 (152-230)	138 (106-165)	<0.001
Albumin, (g/dL)	3.9 (3.6-4.2)	4.0 (3.7-4.2)	3.6 (2.9-3.9)	<0.001
Alanine aminotransferase, U/L	24 (16-38)	24 (16-38)	22 (16-36)	0.685
Aspartate aminotransferase, U/L	31 (23-44)	30 (23-42)	38 (29-53)	0.005
Serum creatinine, mg/dL	0.86 (0.71-1.02)	0.84 (0.71-0.99)	0.96 (0.80-1.31)	0.002
C-reactive protein, mg/dL	2.2 (0.9-7.5)	1.8 (0.8-6.2)	7.6 (3.4-15.5)	<0.001
Ferritin, ng/mL	155 (64-365)	138.2 (56.5-315.5)	438.1 (124.7-941.6)	<0.001
D-dimer, mg/L	0.54 (0.32-0.90)	0.52 (0.32-0.85)	0.87 (0.50-2.30)	<0.001
Fibrinogen, mg/dL	405 (323-509)	405 (323-509)	416 (332-520)	0.475
CONUT score CONUT category Normal Mild Moderate Severe	2 (1-4) 75 (26.7) 163 (58.0) 39 (13.9) 4 (1.4)	2 (1-3) 75 (28.6) 153 (58.4) 32 (12.2) 2 (0.8)	4 (3-5) 0 (0) 10 (52.6) 7 (36.8) 2 (10.5)	<0.001 <0.001
PNI score PNI category Normal Moderate Severe	45.0 (41.3-48.5) 325 (88.3) 20 (5.4) 23 (6.3)	45.8 (41.9-49.0) 292 (90.4) 19 (5.9) 12 (3.7)	41.2 (36.1-44.3) 33 (73.3) 1 (2.2) 11 (24.4)	<0.001 <0.001
Abnormal CT imaging findings	274 (84)	238 (83.5)	36 (87.8)	0.482
COVID-19 pneumonia (n=327)	323 (98.8)	284 (99.3)	39 (95.1)	0.078

CONUT: Controlling nutritional status score, COPD: Chronic obstructive pulmonary disease, PNI: Prognostic nutritional index. Numbers were presented as means ± SD, medians (25th-75th percentiles), or frequencies n (%), as appropriate. SD: Standard deviation, CT: Computed tomography, COVID-19: Coronavirus disease-2019

was shown to be an independent risk factor for COVID-19 (31). Another parameter used in the calculation of CONUT score is cholesterol level and it is a nutritional indicator, too. A reduced level of cholesterol is associated with an impaired immune response (32). Not only being a nutritional indicator but also an immune-inflammatory index; both PNI and CONUT are valuable, especially in the COVID-19 pandemic area. However, the cut-off values of PNI and the CONUT scores need to be updated for COVID-19 patients and older adults, separately, evaluating the confounders and taking comprehensive geriatric assessment into consideration.

Table 2. Baseline characteristics of patients according to age categories

	Total	≥65 years (n=112)	<65 years (n=256)	p-value
Age	57.1±15.7	75.4±6.8	49.1±11.1	<0.001
Sex, male	172 (46.7)	51 (45.5)	121 (47.3)	0.760
Follow-up time	16.1 (13.1-17.4)	15.1 (12.0-16.7)	16.6 (14.0-17.6)	<0.001
Length of stay	6.0 (4.0-10.0)	9.0 (5.0-16.2)	5.0 (4.0-8.0)	<0.001
Comorbidities				
Diabetes mellitus	83 (25.4)	41 (42.7)	42 (18.2)	<0.001
Hypertension	129 (39.4)	67 (69.8)	62 (26.8)	<0.001
COPD	19 (5.8)	11 (11.5)	8 (3.5)	0.005
Coronary artery disease	53 (16.2)	35 (36.5)	11 (11.5)	<0.001
Cerebrovascular disease	15 (4.6)	10 (10.4)	5 (2.2)	0.001
Malignancy	34 (10.4)	11 (11.5)	23 (10)	0.685
Laboratory indices				
White blood cell, $\times10^3/\mu L$	4.8 (3.2-6.1)	4.7 (3.2-6.0)	4.9 (3.3-6.1)	0.864
Neutrophils, $x10^3/uL$	2.9 (1.8-4.3)	2.9 (1.9-4.6)	2.9 (1.8-4.2)	0.718
Lymphocyte, $x10^3/uL$	1.0 (0.7-1.4)	0.9 (0.7-1.3)	1.0 (0.7-1.5)	0.076
Fasting plasma glucose, mg/dL	105 (90-131)	118 (92-159)	101 (90-122)	0.007
Total cholesterol, mg/dL	188 (146-227)	173 (137-214)	190 (148-233)	0.018
Albumin, g/dL	3.9 (3.6-4.2)	3.7 (3.5-4.0)	4.0 (3.7-4.2)	<0.001
Alanine aminotransferase, U/L	24 (16-38)	21 (16-29)	25 (16-41)	0.014
Aspartate aminotransferase, U/L	31 (23-44)	31 (25-43)	31 (22-44)	0.353
Serum creatinine, mg/dL	0.86 (0.71-1.02)	0.95 (0.81-1.29)	0.82 (0.67-0.96)	<0.001
C-reactive protein, mg/dL	2.2 (0.9-7.5)	3.0 (1.2-9.1)	1.9 (0.8-6.3)	0.004
Ferritin, ng/mL	155 (64-365)	158 (71-367)	151 (59-359)	0.559
D-dimer, mg/L	0.54 (0.32-0.90)	0.81 (0.50-1.21)	0.45 (0.28-0.74)	<0.001
Fibrinogen, mg/dL	405 (323-509)	424 (349-527)	395 (311-497)	0.090
CONUT score CONUT category Normal Mild Moderate Severe	2 (1-4) 75 (26.7) 163 (58.0) 39 (13.9) 4 (1.4)	3(2-4) 12 (16.4) 45 (61.6) 14 (19.2) 2 (2.7)	2 (1-3) 63 (30.3) 118 (56.7) 25 (12.0) 2 (1.0)	 0.008 0.063
PNI score PNI category Normal Moderate Severe	45.0 (41.3-48.5) 325 (88.3) 20 (5.4) 23 (6.3)	42.9 (39.6-46.4) 93 (83) 8 (7.1) 11 (9.8)	46.2 (42.0-49.2) 232 (90.6) 12 (4.7) 12 (4.7)	<0.001 0.097
Abnormal CT imaging findings (n=324)	274 (84)	83 (87.4)	191 (82.7)	0.294
COVID-19 pneumonia (n=327)	323 (98.8)	95 (99)	228 (98.7)	0.753
Mortality rate 3-months 6-months 1-year	 35 (9.5) 38 (10.3) 45 (12.2)	 20 (17.9) 22 (19.6) 26 (23.2)	 15 (5.9) 16 (6.3) 19 (7.4)	 <0.001 <0.001 <0.001

CONUT: Controlling nutritional status score, COPD: Chronic obstructive pulmonary disease, PNI: Prognostic nutritional index. Numbers were presented as means ± SD, medians (25^{th}-75^{th} percentiles) or frequencies n (%), as appropriate. SD: Standard deviation, CT: Computed tomography, COVID-19: Coronavirus disease-2019

Study Limitations

This study has some limitations. First of all, it has a retrospective design so we could not perform comprehensive geriatric assessment including the functional, cognitive, and frailty status of patients. Therefore, malnutrition risk screening of patients by using short-form mini-nutritional assessment, nutritional

risk screening (NRS 2002) etc. was not available. Secondly, the number of older patients was low and the effect of comorbidities was not evaluated separately. On the other hand, we did not exclude patients who use lipid-lowering therapy, and it might affect the total cholesterol results also CONUT scores.

Conclusion

PNI and CONUT scores as indicators of nutritional and immune status, predicted 1-year mortality in hospitalized COVID-19 patients when all patients were analyzed. However, their prognostic effects in geriatric patients may be different especially for COVID-19 patients. Future and large sample size studies are needed to provide data about the use of these indices in geriatric COVID-19 patients adjusting for other confounders.

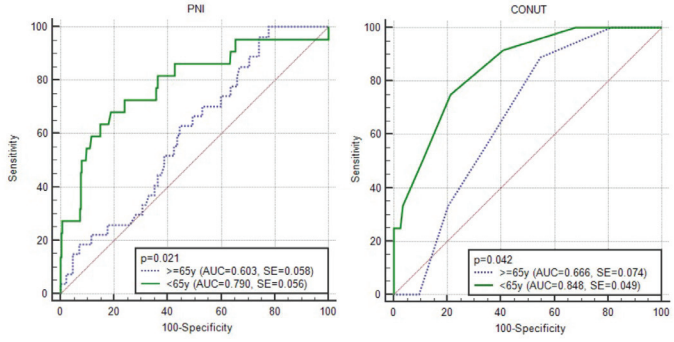

Figure 1. Comparisons of ROC curves for PNI and CONUT according to age categories

CONUT: Controlling nutritional status score, PNI: Prognostic nutritional index

Ethics

Ethics Committee Approval: The study protocol was approved by the Local Ethics Committee of Hacettepe University (Ankara, Turkey), and written informed consent was obtained from all participants (no: GO 21/818). All the procedures were in accordance with the ethical standards established by the 1964 Declaration of Helsinki.

Informed Consent: Informed consent was obtained from all participants. All the procedures were in accordance with the ethical standards established by the 1964 Declaration of Helsinki.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Y.Ö., M.G.O., S.C., M.H., Design: Y.Ö., M.Ö., O.A.U., M.H., Data Collection or Processing: Y.Ö., M.Ö., O.A.U., M.G.O., S.C., M.H., Analysis or Interpretation: Y.Ö., M.G.O., S.C., M.H., Literature Search: Y.Ö., M.H., Writing: Y.Ö., M.H.

Conflict of Interest: No conflict of interest was declared by the authors.

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Table 3. Univariable analysis of two malnutrition indices to predict mortality

Variables	All patients		≥65 years		<65 years	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.058 (1.036-1.081)	<0.001	1.088 (1.035-1.144)	0.001	1.052 (1.002-1.105)	0.043
Sex	2.657(1.413-4.995)	0.002	3.685 (1.548-8.773)	0.003	1.960 (0.772-4.979)	0.157
CONUT score	1.543 (1.304-1.826)	<0.001	1.147 (0.865-1.522)	0.340	1.948 (1.519-2.498)	<0.001
PNI score	0.890 (0.848-0.935)	<0.001	0.923 (0.859-0.991)	0.028	0.884 (0.823-0.950)	0.001

CONUT: Controlling nutritional status score, PNI: Prognostic nutritional index, CI: Confident interval, HR: Hazard ratio

Table 4. Multivariable analysis of two malnutrition indices to predict mortality

Variables	All patients (n=368)		≥65 years (n=112)		<65 years (n=256)	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Model 1						
Age	1.036 (1.001-1.072)	0.043	1.042 (0.958-1.134)	0.336	1.051 (0.981-1.126)	0.154
Sex	2.674 (0.870-8.220)	0.086	9.599 (1.142-80.720)	0.037	0.660 (0.128-3.391)	0.618
CONUT score	1.423 (1.194-1.696)	<0.001	-	-	1.944 (1.478-2.557)	<0.001
Model 2						
Age	1.052 (1.029-1.075)	<0.001	1.077 (1.030-1.127)	0.001	1.042 (0.990-1.097)	0.116
Sex	2.538 (1.340-4.808)	0.004	3.770 (1.572-9.039)	0.003	1.507 (0.579-3.920)	0.401
PNI score	0.924 (0.877-0.974)	0.003	0.955 (0.885-1.031)	0.236	0.899 (0.836-0.966)	0.004

CONUT: Controlling nutritional status score, PNI: Prognostic nutritional index, CI: Confident interval, HR: Hazard ratio, Model 1: Age, sex, CONUT, Model 2: Age, sex, PNI

References

1. Semenzato L, Botton J, Drouin J, Cuenot F, Dray-Spira R, Weill A, Zureik M. Chronic diseases, health conditions and risk of COVID-19-related hospitalization and in-hospital mortality during the first wave of the epidemic in France: a cohort study of 66 million people. Lancet Reg Health Eur 2021;8:100158.
2. Surendra H, Elyazar IR, Djaafara BA, Ekawati LL, Saraswati K, Adrian V, Widyastuti, Oktavia D, Salama N, Lina RN, Andrianto A, Lestari KD, Burhan E, Shankar AH, Thwaites G, Baird JK, Hamers RL. Clinical characteristics and mortality associated with COVID-19 in Jakarta, Indonesia: A hospital-based retrospective cohort study. Lancet Reg Health West Pac 2021;9:100108.
3. Polidori MC, Sies H, Ferrucci L, Benzing T. COVID-19 mortality as a fingerprint of biological age. Ageing Res Rev 2021;67:101308.
4. Panagiotou OA, Kosar CM, White EM, Bantis LE, Yang X, Santostefano CM, Feifer RA, Blackman C, Rudolph JL, Gravenstein S, Mor V. Risk Factors Associated With All-Cause 30-Day Mortality in Nursing Home Residents With COVID-19. JAMA Intern Med 2021;181:439-448.
5. Goodman KE, Magder LS, Baghdadi JD, Pineles L, Levine AR, Perencevich EN, Harris AD. Impact of Sex and Metabolic Comorbidities on Coronavirus Disease 2019 (COVID-19) Mortality Risk Across Age Groups: 66 646 Inpatients Across 613 U.S. Hospitals. Clin Infect Dis 2021;73:e4113-e4123.
6. Pietrobon AJ, Teixeira FME, Sato MN. I mmunosenescence and Inflammaging: Risk Factors of Severe COVID-19 in Older People. Front Immunol 2020;11:579220.
7. Damayanthi H, Prabani KIP. Nutritional determinants and COVID-19 outcomes of older patients with COVID-19: A systematic review. Arch Gerontol Geriatr 2021;95:104411.
8. Ali AM, Kunugi H. Approaches to Nutritional Screening in Patients with Coronavirus Disease 2019 (COVID-19). Int J Environ Res Public Health 2021;18:2772.
9. Ali AM, Kunugi H. Skeletal Muscle Damage in COVID-19: A Call for Action. Medicina (Kaunas) 2021;57:372.
10. Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. Am J Surg 1980;139:160-167.
11. Salinas M, Flores E, Blasco A, López-Garrigós M, Puche C, Asencio A, Leiva-Salinas C. CONUT: a tool to assess nutritional status. First application in a primary care population. Diagnosis (Berl) 2021;8:373-376.
12. Yuan K, Zhu S, Wang H, Chen J, Zhang X, Xu P, Xie Y, Zhu X, Zhu W, Sun W, Xu G, Liu X. Association between malnutrition and long-term mortality in older adults with ischemic stroke. Clin Nutr 2021;40:2535-2542.
13. Liao G, Zhao Z, Yang H, Chen M, Li X. Can Prognostic Nutritional Index be a Prediction Factor in Esophageal Cancer?: A Meta-Analysis. Nutr Cancer 2020;72:187-193.
14. Li S, Tian G, Chen Z, Zhuang Y, Li G. Prognostic Role of the Prognostic Nutritional Index in Pancreatic Cancer: A Meta-analysis. Nutr Cancer 2019;71:207-213.
15. Bullock AF, Greenley SL, McKenzie GAG, Paton LW, Johnson MJ. Relationship between markers of malnutrition and clinical outcomes in older adults with cancer: systematic review, narrative synthesis and meta-analysis. Eur J Clin Nutr 2020;74:1519-1535.
16. Wang X, Wang Y. The prognostic nutritional index is prognostic factor of gynecological cancer: A systematic review and meta-analysis. Int J Surg 2019;67:79-86.
17. Wang QQ, Zheng GQ, Yang DL, Liang YF, Yin WJ, Su SS. Pretreatment Controlling Nutritional Status Score and Lactate Dehydrogenase as Predictive Markers of Survival in Patients with Malignant Peritoneal Mesothelioma. Nutr Cancer 2018;70:1264-1274.
18. Xue W, Hu X, Zhang Y. The Association of Controlling Nutritional Status (CONUT) Score with Survival in Patients with Surgically Treated Renal Cell Carcinoma and Upper Tract Urothelial Carcinoma: A Systematic Review and Meta-Analysis. Nutr Cancer 2021;74:1907-1916.
19. Terasaki F, Sugiura T, Okamura Y, Ito T, Yamamoto Y, Ashida R, Ohgi K, Uesaka K. The preoperative controlling nutritional status (CONUT) score is an independent prognostic marker for pancreatic ductal adenocarcinoma. Updates Surg 2021;73:251-259.
20. Komici K, Vitale DF, Mancini A, Bencivenga L, Conte M, Provenzano S, Grieco FV, Visaggi L, Ronga I, Cittadini A, Corbi G, Trimarco B, Morisco C, Leosco D, Ferrara N, Rengo G. Impact of Malnutrition on Long-Term Mortality in Elderly Patients with Acute Myocardial Infarction. Nutrients 2019;11:224.
21. Li H, Zhou P, Zhao Y, Ni H, Luo X, Li J. Prediction of all-cause mortality with malnutrition assessed by controlling nutritional status score in patients with heart failure: a systematic review and meta-analysis. Public Health Nutr 2021;1-8.
22. Rashedi S, Keykhaei M, Pazoki M, Ashraf H, Najafi A, Kafan S, Peirovi N, Najmeddin F, Jazayeri SA, Kashani M, Moharari RS, Montazeri M. Clinical significance of prognostic nutrition index in hospitalized patients with COVID-19: Results from single-center experience with systematic review and meta-analysis. Nutr Clin Pract 2021;36:970-983.
23. Bengelloun AK, Ortega GJ, Ancochea J, Sanz-Garcia A, Rodríguez-Serrano DA, Fernández-Jiménez G, Girón R, Ávalos E, Soriano JB, Ulíbarri JI. Usefulness of the CONUT index upon hospital admission as a potential prognostic indicator of COVID-19 health outcomes. Chin Med J (Engl) 2021;135:187-193.
24. Song F, Ma H, Wang S, Qin T, Xu Q, Yuan H, Li F, Wang Z, Liao Y, Tan X, Song X, Zhang Q, Huang D. Nutritional screening based on objective indices at admission predicts in-hospital mortality in patients with COVID-19. Nutr J 2021;20:46.
25. Hu X, Deng H, Wang Y, Chen L, Gu X, Wang X. Predictive value of the prognostic nutritional index for the severity of coronavirus disease 2019. Nutrition 2021;84:111123.
26. Wei W, Wu X, Jin C, Mu T, Gu G, Min M, Mu S, Han Y. Predictive Significance of the Prognostic Nutritional Index (PNI) in Patients with Severe COVID-19. J Immunol Res 2021;2021:9917302.
27. Çınar T, Hayıroğlu M, Çiçek V, Kılıç Ş, Asal S, Yavuz S, Selçuk M, Yalçınkaya E, Keser N, Orhan AL. Is prognostic nutritional index a predictive marker for estimating all-cause in-hospital mortality in COVID-19 patients with cardiovascular risk factors? Heart Lung 2021;50:307-312.
28. Owen RK, Conroy SP, Taub N, Jones W, Bryden D, Pareek M, Faull C, Abrams KR, Davis D, Banerjee J. Comparing associations between frailty and mortality in hospitalised older adults with or without COVID-19 infection: a retrospective observational study using electronic health records. Age Ageing 2021;50:307-316.
29. Blomaard LC, van der Linden CMJ, van der Bol JM, Jansen SWM, Polinder-Bos HA, Willems HC, Festen J, Barten DG, Borgers AJ, Bos JC, van den Bos F, de Brouwer EJM, van Deudekom FJA, van Dijk SC, Emmelot-Vonk MH, Geels RES, van de Glind EMM, de Groot B, Hempenius L, Kamper AM, Kampschreur LM, de Koning MMM, Labots G, Looman R, Lucke JA, Maas H, Mattace-Raso FUS, El Moussaoui R, van Munster BC, van Nieuwkoop C, Oosterwijk L, Regtuijt MEM, Robben SHM, Ruiter R, Salarbaks AM, Schouten HJ, Smit OM, Smits RAL, Spies PE, Vreeswijk R, de Vries OJ, Wijngaarden MA, Wyers CE, Mooijaart SP. Frailty is associated with in-hospital mortality in older hospitalised COVID-19 patients in the Netherlands: the COVID-OLD study. Age Ageing 2021;50:631-640.
30. Welch C. Age and frailty are independently associated with increased COVID-19 mortality and increased care needs in survivors: results of an international multi-centre study. Age Ageing 2021;50:617-630.
31. Jafarzadeh A, Jafarzadeh S, Nozari P, Mokhtari P, Nemati M. Lymphopenia an important immunological abnormality in patients with COVID-19: Possible mechanisms. Scand J Immunol 2021;93:e12967.
32. Aguilar-Ballester M, Herrero-Cervera A, Vinué Á, Martínez-Hervás S, González-Navarro H. Impact of Cholesterol Metabolism in Immune Cell Function and Atherosclerosis. Nutrients 2020;12:2021.

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Evaluation of the Effects of Being Over 65 Years of Age on Different Clinical Outcomes in Diabetic Patients with COVID-19

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Abstract

Objective: The Coronavirus disease-2019 (COVID-19) pandemic has affected the entire population, with the most damaging effects among the elderly. The elderly, especially those with diabetes, are at the highest risk for adverse outcomes. We aimed to evaluate the laboratory findings of diabetic patients with COVID-19 from different clinical courses, and to investigate whether being over or under 65 years of age has an effect on the clinical outcome.

Materials and Methods: The demographic data and biochemical results of the patients were examined and recorded. Clinical outcomes, namely hospital discharge, transfer to intensive care unit (ICU) and death, were recorded at the end of the study period. The patients were divided into two groups according to being over or under 65 years of age.

Results: Overall, 122 participants (47 females, 75 males; mean age: 57±13.5 years) were included in the analyses. Age and lactate dehydrogenase (LDH) values were significantly higher in the death group than in the discharged group ($p<0.05$). Ferritin, D-dimer and C-reactive protein (CRP) values of the death and ICU groups were statistically significantly higher than the discharge group ($p<0.05$). The hemoglobin a1c (Hba1c) values of the ICU group were found to be significantly higher than those of the discharged group ($p<0.05$). D-dimer and CRP values were significantly higher in diabetic patients aged >65 years ($p<0.05$). >65 age group, the CRP value of the death group was statistically significantly higher than the discharge group, while the Hba1c value of the ICU group was higher than those of the discharged group. The Spearman correlation analysis showed that there was a negative correlation between HbA1c and lymphocyte ($r=-0.23$, $p=0.030$), HbA1c and white blood cells ($r=-0.22$, $p=0.042$) in patients aged >65 years ($p<0.05$). Age, ferritin, D-dimer, CRP, LDH and Hba1c values of the death/ICU transfer group were significantly higher than the discharged group ($p<0.05$). According to the logistic regression analysis; age, D-dimer, CRP and Hba1c values were found as a statistically significant risk factors for death and transfer to the ICU.

Conclusion: Early intervention and treatment are vital, especially in the presence of elevated inflammatory parameters in uncontrolled diabetic patients aged >65 years with COVID-19 to prevent poor clinical outcomes.

Keywords: Diabetes, COVID-19, older adults

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), defined as a new type of coronavirus, is a curse that causes coronavirus disease (COVID-19), which threatens human public health all over the world and has become a pandemic (1). Patients with COVID-19 have clinical manifestations ranging from mild upper respiratory tract infection symptoms to possibly fatal outcomes due to diffuse respiratory disorders and multi-organ complications (2). The complexity of COVID-19 results from the unpredictable clinical course of the disease, and therefore it is crucial to identify risk factors associated with poor clinical outcomes. Various studies have been carried out in order to predetermine vulnerable groups that may have a poor clinical course of COVID-19 and to reverse the process with early intervention (2). In the face of this pandemic that has taken hold of the world, the need to put an end to the vulnerability

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to the serious COVID-19 disease faced by elderly and chronically ill adults is essential since age has been shown to be a risk factor of poor outcomes of patients with COVID-19 (3). Elderly patients have relatively higher mortality and morbidity than younger patients infected with SARS-CoV-2 (4,5). This can be attributed to the physiological changes of aging; comorbidities such as cardiopulmonary disease, diabetes, neurodegenerative diseases, demantia: and associated polypharmacy are factors that contribute to negative health outcomes. Moreover, immune aging, characterized by reduced ability to mount an adequate immune response to infection and susceptibility to an inflammatory condition, also contributes to the advanced vulnerability of older adults (6,7).

Elderly patients with COVID-19 are very frail and have a high complication burden due to their variable comorbidities. One of the most serious comorbidities accompanying elderly patients is diabetes mellitus (DM) (8). Actually, DM is another pandemic characterized by chronic hyperglycemia, multiple organ dysfunctions, and systemic complications involving the cardiovascular, nervous and renal systems. Inflammation and endothelial dysfunction are the main pathophysiological disorders in the development of DM and associated cardiovascular complications (9). The fact that SARS-CoV-2 causes inflammatory cascades, cytokine storms and coagulation cascade activation through pathogenetic mechanisms after entering the human body, and the aggressive inflammatory responses in SARS-CoV-2 infection cause damage to the airways (10), results in poor clinical outcomes in diabetic patients with COVID-19 (11,12). Both COVID-19 itself and the treatment modalities given impair glucose regulation and complicate glycemic control (13,14). It is known that DM increases the severity and mortality of COVID-19, especially in patients with uncontrolled hyperglycemia (15). In addition, mortality in diabetic patients with COVID-19 is 3 times higher than that in patients without diabetes (16).

Identifying cases that may lead to potentially serious complications and death with rapid progression of the disease is critical for prompt initiation of treatment in high-risk elderly patients. Therefore, in this study, we aimed to investigate whether being over or under the age of 65 has an effect on clinical outcome in COVID-19 patients with DM.

Materials and Methods

Study population and design

This study was carried out by retrospectively scanning the data of 122 patients with DM, who were followed up due to the SARS-CoV-2 infection in the Internal Medicine Clinic of İstanbul Aydın University Hospital between 1.11.2020 and 1.11.2021. The demographic data and biochemical results of the patients were examined and recorded. Clinical outcomes, namely hospital discharge, transfer to intensive care and death, were recorded until the end of the study period. SARS-CoV-2 infection was confirmed by real-time reverse transcription polymerase chain reaction analysis of nasal and pharyngeal swab samples at admission. The patients were divided into two groups according to being over or under 65 years of age.

Patients with a history of acute and/or chronic inflammatory, autoimmune or infectious disease, hematological disease, malignancy, renal and hepatic injury, documented cardiovascular disease, and a history of major surgery or trauma were not included in the study.

In order to prevent the effect of antiviral treatment on laboratory results, laboratory results at the time of first admission before the start of treatment were evaluated. Laboratory blood tests including complete blood count, glucose, hemoglobin a1c (Hba1c), total cholesterol (TC), triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), aspartat aminotransferase, alanine aminotransferase, ferritin, D-dimer, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and lactate dehydrogenase (LDH) levels were evaluated. The time elapsed since the first diagnosis of diabetes was recorded as diabetes age (years).

Statistics

The data were collected by the relevant researchers through clinical studies, transferred to the Microsoft Excel program, organized, cleaned and made suitable for analysis. Data analyzes were tested using the IBM SPSS Statistics 26.0 (Statistical Package for Social Science) package programs. Descriptive statistics were expressed as numbers and percentages for categorical variables, mean, standard deviation, minimum and maximum values for numerical variables. In the normality test applied to the variables in age groups, while age, Hb, Hct, TC, LDL-C, and glucose were normally distributed in the <65 age group ($p>0.05$), in the >65 age group, age, Hb, Hct, monocytes, CRP, ESR, TC, LDL-C, HDL-C and Hba1c were normally distributed ($p>0.05$). It was determined that other variables were not normally distributed in both age groups ($p<0.05$). According to these results, parametric tests were used in the analysis of normally distributed variables, and non-parametric tests were used in the analysis of non-normally distributed variables. T-test, Mann-Whitney U test, ANOVA, Kruskal-Wallis, Tukey post-hoc, Dunn-Benforonni post-hoc and Spearman correlation test was used in the analysis. Multivariable logistic regression modeling was used to explore independent risk factors for death and transfer to the ICU. We performed a receiver operating characteristic (ROC) curve analysis to evaluate accuracy of risk factors. The area under the curve (AUC) was then estimated with a 95% confidence interval (CI) p-value of <0.05 was considered statistically significant.

Results

Overall, 122 participants (47 females, 75 males; mean age: 57±13.5 years) were included in the analyses. 27% (n=33) of patients included in the analyzes were over 65 years of age, while 73% (n=89) of the patients were under 65 years old. Of the patients included in the study, 4.1% (n=5) were dead and 7.4% (n=9) were admitted to the intensive care unit (ICU), while 88.5% (n=108) were discharged. The mean age of patients who died was 71.4±11.5. The mean age of diabetes was 6 years. Of the patients under 65 years of age, 2 (2.2%) died, 5 (5.6%) were transferred to the ICU, and 82 (92.1%) were discharged. As for patients over 65 years of age, 3 (9.1%) died, 4 (12.1%) were transferred to the ICU and 26 (78.8%) were discharged.

Demographics and laboratory findings of diabetic patients with COVID-19 in terms of clinical outcomes were shown in Table 1. There was a significant difference in terms of age, ferritin, and D-dimer, CRP, LDH and Hba1c between the groups who were discharged, admitted to the ICU, and died (p<0.05). Age and LDH values were significantly higher in the death group than in the discharged group (p<0.05). Ferritin, D-dimer and CRP values of the death and ICU groups were statistically significantly higher than the discharge group (p=0.002, p=0.000, p=0.000, respectively). The Hba1c values of the ICU group were found to be significantly higher when compared to the Hba1c values of the discharged group (p=0.009).

Table 2 demonstrates the demographic and laboratory findings of diabetic patients with COVID-19 according to being under or over the age of 65. There was a significant difference between these age groups in D-dimer, CRP and onset of diabetes years variables (p<0.05). D-dimer, CRP values, and onset of diabetes years were significantly higher in the group over 65 years of age (p=0.008, p=0.008 p<0.001, respectively).

Diabetic patients under 65 years of age with COVID-19 were examined according to their clinical outcome. As shown in Table 3, statistically significant differences were found in lymphocyte, ferritin, D-dimer, CRP, ESR, LDH and Hba1c variables between clinical groups ≤65 years of age. Ferritin, ESR and CRP values of the death group were significantly higher than the discharge group, while the lymphocyte value was lower (p<0.05). D-dimer and LDH values of the death and ICU groups were significantly higher than those of the discharged group (p<0.05). The Hba1c and CRP values of the ICU group were statistically significantly higher than the discharged group (p<0.05). As shown in Table 4, for the >65 age group, the CRP value of the death group

Table 1. Demographics and laboratory findings of diabetic patients with COVID-19 in terms of discharge, intensive care unit and death

Laboratory results, mean ± SD	All patients (n=122)	Discharge (n=108)	Intensive care unit (n=9)	Death (n=5)	p
Age (years)	56.95±13.56	55.79±13.04	62.89±15.81	71.4±11.5	0.015
Hemoglobin, g/dL	13.32±1.75	13.28±1.72	13.68±2.21	13.38±1.76	0.810
Hemotocrit %	39.88±4.97	39.74±4.78	41.4±7.12	40.2±5.47	0.626
WBC, 10^3/µL	7.69±3.7	7.56±3.68	7.09±2.22	11.6±4.55	0.133
Neutrophil, 10^3/µL	6.44±7.1	6.33±7.43	5.43±2.19	10.56±4.03	0.065
Lymphocyte, 10^3/µL	2.63±4.41	2.75±4.57	1.17±0.41	2.73±4.92	0.145
PLT, 10^3/µL	232.75±81.02	230.02±76.83	210.44±59.89	331.8±141.17	0.124
Monocyte, 10^3/µL	0.44±0.24	0.45±0.24	0.45±0.19	0.25±0.15	0.081
AST, IU/L	35.73±26.11	36.42±27.29	30.11±14.87	31±12.08	0.986
ALT, IU/L	42.43±32.76	43.55±34.27	35.22±16.24	31.4±14.99	0.907
Ferritin, ng/mL	489.92±569.21	425.74±528.41	744.33±596.14	1418.21±535.92	**0.002**
D-dimer, mg/L	902.62±1594.26	632.9±895.18	2745.78±3421.54	3411.02±3816.1	**<0.001**
CRP, mg/L	57.33±61.42	48.22±55.69	113.38±36.25	153.3±87.74	**<0.001**
ESR, mm/h	30.6±21.35	29.25±20.34	35.78±23.71	50.4±31.67	0.196
LDH, U/L	274.37±119.87	260.89±109.63	337.67±124.95	451.6±169.45	**0.004**
Glucose, mg/dL	160.89±61.27	156.73±54.81	210.11±95.65	162±94.88	0.164
HbA1c, %	7.98±1.69	7.81±1.56	9.89±2.15	8.14±1.75	**0.009**
TC, mg/dL	163.23±40.55	165.06±41.56	143.78±22.87	158.6±38.94	0.310
LDL-C, mg/dL	99.74±31.52	100.75±31.81	89.82±25.59	95.9±37.37	0.588
TG, mg/dL	149.91±104.23	154.05±108.56	105.56±36.54	140.4±75.63	0.348
HDL-C, mg/dL	37.38±11.85	37.9±12.01	30.26±6.51	39.04±13.57	0.160

COVID-19: Coronavirus disease-2019, SD: Standard deviation, WBC: White blood cell, PLT: Platelet, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, LDH: Lactate dehydrogenase, HbA1c: Hemoglobin A1c, TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglyceride, significant p-values are bolded. P<0.05 was considered statistically significant. Data are presented as mean ± standard deviation

Table 2. Demographics and laboratory findings of diabetic patients with COVID-19 by age groups

Laboratory results, (mean ± SD)	All patients (n=122)	≤65 years (n=89)	>65 years (n=33)	p
Sex Male (%) Female (%)	 75 (61.5%) 47 (38.5%)	 56 (62.9%) 33 (37.1%)	 19 (57.6%) 14 (42.4%)	 0.087
Hemoglobin g/dL	13.32±1.75	13.48±1.62	12.87±2.01	0.087
Hemotocrit %	39.88±4.97	40.34±4.44	38.64±6.09	0.094
WBC, 10^3/µL	7.69±3.7	7.69±3.78	7.68±3.52	0.809
Neutrophil, 10^3/µL	6.44±7.1	6.61±8.07	5.98±3.38	0.547
Lymphocyte, 10^3/µL	2.63±4.41	2.71±4.68	2.43±3.64	0.568
PLT, 10^3/µL	232.75±81.02	228.18±74.35	245.06±97	0.682
Monocyte, 10^3/µL	0.44±0.24	0.45±0.24	0.42±0.22	0.665
AST, IU/L	35.73±26.11	34.29±24.99	39.61±28.97	0.234
ALT, IU/L	42.43±32.76	45.06±34.84	35.36±25.51	0.184
Ferritin, ng/mL	489.92±569.21	463.64±564.64	560.79±584.19	0.146
D-dimer, mg/L	902.62±1594.26	825.99±1643.52	1109.29±1456.75	**0.008**
CRP, mg/L	57.33±61.42	49.96±59.35	77.22±63.38	**0.008**
ESR, mm/h	30.6±21.35	28.55±20.01	36.12±24.08	0.095
LDH, U/L	274.37±119.87	265.85±123.47	297.33±107.99	0.082
Glucose, mg/dL	160.89±61.27	165.73±60.76	147.82±61.67	0.081
HbA1c, %	7.98±1.69	8.16±1.74	7.49±1.47	0.059
Onset of diabetes, years	5.93±4.81	4.92±3.97	8.67±5.79	**<0.001**
TC, mg/dL	163.23±40.55	165.37±42.29	157.45±35.36	0.340
LDL-C, mg/dL	99.74±31.52	101.41±32.67	95.24±28.13	0.339
TG, mg/dL	149.91±104.23	155.1±108.09	135.91±93.13	0.590
HDL-C, mg/dL	37.38±11.85	37.2±11.81	37.86±12.15	0.714

COVID-19: Coronavirus disease-2019, SD: Standard deviation, WBC: White blood cell, PLT: Platelet; AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, LDH: Lactate dehydrogenase, HbA1c: Hemoglobin A1c, TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglyceride. Significant p-values are bolded. P<0.05 was considered statistically significant. Data are presented as mean ± standard deviation or n (%).

was statistically significantly higher than the discharge group, while the Hba1c value of the ICU group was higher than that of the discharged group. The Spearman correlation analysis of associated factors for HbA1c by age groups was given in Table 5. Correlation analysis showed that there was a negative correlation between HbA1c and lymphocyte (r=-0.23, p=0.030), HbA1c and white blood cell (WBC) (r=-0.22, p=0.042) in patients >65 years (p<0.05). Lastly, there was a positive high-level (r=0.69) significant correlation between Hba1c and glucose in >65 years patients (p<0.05).

Table 6 demostrates the analysis of biochemical variables by clinical groups of death/ICU transfer and discharged. There was a significant difference between clinical groups in age, ferritin, D-dimer, CRP, LDH and Hba1c variables (p<0.05). Ages, ferritin, D-dimer, CRP, LDH and Hba1c values of the death/ICU transfer group were significantly higher than the discharged group. According to the logistic regression analysis; age [Odds ratio (OR) 21.515 (95%) confidence interval (CI) 1.898-243.912, p=0.013], D-dimer [OR 1.001, (95%) CI 1.000-1.001, p=0.003], CRP [OR 1.038, (95%) CI 1.016-1.061, p=0.001] and Hba1c [OR 4.128, (95%) CI 1.792-9.509, p=0.001] values were found as a statistically significant risk factor for death and transfer to the ICU (Table 7).

A ROC curve analysis was undertaken. We demonstrated that the area under the ROC curve (AUC) of age 0.716 (p=0.009, 95% CI 0.569-0.862), Hba1c 0.720 (p=0.007, 95% CI 0.579-0.860), CRP 0.842 (p<0.001, 95% CI 0.762-0.922) and D-dimer 0.830 (p<0.001, 95% CI 0.725-0.934) (Figure 1).

Discussion

Identifying potential risk factors predicting the course of COVID-19, effectively triage patients, and individualizing treatment are of great benefit to healthcare professionals to ensure optimal clinical outcomes. Various studies have revealed that advanced age, comorbidities, and a wide range of different laboratory parameters are associated with a poor clinical course of the disease (3,4). As age has been shown to be one of the major risk factors for poor outcomes of COVID-19 patients, the vulnerability of the elderly and chronically ill adults to the serious COVID-19 disease faced should be taken seriously, and it

Table 3. Demographics and clinical findings of diabetic patients with COVID-19 by age of ≤65 years according to the clinical outcomes

Laboratory results, mean ± SD	All patients (n=89)	Discharge (n=82)	Intensive care unit (n=5)	Death (n=2)	p
Age (years)	50.58±9.31	50.21±9.14	53±12.47	60±4.24	0.287
Hemoglobin, g/dL	13.48±1.62	13.49±1.63	13.14±1.84	13.85±1.34	0.851
Hemotocrit %	40.34±4.44	40.35±4.46	39.68±5.23	41.4±3.39	0.896
WBC, 10^3/µL	7.69±3.78	7.61±3.84	7.73±2.93	11.12±1.11	0.253
Neutrophil, 10^3/µL	6.61±8.07	6.54±8.36	6.14±2.83	10.62±0.72	0.171
Lymphocyte, 10^3/µL	2.71±4.68	2.86±4.85	1.1±0.32	0.37±0.28	**0.046**
PLT, 10^3/µL	228.18±74.35	224.67±72.1	231.2±70.5	364.5±85.56	0.110
Monocyte, 10^3/µL	0.45±0.24	0.45±0.24	0.46±0.25	0.13±0.11	0.075
AST, IU/L	34.29±24.99	34.46±25.69	36.4±17.24	22±1.41	0.506
ALT, IU/L	45.06±34.84	45.17±36.2	47.6±7.2	34±12.73	0.427
Ferritin, ng/mL	463.64±564.64	415.05±533.72	811.2±643.62	1587±59.4	**0.022**
D-dimer, mg/L	825.99±1643.52	531.29±592.18	3690.6±4374.23	5747.5±6013.94	**0.009**
CRP, mg/L	49.96±59.35	43.98±54.99	107.72±27.22	150.65±148.99	0.017
ESR, mm/h	28.55±20.01	26.16±17.48	47.2±26.68	80±11.31	**0.012**
LDH, U/L	265.85±123.4	252.15±108.67	380.6±150.32	541±248.9	**0.015**
Glucose, mg/dL	165.73±60.76	162.98±57.61	220.4±90.62	142±80.61	0.103
HbA1c, %	8.16±1.74	7.99±1.58	10.43±2.67	9.05±1.91	**0.048**
Onset of diabetes, years	4.92±3.97	5.1±4.06	2.4±2.07	4±1.41	0.286
TC, mg/dL	165.37±42.29	166.43±43.33	142.8±23.57	178.5±12.02	0.439
LDL-C, mg/dL	101.41±32.67	101.81±33.3	87.44±22.96	120±7.07	0.460
TG, mg/dL	155.1±108.09	159.21±111.27	99.4±24.32	126±66.47	0.383
HDL-C, mg/dL	37.2±11.81	37.54±11.81	30.94±4.43	38.8±26.16	0.508

COVID-19: Coronavirus disease-2019, SD: Standard deviation, WBC: White blood cell, PLT: Platelet, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, LDH: Lactate dehydrogenase, HbA1c: Hemoglobin A1c, TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglyceride. Significant p-values are bolded. P<0.05 was considered statistically significant. Data are presented as mean ± standard deviation

Table 4. Demographics and clinical findings of diabetic patients with COVID-19 by age of >65 years according to the clinical outcomes

Laboratory results, mean ± SD	All patients (n=33)	Discharge (n=26)	Intensive care unit (n=4)	Death (n=3)	p
Age (years)	74.12±6.34	73.38±5.79	75.25±9.64	79±6.24	0.334
Hemoglobin, g/dL	12.87±2.01	12.62±1.87	14.35±2.73	13.07±2.21	0.283
Hemotocrit %	38.64±6.09	37.8±5.3	43.55±9.37	39.4±7.18	0.212
WBC, 10^3/µL	7.68±3.52	7.4±3.17	6.28±0.36	11.92±6.35	0.388
Neutrophil, 10^3/µL	5.98±3.38	5.68±3.01	4.54±0.5	10.52±5.68	0.304
Lymphocyte, 10^3/µL	2.43±3.64	2.39±3.63	1.27±0.54	4.3±6.25	0.892
PLT, 10^3/µL	245.06±97	246.88±89.64	184.5±36.37	310±185.52	0.305
Monocyte, 10^3/µL	0.42±0.22	0.43±0.24	0.44±0.09	0.33±0.12	0.748
AST, IU/L	39.61±28.97	42.58±31.6	22.25±6.7	37±12.49	0.284
ALT, IU/L	35.36±25.51	38.42±27.29	19.75±7.72	29.67±18.9	0.287
Ferritin, ng/mL	560.79±584.19	459.46±520.12	660.75±615.3	1305.68±724.68	0.089
D-dimer, mg/L	1109.29±1456.75	953.36±1467.26	1564.75±1535.9	1853.37±1393.9	0.167
CRP, mg/L	77.22±63.38	61.58±56.84	120.45±48.95	155.07±65.47	**0.014**
ESR, mm/h	36.12±24.08	39±25.49	21.5±7.77	30.67±21.94	0.380
LDH, U/L	297.33±107.99	288.45±110.17	284±67.78	392±114.58	0.335
Glucose, mg/dL	147.82±61.67	137.04±39.66	197.25±114.25	175.33±118.7	0.396
HbA1c, %	7.49±1.47	7.22±1.33	9.22±1.32	7.53±1.7	**0.035**
Onset of diabetes, years	8.67±5.79	9.08±6.29	7.25±4.35	7±1.73	0.916
TC, mg/dL	157.45±35.36	160.77±35.84	145±25.5	145.33±47.96	0.598
LDL-C, mg/dL	95.24±28.13	97.4±26.69	92.8±31.96	79.83±42.43	0.597
TG, mg/dL	135.91±93.13	137.77±99.83	113.25±51.29	150±94.25	0.822
HDL-C, mg/dL	37.86±12.15	39.01±12.79	29.4±9.23	39.2±5.11	0.342

COVID-19: Coronavirus disease-2019, SD: Standard deviation, WBC: White blood cell, PLT: Platelet, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, LDH: Lactate dehydrogenase, HbA1c: Hemoglobin A1c, TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglyceride. Significant p-values are bolded. P<0.05 was considered statistically significant. Data are presented as mean ± standard deviation

Table 5. Spearman correlation analysis of associated factors for Hba1c by age groups (r (p))

	hba1c (r (p)) >65 years (n=33)	hba1c (r (p)) ≤65 years (n=89)
Age (years)	0.17 (p=0.116)	0.32 (p=0.071)
Hemoglobin, g/dL	-0.12 (p=0.256)	0.18 (p=0.311)
Hemotocrit %	-0.15 (p=0.153)	0.21 (p=0.252)
WBC, 10^3/µL	-0.23 (p=0.030)	-0.11 (p=0.539)
Neutrophil, 10^3/µL	-0.12 (p=0.258)	-0.12 (p=0.492)
Lymphocyte, 10^3/µL	-0.22 (p=0.042)	0.18 (p=0.323)
PLT, 10^3/µL	-0.07 (p=0.502)	-0.02 (p=0.920)
Monocyte, 10^3/µL	-0.19 (p=0.082)	0.07 (p=0.713)
AST, IU/L	0.01 (p=0.891)	-0.14 (p=0.450)
ALT, IU/L	-0.06 (p=0.596)	-0.16 (p=0.374)
Ferritin, ng/mL	-0.08 (p=0.464)	0.05 (p=0.775)
D-dimer, mg/L	-0.06 (p=0.596)	-0.01 (p=0.947)
CRP, mg/L	0.00 (p=0.963)	0.11 (p=0.552)
ESR, mm/h	0.20 (p=0.059)	-0.18 (p=0.319)
LDH, U/L	0.00 (p=0.979)	-0.26 (p=0.144)
HbA1c, %	-	-
Onset of diabetes, years	0.09 (p=0.378)	-0.15 (p=0.411)
TC, mg/dL	-0.13 (p=0.215)	-0.09 (p=0.610)
LDL-C, mg/dL	-0.16 (p=0.146)	-0.13 (p=0.454)
TG, mg/dL	-0.07 (p=0.515)	-0.16 (p=0.374)
HDL-C, mg/dL	-0.06 (p=0.573)	-0.04 (p=0.822)

WBC: White blood cell, PLT: Platelet, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, LDH: Lactate dehydrogenase, HbA1c: Hemoglobin A1c, TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglyceride. Significant p-values are bolded. P<0.05 was considered statistically significant

is important to understand the mechanisms underlying this age-related vulnerability. Age-related immune system remodeling or immune aging is considered the main cause of increased susceptibility to infection, particularly respiratory infections (6).

In this study, demographic and laboratory data of patients with diabetic COVID-19 and the variability of laboratory parameters in different clinical outcomes in patient groups over and under 65 years of age were examined. The results of our study revealed that age, ferritin, D-dimer, CRP and LDH values were higher in the death and ICU groups than in those who were discharged. In addition, D-dimer and CRP were higher in diabetic COVID-19 patients aged >65 years compared to those aged ≤65 years. In addition, Hba1c was found to be higher in the ICU group than in those discharged, and this result was valid for diabetic COVID-19 patients in the ICU group both under and over the age of 65. Moreover, ages of the patients who died and were transferred to the ICU were higher than those who were discharged. According to the logistic regression analysis, we obtained the result that the patient's age over 65 increased the risk of death/transfer to the ICU 21.5 times.

Vasculitic processes that develop on the background of organ damage caused by activation of inflammatory cascades, complement activation and proinflammatory cytokines in severe COVID-19 patients have been described. Vasculitic injury causes pulmonary edema and acute respiratory distress syndrome and plays an important role in cardiovascular and brain injuries such as ischemia, deep vein thrombosis and pulmonary thromboembolism (6). Various studies have been conducted to investigate the roles of inflammatory parameters in predicting disease progression (3,4). In this study, we showed that ferritin, D-dimer, CRP and LDH values were higher in the patient groups who died and needed ICU. Supporting our study in the literature, various studies indicate that laboratory parameters such as CRP, ferritin, LDH and D-dimer, which are associated with death, are higher in patients with poor prognosis (17,18).

When patients were classified according to whether they were elderly or not, D-dimer and CRP values were higher in diabetic COVID-19 patients over 65 years of age compared to younger patients. Moreover, CRP values were higher in patients who died >65 years than those who were discharged. Therefore, according to this study, it can be suggested that age is associated with an increased risk of inflammation and death. The results of our study are similar to previous studies in the literature (19-21). However, we obtained another interesting result that was beyond our expectation. In the general population of our study, ferritin, D-dimer, CRP and LDH values were higher in patients who died and required ICU, compared to patients who were discharged without complications. Actually, our expectation was that these higher values would be more pronounced over the age of >65. However, contrary to our hypothesis, interestingly, these values, excluding CRP, were higher in the group of patients ≤65 years of age who died and/or were admitted to the ICU. This unexpected result can be attributed to the relatively small sample size of our study and the smaller number of elderly participants.

DM is a chronic, progressive disease that is common in society with lifetime effects on patients. DM is one of the most common comorbidities of COVID-19, with a prevalence ranging from 6% to 50% (13). Diabetes has been associated with increased mortality in previous viral outbreaks such as the SARS-CoV-1 and Middle East respiratory syndrome coronavirus outbreak (22,23). Data from other viral outbreaks such as SARS and influenza H1N1 have shown that patients with poor glycemic control have a higher risk of mortality (22,24). As for SARS-CoV-2 pandemic, data on the impact of diabetes on the prognosis of COVID-19 patients are inconclusive and controversial, as some studies suggest that diabetes is a risk factor for the poor prognosis of COVID-19 (25,26), while some studies have reported that patients with diabetes do not appear to have a higher risk of mortality (27,28). In our study, regardless of the age group, HbA1c levels were found to be higher in both age groups who died and needed intensive care. Thus, our results revealed an

Table 6. Analysis of biochemical variables by clinical groups (mean ± SD/median-range)

	Death/intensive care unit transfer (n=14)	Discharged (n=108)	Total (n=122)	p
Age (years)**	65.93±14.58/65-52	55.79±13.04/55-58	56.95±13.56/57-58	0.008*
Hemoglobin, g/dL **	13.57±2/13.25-6.7	13.28±1.72/13.35-8.7	13.32±1.75/13.3-9.3	0.565
Hemotocrit %**	40.97±6.39/39.75-22.2	39.74±4.78/39.9-24.1	39.88±4.97/39.9-29.1	0.385
WBC, 10^3/µL	8.7±3.8/7.29-12.43	7.56±3.68/6.7-17.65	7.69±3.7/6.7-17.65	0.225
PLT, 10^3/µL	253.79±109.46/229.5-371	230.02±76.83/217-417	232.75±81.02/218.5-453	0.697
Monocyte, 10^3/µL	0.38±0.2/0.38-0.73	0.45±0.24/0.41-1.3	0.44±0.24/0.41-1.32	0.429
Neutrophil, 10^3/µL	7.26±3.8/5.78-11.65	6.33±7.43/4.79-72.39	6.44±7.1/4.87-72.39	0.131
Lymphocyte, 10^3/µL	1.73±2.85/0.99-11.33	2.75±4.57/1.34-24.47	2.63±4.41/1.32-24.63	0.069
Ferritin, ng/mL	985±647.57/910-1915	425.74±528.41/248.63-1990.67	489.92±569.21/281-1990.67	0.001*
D-dimer, mg/L	2983.37±3434.31/1342-9724	632.9±895.18/361-7690	902.62±1594.26/445.16-9990	0.000*
CRP, mg/L	127.64±59.76/119.25-210.7	48.22±55.69/21.5-196.8	57.33±61.42/31.75-255.8	0.000*
ESR, mm/h	41±26.59/36.5-82	29.25±20.34/24-106	30.6±21.35/25.5-106	0.107
LDH, U/L	378.36±147.15/357.5-527	260.89±109.63/243-639	274.37±119.87/257.5-639	0.002*
TC, mg/dL **	149.07±29.03/151-97	165.06±41.56/164.5-182	163.23±40.55/163-182	0.166
LDL-C, mg/dL **	91.99±29.01/86.3-106.4	100.75±31.81/97.7-155.1	99.74±31.52/97.35-163.4	0.330
TG, mg/dL	118±53.68/97.5-188	154.05±108.56/134-553	149.91±104.23/131-553	0.278
HDL-C, mg/dL	33.39±10.09/32.15-37.3	37.9±12.01/34.9-56.7	37.38±11.85/34.4-56.7	0.219
AST, IU/L	30.43±13.46/25.5-53	36.42±27.29/27.5-163	35.73±26.11/27-163	0.942
ALT, IU/L	33.86±15.33/34-45	43.55±34.27/32-157	42.43±32.76/32-157	0.772
Glucose, mg/dL	192.93±94.73/158-282	156.73±54.81/142-242	160.89±61.27/150-297	0.251
HbA1c, %	9.27±2.13/9.04-7.9	7.81±1.56/7.41-7.9	7.98±1.69/7.53-9.4	0.007*
Onset of diabetes, years	5±3.4/4.5-11	6.06±4.96/5-25	5.93±4.81/5-25	0.646

WBC: White blood cell, PLT: Platelet, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, LDH: Lactate dehydrogenase, HbA1c: Hemoglobin A1c, TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglyceride, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase. *Statistically significant at the 0.05 level. **T-test, all other variables were analyzed with Mann-Whitney U test

Table 7. Effect of variables on clinical groups (death/intensive care unit transfer and discharged) - logistic regression analysis

	B	S.E.	Wald	df	p	OR	95% CI
Age groups (65+)	3.069	1.239	6.136	1	0.013*	21.515	1.898-243.912
D-dimer	0.001	0.000	8.826	1	0.003*	1.001	1.000-1.001
CRP	0.037	0.011	11.650	1	0.001*	1.038	1.016-1.061
Hba1c	1.418	0.426	11.089	1	0.001*	4.128	1.792-9.509

*Statistically significant at the 0.05 level, CI: Confidence interval, CRP: C-reactive protein, OR: Odds ratio, HbA1c: Hemoglobin

increased risk of disease worsening in COVID-19 patients with diabetes. Liu et al. (25) found that COVID-19 patients with diabetes had a higher risk of worsening, especially those with poorly-controlled HbA1c, with an optimal cut-off value of 8.6%. In another study, it was demonstrated that high HbA1c level was associated with inflammation, hypercoagulability, and low SaO_2 in COVID-19 patients, and the mortality rate (27.7%) was higher in patients with diabetes (29). In that study, there was a linear negative correlation between SaO_2 and HbA1c, while there was a linear positive correlation between serum ferritin, CRP, fibrinogen, and ESR levels and HbA1c. Besides, it has been shown that generally decreased lymphocytes in severe COVID-19 patients with DM, especially in T and B subgroups, are closely associated with poor prognosis and disease severity (29). In our study, variables that could correlate with Hba1c were examined in the groups above and below 65 years of age, and it was observed that Hba1c was negatively correlated with WBC and lymphocytes in the >65 age group. It is of great importance to state that this correlation did not appear in diabetic patients with COVID-19 under the age of <65 years.

In this study, when we divided the patients into death/ICU transfer and discharge groups and analyzed the analysis of demographic and biochemical variables, we observed that the patients in the death/ICU transfer group had higher age, ferritin, D-dimer, CRP, LDH and Hba1c variables compared to those in the discharged group. Moreover, in the logistic regression analysis that we created to evaluate the effect of the variables on the death/intensive care transfer and discharge clinical groups, we obtained the result that the patient's age over 65 increased the risk of death/transfer to the ICU 21.5 times. Clinical experience

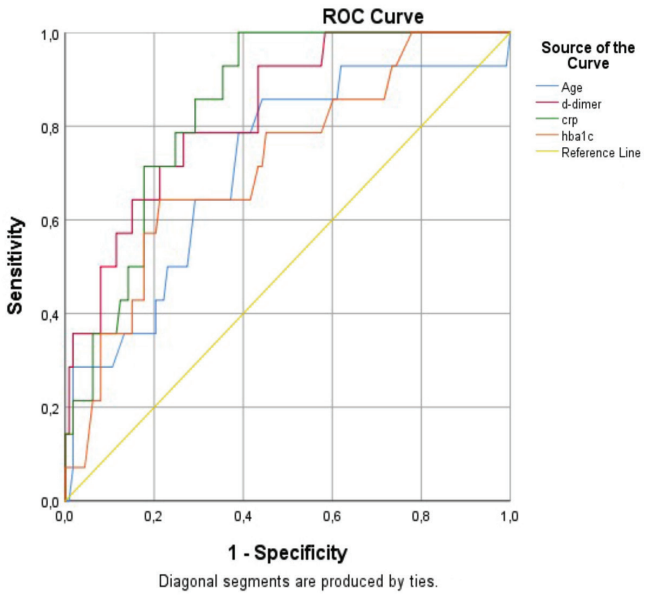

Figure 1. Receiver-operating characteristic (ROC) curve analysis of variables on death and transfer to the intensive care unit. Area under the ROC curve (AUC) for age 0.716 (p=0.009, 95% CI 0.569-0.862), for hba1c 0.720 (p=0.007, 95% CI 0.579-0.860), for CRP 0.842 (p<0.001, 95% CI 0.762-0.922), for D-dimer 0.830 (p<0.001, 95% CI 0.725-0.934)

CI: Confidence interval, CRP: C-reactive protein

to date shows that COVID-19 is highly heterogeneous, ranging from asymptomatic and mild to severe and fatal. Host factors, including age, gender, and comorbid conditions, are key determinants of disease severity and progression. Aging itself is a leading risk factor for serious illness and death from COVID-19. Age-related decline and dysregulation of immune function, i.e. immune aging and inflammation, is thought to play an important role in contributing to the increased vulnerability to serious COVID-19 outcomes in older adults (27,28). The results of our study mentioned above are consistent with previous studies showing that advanced age is a risk factor for worsening clinical outcome (4,6,19,20). Surely, there is much to learn about immune responses to COVID-19. Studies that separate and evaluate all immunological outcome data by age are needed to better understand disease heterogeneity and aging. Taken together, it is clear that aging is an important risk factor for adverse health outcomes, particularly severe COVID-19 disease and the need for hospitalization and ICU.

Study Limitations

This study has several limitations. First, the interpretation of our results might be limited by the small sample size and less number of older participants. Second, medical history was not taken in detail in all patients.

Conclusion

In conclusion, advanced age, Hba1c and inflammatory parameters including D-dimer and CRP are associated with poor clinical outcome such as death and transfer to ICU in COVID- 19 patients with diabetes. Furthermore, since there were increased Hba1c levels in the patient group requiring ICU, the increase in Hba1c levels, which is accepted as an indicator of uncontrolled diabetes, is associated with the need for transfer to the ICU. Finally, aging is an important risk factor for adverse health outcomes, particularly severe COVID-19 disease with diabetes and the need for hospitalization and ICU. In the light of all this information, early intervention and treatment are vital, especially in the presence of elevated inflammatory parameters in uncontrolled diabetic patients aged >65 years with COVID-19 to prevent poor clinical outcomes.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee (approval number: 2973).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.U.A., D.A., Design G.U.A., Data Collection or Processing: G.U.A., D.A., Analysis or Interpretation: D.A., Literature Search: G.U.A., D.A., Writing: G.U.A., D.A.

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References

1. Zheng J. SARS-CoV-2: an emerging coronavirus that causes a global threat. Int J Biol Sci 2020;16:1678-1685.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506.
3. Zhou F, Tu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-1062.
4. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020;46;:846-848.
5. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323:1061-1069.
6. Nidadavolu LS, Walston JD. Underlying Vulnerabilities to the Cytokine Storm and Adverse COVID-19 Outcomes in the Aging Immune System. J Gerontol A Biol Sci Med Sci 2021;76:e13-e18.
7. Dent E, Morley JE, Cruz-Jentoft AJ, Woodhouse L, Rodríguez-Mañas L, Fried LP, Woo J, Aprahamian I, Sanford A, Lundy J, Landi F, Beilby J, Martin FC, Bauer JM, Ferrucci L, Merchant RA, Dong B, Arai H, Hoogendijk EO, Won

CW, Abbatecola A, Cederholm T, Strandberg T, Gutiérrez Robledo LM, Flicker L, Bhasin S, Aubertin-Leheudre M, Bischoff-Ferrari HA, Guralnik JM, Muscedere J, Pahor M, Ruiz J, Negm AM, Reginster JY, Waters DL, Vellas B. Physical Frailty: ICFSR International Clinical Practice Guidelines for Identification and Management. J Nutr Health Aging 2019;23:771-787.

8. Sesti G, Antonelli Incalzi R, Bonora E, Consoli A, Giaccari A, Maggi S, Paolisso G, Purrello F, Vendemiale G, Ferrara N. Management of diabetes in older adults. Nutr Metab Cardiovasc Dis 2018;28:206-218.
9. Argun D, Argun F, Borku Uysal B. Evaluation of salusin-α and salusin-β levels in patients with type 2 diabetes mellitus and determination of the impact of severity of hyperglycemia on salusin levels. Ir J Med Sci 2021;190:1403-1411.
10. Henderson LA, Canna SW, Schulert GS, Volpi S, Lee PY, Kernan KF, Caricchio R, Mahmud S, Hazen MM, Halyabar O, Hoyt KJ, Han J, Grom AA, Gattorno M, Ravelli A, De Benedetti F, Behrens EM, Cron RQ, Nigrovic PA. On the alert for cytokine storm: immunopathology in COVID-19. Arthritis Rheumatol 2020;72:1059-1063.
11. Roncon L, Zuin M, Rigatelli G, Zuliani G. Diabetic patients with COVID-19 infection are at higher risk of ICU admission and poor short-term outcome. J Clin Virol 2020;127:104354.
12. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, Lei F, Wang H, Xie J, Wang W, Li H, Zhang P, Song X, Chen X, Xiang M, Zhang C, Bai L, Xiang D, Chen MM, Liu Y, Yan Y, Liu M, Mao W, Zou J, Liu L, Chen G, Luo P, Xiao B, Zhang C, Zhang Z, Lu Z, Wang J, Lu H, Xia X, Wang D, Liao X, Peng G, Ye P, Yang J, Yuan Y, Huang X, Guo J, Zhang BH, Li H. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab 2020;31:1068-1077.e3.
13. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr 2020;14:303-310.
14. Barron E, Bakhai C, Kar P, Weaver A, Bradley D, Ismail H, Knighton P, Holman N, Khunti K, Sattar N, Wareham NJ, Young B, Valabhji J. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: A whole-population study. Lancet Diabetes Endocrinol 2020;8:813-822.
15. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia. A systematic review, meta-analysis, and meta-regression. Diabetes Metab Syndr 2020;14:395-403.
16. Bloomgarden ZT. Diabetes and COVID-19. J Diabetes 2020;12:347-348.
17. Wang K, Zuo P, Liu Y, Zhang M, Zhao X, Xie S, Zhang H, Chen X, Liu C. Clinical and Laboratory Predictors of In-hospital Mortality in Patients With Coronavirus Disease-2019: A Cohort Study in Wuhan, China. Clin Infect Dis 2020;71:2079-2088.
18. Bousquet G, Falgarone G, Deutsch D, Derolez S, Lopez-Sublet M, Goudot FX, Amari K, Uzunhan Y, Bouchaud O, Pamoukdjian F. ADL-dependency, D-Dimers, LDH and absence of anticoagulation are independently associated with one-month mortality in older inpatients with Covid-19. Aging (Albany NY) 2020;12:11306-11313.
19. Sun H, Ning R, Tao Y, Yu C, Deng X, Zhao C, Meng S, Tang F, Xu D. Risk factors for mortality in 244 older adults with COVID-19 in Wuhan, China: A retrospective study. J Am Geriatr Soc 2020;68:E19-E23.
20. CDC COVID-19 Response Team. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) - United States, February 12-March 16, 2020. MMWR Morb Mortal Wkly Rep 2020;69:343-346.
21. Wu Z, McGoogan JM. Characteristics of and ımportant lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a Report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020;323:1239-1242.
22. Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, Wu BY, Sun GZ, Yang GR, Zhang XL, Wang L, Xu X, Xu XP, Chan JCPlasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabet Med 2006;23:623-628.
23. Al-Tawfiq JA, Hinedi K, Ghandour J, Khairalla H, Musleh S, Ujayli A, Memish ZA. Middle East respiratory syndrome coronavirus: a case-control study of hospitalized patients. Clin Infect Dis 2014;59:160-165.
24. Badawi A, Ryoo SG. Prevalence of Diabetes in the 2009 Influenza A (H1N1) and the Middle East Respiratory Syndrome Coronavirus: A Systematic Review and Meta-Analysis. J Public Health Res 2016;5:733.
25. Liu Z, Bai X, Han X, Jiang W, Qiu L, Chen S, Yu X. The association of diabetes and the prognosis of COVID-19 patients: A retrospective study. Diabetes Res Clin Pract 2020;169:108386.
26. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, Qin R, Wang H, Shen Y, Du K, Zhao L, Fan H, Luo S, Hu D. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev 2020;36:e3319.
27. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Zhou X, Chen D, Xiong W, Xu L, Zhou F, Jiang J, Bai C, Zheng J, Song Y. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan China. JAMA Internal Med 2020;180:934-943.
28. Yang X. Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y, Pan S, Zou X, Yuan S, Shang Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respirat Med 2020;8:475-481.
29. Wang Z, Du Z, Zhu F. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients. Diabetes Res Clin Pract 2020;164:108214.

ORIGINAL RESEARCH

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A Prevalent Sleep Disorder in Older Adults: Restless Legs Syndrome (Is There Any Association with Other Geriatric Syndromes?)

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Abstract

Objective: Restless legs syndrome (RLS) is a common sleep disorder which affects quality of life in older individuals. We aimed to find out the geriatric syndromes and other factors significantly associated with RLS in an older study population.

Materials and Methods: This was a retrospective, cross-sectional study conducted with the participants ≥60 years old who admitted to the geriatric outpatient clinic of a tertiary hospital. The essential clinical features of RLS had to be present for diagnosis of RLS. We assessed geriatric syndromes like sleep disturbance, falls, polypharmacy (≥5 medications/day), constipation, chronic pain, cognitive impairment, depression, dysphagia, urinary and fecal incontinence, malnutrition, sarcopenia, frailty, dependency in basic and instrumental activities of daily living and reduced quality of life.

Results: There was a female predominance (67.7%) in the overall study group (n=492). Median age was 73 (69-78). RLS was seen in 28.5% and it was significantly higher in female participants (p=0.03). Sleep disturbance, depressive mood, fear of falling, reduced quality of life, frailty and polypharmacy were significantly more prevalent in the RLS group (p<0.001, 0.001, 0.04, 0.004, 0.01 and 0.02, respectively). Multivariate analysis revealed that the only factor independently associated with RLS was age [odds ratio (95% confidence interval) =0.9 (0.87-0.96); p<0.001].

Conclusion: Although depression, fear of falling, frailty, polypharmacy, sleep disturbance and reduced quality of life were more prevalent in the RLS group, none of them were independently associated with RLS. Advanced age in the older population might be protective for RLS.

Keywords: Aging, geriatric assessment, geriatric syndromes, restless legs syndrome, sleep disorders

Introduction

Restless legs syndrome (RLS), also known as Willis-Ekbom disease, is a neurological movement disorder characterised by an uncontrollable urge to move (mainly the legs), exclusively during times of inactivity/rest (1). It was introduced by Sir Thomas Willis as a clinical condition in 1685 and the term RLS was coined and clinical features described by Karl-Axel-Ekbom in 1944 (2). It was suggested that RLS was associated with low intracerebral iron stores and downregulation of striatal dopamine receptors. Therefore, dopaminergic medications have been the basis of RLS treatment for years (3).

The prevalence of RLS was reported to be 5-15% and women are affected as twice as men (4). The prevalence increases with age, as it has been reported up to 35% in older adult population (4,5). Besides from well-known risk factors like iron deficiency and uremia, several other medical conditions including arthritis, sensory neuropathy and neurodegenerative diseases are associated with RLS and are also more prevalent in older adults (3). As a frequent but mostly undiagnosed sleep disorder, RLS was reported to have significant relationship with negative outcomes like decrease in quality of life, impaired daytime functioning, falls and impaired cognitive performance in older adults (6-8). Although these findings might be in line

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with expectations, the results are not always consistent in the literature (9,10). Apart from dependency in activities of daily living, falls, or impaired cognitive functioning, there are also other common clinical conditions in older adults, called geriatric syndromes, whose relationship with RLS needs to be clarified. In fact, there is a lack of studies in the literature regarding relationship between RLS and geriatric syndromes, identified by a comprehensive geriatric assessment (CGA).

Therefore, this study aims to detect RLS prevalence, and find out the RLS associated geriatric syndromes and other clinical conditions in community dwelling older adults.

Materials and Methods

Population and setting

This study is a retrospective, cross-sectional study conducted in a tertiary health clinic. We included the patients aged ≥60 years who admitted to the geriatric outpatient clinic between November 2012-December 2019. The exclusion criteria were: i. Being younger than 60 years, ii. Refusal to participate, iii. Moderate to severe dementia or getting ≤20 points from mini-mental state examination, iv. Communicative problems (like severe hearing loss), severe form of depression or psychosis that would prevent establishing healthy communication and getting reliable information. We obtained informed consent from all of the participants. The İstanbul University Local Ethics Committee approved the study (reference: 905400/2022).

RLS diagnosis and CGA

We obtained demographic (age, gender, education level and marital status) and clinical (chronic diseases, number of medications, tobacco use and alcohol intake) characteristics of the study population. We assessed for RLS based on the International Restless Legs Syndrome Study Group (IRLSSG) diagnostic criteria (11). We performed CGA to all of the participants. We asked for sleep disorders, by asking whether they had trouble falling asleep, staying asleep, or if they thought they were having insufficient sleep or excessive sleepiness. We assessed falls during previous year (if yes, how many times), and fear of falling. We asked for chronic constipation using the Rome IV criteria for the definition (12). We evaluated whether they had urinary and/or fecal incontinence affecting daily life. Also, we asked whether they suffer chronic pain that last for at least three months. We checked all of the prescribed medications, over-the-counter drugs and supplements and considered taking ≥5 medications/day as polypharmacy. We assessed dysphagia by simply asking whether subjects had difficulty in swallowing food and/or drink.

We assessed basic Activities of Daily Living (ADL) via Katz ADL index and Instrumental ADL by Lawton IADL scale (13,14). Katz ADL is six-itemed and Lawton IADL is 8-itemed scales with a score of zero means complete dependency and full points mean complete independency, for both tests. We checked for frailty via FRAIL (Fatigue, Resistance, Ambulation, Illnesses, Loss of weight) scale. FRAIL scale is a five-itemed questionnaire with a scoring system of: 0 point means robustness, 1-2 points pre-frailty and 3 or more points frailty (15). We assessed nutritional status via Mini-Nutritional Assessment-Short Form (MNA-SF). An MNA-SF score of <8 was interpreted as malnutrition, and 8-11 was interpreted as malnutrition risk (16). We evaluated cognitive status via Mini-Mental State Examination (MMSE), with a threshold of ≤24 points regarded as cognitive impairment (17). We determined the degree of cognitive impairment according to MMSE scores as follows: 21-24 points meant mild, 10-20 points moderate, and <10 points severe dementia. We used Geriatric Depression Scale to screen depressive mood and a threshold of ≥10 points was regarded as positive for depressive mood (18). We also evaluated quality of life via EuroQol-5 Dimension-3 Levels questionnaire (EQ-5D-3L) descriptive system. It consists of five domains (i.e., mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with three levels of functioning (i.e., no problems, some problems or severe problems). Higher scores reflect a reduced quality of life (19).

Measurements

We measured height and weigth using a standardized stadiometer with participants wearing light clothing and no shoes. We measured body weight and height to the nearest 0.1 kg and 0.1 cm. We calculated body mass index (BMI) as weight (kilograms) divided by height^2 (meters). We evaluated sarcopenia in line with the European Working Group on Sarcopenia in Older People (EWGSOP2) guideline (20). Accordingly, we measured handgrip strength via Jamar hydraulic hand dynamometer in the sitting position, elbows in 90° flexion and wrist in neutral position. We asked the participants to apply maximum grip strength for three times with both hands. We considered maximal grip strength as the grip strength value (21,22). We used the cut-offs recommended by the EWGSOP2 for low muscle strength (<27 kg and 16 kg for males and females, respectively) and defined having low muscle strength as "probable sarcopenia" (20). We measured muscle mass via Tanita BC-532 bioimpedance analyzer (BIA). BIA provided fat-free mass (FFM) and we calculated total skeletal muscle mass (SMM) by the following equation: SMM (kg)=FFM x 0.566 (23). We adjusted SMM for BMI to identify decreased muscle mass. Although EWGSOP2 recommends the use of standard cut-off values for appendicular SMMI, use of national total SMMI thresholds, if available, is suggested for total SMM evaluation (24). The Turkish older population SMMI thresholds was reported as 1.049/0.823 kg/BMI, for males and females, respectively (25). The presence of both low muscle strength and low muscle mass was defined as "confirmed sarcopenia". We excluded the patients having certain conditions that might prevent reliable assessment of handgrip

strength (hand osteoarthritis, peripheral artery disease, stroke, etc.) or FFM (metal implants, cardiac pacemakers, etc) from the measurements stated. The geriatricians performed all of the questionnaires and assessments on geriatric syndromes and a qualified physiotherapist performed all of the measurements.

Statistics

We investigated whether the numerical variables distributed normally or skew using visual (histograms and probability plots) and analytical methods. We presented parametrical variables as mean ± standard deviation and non-parametrical variables as median and interquartile range. We presented categorical variables as numbers and percentages. We used the chi-square test with Yates correction and Fisher's Exact test as appropriate for categorical variables. We used independent samples t-test or Mann-Whitney U test in order to compare differences between two independent groups. We performed logistic regression analyses to identify factors independently associated with RLS. Before running regression analyses, we performed Pearson, Spearman or Kendall's tau-b correlation analyses to check for multicollinearity between independent variables expected to have a close relationship with each other. We accepted a cut-off p-value of <0.05 for statistical significance. We used the Statistical Package for Social Sciences (SPSS) for Windows 21.0 program for statistical analysis.

Results

We included 492 older adults with 333 (67.7%) being female. Median age was 73 (69-78). One-hundred fourty patients (28.5%) had RLS diagnosis. Demographic and clinical characteristics of the study group can be found in Table 1.

Table 1. Demographic and clinical characteristics of the study population (n=492)

Age (years) (med; IQR)	**73 (69-78)**
Gender (female) (n, %)	333 (67.7%)
Education level (n, %)	
Illiterate	133 (27.2%)
Primary school	197 (40.3%)
Secondary school	37 (7.6%)
High school	51 (10.4%)
University	71 (14.5%)
Marital status	
Single	6 (1.3%)
Married	279 (58.4%)
Divorced	10 (2.1%)
Widow	183 (38.3%)
Tobacco use (n, %)	43 (9.1%)
Alcohol use (n, %)	18 (4.7%)
Number of chronic illnesses (med; IQR)	4 (2-5)
Number of regular drugs (med; IQR)	6 (4-8)
BMI (kg/m²) (mean ± standard deviation)	30.4±5.9

BMI: Body mass index, med: Median, IQR: Interquartile range

Subjects with RLS were younger; had higher percentage of female gender, higher number of chronic illnesses and regular drugs, and higher BMI (p-values were 0.007, 0.03, 0.02, 0.03, and 0.03, respectively). According to the CGA findings, RLS group had significantly higher prevalence of depressive mood, fear of falling, frailty, reduced quality of life, polypharmacy and sleep disturbance (p-values were 0.001, 0.04, 0.01, 0.004, 0.02 and <0.001; respectively). CGA findings can be found in Table 2.

We ran a multivariate analysis, defining the factors associated with RLS (according to the univariate analyses) as independent variables and found out that "age" was the only factor independently associated with RLS [Odds Ratio (95% Confidence Interval) =0.9 (0.87-0.96); p<0.001]. Logistic regression analysis findings are presented in Table 3.

Discussion

In this study, we found out that RLS patients had significantly higher prevalence of geriatric syndromes like depression, fear of falling, frailty, polypharmacy and sleep disturbance; and their quality of life significantly reduced compared to the subjects without RLS. According to the logistic regression analysis, age was the only independent factor associated with RLS, and it seemed that individuals with very advanced age might be suffering less from RLS in the older adult community.

RLS prevalence in our study was in line with the literature. There are a few studies on RLS from Turkey reported a prevalence range of 15-28% (7,26,27) in older population. The prevalence and severity of RLS has known to be increased with increasing age, as certain conditions that accompany RLS are seen more frequent in advanced age; like chronic kidney disease, chronic neurological disorders and use of medications that are considered to exacerbate RLS. Likewise, "age" was the only factor independently associated with RLS in our study, but in an unexpected manner: Older age seemed protective for RLS. In fact, there are a plenty of studies reporting increasing prevalence by age (28,29), however this does not seem to be the case in older adult population. Some studies reported an increase up to 70 years and then a decrease in RLS prevalence in older subjects (30-32). Also, certain studies conducted on specifically older populations did not report an increase in RLS prevalence with increasing age as well (33). Advanced age being a favorable trait for RLS may be explained by "survival effect". It is well-known that certain comorbidities like chronic kidney disease or diabetes mellitus are companions of RLS, especially when RLS is a late onset. Patients with these comorbidities would have ended up with early mortality and the rest of the long living seniors are probably more healthy and have less

Table 2. Comprehensive geriatric assessment findings of the study population

Geriatric syndrome	Total	RLS (-)	RLS (+)	p-value
Sleep disturbance	195 (39.6%)	117 (33.2%)	78 (55.7%)	**<0.001**
Falls in the previous year	198 (40.4%)	139 (39.6%)	59 (42.4%)	0.6
Fear of falling	219 (44.7%)	146 (41.7%)	73 (52.1%)	**0.04**
Malnutrition	125 (25.4%)	86 (24.4%)	39 (27.9%)	0.4
Frailty	99 (20.7%)	61 (17.8%)	38 (27.9%)	**0.01**
Sarcopenia (probable)	60 (12.5%)	17 (12.6%)	43 (12.4%)	0.9
Sarcopenia (confirmed)	31 (6.5%)	22 (6.4%)	9 (6.7%)	0.9
Dependency in ADL	139 (28.3%)	95 (27.0%)	44 (31.4%)	0.3
Dependency in IADL	154 (31.3%)	114 (32.4%)	40 (28.6%)	0.4
Dysphagia	40 (10.1%)	25 (8.9%)	15 (13.0%)	0.2
Urinary incontinence	200 (40.7%)	140 (39.8%)	60 (42.9%)	0.5
Fecal incontinence	22 (4.5%)	16 (4.5%)	6 (4.3%)	0.9
Constipation	129 (26.4%)	85 (24.4%)	44 (31.4%)	0.1
Cognitive impairment	44 (8.9%)	34 (9.7%)	10 (7.1%)	0.4
Depression	154 (48.3%)	94 (42.3%)	60 (61.9%)	**0.001**
Polypharmacy	309 (65.1%)	211 (61.9%)	98 (73.1%)	**0.02**
Chronic pain	287 (58.6%)	196 (56%)	91 (65%)	0.07
Reduced QoL	359 (80.0%)	244 (76.5%)	115 (88.5%)	**0.004**

ADL: Activities of daily living, IADL: Instrumental activities of daily living, QoL: Quality of life

Table 3. Multivariate analysis regarding factors independently associated with RLS

Variables	OR (95% CI)	p-value
Age	0.9 (0.87-0.96)	**<0.001**
BMI	1.01 (0.9-1.1)	0.8
Depression	1.4 (0.8-2.5)	0.3
Decreased QoL	1.8 (0.8-4.3)	0.2
Fear of falling	0.9 (0.6-1.8)	0.9
Female gender	0.6 (0.31-1.14)	0.12
Frailty	1.7 (0.9-3.5)	0.1
Number of chronic diseases	1.02 (0.9-1.2)	0.8
Polypharmacy	1.7 (0.9-3.1)	0.1
Sleep disturbance	1.6 (0.9-2.8)	0.1

BMI: Body mass index, CI: Confidence interval, OR: Odds ratio, QoL: Quality of life, RLS: Restless leg syndrome, p-value of less than 0.05 was accepted as statistically significant

comorbidity burden in their ageing period. In addition, the older adults who applied to our outpatient clinic were mostly those under the long-term follow-up of our clinic and whose treatments for secondary causes of RLS are optimally arranged. Apart from all these, some older adults in very old age might have neglected their symptoms, or showed a stoic approach that those sensations were a natural part of normal ageing process, like chronic pain. Therefore, symptoms might be underreported by older subjects.

Female predominance in RLS diagnosis in our study was also consistent with the previous studies (28,30). Estrogens, dopamine and RLS have a close relationship with each other; as the prevalence of RLS significantly increases with pregnancy as estrogen levels are rising (34). Estrogen acting as a dopamine antagonist has been hypothesized as its role in RLS. However, it was also suggested that fluctuations rather than absolute level (as in pregnancy or perimenopausal period) might be the main reason behind RLS tendency in female individuals (35). In fact, there are surveys manifesting that nulliparous women were at the same risk of RLS as same aged men, while the risk was increased in direct proportion as the number of pregnancies increased (36,37). There are other RLS studies reporting male predominance as well (38). Although female subjects had significantly higher numbers of RLS diagnosis, "female gender" was not a risk factor for RLS, according to our regression analysis.

The secondary outcome of our study was to investigate the relationship between RLS and geriatric syndromes and we found out that older adults suffering RLS had higher prevalence of sleep disturbance, depression, fear of falling, frailty, polypharmacy and reduced QoL. RLS and mental health are considered to have a "chicken and egg" relationship: People with RLS often have depression, anxiety, and other mental health issues. And, people with depression or anxiety often have restless legs (39). Clinical and epidemiological studies have reported data supportive of this hypothesis (40). Increase in depressive mood has been attributed to the RLS related sleep impairment and its sequlae; as impaired sleep can create a loss of energy and decreased daytime functionality, which are the somatic symptoms of depression. Dopamine was also implicated in the

causation of depression and treatment of RLS is thought to improve depression in RLS (41). Several antidepressants that are frequently been used in treatment of depression, like selective serotonin re-uptake inhibitors or atypical antidepressants like mirtazapine, were also reported to aggrevate RLS symptoms (42). In our study, although there were significant relationships between depressive mood and RLS, depression was not an independent factor related to RLS.

Fear of falling has a significant importance in geriatric health. It may develop after falls or without any falling experience and may bring out significant negative outcomes like deconditioning, decreased muscle strength and mass, increased risk of future falls and mood disorders like depression and anxiety (43). Although we did not find any relationship between RLS and falls during past year, fear of falling was significantly more prevalent in patient suffering RLS. This might be attributed to the certain factors strongly associated with RLS that might also be facilitators of previous falling episodes, like neuropathies or Parkinson's disease. Again, the significant relationship between fear of falling and RLS was disappeared after regression analysis.

Apart from depression and anxiety (fear of falling); RLS was also significantly associated with reduced QoL, which is an expected finding and consistent with the previous studies (6). EQ-5D-3L has parameters assessing mobility, self-care, day-time functionality, pain/discomfort and anxiety/depression, and most of them were already demonstrated to have a close relationship with RLS (8).

According to our findings, older patients with RLS were more frail than subjects without RLS. To the best of our knowledge, there is no study in the literature investigating the relationship between these two common conditions in older adult population. We screened frailty via FRAIL scale; which comprises five items questioning fatigue, resistance, ambulance, diseases and weight loss. Patients with RLS have sleep disturbance, decreased sleep quality, daytime sleepiness, fatigue and tiredness (8). Fatigue and tiredness might affect daytime functioning and cause difficulty and trouble in ambulation and climbing stairs. Furthermore, we found out that RLS patients had higher number of chronic comorbidities; therefore certain ones that are known to be associated with RLS might have caused fourth item of FRAIL to be positive. Finally, although there was no significant difference between RLS and non-RLS groups in terms of MNA-SF results, patients who had weight losses, but not malnourished according to MNA-SF, might have iron, vitamin B12 or folate deficiencies, which are known to be associated with RLS symptoms as well (1). Indirect relationships stated above might have caused the significant association found in univariate analysis; as the relationship disappeared after adjustments in regression analysis.

Our analysis showed that the RLS group had a higher number of medications and polypharmacy prevalence. Polypharmacy has a strong relationship with adverse outcomes like decreased physical performance, falls, fractures, disabilities, increased hospitalizations and even mortalities in older adult population (44,45). Several medications commonly used in the older adult population are known to aggrevate RLS. According to a literature review including 32 articles related to RLS, the strongest evidence available for drug induced RLS are for the following drugs: Escitalopram, fluoxetine, L-dopa/carbidopa, pergolide, L-thyroxine, mianserin, mirtazapine, olanzapine and tramadol (46). Commonly used medications in geriatric practice (like metformin or proton-pump inhibitors) can cause decreased appetite and oral intake or iron and vitamin B12 malabsorption, hence develop RLS symptoms (47). Evaluating "the use of drugs that might predispose to RLS" or "inappropriate medication use", rather than "polypharmacy" might reveal a significant relationship with RLS, as the regression analysis revealed that polypharmacy was not an independently associated factor with RLS.

We found no relationship between RLS and urinary/fecal incontinence, constipation and dysphagia. Similar to our results, a retrospective analysis of a data deriven from older adults have reported that although autonomic complaints were significantly increased in RLS patients, there were no differences between RLS and control groups in terms of urinary/fecal incontinence, constipation and dysphagia (48). Finally, we found out that RLS did not demonstrate an association with sarcopenia, whether it was probable or confirmed. There are very limited studies regarding sarcopenia and RLS relationship in the literature. Giannaki et al. (49) conducted a study on uremic RLS patients and assessed total muscle mass via dual energy X-ray absorpsiometry and regional (thigh) muscle mass via computerized tomography. They found out that total body composition assessment did not show any differences between the RLS and non-RLS groups; but thigh muscle total area, muscle cross sectional area (CSA) and the level of muscle fat infiltration were significantly reduced in the RLS group. There were no differences in terms of physical performance (evaluated via walking test and sit-to-stand tests) (49). According to a Japanese study conducted on 1592 older adults, sarcopenia (evaluated via Asian Working Group for Sarcopenia definitions) was significantly associated with difficulty initiating and/or maintaining sleep; but there was no subgroup analysis for RLS patients (50). In fact, the relationship between RLS and incontinence, constipation, dysphagia and sarcopenia might seem a little bit forced. However, as previously mentioned, there are studies reporting autonomic dysfunction in RLS patients and this might end up with dysphagia, incontinence or constipation (48). In addition, several conditions like neurodegenerative disorders (like Parkinson's disease) or neuropathies might also

be underlying causes for sarcopenia. Therefore, we wanted to include these geriatric syndromes in the CGA and search whether they have an independent association with RLS. As such, further studies are needed to clarify the exact relationship between RLS and stated geriatric syndromes.

Although there is no study that comprehensively examines the relationship between RLS and geriatric syndromes like our study, some of them studied RLS and certain geriatric syndromes relationship in older adults. In a Turkish study; depressive mood, sleep quality, sleep duration, and difficulty in falling asleep were all significantly associated with RLS; but the relationship did not persist in regression analysis, except for sleeping less than 6 hours/day (26). An American study including 1008 older adults reported that patients with RLS demonstrated increased risk of chronic pain, three or more chronic medications, frequent falls, sleep disturbances and decreased functionality (51). According to a French study comprising of 318 older subjects, participants with RLS had significantly higher anxiety and depression scores, lower cognitive performances and greater hypnotic and antidepressant medications (4). A cross-sectional case-control study from China reported similar results, as RLS patients had higher prevalence of anxiety and depression and to some extent, cognitive impairment (8). In fact, there was no significant difference between MMSE scores of the RLS and control groups; however Montreal Cognitive Assessment (MoCA) performance was poorer in subjects with RLS. Authors discussed this finding as MoCA had a greater sensitivity in identifying mild cognitive impairment compared to MMSE, and it may have detected some of the subjects with mild cognitive impairment in this group (8). In fact, the relationship between RLS and cognitive function is controversial in the literature. Some studies have reported that cognitive decline caused by RLS was related to sleep disturbance or depression, while others have shown that there is no clear relationship between them and that the exact mechanism is unknown (52). In our study, there was no significant relationship between RLS and MMSE performance. Hence, more studies are needed to identify whether RLS has an effect on cognitive functions.

Study Limitations

This study has some limitations. Firstly, because of its cross-sectional design, a causal-effect relationship cannot be claimed. The study population consisted of the older adults admitted to an outpatient clinic of a tertiary hospital, and most of them were under long-term follow-up. Therefore, the findings of this study cannot be generalized to the whole older adult community. Furthermore, due to the subjective evaluation of RLS, "recall bias" might have affected the results. In order to minimize it, we used the most commonly used diagnostic criteria for RLS diagnosis, and excluded individuals getting MMSE scores lower than 21. To the best of our knowledge, this is the first study assessing the relationship between RLS and a list of geriatric syndromes as a whole, in an older adult population.

Conclusion

RLS is a prevalent, but mostly unquestioned and underdiagnosed sleep disorder in older adults. According to our analyses, RLS had a significant relationship with certain geriatric syndromes like depression, fear of falling, frailty, polypharmacy and sleep disturbance and it was closely related to reduced QoL. Although RLS prevalence is known be increasing by age, this may not apply to very old ages and advanced age in this particular population may be somewhat protective for suffering RLS. Further comprehensive studies with larger older adult populations are warranted in order to identify exact relationships and underlying mechanisms.

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Ethics

Ethics Committee Approval: The İstanbul University Local Ethics Committee approved the study (reference: 905400/2022).

Informed Consent: We obtained informed consent from all of the participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.Ö., Design: S.Ö., C.K., M.A.K., Data Collection or Processing: S.Ö., Ç.Ö.A., D.E.S., N.M.Ç., T.E., Analysis or Interpretation: S.Ö., M.A.K., Literature Search: S.Ö., Editing: G.B., Writing: S.Ö., M.A.K.

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References

1. Klingelhoefer L, Bhattacharya K, Reichmann H. Restless legs syndrome. Clin Med (Lond) 2016;16:379-382.
2. Coccagna G, Vetrugno R, Lombardi C, Provini F. Restless legs syndrome: an historical note. Sleep Med 2004;5:279-283.
3. During EH, Winkelman JW. Drug Treatment of Restless Legs Syndrome in Older Adults. Drugs Aging 2019;36:939-946.
4. Celle S, Roche F, Kerleroux J, Thomas-Anterion C, Laurent B, Rouch I, Pichot V, Barthélémy JC, Sforza E. Prevalence and Clinical Correlates of Restless Legs Syndrome in an Elderly French Population: The Synapse Study. J Gerontol A Biol Sci Med Sci 2010;65:167-173.
5. Association ASD. International classification of sleep disorders. Revised: diagnostic and coding manual. Available from: http://www absm org/PDF/ICSD pdf 1997.

6. Cuellar NG, Strumpf NE, Ratcliffe SJ. Symptoms of restless legs syndrome in older adults: outcomes on sleep quality, sleepiness, fatigue, depression, and quality of life. J Am Geriatr Soc 2007;55:1387-1392.
7. Sılay K, Özkaya H, Yalçın A, Akıncı S, Ulaş A, Öztürk E, Canbaz M, Yalçın B. Assessment of Falls In Older People: Is There Any Association Between Restless Leg Syndrome and Falls? Ankara Med J 2016;16:13-19.
8. Xu Y, Wen H, Li J, Yang J, Luo K, Chang L. The relationship between sleep disorders, anxiety, depression, and cognitive function with restless legs syndrome (RLS) in the elderly. Sleep Breath 2022;26:1309-1318.
9. Trenkwalder C, Tinelli M, Sakkas G, Dauvilliers Y, Ferri R, Rijsman R, Oertel W, Jaarsma J. Socioeconomic impact of restless legs syndrome and inadequate restless legs syndrome management across European settings. Eur J Neurol 2021;28:691-706.
10. Lee HB, Ramsey CM, Spira AP, Vachon J, Allen R, Munro CA. Comparison of cognitive functioning among individuals with treated restless legs syndrome (RLS), untreated RLS, and no RLS. J Neuropsychiatry Clin Neurosci 2014;26:87-91.
11. 2012 Revised IRLSSG Diagnostic Criteria for RLS: International Restless Legs Syndrome Study Group; [cited 2022 April, 4]. Available from: http://irlssg.org/diagnostic-criteria
12. Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel Disorders. Gastroenterology 2016;S0016-5085(16)00222-5.
13. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. J Am Geriatr Soc 1983;31:721-727.
14. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179-186.
15. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012;16:601-608.
16. Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol A Biol Sci Med Sci 2001;56:M366-372.
17. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. [Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population]. Turk Psikiyatri Derg 2002;13:273-281.
18. Yesavage JA. Geriatric Depression Scale. Psychopharmacol Bull 1988;24:709-711.
19. Brooks R. EuroQol: the current state of play. Health Policy 1996;37:53-72.
20. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16-31.
21. Massy-Westropp NM, Gill TK, Taylor AW, Bohannon RW, Hill CL. Hand Grip Strength: age and gender stratified normative data in a population-based study. BMC Res Notes 2011;4:127.
22. Fess EE. Grip strength. In: Casanova JS, editor. Clinical assessment recommendations. 2nd ed. Chicago: American Society of Hand Therapists; 1992. p. 41-5.
23. Deurenberg P, Pietrobelli A, Wang Z, Heymsfield S. Prediction of total body skeletal muscle mass from fat-free mass or intra-cellular water. IJBCR 2004;2:107-114.
24. Bahat G, Cruz-Jentoft A. Putting Sarcopenia at the Forefront of Clinical Practice. Eur J Geriatr Gerontol 2019;1:43-45.
25. Bahat G, Tufan A, Kilic C, Aydın T, Akpinar TS, Kose M, Erten N, Karan MA, Cruz-Jentoft AJ. Cut-off points for height, weight and body mass index adjusted bioimpedance analysis measurements of muscle mass with use of different threshold definitions. Aging Male 2020;23:382-387.
26. Safak ED, Gocer S, Mucuk S, Ozturk A, Akin S, Arguvanli S, Mazicioglu MM. The prevalence and related factors of restless leg syndrome in the community dwelling elderly; in Kayseri, Turkey: A cross-sectional study. Arch Gerontol Geriatr 2016;65:29-35.
27. Türkmen BÖ. Evaluation of Self-reported Insomnia and Its Association with Some Geriatric Syndromes in Older Adults. Eur J Geriatr Gerontol 2019;1:11-16.
28. Fereshtehnejad S-M, Rahmani A, Shafieesabet M, Soori M, Delbari A, Motamed MR, Lökk J. Prevalence and associated comorbidities of restless legs syndrome (RLS): Data from a large population-based door-to-door survey on 19176 adults in Tehran, Iran. PLoS One 2017;12:e0172593.
29. Lajous M, Kurth T, Catzin-Kuhlmann A, Romieu I, Lopez-Ridaura R. [Prevalence of restless legs syndrome in 69,830 Mexican women]. Rev Invest Clin 2014;66:303-306.
30. Allen RP, Bharmal M, Calloway M. Prevalence and disease burden of primary restless legs syndrome: Results of a general population survey in the United States. Mov Disord 2011;26:114-120.
31. Kim TJ, Yoon JE, Park JA, Lee SK, Chu MK, Yang KI, Kim WJ, Park SH, Thomas RJ, Shin C, Yun CH. Prevalence and Characteristics of Restless Legs Syndrome in Korean Adults: A Study in Two Independent Samples of the General Population. Neuroepidemiology 2019;52:193-204.
32. Allen RP, Walters AS, Montplaisir J, Hening W, Myers A, Bell TJ, Ferini-Strambi L. Restless Legs Syndrome Prevalence and Impact: REST General Population Study. Arch Intern Med 2005;165:1286-1292.
33. Kim KW, Yoon IY, Chung S, Shin YK, Lee SB, Choi EA, Park JH, Kim JM. Prevalence, comorbidities and risk factors of restless legs syndrome in the Korean elderly population - results from the Korean Longitudinal Study on Health and Aging. J Sleep Res 2010;19:87-92.
34. Seeman MV. Why Are Women Prone to Restless Legs Syndrome? Int J Environ Res Public Health 2020;17:368.
35. Baker JM, Hung AY. Movement Disorders in Women. Semin Neurol 2017;37:653-660.
36. Pantaleo NP, Hening WA, Allen RP, Earley CJ. Pregnancy accounts for most of the gender difference in prevalence of familial RLS. Sleep Meds 2010;11:310-313.
37. Berger K, Luedemann J, Trenkwalder C, John U, Kessler C. Sex and the risk of restless legs syndrome in the general population. Arch Intern Med 2004;164:196-202.
38. Kageyama T, Kabuto M, Nitta H, Kurokawa Y, Taira K, Suzuki S, Takemoto T. Prevalences of periodic limb movement-like and restless legs-like symptoms among Japanese adults. Psychiatry Clin Neurosci 2000;54:296-298.
39. Team E. Restless Legs Syndrome and Mental Health 2020 [cited 2022 April, 20]. Available from: https://restlesslegssyndrome.sleep-disorders.net/coping-mental-health
40. Kallweit U, Werth E, Seiz A, Sefidan S, Dahmen N, Manconi M, Ehlert U, Bassetti CLA. Psychiatric Comorbidities in Restless Legs Syndrome. J Neuropsychiatry Clin Neurosci 2016;28:239-242.
41. Benes H, Mattern W, Peglau I, Dreykluft T, Bergmann L, Hansen C, Kohnen R, Banik N, Schoen SW, Hornyak M. Ropinirole improves depressive symptoms and restless legs syndrome severity in RLS patients: a multicentre, randomized, placebo-controlled study. J Neurol 2011;258:1046-1054.
42. Kolla BP, Mansukhani MP, Bostwick JM. The influence of antidepressants on restless legs syndrome and periodic limb movements: A systematic review. Sleep Med Rev 2018;38:131-140.
43. Auais M, French S, Alvarado B, Pirkle C, Belanger E, Guralnik J. Fear of Falling Predicts Incidence of Functional Disability 2 Years Later: A Perspective From an International Cohort Study. J Gerontol A Biol Sci Med Sci 2018;73:1212-1215.

44. Ozkok S, Aydin CO, Sacar DE, Catikkas NM, Erdogan T, Kilic C, Karan MA, Bahat G. Associations between polypharmacy and physical performance measures in older adults. Arch Gerontol Geriatr 2022;98:104553.

45. Chang TI, Park H, Kim DW, Jeon EK, Rhee CM, Kalantar-Zadeh K, Kang EW, Kang SW, Han SH. Polypharmacy, hospitalization, and mortality risk: a nationwide cohort study. Sci Rep 2020;10:18964.

46. Hoque R, Chesson AL Jr. Pharmacologically induced/exacerbated restless legs syndrome, periodic limb movements of sleep, and REM behavior disorder/REM sleep without atonia: literature review, qualitative scoring, and comparative analysis. J Clin Sleep Med 2010;6:79-83.

47. Bahat G, Ilhan B, Erdogan T, Halil M, Savas S, Ulger Z, Akyuz F, Bilge AK, Cakir S, Demirkan K, Erelel M, Guler K, Hanagasi H, Izgi B, Kadioglu A, Karan A, Kulaksizoglu IB, Mert A, Ozturk S, Satman I, Sever MS, Tukek T, Uresin Y, Yalcin O, Yesilot N, Oren MM, Karan MA. Turkish inappropriate medication use in the elderly (TIME) criteria to improve prescribing in older adults: TIME-to-STOP/TIME-to-START. Eur Geriatr Med 2020;11:491-498.

48. Shneyder N, Adler CH, Hentz JG, Shill H, Caviness JN, Sabbagh MN, Beach TG, Driver-Dunckley E. Autonomic complaints in patients with restless legs syndrome. Sleep Med 2013;14:1413-1416.

49. Giannaki CD, Sakkas GK, Karatzaferi C, Hadjigeorgiou GM, Lavdas E, Liakopoulos V, Tsianas N, Koukoulis GN, Koutedakis Y, Stefanidis I. Evidence of increased muscle atrophy and impaired quality of life parameters in patients with uremic restless legs syndrome. PLoS One 2011;6:e25180.

50. Nagaura Y, Kondo H, Nagayoshi M, Maeda T. Sarcopenia is associated with insomnia in Japanese older adults: a cross-sectional study of data from the Nagasaki Islands study. BMC Geriatrics 2020;20:256.

51. Cirillo DJ, Wallace RB. Restless legs syndrome and functional limitations among American elders in the Health and Retirement Study. BMC Geriatr 2012;12:39.

52. Jung KY. Cognition in Restless Legs Syndrome. J Sleep Med 2015;12:1-6.

ORIGINAL RESEARCH

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Assessment of the Relationship Between Anorexia of Aging and Dietary Intake

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Abstract

Objective: People tend to have less food consumption and energy intakes during old age. Anorexia of aging is one of the major factors reducing energy intake. The aim of this study is to examine the relationship between anorexia of aging and dietary intake among Turkish elderly adults.

Materials and Methods: In the study, the simplified nutritional appetite questionnaire was used to assess the anorexia of aging and a 24-hour recall was employed to evaluate dietary intake. The participants' socio-demographic characteristics (age, sex, and education) as well as their medical history (medication and chronic disease history) lifestyle-related characteristics (smoking and drinking habits and living arrangement), body mass index, and depressive symptoms were analyzed. Binary logistic regression was used to determine risk factors in predicting the anorexia of aging.

Results: A total of 183 Turkish elderly adults were included in the study (mean age of 71.49±5.49 years; female, 56.3%). The prevalence rate of anorexia of aging was 22.4% in the present study. Elderly adults with anorexia of aging had a lower intake of both energy and all macronutrients (proteins, fats, carbohydrates) ($p<0.05$). Furthermore, among micronutrients, elderly adults with anorexia of aging had lower consumption of iron, zinc, calcium, sodium, potassium and magnesium. Moreover, vitamin A, vitamin E, vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12 decreased significantly in those with anorexia of aging ($p<0.05$). Living arrangement, depression status, and protein intake were the important predictors in the multivariate model for anorexia of aging.

Conclusion: This study revealed that elderly adults with anorexia of aging had less intake of macro and micronutrients.

Keywords: Anorexia of aging, dietary intake, loss of appetite, elderly adults

Introduction

The rate of elderly population has increased considerably in Turkey in recent years. This rate was 6.7% of the total population in 2000, but increased to 9.7% in 2021, reaching more than 8 million (1). As the elderly population grows, it becomes increasingly important to encourage health protection in this group (2).

Appetite is defined as the natural urge to consume food, which decreases and changes with increasing age and possibly causes severe weight loss (3). The term "anorexia of aging" refers to decreased appetite and/or decreased food intake in old age (3) and is regarded as a geriatric syndrome, today (4-6). Anorexia of aging causes many adverse outcomes including frailty, sarcopenia, decreased physical and cognitive functions, cachexia, malnutrition, reduced bone mass, micronutrient deficiency, impaired quality of life, and increased mortality (7-11). Screening, early diagnosis, and treatment of anorexia are likely to prevent weight loss and malnutrition, improve health outcomes, and decrease mortality rates. Thus, elderly adults may be periodically screened for poor appetite (12). A validated screening tool on appetite is thought to be an early indicator of malnutrition risk in elderly adults by creating opportunities for early intervention (13). The Simplified Nutritional Appetite Questionnaire (SNAQ) has a high level of reliability, sensitivity, and specificity for predicting malnutrition in elderly populations (14-17) and is a rapid screening tool used in clinical settings

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(18). This tool is applied in a relatively short time to predict possible weight loss in the future (2).

Nutrition is regarded as one of the important elements within the scope of geriatric assessment. Being described as the urge to ingest food, appetite significantly influences nutritional intake (18). The aim of this study is to examine the relationship between anorexia of aging and dietary intake in elderly adults.

Materials and Methods

Participants

This was a single-center, cross-sectional study. The sample consisted of a total of 183 elderly adults who were aged ≥65 years and living in Gaziantep. The people who were enterally or parenterally fed, were bedridden, had terminal diseases or mental disturbances, had any neurological disease or declined to participate in the study were excluded from the study.

For this study, approval was obtained from the Gaziantep Islam Science and Technology University Ethics Committee (2022/102). The principles of the Declaration of Helsinki were followed to conduct the study. All of the participants signed the informed consent form.

Anorexia of aging

SNAQ was developed to assess the anorexia of aging (2). It was adapted into Turkish and its validity was conducted for the elderly population in Turkey (19). The SNAQ is a 5-point Likert-type scale with four items and a single domain: 1) My appetite is (a. very poor, b. poor, c. average, d. good, e. very good); 2) When I eat (a. I feel full after eating only a few mouthfuls, b. I feel full after eating about a third of a meal, c. I feel full after eating over half a meal, d. I feel full after eating most of the meal, e. I hardly ever feel full); 3) Food tastes (a. very bad, b. bad, c. average, d. good, e. very good); 4) Normally I eat (a. less than one meal a day, b. one meal a day, c. two meals a day, d. three meals a day, e. more than three meals a day). Each item is rated from 1 point (the lowest score) to 5 points (the highest score). The total score is the sum of the answers to the four items. The lowest and highest scores of the scale are 4 and 20, respectively. Scores of ≤14 points signify the presence of anorexia of aging (19,20).

Assessment of food intake

The 24-hour dietary recall (24HR) method was used to evaluate the dietary intake of the participants. The 24HR is a simple and affordable scale and can also be applied to illiterate elderly adults (21). The dietary recalls were performed through face-to-face interviews to assess the amount of food and beverage intakes respondents consume the day before the interview-from the time they woke up until bedtime through household measures (cups, spoons) and mL or grams. Also, the food portion sizes are detected by employing a photographic atlas (22). BEBIS 8 software (Ebispro for Windows, Germany; Turkish version/ BeBiS 8) was used to determine mean energy and macronutrient and micronutrient intakes of elderly adults.

Depressive symptoms

Depressive mood of the participants was assessed using the geriatric depression scale (GDS) (23). Total score of the scale ranges between 0-30 points. Turkish validity and reliability study of this scale was conducted and its cut-off point was 14 for the Turkish elderly adults (24).

Socio-demographic variables

Demographic (age, gender, marital status, education level), medical history (number of medications and chronic disease history), and lifestyle-related characteristics (smoking, alcohol consumption, and living arrangement) of the participants were examined using face-to-face interviews.

Also, height (cm) and weight (kg) of the participants wearing light clothes and no shoes were measured. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

Statistics

The data were analyzed using SPSS version 22.0 (SPSS Inc. Chicago, IL, USA). The data were presented as number (n), percentage (%), mean ($\bar{X}$), standard deviation, and median values. The participants were assigned to two groups; group without anorexia of aging and a group with anorexia of aging. Polypharmacy was defined as drug administration of ≥5 (25). Differences between categorical variables were detected through Pearson's chi-square test or Fisher's Exact test. Whether or not the variables were normally distributed was checked with the Shapiro-Wilk test. Quantitative data were compared through independent samples t-test for normal distributed variables. Variables that were non-normally distributed were analyzed via Mann-Whitney U test. Odds ratios (OR) and confidence interval of 95% were used with univariate binary logistic regression and multivariate binary logistic regression (enter method) models to estimate the risk factors for anorexia of aging. A value of $p<0.05$ was set as statistically significant.

Results

The data of 183 elderly adults (80 men, 103 women) having a mean age of 71.49±5.49 years (range, 65-89 years) were analyzed in the current study. The prevalence of anorexia of aging was 22.4%. There were significant differences between the groups for age, GDS score, and BMI ($p<0.001$; $p<0.001$; $p=0.020$, respectively). The rate of the diabetic participants was higher in the group without anorexia of aging. Furthermore, the rate of the participants who had hyperlipidemia, hypertension

or other chronic disease did not vary significantly between the groups. Table 1 shows the demographic characteristics and scale scores of the groups.

Elderly adults with anorexia of aging had lower energy intakes (992.53 kcal vs. 1575.48 kcal, p<0.001) and also lower intakes of all macronutrients such as proteins (35.53 g vs. 63.39 g, p<0.001), fats (46.88±12.97 g vs. 65.47±18.03 g, p<0.001) and carbohydrates (107.96 g vs. 169.98 g, p<0.001) in terms of the

Table 1. Characteristics of the participants

	Total (n=175)		Without an anorexia of aging (n=142)		With an anorexia of aging (n=41)		p
	n	%	n	%	n	%	
Gender							
Female	103	56.3	75	52.8	28	68.3	0.078*
Male	80	43.7	67	47.2	13	31.7	
Age (year) (X ± SD)	71.49±5.49		70.02±4.16		76.59±6.50		<0.001**
Marital status							
Married	105	57.4	82	57.7	23	56.1	0.240*
Single	15	8.2	10	7	5	12.2	
Divorced/widowed	63	34.4	50	35.2	13	31.7	
Educational status							
Illiterate	45	24.6	32	22.5	13	31.7	0.051*
Literate	30	16.4	20	14.1	10	24.4	
Primary school	11	6.0	7	4.9	4	9.8	
Secondary school	16	8.7	11	7.7	5	12.2	
High school or equivalent	58	31.7	52	36.6	6	14.6	
College or university	23	12.6	20	14.1	3	7.3	
Living arrangement							
Living alone	26	14.2	19	13.4	7	17.1	0.481*
Living with family	113	61.7	91	64.1	22	53.7	
Living with relatives	44	24.0	32	22.5	12	29.3	
Presence of chronic disease							
Hypertension	81	44.3	68	47.9	13	31.7	0.076***
Diabetes	78	42.6	70	49.3	8	19.5	<0.001***
Hyperlipidemia	78	42.6	64	45.1	14	35.1	0.213***
Other	45	24.6	33	23.2	12	29.3	0.430***
Polypharmacy	42	23.0	32	22.5	10	24.4	0.804*
Drinking habit							
Never drinking	150	82.0	123	86.6	27	65.9	<0.001*
Stopped drinking	27	14.7	13	9.2	14	34.1	
Current drinking	6	3.3	6	4.2	-	-	
Smoking habit							
Never smokers	106	57.9	84	59.2	22	53.7	0.746*
Stopped smoking	19	10.4	15	10.6	4	9.9	
Current smokers	59	31.7	43	30.3	15	36.6	
SNAQ score (X ± SD)	15.36±2.32		16.28±1.25		11.68±1.87		<0.001**
GDS score (X ± SD)	11.74±4.99		19.17±5.81		10.08±4.96		<0.001**
BMI (X ± SD)	25.40±3.61		25.73±3.69		24.25±3.08		0.020**

SNAQ: Simlified nutritional appetite questionnaire, GDS: Geriatric depression score, BMI: Body mass index, SD: Standard deviation, * Pearson chi-square test, **Independent samples t-test (X ± SD), ***Fisher's Exact test

amount of energy and macronutrients intake. This difference was maintained between the groups in term of body weight (as kcal/kg or g/kg) (p<0.05). The participants also had a lower consumption of fibers (12±5.56 g vs. 19.65±7.36 g, p<0.001). In addition, elderly adults with anorexia of aging consumed less lipid fractions: polyunsaturated fats (10.66 g vs. 14.94 g, p<0.001), monounsaturated fats (14.48 g vs. 20.82 g, p<0.001), saturated (15.04±5.88 g vs. 21.36±7.04 g, p<0.001) and cholesterol (133.30±109.03 g vs. 262.19±159.77 g; p<0.001). When it comes to micronutrients, elderly adults with anorexia of aging had lower consumption of iron zinc, calcium sodium, potassium and magnesium (p<0.05). Moreover, intake of vitamin A, vitamin E, vitamin B1, vitamin B2, niacin, vitamin B6, folate and vitamin B12 decreased significantly in anorexia of aging group (p<0.05). The daily energy and nutrient intakes of the elderly adults based on presence of anorexia of aging is summarized in Table 2.

The univariate binary logistic regression analysis indicated that age, depression, BMI, energy, daily protein, fat and carbohydrate intake were associated with anorexia of aging (OR=1.26;

Table 2. Daily energy and nutrient intakes of the participants in terms of the presence of anorexia of aging

	Without anorexia of aging		With anorexia of aging		U^A/t^B	p
	X ± SD	Median	X ± SD	Median		
Energy (kcal)	1548.83±249.47	1575.48	1028.63±235.13	992.53	U=401.00	<0.001
Energy (kcal/kg)	24.96±5.13	24.77	16.62±4.16	16.61	t=-7.242 df=181	<0.001
Protein (g)	63.39±16.01	62.11	36.76±12.70	35.53	U=478.50	<0.001
Protein (g/kg)	0.94±0.26	0.93	0.59±0.19	0.55	t=-9.316 df=181	<0.001
Protein (% energy)	16.91±4.02	17.00	14.93±5.60	14.00	U=1756.00	0.010
Carbohydrate (g)	172.63±45.81	169.98	110.81±34.33	107.96	U=807.00	<0.001
Carbohydrate (g/kg)	2.57±0.84	2.46	1.79±0.59	1.77	U=1326.00	<0.001
Carbohydrate (% energy)	45.47±9.37	46.00	43.83±8.16	45.00	U=2690.50	0.460
Fat (g)	65.47±18.03	65.94	46.88±12.97	48.71	t=-6.15 df=181	<0.001
Fat (g/kg)	0.97±0.30	0.95	0.76±0.22	0.77	t=-4.213 df=181	<0.001
Fat (% energy)	37.51±8.21	38.00	40.32±7.01	41.00	t=1.99 df=181	0.030
SFA (g)	21.36±7.04	21.25	15.04±5.88	13.70	t=-5.24 df=181	<0.001
SFA (g/kg)	0.32±0.12	0.31	0.24±0.10	0.21	t=-4.094 df=181	<0.001
MUFA (g)	21.85±7.90	20.82	16.55±6.21	14.48	U=1449.50	<0.001
MUFA (g/kg)	0.32±0.12	0.30	0.27±0.10	0.27	U=2175.00	0.014
PUFA (g)	16.51±8.19	14.94	11.42±5.72	10.66	U=1779.00	<0.001
PUFA (g/kg)	0.24±0.12	0.22	0.19±0.10	0.17	t=1.13 df=181	0.010
Dietary cholesterol (mg)	262.19±159.77	245.12	133.30±109.03	75.65	U=2668.00	<0.001
Fiber (g)	19.65±7.36	19.07	12.00±5.56	11.90	t=-6.16 df=181	<0.001
Vitamin A (µg)	885.79±720.42	645.82	598.07±450.31	457.19	U=1994.50	0.020
Vitamin E (mg)	16.20±8.97	14.72	11.24±6.45	10.43	U=1941.00	0.010
Vitamin B1 (mg)	0.81±0.26	0.78	0.48±0.19	0.46	t=-7.47 df=181	<0.001
Vitamin B2 (mg)	1.21±0.42	1.15	0.73±0.31	0.71	U=945.50	<0.001
Niacin (mg)	12.88±6.26	11.59	7.11±3.67	5.96	U=1035.50	<0.001
Vitamin B6 (mg)	1.21±0.43	1.13	0.71±0.39	0.65	U=1020.50	<0.001
Folate (µg)	279.88±120.38	263.40	182.17±100.72	159.67	U=1381.00	<0.001
Vitamin B12 (mg)	4.10±3.07	3.28	2.28±1.69	1.85	U=1594.00	<0.001
Sodium (mg)	1557.29±802.74	1399.80	1234.21±504.81	1118.55	U=2223.00	0.030
Potassium (mg)	2219.02±773.89	2120.06	1428.82±690.11	1325.10	U=2253.00	0.030
Calcium (mg)	653.38±256.92	635.48	445.89±188.6	443.69	U=131.00	<0.001
Magnesium (mg)	259.55±91.35	239.62	163.13±67.45	150.60	t=-6.28 df=181	<0.001
Iron (mg)	9.94±3.31	9.68	6.01±2.60	5.26	U=1033.00	<0.001
Zinc (mg)	9.20±2.59	8.69	6.11±2.58	5.73	U=927.50	<0.001

[A]: Mann-Whitney U test, [B]: Independent samples t-test

p<0.001, OR=4.111; p<0.001, OR=0.887; p<0.05, OR=0.992; p<0.001, OR=0.853; p<0.001, OR=0.931; p<0.001, OR=0.964; p<0.001, respectively); however, multivariate analysis (enter method) revealed that depression, daily protein intake, and living arrangement are correlated with anorexia of aging (OR=3.919, p=0.004; OR=0.331 p=0.037; OR=0.035, p=0.043). Table 3 summarizes the results of binary logistic regression analysis.

Discussion

The relationship between anorexia of aging and dietary intake was examined in the current study. Elderly adults with anorexia of aging had a lower intake of macronutrients and micronutrients than their counterparts without anorexia of aging. Moreover, multivariate logistic regression analysis revealed that anorexia of aging had an effect on living arrangement, depression, and daily protein intake. The prevalence rate of anorexia was 22.4% among elder adults in this study. In a systematic review, it was determined that the prevalence rate of anorexia of aging ranged between 13.0% and 21.2% in this population (26). This finding is compatible with previous studies reporting that 21.5-30.1% of community dwelling elder adults in Turkey suffered from poor appetite (19,20,27).

The presence of acute and chronic diseases and the related medication may affect the anorexia of aging (28). The rate of diabetic elderly adults was higher in the participants without anorexia of aging. This may be due to the type of diabetes drugs of the participants. For instance, insulin may result in weight gain and control blood glucose levels. This can be associated with reduction in energy loss via glycosuria, the anabolic effects of insulin, and a resulting increase in food intake (29). However, metformin or glucagon-like peptide-1 receptor agonists (GLP-1 RAs) used to treat type 2 diabetes may lead to weight loss. Metformin-associated weight loss is caused by the modulation of hypothalamic appetite-regulatory centers and alteration in the gut microbiome. GLP-1RAs suppress the appetite and feeling of hunger, slow the release of food from the stomach, and boost the feeling of fullness after eating (30).

Table 3. Risk factors predicting anorexia aging by binary logistic regression analysis

	Univariate		Multivariate (enter)	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.26 (1.163-1.365)	**<0.001**	1.473 (0.989-2.193)	0.052
Gender (Ref.=Male)				
Female	1.924 (0.922-4.015)	0.081	3.142 (0.027-3.872)	0.317
Marital status (Ref.= single)				
Married	0.393 (0.114-1.353)	0.139	0.016 (0-1.466)	0.073
Divorced/widowed	0.343 (0.094-1.258)	0.107	0.073 (0.002-3.314)	0.179
Living arrangements (Ref: Living alone)				
Living with someone	0.750 (0.291-1993)	0.552	0.035 (0.001-0.904)	**0.043**
Polypharmacy (Ref: Four or less medication)				
Five or more medication	1.109 (0.491-2.503)	0.804	0.574 (0.027-12.087)	0.721
Depression (Ref: Absent)				
Present	4.111 (2.199-7.122)	**<0.001**	3.919 (2.755-6.738)	**0.004**
Hypertension (Ref: Absent)				
Present	0.505 (0.242-1.054)	0.069	4.775 (0.692-7.474)	0.085
Hyperlipidemia (Ref: Absent)				
Present	0.632 (0.306-1.305)	0.215	0.493 (0.123-2.618)	0.355
Diabetes (Ref: Absent)				
Present	0.249 (0.108-0.577)	0.081	0.002 (0.003-0.124)	0.062
BMI	0.887 (0.800-0.983)	**0.022**	1.229 (0.869-1.770	0.195
Energy	0.992 (0.990-0.994)	**<0.001**	1.219 (0.978-1.521)	0.267
Protein	0.853 (0.811-0.899)	**<0.001**	0.331 (0.117-0.936)	**0.037**
Fat	0.931 (0.906-0.957)	**<0.001**	0.166 (0.023-1.173)	0.072
Carbohydrate	0.964 (0.953-0.976)	**<0.001**	0.432 (0.175-1.069)	0.069

Ref: Reference group, BMI: Body mass index, CI: Confidence interval, OR: Odds ratio, **bold values are for p<0.05**

Decreasing dietary intake induced by anorexia of aging has been investigated in a limited number of studies (31-33) on dietary issues and loss of appetite. Van Der Meij et al. (33), reported that intake of calories, proteins, and fibers was lower in elderly adults with poor appetite. Another study revealed that Brazilian elderly adults with anorexia of aging had lower intake of energy, carbohydrates, proteins and lipids as well as fibers, iron and zinc (32). In their study, Donini et al. (31), determined that patients suffering from anorexia of aging consumed less mainly meat, fish, eggs, and fruit and vegetables, and slightly cereals. Results of this study are compatible with these previous reports saying that elderly adults with anorexia of aging had the decreased dietary intake of energy, protein, fat, carbohydrate, vitamin A, vitamin E, vitamin B1, vitamin B2, niacin, vitamin B6, Vitamin B12, and folate as well as calcium, sodium, potassium, iron, and zinc.

The related studies have reported that reduced food intake is frequently seen with aging thus it is crucial for this vulnerable group to achieve optimal nutritional intake in order to satisfy macronutrient and micronutrient needs and achieve maximum prospects of good health (34). elderly adults are suggested to have an energy intake of approximately 30 kcal/kg/day (24-36 kcal/kg/day) and if they are underweight, then more than 30 kcal/kg/day may be suitable to meet energy requirements (35). Energy intake, when compared with the recommended energy intake, was lower in elderly adults with anorexia of aging (16.62±4.16 kcal/kg/day); whereas, elderly adults without anorexia of aging had an energy intake at its lower limit (24.96±5.13 kcal/kg/day).

Dietary protein is crucial to maintain muscle mass through the promotion of muscle protein synthesis, cognitive and body functions and the immune system (36). The recommendations of the PROT-AGE study group and the European Society for Clinical Nutrition and Metabolism are intakes of 1-1.2 g/kg/day for healthy elderly adults, up to 1.5 g/kg/day for elderly people with acute or chronic disease and up to 2 g/kg/day for elderly people suffering from malnourishment (37). Elderly adults with anorexia of aging consumed almost half the recommended protein intake, while elderly adults without anorexia of aging consumed the lower limit of the recommended protein intake.

During the early stages of age-related anorexia, people tend to lose weight, body fat, muscle/bone mass, bodily functions, and even micronutrients because they consume less energy and fewer nutrients (38). Deficiency of vitamin B6, B12 and folate influences cognitive functioning and depressive symptoms are also prevalent among elderly adults (39,40). Low calcium intake is more likely to cause osteoporosis and cardiovascular diseases (41). Magnesium deficiency results in low bone mineral density, high levels of C-reactive protein indicative of systemic inflammation, and an increased risk for the metabolic syndrome (42,43). Iron deficiency causes numerous health complications, such as deterioration of physical functions, increased occurrence of falls, frailty, cognitive impairment, and mortality (44). Zinc is mostly used by the body takes part in immune responses, hormone production, bone mineralization, cognitive functions, taste and many other functions. A considerably zinc deficiency in the elderly adults may bring along many complications and increase the risk of morbidity (45).

Anorexia of aging is considered as one of indicators for a variety of geriatric syndromes. Since decreased dietary intake in elderly individuals frequently results in decreased physical activity and reduced muscle mass, they become more vulnerable and may develop secondary complications (e.g., sarcopenia, frailty, comorbidities or disability) (10,11,38). Therefore, adequacy of food intake is essential to slow down the process resulting in anorexia of aging (32).

Moreover, living arrangement, depression and protein intake were the important predictors in multivariate model for anorexia of aging. In a previous study (46), it was determined that elderly adults who were living alone and so eating alone had poor appetite 1.75 times more. Likewise, in this study, it was found that people living alone had a more poor appetite than those living with someone. Mudge et al. (47), stated that nutritional intake was assessed by measuring plate waste, and in a multivariate reported, poor appetite was the strongest predictor of inadequate nutritional intake. Poor appetite can lead to low dietary intake and malnutrition among elderly adults (13) and psychological factors such as depression and well-being are related to appetite (14).

Although previous studies conducted with different populations have yielded similar results, the findings of this study would contribute to the current literature since they reveal that elderly adults with anorexia of aging had lower intake in terms of macronutrients and micronutrients.

Study Limitations

The most important limitation of this study is that the analyses were performed with data from a relatively small sample. It is recommended to conduct prospective studies examining the effects of specific nutrition interventions on anorexia of aging and to support them by laboratory and clinical data in larger populations.

Conclusion

In this study, elderly adults with anorexia of aging had a lower food intake of macronutrients and micronutrients. Optimizing nutritional status is and also improving other factors affecting anorexia of aging can reduce the risk of functional decline in the elderly population. That, in turn, means that anorexia would no longer be inevitable.

Ethics

Ethics Committee Approval: The protocol of the study was approved by the Gaziantep Islam Science and Technology University Ethics Committee (2022/102). The principles of the Declaration of Helsinki were followed to conduct the study.

Informed Consent: All participants signed the informed consent form.

Peer-review: Externally peer-reviewed.

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References

1. TÜİK. Available from: https://data.tuik.gov.tr/Bulten/Index?p=Istatistiklerle-Yaslilar-2021-45636
2. Wilson M-MG, Thomas DR, Rubenstein LZ, Chibnall JT, Anderson S, Baxi A, Diebold MR, Morley JE. Appetite assessment: simple appetite questionnaire predicts weight loss in community-dwelling adults and nursing home residents. Am J Clin Nutr 2005;82:1074-1081.
3. Di Francesco V, Fantin F, Omizzolo F, Residori L, Bissoli L, Bosello O, Zamboni M. The anorexia of aging. Dig Dis 2007;25:129-137.
4. Landi F, Calvani R, Tosato M, Martone AM, Ortolani E, Savera G, Sisto A, Marzetti E. Anorexia of aging: risk factors, consequences, and potential treatments. Nutrients 2016;8:69.
5. Merchant RA, Woo J, Morley J. Anorexia of Ageing: Pathway to Frailty and Sarcopenia. J Nutr Health Aging 2022;26:1-3.
6. Morley J, Silver AJ. Anorexia in the elderly. Neurobiol Aging 1988;9:9-16.
7. Morley JE. Anorexia, sarcopenia, and aging. Nutrition 2001;17:660-663.
8. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-M157.
9. Tsutsumimoto K, Doi T, Makizako H, Hotta R, Nakakubo S, Makino K, Suzuki T, Shimada H. The association between anorexia of aging and physical frailty: Results from the national center for geriatrics and gerontology's study of geriatric syndromes. Maturitas 2017;97:32-37.
10. Tsutsumimoto K, Doi T, Makizako H, Hotta R, Nakakubo S, Makino K, Suzuki T, Shimada H. Aging-related anorexia and its association with disability and frailty. J Cachexia Sarcopenia Muscle 2018;9:834-843.
11. Tsutsumimoto K, Doi T, Nakakubo S, Kim M, Kurita S, Ishii H, Suzuki T, Shimada H. Association between anorexia of ageing and sarcopenia among Japanese older adults. J Cachexia Sarcopenia Muscle 2020;11:1250-1257.
12. Morley JE. Pathophysiology of the anorexia of aging. Curr Opin Clin Nutr Metab Care 2013;16:27-32.
13. Lau S, Pek K, Chew J, Lim JP, Ismail NH, Ding YY, Cesari M, Lim WS. The simplified nutritional appetite questionnaire (SNAQ) as a screening tool for risk of malnutrition: optimal cutoff, factor structure, and validation in healthy community-dwelling older adults. Nutrients 2020;12:2885.
14. Rolland Y, Perrin A, Gardette V, Filhol N, Vellas B. Screening older people at risk of malnutrition or malnourished using the simplified nutritional appetite questionnaire (SNAQ): A comparison with the mini-nutritional assessment (MNA) tool. J Am Med Dir Assoc 2012;13:31-34.
15. Wang T, Shen J. Usefulness of simplified nutritional appetite questionnaire (SNAQ) in appetite assessment in elder patients with liver cirrhosis. J Nutr Health Aging 2018;22:911-915.
16. Wleklik M, Lisiak M, Andreae C, Uchmanowicz I. Psychometric evaluation of appetite questionnaires in elderly polish patients with heart failure. Patient Prefer Adherence 2019;13:1751.
17. Yaxley A, Crotty M, Miller M. Identifying malnutrition in an elderly ambulatory rehabilitation population: agreement between mini nutritional assessment and validated screening tools. Healthcare (Basel) 2015;3:822-829.
18. Hanisah R, Shahar S, Lee F. Validation of screening tools to assess appetite among geriatric patients. J Nutr Health Aging 2012;16:660-665.
19. İlhan B, Bahat G, Oren M, Kiliç C, Durmazoglu S, Karan M. Reliability and validity of Turkish version of the simplified nutritional appetite questionnaire (SNAQ). J Nutr Health Aging 2018;22:1039-1044.
20. Akın S, Ozer FF, Zararsız GE, Şafak ED, Mucuk S, Göçer Ş, Mazıcıoğlu M. Validity of simplified nutritional appetite questionnaire for Turkish community-dwelling elderly and determining cut-off according to mini nutritional assessment. Arch Gerontol Geriatr 2019;83:31-36.
21. Fisberg RM, Marchioni DML, Colucci ACA. Assessment of food consumption and nutrient intake in clinical practice. Arq Bras Endocrinol Metabol 2009;53:617-624.
22. Rakıcıoğlu N, Acar Tek N, Ayaz A, Pekcan G. Yemek ve Besin Fotoğraf Kataloğu Ölçü ve Miktarlar, 4th ed. Ata Ofset Matbaacılık, Ankara, 2014.
23. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, Leirer VO. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982;17:37-49.
24. Ertan T, Eker E. Reliability and validity of the geriatric depression scale in Turkish elderly population. Int Psychogeriatr 2000;12:163-172.
25. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatr 2017;17:1-10.
26. Malafarina V, Uriz-Otano F, Gil-Guerrero L, Iniesta R. The anorexia of ageing: physiopathology, prevalence, associated comorbidity and mortality. A systematic review. Maturitas 2013;74:293-302.
27. Acar Tek N, Karaçil-Ermumcu M. Determinants of health related quality of life in home dwelling elderly population: appetite and nutritional status. J Nutr Health Aging 2018;22:996-1002.
28. Landi F, Picca A, Calvani R, Marzetti E. Anorexia of aging: assessment and management. Clin Geriatr Med 2017;33:315-323.
29. Schneider E, Spetter MS, Martin E, Sapey E, Yip KP, Manolopoulos KN, Tahrani AA, Thomas JM, Lee M, Hallschmid M, Rotshtein P, Dourish CT, Higgs S. The effect of intranasal insulin on appetite and mood in women with and without obesity: an experimental medicine study. Int J Obes (Lond) 2022;46:1319-1327.
30. Ard J, Fitch A, Fruh S, Herman L. Weight loss and maintenance related to the mechanism of action of glucagon-like peptide 1 receptor agonists. Adv Ther 2021;38:2821-2839.
31. Donini LM, Poggiogalle E, Piredda M, Pinto A, Barbagallo M, Cucinotta D, Sergi G. Anorexia and eating patterns in the elderly. PLoS One 2013;8:e63539.
32. Hara L, Freiria C, Silva G, Fattori A, Corona L. Anorexia of aging associated with nutrients intake in brazilian elderly. J Nutr Health Aging 2019;23:606-613.
33. Van Der Meij BS, Wijnhoven HA, Lee JS, Houston DK, Hue T, Harris TB, Kritchevsky SB, Newman AB, Visser M. Poor appetite and dietary intake in community-dwelling older adults. J Am Geriatr Soc 2017;65:2190-2197.
34. O'Connell ML, Coppinger T, Lacey S, Arsenic T, McCarthy AL. The nutritional status and dietary intake of free-living seniors: A cross-sectional study. Clin Nutr ESPEN 2021;43:478-486.
35. Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, Kiesswetter E, Maggio M, Raynaud-Simon A, Sieber CC, Sobotka L, van Asselt D, Wirth R, Bischoff SC. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr 2019;38:10-47.
36. Tuttiett ER, Green DJ, Stevenson EJ, Hill TR, Corfe BM, Williams EA. Short-term protein supplementation does not alter energy intake, macronutrient intake and appetite in 50-75 year old adults. Nutrients 2021;13:1711.

37. Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft AJ, Morley JE, Phillips S, Sieber C, Stehle P, Teta D, Visvanathan R, Volpi E, Boirie Y. Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. J Am Med Dir Assoc 2013;14:542-559.

38. Muscaritoli M, Anker S, Argilés J, Aversa Z, Bauer JM, Biolo G, Boirie Y, Bosaeus I, Cederholm T, Costelli P, Fearon KC, Laviano A, Maggio M, Rossi Fanelli F, Schneider SM, Schols A, Sieber CC. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG)"cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics". Clin Nutr 2010;29:154-159.

39. Beydoun MA, Shroff MR, Beydoun HA, Zonderman AB. Serum folate, vitamin B-12 and homocysteine and their association with depressive symptoms among US adults. Psychosom Med 2010;72:862.

40. Kennedy DO. B vitamins and the brain: mechanisms, dose and efficacy-a review. Nutrients 2016;8:68.

41. Nieves JW. Osteoporosis: the role of micronutrients. Am J Clin Nutr 2005;81:1232-1239.

42. Ryder KM, Shorr RI, Bush AJ, Kritchevsky SB, Harris T, Stone K, Cauley J, Tylavsky FA. Magnesium intake from food and supplements is associated with bone mineral density in healthy older white subjects. J Am Geriatr Soc 2005;53:1875-1880.

43. Song Y, Ridker PM, Manson JE, Cook NR, Buring JE, Liu S. Magnesium intake, C-reactive protein, and the prevalence of metabolic syndrome in middle-aged and older US women. Diabetes Care 2005;28:1438-1444.

44. Price EA, Mehra R, Holmes TH, Schrier SL. Anemia in older persons: etiology and evaluation. Blood Cells Mol Dis 2011;46:159-165.

45. Stewart-Knox B, Simpson E, Parr H, Rae G, Polito A, Intorre F, Meunier N, Andriollo-Sanchez M, O'Connor JM, Coudray C, Strain JJ. Zinc status and taste acuity in older Europeans: the ZENITH study. Eur J Clin Nutr 2005;59:31-36.

46. Mikami Y, Motokawa K, Shirobe M, Edahiro A, Ohara Y, Iwasaki M, Hayakawa M, Watanabe Y, Inagaki H, Kim H, Shinkai S, Awata S, Hirano H. Relationship between eating alone and poor appetite using the simplified nutritional appetite questionnaire. Nutrients 2022;14:337.

47. Mudge AM, Ross LJ, Young AM, Isenring EA, Banks MD. Helping understand nutritional gaps in the elderly (HUNGER): a prospective study of patient factors associated with inadequate nutritional intake in older medical inpatients. Clin Nutr 2011;30:320-325.

ORIGINAL RESEARCH

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Sleep Quality and Factors Affect It in Caregivers of People with Dementia: A Cross-sectional Study

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Abstract

Objective: The aim of this study was to determine the sleep quality of caregivers of people with dementia (PwD) and the factors affecting it.

Materials and Methods: A cross-sectional study design was used. A total of 119 home-dwelling PwD and their primary caregivers were recruited from February-July 2019. Socio-demographic characteristics form, Pittsburg sleep quality, mini mental state examination (MMSE), neuropsychiatric inventory (NPI), activities of daily Living (ADL) and instrumental ADL (IADL), perceived stress scale (PSS), caregiver burden inventory (CBI), Beck depression inventory (BDI), and Charlson comorbidity index (CCI) were used. Descriptive statistics, t-test, Pearson's correlation and multinominal regression analysis were performed using SPSS version 25.0.

Results: The sleep quality of the caregivers was poor (10.70±3.663). Patients' MMSE, NPI, ADL and IADL; caregivers' PSS, CBI, BDI, and CCI together were a significant predictor of caregiver sleep quality ($F=17.020$; $p<0.001$). Eight variables together account for 55% of the variance in sleep quality. Predictive order of importance of variables on caregiver sleep quality was in the form of CCI ($\beta=-0.396$), BDI ($\beta=0.292$), MMSE score ($\beta=-0.284$), NPI ($\beta=-0.239$), PSS ($\beta=0.196$), CBI ($\beta=0.108$), ADL ($\beta=-0.080$), and IADL ($\beta=0.052$).

Conclusion: By determining the sleep quality and factors affecting of caregivers, it is considered that the caregivers will provide an opportunity for projects that will increase the sleep quality interventionally. Interventions to reduce caregiver depression, stress and burden can improve caregiver sleep quality; in addition, it is suggested that they will contribute to the sleep quality of caregivers in their attempts to improve the behavioral and cognitive functions of PwD.

Keywords: Sleep, caregivers, dementia

Introduction

The caregiving experience is usually seen as a chronic stressor with physical and psychological consequences (1). Caring for people with dementia (PwD) is like working in a full-time job, with family members spending an average of 21.9 hours per week caring for PwD. Caring is both emotionally and cognitively demanding and negatively affects caregivers' health (2). Sleep disturbance is a one of the significant health problems for a majority of caregivers of PwD (2,3). The prevalence rate of sleep problems was 9.4% among caregivers of PwD (4).

Since PwD stay awake at night and sleep during the day, their sleep-wake rhythms are disrupted, so when caregivers try to persuade the dementia patient to go back to bed, they will have to wake up many times and renounce their own sleep (5,6). When the caregivers cannot get enough sleep, their quality of life decreases, health indicators such as cortisol levels are adversely affected, and the risk of cardiovascular disease, obesity and diabetes increases (7). The frequency of depression and anxiety increases and cognitive function declines in caregivers with poor sleep quality (8-10). Sleep problems are significantly and positively associated with care recipients' disruptive behaviors (11). In addition these, it is stated that the main factor for 70% of caregivers to move their loved ones away from home and place them in nursing homes is insomnia (6). In a study conducted with individuals who had previously

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given care to PwD, caregivers quoted that they experienced insomnia, had nightmares, and could not reach pre-care sleep quality for ten years after care (7). Demographic characteristics of caregivers such as being female, highly educated caregivers are also independent predictors for carers' reporting greater sleep disturbance (5,9).

There is many of research have been found to determine the sleep of caregivers and the factors affecting it. But there are very few studies indicated both patients' and caregivers' related variables (8,11). Thus, in this study focused to identify the comprehensive factors of caregivers' sleep quality. In addition to this, there is a current systematic review which was investigate the effects of the sleep interventions for informal caregivers of PwD and none of the studies which was examined on the review from Turkish population (12). To the best of our knowledge, only one study (13) has reported findings of sleep quality of caregivers of PwD in Turkey. This can be a reason in the systematic review, there were no results of sleep interventions for caregivers of PwD from Turkey. In order to plan interventions to regulate and improve the sleep quality in caregivers PwD, it is necessary to determine the sleep quality of the caregivers and the comprehensive factors affecting them.

Materials and Methods

A cross sectional study design was used in this study.

Participants

Non-probability convenience sampling was used. Family members who gave primary care to PwD according to DSM-IV diagnostic criteria, lived in the same house with the patients, provided care for at least six months, and volunteered to participate in the study were included. The sample of the study consisted of 119 caregivers who applied to the dementia outpatient clinic of a university hospital between February-July 2019. A sample size of 119, effect size of 0.20, and alpha value of 0.05 were considered, and the power of study was found to be 0.83 by using G. Power.

Measures

Socio-demographic characteristics form

The form was prepared to obtain the socio-demographic information pf PwD and their caregivers (2,3,7,8,13).

Collected from PwD

Mini mental state examination (MMSE): It is used to access the cognitive function comprises orientation, learning, short-term memory, language use, comprehension, and basic motor skills. The total score ranges from 0 to 30. A low score indicates high cognitive impairment (14).

Neuropsychiatric inventory (NPI): NPI was used to evaluate the presence and severity of neuropsychiatric symptoms. The scores range from 0 to 144, with high scores corresponding to severe behavioral disorders (15).

Activities of daily living (ADL) and instrumental ADL (IADL): The ability of PwD to perform functional activities was assessed with Barthel ADL and Lawton's IADL.

Collected from Caregivers

Charlson comorbidity index (CCI): It was scored according to the weighted comorbidity index developed by Charlson et al. (16). The score obtained as a result of the scoring process for a patient to have more than one disease is called the Charlson comorbidity score (16).

Beck depression inventory (BDI): It was developed by Beck et al. (17) to measure the emotional, cognitive and motivational symptoms of depression in adolescents and adults. A minimum of zero and a maximum of 63 points can be obtained in the BDI inventory, and a high score indicates an excess of depression severity (18).

Perceived stress scale (PSS): It was developed by Cohen et al. (19). Consisting of 14 items in total, PSS is designed to measure how stressful a person's life is perceived to be. A score of 0-56 can be obtained in the PSS, and a high score indicates an excess of stress perception (19).

Caregiver burden inventory (CBI): It is a tool developed to measure the impact of caregiving on caregivers and their relatives (20). The inventory is a 24-item Likert-type (0-4) scale. The total score of each individual varies between 0 and 100. A high score indicates a high degree of burden, and a low score indicates a low degree of burden (21).

Pittsburg sleep quality (PSQ): It was developed by Buysse et al. (22) to determine sleep quality. The scale includes a total of 24 questions (19 of these self-evaluation). They determine the duration of sleep, the frequency and severity of special problems related to sleep latensive sleep. The 18 items scored were grouped into 7 component scores. Some of the components consist of a single substance, while others are obtained by grouping several substances. Each item is evaluated with a score between 0-3 points. A 0-21 points can be obtained from the scale. A total PSQI score of 5 or more indicates poor sleep quality.

Data collection

The study was conducted at a dementia outpatient clinic during follow-up of the PwD in the west part of Turkey. The caregivers had a face-to-face contact with the researchers lasted for 50 min. In the scales collected from PwD, the scores of the mental, behavioral and functional status evaluation scales made by

their neurologist during the outpatient clinic visits were taken into account.

Statistics

Descriptive statistics, number, percentage distributions and correlation coefficients were evaluated. Multiple regression analysis was performed to determine the factors affecting the sleep quality of caregivers. Before the multiple regression analysis, the correlation of the influencing factors and the dependent variable with each other was determined using the multiple correlation test. The variance inflation factor (VIF) and tolerance were used to detect multicollinearity between the independent variables in the regression model. The independent variables with VIF>10 were removed from the model, and tolerance was less than 0.20. For all analysis, the level of statistical significance was set at $p \leq 0.05$. The SPSS 25.0 program was used to evaluate the data in the study.

Ethics

This study was carried out according to the Declaration of Helsinki (as revised 2013). This study was approved by the Ethics Committee of Dokuz Eylül University (2019/12-17, 2019.05.08). The purpose was explained to the caregivers participating in the study and their verbal and written consent were obtained.

Results

The socio-demographic and clinical characteristics of the PwD and their caregivers were shown in Table 1. The PSQ score of 119 caregivers of PwD was determined as 10.70±3.66 (1-17). A total PSQ score of five or more indicates poor sleep quality. The sleep quality of caregivers was compared according to the descriptive characteristics of PwD, and the results were given in Table 2. Sleep quality among the descriptive characteristics of caregivers were compared and the results were given in Table 3.

The relationship and significance between the clinical characteristics of PwD and their caregivers and sleep quality scores were shown in Table 4. A weak negative correlation was found between the MMSE of PwD and the sleep quality of caregivers (r=-0.333; p=0.000). A weak positive correlation was found between the sleep quality of NPI, ADL and IADL caregivers of PwD (r=0.302; r=0.234; r=0.269; p=0.001; p=0.015; p=0.003). A moderate positive correlation was found between caregivers' PSS, BDI and CCI and sleep quality (r=0.430; r=0.498; r=0.436; p<0.001). There was a weak positive correlation between CBI and sleep quality (r=0.397; p<0.001).

Multiple regression analysis was performed to predict the sleep quality of the caregivers according to the MMSE, NPI, ADL/IADL of PwD and the caregivers' PSS, CBI, BDI and CCI, and the results were given in Table 5. According to the results obtained, patients' MMSE, NPI, IADL, ADL, caregivers' PSS, CBI, BDI and

Table 1. Descriptive characteristics of people with dementia and caregivers

People with dementia	n	%	
Age			
65-69	13	10.9	
70-74	22	18.5	
75-79	29	24.4	
80 and above	55	46.2	
Gender			
Female	78	65.5	
Male	41	34.5	
Education level			
Illiterate	10	8.4	
Literate	13	10.9	
Primary school	31	26.1	
Secondary school	14	11.8	
High school graduate	27	22.7	
University graduate	24	20.2	
Marital status			
Married	58	48.7	
Divorced/widowed/living apart	60	50.4	
Acute/chronic disease			
Yes	59	49.6	
No	60	50.4	
Dementia stage			
1. Stage	48	40.3	
2. Stage	35	29.4	
3. Stage	36	30.3	
Years of diagnosed with dementia			
Less than 1 year	36	30.3	
1-5 years	51	42.9	
6 years and above	32	26.9	
Total	**119**	**100**	
	X ± SD	**Min**	**Max**
Mini mental state examination	16.65±6.68	0	28
Neuropsychiatric inventory	50.20±28.19	10	130
Barthel activities of daily living	12.74±6.45	3	24
Lawton's instrumental activities of daily living	8.96±4.62	1	18
Caregivers	**n**	**%**	
Age			
30-39	12	10.0	
40-49	22	18.5	
50 and above	85	71.4	
Gender			
Female	91	76.5	
Male	28	23.5	

Table 1. Continued			
Education level			
Literate	8	6.7	
Primary school	10	8.4	
Secondary school	14	11.8	
High school	25	21.0	
University	62	52.1	
Marital status			
Never married	21	17.6	
Married	79	66.4	
Divorced/widowed/living apart	19	16.0	
Antidepressant use			
Yes	20	16.8	
No	99	83.2	
Acute/chronic disease			
Yes	89	74.8	
No	30	25.2	
Relationship with patient			
Daughter	48	40.3	
Son	17	14.3	
Wife	28	23.5	
Brother	26	21.8	
Duration of living with the patient			
Since birth	11	9.2	
1-10 years	72	60.5	
11-20 years	9	7.6	
21-30 years	13	10.9	
31 years and above	14	11.8	
	X ± SD	**Min**	**Max**
Beck depression inventory	33.33±7.857	4	47
Perceived stress scale	44.02±15.405	3	74
Caregiver burden inventory	25.72±11.938	0	45
Charlson comorbid index	1.84±0.850	0	3
Pittsburgh sleep quality	10.70±3.663	1	17
SD: Standard deviation			

CCI together were a significant predictor of caregiver sleep quality (F=17,020; p<0.001). Eight variables together account for 55% of the variance in sleep quality. Predictive order of importance of variables on caregiver sleep quality was in the form of CCI (β=-0.396), BDI (β=0.292), MMSE score (β=-0.284), NPI (β=-0.239), PSS (β=0.196), CBI (β=0.108), ADL (β=-0.080), and IADL (β=0.052).

Discussion

Sleep quality of the caregivers of the PwD in this study was poor. This finding is similar to other studies (2,3,5,7,8,10). Goa et al. (2) reported that the sleep quality of caregivers of PwD was significantly lower than that of non-caregivers in their meta-analysis. Obtaining similar results in the international literature is thought to be closely related to the dementia care process. Having a PwD in the same house undoubtedly requires day and night care. Since caregivers are constantly on the alert for their patients, it is considered that they experience constant interruptions in their sleep. In addition, the challenges of caregiving are well-known in the literature. It is thought that the difficulties and psychological outcomes of care may adversely affect the sleep quality of caregivers. In the current

Table 2. Comparison of caregivers' Pittsburgh sleep quality scale scores based on descriptive characteristics of people with dementia

Characteristics of people with dementia	Pittsburgh sleep quality scale			Z/X²	p
	X ± SD	Min	Max		
Age					
65-69	8.15±3.43	2	15	7.894[b]	0.048
70-74	10.32±3.83	4	16		
75-79	11.28±3.59	3	16		
80 and above	11.15±3.50	1	17		
Gender					
Female	10.60±3.90	1	17	-0.104[a]	0.917
Male	10.88±3.19	4	16		
Education level					
Illiterate	10.60±4.81	2	17	2.829[b]	0.729
Literate	10.08±5.25	1	16		
Primary school	11.23±3.21	3	16		
Secondary school	9.36±3.50	4	15		
High school graduate	10.78±3.65	4	16		
University graduate	11.08±2.84	5	16		
Marrital status				1.933[b]	0.380
Married	11.10±3.62	2	17		
Divorced/widowed/ living apart	10.27±3.70	1	16		
Acute/chronic disease					
Yes	11.08±3.60	3	17	-1.070[a]	0.285
No	10.32±3.70	1	16		
Dementia stage					
CDR[c] 1	8.96±3.47	2	16	19.862[b]	0.000
CDR 2	11.97±3.57	1	16		
CDR 3	11.78±3.09	4	17		
Year duration with Dementia					
Less than 1 years	9.03±3.722	2	17	12.807[b]	0.002
1-5 years	11.67±3.502	1	16		
6 years and above	11.03±3.277	3	15		

[a]Mann-Whitney U test, [b]Chi-square test, [c]Clinical dementia rating, SD: Standard deviation

Table 3. Comparison of sleep quality according to the descriptive characteristics of caregivers

Characteristics of caregivers	Pittsburgh sleep quality scale			Z/X^2	p
	X ± SD	Min	Max		
Age					
30-39	10.09±3.70	5	15	6.301[b]	0.098
40-49	8.91±4.12	1	15		
50 and above	11.24±3.43	3	17		
Gender					
Female	10.51±3.79	1	17	-0.934[a]	0.350
Male	11.32±3.17	3	15		
Education level					
Literate	11.43±4.86	3	17	2.746[b]	0.739
Primary school	11.40±4.11	2	16		
Secondary school	10.07±3.33	4	15		
High school graduate	10.36±3.94	1	16		
University graduate	10.73±3.48	3	16		
Marital					
Never married	10.52±3.78	3	16	1.833[b]	0.400
Married	10.95±3.72	1	17		
Divorced/widowed/ living apart	9.84±3.27	2	14		
Acute/chronic disease					
Yes	10.54±3.36	2	17	-1.275[a]	0.202
No	11.17±4.45	1	16		
Antidepressant use					
Yes	12.15±3.45	5	17	-1.852[a]	0.064
No	10.40±3.65	1	16		
Relationship with patients					
Daughter	10.90±4.08	1	17	3.609[b]	0.307
Son	11.94±2.56	8	15		
Wife	10.43±3.43	3	16		
Brother	9.81±3.61	3	15		
Duration of living with the elderly					
Since birth	9.64±4.82	3	16	1.308[b]	0.860
1-10 years	10.85±3.53	1	16		
11-20 years	10.00±4.30	2	16		
21-30 years	11.62±2.75	7	16		
31 years and above	10.36±3.83	3	17		

[a]Mann-Whitney U test, [b]Chi-square test, SD: Standard deviation

study, most of the caregivers are over 50 years old and it is known that depending on aging, sleep quality decreases, total sleep duration shortens, night awakenings increase, rapid eye movement and slow wave sleep decreases (23). Therefore, it may be concluded that the sleep quality of the caregivers is low.

There was no significant relationship between the age, gender, educational status, marital status, presence of acute/chronic disease parameters and total PSQ scores of PwD similar to the findings of Chiu et al. (24) and Simpson and Carter (25). Rather than descriptive characteristics of the PwD, such as age, gender, and educational status, the variables of dementia stage and the duration of diagnosis affect the sleep of caregivers.

Table 4. The relationship between the quality of sleep of the caregiver and the determined clinical characteristics of people with dementia and caregivers

Scales of determined clinical characteristics	Pittsburgh sleep quality	
	r	p
Mini mental state examination	-0.333	0.000
Neuropsychiatric inventory	0.302	0.001
Lawton's instrumental activities of daily living	0.269	0.003
Barthel activities of daily living	0.234	0.010
Perceived stress scale	0.430	0.000
Beck depression inventory	0.498	0.000
Caregivers burden inventory	0.397	0.000
Charlson comorbidity index	0.436	0.000

For caregivers, there was no statistically significant difference was found according to the age, gender, education level, marital status, presence of acute/chronic disease, antidepressant use, degree of closeness with the elderly cared for, duration of living with the elderly. In the current literature, studies examining the effects of descriptive characteristics of caregivers of PwD on the sleep quality of caregivers are limited and controversial (5,8,25). Park et al. (8) found the caregivers education was a significant factor on sleep quality. On the other hand, Gibson et al. (5) and Simpson and Carter (25) stated that like in this study caregiver education was not predictor for caregivers sleep quality.

In the study, although there was a weak negative correlation between the MMSE score of PwD and the sleep quality of their caregivers, a weak positive correlation was found between the scores obtained from NPI, from ADL and from IADL, and the sleep quality of caregivers.

Sleep problems of caregivers are strongly positively correlated with patients' neuropsychiatric symptoms (11). Specifically, caregiver sleep disturbance has been associated with patients' sleep disturbances, delusions, hallucinations, and emotional behavioral symptoms (irritation/aggression, depression, and anxiety). Decreased cognitive function and increased behavioral symptoms of PwD can be meaning that there is more and more need for support for patients about assisting personal care, monitoring their safety, comforting them to sleep. It is inevitable that PwD who have decreased cognitive functions, increased behavioral symptoms, and cannot perform their daily living activities are those who are in need of more care. It was concluded that sleep quality might be worse as caregivers may have more difficulty in the face of worsening cognitive,

Table 5. Multiple linear regression analysis to estimate the quality of sleep of the caregiver according to the determined clinical characteristics of individuals with dementia and caregivers

	B	Sh.	β	t	p	R	R^2	F	p
Mini mental state examination	-0.156	0.066	-0.284	-2.343	0.021	0.744	0.553	17.020	0.000
Neuropsychiatric inventory	-0.031	0.020	-0.239	-1.548	0.125				
Lawton's instrumental activities of daily living	0.029	0.165	0.052	0.178	0.859				
Barthel activities of daily living	-0.063	0.200	-0.080	-0.316	0.753				
Perceived stress scale	0.091	0.038	0.196	2.371	0.019				
Beck depression inventory	0.026	0.019	0.108	1.340	0.183				
Caregivers burden inventory	0.090	0.027	0.292	3.346	0.001				
Charlson comorbidity index	5.765	1.026	0.396	5.617	0.000				

functional and behavioral condition.

A moderate positive correlation was determined between the scores of the caregivers from the perceived stress and depression scale and the total score of the PSQ, and the difference was statistically significant. Similarly, Wang et al. (10) showed a weak positive correlation between caregivers' mean total score on PSQ and the score they obtained from the perceived stress scale, and found this relationship statistically significant. Consistently with this research, Park et al. (8) found that the depression was a significant factor on sleep quality in caregivers of PwD. Hamamcı et al. (13) revealed that the depression and anxiety levels of caregivers were related to their PSQ scores. A current, large and robust literature document emphasized the important rate of psychological distress (stress or depressive symptoms) among caregivers of PwD (1).

Peng et al. (3) examined sleep-related factors in caregivers of PwD and concluded that the sleep of caregivers is affected by chronic disease status, depression, caregiver burden, sleep hygiene behaviors. They also reported that caregivers with more chronic diseases and poor sleep hygiene conveyed worse sleep quality, and that poor sleep quality of caregivers disrupted their daytime functionality, causing them to use sleeping pills. Simón et al. (26) showed that the group of family caregivers who perceived the caregiving burden as high had a higher PSQ total score than the control group and the group of family caregivers who perceived the caregiving burden as low. These results are consistent with the current study. The Burden and comorbidity were associated with caregivers sleep quality. The caregivers have to manage their own illnesses. But most caregivers live more patient-oriented lives than their own. It is thought that this causes more burden and negatively affects the sleep quality of caregivers.

Study Limitations

Data on caregivers' sleep quality were collected through self-reported sleep. Dementia type was not assessed in the study; however, the sleep quality of caregivers may vary depending on the type of dementia. It did not identify exogenous variables such as caffeine intake and environmental factors. In this study, the sleep quality of the patients was not measured. The sample was limited to monocentrically, and therefore the findings may not be generalizable to other parts of Turkey. These limitations could be taken into account in future studies.

Conclusion

It was concluded that the sleep quality of caregivers of PwD was poor. It was found that the sleep quality of the caregivers was not affected by the socio-demographic characteristics of the PwD and the caregivers, but by the MMSE, ADL, IADL and NPI scores of the PwD and the BDI, CBI, PSS, CCI scores of the caregivers.

It is recommended that health professionals should consider the needs of not only the patient but also the caregivers, and that they should pay more attention to their sleep problems by deeming the caregiver as a component in the difficult care process of the PwD. Caregiver burden, stress and depression should be evaluated, and it should be taken into account that the sleep quality of caregivers of PwD who have more behavioral symptoms with increased cognitive impairment and decreased functionality may be worse. Interventions to improve these factors, which we identified as a result of our study, may help improve the sleep quality of caregivers.

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Ethics

Ethics Committee Approval: This study was carried out according to the Declaration of Helsinki (as revised 2013). This study was approved by the Ethics Committee of Dokuz Eylül University (2019/12-17, 2019.05.08).

Informed Consent: The purpose was explained to the caregivers participating in the study and their verbal and written consent were obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.A.S., Concept: B.A.S., Design: B.A.S., Data Collection or Processing: B.E., Analysis or Interpretation: B.A.S., B.E., Literature Search: B.A.S., B.E., Writing: B.A.S., B.E.

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References

1. Schulz R, Beach SR, Czaja SJ, Martire LM, Monin JK. Family caregiving for older adults. Annu Rev Psychol 2020;71,635-659.
2. Goa C, Chapagain NY, Scullin MK. Sleep duration and sleep quality in caregivers of patients with dementia. JAMA Network Open 2019;2:1-15.
3. Peng HL, Lorenz RA, Chan YP. Factors associated with sleep in family caregivers of individuals with dementia. Perspect Psychiatr Care 2018;55:95-102.
4. Li X, Ding D, Zhao Q, Wu W, Xiao Z, Luo J, Yaffe K, Leng Y. Sleep Timing and Risk of Dementia Among the Chinese Elderly in an Urban Community: The Shanghai Aging Study. Front Neurol 2021;12:629507.
5. Gibson R, Helm A, Breheny M, Gander P. "My quiet times": Themes of sleep health among people caring for a family member with dementia. Dementia 2021;20:2024-2040.
6. Ehleringer EH, Kim SJ. The Wearable Lullaby: Improving sleep quality of caregivers of dementia patients. In CHI'13 Extended Abstracts on Human Factors in Computing Systems, 2013;409-414.
7. Corey KL, McCurry MK, Sethares KA, Bourbonniere M, Hirschman KB, Meghani SH. Predictors of psychological distress and sleep quality in former family caregivers of people with dementia. Aging Ment Health 2018;24:233-241.
8. Park H, Kim EK, Jeoung SY, Moon KJ, Lee ES. The comprehensive factors affecting the sleep quality in family caregivers of patients with dementia in the community of South Korea. J Korean Gerontol Nurs 2021;23:85-95.
9. Brewster GS, Molinari V, McCrae C, Beckstead J, D'Aoust R, Rowe M. Cognitive Function and Sleep in Caregivers of Persons Living with Dementia. West J Nurs Res 2022;44:260-268.
10. Wang PC, Yip PK, Chang Y. Self-Efficacy and sleep quality as mediators of perceived stress and memory and behavior problems in the link to dementia caregivers' depression in Taiwan. Clin Gerontol 2016;39:222-239.
11. Jiménez-Gonzalo L, Romero-Moreno R, Pedroso-Chaparro MDS. The role of caregivers' sleep problems in the association between behavioral symptoms of dementia and caregiving depression and anxiety. Behav Sleep Med 2021;19:640-651.
12. Pignatiello GA, Martin R, Kraus N, Gutierrez A, Cusick R, Hickman RL. Sleep Interventions for Informal Caregivers of Persons with Dementia: A Systematic Review. West J Nurs Res 2021;01939459211019033.
13. Hamamcı M, Hacimusalar Y, Karaaslan Ö, İnan LE. [The evaluation of sleep quality of caregivers of dementia patients]. Bozok Medical Journal 2019;9:88-93.
14. Keskinoğlu P, Ucku R, Yener G, Yaka E, Kurt P, Tunca Z. Reliability and validity of revised Turkish version of Mini Mental State Examination (rMMSE-T) in community-dwelling educated and uneducated elderly. Int J Geriatr Psychiatry 2009;24:1242-1250.
15. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The neuropsychiatric inventory: Comprehensive assessment of psychopathology in dementia. Neurology, 1994;44:2308-2314.
16. Charlson MA, Pompei P, Ales KL, MacKenzie R. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis 1987;40:373-383.
17. Beck AT, Ward C, Mendelson M. Beck depression inventory (BDI). Arch Gen Psychiatry 1961;4:561-571.
18. Hisli N. [A reliability and validity study of Beck Depression Inventory in a university student sample]. Turkish Journal of Psychology 1988;6:3-13.
19. Cohen S, Kamarck T, Mermelstein RA. Global measure of perceived stress. J Health Soc Behav 1983;24:385-396.
20. Novak M, Guest C. Application of a multidimensional caregiver burden inventory. The Gerontologist 1989;29:798-803.
21. Küçükgüçlü Ö, Esen Y, Yener G. The reliability and validity of the caregiver burden inventory in Turkey. J Neurol Sci 2009;26:60-73.
22. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213.
23. Kuang H, Zhu YG, Zhou ZF, Yang MW, Hong FF, Yang SL. Sleep disorders in Alzheimer's disease: the predictive roles and potential mechanisms. Neural Regen Res 2021;16:1965-1972.
24. Chiu YC, Lee YN, Wang PC, Chang TH, Li CL, Hsu WC, Lee SH. Family caregivers' sleep disturbance and its associations with multilevel stressors when caring for patients with dementia. Aging Ment Health 2014;18:92-101.
25. Simpson C, Carter P. The impact of living arrangements on dementia caregiver's sleep quality. Am J Alzheimers Dis Other Demen 2015;30:352-359.
26. Simón MA, Bueno AM, Otera P, Blanco V, Vázquez FL. Caregiver burden and sleep quality in dependent people's family caregivers. J Clin Med 2019;8:1072.

ORIGINAL RESEARCH

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Challenges of Providing Nursing Care to Patients with Dementia: A Qualitative Study

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Abstract

Objective: The aim of this study was to identify the challenges faced by nurses while providing care to patients with dementia.

Materials and Methods: This study was a descriptive and qualitative study conducted between 10 December 2017 and 1 March 2018. In-depth interviews were conducted with ten nurses. Data were analyzed using the inductive content analysis method.

Results: Four themes and eight subthemes were identified. The themes were: the perception of dementia, the meaning attributed to caring for patients with dementia, challenges of nursing care in dementia, and empowerment in care practices.

Conclusion: Nurses must understand the complex needs of people with dementia in hospitals and clinics. Because these patients need person-centered care that requires special communication and behavior. Nurses should be supported to provide this care to patients with dementia and manage the symptoms of patients with dementia. It contributes to providing individual and institutional support to nurses who care for patients with dementia, improving their communication skills, and coping with the difficulties and difficulties faced by nurses.

Keywords: Dementia, nurse, nursing care, qualitative study

Introduction

Patients with dementia are often older adults with chronic diseases, have complex needs and symptoms, and are difficult to care for (1,2). Therefore, the care of these patients is a difficult and exhausting process.

In the care of patients with dementia, it is among the responsibilities of the nurse to regulate the environment and relationships to preserve the patient's functionality and stability, compensate for the losses associated with the disease, and to provide therapeutic environments that help maintain their privacy and quality of life (3). However, unsuitable hospital environments and an inadequate number of nurses are important barriers to patient management and the provision of quality care (4,5). However, nurses may not be well prepared or experienced in caring for patients with dementia. Several studies have shown that nurses have insufficient knowledge, skills, confidence, and safety awareness about dementia and its care (2,6). Nurses who care for patients with dementia experience negative emotions due to memory and behavior problems (agitation, hallucination, confusion, etc.), which are the most common symptoms of dementia. Nurses have difficulty managing dementia-related symptoms and suffer from job dissatisfaction and experience feelings of fear, anxiety, frustration, burnout, weakness, and guilt; these lead to ineffective coping strategies to overcome the challenges faced (4,7).

Unfamiliar hospital environments and caregivers lead to anxiety, agitation, and aggressive behavior in patients with dementia, making nursing care more challenging (8). Therefore, it is recommended that patients with dementia are approached and provided with person-centered care. Person-centered care is a holistic and integrative approach designed to maintain the well-being and quality of life of people with dementia. The main purpose of person-centered care is to respect the

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patient's autonomy and maintain dignity even though his/her cognitive abilities are impaired. A patient with dementia whose personality is recognized and valued feels respected and honored in social settings; therefore, he/she acquires a sense of belonging, confidence, and comfort, and is willing to participate in activities. It takes time to develop person-centered care for patients with dementia; however, collaboration with the patient's family can facilitate this challenging aspect of care (8,9).

The relationship between the dementia patient and the nurse is critical in clinical settings because familiar caregivers and members are not present to help the patient. Nurses should be able to use appropriate interpersonal communication, empathy skills, and emotional intelligence to make a positive impression on patients with dementia (8,10). Training programs should, therefore, be held to improve the knowledge and confidence of nurses caring for patients with dementia. Research has shown that although nurses have a basic knowledge of the care required by patients with dementia, they know little about the early diagnosis of dementia, and effective communication strategies, and are unable to encourage the participation of patients in activities and manage treatment-resistant patients (8-11). Marx et al. (7) conducted a study to assess the level of knowledge and working status of nurses and reported that nurses had difficulty in managing the behaviors of patients with dementia, securing and providing care, and getting them to accomplish daily tasks. Fukuda et al. (3) reported that nurses caring for patients with dementia have difficulty managing patient behavior, reducing patients' and their families' anxiety and fear, communicating with patients, and providing care and safety due to shortcomings in hospital organizations, such as nursing shortages and inadequate cooperation with professionals in other medical fields.

In Turkey, patients with dementia are hospitalized or admitted to appropriate clinics according to the health problem experienced. Although nurses working in hospitals and clinics provide care to patients with dementia, little is known about nurses' experiences of caring for patients with dementia and the associated problems. Therefore, the aim of this study was to explore nurses' perceptions of the challenges they face in the care of patients with dementia in hospital and clinical settings.

Materials and Methods

Design and participants

This descriptive qualitative study focused on offering a realistic perspective on the difficulties encountered by nurses while providing care for patients with dementia in hospital settings. Participants were recruited from a university hospital using snowball sampling. Participation was voluntary. Data collection was terminated when further data did not provide any new information or insight. The study sample consisted of ten nurses. The inclusion criteria were as follows: (a) The participants should have a bachelor's degree; (b) the participants should have had at least one year of work experience in an adult ICU and/or inpatient clinics; (c) the participants should have had cared for at least one patient(s) with dementia; and, (d) the study required voluntary participation. A profile of study participants is presented in Table 1 and outlines the information regarding their age, gender, education status, working place, and employment year.

Data collection

After obtaining permission from the institution, data were collected between December 10, 2017, and March 1, 2018. A semi-structured interview form consisting of five questions was used (Box 1). Participants were informed about the procedure, confidentiality of the data, and that the interviews would be audio-recorded. The interviews were conducted by two researchers (first and third author) in a quiet room. Each interview lasted 35 minutes (minimum: 20 minutes; and, maximum: 50 minutes) on average. One researcher conducted the interviews while the other observed and took notes. New

Table 1. Demographic features of the nurses

Participant	Age	Gender	Education status	Years of employment	Working place
N1	39	Male	Undergraduate	12	Intensive care
N2	35	Female	Undergraduate	14	Intensive care
N3	50	Female	Undergraduate	27	Clinic
N4	37	Female	Undergraduate	14	Clinic
N5	40	Female	Undergraduate	20	Intensive care
N6	28	Female	Undergraduate	4	Clinic
N7	24	Female	Undergraduate	1	Intensive care
N8	28	Female	Undergraduate	4	Clinic
N9	30	Female	Undergraduate	9	Clinic
N10	24	Female	Undergraduate	2	Clinic

participants were recruited until data saturation was reached, and ten nurses were interviewed in total.

Statistics

Data were analyzed using qualitative inductive content analysis. The interviews were transcribed with no corrections. To ensure confidentiality, participants were coded as N1, N2, N3, N4…. N10. For analysis, first, three authors separately coded the transcripts line-by-line to ascertain the meaning of the sentences during analysis. Similar conceptual expressions were grouped into a list of codes, classified, and labeled. Finally, subthemes were combined and the main themes were created (12).

Trustworthiness: During each interview, the researcher summarized the interview and asked the participant if he/she had anything more to add. The interview was terminated after the participant confirmed that he/she did not have anything further to add. Participants read the themes and subthemes and confirmed the validity of the same, with no further recommendations. Themes and subthemes were discussed by a research team to improve reliability. The methods were reported in accordance with the principles of consolidated criteria research qualitative research (13).

Results

They all had bachelor's degrees. Nine of the participants were female. Six of them worked in inpatient clinics, and the remaining worked in adult ICUs. Participants' mean age was 33.5±8.2 years (minimum: 24 years; maximum: 50 years), and they had a mean of 10.7±8.4 years (minimum: 1 year; maximum: 27 years) of work experience. Data analysis yielded four themes and eight sub-themes. The themes were: (1) the perception of dementia; (2) the meaning attributed to caring for patients with dementia; (3) challenges of nursing care in dementia; and, (4) empowerment in care practices. The second theme comprised two sub-themes: (1) Difficulty in providing care; and, (2) uplifts of caregiving. The third theme consisted of four subthemes: (1) Inability to communicate; (2) difficulty in managing patient behavior; (3) burden of care; and, (4) inability to manage time. The fourth theme comprised two subthemes: (1) Individual empowerment and (2) administrative empowerment (Table 2). The themes and subthemes are discussed in the following section.

Box 1. Questions on the semi-structured interview form
1. What does dementia mean to you?
2. What does care for patients with dementia mean to you?
3. What kind of challenges (psychological, physical etc.) do you face when caring for patients with dementia?
4. How does caring for patients with dementia affect you?
5. What are your recommendations for nurses caring for patients with dementia?

Perception of dementia

Participants were asked what the word "dementia" meant to them. They associated it with deterioration in cognitive processes (7/10), forgetfulness (6/10), difficult patients (6/10), and need for caregiver support (5/10) (Table 3). Participants shared the following experiences regarding their perception of dementia:

……. "To begin with, they are difficult patients; not being able to communicate, there is no way to establish a social… how should I put it? not being able to connect the patient socially to a… The fact that he/she refuses to eat, has no conception of time… It is tough, because, his consciousness is not completely intact, so it is hard to involve him in activities, which increases our workload and exhausts our patience." (N1)

….."Old, forgetting what he/she does and inability to adapt to the environment…"(N6)

….."I can refer to it as a deterioration in cognitive processes….." (N4)

….."The patient's consciousness has deteriorated completely… he isn't adapting to the external environment." (N1)

Most participants associated dementia with a deterioration in cognitive processes and forgetfulness. Nurses who define dementia as a deterioration in cognitive processes have more experience in the profession. Nurses with less experience in the profession (4/6) and those working in ICUs (3/4) stated that patients with dementia are difficult patients and in need of specialized care due to symptoms resulting from a deterioration in cognitive processes.

Meaning attributed to caring for patients with dementia

This theme consisted of two sub-themes: (1) Difficulty in providing care; and, (2) uplifts of caregiving.

Difficulty in providing care

Participants stated that they had difficulty meeting the care needs of patients, communicating and performing activities

Table 2. Categories
Themes and subthemes
1. Perception of dementia
2. Meaning attributed to caring for patients with dementia
a. Difficulty in providing care b. Uplifts of caregiving
3. Challenges
a. Inability to communicate b. Difficulty in managing patient behavior c. Burden d. Inability to manage time.
4. Empowerment
a. Individual empowerment b. Administrative empowerment

Table 3. Nurses' perception of dementia

Perception of dementia	N1	N2	N3	N4	N5	N6	N7	N8	N9	N10
Forgetfulness	√	√		√		√	√	√	√	√
Deterioration in cognitive processes	√	√			√				√	
Need for caregiver support			√	√	√		√		√	√
Difficult patient	√	√	√	√		√		√		√

with them, and concentrating their attention socially and mentally on the reality of the world due to fluctuations in their consciousness and orientation; this caused them to spend most of their time with those patients and sometimes be subjected to physical or verbal violence. One particular nurse characterized her experience as follows:

….."Trying to persuade them is another challenge, there are some things that have to be done, such as vascular access and drawing blood, but the patient just wouldn't let you." (N8)

Uplifts of caregiving

Four participants were satisfied with their job because they knew that patients with dementia needed them and they were able to help the patients. Earning the trust of patients with dementia, cooperating with them and paying more attention to their needs made these participants happy.

……."I love caring for patients with dementia because I know that they need me. Helping them, communicating with them and caring for them make me happy… I give them some time to get to know me… I know that I have to spend more time with them." (N2)

"…I feel satisfied knowing that I have been helpful to them..." (N4)

" … When I see the positive changes in the facial expressions of the patient I cared for, I feel satisfied." (N5)

Challenges of nursing care in dementia

Participants were asked about the challenges they faced while caring for patients with dementia. All participants stated that it posed both physical and psychological challenges, which were grouped under the subthemes of "inability to communicate", "difficulty in managing patient behavior", "inability to manage time", and "burden of care".

Inability to communicate

Seven participants stated that they had difficulty communicating with patients with dementia during their care and medical treatment, in the absence of family, or when the patients were agitated. The experiences of some participants are directly quoted as follows:

……"Patients never understand the procedures, and it is very difficult for us to explain them all. Patients are always agitated, and they don't get us… My biggest communication problem is that they talk about things that never actually happened." (N9)

……"I have a hard time communicating (with patients with dementia), they snap at me…They forget the things that we talked about an hour or a day before, we always have to say the same things over and over again." (N6)

Participants who had difficulty communicating with their patients stated that they did not know how to communicate with them and were tired of having to say the same things repeatedly. They also stated that from time to time, there were some misunderstandings due to deterioration in orientation and perceptions. Families believe what patients say, and therefore, arguments break out or nurses find themselves in a situation where they have to defend themselves.

Difficulty in managing patient behavior

Five participants reported that they had difficulty managing patient behavior. Protecting agitated patients from falling or trauma, while ensuring their own safety, led to nurses' often subjection to verbal and physical violence.

….."We try to help them, but they react negatively like they hit us or display aggressive behavior." (N1)

……"It is a challenge for me, I am scared because I don't know how they will react. I am especially scared when it is a challenging physical task." (N2)

Inability to manage time

Eight participants reported that they had difficulty managing time when there were patients with dementia in their clinics and that it took a lot of time and effort to care for them and to manage their agitated behavior, due to changes in their cognitive processes (8/10). They also stated that they had difficulty ensuring the safety of patients and managing time during their shifts because they had to say the same things repeatedly during treatment and care.

……"I don't want to care for a patient with dementia that I have to deal with during my shift. I'd rather have completely dependent patients instead of patients with dementia because I can care for and treat them and plan their safety easily. But it's not the case with patients with dementia. I just can't leave the patient's room and can't spend any time with my other patients" (N5).

Burden of care

Seven participants suffered from the burden of care because they had to say the same things to patients with dementia repeatedly, and spend most of their time with them. They stated that they were not able to leave their patients with dementia despite their busy shifts, experienced communication problems and had to deal with other patients who did not appreciate the care they provided and the conflicts that arose thereby. They felt exhausted because the care they provided was not visible and they always had to persuade their patients to undergo care and treatment. They stated that they suffered from stress during their shifts since they had to provide safety and physical care for patients with dementia, with whom they were unable to communicate effectively. This resulted in fatigue and exhaustion.

"…We sometimes don't know how to approach our patients. Sometimes I have to give them a command, and sometimes I raise my voice, I mean it's not like I yell at them, but I find myself in conflict situations, which is exhausting to me…" (N6)

Empowerment in care practices

Participants were asked what their recommendations would be for nurses caring for patients with dementia. Their suggestions were grouped under two sub-themes: Individual empowerment and administrative support.

Individual empowerment

Participants stated that they had difficulty caring for patients with dementia and that they should be empowered in that regard. They recommended that communication techniques with patients with dementia be developed (8/10), care is provided by experienced nurses (5/10), and nurses be supported during physical care (4/10). They stated that nurses caring for patients with dementia should be calm and patient, which requires good communication skills and experience in patient-centered care.

……"Nurses should be provided with training on how to approach patients with dementia and how to communicate with agitated patients who refuse treatment and how to make them feel safe." (N6)

….."Be patient, trying to provide treatment and care over and over again ..... Every dementia patient is unique … try to understand as a person and establish a contact point." (N3)

Administrative empowerment

According to participants, what should be done managerially are as follows: Patients with dementia should stay in clinics designed especially for them (8/10); their families should stay with them (7/10); experienced medical teams should provide care for them (7/10); health professionals should be provided with in-service training on caregiving for patients with dementia at regular intervals (5/10); and, the care needs of patients with dementia should be taken into consideration when planning the care process and organizing the workforce or the required number of nurses (4/10).

……"Family members should definitely stay with patients with dementia in the intensive care unit because patients trust their families and express their needs to them more than they do to us." (N4).

Discussion

This study investigated nurses' perceptions of patients with dementia and provided insights into nurses' experiences and recommendations for care processes in hospitals and clinics. The findings revealed that nurses associated dementia with deterioration in cognitive processes, forgetfulness, need for caregiver support, and difficult patients. In particular, experienced nurses defined dementia as a deterioration in cognitive processes and forgetfulness, while others associated dementia with difficult patient(s) and need for caregiver support. Nurses who do not have sufficient theoretical knowledge and/or practical skills to manage the behaviors of patients with dementia, label them as "difficult patients". Therefore, experienced nurses can manage the behaviors of patients with dementia, and care for them successfully. These results are similar to the findings of other studies that reported that caregivers of patients with dementia associated dementia with forgetfulness, irritability, hyperactivity, and aggression (10-13). Clinical management and care of patients with dementia is difficult because of the behavioral and psychological symptoms of dementia.

Nurses are responsible for ensuring the physical, social, spiritual well-being and safety of patients with dementia. Hospitalization of patients with dementia has different negative implications for patients, their families, and nurses (10,13-15). Nurses experience frustration and negative feelings resulting from not having enough resources, opportunities, or abilities to perform quality care for patients with dementia. Additionally, a lack of knowledge of the complex needs of patients with dementia causes frequent emotional exhaustion and stress for nurses. Nurses who work with a deficit in knowledge and skills might feel a sense of professional failure and frustration while providing care for patients with dementia (10,13). Previous studies have also highlighted that nurses with adequate knowledge of dementia and its characteristics can provide better nursing interventions (10,14-18). In their study, Scerri et al. (19) investigated the effect of person-centered dementia care on employees' knowledge and attitudes in acute hospital wards; they stated that training programs were necessary to improve nurses' knowledge attitudes and interpersonal skills. Pinkert et al. (14) reported that it is important to sensitize nurses and provide them with sufficient training and education to enable

them to care for patients with dementia. In this study, nurses expressed those various types of educational activities relating to dementia care (engaging in role-play, watching videos, studying case examples, etc.) helped them develop abilities and strategies, such as viewing reality from the patients' perspective.

Dementia-related behavioral symptoms such as communication problems, conflict, and aggression during care have negative effects on nurses (1,2,10,13,15). Ostaszkiewicz et al. (16) argue that nurses are constantly at risk of physical and verbal abuse, and thus feel insecure and worthless while handling dementia patients. McPherson et al. (18) reported that nurses who work in inpatient dementia care wards experienced work stress caused by structural and interpersonal factors such as the nature of dementia patients, lack of resources, high demand, aggression, and fear. In this study, nurses stated that they suffered from stress and the burden of care because they had to say the same things to patients with dementia over and over again and spend most of their time with them. In addition, they were not able to leave their patients with dementia, despite their busy shifts. Moreover, nurses stated that they experienced difficulty in communicating with patients with dementia and managing their behavior because they do not comprehend as well as other patients. Thus, it is more time-consuming to assess their needs (e.g., pain identification).

Another sub-theme in study was "uplifts of caregiving", which plays a key role in protecting nurses from stress and fatigue; research shows that nurses experience stress, emotional overload and burnout when caring for patients with dementia (2,6). Nurses are less likely to be personally affected by patient behavior if they can associate it with the symptoms of dementia because; in this way, they can feel satisfied with the care they provide and manage the symptoms of dementia (17). Nurses in this study were aware that patients with dementia needed them and stated that they wanted to help patients with dementia and gain their trust and that they were satisfied with their job because they provide meticulous care that maintained patient dignity.

The results of this study showed that experienced nurses expressed more positive statements regarding the care processes of patients with dementia. Previous studies have similarly reported that experienced nurses communicate with dementia patients more easily, have less difficulty in managing routines, and cope with patients and their relatives (2,6,8,20). Burns and McIlfatrick (8) expressed that nurses indicated that having long and persistent contact with dementia patients gave them the ability to realize patients' pain and other needs through their behavioral symptoms, which is quite challenging for less experienced workers or staff. Nurses encountered with dementia patients for the first time in the clinic may feel that lack the expertise required to care for such patients. Therefore, nurses who have had previous experience in providing care for people with dementia can provide more appropriate care.

Sensing and understanding the patients' emotional and physical expressions are ways to extend high-quality care (14,17,19). In addition, viewing the dementia patient as a person and providing holistic care for them were the two most important elements that positively improved care processes. Furthermore, person-centered care is stressed on as the foundation of care for patients with dementia. Therefore, it is recommended that patients with dementia be admitted to specialized clinics (15,17-19). In this study, nurses expressed those demented patients should be in clinics specially designed for them and that the number of nurses required should be outlined in the care plan. However, in Turkey, there are no dementia-friendly hospitals where such patients can be hospitalized. Additionally, due to the increasing number of patients with dementia, nurses in acute hospitals face great uncertainty when caring for patients with dementia.

Nurses who care for patients with dementia should be supported both emotionally and physically. Research shows that nurses caring for patients with dementia should receive guidance and support from experienced nurses and training on effective communication techniques (10,11,14,19). Nurses who are supported and valued by other health professionals and the institution(s) they work for, experience more job satisfaction and less fatigue. Nurses supported by their institutions and managers experience high levels of satisfaction, which, in turn, increases patient satisfaction (21). Sjögren et al. (17) stated thatshigher levels of person-centered care are associated with higher levels of satisfaction with work and care, lower levels of job strain, and a more supportive psychosocial climate. According to the participants, administrative empowerment can be achieved by ensuring that patients with dementia stay with their families in clinics specifically designed for them and are provided with care by experienced teams and nurses who undergo in-service training at regular intervals, on the caregiving requirements of patients with dementia. Research also suggests that nurses or healthcare teams caring for patients with dementia receive education and training on aspects of dementia, such as psychotic symptoms and depressive characteristics of dementia, behavioral disorders, and maladaptive aggressive behavior management and communication skills (8,16,17,19).

Study Limitations

The most important limitations of our study are that it was conducted in a single-center institution and its small sample size. The common aspects and solutions of the difficulties experienced by nurses in the care of patients with dementia can be revealed through studies conducted in large samples and multi-centre institutions.

Conclusion

Achieving person-centered care for patients with dementia in acute hospital settings is complex, and multiple factors need

to be addressed. Most nurses lack the specialist knowledge and skills required for dementia care. The findings of the study revealed that nurses face many different challenges while taking care of patients with dementia. Nurses stated that they suffered from psychological, communication, and time management problems while providing care to patients with dementia, and that experienced and trained nurses should care for patients with dementia. Participants had difficulty communicating with their patients and managing their behavior. Providing them with education and training programs on these issues can help them understand dementia and help them assess patient behavior and manage the behavioral symptoms of dementia. It can also help them adopt an empathic approach to challenging behavior and develop the skills necessary to cope with related stress and emotional problems.

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Ethics

Ethics Committee Approval: Ethical principles were maintained throughout the study. Permission (KA17/313) was obtained from the Medical and Health Sciences Research Board of Başkent University and from the Ethics Committee of Başkent University prior to the study.

Informed Consent: Informed consent was obtained from them prior to participation.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.Ç., S.K., Design: B.Ç., S.K., Data Collection or Processing: B.Ç., E.A.Ç., E.A., A.A., Analysis or Interpretation: B.Ç., E.A.Ç., E.A., A.A., Literature Search: B.Ç., S.K., E.A., Writing: B.Ç., S.K.

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References

1. Meyer OL, Nguyen KH, Dao TN, Vu P, Arean P, Hinton L. The Sociocultural Context of Caregiving Experiences for Vietnamese Dementia Family Caregivers. Asian Am J Psychol 2015;6:263-272.
2. Smythe A, Jenkins C, Harries M, Atkins S, Miller J, Wright J, Wheeler N, Dee P, Bantham P, Orebody J. Evaluation of dementia training for staff in acute hospital settings. Nurs Older People 2014;26:18-24.
3. Fukuda R, Shimizu Y, Seto N. Issues experienced while administering care to patients with dementia in acute care hospitals: a study based on focus group interviews. Int J Qual Stud Health Well-being 2015;10:25828.
4. Houghton C, Murphy K, Brooker D, Casey D. Healthcare staffs' experiences and perceptions of caring for people with dementia in the acute setting: Qualitative evidence synthesis. Int J Nurs Stud 2016;61:104-116.
5. Clissett P, Porock D, Harwood RH, Gladman JR. The responses of healthcare professionals to the admission of people with cognitive impairment to acute hospital settings: an observational and interview study. J Clin Nurs 2014;23:1820-1829.
6. Turner A, Eccles FJ, Elvish R, Simpson J, Keady J. The experience of caring for patients with dementia within a general hospital setting: a meta-synthesis of the qualitative literature. Aging Ment Health 2017;21:66-76.
7. Marx KA, Stanley IH, Van HK, Moody J, Alonzi D. Hansen BR, Gitlin LN. Knowing versus doing: education and training needs of staff in a chronic care hospital unit for individuals with dementia. J Gerontol Nurs 2014;40:26-37.
8. Burns M, McIlfatrick S. Palliative care in dementia: a literature review of nurses' knowledge and attitudes towards pain assessment. Int J Palliat Nurs 2015;21:400-407.
9. Backhouse T, Killett A, Penhale B, Burns D, Gray R. Behavioral and psychological symptoms of dementia and their management in care homes within the East of England: a postal survey. Aging Ment Health 2014;18:187-193.
10. Digby R, Lee S, Williams A. The experience of people with dementia and nurses in hospital: an integrative review. J Clin Nurs 2017;26:1152-1171.
11. Vaismoradi M, Jones J, Turunen H, Snelgrove S. Theme development in qualitative content analysis and thematic analysis. Journal of Nursing Education and Practice 2016;6:100-110.
12. Tong A, Sainsbury P, Craig J. Consolidated Criteria for Reporting Qualitative Research (COREQ): A 32-Item Checklist for Interviews and Focus Groups. Int J Qual Health Care 2007;19:349-357.
13. Lök N, Günbayı İ, Buldukoğlu K. Living with A Person Who Has Dementia: A Study of Phenomenology. Journal of Psychiatric Nursing 2015;6:91-99.
14. Pinkert C, Faul, Saxer S, Burgstaller M, Kamleitner, D, Mayer H. Experiences of nurses with the care of patients with dementia in acute hospitals: A secondary analysis. J Clin Nurs 2018;27:162-172.
15. Griffiths A, Knight A, Harwood R, Gladman JR. Preparation to care for confused older patients in general hospitals: a study of UK health professionals. Age Ageing 2014;43:521-527.
16. Ostaszkiewicz J, Lakhan P, O'Connell B, Hawkins M. Ongoing challenges responding to behavioral and psychological symptoms of dementia. International Nursing Review 2015;62:506-516.
17. Sjögren K, Lindkvist M, Sandman PO, Zingmark K, Edvardsson D. To what extent is the work environment of staff related to person-centered care? A cross-sectional study of residential aged care. J Clin Nurs 2015;24:1310-1319.
18. McPherson S, Hiskey S, Alderson Z. Distress in working on dementia wards - A threat to compassionate care: A grounded theory study. Int J Nurs Stud 2016;53:95-104.
19. Scerri A, Innes A, Scerri C. Person-centered dementia care in acute hospital wards-The influence of staff knowledge and attitudes. Geriatr Nurs 2020;41:215-221.
20. Nakanishi M, Hirooka K, Morimoto Y, Nishida, A. Quality of care for people with dementia and professional caregivers' perspectives regarding palliative care in Japanese community care settings. Int J Geriatr Psychiatry 2017;32:1342-1351.
21. Chenoweth L, Merlyn T, Jeon YH, Tait F, Duffield C. Attracting and retaining qualified nurses in aged and dementia care: outcomes from an Australian study. J Nurs Manag 2014;22:234-247.

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