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European Journal of Geriatrics and Gerontology is the official open access scientific publication organ of the Academic Association of Geriatrics. It is a double peer-reviewed journal published quarterly in April, August and December.

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 editorial processes of the journal are shaped in accordance with the guidelines of the international organizations such as the International Council of Medical Journal Editors (ICMJE) (http://www.icmje.org) and the Committee on Publication Ethics (COPE) (http://publicationethics.org).

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Instructions to Authors

European Journal of Geriatrics and Gerontology is the official publication of Academic Association of Geriatrics. The publication language of the journal is English.

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Following receiving of each manuscript, a checklist is completed by the Editorial Assistant. The Editorial Assistant checks that each manuscript contains all required components and adheres to the author guidelines, after which time it will be forwarded to the Editor in Chief. Following the Editor in Chief's evaluation, each manuscript is forwarded to the Associate Editor, who in turn assigns reviewers. Generally, all manuscripts will be reviewed by at least three reviewers selected by the Associate Editor, based on their relevant expertise. Associate editor could be assigned as a reviewer along with the reviewers. After the reviewing process, all manuscripts are evaluated in the Editorial Board Meeting.

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

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The title page should include the authors' names, degrees, and 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, which is listed separately. Please provide contact information for the corresponding author, including name, e-mail address, and telephone and fax numbers.

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Abstract

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Original articles should have the following sections;

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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 information that was available at the time 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 important 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 important findings, results, and observations in the text. For 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 important values (i.e. p value and confidence interval) should be provided.

Discussion: This section should include a discussion of the data. New and important findings/results, and the conclusions they lead to should be emphasized. Link the conclusions with the goals of the study, 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.

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Examples of References:

1. List All Authors

Ghoneim IA, Miocinovic R, Stephenson AJ, Garcia JA, Gong MC, Campbell SC, Hansel DE, Fergany AF. Neoadjuvant systemic therapy or early cystectomy? Singlecenter analysis of outcomes after therapy for patients with clinically localized micropapillary urothelial carcinoma of the bladder. Urology 2011;77:867-870.

2. Organization as Author

Yaycioglu O, Eskicorapci S, Karabulut E, Soyupak B, Gogus C, Divrik T, Turkeri L, Yazici S, Ozen H; Society of Urooncology Study Group for Kidney Cancer Prognosis. A preoperative prognostic model predicting recurrence-free survival for patients with kidney cancer. Jpn J Clin Oncol 2013;43:63-68.

3. Complete Book

Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA. Campbell-Walsh Urology, 10th ed. Philadelphia, Elsevier&Saunders, 2012.

4. Chapter in Book

Pearle MS, Lotan Y Urinary lithiasis: etiology, epidemiology, and pathogenesis. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA. Campbell-Walsh Urology, 10th ed. Philadelphia, Elsevier&Saunders, 2012, pp 1257-1323.

5. Abstract

Nguyen CT, Fu AZ, Gilligan TD, Kattan MW, Wells BJ, Klein EA. Decision analysis model for clinical stage I nonseminomatous germ cell testicular cancer. J Urol 2008;179:495a (abstract).

6. Letter to the Editor

Lingeman JE. Holmium laser enucleation of the prostate-If not now, when? J Urol 2011;186:1762-1763.

7. Supplement

Fine MS, Smith KM, Shrivastava D, Cook ME, Shukla AR. Posterior Urethral Valve Treatments and Outcomes in Children Receiving Kidney Transplants. J Urol 2011;185(Suppl):2491-2496.

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

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

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Each author should have participated sufficiently in the work to assume public responsibility for the content. Any portion of a manuscript that is critical to its main conclusions must be the responsibility of at least 1 author.

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Acknowledgments

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4. All authors are responsible for the manuscript's content
5. All authors participated in the study concept and design, analysis and interpretation of the data, drafting or revising of the manuscript, and have approved the manuscript as submitted. In addition, all authors are required to disclose any professional affiliation, financial agreement, or other involvement with any company whose product figures prominently in the submitted manuscript.

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EDITORIAL

Dear Colleagues,

As the publication organ of the Academic Geriatrics Society, we are pleased to see the publication of "European Journal of Geriatrics and Gerontology". There are more older adults in the world than ever before, and information in the field of geriatrics and gerontology is also increasing in parallel with this fact. In the last 20 years, studies on this subject have also accelerated in our country. Science is universal, and researchers and scientists in our country both follow current developments in the world and contribute to science with their scientific studies. This international scientific journal emerged as a result of a need.

Sarcopenia, fragility, polypharmacy, falls, urinary and fecal incontinence, dementia, depression, delirium, pressure sores, sleep disorders, Parkinson's disease, diabetes mellitus, hypertension, cardiovascular and cerebrovascular diseases, osteoarthritis, osteoporosis and other subjects are constantly being studied. In addition, the journal will include aging biology and healthy aging, demographic information, palliative care, long-term care, urology, ophthalmology, otolaryngology, geropsychiatry, gynecology, urology, trauma, emergency medicine, orthogeriatrics, and physical medicine and rehabilitation. Geriatrics is an area that requires multidisciplinary teamwork, so gerontological researches in geropsychology, pharmacology, nursing, dietary expertise, physiotherapy and social work, and developments in gerotechnology are our main fields.

The journal is open-access and accessible free of charge. We believe that we will perform a useful activity in the field of gerontology and geriatrics with our editorial board and referees, including respected names from the international community. We are expecting submissions from clinicians and researchers in our country and other countries. We hope to take our place in national and international indexes such as ULAKBIM, PubMed and Science Citation Index Expanded.

I would like to thank my colleagues, Academic Geriatrics Society and the entire Geriatrics-Gerontology community for their great efforts in the preparation of the journal. I thank you in advance for your support on the behalf of our editorial board, and we believe that we will achieve our goals with your support.

Prof. Dr. Mehmet Akif KARAN
Editor in Chief

REVIEW

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Eur J Geriatr Gerontol 2019;1(1):1-10

Poly-De-prescribing vs Polypharmacy - The Weapon to Fight an Iatrogenic Epidemic: An Overview

Doron Garfinkel[1,2]

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[2]IGRIMUP - The International Group for Reducing Inappropriate Medication Use & Polypharmacy, Bat Yam, Israel

Abstract

This review will focus on the topic of de-prescribing, including factors which impede and promote its implementation, the attitudes of physicians and patients towards it, as well as the core recommendations of the International Group for Reducing Inappropriate Medication Use and Polypharmacy that were recently published as a position statement. Finally, I will delineate a comprehensive geriatric-palliative approach to inappropriate medication use and polypharmacy (IMUP) utilizing poly-de-prescribing-cessation of as many nonessential medications as possible. The overarching goal of this approach is minimizing harm, and improving quality of life in the twilight of life for many elderly patients. I will only briefly touch upon the problematic definitions of IMUP, the variety of their negative clinical consequences, and the key tools previously suggested for combating the epidemic, issues which have been extensively discussed and evaluated in past reviews.

Keywords: Poly-De-prescribing, polypharmacy, inappropriate medication use, palliative, dementia, frailty, quality of life, life expectancy

Introduction

Medical interventions are an inseparable part of the human experience. Using a paradigm from Genesis, the creation of Eve from Adam's rib can represent the ideal benefit/risk ratio (number needed to treat = 1), while the fall from the Garden after eating from the Tree of Knowledge can represent the opposite (number needed to harm= 1). Clinicians strive for the divine achievement of an ideal benefit/risk ratio, but often do not succeed, especially with regards to older patients. One particular challenge is the phenomenon of inappropriate medication use and polypharmacy (IMUP), the negative clinical, economic and social ramifications of which can be regarded as an "Iatrogenic epidemic" (1,2) and have been reviewed extensively (3,4). Given its wide-ranging importance for multiple professional fields, an improved understanding of this problem among geriatricians, internists, and generalists, as well as among non-physicians (pharmacists, nurses, policymakers, etc.) is essential. The harmful consequences of IMUP are particularly devastating in the rapidly increasing, most vulnerable geriatric subpopulations, which I have previously termed VOCODFLEX (very old, with comorbidity, dementia, frailty/disability, and limited life expectancy) (3-5). The inability of the workforce to balance the unprecedented medical, economic, and social needs of VOCODFLEX presages a "geriatric boom catastrophe", or burden (5), and a "Tsunami in 21st century Healthcare" (6).

It has become clear to most health professionals that IMUP are associated with diverse negative clinical outcomes that include cognitive and functional impairments, delirium, malnutrition and weight loss, falls and hip fractures, incontinence, hospitalizations, nursing home placement, decrease in quality of life (QoL) and quality of death, as well as medication nonadherence. Furthermore, IMUP begets IMUP in a vicious cycle of over-diagnosis and over-treatment, with the spiraling cost of drugs and hospitalizations related to adverse drug events placing unsustainable financial burdens on healthcare systems (7-17). Catastrophes and tsunamis aside, I believe that most health professionals consider IMUP to represent a major hazard to patients and health care systems. However, we as

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clinicians suffer from the illusion that we do not have a hand in propagating the problem. In reality, as I will expand upon further, we are all to blame in routinely prescribing too many medications, recommended by too many specialists, to mostly older patients, until death.

This review will focus on the topic of de-prescribing, including factors which impede and promote its implementation, the attitudes of physicians and patients towards it, as well as the core recommendations of IGRIMUP, the ''International Group for Reducing Inappropriate Medication Use and Polypharmacy'' that were recently published as a position statement (18). Finally, I will delineate a comprehensive Geriatric-palliative approach to IMUP utilizing poly-de-prescribing the cessation of as many nonessential medications as possible. The overarching goal of this approach is minimizing harm, and improving QoL in the twilight of life for many older patients. I will only briefly touch upon the problematic definitions of IMUP, the variety of their negative clinical consequences, and the key tools previously suggested for combating the epidemic, issues which have been extensively discussed and evaluated in past reviews.

Why is the Epidemic of IMUP Emerging Now?

The increase in average lifespan in the last century is a result of several advances in the medical sciences: improved preventative medicine, the curing of life-threatening acute illnesses, and improved management of chronic diseases. In spite of this boon, most older adults will experience a time-related increase in the number of incurable comorbidities and disability, and the suffering they engender for prolonged periods of time prior to death (1,3-5). These circumstances have yielded a rapidly-growing population of VOCODFLEX with its incumbent increase in the number of specialists involved in their care, each of whom recommend interventions based on the clinical practice guidelines of their field of expertise. Increasing sub-specialization and super-specialization within a healthcare system has clear advantages. However, when the system is fragmented, with little or no direct communication between case manager and specialist, multiple problems ensue, especially for the multi-morbid patient. From the specialist's perspective, the paramount concern is preventing morbidity or mortality from "their" disease. GPs for their part will mostly adopt the specialist's recommendations and rarely interfere or stop these treatments. The absence of a single, assertive case manager capable of looking at the big picture for VOCODFLEX, promotes confusion among patients, families, and caregivers. Lacking a multi-disciplinary or integrative approach, the physicians involved assume a passive role, projecting the burden of authority onto others (19). The result of this diffusion of responsibility is the proliferation of drugs and the interactions and adverse events that come part and parcel with them. But it doesn't end there.

The Twisted Lens with which We View the Vulnerable

Many of the great advances in medicine in the past decades are in large part due to the development and propagation of evidence-based medicine (EBM), the principles of which have led the medical community to adopt the randomized-controlled trial (RCT) as the gold standard of clinical research. The strongest guidelines developed by professional societies rest upon the results of multiple, large RCTs. As such, we feel secure in prescribing based upon EBM guidelines, knowing that our practice is based upon "scientific truth." While this may be true for younger, healthier patients with one, two (or even a few) medical problems, the waters become murky with regards to VOCODFLEX. Very-old age and multiple co-morbidities are usually exclusion criteria in RCTs. Even when trials do include some older patients (as has recently become an FDA requirement) these patients typically do not represent the tremendous heterogeneity of VOCODFLEX (20-22). Furthermore, the same diseases in these populations behave differently. Let alone the changes in disease presentation and the physiological alterations that occur in geriatric populations, there is no longer such a thing as ''natural history'' of a disease as studied in medical school. These populations experience a natural history of multi-morbidity in combination with polypharmacy, a reality which changes the disease in unique ways, about which we have little to no concrete knowledge. In multi-morbid geriatric populations, this is the new norm (1). An additional key factor is that the positive benefit/risk ratio of most interventions decreases or becomes negative as older patients join the ranks of VOCODFLEX and near the end of their life expectancy. Boyd et al. (an IGRIMUP member, John Hopkins University, US) thus conclude that adhering to current guidelines in elders with co-morbidities may lead to inappropriate clinical judgment, creates perverse incentives to care, and diminishes the quality of care (23). This situation is particularly prevalent and inappropriate in the frailest elderly, and in end-stage populations - where palliative care should be the main focus - it borders on the absurd (24-28). And so, despite the tenuous evidence base, we continue to implement multiple specialty-specific interventions to older patients, irrespective of extreme age and patient characteristics, and often into the palliative stages prior to death. In this way, the epidemic of IMUP was born, and nothing short of a revolution in our clinical thinking will suffice to stem the tide of this lethal problem.

Defining IMUP: A Futile Debate

Although the epidemic of IMUP has been recognized for several decades, the community of clinicians sounding the alarm has devoted an excessive amount of time and effort attempting to define the problem precisely. This includes drawing up many lists of ''inappropriate drugs''. While nosology is important, this approach creates a fallacy suggesting that medications

not appearing on these lists are unconditionally "appropriate". Some use the term, ''potentially inappropriate medications'' (PIM). However, all medications are ''potentially inappropriate" when given for the wrong indication in patients with the wrong clinical characteristics. The lack of agreement on the definition of polypharmacy - what specific number of drugs should be considered a disease in and of itself - has contributed to a long period of sterile and stagnant discussion on the topic. Polypharmacy has been vaguely defined as the ''administration of more medications than are clinically indicated''; IMU as ''medication use that has more potential risk for harming than potential benefit or does not agree with accepted medical standards'' (29). Phrases such as "clinically-indicated" and "accepted medical standards" are problematic and dangerous in a population with a fragile evidence base. There is a fair consensus adopting the definition of Gnjidic et al. (30) (both IGIMUP members, university of Sydney, Australia) as five drugs representing the cut-off for polypharmacy, as beyond this standard, older people experience increased risk of mortality, disability, frailty and falls. However, this definition encompasses vast swathes of the population: 50% of Medicare beneficiaries receive five or more medications (31), as do 84% of older adults with cancer, 43% receive 10 medications or more (32). In my view, cutoff numbers should not be the main concern, since IMUP can occur with even a single medication and the risk of IMUP increases in a direct relationship with the number of medications prescribed (30,33-36). Given its futile nature, the time has come to close the door on the debate surrounding the definition of IMUP, and move the discourse decisively towards its effective treatment.

De-prescribing in the Elderly: A Variety of Approaches

There is no global consensus regarding the best method to combat the IMUP epidemic, but most involve de-prescribing. First introduced in 2003 by Woodward (37), the term "de-prescribing" was defined as ''achieving better health outcomes for older people through reducing medications". Wisely worded, this definition attacks the dogma that "the drugs are always good", and highlights the risk of too many drugs becoming a disease in itself. Reeve et al. (38) (IGRIMUP members, University of Sydney, Australia) adjusted Woodward's (37) definition, stating that de-prescribing is "the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes". As I will expand upon later, this alteration may actually introduce greater confusion, given the lack of clarity as to who adjudicates what is regarded as an IMU in an individual patient. I recommend adhering to Woodward's original definition.

Approaches to de-prescribing are traditionally classified as explicit (criteria-based) or implicit (judgment-based). Explicit tools such as lists of ''Drugs to avoid'' have been reviewed extensively elsewhere (1,3,4) as well as in IGRIMUP's position statement (18) and will be mentioned only briefly here. Beer's lists were compiled in an attempt to quantify IMUP and have been repeatedly updated (39), but there are no controlled trials showing improved outcomes using Beers criteria. The START/STOPP criteria (40) developed by O'Mahony et al. (41) (IGRIMUP member, Cork University, Ireland) recognize the dual nature of inappropriate prescribing by including a list of both IMU (STOPP) and the omission of potentially beneficial medications (START); they too have been updated. When applied during hospitalization STOPP/START criteria improve medication appropriateness in a statistically-significant fashion (42,43). The ''Fit for the Aged Criteria'' (FORTA) drug classification, developed by Wheling (IGRIMUP member, University of Heidelberg Germany) ranks drugs into risk groups from A to D (44). Applying FORTA to hospitalized geriatric patients (VALFORTA) was associated with improvement of medication quality and may improve secondary clinical end points (45). This approach has already been extended to include seven European countries (EURO - FORTA) (46). Several country-specific lists have also been developed, often with a focus on the number of medications and the extent of anticholinergic effects Garfinkel et al. (3). These suffer from scant evidence of improved clinical outcomes. Steinman (IGRIMUP member, UCSF, US) concluded that while explicit tools are helpful in highlighting prescribing errors, they have several shortcomings, which render them insufficient to be considered adequate in their approach to IMUP (47). Firstly, for the most part, they have not been demonstrated in trials to improve clinical outcomes. Furthermore, in many cases of polypharmacy, it is unclear which particular drug is responsible for a given adverse effect. As well, as mentioned previously, lists of "drugs to avoid" nurture a fallacy that any drug not found on such lists is automatically appropriate.

An upgrade on the explicit approach can be found in computerized decision-making support systems. Topinkova (IGRIMUP member, Charles University, Czech Republic) (48), have demonstrated some efficacy in reducing IMUP and improved prescribing quality, claiming modest improvements in primary outcomes. The PRIMA-eDS electronic decision support tool for polypharmacy is a multinational European project led by Sönnichsen (IGRIMUP member, Witten University, Germany) and other IGRIMUP members from Finland and Spain (49). The European-funded SENATOR project developed a software engine for the assessment and optimization of drug and non-drug therapy in multi-morbid older people with polypharmacy; it was summarized in part by Soiza et al. (50) (IGRIMUP member, Aberdeen Royal Infirmary, Scotland) and other IGRIMUP members from Ireland, Spain and Belgium. While the computerized approach is a substantial leap forward in tackling the complexity of drug-drug and drug-disease interactions,

such an approach does not address specific patient factors (pharmacogenetics, behavioral factors, etc.) which are central to the etiology of IMUP. While such programs are a useful adjunct, overreliance on them may be misleading and even harmful to elderly patients (51,52).

In comparison with the explicit methods mentioned above, implicit tools are more sophisticated. They take into consideration the evidence base, clinical circumstances, and in some cases also patient preferences. The medication appropriateness index consists of ten elements considered necessary for appropriate prescribing, and demands a degree of clinical judgment. It was proven to have higher reliability and more frequently detect IMU than explicit criteria (53). The ARMOR tool incorporates patients' clinical profiles and functional status with decision-making and has been shown to reduce polypharmacy, healthcare costs and hospitalizations (54). The Palliative and Therapeutic Harmonization (PATH) tool has been developed by Moorhouse and Mallery (IGRIMUP members, Dalhousie University, Canada) to provide frailty-specific treatment guidelines that consider the clinical relevance of commonly-accepted outcomes in the face of multiple competing risks for mortality. Some examples of the guidance provided by this framework include cessation of medications to permit more lenient blood pressure (BP) and A1C targets, as well statin discontinuation (55-57).

Most intrinsic methods channel the principles of the Holmes (58) framework. Of its four parameters, "Treatment target" and "Goals of care" become vague in VOCODFLEX, and when "Time until benefit" for the intervention exceeds "Remaining life expectancy", preventative interventions become irrelevant. I argue that this approach should be extended to include most VOCODFLEX subgroups, which I will demonstrate in my own method later in this review.

Barriers to Routine De-prescribing

Despite the availability of multiple tools to assist the clinician in de-prescribing, this critical practice remains woefully underused. Several obstacles to de-prescribing were identified (by IGRIMUP members from İstanbul, Turkey along with myself), the main obstacle being the psychological difficulty involved in making complex treatment decisions in the face of uncertainty (3); this holds true for both practitioners and patients (3,59). In the patient's perspective, the centrality of "drugs=health" can be a deep-rooted value, and de-prescribing may automatically be perceived negatively. In a given health-care encounter, patients often expect to receive a prescription at the conclusion of a medical transaction, and patient satisfaction frequently depends on this (60). Some of the fears associated with a patient's decision to discontinue a medicine may include fear of their doctor's response, of relapsing into illness, of being denied the option of subsequently resuming the medication, and of abandonment by their physician (61,62). Even when physicians recommend de-prescribing, the patient may disregard this advice without specialist approval. Some even suspect attempts to de-prescribe as having economic incentives: pressure from their Healthcare organization or insurance companies to save money (3).

Physicians have their own barriers to de-prescribing. These include uncertainty over the indication for the drug (63), the excess time needed to safely de-prescribe, including discussing these complex issues with the patient/family (64,65), fear of not following guidelines or specialists' recommendations, pressure due to pay-for-performance, fear of lawsuits, and fear of the patient/family's reaction (3). Some clinician responses to these issues include "I have to give the patient something", "the patient is afraid to stop medications", "if I do not prescribe, someone else will", or "having no EBM guidelines in this population, at least I adhere to guidelines that were proven in another population". All of these statements are unethical, unprofessional, and deceptive.

These various barriers may lead clinicians to a feeling of being trapped. Anthierens et al. (66) (including two IGRIMUP members from Ghent University, Belgium, stress that in spite of being aware of IMUP, and that certain treatment decisions in older patients do not represent good medical practice or beneficial patient care, GPs feel frustrated and "powerless to tackle the problem" due to the lack of guidelines for rational de-prescribing. They conclude that there is a need for simple GP-friendly tools, and access to pharmacotherapy advice to address this problem. In light of these factors, it seems likely that without the evidence and systematic frameworks to reduce IMUP, even knowledgeable and ethical clinicians lack the confidence to de-prescribe (62,67-70), and thus continue to harm their most vulnerable patients, despite the very best of intentions.

Moving Forward: Overcoming the Barriers

Despite the grim picture painted above, there are signs of light on the horizon. The factors which influence effective clinical decision-making in the frail elderly are crystallizing. Lundby et al. (71) identified four themes related to health care professionals' attitudes towards de-prescribing in older people with limited life expectancy: patient and relative involvement, the importance of teamwork, health care professionals' self-assurance and skills, and the impact of organizational factors. There is a sea change in patients' attitudes as well. In contrast to a generation ago, more patients today believe that they are taking too many medications (61,72) and may be open to de-prescribing. Attitudes toward IMUP have also begun to change, with drug reduction becoming increasingly recognized as a global goal of the highest priority. Several studies and reviews highlight the

trend towards increased de-prescribing. A US-population based study evaluated the attitudes of older adults toward prescribing using a revised version of the Patients' Attitudes Towards De-prescribing questionnaire. The majority of older adults were willing to have at least one medicine de-prescribed and did not report distress surrounding this decision. Taking six or more medications was significantly associated with willingness to de-prescribing (73). Todd et al. (74) (IGRIMUP member, Newcastle University, UK) have investigated de-prescribing in the palliative setting, finding that patients who have come to accept the progression of their disease tend to place less importance on their medications and less reluctant to cease them.

Education, of clinicians and patients alike, is another essential component in the fight against IMUP. In a recent systematic review, Hansen et al. (75) evaluated behavior change techniques in de-prescribing interventions.

In another review, Reeve et al. (76) concluded: "an effective patient-centered de-prescribing process will need to involve patient education on the risks and benefits of ongoing medication use, allaying any fears that patients have about medication cessation, and employing a process that includes support, monitoring and follow-up". Reeve et al. (77) also found that patient resistance to de-prescribing may be influenced by family members' attitudes as well as information acquired through the media. They recommended raising awareness about de-prescribing, discussing with the patient potential harms and benefits of given medications, informing patients about different treatment options, and culminating in joint decision-making. By applying these steps, patients gain confidence in the de-prescribing process (77). Sidorkiewicz et al. (78) also stress the need for continual doctor-patient dialogue to strengthen trust in the decision-making process. I would expand on these notions and claim that education about de-prescribing must begin earlier. Medical schools and residency-training programs must teach clinicians more about IMUP as well as the methods to combat it (Figure 1). These topics must become part of the core curriculum. With regards to patient education, the idea that drugs can be harmful, and may eventually need to be stopped, should be instilled early. Public awareness campaigns should be waged about the harms of IMUP and the need to de-prescribe. Combined, these strategies will have a large impact on the attitudes of both clinicians and patients.

Putting It All Together

From stagnant debate about definitions and the publication of exhaustive lists, the discourse on this problem is finally starting to move into a more practical realm - how to counter the IMUP epidemic. I argue that this must take the form of the aggressive use of poly-de-prescribing - the discontinuation of as many medications as possible. To paraphrase a line from a well-known Western: "When you have to stop - STOP, don't talk". It is with this proactive attitude which I encourage the adoption of my own approach - the Garfinkel Palliative-Geriatric Practice (GPGP) method (Figure 2). While realizing that the single, most important predictor of inappropriate prescribing is the number of prescribed medications, my approach offers an effective solution, as well as provides an appropriate definition of poly-de-prescribing: "stopping as many non-life-saving drugs as possible with the approval of the patient/family".

This algorithm is simple and applicable to all patients, with any combination of comorbidities and medication, and conducive to adoption in a wide range of clinical scenarios. It emulates the original definition of EBM by Sackett et al. (79): "the integration of best research evidence, clinical expertise and patient values". The search for reliable best-evidence in VOCODFLEX may ultimately be fruitless. As such, the GPGP re-emphasizes the prominence originally intended to the latter two, forgotten pillars. GPGP combines EBM knowledge with clinical judgment, and gives high priority to patient/family preferences. It is a palliative approach in line with the Holmes (58) framework in which medications with preventive/curative intention of questionable value in their impact on suffering or QoL are stopped. In addition, GPGP addresses under-prescribing of potentially helpful medications. Like PATH, it calls for a less aggressive approach in reaching rigid target goals (BP, serum glucose, and lipid concentrations). Given the bold nature of this intervention, all recommendations for drug discontinuation must be explained in depth and approved by the patient/family (1-4,51). The high degree of involvement by the patient and families can potentially be time-consuming, but this element (in my experience) reduces the likelihood of lawsuits.

GPGP has already been implemented in both nursing departments (80) and in community-dwelling elders (51) and was beneficial in both. It has been suggested by others as a basic paradigm for addressing IMUP (81-84). The validity of the method was borne out recently in a study demonstrating improved clinical outcomes and quality of life comparing VOCODFLEX treated with GPGP with those receiving standard care (1). In this longitudinal, prospective, nonrandomized study in Israel, Poly-de-prescribing (PDP) of as many prescription drugs as possible was recommended. Poly-de-prescribing of ≥3 drugs was achieved by 122 participants (PDP group); two or less drugs were stopped by 55 "non-responders" (NR group). These two groups were then compared over time. The average age was 83.4±5.3, and 80.8±6.3, respectively (p=0.0045), and follow-up was ≥ three years, 43.6±14, and 39.5±16.6 months, respectively (p=0.09). The main barrier to de-prescribing was the GPs' unwillingness to adopt PDP recommendations (p<0.0001). The baseline number of medications taken by both groups was 10 (IQR 8 to 12). On the last follow up, the drug count was 11 (IQR 8 to 12) in the NR group and 4 (IQR 2 to 5)

in the PDP group (p=0.0001). At the end of follow-up, patient/family satisfaction, as well as clinical outcomes were evaluated based on a Likert-scale questionnaire. The PDP group showed significantly less deterioration, and sometimes improvement in the following areas: General satisfaction, functional, mental and cognitive status, sleep quality, appetite, and sphincter control. The number of major complications was significantly reduced (p<0.002 in all). The rate of hospitalizations and mortality was comparable. Health improvement occurred within three months after de-prescribing in 83%, and persisted for ≥ two years in 68%. This longitudinal study demonstrates in a self-selected sample that poly-de-prescribing is not only well tolerated, but also associated with improved clinical outcomes, compared with those who adhered to standard recommendations. Although cost-effectiveness has yet to be studied, intuitively GPGP seems likely to provide substantial financial savings for patients and healthcare systems alike.

The fact that this study is not a double-blinded RCT may be considered a weakness. However, I argue that researching interventions for IMUP may need different standards than those applied to trials for drugs funded by pharmaceutical companies. A "traditional" RCT in VOCODFLEX would be practically impossible. One would need to find a large cohort of demographically similar patients, stop the same X number of medications within the same list of Y medications prescribed for the same medical conditions, then follow both groups for several years. Logistically, the sample sizes necessary for this sort of study would be prohibitive given the great heterogeneity of VOCODFLEX, and needless to say, funding would be sparse. Yet this cannot be an excuse; we must proceed with innovative approaches for treating one of the most devastating problems our vulnerable patients face. My intention is that this study should provide a modicum of confidence to clinicians to overcome the manifold barriers to de-prescribing - and get on with this critical task.

1. Perform a medication review on all older adults, particularly on vulnerable subpopulations (VOCODFLEX, D.G.) and those with polypharmacy, with an eye for de-prescribing. The need to re-prescribe discontinued medications should not be regarded as a failure.

2. Consider the generalizability of the evidence: There is underrepresentation of older adults in general, and VOCODFLEX in particular, in clinical trials. Therefore, before initiating 'appropriate' medications, consider the generalizability of the evidence for the specific patient (as also stressed in Figure 1).

3. Consider each medication for de-prescribing, extending beyond standardized lists of "inappropriate medications". Using all potentially 'helpful' medications may not be appropriate and these medications should be prioritized; in some patients, 'under-prescribing' may actual be ideal.

4. Employ mixed implicit and explicit approaches: lists of "drugs to avoid" may be helpful, but may ultimately give false assurance; other drugs that can be de-prescribed, which do not appear on the list, may be missed.

5. Communicate about the knowledge gap: Approaches to enhance de-prescribing should include recognition of the knowledge gap regarding the dose-effect curve and benefit/risk ratio of drugs used by older adults, and this uncertainty should be communicated to the patient and family.

6. Acknowledge commercial influences on polypharmacy: Publication bias and overhyping of new or immature research results by media and pharmaceutical companies result in a research narrative that overestimates efficacy, underestimates harms, and fuels IMUP. Trial results should not be implemented in older adults unless appropriate clinical outcome are proven in older populations.

7. Medical education needs a stronger focus on IMUP and its potential negative impact. Currently these topics are inadequately emphasized in the curriculum for doctors, nurses, and pharmacists. Education is insufficient regarding the harm of polypharmacy, specific drug-class ADEs, the importance of medication reviews, and how specialty prescribing may increase IMUP and lead to prescribing cascades.

8. Medical education needs a stronger focus on combatting IMUP, including teaching methods to de-prescribe.

9. Medical education should expand teaching on VOCODFLEX and multi-morbidity models. Current medical education places undue focus on single-disease models, and the treatment paradigms which evolve from these models may be harmful in multi-morbid patients.

10. Individualized care models for VOCODFLEX need to be developed: decision-making in older complex patients should be personalized, and must consider life expectancy, quality of life vs. burden of treatment, potential harms and benefits, and should give the highest priority to patient/family preferences. A single case manager should coordinate decisions within a shared framework, preferably in a generalist setting and ideally with the input of a pharmacist.

Figure 1. Short version of IGRIMUP 10 recommendations for action (18)

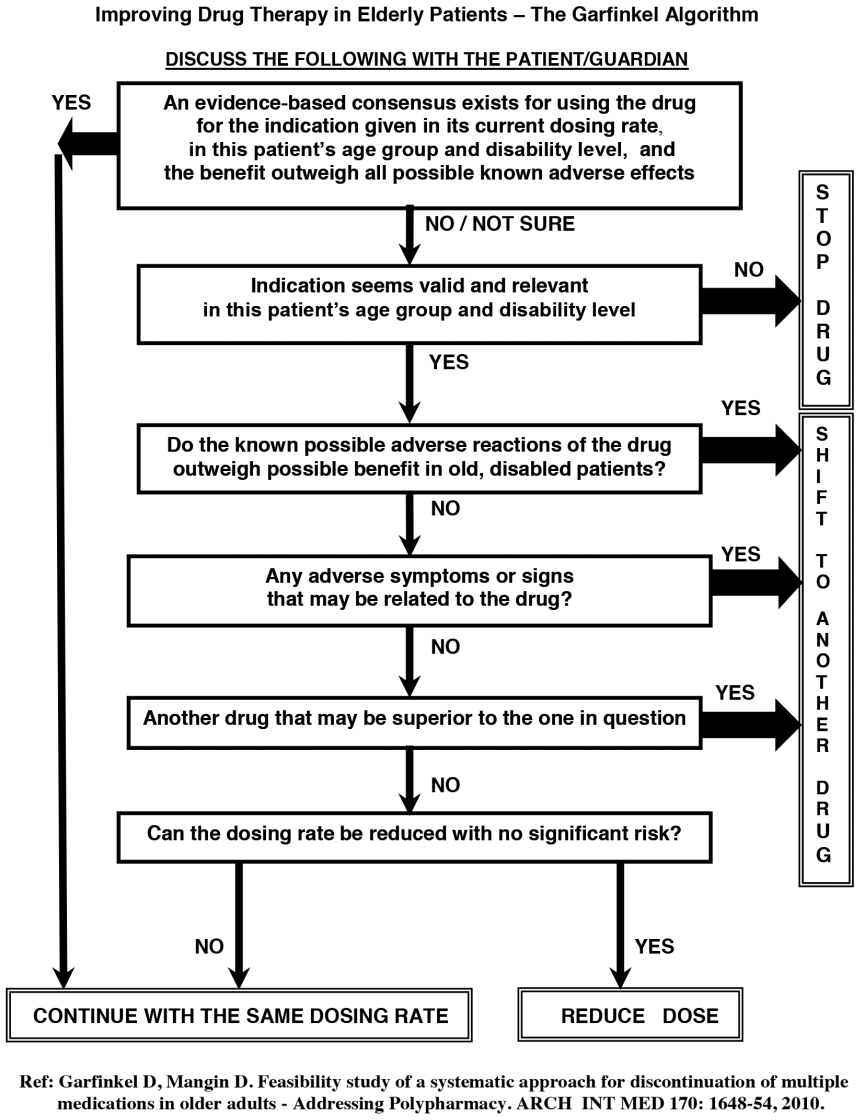

Figure 2. Improving Drug Therapy in Elderly Patients - The Garfinkel Algorithm

A Community of Clinicians Fighting IMUP

A milestone in the fight against the IMUP epidemic and the promotion of rational de-prescribing, was the establishment of IGRIMUP - the International Group for Reducing Inappropriate Medication Use & Polypharmacy in 2013. Our organization's goal is to combat IMUP, via interdisciplinary communication and collaboration. IGRIMUP's membership currently numbers more than 130 leading health professionals from 30 countries joining together as a think-tank strategizing "the war against IMUP" in the conviction that, due to the tremendous extent of the problem, it should be addressed as a global pandemic (1,2,18). Researchers are currently developing strategic approaches to prevent and treat IMUP in its many forms. A number of "5-step de-prescribing protocols" have been proposed by several IGRIMUP members (64,85), leading to a preliminary consensus regarding the principles of de-prescribing. These include reviewing all medications, identifying drugs to be stopped, substituted, or reduced, planning a de-prescribing regimen in partnership with the patient and frequently reviewing and supporting the patient (85). Recently, IGRIMUP has proposed ten comprehensive Action Recommendations, briefly summarized in figure 1. The Garfinkel GPGP method is in agreement with, and may help achieve most of these recommendations.

Conclusion

Towards a New Medical Approach for the Vulnerable Elderly

The time has come to decisively shift the focus of discourse on IMUP from definitions, evaluations, and lists of drugs to avoid towards active, rational de-prescribing. According to Scott

(IGRIMUP member, University of Queensland, Australia), in today's atmosphere of defensive medicine and guideline-based prescribing, a large part of "doing no harm" in the geriatric population must focus on de-prescribing. We must acknowledge the knowledge gap about our patients, and avoid interventions with questionable benefit. Complex elderly patients have a vastly altered pharmacokinetic and pharmacodynamic profile, especially in the presence of comorbidity and polypharmacy; treatment decisions must be made accordingly. Partnership with the patient and family in decision-making is essential in the geriatric-palliative approach, and is key to overcoming barriers to de-prescribing. In line with these perspectives and the IGRIMUP recommendations (18), my proposed GPGP approach provides a simple and practical tool for rational, patient-centred de-prescribing. I have also provided initial evidence for the safety and practicability of the approach, as well as the many positive clinical outcomes realized by the application of GPGP.

Beyond specific definitions of IMUP and methods to combat it, a revolution in our medical paradigm in treating the elderly is of the essence. IMUP is a 21st-century iatrogenic pandemic. Like other pandemics, international efforts must be mobilized in order to manage the problem effectively, and it is in this spirit that IGRIMUP was established and has begun sowing the seeds of global collaboration of clinicians and researchers. To borrow the language of epidemics, curing the "infected", i.e. treating polypharmacy with poly-de-prescribing, is necessary but insufficient. In this review, I also emphasized "immunization", i.e. the need to educate professionals and laymen alike about this critical issue, in an attempt to stem the rising tide. The IGRIMUP principles for research, education, diagnosis, and treatment (18), are based on palliative, geriatric and ethical principles, as well as highlighting patient and family preferences, which differ in goal and in ethos from the principles of the single-disease model. We are practicing in an era when a multitude of guidelines exhort us to do a great deal of good, but we are not taught to discern when too much good becomes harm. We must uphold the legacy of generations of physicians who strove for the highest ethical standards in medical practice, and keep alight the venerable torch of "primum non-nocere".

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Ethics

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References

1. Garfinkel D. Poly-de-prescribing to treat polypharmacy: efficacy and safety. Ther Adv Drug Saf 2018;9:25-43.
2. Barnett N, Garfinkel D. Deprescribing one year on: challenging the first iatrogenic epidemic. Eur J Hosp Pharm Sci Pract 2018;25:63-64.
3. Garfinkel D, Ilhan B, Bahat G. Routine de-prescribing of chronic medications to combat polypharmacy. Ther Adv Drug Saf 2015;6:212-233.
4. Garfinkel D; IGRIMUP. Overview of Current and future research and clinical directions for drug discontinuation psychological, traditional and professional obstacles to de prescribing. Eur J Hosp Pharm Sci Pract 2017;24:16-20.
5. Garfinkel D. Geriatric Boom Catastrophe - A major medical, economic and social nightmare of the 21st century [abstract]. Proc 6th. Congress Intern Ass Gerontol Geriatr 1997:364.
6. 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.
7. Rochon PA, Gurwitz JH. Optimising drug treatment for elderly people: the prescribing cascade. BMJ 1997;315:1096-1099.
8. Gill SS, Mamdani M, Naglie G, Streiner DL, Bronskill SE, Kopp A, Shulman KI, Lee PE, Rochon PA. A prescribing cascade involving cholinesterase inhibitors and anticholinergic drugs. Arch Intern Med 2005;165:808-813.
9. Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, Hanlon JT. Appropriate prescribing in elderly people: how well can it be measured and optimised? Lancet 2007;370:173-184.
10. Ernst FR, Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. J Am Pharm Assoc (Wash) 2001;41:192-199.
11. Hoonhout LH, de Bruijne MC, Wagner C, Zegers M, Waaijman R, Spreeuwenberg P, Asscheman H, van der Wal G, van Tulder MW. Direct medical costs of adverse events in Dutch hospitals. BMC Health Serv Res 2009;9:27.
12. Stark RG, John J, Leidl R. Health care use and costs of adverse drug events emerging from outpatient treatment in Germany: a modelling approach. BMC Health Serv Res 2011;11:9.
13. Rottenkolber D, Hasford J, Stausberg J. Costs of adverse drug events in German hospitals a microcosting study. Value Health 2012;15:868-875.
14. Health Data from Turkish Health Ministry (2005/2006). [http://www.sb.gov.tr/TR/hata/1-0/edomy1fl1cwueh4500xyppma.ex]
15. Santibanez-Beltran S, Villarreal-Rios E, Galicia-Rodriguez L, Martinez-Gonzalez L, Vargas-Daza ER, Ramos-Lopez JM. Economic cost of polypharmacy in the elderly in primary health car]. Rev Med Inst Mex Seguro Soc 2013;51:192-199.
16. Hovstadius B, Petersson G. The impact of increasing polypharmacy on prescribed drug expenditure-a register-based study in Sweden 2005-2009. Health Policy 2013;109:166-174.
17. Gnjidic D, Le Couteur DG, Pearson SA, McLachlan AJ, Viney R, Hilmer SN, Blyth FM, Joshy G, Banks E. High risk prescribing in older adults: prevalence, clinical and economic implications and potential for intervention at the population level. BMC Public Health 2013;13:115.
18. 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 Ten Recommendations for Action. Drugs Aging 2018;35:575-587.
19. Stavert RR, Lott JP. The bystander effect in medical care. N Engl J Med 2013;368:8-9.
20. Golomb BA, Chan VT, Evans MA, Koperski S, White HL, Criqui MH. The older the better: are elderly study participants more non-representative? A cross-sectional analysis of clinical trial and observational study samples. BMJ Open 2012:2.
21. de Souto Barreto P, Ferrandez AM, Saliba-Serre B. Are older adults who volunteer to participate in an exercise study fitter and healthier than nonvolunteers? The participation bias of the study population. J Phys Act Health 2013;10:359-367.

22. Sugisawa H, Kishino H, Sugihara Y, Shibata H. Characteristics of dropouts and participants in a twelve-year longitudinal research of Japanese elderly. Nippon Koshu Eisei Zasshi 2000;47:337-349.

23. Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA 2005;294:716-724.

24. Garfinkel D, Ilin N, Waller A, Torkan- Zilberman A, Zilberman N, Gurta I. Inappropriate Medication Use and Polypharmacy in end stage cancer patients: Isn't it the family doctor's role to de-prescribe much earlier?" Int J Clin Pract 2018;72:e13061.

25. Kotlinska-Lemieszek A, Paulsen O, Kaasa S, Klepstad P. Polypharmacy in patients with advanced cancer and pain: a European cross-sectional study of 2282 patients. J Pain Symptom Manage 2014;48:1145-1159.

26. Sanz Ortiz J. Chemotherapy at the end of life: up until when? Clin Transl Oncol 2012;14:667-674.

27. Cruz-Jentoft AJ, Boland B, Rexach L. Drug therapy optimization at the end of life. Drugs Aging 2012;29:511-521.

28. O'Brien CP. Withdrawing medication. Managing medical comorbidities near the end of life. Can Fam Physician 2011;57:304-307.

29. Hanlon JT, Schmader KE, Ruby CM, Weinberger M. Suboptimal prescribing in older inpatients and outpatients. J Am Geriatr Soc 2001;49:200-209.

30. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, McLachlan AJ, Cumming RG, Handelsman DJ, Le Couteur DG. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol 2012;65:989-995.

31. Tinetti ME, Bogardus ST Jr, Agostini JV. Potential pitfalls of disease-specific guidelines for patients with multiple conditions. N Engl J Med 2004;351:2870-2874.

32. Nightingale G, Hajjar E, Swartz K, Andrel-Sendecki J, Chapman A. Evaluation of a pharmacist-led medication assessment used to identify prevalence of and associations with polypharmacy and potentially inappropriate medication use among ambulatory senior adults with cancer. J Clin Oncol 2015;33:1453-1459.

33. Zhang X, Zhou S, Pan K Li X, Zhao X, Zhou Y, Cui Y. Potentially inappropriate medications in hospitalized older patients: a cross-sectional study using the Beers 2015 criteria versus the 2012 criteria. Clin Interv Aging 2017;12:1697-1703.

34. Chang CB, Lai HY, Hwang SJ, Yang SY, Wu RS, Liu HC, Chan DC. Prescription of potentially inappropriate medication to older patients presenting to the emergency department: a nationally representative population study. Sci Rep 2018;8:11727.

35. Viktil KK, Blix HS, Moger TA, Reikvam A. Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. Br J Clin Pharmacol 2007;63:187-195.

36. Rausch C, Laflamme L, Bültmann U, Möller J. Number of medications and adverse drug events by unintentional poisoning among older adults in consideration of inappropriate drug use: a Swedish population-based matched case-control study. Eur J Clin Pharmacol 2017;73:743-749.

37. Woodward MC. Deprescribing: Achieving Better Health Outcomes for Older People through Reducing Medications. J Pharm Pract Res 2003;33:323-328.

38. Reeve E, Gnjidic D, Long J, Hilmer S. A systematic review of the emerging definition of 'deprescribing' with network analysis: implications for future research and clinical practice. Br J Clin Pharmacol 2015;80:1254-1268.

39. 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.

40. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing 2008;37:673-679.

41. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing 2015;44:213-218.

42. Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. Arch Intern Med 2011;171:1013-1019.

43. Bravo C, Peña A, Molina M, Sanfeliu J. Application of the STOPP criteria in hospitalised elderly patients to detect and optimise inappropriate psychopharmaceutical prescriptions. European Geriatric Medicine 2018;9:597-602.

44. Wehling M. Multimorbidity and polypharmacy: how to reduce the harmful drug load and yet add needed drugs in the elderly? Proposal of a new drug classification: fit for the aged. J Am Geriat Soc 2009;57:560-561.

45. Wehling M, Burkhardt H, Kuhn-Thiel A, Pazan F, Throm C, Weiss C, Frohnhofen H. VALFORTA: a randomised trial to validate the FORTA (Fit fOR The Aged) classification. Age Ageing 2016;45:262-267.

46. Pazan F, Weiss C, Wehling M; FORTA. Correction to: The EURO-FORTA (Fit fOR The Aged) List: International Consensus Validation of a Clinical Tool for Improved Drug Treatment in Older People. Drugs Aging 2018;35:677.

47. Steinman MA, Rosenthal GE, Landefeld CS, Bertenthal D, Kaboli PJ. Agreement between drugs-to-avoid criteria and expert assessments of problematic prescribing. Arch Intern Med 2009;169:1326-1332.

48. Topinkova E, Baeyens JP, Michel JP, Lang PO. Evidence-based strategies for the optimization of pharmacotherapy in older people. Drugs Aging 2012;29:477-494.

49. Renom-Guiteras A, Kunnamo I, Reeves D, Höck J, Johansson T, Sönnichsen A. The PRIMA-eDS electronic decision support tool for polypharmacy - a multinational European project. IN: Proceedings of 2017 International Association of Gerontology and Geriatrics (IAGG) 21st Word Congress; 2017 Jul 23-27, San Francisco, USA. Oxford University Press on behalf of The Gerontological Society of America, 2017.

50. Soiza RL, Subbarayan S, Antonio C, Cruz-Jentoft AJ, Petrovic M, Gudmundsson A, O'Mahony D. The SENATOR project: developing and trialling a novel software engine to optimize medications and nonpharmacological therapy in older people with multimorbidity and polypharmacy. Ther Adv Drug Saf 2017;8:81-85.

51. Garfinkel D, Mangin D. Feasibility study of a new systematic approach for discontinuation of multiple medications in older adults. Addressing polypharmacy. Arch Int Med 2010;170:1648-1654.

52. Garfinkel D. Digital methods for medication review - Less is more - customizing drug therapy in the elderly. Europian Union Geriatric Medicine 2014;5(Suppl 1):22.

53. Hanlon JT, Schmader KE. The medication appropriateness index at 20: where it started, where it has been, and where it may be going. Drugs Aging 2013;30:893-900.

54. ARMOR: A Tool to Evaluate Polypharmacy in Elderly Persons | Annals of Long Term Care [http://www.annalsoflongtermcare.com/content/armor-a-tool-evaluate-polypharmacy-elderly-persons]

55. Moorhouse P, Koller K, Mallery L. End of Live Care in Frailty. Interdiscip Top Gerontol Geriatr 2015;41:151-160.

56. Mallery LH, Ransom T, Steeves B, Cook B, Dunbar P, Moorhouse P. Evidence-informed guidelines for treating frail older adults with type 2 diabetes: from the Diabetes Care Program of Nova Scotia (DCPNS) and the Palliative and Therapeutic Harmonization (PATH) program. J Am Med Dir Assoc 2013;14:801-808.

57. Mallery LH, Allen M, Fleming I, Kelly K, Bowles S, Duncan J, Moorhouse P. Promoting higher blood pressure targets for frail older adults: a consensus guideline from Canada. Cleve Clin J Med 2014;81:427-437.

58. Holmes HM, Hayley DC, Alexander GC, Sachs GA. Reconsidering medication appropriateness for patients late in life. Arch Intern Med 2006;166:605-609.

59. Reeve E, Shakib S, Hendrix I, Roberts MS, Wiese MD. The benefits and harms of de-prescribing. Med J Aust 2014;201:386-389.

60. Drug prescribing for older adults [http://www.uptodate.com/contents/drug-prescribing-for older-adults?topicKey=PC%2F3013&elapsedTimeMs=4&view=print&displayedView=full

61. Linsky A, Simon SR, Bokhour B. Patient perceptions of proactive medication discontinuation. Patient Educ Couns 2015;98:220-225.

62. Scott IA, Anderson K, Freeman CR, Stowasser DA. First do no harm: a real need to de-prescribe in older patients. Med J Aust 2014;201:390-392.

63. Plakiotis C, Bell JS, Jeon YH, Pond D, O'Connor DW. Deprescribing Psychotropic Medications in Aged Care Facilities: The Potential Role of Family Members. Adv Exp Med Biol 2015;821:29-43.

64. Scott IA, Hilmer SN, Reeve Potter K, Le Couteur D, Rigby D, Gnjidic D, Del Mar CB, Roughead EE, Page A0, Jansen J, Martin JH. Reducing inappropriate polypharmacy: the process of de-prescribing. JAMA Intern Med 2015;175:827-834.

65. Reeve E, Turner JP. Patients' perspectives on the brave new word 'deprescribing'. Int J Pharm Pract 2015;23:90-91.

66. Anthierens S, Tansens A, Petrovic M, Christiaens T. Qualitative insights into general practitioners views on polypharmacy. BMC Fam Pract 2010;11:65.

67. Schuling J, Gebben H, Veehof LJ, Haaijer-Ruskamp FM. Deprescribing medication in very elderly patients with multimorbidity: the view of Dutch GPs. A qualitative study. BMC Fam Pract 2012;13:56.

68. Ostini R, Hegney D, Jackson C, Tett SE. Knowing how to stop: ceasing prescribing when the medicine is no longer required. J Manag Care Pharm 2012;18:68-72.

69. Anderson K, Stowasser D, Freeman C, Scott I. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. BMJ Open 2014;4:e006544.

70. Nixon M, Kousgaard MB. Organising medication discontinuation: GP decision making when de-prescribing statins. BMC Health Services Research 2016) 16:226 Denmark: Copenhagen University, 2014.

71. Lundby C, Graabæk T, Ryg J, Søndergaard J, Pottegård A, Nielsen DS. Health care professionals' attitudes towards deprescribing in older patients with limited life expectancy: a systematic review. Br J Clin Pharmacol 2019;85:868-892.

72. Reeve E, Shakib S, Hendrix I, Roberts MS, Wiese MD. Review of de-prescribing processes and development of an evidence-based, patient-centred de-prescribing process. Br J Clin Pharmacol 2014;78:738-747.

73. Reeve E, Wolff JL, Skehan M, Bayliss EA, Hilmer SN, Boyd CM. Assessment of Attitudes Toward Deprescribing in Older Medicare Beneficiaries in the United States. JAMA Intern Med 2018;178:1673-1680.

74. Todd A, Holmes H, Pearson S, Hughes C, Andrew I, Baker L, Husband A. 'I don't think I'd be frightened if the statins went': a phenomenological qualitative study exploring medicines use in palliative care patients, carers and healthcare professionals. BMC Palliat Care 2016;15:13.

75. Hansen CR, O'Mahony D, Kearney PM, Sahm LJ, Cullinan S, Huibers CJA, Thevelin S, Rutjes AWS, Knol W, Streit S, Byrne S . Identification of behaviour change techniques in deprescribing interventions: a systematic review and meta-analysis. Br J Clin Pharmacol 2018;84;2716-2728.

76. Reeve E, To J, Hendrix I, Shakib S, Roberts MS, Wiese MD. Patient barriers to and enablers of de-prescribing: a systematic review. Drugs Aging 2013;30:793-807.

77. Reeve E, Thompson W, Farrell B. Deprescribing: A narrative review of the evidence and practical recommendations for recognizing opportunities and taking action. Eur J Intern Med 2017;38:3-11.

78. Sidorkiewicz S, Tran VT, Cousyn C, Perrodeau E, Ravaud P. Discordance between drug adherence as reported by patients and drug importance as assessed by physicians. Ann Fam Med 2016;14:415-421.

79. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ 1996;312:71-72.

80. Garfinkel D, Zur-Gil S, Ben-Israel J. The war against Polypharmacy. A new, cost Effective Geriatric - Palliative approach for improving drug therapy in disabled elderly people. Israel Med Assoc J 2007;9:430-434.

81. Sengstock D, Zimmerman J. 53. Addressing Polypharmacy & Improving Medication Adherence in Older Adults. In: Current Diagnosis and Treatment: Geriatrics 2e. In: Williams BA, Chang A, Ahalt C, Chen H, Conant R, Landefeld CS, Ritchie C, Yukawa M. 2nd ed. McGraw-Hill Education Medical, 2014:608.

82. Ozturk Bahat G, Ozkaya H, Kılıc C, Muratli S, Ilhan B, Tufan A, Tufan F, Horasan Z, Dogan H, Erten N, Karan MA, Garfinkel D. P-134: Efficacy and safety of training program concentrating on the Garfinkel method as a tool for reducing polypharmacy in nursing home residents. Europ Geriat Med 2015;6(Suppl 1):1-201,

83. Scott IA, Anderson K, Freeman C. Evidence-Based Deprescribing: Reversing the Tide of Potentially Inappropriate Polypharmacy. J Clin Outc Manag (JCOM) 2016;23:359-369.

84. Campins L, Serra-Prat M, Gózalo I, Lopez D, Palomera E, Augsti C, Carbe M; REMEI Group. Randomized controlled trial of an intervention to improve drug appropriateness in community-dwelling polymedicated elderly people. Fam Prac 2016;34:36-42.

85. Farrel B, Mangin D. Deprescribing is an essential part of good prescribing. Am Fam Physician 2019;99:7-9.

ORIGINAL RESEARCH

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Evaluation of Self-reported Insomnia and Its Association with Some Geriatric Syndromes in Older Adults

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Abstract

Objective: Sleep is a reversible state of altered consciousness, characterized by decreased response to environmental stimuli. The American Academy of Sleep Medicine Guideline 2017 defined insomnia as the subjective perception of problems with initiation, duration and quality of sleep leading to daytime impairment. Sleep problems are common among adults over the age of 65, with a reported prevalence of 50-70%. In the older population, sleep disorders have been associated with poor quality of health, falls, inappropriate medication use and higher rates of morbidity and mortality. In our study, we aimed to evaluate the frequency of sleep problems and their relationship with some geriatric syndromes.

Materials and Methods: Medical reports of patients who presented to our outpatient clinic between November 2013 and November 2016 were retrospectively analysed and the association of sleep problems with age, gender, falls, frailty, and restless leg syndrome (RLS) was evaluated.

Results: A total of 295 geriatric patients were included in the study. Sixty-six percent of the patients (n=196) were female and 34% (n=99) were male. The mean age was 75.6±6.8 years. The prevalence of sleep problems was 47.8%. Bivariate analysis showed that insomnia was significantly related with age, polypharmacy and RLS. There was no statistically significant difference between genders. In regression analysis, age, polypharmacy and RLS were independently associated with insomnia.

Conclusion: Sleep disorders in the older adults is a major health problem affecting the quality of life and should be questioned during outpatient clinic visits. It should be kept in mind that sleep problems may be related to important geriatric syndromes.

Keywords: Insomnia, older population, restless leg syndrome

Introduction

Sleep is a reversible state of altered consciousness, characterized by decreased response to environmental factors and stereotypical electroencephalography changes (1,2). Age-associated changes in sleep and circadian rhythm start in early as in forties and increase with age (3). Older people tend to have a disrupted sleep efficiency, and frequency of sleep disorders raises with aging (4). Insomnia disorder is defined as the subjective report of the problems with falling asleep, duration and quality that cause daytime impairment. Insomnia is identified as chronic, if it persists for at least three months three times per a week (5). The prevalence of short-term insomnia is reported 30%-50% in adults and chronic insomnia is reported as at least 5-10% in industrialized countries (5-7). The prevalence of insomnia in older population varies between 18%-65% (8-11). Restless leg syndrome (RLS) is the unpleasant feeling (numbness, ache, tingling) in the legs that cause urge to move, especially in the evening. It is also related with insomnia and sleep disruption and reported more prevalent in older adults (8,12). RLS is reported as a common cause of insomnia; as much as 85% of patients with RLS were reported to have insomnia (13).

Sleep is essential and important in every stage of life. Sleep disorders were found to be related with many undesirable health outcomes significant for the older adults such as cognitive problems, depression, fatigue, falls, metabolic syndrome, cardiovascular problems, polypharmacy and inappropriate medication use (14-18)

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A few published studies evaluated the prevalence of insomnia and RLS among older adults in Eastern Europe. On the other hand, the number of the studies investigating the relation between sleep disorders and polypharmacy and inappropriate medication use is limited. In this study, we aimed to evaluate the prevalence of insomnia and RLS among older patients admitted to our outpatient clinic in Turkey and examine the relation between insomnia/RLS and demographic data (gender and age), frailty, falls and polypharmacy.

Materials and Methods

The medical records of patients, aged ≥60 years admitted to geriatric outpatient clinic at İstanbul University İstanbul Faculty of Medicine between November 2013-November 2016 were evaluated retrospectively. Patients who were questioned for insomnia, RLS and falls were included. Exclusion criteria were age <60 years, any missing data on sleep, RLS or falls.

Gender, age, presence of insomnia, restless leg symptoms, history of falls, presence of polypharmacy and frailty status were noted from the patient files.

Insomnia was assessed by asking the patients if they experienced difficulty in falling sleep and/or maintaining sleep (19). For evaluating RLS a single question was asked; do you experience unpleasant and restless feeling in your legs which is relieved by walking or movement (20). Patients were asked if they had experienced any fall during the last year. Polypharmacy was defined as the use of ≥4 medications (21). Frailty was assessed by FRAIL scale which includes five components; fatigue, resistance, ambulation, illness and loss of weight. Frail scale scores range 0-5; ≥3 represents frail, 1-2 pre-frail and 0 for robust health status (22). In our study FRAIL score ≥3 was accepted frail and scores <3 non-frail. This study has been evaluated and approved by the İstanbul University faculty of medicine ethics committee on June 28, 2018 (Number: 956).

Statistics

Descriptive statistics were generated for all study variables. Kolmogorov-Smirnov test was used to determine normal or non-homegoneous distribution. All the numerical parameters revealed nonparametric with non-homogenous distribution. Numerical variables were given as median, mean and standard deviation and relative frequencies were given for categorical (qualitative) variables. The two independent groups were compared by Mann-Whitney U test. Chi-square test with Yates's correction and Fisher's exact test was used for 2×2 contingency tables when appropriate for nonnumeric data. For further evaluation of the statistically significant data in univariate analysis, binary logistic regression analysis was used. P<0.05 was accepted statistically significant. SPSS version 21 (IBM corporation, Armonk, NY, USA) was used for all statistical analysis in this study.

Results

Among a total of 1034 patients, 295 participants aged ≥60 were included in this study (196 female and 99 male). Mean age was 75.6±6.8 years. One hundred and forty-one patients (47.8%) reported having insomnia. 28.3% of the patients had RLS and 39% of the patients reported at least one fall in the previous year. Prevalence of polypharmacy was found 82.7% and 16.7% of the patients were frail (Table 1). The relationship between insomnia and demographic data (gender and age), RLS, falls, frailty and polypharmacy are given in Table 2. There was no statistically significant difference between genders in terms of insomnia (p=0.07). There was a borderline significant relation between age and insomnia (p=0.05). There was no significant relationship between sleep and falls or frailty (p=0.26 and 0.31, respectively). The relations between insomnia and polypharmacy and insomnia and RLS were found statistically significant (p=0.01). There was higher prevalence of RLS and lower prevalence of polypharmacy in patients with insomnia (p=0.01 for both).

We performed regression analysis to find independent factors associated factors with insomnia. In regression analysis, the dependent variable was the presence of insomnia, independent variables were age, presence of RLS, falls and polypharmacy. Although we didn't find any relation between insomnia and falls in univariate analysis, we put it in regression analysis, as there are studies documenting independent relation between falls and insomnia in the older adults (18). A statistically significant relationship was found between insomnia and age, polypharmacy and RLS. Increased age, presence of polypharmacy and RLS were associated with higher rates of insomnia (Odd's ratios were 1.04, 1.83, 2.08, respectively) (Table 3)

Table 1. General demographic and geriatric syndrome data of the participants

Male	99 (34%)
Female	196 (66%)
Age (years)	75.6±6.8
Insomnia	141 (47.8%)
RLS	83 (28.3%)
Falls	115 (39%)
Polypharmacy	244 (82.7%)
Frailty	49 (16.7%)

RLS: Restless leg syndrome; Data are given as number (%) or mean ± standard deviation as appropriate

Table 2. Univariate analyses for insomnia and related factors				
Gender	**Total**	**Insomnia (+)**	**Insomnia (-)**	**p**
Male [%, (n)]	100% (99)	41.4% (41)	58.6% (58)	0.07
Female [%, (n)]	100% (196)	51% (100)	49% (96)	0.07
Age	75.6±6.8	76.3±7.0	74.9±6.4	0.05
RLS symptom (+)	100% (85)	58% (49)	42% (36)	0.01*
[%, (n)] Fall in the previous year	100% (112)	50% (56)	50% (56)	0.3
[%, (n)] Polypharmacy (+)	100% (244)	51.3% (125)	48.7% (119)	0.01*
[%, (n)] Polypharmacy (-)	100% (51)	31.4% (16)	68.6% (35)	0.01*
Frailty	100% (41)	51.2% (21)	48.8% (20)	0.26
n: Number, *: Statistically significant, RLS: Restless leg syndrome				

Table 3. Logistic regression analysis for factors associated with insomnia			
Factor	**Odd's ratio**	**95% confidence interval**	**p**
Age	1.04	1.01-1.08	0.029
Restless leg syndrome	1.83	1.05-3.19	0.033
Polypharmacy	2.08	1.04-4.17	0.038
Dependent variable was the presence of insomnia; independent variables were age, presence of restless leg syndrome, falls and polypharmacy			

Discussion

Insomnia is a very prevalent problem in older age. In our study the prevalence of insomnia was found as 47.8%. So far, the prevalence of insomnia in geriatric ages was reported between 18-65% (8-11). Hence, our insomnia prevalence is in accordance with the literature documenting that nearly half of the older patients admitting to geriatric outpatient clinics have insomnia in Turkey.

We found the prevalence of RLS as 28.3% and presence of RLS was associated with the presence of insomnia (p=0.01). RLS is defined as the unpleasant feeling that urges to move the limbs especially while resting and in the evening. RLS is highly prevalent among older adults and may contribute to difficulty in initiating and maintaining sleep (23). In a review the prevalence of RLS among older adults has been reported 9-20% and mentioned as a good predictor for impaired sleep quality (23-24). In a study performed in Kayseri in Turkey, 665 cognitively intact older participants (aged ≥60 years) were evaluated and the prevalence of RLS was estimated %15.8 according to the criteria of International RLS group. RLS was significantly associated with impaired self-reported sleep quality and difficulty in falling asleep (25). Prevalence of RLS varies due to population characteristics and assessment method; either a single question or criteria. Our 28.3% prevalence was similar to the previous studies. RLS was found to be associated with insomnia (p=0.01) as expected. Therefore, we suggest that symptoms of RLS is better questioned as maybe a routine part of geriatric assessment. RLS may be a consequence of organic diseases (iron deficiency, neuropathy, renal failure) that are not uncommonly seen in the older adults and can lead to impairment in sleep quality.

In our study we didn't find a statistically significant a relationship between genders and insomnia (p=0.07). Poorer subjective sleep quality in older women was reported in previous studies. In a meta-analysis a risk ratio of 1.41 for female versus male was found for the risk of insomnia (26). The gender effect was found stronger in the youngest population (27,28). In a study Bonanni et al. (10) evaluated 1427 older patients and reported that while the prevalence of insomnia as a syndrome was higher in women than in men, it was not statistically significant. Also, there was found no significant different between both genders in a study conducted in Taiwan among 2045 noninstitutionalized older patients (29). In our study in older adults, insomnia was also more frequent in women (50.1%) than men (41.4%) but it did not reach statistical significance. So, our study also supports that the effect of gender on insomnia may decrease by ageing.

In our study, the relationship between age and insomnia was found borderline significant in univariate analysis and significant in the regression analysis. Our results are in line with the literature. Age is known as a risk factor for insomnia due to the multiple changes in sleep physiology. Older age was reported to be associated with higher frequency of insomnia. In a study, 2095 participants aged ≥18 years (range: 18-100) were evaluated and a statistically strong association between age and insomnia (p=0.001) was detected (30). In another study, data were extracted from a wide group (n=1423) of old participants (aged ≥60 years, age was found to be related with worse sleep complaints.

In our study, the prevalence of frailty was 16.7%. Frailty is a common geriatric syndrome, particularly among older adults population and characterised with increased vulnerability to negative health outcomes, morbidity and mortality (31,32). As sleep is an essential need for overall well-being, one could expect association between insomnia and frailty. In the literature some studies suggested association between frailty and insomnia (32), some did not (33). We did not find a significant association between frailty and insomnia. One could expect more severe problems related with sleep be more associated with frailty but we did not have severity grade for insomnia in this study. More studies are needed to state if there is a relation between frailty and insomnia.

We did not find a significant association between falls and insomnia but we found a significant relation between polypharmacy and insomnia. Falls are also common among older adults and a leading cause of morbidity and mortality. Falls have been thought to be related with sleep disturbances, as a consequence impaired attention and presence of sleepiness due to the effects of sleep disturbances (34). Also, the use of potentially inappropriate medications (i.e. benzodiazepines, antipsychotics, antidepressants) may be the cause of increased fall risk (35,36). While some studies denoted independent relation between falls and insomnia (18,36), more studies denoted that the relation between falls and insomnia revealed nonsignificant after adjustment with potential confounders (18,37). As we found relation between polypharmacy and insomnia, maybe rather than the problems related to sleep, the use of inappropriate medications as hypnotics more related with the falls seen in subjects with insomnia.

Our patients had a high rate (82.7%) of polypharmacy and the relation between insomnia and polypharmacy was significant. Different mechanisms are suggested to contribute to the relationship between polypharmacy and insomnia. Prevalence of chronic health conditions increases with age and the high number of comorbidities is a risk factor for polypharmacy. Some prevalent chronic diseases (e.g. diabetes mellitus, chronic heart failure, chronic renal disease, chronic pain) are related with the development of insomnia. So, polypharmacy may be the cause of insomnia indirectly due to the accompanying comorbidities. The number of medications can reflect underlying health problems as a consequence (24,38). On the other hand, insomnia may be a side effect of medications. Some drugs are known to carry the risk of impairing sleep quality. Selective serotonin receptor inhibitors, selective serotonin noradrenaline reuptake inhibitors and tricyclic antidepressants can cause sleep disruption by suppressing Rapid eye movement (REM) sleep and increasing REM latency (39-41). Acetylcholine esterase inhibitors are reported as associated with sleep disturbances (42,43). Alpha blockers, frequently prescribed to treat hypertension or prostatism may also impair sleep quality as they can trigger nightmares and day time sleepiness (44,45) corticosteroids, beta-blockers, teophylline, diuretics, levodopa are the other possible drugs contributing to impaired sleep quality and insomnia in older patients (46-48). Also, the mechanism of polypharmacy in sleeping problems may also be a consequence of a cascade effect. Insomnia may be a side effect of a previously used medication and another drug may be prescribed to improve sleep (24,49). To our knowledge, there is only one study looking for the relationship between polypharmacy and insomnia. In that recently published study, 379 participants aged between 78-102 were evaluated and no significant relation between insomnia polypharmacy was found after adjustment for potential confounders including the medical conditions (50). Our study suggested positive relation between polypharmacy and insomnia. However, we did not specify the type or number of chronic diseases or use of specific medications and adjust our results for them. The chronic diseases or medications themselves maybe the reason of association between polypharmacy and insomnia in our study.

Study Limitations

There are a number of limitations of this study. The sample size was not very large and the assessment for insomnia was performed with a single question. Also we didn't further analyses the concomitant illnesses and other possible related factors with insomnia (e.g. depression, anxiety disorder, chronic pain etc.) On the other hand, there are few studies evaluating the prevalence of insomnia and possible related factors among community-dwelling older persons in Eastern Europe. Polypharmacy is a highly prevalent medical burden with an increasing awareness and known many worse health outcomes. We found only one study evaluating the association between insomnia and polypharmacy. Our study stands as one of the few examples in this area.

Conclusion

In our study we found high prevalence of self-reported insomnia and RLS among older adults in Turkey as much as 47.8% and 39%, respectively. Self-reported insomnia was associated with higher age, presence of RLS and polypharmacy. We suggest that insomnia and RLS maybe better questioned in routine health care of the older adults. Patients with higher age, polypharmacy and RLS seem to be at more risk to have insomnia and therefore shall be paid more attention.

Ethics

Ethics Committee Approval: This study has been evaluated and approved by the İstanbul University faculty of medicine ethics committee on June 28, 2018 (Number: 956).

Informed Consent: Because of this study is a retrospective study, informed consent form was not taken.

Peer-review: Internally and externally peer-reviewed.

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References

1. Ryden A, Alessi C. Sleep disorders. In: Halter JB, Ouslander JG, Tinetti ME, Studenski S, High KP, Asthana S. Hazzard's Geriatric Medicine and Gerontology, 7th ed. New York, The McGrawHill Companies, 2016, pp 733.
2. Prerau MJ, Brown RE, Bianchi MT, Ellenbogen JM, Purdon PL. Sleep Neurophysiological Dynamics Through the Lens of Multitaper Spectral Analysis. Physiology (Bethesda) 2017;32:60-92.
3. Phillips B, Mannino D. Correlates of sleep complaints in adults: the ARIC study. J Clin Sleep Med 2005;1:277-283.
4. Zdanys KF, Steffens DC. Sleep Disturbances in the Elderly. Psychiatr Clin North Am 2015;38:723-741.
5. Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia in Adults: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med 2017;13:307-349.
6. Ellis JG, Perlis ML, Neale LF, Espie CA, Bastien CH. The natural history of insomnia: focus on prevalence and incidence of acute insomnia. J Psychiatr Res 2012;46:1278-1285.
7. Ohayon MM. Observation of the natural evolution of insomnia in the American general population cohort. Sleep Med Clin 2009;4:87-92.
8. Bloom HG, Ahmed I, Alessi CA, Ancoli-Israel S, Buysse DJ, Kryger MH, Phillips BA, Thorpy MJ, Vitiello MV, Zee PC. Evidence-based recommendations for the assessment and management of sleep disorders in older persons. J Am Geriatr Soc 2009;57:761-789.
9. Liang Y, Rausch C, Laflamme L, Möller J. Prevalence, trend and contributing factors of geriatric syndromes among older Swedes: results from the Stockholm County Council Public Health Surveys. BMC Geriatr 2018;18:322.
10. Bonanni E, Tognoni G, Maestri M, Salvati N, Fabbrini M, Borghetti D, Di Coscio E, Choub A, Sposito R, Pagni C, Iudice A, Murri L. Sleep disturbances in elderly subjects: an epidemiological survey in an Italian district. Acta Neurol Scand 2010;122:389-397.
11. Voyer P, Verreault R, Mengue PN, Morin CM. Prevalence of insomnia and its associated factors in elderly long-term care residents. Arch Gerontol Geriatr 2006;42:1-20.
12. Tufan A, Ilhan B, Bahat G, Karan MA. An under-diagnosed geriatric syndrome: sleep disorders among older adults. Afr Health Sci 2017;17:436-444.
13. Montplaisir J, Allen RP, Walters AS, Ferini-Strambi L. Restless legs syndrome and periodic limb movements during sleep. In: Kryger M, Roth T, Dement WC. Principles and Practice of Sleep Medicine, 4th ed. Saunders, New York, 2005, pp 839.
14. Cooper CB, Neufeld EV, Dolezal BA, Martin JL. Sleep deprivation and obesity in adults: a brief narrative review. BMJ Open Sport Exerc Med 2018;4:e000392.
15. Tobaldini E, Costantino G, Solbiati M, Cogliati C, Kara T, Nobili L, Montano N. Sleep, sleep deprivation, autonomic nervous system and cardiovascular diseases. Neurosci Biobehav Rev 2017;74:321-329.
16. Kreutzmann JC, Havekes R, Abel T, Meerlo P. Sleep deprivation and hippocampal vulnerability: changes in neuronal plasticity, neurogenesis and cognitive function. Neuroscience 2015;309:173-190.
17. Stone KL, Ensrud KE, Ancoli-Israel S. Sleep, insomnia and falls in elderly patients. Sleep Med 2008;9(Suppl 1):18-22.
18. Garfinkel D. Poly-de-prescribing to treat polypharmacy: efficacy and safety. Ther Adv Drug Saf 2018;9:25-43.
19. Roth T. Insomnia: definition, prevalence, etiology, and consequences. J Clin Sleep Med 2007;3(5 Suppl):7-10.
20. Ohayon MM, O'Hara R, Vitiello MV. Epidemiology of restless legs syndrome: a synthesis of the literature. Sleep Med Rev 2012;16:283-295.
21. Cadogan CA, Ryan C, Hughes CM. Appropriate Polypharmacy and Medicine Safety: When Many is not Too Many. Drug Saf 2016;39:109-116.
22. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Ameris. J Nutr Health Aging 2012;16:601-608.
23. 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.
24. Miner B, Kryger MH. Sleep in the Aging Population. Sleep Med Clin 2017;12:31-38.
25. 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.
26. Zhang B, Wing YK. Sex differences in insomnia: a meta-analysis. Sleep 2006;29:85-93.
27. Li RH, Wing YK, Ho SC, Fong SY. Gender differences in insomnia a study in the Hong Kong Chinese population. J Psychosom Res 2002;53:601-609.
28. Luca G, Haba Rubio J, Andries D, Tobback N, Vollenweider P, Waeber G, Marques Vidal P, Preisig M, Heinzer R, Tafti M. Age and gender variations of sleep in subjects without sleep disorders. Ann Med 2015;47:482-491.
29. Su TP, Huang SR, Chou P. Prevalence and risk factors of insomnia in community-dwelling Chinese elderly: a Taiwanese urban area survey. Aust N Z J Psychiatry 2004;38:706-713.
30. Ahmed AE, Al-Jahdali H, Fatani A, Al-Rouqi K, Al-Jahdali F, Al-Harbi A, Baharoon S, Ali YZ, Khan M, Rumayyan A. The effects of age and gender on the prevalence of insomnia in a sample of the Saudi population. Ethn Health 2017;22:285-294.
31. 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;56:146-156.
32. Graham JE, Snih SA, Berges IM, Ray LA, Markides KS, Ottenbacher KJ. Frailty and 10-year mortality in community-living Mexican American older adults. Gerontology 2009;55:644-651.
33. Vaz Fragoso CA, Gahbauer EA, Van Ness PH, Gill TM. Sleep-wake disturbances and frailty in community-living older persons. J Am Geriatr Soc 2009;57:2094-2100.
34. Chen TY, Lee S, Buxton OM. A Greater Extent of Insomnia Symptoms and Physician-Recommended Sleep Medication Use Predict Fall Risk in Community-Dwelling Older Adults. Sleep 2017:40.
35. Machado-Duque ME, Castaño-Montoya JP, Medina-Morales DA, Castro-Rodríguez A, González-Montoya A, Machado-Alba JE. Association between the use of benzodiazepines and opioids with the risk of falls and hip fractures in older adults. Int Psychogeriatr 2018;30:941-946.
36. Martinez-Ramirez D, Giugni JC, Almeida L, Walz R, Ahmed B, Chai FA, Rundle-Gonzalez V, Bona AR, Monari E, Wagle Shukla A, Hess CW, Hass CJ, Okun MS. Association between antidepressants and falls in Parkinson's disease. J Neurol 2016;263:76-82.
37. Helbig AK, Döring A, Heier M, Emeny RT, Zimmermann AK, Autenrieth CS, Ladwig KH, Grill E, Meisinger C. Association between sleep disturbances and falls among the elderly: results from the German Cooperative Health Research in the Region of Augsburg-Age study. Sleep Med 2013;14:1356-1363.

38. Sirois C, Laroche ML, Guénette L, Kröger E, Cooper D, Émond V. Polypharmacy in multimorbid older adults: protocol for a systematic review. Syst Rev 2017;6:104.

39. Molokhia M, Majeed A. Current and future perspectives on the management of polypharmacy. BMC Fam Pract 2017;18:70.

40. Wichniak A, Wierzbicka A, Jernajczyk W. Sleep and antidepressant treatment. Curr Pharm Des 2012;18:5802-5817.

41. Wilson S, Argyropoulos S. Antidepressants and sleep: a qualitative review of the literature. Drugs 2005;65:927-947.

42. Kazui H, Adachi H, Kanemoto H, Yoshiyama K, Wada T, Tokumasu Nomura K, Tanaka T, Ikeda M. Effects of donepezil on sleep disturbances in patients with dementia with Lewy bodies: An open-label study with actigraphy. Psychiatry Res 2017;251:312-318.

43. Boot BP. Comprehensive treatment of dementia with Lewy bodies. Alzheimers Res Ther 2015;7:45.

44. Roepke S, Danker-Hopfe H, Repantis D, Behnia B, Bernard F, Hansen ML, Otte C. Doxazosin, an α-1-adrenergic-receptor Antagonist, for Nightmares in Patients with Posttraumatic Stress Disorder and/or Borderline Personality Disorder: a Chart Review. Pharmacopsychiatry 2017;50:26-31.

45. Kosari S, Naunton M. Sleep Disturbances and Nightmares in a Patient Treated with Prazosin. J Clin Sleep Med 2016;12:631-632.

46. Dokoohaki S, Ghareghani M, Ghanbari A, Farhadi N, Zibara K, Sadeghi H. Corticosteroid therapy exacerbates the reduction of melatonin in multiple sclerosis. Steroids 2017;128:32-36.

47. Scheer FA, Morris CJ, Garcia JI, Smales C, Kelly EE, Marks J, Malhotra A, Shea SA. Repeated melatonin supplementation improves sleep in hypertensive patients treated with beta-blockers: a randomized controlled trial. Sleep 2012;35:1395-1402.

48. Kamel NS, Gammack JK. Insomnia in the elderly: cause, approach, and treatment. Am J Med 2006;119:463-469.

49. Barczi SR, Teodorescu MC. Psychiatric and Medical Comorbidities and Effects of Medications in Older Adults. In: Kryger MH, Roth T, Dement WC. Principles and Practices of Sleep Medicine.6th ed. Philadelphia, PA: Elsevier, 2016.

50. Miner B, Gill TM, Yaggi HK, Redeker NS, Van Ness PH, Han L, Fragoso CAV. Insomnia in Community-Living Persons with Advanced Age. J Am Geriatr Soc 2018;66:1592-1597.

ORIGINAL RESEARCH

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Relationship Between Frailty and Inflammation

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Abstract

Objective: It has been suggested that inflammation plays a role in the pathogenesis of frailty and many studies have been carried out to understand the underlying mechanism. In this study, the relationship between frailty and inflammation was examined.

Materials and Methods: Eight hundred and seventeen patients over 65 years of age were evaluated in this study. Comprehensive geriatric assessment was performed in each patient and the Fried frailty criteria were used to assess physical frailty. Neutrophil count, lymphocyte count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin, mean platelet volume and CRP-to-albumin ratio (CAR) and neutrophil-to-lymphocyte ratio (NLR) were recorded as inflammatory markers.

Results: The median age of the patients was 73 years (minimum-maximum: 65-94). 61.9% of patients were female (n=506) and 10.8% were frail (n=88). The median CRP was 0.49 mg/L (minimum-maximum: 0.10-7.67) in frail group (p=0.167). The CAR was higher in the frail group but there was no significant correlation between high CAR and frailty (p=0.07). The median NLR was 2.17 (minimum-maximum: 0.21-10.17) in the non-frail group and 2.41 (minimum-maximum: 0.62-18.20) in the frail group and the difference between the two groups was significant (p=0.014). ESR was significantly higher in the frail group (p<0.001). In multivariate analysis, when models with independently related factors were studied, ESR was found to be significantly related with frailty (OR: 1.026, 95% CI: 1.005-1.047, p=0.015).

Conclusion: Chronic inflammation has been shown to cause frailty directly or indirectly through its destructive effects on the musculoskeletal, respiratory, and hematological systems as well as other physiological intermediate systems. The findings of this study suggest that there may be a relationship between frailty and inflammation.

Keywords: Frailty, inflammation, older adults

Introduction

The aging of the population brings along health problems. Frailty is a geriatric syndrome defining the physical, functional and cognitive decline that appears as a sequel of particular diseases (e.g., cancer, chronic infection, cardiovascular disease, etc.) but which can also occur in the absence of disease. Frailty is characterized by a high incidence of falls or fractures and increased risk of poor outcomes such as disability, comorbidity, health care expenditures, and premature death (1,2). The frailty notion has gained importance to better understand the health directive of older people and to avoid or at least delay the dependence in late life (3). Fried et al. (1) presented a definition of frailty involving the evaluation of five specific criteria which are weight loss, exhaustion, weak grip strength, slow walking speed, and low physical activity, based on a large data obtained from older individuals.

Although the etiology of frailty is not well known, it has been associated with changes in physiological systems such as brain, immune, endocrine, and skeletal muscle, as well as affecting micronutrients and vitamins in older adults (4). Increased inflammatory markers and cytokines are thought to be major contributors to this process (5). White blood cells (WBCs) and their subpopulation constitute an important part of the inflammation system, and high WBCs counts are associated

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with increased disability and mortality risk (6,7). In the Women's Health and Aging Studies, in which a five-year mortality follow-up was performed, it was shown that increases in neutrophil and decreases in lymphocyte counts were associated with mortality (8). However, the relationship between WBCs and frailty is controversial. While a relationship was found in some of the previous studies, there was no significant relationship in some of the studies. These different results between the studies are based on the small sample size of the studies and the lack of exclusion criteria (9-12).

Chronic inflammatory markers were examined widely in terms of frailty mechanism (13-16). C-reactive protein (CRP), which was found in 1930, is a classical molecule in the circulation of systemic inflammation (17). Studies comparing various inflammatory markers support the role of CRP in frailty etiology (4,15). However, there are also contradictory studies on this subject due to the specific characteristics of the study population (4,13,15,18).

In this study, the relationship between and WBCs count, its subpopulation constitutes, CRP levels were investigated.

Materials and Methods

Study Population and Procedures

Eight hundred and seventeen patients who were admitted to our geriatric medicine outpatient clinic were included in this study. The study was designed as a retrospective cohort. Patients over 65 years of age and suitable for the evaluation of frailty status with Fried criteria were included in the study. Participants who met the following criteria were excluded: 1) patients with rheumatic diseases, active infection, malignancy 2) being on corticosteroids for any reason 3) to have received antibiotic treatment up to a month ago. Age, sex, whom living with, education level, chronic diseases, number of drugs, number of falls and history of fracture in the past year, incontinence data were collected. Height (m) and weight (kg) were measured for each participant, body mass index was calculated. Behavioral factors (smoking, alcohol use) were questioned.

The study protocol has been evaluated and approved by the local Ethics Committee. Informed consent was obtained from all the patients or next of kin.

Physical Frailty Definition

The definition of frailty was established by the Fried frailty criteria, which included the following five elements. 1) Weight: unintentional weight loss of ≥5% in the past year. 2) Weakness: determining the maximal strength of the dominant hand by gender (Three consecutive measurements were taken). Grip strength was determined by using a hand-held dynamometer (Takei A5401). 3) Slowness: determining 15 feet walking time, adjusted for sex and height. 4) Low physical activity: the lowest quintile of International Physical Activity Questionnaire-Short Formscore, which was used to assess weekly energy spending in kcal based on self-reported physical activities. 5) Exhaustion: Fatigue was point out by two questions from the Center for Epidemiologic Studies Depression Scale, including "I felt everything I did was an effort" and "I could not get going". Exhaustion was defined as a positive response to one of these two questions more than 3-4 days per week. The individuals having three or more of these characteristics were considered frail, having one or two characteristics were pre-frail, and without any characteristics were determined as robust (1).

Comprehensive Geriatric Assessment

Basic activities of daily living (ADL) and instrumental ADL (IADL) were used to evaluate the functional capacity of patients. ADL was evaluated with the Katz Scale which assesses the degree of dependence on six basic activities: feeding, sphincter control, transferring, personal hygiene, dressing, and bathing (19-21). The Lawton Brody scale was used for the evaluation of IADL; this scale assesses eight activities: using a telephone, using transportation, shopping, making meals, doing household chores, taking medications, and managing money (22). Cognition was evaluated clinically and by performing the standardized The Mini-Mental State Examination (MMSE) and The Clock Drawing Test (CDT). The MMSE, developed by Folstein in 1975, is widely used to measure cognitive functions (23). Low scores indicate increased dependence in both tests. Nutritional status of the patients was evaluated by Mini Nutritional Assessment short form and having a total score ≤11 was defined to have a high risk of malnutrition (24). Depressive symptoms were assessed by performing Yesavage Geriatric Depression scale (GDS) short form which total score ranges from zero to fifteen. Scoring six point and above from GDS is interpreted as a symptom of depression (25).

Inflammatory Markers

White blood cells, lymphocyte, neutrophil counts, mean platelet volume (MPV), albumin levels, CRP and ESR rate of the patients were recorded. C-reactive protein values of two hundred eighty-eight patients were achieved. Neutrophil/lymphocyte and CRP/albumin ratios were calculated.

Statistics

"Statistical Package for Social Sciences" (SPSS) 22.0 version was used for the statistical analyses. Descriptive statistical analyses were given as frequencies and percentage for categorical variables. Histograms and Kolmogorov-Smirnov tests were used to determine whether the parameters had normal distribution. It was seen that the parameters were not distributed normally and were presented as median (minimum-maximum). Chi-square or

Fischer exact tests were used for the comparison of categorical variables between groups. The skew distributed continuous variables were analyzed between two groups by Mann-Whitney U test. The parameters those had significant differences or had p value lower than 0.20 between frail and non-frail patients in univariate analysis were included in Logistic Regression analysis to detect the independently associated parameters for frailty. P value lower than 0.05 was considered as statistically significant.

Results

General Characteristics and Comprehensive Geriatric Assessment

Eight-hundred and seventeen patients aged 65 years and older were included in this study. The median age was 73 years (range 65-94) and 61.9% (n=506) were female. 16.3% (n=131) of the patients were university graduates. Most of them were living with their partners or families (the frequencies were 59.3% and 25.1%, respectively) and 15.3% of the participants were living alone. The three most common comorbid conditions were hypertension (69.2%), diabetes mellitus (35.9%) and urinary incontinence (35.2%). 13.3% (n=109) of the patients were detected to be frail. When the comprehensive geriatric assessment components were evaluated, it was observed that the ADL, IADL, MMSE, CDT, MNA and GDS test scores of the patients in the frail group were significantly worse (p<0.001). Same as, the frail patient group was found to have lower hand grip strength and a slower walking speed of 15 feet (p<0.001). The frequencies of comorbid diseases, geriatric syndromes and comprehensive geriatric assessment are shown in Table 1.

Association Between Inflammatory Markers and Frailty

When the frail and non-frail groups were compared, albumin levels were significantly lower (p<0.001), ESR (p<0.001) and neutrophil/lymphocyte ratio (p=0.014) were significantly higher in the frail group. There was no significant relationship regarding CRP (p=0.167), CRP/albumin ratio (p=0.07) and MPV (p=0.495)

Table 1. The frequencies of comorbid diseases, geriatric syndromes and comprehensive geriatric assessment between groups determined by the Fried's Frailty Index

	Total (n=817)	Robust/Pre-frail (n=708)	Frail (n=109)	p value
Age, year, median (min-max)	73 (65-94)	72 (65-94)	78 (65-94)	**<0.001**
Female, n (%)	506 (61.9)	425 (60)	81 (74.3)	**0.002**
Education level, university graduate, n (%)	131 (16.3)	128 (18.3)	3 (2.8)	**<0.001**
BMI, kg/m^2, median (min-max)	27.5 (11.7-50.2)	27.6 (17-50.2)	27 (11.7-40)	0.515
Hypertension, n (%)	565 (69.2)	480 (67.6)	85 (78.0)	**0.032**
Diabetes mellitus, n (%)	293 (35.9)	248 (35)	45 (41.3)	0.205
Osteoporosis, n (%)	197 (24.1)	165 (23.3)	32 (29.4)	0.106
Coronary artery disease, n (%)	167 (20.4)	133 (18.8)	34 (31.2)	**0.003**
Chronic obstructive pulmonary disease, n (%)	54 (6.6)	42 (5.2)	12 (11.0)	**0.047**
Congestive heart failure, n (%)	38 (4.7)	24 (3.4)	14 (12.8)	**<0.001**
Dementia, n (%)	67 (8.2)	43 (6.1)	24 (22.0)	**<0.001**
Depression, n (%)	174 (21.3)	45 (41.3)	129 (18.2)	**<0.001**
History of falls, n (%)	228 (28.5)	180 (26)	48 (44.9)	**<0.001**
Fracture, n (%)	88 (11.1)	69 (10)	19 (17.8)	**0.017**
Urinary incontinence, n (%)	287 (35.2)	226 (31.9)	61 (56.5)	**<0.001**
Number of drugs, median (min-max)	5 (0-17)	4 (0-16)	6 (0-17)	**<0.001**
Katz ADL score, median (min-max)	6 (0-6)	6 (1-6)	5 (0-6)	**<0.001**
Lawton IADL score, median (min-max)	8 (0-8)	8 (0-8)	6 (0-8)	**<0.001**
Clock drawing test score, median (min-max)	5 (0-6)	6 (0-6)	3 (0-6)	**<0.001**
Mini-Mental State Examination score, median (min-max)	28 (5-30)	28 (6-30)	25 (5-30)	**<0.001**
Mini nutritional assessment test short form score, median (min-max)	13 (0-14)	14 (0-14)	10 (2-14)	**<0.001**
Yesavage geriatric depression scale score, median (min-max)	2 (0-15)	1 (0-15)	7 (0-15)	**<0.001**
15 feet walking speed, m/s, median (min-max)	1.01 (0.12-3.07)	1.02 (0.26-3.07)	0.50 (0.12-1.18)	**<0.001**
Handgrip, kg, median (min-max)	21.6 (2.8-53.2)	22.6 (5.7-53.2)	14.1 (2.8-33.3)	**<0.001**

n: Number, BMI: Body mass index, ADL: Basic activities of daily living, IADL: Instrumental activities of daily living, min: Minimum, max: Maximum

levels. The relationship between frailty and inflammatory markers is shown in Table 2.

In the logistic regression analysis, models were created in order to determine the independently associated factors of frailty. In Model 1, higher ESR was positively associated with greater frailty states (OR: 1.026, 95% CI: 1.005-1.047, p=0.015). There was no significant difference in neutrophil/lymphocyte ratio (OR: 1.203, 95% CI: 0.986-1.468, p=0.068) in Model 2. In Model 3, a positive significance was observed in ESR (OR: 1.023, 95% CI: 1.002-1.045, p=0.031). The evaluation of the factors related to frailty by multivariate analysis is shown in Table 3.

Discussion

This study examined the association of neutrophil count, neutrophil/lymphocyte ratio, ESR and CRP levels with frailty. In our study, neutrophil/lymphocyte ratio and ESR, but not CRP, were found to be significantly related to frailty.

Table 2. The relationship between the frailty with inflammatory markers

	Total (n=817)	Robust/Pre-frail (n=708)	Frail (n=109)	p value
Albumin, g/dL, median (min-max)	4.29 (3.02-5.09)	4.31 (3.02-5.09)	4.1 (3.06-4.68)	**<0.001**
CRP, mg/dL, median (min-max)	0.43 (0.10-7.67)	0.41 (0.10-3.19)	0.49 (0.1-7.67)	0.167
Leukocyte, e^3/mL, median (min-max)	7100 (3000-14800)	7100 (3000-14800)	7400 (3100-12600)	0.435
Sedimentation rate, mm/st, median (min-max)	12 (2-59)	11 (2-59)	17 (2-56)	**<0.001**
MPV, fL, median (min-max)	8.7 (5.8-12.4)	8.7 (5.8-12.4)	8.7 (6.9-12)	0.495
CRP/Albumin, median (min-max)	0.01 (0.0-0.20)	0.01 (0.0-0.09)	0.01 (0.0-0.2)	0.07
Neutrophil/Lymphocyte, median (min-max)	2.21 (0.21-18.20)	2.17 (0.21-10.2)	2.41 (0.62-18.2)	**0.014**

CRP: C-reactive protein, MPV: Mean platelet volume, min: Minimum, max: Maximum

Table 3. Evaluation of the factors related to frailty by multivariate analysis

	OR	95% CI	p
Model 1			
Age	1.094	1.048-1.141	**<0.001**
MMSE score	0.917	0.875-0.960	**<0.001**
GDS score	1.242	1.163-1.325	**<0.001**
Coronary artery disease	2.080	1.129-3.831	**0.019**
Sedimentation rate	1.026	1.005-1.047	**0.015**
Hyperlipidemia	0.488	0.271-0.879	**0.017**
Model 2			
Age	1.084	1.041-1.128	**<0.001**
MMSE score	0.923	0.884-0.964	**<0.001**
GDS score	1.202	1.133-1.275	**<0.001**
Being a university graduate	0.231	0.054-0.986	**0.048**
Hyperlipidemia	0.529	0.306-0.915	**0.023**
Neutrophil/Lymphocyte ratio	1.203	0.986-1.468	0.068
Model 3			
Age	1.089	1.042-1.137	**<0.001**
MMSE score	0.923	0.880-0.967	**0.001**
GDS score	1.235	1.156-1.319	**<0.001**
Coronary artery disease	2.050	1.093-3.842	**0.025**
Being a university graduate	0.271	0.062-1.191	0.084
Hyperlipidemia	0.505	0.278-0.917	**0.025**
Neutrophil/Lymphocyte ratio	1.175	0.960-1.437	0.118
Sedimentation	1.023	1.002-1.045	**0.031**

OR: Odds ratio, CI: Confidence interval, MMSE: Mini-mental State Examination, GDS: Geriatric depression scale

It has been previously demonstrated that aging is associated with high levels of serum inflammatory markers and inflammatory cytokines, and this chronic inflammation is playing an important role in becoming frail (13,15). The interaction between inflammation and frailty could be both direct and indirect. Chronic diseases such as diabetes, chronic kidney disease and ischemic heart disease, with increasing incidence in aging, could lead to chronic inflammation. This inflammation could result in frailty. In contrast, frailty could be associated with chronic inflammation as a result of immobilization and weakness. In addition, CRP gene polymorphism has been shown to change the inflammatory response and increase the risk of developing frailty. Therefore, the combination of these risk factors might contribute to the development of frailty or may lead to an aggravation of frailty (13,15,26-28).

White blood cells and their subpopulations, including neutrophils, lymphocytes, and monocytes, are well known cellular components of the inflammation system. Leng et al. (29) found a significant relationship between the number of neutrophil and monocyte counts with frailty in community-dwelling disabled women. These findings indicate significant risk for frailty even within the normal range of total WBCs counts. Another study investigating the relationship between inflammation and frailty demonstrated that high WBCs counts were associated with increased frailty prevalence in community-dwelling older women, and the next study with the same cohort found that neutrophil and monocyte counts were positively related to frailty. Moreover, in a cross-sectional study involving older patients, high neutrophil and low lymphocyte counts were associated with low physical activity, whereas low lymphocyte counts were associated with poor muscle strength (29-31). In our study, while the total WBCs count was not elevated in the frail group, neutrophil/lymphocyte ratio increased significantly. We think that NLR is a better marker for frailty than WBCs, neutrophil and lymphocyte count, as it reflects the combination of two markers.

The relationship between CRP and frailty is not clear. C-reactive protein elevation can be seen in a diversity of other conditions like cancer, cardiovascular diseases, metabolic syndrome, and comorbidity. In some studies, there are no clear disease exclusions as in our study and therefore, as a result of these studies, the relationship between CRP and frailty may be found (5,32). In a study, involving patients with acquired immunity deficiency syndrome, high CRP levels have been associated with skeletal muscle loss (33). Patients were followed-up for nine years in the Cardiovascular Health Study, and CRP independently predicted incident frailty (34). Similarly, elevated levels of CRP were associated with 3-year incident frailty, in the Longitudinal Aging Study of Amsterdam (15). In a recent study procalcitonin, but not IL-6 or CRP, was associated with frailty among older inpatients without infection (35). In our study, there was no significant relationship between CRP and frailty. However, these results were at a borderline value in CRP/albumin ratio. This can be attributed to the low number of patients with CRP. This is a limitation of the study.

The role of inflammation in the development of frailty can be explained by a few mechanisms. The first and major role is mainly based on catabolic effect of pro-inflammatory cytokines on muscles. Studies on this subject have been reported that inflammatory cytokines affect muscle protein synthesis and thus lead to frailty (36,37). The second mechanism is that inflammation may reflect compensatory state in the pathophysiology of frailty (38). The third mechanism is inflammation may be an epiphenomenon, only a marker of causal mechanism (39,40). Excessive and unopposed oxidative stress may be the core mechanism in the development of age-related frailty (41). Oxidative stress with age is sufficient to cause DNA, lipid and muscle damage and this results in cellular and organ dysfunction (42). These findings suggest that inflammation directly or indirectly contributes to the frailty pathophysiology of inflammation.

In our study, age was found to be increasing as the frailty group worsened. Previous studies have supported this relationship between frailty and age (43,44). Physiological changes that occur with aging and the interaction of these changes with pathological mechanisms make aging a predisposing factor for frailty (1). According to the results of our study, as the category of frailty deteriorated, the low level of education increased. Hoogendijk et al. (45) found similar results and emphasized the need to focus on the education level of patients in combating frailty. In our study, we demonstrated that all of the comprehensive geriatric assessment tests were worse in the frail group. In multivariate analyzes, MMSE and GDS have found to be independent related factors with frailty which is in accord with the findings of previous studies (46). With this, the number of comorbid diseases and drug use in the frail group patients is also higher. These results assistance the hypothesis of the ''cycle of frailty'' which may appear as a result of comorbidities, malnutrition, dementia and depression. Polypharmacy is contemplated to be a risk factor for frailty in the elderly, in which interactions of more than one drug, random drug use and related side effects are likely to aggravate this situation (47,48).

The superior aspects of the study are the involvement of the large number of older patients and the wide exclusion criteria, as presence of malignancy, diagnosis of rheumatologic disease, presence of active infection and removal of patients using steroids for any reason. In addition to healthy individuals living in the community, people with disability

were also included in the study to generalize study results to the geriatric population.

Study Limitations

The limitations of the present study were retrospective design and therefore the inability to obtain CRP levels for all patients. In our study, both sexes were evaluated but some studies were evaluated by grouping and significant results were obtained in female gender, there was no significant difference in male sex. Finally, another biomarker, helping to explain the mechanism between frailty and inflammation (e.g., interleukin-6), was not used in the study.

Conclusion

In our study, there was a significant relationship between frailty and inflammation. Even though the exact relationship has not yet been established, there is increasing evidence that correlates inflammation with frailty in older people. There is a need for multiple strategies for the prevention and treatment of frailty that occurs after the interaction of different system abnormalities.

Ethics

Ethics Committee Approval: The study protocol has been evaluated and approved by the Hacettepe University Ethics Committee.

Informed Consent: Informed consent was obtained from all the patients or next of kin.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.T.D., Concept: R.T.D., M.C.K., B.B.Y., Design: R.T.D., M.C.K., B.B.Y., Data Collection or Processing: R.T.D., H.D.V., M.C.K., M.K.K., G.A., Ö.K., M.H., M.C., B.B.Y., Analysis or Interpretation: R.T.D., M.C.K., B.B.Y., Literature Search: R.T.D., B.B.Y., Writing: R.T.D., M.C.K., B.B.Y.

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References

1. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-156.
2. Woods NF, LaCroix AZ, Gray SL, Aragaki A, Cochrane BB, Brunner RL, Masaki K, Murray A, Newman AB. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. J Am Geriatr Soc 2005;53:1321-1330.
3. Wyman JF, Henly SJ. Advancing nursing science through health trajectory research: an introduction. Nurs Res 2011;60(3 Suppl): S1-4.
4. Walston J, McBurnie MA, Newman A, Tracy RP, Kop WJ, Hirsch CH, Gottdiener J, Fried LP. Frailty and activation of the inflammation and coagulation systems with and without clinical comorbidities: results from the Cardiovascular Health Study. Arch Intern Med 2002;162:2333-2341.
5. Michaud M, Balardy L, Moulis G, Gaudin C, Peyrot C, Vellas B, Cesari M, Nourhashemi F. Proinflammatory cytokines, aging, and age-related diseases. J Am Med Dir Assoc 2013;14:877-882.
6. Gillum RF, Ingram DD, Makuc DM. White blood cell count, coronary heart disease, and death: the NHANES I Epidemiologic Follow-up Study. Am Heart J 1993;125:855-863.
7. Furlan JC, Vergouwen MD, Fang J, Silver FL. White blood cell count is an independent predictor of outcomes after acute ischaemic stroke. Eur J Neurol 2014;21:215-222.
8. Leng S, Xue QL, Huang Y, Semba R, Chaves P, Bandeen-Roche K, Fried L, Walston J. Total and differential white blood cell counts and their associations with circulating interleukin-6 levels in community-dwelling older women. J Gerontol A Biol Sci Med Sci 2005;60:195-199.
9. Collerton J, Martin-Ruiz C, Davies K, Hilkens CM, Isaacs J, Kolenda C, Parker C, Dunn M, Catt M, Jagger C, von Zglinicki T, Kirkwood TB. Frailty and the role of inflammation, immunosenescence and cellular ageing in the very old: cross-sectional findings from the Newcastle 85+ Study. Mech Ageing Dev 2012;133:456-466.
10. Gibson KL, Wu YC, Barnett Y, Duggan O, Vaughan R, Kondeatis E, Nilsson BO, Wikby A, Kipling D, Dunn-Walters DK. B-cell diversity decreases in old age and is correlated with poor health status. Aging Cell 2009;8:18-25.
11. Semba RD, Margolick JB, Leng S, Walston J, Ricks MO, Fried LP. T cell subsets and mortality in older community-dwelling women. Exp Gerontol 2005;40:81-87.
12. De Fanis U, Wang GC, Fedarko NS, Walston JD, Casolaro V, Leng SX. T-lymphocytes expressing CC chemokine receptor-5 are increased in frail older adults. J Am Geriatr Soc 2008;56:904-908.
13. Baylis D, Bartlett DB, Syddall HE, Ntani G, Gale CR, Cooper C, Lord JM, Sayer AA. Immune-endocrine biomarkers as predictors of frailty and mortality: a 10-year longitudinal study in community-dwelling older people. Age (Dordr) 2013;35:963-971.
14. Gale CR, Baylis D, Cooper C, Sayer AA. Inflammatory markers and incident frailty in men and women: the English Longitudinal Study of Ageing. Age (Dordr) 2013;35:2493-2501.
15. Puts MT, Visser M, Twisk JW, Deeg DJ, Lips P. Endocrine and inflammatory markers as predictors of frailty. Clin Endocrinol (Oxf) 2005;63:403-411.
16. Salanitro AH, Ritchie CS, Hovater M, Roth DL, Sawyer P, Locher JL, Bodner E, Brown CJ, Allman RM. Inflammatory Biomarkers as Predictors of Hospitalization and Death in Community-Dwelling Older Adults. Arch Gerontol Geriatr 2012;54:e387-391.
17. Tillett WS, Francis T Jr. Serological Reactions In Pneumonia with A Non-Protein Somatic Fraction of Pneumococcus. J Exp Med 1930;52:561-571.
18. Lai HY, Chang HT, Lee YL, Hwang SJ. Association between inflammatory markers and frailty in institutionalized older men. Maturitas 2014;79:329-333.
19. 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.
20. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. Gerontologist 1970;10:20-30.
21. 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.
22. Graf C. The Lawton instrumental activities of daily living scale. Am J Nurs 2008;18:315-316.

23. 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.

24. 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.

25. Yesavage JA. Geriatric Depression Scale. Psychopharmacol Bull 1988;24:709-711.

26. Brüünsgaard H, Pedersen BK. Age-related inflammatory cytokines and disease. Immunol Allergy Clin North Am 2003;23:15-39.

27. Fulop T, Larbi A, Witkowski JM, McElhaney J, Loeb M, Mitnitski A, Pawelec G. Aging, frailty and age-related diseases. Biogerontology 2010;11:547-563.

28. Almeida OP, Norman PE, van Bockxmeer FM, Hankey GJ, Flicker L. CRP 1846G>A polymorphism increases risk of frailty. Maturitas 2012;71:261-266.

29. Leng SX, Xue QL, Tian J, Walston JD, Fried LP. Inflammation and frailty in older women. J Am Geriatr Soc 2007;55:864-871.

30. Leng SX, Xue QL, Tian J, Huang Y, Yeh SH, Fried LP. Associations of neutrophil and monocyte counts with frailty in community-dwelling disabled older women: results from the Women's Health and Aging Studies I. Exp Gerontol 2009;44:511-516.

31. Fernández-Garrido J, Navarro-Martínez R, Buigues-González C, Martínez-Martínez M, Ruiz-Ros V, Cauli O. The value of neutrophil and lymphocyte count in frail older women. Exp Gerontol 2014;54:35-41.

32. Puzianowska- Kuźnicka M, Owczarz M, Wieczorowska-Tobis K, Nadrowski P, Chudek J, Slusarczyk P, Skalska A, Jonas M, Franek E, Mossakowska M. Interleukin-6 and C-reactive protein, successful aging, and mortality: the PolSenior study. Immun Ageing, 2016;13:21.

33. Kotler DP. Cachexia. Ann Intern Med 2000;133:622-634.

34. Barzilay JI, Blaum C, Moore T, Xue QL, Hirsch CH, Walston JD, Fried LP. Insulin resistance and inflammation as precursors of frailty: the Cardiovascular Health Study. Arch Intern Med 2007;167:635-641.

35. Yang Y, Hao Q, Flaherty JH, Cao L, Zhou J, Su L, Shen Y, Dong B. Comparison of procalcitonin, a potentially new inflammatory biomarker of frailty, to interleukin-6 and C-reactive protein among older Chinese hospitalized patients. Aging Clin Exp Res 2018;30:1459-1464.

36. Hubbard RE, O'Mahony MS, Calver BL, Woodhouse KW. Plasma esterases and inflammation in ageing and frailty. Eur J Clin Pharmacol 2008;64:895-900.

37. Toth MJ, Matthews DE, Tracy RP, Previs MJ. Age-related differences in skeletal muscle protein synthesis: relation to markers of immune activation. Am J Physiol Endocrinol Metab 2005;288:E883-891.

38. Hubbard RE, Woodhouse KW. Frailty, inflammation and the elderly. Biogerontology 2010;11:635-641.

39. Serviddio G, Romano AD, Greco A, Rollo T, Bellanti F, Altomare E, Vendemiale G. Frailty syndrome is associated with altered circulating redox balance and increased markers of oxidative stress. Int J Immunopathol Pharmacol 2009;22:819-827.

40. Wu IC, Shiesh SC, Kuo PH, Lin XZ. High oxidative stress is correlated with frailty in elderly chinese. J Am Geriatr Soc 2009;57:1666-1671.

41. Maggio M, Guralnik JM, Longo DL, Ferrucci L. Interleukin-6 in aging and chronic disease: a magnificent pathway. J Gerontol A Biol Sci Med Sci 2006;61:575-584.

42. Ershler WB. A gripping reality: oxidative stress, inflammation, and the pathway to frailty. J Appl Physiol (1985) 2007;103:3-5.

43. Alvarado BE, Zunzunegui MV, Béland F, Bamvita JM. Life course social and health conditions linked to frailty in Latin American older men and women. J Gerontol A Biol Sci Med Sci 2008;63:1399-1406.

44. Sánchez-Garcia S, Sánchez-Arenas R, García-Peña C, Rosas-Carrasco O, Avila-Funes JA, Ruiz-Arregui L, Juárez-Cedillo T. Frailty among community-dwelling elderly Mexican people: prevalence and association with sociodemographic characteristics, health state and the use of health services. Geriatr Gerontol Int 2014;14:395-402.

45. Hoogendijk EO, van Hout HP, Heymans MW, van der Horst HE, Frijters DH, Broese van Groenou MI, Deeg DJ, Huisman M. Explaining the association between educational level and frailty in older adults: results from a 13-year longitudinal study in the Netherlands. Ann Epidemiol 2014;24:538-544.e2.

46. Kim S, Park JL, Hwang HS, Kim YP. Correlation between Frailty and Cognitive Function in Non-Demented Community Dwelling Older Koreans. Korean J Fam Med 2014;35:309-320.

47. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Cumming RG, Handelsman DJ, McLachlan AJ, Abernethy DR, Banks E, Le Couteur DG. High-risk prescribing and incidence of frailty among older community-dwelling men. Clin Pharmacol Ther 2012;91:521-528.

48. Weiss CO. Frailty and chronic diseases in older adults. Clin Geriatr Med 2011;27:39-52.

ORIGINAL RESEARCH

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Public Awareness of Geriatrics in the 50th Year of Geriatrics in Turkey

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Abstract

Objective: Geriatrics focuses on health care of the elderly. Geriatrics has a history of about 50 years in Turkey. In order to increase the quality and quantity of geriatric services, geriatric awareness needs to be increased. This is possible only when the government, health workers and the community work together. We decided to do this study to determine the level of public awareness of geriatrics among elderly population in Turkey.

Materials and Methods: Between January 2018 and March 2019, we reached a total of 314 people over 60 years of age living in eight different districts of Ankara. It was questioned whether the patients knew geriatrics, and if they knew and truly described geriatrics, and they were asked how they had learned. Patients who knew geriatrics were asked whether they applied to any of the centers with a geriatrician in Ankara.

Results: Only 2.88% of the study population had geriatrics awareness. In general, participants with geriatrics awareness were found to be older in age, having higher mental scores and having less children.

Conclusion: In our country, the level of awareness of geriatrics is very low in its 50th year.

Keywords: Geriatric awareness, geriatric, elderly

Introduction

Geriatrics focuses on health care of the older adults. It aims to either prevent, to treat or to control diseases and disabilities in older adults. Although The United Nations declared the age cutoff as 60+ years to refer to the older adults, there is no set age at which adults may be under the care of a geriatrician. Rather, this decision is given by the individual's health needs, and the availability of a specialist. The term geriatrics comes from the Greek geron meaning "old man", and iatros meaning "healer".

Traditional Indian system of medicine, Ayurveda, is the first known health system similar to geriatrics. Here fatigue and physical exhaustion is described as the result of poor diet secondary to aging, and the older adults are recommended to avoid excessive physical or mental strain and consume a light but nutritious diet (1). Arabic physician Algizar (A.C. 898-980) wrote a book on the health of the older adults; sleep disorders, forgetfulness and causes of mortality were among the titles (2). Avicenna in 1025 was concerned with sleep, exercises, diet and constipation of the older adults (3). Byzantine Empire viewed aging as a natural and inevitable form of marasmus, caused by the loss of moisture in body tissue, they described the mental and physical symptoms of aging, recommending a diet rich in foods that provide heat and moisture, frequent bathing, massaging, rest, and low-intensity exercise regimens (4).

One of the first publications about geriatric medicine was published in 1849 by George Day, Diseases of Advanced Life (5). The first geriatric hospital was founded in Belgrade, Serbia and the term geriatrics was proposed in 1909 by Ignatz Leo Nascher (6).

Geriatrics began to spread in Northern Europe, America, Canada, Japan, Australia and Western Europe since the 1970s. As in the

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rest of the world, only internal medicine specialists in Turkey have the opportunity to be a geriatrician.

Geriatrics has about 50 years of history in Turkey. Prof. Dr. Şefik Ayhan is known as the first Turkish doctor to be interested in geriatrics (7). First geriatrics department in Turkey was inaugurated at Cerrahpaşa Faculty of Medicine in 1987, Ankara University in 1992 started to accept geriatric patients in 1992. According to Turkish Statistical Institute (TURKSTAT) March 2019 data, geriatricians work only in 16 cities in Turkey.

As of the end of 2018, there are totally 109 geriatricians and geriatrics fellows working privately or publicly working at 41 different centers in Turkey; 11 in Istanbul and Ankara, two in İzmir, Adana, Gaziantep, Kayseri and Erzurum, Bursa, Antalya, Konya, Mersin, Diyarbakır, Eskişehir, Malatya, Isparta and Kırıkkale. According to TURKSTAT data, no geriatrician employment was planned in 46 provinces as of March 2019.

According to TURKSTAT data, as the end of December 2018, Turkey's population has exceeded 80 million and nearly 10% of this population is over 65 years of age. This means that the number of patients per geriatrician is approximately 800,000 in Turkey. According to the World Health Organization statistics, there are approximately 17 doctors per 10,000 patients in Turkey in 2014, indicating that the number of geriatricians should increase by more than 100 times to reach the average for this rate.

In order to increase the quality and quantity of geriatric services, geriatric awareness needs to be increased. And this is possible only when the government, health workers and the community work together. After 20 years from the inauguration of the first geriatric outpatient clinic, we decided to do this study to determine the prevalence of geriatrics awareness among older adults in the community in Turkey.

Materials and Methods

Between January 2018 and March 2019, we reached a total of 314 people over 60 years of age living in eight different districts of Ankara. Individuals over the age of 60 were called to the cultural centers by the municipal employees. Each person who was called and accepted to participate in the study was included in the study. Three doctors, two geriatrics nurses, one geriatrics technician and a geriatrics psychologist took part in the study. Demographic characteristics, diseases, medications, daily living activities (Katz), instrumental daily living activities (Lawton), nutritional status, mini mental scores, and geriatric syndromes like osteoporosis, incontinence, falls etc. were recorded. It was questioned whether if patients knew geriatrics, and if they knew and truly described geriatrics, they were asked how they had learned. Patients who knew the geriatrics were asked whether they applied to any of the centers with a geriatrician Ankara. Ankara University Ethical committee 25.06.2018 (No: 11-747-18).

Statistics

Statistical analysis was performed using SPSS version 22.0. Data was expressed as mean ± standard deviation (SD). The strength of association between variables was tested by Pearson's correlation coefficient. The statistical significance between groups was determined with Student's t-test. Chi-square test was used for the proportional correlations. P values of less than 0.05 were considered as significant.

Results

A total of 314 patients were included in the study. The mean age of the participants was 68.96±5.77. 158 (50.31%) of the participants were female and 156 (49.68%) were male. Of the participants, 235 (74.84%) were married and 79 (25%) were widowed/unmarried (Table 1).

Of the participants, 158 (50.31%) were living with their spouse, 76 (24.20%) with their spouse and children, 45 (14.33%) with their children, and 44 (14.01%) were living alone (Table 1).

Of the participants, 244 (77.70%) were living in their own house, 43 (13.70%) were living in a rented house, 26 (8.30%) were leaving in a relative's home and 1 (0.30%) lived in a nursing home (Table 1).

Ninety-three (29.60%) of the participants were not literate, 45 (14.30%) were literate, 104 (33.10%) were primary school graduates, 20 (6.40%) were secondary school graduates, and 36 (11.50 %) were high school graduates and 16 (5.10%) had university or higher education (Table 1).

The participants' number of medicines was 3.37±2.76, Katz's daily living activities score was 5.86±0.514, Lawton instrumental activity of daily living scores 7.75±7.8, mini nutritional assessment scores 13.61±1.95, mini mental evaluation scores 24, 16±4.33 and geriatric depression scores were found as 4.68±3.77 (Table 1).

According to verbal statements and medications, 173 (55.1%) of the participants had hypertension, 101 (32.20%) had diabetes mellitus, 67 (21.50%) had coronary artery disease, 58 (18.60%) had hyperlipidemia, 52 (16.60%) had asthma/ COPD, 43 (13.70%) had benign prostatic hypertrophy, 29 (9.20%) had hypothyroidism, 25 (8.0 %) had osteoporosis, 16 (5.10%) had rheumatological disease, 13 (4.10%) had atrial fibrillation, 12 (3.80%) had depression, 11 (3.50 %) had malignancy, 10 (3.20%) had cerebrovascular disease, eight (2.60%) had congestive heart failure, three (1.00%) had peripheral arterial disease and two (0.60%) had chronic kidney disease (Table 2).

Only 14 of the participants said they knew geriatrics, but only nine (2.88%) were able to correctly identify what geriatrics is.

While four of these participants (1.70%) had education level less than five years, five (6.90%) of the participants were educated for six and more years (p=0.032).

Table 1. General characteristics	
n=314	
Age (Mean ± SD)	68.96±5.77
Sex (n %)	
Female	158 (50.20)
Male	157 (49.80)
Marital status (n %)	
Married	236 (74.90)
Widowed/unmarried	79 (25.10)
Household (n %)	
Alone	45 (14.40)
Spouse	159 (50.80)
Spouse and children	78 (24.90)
Children	31 (9.90)
Living arrangements (n %)	
Rent	43 (13.70)
Own	244 (77.70)
Relative/friend	26 (8.30)
Nursing home	1 (0.30)
Education (n %)	
Not literate	93 (29.60)
Literate	45 (14.30)
Primary school	104 (33.10)
Secondary school	20 (6.40)
High school	36 (11.50)
University/higher	16 (5.10)
Medicine number (mean - SD)	3.37±2.76
Katz (mean - SD)	5.86±5.14
Lawton (mean - SD)	7.75±7.8
Mini nutritional assessment (mean - SD)	13.61±1.95
Mini mental score (mean - SD)	24.16±4.33
Geriatric depression score (mean - SD)	4.68±3.77
n: Number of the patients, SD: Standard deviation	

Older adults, those who know geriatrics are statistically significantly older, respectively 75 vs 68 years of age (p=0.012); had fewer children, respectively two vs three (p=0.016); higher mini mental scores, respectively 29 vs 25 (p=0.002). (Table 3)

Discussion

Altindag (8) is a district with a population of 10.91% older adults. 50.7 % of the population are females. 62.2% of the population is married. 58% are primary, middle and high school graduates, 15% are university graduates and 15% are in other education. These rates seem to coincide with our data.

To compare the characteristics and rates of geriatric awareness in the literature, we searched the terms "geriatrics" and "awareness" in Web of Sciences, Pubmed, EBSCO, Library of congress, California state Library, Acad Search Prem, Google and Yandex. We did not find any community-based or hospital-based study in the literature. In the literature, which is made of publications close to the property we were looking for was from Turkey, which was published from Ankara Gazi University. Here around 200 patients in the waiting rooms of the hospital

Table 2. Diseases	
	n (%)
Hypertension	173 (55.10)
Diabetes mellitus	101 (32.20)
Coronary artery disease	67 (21.50)
Hyperlipidemia	58 (18.60)
Asthma/Chronic obstructive pulmonary disease	52 (16.60)
Benign prostatic hypertrophy	43 (13.70)
Hypothyroidism	29 (9.20)
Osteoporosis	25 (8.00)
Rheumatological disease	16 (5.10)
Atrial fibrillation	13 (4.10)
Depression	12 (3.80)
Malignancy	11 (3.50)
Cerebrovascular disease	10 (3.20)
Congestive heart failure	8 (2.60)
Peripheral arterial disease	3 (1.00)
Chronic renal disease	2 (0.60)
Osteoporosis	25 (8.00)
Malignancy	11 (3.50)
n: Number of the patients	

Table 3. Statistically significant factors between subjects that are aware and unaware of geriatrics			
	Aware n (%), 9 (2%)	**Unaware n (%), 305 (97%)**	**p value**
Age	75 (67-88)	68 (55-86)	0.012*
Number of children	2 (1-5)	3 (0-8)	0.016*
Mini mental score	29 (24-30)	25 (10-30)	0.002*

were included in the survey, and awareness rate hit 11.6% (9). In comparison, this study population has a mean age of around 40 in a university, with a center of geriatrics, and the rate is quite low. We can argue that this is the first community-based study evaluating geriatrics awareness.

Since we could not compare the awareness rate, we wanted to have an idea about whether we go to a relatively homogenous group by evaluating the prevalence of diseases in the older adults. In our study, diabetes mellitus prevalence is 30%, recently Gümüşsoy et al. (10) published a study from Turkey with similar diabetes prevalence rates in the older adults population, also TURDEP study had similar diabetes prevalence rates among Turkish older adults patients (11). Similarly, the prevalence of hypertension in our study was 55.1%, which is consistent with the Turkish hypertension prevalence study (12). Finally, the total asthma/COPD prevalence was similar to the literature (13). Since we could not reach the data that we could refer to the geriatric awareness in the literature, we compared the chronic diseases of the patients, we thought that we obtained similar results in the literature, so that the population we screened could represent or at least form an opinion about geriatric awareness of the older adults living in the community.

When we compared those, who knew the geriatrics and those who did not know what the geriatrics is, we found that those who knew what geriatrics were statistically significantly older than those who did not know, 75 years of age vs 68 years of age respectively (p=0.012). This may be due to the fact that more geriatric syndrome emerged with advanced age and there being 10 years vs three years for the possibility of intersection with a geriatrician.

We found that participants who knew what geriatrics has statistically fewer number of children when compared with the ones who did not knew, two children vs three children (p=0.016) respectively. Although statistically significant we have some doubts. First, we have limited number of samples in this group. Secondly, having less number of children may be a sign of another situation like higher education level. Also, these group of participants are found to be the ones living with their spouse only in subgroup analysis. For this reason, although this group may be more likely to seek better quality medical care because of the limited availability of social support, we cannot support this view and suggest that more participants should be reached, since only two of the participants who knew what geriatrics is under a geriatrician follow up.

Lastly, we found that those who knew what geriatrics has significantly higher scores in mini mental test when compared with the ones who did not knew, 29 vs 25 (p=0.002) respectively. We can comment that mini mental score may be a sign of any participants' general awareness. We can support this view: We detected that three participants who were detected that they did not know what geriatrics had geriatrician examination in the last three years and their median of mini mental score was 21. According to this result, any participant may still be unaware of what geriatrics is despite being under follow up as mini mental score lowers.

In general, participants with geriatrics awareness were found to be older in age, have higher mental scores and have less children. In subgroup analysis of all nine participants with geriatrics awareness, only education more than five years was statistically significant variable. The prevalence of geriatrics awareness was increased in those with higher education. We think that it would not be wrong to interpret that the "white collared" of the older adults are more aware of geriatrics.

If we revert to the main goal of the study, geriatrics awareness; the prevalence of geriatrics awareness was only 2.88% in this study. Two of these nine people who knew the geriatrics were a man and his wife working in Hacettepe University Anatomy department, which is close to geriatrics department. The remaining seven people were in two districts among eight different districts of Altındağ. Four of them in one district and three of them in another district. And all these four and three participants were the ones participating the survey respectively making us doubt if they were aware or they learned from each other. Lastly, six out of nine patients were detected to have an at least one admission to a medical center with a geriatrician. Five of these nine participants did not know how they learned about geriatrics, two were a married couple who retired from a university with a geriatrics department and they were under follow up there, one had lost his mother in a geriatrics clinic and one had heard from news.

Finally, as we stated in the introduction and aim, as the end of 2018, total number of geriatricians is only 1% of optimal need of Turkey. In our study, we found only 3% geriatrics awareness among target population in the community. This study can be accepted as the main reflection of this insufficiency on the community.

In the 20th year, in the capital city of Turkey, with the highest number of geriatrician and geriatric centers per population, awareness of geriatrics is found to be too low. We are aware that, to generalize all these results to whole country and to be able to detect their consistency, we need more community-based surveys. But here concluding that it is only the community that is not aware of geriatrics will not be fair. Considering that less than 5% of these participants do not have any chronic diseases, it will not be wrong to think that as much as the community, health personnel also is not aware of importance of or geriatrics itself, since 95% of these participants admit to a physician at least every three months for their prescribed medicines, and it seems that most of them have never heard

about geriatrics. Again, looking at the number of geriatricians in the 20th year of geriatric practice in Turkey, state policies should work harder like geriatricians in order to make the geriatrics more known, functional and more preferable by physicians as a specialty.

Study Limitations

We reached to the older adults in eight districts so the data is hard to generalize and since awareness prevalence is so low it is hard to make comparative statistics between the older adults that is aware and unaware of geriatrics.

Conclusion

In our country, awareness of geriatrics is very low in its 50th year. In order to increase the awareness of geriatrics, we think primarily geriatricians should find ways to increase awareness by the government, physicians and community.

Ethics

Ethics Committee Approval: Ankara University Ethical committee 25.06.2018 (No: 11-747-18).

Informed Consent: Informed consent was taken from every patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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References

1. Devi D, Srivastava R, Dwivedi BK. A critical review of concept of aging in Ayurveda. Ayu 2010;31:516-519.
2. Gerrit B, Jazzar I, Isyan R. (treatise on forgetfulness), London, 1995.
3. Pitskhelauri GZ, Dzhorbenadze DA. [Gerontology and geriatrics in the works of Abu Ali Ibn Sina (Avicenna) (on the 950th anniversary of the manuscript, Canon of Medical Science)]. Sov Zdravookhr 1970;29:68-71.
4. Lascaratos J, Poulacou-Rebelacou E. The roots of geriatric medicine: care of the aged in Byzantine times (324-1453 AD). Gerontology 2000;46:2-6.
5. Barton A, Mulley G. History of the development of geriatric medicine in the UK. Postgrad Med J 2003;79:229-234.
6. Vladimir I, Vladimir P. New bibliography of scientific papers by Dr. Laza K. Lazarević. Glas SANU - Medicinske Nauke, 2002:37-51.
7. Hatemi H. Geriatri'nin Türkiye'de "İlk" lerinden Prof. Dr. Şefik KAYAHAN. Turkish Journal of Geriatrics 1998;1:43.
8. https://www.endeksa.com/tr/analiz/ankara/altindag/demografi.
9. Kızılarslanoğlu MC, Kılıç MK, Özsürekci C, Köklü H, Ülger Z. Geriatri Bilim Dalı Olan Bir Üniversite Hastanesinde Geriatri Tanınma Oranları. İç Hastalıkları Dergisi 2013;20:135-140.
10. Gümüşsoy M, Bahşi R, Mut Sürmeli D, Turgut T, Selvi Öztorun H, Atmış V, Varlı M, Aras S. Insulin Misusage and Affect of Insulin Education in the Elderly. Van Med J 2018;25:323-331.
11. Satman I, Omer B, Tutuncu Y, Kalaca S, Gedik S, Dinccag N, Karsidag K, Genc S, Telci A, Canbaz B, Turker F, Yilmaz T, Cakir B, Tuomilehto J; TURDEP-II Study Group. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol 2013;28:169-180.
12. Sengul S, Akpolat T, Erdem Y, Derici U, Arici M, Sindel S, Karatan O, Turgan C, Hasanoglu E, Caglar S, Erturk S; Turkish Society of Hypertension and Renal Diseases. Changes in hypertension prevalence, awareness, treatment, and control rates in Turkey from 2003 to 2012. J Hypertens 2016;34:1208-1217.
13. Murtagh E, Heaney L, Gingles J, Shepherd R, Kee F, Patterson C, MacMahon J. Prevalence of obstructive lung disease in a general population sample: the NICECOPD study. Eur J Epidemiol 2005;20:443-453.

ORIGINAL RESEARCH

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Impact of Oral Health on Nutritional Status in Community-dwelling Older Adults in Turkey

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Abstract

Objective: To determine the association between oral health and nutritional status in community-dwelling older adults in Turkey. A population-based cohort study using data obtained from the Kayseri Elderly. Health Study.

Materials and Methods: Nutritional status was assessed using the Mini Nutritional Assessment. In oral examination, number of decayed permanent teeth, use of dental prostheses, number of natural teeth, use of toothpaste and tooth brushing frequency were noted. Oral health-related quality of life and periodontal status were assessed by the Oral Health Impact Profile (OHIP-14) questionnaire and the Community Periodontal Index, respectively.

Results: A total of 476 older adults, whose oral health data were available, were included in this study. The mean age of the participants was 71.8±5.6 years and 52.3% were female. The prevalence rate for normal nutritional status was 52.2%. The remaining 44.2% of the older adults were determined to be at risk of malnutrition and 3.6% had malnutrition. In multivariate analysis, depressive mood (OR: 2.54 95% CI: 1.59-4.06), use of toothpaste (OR: 0.58 95% CI: 0.38-0.88) and OHIP scores (OR: 1.03 95% CI: 1.01-1.06) were detected to be independent determinants of nutritional status.

Conclusion: Depressive mood, not using toothpaste and high OHIP scores were found to be significant risk factors for malnutrition.

Keywords: Older adults, community-dwelling, malnutrition, oral health status, mini nutritional assessment

Introduction

Malnutrition is frequent in older individuals, and has particular relevance in individuals with the advancing age. Studies have shown that the prevalence of malnutrition is approximately 2-8% in the community-dwelling older adults (1). The reported prevalence of malnutrition in the community-dwelling Turkish older adult population is in a broad range of 3.3 to 19% (2, 3). Malnutrition is one of the most relevant conditions that negatively affects the health of the older adults. Decline in nutritional quality is one of the complications of old aging (4). Poor oral health, comorbidities, use of medication, social, psychological and cultural factors are other contributing factors to the poor nutritional status of the older adults (5). Oral health problems related with teeth loss, lack of or inadequate prosthesis, the presence of pain related to caries and periodontal diseases are fundamental health problems which may have a high impact on nutrition, primarily in the older adults. These oral health-related problems may cause consumption of a diet low in fiber, and difficulty in fragmentation and grinding of food in the mouth. As a result, decreasing amount of fruit, vegetable, meat and bean consumption in diet may lead primarily increase in carbohydrate and sugar consumption (6). A relatively small number of studies have evaluated whether oral health problems are predictors of nutritional status among community-dwelling older adults by using measurements that assess the risk of malnutrition, especially assessment of malnutrition with Mini-Nutritional Assessment (MNA). The assessment of malnutrition can be done with anthropometric measurements or indexes' derived from these measures and with various scales. The most frequently used

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scale to assess nutritional status is the MNA. It is a noninvasive, well-validated, and simple test which is recommended for nutritional assessment in the older adults (1).

To our knowledge, there are studies about the oral health status of the elderly but studies that focus on the association between oral health and nutritional status in the older adults in Turkey are limited. Thus, the aim of this study is both to describe oral health status with reliable measures and to determine whether poor oral status is a contributing factor in the development of malnutrition in the community-dwelling older adults in Turkey.

Materials and Methods

To assess the relationship between oral health and nutritional status in the community dwelling older adults we used the Kayseri Elderly Health Study (KEHES) data (2). This is a cross-sectional population-based study that was conducted from August 2013 to December 2013. Number of older adults in this study constitutes at least 1% of the community-dwelling older adults in the Kayseri (a city in Central Anatolia in Turkey, with an estimated total population of 1.400.000). Data were collected from 21 Family Health Care Centers (FHCC). The distribution of health centers included in the study was stratified according to socio-economic level; low, moderate and good with respect to socio-economic status in general population. Family physicians in each FHCC was requested to randomly invite six older adults (three male and three female) from each age group who were 65-74, 75-84 and older than 85 years.

Nutritional status was assessed by the Turkish version of MNA long form (7). The MNA is developed by Guigoz et al. (8), which is the most established, best validated and widespread nutritional assessment tool used in geriatric population. Based on the total score, MNA scores of the subjects were classified into three categories. A score of less than 17 points (out of total 30) is regarded as malnutrition, 17-23.5 points at risk for malnutrition and >23.5 points at normal nutritional status. Geriatric Depression scale (GDS) (9) and Mini-mental State Examination (MMSE) (10) scores were obtained to screen depression and cognition respectively.

The GDS cut-off point was 14 for Turkish older adults (11) and cognitive impairment was defined as an MMSE score less than 24/30 in the illiterate and 25/30 in the literate individuals (12). Length of education was assessed according to the last school graduated. The level of education was grouped as illiterate, literate (<1 years), ≥1-8 years and >8 years (Illiterate, primary, secondary and over). Income was grouped as good, moderate, and low according to self-report of older adults, since income level is considered as a range of perception rather than a quantity.

All dental examinations were performed by an experienced dentist. The oral health status assessment compromised of the number of decayed, missing and filled teeth; periodontal status, Community Periodontal Index (CPI), and use of dental prosthesis (None, fixed, removable).

Subjective oral health-related quality of life was assessed by oral health impact profile (OHIP-14), which was validated for Turkish population (13). This is a 14-item questionnaire that includes seven dimensions and detects an individual's perception of functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. Subjects are asked if they have always/very often, often, sometimes, seldom or never experienced any of those problems in the previous three months. Responses are scored on a scale ranging from 1 to 5 (14). Higher scores indicate worse oral health-related quality of life.

Periodontal status was assessed by the CPI as it is recommended by World Health Organization. The null CPI score corresponds to healthy periodontal condition. Increasing CPI scores, according to the severity of periodontal status, are described as 1: gingival bleeding; 2: calculus and bleeding; 3: shallow periodontal pockets (Pockets 4-5 mm); 4: deep periodontal pockets (6 millimeters or more) (15). CPI score 1 corresponds to periodontal disease which can be improved with domestic oral hygiene; a score of 2 or 3 needs intervention by a dentist. The most severe condition, CPI 4, means that an individual requires additional periodontal surgery. Participants were categorized according to dentures: none, fixed and removable dentures. The entire study protocol was approved by the Medical Ethics Committee of Erciyes University Medical Faculty (No: 2013/441). Participants without severe cognitive impairment and who gave their informed consent were recruited; for participants with mild or moderate cognitive impairment, consent was obtained from a proxy.

Statistics

Descriptive characteristics of demography, cognitive status and depressive symptoms of community dwelling older adults were determined. These parameters were compared in our study group according to the nutritional status by chi-square test. Another comparison between normal nutritional status and poor nutrition (malnutrition/malnutrition risk) were done for oral health status; number of natural teeth, frequency of tooth brushing, decayed teeth, periodontal status, use of dental prosthesis, and oral health-related quality of life. Each parameter related with nutritional status then analyzed with logistic regression as uni-, and multivariate dependent variable. $P<0.05$ value was considered statistically significant. Data were analyzed by IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY, USA)

Results

We included 468 community-dwelling older adults with a mean age of 71.8 (SD±5.6) years and their age range was 60 to 91years. Of these 52.3% were females and 47.7% were males. We found that 52.1% (n=244) of subjects were at normal nutritional status, 44.2% (n=207) had Ministry of Natural Resources (MNR) status and 3.7 % (n=17) had membranous nephropathy (MN) according to Medical Nurse Associate (MNA). Since only 17 of the older participants were classified as malnourished, we combined the MN/MNR groups. The characteristics of the study group according to nutritional status are summarized in Table 1.

When compared normal nutritional status and MN/MNR subjects by sex, MN/MNR was prevalent in the female gender. Age was a significant indicator of being poor or normal nutritional status, 72.5 (SD±5.9) years for poor and 70.8 (SD=5.3) years for normal nutritional status. The MN/MNR were about two times higher in illiterate than literate older adults and normal nutritional status were two times higher in 1-8 years of educated older adults than literate. The ratio of older adults with cognitive impairment was about two times

Table 1. Comparison of community-dwelling elderly demographical characteristics for nutritional status

Socio-demographic variables	All n (%)	Malnutrition/ Malnutrition risk n (%)	Normal nutritional status n (%)	p values
Age				
Mean ± SD	71.8 (5.6)	72.5 (5.9)	70.8 (5.3)	<0.001
Age groups	-	-	-	
60-64	14 (2.9)	7 (3.1)	7 (2.9)	
65-74	320 (67.2)	144 (64.3)	169 (69.3)	0.721
75-84	132 (27.7)	68 (30.4)	63 (28.3)	
≥85	10 (2.1)	5 (2.2)	5 (2.0)	
Sex				
Female	245 (52.3)	134 (54.7)	111 (45.3)	0.002
Male	223(47.7)	90 (40.4)	133 (59.6)	
Smoking				
Yes	166 (34.9)	70 (31.2)	94 (38.5)	0.099
No	310 (65.1)	154 (68.8)	150 (61.5)	
Education level				
Illiterate	172 (36.1)	107 (47.8)	62 (25.4)	<0.001
Literate	98 (20.6)	45 (20.1)	52 (21.3)	
1-8 years	173 (36.3)	62 (27.7)	107 (43.9)	
>8 years	33 (6.9)	10 (4.5)	23 (9.4)	
Income				
Low	144 (30.6)	78 (35.5)	61 (25.2)	0.040
Moderate	239 (50.9)	107 (48.6)	129 (53.3)	
Good	87 (18.5)	35 (15.9)	52 (21.5)	
Cognitive impairment				
Yes	124 (26.2)	73 (32.6)	48 (19.8)	0.002
No	350 (73.8)	151 (67.4)	194 (80.2)	
Depression				
Yes	138 (29.1)	94 (42.0)	40 (16.5)	<0.001
No	336 (70.9)	130 (58.0)	202 (83.5)	

SD: Standard deviation

high in MN/MNR. Depressive symptoms were also indicator of malnutrition both in normal and poorly (MN/MNR) nourished older adults. Additionally, we detected the ratio of non-depressive was higher in normal nutritional status compared with poorly nourished (Table 1).

The average number of teeth in the studied sample was 3.2 (SD=4.0) and 37.4% of the subjects were edentulous. The edentulous older adults comprised about one fourth of our sample (n=178). In a comparison of the normal nutritional status and MN/MNR older adults, about 1/3 of the normal nutritional status and half of MN/MNR were edentulous. Using toothpaste and brushing teeth rate was about 50%. MN/MNR was higher in non-toothpaste users (59.4 %) than non-toothbrushers (53.1%) (Table 2).

The mean score of OHIP was 12.7 (SD=11.8) in MN/MNR and 7.1 (SD=7.7) for normal nutritional status older adults. Impairment in oral health-related quality of life (increased OHIP score) was at least 50% high in MN/MNR. Periodontal evaluation was done in 295 non-edentulous older adults. We found that just 8.8% of them were healthy. The frequency of periodontal pathologies was as follows: bleeding 1.0%, calculus 8.0% and sulcus 81.2%. We could not find any difference in CPI scores between the MN/MNR and normal nutritional status.

In bivariate analyses, demographical characteristics (gender, educational levels, and income), cognitive impairment, depression, oral health indicators (use of toothpaste, tooth-brushing and oral health-related quality of life) were tested. In multivariate analysis among the above-mentioned independent variables only depressive mood (OR: 2.54 95% CI: 1.59-4.06), use of toothpaste (OR: 0.58 95% CI: 0.38-0.88) and OHIP (OR: 1.03 95% CI: 1.01-1.06) were detected as independent determinants of nutritional status (Table 3).

Discussion

Malnutrition is one of the major geriatric problems associated with functional decline, poor health status and high mortality (4). Oral health status can be considered as a significant parameter that determines the nutritional level. Oral health status determines both the selection and consumption of food particularly in older adults. Certain types of food (difficult to chew and grind) ingestion may be avoided because of decayed, lost teeth and prosthesis (16). These limitations then may lead decrease in intake of products such as meat, fruit,

Table 2. Comparison of community-dwelling elderly oral health parameters for nutritional status

Oral health status	All n (%)	Malnutrition/Malnutrition risk n (%)	Normal nutritional status n (%)	p values
Number of natural teeth				
Edentulous	178 (37.4)	93 (41.5)	80 (32.8)	**0.054**
1-9	256 (53.8)	117 (52.2)	137 (56.1)	
≥10	42 (8.8)	14 (6.2)	27 (11.1)	
Tooth brushing frequency				
No brushing	218 (45.8)	119 (53.1)	93 (38.1)	**0.005**
≤ Once a day	175 (36.8)	70 (31.2)	103 (42.2)	
> Once a day	83 (17.4)	35 (15.6)	48 (19.7)	
Use of toothpaste				
Yes	239 (50.2)	91 (40.6)	144 (59.0)	**<0.001**
No	237 (49.8)	133 (59.4)	100 (41.0)	
Decay				
Yes	176 (37.0)	84 (37.5)	89 (36.5)	0.819
No	300 (63.0)	140 (62.5)	155 (63.5)	
Dental Prosthesis				
No	83 (17.6)	43 (19.3)	39 (16.2)	**0.077**
Fixed prosthesis	41 (8.7)	13 (5.8)	28 (11.6)	
Removable prosthesis	348 (73.7)	167 (74.9)	174 (72.2)	
OHIP	9.8 (10.2)	12.7 (11.8)	7.1 (7.7)	**<0.001**
Periodontal status				
(CPI scores)	5.2 (5.5)	4.5(5.2)	5.8(5.6)	0.206

OHIP: Oral Health impact profile, CPI: The consumer price index

Table 3. Univariate and multivariate analysis to assess to nutritional status with gender, educational level, income, cognitive impairment, tooth brushing frequency, use of toothpaste, OHIP and CPI score

Variables	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	p*	HR (95% CI)	p**
Sex				
Female	1	-	-	-
Male	1.076 (0.657-1.761)	**0.771**	-	
Education level				
Illiterate	1	-	-	-
Literate	0.56 (0.31-0.99)	0.04	-	
1-8 years	0.50 (0.28-0.88)	0.01	-	
>8 years	0.57 (0.22-1.49)	0.25	-	
Income				
Good	1	-	-	-
Moderate	1.03 (0.60-1.79)	0.89	-	
Low	1.14 (0.61-2.09)	0.67	-	
Cognitive impairment				
No	1	-	-	-
Yes	1.25 (0.75-2.05)	0.38		
Depressive mood				
No	1	-		<0.001
Yes	2.47 (1.52-4.04)	<0.001	**2.54 (1.59-4.06)**	
Tooth brushing frequency				
No brushing	1	-	-	-
≤ Once a day	1.09 (0.60-1.95)	0.76	-	
> Once a day	0.59 (0.25-1.42)	0.24	-	
Use of toothpaste				
No	1	-	**0.58 (0.38-0.88)**	**0.01**
Yes	0.40 (0.17-0.94)	0.037		
OHIP	1.03 (1.01-1.06)	0.002	**1.03 (1.01-1.06)**	**<0.001**
CPI	0.98 (0.94-1.02)	0.43	-	-

OHIP: Oral Health impact profile, CPI: The consumer price index, HR: Hazard ratio
p* value for comparison between "MN/MNR" and "normal nutritional status" groups: Univariate Logistic Regression test variable. p** value for comparison between "MN/MNR" and "normal nutritional status" groups: Multivariate Logistic Regression test variable.

and vegetables. Even low intake of protein may solely give rise to loss of muscle mass and strength that is a significant determinant of sarcopenia. Ruling out limitations leading to food restriction may prevent increased incidence of falls and fractures, functional impairments and disability related with sarcopenia (5). Above-mentioned conditions about the relationship between oral health and nutrition in older adults are not shown in national studies.

In our study, independent of age and gender, we found that 52.1% of the older adults were classified as normal nutritional status; 44.2% as MNR and 3.7% as having malnutrition according to the MNA test. To our knowledge this is the first study that used MNA to assess the relationship between oral health and nutritional status in the community-dwelling older adults in Turkey in a quite big sample.

Although in many studies abroad MNA have been used to assess the nutritional status in the older adults, few of these examined the relation with both teeth and periodontal pathologies. Additionally, in most of these studies subjects were institutionalized older adults. Similar with this study

our data support the hypothesis that existing number of natural, non-decayed teeth are not determinants of nutritional status (17,18). The finding that more than one-third of older adults in our study was edentulous supports the consideration that oral health status may be related with malnutrition but tremendous number of older adults with worst oral health condition prevented us to make this discrimination. There are several studies indicating that being edentulous and decreased masticatory capacity is related with malnutrition (19,20). Since we did not collected information about masticator and salivation capacity, we cannot make any evaluation about the effects of these characteristics on malnutrition in the older adults. The major discriminative contribution of our study was the recruitment of community-dwelling elderly who were relatively younger compared to similar studies.

Another contribution of our study was using OHIP-14 to reflect older adults view of quality of life related with oral health in the community-dwelling older adults in Turkey. In the current literature, Barrios et al. (21) shows the association of oral health-related quality of life (OHIP-14) and nutritional status in older adults who has oropharyngeal carcinoma. They found that older adults patients with MN or MNR had considerably worse oral health-related quality of life than those with adequate nutrition. Our findings were consistent with the Barrios et al. (21) study indicating that odds of OHIP on MN/MNR was 1.03 when compared with normal nutritional status. Then we may conclude that OHIP can be a tool of discrimination between MN/MNR and normal nutritional status.

The strong correlation between OHIP and Geriatric Oral Health Assessment Index (GOHAI) provides the opportunity of including another tool for older adults for assessment of oral health related nutritional status. The characteristics of OHIP-14 in determining social impact, and GOHAI in physical function show the significant contribution of this study (22).

Although there are several studies about the inverse relationship between body mass index (BMI) and periodontal health, there are very few about the relationship between MNA and periodontal health. Although BMI may be considered as a simple and basic method to assess nutritional and oral health status it has a limitation in older adults because kyphosis is frequent in older adults (23). We consider that the limitation of BMI may be a good reason to use MNA in assessment of periodontal health in the older adults. However, we could not find any difference between MN/MNR and normal nutritional status in terms of periodontal health.

The limitations of our study can be listed as lack of data in the KEHES study about chewing, swallowing functions and type of consumed food (meat, vegetables and grain).

Conclusion

The relationship between oral health and nutritional status in older adults is well known. According to our findings we may conclude that depressive mood, perception of oral health quality may be the prominent determinants in nutritional status of older adults. Contribution of this study may then be concentrating on relieving depressive state and improving personal oral health care measures may be the most promising clinical approach for older adults.

Ethics

Ethics Committee Approval: The entire study protocol was approved by the Medical Ethics Committee of Erciyes University Medical Faculty.

Informed Consent: Participants without severe cognitive impairment and who gave their informed consent were recruited; for participants with mild or moderate cognitive impairment, consent was obtained from a proxy.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.A., Design: S.A., M.M., S.K., Data Collection or Processing: S.A., S.K., T.Y.M., E.Ş.D., M.M., F.Ö.F., Analysis or Interpretation: A.Ö., Literature Search: S.A., Writing: S.A.

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

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References

1. Guigoz Y. The Mini Nutritional Assessment (MNA) review of the literature-What does it tell us? J Nutr Health Aging 2006;10:466-487.
2. Akin S, Safak ED, Coban SA, Mucuk S, Kiris Y, Ozturk A, Mazıcıoğlu M, Göçer S. Nutritional status and related risk factors which may lead to functional decline in community-dwelling Turkish elderly. Eur Geriatr Med 2014;5:294-297.
3. Gündüz E, Eskin F, Gündüz M, Bentli R, Zengin Y, Dursun R, İçer M, Durgun HM, Gürbüz H, Ekinci M, Yeşil Y, Güloğlu C. Malnutrition in Community-Dwelling elderly in Turkey: A Multicenter, Cross-Sectional Study. Med Sci Monit 2015;15:2750-2756.
4. Kaiser MJ, Bauer JM, Rämsch C, Uter W, Guigoz Y, Cederholm T, Thomas DR, Anthony PS, Charlton KE, Maggio M, Tsai AC, Vellas B, Sieber CC; Mini Nutritional Assessment International Group. Frequency of malnutrition in older adults: a multinational perspective using the mini nutritional assessment. J Am Geriatr Soc 2010;58:1734-1738
5. Brownie S. Why are elderly individuals at risk of nutritional deficiency? Int J Nurs Pract 2006;12:110-118.
6. Savoca MR, Arcury TA, Leng X, Chen H, Bell RA, Anderson AM, Kohrman T, Frazier RJ, Gilbert GH, Quandt SA. Severe tooth loss in older adults as a key indicator of compromised dietary quality. Public Health Nutr 2010;13:466-474.
7. Sarikaya D, Halil M, Kuyumcu ME, Kiliç MK, Yesil Y. A Validity Study of Long and Short (MNA-SF) Forms of Mini Nutritional Assessment (MNA) Test in Geriatric Patients. Presented in the 7th Academic Geriatrics Congress Abstract, Antalya, Turkey, 2014.

8. Guigoz Y, Vellas B, Garry PJ. Assessing the nutritional status of the older adult: the mini nutritional assessment as part of the geriatric evaluation. Nutr Rev 2014;54:59-65.
9. 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 1982-1983;17:37-49.
10. 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.
11. Ertan T, Eker E. Reliability, validity, and factor structure of the Geriatric Depression Scale in Turkish older adult: are there different factor structures for different cultures? Int Psychogeriatr 2000;12:163-172.
12. Ertan E, Eker E, Gurgen C. The Standardized Mini-mental State Examination for illiterate Turkish older adult populations. Presented at the second International Symposium on Neuropsychological Assessment of Mental and Behavioral Disorders. Abstract, Bursa, Turkey, 1999.
13. Mumcu G, Inanc N, Ergun T, Ikiz K, Gunes M, Islek U, Yavuz S, Sur H, Atalay T, Direskeneli H. Oral health related quality of life is affected by disease activity in Behcet's disease. Oral Dis 2006;12:145-151.
14. Slade GD. Derivation and validation of a short-form oral health impact profile. Community Dent Oral Epidemiol 1997;25:284-290.
15. WHO Scientific Group on Epidemiology, Etiology and Prevention of Periodontal Diseases: WHO Technical Report Series, No. 621 Geneva, World Health Organization; 1978:7-9.
16. Mesas AE, Andrade SM, Cabrera MA, Bueno VL. Oral health status and nutritional deficit in noninstitutionalized older adults in Londrina, Brazil. Rev Bras Epidemiol 2010;13:434-445.
17. Lamy M, Mojon P, Kalykakis G, Legrand R, Butz-Jorgensen E. Oral status and nutrition in the institutionalized older adult. J Dent 1999;27:443-448
18. Griep MI, Mets TF, Collys K, Ponjaert-Kristoffersen I, Massart DL. Risk of malnutrition in retirement homes older adult persons measured by the "Mini-Nutritional Assessment". J Gerontol A Biol Sci Med Sci 2000;55:57-63.
19. Soini H, Muurinen S, Routasalo P, Sandelin E, Savikko N, Suominen M, Ainamo A, Pitkala KH. Oral and nutritional status is the MNA a useful tool for dental clinics. J Nutr Health Aging 2006;10:495-499.
20. Dion N, Cotart JL, Rabilloud M. Correction of nutrition test errors for more accurate quantification of the link between dental health and malnutrition. Nutrition 2007;23:301-307.
21. Barrios R, Tsakos G, García-Medina B, Martínez-Lara I, Bravo M. Oral health-related quality of life and malnutrition in patients treated for oral cancer. Support Care Cancer 2014;22:2927-2933
22. El Osta N, Tubert-Jeannin S, Hennequin M, Bou Abboud Naaman N, El Osta L, Geahchan N. Comparison of the OHIP-14 and GOHAI as measures of oral health among older adult in Lebanon. Health Qual Life Outcomes 2012;30:131.
23. Cook Z, Kirk S, Lawrenson S, Sandford S. Use of BMI in the assessment of undernutrition in older subjects: reflecting on practice. Proc Nutr Soc 2005;64:313-317.

CASE REPORT

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Celiac and Crohn's Disease in an Elderly Patient

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Abstract

One of the causes of chronic diarrhea in the elderly is Celiac disease, which is an autoimmune disease that particularly common in children and young adults as well as among the elderly population. Diagnosis is often delayed due to atypical presentation in the elderly. There are only a few studies in the literature linking Celiac disease to inflammatory bowel disease. In the present study, we aimed to draw attention to the rare coexistence of Celiac disease and Crohn's disease presenting with chronic diarrhea and severe malnutrition in a geriatric patient.

Keywords: Celiac disease, diarrhea, Crohn's disease

Introduction

The causes of chronic diarrhea vary according to the socioeconomic status of the population. Chronic diarrhea is frequently associated with bacterial, mycobacterial and parasitic infections in developing countries. In developed countries it is caused by irritable bowel disease, inflammatory bowel disease, chronic infections and malabsorption syndromes. Celiac disease, which is one of the malabsorption syndromes, is often underdiagnosed. It is an autoimmune disease caused by an immun response to the gliadin found in gluten. Incidence of the disease in the population is around one percent (1,2), with the first peak being experienced between the first 8-12 months of life, and the second peak seen in the 3-4 decades (3). Although more common in children and young adults, an increase has been seen in the rate of detection in the elderly population (4,5), and studies have shown that in some countries, 25 percent of Celiac patients receive their first diagnosis in the seventh decade (1,6,7). Celiac disease affects primarily the intestinal system, although it can manifest in a very different clinic in the presence of extra-intestinal symptoms. Classical findings include chronic diarrhea, weight loss, and nutrient deficiencies such as iron and calcium, while exra-intestinal findings include anemia, osteoporosis, increased transaminase levels, neurological symptoms and infertility.

There are a number of studies reporting Celiac disease accompanying inflammatory bowel disease. We present a rare case of Celiac disease and Crohn's disease in the geriatric age group. Our goal is to emphasize Celiac disease from the causes of malnutrition, in that it can be underdiagnosed.

Case Presentation

A 72-year-old female patient visited our hospital with complaints of malaise, nausea, diarrhea and appetite loss. She had complained of diarrhea for seven years. The diarrhea was watery, 9-10 times a day and bloodless. Over the last five years, she has lost more than 20 kilograms. Her medical history includes osteoporosis, psoriasis and a cholecystectomy, although there is no known family history of gastrointestinal disorders. She had psoriasis and treated with methotrexate until 2010. Her medication includes a calcium preparation and bisphosphonate. On examination, temperature was recorded at 36.5 °C, heart rate 102 beats per minute and blood pressure was of 95/60 mmHg. The patient's appearance was cachectic and dehydrated. She measured 148 cm tall, 28 kilograms in weight and body mass

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index was 12.7 kg/m^2. She had a palpable liver edge 4 cm below the right costal margin and her skin was pale; other system examinations were normal. Laboratory studies revealed a serum sodium level of 124 mEq/L, potassium 1.8 mEq/L, phosphorus 1.2 mg/dL, calcium 4.3 mg/dL, albumin 2.4 g/dL, Ast 43 U/L, Alt 56 U/L and 25 hydroxyvitamin D 12 nmol/L (Table 1). Celiac markers Anti-endomysium IgA (+++), Tissue transglutaminase IgA 98 U/mL (reference range 0-10 U/mL) and Anti-deamidated gliadin IgA 41 U/mL (reference range 0-10 U/mL) were positive. A gastroscopic examination revealed hyperemic antrum, a mildly pale bulbi duodeni and occasional atrophy areas (Figure 1).

Pathological examination showed villous blunting, villous flattening, crypt hyperplasia and a small area of gastric metaplasia in both bulbus and duodenum mucosa. Increased intraepithelial CD3 positive T-lymphocyte infiltration exceeding 40 lymphocyte/100 enterocyte was also noted which was compatible with Celiac disease.

Colonoscopy revealed a 20 mm diameter lesion on the pili that is suspicious for a ulcerovegetan lateral spreading tumor in caecum, and a number of white exudate ulcers measuring between 3 and 15 mm in diameter in ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, and sigmoid column. However, no neoplastic lesion but only pseudopolypoid ulcerated and regenerated mucosa was observed in pathological examination. Ileocecal biopsy also showed an ulcerated mucosa while the other parts of colon were normal.

Magnetic resonance enteroclisis reported an increase in number of pleats and wall thickness of intestinal segments in axial sections passing through inferior of the umblicus (Figure 2).

Celiac disease was diagnosed and Crohn's disease was suspected clinically. Crohn disease activity index was 336 points at admission time. A gluten-free diet started with prednol 20 mg/day, oral nutritional support was added. Potassium, vitamin D, vitamin K and vitamin E were given. After vitamin K replacement, the INR level returned to normal. Mesalazine 500 mg 3x2/day peroral and Methotrexate 12.5 mg/week were added. The patient was discharged when her symptoms diminished. She weighed 41 kg, her body mass index was 18.71 kg/m^2 and Crohn disease activity index was 88 points at the time of discharge. Her laboratory results returned to normal range when she discharged (Table 1). At outpatient follow up prednol dosage was reduced

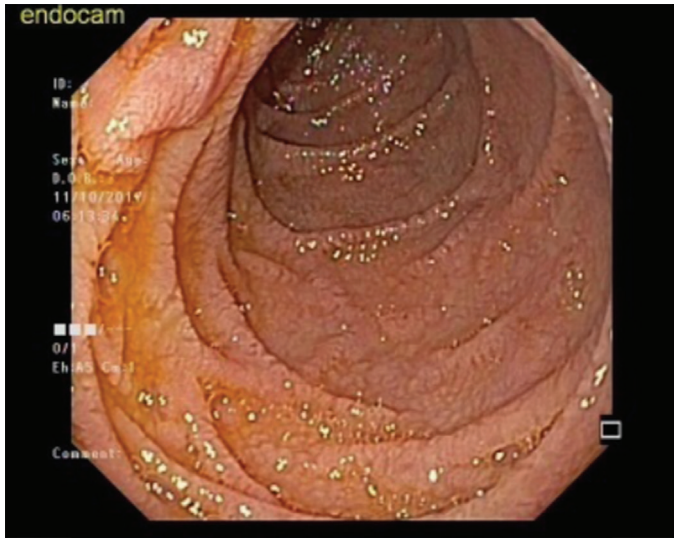

Figure 1. Second segment of duodenum

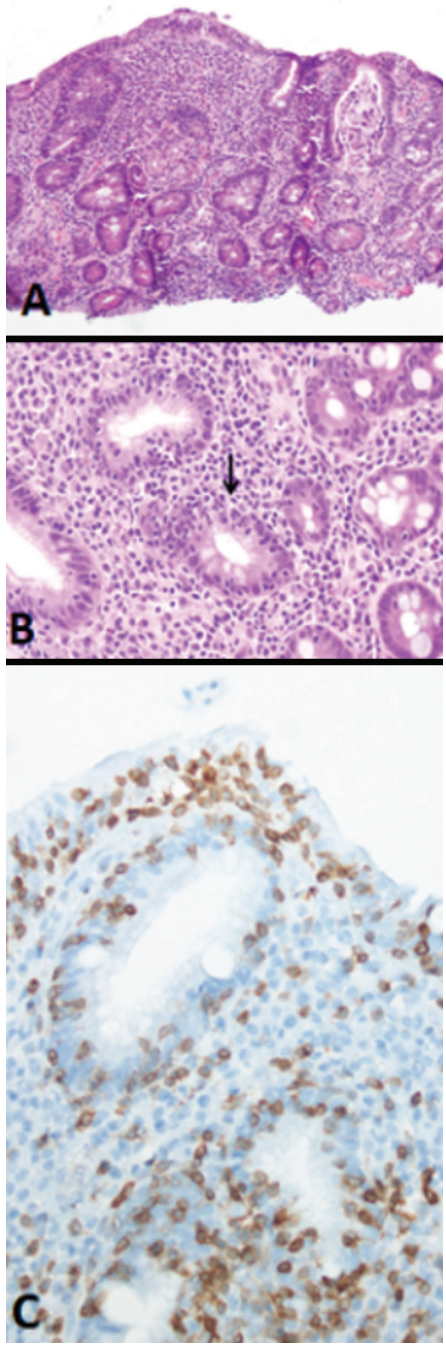

Figure 1. Bulbus biopsy. **A)** Flattened villi and crypts hiper plasia. (Haematoxylin and eosin, x4), **B)** Intraepithelial lymphocyte infiltration (arrow) (Haematoxylin and eosin, x20), **C)** CD3 (+) T-lymphocytes infiltration in the surface epithelium and glands exceeding x40 lymphocytes /100 enterocyte (anti CD3 antibody, x20)

and stopped. She uses mesalazine and methotrexate for 1.5 years and she is asymptomatic now.

Discussion

There have been a number of studies associating Celiac disease with inflammatory bowel disease, although the prevalence is not fully known (8-13). Yang et al. (13) found that inflammatory bowel disease was more common in Celiac disease patients than in the general population (13). In another study investigating this association, the prevalence of inflammatory bowel disease in Celiac disease patients was found to be 10 times higher than the control group (14). A prospective study in 2005 found that Celiac disease was more common in those with Crohn's disease, while another study found that Crohn's disease was more common in those who had Celiac disease (15,16). There have also been studies emphasizing that the prevalence of Celiac disease is similar in those with inflammatory bowel disease and in the general population (17). There is a lack of consensus in the literature regarding the association between inflammatory bowel disease and Celiac disease.

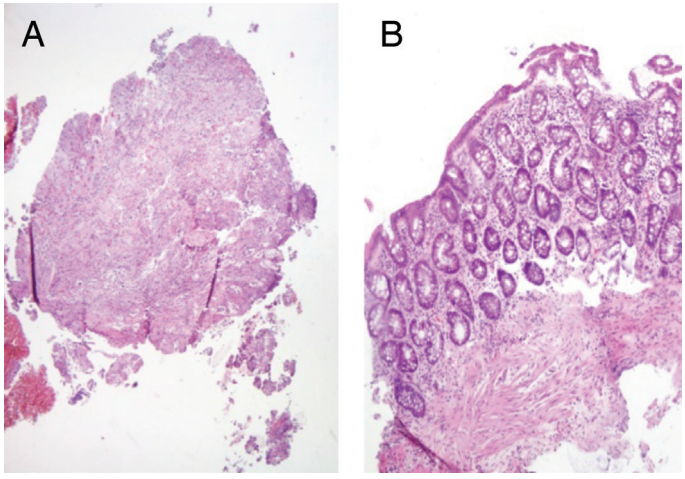

Figure 2. A) Ileocecal biopsy. The mucosa is ulcerated. Normal mucosa is not visible. (Haematoxylin and eosin, x4). **B)** Normal mucosa in other parts of the colon (Haematoxylin and eosin, x4)

In our patient, chronic diarrhea had been accompanied by malnutrition for the last one year, resulting in serious weight loss. The patient was 28 kg at the time of hospital admission. Studies have shown that involuntary weight loss is associated with increased mortality in elderly patients. It is known that five percent weight loss in three years is associated with increased mortality.

There may be many reasons for involuntary weight loss in old age, with malignant disease, psychological and social problems, gastrointestinal problems and end organ failure being just

Table 1. Laboratory results

Variable	Reference Range	Results	Results at hospital discharge time
Hemoglobin (g/dL)	11.7-16.1	11.9	11.9
Hematocrit (%)	35-47	31.7	34.9
White cell count (103/µL)	4.5-11.0	7.580	8.56
Platelet (103/µL)	150-450	293	412
Sodium (mEq/L)	136-145	124	136
Potassium (mEq/L)	3.5-5	1.8	4.3
Chloride (mEq/L)	96-110	86	103
Urea (mg/dL)	10-50	11	22
Creatinine (mg/dL)	0.6-1.1	0.55	0.5
25 hydroxyvitamin D (nmol/L)	10-19 light-medium	12	33
Aspartate aminotransferase (U/L)	<31	43	45
Alanine aminotransferase (U/L)	<34	56	56
International normalized ratio	0.9-1.2	2.1	1.1
C-reactive protein	0-0.5	<0.03	<0.03
Albumin (g/dL)	3.5-5.2	2.4	3.7
Calcium (mg/dL)	8.6-10.2	4.3	8.9
Phosphorus (mg/dL)	2.3-4.5	1.2	3.9
Erythyrocyte sedimentation rate (mm)	<30	7	25
Ferrum (µg/dL)	37-145	105	71
Total iron binding capacity (µg/dL)	228-428	139	146
Ferritin (ng/mL)	13-150	346.7	300.2
Folic acid (ng/mL)	3.89-26.8	2.24	>20

some of these. In general, malignancy is considered in cases of involuntary weight loss, and other causes, such as Celiac disease, can be overlooked. Up to 20 percent of Celiac patients may have abnormal liver function tests, which is known as Celiac hepatitis (18). Liver tests ALT, AST were also high in our case. After excluding the underlying viral and autoimmune hepatitis, abnormality in liver tests was thought to be secondary to Celiac disease.

The onset of diarrhea following the cessation of methotrexate due to psoriasis is thought to be a result of inflammatory bowel disease. In addition, pseudopolyps and ulcers seen in colonoscopy supported inflamatuary bowel disease.

In our opinion, celiac disease rarely conceive as a cause of chronic diarrhea in old age and diagnosis could be delayed.

At the point of this view, Celiac disease should be kept in mind in the presence of chronic diarrhea, weight loss and electrolyte imbalance in the geriatric age group, and it should be remembered that Crohn's disease may accompany Celiac disease.

Ethics

Informed Consent: Informed consent was taken from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.Ş., S.Ş., Z.F.S., R.V., B.D., S.F.A., F.Ö.K.K., B.G., O.Ö., Concept: : S.Ş., S.Ş., Z.F.S., R.V., B.D., S.F.A., Design: S.Ş., Data Collection or Processing: S.Ş., R.V., B.D., Analysis or Interpretation: S.Ş., Literature Search: S.Ş., Writing: S.Ş.

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

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References

1. Rubio-Tapia A, Ludvigsson JF, Brantner TL, Murray JA, Everhart JE. The prevalence of Celiac disease in the United States. Am J Gastroenterol 2012;107:1538-1544.
2. Choung RS, Larson SA, Khaleghi S, Rubio-Tapia, Ovsyannikova IG, King KS, Larson JJ, Lahr BD, Poland GA, Camilleri MJ, Murray JA. Prevalence and Morbidity of Undiagnosed Celiac Disease from a Community-Based Study. Gastroenterology 2017;152:830-839.
3. Schuppan D, Junker Y, Barisani D. Celiac disease: from pathogenesis to novel therapies. Gastroenterology 2009;137:1912-1933.
4. Freeman H, Lemoyne M, Pare P. Coeliac disease. Best Pract Res Clin Gastroenterol 2002;16:37-49.
5. Vilppula A, Kaukinen K, Luostarinen L, Krekelä I, Patrikainen H, Valve R, Mäki M, Collin P. Increasing prevalence and high incidence of Celiac disease in elderly people: a population-based study. BMC Gastroenterol 2009;29:49.
6. Freeman HJ. Clinical Spectrum of Biopsy-Defined Celiac Disease in the Elderly. Can J Gastroenterol 1995;9:42-46.
7. Greco L. Epidemiology of coeliac disease. Proceedings of the Seventh International Symposyum on Coeliac Disease. Tampere: Finland: 1996.
8. Cottone M, Cappello M, Puleo A, Cipolla C, Filippazzo MG. Familial association of Crohn's and coeliac diseases. Lancet 1989;2:338.
9. Cottone M, Marrone C, Casà A, Oliva L, Orlando A, Calabrese E, Martorana G, Pagliaro L. Familial occurrence of inflammatory bowel disease in Celiac disease. Inflamm Bowel Dis 2003;9:321-323.
10. Euler AR, Ament ME. Celiac sprue and Crohn's disease: an association causing severe growth retardation. Gastroenterology 1977;72:729-731.
11. Gillberg R, Dotevall G, Ahrén C. Chronic inflammatory bowel disease in patients with coeliac disease. Scand J Gastroenterol 1982;17:491-496.
12. Kitis G, Holmes GK, Cooper BT, Thompson H, Allan RN. Association of coeliac disease and inflammatory bowel disease. Gut 1980;21:636-641.
13. Yang A, Chen Y, Scherl E, Neugut AI, Bhagat G, Green PH. Inflammatory bowel disease in patients with Celiac disease. Inflamm Bowel Dis 2005;11:528-532.
14. Leeds JS, Höroldt BS, Sidhu R, Hopper AD, Robinson K, Toulson B, Dixon L, Lobo AJ, McAlindon ME, Hurlstone DP, Sanders DS. Is there an association between coeliac disease and inflammatory bowel diseases? A study of relative prevalence in comparison with population controls. Scand J Gastroenterol 2007;42:1214-1220.
15. Tursi A, Giorgetti GM, Brandimarte G, Elisei W. High Prevalence of Celiac Disease Among Patients Affected by Crohn's Disease. Inflamm Bowel Dis 2005:11:662-666.
16. Masachs M, Casellas F, Malagelada JR. Inflammatory bowel disease in Celiac patients. Rev Esp Enferm Dig 2007;99:446-450.
17. Casella G, D'Incà R, Oliva L, Daperno M, Saladino V, Zoli G, Annese V, Fries W, Cortellezzi C. Prevalence of Celiac disease in inflammatory bowel diseases: An IG-IBD multicentre study. Dig Liver Dis 2010;42:175-178.
18. Rubio-Tapia A, Murray JA. Liver involvement in celiac disease. Minerva Med 2008;99:595-604.

CASE REPORT

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An Atypical Case of Psoas Abscess in an Elderly Patient

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Abstract

Psoas abscess (PA), the accumulation of suppurative fluid in the fascia surrounding the psoas muscle, is a rare condition, with difficult diagnosis. Pain, fever, and limping are its main symptoms. In this paper, we report a case of PA presenting with non-specific symptoms, such as pain and fatigue. After the diagnosis, drainage of PA was performed, and intravenous antibiotic treatment was started immediately. The patient was discharged with improvements in his general condition after three weeks of treatment. This case suggests that PA should be considered in geriatric patients presenting with nonspecific symptoms such as fatigue, loss of appetite and weight loss as well as waist and hip pain. Early diagnosis may significantly decrease the risk of morbidity and mortality.

Keywords: Psoas abcess, fever, hip pain, fatigue, weight loss

Introduction

Psoas abscess (PA) is a condition due to accumulation of suppurative fluid in the fascia surrounding the psoas muscle, which has an important role in the flexion of the trunk (1). It is rarely encountered and difficult to diagnose. For example, it is reported in a study (2) that the mean time span between the onset of symptoms and PA diagnosis was found to be 22 days with one third of patients diagnosed after 42 days. PA may be classified as primary or secondary, depending on the original location of the underlying infection. Primary PA usually occurs as a result of the transport of an infection via a hematogenous or lymphogenesis route from a remote infection site in the body (3). Its main risk factors are diabetes mellitus, intravenous drug use, human immunodeficiency virus infection, and renal failure (4). On the other hand, secondary PA is caused by the spread of an infection in the neighborhood of psoas muscle such as sigmoid colon, jejunum, ureter, abdominal aorta, kidneys and vertebrae. Main risk factors of secondary PA are trauma and interventional procedures (5).

While, the most common bacterial cause of PA is *Staphylococcus aureus* worldwide, *Mycobacterium tuberculosis* is also seen commonly in developing countries. Pain (91%) and fever (75%) are two most common complaints of patients applying to the clinic. Furthermore, limping, weight loss, and weakness can be seen in these patients (4). PA is treated with the use of appropriate antibiotics along with drainage of abscess. Even though prognosis of PA is good in cases with early treatment, mortality rate increases if diagnosis is delayed or unless drainage is successfully done.

Case Presentation

A 78-year-old male patient admitted to our clinic with pain in his left hip that had begun one month ago. The patient, who had been functionally independent before pain, stated that he could not perform instrumental activities of daily living anymore and that there had been a loss of appetite accompanied by approximately weight loss of 5 kgs (i.e., 7% of his body weight). As opposed to common characteristics of PA, the patient did not have a fever. Furthermore, the patient did have neither night sweats nor morning stiffness.

Before applying to our clinic, the patient had presented to physical therapy and rehabilitation, orthopedics and neurosurgery clinics with the same complaints. There, the patient had been diagnosed with lumbar disc herniation and osteoporosis for which calcium and vitamin D had been started as a treatment. Then, he admitted to our clinic with no regression

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in his complaints. Past medical history of the patient includes vitiligo diagnosed 50 years ago and cataract surgery as the only operation. The patient had no history of prostate cancer or prostate biopsy. It was found in the geriatric assessment that the patient did not have forgetfulness, depression, falls, urinary incontinence and constipation. On physical examination, blood pressure was 120/80 mmHg, pulse was 65 beats/min, body temperature was 36.8 °C, muscle strength in left hip flexion was 4/5, left hip movements were painful, and there was no heat increase, redness and swelling on hip. There were no significant features in other system examinations.

Comprehensive geriatric assessment was done. Laboratory values are presented in Table 1. Results of microbiological cultures, brucella, and tuberculosis screening tests were negative. No abnormalities were found in radiographs of chest, sacroiliac, and pelvis. Screening for malignancy was planned from the patient who had high sedimentation rate, weight loss and iron deficiency. Multiple myeloma was not detected. Rheumatologic markers were negative except weak antinuclear antibody positivity. Because of the lumbar disc herniation, he was referred to neurosurgery where analgesic was recommended. The hip ultrasound revealed that there was a septated cystic structure with hypoechoic and hyperechoic areas on the medial side of iliopsoas muscle, which implies the PA. Diagnosis of PA was then confirmed by the computed tomography (CT), which is given in Figure 1. CT-guided drainage was performed. Cell count of the sample taken from abscess drainage revealed that there exists 35000/mm^3 leukocytes. Acid resistant bacteria and cytology results were negative. He was started on sulbactam-ampicillin. *S. aureus* was the etiologic agent in abscess culture. Upper and lower gastrointestinal endoscopy was performed to investigate iron deficiency and primary focus of PA. Multiple diverticula were found in the entire colon. He started to walk without pain after abscess drainage and antibiotic treatment. Patient discharged after three weeks of antibiotic therapy. One month later, patient admitted to outpatient clinic, control laboratory values are presented in Table 1.

Discussion

In this case, clinical features of PA, which are difficult to diagnose and which may be atypical in geriatric age group,

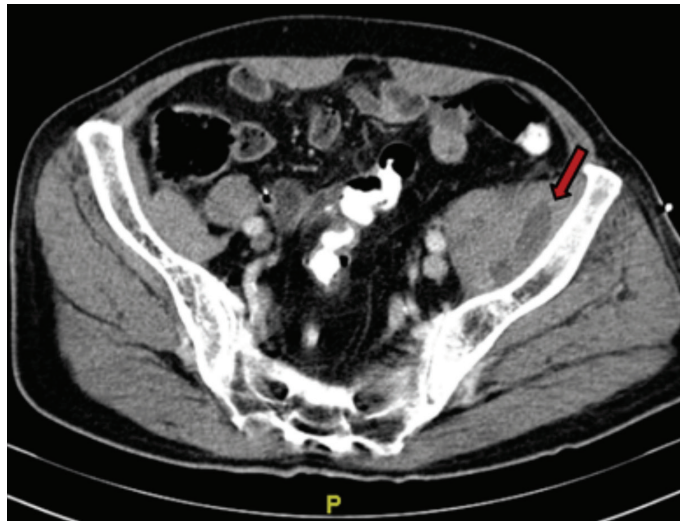

Figure 1. Psoas abscess in the transverse section of computed tomography image at the S2-S3 level

Table 1. Laboratory values of admission and control of the patient

	Admission	Control	Normal range
Hemoglobin (g/dL)	11	12.9	12.6-17.4
MCV (fL)	93.6	93	81-103
WBC (x10^9/L)	8.09	9.04	4.5-11
Platelet (x10^9/L)	376	265	150-400
FPG (mg/dL)	98	96	74-100
Creatinin (mg/dL)	1.08	1.05	0.67-1.17
BUN (mg/dL)	26	17	8-23
GFR (mL/min/1.73 m^2)	65	68	>60
ALT (U/L)	49	13	<50
AST (U/L)	30	23	<50
GGT (U/L)	144	55	<55
ALP (U/L)	206	191	30-120
Sedimentation (mm/hr)	102	40	<20
CRP (mg/L)	178	9	<5
Ferritin (ng/mL)	723	703	23-336
Transferrin saturation (%)	8	24	13-45

MCV: Mean corpuscular volume, WBC: White blood cell, FPG: Fasting plasma glucose, BUN: Blood urea nitrogen, GFR: Glomerular filtration rate, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma glutamyl transferase, ALP: Alkaline phosphatase, CRP: C-reactive protein, min: Minimum

are emphasized. Our case admitted with complaints of severe hip pain, weakness, and loss of appetite. There were no risk factors such as immune suppression, diabetes, and renal failure, which facilitate PA development. Furthermore, the patient did not have fever which is actually a classical symptom of PA (6). Generally, absence of symptoms such as fever, shivering or sweating may suggest no infection which makes diagnosis of PA difficult in our case. This is in line with the general situation of PA diagnosis in older population due to its atypical course and complications such that even sepsis can be seen in some cases (6). Therefore, in older patients with severe abdominal and low back pain, PA should be considered even if there is no fever. Imaging must be performed for definitive diagnosis. Among available techniques, CT is the most appropriate method being able to provide information about causes of secondary PA in addition to diagnosis (7). Alternatively, magnetic resonance imaging can be used since it identifies soft tissues well without any use of contrast. However, ultrasound is not suggested due to its lower diagnostic rate reported to be 48% in a study (8).

In our case, we think that PA was secondary occurring as a result of diverticulosis. Colon pathologies are the second most common cause of secondary PA following the infection of the spine as the number one reason (9). Finally, after diagnosis is made quickly, open or percutaneous abscess drainage should be performed for treatment along with the use of antibiotics against the infectious agent, as we did in our case.

In this paper, we reported a case of a 78-year old male with PA which is a rare condition that might present with an atypical clinical course in geriatric age group compared to young people. Although fever and pain are its most common symptoms, fever may not be seen in older patients. Furthermore, patients with nonspecific symptoms such as fatigue, loss of appetite, waist and hip pain may be suffering from PA. Therefore, atypical presentations should always be kept in mind in geriatric age group, as presented in our case of a PA without fever.

Ethics

Informed Consent: Informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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References

1. Mallick IH, Thoufeeq MH, Rajendran TP. Iliopsoas abscesses. Postgrad Med J 2004;80:459-462.
2. Navarro López V, Ramos JM, Meseguer V, Pérez Arellano JL, Serrano R, García Ordóñez MA, Peralta G, Boix V, Pardo J, Conde A, Salgado F, Gutiérrez F; GTI-SEMI Group. Microbiology and outcome of iliopsoas abscess in 124 patients. Medicine (Baltimore) 2009;88:120-130.
3. Mückley T, Schütz T, Kirschner M, Potulski M, Hofmann G, Bühren V. Psoas abscess: the spine as a primary source of infection. Spine (Phila Pa 1976) 2003;28:106-113.
4. Denis Spelman. Psoas abscess. In: UpToDate, Sexton Daniel (Ed), UpToDate, Waltham, MA, 2019.
5. Buttaro M, González Della Valle A, Piccaluga F. Psoas abscess associated with infected total hip arthroplasty. J Arthroplasty 2002;17:230-234.
6. Deng Y, Zhang Y, Song L, Zhang X, Shen Z, Li Z, Zhang L, Peng A. Primary iliopsoas abscess combined with rapid development of septic shock: Three case reports. Medicine (Baltimore) 2018;97:e13628.
7. Agrawal SN, Dwivedi AJ, Khan M. Primary psoas abscess. Dig Dis Sci 2002;47:2103-2105.
8. Huang JJ, Ruaan MK, Lan RR, Wang MC. Acute pyogenic iliopsoas abscess in Taiwan: clinical features, diagnosis, treatments and outcome. J Infect 2000;40:248-255.
9. Navarro López V, Ramos JM, Meseguer V, Pérez Arellano JL, Serrano R, García Ordóñez MA, Peralta G, Boix V, Pardo J, Conde A, Salgado F, Gutiérrez F; GTI-SEMI Group. Microbiology and outcome of iliopsoas abscess in 124 patients. Medicine (Baltimore) 2009;88:120-130.