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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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Preparation of Manuscript

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

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

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

Title Page

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

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.

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

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Abstract and Keywords: The second page should include an abstract that does not exceed 300 words. Moreover, as various electronic databases integrate only abstracts into their index, important findings should be presented in the abstract.

Abstract

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

Materials and Methods: Important methods should be written respectively.

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Original Articles

Original articles should have the following sections;

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

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

Conclusion: The conclusion of the study should be highlighted.

References

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

Examples of References:

1. List All Authors

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

2. Organization as Author

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

3. Complete Book

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

4. Chapter in Book

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

5. Abstract

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

6. Letter to the Editor

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

7. Supplement

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

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Case reports should be structured as follows:

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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.

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

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

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Tables: Supply each table on a separate file. Number tables according to the order in which they appear in the text, and supply a brief caption for each. Give each column a short or abbreviated heading. Write explanatory statistical measures of variation, such as standard deviation or standard error of mean. Be sure that each table is cited in the text.

Figures: Figures should be professionally drawn and/or photographed. Authors should number figures according to the order in which they appear in the text. Figures include graphs, charts, photographs, and illustrations. Each figure should be accompanied by a legend that does not exceed 50 words. Use abbreviations only if they have been introduced in the text. Authors are also required to provide the level of magnification for histological slides. Explain the internal scale and identify the staining method used. Figures should be submitted as separate files, not in the text file. High-resolution image files are not preferred for initial submission as the file sizes may be too large. The total file size of the PDF for peer review should not exceed 5 MB.

Article Type	Abstract (words)	Document (words) (excluding references)	References	Total Tables and Figures
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Review Articles	300	3500	75	5
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Authorship

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
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CONTENTS

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Can We STOPP Falls?

Nathalie van der Velde, Lotta Seppala

Amsterdam University Medical Centers, Amsterdam, Netherlands

Keypoints

- Falls are under-recognized as adverse drug events (ADEs),
- Healthcare professionals are reluctant to deprescribe fall-risk increasing drugs,
- A European expert consensus list of fall-risk increasing drugs was developed to aid healthcare professionals in identifying fall-risk increasing drugs,
- The STOPP falls deprescribing instrument was developed to assist health care professionals to assist clinical decision making and facilitate appropriate deprescribing of fall-risk increasing drugs,
- STOPP falls is more comprehensive than most national falls prevention guideline listings,
- STOPP falls is a first step toward harmonizing practice and guidelines on drug-related falls in Europe.

Occurrence of harm from medication use is rapidly increasing, especially in older persons, and so is harm resulting from fall incidents in this age group (1,2). Although at first sight these two rising health care problems appear to be separate harms, they are in fact strongly interrelated. In the majority of cases, falls result from interacting risks; and certain medication classes are a significant risk factor for falls (3-5). Thus, falls, widely acknowledged as a geriatric syndrome, should also be recognized as a commonly occurring ADE in the older population (6). Given the fact that approximately 0.9 to 1.5% of the total health care budget in Western countries is spent on fall-related costs (7), there is a great need to prevent unnecessary falls and related injury. This includes minimization of the ADE "falls".

Since the use of fall-risk-increasing drugs (FRIDs) is one of the most prominent fall risk factors, a medication review -aimed at deprescribing FRIDs- is considered an essential component of the multifactorial falls intervention in (inter)national falls prevention guidelines (8,9). In general it is acknowledged that the major groups of medications that can increase fall risk are psychotropic drugs and cardiovascular drugs. Three recent systematic reviews and meta-analyses confirmed the association between psychotropics [antidepressants (selective serotonin reuptake inhibitors, tricyclic antidepressants), antipsychotics, benzodiazepines] and fall risk (4). Moreover, consistent associations were reported for loop diuretics, antiepileptics, opioids, and polypharmacy (3,5). Digitalis, non-selective beta-blocking agents, antiarrhythmics, diuretics in general, antihypertensives, anticholinergics, non-steroidal anti-inflammatory drugs, analgesics, laxatives, long-term proton pump inhibitors, and antiplatelets were also identified as possible FRIDs (3,5). However, although FRIDs use is common in older persons, health care professionals are often reluctant to deprescribe FRIDs (6). Knowledge is lacking among both health care professionals and older people and their caregivers concerning the role of medication as a fall risk factor. The members of the European Geriatric Medicine Society (EuGMS) task and finish group on FRIDs have taken it upon themselves to facilitate appropriate (de)prescribing in older persons at risk of falls through raising public awareness, knowledge dissemination activities, update of knowledge, development of personalized and effective deprescribing interventions, all aimed at optimizing and harmonizing practices among Europe (10). The group was founded by us in 2016 and by now includes 30 members from 14 European countries. On the website of the EuGMS all publications, developed materials as well as symposium presentations can be found and downloaded.

The main objectives of the T&F group on FRIDs are:

- To update knowledge related to FRIDs.

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- To successfully disseminate knowledge on FRIDs and FRIDs withdrawal to health care workers, students and the older population at risk and thus lessen the use of unnecessary FRIDs in older persons at risk.
- To develop drug withdrawal interventions that are personalized and effective.
- To harmonize practice on this topic across Europe.

The latest accomplishment of our group, in collaboration with the EuGMS SIG on pharmacology, is the development of the STOPP falls deprescribing instrument, which was recently published in age and ageing (11). The tool provides practical guidance to simplify and structure FRIDs deprescribing in clinical practice and it has been translated to a freely available online available digital deprescribing decision support tool (STOPP falls online tool).

STOPP falls was built through a Delphi process of European experts and resulted in an agreed on list of 14 FRIDs, in majority psychotropic medication and furthermore cardiovascular and other drug groups such as anticholinergics (11). Also 18 differences between pharmacological subclasses were identified with regard to fall-risk-increasing properties and practical deprescribing guidance to assist clinical decision making. This information was summarized in overview tables and made easily interpretable by providing decision trees per medication group. Remarkably, the STOPP fall list is more comprehensive than most national falls prevention guideline listings.

The drug groups that consensus was reached on as being fall-risk increasing are:

- Benzodiazepines and benzodiazepine related drugs,
- Antipsychotics,
- Antidepressants,
- Diuretics,
- Alpha-blockers used as antihypertensives,
- Centrally-acting antihypertensives,
- Vasodilators used in cardiac diseases,
- Opioids,
- Antiepileptics,
- Anticholinergics,
- Alpha-blockers used for prostate hyperplasia,
- Overactive bladder and incontinence medications,
- Sedative antihistamines.

In the final consensus step of the Delphi effort, consensus was reached on guidance advice of deprescribing, which was translated to a stepwise deprescribing tool, that can also be found online (12). The deprescribing guidance includes information on when and how to deprescribe with relevant references and links to general deprescribing guidelines, specifically is addressed:

- In which cases to consider deprescribing (symptoms and/or indications),
- If stepwise withdrawal is needed,
- If monitoring after deprescribing is necessary (including symptoms and frequency).

STOPP falls is formally part of the STOPP/START series and the results will be included in the draft criteria for the anticipated STOPP/START version 3, to be further validated by the STOPP/START panelists. A next step of our group will be to obtain funding to validate the tool and assess its effectiveness on falls prevention, preferably in a European, multicenter and multi-country randomized controlled study. But in between we are performing a systematic review and meta-analysis to summarize evidence on the effectiveness of different deprescribing tools (including general ones) on fall risk and related injury. This paper is anticipated to be published second part of 2021 and will inform the recommendations of the ongoing word falls guideline effort (13).

Keywords: Deprescribing, older people, falls, prevention, medication review

Ethics

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An Apple of Eye Legacy to the Humanity from Istanbul Medical Faculty: Professor Dr. Cemil Taşçıoğlu

Gülistan Bahat

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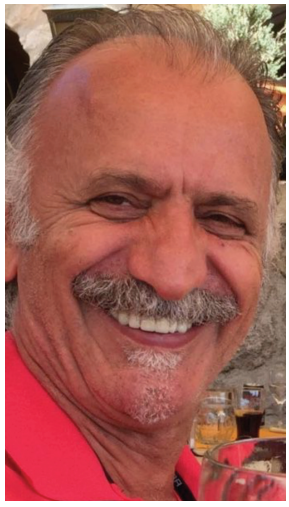

Born in Turkey, Rize in 1952, he has settled in Istanbul, Çengelköy in 1954 with his family. This is where he cultivated a personality since adolescence full of love, liberty and self-reliance, perhaps inspired by the Bosphorus. Graduating from Istanbul University, Istanbul Medical Faculty in 1977, he has completed his specialty education in internal diseases under the roof of the same institution. In 1982, after being entitled a specialist in internal diseases, he was conscripted and fulfilled his duty in Kars/Sarıkamış. Although he was appointed to Şanlıurfa as part of the "obligatory service," he "voluntarily" extended his practice there until 1989. His career advance continued with chief assistantship in Istanbul Medical Faculty, Department of Internal Medicine, General Internal Medicine in 1989; associate professorship in 1993; professorship in 1998. Though retired in 2019 due to age limit, he did not interrupt his prolific career and was employed as an adjunct professor in his home institution.

I am so lucky and have the great honor that I met him in Istanbul Medical Faculty on 1999, at the time that I have begun my residency in internal medicine. The first thing I remember with him was his generous help, emphasizing the ethical and deontological respect to his colleague. I have continued as an academician in this university in the division of geriatrics. It is our privilege and exclusive feature that the geriatrics has taken root from the division of general internal medicine in this faculty so that a geriatrician has all the skills to manage the complex needs of the older adults, not focusing on an organ but on the whole picture of the patient. We worked and studied with him hand to hand to diagnose and treat the most complex cases of Turkey, with great enthusiasm in general internal medicine and geriatrics.

"Cemil Taşcıoğlu" has been an epitome of excellence in clinician medicine. Full of modesty and curiosity, he was particularly keen in helping the patients whose diagnoses were rather enigmatic. Throughout Turkey, from east or west, it has been a custom, to transfer those patients failing to be diagnosed, to his examination. The "stepping stones" he used in the journey from symptoms to diagnosis provided him clarity and direction amidst the complicated diagnosis algorithm. Traces of vitality of a sound knowledge of semiology/symptomatology would be felt in professor's every discussion. Relentlessly accumulating his knowledge, Professor would always integrate new diseases, diagnostic and treatment methods into the classical wisdom and you would always be enriched by observing such amalgamation in his visits.

In his evaluations of the patients, impeccable physical examination was always accompanied by a probe into the patients' family structure, mental situation and social life. He did not perceive his patients as only corporal beings but as mental and social beings as well. Prominent with his clinician identity, he used to have a critical attitude towards laboratory medical practice. Perfection in his diagnoses was also a product of his life-long emphasis on communication

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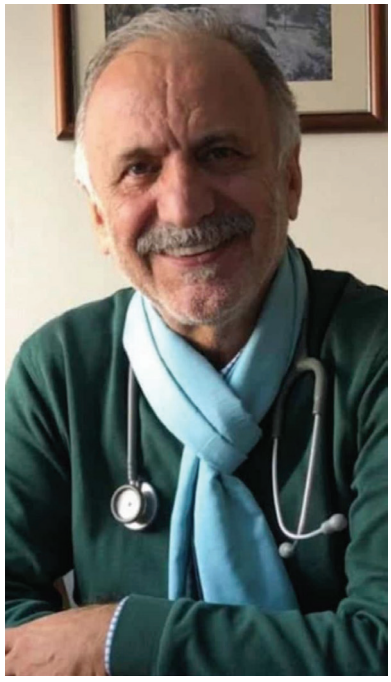

and collaboration as he always gave the verdict on diagnosis questions after intense consultations with his colleagues. He had a daily routine of selecting a patient with the most peculiar physical findings and studying her/him with his students. His students had such unique experience of diagnosing the hardest cases, giving them a sense of how medical contentedness could result from original thinking, cleverness and embracing complexity.

Professor Taşçıoğlu would transform his students and fellows into individuals with confidence and bright ideas, giving them full voice. We know that his happiest moments were when a controversial case presented itself and his students or assistants could point out the differential diagnosis before himself. Such precedents' validity did not matter to him; he was happy to see confident, intelligent beings who could give a judgment in a timely manner. Whenever such a judgment turned out to be true, he would always name its owner in all his visits, honoring hard work and complex thinking. He valued esteem and confidence; he very well knew that the students needed guidance in overcoming their social problems as well. And this he did not spare; he used all his power to support future generations' well-being and intellectual prowess.

He was a truly great instructor and professor. He treated his students and assistants as brothers/sisters and sons/daughters. He did not refrain from sharing his sincere feelings, creating ease and joy around himself. It was a routine for him to emanate artistic and humane messages every single day before starting his daily visits. He would repeat that "life was not long enough to postpone your ordained actions" and that one should not "put his/her dreams off." This motto was also a summary of his life style as he was always busy and energetic. Full of spirit, he would always smile and express himself strenuously, again a reflection of a mind that worked with speed. We have not witnessed any moment of aggression; if there is one thing he did not tolerate, it was languidness and lack of confidence.

Professor Taşçıoğlu's girth and joviality were reflected in his majestic medical and educational practice. Alive or inanimate, everything created was a target of his keen gaze and expression of love. Not only his students, assistants, colleagues but also animals, flowers, art -all that is part of the nature and culture- were dearest to him. His unstinting cordialness to the patients was so ample to attract jealousy of us, his colleagues. Humane exchanges of a few minutes on art, sports, cinema and painting preceding the visits would brighten our days and remind that medical excellence did not have the luxury to exclude intellectual fulfillment in various areas of arts and sciences. Art without science, and vice versa, was unthinkable to him. He would dress exquisitely with vivid colors, wrapping his foulard.

Professor Cemil Taşçıoğlu will always be alive in our memories. His marvel will live with us and future generations, his jollainess and colorful foulards will accompany in our minds his teachings. He taught us to think, speak up, heal and most importantly, to love our patients and each other.

He is a legendary clinician physician and one of the most beloved value of Istanbul Medical Faculty. He was actively working and sadly lost at Coronavirus disease-2019 pandemic in Turkey as the very first physician and health care worker on April 1, 2020 despite great efforts that has been put by his colleagues that love him by heart.

His loss overwhelmed his colleagues, his students, his patients and his lovers in the way that we have not experienced before. We revere the memory of his life of great teaching and clinical wisdom in medicine. We would kindly like to express our gratitudes and thanks to Professor Cemil Taşçıoğlu because meeting, studying, living with him and learning from him was an exceptional honour. He will be missed too much as an exceptional friend, an exceptional clinician and an exceptional teacher.

Both to honour his great legacy and to contribute to his immortality, a newly built, modern and high-capacity hospital was named after Professor Taşçıoğlu. Each medical facility and the individuals within will surely be effectively at the service of the patients who the Professor approached not as professional subjects but as friends. His colleagues -as his spirit will always be alive- will be inspired every time they hear the professor's name referred to. From now on, he has remained as an invaluable, apple of eye legacy to us, to Turkey, and to the humanity, believing sincerely that he has begun a new journey in the beauties already deserved by him.

Keywords: COVID-19, internal medicine, mentor, obituary, Prof. Tascioglu

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An Echo: Professor Tascioglu

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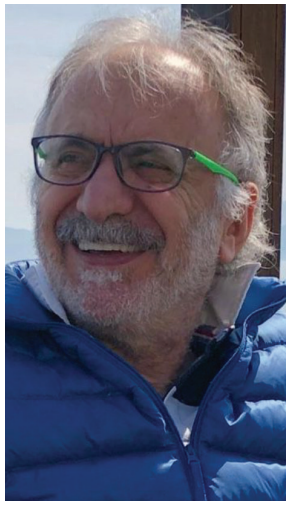

Professor Tascioglu greets the patient with a warm handshake. My coresident presents the history of the patient, leaving us with an extensive differential diagnosis. He silently listens till the end. Of all the possible next steps, he chooses to palpate the patient's spleen. We are all the more astonished when he comes up with a diagnosis on the spot. He turns to us to explain. "the size and the elasticity of the spleen is almost specific" (I am familiar with causes of splenomegaly, but spleen elasticity?). At the end of two weeks of laboratory tests, cytogenetic testing, scans, and biopsies, he proves right yet again.

Learning to become a doctor is certainly an arduous climb. In ancient Greece and Rome, the practice of medicine was considered a craft that required an apprenticeship. Although clinical guidelines on almost every subject are increasingly enmeshed in our practice, we still need experienced seniors to help master the many facets of this "craft." Personally, I have had the privilege of getting to know invaluable professors over the course of my career, who helped me become the physician that I am today. Professor Tascioglu was one of them.

I first met him when I was a third-year medical student. The joy of teaching was almost tangible in his overcrowded lectures. He brought intriguing cases to discuss, asked questions with just the right amount of challenge, and never put us under too much stress. Whenever we got a question right, his eyes would beam like a father proud of his children.

Once I consulted the professor about my mother for what I would now call a trivial problem. I knew he never turned down relatives of students or hospital staff who sought his medical advice. His kindness and humility that day taught me more than any textbook on medical ethics and deontology.

Honestly, he was the reason why most of us chose internal medicine for a residency, me included. He was the head of the general medicine ward, which was on the fourth floor, above hematology. There were more than thirty beds on the ward, which consisted of rooms aligned on an unreasonably long corridor. His room was located at the entrance, where he ran an outpatient clinic, outside of which a queue of patients was always present. Sometimes he would call our names one by one to come see a rare sign, his voice echoing throughout the corridor. During ward rounds, we listened attentively as he enthusiastically led the crowd of interns, residents, and fellows from bedside to bedside. It was not stress or fear that motivated us to work; it was the pleasure of learning (the head nurse scared us a bit, though).

His skills in diagnostics were exceeded only by his humanity and compassion. Anyone could tell that he loved his job, that he loved people. He would hold the hands of the octogenarian patient and chat with her for fifteen minutes about her grandkids like it was the most natural thing to do during a ward round. Where we saw the skin rash of vasculitis, he saw a fragile woman who needed cheering up. Sometimes he would criticize the latest novel he read before going on to explain why he thought sarcoidosis was the most likely diagnosis for the lady who looked exactly like his niece!

He had a genuine smile on his face no matter what. He exuded positivity to every patient, nurse, doctor, and orderly around him, and we could not help but smile back. He appreciated every member of his team and had their back.

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We learned from his colleagues that when the professor was a young resident, he used to stay late to do extra work and never got home earlier than 8:00 o'clock in the evening. After forty years in practice, he could have considered retirement, but he preferred to impart his knowledge and experience to the younger generation instead.

March 2020 marked the beginning in Turkey of the Coronavirus disease-2019 outbreak, which he never braced for. He is believed to have contracted the virus from one of the first patients in the country. He kept assuring everyone around him that he was going to be OK, although deep down, his amazing clinical intuition must have told him otherwise. Right before he was admitted to the intensive care unit, while still conscious, he encouraged the intensive care team to test experimental drugs on him. It was an exemplary end to an exemplary life. Even people who hadn't ever met the professor in person shed tears of grief.

In the ancient city of İstanbul, where I live, historical monuments perpetuate memories of the past. Like an architect who makes timeless buildings, I believe a teacher achieves immortality through his students. It has been a year since we lost Professor Tascioglu, but "deceased" he is not.

He is there when I diagnose a subtle malignancy. He is there when I congratulate an intern. He is there when I hold the trembling hands of a frail octogenarian and ask after her grandkids. His familiar voice will continue to echo in the neuronal network of medical students from generation to generation. Timeless, like the ancient city.

Keywords: COVID-19, internal medicine, mentor, obituary, Prof. Tascioglu

Ethics

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INVITED REVIEW

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Presenting Turkish Inappropriate Medication Use in the Elderly (TIME) Criteria Set in Turkish

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Keywords: Elderly, inappropriate medication use, polypharmacy, prescribing, TIME criteria

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Introduction

Older adults are mostly exposed to polypharmacy and inappropriate medication use (IMU) due to the increasing incidence of chronic diseases and geriatric syndromes with aging. Polypharmacy and IMU use are well-known risk factors for adverse drug reactions (1,2).

Although the prevalence and negative consequences of polypharmacy and IMU in older adults have been known for many years, inappropriate drug use in many older adults continues even in first-line treatment. Consideration of pharmacokinetic/pharmacodynamic changes, functional impairment of organs, and the drugs most commonly associated with adverse outcomes can help reduce polypharmacy and inappropriate drug use in older adults. In this context, strategies are developed to prevent inappropriate drug use and polypharmacy in older adults worldwide. Explicit (criteria-based) screening tools and implicit (judgmental) assessment methods are among the tools developed to assist in the management of drug therapy in older adults. Explicit tools provide the user algorithmic approaches that include lists of drugs to avoid or specific indicators of inappropriate drug use (3). They provide information and guidance on optimal drug use. Implicit approaches evaluate the patient with a much broader concept. Research data, clinical conditions, and patient/family preferences are also considered (4). Therefore, implicit assessments offer the most appropriate assessment for the detection of IMU but are difficult to standardize and require much more time, background knowledge, and judgment. For these reasons, explicit rather than implicit approaches have been more widely studied to guide clinicians in the management of the IMU. More than 70 tools from many different countries are described in literature for the assessment of inappropriate prescribing (5-10). Highlights from internationally accepted recommendations to reduce inappropriate drug use include the drug burden index, Beer's criteria, medication appropriateness index, assessing care of elders project, elderly complex appropriate drug use in patients [criteria to assess appropriate medication use among elderly complex patients (CRIME)] (11) STOPP/START criteria (12) among many others. The most commonly used and studied such criteria are the Beers and STOPP/START criteria.

Prescribing habits differ between the countries and so does the medications available in the market. As such, while the available explicit criteria set for assessing IMU in older adults have provided some important guidance, they had limited benefits due to lack of consideration of circumstances in the countries other than the tool was originated from. To date, there was not any criteria specifically designed from Eastern Europe to aid health care professionals in a better way for optimum prescribing.

Based on this background, we have established Turkish Inappropriate Medication Use in the Elderly (TIME) Criteria with the participation of experienced and expert in the clinical practice of elderly adults in Turkey under the leadership of Rational Drug Use Working Group of the Turkish Academic Geriatrics Society (13). We applied the methodology used to create the STOPP/START tool and classified the criteria as the TIME-to-STOP and TIME-to-START criteria. TIME study group-comprising a national expert group of 49 academics and a national working group of 23 academics conducted the study. The academics were from a wide range of specialties dealing with the care of older adults; 17 members from geriatric medicine; four members from psychiatry; three members each from, general internal medicine, gastroenterology, neurology, cardiology, and pharmacology; two members each from endocrinology, nephrology, urology, physical therapy and rehabilitation; and one member each from clinical pharmacology, pulmonology, infectious diseases, gynecology and ophthalmology. The study was carried out in three phases. In the first phase, STOPP/START v2 and CRIME criteria were combined, and the first draft consisting of 133 criteria was created. At the end of the third phase of the study, 55 new criteria were added, 17 existing criteria were removed, and 60 criteria were modified. Accordingly, the final set of TIME criteria was composed of a total of 153 criteria (112 TIME-to-STOP and 41 TIME-to-START criteria) (13). The fourth phase was the Delphi validation process that validate the tool internationally. An internationally validated TIME criteria set was obtained through a Delphi validation study involving 11 recognized experts who took part in the study from start to finish. The validated TIME list comprised 134 criteria (101 TIME-to-STOP and 33 TIME-to-START criteria) (14). This validation study supports the claim that the TIME set can be regarded as a widened and most up-to-date explicit tool for applications with older adults not only from Turkey and East European region, but also from the other regions across Europe. TIME Criteria mobile application was developed to facilitate the use of Turkish IMU in the elderly criteria in clinics in May 19, 2021. The TIME Criteria application is available now to help health care professionals in reviewing their older patients' medications in the context of this most update explicit IMU tool.

In Turkey, the official language is Turkish. The rate of knowing the English language in the general population is limited. According to the English proficiency index 2020 report, Turkey ranks 69th in the list of 100 countries. With an index score of 465 points, Turkey is among the countries with "low" qualification levels. While the physicians and health care professionals are expected to have better knowledge on the English language due to their education background, a considerable proportion may have problems in following the English text with confidence. Therefore, hereby, we present the TIME criteria in Turkish language to help the healthcare professionals during their application in their everyday practice.

The final list of TIME-to-STOP and TIME-to-START criteria in Turkish is given in Suplementary file 1 and Suplementary file 2, the final list of TIME-to-STOP and TIME-to-START criteria in Turkish with full list of references and accompanying explanations added to some criteria is given in Suplementary file 3 and Suplementary file 4, respectively. The 19 criteria that were not accepted in the international Delphi validation phase are indicated within the supplementary file. Seven criteria were rejected and 12 criteria were neither rejected nor accepted, and were therefore removed. Of note, as can be understood from the panelists' comments in the survey, some criteria were not accepted because the panelists felt they were not sufficiently familiar with the situation or medication in the criterion in their respective clinical practices and personal experiences.

Conclusion

Optimizing the medication use stands as one of the main goals in geriatrics practice. Explicit IMU criteria are important tools to help managing medication use and polypharmacy in older adults. Turkish Inappropriate Medication Use in the Elderly-(TIME criteria), is an up-to-date explicit IMU tool to guide national and international health care professionals in their everyday practice.

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TIME to STOP- YAŞLIDA KULLANIMI ÖNERİLMEYEN İLAÇLAR

Bu grup ilaçların, kriter içeriğindeki durumlarda kullanımı yaşlılarda ilaç-hastalık, ilaç-geriatrik sendrom ve/veya ilaç-ilaç etkileşimi nedeniyle "yüksek" yan etki potansiyeli taşımaktadır ve "potansiyel uygunsuz ilaç kullanımı" olarak nitelendirilmektedirler. Klinisyenler hastanın tüm özellikleriyle ilacın hastasındaki potansiyel fayda ve zararını (kar-zarar dengesini) ve hasta/bakımveren tercihleri doğrultusunda saptanan tedavi hedeflerini göz önünde bulundurarak karar vermelidir. Bu grup ilaçları klinisyenler bazı olgularda kullanmayı yine de uygun bulabilir. Kullanımı tercih edildiğinde dikkatle kullanılması, yan etki varlığı açısından klinik olarak yakın takip edilmesi gereken ilaçlardır.

TIME-to-STOP Kriterleri

A: Kardiyovasküler Sistem Kriterleri

A1. AF tedavisinde 1. basamakta digoksin kullanımı uygun değildir

A2. Digoksin'in 0,125 mg/gün'den yüksek dozda kullanımı uygun değildir (toksisite riski)

A3. Korunmuş (normal) EF'li kalp yetersizliği endikasyonuyla digoksin kullanımı uygun değildir

A4. Düşük EF'li kalp yetersizliğinde diltiazem veya verapamil kullanımı uygun değildir

A5. Bradikardi (<50/dk), tip 2 kalp bloğu veya tam kalp bloğu olanlarda hız kısıtlayıcı tedavi (beta bloker, verapamil, diltiazem, digoksin) başlanması uygun değildir

A6. Kalp yetersizliği, karaciğer yetersizliği, nefrotik sendrom veya böbrek yetersizliğinin klinik, biyokimyasal veya radyolojik bulguları olmadan ayak bileği ödemi için loop diüretiği kullanımı uygun değildir (bacak elevasyonu ve/veya kompresyon çorapları genellikle daha uygundur)

A7. Özel bir endikasyon bulunmadığı halde esansiyel HT tedavisi için ilk basamakta beta-blokerlerin kullanımı uygun değildir (kalp bloğu riskinde artış, halsizlik-yorgunluk, seksüel disfonksiyon ve inmeden korunmada az etkinlik nedeniyle; ek olarak yaşlanmayla β-adrenerjik reseptör fonksiyonunda azalma olur)

A8. Üriner inkontinansı olanlarda esansiyel HT tedavisi için ilk basamakta diüretik kullanımı uygun değildir (inkontinansı ve sıkışma hissini artırarak yaşam kalitesini bozabilir, düşmeleri artırabilir)

A9. Diğer sınıf antihipertansiflerin tolere edilemediği veya etkisiz kaldığı durumlar hariç HT tedavisinde alfa-1 bloker veya santral etkili antihipertansiflerin (örn. metildopa, rilmenidin, rezerpin) kullanımı uygun değildir (alfa-1 bloker antihipertansifler ile kalp yetersizliği ve kardiyovasküler olaylarda artış, ortostatik hipotansiyon, düşme, senkop, kadınlarda üriner inkontinansın kötüleşmesi; santral etkili antihipertansiflerin MSS yan etkileri, sedasyon-depresyon-parkinsonizm ve ortostatik hipotansiyon, bradikardi yan etkileri)

A10. Ortostatik hipotansiyon (sistolik kan basıncında>=20 mmHg düşüş veya diastolik kan basıncında >=10 mmHg düşüş) olanlarda vazodilatör antihipertansiflerin (alfa-1 blokerler)/ nitratların kullanımı uygun değildir (ortostatik hipotansiyonda artış riski)

A11. Ortostatik hipotansiyonu/bilişsel yetersizliği (örn. demans) /fonksiyonel kısıtlılığı/düşük yaşam beklentisi (<2 yıl)/düşme riski yüksek olan hastalarda sıkı kan basıncı kontrolu (<140/90 mmHg) uygun değildir

A12. Sekonder faktörler dışlanmadan ve ilaç dışı yaklaşımlar uygulanmadan ortostatik hipotansiyon tedavisi için fludrokortizon kullanımı uygun değildir

A13. HT olgularında beta bloker ve verapamil/diltiazem kombinasyonu kullanımı uygun değildir (kalp bloğu riski)

A14. Serum potasyum düzeyi 5.5 mEq/L'nin üzerinde olan olgularda RAS blokeri (ACE inhibitörü, ARB, direkt renin inhibitörü) veya potasyum tutucu diüretik (spironolakton, eplerenon, amilorid, triamteren) başlanması uygun değildir

A15. Serum potasyum düzeyi takip edilmeden RAS blokeri (ACEİ, ARB, direkt renin inhibitörü) ve potasyum tutucu diüretiklerin (spironolakton, eplerenon, amilorid, triamteren) kombine edilmesi uygun değildir (tehlikeli hiperpotasemi riski)

A16. GFR<30 mL/dk/1,73 m^2 olan ve serum potasyum düzeyi yakın takip edilemeyecek hastalarda, potasyum tutucu ilaçların (aldosteron antagonistleri, triamteren, amilorid, ACEİ, ARB) kullanımı uygun değildir (hiperpotasemi riski)

A17. Belirgin hipopotasemi (serum K<3,0 mg/L), hiponatremi (serum Na < 130 mEq/L), hiperkalsemi (düzeltilmiş serum Ca>10,6 mg/dL) veya gut hikayesi olan hastalarda tiazid diüretiklerinin kullanımı uygun değildir

A18. Kardiyovasküler hastalığı (ciddi HT, kalp yetersizliği veya geçirilmiş Mİ, inme) olan olgularda NSAİİ kullanımı uygun değildir (artmış kardiyovasküler olay: Mİ, inme, kalp yetersizliği ve ölüm riski)

A19. Sık hipoglisemi atakları olan DM hastalarında beta bloker kullanımı uygun değildir (hipoglisemik semptomları baskılama riski)

A20. Astım öyküsü olanlarda nonselektif beta bloker (oral veya glokom için topikal) kullanımı uygun değildir (bronkospazmda artış riski)

A21. Primer veya sekonder kardiyovasküler korumada aspirin'in 75-150 mg/gün'den yüksek dozda kronik kullanımı uygun değildir (kanıtlanmış ek faydası yok ve kanama riskini artırıyor)

#A22. Aspirin, klopidogrel, dipiridamol ve OAK'ların (Vitamin K antagonistleri, direkt trombin inhibitörü veya faktör Xa inhibitörleri) eşlik eden anlamlı kanama riski varlığında (örneğin kontrolsüz ciddi HT, kanama diyatezi, spontan anlamlı kanaması olanlarda) kullanımı uygun değildir (yüksek kanama riski)

A23. Aspirin ve klopidogrelin birlikte kullanımı için spesifik bir endikasyon yoksa, sekonder inme proflaksisinde aspirin ve klopidogrelin birlikte kullanımı uygun değildir

A24. Kronik AF veya başka bir sebeple OAK kullanan hastalarda aspirin/klopidogrel kullanımı için ek endikasyon yok ise tedaviye aspirin/klopidogrel eklenmesi uygun değildir (aspirin ile ek fayda yok)

A25. OAK'ların (vitamin K antagonistleri, direkt trombin inhibitörleri veya faktör Xa inhibitörleri), devam eden risk faktörleri olmaksızın ilk kez olan derin ven trombozunda 6 aydan uzun süre kullanımı uygun değildir (kanıtlanmış ek yararı yok)

#A26. OAK'ların (vitamin K antagonistleri, direkt trombin inhibitörleri veya faktör Xa inhibitörleri), devam eden risk faktörleri olmaksızın ilk kez olan pulmoner embolide 12 aydan uzun süre kullanımı uygun değildir (kanıtlanmış ek yararı yok)

#A27. OAK'ların (vitamin K antagonistleri, direkt trombin inhibitörleri veya faktör Xa inhibitörleri) kontrendike olduğu kronik AF hastalarında, aspirin veya klopidogrel monoterapisinin kullanımı uygun değildir

A28. Dabigatran'ın GFR <30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir

#A29. Non-valvular AF'si olup malnütre olan veya besin alımı düzensiz olan hastalarda varfarin kullanımı uygun değildir

A30. İlaçlarını kullanmakta, yönetmekte güçlük çeken (öm. bilişsel bozukluğu olan hastalar) ve yardımcı olacak kimselerin (örn. bakıcı) olmadığı hastalarda varfarin ve digoksin gibi dar terapötik indeksi olan ilaçların kullanımı uygun değildir (hayatı tehdit edebilecek toksisite riski)

#A31. Prasugrel'in 75 yaş ve üzeri hastalarda veya GİA/inme geçirmiş olgularda kullanımı uygun değildir

A32. Tiklopidin antitrombosit olarak kullanımı uygun değildir (klopidogrel veya tikagrelor veya prasugrel'in daha yüksek etkinliği vardır, daha çok kanıtı vardır ve daha az yan etkisi vardır)

A33. Antitrombosit-antiagregan etki için kısa etkili dipiridamol kullanımı uygun değildir (ortostatik hipotansiyon yan etkisi ve daha etkili ajanların bulunması)

A34. Yaşam beklentisi düşük olan (<2 yıl) veya ileri evre demanslı yaşlılarda primer koruma amaçlı statin kullanımı uygun değildir

A35. Asemptomatik hiperürisemi (gut veya nefrolitiazisi olmayan olgular) için allopurinol başlanması uygun değildir (fayda için kanıt yok, ksantin oksidaz inhibitörleri kullanımıyla yan etki riski) (tedavinin kardiyovasküler riski veya gut hastalığını azalttığına dair kanıt yok)

B: Santral Sinir Sistemi Kriterleri

B1. Trisiklik antidepresan kullanımı uygun değildir (yüksek antikolinerjik etki, kognitif kötüleşme, kalp iletim bozukluğu, ortostatik hipotansiyon, üriner retansiyon, prostatizmde kötüleşme, dar açılı glokomda kötüleşme)

B2. SSRI tedavisi başlanacak olgularda paroksetin, fluoksetin ve fluvaksaminin ilk basamakta tercih edilmesi uygun değildir (paroksetinin yüksek antikolinerjik etkisi, fluoksetinin uzun yarı ömrü, fluoksetin ve fluvaksaminin sık ilaç etkileşimi nedeniyle)

B3. Yakın geçmişte veya halihazırda anlamlı hiponatremi (serum Na< 130 mEq/L) hikayesi olanlarda SSRI kullanımı uygun değildir (SSRI kullanımı ile artan hiponatremi riski)

#B4. Kontrolsüz HT varlığında SNRI kullanımı uygun değildir

B5. GFR<30 mL/dk/1,73 m^2 olanlarda duloksetin kullanımı uygun değildir (artmış GİS yan etkisi)

B6. GFR<60 mL/dk/1,73 m^2 olması durumunda pregabalin ve gabapentin'in doz azaltımı yapılmadan kullanımı uygun değildir

B7. Deliryum veya demansı olanlarda yüksek antikolinerjik etkili ilaçların (amitriptilin, paroksetin, disiklomin, L-hiyosiyamin, tioridazin, klorpromazin, klozapin, olanzapin, üriner antimuskarinikler, H1 reseptör blokerleri-özellikle 1. jenerasyon H1 reseptör blokerleri (difenhidramin, siproheptadin, feniramin), H2 reseptör blokerlerinin kullanımı uygun değildir (kognitif kötüleşme riski)

B8. Parkinson Hastalığı'nın tedavisinde antikolinerjik ajan kullanımı uygun değildir (artmış yan etki riski; daha etkin ve daha az yan etkisi olan ilaç seçenekleri var)

B9. Nöroleptiklerin ekstrapiramidal yan etkilerini tedavi etmek için antikolinerjik ilaç kullanımı uygun değildir (antikolinerjik toksisitesi riski)

B10. Demans hastalarında davranışsal ve psikolojik semptomların giderilmesinde ilaç dışı tedavilerin etkisiz kaldığı ve semptomların ciddi olduğu durumlar hariç nöroleptiklerin/antipsikotiklerin kullanımı uygun değildir (artmış inme, kalp yetersizliği, pnömoni-infeksiyon, ölüm riski)

B11. Nöroleptiklerin/antipsikotiklerin hipnotik amaçlı kullanımı uygun değildir (artmış konfüzyon, hipotansiyon, ekstrapiramidal yan etkiler, düşme riski)

B12. Parkinsonizm veya Lewy cisimcikli demansı olanlarda nöroleptiklerin/antipsikotiklerin (ketiapin veya klozapin hariç) kullanımı uygun değildir (ağır ekstrapiramidal semptom riski)

B13. Düşme riski yüksek olan hastalarda nöroleptiklerin/antipsikotiklerin (ekstrapiramidal yan etki), benzodiazepinlerin (sedasyon, denge bozukluğu) ve Z tipi hipnotiklerin (ör. zopiklon, zolpidem, zaleplon) (gün içerisinde uzamış sedasyona, ataksi) kullanımı uygun değildir

B14. Benzodiazepin'lerin 4 haftadan uzun süre kullanımı uygun değildir (uzamış sedasyon, konfüzyon, denge bozukluğu, düşme, trafik kazaları riski)

B15. Benzodiazepinlerin akut ve kronik solunum yetersizliğinde (PO_2<60 mmHg ve/veya PCO_2>50 mmHg) kullanımı uygun değildir (solunum yetersizliğinde artış riski)

B16. Persistan bradikardi (<50/dk), 2. veya 3. derece kalp bloğu veya açıklanamayan senkopu olan hastalarda, uzamış QTc olan hastalarda (kadında> 470 msn, erkekte> 450 msn) ChEi kullanımı uygun değildir (kalp iletim defekti, senkop, yaralanma riski)

B17. Esansiyel tremor tedavisi için levodopa veya dopamin agonistlerinin kullanımı uygun değildir (kanıtlanmış etkinliği yoktur)

B18. Vertigo tedavisinde betahistin, trimetazidin, dimenhidrinat gibi ilaçların aralıksız ve uzun süreli olarak kullanımı uygun değildir (kanıta dayalı faydalı etkilerinin olmaması)

#B19. Sinnarizin kullanımı uygun değildir (ekstrapiramidal yan etkiler, sınırlı faydalanım)

B20. Pirasetam kullanımı miyoklonik konvülzüyon tedavisi dışında uygun değildir (kanıtlanmış klinik etkinlik yok, maliyet yükü ve yan etki potansiyeli nedeniyle)

B21. Epilepsinin kronik tedavisinde karbamazepin, fenitoin, fenobarbital veya valproat'ın ilk basamakta kullanımı uygun değildir (vitamin D üzerine olumsuz etkileri, enzim indüksiyonu, düşme riski nedeniyle; ayrıca daha güvenli alternatifleri var)

B22. Epilepsi hastalarında tramadol, nöroleptikler/antipsikotikler (klozapin, olanzapin, klorpromazin, tioridazin), bupropion ve maprotilin kullanımı uygun değildir.

B23. Öncesinde konvülzüyon geçirmemiş bir hastada iskemik/hemorajik inme varlığı nedeniyle nöbet proflaksisi için antiepileptik tedavi kullanımı uygun değildir

B24. Yaşlılarda sitalopram'ın 20 mg/gün, essitalopram'ın 10 mg/gün üzerindeki dozlarda kullanımı uygun değildir (QTc uzama riski nedeniyle)

C: Gastrointestinal Sistem Kriterleri

C1. NSAİİ'lerin OAK'lar (vitamin K antagonistleri, direkt trombin inhibitörleri, faktor Xa inhibitörleri) ile birlikte kullanımı uygun değildir (GİS kanama riski)

C2. Aspirin, klopidogrel, NSAİİ veya steroidlerin; ülser öyküsü olan hastalarda, ek antiplatelet tedavi alan hastalarda, eş zamanlı antikoagülan alan hastalarda, steroid kullanan hastalarda, dispepsi-GÖR semptomları olan hastalarda PPİ verilmeden kullanımı uygun değildir

#C3. Aspirin veya NSAİİ'lerin; peptik ülser (komplike veya komplike olmayan, gastrik veya duodenal) öyküsü olan hastalarda Helicobacter pylori testi yapılmadan kronik kullanım için başlanması uygun değildir

C4. PPİ'ların komplike olmayan peptik ülser veya erozif peptik özofajit tedavisinde tam terapötik dozda 8-12 haftadan uzun süreli kullanımı uygun değildir (doz azaltımı veya daha kısa sürede kesme endikasyonu vardır)

C5. Çoklu ilaç kullanımı nedeniyle PPİ kullanımı uygun değildir (faydası yok, potansiyel zararı var)

C6. Antikolinerjik etkili GİS antispazmotiklerinin (örn. hiyosiyamin) kullanımı uygun değildir [yaşlıda artmış antikolinerjik yan etki (sersemlik, bilişsel kabiliyetlerde azalma, görme bulanıklığı, aritmi, şişkinlik-konstipasyon) ve sınırlı faydalanım]

C7. Kronik konstipasyonu olan hastalarda, bu yan etkiye sahip olmayan alternatifleri varsa, konstipasyona sebep olma ihtimali yüksek olan ilaçların (yüksek antikolinerjik etkili ilaçlar, oral demir, opioidler, verapamil, alüminyum antiasitleri) kullanımı uygun değildir (konstipasyonda artış riski)

C8. Yaşlılarda antiemetik tedavide ilk basamakta metoklopramid veya trimetobenzamid kullanımı uygun değildir (ekstrapiramidal yan etki, huzursuzluk yan etkisi nedeniyle)

C9. GFR< 30 mL/dk/1,73 m^2 olan hastalarda laksatif veya antiasit olarak magnezyum preperatlarının kullanımı uygun değildir (hipermagnezemi riski)

D: Solunum Sistemi Kriterleri

D1. Dar açılı glokom veya üriner çıkış yolu obstrüksiyonu olan hastalarda antimuskarinik bronkodilatör ilaçların (ipratropium, tiotropium) kullanımı uygun değildir (glokomda kötüleşme ve üriner retansiyon riski)

D2. KOAH'ın veya astım bronşialenin idame tedavisinde teofilin kullanımı uygun değildir (dar terapötik indeks ve yaşlıda yüksek insomni, aritmi riski nedeniyle)

D3. Orta-ağır KOAH'ta idame tedavi için inhaler kortikosteroid yerine sistemik kortikosteroid kullanımı uygun değildir (sistemik kortikosteroidlerine uzun süre gereksiz maruziyet; etkin inhale tedaviler mevcut)

E: Kas İskelet Sistemi Kriterleri ve Analjezik İlaçlar

E1. NSAİİ'lerin, alternatif tedavi varken, 3 aydan uzun süreli kullanımı uygun değildir

E2. NSAİİ'lerin GFR< 50 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir (renal fonksiyonlarda kötüleşme riski)

E3. Osteoartrit tedavisinde sistemik steroid kullanımı uygun değildir (sistemik kortikosteroidler ile yan etki riski)

E4. Romatoid artritte 3 aydan uzun süreli kortikosteroid monoterapisi kullanımı uygun değildir (sistemik kortikosteroidler ile yan etki riski)

E5. Gut hastalığının kronik tedavisi için ksantin oksidaz inhibitörleri (örn. allopurinol, febuksostat) kullanımının kontrendike olmadığı durumlarda, uzun süreli NSAİİ veya kolşisin kullanımı uygun değildir (gut hastalığının profilaksisinde ksantin oksidaz inhibitörleri ilk seçenek ilaçlardır)

E6. Kolşisin'in GFR< 10 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir (kolşisin toksisitesi riski)

E7. Metotreksat'ın GFR< 30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir

E8. Ağrı tedavisinde meperidin kullanımı uygun değildir (diğer opioidlere göre artmış nörotoksisite, deliryum riski; daha güvenilir alternatifleri var. Özellikle böbrek yetersizliği varlığında kullanımı risklidir)

E9. Uzamış salınımlı tramadol'ün GFR< 30 mL/dk/1,7 m^2 olan hastalarda kullanımı uygun değildir

E10. Opioidlerin kronik kullanımda eş zamanlı laksatif verilmeden kullanımı uygun değildir (ciddi konstipasyon riski)

E11. Kas iskelet sistemi ağrıları için sistemik kas gevşetici (iskelet kası) ajanların (tiyokolşikosid, tizanidin, klorzoksazon, karisoprodol, klorfenezin karbamat, siklobenzaprin, metaksalon, metokarbamol ve orfenadrin vb.) kullanımı uygun değildir (sedasyon, sersemlik, baş dönmesi, ağız kuruluğu, konstipasyon, bilişsel yan etkileri nedeniyle)

#E12. Osteomalazi tanısı dışlanmadan osteoporoz tedavisi başlanması uygun değildir

E13. Vitamin D "idame" tedavisinde, aralıklı olarak yüksek dozda (300.000 İÜ) konvansiyonel vitamin D kullanımı uygun değildir (artmış düşme riski, kas-iskelet sistemi üzerine ek faydasının olmaması)

E14. Hiperfosfatemi ve/veya hiperkalsemi varlığında aktif (kalsitriol) (1-25(OH)2kolekalsiferol) veya konvansiyonel (25(OH) kolekalsiferol) vitamin D kullanımı uygun değildir

E15. Üst GİS hastalığı (örn. disfaji, özofajit, peptik ülser, üst GİS kanama veya tedavi ile kontrol altına alınamamış GÖR) anamnezi olanlarda ve/veya fiziksel olarak dik duramayacak hastalarda oral bifosfonat kullanımı uygun değildir (özofajit, özofageal ülser, özofageal strüktürde relaps/alevlenme riski)

E16. Bifosfonatlar'ın GFR< 30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir (artmış akut böbrek yetersizliği riski)

E17. Tedavi öncesi serum kalsiyum düzeyi tayin edilmeden ve yeterli düzeyde kalsiyum/vitamin D alımı sağlanmadan zoledronat, denosumab veya teriparatid kullanımı uygun değildir

F: Ürogenital Sistem Kriterleri

F1. Benign prostat hiperplazisine bağlı LUTS semptomları olan erkeklerde PMR>150 mL ise mesaneye yönelik antikolinerjik ilaç kullanımı uygun değildir

F2. Kronik dar açılı glokom hastalarında mesaneye yönelik antikolinerjik ilaç kullanımı uygun değildir

F3. Prostat hiperplazisi olan (obstrüksiyon riski) veya diabetes mellitus komplikasyonları gelişmiş olan (nörojen mesane riski) veya kırılgan olan yaşlılarda (detrusor hiperaktivitesi ile birlikte azalmış kontraktilite riski) PMR tayini yapılmadan mesaneye yönelik antikolinerjik ilaç kullanımı uygun değildir (üriner retansiyon ve postrenal böbrek yetersizliği riski)

F4. Kan basıncı< 90/50 mmHg veya > 170/100 mmHg olan/ unstabil anginası olan/ cinsel ilişki sırasında anjinası olan/ NYHA sınıf 4 kalp yetersizliği olan/ anjina için nitrat tedavisi alan/ alfa-1 bloker tedavisi alan/geçirilmiş Mİ (<3 ay) öyküsü olan/ geçirilmiş inme (<6 ay) öyküsü olan hastalarda fosfodiesteraz tip-5 inhibitörlerinin (örn. sildenafil, tadalafil, vardenafil) kullanımı uygun değildir

F5. Ortostatik hipotansiyonu olan hastalarda benign prostat hiperplazisine bağlı LUTS semptomlarının tedavisinde üroselektif olmayan alfa 1 blokerlerin (örn. doksazosin, terazosin) kullanımı uygun değildir (ortostatik hipotansiyonda, senkop ve düşmelerde artış)

F6. Mukozaya zarar verebilecek ürolojik girişimler hariç asemptomatik bakteriüride antibiyotik kullanımı uygun değildir

F7. Nitrofurantoin'in GFR< 30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir

G: Endokrin Sistem Kriterleri

G1. Yaşam beklentisi düşük (<5 yıl) veya anamnezde düşme veya bilişsel yetersizliği olan hastalarda sıkı kan şekeri kontrolu (HbA1C< %7) uygun değildir

#G2. Kırılgan veya malnütre yaşlılarda metformin kullanımı uygun değildir (metformin'in GİS yan etkileri ve iştahsızlık etkisi nedeniyle)

G3. Metformin'in GFR< 30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir (laktik asidoz riski)

G4. Tip 2 DM hastalarında glibenklamid ve klorpropamid gibi uzun etkili sulfanilürelerin kullanımı uygun değildir (uzamış hipoglisemi riski)

G5. Dökümante kalp yetersizliği/kırık anamnezi/artmış kırık riski/mesane kanseri anamnezi olan veya insülin tedavisi almakta

olan hastalarda tiazolidinedionların (rosiglitazon, pioglitazon) kullanımı uygun değildir (kalp yetersizliğinde kötüleşme, kırık ve mesane kanser riskinde artış)

G6. Kalp yetersizliği olan olgularda saksagliptin kullanımı uygun değildir

G7. Kanagliflozinin, diyabete bağlı alt ekstremite ampütasyonu komplikasyonu geçirmiş/ciddi periferik arter hastalığı olan/tekrarlayan üriner sistem infeksiyonu/genitoüriner enfeksiyonu olan olgularda kullanımı uygun değildir

G8. SGLT-2 inhibitörlerinin GFR< 45 mL/dk/1,73 m^2 olan olgularda kullanılması uygun değildir

G9. Androjen eksikliği ile ilişkili semptom ve bulguların eşlik etmediği serum testosteron düzeyi düşüklüğü varlığında androjen kullanımı uygun değildir

G10. Meme kanseri veya venöz tromboemboli öyküsü olan hastalarda sistemik östrojen kullanımı uygun değildir

G11. İntakt uterusu olan kadınlarda beraberinde progesteron kullanımı olmadan östrojen kullanımı uygun değildir (endometrial kanser riski)

G12. İştah artırıcı olarak megestrol kullanımı uygun değildir (kilo üzerine minimal etki, protrombotik yan etki)

G13. Subklinik hipotiroidisi olan yaşlılarda (TSH: 4-10 mIU/L; sT4: N), tiroid hormonu kullanımı uygun değildir (ek yararı yok, atrial fibrilasyon ve osteoporoz gibi potansiyel yan etki riski)

H: Antimuskarinik-Antikolinerjik Yük

H1. Yüksek antikolinerjik etkili ilaçların [trisiklik antidepresanlar, klorpromazin, tioridazin, klozapin, olanzapin, hiyosin, oral oksibutinin, 1. jenerasyon antihistaminikler (feniramin, klorfeniramin, hidroksizin, siproheptadin, dimenhidrinat, difenhidramin, meklizin vb.), paroksetin] kullanımı aşağıdaki durumlarda uygun değildir

Düşme/konstipasyon/dar açılı glokom/demans/deliryum/idrar retansiyonu/erkekte obstrüktif LUTS semptomları/eş zamanlı yüksek antikolinerjik etkili ilaç kullanımı

J: Suplemanlar.

J1. Kanama riski olan olgularda (antikoagülan kullanımı, NSAİİ kullanımı, anlamlı kanama öyküsü) gingko biloba ekstraktı kullanımı uygun değidir

J2. Sarı kantaron'un (St. John's Wort) antidepresan kullanan hastalarda (özellikle SSRİ ile serotonerjik sendrom riski) ve sitokrom p450 ile metabolize olan ilaç (örn. digoksin, teofilin, varfarin, karbamazepin, fenitoin, fenobarbital) kullanan hastalarda sistemik kullanımı uygun değildir (sarı kantaron sitokrom p450 aktivasyonu yapar)

#J3. Varfarin kullanan hastalarda supleman kullanımı uygun değildir (kanama riskinde olası artış nedeniyle)

#Uluslararası Delfi paneli çalışmasında konsensus sağlanmayan kriterler

Kısaltmalar:

AF: Atrial fibrilasyon

ACEİ: Anjiotensin konverting enzim inhibitörleri

ARB: Anjiotensin reseptör blokerleri

ChEIs:Asetilkolinesteraz inhibitörleri

DM: Diabetes mellitus

EF: Ejeksiyon fraksiyonu

eGFR: Estimated Glomerular Filtrasyon hızı

GİA: Geçici iskemik atak

GÖR: Gastroözofageal reflü

GİS: Gastrointestinal sistem

H1 receptor: Histamin 1 reseptör

HT: Hipertansiyon

KOAH: Kronik obstrüktif akciğer hastalığı

LUTS: Alt üriner sistem semptomları

Mİ: Miyokard infarktüsü

MSS: Merkezi sinir sistemi

NSAİİ: Non steroidal anti inflamatuar ilaçlar

NYHA: New York Heart Association

OAK: Oral antikoagülan

PMR: Post miksiyonel rezidü

PO_2: Parsiyel oksijen basıncı

PPİ: Proton pompa inhibitörleri

QTc: düzeltilmiş QT Intervali

RAS: Renin anjiotensin sistem

SGLT-2: Sodium-glucose kotransporter-2

SNRIs: Serotonin-norepinefrin geri alım inhibitörleri

SSRIs: Selektif serotonin geri alım inhibitörleri

TSH: Tiroid stimulan hormon

TIME to START- YAŞLIDA BAŞLANMASI UYGUN OLAN İLAÇLAR

Bu grup ilaçların, kriter içeriğindeki durumlarda kullanımının yaşlılarda endikasyonu ve potansiyel faydalanımı vardır ancak klinik pratikte sıklıkla gözden kaçabilmekte veya ileri yaş nedeniyle, geçerli ek bir sebep olmaksızın, verilmemektedir. Bu ilaçların kriter içeriğindeki durumda kullanılmaması "potansiyel uygunsuz ilaç kullanımı" olarak nitelendirilmektedirler. Klinisyenler hastanın tüm özellikleriyle ilacın hastasındaki potansiyel fayda ve zararını (kar-zarar dengesini), beklenen yaşam süresini ve hasta/bakımveren tercihleri doğrultusunda saptanan tedavi hedeflerini göz önünde bulundurarak karar vermelidir. Bu grup ilaçları klinisyenler bazı olgularda kullanmamayı uygun bulabilir.

TIME-to-START Kriterleri

A: Kardiyovasküler Sistem Kriterleri

A1. Dökümante aterosklerotik koroner arter hastalığı (geçirilmiş akut koroner sendrom/koroner anjioplasti veya stentleme/ koroner arter bypass greftleme/abdominal aort anevrizması), dökümante aterosklerotik serebrovasküler hastalık (geçirilmiş iskemik inme/GİA/ geçirilmiş karotis endarterektomi veya stentleme) veya semptomatik alt ekstremite arter hastalığı olan hastalarda sekonder korunma amaçlı antiplatelet tedavi (aspirin veya klopidogrel) başlanması uygundur

A2. Dökümante aterosklerotik koroner arter hastalığı (geçirilmiş akut koroner sendrom/koroner anjioplasti veya stentleme/ koroner arter bypass greftleme/abdominal aort anevrizması), dökümante serebrovasküler hastalık (geçirilmiş iskemik inme/ GİA/geçirilmiş karotis endarterektomi veya stentleme) veya periferik arter hastalığı olan hastalarda sekonder korunma amaçlı statin tedavisi başlanması uygundur

A3. Sistolik kan basıncı sürekli olarak >160 mmHg ve/veya diastolik kan basıncı sürekli olarak >90 mmHg olan hastalarda antihipertansif tedavi başlanması uygundur

A4. Kronik non-valvüler AF varlığında, CHA2DS2-VASc skoru göz önüne alınarak, OAK (vitamin K antagonistleri, direkt trombin inhibitorleri veya faktor Xa inhibitörleri) başlanması uygundur

A5. Sistolik kalp yetersizliği (EF<= %40) veya ST elevasyonlu Mİ varlığında ACEİ tedavisi başlanması uygundur

A6. Sistolik kalp yetersizliği (EF<= %40) veya iskemik kalp hastalığı (kronik iskemik kalp hastalığında antianjinal etki/ Mİ sonrası dönemde mortalite düşürücü etki nedeniyle) varlığında beta-bloker tedavi (sistolik KY'de bisoprolol/uzamış salınımlı metoprolol süksinat/karvedilol/nebivolol; iskemik kalp hastalığında herhangi bir beta-bloker) başlanması uygundur

B Santral Sinir Sistemi Kriterleri

B1. Majör depresif bozukluk varlığında antidepresan tedavi başlanması uygundur

B2. Fonksiyonelliği (işlevselliği) etkileyen persistan, ağır şiddette anksiyete varlığında SSRİ (SSRİ kontrendike ise SNRİ veya pregabalin) tedavisi başlanması uygundur

#B3. Erken-orta evre Alzheimer hastalığında ChEi tedavisi başlanması uygundur

#B4. Orta-ileri evre Alzheimer hastalığında memantin tedavisi başlanması uygundur

#B5. Fonksiyonelliği (işlevselliği) etkileyen esansiyel tremoru olan hastalara propranolol veya pirimidon tedavisi başlanması uygundur

B6. Fonksiyonel (işlevsel) bozukluk ve dizabiliteye sebep olan idiyopatik Parkinson hastalığı varlığında L-dopa tedavisi başlanması uygundur

B7. İdiyopatik Parkinson hastalarında açık-kapalı motor dalgalanmalar başladığında, L-dopa tedavisine MAO-B inhibitörü veya COMT inhibitörü eklenmesi uygundur

B8. Demir eksikliği ve kronik böbrek yetersizliğinin dışlandığı huzursuz bacak sendromu olan hastalarda, semptomlar yaşam kalitesini olumsuz etkiliyorsa, alfa-2-delta kalsiyum kanal blokerleri (pregabalin, gabapentin) veya dopamin agonistleri (pramipeksol/ropinirol/rotigotin) başlanması uygundur

C: Gastrointestinal Sistem Kriterleri

C1. Yaşam tarzı değişikliklerine (diyet-egzersiz) yanıtsız semptomatik konstipasyonu olan olgularda, fekal tıkaç dışlanarak, lif desteği (psilyum, metilselüloz, polikarbofil, buğday dekstrin) veya polietilenglikol başlanması uygundur

D: Solunum Sistemi Kriterleri

D1. Hafif-orta astım veya KOAH'ı olan hastalarda düzenli inhale beta2 agonist veya antikolinerjik tedavi başlanması uygundur

D2. FEV1< %50 olan ve oral steroid tedavisi gerektiren tekrarlayan alevlenmeleri olan orta-ağır astım veya KOAH hastalarında düzenli inhale kortikosteroid tedavisi başlanması uygundur

D3. Kronik hipoksemisi (PO_2<= 55 mmHg veya SO_2<= %88) olan hastalarda evde sürekli oksijen tedavisi başlanması uygundur

E: Kas İskelet Sistemi Kriterleri ve Analjezik İlaçlar

#E1. Günlük diyetle vitamin D alımı <800-1000 İÜ veya elementer kalsiyum alımı <1000-1200 mg olan hastalarda replasman tedavisinin başlanması uygundur

E2. Dökümante osteoporozu olan [frajilite fraktürü ve/veya kemik mineral dansitometri T skoru (femur total, femur boyun

veya lomber < -2,5)] hastalarda anti-rezorptif (bifosfonat, denosumab) veya anabolik ajan (parathormon anoloğu) başlanması uygundur

E3. Uzun süreli (beklenen süre ≥3 ay) sistemik kortikosteroid tedavisi başlanan hastalarda: i) ≥7,5 mg/gün prednizolon veya eşdeğer steroid tedavisi alacaklarda, ii) eğer T skoru < -1 ise dozdan bağımsız steroid tedavisi alacak tüm hastalarda, bifosfonat tedavisi başlanması uygundur

E4. En az iki doz Denosumab tedavisi sonlandırıldıktan sonra uzun etkili antirezorbtif tedavi başlanması uygundur (denosumab kesilmesini takiben rebound BTM'lerde artış, KMD kaybı ve vertebral fraktür riskinde artış olur)

#E5. Teriparatid tedavisi sonrası antirezorbtif tedavi başlanması uygundur

E6. Kronik aktif romatolojik hastalık varlığında hastalığı modifiye edici tedavi başlanması uygundur

E7. Metotreksat alan hastalarda folik asit desteği başlanması uygundur

E8. Tekrarlayan gut atağı olan hastalarda ksantin oksidaz inhibitörü (öncelikle allopürinol) başlanması uygundur

E9. Orta-ağır düzeydeki ağrı tedavisinde diğer analjeziklerin (parasetamol, NSAİİ veya hafif opioidler) yeterli olmadığı durumlarda güçlü etkili opioid tedavisi başlanması uygundur

E10. Kronik ağrılı olan ve uzun etkili opioid kullanan hastalarda, kaçak ağrı varlığında (breakthrough pain: Aralıklarla gelen şiddetli ağrılar) tedaviye kısa etkili opioidlerin eklenmesi uygundur (şiddetli ağrının kontrol edilememe riski)

F: Endokrin Sistem Kriterleri

F1. Diabetes mellitus'lu hastalarda aşikar proteinüri (>300 mg/gün) veya mikroalbuminüri (>30 mg/gün) varlığında, ACEi veya ARB tedavisi başlanması uygundur

G: Ürogenital Sistem Kriterleri

#G1. Prostatektominin endike olmadığı, orta-ağır (IPSS skoru) düzeyde semptomatik LUTS (alt uriner sistem semptomları) mevcut olan hastalarda alfa-1 reseptör blokeri kullanımı uygundur

#G2. Prostatektominin endike olmadığı orta-ağır (IPSS skoru) düzeyde semptomatik LUTS (alt uriner sistem semptomları) mevcut olan hastalarda, prostat hacmi >30-40 mL ise, alfa-1 reseptör blokerine ek olarak 5-alfa redüktaz inhibitörü tedavisi başlanması uygundur

G3. Semptomatik atrofik vajinitte, hormon-dışı tedaviler denendikten sonra, topikal vajinal östrojen tedavisi kullanımı uygundur

H: Aşılar.

H1. Yıllık influenza aşısı yapılması uygundur

H2. 65 yaşından sonra Pnömokok aşısı (13 valan konjuge ve 23 valan polisakkarit aşıdan herbiri için bir doz) yapılması uygundur

H3. Herpes zoster aşısı yapılması uygundur (zona infeskiyonu riskinde ve postherpetik nevralji riskinde azalma sağlar)

H4. 10 yılda bir Td (tetanoz-difteri toksoidi) yapılması uygundur

#H5. Hacca gidecek olgulara meningokok aşısı yapılması uygundur

I: Suplemanlar.

I1. Malnütrisyon (MN) veya malnütrisyon riski (MNR) olan yaşlılarda beslenme danışmanlığı ve besin takviyesi diyetle alımı artırmak ve beslenme hedeflerine ulaşmak için yeterli değil ise oral nütrisyonel suplemanların (ONS) başlanması uygundur

I2. Hastanede yatan MN veya MNR olan yaşlılarda ONS başlanması uygundur (besin alımı ve vücut ağırlığını artırır, komplikasyon ve tekrar başvuru riskini azaltır)

I3. Kalça kırığı olan yaşlı hastalara postoperatif dönemde ONS başlanması (nütrisyonel durumundan bağımsız olarak) uygundur (besin alımını iyileştirir ve komplikasyon riskini azaltır)

I4. Bası yarası mevcut olan hastalarda yeterli protein ve enerji alımını sağlamak için 1,2-2 g/kg/gün protein, 30-35 kcal/kg/gün enerji hedeflenerek ONS başlanması uygundur

#Uluslararası Delfi paneli çalışmasında konsensus sağlanmayan kriterler

Kısaltmalar:

AF: Atrial fibrilasyon

ACEİ: Anjiotensin konverting enzim inhibitörleri

ARB: Anjiotensin reseptör blokerleri

KMD: Kemik mineral dansite

BTM: Kemik Turnover Belirteçleri

ChEi: Kolinesteraz İnhibitörü

COMT: Catechol-O-methyltransferase

KOAH: Kronik obstrüktif akciğer hastalığı

EF: Ejeksiyon fraksiyonu

FEV1: Zorlu Ekspiratuar Volüm

IPSS: Uluslararası Prostat Semptom Skoru

LUTS: Alt üriner sistem semptomları

MAO-B: Monoamin oksidaz-B

Mİ: Miyokard infarktüsü

MN: Malnütrisyon

MNR: Malnütrisyon riski

NSAİİ: Non steroidal anti inflamatuar ilaç

OAK: Oral antikoagülan

ONS: Oral nütrisyonel suplemanlar

PO_2: Parsiyel oksijen basıncı

SaO_2: Oksijen satürasyonu

SNRİ: Serotonin-norepinefrin geri alım inhibitörü

SSRİ: Selektif serotonin geri alım inhibitörü

GİA: Geçici iskemik atak

TIME to STOP- YAŞLIDA KULLANIMI ÖNERİLMEYEN İLAÇLAR

Bu grup ilaçların, kriter içeriğindeki durumlarda kullanımı yaşlılarda ilaç-hastalık, ilaç-geriatrik sendrom ve/veya ilaç-ilaç etkileşimi nedeniyle "yüksek" yan etki potansiyeli taşımaktadır ve "potansiyel uygunsuz ilaç kullanımı" olarak nitelendirilmektedirler. Klinisyenler hastanın tüm özellikleriyle ilacın hastasındaki potansiyel fayda ve zararını (kar-zarar dengesini) ve hasta/bakımveren tercihleri doğrultusunda saptanan tedavi hedeflerini göz önünde bulundurarak karar vermelidir. Bu grup ilaçları klinisyenler bazı olgularda kullanmayı yine de uygun bulabilir. Kullanımı tercih edildiğinde dikkatle kullanılması, yan etki varlığı açısından klinik olarak yakın takip edilmesi gereken ilaçlardır.

*Klinik kullanıma yardımcı olması için bazı kriterlere eklenen açıklamalar kriterden hemen sonra italik karakterde ve önek * ile verilmiştir.*

Referanslar; kriterle ilgili ve mevcut ise açıklamalar ile ilgili referansları içermektedir.

TIME-to-STOP Kriterleri (referanslı ve açıklamalı)

A: Kardiyovasküler Sistem Kriterleri

A1. AF tedavisinde 1.basamakta digoksin kullanımı uygun değildir

**Digoksin kullanımı, AF olgularında, beta-bloker ve kalsiyum kanal blokerlerinin tolere edilemediği olgularda (örn. hipotansiyon) veya bu tedavilerin yeterli olmadığı durumlarda kombinasyon tedavisinde kullanılabilir.*

A1(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29.

A1(ii): Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P; ESC Scientific Document Group. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016 Oct 7;37(38):2893-2962. doi:10.1093/eurheartj/ehw210. Epub 2016 Aug 27.

A2. Digoksin'in 0,125 mg/gün'den yüksek dozda kullanımı uygun değildir (toksisite riski)

A2(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29.

A2(ii): Digoxin: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

A2(iii): British National Formulary vol. 76, September 2018-March 2019: p 28.

A3. Korunmuş (normal) EF'li kalp yetersizliği endikasyonuyla digoksin kullanımı uygun değildir

**Digoksin'in eşlik eden AF için endikasyonu olabilir (bkz A1).*

A3(i): Jessup M, Abraham WT, Casey DE, Feldman AM, Francis GS, Ganiats TG, KonstamMA, Mancini DM, Rahko PS, Silver MA, Stevenson LW, Yancy CW.2009 focused update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. Circulation 2009; 119(14): 1977-2016.

A3(ii): Cheng JW, Nayar M. A review of heart failure management in the elderly population. Am J Geriatr Pharmacother 2009; 7(5): 233-49. Review.

A3(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A4. Düşük EF'li kalp yetersizliğinde diltiazem veya verapamil kullanımı uygun değildir

A4(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29.

A4(ii): Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016 Jul 14;37(27):2129-2200. doi: 10.1093/eurheartj/ehw128. Epub 2016 May 20. Erratum in: Eur Heart J. 2016 Dec 30

A4(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A5. Bradikardi (<50/dk), tip 2 kalp bloğu veya tam kalp bloğu olanlarda hız kısıtlayıcı tedavi (beta-bloker, verapamil, diltiazem, digoksin) başlanması uygun değildir

**Beta-blokerler PR aralığı >240 msn olgularda görece kontrendikedir. Halihazırda beta-bloker, diltiazem, verapamil, digoksin kullanmakta olan olgularda bradikardi (<50/dk) varlığında doz azaltımı yapılmalıdır.*

A5(i): British National Formulary, No. 76, September 2018-March 2019, p 145.

A5(ii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A6. Kalp yetersizliği, karaciğer yetersizliği, nefrotik sendrom veya böbrek yetersizliğinin klinik, biyokimyasal veya radyolojik bulguları olmadan ayak bileği ödemi için loop diüretiği kullanımı uygun değildir (bacak elevasyonu ve/veya kompresyon çorapları genellikle daha uygundur)

A6(i): Wehling M. Morbus diureticus in the elderly: epidemic overuse of a widely applied group of drugs. J Am Med Dir Assoc 2013; 14(6): 437-42. Review.

A6(ii): Sarafidis PA, Georgianos PI, Lasaridis AN. Diuretics in clinical practice. Part I: mechanisms of action, pharmacological effects and clinical indications of diuretic compounds. Expert Opin Drug Saf 2010; 9(2):243-57. Review.

A6(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A6(iv): British National Formulary, No. 76, September 2018-March 2019, p28.

A7. Özel bir endikasyon bulunmadığı halde esansiyel HT tedavisi için ilk basamakta beta-blokerlerin kullanımı uygun değildir (kalp bloğu riskinde artış, halsizlik-yorgunluk, seksüel disfonksiyon ve inmeden korunmada az etkinlik nedeniyle; ek olarak yaşlanmayla β-adrenerjik reseptör fonksiyonunda azalma olur)

A7(i): Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/ PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: ExecutiveSummary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2018 Oct 23;138(17):e426-e483

A7(ii): James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, Le-Fevre ML, MacKenzie TD, Ogedegbe O, Smith SC Jr, Svetkey LP, Taler SJ, Townsend RR, Wright JT Jr, Narva AS, Ortiz E. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014 Feb 5;311(5):507-20.

A7(iii): Alexander K P, Peterson E D, Coronary heart disease in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Haler J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017

A7(iv): Arıcı M, Birdane A, Güler K, Yıldız BO, Altun B, Ertürk Ş, Aydoğdu S, Özbakkaloğlu M, Ersöz HÖ, Süleymanlar G, Tükek T, Tokgözoğlu L, Erdem Y; Türk Kardiyoloji Derneği (TKD); Türk İç Hastalıkları Uzmanlık Derneği (TİHUD); Türkiye Endokrinoloji ve Metabolizma Derneği (TEMD); Türk Nefroloji Derneği (TND); Türk Hipertansiyon ve Böbrek Hastalıkları Derneği. [Turkish Hypertension Consensus Report]. Turk Kardiyol Dern Ars. 2015 Jun;43(4):402-9. doi: 10.5543/tkda.2015.16243. Turkish.

A7(v): Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I; ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018 Sep 1;39(33):3021-3104.

A8. Üriner inkontinansı olanlarda esansiyel HT tedavisi için ilk basamakta diüretik kullanımı uygun değildir (inkontinansı ve sıkışma hissini artırarak yaşam kalitesini bozabilir, düşmeleri artırabilir)

**Genel olarak yaşlılarda diüretikler volüm deplesyonu yaparak/miksiyon sıklığını ve volümünü artırarak ve sıkışma hissine sebep olarak hayat kalitesini bozabilir ve düşme için risk faktörü olabilir. Diüretik kullanan olgular bu açılardan yakın takip edilmelidir.*

A8(i): Lukacz E. Evaluation of women with urinary incontinence. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019

A8(ii): Ekundayo OJ. The association between overactive bladder and diuretic use in the elderly. Curr Urol Rep 2009; 10(6):434-40. Review.

A8(iii): Ekundayo OJ, Markland A, Lefante C, Sui X, Goode PS, Allman RM, Ali M, Wahle C, Thornton PL, Ahmed A. Association of diuretic use and overactive bladder syndrome in older adults: a propensity score analysis. Arch Gerontol Geriatr2009; 49(1):64-8.

A8(iv): Finkelstein MM. Medical conditions, medications, and urinary incontinence. Analysis of a population-based survey. Can Fam Physician 2002; 48:96-101.

A8(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A9. Diğer sınıf antihipertansiflerin tolere edilemediği veya etkisiz kaldığı durumlar hariç HT tedavisinde alfa-1 bloker veya santral etkili antihipertansiflerin (örn. metildopa, rilmenidin, rezerpin) kullanımı uygun değildir (alfa-1 bloker antihipertansifler ile kalp yetersizliği ve kardiyovasküler olaylarda artış, ortostatik hipotansiyon, düşme, senkop, kadınlarda üriner inkontinansın kötüleşmesi; santral etkili antihipertansiflerin MSS yan etkileri, sedasyon-depresyon-parkinsonizm ve ortostatik hipotansiyon, bradikardi yan etkileri)

A9(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29.

A9(ii): Marshall HJ, Beevers DG. Alpha-adrenoceptor blocking drugs and female urinary incontinence: prevalence and reversibility. Br J Clin Pharmacol. 1996 Oct;42(4):507-9

A9(iii): Major cardiovascular events in hypertensive patients randomized to doxazosinvs chlorthalidone: the antihypertensive and lipid-lowering treatment to preventheart attack trial (ALLHAT). ALLHAT Collaborative Research Group. JAMA. 2000 Apr19;283(15):1967-75.

A9(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A10. Ortostatik hipotansiyon (sistolik kan basıncında>=20 mmHg düşüş veya diastolik kan basıncında >=10 mmHg düşüş) olanlarda vazodilatör antihipertansiflerin (alfa-1 blokerler)/ nitratların kullanımı uygun değildir (ortostatik hipotansiyonda artış riski)

**Ortostatik hipotansiyon varlığında vazodilatör antihipertansiflerin kullanımı, sadece ciddi süpin HT diğer antihipertansiflerle kontrol edilemediğinde, uygun olabilir. Kullanılmaları durumunda eş zamanlı olarak ortostatik hipotansiyondan koruyucu tedbirler uygulanmalıdır. Ortostatik hipotansiyon varlığında tüm antihipertansifler doz azaltımı açısından değerlendirilmelidir.*

A10(i): Aronow WS. Treating hypertension in older adults: safety considerations. Drug Saf 2009; 32(2): 111-8.

A10(ii): Verhaeverbeke I, Mets T. Drug-induced orthostatic hypotension in the elderly: avoiding its onset. Drug Saf 1997; 17(2): 105-18. Review.

A10(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A10(iv): Brignole M, Moya A, de Lange FJ, Deharo JC, Elliott PM, Fanciulli A, Fedorowski A, Furlan R, Kenny RA, Martín A, Probst V, Reed MJ, Rice CP, Sutton R, Ungar A, van Dijk JG; ESC Scientific Document Group. 2018 ESC Guidelines for the diagnosis and management of syncope. Eur Heart J. 2018 Jun 1;39(21):1883-1948.

A11. Ortostatik hipotansiyonu/bilişsel yetersizliği (örn. demans) /fonksiyonel kısıtlılığı/düşük yaşam beklentisi (<2 yıl)/düşme riski yüksek olan hastalarda sıkı kan basıncı kontrolu (<140/90 mmHg) uygun değildir

A11(i): Onder G, Landi F, Fusco D, Corsonello A, Tosato M, Battaglia M, Mastropaolo S, Settanni S, Anto-cicco M, Lattanzio F. Recommendations to prescribe in complex older adults: results of the CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) project. Drugs Aging. 2014 Jan;31(1):33-45.Review.

A11(ii): Wu JS, Yang YC, Lu FH. Population-based study on the prevalence and risk factors of orthostatic hypotension in subjects withpre-diabetes and diabetes. Diabetes Care. 2009;32:69–74.

A11(iii): Luukinen H, Koski K, Laippala P, Kivela¨ SL. Prognosis of diastolic and systolic orthostatic hypotension in older persons. ArchIntern Med. 1999;159:273–80.

A11(iv): Hiitola P, Enlund H, Kettunen R. Postural changes in blood pressure and the prevalence of orthostatic hypotension among home-dwelling elderly aged 75 years or older. J Hum Hypertens. 915 2009;23:33–9.

A12. Sekonder faktörler dışlanmadan ve ilaç dışı yaklaşımlar uygulanmadan ortostatik hipotansiyon tedavisi için fludrokortizon kullanımı uygun değildir

**Ortostatik hipotansiyonun yönetimine yönelik ilaç dışı yaklaşımlar şunlardır: Ayağa yavaş kalkmak, alt ekstremite direnç egzersizleri, varis çorabı giymek, yeterli sıvı alımı [2–3*

L/gün], alkolden kaçınmak, az ve sık yemek yemek, yeterli tuz alımı [6-10 g/gün], karbonhidrattan zengin yiyeceklerden uzak durulması, sıcak havada yoğun egzersizden kaçınılması, yatarken başın 30-45 derece yüksekte tutulması

A12(i): Seppi K, Weintraub D, Coelho M, Perez-Lloret S, Fox SH, Katzenschlager R,Hametner EM, Poewe W, Rascol O, Goetz CG, Sampaio C. The Movement DisorderSociety Evidence-Based Medicine Review Update: Treatments for the non-motorsymptoms of Parkinson's disease. Mov Disord. 2011 Oct;26 Suppl 3:S42-80.

A12(ii): Kaufmann H. Treatment of orthostatic and postprandial hypotension. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019

A12(iii): Shibao C, Lipsitz LA, Biaggioni I. ASH position paper: evaluation and treatment of orthostatic hypotension. J Clin Hypertens (Greenwich). 2013 Mar;15(3):147-53.

A13. HT olgularında beta-bloker ve verapamil/diltiazem kombinasyonu kullanımı uygun değildir (kalp bloğu riski)

**Yaşlılarda HT tedavisinde kalsiyum kanal blokerlerinden genellikle uzun etkili dihidropiridin grubu tercih edilmelidir (verapamil/diltiazem kullanımı kalp bloğu riskini artırabilir).*

**Beta-blokerler'in, verapamil/diltiazem ile kombinasyonu bazı supraventriküler taşikardi olgularında uygun olabilir. Bu durumda da dikkatli kullanılmalıdır.*

A13(i): Edoute Y, Nagachandran P, Svirski B, Ben-Ami H. Cardiovascular adverse drug reaction associated with combined beta-adrenergic and calcium entry-blocking agents. J Cardiovasc Pharmacol 2000; 35(4): 556-9.

A13(ii): Egan BM. Treatment of hypertension in older adults, particularly isolated systolic hypertension. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019

A13(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A14. Serum potasyum düzeyi 5.5 mEq/L'nin üzerinde olan olgularda RAS blokeri (ACE inhibitörü, ARB, direkt renin inhibitörü) veya potasyum tutucu diüretik (spironolakton, eplerenon, amilorid, triamteren) başlanması uygun değildir

**Potasyum düzeyi 6 mEq/L'nin üzerinde olan olgularda bu grup ilaçlar kullanılıyorsa kesilmelidir.*

**ACE inhibitörü ve ARB'lerin antihipertansif amaçlı kombine kullanımı uygun değildir.*

A14(i): Izzo JL Jr, Weir MR. Angiotensin-converting enzyme inhibitors. J Clin Hypertens (Greenwich) 2011; 13(9):667-75. Review.

A14(ii): Desai AS, Swedberg K, McMurray JJ, Granger CB, Yusuf S, Young JB, Dunlap ME, Solomon SD, Hainer JW, Olofsson B, Michelson EL, Pfeffer MA; CHARM Program Investigators. Incidence and predictors of hyperkalemia in patients with heart failure: an analysis of the CHARM Program. J Am Coll Cardiol 2007 Nov 13;50(20):1959-66.

A14(iii): Reardon LC, Macpherson DS. Hyperkalemia in outpatients using angiotensin-converting enzyme inhibitors. How much should we worry? Arch Intern Med 1998; 158(1):26-32.

A14(iv): ONTARGET Investigators, Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med. 2008 Apr 10;358(15):1547-59.

A14(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A15. Serum potasyum düzeyi takip edilmeden RAS blokeri (ACEİ, ARB, direkt renin inhibitörü) ve potasyum tutucu diüretiklerin (spironolakton, eplerenon, amilorid, triamteren) kombine edilmesi uygun değildir (tehlikeli hiperpotasemi riski)

**Bu risk özellikle diabetes mellitus hastalarında, böbrek yetersizliği hastalarında, yaşlılarda ve potasyum tuzu takviyeleri kullanmakta olanlarda daha yüksektir.*

A15(i): Bauersachs J, Fraccarollo D. Aldosterone antagonism in addition to angiotensin-converting enzyme inhibitors in heart failure. Minerva Cardioangiol 2003; 51(2):155-64. Review.

A15(ii): Poggio R, Grancelli HO, Miriuka SG. Understanding the risk of hyperkalaemia in heart failure: role of aldosterone antagonism. Postgrad Med J 2010; 86 (1013):136-42. Review.

A15(iii): Wrenger E, Müller R, Moesenthin M, Welte T, Frölich JC, Neumann KH. Interaction of spironolactone with ACE inhibitors or angiotensin receptor blockers: analysis of 44 cases. BMJ 2003; 327(7407):147-9.

A15(iv): Marcy TR, Ripley TL. Aldosterone antagonists in the treatment of heart failure. Am J Health Syst Pharm 2006; 63(1): 49-58.

A15(v): Tang WH, Parameswaran AC, Maroo AP, Francis GS. Aldosterone receptor antagonists in the medical management of chronic heart failure. Mayo Clin Proc 2005; 80(12): 1623-30. Review.

A15(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A16. GFR<30 mL/dk/1,73 m^2 olan ve serum potasyum düzeyi yakın takip edilemeyecek hastalarda, potasyum tutucu ilaçların (aldosteron antagonistleri, triamteren, amilorid, ACEİ, ARB) kullanımı uygun değildir (hiperpotasemi riski)

A16(i): Kidney Disease Outcomes Quality Initiative (K/DOQI). K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis. 2004 May;43(5 Suppl 1):S1-290.

A17. Belirgin hipopotasemi (serum K<3,0 mg/L), hiponatremi (serum Na < 130 mEq/L), hiperkalsemi (düzeltilmiş serum Ca>10,6 mg/dL) veya gut hikayesi olan hastalarda tiazid diüretiklerinin kullanımı uygun değildir

A17(i): Sica DA, Carter B, Cushman W, Hamm L. Thiazide and loop diuretics. J Clin Hypertens (Greenwich) 2011; 13(9):639-43. Review.

A17(ii): Gurwitz JH, Kalish SC, Bohn RL, Glynn RJ, Monane M, Mogun H, Avorn J. Thiazide diuretics and the initiation of anti-gout therapy. J ClinEpidemiol1997; 50(8): 953-9.

A17(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A18. Kardiyovasküler hastalığı (ciddi HT, kalp yetersizliği veya geçirilmiş Mİ, inme) olan olgularda NSAİİ kullanımı uygun değildir (artmış kardiyovasküler olay: Mİ, inme, kalp yetersizliği ve ölüm riski)

**NSAİİ kullanımının klinik olarak endike olduğu durumlarda, yakın klinik takip ile ve mümkün olan en düşük dozda, kısa süreli kullanım tercih edilebilir.*

**NSAİİ'lerin hepsi kardiyovasküler açıdan riskli olmakla birlikte naproksen ve ibuprofen görece daha güvenli olabilirler.*

**Aspirin kullanan hastaya NSAİİ'ler verilecekse, aspirinden en az 2 saat sonra uygulanması daha uygun olabilir.*

A18(i): Pilotto A, Sancarlo D, Addante F, Scarcelli C, Franceschi M. Non-steroidal anti-inflammatory drug use in the elderly. Surg Oncol 2010; 19(3): 167-72. Review.

A18(ii): Strand V. Are COX-2 inhibitors preferable to non-selective non-steroidal anti-inflammatory drugs in patients with risk of cardiovascular events taking low-dose aspirin? Lancet 2007; 370(9605): 2138-51. Review.

A18(iii): White WB. Defining the problem of treating the patient with hypertension and arthritis pain. Am J Med. 2009; 122(5 Suppl): S3-9. Review.

A18(iv): Park KE. Qin Y, Bavry AA.Nonsteroidal anti-inflammatory drugs and their effects in the elderly. Aging Health 2012; 8(2): 167-177.

A18(v): Solomon DH. NSAIDs: Adverse cardiovascular effects. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019

A18(vi): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29.

A18(vii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A19. Sık hipoglisemi atakları olan DM hastalarında beta-bloker kullanımı uygun değildir (hipoglisemik semptomları baskılama riski)

A19(i): Chelliah A, Burge MR. Hypoglycaemia in elderly patients with diabetes mellitus: causes and strategies for prevention. Drugs Aging 2004; 21(8): 511-30. Review.

A19(ii): British National Formulary vol. 76, September 2018-March 2019: p 145.

A19(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A20. Astım öyküsü olanlarda nonselektif beta-bloker (oral veya glokom için topikal) kullanımı uygun değildir (bronkospazmda artış riski)

A20(i): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A20(ii): Kaiserman I, Fendyur A, Vinker S. Topical beta blockers in asthmatic patients-is it safe? Curr Eye Res. 2009 Jul;34(7):517-22.

A20(iii): McNeill RS, Ingram CG. Effect of propranolol on ventilatory function. Am J Cardiol. 1966 Sep;18(3):473-5.

A20(iv): Morales DR, Lipworth BJ, Donnan PT, Jackson C, Guthrie B. Respiratory effect of beta-blockers in people with

asthma and cardiovascular disease: population-based nested case control study. BMC Med. 2017 Jan 27;15(1):18.

A21. Primer veya sekonder kardiyovasküler korumada aspirin'in 75-150 mg/gün'den yüksek dozda kronik kullanımı uygun değildir (kanıtlanmış ek faydası yok ve kanama riskini artırıyor)

A21(i): Task Force Members, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di Mario C, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabaté M, Senior R, Taggart DP, van der Wall EE, Vrints CJ; ESC Committee for Practice Guidelines, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S; Document Reviewers, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Rydén L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013 Oct;34(38):2949-3003.

A21(ii): Hennekens CH.Aspirin for the secondary prevention of atherosclerotic cardiovascular disease. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 23 October 2019

A21(iii): Cucchiara BL.Antiplatelet therapy for secondary prevention of stroke. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 23 Ekim 2019

A21(iv): Spencer FA, Guyatt G, Tampi M, Golemiec B.Aspirin in the primary prevention of cardiovascular disease and cancer. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 23 Ekim 2019

A21(v): Smith SC Jr, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, Gibbons RJ, Grundy SM, Hiratzka LF, Jones DW, Lloyd-Jones DM, Minissian M, Mosca L, Peterson ED, Sacco RL, Spertus J, Stein JH, Taubert KA; World Heart Federation and the Preventive Cardiovascular Nurses Association. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosc-lerotic Vascular Disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011 Nov 29;124(22):2458-73.

A21(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A21(vii): Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; American Heart Association Stroke Council. 2018 Guidelines for the EarlyManagement of Patients With Acute Ischemic Stroke: A Guideline for HealthcareProfessionals From the American Heart Association/American Stroke Association.Stroke. 2018 Mar;49(3):e46-e110.

#A22. Aspirin, klopidogrel, dipiridamol ve OAK'ların (Vitamin K antagonistleri, direkt trombin inhibitörü veya faktör Xa inhibitörleri) eşlik eden anlamlı kanama riski varlığında (örneğin kontrolsüz ciddi HT, kanama diyatezi, spontan anlamlı kanaması olanlarda) kullanımı uygun değildir (yüksek kanama riski)

A22(i): Lip GY. Implications of the CHA(2)DS(2)-VASc and HAS-BLED Scores for thromboprophylaxis in atrial fibrillation. Am J Med. 2011; 124(2):111-4.

A22(ii): Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest 2010; 138(5):1093-100.

A22(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A23. Aspirin ve klopidogrelin birlikte kullanımı için spesifik bir endikasyon yoksa, sekonder inme proflaksisinde aspirin ve klopidogrelin birlikte kullanımı uygun değildir

*Aspirin +klopidogrel kombine kullanımının uygun olduğu durumlar

1. son 12 ay içinde akut koroner sendrom veya koroner girişim geçirmiş olmak (balon ve/veya stent)

2. periferik arter hastalığı nedeniyle son 1 ayda girişim geçirmiş olmak

son bir ayda stent (karotis arter stenozu/alt ekstremite arter hastalığı nedeniyle) yerleştirilmesi

son bir ayda alt ekstremiteye balon uygulaması

3. son 3 hafta-3 ay içinde inme-GİA geçirmiş olmak

intrakranial ateroskleroza bağlı inme veya GİA olgularında 3 ay boyunca

minör inme veya GİA olgularında 3 hafta boyunca

A23(i): Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, Leys D, Matias-Guiu J, Rupprecht HJ; MATCH investigators. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. Lancet 2004; 364(9431):331-7.

A23(ii): Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, Cacoub P, Cohen EA, Creager MA, Easton JD, Flather MD, Haffner SM, Hamm CW, Hankey GJ, Johnston SC, Mak KH, Mas JL, Montalescot G, Pearson TA, Steg PG, Steinhubl SR, Weber MA, Brennan DM, Fabry-Ribaudo L, Booth J, Topol EJ; CHA-RISMA Investigators. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med. 2006; 354(16):1706-17.

A23(iii): Usman MH, Notaro LA, Nagarakanti R, Brahin E, Dessain S, Gracely E, Ezekowitz MD. Combination antiplatelet therapy for secondary stroke prevention: enhanced efficacy or double trouble? Am J Cardiol 2009;103(8):1107-12. Review.

A23(iv): Squizzato A, Keller T, Romualdi E, Middeldorp S. Clopidogrel plus aspirin versus aspirin alone for preventing cardiovascular disease. Cochrane Database Syst Rev 2011;(1):CD005158. Review.

A23(v): Fares RR, Lansing LS, Gallati CA, Mousa SA. Antiplatelet therapy with clopidogrel and aspirin in vascular diseases: clinical evidence for and against the combination. Expert Opin Pharmacother 2008; 9(3): 377-86. Review.

A23(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A23(vii): Valgimigli M. The ESC DAPT Guidelines 2017. Eur Heart J. 2018 Jan 14;39(3):187-188. doi: 10.1093/eurheartj/ehx768.

A23(viii): Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, Collet JP, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzolai L, Naylor AR, Roffi M, Röther J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I; ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2018 Mar 1;39(9):763-816. doi: 10.1093/eurheartj/ehx095.

A24. Kronik AF veya başka bir sebeple OAK kullanan hastalarda aspirin/klopidogrel kullanımı için ek endikasyon yok ise tedaviye aspirin/klopidogrel eklenmesi uygun değildir (aspirin ile ek fayda yok)

**OAK kullanımı olan hastalarda tedaviye aspirin/klopidogrel eklenmesi uygun olan durumlar şunlardır:*

1. son 12 ayda akut koroner sendrom veya koroner girişim geçirmiş olmak (balon ve/veya stent)

2. periferik arter hastalığı nedeniyle son 1 ayda girişim geçirmiş olmak

son bir ayda stent (karotis arter stenozu/alt ekstremite arter hastalığı nedeniyle) yerleştirlmesi

son bir ayda alt ekstremiteye balon uygulaması

**OAK kullanan hastalarda aşağıdaki durumlarda tedaviye aspirin/klopidogrel eklenmesi uygun değildir:*

1. üstteki durumlar haricinde olan periferik arter hastalığı (karotis arter stenozu, alt ekstremite arter hastalığı, intraserebral ateroskleroz)

2. stabil koroner arter hastalığı (örneğin 12 aydan daha uzun zaman önce geçirilmiş akut koroner sendrom veya koroner girişim)

A24(i): Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, Collet JP, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzolai L, Naylor AR, Roffi M, Röther J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I; ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2018 Mar 1;39(9):763-816. doi: 10.1093/eurheartj/ehx095.

A24(ii): Flaker GC, Gruber M, Connolly SJ, Goldman S, Chaparro S, Vahanian A, Halinen MO, Horrow J, Halperin JL; SPORTIF Investigators. Risks and benefits of combining aspirin with anticoagulant therapy in patients with atrial fibrillation: an exploratory analysis of stroke prevention using an oral thrombin inhibitor in atrial fibrillation (SPORTIF) trials. Am Heart J 2006; 152(5):967-73.

A24(iii): Larson RJ, Fisher ES. Should aspirin be continued in patients started on warfarin? J Gen Intern Med 2004; 19(8):879-86. Review.

A24(iv): Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Agewall S, Camm J, Baron Esquivias G,Budts W, Carerj S, Casselman F, Coca A, De Caterina R, Deftereos S, Dobrev D, Ferro JM, Filippatos G, Fitzsimons D, Gorenek B, Guenoun M, Hohnloser SH, Kolh P,Lip GY, Manolis A, McMurray J, Ponikowski P, Rosenhek R, Ruschitzka F, Savelieva I, Sharma S, Suwalski P, Tamargo JL, Taylor CJ, Van Gelder IC, Voors AA, Windecker S, Zamorano JL, Zeppenfeld K. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace. 2016 Nov;18(11):1609-1678.)

A24(v): XU H. Antithrombotic Therapy for Patients With Both Stable Coronary Artery Disease andAtrial Fibrillation-Expert Analysis 2014. Available at:

http://www.acc.org/latest-in-cardiology/articles/2014/07/18/15/34/antithrombotic-therapy-for-patients-with-both-stable-cad-and-afib) (erişim tarihi 28 Ekim 2019)

A24(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A24(vii): Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, HindricksG, Kirchhof P; ESC Committee for Practice Guidelines-CPG; Document Reviewers.2012 focused update of the ESC Guidelines for the management of atrialfibrillation: an update of the 2010 ESC Guidelines for the management of atrialfibrillation--developed with the special contribution of the European HeartRhythm Association. Europace. 2012 Oct;14(10):1385-413.

A24(viii): Smith SC Jr, Benjamin EJ, Bonow RO, et al. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. J Am Coll Cardiol 2011;58:2432-2446.

A24(ix): Yasuda S, Kaikita K, Akao M, Ako J, Matoba T, Nakamura M, Miyauchi K, Hagiwara N, Kimura K, Hirayama A, Matsui K, Ogawa H; AFIRE Investigators. Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease. N Engl J Med. 2019 Sep 19;381(12):1103-1113.

A25. OAK'ların (vitamin K antagonistleri, direkt trombin inhibitörleri veya faktör Xa inhibitörleri), devam eden risk faktörleri olmaksızın ilk kez olan derin ven trombozunda 6 aydan uzun süre kullanımı uygun değildir (kanıtlanmış ek yararı yok)

A25(i): Pinede L, Ninet J, Duhaut P, Chabaud S, Demolombe-Rague S, Durieu I, Nony P, Sanson C, Boissel JP; Investigators of the "Durée Optimale du Traitement AntiVitamines K" (DOTAVK) Study. Comparison of 3 and 6 months of oral anticoagulant therapy after a first episode of proximal deep vein thrombosis or pulmonary embolism and comparison of 6 and 12 weeks of therapy after isolated calf deep vein thrombosis. Circulation 2001; 103(20): 2453-60.

A25(ii): Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, Nelson ME, Wells PS, Gould MK, Dentali F, Crowther M, Kahn SR; American College of Chest Physicians. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2 Suppl): e419S-94S.

A25(iii): Lip GYH, Hull RD. Overview of the treatment of lower extremity deep vein thrombosis (DVT). In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 23 Ekim 2019

A25(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

#A26. OAK'ların (vitamin K antagonistleri, direkt trombin inhibitörleri veya faktör Xa inhibitörleri), devam eden risk faktörleri olmaksızın ilk kez olan pulmoner embolide 12 aydan uzun süre kullanımı uygun değildir (kanıtlanmış ek yararı yok)

A26(i): Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, Nelson ME, Wells PS, Gould MK, Dentali F, Crowther M, Kahn SR; American College of Chest Physicians. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2Suppl): << potentially inappropriate prescribing in older people: version 2. Age Ageing. 2015 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

#A27. OAK'ların (vitamin K antagonistleri, direkt trombin inhibitörleri veya faktör Xa inhibitörleri) kontrendike olduğu kronik AF hastalarında, aspirin veya klopidogrel monoterapisinin kullanımı uygun değildir

*Aspirin veya klopidogrel monoterapisi AF hastalarında inmenin önlenmesi için önerilmez, zararlıdır.

*Kanama riski varlığı nedeniyle OAK kontrendike olan hastalarda dual antiplatelet tedavi de önerilmez.

*Bu hastalarda inme riski yüksek olan durumlarda sol atrium appendiks kapatılması önerilebilir.

A27(i): Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P; ESC Scientific Document Group. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016 Oct 7;37(38):2893-2962. doi:10.1093/eurheartj/ehw210. Epub 2016 Aug 27.

A27(ii): Själander S, Själander A, Svensson PJ, Friberg L. Atrial fibrillation patients do not benefit from acetylsalicylic acid. Europace 2014; 16:631-8.

A27(iii): Olesen JB, Lip GY, Lindhardsen J, Lane DA, Ahlehoff O, Hansen ML, Raunsø J,Tolstrup JS, Hansen PR, Gislason GH, Torp-Pedersen C. Risks of thromboembolism and bleeding with thromboprophylaxis in patients with atrial fibrillation: A net clinical benefit analysis using a 'real world' nationwide cohort study. Thromb Haemost. 2011 Oct;106(4):739-49.

A27(iv): ManningWJ, Singer DE, Lip GYH. Atrial fibrillation: Anticoagulant therapy to prevent thromboembolism. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 23 Ekim 2019

A28. Dabigatran'ın GFR <30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir

**GFR<15 mL/dk/1,73 m^2 ise hiçbir YOAK kullanılmamalıdır.*

**GFR 15-30 mL/dk/1,73 m^2 olan olgularda apiksaban, rivaroksaban ve edoksaban için sınırlı kanıt olmakla birlikte genel olarak kullanımları önerilmemektedir.*

**GFR<30 mL/dk/1,73 m^2 olan AF olgularında, düşme riski yüksek olan hastalarda veya hayatı tehdit eden kanama geçirmiş hastalarda, kanama riskini göze almak istemeyen hastalarda, INR kontrolünde zorlanacak hastalarda, kötü kontrollü HT olgularında, antikoagülan verilmeyebilir.*

**Diyalize giren AF olgularında antikoagülan önerilmez [çok yüksek inme riski olmadıkça: atrial trombüs, geçirilmiş GİA-inme, kapak hastalığı: (orta ciddi MS, protez kapak)]. Antikoagülasyon endike ise varfarin önerilir.*

**İnme riski yüksek olan AF olgularında, OAK'ların kullanılamaması durumunda sol atrium appendiks kapatılması önerilebilir.*

**Edoksaban GFR>95 mL/dk/1,73* m^2 *olan olgularda kullanılmamalıdır.*

A28(i): Hariharan S, Madabushi R. Clinical pharmacology basis of deriving dosing recommendations for dabigatran in patients with severe renal impairment. J ClinPharmacol 2012; 52(1 Suppl):119S-25S.

A28(ii): Samama MM. Use of low-molecular-weight heparins and new anticoagulants in elderly patients with renal impairment. Drugs Aging 2011; 28(3): 177-93.

A28(iii): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

A28(iv): Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P; ESC Scientific Document Group. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016 Oct 7;37(38):2893-2962.

A28(v): Manning WJ, Singer DE, Lip GYH. Atrial fibrillation: Anticoagulant therapy to prevent thromboembolism. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 28 Ekim 2019

A28(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A28(vii): Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, Georg Haeusler K, Oldgren J, Reinecke H, Roldan-Schilling V, Rowell N, Sinnaeve P, Collins R, Camm AJ, Heidbüchel H; ESC Scientific Document Group. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation: executive summary. Europace. 2018 Aug 1;20(8):1231-1242.

#A29. Non-valvular AF'si olup malnütre olan veya besin alımı düzensiz olan hastalarda varfarin kullanımı uygun değildir

A29(i): Onder G, Landi F, Fusco D, Corsonello A, Tosato M, Battaglia M, Mastropaolo S, Settanni S, Antocicco M, Lattanzio F. Recommendations to prescribe in complex older adults: results of the CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) project. Drugs Aging. 2014 Jan;31(1):33-45.Review.

A29(ii): Lurie Y, Loebstein R, Kurnik D, Almog S, Halkin H. Warfarin and vitamin K intake in the era of pharmacogenetics. Br J Clin Pharmacol. 2010;70:164–70. 1092.

A29(iii): Sebastian JL, Tresch DD. Use of oral anticoagulants in older patients. Drugs Aging. 2000;16:409–35. 1094.

A29(iv): Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-

Based Clinical Practice Guidelines (8th Edition). Chest. 2008 Jun;133(6 Suppl):160S-198S.

A29(v): Vranckx P, Valgimigli M, Heidbuchel H. The Significance of Drug-Drug and Drug-Food Interactions of Oral Anticoagulation. Arrhythm Electrophysiol Rev. 2018 Mar;7(1):55-61.

A30. İlaçlarını kullanmakta, yönetmekte güçlük çeken (öm. bilişsel bozukluğu olan hastalar) ve yardımcı olacak kimselerin (örn. bakıcı) olmadığı hastalarda varfarin ve digoksin gibi dar terapötik indeksi olan ilaçların kullanımı uygun değildir (hayatı tehdit edebilecek toksisite riski)

A30(i): Onder G, Landi F, Fusco D, Corsonello A, Tosato M, Battaglia M, Mastropaolo S, Settanni S, Antocicco M, Lattanzio F. Recommendations to prescribe in complex older adults: results of the CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) project. Drugs Aging. 2014 Jan;31(1):33-45.Review.

A30(ii): van Deelen BA, van den Bemt PM, Egberts TC, van 't Hoff A, Maas HA. Cognitive impairment as determinant for sub-optimal control of oral anticoagulation treatment in elderly patients with atrial fibrillation. Drugs Aging.2005;22(4):353-60. Review.

A30(iii): Diug B, Evans S, Lowthian J, Maxwell E, Dooley M, Street A, Wolfe R, Cameron P, McNeil J. The unrecognized psychosocial factors contributing to bleeding risk in warfarin therapy. Stroke. 2011 Oct;42(10):2866-71.

A30(iv): Arlt S, Lindner R, Ro¨sler A, von Renteln-Kruse W. Adherence to medication in patients with demen-tia: predictors and strategies for improvement. Drugs Aging. 2008;25:1033–47.

A30(v): Brauner DJ, Muir JC, Sachs GA. Treating nondementia illnesses in patients with dementia. JAMA. 2000;283:3230–5.

A30(vi): Marvanova M. Drug-induced cognitive impairment: Effect of cardiovascular agents. Ment Health Clin. 2016 Jun 29;6(4):201-206. doi: 10.9740/mhc.2016.07.201.

#A31. Prasugrel'in 75 yaş ve üzeri hastalarda veya GİA/inme geçirmiş olgularda kullanımı uygun değildir

A31(i): Prasugrel: Drug information, Lexicomp Online.Son erişim tarihi 22 Ekim 2019.

A32. Tiklopidin antitrombosit olarak kullanımı uygun değildir (klopidogrel veya tikagrelor veya prasugrel'in daha yüksek etkinliği vardır, daha çok kanıtı vardır ve daha az yan etkisi vardır)

A32(i): Furie KL, Kasner SE, Adams RJ, Albers GW, Bush RL, Fagan SC, Halperin JL, Johnston SC, Katzan I, Kernan WN, Mitchell PH, Ovbiagele B, Palesch YY, Sacco RL, Schwamm LH, Wassertheil-Smoller S, Turan TN, Wentworth D; American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American heart association/American stroke association. Stroke 2011; 42(1):227-76.

A32(ii): Porto I, Giubilato S, De Maria GL, Biasucci LM, Crea F. Platelet P2Y12 receptor inhibition by thienopyridines: status and future. Expert Opin Investig Drugs 2009; 18(9):1317-32. Review.

A32(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A32(iv): Li YH, Fang CY, Hsieh IC, Huang WC, Lin TH, Sung SH, Chiu CZ, Wu CJ, Shyu KG, Chang PY, Fang CC, Lu TM, Chen CP, Tai WC, Sheu CC, Wei KC, Huang YH, Wu HM, Hwang JH. 2018 Expert Consensus on the Management of Adverse Effects of Antiplatelet Therapy for Acute Coronary Syndrome in Taiwan. Acta Cardiol Sin. 2018 May;34(3):201-210.

A33. Antitrombotik antiagregan etki için kısa etkili dipiridamol kullanımı uygun değildir (ortostatik hipotansiyon yan etkisi ve daha etkili ajanların bulunması)

A33(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

A33(ii): Dipyridamole: Drug information, Lexicomp Online. Son erişim tarihi 22 October 2019.

A34. Yaşam beklentisi düşük olan (<2 yıl) veya ileri evre demanslı yaşlılarda primer koruma amaçlı statin kullanımı uygun değildir

A34(i): Onder G, Landi F, Fusco D, Corsonello A, Tosato M, Battaglia M, Mastropaolo S, Settanni S, Antocicco M, Lattanzio F. Recommendations to prescribe in complex older adults: results of the CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) project. Drugs Aging. 2014 Jan;31(1):33-45.Review.

A34(ii): Pignone M. Management of elevated low density lipoprotein-cholesterol (LDL-C) in primary prevention of cardiovascular disease.In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 23 Ekim 2019

A34(iii): Lavan AH, Gallagher P, Parsons C, O'Mahony D. STOPPFrail (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy) consensus validation. Age Ageing. 2017 Jul 1;46(4):600-607.

A35. Asemptomatik hiperürisemi (gut veya nefrolitiazisi olmayan olgular) için allopurinol başlanması uygun değildir (fayda için kanıt yok, ksantin oksidaz inhibitörleri kullanımıyla yan etki riski) (tedavinin kardiyovasküler riski veya gut hastalığını azalttığına dair kanıt yok)

**Serum ürik asit düzeyi, kadınlarda> 10 mg/dl ve erkeklerde> 13 mg/dL ise kronik böbrek hastalığı riski nedeniyle ürik asit düşürücü tedavi önerilebilir.*

A35(i): Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. N Engl J Med. 2008 Oct 23;359(17):1811-21. doi: 10.1056/NEJMra0800885. Review.

A35(ii): Poon SH, Hall HA, Zimmermann B. Approach to the treatment of hyperuricemia. Med Health R I. 2009 Nov;92(11):359-62. Review.

A35(iii): Maria Lorenza Muiesan, Claudia Agabiti-Rosei, Anna Paini, Massimo Salvetti. Uric Acid and Cardiovascular Disease: An Update. European Cardiology Review 2016;11(1):54–9.

A35(iv): Luis Ruilope, César Cerezo. Uric acid and cardiovascular risk considered: an update An article from the e-journal of the ESC Council for cardiology Practice. e-Journal of Cardiology Practice. Vol. 10, N° 21 - 02 Mar 2012. Available at:

https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-10/Uric-Acid-and-Cardiovascular-Risk-Considered-an-Update; son erişim tarihi 28 Ekim 2019

A35(v): Becker MA, Perez-Ruiz F. Pharmacologic urate-lowering therapy and treatment of tophi in patients with gout. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 28 Ekim 2019

A35(vi): Wallace SL, Singer JZ. Therapy in gout. Rheum Dis Clin North Am 1988; 14:441.

A35(vii): Becker MA, Mount DB. Asymptomatic hyperuricemia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 son erişim tarihi 23 Ekim 2019

A35(viii): Fessel WJ. Renal outcomes of gout and hyperuricemia. Am J Med. 1979 Jul;67(1):74-82.

B: Santral Sinir Sistemi Kriterleri

B1. Trisiklik antidepresan kullanımı uygun değildir (yüksek antikolinerjik etki, kognitif kötüleşme, kalp iletim bozukluğu, ortostatik hipotansiyon, üriner retansiyon, prostatizmde kötüleşme, dar açılı glokomda kötüleşme)

B1(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

B1(ii): Sultana J, Spina E, Trifirò G. Antidepressant use in the elderly: the role of pharmacodynamics and pharmacokinetics in drug safety. Expert Opin Drug Metab Toxicol. 2015 Jun;11(6):883-92. doi: 10.1517/17425255.2015.1021684. Epub 2015 Mar 3. Review.

B2. SSRI tedavisi başlanacak olgularda paroksetin, fluoksetin ve fluvaksaminin ilk basamakta tercih edilmesi uygun değildir (paroksetinin yüksek antikolinerjik etkisi, fluoksetinin uzun yarı ömrü, fluoksetin ve fluvaksaminin sık ilaç etkileşimi nedeniyle)

B2(i): Canadian Coalition for Seniors' Mental Health. National guidelines for seniors' mental health: The assessment and treatment of depression. Toronto, ON: Canadian Coalition for Seniors' Mental Health; 2006. Available at: https://ccsmh.ca/wp-content/uploads/2016/03/NatlGuideline_Depression.pdf (son erişim tarihi Ekim 23, 2019).

B2(ii): Bonnie Wiese, MD, MA, FRCPC. Geriatric depression: The use of antidepressants in the elderly. BCMJ, Vol. 53, No. 47, September, 2011, Page(s) 341-347 - Clinical Articles. Available at: http://www.bcmj.org/articles/geriatric-depression-use-antidepressants-elderly (son erişim tarihi Ekim 23, 2019).

B3. Yakın geçmişte veya halihazırda anlamlı hiponatremi (serum Na< 130 mEq/L) hikayesi olanlarda SSRİ kullanımı uygun değildir (SSRİ kullanımı ile artan hiponatremi riski)

**SSRI'larla hiponatremi gelişimi için risk faktörleri ileri yaş, kadın cinsiyet, eş zamanlı diüretik kullanımı, düşük vücut ağırlığı ve düşük bazal Na değeridir.*

**SSRI başlanan veya doz artırımı olan hastalar hiponatremi klinik bulguları açısından bilgilendirilmelidir. İlk 4 hafta en riskli zamandır.*

**Hiponatremi riski olan hastalarda, SSRI yerine mirtazapin veya bupropion tercih edilmesi uygun olabilir.*

B3(i): Jacob S, Spinler SA. Hyponatremia associated with selective serotonin-reuptake inhibitors in older adults. Ann Pharmacother 2006; 40(9):1618-22. Review.

B3(ii): Draper B, Berman K. Tolerability of selective serotonin reuptake inhibitors: issues relevant to the elderly. Drugs Aging 2008; 25(6): 501-19. Review.

B3(iii): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

B3(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B3(v): Fabian TJ, Amico JA, Kroboth PD, et al. Paroxetine-induced hyponatremia in older adults: a 12-week prospective study. Arch Intern Med. 2004;164: 327–332.

B3(vi): Fiske A,Wetherell JL, Gatz M. Depression in older adults. Annu Rev Clin Psychol. 2009;5:363–389.

B3(vii): De Picker L,VanDen Eede F, Dumont G, et al.Antidepressants and the risk of hyponatremia: a class-by-class review of literature. Psychosomatics. 2014;55:536–547.

B3(viii): Leth-Møller KB, Hansen AH, Torstensson M, Andersen SE, Ødum L, Gislasson G,Torp-Pedersen C, Holm EA. Antidepressants and the risk of hyponatremia: a Danishregister-based population study. BMJ Open. 2016 May 18;6(5):e011200.

#B4. Kontrolsüz HT varlığında SNRİ kullanımı uygun değildir

**Venlafaksin'in HT yan etkisi duloksetin'e göre daha belirgindir.*

**Venlafaksinin HT yan etkisi >300 mg/gün dozlarda daha belirgindir.*

B4(i): Breeden M, Brieler J, Salas J, Scherrer JF. Antidepressants and Incident Hypertension in Primary Care Patients. J Am Board Fam Med. 2018 Jan-Feb;31(1):22-28.

B4(ii): Taylor D, Lenox-Smith A, Bradley A. A review of the suitability of duloxetine and venlafaxine for use in patients with depression in primary care with a focus on cardiovascular safety, suicide and mortality due to antidepressant overdose. Ther Adv Psychopharmacol. 2013 Jun;3(3):151-61.

B4(iii): Thase ME. Effects of venlafaxine on blood pressure: a meta-analysis of original data from 3744 depressed patients. J Clin Psychiatry. 1998 Oct;59(10):502-8.

B5. GFR< 30 mL/dk/1,73 m^2 olanlarda duloksetin kullanımı uygun değildir (artmış GİS yan etkisi) **Böbrek yetmezliği durumunda diğer yaygın antidepresanların kullanımı:*

Sitalopram ve essitalopram: hafif-orta böbrek yetersizliğinde doz ayarlaması gerekli değildir. Ciddi (GFR<20 mL/dk/1.73 m^2) böbrek yetersizliğinde doz ayarlaması gerekli değildir ancak dikkatle kullanılmalıdır.

Sertralin: böbrek yetersizliğinde doz ayarlaması gerekli değildir.

Paroksetin: GFR< 30 mL/dk/1,73 m^2 ise hızlı salınımlı tabletlerde maksimum doz 40 mg, uzatılmış salınımlı preperatlarda maksimum doz: 50 mg/gün.

Venlafaksin: GFR< 30 mL/dk/1,73 m^2 ise uzatılmış salınımlı preperatlarda doz %50 azaltılmalıdır; hızlı salınımlı preperatlarda GFR 10-75 mL/dk/1,73 m^2 ise doz %25 azaltılmalıdır.

Mirtazapin: böbrek yetersizliğinde doz ayarlaması gerekli değildir ancak orta-ciddi böbrek yetersizliğinde dikkatle kullanılmalıdır.

Agomelatin: böbrek yetersizliğinde doz ayarlaması gerekli değildir.

Vortioksetin: böbrek yetersizliğinde doz ayarlaması gerekli değildir.

B5(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

B5(ii): Vortioxetine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B5(iii): Paroxetine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B5(iv): Duloxetine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B5(v): Sertraline: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B5(vi): Mirtazapine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B5(vii): Venlafaxine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B5(viii): Escitalopram: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B5(ix): Citalopram: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B6. GFR< 60 mL/dk/1,73 m^2 olması durumunda pregabalin ve gabapentin'in doz azaltımı yapılmadan kullanımı uygun değildir

B6(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

B6(ii):Pregabalin: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B7. Deliryum veya demansı olanlarda yüksek antikolinerjik etkili ilaçların (amitriptilin, paroksetin, disiklomin, L-hiyosiyamin, tioridazin, klorpromazin, klozapin, olanzapin, üriner antimuskarinikler, H1 reseptör blokerleri-özellikle 1. jenerasyon H1 reseptör blokerleri (difenhidramin, siproheptadin, feniramin), H2 reseptör blokerlerinin kullanımı uygun değildir (kognitif kötüleşme riski)

**Parkinson demansı ve Lewy cisimcikli demans gibi ekstrapiramidal sistem bulguları (parkinsonizm bulguları) olan hastalarda demansın/deliryumun ciddi davranışsal semptomlarının tedavisi için klinik pratikte klozapin kullanımı gerekebilmektedir. Bu durumda mümkün olan en kısa süreli, en düşük dozda ve yakın kognitif fonksiyon takibi ile kullanılmalıdır.*

**Parkinson demansı ve Lewy cisimcikli demans gibi ekstrapiramidal sistem bulguları (parkinsonizm bulguları) olan*

hastalarda ciddi davranışsal sepmtomlar nedeniyle nöroleptik kullanımı gerekli olması durumunda klozapin tedavisinden önce ilk basamakta ketiapin tedavisinin kullanımı uygundur.

**Tedavi düşünüldüğünde, Klozapin/ketiapin tedavileri 12,5 mg dozunda başlanarak, yan etkiler yakından izlenmeli, lüzum halinde 12,5-25 mg dozlarında artırılmalıdır. Semptom kontrolü sağlandıktan sonra birkaç hafta içinde azaltılarak kesilmesi denenmelidir.*

B7(i): Pagoria D, O'Connor RC, Guralnick ML. Antimuscarinic drugs: review of the cognitive impact when used to treat overactive bladder in elderly patients. Curr Urol Rep 2011; 12 (5): 351-7. Review.

B7(ii): Gerretsen P, Pollock BG. Drugs with anticholinergic properties: a current perspective on use and safety. Expert Opin Drug Saf 2011; 10(5): 751-65. Review.

B7(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B7(iv): McKeith IG, Boeve BF, Dickson DW, et al., Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology. 2017 Jul 4;89(1):88-100.

B7(v): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694.

B8. Parkinson Hastalığı'nın tedavisinde antikolinerjik ajan kullanımı uygun değildir (artmış yan etki riski; daha etkin ve daha az yan etkisi olan ilaç seçenekleri var)

B8(i): Spindler MA, Tarsy D.Initial pharmacologic treatment of Parkinson disease. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019.

B8(ii): Cummings JL. Behavioral complications of drug treatment of Parkinson's disease. J Am Geriatr Soc. 1991 Jul;39(7):708-16. Review.

B9. Nöroleptiklerin ekstrapiramidal yan etkilerini tedavi etmek için antikolinerjik ilaç kullanımı uygun değildir (antikolinerjik toksisitesi riski)

B9(i): Heinik J. Effects of trihexyphenidyl on MMSE and CAMCOG scores of medicated elderly patients with schizophrenia. Int Psychogeriatr 1998; 10(1): 103-8.

B9(ii): Drimer T, Shahal B, Barak Y. Effects of discontinuation of long-term anticholinergic treatment in elderly schizophrenia patients. Int ClinPsychopharmacol 2004; 19(1):27-9.

B9(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B9(iv): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694.

B10. Demans hastalarında davranışsal ve psikolojik semptomların giderilmesinde ilaç dışı tedavilerin etkisiz kaldığı ve semptomların ciddi olduğu durumlar hariç nöroleptiklerin/antipsikotiklerin kullanımı uygun değildir (artmış inme, kalp yetersizliği, pnömoni-infeksiyon, ölüm riski)

**Demans hastalarında davranışsal ve psikolojik semptomların giderilmesinde ilaç dışı tedavilerin etkisiz kaldığı ve semptomların ciddi olduğu durumlarda nöroleptikle/antipsikotikler kullanılabilir ancak bu durumda semptom kontrolünü sağlayan en düşük dozda ve en kısa süre ile kullanılmalıdır.*

**Demans hastalarında davranışsal ve psikolojik semptomların giderilmesinde öncelikli yaklaşım optimum demans tedavisinin (ChEi/memantin) verilmesidir. Takiben seçilmiş SSRİ'lar (özellikle sitalopram) denenebilir.*

**Sertralin, trazadon ve melatoninin demans hastalarında davranışsal ve psikolojik semptomların giderilmesinde etkinliği ile ilgili çelişkili bilgiler vardır.*

B10(i): Desmidt T, Hommet C, Camus V. Pharmacological treatments of behavioral and psychological symptoms of dementia in Alzheimer's disease: role of acetylcholinesterase inhibitors and memantine. Geriatr Psychol Neuropsychiatr Vieil. 2016 Sep 1;14(3):300-6. doi: 10.1684/pnv.2016.0621. Review.

B10(ii): Campbell N, Ayub A, Boustani MA, Fox C, Farlow M, Maidment I, Howards R. Impact of cholines-terase inhibitors on behavioral and psychological symptoms of Alzheimer's disease: a meta-analysis. Clin Interv Aging. 2008;3(4):719-28.

B10(iii): Tible OP, Riese F, Savaskan E, von Gunten A. Best practice in the management of behavioural and psychological symptoms of dementia. Ther Adv Neurol Disord. 2017 Aug;10(8):297-309. doi: 10.1177/1756285617712979. Epub 2017 Jun 19. Review.

B10(iv): Press D, Alexander M.Management of neuropsychiatric symptoms of dementia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019.

B10(v): Corbett A, Smith J, Creese B, Ballard C. Treatment of behavioral and psychological symptoms of Alzheimer's disease. Curr Treat Options Neurol. 2012 Apr;14(2):113-25. doi: 10.1007/s11940-012-0166-9.

B10(vi): Whitney M. Buterbaugh, Todd Jamrose, Jonathon Lazzara, Lindsay Honaker, and Christopher J. Thomas (2014) Review of antidepressants in the treatmentof behavioral and psychiatric symptoms in dementia (BPSD)Mental Health Clinician: July 2014, Vol. 4, pp 183-188.

B10(vii): Henry G, Williamson D, Tampi RR. Efficacy and tolerability of antidepressants in the treatment of behavioral and psychological symptoms of dementia, a literature review of evidence. Am J Alzheimers Dis Other Demen. 2011 May;26(3):169-83. doi: 10.1177/1533317511402051. Epub 2011 Mar 23. Review.

B10(viii): Seitz DP, Adunuri N, Gill SS, Gruneir A, Herrmann N, Rochon P. Antidepressantsfor agitation and psychosis in dementia. Cochrane Database Syst Rev. 2011 Feb16;(2):CD008191. doi: 10.1002/14651858.CD008191.pub2. Review.

B10(ix): Hersch EC, Falzgraf S. Management of the behavioral and psychological symptoms of dementia. Clin Interv Aging. 2007;2(4):611-21.

B10(x): Sultzer DL, Gray KF, Gnay I, Berisford MA, Mahler ME. A double-blind comparison of trazodone and haloperidol for treatment of agitation in patients with dementia. Am J Geriatr Psychiatry. 1997 Winter;5(1):60-9.

B10(xi): Pazan F, Weiss C, Wehling M; FORTA. 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 Jan;35(1):61-71.

B10(xii): Martinon-Torres G, Fioravanti M, Grimley EJ. Trazodone for agitation indementia. Cochrane Database Syst Rev. 2004 Oct 18;(4):CD004990. Review.

B10(xiii): Alagiakrishnan K. Melatonin based therapies for delirium and dementia. Discov Med. 2016 May;21(117):363-71. Review.

B10(xiv): De Jonghe A, Korevaar JC, Van Munster BC, De Rooij SE. Effectiveness of melatonin treatment on circadian rhythm disturbances in dementia. Are there implications for delirium? A systematic review. Int J Geriatr Psychiatry 2010; 25(12):1201– 1208.

B10(xv): Jansen SL, Forbes DA, Duncan V, Morgan DG: Melatonin for cognitive impairment. Cochrane Database Syst Rev 2006; Jan 25 (1):CD003802. Review.

B10(xvi): Rabins P, Rovner B, Rummans T, Schneider L, Tariot P. Guideline Watch (October 2014): Practice Guideline for the Treatment of Patients with Alzheimer's Disease and Other Dementias. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/alzheimerwatch.pdf (son erişim tarihi 28 Ekim 2019)

B10(xvii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B11. Nöroleptiklerin/antipsikotiklerin hipnotik amaçlı kullanımı uygun değildir (artmış konfüzyon, hipotansiyon, ekstrapiramidal yan etkiler, düşme riski)

**Yaşlıda insomni tedavisinde öncelikle uyku hijyeni düzenlemesi ve bilişsel davranışcı terapiler uygulanmalıdır.*

**Yaşlıda insomni tedavisinde farmakolojik tedaviye ihtiyaç duyulması halinde melatonin, melatonin reseptor agonisti ramelteon kullanılabilir. Eşlik eden depresyon varsa sedatif etkili antidepresanların (mirtazapin, trazadon, agomelatin) kullanımı değerlendirilebilir.*

B11(i): British National Formulary vol. 76, September 2018-March 2019: p 28.

B11(ii): RD McEvoy, KS Nyfort-Hansen. Sleep disorders in the elderly: the pros and cons of prescribing. In: Prescribing for Elderly Patients, eds. S. Jackson, P. Jansen, A. Mangoni. Wiley-Blackwell 2009, pp 45-52.

B11(iii): Alexopoulos GS, Streim J, Carpenter D, Docherty JP. Expert Consensus Panel for Using Antipsychotic Drugs in Older Patients. Using antipsychotic agents in older patients. J Clin Psychiatry 2004; 65 Suppl 2:5-99; discussion 100-102; quiz 103-4. Review.

B11(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B11(v): Schroeck JL, Ford J, Conway EL, Kurtzhalts KE, Gee ME, Vollmer KA, Mergenhag KA. Review of Safety and Efficacy of Sleep Medicines in Older Adults. Clin Ther. 2016 Nov;38(11):2340-2372.

B12. Parkinsonizm veya Lewy cisimcikli demansı olanlarda nöroleptiklerin/antipsikotiklerin (ketiapin veya klozapin hariç) kullanımı uygun değildir (ağır ekstrapiramidal semptom riski)

B12(i): Mena MA, de Yébenes JG. Drug-induced parkinsonism. Expert Opin Drug Saf 2006; 5(6):759-71. Review.

B12(ii): Eng ML, Welty TE. Management of hallucinations and psychosis in Parkinson's disease. Am J Geriatr Pharmacother 2010; 8(4):316-30. Review.

B12(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B12(iv): McKeith IG, Boeve BF, Dickson DW, Halliday G, Taylor JP, Weintraub D, Aarsland D, Galvin J, Attems J, Ballard CG, Bayston A, Beach TG, Blanc F, Bohnen N, Bonanni L, Bras J, Brundin P, Burn D, Chen-Plotkin A, Duda JE, El-Agnaf O, Feldman H, Ferman TJ, Ffytche D, Fujishiro H, Galasko D, Goldman JG, Gomperts SN, Graff-Radford NR, Honig LS, Iranzo A, Kantarci K, Kaufer D, Kukull W, Lee VMY, Leverenz JB, Lewis S, Lippa C, Lunde A, Masellis M, Masliah E, McLean P, Mollenhauer B, Montine TJ, Moreno E, Mori E, Murray M, O'Brien JT, Orimo S, Postuma RB, Ramaswamy S, Ross OA, Salmon DP, Singleton A, Taylor A, Thomas A, Tiraboschi P, Toledo JB, Trojanowski JQ, Tsuang D, Walker Z, Yamada M, Kosaka K. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology. 2017 Jul 4;89(1):88-100.

B13. Düşme riski yüksek olan hastalarda nöroleptiklerin/ antipsikotiklerin (ekstrapiramidal yan etki), benzodia-zepinlerin (sedasyon, denge bozukluğu) ve Z tipi hipnotiklerin (ör. zopiklon, zolpidem, zaleplon) (gün içerisinde uzamış sedasyona, ataksi) kullanımı uygun değildir

**Genel olarak bu grup ilaçlar yaşlılarda düşme riskini artıran ilaçlardır. Yaşlılarda kullanımından mümkün mertebe kaçınılmalıdır.*

B13(i): Huang AR, Mallet L, Rochefort CM, Eguale T, Buckeridge DL, Tamblyn R. Medication-related falls in the elderly: causative factors and preventive strategies. Drugs Aging 2012; 29(5): 359-76. Review.

B13(ii): Woolcott JC, Richardson KJ, Wiens MO, Patel B, Marin J, Khan KM, Marra CA. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med 2009; 169(21): 1952-60. Review. Erratum in: Arch Intern Med 2010 Mar 8;170(5):477.

B13(iii): Hill KD, Wee R. Psychotropic drug-induced falls in older people: a review of interventions aimed at reducing the problem. Drugs Aging 2012; 29(1): 15-30. Review.

B13(iv): Mets MA, Volkerts ER, Olivier B, Verster JC. Effect of hypnotic drugs on body balance and standing steadiness. Sleep Med Rev 2010; 14(4): 259-67.

B13(v): Shuto H, Imakyure O, Matsumoto J, Egawa T, Jiang Y, Hirakawa M, Kataoka Y, Yanagawa T. Medication use as a risk factor for inpatient falls in an acute care hospital: a case-crossover study. Br J Clin Pharmacol 2010; 69(5): 535-42.

B13(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B14. Benzodiazepin'lerin 4 haftadan uzun süre kullanımı uygun değildir (uzamış sedasyon, konfüzyon, denge bozukluğu, düşme, trafik kazaları riski)

**Genel olarak, yüksek yan etki potansiyelleri nedeniyle, benzodiazepin kullanımından kaçınılmalıdır.*

**Kısa etkili benzodiazepinler klinik endikasyon varlığında dikkatle ve kısa süreli (<4 hafta) kullanılabilir (örn. demans ile ilişkili ajitasyonda lorazepam verilebilir).*

**Seçilmiş hastalarda başka ilaçlarla kontrol altına alınamayan REM uykusu davranış bozukluğu için uzun etkili benzodiazepinlerden klonazepam verilebilir ancak bu durumda da yakın klinik takip edilmelidir.*

**2 hafta ve üzeri kullanılan bütün benzodiazepinler "benzodiazepin geri çekilme sendromuna" yol açmamak için birden değil kademeli azaltılarak kesilmelidir.*

B14(i): Madhusoodanan S, Bogunovic OJ. Safety of benzodiazepines in the geriatric population. Expert Opin Drug Saf 2004; 3(5): 485-93. Review.

B14(ii): Glass J, Lanctôt KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics inolder people with insomnia: meta-analysis of risks and benefits. BMJ 2005; 331(7526): 1169. Review.

B14(iii): Barker MJ, Greenwood KM, Jackson M, Crowe SF. Cognitive effects of long-term benzodiazepine use: a meta-analysis. CNS Drugs 2004; 18(1):37-48.

B14(iv): Model DG, Berry DJ. Effects of chlordiazepoxide in respiratory failure due to chronic bronchitis. Lancet 1974; 2(7885): 869-70.

B14(v): Hak E, Bont J, Hoes AW, Verheij TJ. Prognostic factors for serious morbidity and mortality from community-acquired lower respiratory tract infections among the elderly in primary care. Fam Pract 2005; 22(4): 375-80.

B14(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B14(vii): Kotagal V, Bohnen N I. Parkinson Disease and Related Disorders in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017 page 1431.

B14(viii): British National Formulary vol. 76, September 2018-March 2019: p 28.

B15. Benzodiazepinlerin akut ve kronik solunum yetersizliğinde (PO_2< 60 mmHg ve/veya PCO_2> 50 mmHg) kullanımı uygun değildir (solunum yetersizliğinde artış riski)

B15(i): Model DG, Berry DJ. Effects of chlordiazepoxide in respiratory failure due to chronic bronchitis. Lancet 1974; 2(7885): 869-70.

B15(ii): Hak E, Bont J, Hoes AW, Verheij TJ. Prognostic factors for serious morbidity and mortality from community-acquired lower respiratory tract infections among the elderly in primary care. Fam Pract 2005; 22(4): 375-80.

B15(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B15(iv): Overdyk FJ, Dowling O, Marino J, Qiu J, Chien HL, Erslon M, Morrison N, Harrison B, Dahan A, Gan TJ. Association of Opioids and Sedatives with Increased Risk of In-Hospital Cardiopulmonary Arrest from an Administrative Database. PLoS One. 2016 Feb 25;11(2):e0150214.

B16. Persistan bradikardi (<50/dk), 2. veya 3. derece kalp bloğu veya açıklanamayan senkopu olan hastalarda, uzamış QTc olan hastalarda (kadında> 470 msn, erkekte> 450 msn) ChEi kullanımı uygun değildir (kalp iletim defekti, senkop, yaralanma riski)

**Nabız: 50-60/dk olan ve asemptomatik olan hastalarda ChEi başlanabilir. Tedavi başlangıcı veya doz artırımından 1 hafta sonra nabız sayısı ve semptom açısından kontrol edilmelidir.*

**Eş zamanlı hız kısıtlayıcı ilaç alanlarda nabız< 50/dk değilse ve semptom yok ise, dikkatle kullanılabilir. ChEi'leri LBBB veya AF olan hastalarda dikkatli kullanılmalıdır, hastalar takip edilmelidir.*

**ChEi'leri KOAH veya astımı olan hastalarda dikkatle kullanılmalıdır. Bronkospazmı agreve edebilir, takip edilmelidir.*

**ChEi'leri gastik ülser hikayesi olanlarda ve nonsteroid anti inflamatuar ilaç kullananlarda dikkatle kullanılmalıdır. Bu hastalar gastrointestinal kanama açısından takip edilmelidir.*

B16(i): Salarbaks AM, Boomkamp-Snoeren CM, van Puijenbroek E, Jansen PA, van Marum RJ. [Cardiac effects of cholinesterase inhibitors: a reason for restraint?]. Tijdschr Gerontol Geriatr 2009; 40(2):79-84.

B16(ii): Fisher A.A. and Davis M.W. Prolonged QT interval, syncope, and delirium with galantamine Ann Pharmacother 2008 42; 2: 278-283.

B16(iii): Suleyman T, Tevfik P, Abdulkadir G. and Ozlem S. Complete atrioventricular block and ventricular tachyarrhythmia associated with donepezil. Emerg Med J 2006; 23(8): 641-2.

B16(iv): Bordier P, Lanusse S, Garrigue S, Reynard C, Robert F, Gencel L and Lafitte A. Causes of syncope in patients with Alzheimer's disease treated with donepezil. Drugs Aging 2005; 22(8): 687-694.

B16(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B16(vi): Helou R, Rhalimi M. Cholinesterase inhibitors and the risk of pulmonary disorders in hospitalized dementia patients. J Popul Ther Clin Pharmacol. 2010 Fall;17(3):e379-89. Epub 2010 Oct 26.

B16(vii): Thavorn K, Gomes T, Camacho X, Yao Z, Juurlink D, Mamdani M. Upper gastrointestinal bleeding in elderly adults with dementia receiving cholinesterase inhibitors: a population-based cohort study. J Am Geriatr Soc. 2014 Feb;62(2):382-4.

B16(viii): Rivastigmine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B17. Esansiyel tremor tedavisi için levodopa veya dopamin agonistlerinin kullanımı uygun değildir (kanıtlanmış etkinliği yoktur)

B17(i): Zesiewicz TA, Elble RJ, Louis ED, Gronseth GS, Ondo WG, Dewey RB Jr, Okun MS, Sullivan KL, Weiner WJ. Evidence-based guideline update- treatment of essential tremor-report of the Quality Standards sub-committee of the American Academy of Neurology. Neurology 2011; 77(19):1752-5. Review.

B17(ii): Deuschl G, Raethjen J, Hellriegel H, Elble R. Treatment of patients with essential tremor. Lancet Neurol 2011; 10(2): 148-61. Review.

B17(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B18. Vertigo tedavisinde betahistin, trimetazidin, dimenhidrinat gibi ilaçların aralıksız ve uzun süreli olarak kullanımı uygun değildir (kanıta dayalı faydalı etkilerinin olmaması)

B18(i): FurmanJM, Barton JJS.Treatment of vertigo. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 28 Ekim 2019.

B18(ii): Aman Nanda, Richard W. Besdine. Dizziness in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017 page 1086.

#B19. Sinnarizin kullanımı uygun değildir (ekstrapiramidal yan etkiler, sınırlı faydalanım)

B19(i): Shin HW. Drug-induced parkinsonism. J Clin Neurol. 2012 Mar;8(1):15-21.

B20. Pirasetam kullanımı miyoklonik konvülzüyon tedavisi dışında uygun değildir (kanıtlanmış klinik etkinlik yok, maliyet yükü ve yan etki potansiyeli nedeniyle)

**Pirasetam tedavisinden semptomatik fayda görüldüğüne inanılan hastalarda, kar-zarar dengesi göz önünde bulundurularak kullanılabilir.*

**Pirasetamın inme sonrası akut afazi tedavisinde sınırlı yararı olabileceğine dair çalışmalar mevcuttur.*

B20(i): Piracetam for Aphasia in Post-stroke Patients: A Systematic Review and Meta-analysis of Randomized Controlled Trials. CNS Drugs. 2016 Jul;30(7):575-87.

B20(ii): Wright CB. Treatment and prevention of vascular dementia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 28 Ekim 2019.

B20(iii): Flicker L, Grimley Evans G. Piracetam for dementia or cognitive impairment. Cochrane Database Syst Rev. 2001;(2):CD001011. Review.

B21. Epilepsinin kronik tedavisinde karbamazepin, fenitoin, fenobarbital veya valproat'ın ilk basamakta kullanımı uygun değildir (vitamin D üzerine olumsuz etkileri, enzim indüksiyonu, düşme riski nedeniyle; ayrıca daha güvenli alternatifleri var)

**Yaşlılarda kronik epilepsi tedavisinde levatiresetam, lamotrijin, gabapentin gibi yeni ajanlar tercih edilebilir.*

B21(i): Snih T. Seizures and epilepsy in older adults: Treatment and prognosis. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019.

B21(ii): Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk associated with use of antiepileptic drugs. Epilepsia. 2004 Nov;45(11):1330-7.

B21(iii): Vestergaard P, Tigaran S, Rejnmark L, Tigaran C, Dam M, Mosekilde L. Fracture risk is increased in epilepsy. Acta Neurol Scand. 1999 May;99(5):269-75.

B21(iv): Koppel BS, Harden CL, Nikolov BG, Labar DR. An analysis of lifetime fractures in women with epilepsy. Acta Neurol Scand. 2005 Apr;111(4):225-8.

B21(v): Nakken KO, Sætre E, Markhus R, Lossius MI. [Epilepsy in the elderly]. Tidsskr Nor Laegeforen. 2013 Mar 5;133(5):528-31.

B22. Epilepsi hastalarında tramadol, nöroleptikler/antipsikotikler (klozapin, olanzapin, klorpromazin, tioridazin), bupropion ve maprotilin kullanımı uygun değildir.

B22(i): By the American Geriatrics Society 2015 Beers Criteria Update Expert Panel.American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015 Nov;63(11):2227-46.

B22(ii): Habibi M, Hart F, Bainbridge J. The Impact of Psychoactive Drugs on Seizures and Antiepileptic Drugs. Curr Neurol Neurosci Rep. 2016 Aug;16(8):71.

B23. Öncesinde konvülzüyon geçirmemiş bir hastada iskemik/hemorajik inme varlığı nedeniyle nöbet proflaksisi için antiepileptik tedavi kullanımı uygun değildir

B23(i): Hemphill JC 3rd, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, Fung GL, Goldstein JN, Macdonald L, Mitchell PH, Scott PA, Selim MH, Woo D; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2015Jul;46(7):2032-60.

B23(ii): Adams HP Jr, del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, Grubb RL,Higashida RT, Jauch EC, Kidwell C, Lyden PD, Morgenstern LB, Qureshi AI,Rosenwasser RH, Scott PA, Wijdicks EF; American Heart Association/American StrokeAssociation Stroke Council; American Heart Association/American Stroke-Association Clinical Cardiology Council; American Heart Association/AmericanStroke Association Cardiovascular Radiology and Intervention Council;Atherosclerotic Peripheral Vascular Disease Working Group; Quality of CareOutcomes in Research Interdisciplinary Working Group. Guidelines for the earlymanagement of adults with ischemic stroke: a guideline from the American HeartAssociation/American Stroke Association Stroke Council, Clinical CardiologyCouncil, Cardiovascular Radiology and Intervention Council, and theAtherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes inResearch Interdisciplinary Working Groups: The American Academy of Neurologyaffirms the value of this guideline as an educational tool for neurologists. Circulation. 2007 May 22;115(20):e478-534.

B24. Yaşlılarda sitalopram'ın 20 mg/gün, essitalopram'ın 10 mg/gün üzerindeki dozlarda kullanımı uygun değildir (QTc uzama riski nedeniyle)

B24(i): Citalopram: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B24(ii): U.S. Food and Drug Administration. Escitalopram: Highlights Of Prescribing Information by FDA. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021323s047lbl.pdf (son erişim tarihi 28 Ekim 2019.)

B24(iii): October November reports of the European Pharmacovigilance Working Party. Drug Safety Update Vol 5 Issue 5, Dec 2011: A1.

C: Gastrointestinal Sistem Kriterleri

C1. NSAİİ'lerin OAK'lar (vitamin K antagonistleri, direkt trombin inhibitörleri, faktor Xa inhibitörleri) ile birlikte kullanımı uygun değildir (GİS kanama riski)

C1(i): Knijff-Dutmer EA, Van der Palen J, Schut G, Van de Laar MA. The influence of cyclooxygenase specificity of non-steroidal anti-inflammatory drugs on bleeding complications in concomitant coumarine users. QJM 2003; 96(7):513-20.

C1(ii): Peng S, Duggan A. Gastrointestinal adverse effects of non-steroidal anti-inflammatory drugs. Expert Opin Drug Saf 2005; 4(2):157-69. Review.

C1(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

C1(iv): Solomon DH. Nonselective NSAIDs: Overview of adverse effects.In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 28 Ekim 2019.

C1(v): Melcarne L, García-Iglesias P, Calvet X. Management of NSAID-associated peptic ulcer disease. Expert Rev Gastroenterol Hepatol. 2016 Jun;10(6):723-33.

C1(vi): Chinese Rheumatism Data Center; Chinese Systemic Lupus Erythematosus Treatment and Research Group. [Recommendation for the prevention and treatment of non-steroidal anti-inflammatory drug-induced gastrointestinal ulcers and its complications]. Zhonghua Nei Ke Za Zhi. 2017 Jan 1;56(1):81-85.

C1(vii): Masclee GM, Valkhoff VE, Coloma PM, de Ridder M, Romio S, Schuemie MJ, Herings R, Gini R, Mazzaglia G, Picelli G, Scotti L, Pedersen L, Kuipers EJ, van der Lei J, Sturkenboom MC. Risk of upper gastrointestinal bleeding from different drug combinations. Gastroenterology. 2014 Oct;147(4):784-792.e9; quiz e13-4.

C2. Aspirin, klopidogrel, NSAİİ veya steroidlerin; ülser öyküsü olan hastalarda, ek antiplatelet tedavi alan hastalarda, eş zamanlı antikoagülan alan hastalarda, steroid kullanan hastalarda, dispepsi-GÖR semptomları olan hastalarda PPİ verilmeden kullanımı uygun değildir

**Profilaksi amacıyla PPİ kullanımında önerilen PPİ dozu, günde 1 kez tercih edilen PPİ'nin piyasadaki yüksek dozudur.*

**Dispepsi dışındaki komorbid durumlarda, PPİ'nin yüksek dozu ile devam etmek uygundur.*

**Yukarıdaki ilaçların kullanımına eşlik eden dispepsi varlığı nedeniyle PPİ endikasyonu olan olgularda bir süre PPİ yüksek dozu kullanılarak takipte hastanın semptomlarının tekrarlamadığı en düşük PPİ dozuna düşülmesi uygun olabilir.*

**Kronik NSAİİ kullanan yaşlılarda PPİ kullanımı gereklidir. NSAİİ'lerin yaşlıda kronik kullanımlarında, yukarıdaki eşlik eden risk faktörleri olmasa dahi, PPİ/misoprostol verilmelidir.*

**Kısa süreli NSAİİ kullanan yaşlılarda, yukarıdaki risk faktörleri olmasa bile eş zamanlı PPİ vermek uygun olabilir.*

**Tek başına antiagregan dozda aspirin veya klopidogrel kullanan yaşlılarda, yukarıdaki risk faktörlerinin hiçbiri yoksa, PPİ kullanımına muhtemelen gerek yoktur.*

**PPİ'ların klopidogrel ile birlikte kullanıldığında etkinliğinin azaldığına dair çalışmalar mevcuttur. Ancak bu konuda net bir öneri yapılamamaktadır.*

**Varfarin kullanan hastalarda PPİ kullanım endikasyonu varsa omeprazol dışındaki bir PPİ tercih edilmelidir (omeprazol varfarin düzeyini artırır).*

**PPİ tedavisi yerine misoprostol veya yüksek doz H2 reseptör blokerleri de tercih edilebilir.*

C2(i): Lanza FL, Chan FK, Quigley EM; Practice Parameters Committee of the American College of Gastroenterology. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol 2009; 104(3):728-38.

C2(ii): Nardulli G, Lanas A. Risk of gastrointestinal bleeding with aspirin and platelet antiaggregants. Gastroenterol Hepatol 2009; 32(1):36-43. Review.

C2(iii): Zullo A, Hassan C, Campo SM, Morini S. Bleeding peptic ulcer in the elderly-risk factors and prevention strategies. Drugs Aging 2007; 24(10): 815-28. Review.

C2(iv): Abraham NS, Hlatky MA, Antman EM, Bhatt DL, Bjorkman DJ, Clark CB, Furberg CD, Johnson DA, Kahi CJ, Laine L, Mahaffey KW, Quigley EM, Scheiman J, Sperling LS, Tomaselli GF; ACCF/ACG/AHA. ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitors and thienopyridines: a focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastro-intestinal risks of antiplatelet therapy and NSAID use. Am J Gastroenterol. 2010 Dec;105(12):2533-49. doi: 10.1038/ajg.2010.445. Review.

C2(v): Vaduganathan M, Cannon CP, Cryer BL, Liu Y, Hsieh WH, Doros G, Cohen M, Lanas A, Schnitzer TJ, Shook TL, Lapuerta P, Goldsmith MA, Laine L, Bhatt DL; COGENT Investigators. Efficacy and Safety of Proton-Pump Inhibitors in High-Risk Cardiovascular Subsets of the COGENT Trial. Am J Med. 2016 Sep;129(9):1002-5.

C2(vi): Vaduganathan M, Bhatt DL, Cryer BL, Liu Y, Hsieh WH, Doros G, Cohen M, Lanas A, Schnitzer TJ, Shook TL, Lapuerta P, Goldsmith MA, Laine L, Cannon CP; COGENT Investigators.

Proton-Pump Inhibitors Reduce Gastrointestinal Events Regardless of Aspirin Dose in Patients Requiring Dual Antiplatelet Therapy. J Am Coll Cardiol. 2016 Apr 12;67(14):1661-71.

C2(vii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

C2(viii): Feldman M, Das S.NSAIDs (including aspirin): Primary prevention of gastroduodenal toxicity. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 28 Ekim 2019.

C2(ix): Bundhun PK, Teeluck AR, Bhurtu A, Huang WQ. Is the concomitant use of clopidogrel and Proton Pump Inhibitors still associated with increased adverse cardiovascular outcomes following coronary angioplasty?: a systematic review and meta-analysis of recently published studies (2012 - 2016). BMC Cardiovasc Disord. 2017 Jan 5;17(1):3. doi: 10.1186/s12872-016-0453-6. Review.

C2(x): Celebi A, Yilmaz H. When proton pump inhibitors are compared, are there specific cases in which a certain proton pump inhibitors should be particularly preferred? Turk J Gastroenterol. 2017 Dec;28(Suppl 1):S68-S70. doi: 10.5152/tjg.2017.17.

C2(xi): Sutfin T, Balmer K, Boström H, Eriksson S, Höglund P, Paulsen O. Stereoselective interaction of omeprazole with warfarin in healthy men. Ther Drug Monit. 1989;11(2):176-84.

C2(xii): Satoh K, Yoshino J, Akamatsu T, Itoh T, Kato M, Kamada T, Takagi A, Chiba T,Nomura S, Mizokami Y, Murakami K, Sakamoto C, Hiraishi H, Ichinose M, Uemura N,Goto H, Joh T, Miwa H, Sugano K, Shimosegawa T. Evidence-based clinical practice guidelines for peptic ulcer disease 2015. J Gastroenterol. 2016 Mar;51(3):177-94.

C2(xiii): British National Formulary vol. 76, September 2018-March 2019: p 1385.

#C3. Aspirin veya NSAİİ'lerin; peptik ülser (komplike veya komplike olmayan, gastrik veya duodenal) hikayesi olan hastalarda Helicobacter pylori testi yapılmadan kronik kullanım için başlanması uygun değildir

**H. pylori (+) saptanırsa eradikasyon tedavisi verilmelidir.*

**Hasta bir süredir aspirin/NSAİİ alıyorsa, H. pylori eradikasyon tedavisinden beklenen faydalanım azdır fakat pratikte taranıp pozitif saptanması halinde genellikle eradikasyon uygulanması tercih edilmektedir.*

**H. pylori prevalansı yüksek olan popülasyonlarda, anamnezde peptik ülser hikayesi olmayan olgularda da aspirin/NSAİİ kronik kullanımı başlanmadan önce, H. pylori için "test-tedavi" yaklaşımı uygun olabilir.*

**Klopidogrel kronik kullanımı başlanacak hastalarda; anamnezde peptik ülser (komplike veya komplike olmayan, gastrik veya duodenal) hikayesi olsa dahi, H. pylori testi yapılması ve/veya H. pylori eradikasyon tedavisi uygulanması önerilmemektedir (teorik veya pratik uygulama).*

C3(i): Feldman M, Das S. NSAIDs (including aspirin): Primary prevention of gastroduodenal toxicity. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 28 Ekim 2019.

C3(ii): Yazıcı A, Akyuz F, Issever H, Pinarbasi B, Demir K, Ozdil S, Besisik F, Boztas G, Mungan ZA, Kaymakoğlu S, Peptic ulcer disease: Whay did change in Turkey? Gastroenterology 2008;134(4):A328-329.

C3(iii): Malfertheiner P, Megraud F, O'Morain CA, Atherton J, Axon AT, Bazzoli F, Gensini GF, Gisbert JP, Graham DY, Rokkas T, El-Omar EM, Kuipers EJ; European Helicobacter Study Group. Management of Helicobacter pylori infection—the Maastricht IV/ Florence Consensus Report. Gut. 2012 May;61(5):646-64.

C3(iv): Kocazeybek B, Tokman HB. Prevalence of Primary Antimicrobial Resistance of H. pylori in Turkey: A Systematic Review. Helicobacter. 2016 Aug;21(4):251-60. doi: 10.1111/hel.12272. Epub 2015 Sep 23.

C3(v): Thung I, Aramin H, Vavinskaya V, Gupta S, Park JY, Crowe SE, Valasek MA. Review article: the global emergence of Helicobacter pylori antibiotic resistance. Aliment Pharmacol Ther. 2016 Feb;43(4):514-33. doi: 10.1111/apt.13497. Epub 2015 Dec 23. Review.

C4. PPİ'ların komplike olmayan peptik ülser veya erozif peptik özofajit tedavisinde tam terapötik dozda 8-12 haftadan uzun süreli kullanımı uygun değildir (doz azaltımı veya daha kısa sürede kesme endikasyonu vardır)

**8-12 haftalık terapötik doz süresi, H. pylori eradikasyonu için verilen PPİ tedavi süresini içermemektedir.*

**Kesilme döneminde rebound etkiden kaçınmak için PPİ'lerin azaltılarak kesilmesi uygundur. (örneğin 1 hafta yarı doz, 1 hafta günaşırı doz, sonrasında kesilmesi gibi)*

C4(i): British National Formulary vol. 76, September 2018-March 2019: p 78-83.

C4(ii): Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. Clinical guideline. Published: 3 September 2014.Available at:www.nice.org.uk/guidance/cg184 Son erişim tarihi 29 Ekim 2019.

C4(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

C5. Çoklu ilaç kullanımı nedeniyle PPİ kullanımı uygun değildir (faydası yok, potansiyel zararı var)

*PPİ kullanım endikasyonları arasında "çoklu ilaç kullanımı" şeklinde bir endikasyon yoktur. Öte yandan kronik PPİ kullanımı kronik böbrek yetersizliği, fraktürler, demans riskinde artış, C. difficile infeksiyonu sıklığında artış, vitamin B12 eksikliği, hipomagnezemi, enterik infeksiyonlar-bakteriyel aşırı gelişimi için risk faktörüdür.

C5(i): Xie Y. et al. Proton Pump Inhibitors and Risk of Incident CKD and Progression to ESRD. J Am Soc Nephrol.2016 Oct;27(10):3153-3163.

C5(ii): Lazarus B. et al. Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease. JAMA Intern Med. 2016 Feb;176(2):238-46.;

C5(iii): Gomm W. et al. Association of Proton Pump Inhibitors With Risk of Dementia: A Pharmacoepidemiological Claims Data Analysis. JAMA Neurol. 2016 Apr;73(4):410-6.

C5(iv): Cai D, Feng W, Jiang Q. Acid-suppressive medications and risk of fracture: an updated meta-analysis. Int J Clin Exp Med. 2015 Jun 15;8(6):8893-904. eCollection 2015.

C5(v): Trifan A, Stanciu C, Girleanu I, Stoica OC, Singeap AM, Maxim R, Chiriac SA, Ciobica A, Boiculese L. Proton pump inhibitors therapy and risk of Clostridium difficile infection: Systematic review and meta-analysis. World J Gastroenterol. 2017 Sep 21;23(35):6500-6515. doi: 10.3748/wjg.v23.i35.6500. Review.

C5(vi): Scarpignato C, Gatta L, Zullo A, Blandizzi C; SIF-AIGO-FIMMG Group; Italian Society of Pharmacology, the Italian Association of Hospital Gastroenterologists, and the Italian Federation of General Practitioners. Effective and safe proton pump inhibitor therapy in acidrelated diseases - A position paper addressing benefits and potential harms of acid suppression. BMC Med. 2016 Nov 9;14(1):179. Review.

C6. Antikolinerjik etkili GİS antispazmotiklerinin (örn. hiyosiyamin) kullanımı uygun değildir [yaşlıda artmış antikolinerjik yan etki (sersemlik, bilişsel kabiliyetlerde azalma, görme bulanıklığı, aritmi, şişkinlik-konstipasyon) ve sınırlı faydalanım]

C6(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

C6(ii): Hyoscyamine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

C6(iii): Wald A.Treatment of irritable bowel syndrome in adults. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019.

C7. Kronik konstipasyonu olan hastalarda, bu yan etkiye sahip olmayan alternatifleri varsa, konstipasyona sebep olma ihtimali yüksek olan ilaçların (yüksek antikolinerjik etkili ilaçlar, oral demir, opioidler, verapamil, alüminyum antiasitleri) kullanımı uygun değildir (konstipasyonda artış riski)

**Verapamil dışındaki diğer kalsiyum kanal blokeri antihipertansifler de konstipasyona sebep olabilir. Ancak bu etki sırasıyla verapamil ve nifedipinde daha belirgindir.*

C7(i): Meek PD, Evang SD, Tadrous M, Roux-Lirange D, Triller DM, Gumustop B. Overactive bladder drugs and constipation: a meta-analysis of randomized, placebo-controlled trials. Dig Dis Sci 2011; 56(1): 7-18. Review.

C7(ii): Müller-Lissner S. General geriatrics and gastroenterology: constipation and faecal incontinence. Best Pract Res Clin Gastroenterol 2002; 16(1): 115-33. Review.

C7(iii): Harari D, Gurwitz JH, Avorn J, Choodnovskiy I, Minaker KL. Correlates of regular laxative use by frail elderly persons. Am J Med 1995; 99(5): 513-8.

C7(iv): Opie LH. Choosing the correct drug for the individual hypertensive patient. Drugs 1992; 44 Suppl 1: 147-55. Review.

C7(v): Opie LH. Calcium channel antagonists. Part IV: Side effects and contraindications drug interactions and combinations. Cardiovasc Drugs Ther. 1988 Jul;2(2):177-89. Review.

C**7(vi):** Russell RP. Side effects of calcium channel blockers. Hypertension. 1988 Mar;11(3 Pt 2):II42-4. Review.

C7(vii): Poole-Wilson PA, Kirwan BA, Vokó Z, de Brouwer S, van Dalen FJ, Lubsen J; ACTION Investigators. Safety of nifedipine GITS in stable angina: the ACTION trial. Cardiovasc Drugs Ther. 2006 Feb;20(1):45-54.

C7(viii): Acosta A, Tangalos E G, Harari D. Constipation in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017. Page 1956.

C7(ix): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

C7(x): Bulpitt CJ, Connor M, Schulte M, Fletcher AE. Bisoprolol and nifedipine retard in elderly hypertensive patients: effect on quality of life. J Hum Hypertens. 2000 Mar;14(3):205-12.

C7(xi): Elliott WJ, Ram CV. Calcium channel blockers. J Clin Hypertens (Greenwich).2011 Sep;13(9):687-9.

C8. Yaşlılarda antiemetik tedavide ilk basamakta metoklopramid veya trimetobenzamid kullanımı uygun değildir (ekstrapiramidal yan etki, huzursuzluk yan etkisi nedeniyle)

**Antiemetik olarak serotonin 5HT3 reseptor antagonist'leri yaşlılarda en güvenilir ajanlardır.*

**Metoklopramid ve trimetobenzamid parkinsonizm olan hastalarda kontrendikedir.*

C8(i): Glare P, Miller J, Nikolova T, Tickoo R. Treating nausea and vomiting in palliative care: a review. Clin Interv Aging. 2011;6:243-59. doi: 10.2147/CIA.S13109. Epub 2011 Sep 12. Review.

C8(ii): Stephen PJ, Williamson J. Drug-induced parkinsonism in the elderly. Lancet 1984; 2(8411): 1082-3.

C8(iii): Ganzini L, Casey DE, Hoffman WF, McCall AL. The prevalence of metoclopramide-induced tardive dyskinesia and acute extrapyramidal movement disorders. Arch Intern Med 1993; 153(12): 1469-75.

C8(iv): Pasricha PJ, Pehlivanov N, Sugumar A, Jankovic J. Drug Insight: from disturbed motility to disordered movement - a review of the clinical benefits and medicolegal risks of metoclopramide. Nat Clin Pract Gastroenterol Hepatol 2006; 3(3): 138-48. Review.

C8(v): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

C8(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

C9. GFR< 30 mL/dk/1,73 m^2 olan hastalarda laksatif veya antiasit olarak magnezyum preperatlarının kullanımı uygun değildir (hipermagnezemi riski)

C9(i): Yu ASL, Gupta A.Causes, symptoms, and treatment of hypermagnesemia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

C9(ii): Navarro-González JF, Mora-Fernández C, García-Pérez J. Clinical implications of disordered magnesium homeostasis in chronic renal failure and dialysis. Semin Dial. 2009 Jan-Feb;22(1):37-44. doi: 10.1111/j.1525-139X.2008.00530.x. Review.

C9(iii): Rao SSC. Constipation in the older adult. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

C9(iv): Magnesium hydroxide: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

C9(v): Magnesium carbonate: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

D: Solunum Sistemi Kriterleri

D1. Dar açılı glokom veya üriner çıkış yolu obstrüksiyonu olan hastalarda antimuskarinik bronkodilatör ilaçların (ipratropium, tiotropium) kullanımı uygun değildir (glokomda kötüleşme ve üriner retansiyon riski)

**Benign prostat hiperplazisine eşlik eden obstrüktif LUTS semptomları (alt üriner traktus semptomları) yaşlı erkeklerde sıktır. Hafif düzeyde obstrüktif semptomu olan olgularda klinisyen yakın klinik takip ile antimuskarinik bronkodilatör ilaçları kullanabilir. Üriner retansiyon yan etkisi açışından PMR >150 mL olan olgular özellikle risklidir (>150 mL olan olgularda kullanılması uygun değildir).*

D1(i): Gupta P, O'Mahony MS. Potential adverse effects of bronchodilators in the treatment of airways obstruction in older people: recommendations for prescribing. Drugs Aging 2008; 25(5): 415-43. Review.

D1(ii): Oba Y, Zaza T, Thameem DM. Safety, tolerability and risk benefit analysis of tiotropium in COPD. Int J Chron Obstruct Pulmon Dis 2008; 3(4): 575-84. Review.

D1(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

D1(iv): Ah-Kee EY, Egong E, Shafi A, Lim LT, Yim JL. A review of drug-induced acute angle closure glaucoma for non-ophthalmologists. Qatar Med J. 2015 May 10;2015(1):6. doi: 10.5339/qmj.2015.6. eCollection 2015. Review.

D1(v): Vande Griend JP, Linnebur SA. Inhaled anticholinergic agents and acute urinary retention in men with lower urinary tract symptoms or benign prostatic hyperplasia. Ann Pharmacother. 2012 Sep;46(9):1245-9. doi: 10.1345/aph.1R282. Epub 2012 Jul 31. Review.

D1(vi): Carlos Andrés Celis Preciado, Horacio Giraldo, Dario Londoño, Ingrid Rodriguez. Glaucoma risk due to antimuscarinics, not a class effect: A systematic review. European Respiratory Journal 2016 48: PA4069.

D1(vii): British National Formulary vol. 76, September 2018-March 2019: p 247.

D1(viii): Hashimoto M, Hashimoto K, Ando F, Kimura Y, Nagase K, Arai K. Prescription rate of medications potentially contributing to lower urinary tract symptoms and detection of adverse reactions by prescription sequence symmetry analysis. J Pharm Health Care Sci. 2015 Feb 15;1:7.

D2. KOAH'ın veya astım bronşialenin idame tedavisinde teofilin kullanımı uygun değildir (dar terapötik indeks ve yaşlıda yüksek insomni, aritmi riski nedeniyle)

D2(i): Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, Fukuchi Y, Jenkins C, Rodriguez-Roisin R, van Weel C, Zielinski J; Global Initiative for Chronic Obstructive Lung Disease. Global strategy ort he diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007; 176(6): 532-55. Review.

D2(ii): Ramsdell J. Use of theophylline in the treatment of COPD. Chest 1995; 107(5 Suppl): 206S-209S. Review.

D2(iii): Fragoso CAV. Diagnosis and management of asthma in older adults. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

D2(iv): 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 Mar;44(2):213-8. Doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

D2(v): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694. Doi: 10.1111/jgs.15767.

D3. Orta-ağır KOAH'ta idame tedavi için inhaler kortikosteroid yerine sistemik kortikosteroid kullanımı uygun değildir (sistemik kortikosteroidlerine uzun süre gereksiz maruziyet; etkin inhale tedaviler mevcut)

D3(i): Hess MW. The 2017 Global Initiative for Chronic Obstructive Lung Disease Report and Practice Implications ort he Respiratory Therapist. Respir Care. 2017 Nov;62(11):1492-1500.

D3(ii): Wood-Baker R, Walters J, Walters EH. Systemic corticosteroids in chronic obstructive pulmonary disease: an overview of Cochrane systematic reviews. Respir Med 2007; 101(3): 371-7. Review.

D3(iii): 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 Mar;44(2):213-8. Doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E: Kas İskelet Sistemi Kriterleri ve Analjezik İlaçlar

E1. NSAİİ'lerin, alternatif tedavi varken, 3 aydan uzun süreli kullanımı uygun değildir

**Osteoartrit ağrısında ve basit ağrılarda (kas-iskelet sistemi, baş ağrısı vb.) öncelikle parasetamol tedavisi uygulanmalıdır (parasetamol tedavisinin metamizol, düşük doz kodein/ tramadol ile kombinasyonu düşünülebilir).*

**NSAİİ kullanılan olgular yan etkileri açısından (nefropati, HT, kalp yetersizliği, KV olay) yakın klinik takip edilmelidir.*

**NSAİİ kullanılması durumunda indometasin tercih edilmemelidir (yaşlıda diğer NSAİİ'lere kıyasla daha fazla MSS ve diğer sistem yan etkileri)*

**Kronik NSAİİ kullanımı gereken durumlarda NSAİİ'lere ek olarak PPİ/misoprostol kullanılmalıdır.*

E1(i): Nikles CJ, Yelland M, Del Mar C, Wilkinson D. The role of paracetamol in chronic pain: an evidence-based approach. Am J Ther 2005; 12(1): 80-91. Review.

E1(ii): Seed SM, Dunican KC, Lynch AM. Osteoarthritis: a review of treatment options. Geriatrics 2009; 64(10): 20-9. Review.

E1(iii): Jawad AS. Analgesics and osteoarthritis: are treatment guidelines reflected in clinical practice? Am J Ther 2005; 12(1): 98-103. Review.

E1(iv): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

E1(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E2. NSAİİ'lerin GFR< 50 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir (renal fonksiyonlarda kötüleşme riski)

E2(i): Harirforoosh S, Jamali F. Renal adverse effects of non-steroidal anti-inflammatory drugs. Expert Opin Drug Saf 2009; 8(6): 669-81. Review.

E2(ii): Cheng HF, Harris RC. Renal effects of non-steroidal anti-inflammatory drugs and selective cyclooxyge-nase-2 inhibitors. Curr Pharm Des 2005; 11(14): 1795-804. Review.

E2(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E3. Osteoartrit tedavisinde sistemik steroid kullanımı uygun değildir (sistemik kortikosteroidler ile yan etki riski)

E3(i): British National Formulary vol. 76, September 2018-March 2019: p 1058.

E3(ii): Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum 2000; 43(9): 1905-15.

E3(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E4. Romatoid artritte 3 aydan uzun süreli kortikosteroid monoterapisi kullanımı uygun değildir (sistemik kortikosteroidler ile yan etki riski)

E4(i): Onishi S, Iwmoto M, Minota S. Management of elderly-onset rheumatoid arthritis. J Clin Immunol 2010; 33(1): 1-7.

E4(ii): American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 Update. Arthritis Rheum 2002; 46(2): 28-46.

E4(iii): Soubrier M, Mathieu S, Payet S, Dubost JJ, Ristori JM. Elderlyonset rheumatoid arthritis. Joint Bone Spine 2010; 77(4): 290-6. Review.

E4(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E4(v): Burmester GR, Pope JE. Novel treatment strategies in rheumatoid arthritis. Lancet. 2017 Jun 10;389(10086):2338-2348.

E4(vi): Roubille C, Richer V, Starnino T, McCourt C, McFarlane A, Fleming P, Siu S, Kraft J, Lynde C, Pope J, Gulliver W, Keeling S, Dutz J, Bessette L, Bissonnette R, Haraoui B. The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis. Ann Rheum Dis. 2015 Mar;74(3):480-9.

E5. Gut Hastalığı'nın kronik tedavisi için ksantin oksidaz inhibitörleri (örn. allopurinol, febuksostat) kullanımının kontrendike olmadığı durumlarda, uzun süreli NSAİİ veya kolşisin kullanımı uygun değildir (gut hastalığının profilaksisinde ksantin oksidaz inhibitörleri ilk seçenek ilaçlardır)

E5(i): De Leonardis F, Govoni M, Colina M, Bruschi M, Trotta F. Elderly-onset gout: a review. Rheumatol Int 2007; 28(1): 1-6. Review.

E5(ii): Hoskison KT, Wortmann RL. Management of gout in older adults: barriers to optimal control. Drugs Aging 2007; 24(1): 21-36. Review.

E5(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E5(iv): British National Formulary vol. 76, September 2018-March 2019: p 1085-87.

E6. Kolşisin'in GFR< 10 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir (kolşisin toksisitesi riski)

E6(i): Hoskison KT, Wortmann RL. Management of gout in older adults: barriers to optimal control. Drugs Aging 2007; 24(1): 21-36. Review.

E6(ii): Hanlon JT, Aspinall SL, Semla TP, Weisbord SD, Fried LF, Good CB, Fine MJ, Stone RA, Pugh MJ, Rossi MI, Handler SM. Consensus guidelines for oral dosing of primarily renally cleared medications in older adults. J Am Geriatr Soc 2009; 57(2):335-40. Erratum in: J Am Geriatr Soc 2009; 57(11): 2179. Dosage error in article text.

E6(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E6(iv): BritishNational Formulary vol. 76, September 2018-March 2019: p 1085-86.

E7. Metotreksat'ın GFR< 30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir

E7(i): Seyffart's Directory of Drug Dosage in Kidney Disease; (1st ed., 2011) by GünterSeyffart Publisher: Dustri-Verlag Dr. Karl Feistle GmbH & Co. KG, Munich-Orlando; pp: 476-477.

E7(ii): Methotrexate: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

E8. Ağrı tedavisinde meperidin kullanımı uygun değildir (diğer opioidlere göre artmış nörotoksisite, deliryum riski; daha güvenilir alternatifleri var. Özellikle böbrek yetersizliği varlığında kullanımı risklidir)

E8(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

E8(ii): Meperidine (pethidine): Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

E9. Uzamış salınımlı tramadol'ün GFR< 30 mL/dk/1,7 m^2 olan hastalarda kullanımı uygun değildir

**Hızlı salınımlı tramadol için doz azaltımı yapılmalıdır.*

E9(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated

AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

E9(ii): Tramadol: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

E10. Opioidlerin kronik kullanımda eş zamanlı laksatif verilmeden kullanımı uygun değildir (ciddi konstipasyon riski)

E10(i): Forman WB. Opioid analgesic drugs in the elderly. Clin Geriatr Med 1996; 12(3): 489-500. Review.

E10(ii): Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. Pain 2004; 112(3): 372-80.

E10(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E10(iv): Galicia-Castillo MC, Weiner DK. Treatment of persistent pain in older adults. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019.

E11. Kas iskelet sistemi ağrıları için sistemik kas gevşetici (iskelet kası) ajanların (tiyokolşikosid, tizanidin, klorzoksazon, karisoprodol, klorfenezin karbamat, siklobenzaprin, metaksalon, metokarbamol ve orfenadrin vb.) kullanımı uygun değildir (sedasyon, sersemlik, baş dönmesi, ağız kuruluğu, konstipasyon, bilişsel yan etkileri nedeniyle)

**Tizanidin ile hipotansiyon riski de çok belirgindir.*

E11(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

E11(ii): A.R Umarkar, S.R Bavaskar and P.N.Yewale. Thiocolchicoside as muscle relaxant: a review; International Journal of Pharmacy and Biological Sciences (eISSN: 2230-7605). Volume 1, Issue 3, JULY-SEPT, 2011;364-371.Available at: https://www.ijpbs.com/ijpbsadmin/upload/ijpbs_50c8471a463c9.pdf son erişim tarihi 28 Ekim 2019.

E11(iii): Thiocolchicoside: review of adverse effects. Prescrire Int. 2016; Feb;25(168):41-3

E11(iv): Tizanidine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

#E12. Osteomalazi tanısı dışlanmadan osteoporoz tedavisi başlanması uygun değildir

E12(i): Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R; National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014 Oct;25(10):2359-81.

E13. Vitamin D 'idame' tedavisinde, aralıklı olarak yüksek dozda (300.000 İÜ) konvansiyonel vitamin D kullanımı uygun değildir (artmış düşme riski, kas-iskelet sistemi üzerine ek faydasının olmaması)

**"İdame" tedavide kullanılan yüksek doz konvansiyonel vitamin D'nin olumsuz sonuçları gösterilmiştir.*

**"Replasman" tedavisinde kullanılan yüksek doz konvansiyonel vitamin D ile ilişkili olumsuz sonuçlar bildirilmemiştir. Bununla birlikte, yaşlıda ilaç kullanımında genel geçerliliği olan "düşük başla-yavaş artır" ilkesi nedeniyle "replasman" vitamin D tedavisinin de tedrici yapılması uygun olabilir.*

E13(i): Sanders KM, Stuart AL, Williamson EJ, Simpson JA, Kotowicz MA, Young D, Nicholson GC. Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. JAMA. 2010 May 12;303(18):1815-22.

E13(ii): Bischoff-Ferrari HA, Dawson-Hughes B, Orav EJ, Staehelin HB, Meyer OW, Theiler R, Dick W, Willett WC, Egli A. Monthly High-Dose Vitamin D Treatment for the Prevention of Functional Decline: A Randomized Clinical Trial. JAMA Intern Med. 2016 Feb;176(2):175-83.

E13(iii): Smith H, Anderson F, Raphael H, Maslin P, Crozier S, Cooper C. Effect of annual intramuscular vitamin D on fracture risk in elderly men and women—a population-based, randomized, double-blind, placebo-controlled trial. Rheumatology (Oxford). 2007 Dec;46(12):1852-7.

E13(iv): Heikinheimo RJ, Inkovaara JA, Harju EJ, Haavisto MV, Kaarela RH, Kataja JM, Kokko AM, Kolho LA, Rajala SA. Annual injection of vitamin D and fractures of aged bones. Calcif Tissue Int. 1992 Aug;51(2):105-10.

E13(v): Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R; National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014 Oct;25(10):2359-81. doi: 10.1007/s00198-014-2794-2. Epub 2014 Aug 15. Erratum in: Osteoporos Int. 2015 Jul;26(7):2045-7.

E13(vi): Shah S, Chiang C, Sikaris K, Lu Z, Bui M, Zebaze R, Seeman E. Serum 25-Hydroxyvitamin D Insufficiency in Search of a Bone Disease. J Clin Endocrinol Metab. 2017 Jul 1;102(7):2321-2328.

E14. Hiperfosfatemi ve/veya hiperkalsemi varlığında aktif (kalsitriol) (1-25(OH)2kolekalsiferol) veya konvansiyonel (25(OH) kolekalsiferol) vitamin D kullanımı uygun değildir

E14(i): Seyffart's Directory of Drug Dosage in Kidney Disease; (1st ed., 2011) by GünterSeyffart Publisher: Dustri-Verlag Dr. Karl Feistle GmbH & Co. KG, Munich-Orlando; pp: 476-477.

E14(ii): Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice

Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl. 2017;7:1–59.

E15. Üst GİS hastalığı (örn. disfaji, özofajit, peptik ülser, üst GİS kanama veya tedavi ile kontrol altına alınamamış GÖR) anamnezi olanlarda ve/veya fiziksel olarak dik duramayacak hastalarda) oral bifosfonat kullanımı uygun değildir (özofajit, özofageal ülser, özofageal strüktürde relaps/alevlenme riski)

**Oral bifosfonatlar iyi kontrol edilmiş GÖR varlığında dikkatle kullanılabilir.*

E15(i): Pazianas M, Abrahamsen B. Safety of bisphosphonates. Bone 2011; 49(1): 103-10. Review.

E15(ii): Civitelli R, Napoli N, Armamento-Villareal R. Use of intravenous bisphosphonates in osteoporosis. Curr Osteoporos Rep 2007;5(1): 8-13.

E15(iii): Gaudio A, Morabito N. Pharmacological management of severe postmenopausal osteoporosis. Drugs Aging 2005; 22(5): 405-17. Review.

E15(iv): Lewiecki EM. Bisphosphonates for the treatment of osteoporosis: insights forclinicians. Ther Adv Chronic Dis. 2010 May;1(3):115-28.

E15(v): Kennel KA, Drake MT. Adverse effects of bisphosphonates: implications forosteoporosis management. Mayo Clin Proc. 2009 Jul;84(7):632-7; quiz 638.

E15(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E15(vii): Alendronate: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

E15(viii): Risedronate: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

E15(ix): Ibandronate: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

E15(x): RosenHN.The use of bisphosphonates in postmenopausal women with osteoporosis. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 22 Ekim 2019.

E16. Bifosfonatlar'ın GFR< 30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir (artmış akut böbrek yetersizliği riski)

**Zoledronat ve alendronat için eşik GFR değeri daha yüksektir (<35 mL/dk/1,73 m^2).*

E16(i): Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R; National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014 Oct;25(10):2359-81.

E16(ii): Alendronate: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

E16(iii): Risedronate: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

E16(iv): Ibandronate: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

E16(v): RosenHN.The use of bisphosphonates in postmenopausal women with osteoporosis. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 22 Ekim 2019.

E17. Tedavi öncesi serum kalsiyum düzeyi tayin edilmeden ve yeterli düzeyde kalsiyum/vitamin D alımı sağlanmadan zoledronat, denosumab veya teriparatid kullanımı uygun değildir

E17(i): Denosumab: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

E17(ii): Zoledronic acid: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

E17(iii): Teriparatide (recombinant human parathyroid hormone [1-34]) : Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

F: Ürogenital Sistem Kriterleri

F1. Benign prostat hiperplazisine bağlı LUTS semptomları olan erkeklerde PMR>150 mL ise mesaneye yönelik antikolinerjik ilaç kullanımı uygun değildir

**Yaşlı erkeklerde, aşırı aktif mesane tedavisi için mesaneye yönelik antikolinerjik ilaç reçetelemeden önce LUTS semptomları sorgulanmalı ve tüm olgulara PMR tayini yapılmalıdır.*

F1(i): McVary KT, Roehrborn CG, Avins AL, Barry MJ, Bruskewitz RC, Donnell RF, FosterHE Jr, Gonzalez CM, Kaplan SA, Penson DF, Ulchaker JC, Wei JT. Update on AUAguideline on the management of benign prostatic hyperplasia. J Urol. 2011May;185(5):1793-803.

F1(ii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

F1(iii): S. Gravas (Chair), J.N. Cornu, M.J. Drake, M. Gacci, C. Gratzke, T.R.W. Herrmann, S. Madersbacher, C. Mamoulakis, K.A.O. Tikkinen Guidelines Associates: M. Karavitakis, I. Kyriazis, S. Malde, V. Sakkalis, R. Umbach. EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology 2018. Page 25.

F2. Kronik dar açılı glokom hastalarında mesaneye yönelik antikolinerjik ilaç kullanımı uygun değildir

**Mesaneye yönelik antikolinerjik ilaç başlanmadan önce glokom hikayesi sorgulanmalıdır.*

**Mesaneye yönelik antikolinerjik ilaçlar dar açılı glokom lazer iridotomi ile tedavi edilmiş ise kontrendike değildir.*

**Mesaneye yönelik antikolinerjik ilaçlar açık açılı glokomda da kontrendike değildir.*

F2(i): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

F2(ii): Gani J, Perlis N, Radomski SB. Urologic medications and ophthalmologic side effects: a review. Can Urol Assoc J. 2012 Feb;6(1):53-8. doi: 10.5489/cuaj.11037.

F2(iii): Kato K, Yoshida K, Suzuki K, Murase T, Gotoh M. Managing patients with an overactive bladder and glaucoma: a questionnaire survey of Japanese urologists on the use of anticholinergics. BJU Int. 2005 Jan;95(1):98-101.

F2(iv): Oxybutynin: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

F2(v): Darifenacin: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

F2(vi): Tolterodine: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

F2(vii): Trospium: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

F2(viii): Fesoterodine: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

F2(ix): Solifenacin: Drug information, Lexicomp Online. Son erişim tarihi 29 Ekim 2019.

F3. Prostat hiperplazisi olan (obstrüksiyon riski) veya diabetes mellitus komplikasyonları gelişmiş olan (nörojen mesane riski) veya kırılgan olan yaşlılarda (detrusor hiperaktivitesi ile birlikte azalmış kontraktilite riski) PMR tayini yapılmadan mesaneye yönelik antikolinerjik ilaç kullanımı uygun değildir (üriner retansiyon ve postrenal böbrek yetersizliği riski)

F3(i): Taylor JA 3rd, Kuchel GA. Detrusor underactivity: Clinical features and pathogenesis of an underdiagnosed geriatric condition. J Am Geriatr Soc. 2006 Dec;54(12):1920-32. Review.

F3(ii): S. Gravas (Chair), J.N. Cornu, M.J. Drake, M. Gacci, C. Gratzke, T.R.W. Herrmann, S. Madersbacher, C. Mamoulakis, K.A.O. Tikkinen Guidelines Associates: M. Karavitakis, I. Kyriazis, S. Malde, V. Sakkalis, R. Umbach. EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology 2018. Page 25.

F3(iii): Golbidi S, Laher I. Bladder dysfunction in diabetes mellitus. Front Pharmacol.2010 Nov 16;1:136. doi: 10.3389/fphar.2010.00136. eCollection 2010.

F3(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

F4. Kan basıncı <90/50 mmHg veya > 170/100 mmHg olan/ unstabil anginası olan/ cinsel ilişki sırasında anjinası olan/ NYHA sınıf 4 kalp yetersizliği olan/ anjina için nitrat tedavisi alan/ alfa-1 bloker tedavisi alan/geçirilmiş Mİ (< 3 ay) öyküsü olan/ geçirilmiş inme (< 6 ay) öyküsü olan hastalarda fosfodiesteraz tip-5 inhibitörlerinin (örn. sildenafil, tadalafil, vardenafil) kullanımı uygun değildir

F4(i): Kloner RA, Hutter AM, Emmick JT, Mitchell MI, Denne J, Jackson G. Time course of the interaction between tadalafil and nitrates. J Am Coll Cardiol 2003; 42 (10): 1855-60.

F4(ii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

F4(iii): S. Gravas (Chair), J.N. Cornu, M.J. Drake, M. Gacci, C. Gratzke, T.R.W. Herrmann, S. Madersbacher, C. Mamoulakis, K.A.O. Tikkinen Guidelines Associates: M. Karavitakis, I. Kyriazis, S. Malde, V. Sakkalis, R. Umbach. EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology 2018. Page 21.

F4(iv): K. Hatzimouratidis (Chair), F. Giuliano, I. Moncada, A. Muneer, A. Salonia (Vice-chair), P. Verze Guideline Associates: A. Parnham, E.C. Serefoglu. EAU Guidelines on Erectile Dysfunction, Premature Ejaculation, Penile Curvature and Priapism. European Association of Urology 2018. Page 20-21.

F5. Ortostatik hipotansiyonu olan hastalarda benign prostat hiperplazisine bağlı LUTS semptomlarının tedavisinde üroselektif olmayan alfa 1 blokerlerin (örn. doksazosin, terazosin) kullanımı uygun değildir (ortostatik hipotansiyonda, senkop ve düşmelerde artış)

**Ortostatik hipotansiyon riski en düşük üroselektif ajan silodosindir; plaseboya benzer olduğu düşünülmektedir.*

**Üroselektif olmayan alfa-1 blokerlerle tedavi edilen yaşlı hastalar ortostatik hipotansiyon riski için bilgilendirilmelidir.*

F5(i): S. Gravas (Chair), J.N. Cornu, M.J. Drake, M. Gacci, C. Gratzke, T.R.W. Herrmann, S. Madersbacher, C. Mamoulakis, K.A.O. Tikkinen Guidelines Associates: M. Karavitakis, I. Kyriazis, S. Malde, V. Sakkalis, R. Umbach. EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology 2018. Page 17.

F5(ii): Chapple CR, Montorsi F, Tammela TL, Wirth M, Koldewijn E, Fernández Fernández E; European Silodosin Study Group. Silodosin therapy for lower urinary tractsymptoms in men with suspected benign prostatic hyperplasia: results of aninternational, randomized, double-blind, placebo- and active-controlled clinical trial performed in Europe. Eur Urol. 2011 Mar;59(3):342-52.

F5(iii): Welk B, McArthur E, Fraser LA, Hayward J, Dixon S, Hwang YJ, Ordon M. The riskof fall and fracture with the initiation of a prostate-selective α antagonist: a population based cohort study. BMJ. 2015 Oct 26;351:h5398.

F5(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

F5(v): Cho HJ, Yoo TK. Silodosin for the treatment of clinical benign prostatic hyperplasia: safety, efficacy, and patient acceptability. Res Rep Urol. 2014 Sep 26;6:113-9. doi: 10.2147/RRU.S41618. eCollection 2014. Review.

F5(vi): S. Gravas (Chair), T. Bach, M. Drake, M. Gacci, C. Gratzke, T.R.W. Herrmann, S. Madersbacher, C. Mamoulakis, K.A.O. Tikkinen Guidelines Associates: M. Karavitakis, S. Malde, V. Sakkalis, R. Umbach. EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology 2017; Page 14-15.

F5(vii): Chatziralli IP, Sergentanis TN. Risk factors for intraoperative floppy iris syndrome: a meta-analysis. Ophthalmology. 2011 Apr;118(4):730-5.

F5(viii): Cantrell MA, Bream-Rouwenhorst HR, Steffensmeier A, Hemerson P, Rogers M,Stamper B. Intraoperative floppy iris syndrome associated with alpha1-adrenergic receptor antagonists. Ann Pharmacother. 2008 Apr;42(4):558-63. doi:10.1345/aph.1K679. Epub 2008 Mar 25. Review.

F5(ix): Chang DF, Campbell JR. Intraoperative floppy iris syndrome associated with tamsulosin. J Cataract Refract Surg. 2005 Apr;31(4):664-73.

F5(x): Chang DF, Osher RH, Wang L, Koch DD. Prospective multicenter evaluation ofcataract surgery in patients taking tamsulosin (Flomax). Ophthalmology. 2007May;114(5):957-64.

F5(xi): Bell CM, Hatch WV, Fischer HD, Cernat G, Paterson JM, Gruneir A, Gill SS,Bronskill SE, Anderson GM, Rochon PA. Association between tamsulosin and serious ophthalmic adverse events in older men following cataract surgery. JAMA. 2009 May20;301(19):1991-6.

F5(xii): Gani J, Perlis N, Radomski SB. Urologic medications and ophthalmologic side effects: a review. Can Urol Assoc J. 2012 Feb;6(1):53-8.

F6. Mukozaya zarar verebilecek ürolojik girişimler hariç asemptomatik bakteriüride antibiyotik kullanımı uygun değildir

**Mukozaya zarar verebilecek ürolojik girişimler öncesinde asemptomatik bakteriüri taranmalı ve tedavi edilmelidir.*

**Asemptomatik bakteriürinin aşağıdaki hasta gruplarında taranması ve/veya tedavi edilmesi önerilmez:*

Risk faktörü olmayan hastalar

Diyabeti iyi regüle edilmiş hastalar

Bakımevinde yaşayan hastalar

Alt idrar yolu disfonksiyonu/rekonstrüksiyonu olan hastalar

Rekürren idrar yolu infeksiyonu geçiren hastalar

Artroplasti ameliyatlarından önce

Üriner katateri olan hastalar

F6(i): Lindsay E. Nicolle, Suzanne Bradley, Richard Colgan, James C. Rice, Anthony Schaeffer, Thomas M. Hooton, Infectious Diseases Society of America Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults, Clinical Infectious Diseases, Volume 40, Issue 5, 1 March 2005, Pages 643–654.

F6(ii): G. Bonkat (Co-chair), R. Pickard (Co-chair), R. Bartoletti, T. Cai, F. Bruyère, S.E. Geerlings, B. Köves, F. Wagenlehner Guidelines Associates: A. Pilatz, B. Pradere, R. Veeratterapillay. EAU Guidelines on Urological Infections. European Association of Urology 2018.

F7. Nitrofurantoin'in GFR< 30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir

**Nitrofurantoin'in üriner infeksiyonların süpresyon tedavisi amacıyla uzun süreli kullanımı yaşlılarda uygun değildir (uzun süreli kullanımda irreversibl pulmoner fibroz, karaciğer toksisitesi ve periferal nöropati riski nedeniyle)*

F7(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Soci-ety 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019Apr;67(4):674-694.

F7(ii): G. Bonkat (Co-chair), R. Pickard (Co-chair), R. Bartoletti, T. Cai, F. Bruyère, S.E. Geerlings, B. Kö-ves, F. Wagenlehner

Guidelines Associates: A. Pilatz, B. Pradere, R. Veeratterapillay. EAU Guidelines onUro-logical Infections. European Association of Urology 2018.

G: Endokrin Sistem Kriterleri

G1. Yaşam beklentisi düşük (<5 yıl) veya anamnezde düşme veya bilişsel yetersizliği olan hastalarda sıkı kan şekeri kontrolu (HbA1C< %7) uygun değildir

G1(i): Onder G, Landi F, Fusco D, Corsonello A, Tosato M, Battaglia M, Mastropaolo S, Settanni S, Antocic-co M, Lattanzio F. Recommendations to prescribe in complex older adults: results of the CRIteria to assess app-ropriate Medication use among Elderly complex patients (CRIME) project. Drugs Aging. 2014 Jan;31(1):33-45.

G1(ii): Medha M. Treatment of type 2 diabetes mellitus in the older patient. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019.

#G2. Kırılgan veya malnütre yaşlılarda metformin kullanımı uygun değildir (metformin'in GİS yan etkileri ve iştahsızlık etkisi nedeniyle)

*Malnütrisyon riski olan olgularda metformin kullanımına kar-zarar dengesi göz önüne alınarak karar verilmelidir.

G2(i): Haas L. Management of diabetes mellitus medications in the nursing home. Drugs Aging. 2005;22:209–218.

G2(ii): Onder G, Landi F, Fusco D, Corsonello A, Tosato M, Battaglia M, Mastropaolo S, Settanni S, Anto-cicco M, Lattanzio F. Recommendations to prescribe in complex older adults: results of the CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) project. Drugs Aging. 2014 Jan;31(1):33-45.

G3(iii): Bahat G, Erdogan T, Karan MA. Need for increased awareness for avoiding metformin treatment in mal-nourished older adults with diabetes mellitus. Clinical Nutrition, 2019.

G3. Metformin'in GFR< 30 mL/dk/1,73 m^2 olan hastalarda kullanımı uygun değildir (laktik asidoz riski)

**Metformin dozu, GFR: 30-45 mL/dk/1,73 m^2 olan hastalarda %50 azaltılmalıdır.*

**Metformin kullanımı laktik asidoz riskini artıran diğer durumlarda da (kalp yetersizliği, karaciğer yetersizliği, şok veya kalıcı hemodinamik instabilite, KOAH, hipoksi) uygun değildir.*

G3(i): Metformin: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

G3(ii): Germino FW. Non-insulin treatment of type 2 diabetes mellitus in geriatric patients: a review. Clin Ther 2011; 33(12): 1868-82.

G3(iii): Lalau JD. Lactic acidosis induced by metformin: Incidence, management and prevention. Drug Sa-fety 2010; 33(9): 727-40.

G3(iv): 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 Mar;44(2):213-8.

G4. Tip 2 DM hastalarında glibenklamid ve klorpropamid gibi uzun etkili sulfanilürelerin kullanımı uygun de-ğildir (uzamış hipoglisemi riski)

G4(i): David K M. Sulfonylureas and meglitinides in the treatment of diabetes mellitus. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

G4(ii): Graal MB, Wolffenbuttel BH. The use of sulphonylureas in the elderly. Drugs Aging 1999; 15(6): 471-81.

G4(iii): Langtry HD, Balfour JA. Glimepiride. A review of its use in the management of type 2 diabetes melli-tus. Drugs 1998; 55(4): 563-84.

G4(iv): 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 Mar;44(2):213-8.

G5. Dökümante kalp yetersizliği/kırık anamnezi/artmış kırık riski/mesane kanseri anamnezi olan veya insülin tedavisi almakta olan hastalarda tiazolidinedionların (rosiglitazon, pioglitazon) kullanımı uygun değildir (kalp yetersizliğinde kötüleşme, kırık ve mesane kanser riskinde artış)

G5(i): David K M. Thiazolidinediones in the treatment of diabetes mellitus. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

G5(ii): Rosiglitazone: Drug information, Lexicomp Online. Son erişim tarihi 04 Kasım 2019.

G5(iii): Germino FW. Noninsulin treatment of type 2 diabetes mellitus in geriatric patients: a review. Clin Ther 2011; 33(12): 1868-82.

G5(iv): Lago RM, Singh PP, Nesto RW. Congestive heart failure and cardiovascular death in patients with pre-diabetes and type 2 diabetes given thiazolidinediones: a meta-analysis of randomised clinical trials. Lancet 2007; 370(9593): 1129-36.

G5(v): 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 Mar;44(2):213-8.

G6. Kalp yetersizliği olan olgularda saksagliptin kullanımı uygun değildir

G6(i): LeRoith D, Biessels GJ, Braithwaite SS, Casanueva FF, Draznin B, Halter JB, Hirsch IB, McDonnell ME, Molitch ME, Murad MH, Sinclair AJ. Treatment of Diabetes in Older Adults: An Endocrine Society* Cli-nical Practice Guideline. J Clin Endocrinol Metab. 2019 May 1;104(5):1520-1574.

G6(ii): Scirica BM, Braunwald E, Raz I, Cavender MA, Morrow DA, Jarolim P, Udell JA, Mosenzon O, Im K, Umez-Eronini AA, Pollack PS, Hirshberg B, Frederich R, Lewis BS, McGuire DK, Davidson J, Steg PG, Bhatt DL; SAVOR-TIMI 53 Steering Committee and Investigators. Heart Failure, Saxagliptin, and Diabetes Mellitus: Observations from the SAVOR-TIMI 53 Randomized Trial. Circulation. 2015 Oct 13;132(15):e198.

G7. Kanagliflozinin, diyabete bağlı alt ekstremite ampütasyonu komplikasyonu geçirmiş/ciddi periferik arter hastalığı olan/tekrarlayan üriner sistem infeksiyonu/genitoüriner enfeksiyonu olan olgularda kullanımı uygun değildir

**SGLT-2 inhibitörleri dehidratasyona, urgency inkontinansa ve diabetik ketoasidoza sebep olabileceklerinden, yaşlı hastalarda genel olarak dikkatle kullanılmalıdır.*

G7(i): U.S. Food and Drug Administration. FDA confirms increased risk of leg and foot amputations with the diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR). Available at: www.fda.gov/downloads/Drugs/DrugSafety/UCM558427.pdf.Son erişim tarihi 30 Ekim 2019.

G7(ii): Sinclair AJ, Bode B, Harris S, Vijapurkar U, Shaw W, Desai M, Meininger G. Efficacy and Safety of Canagliflozin in Individuals Aged 75 and Older with Type 2 Diabetes Mellitus: A Pooled Analysis. J Am Geri-atr Soc. 2016 Mar;64(3):543-52.

G7(iii): Watts NB, Bilezikian JP, Usiskin K, Edwards R, Desai M, Law G, Meininger G. Effects of Canagliflo-zin on Fracture Risk in Patients With Type 2 Diabetes Mellitus. J Clin Endocrinol Metab. 2016 Jan;101(1):157-66.

G7(iv): Anthony D. Sodium-glucose co-transporter 2 inhibitors for the treatment of hyperglycemia in type 2 diabetes mellitus. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

G7(v): Lupsa BC, Inzucchi SE. Use of SGLT2 inhibitors in type 2 diabetes: weighing the risks and benefits. Diabetologia. 2018 Oct;61(10):2118-2125.

G8. SGLT-2 inhibitörlerinin GFR< 45 mL/dk/1,73 m^2 olan olgularda kullanılması uygun değildir

**Kanagliflozin, empagliflozin, ve ertugliflozin'in GFR< 45 mL/dk/1,73 m^2 olan olgularda öncelikle etkinlikte azalma nedeniyle kullanılması uygun değildir.*

**Dapagliflozin'in GFR<60 mL/dk/1,73 m^2 olan olgularda etkisinin azalması nedeniyle kullanılması uygun değildir.*

**SGLT-2 inhibitörlerinin, GFR 30-60 mL/dk/1,73 m^2 olan hastalarda, nefropati (idrar albümin atılımı> 300 mg/gün) tedavisi için kullanımı değerlendirilebilir.*

G8(i): LeRoith D, Biessels GJ, Braithwaite SS, Casanueva FF, Draznin B, Halter JB, Hirsch IB, McDonnell ME, Molitch ME, Murad MH, Sinclair AJ. Treatment of Diabetes in Older Adults: An Endocrine Society* Cli-nical Practice Guideline. J Clin Endocrinol Metab. 2019 May 1;104(5):1520-1574.

G8(ii): George L B. Treatment of diabetic kidney disease. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

G9. Androjen eksikliği ile ilişkili semptom ve bulguların eşlik etmediği serum testosteron düzeyi düşüklüğü varlığında androjen kullanımı uygun değildir.

*Hipogonadizm tanısı androjen yetersizliğinin semptom ve belirtileriyle birlikte kalıcı düşük serum testosteron düzeyi varlığında koyulur.

G9(i): 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 Mar;44(2):213-8. G9(ii): Bhasin S, Brito JP, Cunningham GR, Hayes FJ, Hodis HN, Matsumoto AM, Snyder PJ, Swerdloff RS, Wu FC, Yialamas MA. Testosterone Therapy in Men With Hypogonadism: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2018 May 1;103(5):1715-1744.

G9(iii): G.R. Dohle, S. Arver, C. Bettocchi, T.H. Jones, S. Kliesch. EAU Guidelines on Male Hypogonadism. In: European Association of Urology 2018, Son erişim tarihi 29 Ekim 2019.

G10. Meme kanseri veya venöz tromboemboli öyküsü olan hastalarda sistemik östrojen kullanımı uygun değil-dir

*Meme kanseri veya venöz tromboemboli öyküsü olan hastalarda vajinal östrojen; atrofik vajinit gibi ürogenital semptomların tedavisinde hormon-dışı tedavilerden sonra, kar-zarar dengesi göz önünde bulundurularak verilebilir.

G10(i): American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice, Farrell R. ACOG Committee Opinion No. 659: The Use of Vaginal Estrogen in Women With a History of Estrogen-Dependent Breast Cancer. Obstet Gynecol. 2016 Mar;127(3):e93-6.

G10(ii): The NAMS 2017 Hormone Therapy Position Statement Advisory Panel. The 2017 hormone therapy position statement of The North American Menopause Society. Menopause. 2017 Jul;24(7):728-753.

G10(iii): Bergendal A, Kieler H, Sundström A, Hirschberg AL, Kocoska-Maras L. Risk of venous thromboem-bolism associated with local and systemic use of hormone therapy in peri- and

postmenopausal women and in relation to type and route of administration. Menopause. 2016 Jun;23(6):593-9.

G10(iv): Calle EE, Feigelson HS, Hildebrand JS, Teras LR, Thun MJ, Rodriguez C. Postmenopausal hormone use and breast cancer associations differ by hormone regimen and histologic subtype. Cancer 2009; 115(5): 936-45. Erratum in: Cancer 2009; 115(7): 1587.

G10(v): Diergaarde B, Potter JD, Jupe ER, Manjeshwar S, Shimasaki CD, Pugh TW, Defreese DC, Gramling BA, Evans I, White E. Polymorphisms in genes involved in sex hormone metabolism, estrogen plus progestin hormone therapy use, and risk of postmenopausal breast cancer. Cancer Epidemiol Biomarkers Prev 2008; 17(7): 1751-9.

G10(vi): 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 Mar;44(2):213-8.

G11. İntakt uterusu olan kadınlarda beraberinde progesteron kullanımı olmadan östrojen kullanımı uygun değil-dir (endometrial kanser riski)

G11(i): Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society. Menopause. 2013 Sep;20(9):888-902; quiz 903-4.

G11(ii): Dick SE, DeWitt DE, Anawalt BD. Postmenopausal hormone replacement therapy and major clinical outcomes: a focus on cardiovascular disease, osteoporosis, dementia, and breast and endometrial neoplasia. Am J Manag Care 2002; 8(1): 95-104.

G11(iii): Furness S, Roberts H, Marjoribanks J, Lethaby A. Hormone therapy in postmenopausal women and risk of endometrial hyperplasia. Cochrane Database Syst Rev 2012 Aug 15;8:CD000402.

G11(iv): Marjoribanks J, Farquhar C, Roberts H, Lethaby A. Long term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev 2012 Jul 11;7:CD004143.

G11(v): 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 Mar;44(2):213-8.

G11(vi): Lindahl SH. Reviewing the options for local estrogen treatment of vaginal atrophy. Int J Womens He-alth. 2014 Mar 13;6:307-12.

G11(vii): US Preventive Services Task Force, Grossman DC, Curry SJ, Owens DK, Barry MJ, Davidson KW, Doubeni CA, Epling JW Jr, Kemper AR, Krist AH, Kurth AE, Landefeld CS, Mangione CM, Phipps MG, Silverstein M, Simon MA, Tseng CW. Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Women: US Preventive Services Task Force Recommendation Statement. JAMA. 2017 Dec12;318(22):2224-2233.

G12. İştah artırıcı olarak megestrol kullanımı uygun değildir (kilo üzerine minimal etki, protrombotik yan etki)

G12(i): By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694.

G12(ii): Wen FK, Millar J, Oberst-Walsh L, Nashelsky J. Clinical Inquiry: Is megestrol acetate safe and effective for malnourished nursing home residents? J Fam Pract. 2018 Feb;67(2):112-113.

G13. Subklinik hipotiroidisi olan yaşlılarda (TSH: 4-10 mIU/L; sT4: N), tiroid hormonu kullanımı uygun değildir (ek yararı yok, atrial fibrilasyon ve osteoporoz gibi potansiyel yan etki riski)

G13(i): Stott DJ, Rodondi N, Kearney PM, Ford I, Westendorp RGJ, Mooijaart SP, Sattar N, Aubert CE, Au-jesky D, Bauer DC, Baumgartner C, Blum MR, Browne JP, Byrne S, Collet TH, Dekkers OM, den Elzen WPJ, Du Puy RS, Ellis G, Feller M, Floriani C, Hendry K, Hurley C, Jukema JW, Kean S, Kelly M, Krebs D, Langhorne P, McCarthy G, McCarthy V, McConnachie A, McDade M, Messow M, O'Flynn A, O'Riordan D, Poortvliet RKE, Quinn TJ, Russell A, Sinnott C, Smit JWA, Van Dorland HA, Walsh KA, Walsh EK, Watt T, Wilson R, Gussekloo J; TRUST Study Group. Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism. N Engl J Med. 2017 Jun 29;376(26):2534-2544.

G13(ii): Selmer C, Olesen JB, Hansen ML, von Kappelgaard LM, Madsen JC, Hansen PR, Pedersen OD, Faber J, Torp-Pedersen C, Gislason GH. Subclinical and overt thyroid dysfunction and risk of all-cause mortality and cardiovascular events: a large population study. J Clin Endocrinol Metab. 2014 Jul;99(7):2372-82.

G13(iii): Waring AC, Arnold AM, Newman AB, Bùzková P, Hirsch C, Cappola AR. Longitudinal changes in thyroid function in the oldest old and survival: the cardiovascular health study all-stars study. J Clin Endocrinol Metab. 2012 Nov;97(11):3944-50.

G13(iv): Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, Pessah-Pollack R, Singer PA, Woeber KA; American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012 Nov Dec;18(6):988-1028. Erratum in: Endocr Pract. 2013 Jan-Feb;19(1):175.

G13(v): Razvi S, Weaver JU, Butler TJ, Pearce SH. Levothyroxine treatment of subclinical hypothyroidism, fatal and nonfatal cardiovascular events, and mortality. Arch Intern Med. 2012 May 28;172(10):811-7.

G13(vi): Pearce SH, Brabant G, Duntas LH, Monzani F, Peeters RP, Razvi S, Wemeau JL. 2013 ETA Guideline: Management of Subclinical Hypothyroidism. Eur Thyroid J. 2013 Dec;2(4):215-28.

H: Antimuskarinik-Antikolinerjik Yük

H1. Yüksek antikolinerjik etkili ilaçların [trisiklik antidepresanlar, klorpromazin, tioridazin, klozapin, olanzapin, hiyosin, oral oksibutinin, 1. jenerasyon antihistaminikler (feniramin, klorfeniramin, hidroksizin, siproheptadin, dimenhidrinat, difenhidramin, meklizin vb.), paroksetin7 kullanımı aşağıdaki durumlarda uygun değildir

Düşme/konstipasyon/dar açılı glokom/demans/deliryum/idrar retansiyonu/erkekte obstrüktif LUTS semptomları/eş zamanlı yüksek antikolinerjik etkili ilaç kullanımı

**Genel olarak yaşlılarda yüksek antikolinerjik etkili ilaçların kullanımı tercih edilmemelidir; klinik gereklilik durumunda yan etki açısından dikkatli takip edilmelidir.*

**1.kuşak antihistaminiklerin akut alerjik reaksiyon varlığında parenteral kullanımı uygundur.*

H1(i): Verhamme KM, Sturkenboom MC, Stricker BH, Bosch R. Drug-induced urinary retention: incidence, management and prevention. Drug Saf 2008; 31(5):373-88.

H1(ii): Feinberg M. The problems of anticholinergic adverse effects in older patients. Drugs Aging 1993; 3(4): 335-48.

H1(iii): Gerretsen P, Pollock BG. Drugs with anticholinergic properties: a current perspective on use and safety. Expert Opin Drug Saf 2011; 10(5): 751-65.

H1(iv): Karimi S, Dharia SP, Flora DS, Slattum PW. Anticholinergic burden: clinical implications for seniors and strategies for clinicians. Consult Pharm 2012; 27(8): 564-82.

H1(v): 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 Mar;44(2):213-8.

H1(vi): Collamati A, Martone AM, Poscia A, Brandi V, Celi M, Marzetti E, Cherubini A, Landi F. Anticholinergic drugs and negative outcomes in the older population: from biological plausibility to clinical evidence. Aging Clin Exp Res. 2016 Feb;28(1):25-35.

H1(vii): Salahudeen MS, Duffull SB, Nishtala PS. Anticholinergic burden quantified by anticholinergic risk scales and adverse outcomes in older people: a systematic review. BMC Geriatr. 2015 Mar 25;15:31. doi: 10.1186/s12877-015-0029-9.

J: Suplemanlar.

J1. Kanama riski olan olgularda (antikoagülan kullanımı, NSAİİ kullanımı, anlamlı kanama öyküsü) gingko biloba ekstraktı kullanımı uygun değidir

**Gingko biloba ile birlikte aspirin kullanımında da kanama riski artar; kombine kullanılmamaları daha uygun olabilir*

J1(i): Robert B S. Clinical use of ginkgo biloba. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

J1(ii): Clinton B W. Treatment and prevention of vascular dementia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

J1(iii): Bent S, Goldberg H, Padula A, Avins AL. Spontaneous bleeding associated with ginkgo biloba: a case report and systematic review of the literature: a case report and systematic review of the literature. J Gen Intern Med 2005; 20:657.

J1(iv): Rosenblatt M, Mindel J. Spontaneous hyphema associated with ingestion of Ginkgo biloba extract. N Engl J Med 1997; 336:1108.

J1(v): Rowin J, Lewis SL. Spontaneous bilateral subdural hematomas associated with chronic Ginkgo biloba ingestion. Neurology 1996; 46:1775.

J1(vi): Gilbert GJ. Ginkgo biloba. Neurology. 1997 Apr;48(4):1137.

J1(vii): Vale S. Subarachnoid haemorrhage associated with Ginkgo biloba. Lancet. 1998 Jul 4;352(9121):36.

J1(viii): Pedroso JL, Henriques Aquino CC, Escórcio Bezerra ML, Baiense RF, Suarez MM, Dutra LA, Braga-Neto P, Povoas Barsottini OG. Ginkgo biloba and cerebral bleeding: a case report and critical review. Neurologist. 2011 Mar;17(2):89-90.

J2. Sarı kantaron'un (St. John's Wort) antidepresan kullanan hastalarda (özellikle SSRİ ile serotonerjik sendrom riski) ve sitokrom p450 ile metabolize olan ilaç (örn. digoksin, teofilin, varfarin, karbamazepin, fenitoin, fenobarbital) kullanan hastalarda sistemik kullanımı uygun değildir (sarı kantaron sitokrom p450 aktivasyonu yapar)

J2(i): Robert B Saper. Clinical use of St. John's wort. In: UpToDate, Poat, TW(Ed), Waltham, MA, 2019 Son erişim tarihi 29 Ekim 2019.

J2(ii): Lantz MS, Buchalter E, Giambanco V. St. John's wort and antidepressant drug interactions in the elderly. J Geriatr Psychiatry Neurol. 1999;12(1):7.

J2(iii): Henderson L, Yue QY, Bergquist C, Gerden B, Arlett P. St John's wort (Hypericum perforatum): drug interactions and clinical outcomes. British Journal of Clinical Pharmacology. 2002;54(4):349-356.

#J3. Varfarin kullanan hastalarda supleman kullanımı uygun değildir (kanama riskinde olası artış nedeniyle)

**Oral olarak kullanılan birçok supleman (örn. ginseng, sarımsak, zerdeçal, zencefil, şeytan pençesi, sarı kantaron, koenzim Q10, yeşil çay vb.) varfarin'in antikoagülan etkisini artırarak kanama riskinde artışa sebep olabilir.*

J3(i): Ge B, Zhang Z, Zuo Z. Updates on the clinical evidenced herbwarfarin interactions. Evid Based Complement Alternat Med. 2014;2014:957362.

J3(ii): Holbrook AM, Pereira JA, Labiris R, McDonald H, Douketis JD, Crowther M, Wells PS. Systematic overview of warfarin and its drug and food interactions. Arch Intern Med. 2005 May 23;165(10):1095-106.

#Uluslararası Delfi paneli çalışmasında konsensus sağlanmayan kriterler

Kısaltmalar:

AF: Atrial fibrilasyon

ACEİ: Anjiotensin konverting enzim inhibitörleri

ARB: Anjiotensin reseptör blokerleri

ChEIs:Asetilkolinesteraz inhibitörleri

DM: Diabetes mellitus

EF: Ejeksiyon fraksiyonu

eGFR: Estimated Glomerular Filtrasyon hızı

FDA: Food and Drug Administration

GIS: Gastrointestinal sistem

GİA: Geçici iskemik atak

GÖR: Gastroözofageal reflü

H1 receptor: Histamin 1 reseptör

HT: Hipertansiyon

INR: International Normalized Ratio

KOAH: Kronik obstrüktif akciğer hastalığı

LUTS: Alt üriner sistem semptomları

Mİ: Miyokard infarktüsü

MSS: Merkezi sinir sistemi

NSAİİ: Non steroidal anti inflamatuar ilaçlar

NYHA: New York Heart Association

OAK: Oral antikoagülan

PMR: Post miksiyonel rezidü

PO_2: Parsiyel oksijen basıncı

PPİ: Proton pompa inhibitörleri

QTc: düzeltilmiş QT Intervali

RAS: Renin anjiotensin sistem

SGLT-2: Sodium-glucose kotransporter-2

SNRIs: Serotonin-norepinefrin geri alım inhibitörleri

SSRIs: Selektif serotonin geri alım inhibitörleri

TSH: Tiroid stimulan hormon

TIME to START- YAŞLIDA BAŞLANMASI UYGUN OLAN İLAÇLAR

Bu grup ilaçların, kriter içeriğindeki durumlarda kullanımının yaşlılarda endikasyonu ve potansiyel faydalanımı vardır ancak klinik pratikte sıklıkla gözden kaçabilmekte veya ileri yaş nedeniyle, geçerli ek bir sebep olmaksızın, verilmemektedir. Bu ilaçların kriter içeriğindeki durumda kullanılmaması "potansiyel uygunsuz ilaç kullanımı" olarak nitelendirilmektedirler. Klinisyenler hastanın tüm özellikleriyle ilacın hastasındaki potansiyel fayda ve zararını (kar-zarar dengesini), beklenen yaşam süresini ve hasta/bakımveren tercihleri doğrultusunda saptanan tedavi hedeflerini göz önünde bulundurarak karar vermelidir. Bu grup ilaçları klinisyenler bazı olgularda kullanmamayı uygun bulabilir.

*Klinik kullanıma yardımcı olması için bazı kriterlere eklenen açıklamalar kriterden hemen sonra italik karakterde ve önek * ile verilmiştir.*

Referanslar; kriterle ilgili ve mevcut ise açıklamalar ile ilgili referansları içermektedir.

TIME-to-START Kriterleri (referanslı ve açıklamalı)

A: Kardiyovasküler Sistem Kriterleri

A1. Dökümante aterosklerotik koroner arter hastalığı (geçirilmiş akut koroner sendrom/koroner anjioplasti veya stentleme/ koroner arter bypass greftleme/abdominal aort anevrizması), dökümante aterosklerotik serebrovasküler hastalık (geçirilmiş iskemik inme/GİA/ geçirilmiş karotis endarterektomi veya stentleme) veya semptomatik alt ekstremite arter hastalığı olan hastalarda sekonder korunma amaçlı antiplatelet tedavi (aspirin veya klopidogrel) başlanması uygundur

**Primer kardiyovasküler korunma amaçlı aspirin başlanması çoğu olguda uygun değildir (intrakranial ve GİS kanama riskinde artış ve sınırlı faydalanım nedeniyle).*

A1(i): Zuckerman IH, Yin X, Rattinger GB, Gottlieb SS, Simoni-Wastila L, Pierce SA, Huang TY, Shenolikar R, Stuart B. Effect of exposure to evidence-based pharmacotherapy on outcomes after acute myocardial infarction in older adults. J Am Geriatr Soc 2012; 60(10): 1854-61.

A1(ii): Alonso-Coello P, Bellmunt S, McGorrian C, Anand SS, Guzman R, Criqui MH, AklEA, Olav Vandvik P, Lansberg MG, Guyatt GH, Spencer FA; American College of Chest Physicians. Antithrombotic therapy in peripheral artery disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2Suppl): e669S-90S.

A1(iii): Fleg JL, Aronow WS, Frishman WH. Cardiovascular drug therapy in the elderly: benefits and challenges. Nat Rev Cardiol 2011; 8(1): 13-28.

A1(iv): Vandvik PO, Lincoff AM, Gore JM, Gutterman DD, Sonnenberg FA, Alonso-Coello P,Akl EA, Lansberg MG, Guyatt GH, Spencer FA; American College of Chest Physicians. Primary and secondary prevention of cardiovascular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2Suppl): e637S-68S. Erratum in: Chest 2012; 141(4): 1129. Dosage error in article text.

A1(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16.

A1(vi): McNeil JJ, Wolfe R, Woods RL, Tonkin AM, Donnan GA, Nelson MR, Reid CM, Lockery JE, Kirpach B, Storey E, Shah RC, Williamson JD, Margolis KL, Ernst ME, Abhayaratna WP, Stocks N, Fitzgerald SM, Orchard SG, Trevaks RE, Beilin LJ, Johnston CI, Ryan J, Radziszewska B, Jelinek M, Malik M, Eaton CB, Brauer D, Cloud G, Wood EM, Mahady SE, Satterfield S, Grimm R, Murray AM; ASPREE Investigator Group. Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly. N Engl J Med. 2018 Oct 18;379(16):1509-1518.

A1(vii): ASCEND Study Collaborative Group, Bowman L, Mafham M, Wallendszus K, Stevens W, Buck G, Barton J, Murphy K, Aung T, Haynes R, Cox J, Murawska A, Young A, Lay M, Chen F, Sammons E, Waters E, Adler A, Bodansky J, Farmer A, McPherson R, Neil A, Simpson D, Peto R, Baigent C, Collins R, Parish S, Armitage J. Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. N Engl J Med. 2018 Oct 18;379(16):1529-1539.

A1(viii): Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, Collet JP, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzolai L, Naylor AR, Roffi M, Röther J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I; ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2018 Mar 1;39(9):763-816.

A1(ix): Authors/Task Force Members:, Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corrà U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FDR, Løchen ML, Löllgen H, Marques-Vidal P, Perk J, Prescott E, Redon J,

Richter DJ, Sattar N, Smulders Y, Tiberi M, Bart van der Worp H, van Dis I, Verschuren WMM. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Atherosclerosis. 2016 Sep;252:207-274.

A2. Dökümante aterosklerotik koroner arter hastalığı (geçirilmiş akut koroner sendrom/koroner anjioplasti veya stentleme/ koroner arter bypass greftleme/abdominal aort anevrizması), dökümante serebrovasküler hastalık (geçirilmiş iskemik inme/ GİA/geçirilmiş karotis endarterektomi veya stentleme) veya periferik arter hastalığı olan hastalarda sekonder korunma amaçlı statin tedavisi başlanması uygundur

**Yaşam beklentisi <2 yıl olan hastalarda, terminal demansı olanlarda, >85 yaş hastalarda statinden beklenen faydalanım düşüktür; statin yan etkileri (miyopati, karaciğer toksisitesi vb.) daha fazladır. *Bu olgularda, statin tedavisi kararı hasta/ hasta yakını bilgilendirmesi ve ortak karar verme ilkesi ile belirlenmelidir.*

A2(i): Mills EJ, Wu P, Chong G, Ghement I, Singh S, Akl EA, Eyawo O, Guyatt G, Berwanger O, Briel M. Efficacy and safety of statin treatment for cardiovascular disease: a network meta-analysis of 170,255 patients from 76 randomized trials. QJM 2011; 104(2): 109-24. Review.

A2(ii): Brugts JJ, Yetgin T, Hoeks SE, Gotto AM, Shepherd J, Westendorp RG, de CraenAJ, Knopp RH, Nakamura H, Ridker P, van Domburg R, Deckers JW. The benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors: meta-analysis of randomised controlled trials. BMJ 2009; 338: b2376. Review

A2(iii): Amarenco P, Labreuche J. Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention. Lancet Neurol 2009; 8(5): 453-63. Review.

A2(iv): Onder G, Landi F, Fusco D, Corsonello A, Tosato M, Battaglia M, Mastropaolo S, Settanni S, Antocicco M, Lattanzio F. Recommendations to prescribe in complex older adults: results of the CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) project. Drugs Aging. 2014 Jan;31(1):33-45. Review.

A2(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A2(vi): Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, Collet JP, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzolai L, Naylor AR, Roffi M, Röther J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I; ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2018 Mar 1;39(9):763-816.

A2(vii): Authors/Task Force Members:, Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corrà U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FDR, Løchen ML, Löllgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, Bart van der Worp H, van Dis I, Verschuren WMM. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Atherosclerosis. 2016 Sep;252:207-274.

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A3. Sistolik kan basıncı sürekli olarak >160 mmHg ve/veya diastolik kan basıncı sürekli olarak >90 mmHg olan hastalarda antihipertansif tedavi başlanması uygundur

A3(i): Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, Sever PS, Thom SM; BHS guidelines working party, for the British Hypertension Society.British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. BMJ 2004; 328(7440):634-40. Erratum in: BMJ 2004; 328(7445): 926.

A3(ii): Papademetriou V, Farsang C, Elmfeldt D, Hofman A, Lithell H, Olofsson B, Skoog I, Trenkwalder P, Zanchetti A;

Study on Cognition and Prognosis in the Elderly study group. Stroke prevention with the angiotensin II type 1-receptor blocker candesartan in elderly patients with isolated systolic hypertension: the Study on Cognition and Prognosis in the Elderly (SCOPE). J Am Coll Cardiol 2004; 44(6): 1175-80.

A3(iii): Bejan-Angoulvant T, Saadatian-Elahi M, Wright JM, Schron EB, Lindholm LH, Fagard R, Staessen JA, Gueyffier F. Treatment of hypertension in patients 80years and older: the lower the better? A meta-analysis of randomized controlled trials. J Hypertens 2010; 28(7): 1366-72.

A3(iv): George L B. Treatment of hypertension in patients with diabetes mellitus. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 23 Ekim 2019.

A3(v): Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement D, Coca A, De Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen S, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder R, Shlyakhto E, Tsioufis K, Aboyans V, Desormais I. 2018 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC). Blood Press. 2018 Dec;27(6):314-340.

A3(vi): Paul K. Whelton, Robert M. Carey, Wilbert S. Aronow, Donald E. Casey Jr., Karen J. Collins, Cheryl Dennison Himmelfarb, Sondra M. DePalma, Samuel Gidding, Kenneth A. Jamerson, Daniel W. Jones, Eric J. MacLaughlin, Paul Muntner, Bruce Ovbiagele, Sidney C. Smith Jr., Crystal C. Spencer, Randall S. Stafford, Sandra J. Taler, Randal J. Thomas, Kim A. Williams Sr., Jeff D. Williamson and Jackson T. Wright Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/ AGS/APhA/ASH/ ASPC /NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.. J Am Coll Cardiol 2018;71:e127-e248

A3(vii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A4. Kronik non-valvüler AF varlığında, CHA2DS2-VASc skoru göz önüne alınarak, OAK (vitamin K antagonistleri, direkt trombin inhibitorleri veya faktor Xa inhibitörleri) başlanması uygundur

**Vitamin K antagonistleri yerine non vitamin K antagonisti'nin (YOAK) tercih edilmesi önerilir.*

A4(i): Hughes M, Lip GY; Guideline Development Group, National Clinical Guideline forManagement of Atrial Fibrillation in Primary and Secondary Care, NationalInstitute for Health and Clinical Excellence. Stroke and thromboembolism inatrial fibrillation: a systematic review of stroke risk factors, riskstratification schema and cost effectiveness data. Thromb Haemost 2008; 99(2): 295-304Review.

A4(ii): Dentali F, Riva N, Crowther M, Turpie AG, Lip GY, Ageno W. Efficacy and safetyof the novel oral anticoagulants in atrial fibrillation: a systematic review and meta-analysis of the literature. Circulation 2012; 126(20): 2381-91. Review.

A4(iii): Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have non-valvular atrial fibrillation. Ann Intern Med 2007; 146(12): 857-67.

A4(iv): Aguilar MI, Hart R. Oral anticoagulants for preventing stroke in patients with non-valvular atrial fibrillation and no previous history of stroke or transient ischemic attacks. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD001927.

A4(v): Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Agewall S, Camm J, Baron Esquivias G,Budts W, Carerj S, Casselman F, Coca A, De Caterina R, Deftereos S, Dobrev D, Ferro JM, Filippatos G, Fitzsimons D, Gorenek B, Guenoun M, Hohnloser SH, Kolh P, Lip GY, Manolis A, McMurray J, Ponikowski P, Rosenhek R, Ruschitzka F, Savelieva I, Sharma S, Suwalski P, Tamargo JL, Taylor CJ, Van Gelder IC, Voors AA, Windecker S, Zamorano JL, Zeppenfeld K. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur J Cardiothorac Surg. 2016 Nov;50(5):e1-e88.

A4(vi): 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 Mar;44(2):213-8.

A5. Sistolik kalp yetersizliği (EF<= %40) veya ST elevasyonlu Mİ varlığında ACE inhibitörü tedavisi başlanması uygundur

A5(i): Fleg JL, Aronow WS, Frishman WH. Cardiovascular drug therapy in the elderly: benefits and challenges. Nat Rev Cardiol 2011; 8(1):13-28. Review.

A5(ii): Arif SA, Mergenhagen KA, Del Carpio RO, Ho C. Treatment of systolic heartfailure in the elderly: an evidence-based review. Ann Pharmacother 2010; 44(10): 1604-14. Review.

A5(iii): Lahoud R, Howe M, Krishnan SM, Zacharias S, Jackson EA. Effect of use of combination evidence-based medical therapy after acute coronary syndromes on long-term outcomes. Am J Cardiol 2012; 109(2): 159-64.

A5(iv): Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P. [2017 ESC

Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation.]. Kardiol Pol. 2018;76(2):229-313.

A5(v): Marco Roffi, Carlo Patrono, Jean-Philippe Collet, Christian Mueller, Marco Valgimigli, Felicita Andreotti, Jeroen J. Bax, Michael A. Borger, Carlos Brotons, Derek P. Chew, Baris Gencer, Gerd Hasenfuss, Keld Kjeldsen, Patrizio Lancellotti, Ulf Landmesser, Julinda Mehilli, Debabrata Mukherjee, Robert F. Storey, Stephan Windecker, ESC Scientific Document Group, 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC), European Heart Journal, Volume 37, Issue 3, 14 January 2016, Pages 267–315.

A5(vi): Task Force Members, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di Mario C, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabaté M, Senior R, Taggart DP, van der Wall EE, Vrints CJ; ESC Committee for Practice Guidelines, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S; Document Reviewers, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Rydén L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013 Oct;34(38):2949-3003.

A5(vii): Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, Douglas PS, Foody JM, Gerber TC, Hinderliter AL, King SB 3rd, Kligfield PD, Krumholz HM, Kwong RY, Lim MJ, Linderbaum JA, Mack MJ, Munger MA, Prager RL, Sabik JF, Shaw LJ, Sikkema JD, Smith CR Jr, Smith SC Jr, Spertus JA, Williams SV; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines; American College of Physicians; American Association for Thoracic Surgery; Preventive Cardiovascular Nurses Association; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2012 Dec 18;60(24):e44-e164.

A5(viii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

A6. Sistolik kalp yetersizliği (EF<= %40) veya iskemik kalp hastalığı (kronik iskemik kalp hastalığında antianjinal etki/ Mİ sonrası dönemde mortalite düşürücü etki nedeniyle) varlığında beta-bloker tedavi (sistolik KY'de bisoprolol/uzamış salınımlı metoprolol süksinat/karvedilol/nebivolol; iskemik kalp hastalığında herhangi bir beta-bloker) başlanması uygundur

**Miyokard infarktüsünden 3 yıl sonra beta-bloker tedavi potansiyel kar-zarar dengesi göz önünde bulundurularak kesilebilir.*

A6(i): Theo E M. Initial pharmacologic therapy of heart failure with reduced ejection fraction in adults. Son erişim tarihi 11 Kasım 2019.

A6(ii): Flather MD, Shibata MC, Coats AJ, et al. Randomized trial to determine the effect of nebivolol on mortality and cardiovascular hospital admission in elderly patients with heart failure (SENIORS). Eur Heart J 2005; 26:215.

A6(iii): van Veldhuisen DJ, Cohen-Solal A, Böhm M, et al. Beta-blockade with nebivolol in elderly heart failure patients with impaired and preserved left ventricular ejection fraction: Data From SENIORS (Study of Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors With Heart Failure). J Am Coll Cardiol 2009; 53:2150.

A6(iv): Veldhuisen DJ. Nebivolol in chronic heart failure: current evidence and future perspectives. Expert Opin Pharmacother. 2010 Apr;11(6):983-92.

A6(v): Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V,González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016 Jul 14;37(27):2129-2200.

A6(vi): Joseph P K, Julian M A, Bernard J G. Stable ischemic heart disease: Overview of care. Son erişim tarihi 23 Ekim 2019.

A6(vii): Smith SC Jr, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, Gibbons RJ, Grundy SM, Hiratzka LF, Jones DW, Lloyd-Jones DM, Minissian M, Mosca L, Peterson ED, Sacco RL, Spertus J, Stein JH, Taubert KA; World Heart Federation and the Preventive Cardiovascular Nurses Association. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011 Nov 29;124(22):2458-73.

A6(viii): 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 Mar;44(2):213-8.

B Santral Sinir Sistemi Kriterleri

B1. Majör depresif bozukluk varlığında antidepresan tedavi başlanması uygundur

B1(i): Lebowitz BD, Pearson JL, Schneider LS, Reynolds CF 3rd, Alexopoulos GS, Bruce ML, Conwell Y, Katz IR, Meyers BS, Morrison MF, Mossey J, Niederehe G, ParmeleeP. Diagnosis and treatment of depression in late life.Consensus statementupdate. JAMA 1997; 278(14): 1186-90. Review.

B1(ii): Mottram P, Wilson K, Strobl J. Antidepressants for depressed elderly. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003491. Review.

B1(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B1(iv): Charles F. Reynolds. Evidence-Based Treatment and Prevention of Major Depressive Episodes in Later Life in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017 page1487-1503.

B2. Fonksiyonelliği (işlevselliği) etkileyen persistan, ağır şiddette anksiyete varlığında SSRİ (SSRİ kontrendike ise SNRİ veya pregabalin) tedavisi başlanması uygundur

**Anksiyete tedavisinde, SSRİ'lerden yararlanmayan veya SSRİ'leri tolere edemeyen hastalarda, eşlik eden depresyon yok ise, buspiron monoterapisi kullanılabilir.*

B2(i): Allgulander C, Hartford J, Russell J, Ball S, Erickson J, Raskin J, Rynn M. Pharmacotherapy of generalized anxiety disorder: results of duloxetine treatment from a pooled analysis of three clinical trials. Curr Med Res Opin 2007; 23(6): 1245-52.

B2(ii): National Institute for Health and Clinical Excellence. Generalized anxiety disorder and panic disorder (with or without agoraphobia) in adults. Clinical Guideline 113. 2011. http://guidance.nice.org.uk/CG113 (son erişim tarihi 12 Kasım 2019).

B2(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B2(iv): Bystritsky A. Pharmacotherapy for generalized anxiety disorder in adults. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

B2(v): Brawman-Mintzer O, Knapp RG, Rynn M, et al. Sertraline treatment for generalized anxiety disorder: a randomized, double-blind, placebo-controlled study. J Clin Psychiatry 2006; 67:874.

B2(vi): Dahl AA, Ravindran A, Allgulander C, et al. Sertraline in generalized anxiety disorder: efficacy in treating the psychic and somatic anxiety factors. Acta Psychiatr Scand 2005; 111:429.

B2(vii): Davidson JR, Bose A, Korotzer A, Zheng H. Escitalopram in the treatment of generalized anxiety disorder: double-blind, placebo controlled, flexible-dose study. Depress Anxiety 2004; 19:234.

B2(viii): Davidson JR, Bose A, Wang Q. Safety and efficacy of escitalopram in the long-term treatment of generalized anxiety disorder. J Clin Psychiatry 2005; 66:1441.

B2(ix): Goodman WK, Bose A, Wang Q. Treatment of generalized anxiety disorder with escitalopram: pooled results from double-blind, placebo-controlled trials. J Affect Disord 2005; 87:161.

B2(x): Craske M, Bystritsky A. Approach to treating generalized anxiety disorder in adults. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 erişim tarihi 11 Kasım 2019

B2(xi): Baldwin DS, Anderson IM, Nutt DJ, Allgulander C, Bandelow B, den Boer JA, Christmas DM, Davies S, Fineberg N, Lidbetter N, Malizia A, McCrone P, Nabarro D, O'Neill C, Scott J, van der Wee N, Wittchen HU. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. J Psychopharmacol. 2014 May;28(5):403-39.

B2(xii): Lenze EJ, Rollman BL, Shear MK, Dew MA, Pollock BG, Ciliberti C, Costantino M, Snyder S, Shi P, Spitznagel E, Andreescu C, Butters MA, Reynolds CF 3rd. Escitalopram for older adults with generalized anxiety disorder: a randomized controlled trial. JAMA. 2009 Jan 21;301(3):295-303.

B2(xiii): Andreescu C, Varon D. New research on anxiety disorders in the elderly and an update on evidence-based treatments. Curr Psychiatry Rep. 2015 Jul;17(7):53.

B2(xiv): Daniel D. Sewell, Steve Koh, Jeanne Maglione, Ryan Greytak, Laura Marrone, Dilip V. Jeste. General Topics in Geriatric Psychiatry, ANXIETY DISORDERS. in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017 pages 1532-36.

#B3. Erken-orta evre Alzheimer hastalığında ChEi tedavisi başlanması uygundur

**Alzheimer hastalığında ChEi tedavisi başlanması için kanıt vardır.*

**Erken-orta evre Alzheimer hastalığında her 3 kolinesteraz inhibitörü (donepezil, galantamin, rivastigmin) için kanıt vardır ve FDA onayı mevcuttur*

**İleri evre Alzheimer hastalığında donepezil ile ilgili kanıt ve FDA onayı mevcuttur.*

**Parkinson hastalığı demansında rivastigmin başlanması için kanıt vardır ve FDA onayı mevcuttur. Parkinson hastalığı demansında donepezilin yararlı olabileceğine dair çalışmalar vardır*

**Diğer demans tiplerinden Lewy cisimcikli demans ve vasküler demansta ChEi kullanımına dair kesin kanıtlar yoktur ancak kullanılması önerilebilir.*

**Lewy cisimcikli demansta donepezil ve rivastigminin yararlı olabileceğine dair çalışmalar vardır. Lewy cisimcikli demansta FDA onayı ChEi'lerinin hiçbiri için mevcut değildir*

**Vasküler demansta kolinesteraz inhibitörlerinin yararlı olabileceğine dair çalışmalar vardır. Vasküler demansta FDA onayı ChEi'lerinin hiçbiri için mevcut değildir.*

B3(i): Raina P, Santaguida P, Ismaila A, Patterson C, Cowan D, Levine M, Booker L, Oremus M. Effectiveness of cholinesterase inhibitors and memantine for treating dementia: evidence review for a clinical practice guideline. Ann Intern Med 2008; 148(5): 379-97. Review.

B3(ii): Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev 2006 Jan 25;(1):CD005593. Review.

B3(iii): Rolinski M, Fox C, Maidment I, McShane R. Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. Cochrane Database Syst Rev 2012 Mar 14;3:CD006504.

B3(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B3(v): Press D, Alexander M. Cholinesterase inhibitors in the treatment of dementia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

B3(vi): Press D, Alexander M. Treatment of dementia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

B3(vii): Farlow MR. Prognosis and treatment of dementia with Lewy bodies. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

B3(viii): Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. McKeith I, Del Ser T, Spano P, Emre M, Wesnes K, Anand R, Cicin-Sain A, Ferrara R, Spiegel R Lancet. 2000;356(9247):2031;

B3(ix): Mori E, Ikeda M, Kosaka K, Donepezil-DLB Study Investigators. Donepezil for dementia with Lewy bodies: a randomized, placebo-controlled trial. Ann Neurol 2012; 72:41.

B3(x): Ikeda M, Mori E, Matsuo K, et al. Donepezil for dementia with Lewy bodies: a randomized, placebo-controlled, confirmatory phase III trial. Alzheimers Res Ther 2015; 7:4.

B3(xi): Emre M, Aarsland D, Albanese A, et al. Rivastigmine for dementia associated with Parkinson's disease. N Engl J Med 2004; 351:2509.;

B3(xii): Dubois B, Tolosa E, Katzenschlager R, Emre M, Lees AJ, Schumann G, Pourcher E, Gray J, Thomas G, Swartz J, Hsu T, Moline ML. Donepezil in Parkinson's disease dementia: a randomized, double-blind efficacy and safety study. Mov Disord. 2012 Sep 1;27(10):1230-8

B3(xiii): Malouf R, Birks J. Donepezil for vascular cognitive impairment. Cochrane Database Syst Rev. 2004;(1):CD004395. Review.

B3(xiv): Erkinjuntti T, Kurz A, Gauthier S, Bullock R, Lilienfeld S, Damaraju CV. Efficacy of galantamine in probable vascular dementia and Alzheimer's disease combined with cerebrovascular disease: a randomised trial. Lancet. 2002 Apr 13;359(9314):1283-90.

B3(xv): Auchus AP, Brashear HR, Salloway S, Korczyn AD, De Deyn PP, Gassmann-Mayer C; GAL-INT-26 Study Group. Galantamine treatment of vascular dementia: a randomized trial. Neurology. 2007 Jul 31;69(5):448-58.

B3(xvi): Birks J, McGuinness B, Craig D. Rivastigmine for vascular cognitive impairment. Cochrane Database Syst Rev. 2013 May 31;(5):CD004744. Review.

B3 (xvii): Ballard C, Sauter M, Scheltens P, He Y, Barkhof F, van Straaten EC, van der Flier WM, Hsu C, Wu S, Lane R. Efficacy, safety and tolerability of rivastigmine capsules in patients with

probable vascular dementia: the VantagE study. Curr Med Res Opin. 2008 Sep;24(9):2561-74.

B3(xviii): Mok V, Wong A, Ho S, Leung T, Lam WW, Wong KS. Rivastigmine in Chinese patients with subcortical vascular dementia. Neuropsychiatr Dis Treat. 2007 Dec;3(6):943-8.

B3(xix): Narasimhalu K, Effendy S, Sim CH, Lee JM, Chen I, Hia SB, Xue HL, Corrales MP, Chang HM, Wong MC, Chen CP, Tan EK. A randomized controlled trial of rivastigmine in patients with cognitive impairment no dementia because of cerebrovascular disease. Acta Neurol Scand. 2010 Apr;121(4):217-24.

B3(xx): U.S. Food and Drug Administration. Donepezil hydrochloride: Highlights of prescribing information by FDA. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/020690s035,021720s008,022568s005lbl.pdf erişim tarihi 11 Kasım 2019.

B3(xxi): U.S. Food and Drug Administration. Rivastigmine tartrate: Highlights of prescribing information by FDA Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/020823s016,021025s008lbl.pdf erişim tarihi 11 Kasım 2019.

B3(xxii): U.S. Food and Drug Administration. Galantamine hydrobromide: Highlights of prescribing information by FDA Available at: https://www.acce ssdata.fda.gov/d rugsatf da_docs/l abel/2017/021 169Orig 1s032,02 1224O ri g1s030,02161 5Or ig1s023lbl.pdf erişim tarihi 11 Kasım 2019

B3(xxiii): Birks JS, Harvey RJ. Donepezil for dementia due to Alzheimer's disease. Cochrane Database Syst Rev. 2018 Jun 18;6:CD001190.

B3(xxiv): Birks JS, Grimley Evans J. Rivastigmine for Alzheimer's disease. Cochrane Database Syst Rev. 2015 Apr 10;(4):CD001191.

#B4. Orta-ileri evre Alzheimer hastalığında memantin tedavisi başlanması uygundur

**Memantin'in vasküler demansta da etkinliği olabilir.*

**Memantin, demansın davranışsal ve psikiyatrik semptomlarında (BPSD) faydalı olabilir.*

B4(i): Memantine: Drug information, Lexicomp Online. Son erişim tarihi 22 Ekim 2019.

B4(ii): California ADS Tx guideline; Geldmacher DS. Treatment Guidelines for Alzheimer's Disease: Redefining Perceptions in Primary Care. Primary Care Companion to The Journal of Clinical Psychiatry. 2007;9(2):113-121

B4(iii): Press D, Alexander M. Treatment of dementia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

B4(iv): Reisberg B, Doody R, Stöffler A, Schmitt F, Ferris S, Möbius HJ; Memantine Study Group. Memantine in moderate-to-severe Alzheimer's disease. N Engl J Med. 2003 Apr 3;348(14):1333-41.

B4(v): Howard R, McShane R, Lindesay J, Ritchie C, Baldwin A, Barber R, Burns A, Dening T, Findlay D, Holmes C, Hughes A, Jacoby R, Jones R, Jones R, McKeith I, Macharouthu A, O'Brien J, Passmore P, Sheehan B, Juszczak E, Katona C, Hills R, Knapp M, Ballard C, Brown R, Banerjee S, Onions C, Griffin M, Adams J, Gray R, Johnson T, Bentham P, Phillips P. Donepezil and memantine for moderate-to-severe Alzheimer's disease. N Engl J Med. 2012 Mar 8;366(10):893-903.

B4(vi): Chen R, Chan PT, Chu H, Lin YC, Chang PC, Chen CY, Chou KR. Treatment effects between monotherapy of donepezil versus combination with memantine for Alzheimer disease: A meta-analysis. PLoS One. 2017 Aug 21;12(8):e0183586.

B4(vii): Orgogozo JM, Rigaud AS, Stöffler A, Möbius HJ, Forette F. Efficacy and safety of memantine in patients with mild to moderate vascular dementia: a randomized, placebo-controlled trial (MMM 300). Stroke. 2002 Jul;33(7):1834-9.

B4(viii): Wilcock G, Möbius HJ, Stöffler A; MMM 500 group. A double-blind, placebo-controlled multicentre study of memantine in mild to moderate vascular dementia (MMM500). Int Clin Psychopharmacol. 2002 Nov;17(6):297-305.

B4(ix): Guidelines for the treatment of Alzheimer's disease. NHS Foundation Trust. Review Jan 2012. Available at: http://www.humber.nhs.uk/Downloads/Services/Pharmacy/Guidelines/Alzheimer%20disease%20treatment%20guidelines.pdf (erişim tarihi 11 Kasım 2019)

B4(x): McShane R, Westby MJ, Roberts E, Minakaran N, Schneider L, Farrimond LE, Maayan N, Ware J, Debarros j. Memantine for dementia. Cochrane Database of Systemic Reviews 2019, Issue 3. Art. No: CD003154.

#B5. Fonksiyonelliği (işlevselliği) etkileyen esansiyel tremoru olan hastalara propranolol veya pirimidon tedavisi başlanması uygundur

**Pirimidon'un FDA onayı yoktur.*

**Pirimidon yan etkileri (sedasyon, vertigo ve bulantı) yaygındır. Kulanıldığında düşük dozda başlanıp yavaş doz artırımı yapılmalıdır.*

B5(i): Zesiewicz TA, Evidence-based guideline update: treatment of essential tremor: report of the Quality Standards subcommittee of the American Academy of Neurology. Neurology. 2011 Nov 8;77(19):1752-5.

B5(ii): Reich SG. Essential Tremor. Med Clin North Am. 2019 Mar;103(2):351-356. doi: 10.1016/j.mcna.2018.10.016. Review.

B5(iii): Haubenberger D, Hallett M. Essential Tremor. N Engl J Med. 2018 May 10;378(19):1802-1810. doi: 10.1056/NEJMcp1707928. Review.

B5(iv): Primidone: Drug information, Lexicomp online. Son erişim tarihi 12 Kasım 2019.

B6. Fonksiyonel (işlevsel) bozukluk ve dizabiliteye sebep olan idiyopatik Parkinson hastalığı varlığında L-dopa tedavisi başlanması uygundur

B6(i): Marjama-Lyons JM, Koller WC. Parkinson's disease. Update in diagnosis and symptom management. Geriatrics 2001; 56(8): 24-5, 29-30, 33-5. Review.

B6(ii): Danisi F. Parkinson's disease. Therapeutic strategies to improve patient function and quality of life. Geriatrics 2002; 57(3): 46-50; quiz 52. Review.

B6(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B6(iv): Ferreira JJ,Summary of the recommendations of the EFNS/MDS-ES review on therapeutic management of Parkinson's disease. Eur J Neurol. 2013 Jan;20(1):5-15

B6(v): Spindler MA, Tarsy D. Initial pharmacologic treatment of Parkinson disease. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 12 Kasım 2019.

B6(vi): Kotagal V, Bohnen NI. Parkinson Disease and Related Disorders in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017. Pages 1422-28.

B6(vii): Connolly BS, Lang AE. Pharmacological treatment of Parkinson disease: a review. JAMA. 2014 Apr 23-30;311(16):1670-83. doi: 10.1001/jama.2014.3654. Review.

B7. İdiyopatik Parkinson hastalarında açık-kapalı motor dalgalanmalar başladığında, L-dopa tedavisine MAO-B inhibitörü veya COMT inhibitörü eklenmesi uygundur

B7(i): Ferreira JJ, Summary of the recommendations of the EFNS/MDS-ES review on therapeutic management of Parkinson's disease. Eur J Neurol. 2013 Jan;20(1):5-15.

B7(ii): Kotagal V, Bohnen NI. Parkinson Disease and Related Disorders in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A; 2017. Pages 1428-30.

B7(iii): Connolly BS, Lang AE. Pharmacological treatment of Parkinson disease: a review. JAMA. 2014 Apr 23-30;311(16):1670-83. doi: 10.1001/jama.2014.3654. Review.

B8. Demir eksikliği ve kronik böbrek yetersizliğinin dışlandığı huzursuz bacak sendromu olan hastalarda, semptomlar yaşam kalitesini olumsuz etkiliyorsa, alfa-2-delta kalsiyum kanal blokerleri (pregabalin, gabapentin) veya dopamin agonistleri (pramipeksol/ropinirol/rotigotin) başlanması uygundur

**L-dopa tedavisi (50-200 mg), özellikle intermitan semptomu olan olgularda uygun olabilir. Böbrek yetersizliği olan semptomatik olgularda da tercih edilebilir.*

B8(i): Zintzaras E, Kitsios GD, Papathanasiou AA, Konitsiotis S, Miligkos M, Rodopoulou P, Hadjigeorgiou GM. Randomized trials of dopamine agonists in restless legs syndrome: a systematic review, quality assessment, and meta-analysis. Clin Ther 2010; 32(2): 221-37. Review.

B8(ii): Hansen RA, Song L, Moore CG, Gilsenan AW, Kim MM, Calloway MO, Murray MD. Effect of ropinirole on sleep outcomes in patients with restless legs syndrome: meta-analysis of pooled individual patient data from randomized controlled trials. Pharmacotherapy 2009; 29(3): 255-62.

B8(iii): Scholz H, Trenkwalder C, Kohnen R, Riemann D, Kriston L, Hornyak M. Dopamine agonists for restless legs syndrome. Cochrane Database Syst Rev. 2011 Mar 16;(3):CD006009. doi: 10.1002/14651858.CD006009.pub2. Review.

B8(iv): Garcia-Borreguero D, Stillman P, Benes H, Buschmann H, Chaudhuri KR, Gonzalez Rodríguez VM, Högl B, Kohnen R, Monti GC, Stiasny-Kolster K, Trenkwalder C,Williams AM, Zucconi M. Algorithms for the diagnosis and treatment of restless legs syndrome in primary care. BMC Neurol. 2011 Feb 27;11:28

B8(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

B8(vi): Silber MH. Treatment of restless legs syndrome and periodic limb movement disorder in adults. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 erişim tarihi 11 Kasım 2019

B8(vii): Trenkwalder C, Stiasny K, Pollmächer T, Wetter T, Schwarz J, Kohnen R, Kazenwadel J, Krüger HP, Ramm S, Künzel M, et al. L-dopa therapy of uremic and idiopathic restless legs syndrome: a double-blind, crossover trial. Sleep. 1995Oct;18(8):681-8.

B8(viii): Garcia-Borreguero D, Silber MH, Winkelman JW, Högl B, Bainbridge J, Buchfuhrer M, Hadjigeorgiou G, Inoue Y, Manconi M, Oertel W, Ondo W, Winkelmann J, Allen RP. Guidelines for the first-line treatment of restless legs syndrome/Willis-Ekbom disease, prevention and treatment of dopaminergic augmentation: a combined task force of the IRLSSG, EURLSSG, and the RLS-foundation. Sleep Med. 2016 May;21:1-11.

B8(ix): Winkelman JW, Armstrong MJ, Allen RP, Chaudhuri KR, Ondo W, Trenkwalder C, Zee PC, Gronseth GS, Gloss D, Zesiewicz T. Practice guideline summary: Treatment of restless legs syndrome in adults: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2016 Dec 13;87(24):2585-2593.

C: Gastrointestinal Sistem Kriterleri

C1. Yaşam tarzı değişikliklerine (diyet-egzersiz) yanıtsız semptomatik konstipasyonu olan olgularda, fekal tıkaç dışlanarak, lif desteği (psilyum, metilselüloz, polikarbofil, buğday dekstrin) veya polietilenglikol başlanması uygundur

C1(i): Rao SSC. Constipation in the older adult.In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019

C1(ii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

C1(iii): Emmanuel A, Mattace-Raso F, Neri MC, Petersen KU, Rey E, Rogers J.Constipation in older people: A consensus statement. Int J Clin Pract. 2017Jan;71(1).

C1(iv): Bharucha AE, Pemberton JH, Locke GR 3rd. American GastroenterologicalAssociation technical review on constipation. Gastroenterology. 2013Jan;144(1):218-38. doi:10.1053/j.gastro.2012.10.028. Review.

D: Solunum Sistemi Kriterleri

D1. Hafif-orta astım veya KOAH'ı olan hastalarda düzenli inhale beta2 agonist veya antikolinerjik tedavi başlanması uygundur

D1(i): Pauwels RA, Buist AS, Ma P, Jenkins CR, Hurd SS; GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: National Heart, Lung, and Blood Institute and World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary. Respir Care 2001; 46(8): 798-825. Review.

D1(ii): Keating GM. Tiotropium bromide inhalation powder: a review of its use in the management of chronic obstructive pulmonary disease. Drugs 2012; 72(2):273-300. Review.

D1(iii): Yohannes AM, Hardy CC. Treatment of chronic obstructive pulmonary disease in older patients: a practical guide. Drugs Aging 2003; 20(3): 209-28. Review.

D1(iv): McCrory DC, Brown CD. Anti-cholinergic bronchodilators versusbeta2-sympathomimetic agents for acute exacerbations of chronic obstructivepulmonary disease. Cochrane Database Syst Rev. 2002;(4):CD003900. Review.

D1(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

D1(vi): Global Initiative For Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease.2018 Report.Available at: https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf son erişim tarihi 23 October 2019.

D1(vii): Anderson GP1.Current issues with beta2-adrenoceptor agonists: pharmacology and molecular and cellular mechanisms. Clin Rev Allergy Immunol. 2006 Oct-Dec;31(2-3): 119-30.

D2. FEV1< %50 olan ve oral steroid tedavisi gerektiren tekrarlayan alevlenmeleri olan orta-ağır astım veya KOAH hastalarında düzenli inhale kortikosteroid tedavisi başlanması uygundur

D2(i): Global Initiative For Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease.2018 Report. Available at: https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf Son erişim tarihi 23 Ekim 2019.

D2(ii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

D3. Kronik hipoksemisi (PO_2<= 55 mmHg veya SO_2<= %88) olan hastalarda evde sürekli oksijen tedavisi başlanması uygundur

D3(i): Tiep BL, Carter R. Long-term supplemental oxygen therapy.In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 erişim tarihi 11 Kasım 2019

D3(ii): 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 Mar;44(2):213-8. Doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

D3(iii): Croxton TL, Bailey WC. Long-term oxygen treatment in chronic obstructive pulmonary disease: recommendations for future research: an NHLBI workshop report. Am J Respir Crit Care Med 2006; 174:373.

D3(iv): Sjöberg F, Singer M. The medical use of oxygen: a time for critical reappraisal. J Intern Med2013; 274:505.

D3(v): Global Initiative For Chronic Obstructive Lung Disease. Global Strategy ort he Diagnosis, Management, and Prevention

of Chronic Obstructive Pulmonary Disease.2018 Report. Available at: https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf Son erişim tarihi 23 Ekim 2019.

E: Kas İskelet Sistemi Kriterleri ve Analjezik İlaçlar

#E1. Günlük diyetle vitamin D alımı <800-1000 İÜ veya elementer kalsiyum alımı <1000-1200 mg olan hastalarda replasman tedavisinin başlanması uygundur

E1(i): Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R; National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014 Oct;25(10):2359-81. doi:10.1007/s00198-014-2794-2. Epub 2014 Aug 15. Erratum in: Osteoporos Int. 2015 Jul;26(7):2045-7.

E1(ii): Rosen HN. Calcium and vitamin D supplementation in osteoporosis. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

E1(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E1(iv): Camacho PM, Petak SM, Binkley N, Clarke BL, Harris ST, Hurley DL, Kleerekoper M, Lewiecki EM, Miller PD, Narula HS, Pessah-Pollack R, Tangpricha V, WimalawansaSJ, Watts NB. American Association Of Clinical Endocrinologists And Americancollege of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2016. Endocr Pract. 2016 Sep2;22(Suppl 4):1-42.

E1(v): Heflin MT. Geriatric health maintenance. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

E1(vi): Stephen R. Lord. Falls.in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017 pages 1032-42.

E1(vii): Dennis H. Sullivan, Larry E. Johnson. Nutrition and Obesityin Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017 page 723-24.

E2. Dökümante osteoporozu olan [frajilite fraktürü ve/veya kemik mineral dansitometri T skoru (femur total, femur boyun veya lomber < -2,5)] hastalarda anti-rezorptif (bifosfonat, denosumab) veya anabolik ajan (parathormon anoloğu) başlanması uygundur

**Tedavi aynı zamanda yeterli D vitamini ve elementer kalsiyum alımını da içermelidir.*

E2(i): Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R; National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014 Oct;25(10):2359-81. doi: 10.1007/s00198-014-2794-2. Epub 2014 Aug 15. Erratum in: Osteoporos Int. 2015 Jul;26(7):2045-7.

E2(ii): O'Donnell S, Cranney A, Wells GA, Adachi JD, Reginster JY. Strontium ranelate for preventing and treating postmenopausal osteoporosis. Cochrane Database SystRev. 2006 Jul 19;(3):CD005326. Review. Update in: Cochrane Database Syst Rev.2006;(4):CD005326.

E2(iii): Rosen HN, Drezner MK. Overview of the management of osteoporosis in postmenopausal women. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

E2(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E2(v): Camacho PM, Petak SM, Binkley N, Clarke BL, Harris ST, Hurley DL, Kleerekoper M, Lewiecki EM, Miller PD, Narula HS, Pessah-Pollack R, Tangpricha V, WimalawansaSJ, Watts NB. American Association of Clinical Endocrinologists and Americancollege of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2016. Endocr Pract. 2016 Sep2;22(Suppl 4):1-42.

E2(vi): Eastell R, Rosen CJ, Black DM, Cheung AM, Murad MH, Shoback D. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society*Clinical Practice Guideline. J Clin Endocrinol Metab. 2019 May 1;104(5):1595-1622.

E3. Uzun süreli (beklenen süre ≥3 ay) sistemik kortikosteroid tedavisi başlanan hastalarda: i) ≥7,5 mg/gün prednizolon veya eşdeğer steroid tedavisi alacaklarda, ii) eğer T skoru < -1 ise dozdan bağımsız steroid tedavisi alacak tüm hastalarda, bifosfonat tedavisi başlanması uygundur

**>=70 yaş olgularda, dozdan bağımsız uzun süreli (>3 ay) steroid tedavisi alacak tüm hastalara da, bifosfonat tedavisi başlanması uygun olabilir.*

**Tedavi aynı zamanda yeterli D vitamini ve temel kalsiyum alımını da içermelidir.*

E3(i): Homik J, Suarez-Almazor ME, Shea B, Cranney A, Wells G, Tugwell P. Calcium and vitamin D for corticosteroid-induced osteoporosis. Cochrane Database Syst Rev 2000; (2): CD000952. Review.

E3(ii): Iwamoto J, Takeda T, Sato Y. Effects of antifracture drugs in postmenopausal, male and glucocorticoid-induced osteoporosis--usefulness of alendronate and risedronate. Expert Opin Pharmacother 2007; 8(16): 2743-56. Review.

E3(iii): Glucocorticoid Induced Osteoporosis. Osteoporosis and metabolic bone disease diagnosis and treatment guidelines of the Society of Endocrinology and Metabolism of Turkey • 2018. Page 59-61. Available at: http://www.temd.org.tr/admin/uploads/tbl_gruplar/20180517113533-2018-05-17tbl_gruplar113531.pdf erişim tarihi 11 Kasım 2019. (Türkçe)

E3(iv): Allen CS, Yeung JH, Vandermeer B, Homik J. Bisphosphonates for steroid-induced osteoporosis. Cochrane Database Syst Rev. 2016 Oct 5;10:CD001347. Review.

E3(v): Rosen HN, Saag KG.Prevention and treatment of glucocorticoid-induced osteoporosis.In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

E3(vi): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E3(vii): Compston J, Cooper A, Cooper C, Gittoes N, Gregson C, Harvey N, Hope S, Kanis JA, McCloskey EV, Poole KES, Reid DM, Selby P, Thompson F, Thurston A, Vine N; National Osteoporosis Guideline Group (NOGG). UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos. 2017 Dec;12(1):43.

E3(viii): Lekamwasam S, Adachi JD, Agnusdei D, Bilezikian J, Boonen S, Borgström F, Cooper C, Diez Perez A, Eastell R, Hofbauer LC, Kanis JA, Langdahl BL, Lesnyak O, Lorenc R, McCloskey E, Messina OD, Napoli N, Obermayer-Pietsch B, Ralston SH, Sambrook PN, Silverman S, Sosa M, Stepan J, Suppan G, Wahl DA, Compston JE; Joint IOF-ECTS GIO Guidelines Working Group. A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis. Osteoporos Int. 2012 Sep;23(9):2257-76.

E4. En az iki doz denosumab tedavisi sonlandırıldıktan sonra uzun etkili antirezorbtif tedavi başlanması uygundur (denosumab kesilmesini takiben rebound BTM'lerde artış, BMD kaybı ve vertebral fraktür riskinde artış olur)

**Rebound etki iki dozdan sonra denosumab tedavisi kesilen olgularda daha belirgindir.*

E4(i): Eastell R, Rosen CJ, Black DM, Cheung AM, Murad MH, Shoback D. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab. 2019 May 1;104(5):1595-1622.

E4(ii): TsourdiE et al. Discontinuation of denosumab therapy for osteoporosis: a systematic review and position statement by ECTS. Bone2017;105:11–17.

E4(iii): Horne AM, Mihov B, Reid IR. Bone loss after romosozumab/denosumab: effects of bisphosphonatesCalcif Tissue Int 2018;103:55–61.

E4(iv): Reid IR, Horne AM, Mihov B, Gamble GD. Bone loss after denosumab: only partial protection with zoledronateCalcif Tissue Int. 2017;101:371–374.

#E5. Teriparatid tedavisi sonrası antirezorbtif tedavi başlanması uygundur

E5(i): Camacho PM, Petak SM, Binkley N, Clarke BL, Harris ST, Hurley DL, Kleerekoper M, Lewiecki EM, Miller PD, Narula HS, Pessah-Pollack R, Tangpricha V, WimalawansaSJ, Watts NB. American Association Of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2016. Endocr Pract. 2016 Sep2;22(Suppl 4):1-42.

E5(ii): Meier C, Uebelhart B, Aubry-Rozier B, Birkhäuser M, Bischoff-Ferrari HA, Frey D, Kressig RW, Lamy O, Lippuner K, Stute P, Suhm N, Ferrari S. Osteoporosis drug treatment: duration and management after discontinuation. A position statement from the SVGO/ASCO. Swiss Med Wkly. 2017 Aug 16;147:w14484.

E5(iii): Eastell R, Rosen CJ, Black DM, Cheung AM, Murad MH, Shoback D. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society* Clinical Practice Guideline. J Clin Endocrinol Metab. 2019 May 1;104(5):1595-1622

E6. Kronik aktif romatolojik hastalık varlığında hastalığı modifiye edici tedavi başlanması uygundur

E6(i): Saag KG, Teng GG, Patkar NM, Anuntiyo J, Finney C, Curtis JR, Paulus HE,Mudano A, Pisu M, Elkins-Melton M, Outman R, Allison JJ, Suarez Almazor M,Bridges SL Jr, Chatham WW, Hochberg M, MacLean C, Mikuls T, Moreland LW, O'DellJ, Turkiewicz AM, Furst DE; American College of Rheumatology. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum 2008; 59(6): 762-84.

E6(ii): Köller MD, Aletaha D, Funovits J, Pangan A, Baker D, Smolen JS. Response of elderly patients with rheumatoid arthritis to methotrexate or TNF inhibitors compared with younger patients. Rheumatology (Oxford) 2009; 48(12): 1575-80.

E6(iii): Fleischmann R, Baumgartner SW, Weisman MH, Liu T, White B, Peloso P. Long term safety of etanercept in elderly subjects with rheumatic diseases. Ann Rheum Dis 2006; 65(3): 379-84.

E6(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E6(v): Smolen JS, Landewé R, Bijlsma J, Burmester G, Chatzidionysiou K, Dougados M, Nam J, Ramiro S, Voshaar M, van Vollenhoven R, Aletaha D, Aringer M, Boers M, Buckley CD, Buttgereit F, Bykerk V, Cardiel M, Combe B, Cutolo M, van Eijk-Hustings Y, Emery P, Finckh A, Gabay C, Gomez-Reino J, Gossec L, Gottenberg JE, Hazes JMW, Huizinga T, Jani M, Karateev D, Kouloumas M, Kvien T, Li Z, Mariette X, McInnes I, Mysler E, Nash P, Pavelka K, Poór G, Richez C, van Riel P, Rubbert-Roth A, Saag K, da Silva J, Stamm T, Takeuchi T, Westhovens R, de Wit M, van der Heijde D. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76(6):960-977. doi: 10.1136/annrheumdis-2016-210715. Epub 2017 Mar 6. Review.

E7. Metotreksat alan hastalarda folik asit desteği başlanması uygundur

E7(i): Visser K, Katchamart W, Loza E, Martinez-Lopez JA, Salliot C, Trudeau J,Bombardier C, Carmona L, van der Heijde D, Bijlsma JW, Boumpas DT, Canhao H,Edwards CJ, Hamuryudan V, Kvien TK, Leeb BF, Martín-Mola EM, Mielants H,Müller-Ladner U, Murphy G, Østergaard M, Pereira IA, Ramos-Remus C, Valentini G, Zochling J, Dougados M. Multinational evidence-based recommendations for the use of methotrexate in rheumatic disorders with a focus on rheumatoid arthritis: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative. Ann Rheum Dis 2009; 68(7): 1086-93.

E7(ii): Ortiz Z, Shea B, Suarez Almazor M, Moher D, Wells G, Tugwell P. Folic acid and folinic acid for reducing side effects in patients receiving methotrexate for rheumatoid arthritis. Cochrane Database Syst Rev 2000; (2):CD000951. Review.

E7(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E7(iv): Shea, B., Swinden, M. V., Ghogomu, E. T., Ortiz, Z., Katchamart, W., Rader, T.,... & Tugwell, P. (2014). Folic acid and folinic acid for reducing side effects in patients receiving methotrexate for rheumatoid arthritis. The Journal of rheumatology, 41(6), 1049-1060.

E7(v): British National Formulary vol. 76, September 2018-March 2019: p 993, 888-89.

E7(vi): Smolen JS, Landewé R, Bijlsma J, Burmester G, Chatzidionysiou K, Dougados M,Nam J, Ramiro S, Voshaar M, van Vollenhoven R, Aletaha D, Aringer M, Boers M,Buckley CD, Buttgereit F, Bykerk V, Cardiel M, Combe B, Cutolo M, vanEijk-Hustings Y, Emery P, Finckh A, Gabay C, Gomez-Reino J, Gossec L, Gottenberg JE, Hazes JMW, Huizinga T, Jani M, Karateev D, Kouloumas M, Kvien T, Li Z,Mariette X, McInnes I, Mysler E, Nash P, Pavelka K, Poór G, Richez C, van Riel P,Rubbert-Roth A, Saag K, da Silva J, Stamm T, Takeuchi T, Westhovens R, de Wit M, van der Heijde D. EULAR recommendations for the management of rheumatoidarthritis with synthetic and biological disease-modifying antirheumatic drugs:2016 update. Ann Rheum Dis. 2017 Jun;76(6):960-977. doi:10.1136/annrheumdis-2016-210715. Epub 2017 Mar 6. Review.

E8. Tekrarlayan gut atağı olan hastalarda ksantin oksidaz inhibitörü (öncelikle allopürinol) başlanması uygundur

E8(i): Fravel MA, Ernst ME. Management of gout in the older adult. Am J Geriatr Pharmacother 2011; 9(5): 271-85. Review.

E8(ii): Zhang W, Doherty M, Bardin T, Pascual E, Barskova V, Conaghan P, Gerster J,Jacobs J, Leeb B, Lioté F, McCarthy G, Netter P, Nuki G, Perez-Ruiz F, Pignone A,Pimentão J, Punzi L, Roddy E, Uhlig T, Zimmermann-Gòrska I; EULAR Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2006; 65(10): 1312-24. Review.

E8(iii): Tayar JH, Lopez-Olivo MA, Suarez-Almazor ME. Febuxostat for treating chronic gout. Cochrane Database Syst Rev. 2012 Nov 14;11:CD008653. Review.

E8(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E8(v): British National Formulary vol. 76, September 2018-March 2019: p 1085-87.

E8(vi): Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castañeda-Sanabria J, Coyfish M, Guillo S, Jansen TL, Janssens H, Lioté F, Mallen C, Nuki G, Perez-RuizF, Pimentao J, Punzi L, Pywell T, So A, Tausche AK, Uhlig T, Zavada J, Zhang W,Tubach F, Bardin T. 2016 updated EULAR evidence-based recommendations for themanagement of gout. Ann Rheum Dis. 2017 Jan;76(1):29-42. doi:10.1136/annrheumdis-2016-209707. Epub 2016 Jul 25. Review.

E9. Orta-ağır düzeydeki ağrı tedavisinde diğer analjeziklerin (parasetamol, NSAİİ veya hafif opioidler) yeterli olmadığı durumlarda güçlü etkili opioid tedavisi başlanması uygundur

E9(i): Papaleontiou M, Henderson CR Jr, Turner BJ, Moore AA, Olkhovskaya Y, Amanfo L,Reid MC. Outcomes associated with opioid use in the treatment of chronic non-cancer pain in older adults: a systematic review and meta-analysis. J Am Geriatr Soc 2010; 58(7): 1353-69. Review.

E9(ii): van Ojik AL, Jansen PA, Brouwers JR, van Roon EN. Treatment of chronic pain in older people: evidence-based choice of strong-acting opioids. Drugs Aging 2012; 29(8): 615-25. Review.

E9(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E9(iv): Guerriero F. Guidance on opioids prescribing for the management of persistent non-cancer pain in older adults. World J Clin Cases. 2017 Mar 16;5(3):73-81.

E9(v): Bruce A. Ferrell. Pain Management in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017.

E10. Kronik ağrılı olan ve uzun etkili opioid kullanan hastalarda, kaçak ağrı varlığında (breakthrough pain: aralıklarla gelen şiddetli ağrılar) tedaviye kısa etkili opioidlerin eklenmesi uygundur (şiddetli ağrının kontrol edilememe riski)

E10(i): Portenoy RK, Mehta Z, Ahmed E. Cancer pain management with opioids: Optimizing analgesia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

E10(ii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

E10(iii): John G. Cagle, Eric W. Widera. Geriatrics and Palliative Care in Current Diagnosis and Treatment: Geriatrics Second edition. Eds. Brie Williams, Anna Chang, C. Seth Landefeld, Cyrus Ahalt, Rebecca Conant, Helen Chen.; 2014 page 65.

E10(iv): Bruce A. Ferrell. Pain Management in Hazzards Geriatric Medicine and Gerontology Seventh edition. Eds. Halter J B, Ouslander J G, Studenski S, High K P, Asthana S, Ritchie C S, Supiano M A,; 2017 page 1204-1211.

F: Endokrin Sistem Kriterleri

F1. Diabetes mellitus'lu hastalarda aşikar proteinüri (>300 mg/gün) veya mikroalbuminüri (>30 mg/gün) varlığında, ACEi veya ARB tedavisi başlanması uygundur

**Böbrek yetersizliği olan olgularda ACEi veya ARB tedavisinin başlangıç döneminde serum kreatinin düzeyinde artış beklenir.*

**Bu artış %30'dan az ise tedaviye devam edilmesi önerilir.*

**ACEi veya ARB başlanması açısından mutlak kontrendike bir bazal kreatinin düzeyi olmamakla birlikte serum kreatinin düzeyi >3,0 mg/dl olan hastalarda başlanmaması önerilebilir.*

**Diabetes mellitus'lu hastalarda ACEİ-ARB tedavisi başlangıcından sonraki 1-2 hafta içinde, her doz artışında ve en az yılda 1 defa serum kreatinin ve potasyum düzeyi monitörize edilmelidir (hiperpotasemi ve renal bozulma riski)*

F1(i): Schmidt M, Mansfield KE, Bhaskaran K, Nitsch D, Sørensen HT, Smeeth L, Tomlinson LA. Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: cohort study. BMJ. 2017 Mar 9;356:j791.

F1(ii): Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor-associated elevations in serum creatinine: is this a cause for concern? Arch Intern Med. 2000 Mar 13;160(5):685-93.

F1(iii): Bicket DP. Using ACE inhibitors appropriately. Am Fam Physician. 2002 Aug 1;66(3):461-8. Review.

G: Ürogenital Sistem Kriterleri

#G1. Prostatektominin endike olmadığı, orta-ağır (IPSS skoru) düzeyde semptomatik LUTS (alt uriner sistem semptomları) mevcut olan hastalarda alfa-1 reseptör blokeri kullanımı uygundur

G1(i): Lowe FC. Role of the newer alpha, -adrenergic-receptor antagonists in the treatment of benign prostatic hyperplasia-related lower urinary tract symptoms. Clin Ther 2004; 26(11): 1701-13. Review.

G1(ii): Schwinn DA, Roehrborn CG. Alpha1-adrenoceptor subtypes and lower urinary tractsymptoms. Int J Urol. 2008 Mar;15(3):193-9. doi:10.1111/j.1442-2042.2007.01956.x. Review.

G1(iii): Dunn CJ, Matheson A, Faulds DM. Tamsulosin: a review of its pharmacology and therapeutic efficacy in the management of lower urinary tract symptoms. Drugs Aging 2002; 19(2):135-61. Review.

G1(iv): Cunningham GR, Kadmon D. Medical treatment of benign prostatic hyperplasia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

G1(v): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

G1(vi): S. Gravas (Chair), J.N. Cornu, M.J. Drake, M. Gacci, C. Gratzke, T.R.W. Herrmann, S. Madersbacher, C. Mamoulakis, K.A.O. Tikkinen Guidelines Associates: M. Karavitakis, I. Kyriazis, S. Malde, V. Sakkalis, R. Umbach. EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology 2018. Page 17-18.

#G2. Prostatektominin endike olmadığı orta-ağır (IPSS skoru) düzeyde semptomatik LUTS (alt uriner sistem semptomları) mevcut olan hastalarda, prostat hacmi >30-40 mL ise, alfa-1 reseptör blokerine ek olarak 5-alfa redüktaz inhibitörü tedavisi başlanması uygundur

G2(i): Cunningham GR, Kadmon D. Medical treatment of benign prostatic hyperplasia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

G2(ii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

G2(iii): S. Gravas (Chair), J.N. Cornu, M.J. Drake, M. Gacci, C. Gratzke, T.R.W. Herrmann, S. Madersbacher, C. Mamoulakis, K.A.O. Tikkinen Guidelines Associates: M. Karavitakis, I. Kyriazis, S. Malde, V. Sakkalis, R. Umbach. EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). European Association of Urology 2018. Page 18-19.

G3. Semptomatik atrofik vajinitte, hormon-dışı tedaviler denendikten sonra, topikal vajinal östrojen tedavisi kullanımı uygundur

G3(i): Lynch C. Vaginal estrogen therapy for the treatment of atrophic vaginitis. J Womens Health (Larchmt) 2009; 18(10): 1595-606. Review.

G3(ii): Bachmann G, Bouchard C, Hoppe D, Ranganath R, Altomare C, Vieweg A, Graepel J, Helzner E. Efficacy and safety of low-dose regimens of conjugated estrogens cream administered vaginally. Menopause 2009; 16(4): 719-27.

G3(iii): Mainini G, Scaffa C, Rotondi M, Messalli EM, Quirino L, Ragucci A. Local estrogen replacement therapy in postmenopausal atrophic vaginitis: efficacy and safety of low dose 17beta-estradiol vaginal tablets. Clin Exp Obstet Gynecol 2005; 32(2): 111-3.

G3(iv): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

G3(v): The use of vaginal estrogen in women with a history of estrogen-dependent breast cancer. Committee Opinion No. 659. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;127:e93–6.

G3(vi): The NAMS 2017 Hormone Therapy Position Statement Advisory Panel. The 2017 hormone therapy position statement of The North American Menopause Society.Menopause. 2017 Jul;24(7):728-753.

G3(vii): Bergendal A, Kieler H, Sundström A, Hirschberg AL, Kocoska-Maras L. Risk ofvenous thromboembolism associated with local and systemic use of hormone therapy in peri- and postmenopausal women and in relation to type and route ofadministration. Menopause. 2016 Jun;23(6):593-9.

G3(viii): Calle EE, Feigelson HS, Hildebrand JS, Teras LR, Thun MJ, Rodriguez C. Postmenopausal hormone use and breast cancer associations differ by hormone regimen and histologic subtype. Cancer 2009; 115(5): 936-45. Erratum in: Cancer 2009; 115(7): 1587.

G3(ix): Diergaarde B, Potter JD, Jupe ER, Manjeshwar S, Shimasaki CD, Pugh TW, Defreese DC, Gramling BA, Evans I, White E. Polymorphisms in genes involved in sex hormone metabolism, estrogen plus progestin hormone therapy use, and risk of postmenopausal breast cancer. Cancer Epidemiol Biomarkers Prev 2008; 17(7): 1751-9.

H: Aşılar.

H1. Yıllık influenza aşısı yapılması uygundur

**Trivalan yüksek doz ve tetravalan influenza aşılarının yaşlıda etkinlikleri standart doz trivalan aşıya göre daha fazladır, tercih edilebilir.*

** Tetravalan, trivalan ve yüksek doz trivalan influenza aşılarının FDA onayı vardır.*

H1(i): Hibberd PL. Seasonal influenza vaccination in adults. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 erişim tarihi 11 Kasım 2019

H1(ii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

H1(iii): U.S. Food and Drug Administration. Vaccines Licensed for Use in the United States. Content current as of: 05/09/2019. Available at: https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states (erişim tarihi 10 Kasım 20192019)

H1(iv): Grohskopf LA, Alyanak E, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and Control of Seasonal Influenza with

Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2019–20 Influenza Season. MMWR Recomm Rep 2019;68(No. RR-3):1–21.

H2. 65 yaşından sonra Pnömokok aşısı (13 valan konjuge ve 23 valan polisakkarit aşıdan herbiri için bir doz) yapılması uygundur

i) *Daha önce pnömokok aşısı yapılmamış bireylerde ilk doz aşı olarak 13 valan konjuge aşı, takiben en az 1 yıl sonra 23 valan polisakkartd aşı uygulanmalıdır.*

ii) *Daha önce 23 valan polisakkarit aşı yapılmış bireylerde 1 yıl sonra 13 valan konjuge aşı yapılmalıdır.*

**23 valan polisakkarit aşı 65 yaş öncesinde uygulanmışsa, 65 yaş üstünde ilk aşıdan en az 5 yıl sonra tekrarlanmalıdır*

**23 valan polisakkarit aşının 65 yaş üzeri 10 yılda bir tekrarlanması önerilebilir*

H2(i): Advisory Committee on Immunization Practices. Recommended Adult Immunization Schedule, United States, 2019.Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf. (erişim tarihi 10 Kasım 2019 2019)

H2(ii): An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Update on the use of 13-valent pneumococcal conjugate vaccine (PNEU-C-13) in addition to 23-valent pneumococcal polysaccharide vaccine (PNEU-P-23) in immunocompetent adults 65 years of age and older – Interim Recommendation. Date published: October 2016. Available at: https://www.canada.ca/en/public-health/services/publications/healthy-living/update-use-of-13-valent-pneumococcal-conjugate-vaccine-pneu-c-13-in-addition-to-23-valent-pneumococcal-polysaccharide-vaccine-pneu-p-23-immunocompetent-adults-65-years-and-older-interim-recommendation.html (erişim tarihi 10 Kasım 2019)

H2(iii): 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 Mar;44(2):213-8. doi: 10.1093/ageing/afu145. Epub 2014 Oct 16. Review.

H2(iv): U.S. Food and Drug Administration. Vaccines Licensed for Use in the United States. Content current as of: 05/09/2019. Available at: https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states (Son erişim tarihi 10 Kasım 2019.)

H2(v): Heflin MT. Geriatric health maintenance. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 Son erişim tarihi 11 Kasım 2019.

H3. Herpes zoster aşısı yapılması uygundur (zona infeskiyonu riskinde ve postherpetik nevralji riskinde azalma sağlar)

**Daha önce zona infeksiyonu veya su çiçeği geçirmiş olguların da aşılanması önerilir.*

**RZV, ZVL'den daha fazla koruma sağlar.*

**RZV, ZVL'ye tercih edilir.*

**RZV intramüsküler olarak iki dozda uygulanır. İkinci doz, ilk dozdan 2-6 ay sonra verilmelidir. Bu program, önceden herpes zoster öyküsü olanlar ve daha önce ZVL almış olanlar dahil tüm hastalar için kullanılmalıdır.*

**Zona infeksiyonu geçiren olgularda aşılama en erken 6-12 ay sonra önerilir.*

H3(i): Oxman MN, Levin MJ, Shingles Prevention Study Group. Vaccination against Herpes Zoster and Postherpetic Neuralgia. J Infect Dis 2008; 197 Suppl 2:S228.

H3(ii): Albrecht MA, Levin MJ. Vaccination for the prevention of shingles (herpes zoster).In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 erişim tarihi 10 Kasım 2019

H3(iii): Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, Arbeit RD,Simberkoff MS, Gershon AA, Davis LE, Weinberg A, Boardman KD, Williams HM, Zhang JH, Peduzzi PN, Beisel CE, Morrison VA, Guatelli JC, Brooks PA, Kauffman CA,Pachucki CT, Neuzil KM, Betts RF, Wright PF, Griffin MR, Brunell P, Soto NE,Marques AR, Keay SK, Goodman RP, Cotton DJ, Gnann JW Jr, Loutit J, Holodniy M,Keitel WA, Crawford GE, Yeh SS, Lobo Z, Toney JF, Greenberg RN, Keller PM,Harbecke R, Hayward AR, Irwin MR, Kyriakides TC, Chan CY, Chan IS, Wang WW,Annunziato PW, Silber JL; Shingles Prevention Study Group. A vaccine to preventherpes zoster and postherpetic neuralgia in older adults. N Engl J Med. 2005 Jun 2;352(22):2271-84.

H3(iv): Heflin MT. Geriatric health maintenance. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 erişim tarihi 11 Kasım 2019

H3(v): Kimberlin DW, Whitley RJ. Varicella-zoster vaccine for the prevention ofherpes zoster. N Engl J Med. 2007 Mar 29;356(13):1338-43. Review.

H3(vi): Curran D, Patterson BJ, Van Oorschot D, Buck PO, Carrico J, Hicks KA, Lee B,Yawn BP. Cost-effectiveness of an adjuvanted recombinant zoster vaccine in older adults in the United States who have been previously vaccinated with zostervaccine live. Hum Vaccin Immunother. 2019;15(4):765-771. doi:10.1080/21645515.2018.1558689. Epub 2019 Feb 20.

H3(vii): U.S. Food and Drug Administration. Vaccines Licensed for Use in the United States. Content current as of: 05/09/2019. Available at: https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states (erişim tarihi 10 Kasım 2019)

H3(viii): An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Updated Recommendations on the Use of Herpes Zoster Vaccines. Date published: 2018-08-30.

H4. 10 yılda bir Td (tetanoz-difteri toksoidi) yapılması uygundur

**Pertusis aşısı 1 yaşından büyük infantlarla yakın teması olan yaşlılarda (dede, nine gibi) önerilebilir. Bu durumda tek doz TdaP şeklinde uygulanabilir*

H4(i): Recommended Adult Immunization Schedule for ages 19 years or older. https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf. erişim tarihi 23 Ekim 2019

H4(ii): Ridda I, Yin JK, King C, Raina MacIntyre C, McIntyre P. The importance ofpertussis in older adults: a growing case for reviewing vaccination strategy in the elderly. Vaccine. 2012 Nov 6;30(48):6745-52.

H4(iii): Centers for Disease Control and Prevention (CDC). Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine from the Advisory Committee on Immunization Practices, 2010. MMWR Morb Mortal Wkly Rep 2011; 60:13.

H4(iv): Heflin MT. Geriatric health maintenance. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 erişim tarihi 11 Kasım 2019

H4(v): Liang JL, Tiwari T, Moro P, Messonnier NE, Reingold A, Sawyer M, Clark TA. Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the UnitedStates: Recommendations of the Advisory Committee on Immunization Practices(ACIP). MMWR Recomm Rep. 2018 Apr 27;67(2):1-44.

H4(vi): Diphtheria, tetanus toxoids, and acellular pertussis vaccine (DTaP and Tdap): Drug information, Lexicomp online. erişim tarihi 11 Kasım 2019.

#H5. Hacca gidecek olgulara meningokok aşısı yapılması uygundur

**Hacdan en az 10 gün önce önerilir.*

**5 yıldan sonra tekrar seyahat edilecekse doz tekrarlanmalıdır.*

H5(i): Recommended Adult Immunization Schedule for ages 19 years or older. https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf. erişim tarihi 23 Ekim 2019

H5(ii): David O F, Karin L. Immunizations for travel. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2019 erişim tarihi 10 Kasım 2019

H5(iii): Kim DK, Riley LE, Hunter P; Advisory Committee on Immunization Practices. Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States, 2018. Ann Intern Med. 2018 Feb 6;168(3):210-220.

I: Suplemanlar.

I1. Malnütrisyon (MN) veya malnütrisyon riski (MNR) olan yaşlılarda beslenme danışmanlığı ve besin takviyesi diyetle alımı artırmak ve beslenme hedeflerine ulaşmak için yeterli değil ise oral nütrisyonel suplemanların (ONS) başlanması uygundur

**Kronik hastalığı olan yaşlılarda ONS başlanması ile ilgili daha çok kanıt vardır.*

**ONS içeriğinin günlük en az 400 kcal enerji ve 30 g protein içermesi ve ONS'nin en az 1 ay devam edilmesi önerilir.*

**ONS verilen olguların ayda 1 değerlendirilmesi uygundur.*

**Tedavide rehberlik etmesi açısından yaşlı bireylerde enerji alımı için tavsiye edilen değer 30 kcal/kg/gün'dür.*

**Sağlıklı yaşlı bireylerde protein alımı 1,0-1,2 g/kg/gün önerilmektedir*

**Akut veya kronik hastalığı olan yaşlı bireyler için protein alımı 1,2-1,5 g/kg/gün önerilmektedir.*

**Ciddi hastalığı, yaralanma veya malnütrisyonu olan yaşlı bireyler için protein alımının 1,5 g/kg/gün'ün üzerine 2,0 g/kg/gün'e kadar çıkarılması gerekebilir.*

I1(i): LLLnutrition Topic 8. Approach to Oral and Enteral Nutrition in Adults. Module 8.1. Indications, Contraindications, Complications and Monitoring of EN. Zanetti M. Available at: https://lllnutrition.com/mod/page/view.php?id=2654; (erişim tarihi 10 Kasım 2019.)

I1(ii): Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. Clin Nutr 2008; 27: 5-15.

I1(iii): Stratton RJ, Green CJ, Elia M. Disease-related malnutrition: an evidence-based approach to treatment. First Edition. CABI; First edition (January 30, 2003)

I1(iv): Guest JF, Panca M, Baeyens JP, de Man F, Ljungqvist O, Pichard C, Wait S, Wilson L. Health economic impact of managing patients following a community-based diagnosis of malnutrition in the UK. Clin Nutr. 2011; 30: 422-429.

I1(v): lllnutrition: Topic 36. Nutrition in OlderAdults. Module 36.1 Epidemiology, Aetiology and Consequences of Malnutrition in Older Adults: Cederholm T. Available at: https://lllnutrition.com/mod/page/view.php?id=2685#u361p4 (erişim tarihi 10 Kasım 2019)

I1(vi): Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, Kiesswetter E, Maggio M, Raynaud-Simon A, Sieber CC, Sobotka L, van Asselt D, Wirth R, Bischoff SC. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr. 2018 Jun 18.pii: S0261-5614(18)30210-3.

I2. Hastanede yatan MN veya MNR olan yaşlılarda oral nutrisyonel suplemanların (ONS) başlanması uygundur (besin alımı ve vücut ağırlığını artırır, komplikasyon ve tekrar başvuru riskini azaltır)

**Spontan oral enerji alımı akut hastane yatışı olan yaşlılarda genellikle düşüktür ve gereksinimleri karşılamamaktadır.*

**Hastaneden çıktıktan sonra çoğu olguda ONS kullanımına devam etmek uygun olabilir.*

I2(i): Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, Kiesswetter E, Maggio M, Raynaud-Simon A, Sieber CC, Sobotka L, van Asselt D, Wirth R, Bischoff SC. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr. 2018 Jun 18.pii: S0261-5614(18)30210-3.

I3. Kalça kırığı olan yaşlı hastalara postoperatif dönemde ONS başlanması (nütrisyonel durumundan bağımsız olarak) uygundur (besin alımını iyileştirir ve komplikasyon riskini azaltır)

**Spesifik bir ONS (standart veya yüksek proteinli) önerisi yoktur.*

**ONS'nin en az 1 ay verilmesi uygun olabilir. Çalışmalarda, kalça kırığı sonrası ONS 1-6 ay arası kullanılmıştır.*

**Preoperatif başlanması da düşünülebilir.*

I3(i): Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, Kiesswetter E, Maggio M, Raynaud-Simon A, Sieber CC, Sobotka L, van Asselt D, Wirth R, Bischoff SC. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr. 2018 Jun 18.pii: S0261-5614(18)30210-3.

I4. Bası yarası mevcut olan hastalarda yeterli protein ve enerji alımını sağlamak için 1,2-2 g/kg/gün protein, 30-35 kcal/kg / gün enerji hedeflenerek ONS başlanması uygundur

**Bası yarası olan malnütre hastalarda, arjinin, çinko ve antioksidanlarla zenginleştirilmiş yüksek protein ve enerji içeriğine sahip ONS kullanımı daha faydalı olabilir.*

**Bası yarası olan hastalarda beslenme ürünlerine arjinin, glutamin ve HMB eklenmesinin olumlu sonuçları olabilir.*

I4(i): Gomes F, Schuetz P, Bounoure L, Austin P, Ballesteros-Pomar M, Cederholm T, Fletcher J, Laviano A, Norman K, Poulia KA, Ravasco P, Schneider SM, Stanga Z, Weekes CE, Bischoff SC. ESPEN guidelines on nutritional support for polymorbid internal medicine patients. Clin Nutr. 2018 Feb;37(1):336-353.

I4(ii): Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, Kiesswetter E, Maggio M, Raynaud-Simon A, Sieber CC, Sobotka L, van Asselt D, Wirth R, Bischoff SC. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr. 2018 Jun 18.pii: S0261-5614(18)30210-3.

I4(iii): Stratton RJ, Ek AC, Engfer M, Moore Z, Rigby P, Wolfe R, Elia M. Enteralnutritional support in prevention and treatment of pressure ulcers: a systematic review and meta-analysis. Ageing Res Rev. 2005 Aug;4(3):422-50. Review.

I4(iv): Volkert D, Berner YN, Berry E, Cederholm T, Coti Bertrand P, Milne A, Palmblad J, Schneider S, Sobotka L, Stanga Z; DGEM (German Society for Nutritional Medicine), Lenzen-Grossimlinghaus R, Krys U, Pirlich M, Herbst B, Schütz T, Schröer W, Weinrebe W, Ockenga J, Lochs H; ESPEN (European Society for Parenteral and Enteral Nutrition). ESPEN Guidelines on Enteral Nutrition: Geriatrics. Clin Nutr. 2006 Apr;25(2):330-60.

I4(v): Cereda E, Klersy C, Serioli M, Crespi A, D'Andrea F; OligoElement Sore Trial Study Group. A nutritional formula enriched with arginine, zinc, and antioxidants for the healing of pressure ulcers: a randomized trial. Ann Intern Med. 2015 Feb 3;162(3):167-74. doi: 10.7326/M14-0696. Erratum in: Ann Intern Med. 2015 Dec 15;163(12):964.

I4(vi): Liu P, Shen WQ, Chen HL. Efficacy of arginine-enriched enteral formulas for the healing of pressure ulcers: a systematic review. J Wound Care. 2017 Jun 2;26(6):319-323.

I4(vii): Wong A, Chew A, Wang CM, Ong L, Zhang SH, Young S. The use of a specialised amino acid mixture for pressure ulcers: a placebo-controlled trial. J Wound Care. 2014 May;23(5):259-60, 262-4, 266-9.

Kısaltmalar:

ACEİ: Anjiotensin konverting enzim inhibitörleri

ARB: Anjiotensin reseptör blokerleri

BTM: Kemik turnover belirteçleri

ChEİ: Asetilkolinesteraz inhibitörleri

COMT: Catechol-O-methyltransferase

EF: Ejeksiyon fraksiyonu

eGFR: Estimated Glomerular Filtrasyon hızı

FDA: Food and Drug Administration

FEV1: Zorlu ekspiratuvar volüm

GİS: Gastrointestinal sistem

IPSS: Uluslararası Prostat Semptom Skoru

KOAH: Kronik obstrüktif akciğer hastalığı

KMD: Kemik mineral dansitesi

LUTS: Alt üriner sistem semptomları

MAO-B: Monoamine oxidase-B

Mİ: Miyokard infarktüsü

MN: Malnürisyon

MNR: Malnütrisyon riski

NSAİİ: Non steroidal anti inflamatuar ilaçlar

OAK: Oral antikoagülan

ONS: Oral nütrisyonel supleman

RZV: Rekombinant zoster aşısı

SaO_2: Oksijen saturasyonu

SNRIs: Serotonin-norepinefrin geri alım inhibitörleri

SSRIs: Selektif serotonin geri alım inhibitörleri

TdaP: Tetanoz, difteri, and aselüler pertussis

ZVL: Canlı zoster aşısı

#Uluslararası Delfi paneli çalışmasında konsensus sağlanmayan kriterler

ORIGINAL RESEARCH

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Post-COVID-19 Management: Comprehensive Assessment at Post-COVID-19 Monitoring Centre

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Abstract

Objective: The 2019 Coronavirus disease-2019 (COVID-19) is a novel disease that affects multiple systems. Several details about its long-term effects are unknown. Follow-up and early detection of post-COVID conditions could help improve outcomes. We established a multidisciplinary "Post-COVID-19 Monitoring Centre" in İstanbul University Medical School Hospital and aimed to introduce this centre to represent a model for centres that would provide post-COVID care.

Materials and Methods: We outlined the multidisciplinary healthcare team professions, the schedule for organising the appointments and specific intervals, and the items of comprehensive assessment and the consultant services at the centre.

Results: The first appointment for inpatients and outpatients are scheduled at first month after discharge and 1 month after symptoms have resolved, respectively, and at 3-month intervals thereafter unless necessitated more often. The specialists involved in post-COVID-19 care are internal medicine, respiratory medicine, infection disease, geriatrics and nutrition, psychiatry, public health medicine and consultant specialists (radiology, ophthalmology, gastroenterology, cardiology and neurology). Geriatricians come at the forefront as experts and case managers that can integrate and manage the multidisciplinary team because of their experience and practices in routine care.

Conclusion: Comprehensive assessment and follow-up of COVID-19 recovery patients would help us understand the long-term consequences of the disease. We reveal that multidisciplinary management of COVID-19 survivors may greatly improve outcomes in several aspects. Moreover, we suggest that setting up similar centres for post-COVID-19 care contributes to the management of this pandemic globally.

Keywords: Post-COVID-19, multidisciplinary team, long-term consequences, care, follow-up

Introduction

New coronavirus, Severe Acute Respiratory syndrome-coronavirus-2 (SARS-Cov-2), is an important human and animal pathogen which has been identified at the end of the 2019 in Wuhan (China) and has rapidly spread to all countries throughout world. This pandemic related to Coronavirus disease-2019 (COVID-19) has resulted in more than 27 million confirmed cases and more than 890,000 deaths worldwide (1). Although most people are asymptomatic, symptomatic infection occasionally occur and the symptoms vary among patients. The respiratory system is the most effected system with common symptoms of dry cough, fever, fatigue, shortness of breath (2). Previous evidence demonstrated that the virus can be more than just respiratory symptoms that can also attack the other systems including cardiovascular, gastrointestinal, urinary system, coagulopathies, cutaneous

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manifestations, neurological system. In addition, there are comorbidities and conditions that affect severity of COVID-19, i.e., age, diabetes mellitus, hypertension, cancer and obesity (3,4). Moreover, information and experience about long-term consequences of COVID-19 is not enough known yet, as it is a very new disease with only a few months history. On the other hand, evidence from two previous outbreaks of other coronaviruses (SARS and MERS) could help guiding scientists for potential long-term sequels of it (5,6). With the light of this background, multidisciplinary attitude is important in management and follow-up of the COVID-19.

The main aim after acute-term treatment of the disease should be identifying and following the biological and psychosocial long-term consequences, as well. Based on acute term data and previous coronaviruses outbreaks' evidence, a comprehensive assessment of the individuals is required to understand and manage the long-term effects. At this aspect, geriatricians are the experts that can integrate and manage the multidisciplinary team as case managers because they are very experienced in this regard and involved in similar practices in their routine care. For this purpose, İstanbul University Medical Hospital (İstanbul, Turkey) has constituted a multidisciplinary healthcare service called "Post-COVID-19 Monitoring Centre". To our knowledge, this is the second multidisciplinary center dedicated to this purpose (7). Geriatricians, the specialties that take part in acute management of COVID-19, i.e., emergency medicine, internal medicine, infectious diseases, pulmonary diseases, radiology, and intensive care are involved in this center together with the specialties from public health, psychiatry, ophthalmology, gastroenterology, cardiology and neurology to display multidisciplinary examination in the post-COVID-19 Monitoring Centre (Table 1).

Table 1. Specialties take part at post-COVID assessment	
Internal medicine	
Respiratory medicine	
Infectious diseases	
Geriatrics and nutrition	
Psychiatry	
Radiology	
Public health medicine	
Consultant specialties	Radiology Ophthalmology Gastroenterology Cardiology Neurology
COVID-19: Coronavirus disease-2019	

Materials and Methods

The Methods of Care in the Post-COVID-19 Center

Appointment for post-COVID-19 monitoring centre

COVID-19 patients present with variety of symptoms amongst individuals, ranging from asymptomatic infection to severe respiratory failure. Recovery duration depends on preexisting illnesses and comorbidities and their severity and patient ages. However, COVID-19 is a new worldwide disease, there is no data about its long-term complications of inpatient and outpatient patients. Persistent symptoms after recovery were reported (8,9). İstanbul University post-COVID-19 Monitoring Center has been established for the purpose to identify the problems that may develop in the short and long term of inpatient and outpatient patients who survived the acute phase.

1. Patients who were hospitalized and monitored at the İstanbul Medical Faculty pandemic wards and were followed up at home with a diagnosis of COVID-19 are called by phone and arranged an appointment to the monitoring center. Additionally, patients who were treated in a different hospital can also apply to the monitoring center by making an appointment by phone.

2. The first appointment for the inpatients is created after the first month after discharge.

3. The first appointment for the patient's followed up at home is created one month after symptoms have resolved.

4. Patients who require close monitoring after the first monitoring center assessment, the second appointment is made according to the physician's decision. If there is no special condition, the second appointment is made for 3 months later, and the patient is notified before leaving the center.

Statistics

Quantitative variables are expressed as mean ± standard deviation if they contain continuous data. If they contain categorical data, they are expressed as percentage (%) and frequency (n).

Comparison of qualitative variables was analyzed using the Pearson chi-square test. The normal distribution, which was used to question the presence of parametric data in the data containing the measurement, was examined by Kolmogrov-Smirnov and Curtosis-Skewness tests. Age showed normal distribution, which could be parametric. A Student's t-test was used to compare parameters including only age.

Kruskal-Wallis test was used for the analysis of continuous and more than two independent non-parametric groups (Bonferroni correction was used when necessary) and Mann-Whitney U test was used for post-hoc analysis. receiver operating characteristic (ROC) curves dependent groups were handled one by one, ROC

curves were drawn and "area under the curve (AUC)", "sensitive (sens) and specificity (spes) of cut-off values" were shown. Additionally, the optimum cut-off point suggestions were given for the parameters. Patient data that exceeds the cut-off value indicates that it involves a high risk in that parameter. The closer the AUC value is to 100, the better the cut-off points are, in that regard. This study suggested that these cut-off values can be used for these parameters in healthcare facilities, which are considered to include practically similar patients. The results were evaluated in 95% confidence interval and statistical significance level was defined as $p<0.05$. The analyzes were performed using IBM SPSS-21 (Statistical Package for Social Sciences, Chicago, IL, USA).

Comprehensive Assessment at the Post COVID-19 Monitoring Center

During comprehensive assessment, a number of CGA components have been applied by different specialists at post- COVID-19 care center (Table 2).

General Assessment

Vital signs and blood collection

The patient, after ID check is completed, is directed to the blood drawing unit. The patient's fever, blood pressure, pulse, oxygen saturation measurement is recorded, and blood drawing is performed by the nurse in charge.

Laboratory

Recent studies have shown reinfection with coronavirus, re-hospitalization need, long-term pulmonary sequalae, and post-traumatic stress disorder (10,11). Common laboratory abnormalities among hospitalized patients with COVID-19 include lymphopenia, elevated aminotransaminase levels, elevated lactate dehydrogenase levels, elevated inflammatory markers (e.g., ferritin, C-reactive protein, and erythrocyte sedimentation rate), and abnormalities in coagulation tests (12). In addition to these laboratory parameters, lipid profile and thyroid function tests and parathormone level are checked at the first visit. Quarantine itself and long-term hospitalization are associated with decreased physical activity and unhealthy diet that could provoke cardiovascular disease (13). Evaluating blood lipid profile at the early stage could guide physicians. Previous evidence of other coronaviruses showed that thyroid follicular cells and parafollicular cells were also injured, thus could reflect with abnormalities of the TT3, TT4, TSH and PTH levels (14,15). Thyroid functional abnormalities may be correlated with the severity of COVID-19 (16).

Table 2. Components and methods of the comprehensive geriatric assessment for post-COVID-19 follow-up

Frailty	FRAIL
Malnutrition	GLIM and MNA-SF
Sarcopenia	SARC-F, BIA (skeletal muscle mass index (SMM/height^2)
Physical performance	Hand grip
Anthropometric evaluation	Body weight, BMI
Geriatric syndromes	Falls, sleep disorder, urinary and fecal incontinence, constipation, vertigo, forgetfulness, anhedonia
Activities of daily living	Katz-ADL, Lawton&Brody-IADL

FRAIL. Simple frailty questionnaire, GLIM: Global Leadership Initiative on Malnutrition, MNA-SF: Mini nutritional assessment-short form, SARC-F: Simple frailty questionnaire, BIA: Bioelectrical impedance analyses, BMI: Body mass index, ADL: Activities of daily living, IADL: Instrumental activities of daily living, COVID-19: Coronavirus disease-2019

Antibody tests are important for determining seroprevalence in a particular population, detecting and monitoring population immunity (17). All recovered patients' blood are collected for assessing antibodies

Internal Medicine Assessment

The patient is directed to the internal medical specialist after vital signs monitoring and blood sample collection. Patients' past records during the hospitalization at the İstanbul Medical Hospital pandemic services are checked before the assessment. Comprehensive medical assessment including detailed clinical and pharmacologic history, physical examination, anthropometric measurements were performed to the patients by the internal medical specialist. COVID-19 symptoms such as cough, chest pain, shortness of breath, nausea and diarrhea are asked using a standard questionnaire enrollment. The presence of an additional or new onset complaint of recovery COVID-19 patients is also recorded. Previous study reported post-COVID-19 patients had persistence of at least 1 symptom, mainly fatigue and dyspnea (8).

Respiratory Medicine Assessment

The spectrum of symptomatic infection ranges from mild to severe, as pneumonia appears to be the most common severe manifestation of COVID-19 infection, mostly characterized by fever, cough, shortness of breath. Computed tomography (CT) findings may differ depending on time points and severity of the diseases. Typical chest imaging findings are usually multifocal, bilateral and peripheral ground-glass opacification with or without consolidative abnormalities, consistent with viral pneumonia (18). However, the early phase of the disease may present as a single lesion, most commonly located in the inferior lobe of the right lung (19).

Previous early study has found decreased lung function and residual imaging abnormalities at the first month after discharge (20). Decreased lung function might not be reversible. Although not much is known about long-term respiratory complications for COVID-19 patients, there are a lot of information for other coronaviruses SARS and MERS. Experience showed that the impact of the new coronavirus

on the pulmonary system is similar with those of SARS and MERS (21). Persistent lung injury was detected at the previous epidemics (6,22).

In the light of these, the long-term following up of pulmonary function will be important for reducing pulmonary functional impairment by making an early decision to consult the patient on chest physiotherapy and functional rehabilitation. After the acute phase of COVID-19, 6-minute walking test and spirometry are planned on the sixth month.

Patients with severe pulmonary findings at the initial diagnosis of COVID-19 have a control low-density thoracic CT at the same day in the post-COVID-19 monitoring center. The patients who have severe respiratory distress and newly developed suspicious opacification are directed to hospitalization.

Geriatrics' Assessment

COVID-19 is typically more severe and lethal among older people and they are at significantly increased risk for morbidity and mortality (12). However, older adults with chronic conditions (e.g., diabetes, chronic pulmonary disease, heart failure, cancer, dementia, polypharmacy) have greater impairment in immunity. Even more physiological chances of aging itself causes a decrease in the cell-mediated and humoral immune system (23), resulting in greater sensitivity to common infections. In addition, older adults with COVID-19 or other infection diseases may present with subtle findings. Clinicians should bear in mind the illnesses could present in older adults with non-specific symptoms such as falls, confusion or worsening functional impairment (24). Any preexisting medical condition could be worsened at infected older patients. The presence of multiple factors of COVID-19 in elderly patients could influence the physical or cognitive frailty that complicates patient prognosis. Therefore, it requires a multidisciplinary assessment and management for elderly patient's demands. In this regard, geriatricians are probably best doctors on management of elderly COVID-19 patients. Geriatricians at İstanbul University post-COVID-19 Monitoring Centre work in teams with internal medicine specialists, infection disease specialists, pneumonologists, and psychiatrists. COVID-19 patients over the age of 65 are examined by the geriatricians in this unit, in terms of evaluating their nutritional status and geriatrics syndromes. A meta-analysis demonstrated that comprehensive geriatric assessments (CGA) benefit on physical and functional status and mortality (25). Detailed model is organized for the assessment of elderly COVID-19 people in purpose of providing them the most suitable treatment and care for their needs (Table 3). The components of CGA chosen for post-COVID-19 care were screening/assessments of physical frailty, nutritional status, sarcopenia, physical performance, anthropometric evaluation, geriatric

Table 3. Components of care applied in post-COVID-19 care center

General assessment	**Vital signs:** Fever, oxygen saturation, heart rate, blood pressure **Laboratory assessment:** Glucose, creatinine, BUN, electrolytes, uric aside, liver enzymes (AST, ALT, GGT, LDH) cholesterol levels (LDL, HDL, total cholesterol, triglycerides), CK, albumin, total protein, troponin, D-dimer, pro-BNP, INR, aPTT, ferritin, fibrinogen, hemogram, inflammatory markers (CRP), thyroid function test and antibodies, Antibody of SARS-CoV-2 infection
Internal medicine	Medical, clinical and drug history Allergy Vaccination history (BCG) Lifestyle (smoking) Past and present signs and symptoms of COVID-19 Treatment received for COVID-19 (supplemental oxygen, antibiotics, anti-retroviral, hydroxychloroquine, immunomodulators) Use of personal protective equipment (PPE): gloves, eye protection, facemasks Electrocardiogram
Respiratory medicine	Respiratory symptoms Chest X-ray and/or chest CT scan 6-min walking test Spirometry (lung capacity for carbon monoxide) Borg scale
Infection diseases	Detecting for reinfection
Geriatrics	Anthropometric evaluation (weight, BMI) Bioelectric impedance analysis (BIA) Comprehensive geriatric assessment (fall, sleep disorder, urinary incontinence, constipation, malnutrition, sarcopenia, frailty) **Tests:** FRAIL, MNA, SARC-F, the Barthtel ADL, the Lawton IADL index, GLIM Physical performance (hand grip)
Psychiatry	Psychiatric disorders (hospital anxiety and depression scale (HADS), impact of event scale-revised (IES-R)
Radiology	Chest X-ray and or chest CT scan
Cardiovascular assessment	Echocardiography
Gastroenterology	Gastrointestinal symptoms or history of chronic gastrointestinal diseases
Ophthalmology	Ophthalmological assessment
Public health medicine	Socio-demographic status Socio-economic status Self-determinations/fears/self-confidence
Neurology	Central and peripheral neurvous system evaluation (if necessary cranial MR, cranial CT) and cognitive function

CT: Computed tomography, MR: Magnetic resonance, COVID-19: Coronavirus disease-2019, SARS-CoV-2: Severe Acute Respiratory syndrome-coronavirus-2

syndromes and functional status. These components were selected because COVID-19 is very likely to result in frailty, malnutrition, sarcopenia, physical performance deterioration, progression in geriatric syndromes and impairments in functional abilities (26).

Psychiatric Assessment

The COVID-19 pandemic may be associated with psychiatric symptoms in the general population because of the uncertainty about the consequences of the duration of the pandemic, symptoms, high mortality rates and high risk of transmission. Previous data suggest that patient with COVID-19 might experience significant psychiatric symptoms of anxiety, depression, distress, insomnia and post-traumatic stress disorder (27,28). For patients recovering from COVID-19, the psychological dimension of this pandemic has been much more dramatic. During their hospitalization these patients are isolated for long-term due to biological risk from COVID-19. There are only a few data available on psychiatric illness in COVID-19 patients. However, research on previous coronavirus outbreaks (SARS and MERS) suggest that many patients with COVID-19 will show psychiatric symptoms and disorders (28). A study investigating psychopathology in COVID-19 survivors at one-month follow-up after hospital treatment showed a high prevalence of pathological score for at least one psychiatric disorder. They predict that higher incidence of PTSD, major depression, and anxiety are expected in survivors (29). In the light of these, mental health support is important for the COVID-19 survivors to prevent the possible development of serious psychiatric disorders in the future. In order to prevent chronic psychiatric disorder, hospital anxiety and depression scale and impact of event scale-revised test are applied by the psychiatrist with patient's approval who apply to the post-COVID-19 monitoring center.

Public Health Medicine

Public health specialists are the doctors who are responsible of improving and protecting the health of people and the communities in which they live. They research diseases and illnesses; detect and try to find to prevention measures for infectious diseases. Additionally, the aim of public health is finding a way to decrease health disparities and promoting healthier lifestyles.

Public health specialists make calls for the appointment at the İstanbul University post COVID-19 monitoring center. Psychosocial questionnaire is formed for the recovered patients that involves questions about their socio-demographic analyze, physiological and socio-economical status. Patients are directed to appropriate unit (e.g., social workers specialists, psychiatrists) after the public health specialists' assessment if they needed.

Specialist Consultations

Radiology

Patients with severe pulmonary findings at the initial diagnosis of COVID-19 have control low-density chest CT on the same day at the post-COVID-19 monitoring center. Primary evaluation of chest CT is made by respiratory medicine specialist. Most commonly findings at chest CT are ground-glass opacifications (83%), ground-glass opacifications with mixed consolidation (58%), pleural thickening (52%), interlobular septal thickening (48%) and air bronchograms (46%) (30). Chest CT of COVID-19 patient is consulted to a radiologist if there are less common, unusual and unexpected findings.

Ophthalmology

There are few reports on the association of COVID-19 with ocular abnormalities as conjunctivitis, including conjunctival hyperemia, chemosis, epiphora or increased secretions (31). COVID-19 patients may have a number of complex and varied systemic coagulation abnormalities. Ocular intravascular hypercoagulation is possible situation. If required, the ophthalmology specialist will complete all ophthalmological evaluation for a possible ocular complication.

Gastroenterology

COVID-19 patients could present with gastrointestinal symptoms (e.g., nausea and diarrhea). The prevalence gastrointestinal symptoms (diarrhea, nausea/vomiting or abdominal pain) was overall stated as 18 percent (32). Post COVID-19 patients are consulted to gastroenterologist if needed especially for persistent gastrointestinal symptoms, infection related gastrointestinal complications, past history of chronic gastrointestinal diseases or an adverse drug effect.

Cardiology

Previous studies have shown interplay between cardiovascular events and COVID-19 (33,34). Different mechanisms are responsible of its effects. Hemodynamic instability and hypoxemia during acute phase could reduce myocardial oxygen demand-supply balance that lead to acute myocardial injury and toxic inflammatory cytokines may cause inflammatory myocarditis, microvascular dysfunction or prothrombotic events which may result as venous and arterial thrombosis (35). Patients with history of cardiovascular disease and risk factors including diabetes, hypertension, obesity are at high risk to develop CVD related COVID-19 (3). Based on evidence of previous coronaviruses it is not hard to predict long-term sequels of COVID-19. Trans-thoracic echocardiography is performed to patients who experienced CVD during acute-phase of COVID-19 or to patient with new onset cardiovascular symptoms during the post-COVID assessment.

Neurology

Both central and peripheral nervous system are reported to be involved during COVID-19 (36). Most common central nervous system symptoms are dizziness, headache, impaired consciousness, acute cerebrovascular disease, ataxia and seizure. Most common peripheral nervous system symptoms are disorders of taste and smell, visual impairment and nerve pain. Anosmia and dysgeusia were reported as common early symptoms (37). Neurological complications occur nearly in half of the hospitalized patients (38). Cerebrovascular diseases are infrequent and common in those with comorbidities e.g., hypertension, diabetes mellitus, cancer which also increase the occurrence and severity of COVID-19. It seems both stroke and COVID-19 have similar risk factors (39).

All neurological complications related COVID-19 are likely to have long-term consequences. Follow-up of the patients with neurological complications of COVID-19 could help to understand the viral disease better and enable physicians to take early precautions for the possible severe long-term neurological complications. Neurologists, in monitoring center, take part as consultant to evaluate patients with acute phase neurological complications or new onset neurological symptoms.

Identifying and following the biological and psychosocial long-term consequences will help to survive the COVID-19 with fewer side effects. To our knowledge, this is the second multidisciplinary center for post-COVID-19 follow-up. Similar multidisciplinary center has been established at the Fondazione Policlinico Universitario A. Gemelli IRCSS (Rome, Italy) (7). These two centers persuade same goal with minor differences. It has been reported that, in Italy, the center that represents the first multi-disciplinary post-COVID-19 follow-up center, four visits have been planned with different regular components. In our center, first visit has been planned after first month of recovery. Consequently, three more regular follow-up visits (at 3rd, 6th and 12th months) have been organized. Moreover, the internal specialist in charge directs the patients for more frequent visits in case of possible need. After multisystem evaluation, the consultation is made in case of need by guidance of the responsible physicians. The Italy center applies routine otorhinolaryngological assessment, stool and urine analyses to the all follow-up patients. Public health specialists have been taking active role in our center aiming to find a solution to decrease health disparities and promote healthier lifestyles.

Conclusion

Information and experience about long-term consequences of COVID-19 is limited yet, worldwide, as it is a very new disease with only a few months' history. Comprehensive assessment and follow-up recovery COVID-19 patients would help us to understand about its long-term consequences. We suggest that multidisciplinary management of COVID-19 survivors could improve the quality of our care, lives of our patients in the deep sea of uncertainties. Geriatricians are the experts that come in front with their distinguished skills in managing multidisciplinary aspects and teams.

Ethics

Ethics Committee Approval: Institutional review board approved the study with the number of 28/09/2020-164155.

Informed Consent: Written consent was obtained from the participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.Ç., N.Ş., S.B., M.K., Concept: G.B., A.M., M.A.K., T.T., M.K., Design: G.B., A.M., M.A.K., T.T., M.K., Data Collection or Processing: S.G., Y.Ç., N.Ş., S.B., Analysis or Interpretation: M.M.Ö., M.K., Literature Search: S.G., Writing: G.B.

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ORIGINAL RESEARCH

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Handgrip Strength and Ultrasonographically-measured Lower Arm Muscle Thickness in Hospitalised Older Adults: The SARCopenia and Ultrasound 3rd Pilot Study

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Abstract

Objective: The SARCopenia and UltraSound 3rd (SARCUS3) pilot study aims to determine the relationship between ultrasound (US)-based lower arm muscle thickness and handgrip strength in hospitalised older adults.

Materials and Methods: SARCUS3 is a single-centre cross-sectional study (Ziekenhuis Netwerk Antwerpen, Campus Middelheim, Antwerp, Belgium). For inclusion, all patients admitted to a geriatric ward were screened. US was used to measure the thickness of the lower arm muscles. On the other hand, a Jamar dynamometer was used to measure handgrip strength.

Results: A total of 83 patients were included in the data analysis (48 women, 35 men, mean age 84 years). According to the Shapiro-Wilk test, the lower arm muscle thickness and square root of handgrip strength had a normal distribution. The scatterplot and line of best fit suggested that the two variables had a linear relationship. Pearson's correlation coefficient was 0.287 (p=0.051) for women and 0.361 (p=0.036) for men for the US-measured muscle thickness of the lower arm and square root of handgrip strength. A linear regression analysis of the data from the participating men revealed that the best estimate for handgrip strength can be calculated using the formula: handgrip strength (kg) = [2.773+0.061 × lower arm muscle thickness (mm^2)], with an adjusted R square of 0.103.

Conclusion: This pilot study, using US-based muscle measurements, discovered a significant positive relationship for men and a borderline nonsignificant relationship for women between lower arm muscle thickness and handgrip strength. Furthermore, muscle thickness alone can explain up to 10.3% of the measured variability of handgrip strength in men. To our knowledge, this study is the first to show that US-based measurements of the lower arm are related to handgrip strength in a group of hospitalised older people. More research is required to identify other factors that influence lower arm muscle strength in hospitalised older adults.

Keywords: Sarcopenia, grip strength, muscle thickness, ultrasound, older adults, age-related changes, frailty

Introduction

Sarcopenia was first described by Irwin Rosenberg in 1989 as a deficiency of muscle mass (1). During the following years, the terminology for sarcopenia changed according to the continuous increase in knowledge about the syndrome (2-4). In 2010 the European Working Group on Sarcopenia in Older People (EWGSOP) published a consensus definition and diagnostic criteria for age-related sarcopenia, with an update (EWGSOP2) in 2019 (5,6). The EWGSOP2 definition states that sarcopenia is a progressive and generalized skeletal muscle disorder that is associated with an increased likelihood of adverse outcome including falls, fractures, physical disability and mortality (6). Low muscle strength is used as the main parameter of sarcopenia according the EWGSOP2 (6). Whenever low muscle strength is present, the term "probable sarcopenia" can be used according EWGSOP2 criteria (6). If there is additionally either low muscle quantity or quality present, the diagnose of sarcopenia is conformed (6). Low physical performance is furthermore used to grade the severity of sarcopenia (6).

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Defining the standard methods to measure muscle strength, quantity or quality remains subject of discussion (6). Handgrip strength was acknowledged by the EWGSOP2 as a convenient method to evaluate low muscle strength. The method is standardized and cut-off points for men and women were confirmed (6,7). A measured handgrip strength <27 kg for men and <16 kg for women indicates the presence of low handgrip strength (6). Handgrip strength is a well-studied variable (8). Similar to sarcopenia, low handgrip strength has been associated with an increased likelihood of adverse outcome including falls (9), fractures (10), physical disability (11) and mortality (12,13).

On the other hand, a suitable method to measure the muscle quality and muscle quantity in daily clinical practice is still undetermined. To date, computed tomography (CT) and magnetic resonance imaging (MRI) based measurements are regarded as the gold standard and dual-energy X-ray absorptiometry (DXA) as the preferred alternative for measuring muscle mass (6). However, these techniques are complex, expensive and unavailable in many centers making them of little use in daily clinical practice. Bioelectrical impedance analysis (BIA) is an additional, upcoming technique for measuring muscle mass (6,14). Due to a lack of standardization and validation of the prediction equations in specific populations, its use in daily clinical practice remains rather limited (6,14). Furthermore, BIA-equations strongly depend on the patients fluid balance, which can greatly differ between healthy subjects and hospitalized older adults (15). The EWGSOP2 provides cut-off points for BIA and DXA - but not for CT or MRI-that indicate the presence of low muscle quantity (6). With an appendicular skeletal muscle mass (ASM) <20 kg for men and <15 kg for woman or an ASM/height^2 <7.0 kg/m^2 for men and <5.5 kg/m^2 conforming the presence of low muscle quantity (6,16,17).

Despite a wide range of available technics and even recognized cut-off points for some of them, it remains unfeasible to measure muscle mass in daily clinical practice. An alternative for the aforementioned techniques however, might be found in ultrasonography (6,18).

Ultrasound (US) is an inexpensive, portable, non-invasive technique without the need for ionizing radiation (18). Previous studies on US-based measurements of muscle quantity suggest a significant correlation with CT and MRI based measurements (19-21). In regard to the lower arm muscles, a recent study observed a strong correlation between the lower arm muscle thickness, measured as the distance between the subcutaneous adipose tissue-muscle interface and the muscle-bone interface of the ulnae/radius, and MRI-measured cross- sectional area of the flexor and extensor components of the lower arm (22). Multiple studies have shown a good intra- and inter-observer, test-retest reliability (23-26), and feasibility in assessing small muscle groups with the use of US (18,27-29).

Recommendations about the measurement of muscle quality in daily clinical remain scarce (6). As to date, mostly CT and MRI based measurement have been used in research to asses muscle quality (6). Similar to CT and MRI-based measurements, US can assess muscle quality directly via specific tissue characteristics (18,30). Cadaver studies have shown that US is a valid tool for assessing basic architectural parameters (31,32). As yet, there is no consensus as to which technique is to be used to provide qualitative information on muscles (6). The EWGSOP2 doesn't make any recommendations nor provides cut-off points for any qualitative muscle parameter (6). US-based measurements could play a major future role in the evaluation of sarcopenia as it combines muscle quality and quantity assessment without the downsides of CT, MRI, DXA or BIA (18).

Confirming the viability of use of this new US-based strategy could improve the diagnostic process of sarcopenia in regular practice. This includes describing the ideal detection area in older patients and gaining further insights in the relationship between muscle quality, quantity and muscle strength. Previous studies examining the muscle quantity and muscle strength relationship solely focused on healthy community dwelling older adults (33,34). Therefore, the aim of this study is to question the relationship between US based measurements of lower arm muscle quantity and handgrip strength in hospitalized older adults.

Materials and Methods

Study design

The SARCopenia and UltraSound 3rd study (SARCUS3) was a single centre cross-sectional study. This study was approved by our Local Hospital's Ethics Committee (approval no: 5226).

Study population

All patients admitted to the acute and orthogeriatric wards of the Ziekenhuis Netwerk Antwerpen campus Middelheim (Antwerp, Belgium) between the 1st of May 2019 until the 31th of December 2019 were eligible and screened for inclusion. Patient had to be over 65 years old and be able to comply with the study protocol to be included.

All patients with known cognitive problems (either mild cognitive impairment or dementia) or who were diagnosed with cognitive problems (either mild cognitive impairment, dementia or delirium) during hospitalization were excluded. Additionally, all patient with recent surgery or trauma (<3 months) of the dominant arm, severe electrolyte disturbances, hyper- or hypovolemia or neuromuscular disease were excluded. A full list of the exclusion criteria is provided in the supplementary material. Written informed consent was obtained from all subjects.

Collection of descriptive data

All information on the reason for admission, substance use, biometrical information, medication use and length of stay was either retrieved from the patient themselves or the patient's medical record. The Cumulative Illness Rating Scale-Geriatric (CIRS-G) was used to asses co-morbidity. It rates 14 different organ systems (score 0 to 4), with a higher score implying a higher disease burden and with a maximum score of 56 (35). The mini nutritional assessment-short form (MNA-SF), a 6 item questionnaire, was used to identify patients who were are either at risk or had malnutrition (36). A score of 0 to 7 implying malnutrition, a score of 8 to 11 being at risk of malnutrition and a score of 12 to 14 meaning a normal nutritional status. The SARC-F score was used to screen for sarcopenia. The SARC-F rates 5 components (Strength, Assistance in walking, Rise from a chair, Climb stairs, Falls) and ranges from 0 to 10. A score of 0 meaning no characteristics of sarcopenia are present (37). In accordance with the EWGSOP2 criteria, probable sarcopenia was present when low handgrip strength (<27 kg for men and <16 kg for women) was confirmed (6). The FRAIL scale, a frailty screening stool ranging from 0 to 5, was used to describe the presence of frailty in the study population (38,39). A score of 3-5 indicating the presence of frailty, a score of 1-2 pre- frailty, and a score of 0 a health status.

US based muscle measurements

US based measurements of muscle thickness were used to quantify lower arm muscles. As these muscles are rather small, especially in older adults, measuring the thickness of an entire muscle compartment was chosen rather than measuring individual muscles. This approach deemed more straightforward than the more complex volume-based measurement of a single muscles. The dominant forearm muscles were measured while the participants were seated. The forearm was placed on a table to rest. The elbow was flexed to 120° and the forearm put in midprone (neutral position). The wrist was at 15-30° of extension (dorsiflexion). Patients were asked to hold a Wilson US 4 tennis ball (Wilson Sporting Goods Company, United States of America) without squeezing it, to ensure correct positioning. A tennis ball was used as this is a standardized measure throughout the world. Muscle thickness was measured using brightness (B)-mode on an Aplio 300 (Canon Medical Systems Europe, the Netherlands). A 5 cm wide, 7.5 and 10 MHz linear transducer with a scanning head coated with water-soluble transmission gel was used. Muscle thickness was measured at the proximal 1/3 of the distance between the tip of the olecranon and the ulnar styloid process. An example of probe and patient positioning is shown in Figure 1. The probe was placed perpendicular on the medial side of the forearm. The distance between the subcutaneous adipose tissue-muscle interface and muscle-bone interface of the ulna was measured (Figure 2). All measurements were repeated three times and the mean value of these measurements was used. Muscle thickness was measured within 4 days of admission in order to minimize the risk of acute hospital admission related muscle wasting (40). Furthermore, in order to comply with the US study protocol patients had to be able to walk and sit up in a chair. Thus, reducing the risk of acute bed rest-induced muscle loss.

Handgrip strength

Handgrip strength was measured using a Jamar hydraulic hand dynamometer (Lafayette Instrument Company, United States of America), according to the American Society of Hand Therapists protocol (ASHT) (41,42). Patients were seated in a chair without arm rests. There feet had to be on the ground. Hips had to be as far back in the chair as possible and the hips and knees positioned at approximately 90°. Shoulders had to be adducted and in a neutral position. The elbow had to be flexed at 90° angle and the forearm was held in a midprone (neutral position). The wrist was held between 15 to 30° of extension (dorsiflexion) and 0 to 15° of ulnar deviation. The mean of three consecutive trials

Figure 1. Probe (left) and patient (right) positioning

was used. A rest of at least 15 seconds was allowed between trials. Instructions to the patient were provided according to the ASHT-protocol.

Statistics

Statistical analysis was done by using Statistical Product and Service Solutions (SPSS) Statistics (International Business Machines Corporation, United States of America) version 26 software. Continuous variables are expressed as mean and standard deviation. Nominal variables are presented as percentages. Ordinal variables are presented as median and interquartile range. Handgrip strength and lower arm muscle thickness were checked for a normal distribution with a Shapiro-Wilk test. Data of muscle quantity and handgrip strength were plotted in a scatterplot and the correlation examined by calculation of the Pearson's correlation coefficient. The null hypothesis being that there is no relationship between muscle quantity and handgrip strength. The correlation was deemed significant at a 0.05 level (two tailed). In case of a significant correlation, a simple linear regression analysis will be performed. An additional bivariate analysis was performed using a correlation matrix. In case of multiple variables that correlated (Spearman's rho >0.250, p>0.05) to handgrip strength, a multiple regression analyze will be performed to further explore the relationship between lower arm muscle thickness and handgrip strength.

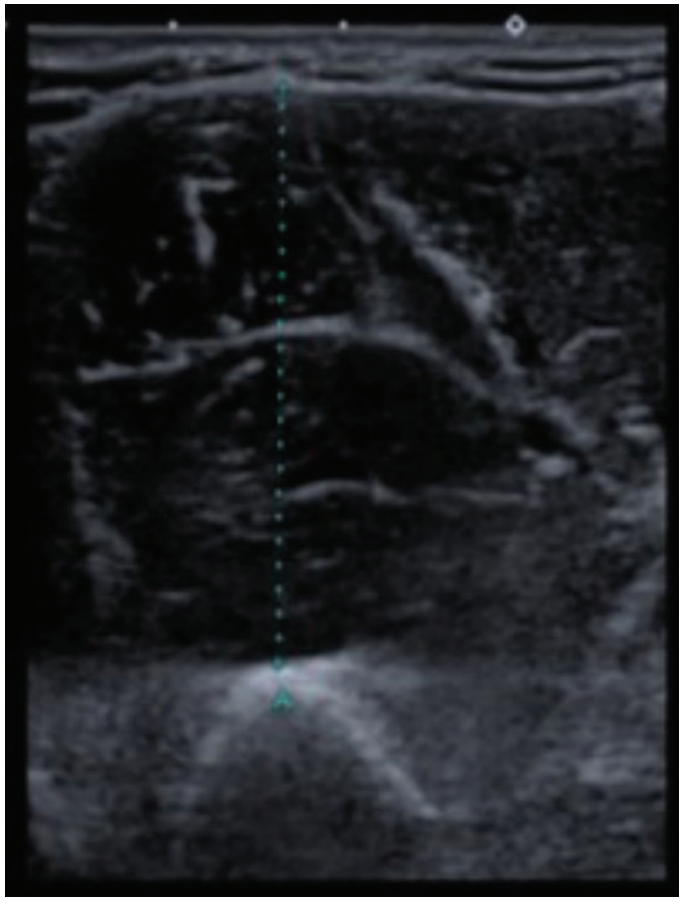

Figure 2. Muscle thickness. Dotted line: the distance between the subcutaneous adipose tissue- muscle interface (top) and muscle-bone interface of the ulna (bottom)

Before the start of the study a power analysis was performed using G*Power version 3.1.9.3 software (Heinrich Heine-Universiteit Düsseldorf, Germany) presuming there would be a weak correlation (0.3) between handgrip strength and lower arm muscle thickness. A required sample size of 82 patients was calculated.

Results

Patient characteristics

In total, 100 patients were included in the SARCUS3 study between the 1st of May 2019 and the 30th of November 2019. Seventeen patients had to be excluded: fifteen patients due to a new diagnose of either mild cognitive impairment or dementia, one patient because of a new diagnose of multiple sclerosis and one patient because of generalized edema caused by heart failure. After all exclusions, a total of 83 patients remained for data analysis. A summary of the patient characteristics is shown in Table 1. The mean age for women was 84.51±5.29 years and for men 84.19±6.01 years. Women represented 57.8% of the total population. On average, patients had serious co-morbidities as is expressed by a high mean CIRS-G score of 10.08±4.20 for men and 12.71±5.15 for women. Patients where admitted for various reasons, mostly because of infections (20 patients), gait and balance problems (12 patients) and fractures (8 patients). In the cohort 79.9% of women and 88.6% of men were right handed. Using the EWGSOP2 provided cut-off points for low hand grip strength, 39.58% of the women and 42.86% of the men were classified to have probable sarcopenia. In both men and women, 56% had either malnutrition or were at risk of malnutrition according the MNA- SF. The mean length of stay was 10 days. The median SARC-F score of 3 for women and 4 for men indicates a relatively high presence of self-reported characteristics of sarcopenia. A median score of 1.50 for women and 2 for men, on the FRAIL scale, indicates the presence of multiple characteristics of frailty.

Correlation between lower arm muscle thickness and handgrip strength

The mean handgrip strength was 16.75±4.82 kg for women and 28.60±9.32 kg for men. The mean lower arm muscle thickness was 37.28±5.91 mm for women and 41.61±4.94 mm for men. The square root of the handgrip strength had to be taken to correct for skewness and ensure a normal distribution according the Shapiro-Wilk test. The scatterplot and fit line for lower arm muscle thickness and the square root of the handgrip strength suggested a linear relationship between the two variables

Table 1. Patient characteristics

	Women	Men
Gender-n (%)	48 (57.8)	35 (42.2)
Age-years	84.51±5.29	84.19±6.01
CIRS-G score-median (IQR)	10 (6)	13 (8)
Alcohol-n (%)		
Total abstinence	23 (48.9)	11 (31.4)
Weekly	24 (51.1)	21 (60.0)
Daily	0 (0)	3 (8.6)
Smoking-n (%)		
Non-smoker	31 (64.4)	16 (45.7)
Ex-smoker	15 (31.3)	18 (51.4)
Active smoker	2 (4.2)	1 (2.9)
Reason for admission-n (%)		
Respiratory infection	4 (8.3)	3 (8.6)
Urinary tract infection	0	3 (8.6)
Other infections	7 (14.6)	3 (8.6)
Gait and balance problem	10 (20.8)	2 (5.7)
Hip fracture	1 (2.1)	2 (5.7)
Other fracture	4 (8.3)	1 (2.9)
Neoplasm related	4 (8.3)	1 (2.9)
Gastrointestinal bleeding	2 (4.2)	1 (2.9)
Other gastrointestinal disease	3 (6.3)	4 (11.4)
Transcatheter aortic valve implantation	2 (4.2)	6 (17.1)
Other cardiovascular disease	2 (4.2)	3 (8.6)
Adverse drug event	1 (2.1)	3 (8.6)
Pain problem	1 (2.1)	2 (5.7)
Other	7 (14.6)	3 (8.6)
Handedness-right/left %	97.9/2.1	88.6/11.4
Weight-kg	63.06±14.50	75.79±11.91
Length-cm	159.34±7.88	174.06±6.40
Body mass index-kg/m²	24.80±5.28	24.95±3.22
Length lower arm-mm	253.27±14.66	274.72±15.29
Muscle thickness-mm	37.28±5.91	41.61±4.94
Handgrip strength dominant hand-kg	16.75±4.82	28.60±9.32
Presence sarcopenia (EWGSOP2-criteria) No sarcopenia-n (%) Probable sarcopenia-n (%)	 29 (60.42) 19 (39.58)	 20 (57.14) 15 (42.86)
Albumin-g/dL	35.90±4.04	36.59±5.07
Prealbumin-mg/dL	0.192±0.051	0.213±0.057
SARC-F score-median (IQR)	3 (4)	4 (5)
FRAIL scale-median (IQR)	1.5 (1)	2 (2)
MNA-SF-median (IQR)	11 (5)	10 (4)
Malnutrition (score 0-7) - n (%)	10 (20.8)	3 (8.8)
Risk of malnutrition (score 8-11) - n (%)	17 (35.4)	16 (47.0)
Normal nutritional status (score 12-14) - n (%)	21 (43.9)	15 (44.1)
Length of stay-days	10.88±6.71	10.11±8.12
Medication on admission-n	6.77±3.79	7.29±3.38

Data shown as mean ± standard deviation unless otherwise indicated.
IQR: Interquartile range, MNA-SF: Mini nutritional assessment-short form, EWGSOP2: European Working Group on Sarcopenia in Older People

(Figure 3, 4). The calculated Pearson's correlation coefficient between the square root of handgrip strength and lower arm muscle thickness was 0.287 (p=0.051) for women and 0.361 (p=0.036) for men. To further explore the relationship between handgrip strength and muscle thickness, an additional linear regression analysis was performed. Hereby only the data of the participating men was used since only the men's calculated Pearson's correlation coefficient (0.361, p=0.036) was significant. Regression analysis showed that handgrip strength in men can be estimated using the following formula:

handgrip strength (kg) = [2.773+0.061 x lower arm muscle thickness (mm^2)].

The adjusted R square of the linear regression analysis was 0.103. An additional bivariate correlation analysis (including: age, CIRS-G, weight, length,) was performed using a correlation matrix. No additional variables significantly correlated (Spearman's rho, p>0.05) to handgrip strength were found (Table 2).

Discussion

Using US-based muscle measurements, the SARCUS3 pilot study found a positive linear relationship between lower arm muscle quantity and handgrip strength in hospitalized older adults. The results were significant for men and borderline non-significant for women. Handgrip strength in men could be estimated using the following formula:

handgrip strength (kg) = [2.773+0.061 x lower arm muscle thickness (mm^2)]

Although there is some data on the relationship between lower arm muscle quantity and handgrip strength in healthy community dwelling adults (22,33,34,43), this study provides for the first-time confirmation of this relationship in hospitalized older adults with serious co- morbidities.

There are multiple reasons however why the correlation was not as pronounced as one might expect. First of all, as noted by previous auteurs, there is an age-related decrease in the correlation between lower arm muscle thickness and handgrip strength (22,33,34,43). As the population in our study [mean

age in years: women 84.51±5.29, men 84.19±6.01) was significant older than in previous studies (mean age in years for women and men: 23±3, 24±4 (43); 73±3, 74±3 (34); women/men together 31±14 (22); and women/men together aged 20 to 89 (33)] it was expected that the correlation between lower arm muscle mass and handgrip strength would be lower as well.

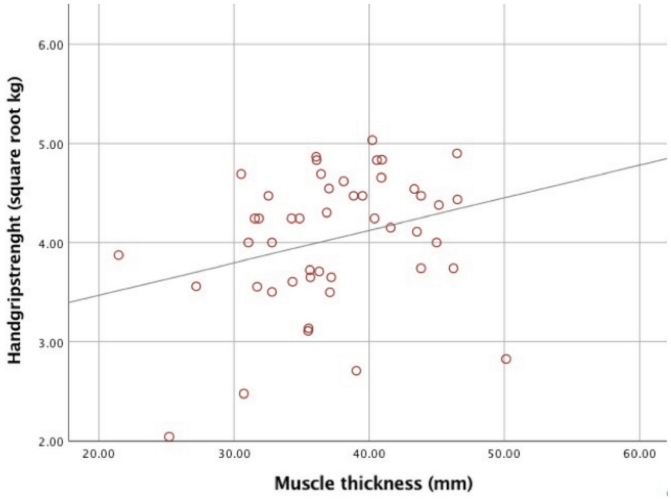

Figure 3. Scatterplot of the muscle thickness and the square root of handgrip strength (women). The square root of the handgrip strength had to be taken to correct for skewness and ensure a normal distribution according the Shapiro-Wilk test

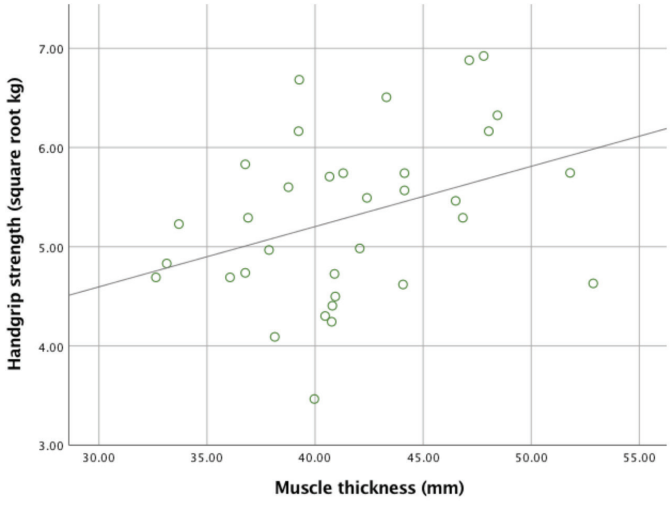

Figure 4. Scatterplot of the muscle thickness and the square root of handgrip strength (men). The square root of the handgrip strength had to be taken to correct for skewness and ensure a normal distribution according the Shapiro-Wilk test

Table 2. Bivariate correlations

Independent variable	Women	Men
Age	-0.105 (0.478)	-0.336 (0.52)
CIRS-G	-0.110 (0.456)	-0.163 (0.356)
Length	0.120 (0.421)	0.209 (0.237)
Weight	0.256 (0.083)	0.331 (0.056)

Data shown as Spearman's rho correlation coefficient (p-value) between independent variable and handgrip strength

Another reason for the weak relationship observed between lower arm muscle quantity and handgrip strength is certainly the absence of clear qualitative muscle measurements (44-46). Qualitative determinants like age-related adipose or connective tissue infiltration of the muscle, changes in myofiber size, changes in muscle metabolism, a reduced capillary density or neural changes that have been described in previous studies might be equally important as a decline in muscle quantity, certainly in an older age cohort (47). The calculated linear regression analysis in men showed an adjusted R square of 0.103. This means that only 10.3% of the witnessed variability in handgrip strength can be explained by the muscle thickness.

This showing a certain margin of error for the current formula [handgrip strength (kg) = [2.773+0.061 x lower arm muscle thickness $(mm)^2$]. The absence of a significant correlation in the additional bivariate analysis suggests other variables, for example muscle quality, must therefore contribute to the witnessed variability in handgrip strength.

Previous studies have shown an age-related decline in handgrip strength (7). Our results on handgrip strength (mean handgrip strength 16.75±4.82 kg for women and 28.60±9.32 kg for men) are, both for men and woman, within the 25-50th percentile of the age and gender specified reference range (7). As expected a significant portion of the patients was diagnosed with probable sarcopenia according the EWGSOP2 criteria (39.58% women, 42.86% men) on account of having low handgrip strength (6). The absence of a significant correlation between age and handgrip strength in the bivariate analysis is probably due to the small sample size and limited age-range of the study population.

The observed relationship between lower arm muscle thickness and handgrip strength was lower in our study than in previous US-based observations regarding lower limb muscle (48,49). Prior studies reported on the relationship between muscle thickness of the quadriceps and muscle strength (correlation coefficient: 0.422, p<0.001) (48) and the thickness of the musculus rectus femoris and maximum isometric voluntary contraction (Pearson correlation coefficients: 0.834, p<0.001) (49). A study investigating age-related site-specific muscle wasting showed an age-related increased muscle loss in the upper leg muscles (50). However, the age-related effect on lower arm muscles was rather small. The absence of significant age- related lower arm muscle loss combined with an age-related decline in handgrip strength further emphasizes the importance of muscle quality as a predictor of lower arm muscle strength in later life.

Although this was not the primary aim of our study, the SARCUS3 study showed that US- based measurements of the lower arm

muscles in older adults are feasible to obtain in regular clinical practice and could therefore be useful for the screening of low muscle mass in this cohort. In contrast to previous studies, a seated patient position was chosen with a flexed arm (elbow 120°) on the table instead of a standing position with stretched arms (22,33,34,43). This new approach is more appropriate for studies in older adults for several reasons. First of all, a seated position is physical less demanding for older adults than a standing position. Secondly, a rested flexed arm position is a more natural body posture in contrast to a stretched arm, making it easier for patients to maintain the same posture for the duration of the examination. In a standing position, test subjects always need to contract muscles to maintain the "ideal" test position. This is not the case in a seated position, leading to less variation in measurements. Finally, the table surface can be used to rest the probe, reducing the risk of vertical probe displacement when taking repetitive measurements.

Similar to previous studies the choice was made to measure an entire muscle compartment rather than a single muscle (22,33,34,43). Although this increases the risk of including non-muscle tissue as part of the measurement, this is a more feasible approach for the screening of sarcopenia in older adults. As a consequence of the difference in our study protocol to previous studies, a direct comparison between the measured muscle thickness was not possible (22,33,34,43).

The SARCUS 3 study had several strengths. All measurements were acquired using a strict protocol, with special attention for standardization. All data and measurements were obtained by one trained researcher, excluding any inter-observer disagreement.

Study Limitations

The SARCUS3 study has some limitations. First of all, the reason for admission could have influenced patient's handgrip strength and lower arm muscle thickness. We tried to minimize this by excluding severely ill patients who were not able to comply with the study protocol. Furthermore, we believe that the impact of acute muscle wasting would have been limited.

Experimental research showed that older adults have a total lean mass decreased of ± 4% after 5 days of total bed rest (51). Patients where however not allowed to be bedridden in order to comply with the study protocol, additionally early mobilization is regarded as usual care on our geriatric ward. Secondly, we excluded patients with cognitive problems to ensure correct data collection and adherence to the study protocol. Thus, making it unsure if our findings apply to all hospitalized older adults. Lastly, a direct comparison between US and CT, MRI, CT or BIA based measurement would have given additional insight on potential US based muscle measurement of variables like pennation angle (the angle formed between fiber insertions and the aponeurosis in penniform muscles), fascicle length or echo intensity (15,18). This was however beyond the scope of this pilot study, primarily because the focus was placed on feasibility in clinical practice.

Conclusion

The results of this study show for the first time a significant positive relationship for men and a borderline significant relationship for women between lower arm muscle thickness and handgrip strength in hospitalized older adults. Up to 10.3% of the measured variability of the handgrip strength in men can be explained by muscle thickness alone. Further research is necessary to look into other relevant factors.

Ethics

Ethics Committee Approval: This study was approved by our Local Hospital's Ethics Committee (approval no: 5226).

Informed Consent: Written informed consent was obtained from all subjects.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.A., A.M.D.C., V.M., S.P., Concept: T.A., A.M.D.C., V.M., S.P., Design: T.A., A.M.D.C., V.M., S.P., Data Collection or Processing: T.A., A.M.D.C., S.P., Analysis or Interpretation: T.A., A.M.D.C., S.P., Literature Search: T.A., A.M.D.C., S.P., Writing: T.A., A.M.D.C., S.P.

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

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Supplementary Material

Exclusion criteria

All patients with a history of/or the presence of a paresis/paralysis of the dominant upper limb due to a stroke will be excluded. All patient with severe electrolyte disturbances at admission will be excluded because of the potential effect on muscle contraction. Patients who are clinically either hyper- or hypovolemic will be excluded because fluid shifts could influence the US measurement results. All patients who are unable to comply with the given instructions about limb positioning will be excluded. Patients with a history of systemic connective tissue disorders, myositis, calcification and ossification of muscle, systemic atrophies primarily affecting the central nervous system and demyelinating diseases of the central nervous system will be excluded because of the uncertain effect muscle quantity and function. All patient with partial or total parenteral and/or intravenous nutrition will be excluded.

ORIGINAL RESEARCH

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Breast Cancer in Women Aged 75 Years and Older

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Abstract

Objective: Breast cancer is the most common cancer in women, with incidence and mortality increasing dramatically with age. Applying data of younger patients to the geriatric age group indicates "evidence biased medicine". Therefore, this study aimed to present the clinical and pathological features of breast cancer and treatment choices in older patients.

Materials and Methods: This study included 72 patients aged 75 years and older with breast cancer who were admitted to our medical oncology clinic between 2005 and 2013. Clinicopathological and demographic features, progression-free survival and overall survival and adjuvant and palliative treatments were recorded retrospectively. Categorical variables were presented as number (n) and percentage (%) and continuous variables as median and minimum-maximum. Survival curves were drawn using the Kaplan-Meier method. $P<0.05$ was considered as statistically significant.

Results: The study population consisted of 72 patients, with a median age of 78 (minimum-maximum: 75-88). The most common pathological type of breast cancer was invasive ductal carcinoma, followed by infiltrative lobular carcinoma. Steroid receptor positivity rates were high, and the cerbB2 status was mostly negative; older patients had favourable tumours. Endocrine therapy was the most preferred option in this geriatric patient group, and aromatase inhibitors were the most commonly chosen hormonotherapy. Endocrine therapy is the first choice in palliative treatment; however, chemotherapy was preferred in second- and third-line treatment in metastatic diseases.

Conclusion: According to available literature, geriatric patients show similarities in histologic and intrinsic subtypes with postmenopausal women, except for frailty and comorbidities. However, in geriatric patients, endocrine therapy is preferred as adjuvant and/or metastatic treatment because they are more susceptible to chemotherapeutic agents. Oncologists should consulate every older patient to geriatric medicine, and comprehensive geriatric assessment should be done to decide and continue treatment. Age should not be the only factor in decision-making.

Keywords: Geriatric patients, older women, breast cancer, aged women, decision-making, endocrine therapy, postmenopausal women

Introduction

Breast cancer is the most common cancer in women, the incidence and mortality increase dramatically by ageing (1). The average age at diagnosis of breast cancer is 61 years, and the majority of women who die because of breast cancer are aged 65 years and older (2). Major improvements in public health like routine screening with mammography, and better treatment options like endocrine therapies or targeted therapies, better medical care after surgery have resulted in increased survival of patients with breast cancer. However, age-related disparity is seen in these improvements. In one study, the absolute risk of breast cancer death decreased by 15.3% for women aged 50 to 64 years but only 7.5% for women 75 years and older (3). This may be related to that there are no screening guidelines in older women and routine mammography screening is ended after 74 years of age according to USPTF and American College of Physicians Guidelines. Older women were self-admitted to medical care with a palpable mass, however, they have more favorable tumors and early-stage disease (4).

The treatment of individuals who are aged 75 years and older is complicated and the goals of the treatment should be well-defined. It is important to guide the treatments by evaluating

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possible toxicities, functional loss, and quality of life. In data from clinical trials that enroll primarily younger patients, older patients with breast cancer are underrepresented (5,6). Therefore, evidence-based treatment guidelines are limited. Applying the data of younger patients to geriatric age group cause "evidence biased medicine". Lack of information needed to estimate the likelihood of toxicity can lead to life-changing results in older adults. It is essential to personalize management for geriatric patients. In the current study, it is aimed to present the clinical and pathological features of breast cancer and choices of the treatment in older patients.

Materials and Methods

Our study was conducted by Declaration of Helsinki. This study was reviewed by the approval (date: 12.07.12, decision number: 12-6.1/7) of the local Ethics Committee of the Ege University (İzmir/Turkey). The participants provided informed consent.

Study population

Patients who were admitted to the medical oncology clinic between 2005-2013 were evaluated, and 72 patients diagnosed with breast cancer aged 75 years and older were included. Clinicopathological features, demographic features, comorbidities, family history of malignancy, metastasis date and regions, progression status, progression-free survival and overall survival, adjuvant and palliative treatment regimens were recorded retrospectively.

Adjuvant treatment was given after surgery in order to reduce the chance of cancer coming back by destroying any remaining cancer cells. It usually refers to chemotherapy, radiation therapy, hormone therapy, and/or immunotherapy. Palliative treatment is the systemic treatment given to metastatic disease, which may include hormone therapy, chemotherapy, targeted therapy, or some combination of these.

Stage of the disease was established through the tumor, node and metastasis classification system. Early stage breast cancer includes ductal carcinoma *in situ*, stage 1 and stage 2a. Locally advanced breast cancer includes stage 2b, stage 3a, 3b and 3c. Vital status, date, and the cause of the death were determined through linkage with the Turkish national death registry.

Estrogen receptor (ER) and/or progesterone receptor (PR) positive, Cerb-2 negative, and proliferation rate of ki-67 lower than 14% were accepted as Luminal A subgroup. Luminal B subgroup was defined as either ER and/or PR positive, Cerb-2 positive; or ER and/or PR positive, C-erb2 negative, and proliferation rate of ki-67 status equal or higher than 14%. ER, PR and C-erb2 negative ones were described as a basaloid subtype. HER2 subtype defined as ER and PR negative and C-erb2 positive.

Statistics

Categorical variables were given as number (n) and percentage (%). Continuous variables that followed a normal distribution was given as mean ± standard deviation values. Median and minimum-maximum values were presented for the variables where normal distribution was not observed.

Overall survival was defined as the time from diagnosis to death or the last follow-up examination. The effect of the subtype on survival of breast cancer patients was investigated using the log-rank test, and the Kaplan-Meier survival estimates were calculated. A value of $p<0.05$ was accepted as statistically significant. The data obtained in the study were analyzed using IBM SPSS Statistics vn. 24.0 software (IBM Co., Armonk, NY, USA).

Results

The study population was composed of 72 patients, with a median age of 78 (minimum-maximum: 75-88). The n of patients who had at least one comorbidity was 58 (80.6%), and the most common disease was hypertension followed by diabetes mellitus. The study sample was mostly overweight or obese. The demographic properties, general characteristics, and comorbidities are summarized in Table 1.

The most common pathological type of breast cancer was invasive ductal carcinoma (IDC), and the second one was infiltrative lobular carcinoma. ER and PR positivity rates were high and cerbB2 status was negative mostly, thus, older patients had favorable tumors. Hormone receptor status, subtypes of the diseases, and ki-67 status are given in Table 1. The most common subtype was luminal A disease. HER2 receptor positivity of immunohistochemistry and FISH method in the luminal b diseases are shown in Table 2.

The majority of the patients had a locally-advanced disease or early-stage disease at the time of diagnosis. The n of metastatic patients at diagnosis or during follow-up was 29 (40.3%). Most common metastasis regions were bone, lymph nodes, and lung.

The majority of the patients died within the follow-up time. When the registry of the Ministry of Health was controlled, it was revealed that cancer-related death occurred in 30 patients. Overall and progression-free survival according to subtypes and the whole group are shown in Table 3, Figures 1, 2.

Adjuvant and palliative therapies given to the patients were recorded. Endocrine therapy was the most preferred option in this geriatric patient group, that it is followed by radiotherapy and chemotherapy. Taxan-based chemotherapies were preferred as adjuvant chemotherapy in many patients, however, there are no major differences between chemotherapy regimens. Aromatase inhibitors were the most commonly chosen hormonotherapy. Only three patients received

Table 1. Demographic and clinicopathological features of the patients

	Total sample (n=72)
Age	78 (75-88)
BMI	29.67 (17.78-39.80)
Comorbidities*	58
Hypertension	43 (39.1)
Diabetes mellitus	20 (18.2)
Atherosclerotic heart disease	10 (9.1)
Congestive heart failure	4 (3.6)
Osteoporosis	3 (2.7)
Dementia	8 (7.3)
Depression	1 (0.9)
Cerebrovascular disease	2 (1.8)
COPD-asthma	3 (2.7)
Hyperlipidemia	4 (3.6)
Thyroid disease	3 (2.7)
Malignancy	5 (4.5)
Papillary thyroid cancer	2 (1.8)
Endometrial cancer	1 (0.9)
Colorectal cancer	1 (0.9)
Hepatocellular cancer	1 (0.9)
Rheumatological disease	4 (3.6)
Metastases status	
Absent	43 (59.7)
Present	29 (40.3)
Bone	21 (45.7)
Lymph nodes	11 (23.9)
Lung	7 (15.2)
Liver	5 (10.9)
Skin	1 (2.2)
Adrenal	1 (2.2)
ER	
Negative	18 (25)
1+	4 (5.6)
2+	9 (12.5)
3+	41 (56.9)
PR	
Negative	31 (43.1)
1+	11 (15.3)
2+	9 (12.5)
3+	21 (29.2)
CERB2	
Negative	50 (69.4)
1+	1 (1.4)
2+	9 (12.5)
3+	12 (16.7)
HER2-FISH	
Negative	49 (94.2)
Positive	3 (5.8)
Ki-67	
<14%	27 (67.5)
≥14%	13 (32.5)
Subtype	
Basaloid	10 (13.9)
Luminal A	30 (41.7)
Luminal B	20 (27.8)
HER2	12 (16.7)
Stage	
Unknown	5 (6.9)
Early-stage	26 (36.1)
Local-advanced	30 (41.7)
Metastatic	11 (15.3)
Histology	
IDC	47 (66.2)
ILC	8 (11.3)
Others	15 (21.1)
Basaloid	1 (1.4)
Unspecified	1 (1.4)
Outcome	
Exitus	52 (72.2)
Cancer-death	40 (76.9)
Other causes	12 (23.1)
Follow-up	20 (27.8)

*Because of the retrospective design of the study, comorbidty data of some patients were missing
ILC: Infiltrative lobular carcinoma, BMI: Body mass index, IDC: Invasive ductal carcinoma

tamoxifen. Eight patients were treated with trastuzumab for adjuvant therapy.

Endocrine therapy is the first choice in palliative treatment, however, chemotherapy was preferred as second and third-line treatment in metastatic diseases. Detailed treatment options are shown in Table 4. In luminal A disease, the majority of the patients received endocrine therapy. Only two of the patients did not receive anti-estrogen therapy. All of the patients except one with luminal B disease received anti-estrogen treatment for adjuvant therapy. Treatment regimens are given in Table 4.

Discussion

In our study, breast tumors in patients aged 75 years and older showed high rates of ER/PR content, low ki-67 proliferation, and low cerbB2 positivity. Geriatric patients had less aggressive tumors like postmenopausal women, and steroid receptor positivity rates increase with age (7,8). The hormone-negative disease is relatively uncommon in older women according to several studies in the literature (9,10). In our study, it is found that hormone-negative disease is also rare. The subtypes in older women resemble postmenopausal women defined many studies in literature.

The most common histologic type was IDC in compliance with the literature (11,12). However, other rare histopathologies like mucinous or medullary carcinoma were also seen. It was found that older patients with breast cancer are more likely to present with earlier stages. In a study which was performed in women 70 years of age and older, it was found that older patients with breast cancer presented at early stages (13). Obesity is one of the risk factors of breast cancer (14). In our study the population was overweight or obese.

In the early stage of the disease, the main treatment choice is surgery. Older patients with breast cancer have not undergone surgery according to many studies (15-17), because of comorbidities (11,18,19). On the other hand, a study has shown that there is no difference regarding comorbidities in older women with and without breast cancer. A review from the Cochrane database has found that there is no survival benefit between undergoing surgery and not (20). In our study, most of the patients had at least one comorbid disease, but the primary surgery rate was not recorded. So,

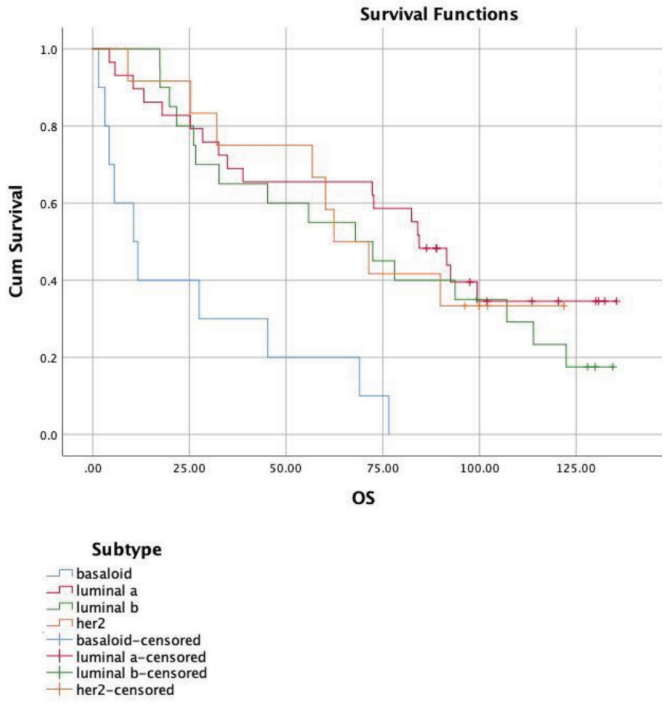

Figure 1. Overall survival (OS) (in months) curves according to subtypes

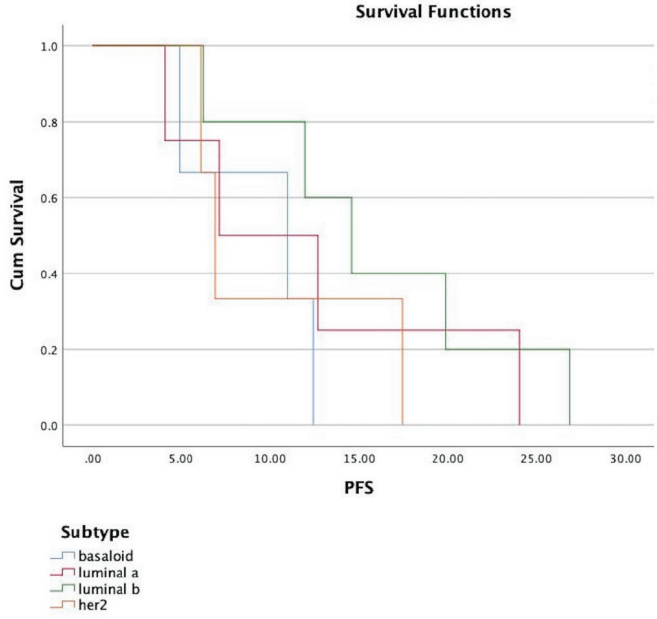

Figure 2. Progression-free survival (in months) curves according to tumor subtypes

Table 2. Immunohistochemistry and FISH positivity of HER2 receptor in luminal B disease

Luminal B	Immunohistochemistry			FISH	
	HER2 0/1+	HER2 2+	HER2 3+	HER-2 positive	HER-2 negative
N	15	5	0	1	15
%	75	25	0	6.3	93.8

Table 3. Medians for overall and progression-free survival time in months according to molecular subtypes

Overall survival						Progression-free survival				
			95% CI		p			95% CI		p
	Est	Std. error	Lower bound	Upper bound		Est	Std. error	Lower bound	Upper bound	
Basaloid	10.586	4.860	1.060	20.113	<0.001	10.981	4.966	1.247	20.714	0.435
Luminal A	84.460	7.515	69.731	99.190		7.134	4.307	.000	15.576	
Luminal B	67.923	18.599	31.469	104.378		14.597	2.881	8.950	20.244	
HER2	62.400	9.681	43.426	81.374		6.904	0.644	5.641	8.167	
Total	71.375	9.264	53.218	89.533		11.967	3.409	5.385	18.649	

CI: Confidence interval

the authors could not report a relationship with surgery and comorbidities among patients.

Endocrine therapy is the main treatment option in older patients, and aromatase inhibitors are preferred to tamoxifen (21). In BIG 1-98 study by Crivellari et al. (22) has stated that letrozole is superior to tamoxifen regardless of the age of the patient. Aromatase inhibitors are well-tolerated in geriatric patients with less adverse reactions like thromboembolic events, endometrial cancers, and impaired cognition than tamoxifen which is essential for this age group (21).

Pooled clinical trial data within the Alliance for Clinical Trials in Oncology and studies using surveillance, epidemiology, and end results data suggest that older patients benefit from chemotherapy as much as younger patients (23,24) but, they may experience higher rates of treatment-related toxicity, including cardiotoxicity and bone marrow disorders (24). Albeit that chemotherapy benefit, some other studies determined a decline in the choice of chemotherapy when the patients become older (11,22). In the present study, it was found that chemotherapy is the least chosen treatment pattern in the advanced-geriatric patient group.

Table 4. Adjuvant and palliative treatments of the patients

Adjuvant therapy Chemotherapy Radiotherapy Hormonotherapy	65 (100) 15 (23.1) 16 (24.6) 34 (52.3)
Adjuvant chemotherapy regimen	15 (100)
Anthracycline-based	3 (20)
Taxan-based	5 (33.3)
Other	1 (6.7)
Unknown	6 (40)
Adjuvant hormonotherapy	34 (100)
AIs	22 (64.7)
TMX	3 (8.8)
Unknown	9 (26.4)
First-line therapy*	27 (100)
Chemotherapy	7 (25.9)
AIs	15 (55.6)
TMX	2 (7.4)
Trastuzumab	3 (11.1)
Second-line therapy	14 (100)
AIs	4 (28.6)
GnRH agonists	2 (14.3)
Chemotherapy	6 (42.9)
Trastuzumab	2 (14.3)
Third-line therapy	11 (100)
AIs	1 (9.1)
GnRH analogs	2 (18.2)
Chemotherapy	6 (54.5)
Tamoxifen	2 (18.2)

*First-line therapy regimens of two metastatic patients were missing

Adjuvant radiotherapy in geriatric patients is a well-discussed topic and plays an important role in early-stage breast cancer for local recurrence. There are at least four large randomized clinical trials that were researching the beneficial effect of radiotherapy. Despite the fact that radiotherapy is beneficial for local recurrence, no benefit is observed in disease-free survival and overall survival (25-28). In the current study, the quarter of the patients was treated with radiation, however, radiotherapy decision should be personalized.

Independent from age, metastatic disease remains incurable and the main goal of the treatment is the control of the disease and gain the highest function (29). Even though they have metastatic disease, in one study it was shown that one-fifth of the patients died from non-breast cancer causes (30). In our study this ratio was 23%. For hormone-receptor positive and HER2 negative metastatic disease endocrine therapy is the mainstay of the treatment. For triple-negative disease, which is resistant to hormonotherapy, chemotherapy should be given in older patients. In HER2 disease, trastuzumab plus chemotherapy improved survival compared with chemotherapy alone at first-line treatment (31). Even though older women can tolerate anti- HER2 regimens, there is an increased risk of cardiotoxicity (32).

The triple-negative disease has the worst overall survival among the molecular subtypes (33) as in the current study. The longest survival is seen in luminal A subtype in compatible with the literature (34). In a study done in postmenopausal women, it was found that age is the most determinant factor of decreased survival in early-stage disease. However, comorbidity rather than age has a bigger impact on survival in stage 3 disease and metastatic disease (35).

Study Limitations

There are some limitations in this study. This study had retrospective design and data was collected from single center. Another limitation of the study was some of the patients had missing data like ECOG and Karnofsky scores, comorbidities, and treatment choices. The study group included 75 years and older women; therefore, the results of the study population were compared with the literature, control group was not formed. Nevertheless, the aim of the study was not performing comprehensive geriatric assessment, so that the frailty scores, nutritional and cognitive status of the patients were missing. Further studies examining the association of frailty with management decisions and outcomes will clarify this point.

Conclusion

Treatment patterns should be planned by calculating the expected life-time other than cancer in older women. The geriatric patient group shows similarities in histologic and intrinsic subtypes with postmenopausal women according to the literature except for their frailty and comorbidities, however in geriatric patients endocrine therapy is preferred as adjuvant and/or metastatic treatment due to their susceptibility to chemotherapeutic agents. Patient preferences should be evaluated during the oncologist's decision- making process of adjuvant therapy. Chemotherapy should be tailored according to benefits and toxicities in the aged group.

This study shows geriatric women have similar tumors like postmenapausal women, however they are treated differently. It is known that geriatric patients is more fragile to anti-cancer treatments, and oncologist are afraid of their ages beside from their clinical, physical and psychological status. Oncologists should consulate every older patient to geriatric medicine and comprehensive geriatric assessment should be done to decide and continue treatment. Moreover, this study shows ageism should not be interfered in anti-cancer therapy and geriatrician should be included to decision-making process. Age should not be the only factor for decision-making.

Ethics

Ethics Committee Approval: This study was reviewed by the approval (date: 12.07.12, decision number: 12-6.1/7) of the Local Ethics Committee of the Ege University (İzmir/Turkey).

Informed Consent: The participants provided informed consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.B., E.A., B.K., Concept: G.B., E.A., B.K., Design: G.B., M.G.O., E.A., B.K., Data Collection or Processing: G.B., E.A., Analysis or Interpretation: G.B., M.G.O., B.B.D., Literature Search: G.B., M.G.O., B.B.D., B.K., Writing: G.B., M.G.O., B.B.D., B.K.

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ORIGINAL RESEARCH

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Socio-demographic and Subjective Factors Related to a Psychosocial and Biomedical Model of Successful Ageing

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Abstract

Objective: With the number and proportion of older adults increasing worldwide, successful ageing (SA) has become a global goal. This study aimed to examine the association of subjective age, health and socio-demographic factors with the biomedical and psychosocial dimensions of SA.

Materials and Methods: A total of 61 adults, aged ≥50 (mean age 67.1±9.4) years, living in nursing homes or in the community, were asked to answer a series of questions. A biomedical model of SA was measured by Rowe and Kahn's criteria (i.e. being free of disease and disability, having high physical and cognitive functioning and being actively engaged in life). A psychological well-being scale was used as an indicator of successful psychosocial ageing.

Results: Our analysis revealed that being married and younger by chronological age, having a high educational level, having a younger subjective age and having better subjective health are correlated with both the biomedical and psychosocial dimensions of SA. Neither gender nor the number of children was correlated with these dimensions.

Conclusion: The biomedical and psychosocial dimensions of SA are associated with similar socio-demographic factors along with subjective health and age. These findings suggest that subjective age and health status, which are changeable and relatively under the control of the individuals, are important to promote SA. Future research in this field can measure SA by creating an index that includes components of Rowe and Kahn's model and psychosocial indicators of SA.

Keywords: Healthy ageing, Rowe and Kahn's model, successful ageing

Introduction

Successful aging (SA) is worldwide and an important concept that is widely discussed in gerontology today (1). As the number and the proportion of older adults continue to grow around the world as well as in Turkey (2), this concept draw great interest both to individuals and societies.

Over the past few decades, SA has been studied from different vantage points which reflected psychosocial or biomedical approaches or combinations of the two (3). One of the most influential conceptualisations of SA in a biomedical model was put forth by McLaughlin et al. (4) in the late 1980s, and this model has played a major role in the literature. In the year 1997, Rowe and Kahn (5) more explicitly defined the three main components of SA, including: (a) the absence of chronic disease and disability; (b) high physical and cognitive functioning; and (c) active engagement with life. To be a successful adult, an individual had to meet all three criteria. While the biomedical model emphasises the maintenance of mental and physical functioning as the keys to aging successfully, psychosocial models emphasize psychological resources, well-being and life satisfaction, including contentment and happiness (3).

There are an increasing number of studies on the factors that influence SA, and most of them have examined only the biomedical dimension (i.e., Rowe and Kahn's components, either singularly or in various combinations) or the psychosocial dimension (i.e., well-being and life satisfaction) of SA (6). However, there are very few studies which examined factors related to SA in terms of both the biomedical and psychosocial approaches. In addition, longitudinal and cross-sectional studies

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conducted in line with this purpose have mainly focused on socio-demographic factors (e.g., educational level, age, and marital status). There is very little known about the relationship between subjective health, age, and the dimensions of SA. For that reason, the purpose of the current study was to examine how current socio-demographic variables, subjective age and health are related to both the biomedical and the psychosocial models of SA. In that respect, our findings are inclusive of different dimensions of SA; therefore, they must be seen as exploratory.

Materials and Methods

The study included adults who lived in private nursing homes or who lived in the larger community in Turkey between April and June of 2019. Adults were considered eligible for participation if they: a) were aged 50 or older; and b) scored more than 19 points on the "standardized mini mental state examination test (SMMSE)".

A total of 68 participants were identified who were eligible for participation. Four adults didn't complete some of the items and were thus excluded from the analyses. Three participants were regarded as outliers on one or more variables and were therefore excluded. As a result, all analyses were performed on the data from 61 participants. The baseline characteristics of the participants are showned in Table 1.

The study was approved by the Ethics Board and Commission of Ege University in Turkey (approval number=204-2019). All participants provided written and verbally informed consent.

Subjective age and health

Similar to Stephan et al. (7) study, participants were asked to specify, in years, how old they felt most of the time. A subjective age score was computed by subtracting one's perceived age from one's chronological age. Higher scores reflected a younger age identity. In line with previous studies (8,9), subjective health was assessed using one item: "How would you describe your current health?". Participants rated their current health status on a five-point rating scale, from 1 (very bad) to 5 (very good).

Table 1. Factors related to biomedical model of successful aging in all patients based on the Rowe and Kahn's definition

	Usual aging (n=26)	Successful aging (n=35)	Total participants (n=61)		
Associated factors	**n (%)**	**n (%)**	**n (%)**	**χ^2**	**p**
Living space	-	-	-	20.71	<0.001
Nursing home residents	22 (71.0)	9 (29.0)	31 (50.8)	-	-
Community-dwelling adults	4 (13.3)	26 (86.7)	30 (49.2)	-	-
Age	-	--		4.18	0.041
50-64	8 (28.6)	20 (71.4)	28 (45.9)	-	-
65 or more	18 (54.5)	15 (45.5)	33 (54.1)	-	-
Gender	-	-	-	0.231	0.631
Female	12 (46.2)	14 (53.8)	26 (42.6)	-	-
Male	14 (40.0)	21 (60.0)	35 (57.4)	-	-
Marital status	-	-	-	9.35	0.002
Single*	25 (53.2)	22 (46.8)	47 (77.0)	-	-
Married	1 (7.1)	13 (92.9)	14 (23.0)	-	-
Number of children	-	-	-	4.98	0.174
0	5 (71.4)	2 (28.6)	7 (11.5)	-	-
1	4 (26.7)	11 (73.3)	15 (24.6)	-	-
2	9 (37.5)	15 (62.5)	24 (39.3)	-	-
3 or more	8 (53.3)	7 (46.7)	15 (24.6)	-	-
Education	-	-	-	18.26	0.001
Literature	6 (54.5)	5 (45.5)	11 (18)	-	-
Primary school	9 (75.0)	3 (25.0)	12 (19.7)	-	-
Secondary school	7 (63.6)	4 (36.4)	11 (18)	-	-
College	1 (8.3)	11 (91.7)	12 (19.7)	-	-
Associate degree or more	3 (20.0)	12 (80.0)	15 (24.6)	-	-

*Includes separated, divorced, and widowed

Chronic diseases and disability

To assess the number of chronic health conditions, participants were asked whether they had any chronic diseases (e.g., cholesterol or osteoporosis). The number of chronic health conditions was added, and a dichotomous variable (≤2 chronic diseases and ≥3 chronic diseases) was created.

Disability levels were measured using the Katz index of independence in activities of daily living scale (Katz et al., 10). The scale measures self-care tasks including bathing, dressing, toileting, transferring to and from a chair, feeding, and maintaining continence. The Turkish version of this scale was assessed by Pehlivanoğlu et al. (11) for its validity and reliability, and the Cronbach alpha coefficient was 0.83. The Cronbach alpha coefficient was 0.85 in this study.

Cognitive and physical functioning

The Lawton instrumental activities of daily living scale was developed by Lawton and Brody (12) to assess independence level and physical functioning. It contains eight items which are rated trichotomously (i.e., 1=unable, 2=able with help, 3=able without help). Reliability and validity of the Turkish version was assessed in the present study, and the Cronbach alpha coefficient was 0.95.

SMMSE was originally developed by Folstein et al. (13). The SMMSE measures different domains of cognitive function such as orientation to time and place, short-term recall, and construct a diagram. The validity and reliability of the Turkish version of the SMMSE was determined by Güngen et al. (14). It had high valid and reliable properties for the diagnosis of mild dementia in the Turkish population.

Social engagement with life

In line with existing research (15,16), participants were defined as being actively engaged if they reported, first, having provided any grandchild care during the past 12 months or having done "any paid work" or "voluntary or charity work" in the year preceding the interview, and second, if they reported having "spent time with their neighbours" for a social visit or a chat at least once a week or having "providing assistance to family, friends or neighbors or attending a sports, social or other type of club" in the month preceding the interview.

Psychological well-being

This scale consists of 18 items with 5 rating points ranging from 1 to 5 (17). The obtainable total score varies between 18 and 90. A high score indicates the higher psychological well-being. This measurement tool was adapted for Turkey by Imamoglu (18), and its Cronbach alpha coefficient was reported to be 0.79. The Cronbach alpha was 0.94 in this study.

Dependent variable

Consistent with Rowe and Kahn (5), SA was defined as having a) high physical and cognitive functioning b) no chronic disease [Similar to Wu et al. (19) study, we revised the range of this criterion and classified adults with no more than two chronic diseases as successful adults] and disability c) being actively engaged with life. In order to determine the number of successful agers, in the first step, each criterion were scored as 1 or 0 for meeting or not meeting criteria for each participants (see Table 2). In the second step, we created a dichotomous/binary variable of having all five (1) or fewer than five (0) indicators. In other words, the participants with high physical and cognitive functioning, and few chronic diseases and no disability and active social engagement were classified as aging successfully. Psychological well-being was taken as an indicator of psychosocial SA.

Statistics

Prior to the data analyses, recommended assumptions of univariate and multivariate outliers, normality and multicollinearity were checked for each scale. The distribution and normality of the variables were assessed by graphical and statistical methods (20). Mann-Whitney U and Kruskal-Wallis test were used to compare the psychological well-being scores according to the socio-demographic data of the adults. In cases of a significant difference between three or more groups,

Table 2. Frequency and percentage of adults who meet each successful aging criterion and all the criteria

Indicators of successful aging	n (%)
The number of chronic diseases	
≤2 chronic diseases*	41 (67.2)
≥3 chronic diseases**	20 (32.8)
Katz ADL	
Independent/no disability*	47 (77.0)
Moderate or severe functional impairment**	14 (23.0)
Lawton IADL	
High physical functioning*	44 (72.1)
Moderate or low physical functioning**	17 (27.9)
SMMSE	
Normal cognitive functioning*	40 (65.6)
Mild cognitive impairment**	21 (34.4)
Social engagement with life	
Yes*	54 (88.5)
No**	7 (11.5)
Successful aging	
Yes*	35 (57.4)
No**	26 (42.6)

*: Proportion of successful agers, **: Proportion of usual agers, SMMSE: Standardized mini mental state examination test, IADL: Instrumental activities of daily living, ADL: Activities of daily living

using a Bonferonni corrected p-value, follow-up post-hoc tests applied. The relationship between categorical data was assessed using the chi-square test. In order to assess correlations among subjective health, subjective age and dimensions of SA, Spearman rho statistic was computed. All data was analysed using R (21). A p-value less than 0.05 ($p<0.05$) was taken to indicate statistical significance.

Results

67.2% of the participants had fewer than three chronic diseases, and 77.0% of those with no disability (Table 2). Slightly two-thirds of participants met the physical and cognitive functioning criterion (72.1% and 65.6%, respectively). The majority of the participants (88.5%) met the social engagement criteria and were socially active. According to these five criteria, 35 (57.4%) participants were successful in aging.

Table 1 and Table 3 summarise the results of all relationships between the independent variables and dependent variables. As seen in Table 1, the community-dwelling adults were more likely to experience SA than the adults who were living in nursing homes (86.7 vs. 29.0%) χ^2 (1) =20.71, $p<0.001$. Adults ages 50 to 64 were more likely to experience SA than the adults who were 65 or older (71.4 vs. 45.5%) χ^2 (1) =4.18, p=0.041. Furthermore, the married adults were more likely to experience SA than the single adults (92.9 vs. 46.8%) χ^2 (1) =9.35, p=0.002. A difference was also observed in the educational levels χ^2 (4) =18.26, p=0.001. Post hoc tests using a Bonferroni correction indicated that adults having college (91.7%) and associate degrees or more educated adults (80.0%) were more likely to experience SA than the adults having only literature (45.5%), primary (25.0%) and secondary (36.4%) educations. However, in this study, we did not find any differences based on gender or the number of children an individual had ($p>0.05$).

As seen in Table 3, the Mann-Whitney U test showed that psychological well-being scores of adults ages 50-64 (Mdn.=58.0) were higher than the scores of adults ages 65 or older (Mdn.=42.0) U=297.00, p=0.017. In addition, psychological well-being scores of married adults (Mdn.=69.5) were higher than those of single adults (Mdn.=44.0) U=182.50, p=0.012. A Kruskal-Wallis test indicated that the adult's educational groups differed significantly in terms of SA χ^2 (4) =13.40, p=0.009. Post-hoc Mann-Whitney U tests indicated that the psychological well-being scores of adults who had associate degrees or higher (Mdn.=68.0) was significantly better than that of literature

Table 3. Factors related to psychosocial successful aging in all patients based on the psychological well-being scale

Associated factors	Mean rank	Median	Min.	Max.	χ^2/U	p
Living space*	-	-	-	-	384.50	0.245
Nursing home residents	28.4	50.0	26.0	73.0	-	-
Community-dwelling adults	33.7	60.0	27.0	80.0	-	-
Age*	-	-	-	-	297.00	0.017
50-64	36.9	58.0	27.0	80.0	-	-
65 or more	26.0	42.0	26.0	76.0	-	-
Gender*	-	-	-	-	399.50	0.418
Female	28.9	43.0	26.0	80.0	-	-
Male	32.6	54.0	27.0	77.0	-	-
Marital status*	-	-	-	-	182.50	0.012
Single**	27.9	44.0	26.0	76.0	-	-
Married	41.5	69.5	29.0	80.0	-	-
Number of children***	-	-	-	-	4.24	0.236
0	19.0	32.0	26.0	69.0	-	-
1	33.2	64.0	29.0	76.0	-	-
2	34.1	50.0	30.0	80.0	-	-
3 or more	29.5	48.0	27.0	73.0	-	-
Education***	-	-	-	-	13.40	0.009
Literature	20.5	38.0	26.0	65.0	-	-
Primary school	25.3	43.5	30.0	72.0	-	-
Secondary school	28.2	48.0	30.0	71.0	-	-
College	32.8	53.5	27.0	80.0	-	-
Associate degree or more	43.9	68.0	34.0	76.0	-	-

*Mann-Whitney U test, **Includes separated, divorced, and widowed, ***Kruskal-Wallis test

(Mdn.=38.0) p<0.001 and primary school graduates (Mdn.=43.5) p=0.003.

Lastly, psychological well-being is positively correlated with the biomedical dimension of SA (r=0.54, p<0.001), subjective age (r=0.31, p=0.017) and subjective health (r=0.59 p<0.001). Moreover, the biomedical dimension of SA is positively related to subjective age (r=0.26 p=0.045) and subjective health (r=0.66 p<0.001) (Table 4).

Discussion

This research represents an early step in the determination of related factors with two main approaches to SA. One of the most interesting findings is that living space is srelated to Rowe et al. (5) SA model, but not to psychological well-being. This finding can be explained by the fact that the health status of adults living in nursing homes is worse than that of the community-dwelling adults. However, well-being is a more subjective and person-centered concept as compared to health status; therefore, we may not have found a significant difference between the two groups for well-being. Consistent with our study, Scheidt et al. (22) indicated that Rowe and Kahn's definition is very narrow, and there may be adults who do not meet these criteria but who are successful agers. This finding is especially noteworthy and should be addressed in future research. Those adults who were inconsistent in terms of the two conceptual definitions may hold the key to understanding what SA is really all about.

Some researchers found that men were more successful than women meet the criteria of Rowe et al.'s SA (1). However, other studies have suggest that more women than men have a higher prevalence of SA (23). The results of our study showed no significant gender differences in SA. This result is consistent with those of McLaughlin et al. (4) specifying that no significant gender difference was observed in SA among United States adults.

In line with previous studies (24), we speculated that adults with more children may have more physical and social support from their children, as compared to those who have fewer children, and therefore, we expected that the number of children would positively affect SA. However, we did not find SA benefits with regard to a greater number of children. We also conducted additional analysis and found no significant difference in SA rates among adults with and without children. The reason why these variables are not related to SA may be the relatively small sample size.

Ferri et al. (9) suggest that better health is associated with higher ratings on SA. Similarly, Whitley et al. (25) explored associations between Rowe-Kahn SA components and subjective health and concluded that all individual positive SA components were associated with better subjective health. In line with these studies, we found that as the evaluations of subjective health moved from very good to very bad, the level and proportion of those aging successfully decreased. This finding is important and noteworthy. How an individual feels about herself/himself in terms of health status may be the predictor of SA, and there may be a causal relationship between the two. Therefore, future research should evaluate these relationships longitudinally.

In light of the Palgi et al. (26) study, we expected there to be a relationship between subjective age and SA, and we found that younger subjective age is related to better SA. This result might be based on several factors. First of all, individuals who feel younger may be involved in more physical and social activities, and this may make them feel like successful agers. Another factor may be that a younger subjective age provides a positive psychological environment by increasing self-esteem and coping skills in the face of increasing problems with age, which may, in turn, promote SA.

An earlier study regarding the marital status and SA that was conducted in 2006 found that being currently married contributed to successful aging (27). A recent study conducted in 2018 reported that married participants are more likely to be successful agers (28). In accordance with those studies, our data revealed that the rate of successful aging was higher in married individuals. This result might be based on several factors. First of all, many researchers show that being

Table 4. The relationship between dimensions of successful aging and potential independent variables

	Mean ± SD	Median (Min-max)		1	2	3	4
1. Psychological well-being	51.3±16.9	50.0 (26.0-80.0)	**r**	-	-	-	-
	-	-	**p**	-		-	-
2. Biomedical model of successful aging*	-	-	**r**	0.536	-	-	-
	-	-	**p**	0.000	-	-	-
3. Subjective age	6.3±8.0	4.0 (-9.0-25.0)	**r**	0.305	0.258	-	-
	-	-	**P**	0.017	0.045	-	-
4. Subjective health	3.2±1.2	3.0 (1.0-5.0)	**r**	0.588	0.664	0.413	-
	-	-	**p**	0.000	0.000	0.001	-

*0 indicatesusual aging; 1 indicates successful aging, r=Spearman rho correlation coefficient, SD: Standard deviation

married is associated with many health benefits (29,30). Another possible explanation for this result is that married adults might be more likely to engage social activities (e.g., visiting relatives) and may also be less exposed to stressful life situations than single adults due to their greater financial power which may, in turn, promote SA. However, it should be note that some researchers indicated that high marital quality was associated lower stress, less depression, and higher satisfaction with life, therefore, marriage must be of a high quality to be advantageous. In other words, one is better off single than unhappily married (31).

Consistent with previous studies (1,23,32,33), this study shows that SA was related to age, educational level and marital status. More specifically, there was a higher rate of successful aging among those in the younger age category, those with higher education levels, and those who were married. As a matter of fact, these findings are well known from previous studies, and a consensus has been reached in many studies, as noted above.

Study Limitations

This study has some limitations. The first limitation of the present study was the relatively small number of participants, and future research for a similar purpose should include larger samples. Second, the study had a cross-sectional design which provides no information on causal relationships; therefore, longitudinal studies are required to more clearly establish the causal relationship between socio-demographic factors and SA. Moreover, the depression status of the patients may have affected answers to all subjective questions, but we did not investigate this variable. For this reason, the depression status should be included in future research as a covariate or control variable. On the other hand, our study's strengths include its comprehensive, two main approaches to SA based on a large set of objective and subjective functioning measures.

Conclusion

Overall, our study demonstrated that the biomedical and psychosocial dimensions of SA are related to the similar socio-demographic factors along with subjective health and age. These findings suggest that subjective age and health status, which are changeable and relatively under the control of the individuals, are important to promote SA. However, it is important to avoid blaming adults for their unsuccessful aging status, as having these socio-demographic factors is not under the control of most adults. However, social, cultural and psychological opportunities that increase individuals' ability to feel they are younger and better health should not be abandoned, multipronged approaches are needed to enhance SA. These methods should include policies to reduce socio-economic inequalities and related health disparities.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Board and Commission of Ege University in Turkey (approval number: 204-2019).

Informed Consent: Written informed consent was obtained from participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: C.S., T.Y.I., Design: C.S., T.Y.I., Data Collection or Processing: C.S., Analysis or Interpretation: C.S., T.Y.I., Literature Search: C.S., Writing: C.S.

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