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THE FEATURES OF COMORBIDITY AMONG ELDERLY AND SENILE PATIENTS

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This study presents an analysis of modern scientific literary sources on multimorbidity among the elderly, which has a growing tendency, despite significant differences between countries. Geriatric comorbidity usually leads to poorer health, especially increased disability and mortality in the elderly. The presence of comorbid pathology additionally complicates the treatment of the disease and rehabilitation, increases the risk of mental and physical complications. Senile asthenia is a leading geriatric syndrome and characterizes the most vulnerable group of patients in older age groups. At the same time, senile asthenia is closely related to other common geriatric syndromes, such as sarcopenia, malnutrition, reduced mobility and falls, cognitive impairment, and depression. The development and progression of senile asthenia increase the risk of dependence on external care and worsens the patient's prognosis. Comorbidity can accelerate the development of senile asthenia and its progression, but a large number of concomitant diseases cannot be identified with this age-associated syndrome. Despite their widespread distribution, geriatric syndromes often remain undiagnosed, leading to the development of patients' functional dependence and reduced quality of life, increasing the number of hospitalizations and the risk of death. Doctors of all specialties must have the skills to detect the syndrome of senile asthenia, know the algorithm of joint management of such patients with a geriatrician, and have the skills to detect polypharmacy and assess the risk of adverse drug reactions. Prophylactic and screening programs aimed at preventing premature aging of the population and early detection of patients with risk factors for the development of senile asthenia or its manifest signs are necessary.

Key words: multimorbidity, senile asthenia, geriatric syndromes, polypharmacy, active longevity.

Connection of the publication with planned research works.

The paper has been written within the research scientific work, entitled "The peculiarities of the course of cardiovascular pathology in patients of different age categories depending on the presence of components of metabolic syndrome and comorbital conditions, the way of correction of detected disorders and prevention", state registration № 0119U1028.

Introduction.

Aging is a global demographic phenomenon. Chronic diseases have become the most important disease burden and the main cause of death for the global population. It is estimated that chronic disease-related deaths accounted for 73.9% of the total deaths in 2019, ranking first among the causes of death [1]. Nowadays, more and more elderly people suffer from multiple chronic diseases at the same time because of the high prevalence and long course of chronic diseases. According to the definition of the American Geriatrics Association, multimorbidity in the elderly refers to the existence of two or more chronic medical conditions, including com-

mon chronic diseases, geriatric syndromes, and geriatric problems [2]. Elderly and senile patients make up the majority of outpatient admissions in medical institutions and lead in terms of the number of hospitalizations, so choosing the optimal approach to their management can significantly reduce the economic burden on healthcare by reducing visits to the doctor and hospitalizations. The goal, tasks, and methods of management of an elderly patient with comorbid pathology are significantly different from those in young and middle age [3]. In the past two decades, the global prevalence of multimorbidity among the elderly has shown an upward trend despite the large differences between countries [4, 5, 6, 7, 8, 9, 10].

With the increase in elderly people having multimorbidity, the substantive research literature has been published on the burden of disease caused by comorbid conditions [11, 12, 13, 14]. Additionally, geriatric multimorbidity usually leads to poor health, especially increasing disability and mortality in the elderly [15]. As huge research has been published on senile syndromes and common problems in the elderly, common chronic

diseases and weakness [16, 17, 18], multiple medications [19, 20, 21, 22, 23], malnutrition [24, 25, 26], falls [27], gradually became hot research topics for scientists studying the course of COVID-19 [28, 29, 30, 31, 32]. In addition, multimorbidity further complicates disease treatment and rehabilitation and increases the risk of mental and physical complications [33, 34].

In total of 3857 articles in English were published in 530 journals, among which the three most published journals are *Value in Health* (200 articles, 5.19%), *BMJ Open* (184 articles, 4.77%) and *Journal of General Internal Medicine* (145 articles, 3.76%). Articles about comorbid elderly patients are quite diverse in subject matter. Although most are published in the fields of public health and population health, some of them involve internal medicine, nursing, and other fields [35].

In general, the scope of research about multimorbidity in the elderly is gradually expanding and deepening, covering the entire process of chronic diseases from diagnostics to further treatment, including epidemiology, pharmacology, gerontology and other disciplines.

The aim of the study.

To analyse literary sources with the learning modern views on the features of comorbidity among elderly and senile patients to improve physicians' awareness of potential risks, to improve diagnostics.

Object and research methods.

We conducted a review and analysis of scientific and medical literature relying on databases Scopus, Web of Science, MedLine, and PubMed.

Main part.

Nowadays and for the foreseeable future, process of the aging is the dominant of demographic dynamics in Ukraine. This process, as an objective and natural result of the evolution of demographic processes, an indispensable attribute and satellite of socio-economic progress that is the most significant feature of long-term changes in the age composition of the population everywhere in the developed world. However, depopulation causes the most acute problems precisely in countries with a high level of demographic aging. Ukraine belongs to the thirty countries of the world with the oldest population, which determines both the inevitability of large-scale depopulation in the country and the severity of the socio-economic challenges of the progressive aging of the population [36].

As of the beginning of 2020, the proportion of persons aged 65 years and older in Ukraine is 17.1% with a significant gender differentiation of the level of aging: if among women the proportion of persons who crossed the above age threshold reached 21.2%, among men it is at the level of 12.4%.

The experiment showed that traditionally observes a higher rate of aging of the population and a lower part of the working-age contingent in rural areas in Ukraine. In Ukraine, there is traditionally a higher level of population aging and a lower share of the working-age contingent in rural areas. This causes a higher intensity of depopulation than in urban areas (-8.7% versus -5.5% in 2019). Protracted depopulation in the villages of Ukraine is combined with a long migration outflow of the rural population of the city.

As a result, from 2002 to 2019 life expectancy at birth in Ukraine increased by 4.8 years for men and 3.3 years for women and amounted to 66.9 and 77.0 years

for men and women in 2019, respectively. However, given that this is an 18-year period, this increase does not look like a significant achievement, and Ukraine is still one of the outsiders in terms of life expectancy in the European region. Compared to developed countries, life expectancy in Ukraine is lower by an average of 10-12 years for men and 6-7 years for women.

We reviewed the distribution of deceased older ages (80 and older) for the selected causes of death (exception: circulatory system diseases) in Ukraine. Thus, we can see how the proportion of such a cause of death as old age increases with age (from 2.2 to 16.9%), and the number of deaths from such increasingly dependent pathologies as neoplasm (from 7.1 to 0.4%) and remains consistently scarce (0.2-0.3%) diseases of the nervous system. We want to emphasize that we have a consistently ultra-high proportion of deaths registered from cardiovascular diseases (more than 80%).

According to the State Statistics Service of Ukraine in 2019, as in previous years, the proportion of premature deaths (before reaching 65 years old) was almost a third (29%) of the deaths of both genders in Ukraine (total – 581,114 people). Some men turned out to be much more significant – 42.0% versus 16.4% in women. This shows the highest significance of the problem of a high level of premature mortality for the male population of our country. High premature mortality, primarily in men, is an acute social problem in modern Ukraine: 29% of those who died in 2019 did not live to the age of 65. The mortality rate before reaching 65 years of age remains higher than in the developed countries of the world (in particular, in 2019, the figure was 3.4 times higher than in Sweden). Ukraine is characterized by an excessively high ratio of male and female premature all-cause mortality (one of the highest among countries in the WHO European Region).

The quality of life of older people and the prognosis for their life and health are determined by the presence of chronic diseases and the severity of geriatric syndromes.

Senile asthenia (SA) is the leading geriatric syndrome which characterizes the most vulnerable group of older patients. At the same time, senile asthenia is closely associated with other common geriatric syndromes, such as sarcopenia, malnutrition, reduced mobility and falls, cognitive impairment and depression. Despite widespread adoption, geriatric syndromes often remain undiagnosed. It is leading to the patient functional dependence and reduced quality of life, increasing the number of hospitalizations and the risk of death. Doctors of all specialties should have skills in detecting the syndrome of senile asthenia, know the algorithm for joint management of such patients with geriatric, have skills in detecting polypharmacy and assessing the risk of adverse drug reactions. The detection of senile asthenia can be a necessary tool to solve problem of treatment tactics a particular disease in an elderly patient with comorbidity [37].

Senile asthenia syndrome (frailty) is an age-related syndrome characterized by five main clinical manifestations (by Fried L. et al.):

1. Loss of muscle mass (sarcopenia).
2. Proven dynamometric decrease in hand strength.
3. Pronounced weakness and increased fatigue.
4. Decrease in movement speed.

5. Significant decrease in physical activity.

Taking into account the above, the syndrome of senile asthenia (SA) is diagnosed in the presence of three or more of the above symptoms, senile preasthenia – in the case of one or two [38].

At the basis of the course of SA are distinguished three interdependent age-related conditions [39]: 1. Malnutrition syndrome. 2. Sarcopenia (loss of muscle mass). 3. Decrease in metabolic index and physical activity. With minimal external or internal influences, this unfavorable pathological circle (the syndrome of malnutrition, sarcopenia and a decrease in the metabolic index and the level of physical activity) can lead to deterioration of health, disability and death in the shortest possible time.

The development and progression of senile asthenia increases the risk of dependence on external care and worsens the patient's prognosis. Comorbidity can accelerate and progressive the course of the senile asthenia, but a large number of comorbidities cannot be identified with this age-associated syndrome.

In conditions of limited significance or even inapplicability of stratification systems, that widely use terms of risk to various conditions for elderly and senile patients. Detection of senile asthenia can become the most important stage for deciding the choice of treatment tactics (for example, prescribing antihypertensive therapy and target blood pressure levels in patients 80 years and older, deciding on a method of treating cancer) [40, 41].

Fall syndrome should be considered separately. It is a polyfactor syndrome encompassing a complex of biological, behavioral, environmental, and socioeconomic factors. It must be taken into account that the risk of falls increases as a result of taking some drugs. At the same time, injuries got due to the fall syndrome occupy the fifth place among the causes of death in the elderly (due to cardiovascular diseases, tumors, stroke and bronchopulmonary pathology).

The specialized geriatric diagnostics of SA (interdisciplinary diagnostic process based on a comprehensive geriatric assessment (CGO)) is used to develop a set of measures for the long-term support of elderly and senile patients and create a coordinated treatment plan using [42, 43, 44]. The CGO is based on the use of questionnaires and scales: estimating the degree of nutritional disorders and the risk of developing malnutrition syndrome (questionnaire Mini nutritional assessment (MNA), assessment tests for evaluating mobility of elderly people (according to Tinetti M.), questionnaire Mini-mental state examination, the depression score (Beck's scale), assessment and determination of moral status (questionnaire Philadelphia Geriatric Morale Scale), assessment of independence in everyday life (Barthel scale).

Detection of senile asthenia in a patient implies, on one hand, lower expected life expectancy and increase in severity of diseases, and, on the other hand, it is this group of patients who can benefit the most from comprehensive geriatric assessment and application of a holistic geriatric approach [43, 44]. The diagnosis of senile asthenia may necessitate correction of patient care goals and treatment tactics.

The principles of medication therapy in elderly patients with comorbidity and senile asthenia differ from

“standard” approaches, and these differences imply not only the peculiarities of medication dosage related to age and kidney and liver function. A practical approach to prescribing medicines for such patients involves selection of a priority disease, treatment of which will currently improve the patient's quality of life and the prognosis of the patient's health. Emergence and progression of geriatric syndromes should be monitored. For example, it is necessary to remember that prescribing or increasing the dose of any antihypertensive medicine increases the risk of falling in the first two weeks, that excessive decrease in blood pressure can lead to worsening of cognitive deficits and requires reduction in antihypertensive therapy.

Polypharmacy is an essential companion of comorbid pathology, therefore one of manifestations of the professional skill of a family doctor is the ability to distribute the courses of treatment of various diseases in time, or (if the latter is impossible) adequately combine them. For this, peculiarities of interactions of pharmacological medicines should be taken into account. It is advisable to use medicines that simultaneously affect various diseases that the patient has. This will allow reducing the total number of medicines without harming the patient. When choosing medicines for patients over 65 years of age, the updated Beers criteria will help the family doctor. The main purpose of their use is to prevent unwanted side reactions in elderly patients, to optimize medication therapy. The Beers criteria were first published in 1991 and last revised in 2019. These recommendations were created by a group of experts taking into account the principles of evidence-based medicine and consist of the following sections: – medicinal products that are potentially not recommended for elderly patients; – medicinal products that are potentially not recommended for elderly patients with certain diseases and syndromes; – medicines that should be used with caution in elderly patients; – medicines that should be avoided in elderly patients or require dose correction taking into account the kidney function. The prognosis of comorbid diseases largely depends on the behavior of the patient, but it can be adjusted to a large extent by a family doctor who, owing to his or her understanding of characteristics of the persons under the doctor's care, has the best opportunities for this compared to other doctors. This will allow achieving the best results not only in increasing life expectancy, but also in improving its quality in comorbid patients.

Senile asthenia is not an integral part of aging. Such concepts as active longevity and healthy aging are more and more widely used in the society for developing action strategies aimed at supporting the elderly and senile population. The modern understanding of successful aging includes psychological, physical, and social health, functioning, life satisfaction, sense of purpose, financial stability, learning, achievement, appearance, activity, sense of humor, and spirituality. Preventive and screening programs directed at preventing premature aging of the population and early detection of patients with risk factors for development of senile asthenia or its manifest signs are necessary. Starting in 2020, the 73rd World Health Assembly approved the launch of the Decade of Healthy Aging (2020-2030), which will help bringing together UN experts, civil society, government and medical professionals to discuss the five strategic

goals of the Global Strategy and Action Plan on Aging and Health.

Conclusions.

Thus, the management of elderly and senile patients with polymorbidity should take into account the presence of senile asthenia, the patient's life priorities and

be focused on the optimal quality of life and supporting the patient's independence from outside assistance.

Prospects for further research.

Further research will focus on the study of compliance of elderly and senile age with comorbid pathology.

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ОСОБЛИВОСТІ КОМОРБІДНОСТІ СЕРЕД ПАЦІЄНТІВ ПОХИЛОГО ТА СТАРЕЧОГО ВІКУ

Трибрат Т. А., Шуть С. В., Іваницька Т. А., Сакевич В. Д., Боряк В. П.

Резюме. Мета дослідження. Аналіз літературних джерел з вивченням сучасних поглядів особливостей коморбідності серед пацієнтів похилого та старечого віку з метою поліпшення інформованості лікарів щодо потенційних ризиків, покращення діагностики, своєчасного призначення відповідного лікування і поліпшення якості життя.

Об'єкт і методи дослідження. Огляд та аналіз наукової та медичної літератури на основі баз даних Scopus, Web of Science, MedLine, PubMed.

Основна частина. Постаріння є глобальним демографічним феноменом. Хронічні захворювання стали найважливішим тягарем захворювань і основною причиною смерті населення планети. За останні два десятиліття глобальна поширеність мультиморбідності серед людей похилого віку продемонструвала тенденцію до зростання, незважаючи на значні відмінності між країнами. Наявність коморбідної патології додатково ускладнює лікування захворювання та реабілітацію, підвищує ризик психічних і фізичних ускладнень.

Якість життя людей похилого віку, а також прогноз для їхнього життя та здоров'я, визначаються не тільки і не стільки наявністю хронічних захворювань, скільки наявністю та тяжкістю геріатричних синдромів.

Стареча астенія (СА) є провідним геріатричним синдромом і характеризує найбільш уразливу групу пацієнтів старших вікових груп. При цьому стареча астенія тісно пов'язана з іншими поширеними геріатричними синдромами, такими як саркопенія, мальнутриція, зниження мобільності, падіння, когнітивні порушення, депресія. Незважаючи на широке поширення, геріатричні синдроми часто залишаються не діагностованими, призводячи до розвитку функціональної залежності пацієнтів та зниження якості життя, підвищуючи кількість госпіталізацій та ризик смерті.

Такі поняття, як активне довголіття та успішне старіння, все ширше використовуються в суспільстві при розробці стратегій дій, спрямованих на підтримання населення похилого та старечого віку. Необхідні профілактичні та скринінгові програми, які спрямовані на запобігання передчасному старінню населення та раннє виявлення пацієнтів із факторами ризику розвитку старечої астениї або її маніфестними ознаками.

Висновки. Таким чином, тактика ведення пацієнтів похилого та старечого віку з поліморбідністю повинна враховувати наявність старечої астениї, життєві пріоритети пацієнта та бути орієнтованою на оптимальну якість життя та підтримання незалежності пацієнта від сторонньої допомоги.

Ключові слова: мультиморбідність, стареча астенія, геріатричні синдроми, поліпрагмазія, активне довголіття.

THE FEATURES OF COMORBIDITY AMONG ELDERLY AND SENILE PATIENTS

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Abstract. The aim of the research. To analyse literary sources with the learning modern views on the features of comorbidity among elderly and senile patients to improve physicians' awareness of potential risks, to improve diagnostics.

Object and research methods. We conducted a review and analysis of scientific and medical literature relying on databases Scopus, Web of Science, MedLine, and PubMed.

Main part. Aging is a global demographic phenomenon. Chronic diseases have become the most important disease burden and the main cause of death for the global population.

In the past two decades, the global prevalence of multimorbidity among the elderly has shown an upward trend despite the large differences between countries.

Multimorbidity further complicates disease treatment and rehabilitation and increases the risk of mental and physical complications.

The quality of life of older people and the prognosis for their life and health is determined by the presence of chronic diseases and the severity of geriatric syndromes.

Senile asthenia (SA) is the leading geriatric syndrome which characterizes the most vulnerable group of older patients. At the same time, senile asthenia is closely associated with other common geriatric syndromes, such as sarcopenia, malnutrition, reduced mobility and falls, cognitive impairment and depression. Despite widespread adoption, geriatric syndromes often remain undiagnosed. As a result, it leads to the patient functional dependence and reduced quality of life, increasing the number of hospitalizations and the risk of death.

Concepts such as active longevity and healthy aging are increasingly used in society to develop action strategies aimed at supporting the elderly and senile age.

Preventive and screening programs directed at preventing premature aging of the population and early detection of patients with risk factors for development of senile asthenia or its manifest signs are necessary.

Conclusions. Thus, the management of elderly and senile patients with polymorbidity should take into account the presence of senile asthenia, the patient's life priorities and be focused on the optimal quality of life and supporting the patient's independence from outside assistance.

Key words: multimorbidity, senile asthenia, geriatric syndromes, polypharmacy, active longevity.

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CONTROL OF THE PHARMACOGENETICS OF ENZYMES' MEDICINE BIOTRANSFORMATION – A TOOL FOR PROVIDING PERSONALIZED MEDICINE

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The review of the literature reflects current ideas about the importance of cytochrome P450 enzymatic systems for the detoxification of endogenous (hormones, signalling molecules, neurotransmitters) and exogenous substrates (food, drugs, toxins), especially for the conversion of lipophilic molecules into water-soluble forms for excretion from the body. The goals of biotransformation correspond to the body's need to remove endo – and exogenous, mainly lipophilic molecules that cross and are retained in cell membranes and the need to ensure the transformation of molecules into a water-soluble form. According to the structure of cytochrome P450, it is a multi-enzyme protein complex embedded in the phospholipid matrix of microsomes. Individual stimuli cause a response specific to different enzyme variants, which depends on genetic control. Genetic polymorphism ensures an individual-sensitive detoxification reaction of various molecules in the body. At the same time, the actual implementation of genetic monitoring methods in medical practice remains insufficient. Moreover, different variants of genes can cover both the pathogenesis of the disease and individual phases of pharmacological intervention (mechanism of action of drugs, their transport and excretion, interaction with medications and unwanted side reactions). The formation of cytochrome P450 enzymes is due to the genetic control of their expression in tissues and organs, and this regulation is individual. It can vary significantly in activity levels (from minimal to ultra-fast). Some variants of genetic polymorphism of cytochrome P450, which most actively affect the metabolism of drugs, are given. Understanding these reactions when conducting genetic analysis in patients will allow us to vary adequate dosage regimens, predict results for obtaining safe, effective pharmacotherapy, and prevent the toxic effects of drugs.

Key words: acogenetics, cytochrome P450, enzyme polymorphism.