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The problem of multimorbidity in a modern therapeutic clinic

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ABSTRACT

A review of modern studies on the problem of multimorbidity, its definition, frequency of occurrence, prevalence, medical and social consequences, factors predisposing to its formation, and approaches to diagnosis, therapy, and rehabilitation is presented. According to modern understanding, multimorbidity is the presence of two and / or more chronic diseases that are pathogenetically interconnected and / or coincide in time in one patient.

Currently, multimorbidity is becoming an epidemic, affecting people of different ages and gender and with various diseases. The literature describes multiple adverse medical and social consequences of multimorbidity, such as increased rates of hospitalization, disability, and mortality, decreased functional capabilities and quality of life in patients, as well as increased volume, timing, and cost of medical care. Today, issues of the unified terminology, identification of multimorbidity, and the structure and clinical manifestations of associated pathology are being studied. There are single works on the study of possible factors contributing to the formation of multimorbidity. Approaches to management of patients in conditions of multimorbidity are being developed. A more detailed study of the mechanisms of multimorbidity formation and common pathogenetic links of associated diseases will make it possible to develop more effective strategies for the diagnosis, treatment and rehabilitation of multimorbid patients.

Keywords: multimorbidity, comorbidity, associated pathology

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Проблема полиморбидности в современной терапевтической клинике

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РЕЗЮМЕ

Представлен обзор современных исследований, посвященных проблеме полиморбидности, ее определению, частоте встречаемости, распространенности, медико-социальным последствиям, факторам, предрасполагающим к ее формированию и подходам к диагностике, терапии и реабилитации. Согласно современным представлениям, полиморбидность представляет собой наличие двух и (или) более хронических заболеваний, патогенетически взаимосвязанных между собой и (или) совпадающих по времени у одного пациента.

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В настоящее время полиморбидность приобретает масштабы эпидемии, затрагивая лиц различного возраста и пола, с различными нозологиями. В литературе описаны множественные неблагоприятные медицинские и социальные последствия полиморбидности: повышение показателей госпитализации, инвалидизации и смертности, снижение функциональных возможностей и качества жизни пациентов, увеличение объема, сроков и стоимости оказания медицинской помощи. В настоящее время активно исследуются вопросы единства терминологии, идентификации полиморбидности, проводится изучение структуры и клинических проявлений сочетанной патологии. Появляются отдельные работы по изучению возможных факторов, способствующих формированию полиморбидности, разрабатываются подходы к ведению больных в условиях множественной сочетанной патологии. Более детальное изучение механизмов формирования полиморбидности, исследование общих патогенетических звеньев сочетанных заболеваний позволит разработать более эффективные стратегии диагностики, лечения и реабилитации полиморбидных пациентов.

Ключевые слова: полиморбидность, коморбидность, мультиморбидность, сочетанная патология

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INTRODUCTION

In recent decades, wide spread and growth of associated pathology, which is considered within the concept of multimorbidity (MM), has become a serious medical, social, organizational, and economic problem [1–5].

A combination of diseases should be taken into account for targeted prevention, adequate treatment, and prediction of complications. At the same time, it should be noted that to date, most studies are predominantly mononosological in nature, and most guidelines have been developed for individual diseases. This presents the greatest difficulties in managing patients with multimorbid pathology, as it does not allow to fully analyze risk factors and prognosis for the development of associated diseases and effectively solve the problems related to their prevention and treatment. A lack of knowledge in this area leads to defects in the organization of medical care. Thus, an analysis of 10 studies conducted in seven countries (Belgium, England, Germany, Ireland, Scotland, the Netherlands, and the USA) showed that most difficulties in the treatment of patients with multimorbidity occurred following disorganization and fragmentation of medical care and inadequacy of guidelines and evidence-based medicine [6].

To solve this problem, a thorough comprehensive study of multimorbidity, its structure, clinical manifestations, risk factors, and features of its formation is required. This review presents current information on the definition, identification, frequency of occurrence, and medical and socioeconomic consequences of multimorbidity. Scientific works on the study of possible mechanisms and factors contributing to the formation of multimorbidity, as well as currently available approaches to the management and treatment of multimorbid patients are also considered.

CONCEPT AND DEFINITIONS OF MULTIMORBIDITY

Currently, multimorbidity is defined as the presence of two and / or more chronic diseases, pathogenetically interrelated and / or coinciding in time in one patient, regardless of the intensity of each of them [3, 7–11]. The term “multimorbidity” has various synonyms: comorbidity, polymorbidity, multifactorial, combined, and associated diseases, polypathia, etc. There is still no mainstay of the definition [9, 10]. Most often, in the Russian-language literature, the terms “polymorbidity” and “comorbidity” are used, in foreign literature – “multimorbidity” and ‘comorbidity”.

Comorbidity is most often defined as the coexistence of 2 and / or more diseases in one patient, pathogenetically and genetically interrelated [12, 13]. Comorbidity can proceed as syntropy – organ damage under the influence of common pathogenetic factors or interference – the occurrence of one disease under the influence of another [14]. Diseases or disorders

that are comorbid with a particular disease are understood as disorders that occur in this disease most often and have some common etiological or pathogenetic mechanisms with it [3].

According to some authors, the term "comorbidity" usually implies interaction of several diseases, one of which being the underlying one [15, 16]. At the same time, multimorbidity is also considered as the presence of two or more diseases that may not be in a cause-and-effect relationship. Consequently, multimorbidity is a broader concept focused on the entire complex of patient's diseases, and not on one underlying disease [15, 16].

It is believed that the relationship of several diseases can be represented by various variants. Thus, one disease may be the cause of another disease. In another variant, associated diseases may have common risk factors and common pathogenetic mechanisms. One more variant suggests that multiple diseases may not have a cause-and-effect relationship or may have only a weak association [17]. Moreover, one disease may be caused by iatrogenic factors, occurring in connection with another disease [18].

Transsystemic, transnosological, and chronological multimorbidity are identified. The first two variants represent the coexistence in one patient of two and / or more syndromes or diseases, pathogenetically interrelated with each other, and the last variant requires their temporal coincidence [19].

In recent years, the concept of "associative multimorbidity" has also emerged, which implies non-random occurrence of a certain complex of diseases that develop together much more often than one would expect from a pure chance [20]. M. van den Akker (1998) [21] and A. Prados-Torres (2014) [20] initiated the cluster theory of multimorbidity, according to which a number of diseases tend to appear in clusters [21].

METHODOLOGICAL APPROACHES TO THE DETERMINATION OF MULTIMORBIDITY PARAMETERS

There are two main groups of multimorbidity parameters. The first group consists of simple counts from various lists of chronic diseases. The second group of measurements introduces weighting for included chronic diseases, thus creating a weighted index of multimorbidity [22].

According to a review article by V. de Groot et al. (2003), there are 13 methods for scoring multimorbidity [23]. Data from a systematic review by A.L. Huntley et al. (2012) [24] cover 17 methods for assessing multimorbidity, of which the estimations of Chronic Disease Score (CDS), Charlson Index, Cumulative Illness Rating Scale (CIRS), and Duke Severity of Illness (DUSOI) indices are the most commonly used methods. The Charlson Index is based on an elaborate list of specific diagnoses. The CIRS system summarizes the state of each system and makes it possible to assess the "ranked" effect of comorbid states on specific organs and systems of the body. The DUSOI scale assesses the severity of the patient's condition according to four scales (symptoms of the disease, complications, prognosis without treatment, and possibility of cure) [25].

PREVALENCE AND FREQUENCY OF MULTIMORBIDITY

Epidemiological studies of recent years convincingly show high prevalence of multimorbidity around the world, associated, among other factors, with population aging and an increase in life expectancy [1, 2, 5, 26]. The global estimates of the multimorbidity prevalence among different age groups vary from 14 to 90% [26]. Such a large difference in magnitude can hardly be associated only with the real difference between populations, but rather with different methodological criteria for its determination. Thus, according to C. Violan et al. [1], the prevalence of multimorbidity varies from 13 to 95% depending on the studied population and the method of collecting and recording incidence data.

According to C. Buffel du Vaure et al. [27], 55% patients with chronic diseases are multimorbid. According to A.L. Vertkina et al. [19], the frequency of comorbidity in patients with decompensation of chronic diseases (average age of 67.8 ± 11.6 years) is 94.2%. Most frequently, in clinical practice, combinations of two and three diseases are observed, however, in 2.7% of cases, up to 6–8 diseases proceed in one patient simultaneously.

In recent decades, there has been a significant increase in the incidence of multimorbidity in a therapeutic clinic [3, 4, 28, 29]. Thus, the analysis of data on the occurrence of multimorbid pathology in patients of a therapeutic clinic in Novosibirsk, carried out by the authors of this review, showed an increase in the degree of transnosological multimorbidity (average number of nosological forms) from 4–6 disorders in one patient in 2003–2005 to 11–14 pathologies in 2015 [30]. The dynamics of transsystemic multimor-

bidity (average number of affected systems) showed an increase in the average number of body systems involved in the pathological process in one patient from 2–4 in 2003–2005 up to 5–6 in the current time period [30].

MEDICAL, SOCIAL, AND ECONOMIC CONSEQUENCES OF MULTIMORBIDITY

The issues of effective prevention, treatment, and long-term follow-up of patients with multiple chronic comorbidities are a major problem facing public health and society [31, 32]. Multimorbidity leads to adverse medical and socioeconomic consequences: an increase in hospitalization, disability, and mortality rates, worsening of disease prognosis, a decrease in functionality and quality of life in patients, and an increase in the volume, timing, and cost of medical care [3, 7, 8, 12, 33].

In patients with associated diseases, diagnosis and choice of treatment methods and strategy become more complicated, or when following the standards of compulsory medical services, the target results are not achieved in patients of this category [34]. All this leads to a decrease in the treatment effectiveness and patient's adherence to therapy, as well as polypharmacy [32, 33, 35, 36]. The interaction of comorbidities changes the classical clinical presentation and the course of diseases, increases the number and severity of complications, and worsens the quality-of-life prognosis [33, 36–38]. Patients with multimorbid pathology are characterized by higher rates of hospitalization and complications, significant deterioration in the prognosis of morbidity, reduced functionality and quality of life, and the highest mortality rates [35–37, 39–44].

Multimorbidity is associated with an increased risk of mortality [36, 39, 41–43]. A systematic review and meta-analysis of 26 articles showed a significant association between multimorbidity and mortality. The number of diseases is also positively associated with the risk of death [36]. Thus, the risk of death in patients with two diseases is 5–10%, while with five or more diseases it increases to 70–80% [21, 45].

Multimorbid pathology is a heavy burden on the country's economy. In the presence of multimorbidity, the costs for diagnosing and treating diseases significantly increase [39, 46, 47]. Thus, 75% of the US budget for medicine is spent on patients with multiple comorbidities. Medical insurance payment for patients with one disease is 211 USD, with four or more diseases – hundreds of times more (13,973 USD) [33]. The Russian National Clinical Guidelines "Comorbid Pathology in Clinical Practice" [46] emphasize the impact of an increase in the prevalence of multimorbidity on the impoverishment of individual families due to catastrophic medical care costs and a high share of costs from family funds.

RISK FACTORS FOR THE FORMATION OF MULTIMORBIDITY

The common risk factors and pathogenetic mechanisms of multimorbidity formation should be identified to develop effective approaches to disease prevention, treatment, and rehabilitation in multimorbid patients. Chronic somatic symptom disorders form the majority of multimorbid pathologies in the therapeutic clinic. The common etiological factors and risk factors are identified, which determine the commonality of some links in the pathogenesis of chronic somatic symptom disorder [48]. The formation and frequency of associated chronic diseases are influenced by many risk factors, including gender, age, social conditions, place of residence, etc. [8, 17, 28, 35, 49, 50].

Many studies have shown the relationship of multimorbidity with age; researchers focus on a significant increase in multimorbidity with increasing age [1, 8, 28, 32, 50–53]. According to M. van den Akker et al. [54], multimorbidity increases from 10% in patients under the age of 19 to 78% in people that are 80 years and older. According to M. Fortin et al. [45], multimorbidity occurs in up to 69% of young patients, in up to 93% of cases among people of middle age, and in up to 98% of patients of older age. At the same time, the average number of chronic diseases varies from 2.8 in young patients to 6.4 in elderly and senile patients.

L.B. Lazebnik et al. [48] analyzed the number of diseases in patients of therapeutic departments of a geriatric hospital depending on age. The authors obtained the following data: the number of diseases per one patient aged 60–65 years was 5.2 ± 1.7; aged 66–70 years – 5.4 ± 1.4; aged 71–75 years – 7.6 ± 1.7; aged 76–80 years – 5.8 ± 1.6; aged 81–85 years – 5.8 ± 1.8; aged 86–90 years – 4.4 ± 1.6; in centenarians aged 91–95 years – 3.2 ± 0.5. According to A. Marengoni et al. [7], the prevalence of multimorbidity in older people varies from 55 to 98%. According to C. Violan et al. [1], in patients aged 18 years and older, the prevalence of multimorbidity is 12.9%, and in patients older than 65 years it reaches 95.1%.

It has been noted that the onset of diseases forming multimorbidity and their chronicity occur mainly in middle age, but the result of their accumulation, that

is, a period of vivid manifestation, begins precisely in old age [51]. Some authors put forward a hypothesis according to which the formation of multimorbidity and aging are based on the same mechanisms, and multimorbidity can be considered as a marker of accelerated aging [55]. There is growing evidence on gender differences in the prevalence of multimorbidity. Most studies have shown that a greater frequency and severity of multimorbidity is associated with the female gender [1, 2, 7, 8, 28, 56, 57].

The formation of multimorbidity is significantly influenced by the socioeconomic status of a person [28]. In this regard, in recent years, the so-called social gradient or socioeconomic risk factors has begun to attract special attention. It includes the level of real income, the structure and standards of consumption, provision with housing and the comfort of life, the degree of cultural development, the social status of a person, the level of education, professional affiliation, etc. [58]. One of the significant social factors is the professional status, which largely forms the individual health of a population [3].

According to a meta-analysis of studies conducted using Medline and Embase databases, low level of education was associated with a 64% increase in the likelihood of multimorbidity, compared with high level of education. An increase in deprivation was consistently associated with an increased risk of multimorbidity, while data on income were ambiguous [59]. Other studies have also shown that the prevalence and severity of multimorbidity are associated with lower socioeconomic status, socioeconomic deprivation [1, 2, 60–63], and lower level of education [2, 7]. L. Mounce et al. [64] noted that individual factors of lifestyle, including obesity, sedentary lifestyle, smoking and excessive alcohol consumption; psychosocial factors (negative life events, external locus of control, and limited social contacts); mental health problems (depression and long-term treatment with certain drugs), also contribute to the formation of multimorbidity.

Modifiable hemodynamic and metabolic risk factors for chronic noncommunicable diseases are of great interest for practical medicine. These factors include high blood pressure, obesity, dyslipidemia, hyperglycemia, hyperuricemia, and others. However, their role in the formation of multimorbidity is much less studied. In recent years, there have been works indicating a possible relationship of multimorbidity formation with an imbalance in metabolic parameters [30, 46, 65] and with behavioral risk factors (smoking, alcohol abuse, low physical activity, overweightness) [1, 60].

Our previous studies have shown a direct relationship between the formation and development of multimorbidity and some of the main risk factors for chronic noncommunicable diseases, such as arterial hypertension, hyperglycemia, dyslipidemia, hyperuricemia, and obesity [30]. It is known that these metabolic and hemodynamic risk factors for chronic noncommunicable diseases, which are also risk factors for cardiovascular diseases, are closely related within the metabolic syndrome [66]. Literature data indicate that metabolic syndrome significantly increases the risk of developing multiple diseases, primarily diseases of cardiovascular and endocrine systems, digestive system, as well as musculoskeletal system, which can serve as a pathogenetic basis for the formation of multimorbidity [46, 67, 68].

APPROACHES TO TREATMENT OF MULTIMORBIDITY

The existing problems and unfavorable trends associated with multimorbidity have necessitated creation of guidelines and national recommendations for management of multimorbid patients.

The American Geriatrics Society developed a concept of individual approach to an elderly patient with multimorbidity. The basic principles of the concept included defining the key role of the patient's values and priorities; building a relationship between the doctor and the patient, ensuring shared decision-making; and a coordinated approach to interdisciplinary care [69]. In this document, particular attention is given to optimization of treatment regimens. It is recommended to avoid polypharmacy in patients with multimorbidity, reduce the number of drugs, especially high-risk drugs, systematically review the list of drugs to eliminate drugs that people no longer need, and select drugs with minimal drug interactions [69].

In 2016, the National Institute for Health and Clinical Excellence (NICE) guidelines "Multimorbidity: Clinical Assessment and Management" were issued [70]. The NICE Guidelines for the management of patients with multimorbidity are based on other guidelines created to provide optimal management of patients with isolated diseases or conditions (that is, for patients without multimorbidity) that require regular medication. The main principle of these guidelines is a personalized assessment and development of an individual management plan; the purpose is to improve the patient's quality of life by reducing the treatment load and unplanned or uncoordinated care.

In accordance with these guidelines, when prescribing research and treatment to multimorbid patients, it is recommended to carefully consider all the risks and advantages of the methods recommended for the diagnosis and treatment of certain diseases and conditions on an individual basis and discuss the risks and advantages with the patient, taking into account their preferences. When analyzing the expected positive and negative effects of treatment methods (including drugs), it is recommended to use databases of treatment method effectiveness. The need to analyze all drugs and non-pharmacological methods of treatment that the patient is already receiving and assess which of them can be canceled and which new treatments are reasonable for prescription is noted. Separately, it is recommended to consider the likelihood of a slight potential benefit of some treatment methods aimed at improving the prognosis in the long term in patients with a limited expected life expectancy or fragility.

In the subsequent Recommendations on the tactics of managing patients with multimorbidity (JA-CHRODIS consensus, 2017), on the basis of expert discussions, 16 principles of providing medical care to patients with multimorbidity were formulated [71]. In this document, tactical and organizational issues of managing multimorbid patients were worked out in detail. Particular attention is paid to the need for a regular comprehensive assessment of the patient's condition, as well as interdisciplinary, coordinated work of a team of specialists.

On the initiative of Academician of the Russian Academy of Sciences, Professor R.G. Oganov, the Working Group developed Russian Clinical Recommendations "Comorbid Pathology in Clinical Practice" (2017) [46], and "Comorbid pathology in clinical practice. Algorithms for diagnosis and treatment" (2019) [13]. The approaches to diagnosis and treatment of multimorbid patients are set out in these Recommendations. Due to the fact that in modern clinical practice multimorbidity is based on chronic diseases, the influence on common risk factors for chronic noncommunicable diseases has been proposed as an effective therapeutic approach in multimorbidity. Among the modifiable risk factors, the largest number of associations with polypathies is noted for behavioral risk factors and obesity. In addition, by the examples of the most common combinations of diseases, it is recommended to conduct a thorough analysis of drug therapy for the underlying disease, taking into account the concomitant disease (the choice of drugs that do not adversely affect the course of the comorbid disease) [13, 46].

In connection with the need to minimize and optimize therapy for multimorbidity (by the example of the gastrointestinal tract disorders), the concept of multitarget therapy of comorbid disorders was developed. In accordance with this concept, in case of comorbidities, it is advisable to use drugs affecting the common links in the pathogenesis of associated diseases and leading to positive changes in the course of all components of comorbid pathology [13].

CONCLUSION

In the modern therapeutic clinic, there is a significant increase in multimorbidity, which significantly affects the course and outcome of many diseases. It is of great medical and social importance and determines the need for a detailed study of risk factors and features of its formation. Due to the prevalence and socioeconomic consequences of multimorbidity, this problem poses a challenge to healthcare in the XXI century. Scientists and specialists are focusing on the need to develop effective strategies for managing multimorbid patients, set treatment priorities in order to improve the quality of life, reduce unwanted interventions and consequences of polypharmacy, and create a network of health professionals.

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