

THERAPEUTIC OPTIONS FOR THE PREVENTION AND TREATMENT OF FRAILTY SYNDROME

Możliwości terapeutyczne w zapobieganiu i leczeniu zespołu kruchości

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SUMMARY

Background. Frailty syndrome is very important in assessing the course of the aging process, as it has long-term health implications. The group of major international scientists defined physical frailty as “a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency and/or death”.

Objectives. The aim of the study was to analyze the literature and collect the most important information on the prevention and treatment of the frailty syndrome.

Discussion. Frailty syndrome is still a studied and diagnosed affliction. Recent recommendations and therapeutic options are not gathered in any guidelines so far, due to the fact there is not enough research on a dedicated group. However, many scientists and researchers report that early diagnosis, physical activity and a change in eating habits can have a positive effect on further prognoses. It is important to make every effort in the diagnosis of the elderly towards the frailty syndrome. As a result, early diagnosis allows for longer independence of the patient and the possibility of ensuring care. A care model that focuses on health promotion and disease prevention can influence decision making and care planning for older people.

Conclusions. 1. Physical activity can potentially prevent and reduce the risk of frailty syndrome. 2. A properly selected diet can relieve the course of frailty syndrome. 3. Monitoring micro and macro levels of elements and blood parameters, hormones help to control the course of frailty syndrome. 4. Early diagnosis and the resulting preventive measures can significantly reduce the incidence of frailty syndrome among the elderly. 5. Adequate care of the primary care giver is able to provide the patient with a better prognosis.

Key words: frailty syndrome, prevention, therapeutic options, treatment, elderly.

STRESZCZENIE

Wstęp. Zespół kruchości jest bardzo ważny w ocenie przebiegu procesu starzenia, ponieważ ma długoterminowe konsekwencje zdrowotne. Grupa najważniejszych międzynarodowych naukowców zdefiniowała zespół kruchości jako „zespół medyczny z wieloma przyczynami i czynnikami wpływu, który charakteryzuje się zmniejszeniem siły, wytrzymałości i ograniczeniem funkcji fizjologicznych, które zwiększają podatność jednostki na rozwój zwiększonej zależności i/lub śmierci”.

Cel pracy. Analiza literatury oraz zebranie najważniejszych informacji na temat profilaktyki i leczenia zespołu kruchości.

Dyskusja. Zespół kruchości jest nadal badaną i diagnozowaną dolegliwością. Najnowsze zalecenia i możliwości terapeutyczne nie są jak dotąd zebrane w żadnych wytycznych, ze względu na fakt, iż nie ma wystarczających badań na dedykowanej grupie. Wielu naukowców i badaczy donosi, że wczesna diagnoza, aktywność fizyczna i zmiana nawyków żywieniowych mogą mieć pozytywny wpływ na dalsze prognozy. Ważne jest, aby dołożyć wszelkich starań w diagnostyce osób starszych w kierunku zespołu kruchości. Dzięki temu wczesna diagnoza pozwala na dłuższą samodzielność pacjenta i możliwość zapewnienia opieki. Model opieki, który koncentruje się na promocji zdrowia i zapobieganiu chorobom, może wpływać na podejmowanie decyzji i planowanie opieki nad osobami starszymi.

Wnioski. 1. Aktywność fizyczna może potencjalnie zapobiegać i zmniejszać ryzyko zespołu kruchości. 2. Odpowiednio dobrana dieta może złagodzić przebieg zespołu kruchości. 3. Monitorowanie poziomów mikro- i makroelementów, parametrów krwi, hormonów pomagają kontrolować przebieg zespołu kruchości. 4. Wczesna diagnoza i wynikające z niej środki zapobiegawcze mogą znacznie zmniejszyć częstość występowania zespołu kruchości wśród osób starszych. 5. Odpowiednia opieka lekarza pierwszego kontaktu jest w stanie zapewnić pacjentowi lepsze rokowania.

Słowa kluczowe: zespół kruchości, zapobieganie, opcje terapeutyczne, leczenie, osoby starsze.

BACKGROUND

Nowadays, due to the increasing life expectancy and societies aging process, diseases of the oldest age groups become significantly more important. Numerous studies aimed at accurately illustrating the problems and ailments of the elderly are currently conducted due to that reasons. One of the important disease units of said group is frailty syndrome, which recently gained more attention from the scientific community and has been studied more frequently in recent years [1]. Despite many attempts to unambiguously define the syndrome, one of the commonly used definitions is one created by Fried et al.: „Frailty is considered highly prevalent in old age and to confer high risk for falls, disability, hospitalization, and mortality. Frailty has been considered synonymous with disability, comorbidity, and other characteristics, but it is recognized that it may have a biologic basis and be a distinct clinical syndrome” [2]. However, since then, the multidimensional aspect of the syndrome has been more widely understood and nowadays more definitions can be found depending on the field. The group of major interna-

tional scientists defined physical frailty as “a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency and/or death” [3]. Both definitions refer to the concept of physical weakness phenotype. It is the best-known concept to this day and from it the research on fragility basically originated, even despite the fact that this concept excludes the effects of cognitive function and mood.

This phenotype or biological model was originally operationalized using the Cardiovascular Health Study (CHS) database, using five practically measurable elements: exhaustion, involuntary weight loss, poor grip strength, slow walking speed and low energy expenditure, and the number of defined positive positions of an individual as brittle (≥ 3), in front of the rail (1–2) and solid (none) [2].

There is also a definition covering the biopsychosocial model and the accumulation deficit model, i.e. covering a large number

of factors such as symptoms, abnormal laboratory test results or medical conditions. Weakness syndrome significantly affects the susceptibility of the individual to stressors.

Frailty syndrome is very important in assessing the course of the aging process, as it has long-term health implications. Today, using several scales (FRAIL scale, Edmonton Frail Scale, Tilburg Frailty Indicator, Kihon Checklist and the five-item frailty screening index, Cardiovascular Health Study criteria) [4], tests (grip strength by dynamometer, time to walk) and determination of levels of certain elements, hormones (raised inflammatory markers including interleukin 6, C-reactive protein, low vitamin D, and testosterone low levels) can confirm frailty syndrome [5–8].

THERAPEUTIC OPTIONS FOR TREATING AND PREVENTING FRAILITY SYNDROME

Therapeutic options will be centered around individual systems in the body. The inclusion of patients with confirmed fragility syndrome with complex treatment can contribute to improving quality of life, avoiding premature aging, reducing hospitalization times and reducing intervention by healthcare professionals.

In the case of frailty syndrome, there are no guidelines dedicated to the disease unit to prevent it. Rather than that, it is a set of recommendations for each body system. As in most diseases, our daily habits have a huge impact on the onset of the syndrome. By leading a balanced lifestyle with common sense and considering cardiac or oncological guidelines, and prevention in general, we may be able to avoid the onset of frailty syndrome in old age.

Patient health deficits accumulate gradually over the entire period of life, rather than only during old age. In the context of cognitive impairment in old age, pointing to a deep relationship between the patient's health condition in late adulthood and his or her history of disease in old age [9]. For the elderly, early diagnosis is crucial. A great emphasis on the detection of frailty syndrome should be implemented by primary care physician. Diagnostics take time and financial resources, but proper diagnostics at an early stage is still much more economically advantageous. One of the most basic diagnostic indicators is to check the gait speed. This examination is painless, does not require specialized equipment and should be carried out by primary care giver. Study conducted by Castell et al. showed that after reaching 75 years old the incidence rate of FS among the subjects was significantly higher (19%) than in other age groups. As a result, the detection of the syndrome increases. Of course, in the current epidemiological situation, it is difficult to perform tests requiring the presence of a patient. In the current situation, tools such as the Tilburg frailty indicator and a thorough interview will work satisfactory [10, 11].

Risk factors for frailty syndrome are associated with lifestyle, polypharmacy, disorders on the levels of certain micro and macro elements, hormones and vitamins. Somatic factors such as extensive pain, civilization or psychological diseases (e.g. depression) can also affect the onset of syndrome [12].

EXERCISE

In 2013 study showed that exercise has a positive effect on patients with frailty syndrome. Strengthening muscles and regular exercise increase mobility and independence of patients and allow them to be maintained for a longer period at a given level of fitness [3]. However, the exact exercise regimen has not yet been developed. Depending on the studies conducted, emphasis was placed on different types of exercises (multi-component, resistance training). It is also worth encouraging patients to be independent and educated about the positive impact of physical activity on daily functioning. Nevertheless, it should not be forgotten that the selection of appropriate exercises should be handled by appropriately trained personnel (e.g. physiotherapist, rehabilitator).

Further studies are needed among patients with this condition in order to establish a thorough investigation. Moreover, the conclusions of previous studies clearly suggest that physical activity appropriate to the patient's capabilities reduces the risk of developing frailty syndrome and improves the patient's quality of life [13].

Regular exercise supports the proper functioning of the muscular, nervous and circulatory systems. Performing such physical activities as dance, aerobics or Tai Chi has a positive effect on our body, improves motor coordination, balance and strengthens individual muscle groups. Maintaining physical activity by the elderly is important because it reduces the risk of falls, increases mobility and allows you to maintain independence longer. Thanks to this, patients have a lower probability of falling and thus can avoid hospitalization, which negatively affects the functioning of the body. Of course, physical activity should always be selected by a specialist and performed under his care, especially by people who already have frailty syndrome. Poorly chosen exercises can lead to injuries and have many associated consequences [14].

According to Rossi's et al. meta-analysis, people with frailty syndrome experience development of their cognitive functions. The data from the meta-analysis showed that physical exercise improves Global Cognition (Mean Difference = 2.26; 95% CI: 0.42–4.09; $p = 0.02$) and mental flexibility (Trail Making Test B) (Mean Difference = -30.45; 95% CI: - 47.72 – -13.19; $p = 0.0005$) [15]. However, research conducted by Dziubek et al. has shown that much better exercise effects are obtained by pre-frail people. People with FS require additional psychological care and the care of support groups. The psyche of the examined patients had a significant impact on the results achieved [16]. The common conclusion of many studies is the fact that early implemented exercises improve and reduce the development of FS. Significant improvement can be expected in groups of pre-frail patients, while patients with a developed syndrome may not achieve the expected results.

POLYPHARMACY

Polypharmacy is nowadays a common phenomenon. Due to the increasing life expectancy and modern methods of treatment of many disease units, patients tend to take many different types of medications per day. According to M. Gutiérrez-Valencia's et al's analysis [17], polypharmacy has a significant impact on the development of frailty syndrome. Modern patient therefore needs a good primary care giver, who can supervise the quantity and quality of the drugs taken. It is nothing new that patients can take antagonistic drugs, take diet supplements on their own or take drugs with the same effect. Often older patients are unable to understand how individual drugs work because there are too many of them. Hence that, i.a. The Edmonton Frail Scale questionnaire asks about how many medicines one is taking. A good practice that can affect the reduced occurrence of frailty syndrome is to supervise and observe patients who tend to abuse medications intake. Additional studies are needed to confirm how polypharmacy affects the development of frailty syndrome and whether properly conducted pharmacotherapy can prevent or delay the development of frailty syndrome [18].

Often, studies conducted on the introduction of drugs exclude patients with frailty syndrome, as a result of which we do not know exactly the effect of drugs on this group. Specialists introducing drugs often deal with the treatment of their disease entity. The effect of drugs on each other is often overlooked and patients take drugs for reactions caused by other medicaments, which only increases the occurrence of polypharmacy. That is why integrated care for the geriatric patient and the huge role of the general practitioner are so important [19, 20].

DIET

Elderly patients' diet is often insufficient. There are large deficiencies in the amount of protein, micro and macro elements, vitamins, etc. supplied. This is due to several factors such as lack

of appetite or insufficient financial resources and restrictions due to individual disease units. For patients diagnosed with frailty syndrome, an increased protein supply of 1.0–1.2 g per kilogram of body weight per 24 h is recommended [21]. Some studies show that there is no effect of increased protein supply on the improvement of patients with this disease unit or the lack of benefit from increased protein intake without physical activity. It is important that the increased amount of protein taken is a conscious decision, which also considers the occurrence of patient other conditions and will bring decisive benefits. Increasing the supply of protein without considering its effects, e.g. on the cardiovascular or renal system, is a short-sighted activity and should be avoided.

Diet therapy should also include the supply of amino acids, elements (selenium, calcium, zinc), omega-3 acids and antioxidants. A Mediterranean diet which is rich in the above-mentioned ingredients is highly recommended and is considered one of the healthier diets found in the world [22, 23].

Due to the rich composition of the Mediterranean diet and the proven effect on reducing the development of cardiovascular or nervous system diseases, Talegakwar et al. conducted a study on 690 Italians over 6 years. Studies have shown that there was a high adherence to a Mediterranean-style diet at baseline was associated with a lower risk of developing frailty both for men and women [24].

The increase in protein demand may be due to the fact that people quite often take less protein than the recommended by WHO RDA standard of 0.8 g/kg/day. Studies in the USA have shown that as many as 1/3 of the female population over 50 years of age and 1/4 of the male population consumed not enough protein. Protein deficiencies significantly affect the development of sarcopenia, which is one of the criteria for determining frailty syndrome. It is important that the diet includes the necessary micro and macro elements at every stage of development. Deficiencies occurring in earlier years may contribute to an increase in the occurrence of frailty syndrome in the future [14].

VITAMIN D

Also, an important aspect in frailty syndrome is monitoring the level and regulating the supply of vitamin D. In many recommendations it occurs as a factor slowing down or reducing the risk of frailty syndrome. The effect of vitamin D deficiencies on the appearance of FS is not fully known. In several international studies conducted by e.g.: Concord Health and Ageing in Men Project, European Male Ageing Study, KORA Age study, has been shown to be the relationship between vitamin D deficiencies and the occurrence of brittleness syndrome or pre-frailty [25]. If this deficiency occurs, the patient should be given the right dose of vitamin and, in combination with calcium supplementation, it could increase survival among the elderly population, who have deficiency of vitamin D commonly present [26, 27]. In a number of studies e.g. The Third National Health and Nutrition surveys (NHANES III), the InCHIANTI study showed that deficiencies of 25(OH)D < 20 ng/ml were associated with an increased risk of frailty syndrome. Regular monitoring of vitamin D levels and appropriately selected doses may prevent the development of frailty syndrome in the future, but appropriate research is still needed to confirm this [14, 28].

CARDIAC PATIENTS AND TREATMENT OPTIONS

Frail patients with CVD have a worse prognosis than non-frail patients. In the European Society of Cardiology (ESC) guidelines published in 2016, recommendations can be found that, in the event of coexistence of vascular diseases with frailty syndrome, when undertaking medicinal measures such as lowering cholesterol or glycated hemoglobin, the standards adopted for other patients should not be applied. It is recommended that patients with frailty syndrome lower high values of said factors gradually and under increased supervision. Thanks to this treatment, patients with frailty syndrome have better prognosis and a longer chance of survival [29, 30]. Patients with cardiac diseases

quite often also develop frailty syndrome. This has a significant importance in the planned prognosis and treatment of a particular individual. In the study, Uchmanowicz and colleagues evaluated patients diagnosed with atrial fibrillation using TFI questionnaire. It turned out that mild FS was found in 38% and moderate FS in 29% of patients [31].

In a meta-analysis of Dawis et al. of patients with heart attack, it was shown that women have a 26% higher risk of developing frailty syndrome than men. He even suggests that when conducting diagnostics in the future, we should pay more attention to gender [32].

Also, the meta-analysis of Uchmanowicz et al. showed that among patients with a heart attack, frailty syndrome increases the risk of mortality and hospitalization by an average of 40% and in 48% of cases FS occurs [33].

All these studies show how often frailty syndrome is associated with cardiac diseases. Therefore, with cardiac diagnostics, diagnostics of frailty syndrome should be carried out immediately. Nowadays, we do not have a unified tool, but perhaps the introduction of FS research in the assessment of other disease entities with which there is a relationship may allow us to develop a new tool for diagnosing FS.

COVID-19

In 2019, the pathogen causing the pandemic – COVID19 – appeared in the world. All over the world, people of all ages began to get sick. In the first months, medics were focused on saving lives, but now by analyzing the data collected, actions taken and sharing information about COVID-19, we can assess the impact of the disease on individual groups. Patients with FS who, because of the disease, are normally exposed to more frequent hospitalizations and multimorbidity may have felt more at risk.

In Yao Ma's et al. study of hospitalized patients with confirmed COVID-19, it was shown that pre-frail and frail patients were more likely to develop chronic disease than non-frail patients [34]. In the study of Woolford et al. frailty and multimorbidity do not seem to help stratify risk in terms of positive and negative COVID-19 test results [35]. In Hägg's et al. study, it was shown that among older patients, FS assessment helped assess the risk of developing COVID-19 outcomes [36]. In Kundi's et al. study, the HFRS tool shows that it is an effective tool for diagnosing COVID-19 patients and helps with risk assessment, categorization and elective treatment [37].

All these studies prove that the possibilities in the face of a new disease entity, which is the cause of the pandemic, are important to determine whether older patients ≥ 60 have FS. If patients are assessed in the context of the occurrence of FS, it gives wider possibilities in making therapeutic decisions, allows to provide adequate care and allows for a real assessment of the effects of given therapies. At the same time, thanks to numerous studies, we are able to provide better care and give patients a sense of better care.

DISCUSSION

Frailty syndrome is still a studied and diagnosed affliction. Many researchers around the world are involved in learning about its effects on the course, quality of life or functioning of patients. In most cases, it is assumed that this condition affects the elderly and the increase in the number of patients with frailty syndrome is due to higher survivability rate of modern society. Recent recommendations and therapeutic options are not gathered in any guidelines so far, due to the fact there is not enough research on a dedicated group. However, many scientists and researchers report that early diagnosis, physical activity and a change in eating habits can have a positive effect on further prognoses. Also, a properly adapted treatment of comorbidities along with frailty syndrome requires an appropriate approach and specific supervision. A large role in the care of such a patient should be played by a primary care giver, who is able to supervise regularly the patient's nutrition status, de-

terioration or improvement of health, assess the progression of the disease and the patient's capabilities, to provide him with adequate care and quality of life. Physician is also able to monitor the number of drugs taken by the patient and prevent the occurrence of drug use abuse [5, 38]. Patients over 70 years of age should be screened for frailty syndrome [3].

Nowadays, the number of elderly people is increasing. Due to their different health status, they become dependent on their caregivers. This has socio-economic consequences and significantly affects the functioning of society, the family and the health system. Therefore, it is important to make every effort in the diagnosis of the elderly towards the frailty syndrome. As a result, early diagnosis allows for longer independence of the patient and the possibility of ensuring care [39]. A care model that focuses on health promotion and disease prevention can influence decision making and care planning for older people. In this way, preventive measures related to FS and cognitive impairment contribute directly into the process of healthy aging [40].

Despite the aforementioned definitions and guidelines, there are studies such as Brummel et al. according to which frailty syndrome is not only an ailment of the elderly, but also of criti-

cally ill people of all ages. This is very important information and the study itself shows how much the human body and frailty syndrome are hiding from us. Determining how many aspects are still to be explored and creating clear definition of the syndrome may take years [41, 42].

CONCLUSIONS

1. Physical activity can potentially prevent and reduce the risk of frailty syndrome.
2. A properly selected diet can relieve the course of frailty syndrome.
3. Monitoring micro and macro levels of elements and blood parameters, hormones help to control the course of frailty syndrome.
4. Early diagnosis and the resulting preventive measures can significantly reduce the incidence of frailty syndrome among the elderly.
5. Adequate care of the primary care giver is able to provide the patient with a better prognosis.

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