Mini Review Article

Frailty and bone health in European men

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Abstract
Frailty is a geriatric syndrome, which is characterized by the decline of the functions of older people systems, resulting in the exposure of one’s health at risk, disability and mortality. Older people lose their autonomy and independence, quality of life and their psychological state is decreased. Frailty is a syndrome with multiple manifestations and with no single feature being enough in its presentation, many signs and symptoms determine it, which frame the “frailty clinical phenotype”. The rates of frailty are constantly increasing, due to the increase of the aging population in Western countries. In Europe, these percentages are higher in the Mediterranean countries, on the contrary to the Nordic countries. For this reason it is important to prevent the syndrome and its effects, in order to improve the elderly population quality of life. The aim of this study is to review assessment tools for frailty, to flag consequences of this syndrome, to mention the epidemiological data in European community-dwelling population and mainly in European men, to accent the correlation between frailty and bone health and to report the treatment of frailty.

Keywords: Frailty, Aging, Male health, Bone health, Epidemiology

Introduction
Consequence of aging is the reduced functional capacity of the individual autonomy and independence, due to malfunctions of the body systems, in cognitive and sensory problems. As life expectancy is increasing, retaining functionality is essential as a public health precedence. It is assumed that by 2025, 1.2 billion people worldwide will be over 60 years old. The majority of European men are estimated to have healthy aging by the age of 67 years, while 40 percent of them will have reduced functionality. The 46% of European women will have functional limitation and they estimated to have healthy aging until 68 years old1. Frailty, disability and functional debility belong to geriatric syndromes and affect the quality of life and older people’s functionality. Disability and frailty present common features, both effects elderly population, depends on a number of factors and pathological mechanisms and some risk factors are common. Disability is defined as the inability of older people to perform everyday life activities, to self-handling and to be independent. A large percentage of disability, is developed slowly and is affected by chronic diseases, comorbidities and weakness. At the beginning of adulthood, the functional capacity reaches top levels and steadily decreases with age, reaching the level of disability. The rate of decline of functional capacity depends on intrinsic factors such as the existence of diseases and environmental factors including social and economic factors. It is noted that in the deterioration of disability contributes the decreased muscle strength, mobility, balance disorders and comorbidity2.

Frailty
Frailty is a common geriatric syndrome that affects nervous, musculoskeletal, endocrine and immune system. Current data show that 10.7% of population suffer from frailty. These people have an increased risk of fall, disability, hospitalization and mortality3. In clinical practice, frailty is a pathophysiological condition that is defined as a loss of functional homeostasis characterized by the accrual of cellular and tissue detriment in different systems of human body1. The frailty syndrome is associated with chronic diseases. Some of the most frequent diseases of elderly are cardiovascular disease, stroke, chronic renal disease, osteoarthritis and depression. The frailty syndrome is a recording and evaluation of deficits related to age. These deficits are related to weight loss, reduced physical stamina,

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slow motion, reduced muscle strength and low physical activity. Other features of the syndrome are disturbances in cognition, mood, vision and hearing, diabetes, vascular problems and sleep disorders. 

Assessment tools to identify frailty

Frailty models have been constructed according to three different models. The first one is the functional model and includes physical, cognitive and sensory function and nutrition. The second model is a frailty index that measures the burden of various defects such as diseases, disability and symptoms. The biological model comprises five criteria, and represent the “frailty clinical phenotype”. None of these models is suitable for widespread clinical use, so the Frail scale has been developed. The Frail Scale is a scale comprising these three models and is widely used in clinical practice. 

Frailty clinical phenotype

The key features of frailty syndrome, that help in diagnosis, are five, and composed the “frailty clinical phenotype”, expressed by Fried. These features are weight loss, exhaustion, weakness, slowness (walking speed) and physical activity. 

The weight loss was evaluated by whether or not the appetite of the patient have been reduced. Exhaustion, was assessed by the positive or negative answer to the question “In the last month, have you had too little energy to do the things you wanted to do?”. A positive answer was recorded by “1” and a negative answer by “0”. Weakness was assessed by measuring the force of the hand grip using a dynamometer. The right and the left hand were measured and the highest measurement was selected. Slowness was determined by whether or not the patient had difficulty walking 100 meters, because of a health problem and if he could climb stairs, without resting. The score “1” was received by one or two positive answers and the score “0” to negative answers. Physical activity was evaluated by the question “How often your activities are required low or moderate level of energy?”. score “1”: more than once time per week, score “2”: one time a week, score “3”: one to three times per a month and “4”: rarely or never.

According to this phenotype, depending on the number of characteristics of each elderly, people are divided into three categories: O: non-frail, 1 or 2: pre-frail, and 3, 4 or 5: frail. 

Frailty index

The Frailty Index is the second most widely used scale to determine the health status of older people. It represents the ratio of number of health deficits present to a number of health deficits measured. The deficits include diseases, symptoms, laboratory findings, cognitive disorders and difficulties in performing daily activities. The rating scale ranges from 0 to 1. 

Frail tool

Frail tool was created to identify the older people, who are at risk for frailty syndrome. It measures five items, which are fatigue, resistance, ambulation, illnesses, and loss of weight. Frailty is defined by the presence of three or more items.

Except of the key factors that constitute frailty clinical phenotype there are more factors that could influence the progress of frailty syndrome. Two more factors that should coexist with the factors of the clinical phenotype for frailty diagnosis, are depression and impaired cognition. These psychological factors could be represented as predictors of frailty syndrome. Frailty is characterized by multiple deficits in different biological systems such as sarcopenia, osteoporosis, metabolic and neuroendocrine dysfunction, high inflammatory factors malnutrition and cardiovascular abnormalities. Sarcopenia is the reduction of muscle mass and functional capacity of the muscle and affects the course of frailty. The results of this situation are the reduced mobility, impaired gait and balance, falls, fractures, reduced functionality and independence of elderly and increased mortality. Three criteria for diagnosing sarcopenia are low muscle mass, low muscle strength and low physical performance. Frail older people exhibit sarcopenia and a percentage of elderly people with sarcopenia are frail.

Osteoporosis is an age related disease that causes reduction of bone mineral density in both trabecular and cortical bone. The 4-6% of men over 50 years have osteoporosis and the 33-47% have osteopenia. Aging and genetic factors, glucocorticoid therapy, anticonvulsant therapy, low levels of androgens and estrogen, smoking and alcohol use, are related with osteoporosis in men. Commonly osteoporotic fractures in men are spine or hip fractures.

Chronic pain is associated with the emergence and worsening weakness in elderly European men, regardless of comorbidities and lifestyle. Other factors that influence the development of the syndrome are smoking, alcohol consumption, depression, eating disorders, diabetes and cardiovascular diseases. Low testosterone levels, low protein intake and excess cytokines and vitamin B12 deficiency are associated with frailty.

Epidemiology

The elder people over 60 years old, all over the world was 600 million in 2000 and expected to reach 2 billion by 2050. 1 in 20 people over 60 years old will be frail and the 20-30% of the population older than 75 years will be frail too. The percentage of frail in elderly Europeans over 65, varies between 5.8% and 27.3%, while the pre-fail varies between 34.6% and 50.9%.

These rates are increasing with age and are higher in women and in people with low income and are increased even more when coexist with chronic diseases. In Southern
European countries, the percentages of frail is higher than the percentages in the North countries\(^1\). The 4.1% of European over 50 years old were frail and 37.4% were prefrail, 5.2% of the women were frail and the 42% pre frail, while men in the same age group, the 2.9% were frail and the 32.7% prefrail. The 17% of people over 65 years old were frail and the 42.3% prefrail. The prevalence of frail Europeans over 65 years old is 17% and the prefrail prevalence is 42.3%. The 21% of women over 65 years old were frail and the 42.7% prefrail, while the 11.9% of men were frail and the 41.9% prefrail.

The frailty and prefrailty syndromes are very common in Spain and to a lesser extent in Italy, unlike in Switzerland and Sweden, where the rates of frailty are low. The highest rates of frailty were observed in southern European countries. More specifically, weight loss, exhaustion, weakness and slowness had higher rates in Spain, while in Italy weakness, slowness and low physical activity had higher prevalence in elders over 65 years old. Regarding disability rates at elders over 65 years old, are higher in Italy, Spain and France. But in people without a disability, frail is still frequent in southern Europe and particularly in Spain rates 21%, in Italy rates 14.3%, in Greece to 11.3% and in France to 9.3\%\(^12\) (Table 1). On the other hand German has the lowest prevalence of frailty in Europe, specifically less than 1% is the prevalence of frailty in Germans over 50 years old\(^13\).

### Consequences of frailty

The consequences of frailty syndrome are falls, disability, hospitalization and mortality. Frailty increases the risk of falls and death in the next five years. At frailty women the risk of death is increasing 6 times more than healthy women and disability risk is increasing 10 times more.

#### Falls

Advancing age increases the risk of falls. The 1% of falls causes hip fractures, 2-6% is related with fractures, while 10-15% is associated with severe injuries. Older people with chronic diseases have high rates of falls compared to healthy subjects. The systems that help to maintain balance and body stability are vision, vestibular Function, peripheral sensation, muscle force and reaction time\(^14\).

Frail people have increased risk of fractures. Frailty is related to low bone mineral density (BMD) of the femoral neck and the vertebrae of the lumbar spine. Maintaining good bone health prevents falls and helps the reduction of fractures of the elders\(^15\). The fracture risk in men increases after the age of 70-75 years, in contrast to women, which increases after age 65. Bone density is one of the factors affecting it, as the others factors such as body type, the way of falling and the size of the bones, are different from men to women. Bone loss with age is different in the two sexes. In men there is loss of trabecular bone, while in women of the cortical. In patients with fractures of the femoral BMD was greater in men compared with women with the same fracture\(^16\).

| Countries  | Pre-frail | Frail |
|------------|----------|------|
| Sweden     | 43.7%    | 5.9% |
| Denmark    | 36.6%    | 8.8% |
| Netherlands| 37.4%    | 8.5% |
| Germany    | 32.9%    | 8.2% |
| Austria    | 41.2%    | 6.6% |
| Switzerland| 45.6%    | 3.9% |
| France     | 44.3%    | 9.3% |
| Italy      | 48.8%    | 14.3%|
| Spain      | 53.7%    | 21%  |
| Greece     | 45.8%    | 11.3%|

**Table 1.** Percentage of the 65 years and older community-dwelling population without a disability classified as prefrail and frail by country in Europe (based on\(^13\)).

The mortality rate of the elderly after a fall is great. The 4% of the falls cause fractures and 11% severe injury to the skull. Those who survive after a fall, have a limitation of their activity because of fractures and injuries of the soft tissues or the fear of falling. The fear of the elderly for a next fall, usually leads to depression and social isolation. Factors that increase the risk of falls and fractures are chronic conditions, activities, living environment of the elder and bone mineral density and bone strength.

### Dealing with frailty

#### Physical activity

The physical activity is very important to prevent frailty, because exercise increases muscle strength, improves cardiovascular endurance, balance, gait, psychology and the general health status of the elderly\(^17\).

The exercise program consists of aerobic exercise 150 minutes/week, because walking 5-7 times/week decreases by 50-80% the risk of mobility impairments and increases the life expectancy by two years. Resistance exercises 60-80% of the maximum force, helps to increase muscle strength and endurance, and improve the mobility of the elderly. The exercises should include muscle strengthening exercises of the trunk and thigh, that will improve balance and prevent falls. Strengthening flexor tred, helps increase the speed of walking and improve the gait. The frequency of these exercises must be 2 -3 times/week, and the duration 45 minutes per session\(^18\).

Regarding skeletal health, it is important to increase the maximum bone density during the growth, for the prevention of osteoporosis and fractures at the age of 65 years and older. Charging and strength engineering exercises, increase bone density during adolescence\(^19\).
Nutrition - Medication

Proper nutrition is very important to weight loss due to frailty syndrome. Elders between meals should take protein supplement, consisted of 1.2-1.5 g per kilogram of body mass per a day. Low vitamin D levels is associated with frailty so 1000 IU/day of vitamin D should be taken. The administration of calcium and vitamin D supplements helps to reduce falls and fractures. Angiotensin converting enzyme (ACE) inhibitors improves the structure and function of skeletal muscle and can slow down the decline in muscle strength with age, improving the quality of life. Testosterone has been found to improve muscle strength, but has effects on the cardiovascular and respiratory systems. Reducing polypharmacy helps the treatment of frailty as well, because it is considered that it probably contributes to the appearance of frailty syndrome.

Conclusion

Frailty syndrome is a major health problem associated with aging. Frail older people have increased susceptibility to falls, fractures, hospitalization and mortality. Early diagnosis is the key of dealing with frailty syndrome and its consequences. The main parts of the treatment are proper nutrition, reducing medication and physical exercise. In Europe the prevalence of frailty is higher in South Europe community-dwelling population and women have higher rates of frailty than men. Health professionals assessment should recognize older people as frail, pre-frail or non-frail, that might result timely treatment of the syndrome. Failure to discover frailty leads to interventions that may harm the patient’s health.

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