Catarina Inês de Jesus Vieira Neves Ferreira

Nutritional interventions in frailty in older adults: a review of the literature

Ciências da Nutrição
Faculdade de Ciências da Saúde
Universidade Fernando Pessoa
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(Catarina Inês de Jesus Vieira Neves Ferreira)

Trabalho apresentado à Universidade Fernando Pessoa como parte dos requisitos para obtenção do grau de licenciado em Ciências da Nutrição.

Orientadora:

Professora Doutora Ana Sofia Sousa

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IV. List of abbreviation and acronyms

LDL- Low- Density Lipoprotein Cholesterol

IGF-1 - Insulin-like growth factor type I

IL-2 - InterLeukine-2

BMI – Body Mass Index

ONS - Oral Nutritional Supplements

EPA - Eicosapentaenoic Acid

DHA - Docosaexaenoic Acid

TNFα - Tumor Necrosis Factor

V. Title/authors/ academic affiliation

Nutritional interventions in frailty in older adults: a review of the literature

Intervenções nutricionais em idosos com fragilidade: revisão da literatura

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VI. Resumo

Nos últimos anos, verificou-se um aumento da população idosa e da prevalência da fragilidade, condição geriátrica caracterizada pelo aumento da vulnerabilidade e incapacidade de responder a factores de stress. Embora não exista definição universal de fragilidade, a mais utilizada é o fenótipo de fragilidade definido por Fried et al. (2001). Sendo uma condição reversível, um de seus fatores modificáveis é a alimentação.

O objetivo desta revisão da literatura é analisar informação relativa ao papel da nutrição na prevenção e tratamento da fragilidade em idosos residentes na comunidade, institucionalizados e hospitalizados.

A pesquisa foi realizada no PubMed, Google Scholar e incluiram-se 70 artigos científicos publicados entre 2001 e 2020.

Em idosos a residir na comunidade, a Dieta Mediterrânea, a fortificação de alimentos, a suplementação e as intervenções multidisciplinares são estratégias importantes para a prevenção e o tratamento da fragilidade. No que diz respeito aos idosos institucionalizados e hospitalizados, o reforço de refeições com alimentos fortificados, a suplementação e as intervenções nutricionais individualizadas e ajustadas às necessidades juntamente com a prática de atividade física são estratégias eficazes para prevenir e tratar a fragilidade nessa população.

Em conclusão, as intervenções nutricionais para a prevenção e tratamento da fragilidade são essenciais. Existem diferentes abordagens em idosos, independentemente do enquadramento. No entanto, são necessários mais estudos que suportem a elaboração de recomendações específicas.

Palavras-chave: fragilidade, intervenções nutricionais, idosos, prevenção, tratamento.

VII. Abstract

In recent years there has been an increase in elderly population and frailty which is a geriatric condition characterized by increased vulnerability and an inability to respond to stressors. Although there is no universal definition of frailty, the most used is the frailty phenotype defined by Fried et al. (2001). Since it is a reversible condition, one of its modifiable factors is food.

The aim of this literary review is to analyse the role of nutrition in the prevention and treatment of frailty in community-dwelling, institutionalized and hospitalized older adults.

Thus, a literary research was carried out at PubMed, Google Scholar and through a "snowball" research that included 70 scientific articles published between 2001 and 2020.

In community-dwelling old individuals, Mediterranean Diet, food fortification, supplementation and multidisciplinary interventions are important strategies for the prevention and treatment of frailty. Regarding institutionalized and hospitalized elderly, the low nutritional quality of meals and the lack of appetite characteristic of this population leads to protein-energy malnutrition. The reinforcement of meals with fortified foods, supplementation and individualized nutritional interventions that are appropriate to the needs together with the practice of physical activity are effective strategies to prevent and treat frailty in this population.

In conclusion, nutritional interventions for the prevention and treatment of frailty are essential. There are different approaches in older adults depending on the setting. Further studies are needed in order to establish specific recommendations.

Keywords: frailty, nutritional interventions, older adults, prevention, treatment.

1. Introduction

Over the past few years, there has been an increase in Average Life Expectancy. In 2050 it is estimated that over two billion people are 65 years old or older (1,2). This gradual aging of the world population leads to major changes in health care and economic systems as conditions associated with aging are emerging (1,3). The aging process differs between individuals (4). Although aging can be a healthy process, with preservation of physical and mental health, in most cases, it can result in physical and psychological decline and compromises the performance of daily activities (4). One of the most problematic condition associated with the aging process is frailty (1).

Frailty is characterized by the decline of different systems associated with age and body's inability to respond to stress factors (5). This vulnerability leads to an increased risk of disability and mortality as well as an increased risk of falls, delirium, fractures, dependence, cognitive impairment, hospitalization, institutionalization and, consequently, poor quality of life (1-5).

Frailty is not considered as a disease but as a syndrome, because this condition does not present a single cause (6). Frailty is usually mistaken with "comorbidity" and "disability" (6). Whereas “disability” is defined as the dependence or difficulty in performing daily basis activities, "comorbidity" is defined by the presence of two or more disorders at the same time (6). In fact, these three conditions are correlated since frailty and comorbidity are predictors of disability (6). Furthermore, comorbidity may cause the development of frailty and disability can worsen the development of frailty and comorbidity (6).
Frailty and sarcopenia are correlated because sarcopenia is an aged-associated progressive decrease of muscle mass and muscle function, resulting in physical frailty (7). Thus, sarcopenia is a key component of frailty (1).

Changes associated with age combined with a sedentary lifestyle, inadequate nutrition, drugs and injuries or illnesses over the years, lead to malnutrition in older individuals (8). Indeed, the deficit of nutrients and energy and weight loss cause a decrease of muscle function and bone mass (8). Thus, sarcopenia along with a decrease of cardiovascular function and muscle storages lead to a higher effort to carry out basic

activities of daily living (8). As far as the practice of physical activities decreases, physical capacity and resting metabolism rate and total energy expendure also decrease which results in an increase of sarcopenia and, consequently, of frailty (8). Therefore, frailty is the interaction of several unbalanced systems (8).

Although it is known that frailty is a condition that combines both physical and psychological factors, there is still no clear definition (5). The definition most commonly used is the frailty phenotype proposed by Fried et al. in 2001 (5). According to the frailty phenotype (5), frailty is a condition characterized by physiological changes such as unintentional weight loss, reported exhaustion, decreased gait speed, decreased physical activity and muscle weakness (5). Older adults who demonstrate at least three of the above-mentioned features are frail and older adults in which one or two of these features have developed are considered pre-frail (5). However, this definition regards only symptoms and physical signs of the condition and does not consider aspects such as mood, cognition, socioeconomic condition and sensory impairments (5).

Rockwood et al. (2011) have reformulated the concept by proposing the frailty index (9) which assesses several factors such as comorbidity, cognitive and nutritional, motivation, emotions, communication capacity, physical function and drug prescriptions (9).

As a result of the increase of the elderly population, there was also an increase in the prevalence of frailty (1). Since there is not a universally accepted definition of frailty, the assessment of its prevalence differs according to the methodologies used (10). According to a cross-sectional analysis published by Santos-Eggimann et al. (2009) that compares the prevalence of this condition among 10 countries in Europe, and considering the frailty phenotype, Southern European countries such as Spain (27.3%), Italy (23.0%), France (15.0%) and Greece (14.7%) have a higher prevalence of frailty compared to countries such as Switzerland (5.8%), Sweden (8.3%), the Netherlands (11.3%), Denmark (12.4%) and Germany (12.1%) (10). Except for Germany, where the prevalence is slightly lower, the percentage of pre-frail people is high in all studied countries (10).

Despite decreasing with aging, physical activity plays an important role in both prevention and management of frailty (9,11). The practice of physical exercise has a positive impact on gait speed, muscle strength, balance and coordination of movements and intensification of bone mineral density leading to a reduction in the occurrence of

falls (11,12). In addition, physical activity promotes cognitive health and, consequently, has a positive impact on depression (12). However, it is worth noticing that the results of physical activity interventions vary according to the duration, intensity and type of exercise (12).

According to a review published by Theou et al. (2011) that assessed the effectiveness of exercise interventions for the management of frailty, a multicomponent training had a greater impact on functional ability and adverse consequences (13). However, resistance training had more positive results than other physical exercises on physical and psychosocial characteristics (13). In fact, according to Tarazona-Santabalbina et al. (2016), in a randomized controlled study conducted in 100 Spanish community-dwelling frail old individuals, after two years of practicing different type of exercises such as aerobic, strength and stretching it was observed a reversal of frailty and an improvement of performance in carrying out daily activities, autonomy, balance, gait speed and muscle strength as well as in cognitive, emotional and social skills (14).

Frailty is a progressive condition characterized by a silent, subclinical phase and difficult to detect phase (6). However, when this syndrome is diagnosed, there is an opportunity to delay the progression of the disease and to avoid negative consequences (15).

Among the various factors that are associated with frailty, nutrition plays a major role (15,16). Regarding the frailty phenotype proposed by Fried et al. (5), the features that identify the presence of frailty are closely related to nutrition: poor eating habits can be seen either as a cause of unintentional weight loss, exhaustion, muscle weakness, decreased walking speed and physical activity or as a consequence of frailty (15,16).

Anorexia of aging, a condition characterized by loss of appetite or reduced food intake associated with advanced age, is a modifiable risk factor of frailty (17). Physiologic factors such as chewing and swallowing problems, slow gastric emptying, modified smell, taste and hormonal responses have a great impact on anorexia of aging (17). Nonetheless, psychosocial factors such as depression and anxiety and social aspects such as social isolation, unwillingness to cook and the lack of independence have a major impact on anorexia of aging because these conditions tend to decrease appetite (17). In addition to those aspects, sedentary lifestyle contributes to weight loss, decrease of muscle mass and muscle function and physical inactivity (17).

There is a consistent body of evidence on the role of nutrition in frailty prevention and management. Therefore, the aim of the present study is to review the literature and to analyse the information regarding nutritional interventions both for prevention and treatment of frailty in hospitalized, institutionalized and community-dwelling older adults.

2. Methodology

A literature review was carried out by searching the PubMed and Google Scholar databases in which scientific articles and review articles published between 2001 and 2020 were identified. All articles carried out in the elderly published in English and Spanish. Articles whose study population was obese, acute patients, diabetics, with fractures, cancerous, surgical, chronic patients with diagnosed depression and dementia were excluded. A total of 23 scientific articles were selected with the expressions "nutrition * intervention * frailty elderly", "Food quality in nursing homes", "Food-enriched in nursing homes", "Food menus in hospital" and "Supplementation in nursing homes". There were 46 scientific articles that were selected by "Snowball". The flow diagram regarding the article selection is presented in Figure 1.

3. Nutritional interventions in frailty in older adults: different approaches

Over the years, different nutritional approaches have been studied concerning the prevention or treatment of frailty in older adults. The strategies differ according to the setting: community-dwelling, hospital and institutional. In the next section these different nutritional strategies are described in detail.

Table 1, displayed in attachment, summarizes the main studies regarding nutritional interventions in frailty in older adults.

3.1. Community dwelling older adults

3.1.1 Prevention of frailty

3.1.1.1 Dietary pattern: Mediterranean diet

The Mediterranean diet is a key dietary pattern for promoting healthy aging since it is nutritious, complete and promotes the consumption of traditional and local food (18). It is characterized by the low consumption of red and processed meat, dairy products, saturated fat and sweets and high consumption of vegetables, fruits, whole grains, fish, nuts, legumes, olive oil as the main source of shortening and moderate consumption of red wine during lunch and dinner (18). Higher adherence to the Mediterranean diet means higher consumption of fruit and vegetables, nuts, fish, monounsaturated fat and legumes (19). Consequently, this dietary pattern leads not only to an increase in energy and macronutrients intake but also b-carotene and equivalents, vitamin E, C, B6 and folic acid (19).

The high consumption of fruit and vegetables, cereals and of the ratio of Unsaturated Fat / Saturated Fat, the moderately consumption of red wine and the low consumption of meat have a positive impact on muscle mass and muscle strength, preventing sarcopenia in older women (20). In fact, the mediterranean diet is shown to contribute to maintain muscle mass and to be inversely associated with muscle weakness and reduced gait speed (21). These two frailty phenotype features have a very significant impact on individuals' social life because the reduced physical capacity leads to a decrease in movement and in elderly's social life and, consequently, to greater isolation (22). The preventive role played by the Mediterranean diet leads to an increase in the ability to move and may also contribute to a more active social life (22). Moreover, the Mediterranean diet as a pattern, and not just isolated food groups, is associated with a decreased risk of low gait speed, weight loss, exhaustion and the low hand grip strength. (21, 22) Thus, a higher adherence to Mediterranean Diet has been inversely associated with development of frailty (18-23).

Food fortification also plays an important role in the prevention of frailty (24). In a randomized controlled published by Ottestad et al. (2016) in 36 healthy community-dwelling elderly, the intake of protein-enriched milk twice a day improved nutritional status since it increased protein intake (24).

3.1.1.2 Supplementation

According to a double-blind randomized controlled trial published by Bo et al. (2017) and performed in a 60 sarcopenic community-dwelling population, Vitamin D, E and whey protein supplementation significantly improved nutritional status by increasing protein intake and serum levels of vitamin D and Vitamin E, improved muscle mass, muscle strength and Insulin-like growth factor type I (IGF-1) (25). The increase of IGF-1 and the decrease in the proinflammatory cytokine InterLeukine-2 (IL-2), led to a decrease in inflammation and, consequently, to an improvement in quality of life (25). As reported in a double-blind randomized placebo-controlled trial by Bauer et al. (2015) conducted in 380 European community-dwelling sarcopenic elderly, vitamin D and whey protein enriched in leucine supplementation increased muscle strength, protein intake, serum levels of Vitamin D and IGF-1 which enhance the protective role of supplementation in preserving muscle mass and muscle function (26). However, in an 80 community-dwelling elderly population assessed in a randomized double-blind, controlled trial by Chalé et al. (2012), when combined with the practice of resistance physical activity, whey protein supplementation does not seem to have any benefit in frailty's prevention (27).

Regarding Vitamin D supplementation, a randomized controlled trial by Hajj et al. (2019) in 128 vitamin D deficient pre-sarcopenic community-dwelling Lebanese elderly, vitamin D supplementation has a frailty's protective role since it improved skeletal muscle mass, reduced fat body mass, body weight and waist circumference regardless their Body Mass Index (BMI) (28). Furthermore, in a randomized controlled trial conducted by Bischoff-Ferrariet al. (2016) with 200 healthy community-dwelling elderly individuals, monthly high doses supplementation of vitamin D resulted in increased serum levels of vitamin D (29). However, it did not lead to a decrease in functional decline and, surprisingly, led to an increase in falls (29).

Sarcopenia is characterized by an increase in proinflammatory cytokines that, in turn, increases the susceptibility to loss of muscle mass and muscle strength (1). Omega-3 fatty acids are anti-inflammatory agents and therefore have a protective role on sarcopenia and frailty (30). In a randomized controlled trial published by Smith et al. (2011), unlike corn oil supplementation, fatty acid supplementation induces protein synthesis and therefore prevents sarcopenia in 16 healthy community-dwelling old adults (30). In 45 community-dwelling healthy old women that took part in a randomized controlled trial conducted by Rodacky et al (2012), fish oil supplementation and the practice of strengthening exercise increased plasma Eicosapentaenoic Acid (EPA) and Docosaexaenoic Acid (DHA) concentrations, promoted muscle activation and muscle function which improved functional capacity and, consequently, the quality of life of old adults (31).

Concerning 113 sarcopenic community-dwelling Chinese elderly population that took part in a randomized controlled trial by Zhu et al. (2018), a protein-energy, vitamin D, Fatty Acid Omega-3 and þ-hydroxy þ-methylbutyrate supplement results in an increase in muscle mass (32) and when combined with the practice of aerobics, resistance and flexibility exercises, increased not only in muscle mass, but also in muscle strength and physical performance (32).

3.1.2 Treatment of frailty

3.1.2.1 Educational strategies

Nutritional education along with the practice of physical activity and social support is an interesting suggestion to reverse frailty in old adults (33-36). Elderly's eating habits tend to be quite monotonous due to the limited knowledge of foods availability, cooking methods and difficulty in preparing (33). Therefore, a controlled randomized study driven by Seino et al. (2017) in 77 pre-frail and frail community-dwelling elderly population, nutritional education sessions that elucidate the elderly about the importance of food, cooking methods, sufficient food intake and food variety, the practice of resistance exercise to improve muscle strength and mobility and the psychosocial help to promote

social interaction, results in an improvement in nutritional status due to the increase of protein and micronutrients intake and greater variety, reduction of frailty, increase functional mobility and greater social interaction (33). Educational sessions on health concepts such as frailty, sarcopenia, healthy eating, the distribution of an informational leaflet, the practice of balance, posture, resistance, stretching and strengthening exercises and psychotherapy sessions, lead to reversal of frailty and sarcopenia (34-36). In a randomized controlled trial published by Chan et al. (2012) conducted in 117 community-dwelling frail elderly, psychotherapy sessions, in particularly, had positive effects on exhaustion and education and physical activity sessions significantly improved frailty phenotype criteria such as low gait speed and low muscle strength and nutritional status (35). According to a randomized controlled trial published by Luger et al. (2016) with 80 frail and pre-frail, at risk of malnutrition and malnourished community-dwelling elderly, multidisciplinary intervention that includes the practice of resistance physical activity, education on the food variety, food fortification and energy and protein intake to elucidate individuals about adequate food intake, also proved to be effective in improving nutritional status and reversing frailty (36).

A randomized controlled trial by Huguet et al. (2018) performed in 200 pre-frail community-dwelling elderly Spanish population highlight the importance of multidisciplinary intervention that includes educational sessions about Mediterranean diet, the practice of strength, endurance, balance and coordination exercises, the evaluation of incorrect prescription of drugs and social support since it reproduces beneficial effects on functional status, adherence to Mediterranean diet, quality of life and functional mobility, thus preventing the progression of early stages of frailty and avoiding negative outcomes (37).

Although educational nutritional interventions reproduce positive results both in improving nutritional status and reversing frailty, interventions that combine food education with oral nutritional supplements and the practice of strength, balance, resistance and flexibility exercises is an equally feasible approach (38). In a four-arm, single blind, randomized controlled trial conducted by Hsieh et al. (2019) with 319 frail and pre-frail elderly community-dwelling population were provided personalized dishes and skimmed milk powder supplement in order to ensure the maintenance of body weight and sufficient food intake (38). After the nutritional intervention, elderly improved their eating habits since they increased the consumption of high protein foods, which,

consequently, led to an increase in energy intake. Concerning physical approach, it led to an improvement in muscle strength and gait speed, reproducing beneficial effects in reversing frailty (38).

3.1.2.2 Supplementation

A randomized controlled study in 241 frail community-dwelling elderly population published by Cameron et al. (2013) demonstrates an interesting individualized intervention to treat frailty (39). In other words, if a person met "weight loss" criteria, nutritional assessment and supplementation were provided. Regarding "exhaustion" criteria, psychological help was provided and if the "weakness", "slowness" or "low energy expenditure" were met, an individualized home exercise plan was performed (39). In fact, this innovative, customized intervention has been shown to be effective in reversing frailty and improving mobility (39). Regarding L-carnitine supplementation, a randomized, double-blind, placebo-controlled trial written by Badrasawi et al. (2016) performed in a 50 prefrail community-dwelling elderly population demonstrated that L-carnitine supplementation not only improved physical function, since it increased muscle strength, reversed exhaustion, weakness, and consequently, reversed frailty but also increased serum IGF-1 levels and decrease IL-6 levels (40). In 187 community-dwelling frail elderly of low socioeconomic status and who live alone and took part in a randomized controlled trial conducted by Jang et al. (2018), the practice of resistance, balance and aerobic exercise along with protein supplementation, control of depression's signs, reduction of medication and home hazards showed positive effects on sarcopenia and frailty as well as in physical function, depressive symptoms, reduced functional decline and symptoms of depression (41). In agreement, a randomized controlled trial by Kim and Lee (2012) with 87 frail, low income community-dwelling population, protein-energy supplementation results in greater protein intake and energy intake and reduces progress of functional decline (42). Multidisciplinary intervention that includes protein supplementation, the practice of aerobic physical exercises, memory exercises and revision of medication proposed by Romera-Liebana et al. (2018) in a randomized controlled trial with 352 frail community-dwelling older adults, showed not only improvement of frailty but also of improvement of aspects that contribute directly or

indirectly to frailty such as improvement of cognitive status and muscle strength, stretching, balance and mobility the reduction of medication, (43). In a randomized controlled trial published by Kang et al. (2019) enrolled in 115 frail community-dwelling chinese old individuals, whey protein supplementation along with resistance exercises led to increased muscle function (44). In agreement, in a randomized controlled trial conducted by Kim et al. (2015) with 131 community-dwelling frail old women, the practice of strength, balance and gait training exercises along with milk fat globule membrane supplementation resulted in a decrease in all frailty phenotype criteria, except muscle strength, and in improvement of physical function (45).

Regarding vitamin supplementation, in a randomized controlled trial by Ng et al. (2015) that assessed 246 community-dwelling frail old individuals, multivitamin nutritional supplementation (iron and folate, vitamin B6 and vitamin B12, calcium and Vitamin D) along with cognitive training to improve short-time memory and balance and strength physical exercise intervention decreased frailty since supplementation increased nutritional intake and, particularly, physical exercise increased gait speed and muscle strength (46). Despite the low serum levels of vitamin D being related to frailty (47), Vaes et al. (2018) demonstrates in a randomized controlled trial with 78 prefrail and frail community-dwelling elderly that vitamin D supplementation has not been shown to reproduce any effect in improving frailty's features such as physical performance and muscle strength (48).

According to a randomized controlled trial conducted by Hutchins-Wiese et al. (2013) with 118 postmenopausal community-dwelling frail and pre-frail women, fish oil with vitamin C and selenium supplementation only improve gait speed (49). The antioxidant action of vitamin C and selenium and the decrease of pro-inflammatory cytokine TNFα, there was an increase in physical performance (49). Strike et al. (2016) shows in a randomized double-blind, placebo-controlled pilot study with 27 healthy, prefrail and frail postmenstrual women that omega-3 fatty acid, multivitamin supplementation improved not only functional mobility due to an increase in gait speed but also improves serum DHA and EPA levels and cognitive status (50).

3.2. Institutionalized older adults

3.2.1 Prevention of frailty

3.2.1.1 Improvement of institutional meals

Food in nursing homes is not always well qualified (51). The meals aren´t varied and do not meet neither micronutrients (Vitamin D, E, B9, fiber, potassium, magnesium, iodine and folate) daily recommendations nor Mediterranean Diet's daily recommendations for the intake of dairy products, legumes, cereals, fruit and vegetables, olive oil and nuts (51,52). Besides that, sarcopenic institutionalized old adults have more difficulty in meeting micronutrients' dietary recommendations since they don´t eat the entire meal due to lack of appetite (53). Low food quality and lack of appetite lead to protein-energy malnutrition or the risk of protein-energy malnutrition (53). In fact, the recommended consumption of 400 g / day of fresh fruit and vegetables not only prevents protein-energy malnutrition, but also guarantees the adequate supply of micronutrients and macronutrients, protecting older adults against health problems (54).

It is important to understand how to increase nutritional density without increasing the amount of food or increasing the consumption of high energy density foods that are easily accepted by older adults (55). Since food fortification is a great strategy to improve nutritional status, it can be useful to recognize which foods are most consumed by home nurses' residents so that they can be fortified. In fact, a randomized controlled trial published by Mila et al. (2012) with 62 institutionalized Spanish old individuals proposes that the best accepted foods are dairy products, cereals and fish, enriched-soups and milk-based products are a possible strategy to increase the nutritional density of foods and to reverse malnutrition (55).

Protein-enriched foods that are familiar to them, such as bread, soup, fruit juices, instant potato puree and yogurt and high protein food can increase protein intake and meet the protein daily recommendations (56,57). Despite the fact that taking oral nutritional supplements (ONS) causes a decrease in meal intake, the treatment of malnutrition can be done through ONS or through the reinforcement of snacks since both lead to an

increase in caloric intake. In addition, snacks are more cost-effective compared to ONS, thus being the favourite way to increase caloric intake (58). A three-armed, multicentre, controlled trial by Wymelbeke et al (2016) with 68 elderly institutionalized individuals at risk of malnutrition or malnutrition proves that they prefer enriched protein-energetic brioche instead of oral nutritional supplements because supplements are still seen as medication and brioche is a familiar, appealing and easy to chew food (59). The consumption of this new food led to an improvement in the nutritional status since there was an increase in plasmatic B2, B6, B9 and B12 vitamins, homocysteine and protein intake (59). Leslie et al. (2012) showed in a cluster randomized controlled trial with 444 nursing homes residents that the addiction of double cream, butter and malted milk to regular foods is also an available approach to prevent frailty because it led not only to an increase of energy intake without the need to increase food intake but also to an increase of body weight (60).

3.2.1.2 Supplementation

Regarding nutritional supplements, a randomized controlled trial conducted by Björkman et al. (2012) in 106 healthy nursing home residents shows that whey protein supplement lead not only to improvement in body weight and preservation of muscle mass, but also to an improvement of IGF-1, insulin and maintenance of well-being, since it seems to have a protective effect against infections (61). Moreover, Rondanelli et al. (2011) shows in a randomized controlled trial with 41 patients with sequalae of coronary artery disease and femoral fracture that essentials amino acids supplement improved nutritional status, muscle strength and serum pre-albumin levels and had a significant impact in depression symptoms which in turn leads to better life's quality (62). In 50 sarcopenic nursing home residents who took part in a randomized and placebo-controlled trial by Martinez-Arnau et al. (2020), leucine supplementation enhances physical performance, especially respiratory muscles function and improved fat-free mass (63). In addition, a randomized controlled trial by Trabal et al. (2015) with 24 Spanish nursing home old residents that combine leucine supplementation with resistance and balance exercises improved physical capacity because there was an increase in protein synthesis and, consequently, in muscle strength (64). According to Lee et al. (2015), in a randomized controlled trial conducted in 92 old institutionalized at risk of malnutrition

population, a soy protein-based protein-energy supplement should be taken until old residents reach an adequate nutritional status and avoid overnutrition (65,66). This represents positive effects on muscle mass and muscle strength (65) and improve nutritional status since it improve biochemical parameters such as serum cholesterol and albumin levels (66).

3.2.2 Treatment of frailty

3.2.2.1 Supplementation

According to a multicentre prospective observational study by Abizanda et al. (2015) with 91 institutionalized frail nursing home residents, Vitamin D, calcium and prebiotic fiber enriched protein-energy supplementation combined with the practice of strength, balance and flexibility physical exercises had a positive impact at different levels that led to a better quality of life. (67). Regarding nutritional status, this multidisciplinary intervention caused an increase in weight and BMI and reduction of malnutrition (67). Concerning functional status, there was observed a significant improvement in balance and gait speed (67). Since older adults have difficulties in chewing and swallowing, the most common oral nutritional supplements (ONS) are the liquid and creamy ones (68). However, to avoid the monotony that can lead to poor appetite, oral nutritional supplements can have other consistencies (68). Therefore, a randomized controlled trial published by Pouyssegurt et al. (2015) with 175 malnourished older nursing home residents, suggests an adapted cookie-shaped protein-energy supplement as an alternative to the liquid or powder supplement usually used (68). In fact, besides increasing appetite, this supplement also increases weight and stimulates senses such as touch and smell (68).

It is known that in frail, at risk of malnutrition and malnourished institutionalized elderly, protein supplementation is an effective intervention (69). Actually, Park et al. (2018) showed in a randomized, double-blind, placebo-controlled trial with 120 undernourished prefrail and frail institutionalized old adults that the higher the protein intake, the greater are muscle strength and gait speed, preventing the progression of frailty and pre-frailty in old individuals (69). Likewise, Stange et al. (2013) determined in a

randomized controlled trial with 286 pre-frail individuals at risk of malnutrition or malnourished, with high level of mental and physical impairment that low volume and high protein-energy density supplementation improved nutritional status since it was observed an increase in energy, protein and micronutrient intake and improved body composition due to the increase in BMI, body weight, and, consequently, improved quality of life (70).

Among other factors, low plasmatic Vitamin D levels are involved with risk of falls among frail individuals, deteriorating their quality of life (71). In this perspective, Imaoka et al. (2016) conducted a randomized controlled trial among 91 frail nursing home residents that concludes that vitamin D supplementation along with low frequency strength, balance and resistance exercises, besides increasing plasmatic vitamin D levels and muscle function, reduced the occurrence of falls (71). Calcium and vitamin D supplementation along with body vibration training assessed in a randomized controlled trial published by Bogaerts et al. (2011) among 113 frail institutionalized women, despite not reproducing any results in reducing falls, it results in an improvement in physical performance (72).

As reported by Abe et al. (2016) in a randomized controlled trial that involved 38 frail nursing home old residents, medium-chain triglycerides with leucine and vitamin D supplementation results in weight gain as well as in an increase of muscle strength and muscle function (73). Buigues et al. (2016) determined in a randomized controlled trial enrolled in 60 frail institutionalized older adults that despite pre-biotic supplementation did not reproduce any nutritional effect, there is a positive correlation with frailty features such as exhaustion and muscle strength leading to prevention of progression of frailty (74).

3.3. Hospitalized patients

3.3.1 Prevention of frailty

3.3.1.1 Improve hospital meals

In hospitalized inpatients, protein recommendations vary between 1.2 g and 1.5 g of protein per kg of body weight per day (75). Since hospitalized inpatients are unable to meet these needs, it is necessary to protein-enriching hospital meals (76). Protein-enrich familiar food such as bread, fruit juices and dairy products significantly increase protein intake to minimum daily recommendations without an increase in the consumption of the amount of food (76). Therefore, a randomized controlled trial presented by Beelen et al. (2018) enrolled with 147 hospitalized old inpatients shows that the use of protein-fortified foods is a positive strategy in improving the nutritional status of the elderly (76). Besides being an easy strategy to implement because there is no need to modify the hospital's menu plan or require much hospital team's effort, it is well- accepted by inpatients (76). Mortensen et al. (2019) proposes in a randomized controlled trial with 92 hospitalized inpatients at risk of malnutrition that protein and energy-enriched snacks are a great intervention because it causes a significant increase in protein and energy intake (77).

Another successful intervention is the reinforcement of hospital meals with high energy ingredients and supplemented with milk protein (78). Compared to the common hospital diet, this one proposed by Munk et al. (2014) with 84 older adults at risk of malnutrition, presented several advantages since patients improved nutritional status by improving protein and energy intake (78). A prospective randomized controlled trial by Bouillanne et al. (2013) which involved 66 at risk of malnutrition and malnourished rehabilitation elderly agrees that in an hospital's diet enriched with milk protein, when most of the protein intake is consumed only in a single meal, there is improvement in fat-free mass, compared with a diet in which the protein intake is equitably distributed among the meals of the day (79).

3.3.1.2 Supplementation

The intake of oral protein-energy, vitamin D nutritional supplementation and a high protein-energy hospital diet that includes fortified foods with extra cream and carbohydrates helps to treat malnutrition (80). In fact, this intervention proposed by Neelemaat et al. (2012) in a randomized controlled trial with 210 malnourished old inpatients, not only improved nutritional status because it increased the protein-energy and vitamin D intake, reflecting on weight gain and BMI increasing, but also reduced the incidence of falls (80). In 180 hospitalized sarcopenic inpatients who were enrolled in a randomized double-blind, placebo-controlled trial published by Rondanelli et al. (2016), the practice of low-intensity physical activity characterized by strength, endurance and walking exercises combined with vitamin D, essential amino acids and whey protein supplement has shown to increase muscle mass, muscle strength, physical function, improve nutritional status, serum IGF-1 hormone levels and quality of life (81). *Per se*, supplementation caused an increase in the IGF-1 hormone and a decrease in C-reactive protein that contributed to reduce inflammation, commonly present in hospitalized patients (81). As stated in a multicentre, randomized controlled trial by Takeuchi et al. (2018) with 68 old post-acute rehabilitation sarcopenic inpatients, along with occupational therapy and low-intensity physical training, Vitamin D and branched-chain amino acids supplement has yielded beneficial results since it shows an increase in protein synthesis and consequently to an improvement in muscle strength and muscle mass, body weight, serum albumin levels and physical performance (82). According to a randomized controlled trial published by Yoshimura et al. (2016) performed in 39 sarcopenic rehabilitation hospital old inpatients, it is important to consider both the amount and distribution of protein during the day. It was realized that the major consumption of the daily intake of protein in one meal and food supplementation with powdered milk protein has shown that a great increase in lean mass, physical performance, muscle strength and serum levels of albumin (83).

3.3.2 Treatment of frailty

3.3.2.1 Individualized nutritional intervention

In both institutionalized and hospitalized older adults, the poor quality of meals is directly related to the deterioration of nutritional status. Thus, it is important to develop appropriate nutritional interventions to improve nutritional status (84).

As reported in a randomized controlled trial published by Schuetz et al. (2019) with 288 frail hospitalized patients at risk of malnutrition, the best nutritional approach is done from admission to discharge and consists in a nutritional plan adjusted to the energy and protein needs and comorbidities of each patient (85). The choices of the patients' favourite foods, additional snacks, the use of oral nutritional supplements or the use of protein-enriched foods and the use of enteral tube or parental feeding when necessary, are feasible approaches to improve the nutritional status of patients since caused improves in weight and in BMI (85). This individualized approach led not only to an increase in energy and protein intake, but also to an improvement in physical capacity, functional status and, consequently, quality of life (85).

3.3.2.2 Supplementation

Malnutrition is very common in a hospital setting, since about half of hospitalized older adults are malnourished (86). Hospitalized frail or pre-frail old individuals have less muscle strength and, consequently, higher risk of falling, less physical capacity and a higher risk of malnutrition (86). In order to improve low physical capacity and muscle strength, whey protein supplementation seems to be beneficial in the elderly in rehabilitation unit (87).

In fact, according to a randomized controlled trial published by Niccoli et al. (2017) in 47 hospitalized frail individuals, whey protein supplementation is accepted by the frail elderly and improve protein intake, usually deficient in this population. In addition to the nutritional benefits, it also shows improvements in physical function, particularly in muscle strength and gait speed, leading to the reversal of frailty. Finally, and equally

important, whey protein supplementation played an important role in controlling inflammation as it led to a decrease in the pro-inflammatory cytokine IL-6 and an increase in serum levels of prealbumin (87).

4. Discussion and Conclusion

The increase in the number of older adults as well as the increase in the prevalence of frailty syndrome in this population leads to deterioration of quality of life. Nutrition plays an important role in both preventing and treating frailty and its consequences. In non-frail community- dwelling old individuals, Mediterranean diet and protein-fortified foods are essential in frailty prevention. The Mediterranean diet is varied, balanced, healthy and characterized by the consumption of seasonal and biological products. In fact, adherence to this dietary pattern has shown to improve nutritional status, which is often depleted in older adults, functional capacity and promotes social life. As well as Mediterranean diet, protein-enriched foods are an effective strategy for preventing frailty since they significantly improve nutritional status. Regarding dietary supplements, protein, vitamins D and E, omega-3 fatty acids and þ-Hydroxy þ-methylbutyrate supplements along with the practice of strength, balance, aerobic, endurance and flexibility exercises improve physical condition, nutritional status and quality of life in healthy, pre sarcopenic and sarcopenic elderly. Multidisciplinary interventions that combine dietary education, the practice of resistance, posture, balance, strength and stretching exercises, psychological support and medication review is the best approach reverse frailty in community-dwelling older people are an effective approach in reversing and preventing the progression of frailty since improves the low physical capacity and food intake in frail and pre-frail elderly. Protein, protein-energy, selenium, vitamin C and D and omega-3 fatty acids supplementation together with the practice of physical exercise has also shown to reverse the frailty, improve nutritional status and functional status and decreased inflammation in frail community-dwelling older adults. In institutionalized old people, besides the fact that the meals served in nursing homes are not of good nutritional quality, the elderly do not always eat everything due to lack of appetite. Therefore, it is important to understand how to increase food intake without increasing the amount of

food or add high energy density foods. One strategy to avoid protein-energy malnutrition, that improve nutritional status, weight gain and, consequently, preventing frailty is to fortify their favourite and familiar foods. Although the elderly prefer food to dietary supplements, protein and leucine supplementation together with the practice of resistance and balance exercises have shown to improve nutritional and functional status and biological markers in healthy and at risk of malnutrition older adults. As far as frailty treatment in institutionalized frail older adults is concerned, protein-energy vitamin D, omega-3 fatty acids and prebiotics supplementation, have both nutritionally and physically benefits, improving the quality of life. However, improving physical status can mean an increase in the frequency of falls.

Similarly to nursing homes, in hospitals older adults does not control the preparation of meals and it do not supply the protein and energy needs. Therefore, protein-energy fortification of the elderly's favourite foods, as well as the addiction of snacks, energy-rich ingredients in meals and the protein-energy fortification of meals are feasible and effective strategies to improve nutritional status and prevent frailty in hospitalized elderly. Furthermore, protein supplementation, vitamin D and essential amino acids along with occupational therapy and physical activity have shown to reduce inflammation levels, that are quite common in this population, improve nutritional status, physical capacity and biochemical markers. The treatment of frailty in hospital setting consists in an individualized intervention according to the needs of each patient and their different comorbidities with of aim of improving their nutritional status as well as whey supplementation demonstrated to be effective in improving nutritional and functional status.

In this review several limitations were observed. The first one is the lack of consensus on the universal definition of frailty. There are several definitions for the concept of frailty, however the most frequently used is the frailty phenotype defined by Fried et al. (2001). As far as nutritional interventions for the prevention of frailty through diet in community-dwelling older adults is concerned, the results are based on observational studies since randomized controlled trials were not found, which can lead to several bias. Another limitation was the lack of scientific evidence of nutritional interventions through food for the treatment of frailty in institutionalized frail people. There was also a lack of scientific evidence regarding nutritional interventions for the treatment of frail hospitalized patients. Despite all the limitations, I enhance that the greatest strength of this study is the

embrace of nutritional interventions since it not only includes independent living elderly people but also includes those who are institutionalized and hospitalized.

However, apart from the setting, multidisciplinary interventions that associate nutrition and physical activity are the most effective ones because they combine different areas that are, directly or indirectly, correlated with frailty. In the future, more research and scientific evidence on the role of nutrition in the treatment and prevention of frailty in community-dwelling, institutionalized and hospitalized older adults would be important in order to allow timely intervention. Dietary strategies throughout the lifecycle are also important to the early prevention of frailty.

In conclusion, nutritional interventions for the prevention and treatment of frailty are essential. There are different approaches in older adults depending on the setting. Further studies are needed in order to establish specific recommendations.

5. Critical Reflection

Nutritionists and other health professionals are of utmost importance both in treating and preventing frailty throughout the lifecycle. It is worth noticing that the implementation of individualized nutritional interventions according to the needs of each older adult is crucial, regardless of the setting.

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7. Attachments

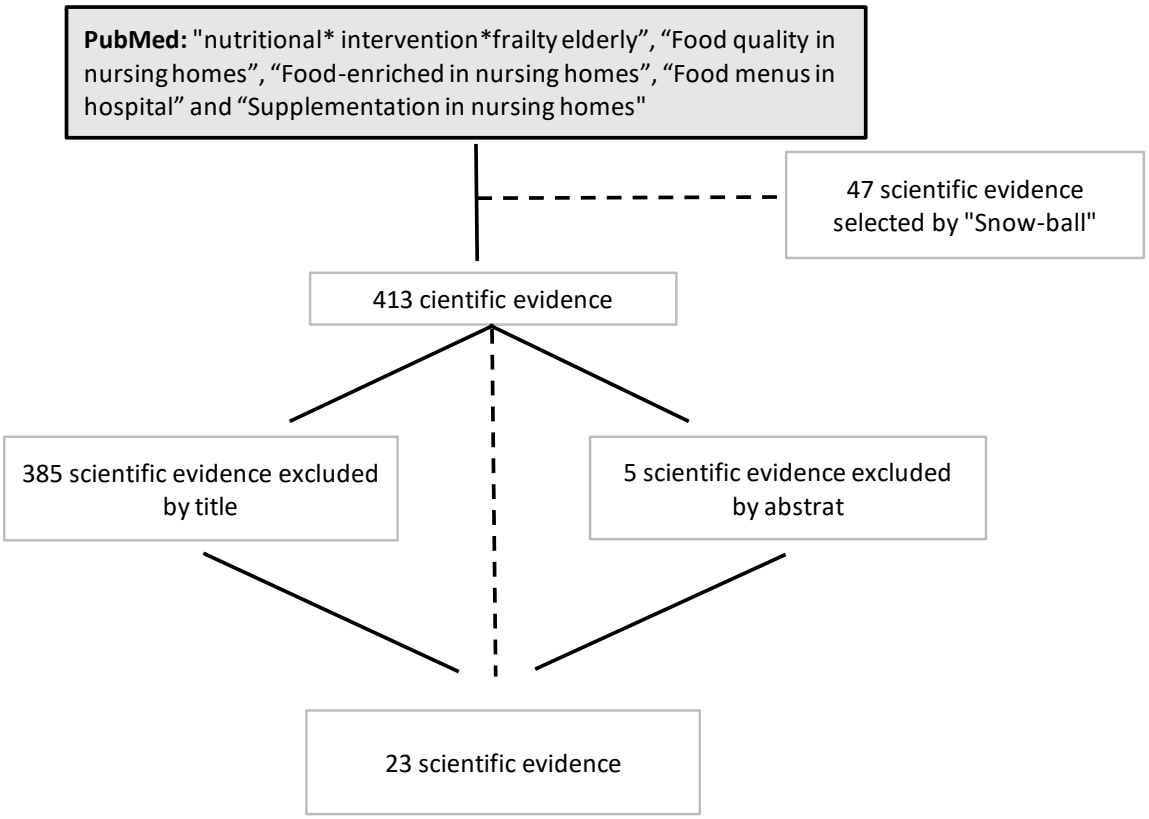

Figure 1. Flow diagram.

Table 1. Summary of the most relevant studies.

Article	Author(s)	Year	Objective	Population	Methods	Main Highlights
Frailty in Older Adults: Evidence for a Phenotype	Linda P. Fried	2001	Provide consistent definition for frailty in community-dwelling older adults	5317 women and men	Data from Cardiovascular Health Study (CHS)	The Frailty Phenotype defines frailty syndrome as the presence, at least of, three out of five components: unintentional weight loss, weakness,slowness, low physical activity and exhaustion.
Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care	Linda P. Fried	2001	Diference between frailty, disability and comorbidity	_	Review	"Comorbidity" is the presence of two or more disorders at the same time.“Disability” refers to the difficulty in carrying out daily basis activities. Frailty and comorbidity predict disability, comorbidity may cause the development of frailty and disability can worsen the development of frailty and comorbidity.
Frailty defined by deficit accumulation and geriatric medicine defined by frailty.	Kenneth Rockwood and Arnold Mitnitski	2011	Provide a definition for frailty in community-dwelling older adults	_	Review	The Frailty Index determines that frailty is the result of the deficits' accumulation over the years. So, the greater the accumulation of deficits, the higher the risk of frailty.
Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries	Brigitte Santos-Eggiman et al	2009	Evaluate the revalence of frailty in ten European countries	18,227 frail community-dwelling individuals	Frail individuals (Frailty Phenotype) were enrolled in the Survey of Health, Aging and Retirement in Europe (SHARE) in 2004.	The prevalence of frail or prefrail individuals is higher in Southern than in Northern Europe.
The effectiveness of exercise interventions for the management of frailty: a systematic review	Olga Theou et al.	2011	Assess the effectiveness of physical exercise interventions for the management of frailty	_	Literature research that include 47 studies	Multicomponent exercise programs helps promoting well-being of frail older adults since it have a great impact on physical mobility frail older adults and it's used as a strategy for the management of frailty.

Table 2. Summary of the most relevant studies (Continuation).

Article	Author(s)	Year	Objective	Population	Methods	Main Highlights
A higher adherence to a Mediterranean-style diet is inversely associated with the development of frailty in community-dwelling elderly men and women.	Sameera A. Talegawkar et al.	2012	Evaluate the association between a Mediterranean-diet with the risk of frailty in community-dwelling older individuals.	690 community-dwelling	The study population was randomly selected and after a 6-year follow-up, they were examined.	Higher adherence to Mediterranean diet is inversely associated the development of frailty and to a lower risk of low physical activity and slowness. However, it's not associated exhaustion and weakness.
Effects of a vitamin D and leucine-enriched whey protein nutritional supplement on measures of sarcopenia in older adults, the PROVIDE study: a randomized, double-blind, placebo-controlled trial	Jürgen M. Bauer MD et al.	2015	Analyse if vitamin D and leucine enriched-whey protein oral nutritional supplement resulted in improvements in sarcopenia in community-dwelling individuals	380 sarcopenic community-dwelling individuals	The intervention group took a vitamin D and leucine-enriched whey protein nutritional supplement twice daily for 13 weeks. The control group received an iso-caloric control product to consume twice daily for 13 weeks.	A vitamin D and leucine-enriched whey protein oral nutritional supplement improved muscle mass and muscle function and played a protective role against inflammation sice it led to an increase of IGF-1 e a decrease in IL-2 among sarcopenic older adults.
Pre frail 80: multifactorial intervention to prevent progression of pre-frailty to frailty in the elderly	L. Gené Huguet et al.	2018	Evaluate the impact of a multifactorial, interdisciplinary primary care intervention in community-dwelling pre-frail old adults	200 pre-frail community-dwelling subjects aged ≥ 80 years	In the intervention group, participants received during 6 months physical exercise, Mediterranean diet advice, assessment of inadequate prescribing in polypharmacy patients and social assessment intervention, while the control group received standard primary healthcare treatment.	A multifactorial,interdisciplinary intervention prevents frailty in pre-frail older community-dwelling individuals and improves improved mobility, quality of life and nutritional status.
Nutritional, physical, cognitive, and combination interventions and frailty reversal among older adults: a randomized controlled trial. The American journal of medicine	Tze Pin Ng et al.	2015	Compared the effects of nutritional supplementation, physical training, cognitive training, and combination treatment vs control during 6 monthsin reducing frailty among community-dwelling prefrail and frail older individuals.	246 community-dwelling older individuals	49 individuals in nutritional supplementation, 50 in cognitive training, 48 in physical training, 49 in combination treatment and 50 in usual care control .	This intervention resulted in a reverse of frailty status, especially in nutritional, cognition, and physical and combination groups.Besides the positive effect in frailty status, there were significant improvements in frailty domains such as knee strength,physical activity, gait speed and energy.
Protein enrichment of familiar foods as an innovative strategy to increase protein intake in institutionalized elderly.	J. Beelen, N.M. De Roos, L.C.P.G.M. De Groot	2015	Analyse if protein enriched-familiar foods and drinks could help institutionalized elderly to reach a protein intake of 1.2gr/kg body weight/ day (g/kg/d).	22 institutionalized elderly	All participants were included in the intervention group where the consumed protein enriched regular foods and drinks, including bread, soups, fruit juices, and instant mashed potatoes.	Despite didn't change the intake of energy and micronutrients, elderly individuals reached dairy recommended protein intake.

Table 3. Summary of the most relevant studies (Continuation)

Article	Author(s)	Year	Objective	Population	Methods	Main Highlights
Effects of an oral nutritional supplementation plus physical exercise intervention on the physical function, nutritional status, and quality of life in frail institutionalized older adults: The ACTIVNES study	Pedro Abizanda et al.	2015	Analyse the effects of a hyperproteic, hypercaloric oral nutritional supplement with prebiotic fiber, vitamin D, and calcium along with a standardized physical intervention, in the functional status, strength, nutritional status, and quality of life of frail institutionalized older adults.	91 nursing home residents	In intervention group, participants take two 200-mL bottles of oral protein-energy oral nutritional supplement with prebiotic fiber, vitamin D, and calcium nutritional supplement along with flexibility, balance and strengthening exercises.	This intervention led to na improvement in nutritional status because it was observed a gain in weight and in Body Mass Index, reducing malnutrition in institutionalized elderly. It also improved functional status.
Protein-enriched familiar foods and drinks improve protein intake of hospitalized older patients: A randomized controlled trial.	Janne Beelen et al.	2018	Analyse if protein-enriched familiar foods and drinks were effective in increasing protein intake of hospitalized older patients.	147 hospitalized older adults	80 older individuals received the standard energy and protein rich hospital menu. 67 older individuals received the same menu with various protein-enriched products replacing regular products or added to the menu.	Protein-enriched familiar foods and drinks such as bread, fruit juice and dairy products as replacement of regular products or as additions to the hospital's menus besides improving nutritional status, is a feasable and well-accepted nutritional intervention by elderly.
Whey protein, amino acids, and vitamin D supplementation with physical activity increases fat-free mass and strength, functionality, and quality of life and decreases inflammation in sarcopenic elderly	Mariangela Rondanelli et al.	2016	Analyse if supplementation whey protein, essential amino acids and vitamin D supplementation along with physical activity would increase fat-free mass, strength, physical function, and quality of life, and reduce the risk of malnutrition in sarcopenic elderly individuals.	130 sarcopenic hospitalized older adults	All participants were included in the supplementation and physical activity group.	Vitamin D, whey protein and essencial amino acids supplementation along with physical activity improved nutritional and functional status and biochemical markers that influence the reduction of inflammation which contributed to improvement in well-being.
Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial.	Schuetz, P et al.	2019	Analyse if individualised nutritional support to reach patients needs reduces the risk of adverse clinical outcomes in medical inpatients at nutritional risk.	2088 hospitalized inpatients	The participants were randomized in a intervention group that receive individualised nutritional support to reach protein and caloric goals or in a control group that receive standard hospital food.	This individualized strategy increased energy and protein intake,improved physical capacity, functional status and, consequently, quality of life.
Whey protein supplementation improves rehabilitation outcomes in hospitalized geriatric patients: a double blinded, randomized controlled trial.	Niccoli, S. et al.	2017	Evaluate the efficacy of Whey protein supplementation a frail, hospitalized elderly population.	47 hospitalized inpatients	The population was randomized in na intervention (whey protein supplement) and a control group (without supplementation).	Whey protein supplementation improved nutritional status and physical condition,namely, gait speed and muscle strength, reduced inflammation and, consequently, improved quality of life.