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Short Review Article Open Access

Recommendation of a Whey Protein Diet Combined with Rehabilitation for Patients with Hip Fracture in the Early Postoperative Period

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Introduction

Sarcopenia is the loss of muscle mass that frequently occurs during aging. Reductions in protein anabolism are caused by chronic inflammation, increased insulin resistance, low sensitivity to amino acids, and reduced physical activity in the elderly [1]. An inadequate protein intake is more common among the elderly, and the synthetic responses of muscle protein to food intake are also impaired. A positive association has been reported between protein intake and muscle mass in the elderly [2]. However, the effects of resistance training on muscle strength and mass were found to be less prominent in the elderly than in young adults [3].

Hip fracture is a common orthopedic condition among the elderly, and surgery is generally regarded as the best treatment. Patients subsequently undergo a rehabilitation program in order to regain their pre-injury ambulatory ability and activity of daily living (ADL) level. However, a large number of patients cannot regain their pre-injury performance when treated with usual care or rehabilitation. Factors, such as pain, dementia, delirium, energy balance, and altered metabolism, have been shown to inhibit improvements in physical function after surgery; of these, protein metabolism and the nutritional status are regarded as important factors for functional recovery. In this review, we discuss protein metabolism after surgery and the combination of nutritional supplementation and rehabilitation among patients with hip fracture in the early postoperative period. We also recommend whey protein as a nutritional supplement.

Protein catabolism and malnutrition after surgery and the importance of a protein diet combined with training for physical function among patients with hip fracture

Patients with hip fracture are at risk of protein catabolism after surgery and a loss in total body weight and lean mass during the first 6 months [4]. Surgical stress results in alternations in total protein metabolism, characterized by an increase in protein catabolism and a negative nitrogen balance. Cortisol increases, insulin resistance, hypoxia, and acidosis in muscle cells cause early proteolysis, and protein catabolism results in marked weight loss and muscle wasting [5]. Additionally, surgical patients are at risk of malnutrition, which has also been identified as one of the risk factors for the poor recovery of physical function. There are many patients with malnutrition or potential malnutrition in hospitals and rehabilitation facilities; those who obtain sufficient nutrition account for only 14% of all hospitalized patients [6]. The prevalence of malnutrition is generally high among patients with hip fracture. More than half of elderly patients with hip fracture are already malnourished on admission [7]. These factors may inhibit the effects of rehabilitation on physical function, which is one of the challenges faced in the early postoperative period (Figure 1).

In recent years, nutritional treatments and exercise have been reported to have positive effects on physical function in the elderly [8,9]. Essential amino acids exert a significant stimulatory effect on muscle protein synthesis and reportedly result in increases in muscle strength, mass, and physical function among the elderly [10]. However, few studies have described positive effects on muscle strength, ADL, or the functional status of nutritional care combined with exercise (rehabilitation) among patients with hip fracture after surgery, specifically within the acute phase. A previous study demonstrated that nutritional support combined with rehabilitation for a maximum duration of four weeks in patients with hip fracture in the postoperative period resulted in increases in body weight and a shorter hospital stay. However, motor function and ADL were not significantly different from those in the control group [11]. In another study, nutritional supplementation (protein and calcium) after surgery for 60 days did not result in improvements in functional recovery [12]. A high-protein diet for 28 days led to greater improvements in serum albumin levels and a slightly shorter hospital stay; however, no outcome differences were observed in ADL in a rehabilitation hospital [13]. These findings indicate that improvements in muscle strength or physical function are difficult to achieve in the postoperative period among patients with hip fracture, even with nutritional interventions. This may have been due

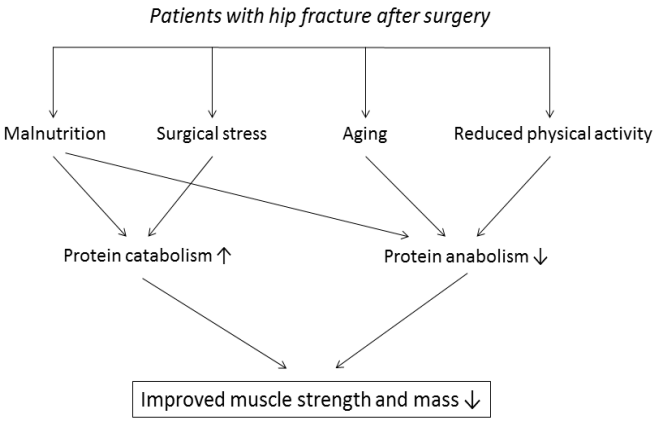

Figure 1: Factor, such as malnutrition, surgical stress, aging, and reduced physical activity affecting recovery in patients with hip fracture after surgery. These factors induce alternations in total protein metabolism, characterized by an increase in protein catabolism and a negative nitrogen balance. Therefore, improvements in muscle strength and mass are inhibited.

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to the insufficient ingestion of proteins, essential amino acids, or the exercise load used in each study. Protein intake is required to improve muscle strength, which is an important factor of physical function, and the quality of proteins needs to be considered for training. The positive effects of proteins, such as soy protein and casein, in combination with resistance training on the muscle protein fractional synthetic rate have already been reported [14]. However, whey protein includes more essential amino acids, particularly valine, leucine, and isoleucine, than other types of proteins; it induces increased muscle protein synthesis, and the combination of a whey protein diet and resistance exercise has resulted in greater improvements in muscle protein synthesis than soy protein, casein, and only dietary whey protein [14-16]. Therefore, patients with hip fracture need to enhance their protein anabolism using an adequate protein diet (if possible, a whey protein diet) combined with physical training.

Effects of whey protein combined with rehabilitation on muscle strength and physical function in the early postoperative period

We previously compared the effects of dietary whey protein combined with rehabilitation versus rehabilitation alone on muscle strength and ADL among patients with hip fracture in the early postoperative period [17]. Our findings demonstrated that dietary whey protein combined with rehabilitation in the early postoperative period had beneficial effects on knee extension strength in operated and non-operated limbs and ADL levels [17] (Figure 2).

The ingestion of whey protein post-exercise has been shown to increase muscle protein synthesis more than exercise without a subsequent whey protein diet or a whey protein diet alone [16] , and the ingestion of whey protein was found to induce increments in plasma levels of phenylalanine and insulin, which stimulate muscle protein synthesis, within one hour in the elderly [16,18]. Resistance training alone promotes muscle protein synthesis and breakdown, and may lead to the negative nitrogen balance associated with muscle protein synthesis; however, resistance training combined with dietary proteins has been shown to have a positive impact on the nitrogen balance [19]. Furthermore, the muscle protein synthesis rate was approximately 200 % higher with an amino acid infusion after exercise than with an amino acid infusion alone, and the rate of arterial amino acid delivery was significantly higher with an amino acid infusion during post-exercise recovery than with an amino acid infusion alone [20]. A relationship has been identified between muscle protein synthesis and blood flow, indicating that an amino acid infusion combined with exercise may accelerate amino acid transport [20]. Furthermore, a previous study reported that the ingestion of a whey protein hydrolysate induced greater changes in post-exercise gene expression profiles in rat skeletal muscle [21]. Therefore, dietary whey protein combined with resistance training is very important for muscle strength and mass, and the combination of a whey protein diet and rehabilitation may have led to the increases in muscle strength observed in our previous study.

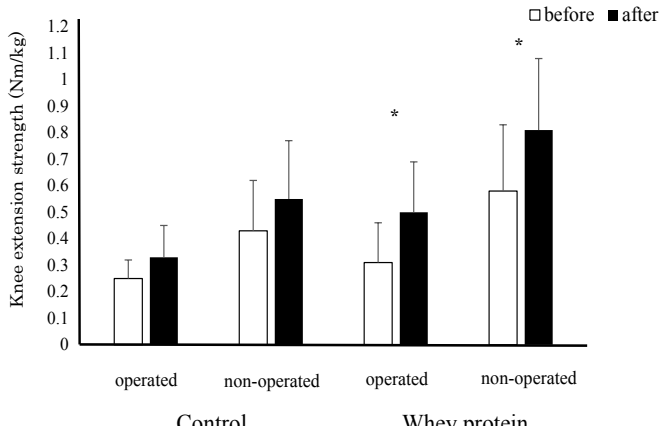

Figure 2: The whey protein group showed greater improvements in knee extension strength in the operated limb and non-operated limb after rehabilitation than the control group, *: Significantly different from the control, $p < 0.05$. Data are taken Niitsu et al., Clin Nutr. pii: S0261-5614(15).

Considerations when using protein

The timing of the ingestion, the amount of protein, and exercise load need to be considered when using protein combined with training in the early postoperative period and short term in order to achieve improvements in muscle strength and physical function. In terms of timing, plasma levels of phenylalanine and insulin, which stimulate muscle protein synthesis, were previously found to reach a peak concentration 30 minutes after the ingestion of whey protein and early protein intake after resistance training bouts in the elderly was reported to be more important for hypertrophy in skeletal muscle than 2 hours post-training; therefore the timing of protein intake in the immediate post-training period is recommended [18,22]. In terms of protein intake, the protein requirements of individuals engaged in strength training are related to the intensity of the training. However, patients with hip fracture need to ingest a high-protein diet regardless of the training intensity after surgery. A high-protein diet results in greater amino acid absorption, plasma insulin and phenylalanine levels, and a significantly higher muscle protein synthesis rate in healthy older adults [16,23]. A high whey protein diet induces greater muscle protein synthesis, and a linear relationship has been identified between protein intake and muscle protein synthesis. However, a high-protein diet may also promote renal disease, and, thus, the continuation of a high-protein diet may damage renal function in healthy individuals [24]. Therefore, renal function, including serum creatinine levels and the glomerular filtration rate (GFR), needs to be monitored in patients as a biochemical factor for risk management. Patients with hip fracture ingested approximately 1.8 g/kg protein per day in our previous studies, and we followed their GFR over time; we did not observed any significant changes [17,25]. The safety of a short-term 1.6-1.8 g/kg per day protein diet among the elderly has already been described [26]. A high-protein diet is not associated with kidney damage in healthy individuals, and hyper filtration is a normal adaptation to a high-protein diet. Evidence to show that a high-protein intake is detrimental to renal function in healthy individuals is limited [24]. However, a high-protein diet may place renal function under stress and accelerate renal disease among patients with kidney disease [24], and, hence, these patients require a lower protein intake. In terms of training, although there are various rehabilitation procedures, patients with hip fracture need to engage in active muscle training in order to improve physical function when combined with protein. Patients with hip fracture mainly performed active training (sit-to-stand training and walking exercise) for rehabilitation in order to promote the effects of whey protein in our previous studies. The acute response of muscle protein synthesis is dependent on exercise intensity, with high intensity exercise increasing muscle protein synthesis more than low intensity in the elderly [27]. Passive exercise, such as stretching and range of motion exercises, may not accelerate protein anabolism. Therefore, we advise the use of progressive exercise to induce hypertrophy and improve

muscle strength and physical function. Progressive resistance training is safe and effective for geriatric rehabilitation after hip surgery [28].

Conclusion

The elderly account for a large proportion of patients with hip fracture, and the effects of training on physical function is less prominent in the elderly than in young adults. Inflammation, malnutrition, and reduced physical activity increase protein catabolism and impose a limitation for improvements in physical function and ADL in the early postoperative period. However, the combination of dietary whey protein and rehabilitation in the early postoperative period has beneficial effects on muscle strength. Nutritional interventions, particularly adequate dietary protein and essential amino acids, are important when combined with rehabilitation among patients with hip fracture after surgery. Protein energy is a major factor influencing the post-discharge functional recovery of elderly patients with hip fracture after surgery. Therefore, in the early postoperative period, we recommend a high whey protein diet for all elderly patients with hip fracture who are not on a restricted protein diet.

Even though the beneficial effects of whey protein combined with rehabilitation on muscle strength and physical function among patients with hip fracture after surgery were demonstrated, further evidence is needed. A large number of uncertainties remain including an appropriate protein intake, the duration of a protein diet during rehabilitation treatment, nutritional supplements that are more effective at improving physical function, and the best training protocol combined with nutritional supplementation. Therefore, further well-designed studies and well-performed randomized control trials with larger sample sizes are needed in order to achieve positive effects.

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