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Review

Aggressive nutrition therapy in malnutrition and sarcopenia

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ABSTRACT

Aggressive nutrition therapy is essential to improve nutrition and function in patients with malnutrition and sarcopenia. Malnutrition and sarcopenia negatively affect functional recovery and activities of daily living. Nutrition improvement is associated with better functional recovery. Target energy intake in aggressive nutrition therapy is defined as total energy expenditure (TEE) plus the amount of energy accumulated. The amount of energy accumulation per 1 kg of body weight is generally 7500 kcal. If the goal is to gain 1 kg of weight over 30 d, TEE + 250 kcal is the target daily energy intake. Aggressive nutrition therapy is implemented using a rehabilitation nutrition care process, which consists of five steps: assessment and diagnostic reasoning, diagnosis, goal setting, intervention, and monitoring. Aggressive nutrition therapy sets clear goals using the Specific, Measurable, Achievable, Relevant, and Time-bound principles. The application and effect of aggressive nutrition therapy differs depending on the etiology and condition of malnutrition. Precachexia, short bowel syndrome, and older people with mild to moderate dementia are indications for aggressive nutrition therapy. Nevertheless, aggressive nutrition therapy is usually contraindicated in cases of refractory cachexia, acute disease or injury with severe inflammation, and bedridden patients with severe dementia and reduced activity. Aggressive nutrition therapy should be combined with aggressive exercise and rehabilitation. Enhanced nutritional therapy combined with rehabilitation in patients with cerebrovascular disease, hip fracture, or acute disease is recommended in the 2018 clinical practice guidelines for rehabilitation nutrition. Further evidence for aggressive nutrition therapy is however required.

Introduction

Malnutrition and sarcopenia are associated with reductions in swallowing function, activities of daily living (ADLs), and home discharge rates. The prevalence of malnutrition and sarcopenia in older adults undergoing rehabilitation has been reported to be 49% to 67% [1] and 40% to 50% [2–4], respectively. A systematic review showed malnutrition in older adults admitted for rehabilitation hospitals affected functional recovery and ADLs after patients were discharged to the community [5]. Sarcopenia was associated with poorer recovery of physical function and dysphagia in hospitalized Japanese adults undergoing rehabilitation and also lower rates of home discharge [6]. Therefore, it is important to improve nutritional status and sarcopenia in patients undergoing rehabilitation.

The practice of rehabilitation nutrition can improve function and ADLs in cases of malnutrition and sarcopenia [7]. Rehabilitation nutrition includes holistic assessment by International Classification of Functioning, Disability and Health; assessment of nutritional disorders, sarcopenia, and excessive or inadequate intake of nutrients; diagnosis of rehabilitation nutrition; and goal setting. There is also evidence that rehabilitation nutrition improves the nutritional status of sarcopenia in individuals with

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disabilities and frail older people in addition to maximizing their functions, activities, participation, and quality of life (QoL). This is achieved by "nutrition management from the perspective of rehabilitation" and "rehabilitation from the perspective of nutrition" [8]. The 2018 clinical practice guidelines of rehabilitation nutrition developed by the Japanese Association of Rehabilitation Nutrition recommended the use of enhanced nutritional therapy in cerebrovascular disease, hip fracture, and acute disease [9].

Swallowing function and ADLs in malnourished patients can be recovered by improving nutritional status. Patients with stroke, hip fracture, or pneumonia who are malnourished are more likely to experience an improvement in their swallowing function and ADLs after nutrition improvement [10–12]. Therefore, in cases of malnutrition and sarcopenia, aggressive nutrition therapy that adds energy and protein to daily energy expenditure is important for improving nutritional status.

Rehabilitation nutrition can be implemented by using the rehabilitation nutrition care process that includes the following five steps: assessment and diagnostic reasoning, diagnosis, goal setting, intervention, and monitoring. The effectiveness of rehabilitation can be improved by setting SMART (Specific, Measurable, Achievable, Relevant, and Time-bound) nutrition goals and using aggressive nutrition therapy [13] (Fig. 1). Reducing energy intake is one of the factors that contribute to weight loss. Similarly, energy gain for increasing weight is essential for improving malnutrition and sarcopenia. This review discusses aggressive nutrition therapy in malnutrition and sarcopenia.

Aggressive nutrition therapy

Aggressive nutrition therapy is a nutritional management method in which daily energy expenditure is considered and the amount of energy accumulation is set as the energy requirement. Generally, energy requirements are composed of resting metabolic rate, diet-induced thermogenesis, and activity- and disease-related energy expenditure. Additionally, in the case of malnutrition and sarcopenia, the energy requirement is set by adding the amount of energy accumulation to that required to recover lean mass. To increase 1 kg of lean mass, 7500 kcal are required for individuals aged 10-40 years [14,15], whereas 8800 to 22600 kcal are needed for older individuals [16].

In cases presenting with malnutrition or sarcopenia, aggressive nutrition therapy can improve nutritional status and promote rehabilitation. Weight gain in underweight patients undergoing acute rehabilitation is associated with better improvement in ADLs [17]. Nutrition improvement and high energy intake improved ADLs more in patients with cerebrovascular disease [18–20]. Similarly, improvement or maintenance of nutritional status is associated with better functional recovery in post-stroke rehabilitation [21].

Based on the importance of nutrition care in rehabilitation, cerebrovascular disease, hip fracture, acute diseases, and cancer were included in the 2018 Clinical Practice Guidelines of Rehabilitation Nutrition developed by the Japanese Association of Rehabilitation Nutrition [9]. These clinical guidelines recommend enhanced nutritional therapy (e.g., standard nutritional care such as the provision

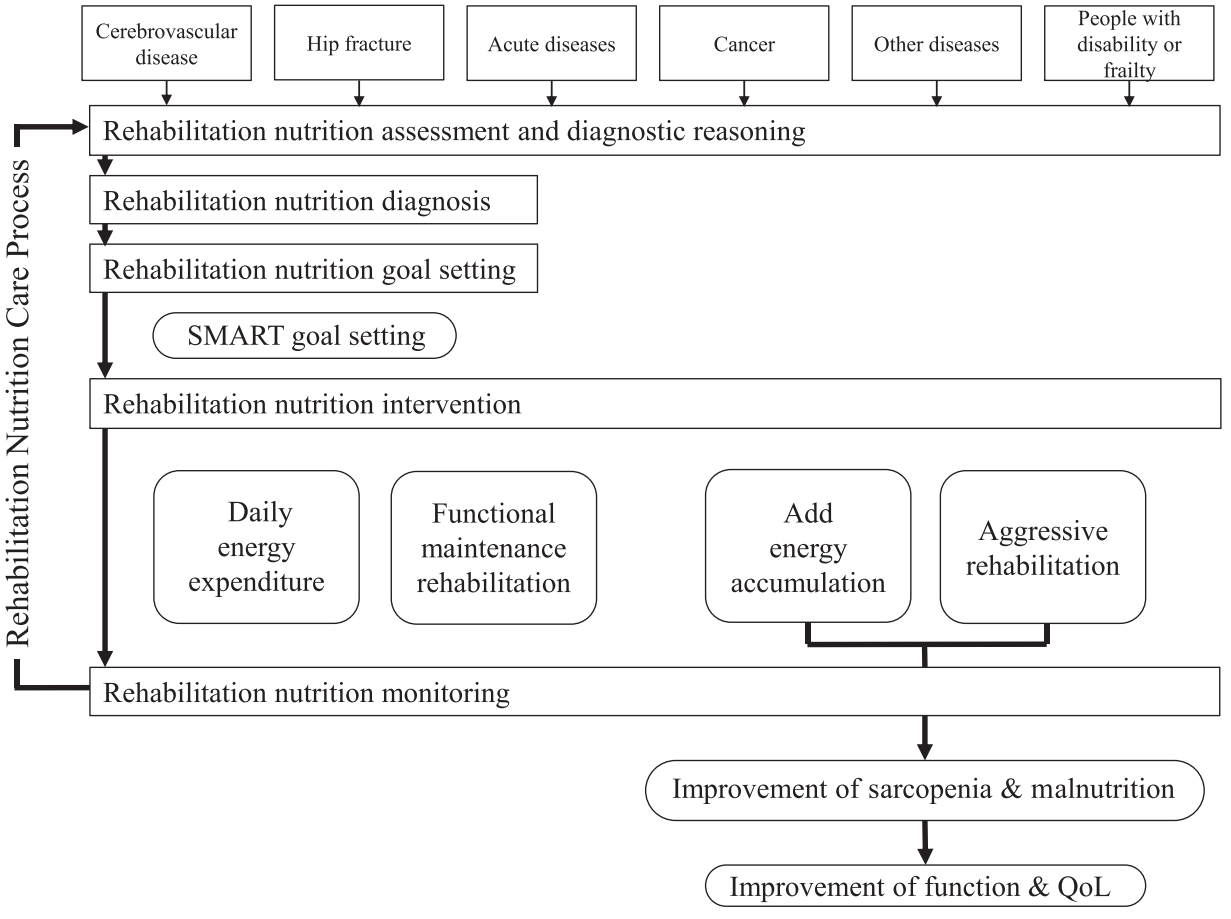

Fig. 1. Rehabilitation nutrition care process and aggressive nutrition therapy. QoL, quality of life; SMART, Specific, Measurable, Achievable, Relevant, and Time-bound.

of hospital meals, or daily dietary intake at home and in institutions, plus nutrition guidance based on individualized patient nutrition assessment, nutritional counseling, provision of oral supplements, and intravenous and enteral nutrition) in patients with cerebrovascular disease, hip fracture, and acute diseases undergoing rehabilitation. Aggressive nutrition therapy described in this review is characterized by the setting of energy requirements based on the amount of energy expenditure per day plus the amount of energy accumulation. This is not the same as enhanced nutrition therapy and instead focuses more on improving malnutrition and sarcopenia.

The practice of aggressive nutrition therapy

Indications and contraindications of aggressive nutrition therapy

The application and effect of aggressive nutrition therapy may differ depending on the etiology and the degree of malnutrition. In 2017, the European Society for Clinical Nutrition and Metabolism (ESPEN) classified conditions of malnutrition into disease-related malnutrition (with or without inflammation) and malnutrition without disease. A diagnosis based on the etiology of malnutrition was also proposed [22]. This led to the Global Leadership Initiative on Malnutrition criteria [23], that divides the malnutrition into four categories:

1. Malnutrition related to chronic disease with inflammation.
2. Malnutrition related to chronic disease with minimal or no perceived inflammation.
3. Malnutrition related to acute disease or injury with severe inflammation.
4. Malnutrition related to starvation without inflammation.

The timing and indication of aggressive nutrition therapy differ in these categories.

The etiology of the first category includes cancer, chronic obstructive pulmonary disease, congestive heart failure, and chronic kidney disease, leading to cachexia. In recent years, palliative care has been classified into three stages as disease-focused, symptom-focused, or no nutrition [24]. Cancer and palliative care are closely related, with cancer cachexia classified into three categories: precachexia, cachexia, and refractory cachexia [25]. Precachexia is a stage of mild metabolic abnormalities. The nutritional management of precachexia is an indication for aggressive nutrition therapy. In cachexia in which metabolic abnormalities and muscle and weight loss occur, aggressive nutritional therapy is indicated because nutrition intervention is known to be effective for improving QoL and loss of appetite [26,27]. In contrast, the goal of nutritional management in refractory cachexia is to maintain or reduce a deterioration in QoL. Aggressive nutrition therapy in refractory cachexia is therefore contraindicated.

The etiology of the second category, malnutrition related to chronic disease with minimal or no perceived inflammation, includes anorexia nervosa, short bowel syndrome (SBS), stroke, amyotrophic lateral sclerosis, and dementia. Jensen et al. reported that in anorexia nervosa, lean body mass may be reduced in the absence of nutritional intervention but improved by nutrition support [28]. SBS with malnutrition requires 30 to 35 kcal/kg daily [29], or 1.4 times as much energy as resting energy expenditure [30]. The use of oral nutritional supplements in older people with malnutrition and mild to moderate dementia improved weight, body mass index, and cognitive function [31]. Therefore, SBS and mild to moderate dementia in older people with malnutrition is an indication for aggressive nutrition therapy. However, in bedridden patients with severe dementia, administration of an excessive amount of nutrition is contraindicated [32].

The etiology of category 3, malnutrition related to acute disease or injury with severe inflammation, includes major infection, burns, trauma, or closed head injury. Metabolic changes during the inflammatory response are categorized into the injury catabolic and anabolic phases. Protein catabolism, insulin resistance, and hyperglycemia occur during these two phases. Overfeeding also causes hyperglycemia, nutritional stress [33,34], and functional suppression of autophagy [35]. For this reason, ESPEN recommends providing <70% of resting energy expenditure in intensive care unit (ICU) patients for at least the first week [36]. The daily nutritional amount recommended for ICU patients should be 20 kcal/kg, or ~80% of the estimated energy requirement for the first week [37]. Therefore, aggressive nutritional therapy is contraindicated in patients with acute diseases or injuries with severe inflammation. In contrast, mildly invasive diseases and transition to the anabolic phase are indications for aggressive nutrition therapy.

The etiology of the final category, malnutrition related to starvation without inflammation in patients who need rehabilitation, involves an insufficient intake of nutrients. Severe starvation should be noted in the refeeding syndrome. According to the American Society for Parenteral and Enteral Nutrition [38] the significant risk for refeeding syndrome is no or very little oral intake for ≥7 d. To prevent the refeeding syndrome, it is recommended to start at 10 to 20 kcal/kg for the first 24 h and increase the amount by 33% of the target energy level every 1 to 2 d [38]. Aggressive nutrition therapy is used when it is confirmed that there are no symptoms or risks for refeeding syndrome.

Setting nutritional goals and energy accumulation

The goal of aggressive nutrition therapy for individuals in need of rehabilitation is to set nutritional and rehabilitation goals based on the concept of International Classification of Functioning, Disability and Health. In aggressive nutrition therapy, goal setting is performed using SMART (Specific, Measurable, Achievable, Relevant, and Time-bound parameters) principles (Table 1) [39].

The accumulation of energy during aggressive nutrition therapy is determined by nutritional goal setting. The target energy amount for patients with malnutrition is calculated by adding energy accumulation to the total energy expenditure (TEE) required to increase weight and muscle mass. TEE is calculated by obtaining the basal energy expenditure using an estimation formula such as the Harris–Benedict method and multiplying the result by stress and activity factors. Alternatively, an indirect calorimeter can be used or by multiplying the result by 30 to 40 kcal/kg body weight. Zanten et al. [40] stated that after discharge from the ICU, 150% of the predictive formula, 150% of the indirect calorimetry result, or 35 kcal/kg of simplified energy is required. The amount of energy accumulation per 1 kg of body weight is generally 7500 kcal [14], although various other theories have been proposed [15,41]. The daily energy accumulation required for a weight gain of 1 kg/mo is 250 kcal, which is 7500 kcal divided by 1 mo. Therefore, if the goal is to gain 1 kg of weight per month, TEE + 250 kcal is the target energy intake per day. However, adjustment for nutritional provisions through regular monitoring is necessary.

Oral aggressive nutrition therapy

A regular balanced diet is the first choice for oral aggressive nutrition therapy. Accurate recording and monitoring of intake

Table 1
SMART principles

Item	Content	Example
S: Specific	• Clear • Concrete	3-kg weight gain not improved nutrition
M: Measurable	• Easy to measure • Quantification of goals	2-kg weight gain/mo
A: Achievable	• Achievable if you try. • Considering the feasibility of the intervention and the time to reach the goal	2-kg weight gain after 1 mo
R: Relevant	For patients and families, • Important content • Improving QoL	2-kg weight gain rather than improvement of blood albumin concentration
T: Time-bound	Clarification of the time of the next evaluation and achievement deadline. • Short-term goal: daily or weekly • Long-term goal: monthly The situation where the outlook is unknown • Discernment is the goal	Short-term goal: 0.5-kg weight gain in 2 wk Long-term goal: 3-kg weight gain after 3 mo

QoL, quality of life.

are fundamental to ensure that patients are eating well. If the patient is unable to meet their nutritional requirements, the causes of the inadequate intake should be assessed by a trained dietitian and multiprofessional team. A recent report described the concept of rehabilitation pharmacotherapy [42]. The concept envisages helping frail older individuals and individuals with disabilities to achieve the highest possible body function, activity level, and QoL. Rehabilitation pharmacotherapy states that inappropriate medications may adversely affect nutritional status [42]. Reviewing prescribed medications and considering the discontinuation of the prescription of medications that cause loss of appetite is another strategy to combat the appetite problem. There are ways to devise a diet and eat more nutritious foods (Table 2). Inpatients may fast or eat late in the day due to medical examinations, surgery, and treatment [43]. Additionally, missing even one meal may reduce energy replacement obtained from oral intake. Therefore, eating three meals a day should be advocated [44]. If patients are not getting their nutritional requirements at basic mealtimes, supplementation between meals and late-evening meals can be effective for increasing nutrient intake [45]. Oral sip feeds are easy to use, inexpensive, and can increase oral intake [46].

Aggressive nutrition therapy with tube feeding

Tube feeding is used as an aggressive nutrition therapy when the gastrointestinal tract is functioning and the patient cannot consume a safe and adequate amount of food orally. Adjustment of nutritional prescriptions is required based on changes in the patients' body weight, muscle mass, and rehabilitation dose. High-energy nutritional supplements administered at a dose of 1 kcal/mL may cause the need for numerous administrations. The amount of protein and lipid needed for each disease should therefore be evaluated. Continuous administration should be considered in patients with gastrointestinal symptoms such as reflux, vomiting, and diarrhea rather than using intermittent administration. If it is difficult to increase the dose of tube feeding, supplemental parenteral nutrition can be introduced [48].

Table 2
Strategy for oral aggressive nutrition therapy according to cause of malnutrition

Factors associated with decreased food intake	Examples
Chewing and swallowing problems	• Determine appropriate food texture to prevent aspiration • Add smoothness to a meal using mayonnaise or oily foods • Use smooth, nutrient-rich foods such as mousse and pudding
Appetite problems	• Change the menu to take into account patient's preferences • Increase the volume of meals at a time of day when the patient has a relatively good appetite In the case of fasting by inspection, serve the meal again as soon as possible • Adjust the eating environment and check the patient's lifestyle. Avoid mealtime interruptions by examinations or other procedures. If inevitable, change the mealtime so that the patient can eat • Adjust the environment to the patient's preferences (e.g., use the patient's tableware) • Use appetizing ingredients such as spices and citrus fruits • Prepare the food when the patient wants to eat
Digestion and absorption problems	• Provide softened, modified, minced, or pureed food • Increase the frequency of meals
Increased energy expenditure	• Neurodegenerative diseases lead to marked muscle tonus, involuntary movements, excessive rehabilitation, and pressure ulcers; thereby increasing the requirement for nutrients • Increase the patient's chance of eating, such as adding opportunities for snacking in addition to the 3 meals/d • Use sip feed and Med pass [46]
Medication problems	• Consider stopping medications that cause loss of appetite (e.g., nonsteroidal anti-inflammatory drugs, bisphosphonates) • Consider stopping medications that cause nausea and vomiting (e.g., opioids, anticancer drugs, digitalis) • Consider stopping medications that cause taste disorders (e.g., angiotensin-converting-enzyme inhibitors, angiotensin II receptor blockers) • Consider prescribing medications that cause an increased appetite (e.g., progesterone analogs, corticosteroids) [47]

Monitoring of aggressive nutrition therapy

Monitoring of aggressive nutrition therapy should include its efficacy, adverse effects, and associated diseases. Nutrition care professionals determine whether aggressive nutrition therapy should be continued or whether the nutritional strategies should be changed. Once-weekly monitoring is more likely than once-monthly monitoring to maintain the weight of patients in convalescent rehabilitation wards [49]. Indicators for monitoring are selected based on the goals set. Body weight can be useful for evaluating nutritional status. Aggressive nutrition therapy should be withdrawn if the patient's fat mass increases markedly. Measurement of body composition is effective for assessing muscle and fat mass. If it is not possible to assess muscle mass using expensive equipment such as dual energy x-ray absorptiometry and bioelectrical impedance analysis, calf circumference can be used as a measure of muscle loss [50]. The adverse effects of aggressive nutrition therapy should be monitored. Hyperglycemia, dyslipidemia, elevated blood urea nitrogen, liver dysfunction, and electrolyte abnormalities such as hypophosphatemia can occur during aggressive nutrition therapy. Table 3 lists other indicators that may be monitored [51].

Combination of aggressive nutrition therapy and rehabilitation/exercise

Aggressive exercise and rehabilitation are necessary when aggressive nutrition therapy is performed. Nutrition care combined with exercise reduces protein breakdown and improves muscle function [52]. In contrast, nutrient supplementation without exercise does not reduce muscle weakness or physical frailty [53,54]. Systematic reviews and meta-analyses have shown that rehabilitation interventions combined with nutritional care improved ADLs and physical functioning of individuals residing in nursing homes [55]. There is also evidence that exercise combined with nutritional therapy improves muscle mass and function in patients with sarcopenia [56–60]. Specifically, exercise in older patients requires a protein intake of 1.2 g/kg body weight to increase lean body mass [61–63]. The Clinical Guide for Frailty strongly recommends exercise therapy combined with nutritional care for frail patients [64]. Therefore, aggressive nutrition therapy should be performed in combination with aggressive exercise and rehabilitation.

Table 3
Indicators for monitoring aggressive nutrition therapy

Malnutrition	Weight Body composition Blood tests (Alb, Hb, TC, CRP, BG, TG, BUN, Cr, eGFR, AST, ALT, Na, Cl, K, P, Mg, Ca)
Sarcopenia	Muscle mass Muscle strength (grip strength) Physical function (walking speed, 5 chair-standing test, SPPB)
Cachexia	In addition to 5% weight loss within 12 mo, 3 or more of the following items: 1. Muscle weakness, 2 Fatigue, 3. Decreased appetite, 4. Low lean body mass, 5. Abnormalities in biochemical data such as CRP, Hb, and Alb [51]
Excess or deficiency of nutrient intake	Nutrient intake, BDHQ
ADL	BI, FIM
IADL	FAI
Swallowing function	Eating Assessment Tool (EAT-10).

ADL, activities of daily living; Alb, albumin; ALT, alanine transaminase; AST, aspartate transaminase; BDHQ, Brief-type self-administered diet history questionnaire; BI, Barthel Index; BG, blood glucose level; BUN, blood urea nitrogen; Ca, calcium; Cl, chloride; Cr, creatinine; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; FAI, Frenchay Activities Index; FIM, Functional Independence Measure; Hb, hemoglobin; IADL, instrumental activities of daily living; K, potassium; Mg, magnesium; Na, sodium; P, phosphate; SPPB, Short Physical Performance Battery, TC, total cholesterol; TG, triacylglyceride.

Conclusion

Aggressive nutrition therapy is important for improving nutritional status and function in patients with malnutrition and sarcopenia. Aggressive nutrition therapy should be provided after assessment of indications and SMART goal setting. The 2018 Clinical Practice Guidelines for Rehabilitation Nutrition recommend enhanced nutrition therapy for patients with cerebrovascular disease, hip fracture, and acute illnesses. However, evidence in support of aggressive nutritional therapy is not sufficient. Further clinical studies are needed to validate the effectiveness of aggressive nutrition therapy.

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