

## Special Review



# Nutritional Supplementation in Stroke Rehabilitation: A Narrative Review

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## HIGHLIGHTS

- In stroke rehabilitation, nutritional supplementation for malnutrition is required.
- Nutritional supplementation may affect positive outcomes after stroke.

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# Nutritional Supplementation in Stroke Rehabilitation: A Narrative Review

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## ABSTRACT

Malnutrition is associated with increased mortality and poor functional recovery after stroke. Most guidelines for stroke rehabilitation strongly recommend nutritional screening for malnutrition. Nutritional status after stroke is related to long-term outcomes, and nutritional supplementation is recommended for stroke patients with malnutrition and those at risk of malnutrition. However, routine nutritional supplementation in stroke patients, regardless of nutritional status, is not correlated with improved functional outcomes, and nutritional supplementation is not recommended if the nutritional status is adequate. Nutritional supplementation with protein, amino acids, vitamins, and minerals positively affects recovery after stroke, with improvements seen in motor function, cognition, activities of living, and mood. However, the evidence is insufficient due to the small number of studies and the lack of well-designed randomized controlled studies. Therefore, nutritional supplementation for stroke patients in rehabilitation should not be uniform, and individual nutritional interventions based on an assessment of the patient's nutritional status should be provided.

**Keywords:** Dietary Supplements; Malnutrition; Nutritional Status; Stroke; Rehabilitation

## INTRODUCTION

Stroke, which is one of the most common and severe neurological diseases, is among the leading causes of death and disability worldwide. Stroke patients are at risk for dehydration and malnutrition due to dysphagia, cognitive impairment, and decreased consciousness.

Nutritional status may deteriorate during the acute phase after stroke for various reasons, including surgery and energy consumption, and malnutrition is associated with increased mortality and poor functional recovery in stroke patients [1-4]. Malnutrition can also persist after stroke if it is not managed effectively. The key components of nutritional management include nutritional screening, assessment, and supplementation. Many guidelines for stroke rehabilitation recommend screening for malnutrition and providing nutritional supplementation [5-9]. Herein, we review nutritional supplementation in stroke rehabilitation for functional recovery, with a focus on general nutritional supplementation with protein/amino acids, vitamins, and minerals.

**Conflict of Interest**

The first and corresponding authors of this manuscript are the editors of *Brain & NeuroRehabilitation*. The authors did not engage in any part of the review and decision-making process for this manuscript.

**SCREENING OF NUTRITIONAL STATUS**

The prevalence of malnutrition varies from 6% to 62% upon admission to the hospital in stroke patients, and it has been reported to be 25% in the first weeks after stroke [10]. Malnutrition is associated with poor outcomes in terms of mortality, length of hospital stay, and cost of hospitalization compared to normal nutritional status. The Feed Or Ordinary Food (FOOD) trial, a large cohort study, analyzed the association between nutritional status and mortality in 3,012 stroke patients [2], and found higher 6-month mortality in malnourished patients than in patients with normal nutritional status. Another retrospective cohort study involving 540 stroke patients reported that poor nutritional status was a predictor of lower functional outcome improvement in stroke patients [11]. Along with this evidence, most guidelines for stroke rehabilitation strongly recommend nutritional screening and assessment (Table 1). To this end, most hospitals have formed a nutrition support team to provide adequate nutritional interventions and nutritional screening for inpatients as well as stroke patients.

**GENERAL NUTRITIONAL SUPPLEMENTATION**

Guidelines for stroke present recommendations for nutritional supplementation according to stroke patients' nutritional status. In patients with malnutrition, nutritional supplementation is recommended; however, if patients' nutritional status is adequate, it is recommended not to provide supplementation (Table 2).

The FOOD trial comprised three well-designed, large randomized controlled trials (RCTs) on the nutritional management of stroke patients [12-14]. As mentioned above, the FOOD trial provided reliable evidence that nutritional status after stroke is associated with long-

**Table 1.** Recommendations for nutritional screening in stroke patients

Guideline	Recommendation
Clinical Practice Guideline for Stroke Rehabilitation in Korea 2016 [5]	All stroke patients should be screened for malnutrition and nutritional status in the acute-onset stage (recommendation level B, evidence level 2+).
Canadian Stroke Best Practice Recommendations: Rehabilitation, Recovery, and Community Participation Following Stroke. Update 2019 [7]	Patients should be screened for malnutrition, ideally within 48 hours of inpatient rehabilitation admission using a valid screening tool (evidence level C).
(Australian) Clinical Guidelines for Stroke Management (2017) [8]	All stroke patients should be screened for malnutrition at admission and on an ongoing basis (at least weekly) while in hospital (strong recommendation).
ESPEN Guideline Clinical Nutrition in Neurology (2018) [9]	The available evidence suggests that all stroke patients should be screened for risk of malnutrition on admission to hospital (within 48 hours), and the MUST can be used to identify patients who are more likely to benefit from medical nutrition therapy. Grade of recommendation: GPP - strong consensus (100% agreement).

ESPEN, European Society for Clinical Nutrition and Metabolism; MUST, Malnutrition Universal Screening Tool; GPP, good practice point.

**Table 2.** Recommendations for nutritional supplementation in stroke patients

Guidelines	Recommendation
(AHA/ASA) Guidelines for Adult Stroke Rehabilitation and Recovery (2016) [6]	Nutritional supplements are reasonable to consider for patients who are malnourished or at risk of malnourishment (IIa, B)
(Australian) Clinical Guidelines for Stroke Management (2017) [8]	For stroke patients whose nutrition status is poor or deteriorating, nutritional supplementation should be offered (strong recommendation). For stroke patients who are adequately nourished, routine ONS is not recommended (weak recommendation against).
ESPEN Guideline Clinical Nutrition in Neurology (2018) [9]	Routine ONS is not recommended for patients with an acute stroke without dysphagia and who are adequately nourished on admission. Degree of recommendation: GPP - strong consensus (100% agreement). In stroke patients who are able to eat and who have been identified to be malnourished or at risk of malnutrition, ONS is recommended. Degree of recommendation: GPP - strong consensus (100% agreement).

AHA/ASA, American Heart Association/American Stroke Association; ONS, oral nutrition supplementation; ESPEN, European Society for Clinical Nutrition and Metabolism; GPP, good practice point.

term outcomes, supporting the recommendation of nutritional supplementation for stroke patients with malnutrition and those at risk of malnutrition. However, it was found that routine oral nutritional supplementation for stroke patients in the hospital was not correlated with improved functional outcomes 6 months after stroke. Furthermore, routine oral nutritional supplementation in patients with non-malnutrition was found to induce hyperglycemia [14].

In 2012, a Cochrane review reported no significant differences in the case fatality, death, or dependency according to the use of nutritional supplementation in patients with acute and subacute stroke [4]. However, nutritional supplementation was correlated with reduced pressure sores and increased energy and protein intake. A study of 178 patients with malnutrition after stroke found an association between improved nutritional status and activities of daily living [15]. Ha et al. [16] analyzed the effectiveness of individualized nutritional interventions compared to usual care in patients with acute stroke. Patients who received individualized nutrition treatment had significantly lower weight loss and higher quality of life and handgrip strength. A recent study reported the impact of individualized nutritional support during a post-stroke rehabilitation program [17]. Among 454 stroke patients admitted to rehabilitation wards, nutritional management was provided (a high-calorie, high-protein diet for malnourished patients and calorie restriction with an appropriate protein diet for obese patients) nutritional screening and assessment. Multivariate analysis found that frequent and individualized nutritional support was independently associated with improved skeletal muscle mass, motor function, and dysphagia, and a shortened length of stay after stroke.

Therefore, malnourished patients should receive nutritional supplementation, but indiscriminate nutritional supplementation without a nutritional assessment is unnecessary. Providing individualized diet support is essential in stroke rehabilitation.

## PROTEIN/AMINO ACID SUPPLEMENTATION

Supplementation of protein and amino acids could enhance muscle protein synthesis and increase anabolic activity. In stroke patients, rehabilitation with protein/amino acid supplementation may contribute to post-stroke cortical plasticity and the maintenance of muscle mass.

Several studies have reported that protein supplementation had a positive effect on stroke recovery [18-20]. In an RCT of protein supplementation with 42 stroke patients, patients who received 21 days of protein supplementation showed improvements in the National Institute of Health Stroke Scale compared to those who consumed a spontaneous diet [18]. In another study by Aquilani et al. [19], daily high-protein nutritional supplementation improved cognitive function in subacute stroke patients. Rabadi et al. [20] studied the effects of intensive nutritional supplementation with high-energy, high-protein supplements in 58 stroke patients. High-energy, high-protein supplementation showed good outcomes in motor function and ambulation compared to routine nutritional supplementation, but improvements were not found in the length of hospital stay, body weight, or cognitive function.

Recent studies have moved beyond protein supplementation to actively investigate amino acid supplementation in stroke recovery. Aquilani et al. [21] studied 38 dysphagic subacute

stroke patients enrolled and randomized to receive 8 g/day of essential amino acids or an isocaloric placebo. The patients who did not receive essential amino acid supplementation continued to lose muscle mass even 76 days post-stroke, whereas those who received supplementation of essential amino acids did not exhibit unaffected muscle protein over-degradation. Yoshimura et al. [22] reported that the intervention group, which received a leucine-enriched amino acid supplement, showed significantly greater improvements in the Functional Independence Measure, handgrip strength, and skeletal muscle mass than the control group. However, that study of stroke patients with sarcopenia cannot be generalized to all stroke patients. No RCTs have yet investigated the effects of amino acid supplementation on the functional improvement of stroke rehabilitation. The study protocol has been published for a randomized double-blinded placebo-controlled clinical study (AMINO-Stroke Study) of essential amino acid supplementation on muscle strength, muscle function, and physical performance in stroke patients [23]. The results of this study are expected to elucidate the effects of amino acid supplementation on stroke rehabilitation.

Based on previous studies of protein and amino acid supplementation for stroke, nutritional interventions involving protein and amino acid supplementation are expected to be helpful for recovery and functional improvement after stroke. However, there is still insufficient evidence for this possibility. A large-scale RCT is needed to draw evidence-based conclusions.

## VITAMIN SUPPLEMENTATION

Many studies are being conducted on vitamin supplementation in relation to stroke, because the antioxidant and anti-inflammatory effects exerted by vitamins are thought to have positive impacts on stroke patients. Studies on stroke prevention are relatively better known. However, the long-term, large-scale Vitamins to Prevent Stroke (VITATOPS) [24] and Vitamin Intervention for Stroke Prevention (VISP) [25] studies showed that folic acid and vitamin B supplementation did not lead to a significant reduction in risk of secondary stroke among patients with recent stroke. However, few studies have been conducted on vitamin supplementation in the context of stroke recovery compared to those focusing on stroke prevention, and the extant studies are relatively small.

The B vitamins play an important role in brain function, and vitamin B levels may be associated with functional outcomes after stroke [26]. A study of vitamin B in stroke pathology using in vivo and in vitro mouse models reported that vitamin B and choline effectively promoted functional stroke recovery [27]. Another animal study showed that vitamin B promoted the recovery of learning and memory functions of rats with cerebral ischemia [28]. Almeida et al. [29] studied the relation between vitamin B supplementation and post-stroke depression in 273 stroke patients, and found that vitamin B supplementation was associated with a lower hazard of major depression than was observed in participants who received a placebo.

Vitamin D carries out neuromuscular, neuroprotective, and osteoprotective roles. Gupta et al. [30] investigated the effect of vitamin D and calcium supplementation on ischemic stroke in patients with vitamin D deficiency or insufficiency. The proportions of good outcomes (modified Rankin Scale score 0–2) and survival were higher in the supplementation group than in the control group. Sari et al. [31] reported that vitamin D supplementation improved activity levels and balance; however, it did not improve motor function or

ambulation. Another RCT by Torrisi et al. [32] found that vitamin D supplementation affected independence and depression after stroke.

Vitamins C and E have documented positive effects on the antioxidant capacity in patients with acute ischemic stroke [33]. However, the effects of vitamin C supplementation on stroke recovery have only been investigated in a retrospective case-control study [34], which reported that vitamin C supplementation did not enhance functional recovery in stroke patients.

Vitamins B and D have the potential to exert positive effects on emotion and function after stroke. However, the paucity of studies makes it impossible to reach a definitive conclusion on vitamin supplementation for functional recovery after stroke. Nonetheless, vitamin supplementation may be considered in stroke patients to prevent complications due to vitamin deficiency.

## MINERAL SUPPLEMENTATION

Among various minerals, the neuroprotective effect of magnesium sulfate has been documented in animal models [35]. In addition, a meta-analysis confirmed that dietary magnesium intake was associated with a reduced risk of ischemic stroke [36]. A study investigated the effect of magnesium intake on functional improvement after stroke in 291 discharged stroke patients, who were divided into three groups and provided regular salt, potassium-enriched salt, or potassium- and magnesium-enriched salt [37]. After the 6-month intervention, the potassium- and magnesium-enriched salt group showed better neurologic recovery than the potassium-enriched salt group and the regular salt group. Although studies have reported positive findings on magnesium supplementation, more research on mineral supplementation for stroke recovery is needed.

## CONCLUSION

Nutritional status should be assessed in stroke rehabilitation, and appropriate nutritional supplementation is required. Although caloric, protein/amino acid, vitamin, and mineral supplementation may have the potential for positive outcomes in stroke rehabilitation, evidence supporting these interventions is still lacking. Therefore, nutritional support for stroke patients in rehabilitation should not be uniform; instead, individual nutritional interventions should be provided.

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