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How to Increase Muscle Mass in Critically Ill Patients: Lessons Learned from Athletes and Bodybuilders

Khushboo Gala[1] · Viral Desai[1] · Nanlong Liu[2] · Endashaw M. Omer[2] · Stephen A. McClave[2]

Abstract

Purpose of Review Decades of research on nutrition and exercise on athletes and bodybuilders has yielded various strategies to promote anabolism and improve muscle health and growth. We reviewed these interventions in the context of muscle loss in critically ill patients.

Recent Findings For critically ill patients, ensuring optimum protein intake is important, potentially using a whey-containing source and supplemented with vitamin D and leucine. Agents like hydroxyl β-methylbutyrate and creatine can be used to promote muscle synthesis. Polyunsaturated fatty acids stimulate muscle production as well as have anti-inflammatory properties that may be useful in critical illness. Adjuncts like oxandralone promote anabolism. Resistance training has shown mixed results in the ICU setting but needs to be explored further with specific outcomes.

Summary Critically ill patients suffer from severe proteolysis during hospitalization as well as persistent inflammation, immunosuppression, and catabolism syndrome after discharge. High protein supplementation, ergogenic aids, anti-inflammatories, and anabolic adjuncts have shown potential in alleviating muscle loss and should be used in intensive care units to optimize patient recovery.

Keywords Critical care nutrition · Muscle mass · Protein synthesis · Proteolysis · Catabolism · Ergogenic supplements

Introduction

Managing nutrition in patients in the critical care setting is imperative to prevent catabolism and muscle loss associated with hospitalization. During hospitalization in the intensive care unit (ICU), patients suffer from acute severe proteolysis and muscle loss as well as disuse atrophy, with loss of nearly 20% of quadriceps femoris muscle mass within 10 days of ICU stay [1]. It is known that muscle loss is associated with a prolonged period of recovery and a decline in metabolic health [2]. ICU patients are also at risk for developing neuromuscular syndromes like critical illness poly-neuropathy and myopathy (CIPNM), which is another component of ICU-acquired weakness [3, 4]. Post-hospitalization, patients can also suffer from persistent inflammation, immunosuppression, and catabolism syndrome (PICS), which refers to prolonged low-grade inflammation and catabolism with resultant loss of lean body mass [5••]. Inflammation-induced cachexia develops secondary to an inappropriate interplay between cytokines, neuropeptides, stress hormones, and intermediary substrate metabolism [6]. This is similar to "inflammaging"—chronic low-grade inflammation associated with aging that contributes to the development of sarcopenia [7]. Guidelines by multiple societies recommend that all patients staying for more than 24–48 h in the ICU should be considered at risk for malnutrition, and early enteral nutrition should be encouraged in these patients [8, 9••]. Adequate nutrition in critically ill patients requiring prolonged mechanical ventilation has been shown to improve survival time and physical recovery at 3 months post-hospitalization [10]. However, cachexia and

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✉ Khushboo Gala
khushboo.gala@louisville.edu

[1] Department of Internal Medicine, University of Louisville, 550 S Jackson Street, 3rd Floor, Ambulatory Care Building, Louisville, KY 40202, USA

[2] Department of Gastroenterology and Hepatology, University of Louisville, Louisville, KY, USA

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muscle loss from PICS persist despite currently recommended intensive care unit (ICU) nutrition support. The inflammation-induced cachexia in PICS is analogous to that of patients with cancer, major burns, and sarcopenia and may benefit from similar interventions. High protein intake and anti-inflammatories along with anabolic interventions and nutritional rehabilitation are some measures that have been proposed to manage PICS [5••, 11, 12].

Ergogenic supplements are nutritional aids that improve exercise performance capacity or enhance training adaptations. These supplements have been long tested and trialed in athletes and bodybuilders, and retail sales for the same exceeded USD 5 billion in 2016, with a 6.7% growth in sales in 2018 [13]. Ergogenic aids are divided into supplements that improve muscle health and growth and performance enhancers. The International Society of Sports Nutrition (ISSN) has classified these into three categories based on the available evidence, as those with strong evidence to support efficacy with apparent safety, limited or mixed evidence to support efficacy, and little to no evidence to support efficacy and/or safety [14]. There are very few studies involving these supplements to benefit ICU patients to prevent catabolism [15]. We have reviewed ergogenic aids that improve muscle health which have been studied in athletes and bodybuilders and described their significance and possible utility in managing cachexia in the critical care setting.

High Protein Intake

Catabolic critical illness increases protein requirements by increasing obligatory protein loss and decreasing protein synthesis secondary to decreased efficiency of exogenous amino acid deposition into endogenous proteins [16]. A prospective study showed that when both protein and energy targets were reached in mechanically ventilated ICU patients, there was a 50% reduction in 28-day mortality, whereas only reaching energy targets was not associated with a reduction in mortality [17]. Adult medical ICU patients with higher daily protein intake during hospitalization have improved mortality at 3 months post-hospitalization (17% lower mortality for each 1 g/kg increase in daily protein delivery) [18•]. The recommendation for protein requirement for normal or hospitalized adults with normal metabolism is 0.8 g/kg/day [19]. Current American Society for Parenteral and Enteral Nutrition (ASPEN)/Society of Critical Care Medicine (SCCM) guidelines recommend protein requirements of 1.2–2.0 g/kg of ideal body weight per day for all ICU patients, with 2.0 g/kg/day as the minimum amount to provide to patients with severe burns and polytrauma and 2.5 g/kg/day as the minimum amount to provide to critically ill, permissively underfed morbidly obese patients [9••]. European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend 1.3 g/kg of ideal body weight per day for ICU patients [8, 9••]. A systematic review showed that nitrogen balance improves with increasing protein provision to an upper limit of 2.5 g/kg/day, which could be considered as a safe upper limit of protein requirement in critically ill patients [20]. It has been observed that many strength-training athletes consume even as much as 4 g/kg/day protein without reported adverse effects, and as much as 8 g/kg/day has been given for short periods without adverse effects [21]. Unfortunately, most ICU patients receive less than half of the most common current recommendation, 1.5 g/kg/day, for the first week or longer of their hospitalization [22]. A review of available data strongly shows that most ICU patients are provided calorie-rich, protein-deficient supplemental nutrition, when in fact they are protein-starved and overweight [16]. Going by current evidence, adequate protein intake in critical illness strongly improves clinical outcomes. Recently, the PROTINVENT study showed increased mortality in patients treated with high-dose proteins in the first 3 days, although patients with an overall low protein intake (0.8 g/kg/day) had the highest mortality risk [23]. Optimization of enteral nutrition to better accommodate a high ratio of protein to nonprotein calories may be the answer to meeting the protein targets without overfeeding. A recent trial showed that using a very high intact-protein formula (8 g/100 kcal) in overweight patients resulted in higher protein intake and plasma amino acid concentrations than an isocaloric standard high protein formula (5 g/100 kcal), without an increase in energy intake [24]. Other options to meet protein targets are using enteral protein supplements or supplemental amino acid solutions. Further well-conducted studies are needed to evaluate protein intake, timing, and route of administration in the ICU.

Whey

Whey protein is a dairy by-product and one of the most used supplements by athletes and sports nutrition product consumers. It has been found to be the "gold standard" protein in promoting myofibrillar protein synthesis (MPS), and this has been attributed to the high proportion of leucine along with rapid digestibility and high bioavailability within the plasma and muscle tissue [25, 26]. Whey protein has been shown to improve nutritional status and immunity in cancer patients and has been deemed a practical and cost-effective approach to cancer cachexia [27, 28]. Multiple trials including the PROVIDE study have shown that vitamin D and leucine-enriched whey protein resulted in improvements in muscle mass and also attenuated chronic low-grade inflammation in elders with sarcopenia [29–31]. A high whey protein and vitamin D-enriched supplement may be protective against sarcopenia, as it preserved muscle mass in obese older adults during a hypocaloric diet and resistance exercise program [32]. Similarly, adding a vitamin D and leucine-enriched whey protein supplement stimulated postprandial muscle

protein synthesis and increased muscle mass in healthy older adults and may serve as a mode for muscle preservation [33•]. It has also been demonstrated that leucine-rich whey protein have superior anabolic effects on muscle protein kinetics after fasting and can be beneficial during fasting-induced catabolic conditions [34]. Whey protein is widely available and affordable, with a relatively good safety profile. Using whey protein to combat muscle loss and chronic inflammation may be beneficial in critical illness during catabolism and in ICU patients post-hospitalization, particularly those at risk of sarcopenia.

Branched-Chain Amino Acids (BCAA) Including Leucine

Essential amino acids (EAA) are the building blocks of muscle and play an important role in MPS. Among the EAA, the BCAAs (leucine, isoleucine, and valine) have been found to be the most important [35]. BCAAs have been demonstrated to contribute to the formation of glutamine and alanine in the muscle, increase MPS synthesis rates in resistance-trained men, and attenuate exercise-induced muscle damage [36, 37].

Leucine is the most important branched-chain EAA and a key component of muscle protein. It stimulates MPS via the mammalian target of rapamycin (mTOR) signaling pathway and is also associated with the release of gluconeogenic precursors from muscle [38]. Both animal and human models have demonstrated that leucine ingestion drives and extends MPS [39, 40]. The leucine trigger or threshold hypothesis states that the muscle's intracellular leucine concentration needs to reach a given threshold to see a robust increase in MPS following protein consumption [41]. Leucine co-ingestion in elderly subjects who even consume daily protein intakes greater than or equal to the RDA has been shown to enhance rates of MPS [42]. In fact, low protein doses supplemented with a high (5.0 g) amount of leucine were shown to be as effective as high protein doses at stimulating increased MPS rates [43, 44]. The International Society of Sports Nutrition (ISSN) recommends that in healthy, exercising individuals, acute protein doses should contain 0.7–3 g of leucine and/or a higher relative leucine content, in addition to other EAAs [45]. It has been demonstrated that supplementation of leucine with EAAs is associated with improvements in body composition and nutritional status in many groups with muscle wasting illnesses, like chronic diseases and disuse atrophy [15, 46]. A recent systemic review supported use of leucine or leucine-enriched proteins (1.2–6 g leucine/day) to improve sarcopenia in elderly individuals [47]. Studies have also demonstrated the BCAA enriched diets or total parenteral nutrition (TPN) have benefited patients with cancer undergoing surgery, sepsis, and burns [48–50]. Rat models have shown that leucine-stimulated MPS and downstream signaling of the mTOR pathway at the level of S6K1 is impaired by acute metabolic acidosis, which is found in many patients in the ICU; hence, supplementation of leucine may help with ICU-associated muscle wasting [51]. There have been very few studies done on specifically leucine administration in the ICU setting. A recent randomized feasibility study demonstrated that administering a leucine-enriched EAA supplement in ICU patients was practical but posed significant barriers to recruitment and measurement of the chosen outcomes [52].

Hydroxyl β-Methylbutyrate (HMB)

HMB is a transamination product of leucine produced in skeletal muscle and has been shown to enhance MPS by its involvement in the mTOR pathway (similar to leucine), and also attenuates muscle protein breakdown in an insulin-independent manner [53, 54]. Since upwards of 20 g of leucine is metabolized into 1 g of HMB in muscle cells under normal physiologic conditions, HMB provides the potential to affect skeletal muscle turnover more efficiently [55]. HMB has been studied widely as an ergogenic supplement, and it has been shown that in healthy adults in conjunction with resistance training, HMB supplementation augments acute immune and endocrine responses and enhances training-induced muscle mass and strength [56–58]. A recent systematic review demonstrated that HMB may have a small positive impact on fat-free mass in athletes and no significant effect on body mass or fat mass [59]. In the elderly, HMB supplements have been proven to preserve muscle mass, but have conflicting evidence on muscle strength and functional performance [60–62]. There is some evidence that HMB reduces exercise-induced muscle damage, as evidenced by decrease in indirect markers like lactate dehydrogenase and creatine kinase [63]. HMB supplementation has also been shown to prevent the decline in LBM in healthy older adults during 10 days of bed rest [64]. Animal models have demonstrated that there are age-related reductions in conversions of leucine to HMB [65]; hence, supplementation especially to the elderly patients may be crucial. In the critical care setting, HMB supplementation remains questionable. A recent trial with daily HMB complex supplementation (3 g HMB, 14 g arginine, and 14 g glutamine) to ICU patients demonstrated that HMB did not inhibit muscle volume loss in the acute phase of ICU care [66]. Previously, a small trial by Hsieh et al. demonstrated anti-inflammatory and anti-catabolic effects and improvement in pulmonary function of HMB supplementation in COPD patients in the ICU [67]. Another trial in trauma ICU patients demonstrated improved nitrogen balance but no improvement in muscle proteolysis with HMB supplementation (although a biomarker with known limitations, 3-MH was used as the sole marker for muscle proteolysis) [68]. The value of HMB may not be in reducing the catabolism seen in critical illness, but in supporting muscle synthesis to offset muscle loss. HMB is available readily in enteral formulations enhanced with this substrate. In summary, HMB is worth further study for

management of post-ICU cachexia combined with rehabilitation, with potential use in PICS.

Creatine

Creatine is one of the most popular and effective nutritional supplements in athletes and bodybuilders [69]. Creatine supplementation increases availability of creatine and phosphocreatine in muscle, and supports anabolism by promoting the expression of growth factors like insulin growth factor (IGF)-1 and the phosphorylation of signaling proteins [70]. It has been proven to improve muscle mass and enhance exercise capacity in adolescents, adults, and even vulnerable elders and in conjunction with resistance training can result in greater adaptations in skeletal muscle than training alone [71–73]. There is conflicting data showing that creatine supplementation may attenuate muscle atrophy following immobilization and benefit exercise-related rehabilitation. Two trials from the early 2000s showed that creatine supplementation improved losses in muscle mass and strength during immobilization in healthy volunteers [74–76]; however, a recent trial opposed this and showed that creatinine loading before and after immobilization did not attenuate muscle loss [77]. It is unclear if creatine helps with preserving muscle loss, but it may still be beneficial in supporting muscle mass and strength regain during rehabilitation. There is also data showing that creatine may be beneficial in muscle disorders like dystrophies, inflammatory myopathies, and cytopathies [78]. There have not been any studies specifically targeting creatine supplementation in critically ill patients. The strategy of creatine supplementation to improve rehabilitation in injured athletes [79] may be replicated in an ICU and post-ICU cohort in future studies. A combination of 3–10 g/day of creatine and 3 g/day of HMB supplemented chronically has been shown to have positive effects on sport performance and body composition in athletes [80]; a similar combination may be useful in critical care given the ergogenic capabilities of both.

Vitamin D

Vitamin D has varied functions in skeletal muscle, including calcium homeostasis, cell proliferation and differentiation, prevention of fatty degeneration, protection against insulin resistance, and arachidonic acid mobilization [81]. Multiple studies and systematic reviews have found a significant association between low levels of vitamin D and muscle dysfunction and decline in physical performance [82, 83]. Vitamin D has been shown to improve muscle strength in athletes [84, 85]. Multiple nationwide cohort studies have shown an association between low levels of vitamin D and frailty in the elderly [86–88]. A recent review demonstrated that a combination of high-quality proteins, leucine, vitamin D, and n-3 PUFA may be beneficial in the prevention of sarcopenia [89].

There have been very few trials of vitamin D supplementation in the ICU. The largest one, the VITdAL-ICU (Effect of High-dose Vitamin D3 on Hospital Length of Stay in Critically Ill Patients with Vitamin D Deficiency) trial, showed no benefits on mortality in its primary analysis but demonstrated improvement in those patients with severe deficiency (< 12 ng/mL) in its secondary analysis [90]. A recent meta-analysis of these trials showed that vitamin D administration did not have a mortality benefit or improve clinical outcomes [91]. None of these trials have looked at muscle mass or strength as an outcome measure. Currently, the only society recommending vitamin D supplementation in ICU patients is ESPEN, which recommends supplementing severely deficient patients with levels < 12.5 ng/mL within the first week after ICU admission [8, 92]. However, deriving from its benefits in the elderly and on sarcopenia, vitamin D supplementation may play a useful role in alleviating muscle loss both during and post-critical care hospitalization.

Polyunsaturated Fatty Acids (PUFA)

Ω3-PUFAs like eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been shown to stimulate MPS via increased activation of the mTOR-p70s6k signaling pathway and reduction of insulin resistance and anti-inflammatory effects that support anabolic processes [93, 94•]. Animal models have demonstrated that fish oil, which contains a high percentage of PUFAs, stimulates anabolic signaling and muscle protein mass [95, 96]. Studies have shown that PUFA intake promotes muscle anabolism in healthy young and middle-aged adults as well as the elderly [93, 97–99]. Higher intake or increased plasma/RBC levels of omega-3 fatty acids (Ω-3 FAs) are associated with higher muscle mass, strength, and quality and physical performance [94•], and Ω-3 FAs are being studied as a low-cost, low-risk sports performance enhancer [100]. Ω-3 FA supplementation has been shown to augment improved muscle function and quality achieved by resistance training in older women, but not in men [101]. Supplementation with Ω3-PUFAs has been shown to attenuate sarcopenia in advanced cancer, aging, and chronic diseases [102–104]. Additionally, given their anti-inflammatory properties, PUFAs may have a role in protecting against inflammation-induced cachexia and PICS. According to a recent systemic review, a dose of 3 g/day of EPA + DHA is beneficial for muscle health in older adults [89]. Although there have been no trials on solely PUFA supplementation in critically ill patients, it appears to be a promising area, especially when combined with other supplements.

Anabolic Steroids

Anabolic steroids in supraphysiologic doses have been shown to increase bodyweight, fat-free mass, and muscle strength in

healthy people [105] and hence have been used and abused by bodybuilders and athletes [106]. However, the obvious method to counteract catabolism generated in the ICU is the use of anabolic therapies. Several anabolic adjuncts have been studied, especially in patients with burns who are known to have hypercatabolic responses to injury. One of the most efficacious of these is oxandrolone, a synthetic steroid with enhanced anabolic activity and minimal androgenic activity. In murine models of severe burn injury, oxandrolone-treated animals demonstrate improved organ function, attenuated inflammatory response, and accelerated wound healing [107]. Oxandrolone has been widely studied in burn patients and has been shown to decrease catabolism and weight loss, improve MPS and wound healing, and decrease mortality and length of stay in this cohort both during and post-hospitalization [108–110••]. Long-term supplementation of oxandrolone leads to improved lean body mass, bone mineral content, and muscle strength in burn patients [111]. Other anabolic steroids have also been found to improve lean body mass and muscle strength in various cohorts including patients with HIV, chronic obstructive pulmonary disease patients, and patients on hemodialysis [112]. Oxandrolone is an oral supplement and generally well tolerated, and although there are recommendations to monitor hepatic function during administration, rises in aminotransferases have been found to be transient [113, 114]. These factors certainly demonstrate an ease in administration. The timing of administration may be a little more controversial; however, initiating treatment after the initial inflammatory phase, in the so-called recovery phase of critical illness, may be most appropriate. This can be signaled by clinical improvement, absent need for organ support, and decreasing inflammatory markers. Small case series have used anabolic steroids with great success in patients with profound critical illness myopathy and weight loss who were already receiving appropriate nutritional support and physiotherapy [115]. Albeit controversial in the world of competitive sports, anabolic steroids may be one of the most promising therapies in post-ICU care.

Resistance Training

High-intensity resistance training has been shown to be very effective in enhancing muscle strength and performance in athletes [116]. Extensive research has been demonstrated that resistance training even in regular healthy adults increases muscle mass and MPS [117]. In addition, resistance training has been shown to restore bed rest-induced muscle loss and improve strength and in fact has been shown to prevent cardiovascular and skeletal muscle deconditioning during strict bed rest [118, 119]. Acute hospitalization in elderly patients leads to functional decline, but early exercise and rehabilitation protocols with resistance training have been shown to prevent atrophy [120]. Unfortunately, studies exploring early physical and occupational therapy in the ICU have had mixed results, with some showing improved length of stay and functional outcomes at discharge [121, 122], while other studies and meta-analyses show no change in these parameters [123–125]. Even aggressive post-ICU rehabilitation shows mixed results [126, 127]. The RECOVER trial used a multifaceted approach to post-ICU rehabilitation, including increased physical and nutritional therapy and information provision—none of which improved physical recovery or health-related quality of life, but improved patient satisfaction with recovery [127]. Studies looking at electrical muscle stimulation combined with rehabilitation have also not been effective [128, 129]. This might be because of several challenges faced while implementing these programs in critically ill patients—weaning sedation effectively, correct patient selection, inadequate nutritional delivery [130], and poor standardization with regard to timing of initiation. Another consideration before widespread use can be recommended is the overall cost-effectiveness of running these programs without proven improvement in functional outcomes. Participatory exercise is better than passive exercise, all of which is better than nerve stimulation; also in theory, early exercise may be beneficial—hence, resistance training in the ICU needs to be explored in terms of timing, patient selection, and therapy type.

Phosphatidic Acid (PA)

PA is a phospholipid that has been shown to stimulate the mTOR pathway via activation of the substrate S6 kinase and hence influence MPS in vitro [131–133]. However, there are conflicting results in human studies; a recent review analyzed 5 studies with PA supplementation in resistance-trained men and found mixed evidence of influence on muscle mass and strength, with 3 trials showing positive results and the latest trial showing no effects of PA supplementation [134, 135]. A trial that used lower than the standard dose of 750 mg of PA also failed to show results [136]. There have been no trials on PA in the elderly, patients with sarcopenia, or ICU patients. PA presents a potentially useful therapeutic option for management of cachexia but needs much further study to be recommended at this time.

Arginine

Arginine is a conditionally essential amino acid that has multiple functions with ergogenic potential. It stimulates secretion of growth hormone from the anterior pituitary due to suppression of somatostatin; it is one of the AAs involved in the synthesis of creatine and it augments nitric oxide production [137]. However, very few studies have examined arginine supplementation in humans on muscle metabolism and inconclusive results have been observed with respect to improvements in exercise performance and muscle mass [138, 139]. A

recent trial reported no improvement in muscle function with arginine supplementation during recovery following high-intensity resistance exercise [140]. Arginine supplements have controversial use as immune-modulating nutrition in the ICU, with current recommendations recommending use in surgical ICU, but not medical ICU patients [141]. Although its functions seem promising in the management of cachexia and muscle loss, more research is required before it can be recommended as a supplement for muscle preservation in critically ill patients.

Adenosine-5′-Triphosphate (ATP)

Adenosine-5′-triphosphate (ATP) is a purine nucleotide which serves as the primary source of intracellular energy and performs extracellular functions like increasing skeletal muscle calcium permeability and vasodilation. It is currently being investigated as an ergogenic aid, as chronic ATP supplementation minimizes exercise-induced drops in ATP levels as it increases the capacity of erythrocytes to synthesize ATP without increasing resting concentrations in the plasma [142]. Human trials thus far have focused on muscular power and post-exercise hemodynamic and autonomic parameters during single bouts of exercise and have found positive results [142, 143]. Only one trial has looked at chronic (12 weeks) supplementation during a resistance-training program in resistance-trained populations and found that supplementation may enhance muscular adaptations [144]. Given the limited data, it is prudent to wait for more studies and trials on different populations before attempting to supplement ATP in the ICU population.

Other Considerations

Several anabolic adjuncts are under study for patients with hypercatabolic states and cachexia. These include intensive insulin therapy, propranolol, testosterone, metformin, GLP-1, and PPAR agonists. Intensive insulin therapy has been shown to be protective for ICU-acquired weakness, both from achieving euglycemia and insulin-mediated mRNA expression of glucose transporter-4 [145]. Propranolol reduces burn-induced proteolysis and increases muscle anabolism and thus can be used as an anabolic adjunct [146]. Testosterone acts as an anabolic stimulus to skeletal muscle as is evidenced by abuse by bodybuilders, and trials have used them in patients with burns to decrease catabolism with promising results [147]. By inducing adenosine monophosphate-activated protein kinase (AMPK), metformin has been shown to inhibit the production of reactive oxygen species and pro-inflammatory cytokines and may be protective in critical illness [148]. GLP-1 agonists are also being explored in the ICU, given that GLP-1 has positive actions on the myocardium and vasculature as well as improving glycemic control with a low risk of hypoglycemia [149]. Activation of PPAR-γ may attenuate proinflammatory cytokines and apoptosis and hence be used in catabolic states [150]. These therapies hold some promise in critical illness.

Conclusion

Survivors of critical illness are faced with severe muscle loss and catabolic processes, both during and after their stay in the ICU, which leaves them with a reduced quality of life post-hospitalization. Several lessons can be learned from athletes and bodybuilders and extrapolated to improving muscle mass in critically ill patients. High protein intake, with a minimum goal of 2.0 g/kg/day, is key, using a whey-containing protein source early in the acute and immediate post-acute phases, and then adding HMB, creatine, or BCAAs with resistance training in early recovery might be an optimum solution. Anti-inflammatory agents like PUFAs may be used to reduce inflammation in early phases through to recovery phase. Other anabolic interventions like steroids may be used as adjuncts in the recovery phase. Many interventions like ATP, PA, PPAR agonists, or GLP-1 are yet in the earlier phases of research and not ready for widespread use in critically ill patients.

Athletes and bodybuilders are afforded the opportunity to focus on a singular issue—building muscle mass, strength, and function—and hence, results obtained in this cohort are dramatic. Intensivists have to manage multiple aspects of critical care (multiorgan failure, sepsis, metabolic derangements, etc.), and their attention and priorities become divided. Consequently, although important, nutrition and prevention of muscle loss too often is assigned a lower priority. This problem is inconclusive studies for many of the supplements and ergogenic aids in the ICU. Trials with these supplements have been designed with outcomes like ICU and hospital length of stay, mortality, and infection but not as part of an aggressive strategy to promote muscle mass and function. Other factors contributing to inconclusive results from these trials include patient heterogeneity and broad patient selection criteria, disparate timing of interventions, imprecise objective parameters and study endpoints, and evaluating complex interventions which are difficult to execute in an ICU setting. Whether aggressive nutritional support and use of supplements is actually utilized may be more a function of the culture, leadership, and values of the ICU team of physicians, and how much priority they place on these issues. With more research yielding definitive results, and incorporation into guidelines and institutionalized protocols, the lessons learned from athletes and bodybuilders may be incorporated to improve outcomes for survivors of critical illness.

Compliance with Ethical Standards

Conflict of Interest Khushboo Gala declares that she has no conflict of interest.

Viral Desai declares that he has no conflict of interest.

Nanlong Liu declares that he has no conflict of interest.

Endashaw M. Omer has received compensation from AbbVie for service as both an educational consultant and a guest speaker.

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Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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