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Role of Omega-3 Supplementation in Clinical and Athletic Populations

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Abstract: ***Omega-3 fatty acids may play a crucial role in muscle sparing by enhancing muscle protein synthesis and reducing proteolytic breakdown, ultimately supporting lean muscle mass and strength in athletes, particularly those engaged in resistance training. Their antioxidant and anti-inflammatory properties help mitigate post-exercise inflammation, reduce reactive oxygen species (ROS) production, and lessen the severity of delayed onset muscle soreness (DOMS). Omega-3s also influence key biochemical markers of muscle damage, such as lactate dehydrogenase (LDH) and creatine kinase (CK), and activate the mTOR signalling pathway essential for muscle protein synthesis. Additionally, they enhance insulin and amino acid sensitivity in muscle cells, aiding in nutrient retention post-exercise. Given the low bioavailability of omega-3 polyunsaturated fatty acids (PUFAs), fish oil supplementation is often recommended. However, most studies to date have been conducted in amateur athletes or general populations, with a lack of focused research in elite sports contexts. Long-term clinical trials are needed to establish evidence-based guidelines for omega-3 intake to optimize athletic performance and muscle health. This paper touches upon the potential implications of omega-3 that can be followed in sports.***

Keywords: Omega-3, Muscle protein synthesis, sarcopenia, athletes, recovery

1. Introduction

Muscle sparing is a phenomenon in which the body uses carbohydrates and fats as primary fuel sources to protect protein for other essential functions, such as bodybuilding, muscle maintenance, and repair, rather than using it for energy, thereby preventing muscle wasting. Muscle strength has been a determining factor in injuries, fractures, and falls in general and the geriatric population [36], while in athletes, it is a major performance-determining factor, particularly in resistance athletes [32],[33],[37].

Age-related muscle loss and decline in musculoskeletal health are significant concerns in aging populations, where there remains a fear of falls, fractures, and hospitalization. The loss of muscle protein brought about by increased protein breakdown and decreased protein synthesis causes muscular atrophy in people of all ages [34],[39]. Physical exercise and protein supplementation are considered preventive measures against the risks of sarcopenia [3]. Reports show that omega-3 increases muscle size, reduces muscle loss, and prevents mitochondrial respiration from declining when muscles are not being used [34]. A progressive and widespread skeletal muscle condition, sarcopenia is linked to a higher risk of negative consequences such as falls, fractures, physical impairment, and death [31].

The polyunsaturated fatty acid family includes omega-3 fatty acids. The very long-chain fatty acids docosahexanoic acid (DHA, 22:6n-3) and eicosapentanoic acid (EPA, 20:5n-3) are thought to be the most significant, while there exist fatty acids of other lengths [20]. Consuming n-3 PUFAs—mainly EPA and DHA—has attracted attention as a dietary approach to healing muscle injury [24]. Initially, omega-3 fatty acids have been shown to help prevent cardiovascular disease and are known for their anti-inflammatory properties; now, it has been demonstrated that LCn-3s (long-chain omega-3s) also provide protection against proteolysis and muscle wasting [1]. Researchers identified a positive effect of n-3 fatty acids on muscle protein synthesis and breakdown in both subjects with cancer cachexia and healthy volunteers. It showed a positive impact on muscle maintenance and protein synthesis [1], [2].

Out of the three n-3 fatty acids, ALA, DHA, and EPA, animal-derived sources high in DHA and EPA are mostly recommended. Fish oil supplementation has been shown to increase muscle protein synthesis and improve muscle strength and functional capacity in elderly individuals and strength-training athletes [3]. Blood markers such as creatine kinase, interleukin-6, lactate dehydrogenase, and many others demonstrate that muscle damage brought on by unusual eccentric exercises causes several skeletal muscle changes, such as the release of muscle enzymes into the blood, a decrease in muscle strength, an increase in muscle soreness, and the activation of the inflammatory process and oxidative stress [25].

2. Physiology behind Omega-3 and muscle protein

The exact mechanism by which Omega-3 increases MPS is not fully understood. However, it is reported that n-3 supplementation increases anabolic signaling pathways (e.g., the mTOR pathway). The mechanism of omega-3 and skeletal muscle mass, so far understood, states that "The incorporation of EPA and DHA into the membrane phospholipids of the sarcolemma and intracellular organelles is the main way that omega-3 fatty acids have a beneficial effect on skeletal muscle mass. Increased rates of muscle protein synthesis are associated with EPA and DHA enrichment in these membrane phospholipids [34]." A key regulator of skeletal muscle metabolism, the mechanistic target of rapamycin (mTOR) pathway integrates signals from hormones, nutrients, and mechanical stimuli to determine whether muscle protein breakdown (MPB) or muscle protein synthesis (MPS) predominates [42]. Muscle development and sparing are facilitated by the stimulation of downstream effectors such as p70S6 kinase and 4E-BP1 by activation of the mTOR complex 1 (mTORC1) [42],[43]. These effectors encourage translation initiation and protein synthesis. Omega-3 supplementation increases the phosphorylation of mTOR downstream targets, leading to higher MPS rates and lean mass preservation, as shown in human trials (Smith et al., 2011) [34],[41]. Additionally, omega-3s boost mitochondrial function, decrease chronic inflammation by reducing cytokines such as TNF-α and IL-6, and improve insulin and IGF-1 signalling, all of which together reduce the breakdown of muscle proteins [5] Implies that omega-3 fatty acids may aid muscle sparing by activating the mTOR pathway, which is essential for preventing sarcopenia and maintaining lean body mass in athletes [41].

3. Omega-3 supplementation in normal population

In addition to maintaining cell membrane fluidity, reducing inflammation, and supporting cardiovascular health, several studies have examined the benefits of omega-3 supplementation for muscle mass and strength [6],[7]. The studies were conducted in older and younger populations to test whether it can contribute to treating or preventing sarcopenia [9] or other clinical conditions, such as cancer [10].

3.1 Omega-3 and Sarcopenia

In a study in which 12 volunteers received 3.9 g/day of n-3 (2.7 g EPA and 1.2 g DHA) for 16 weeks in an open-label intervention, there was a slight, non-significant increase in myofibrillar protein synthesis without exercise. At the same time, the same group showed a significant increase in protein synthesis in the post-exercise and post-absorptive state [6]. A 6-month RCT in older adults (~71 years) found that 4 g/day of n-3 PUFA significantly improved muscle strength compared to placebo (corn oil), with no effects on mitochondrial function or exercise responses [7]. In a 6-month study of 200 subjects, those receiving 4 g/day fish oil showed significant gains in muscle mass, strength, and physical performance, along with reduced triglycerides and increased HDL. At the same time, total cholesterol and LDL remained unchanged [8]. An 18-week study in older adults (mean age ~70 years) found that 3 g/day of fish oil, combined with resistance exercise, improved muscle quality and isometric torque in women but not in men. n-3 PUFA also lowered plasma triglycerides in both sexes, with no changes in other markers [9].

3.2 Omega-3 and Cancer

In an 8-week study of 200 cachectic pancreatic cancer patients, those receiving an n-3–enriched protein supplement showed increased plasma EPA levels, weight gain, and lean body mass, improving quality of life. In contrast, the control group showed no such effects [10]. In a 4–5 week RCT in 40 stage III NSCLC patients, those receiving an n-3 PUFA–enriched supplement showed better preservation of body weight and fat-free mass, along with higher energy intake and improved physical function and quality of life [11]. A review article also suggested that supplementation with EPA and DHA has shown promise in treating cachexia in patients with various cancer types. It can help stabilise weight, enhance lean mass, improve inflammatory markers, and improve quality of life [12]. Not only in cancer cachexia but also in routine young and older populations, n-3 PUFA has shown a positive impact on muscle maintenance. Both in-vivo and in-vitro studies have shown a significant increase in protein synthesis after an 8-week supplementation. A similar 6-month supplementation (3.36 g/d) has shown a substantial increase in muscle mass and strength [13].

4. Omega-3 supplementation in athletic population

In athletes, Omega-3 PUFAs are said to help in 'recovery' if athletes in the terms of reduction in post-exercise muscle damage [35] and improved skeletal muscle performance which includes modulation in rate of muscle protein synthesis, muscle mass, maximum torque development and biomarkers of muscle damage, improvements in joint flexibility and range of motion, reduction in muscle swelling or soreness.

4.1 Omega-3 Supplementation in Performance

A 12-week study with omega-3 fatty acid supplementation at 2234 mg of EPA and 916 mg of DHA daily showed an increase in the omega-3 index. When this supplementation was given to endurance athletes, it led to increased VO2peak and improved running economy [18]. In a study, 24 runners were tested for changes in performance with supplementation of chia seed oil, and the results were negative for performance improvements [28]. In a group of trained males, 8 weeks of supplementation with 0.56 g EPA and 0.14 g DHA did not affect power output. Still, improvements in cycling economy and an elevation in the omega-3 index were observed. A systematic review suggests that FOS affects endurance athletes' oxygen efficiency but not performance [27].

A 2018 study measured muscle strength in association with n-3 PUFA supplementation (2g/day) and observed an increase in peak torque within 90-150 days; however, the study was conducted in older female athletes, which may not be particularly relevant to the athletic population [14]. Fish oil supplementation (FOS) of 4 g/day [3.85 g EPA+DHA] in a 10-week resistance training trial has shown better results in measures of relative and absolute RM during bench press and back squats [26].

4.2 Omega-3 Supplementation in Muscle damage, and recovery

Eccentric exercises led to decreased range of motion and myofibrillar damage, whereas the omega-3-supplemented group showed an increase in elbow range of motion (ROM)

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that persisted for 3 days. The studies claim that EPA and DHA supplementation benefits joint flexibility, maximal voluntary isometric contraction torque after eccentric exercise [13]. Taking 3 g/day n-3 PUFA supplements for seven days reduced post-exercise muscle damage and soreness, according to a study on muscle healing and soreness following eccentric biceps curls [13]. A study found that 4 weeks of supplementation with 3 g/day of n-3 PUFA mitigates the pain response to exercise-induced muscle damage (EIMD) after a single high-intensity exercise session. However, there were no differences in blood markers, such as creatine kinase (CK) or IL-6, that would indicate muscle damage [22]. A 4-week study found that EPA (600 mg/day) and DHA (260 mg/day) supplementation reduced CK levels and improved range of motion, with no change in IL-6 levels [23]. In trained collegiate athletes, 3 days of Antarctic krill oil supplementation after resistance exercise lowered CK levels at 24 and 48 hours post-exercise, though other results were mixed [24]. A 2023 study conducted with untrained young men for 6 weeks investigated the effects of fish oil supplementation alongside a strength-training protocol. It showed that the combination reduced muscle injury and inflammation caused by strength training [25]. A study found that the full benefits of FOS for muscle recovery can be achieved when combined with other nutrients that affect skeletal muscle remodelling, such as whey protein and vitamin D [26]. Ten weeks of DHA+EPA supplementation in endurance athletes led to lower concentrations of markers of inflammation and muscle soreness. Still, they did not improve the strength deficit after a muscle-damaging eccentric exercise training session [29]. In a study, 24 healthy men were randomly assigned the EPA+DHA supplement and were made to perform eccentric bouts. It was observed that improvements in maximal voluntary contraction (MVC) torque and ROM were greater than in the placebo group [30].

5. Omega-3 dosage for muscle preservation

There is ample evidence of the positive effects of n-3 PUFAs, but the dosages remain unknown. The duration of supplementation is also essential for observing noticeable changes. The dosages reported in various research articles and tested in randomized controlled trials range from 1-4g/day of omega-3, and these dosages have been shown to preserve muscle function in both sarcopenia and cancer patients [10],[11],[13].

In athletes, a study provided athletes with various (2g, 4g, 6g) amounts of fish oil per day after a vigorous lower-body eccentric resistance exercise. It was found that the group taking 6g/day of fish oil (2400 mg/day of EPA and 1800 mg/day of DHA) showed less perceived muscle soreness rating at all post-exercise time points, and it enhanced recovery and statistically seemed to show lower levels of markers of indirect muscle damage [14]. However, many other studies have either shown a decrease in perceived soreness at lower doses (0.8 g/day) or an increase in perceived soreness at 2g/day when given for 21 days, compared to placebo [15]. Studies using 3 g/day for 7 days and 2.7 g/day for 30 days showed reduced muscle soreness, suggesting that fish oil doses of 1.8–6 g/day may aid recovery, though the evidence remains limited and inconsistent [16]. A narrative review indicates that the effect of n-3 PUFA on muscle cells has increased continuously for 4 weeks without a plateau, suggesting that>4 weeks of n-3 supplementation would unleash its benefits [19]. A 2020 study found that supplementation duration affects outcomes, with positive effects becoming more consistent after roughly 6–8 weeks [17]. The same is true for EPA/DHA dosage: levels above 1.5–2.0 g/day yield superior results [17]. Lastly, it seems that amateurs experience the positive effects more frequently; therefore, in general, amateurs may need smaller doses for shorter durations to achieve improvements [20].

Table 1: Comparative analysis of the effect of Omega-3 supplementation in clinical and athletic populations

Analysis of the effect of Omega-3 supplementation Parameter	Athletic population	Clinical population (Older Adults, Sarcopenia, Cancer)
Effect on Muscle Protein Synthesis (MPS)	Mixed results; some improvement when combined with training; no consistent direct increase in MPS	More substantial evidence; increases MPS, especially in older adults and cachectic patients.
Effect on Muscle Mass	Minor or inconsistent improvements; benefits mainly when combined with resistance exercise	Significant improvements reported in sarcopenia and cancer patients after 4–6 months of supplementation
Effect on Muscle Strength	Improvements are seen primarily in trained and resistance-training individuals; some studies show no effect.	Consistent improvements in muscle strength in older adults and clinical populations
Effect on Performance	Improved VO_2 peak and running economy in endurance athletes; no substantial effect on actual performance outcomes	Not applicable; clinical trials focus on functional ability rather than sport performance.
Effect on Recovery / Muscle Damage	Strong evidence of reduced soreness, better ROM, and reduced CK in several studies; benefits appear in 1–8 weeks.	Recovery from muscle wasting rather than acute EIMD; improvements in inflammatory markers and quality of life
Anti-Inflammatory Effect	Lowers IL-6 and CK in some studies; reduces DOMS and swelling	Reduces chronic inflammation; improves markers in cancer cachexia and the elderly
Study Outcomes (Overall)	Mixed and inconsistent; depends on dosage, training, sex, and study design	Stronger, more consistent evidence supporting muscle preservation and improved physical function

6. Future directions and research gaps

There were no discernible impacts on muscle force, training adaptation, or endurance performance [26]. Whether FOS raises lean body mass more than RET does on its own is unknown [28], [47]. So far, FOS has shown effects on

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reducing EIMD, but the evidence is not conclusive [48]. It also shows effects on other physiological stressors; however, it does not prove its precise role in preserving muscle mass [27]. Omega-3 may be a sports supplement and post-exercise recovery aid that enhances performance by maintaining and strengthening skeletal muscle mass and strength. However, there is insufficient data to draw firm conclusions regarding the possible effects of omega-3 on sports performance and post-exercise biomarkers in physically fit individuals [13],[50] due to small sample sizes [13] and varied dosages [49]. Many studies reported mixed results, which may be due to differences in study design, population selection, intervention duration, and dosage across studies [44],[45]. Studies in clinical settings also suggest that more clinical trials and data are needed to support the beneficial role of omega-3 [46]. A study indicated no increase in muscle protein synthesis (MPS) or skeletal muscle composition despite a twofold increase in n-3 supplementation [47], though there were positive effects on anabolic signalling pathways, including PKB activity [48]. However, before using nutritional supplements in clinical therapy, further well-planned experiments are required [45]. Considering the general or athletic population, some questions can be regarded as like: Does the effectiveness of omega-3 fatty acid intake on skeletal muscle depend on sex, and is there a dose-response relationship between omega-3 fatty acid intake and physiological outcomes [34], and what type of n-3 works better?[38]

7. Conclusion

This narrative review compiles information on the effects of omega-3 fatty acids on muscle preservation in both clinical and athletic populations. This review presents both positive and negative studies in both populations. In clinical settings, FOS has shown significant positive results in the majority of the articles reviewed. In the athletic population, there are fewer RCTs than in the general population, and results have been mixed. However, large-sample RCTs in both clinical and athletic populations, examining dosages and durations, and investigating the effects of FOS and differences in impact between endurance and resistance athletes, are yet to be conducted.

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