Check for updates

Scandinavian Journal of Medicine & Science in Sports

WILEY

ORIGINAL ARTICLE

Effects of Protein Supplementation During Early Rehabilitation on Muscle Volume and Function After Acute Muscle Strain Injuries: A Randomized Controlled Trial

Kenneth H. Mertz[1] | Helene H. Sorensen[1] | Charlotte Lorentz[1] | Elena Johansen[1] | Niels U. Fredskild[1] | Mette With Wulff[1] | Rene B. Svensson[1] | Maria B. Kjaer[1] | Frederik Hvid Linden[2] | Michael Kjaer[1] | Monika L. Bayer[1]

[1]Department of Orthopedic Surgery M, Institute of Sports Medicine Copenhagen, Copenhagen University Hospital, Bispebjerg Frederiksberg, Copenhagen, Denmark | [2]Department of Radiology, Copenhagen University Hospital, Bispebjerg Frederiksberg, Copenhagen, Denmark

Correspondence: Kenneth H. Mertz (kenneth.hudlebusch.mertz@regionh.dk)

Received: 10 December 2024 | **Revised:** 13 March 2025 | **Accepted:** 14 March 2025

Funding: This work was supported from Team Danmark, The Novo Nordisk Foundation, and The Danish Ministry of Culture. Further, the protein supplements were kindly sponsored by Arla Foods.

Keywords: aponeurosis | isokinetic | MRI | muscle injuries | whey protein

ABSTRACT

Muscle strain injuries are common in sports, with a high recurrence rate and loss of muscle mass. Whether protein supplementation can counteract the detrimental effects of strain injuries during rehabilitation has not been explored. We investigated the effects of protein supplementation during early rehabilitation of acute strain injuries on muscle volume and function. Fifty recreational athletes were enrolled for a double-blinded, randomized controlled trial comparing the effects of twice-daily whey protein supplementation to isocaloric placebo during early rehabilitation after acute hamstring or calf strain injuries. The primary outcome was changes in muscle volume during the 3 months of intervention, assessed by magnetic resonance imaging. Secondary outcomes included muscle strength, time to return to sport (RTS), and aponeurosis volume. Long-term changes were assessed 12 months after the injury. Muscle volume decreased in the injured muscle compared to the contralateral healthy muscle during the intervention [−9.4% (−13.5% to −5.3%), $p < 0.0001$], and persisted at 12 months. No effects of protein supplementation were observed. Further, there was no effect of protein supplementation on muscle strength or RTS. There was a persistent increase in aponeurosis volume associated with the injured muscle at 3 months [sixfold enlarged, +17.3 cm^3 (+8.3 to 26.3 cm^3), $p = 0.0005$] and 12 months [fivefold enlarged, +10.4 cm^3 (5.3–15.4 cm^3), $p = 0.0003$], but it was unaffected by protein supplementation. In conclusion, muscle strain injuries cause persistent atrophy of the injured musculature and enlargement of the muscle aponeurosis, which was not counteracted by protein supplementation during the rehabilitation period.

Trial Registration: Clinical trial number: NCT04100161; Clinicaltrials.gov

1 | Introduction

Muscle strain injuries constitute a major problem in recreational and professional sports, contributing substantially to injury absence [1, 2]. Despite intensive research on muscle strain prevention, injury rates in professional sports such as soccer are still prominent and, if anything, increasing in incidence [3]. Also, in recreational sports, injury incidence is high, especially in sport activities with rapid/explosive movements. In rapidly growing recreational activities such as paddle tennis and pickleball, muscle injuries are among the most prominent types of injuries amateur players sustain [4, 5]. Further, another complicating factor regarding muscle strain injuries is the high risk of re-injury, especially during the initial phase of return to play [1, 3, 6].

© 2025 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

Despite extensive rehabilitation, muscle strain injuries typically induce a seemingly permanent decrease in muscle volume of the injured muscle [7, 8]. While muscle strength is initially decreased in the injured muscle group in some studies, muscle strength seems to normalize within 6 months after the injury [8, 9]. The normalization of muscle strength without concurrent regain of muscle volume of the injured muscle could be due to compensatory hypertrophy of agonist muscles [7], although this is not a consistent finding [9]. However, as the majority of re-injuries seem to occur in the same location as the index injury [6], the local muscle atrophy might potentially contribute to the high re-injury risk.

A strain injury is associated with a significant acute reduction in muscle loading due to the tissue damage as well as the associated pain during movement. Hence, the injury-induced atrophy could be partly related to local disuse. In healthy immobilized individuals, muscle volume has been shown to decrease by 4% and 10% within 5 and 14 days of disuse, respectively [10–13]. These data suggest a rather rapid loss of muscle mass. Importantly, young healthy individuals regain muscle mass to preimmobilization levels after a 4-week re-training period [14]. In contrast, strain-injured individuals showed no recovery of muscle mass despite extensive rehabilitation and full participation in sports [8]. The lack of recovery following significant muscle atrophy indicates persisting damage to tissues involved in the injury other than just the initial reduction in mobilization following a strain injury.

Muscle atrophy in response to disuse can in some situations be counteracted by protein supplementation [15, 16], although the beneficial effect of protein on the preservation of muscle mass is not a consistent finding [17, 18]. In healthy muscle tissue, sufficient dietary protein intake is a well-established determinant of training-induced hypertrophy [19, 20]. The optimal daily protein intake for training adaptations in healthy tissue is debated, but most available evidence suggests that the majority of the effects of protein supplementation occur up to ~1.6 g/kg bodyweight (BW) per day [19, 20]. A daily protein intake of 1.6 g/kg BW is substantially more than the average consumption in Danish adults [21]. In injured athletes, some reports have even suggested that a protein intake of as much as 2.5 g/kg BW per day is required in order to offset injury-induced muscle atrophy [22].

Recent studies have found substantial thickening of the muscle aponeurosis structure and changes in corresponding muscle fascicle function in patients with a history of muscle strain injuries [23–25], which could potentially be linked to the high risk of re-injury observed after muscle strain injuries. To our knowledge, no evidence exists on the causal link between changes in aponeurosis structure, function, and losses of muscle volume. We speculate that the enlarged aponeurosis is due to a suboptimal healing of the muscle-aponeurosis interface, which is likely linked to the reduced muscle volume. Hence, if protein supplementation has positive benefits on preservation of muscle volume, this could be mediated by improved healing of the muscular part of the muscle-aponeurosis interface and consequently less thickening of the aponeurosis after the injury.

The effect of protein supplementation on the preservation of muscle volume and strength during rehabilitation after an acute muscle strain injury has not been studied, and we therefore tested protein supplementation after strain injuries. We hypothesized that muscle strain injury would lead to a loss of muscle volume of the injured muscle both in the short term (3 months post injury, primary outcome) and long term (12 months post injury, secondary outcome), and that protein supplementation during early rehabilitation of acute strain injuries would counteract the loss of muscle volume, thereby potentially improving function and shortening the time for return to sport (RTS) in physically active individuals.

2 | Methods

2.1 | Participants

This study enrolled 50 sports-active individuals with an acute muscle strain injury in the calf or hamstring musculature. Included patients were recreationally active or competing at the local level (Tier 1–2) [26]. Calf and hamstring musculature have previously been found to have comparable rates of recovery and loss of muscle volume after strain injuries [8]. Patients reported to the staff members within 48 h of an acute muscle injury (defined as a sudden onset of pain and being unable to continue sports participation). Upon arrival at the hospital, patients were clinically examined and diagnosed before inclusion in the study. Participants were included based on clinical history (sudden onset of pain during explosive movement), pain on palpation of the suspected injured muscle(s), and a clear defect at the muscle-connective tissue (aponeurosis) interface on an ultrasound scan. Exclusion criteria included claustrophobia (or other contraindications to MRI scans), daily intake of nonsteroidal anti-inflammatory drugs (NSAIDs) within 3 months prior to the strain injury, smoking, type I or type II diabetes, and rheumatic diseases or organ dysfunctions. The study was approved by the local ethics committee (The Regional Ethical Committee, ref. H-19027293) and registered at clinicaltrials.gov (NCT04100161). All participants gave written informed consent to participate. Study data were collected and managed using REDCap electronic data capture tools [27, 28].

2.2 | Nutritional Supplementation

Upon inclusion in the study, patients were randomized to receive either whey protein supplementation (Lacprodan DI-3091, Arla Foods Ingredients, Denmark) or an isocaloric placebo (maltodextrin, Belgosuc, Belgium) twice-daily throughout the 12-week rehabilitation protocol. Randomization (minimization) of participants was performed using the MinimPy 2 software [29] stratifying the participants by muscle group (hamstring or calf) and sex.

Upon group allocation, patients received the respective supplements and were instructed to consume 20 g of the supplement mid-day and in the evening before bedtime, resulting in a daily supplement dose of 40 g. On training days, patients were instructed to ingest the mid-day supplement in close relation to the rehabilitation session (either before or after). The protein dose was chosen expecting an average BW of ~80 kg and a maximal stimulation of muscle protein synthesis at ~0.24 g/kg BW [30]. Patients were instructed to start supplementation 2 days after the injury. Adherence to the supplements was noted using daily online questionnaires. To control for potential over-reporting of supplementation adherence, participants were initially provided with half the amount of supplement needed for the intervention period.

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Both supplements were provided in taste-neutral variants. To investigate whether the blinding of the supplements had been successful, patients were asked which group they suspected having been allocated to after completing the intervention period. 53% of participants guessed the correct supplement, with no difference between groups ($p = 0.48$) indicating successful blinding. Participants remained blinded until completing the 12-month follow-up.

2.3 | Dietary Assessments

Patients weighed their dietary intakes for four consecutive days, always including two weekend days (e.g., Saturday to Tuesday) and noted their intakes in online food logs (VITAKOST, MADLOG ApS). Dietary assessments were performed in Week 4 or 5 of the intervention. Patients were instructed not to include their daily supplements in the food logs. Total protein and energy intakes were then added by multiplying the compliance to the supplement by the dietary content of the supplement.

2.4 | Rehabilitation

All patients initiated rehabilitation 2 days after injury onset. The rehabilitation protocol was a modified version of a previously published program after strain injuries [8, 31]; the full rehabilitation protocol can be found in Table S1. Briefly, rehabilitation was designed as a four-step regimen: daily repeated stretching (Days 1, 2), daily isometric loading with increasing load (Weeks 1–4), dynamic loading with increasing resistance three times weekly (Weeks 5–8), and functional exercises combined with heavy resistance training three times weekly (Weeks 9–12). Patients reported to the research facilities once-weekly for supervised rehabilitation and completed the remaining training sessions unsupervised. Rehabilitation adherence and external load were recorded in online training diaries sent out after each week. During full COVID-19 lockdowns, weekly supervision was conducted via an online video platform. Return to sports participation was allowed at any point during the rehabilitation regimen when participants were pain-free during the exercises as well as the sports-specific tasks such as repeated sprints and jumps, and this was decided in collaboration with the staff supervising the rehabilitation. The first time of full participation in sports was recorded. Staff supervising the rehabilitation were blinded to the supplementation group of the patients.

2.5 | Muscle Volume and Strength

Total muscle volume was assessed using magnetic resonance imaging (MRI) at baseline, 3 months post injury, and 12 months post injury. The baseline scan was performed as soon as possible after inclusion in the study (mean days after injury ± SD; 7.3 ± 2.6 days).

All patients were MRI-scanned (Philips Ingenia Ambition 1.5T scanner, software version 5.6.1.2, Netherlands) in the first week after the injury, 3 months post (after the rehabilitation period, at least 48 h after the last training session), and again 12 months post injury. The patients were scanned in a supine position with their feet placed against a plastic foot plate. A coronal isotropic 3D T1-weighted sequence (voxel size $0.7 \times 0.7 \times 0.7\,mm^3$) of the calf (calf strain) or hamstrings (hamstring strain) was recorded and used to measure muscle volumes. ITK snap open-source was used for manual muscle segmentation and volume measurement. Trained personnel blinded to the group allocation (Protein/Placebo) of the patients performed the measurements. The same technician performed all segmentation for the individual patients, and subsequent quality control was performed to ensure comparability between technicians. Both the injured and healthy legs were analyzed. For manual segmentation, bony landmarks were used to ensure the exact same length at the acute scan, the 3- and 6 month post injury scans. For orientation on calf scans, the epiphyseal plate of the fibula head was taken; for hamstring scans, the epiphyseal plate of the femur head was taken. Further, for calf scans, segmentation started at the distal site on the first slice on which the medial gastrocnemius was visible and continued proximally to the last slice on which the medial gastrocnemius still was visible. For hamstring scans, segmentation started at the proximal site on the first slice on which the semitendinosus was visible and continued distally to the last slice on which the semitendinosus still was visible.

Aponeurosis thickness was measured based on the signal from the hematoma determined on the STIR sequence recorded on the acute scan. The aponeurosis thickness was measured on both the healthy and injured sites; potential displacements between the two legs were corrected for based on the position of the epiphyseal plate.

Muscle strength was assessed 3- and 12 months post injury. Eccentric and concentric muscle strength was measured in an isokinetic dynamometer (Biodex Multi-Joint System 4, Software version 4.63, Biodex Medical Systems, Shirley NY, USA). Patients performed 5-min warm-up exercise on a bike at a self-selected pace. Assessments were performed in the passive mode and measured at an angular velocity of 60°/s. For hamstring tests, participants were seated with 85° hip flexion, and hamstring strength was assessed from 100° to 20° knee flexion (0° being full extension). For calf tests, patients were seated with 70° hip flexion and full knee extension, and plantar flexor strength was assessed from 20° plantar flexion to 10° dorsiflexion. For both eccentric and concentric tests, sets of five reps were performed, including one submaximal trial set to familiarize the patients with the test, followed by two maximal sets. Sets were separated by 75 s of rest. Data were sampled in the software provided by the manufacturer. The peak torque achieved during the maximal effort sets was used for further analysis.

2.6 | Statistics

All analyses were performed according to a modified intention-to-treat principle, including all participants who returned for the 3-month measurements in the analysis, irrespective of adherence to the training and supplementation. For the primary outcome, the analysis was also performed per protocol, including only patients with training and supplementation adherence ≥ 75%. Data are presented as means and corresponding 95% confidence intervals, unless otherwise stated. Baseline characteristics of the patients included in the analysis, as well as days to RTS, were compared between the two groups using unpaired

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

t-tests or Mann–Whitney tests depending on data distribution. Effect sizes of between-group differences in days to RTS were estimated using Cohen's *d*. Between-group differences in number of re-injuries were analyzed using Fisher's test. Statistics were performed in GraphPad Prism version 9.4.1 for macOS (GraphPad Software, San Diego, CA, USA) except for Fisher's tests, which were performed in R version 4.3.2 [32].

2.6.1 | Primary Outcome

The primary outcome of the study was changes during the 3-month intervention in muscle volume of the injured muscle compared to the changes observed in the same muscle of the healthy limb. To assess statistical differences between Protein and Placebo at this time point, the relative change from baseline was tested using a two-way ANOVA, evaluating supplementation and injury (injured vs. healthy limb) as factors, as well as their interaction. This analysis was also performed for the uninjured agonist muscles, comparing changes in the agonist muscles of the injured limb vs. changes of the same muscles in the healthy limb. For both analyses, effect sizes of the supplementation were also estimated using Cohen's *d*, comparing percentage changes in muscle volume of the injured limb (injured muscle or uninjured agonists) between protein and placebo.

2.6.2 | Multiple Linear Regression Analysis

Further, to investigate the impact of potential covariates, multiple linear regression was performed. Days from injury to baseline scan, injured muscle group (hamstring or calf), total protein and energy intake, training adherence during the intervention, injury recurrence, and days to RTS (as a marker of injury severity) were investigated as potential covariates.

2.6.3 | Secondary Analyses

Further, 3-way mixed model analyses on absolute muscle volumes, aponeurosis volumes, and muscle strength explored differences at baseline, 3 months post injury, and 12 months post injury. Due to a lack of baseline data in aponeurosis volume and muscle strength, the analysis of these data only included data at 3- and 12 months post injury. In these analyses, overall effects of time, supplementation, and injury as well as their interactions were analyzed. In the case of a significant time × supplement, time × injury, or supplement × injury interaction (with no time × supplement × injury interaction), a consolidated 2-way mixed model analysis was applied, with post hoc Tukey's multiple comparisons tests. Due to the lack of baseline data for these outcomes, effect sizes were not estimated.

2.6.4 | Sample Size

Based on previous data [8], 25 participants were recruited for each group in order to detect a 13% between-group difference in changes in muscle volume at the 3-month time point, which we consider clinically relevant ($\alpha = 0.05$, $\beta = 0.80$, SD = 15.4%).

3 | Results

CONSORT flow diagram for participant inclusion is displayed in Figure 1. Recruitment took place from February 2020 to February 2022, and follow-up was finalized in February 2023.

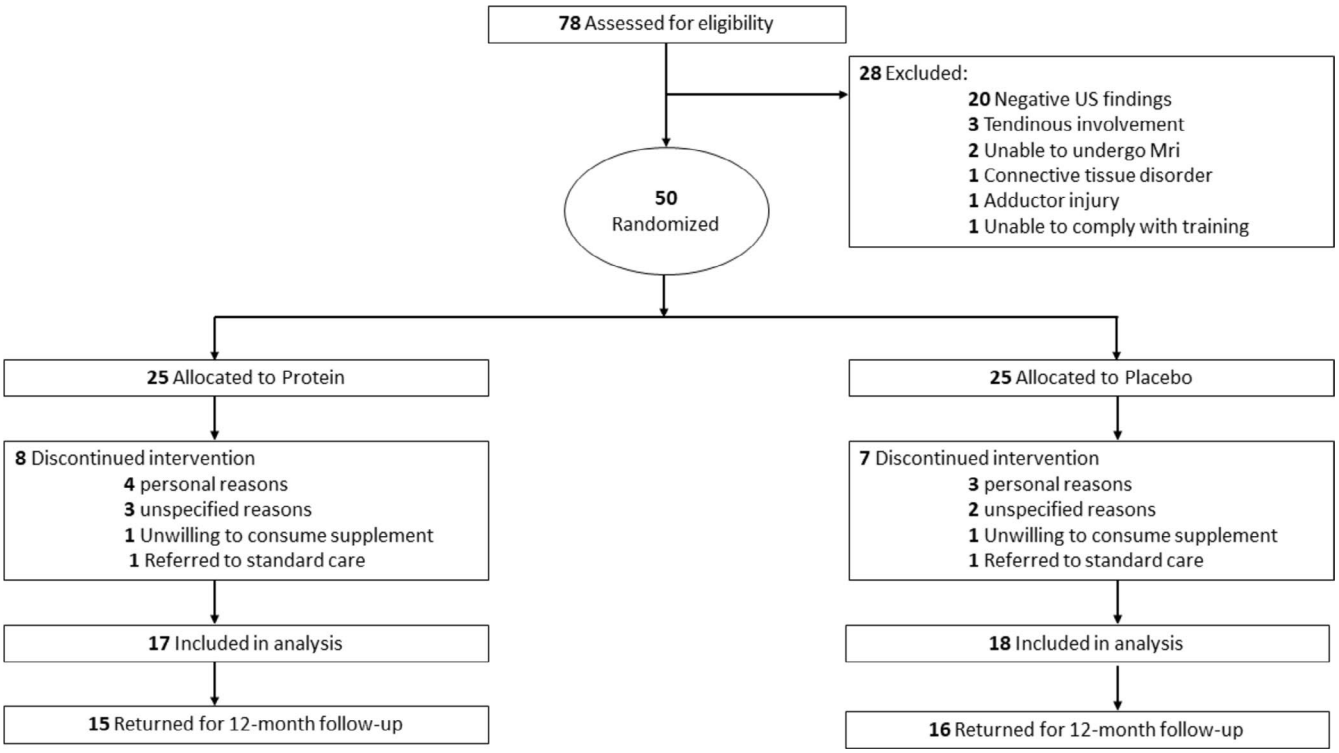

FIGURE 1 | CONSORT flow diagram.

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Briefly, 35 participants completed the intervention (18 placebo, 17 protein), and 15 participants discontinued the intervention. The study started at the beginning of the COVID-19 pandemic, and a large proportion of dropouts were directly related to repeated COVID-19 lockdowns imposed on Danish citizens.

Baseline characteristics of participants included in the analysis can be found in Table 1. No between-group differences were observed at baseline in any parameter. One patient self-reported a high degree of adherence (>75% of provided supplements), but only received the first half of the supplementation and was therefore noted as an over-reporter and not included in per-protocol analysis. Protein intake, including supplements, was higher in the protein group than in placebo group ($p=0.04$). Total intakes of carbohydrate ($p=0.11$) and fat ($p=0.60$) did not differ between groups.

TABLE 1 | Baseline characteristics of the included participants.

	Protein $N=17$	Placebo $N=18$
Demographics		
Age (years)	42.8 ± 10.6	41.0 ± 11.6
Males/females	14/3	17/1
BMI (kg/m^2)	25.4 ± 1.9	26.4 ± 3.4
Injury site		
Hamstring (*N*)	6	4
Calf (*N*)	12	13
Recurrent injury (*N*)	2	4
Diet		
Protein intake excluding supplements (g/kg/day) (Median 1st; 3rd quartile)	1.1 (1.0; 1.2)	1.2 (0.9; 1.5)
Protein intake including supplements (g/kg/day) (Median 1st; 3rd quartile)	1.5 (1.5; 1.6)[a]	1.2 (0.9; 1.5)
Carbohydrate intake excluding supplements (g/kg/day)	2.9 ± 0.6	3.1 ± 1.0
Carbohydrate intake including supplements (g/kg/day)	2.9 ± 0.6	3.5 ± 1.1
Fat intake excluding supplements (g/kg/day)	1.0 ± 0.2	0.9 ± 0.4
Fat intake including supplements (g/kg/day)	1.0 ± 0.2	0.9 ± 0.4
Energy intake excluding supplements (kJ/kg/day)	111.4 ± 17.9	109.8 ± 26.4
Energy intake including supplements (kJ/kg/day)	118.0 ± 17.9	115.4 ± 26.8
Intervention adherence (% of total)		
Supplements (Median 1st; 3rd quartile)	89% (74%; 95%)	85% (60%; 94%)
Rehabilitation exercise (Median 1st; 3rd quartile)	94% (79%; 97%)	88.5% (66%; 100%)

Note: Data are presented as means and standard deviations unless otherwise stated. Between-group differences were tested with unpaired *t*-tests or Mann–Whitney tests depending on the data normality.
[a]Indicates significant ($p<0.05$) between-group difference compared to placebo.

3.1 | Muscle Volume

Changes in muscle volume during the intervention period are shown in Figure 2. In the injured muscle (Figure 2B), no main effect of protein supplementation was observed {[Group difference (95% CI)]; −0.6% (−5.9% to +4.6%), $p=0.81$}, but the injured muscle decreased muscle volume compared to the same muscle of the healthy leg [−9.4% (−13.5% to −5.3%), $p<0.0001$]. No Group × Injury interaction was observed ($p=0.68$). Cohen's *d* estimated effect size of protein vs. placebo changes in muscle volume of the injured muscle was 0.12. In the agonist muscles (Figure 2C), changes in muscle volume were not affected by protein supplementation [+0.1% (−3.1% to +3.2%), $p=0.97$], but muscle volume increased in the agonists in the injured leg compared to the healthy leg [+2.5% (+0.6% to +4.4%), $p=0.01$]. No Group × Injury interaction was observed for the agonist muscles ($p=0.29$). Cohen's *d* estimated effect size of protein vs. placebo changes in muscle volume of the agonist muscle was 0.20. No effects of protein supplementation were observed in per-protocol analyses either (Figure S1).

Multiple linear regression showed a positive association between days from injury to baseline MRI scan, and changes in muscle volume during the intervention ($p=0.02$, Table 2), indicating that a later baseline scan was associated with less detected atrophy from baseline to 3 months. Total daily protein and energy intake (including supplements), injured muscle group (Calf/Hamstring), training adherence, time to RTS, and injury recurrence were not significant factors in the model.

Secondary 3-way mixed-effect model analysis of the absolute injured muscle volumes (Figure 3A) revealed no overall effect of time ($p=0.11$) or supplement ($p=0.51$). A time × injury interaction was observed ($p<0.0001$), whereas no time × supplement interaction ($p=0.79$), supplement × injury ($p=0.10$), and time × supplement × injury ($p=0.82$) were observed. To investigate the time × injury interaction, the supplement groups were pooled in a consolidated 2-way mixed model analysis. Tukey's multiple comparisons tests revealed decreases in muscle volume of the injured leg from baseline to 3 months [−27.0 cm^3 (−41.2 to −12.8 cm^3), $p<0.0001$] and from baseline to 12 months [−26.8 cm^3 (−41.9 to −11.7 cm^3), $p=0.0001$]. No changes were observed from 3 to 12 months [−0.1 cm^3 (−15.3 to +15.0 cm^3), $p=1.00$]. In the healthy leg, no changes in muscle volume were observed from baseline to 3 months [+6.5 cm^3 (−7.7 to 20.7 cm^3), $p=0.52$], 3–12 months [−2.3 cm^3 (−17.4 to +12.8 cm^3),

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

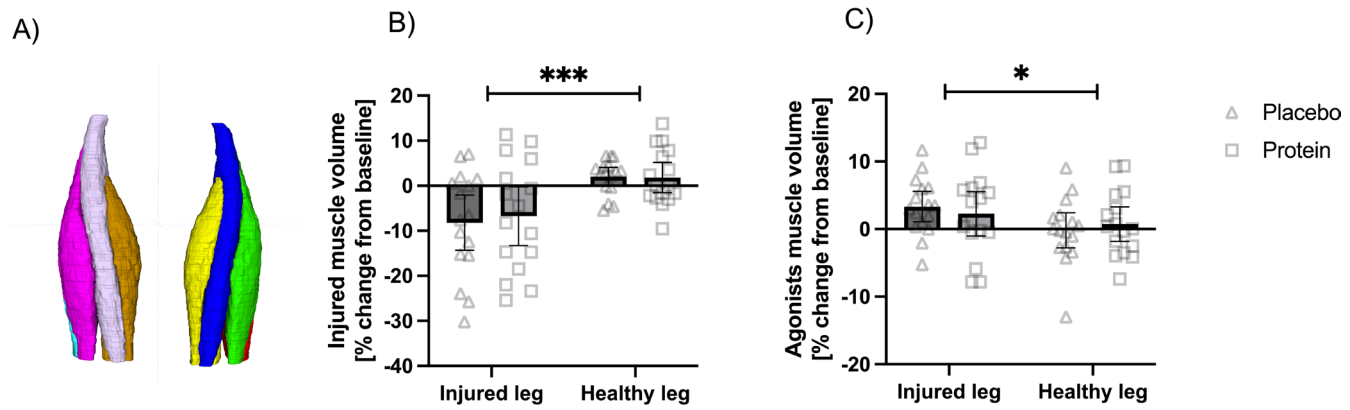

FIGURE 2 | Changes in muscle volume during the intervention period. (A) Illustration of a 3D MRI image of hamstring musculature. (B) Changes in muscle volume of the injured muscle vs. the same muscle in the healthy leg. (C) Changes in muscle volume of uninjured agonists in the injured leg vs. the healthy leg. Data are presented as individual data as well as means with corresponding 95% confidence intervals. Data were analyzed using a 2-way mixed-effects analysis. *$p < 0.05$, ***$p < 0.001$ main effect between injured and healthy limbs.

TABLE 2 | Multiple linear regression on associations between changes in muscle volume of the injured muscle. For muscle group analysis, Calf was imputed as the reference muscle group. For recurrent injury analysis, patients with index injuries were imputed as the reference.

Associations to changes in muscle volume	Estimate	95% CI	*p*	R^2
Regression	—		0.3	0.45
Intercept (mm^3)	−66.3	−125.5 to −7.1	0.03	—
Days from injury to MRI (days)	3.1	+0.6 to +5.6	0.02	—
Muscle group (Hamstring)	2.4	−17.6 to +22.5	0.80	—
Total protein intake (g/kg BW)	8.7	−8.5 to +25.8	0.29	—
Total energy intake (kj/kg BW)	0	−0.4 to +0.3	0.82	—
Training adherence (%)	0.3	−0.2 to +0.7	0.24	—
Recurrent injury (yes)	5.2	−12.7 to +23.1	0.54	—
Time to return to sport (days)	0.1	−0.6 to +0.7	0.87	—

$p = 0.93$], or from baseline to 12 months [+4.2 cm^3 (−10.9 to +19.3 cm^3), $p = 0.79$]. Muscle volume of the affected muscle did not differ between the injured leg and healthy leg at baseline [+16.2 cm^3 (−16.0 to +48.5 cm^3), $p = 0.32$], 3 months [−17.3 cm^3 (−49.5 to +15.0 cm^3), $p = 0.29$], or 12 months [−14.8 cm^3 (−47.7 to +18.0 cm^3), $p = 0.37$].

For the uninjured agonist muscles (Figure 3B), a trend toward an overall effect of time ($p = 0.055$) was observed, with no overall effect of supplement ($p = 0.52$). A time × injury interaction was observed ($p = 0.048$), with no supplement × injury ($p = 0.99$), time × supplement ($p = 0.57$), or time × supplement × injury interaction ($p = 0.82$). To investigate the time × injury interaction, the supplement groups were pooled in a consolidated 2-way mixed model analysis. Tukey's multiple comparisons tests revealed increases in muscle volume on the injured leg from baseline to 3 months [+13.8 cm^3 (+5.1 to +22.5 cm^3), $p = 0.0008$]. No changes were observed from 3 to 12 months [−5.5 cm^3 (−14.8 to +3.8 cm^3), $p = 0.35$] or from baseline to 12 months [+8.3 cm^3 (−1.0 to +17.6 cm^3), $p = 0.09$]. No changes in agonist muscle volume were observed in the healthy leg from baseline to 3 months [+3.0 cm^3 (−5.7 to +11.7 cm^3), $p = 0.69$], 3–12 months [+1.9 cm^3 (−7.4 to +11.2 cm^3), $p = 0.87$], or baseline to 12 months [−1.1 cm^3 (−10.4 to +8.2 cm^3), $p = 0.96$]. Muscle volume of the agonists did not differ between the injured leg and healthy leg at baseline [+7.4 cm^3 (−49.4 to +64.2 cm^3), $p = 0.80$], 3 months [+18.2 cm^3 (−38.6 to +75.0 cm^3), $p = 0.53$], or 12 months [+13.8 cm^3 (−43.1 to +70.7 cm^3), $p = 0.63$].

3.2 | Aponeurosis Volume

An effect of time ($p = 0.006$) and injury ($p = 0.0006$) was observed for aponeurosis volume (Figure 4), with no overall effect of supplement ($p = 0.49$). A time × injury interaction was observed ($p = 0.0081$), with no time × supplement ($p = 0.35$), supplement × injury ($p = 0.32$), or time × supplement × injury ($p = 0.46$) interactions. To investigate the time × injury interaction, the supplement groups were pooled in a consolidated 2-way mixed model analysis. The aponeurosis volume was larger on the injured muscles compared to the contralateral healthy muscles both at 3 months [sixfold enlarged, +17.3 cm^3 (+8.3 to 26.3 cm^3), $p = 0.0005$] and 12 months [fivefold enlarged, +10.4 cm^3 (5.3–15.4 cm^3), $p = 0.0003$]. The volume of the aponeurosis on the injured muscle decreased from 3 to 12 months [−7.3 cm^3 (−13.0 to −1.7 cm^3), $p = 0.01$], with no changes in the aponeurosis of the healthy muscles [−0.4 cm^3 (−1.1 to 0.3 cm^3), $p = 0.24$].

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

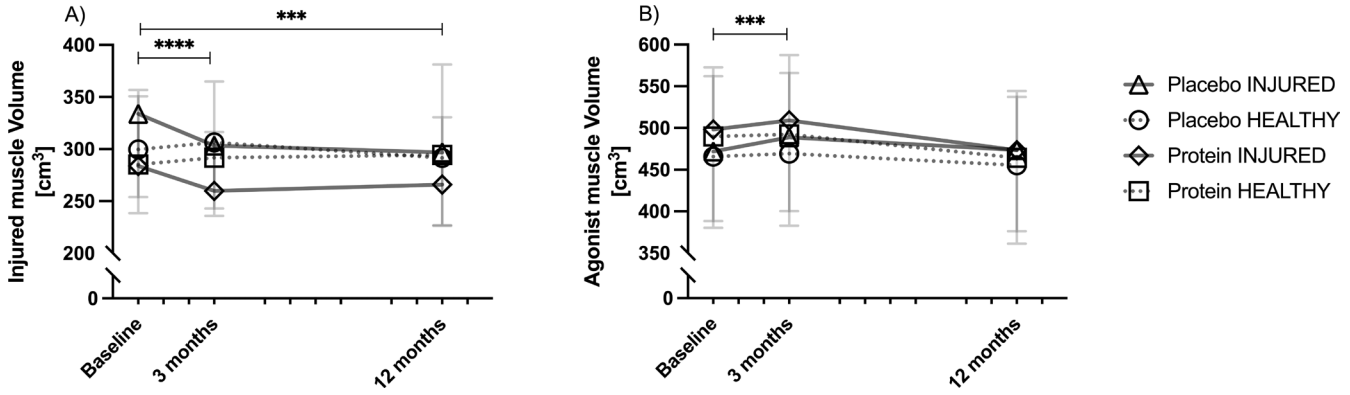

FIGURE 3 | Absolute muscle volume of the injured muscle (A) and the uninjured agonists (B). Data are presented as means with corresponding 95% confidence intervals based on the raw data and were analyzed using a 3-way mixed-effects model. ***$p < 0.001$, ****$p < 0.0001$ between time points within injured muscles.

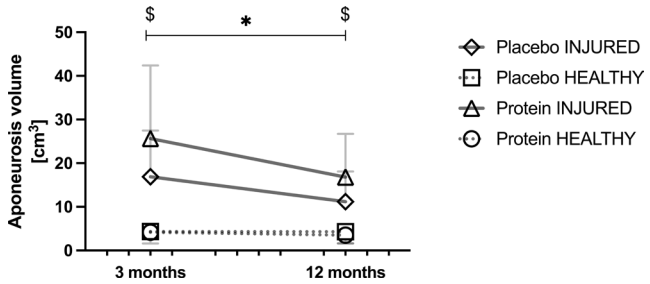

FIGURE 4 | Aponeurosis volume of the injured and healthy legs. Data are presented as means with corresponding 95% confidence intervals based on the raw data and were analyzed using a 3-way mixed-effects model. *$p < 0.05$ between time points within injured muscles. \$$p < 0.05$ between injured and healthy legs.

3.3 | Muscle Strength

For both concentric and eccentric strength (Figure 5A,B), no overall effects of time ($p = 0.89$, $p = 0.32$, concentric and eccentric respectively), supplement ($p = 0.67$, $p = 0.63$), or injury ($p = 0.98$, $p = 0.58$) were observed. Also, no significant time × supplement ($p = 0.63$, $p = 0.12$), time × injury ($p = 0.33$, $p = 0.39$), supplement × injury ($p = 0.97$, $p = 0.71$), or time × supplement × injury ($p = 0.94$, $p = 0.77$) interactions were observed.

3.4 | Clinical Outcomes

Days to RTS did not differ between groups (Figure 6, $p = 0.45$, ES = 0.12). Five participants had strain re-injuries during the follow-up period. The frequency of re-injuries did not differ significantly between groups (1 Placebo, 4 Protein, $p = 0.20$).

4 | Discussion

The present study reports a loss of muscle mass after a strain injury, which is not restored even 1 year post injury. Supplementation with whey protein over the initial 12-week rehabilitation period did not have any positive effect on the loss of muscle mass. Further, there was hypertrophy of the uninjured agonists after 12 weeks, but protein supplementation had no beneficial effect on this gain of muscle mass either. In addition, we did not detect any positive effect of protein supplementation on the time until RTS. Interestingly, both concentric and eccentric muscle strength in participants with a strain injury in either calf or hamstrings was similar in the injured and healthy limbs with no effect of protein supplementation. Finally, the aponeurosis associated with the injured muscle was markedly enlarged in the region where the aponeurosis connects to the muscle, both 3- and 12 months post injury.

The lack of effect on protein supplementation is somewhat surprising, given that the bulk of the literature indicates a positive effect of protein supplementation on training-induced hypertrophy [19]. However, this has only previously been investigated in healthy muscle and might not be applicable to a muscle injury state. Protein supplementation provides an acute anabolic stimulus [33] and seems like a plausible treatment option to reduce muscle atrophy in strain-injured individuals. A systematic review on protein supplementation versus placebo following orthopedic surgery to prevent muscle atrophy reported beneficial effects across different types of surgeries including anterior cruciate ligament reconstruction, total hip arthroplasty, hip fractures, and total knee arthroplasty [34]. The primary benefit was diminished loss of muscle mass assessed as muscle cross-sectional area. However, it is important to note that studies on postoperative protein supplementation target otherwise healthy muscles subjected to less mobilization due to disorders that have not directly included skeletal muscle, whereas in the present study, strain injuries cause a complete loss of tension within the injured areas.

Previous studies on the recovery following muscle strain injuries reported a significant reduction in the mass of the affected muscle [7, 8] and our findings are in line with those data. Despite regular rehabilitation for 3 months, the injured muscle loses on average ~7% of muscle volume over these 3 months. As the present study included the 1-year post injury time point, which did not show any recovery of muscle mass in the injured muscle, it is likely that the loss of muscle mass after strain injuries is permanent. Further, we show that the number of days from injury to the initial MRI scan was positively associated with changes in muscle volume during the intervention—meaning that more atrophy was present the earlier the baseline scan. Although the time course of muscle atrophy was not directly assessed in the

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

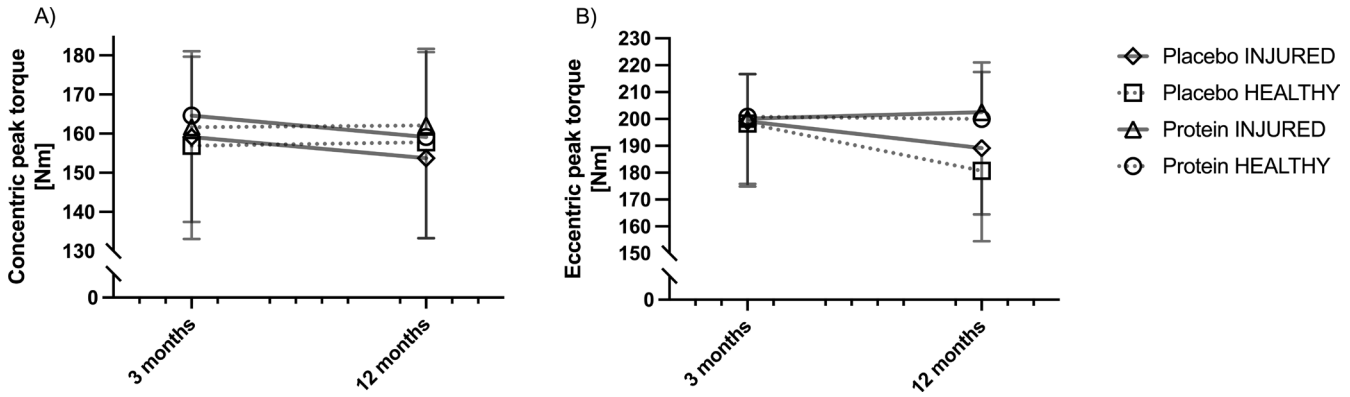

FIGURE 5 | Muscle strength measurements from 3 to 12 months follow-up. (A) Concentric peak torque. (B) Eccentric peak torque. Data are presented as means with corresponding 95% confidence intervals based on the raw data and were analyzed using a 3-way Mixed-effects model.

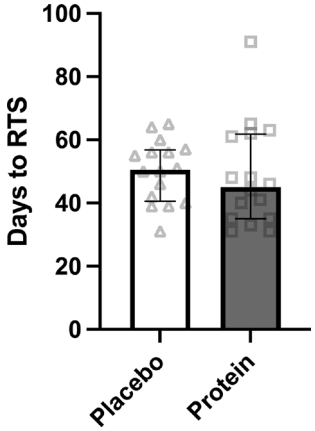

FIGURE 6 | Days to RTS. Between-group differences were tested using the Mann–Whitney test. Data are presented as individual values as well as medians with interquartile ranges.

present study, these findings indicate that a large proportion of the atrophy seen after acute strain injuries is occurring within a few days after the injury.

Strain-injured muscles with a clear defect on an ultrasound/MRI scan present with retracted muscle fascicles from the aponeurosis with more or less damage to the aponeurosis itself [25]. And while the defect itself evidently heals, there is accumulating data that strain-injured muscles and their associated aponeurosis are chronically altered. There are pathologic signs such as fatty infiltration in the muscle long time after the injury [35] and the architecture of the muscle and aponeurosis as well as the fascicle behavior during movement are not normalized years after the injury [23]. These factors likely contribute to the high risk of re-injury [6].

The present manuscript clearly shows structural alterations in the aponeurosis both 3- and 12 months post injury. Even though there is a significant decrease in aponeurosis volume from 3 to 12 months, the volume remains markedly enlarged compared to the healthy side, with no effects of the protein supplementation. The reduction in volume is probably a consequence of re-organization of matrix components, the remaining enlarged aponeurosis 1 year after the injury indicating a permanent change in structure. Muscle strain injuries have historically been presented as injuries that predominantly cause damage to the muscle fibers. Accordingly, the repair of muscle strain injuries has been focused on sequences described in muscle healing following experimental muscle damage [36, 37]. Here, we clearly show that the aponeurosis, that is, the connective tissue to which muscle fibers attach is greatly affected by the injury. Persisting changes to the aponeurosis after a strain injury are backed up by previous data from our group [23] and others [24, 25]. It is therefore pertinent to consider the connective tissue side of the muscle-tendon unit and its repair capacities as well as limitations to repair in the context of muscle strain injuries. In particular, the aponeurosis is not only the site of load transmission between the muscle and tendon but also influences muscle shape, muscle fiber strain distribution, and contractile properties [38, 39]. Hence, the loss of muscle volume in the injured muscle is likely related to changes in load transmission in the muscle-aponeurosis interface.

Interestingly, the present study did not record any deficits in muscle strength of the injured limb. Both the eccentric and concentric components were similar in the affected compared to the unaffected limb. This is in line with a meta-analysis [40] showing conflicting results, with some studies reporting a lower eccentric strength after a hamstring strain injury compared to the uninjured hamstrings. The absence of a lower strength after injury, especially the eccentric component, might be a reflection on successful 12-week rehabilitation, which focuses on resistance training from Week 3. At the same time, similar strength in the injured and healthy limbs might be a result of compensatory hypertrophy of the agonist muscles in the injured limbs.

A limitation to the present study is the low statistical power achieved for the primary outcome. We based our sample size calculation on a large (ES ~ 0.80) reduction in muscle atrophy, as this was what we considered to be of minimal clinical relevance. It could be discussed if smaller reductions would be of interest. The statistical power was further challenged by the high dropout rate. While almost all dropouts were related to logistical constraints for participants during COVID-19 lockdowns imposed by the Danish government, and hence had little to do with the feasibility of interventions under normal circumstances, it caused a lower statistical power than expected for the primary outcome. Further studies with greater statistical power would be needed to fully elucidate this subject, but the present results are

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

not encouraging of a high clinical potential for simple protein supplementation after muscle strain injuries. The present study only assessed dietary intake at a single time point, and hence variation in patients' intake throughout the intervention might have been missed.

Further, variation in time from injury to the baseline MRI scan seems to have affected the results. We show that the number of days from injury to the first MRI scan is associated with changes in muscle volume during the intervention, and hence will affect the primary outcome of the study. However, due to logistical constraints, it was not possible to standardize the timing of the baseline MRI within a narrower time frame in the present study.

In conclusion, acute muscle strain injuries induce severe and persistent atrophy of the injured musculature as well as enlargement of the aponeurosis, which are not counteracted by increasing dietary protein intake through supplementation. Protein supplementation did not benefit time to RTS either.

4.1 | Perspectives

The present study does not indicate any beneficial effects of protein supplementation during rehabilitation of acute muscle strain injuries. We do, however, recognize the limitations of our study, and therefore encourage future research to further investigate this field. The present study did not investigate mechanistic aspects in detail, and while the simple addition of protein had no benefit, it cannot be ruled out that mechanisms exist by which other forms of nutritional interventions could be beneficial.

Our data indicate indirectly that a significant portion of the muscle atrophy and/or remodeling occurs within the first days after the injury. This further not only underlines the necessity of early onset of rehabilitation [31] but also calls for more research aiming at understanding this time period of the injury process. The permanent changes in muscle-tendon unit structure are most likely related to the high risk of re-injury seen for this type of injury. Hence, future research should aim to investigate the mechanisms behind this remodeling, as well as identify the rehabilitation practices best at optimizing muscle-tendon unit structure.

Conflicts of Interest

The present results are presented clearly, honestly, and without fabrication or inappropriate data manipulation. The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available upon request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. B. Green, M. N. Bourne, N. Van Dyk, and T. Pizzari, "Recalibrating the Risk of Hamstring Strain Injury (HSI): A 2020 Systematic Review and Meta-Analysis of Risk Factors for Index and Recurrent Hamstring Strain Injury in Sport," *British Journal of Sports Medicine* 54 (2020): 1081–1088.

2. M. Hägglund, M. Waldén, and J. Ekstrand, "Injury Recurrence Is Lower at the Highest Professional Football Level Than at National and Amateur Levels: Does Sports Medicine and Sports Physiotherapy Deliver?," *British Journal of Sports Medicine* 50 (2016): 751–758.

3. J. Ekstrand, H. Bengtsson, M. Waldén, M. Davison, K. M. Khan, and M. Hägglund, "Hamstring Injury Rates Have Increased During Recent Seasons and Now Constitute 24% of All Injuries in Men's Professional Football: The UEFA Elite Club Injury Study From 2001/02 to 2021/22," *British Journal of Sports Medicine* 57 (2023): 292–298.

4. F. M. Azar, J. D. Lamplot, D. L. Bernholt, and D. D. Spence, "Pickleball: A Standard Review of Injury Prevalence and Prevention in a Rapidly Growing Sport," *Journal of the American Academy of Orthopaedic Surgeons* 10 (2024): 1–12.

5. J. Dahmen, K. S. Emanuel, A. Fontanellas-Fes, E. Verhagen, G. M. M. J. Kerkhoffs, and B. M. Pluim, "Incidence, Prevalence and Nature of Injuries in Padel: A Systematic Review," *BMJ Open Sport & Exercise Medicine* 9 (2023): e001607.

6. A. Wangensteen, J. L. Tol, E. Witvrouw, et al., "Hamstring Reinjuries Occur at the Same Location and Early After Return to Sport: A Descriptive Study of MRI-Confirmed Reinjuries," *American Journal of Sports Medicine* 44 (2016): 2112–2121.

7. A. Silder, B. C. Heiderscheit, D. G. Thelen, T. Enright, and M. J. Tuite, "MR Observations of Long-Term Musculotendon Remodeling Following a Hamstring Strain Injury," *Skeletal Radiology* 37 (2008): 1101–1109.

8. M. L. Bayer, M. Hoegberget-Kalisz, M. H. Jensen, et al., "Role of Tissue Perfusion, Muscle Strength Recovery, and Pain in Rehabilitation After Acute Muscle Strain Injury: A Randomized Controlled Trial Comparing Early and Delayed Rehabilitation," *Scandinavian Journal of Medicine & Science in Sports* 28 (2018): 2579–2591.

9. J. L. Sanfilippo, A. Silder, M. A. Sherry, M. J. Tuite, and B. C. Heiderscheit, "Hamstring Strength and Morphology Progression After Return to Sport From Injury," *Medicine and Science in Sports and Exercise* 45 (2013): 448–454.

10. B. T. Wall, T. Snijders, J. M. G. Senden, et al., "Disuse Impairs the Muscle Protein Synthetic Response to Protein Ingestion in Healthy Men," *Journal of Clinical Endocrinology and Metabolism* 98 (2013): 4872–4881.

11. E. M. P. Backx, A. M. H. Horstman, G. N. Marzuca-Nassr, et al., "Leucine Supplementation Does Not Attenuate Skeletal Muscle Loss During Leg Immobilization in Healthy, Young Men," *Nutrients* 10 (2018): 1–12.

12. B. T. Wall, M. L. Dirks, T. Snijders, J. M. G. Senden, J. Dolmans, and L. J. C. van Loon, "Substantial Skeletal Muscle Loss Occurs During Only 5 Days of Disuse," *Acta Physiologica (Oxford, England)* 210 (2014): 600–611.

13. B. T. Wall, M. L. Dirks, T. Snijders, et al., "Short-Term Muscle Disuse Lowers Myofibrillar Protein Synthesis Rates and Induces Anabolic Resistance to Protein Ingestion," *American Journal of Physiology. Endocrinology and Metabolism* 310 (2016): E137–E147.

14. C. Suetta, L. G. Hvid, L. Justesen, et al., "Effects of Aging on Human Skeletal Muscle After Immobilization and Retraining," *Journal of Applied Physiology* 107 (2009): 1172–1180.

15. P. Vinci, F. G. Di Girolamo, A. Mangogna, et al., "Early Lean Mass Sparing Effect of High-Protein Diet With Excess Leucine During Long-Term Bed Rest in Women," *Frontiers in Nutrition* 9 (2022): 1–11.

16. E. J. Arentson-Lantz, E. Galvan, J. Ellison, A. Wacher, and D. Paddon-Jones, "Improving Dietary Protein Quality Reduces the Negative Effects of Physical Inactivity on Body Composition and Muscle Function," *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences* 74 (2019): 1605–1611.

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

17. C. J. Mitchell, R. F. D'Souza, S. M. Mitchell, et al., "Impact of Dairy Protein During Limb Immobilization and Recovery on Muscle Size and Protein Synthesis; a Randomized Controlled Trial," *Journal of Applied Physiology* 124 (2018): 717–728.

18. M. L. Dirks, B. T. Wall, R. Nilwik, D. H. J. M. Weerts, L. B. Verdijk, and L. J. C. van Loon, "Skeletal Muscle Disuse Atrophy Is Not Attenuated by Dietary Protein Supplementation in Healthy Older Men," *Journal of Nutrition* 144 (2014): 1196–1203.

19. R. W. Morton, K. T. Murphy, S. R. McKellar, et al., "A Systematic Review, Meta-Analysis and Meta-Regression of the Effect of Protein Supplementation on Resistance Training-Induced Gains in Muscle Mass and Strength in Healthy Adults," *British Journal of Sports Medicine* 52 (2018): 376–384.

20. R. Tagawa, D. Watanabe, K. Ito, et al., "Dose-Response Relationship Between Protein Intake and Muscle Mass Increase: A Systematic Review and Meta-Analysis of Randomized Controlled Trials," *Nutrition Reviews* 79 (2020): 66–75.

21. A. N. Pedersen, T. Christensen, J. Matthiessen, et al., "Dietary Habits in Denmark 2011–2013." (2015).

22. B. T. Wall, J. P. Morton, and L. J. C. van Loon, "Strategies to Maintain Skeletal Muscle Mass in the Injured Athlete: Nutritional Considerations and Exercise Mimetics," *European Journal of Sport Science* 15 (2015): 53–62.

23. L. Nielsen, R. Svensson, N. Fredskild, et al., "Chronic Changes in Muscle Architecture and Aponeurosis Structure Following Calf Muscle Strain Injuries," *Scandinavian Journal of Medicine & Science in Sports* 33 (2023): 1–13.

24. S. L. Lazarczuk, T. J. Collings, A. H. Hams, et al., "Biceps Femoris Long Head Muscle and Aponeurosis Geometry in Males With and Without a History of Hamstring Strain Injury," *Scandinavian Journal of Medicine & Science in Sports* 34 (2024): e14619.

25. C. Pedret, R. Balius, M. Blasi, et al., "Ultrasound Classification of Medial Gastrocnemious Injuries," *Scandinavian Journal of Medicine & Science in Sports* 30 (2020): 2456–2465.

26. A. K. A. McKay, T. Stellingwerff, E. S. Smith, et al., "Defining Training and Performance Caliber: A Participant Classification Framework," *International Journal of Sports Physiology and Performance* 17 (2022): 317–331.

27. P. A. Harris, R. Taylor, B. L. Minor, et al., "The REDCap Consortium: Building an International Community of Software Platform Partners," *Journal of Biomedical Informatics* 95 (2019): 103208.

28. P. A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, and J. G. Conde, "Research Electronic Data Capture (REDCap)—a Metadata-Driven Methodology and Workflow Process for Providing Translational Research Informatics Support," *Journal of Biomedical Informatics* 42 (2009): 377–381.

29. M. Saghaei and S. Saghaei, "Implementation of an Open-Source Customizable Minimization Program for Allocation of Patients to Parallel Groups in Clinical Trials," *Journal of Biomedical Science and Engineering* 04 (2011): 734–739.

30. D. R. Moore, T. Churchward-Venne, O. Witard, et al., "Protein Ingestion to Stimulate Myofibrillar Protein Synthesis Requires Greater Relative Protein Intakes in Healthy Older Versus Younger Men," *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences* 70 (2015): 57–62.

31. M. L. Bayer, S. P. Magnusson, M. Kjaer, and Tendon Research Group Bispebjerg, "Early Versus Delayed Rehabilitation After Acute Muscle Injury," *New England Journal of Medicine* 377 (2017): 1300–1301.

32. R Core Team, *R: A Language and Environment for Statistical Computing* (R Core Team, 2019).

33. O. C. Witard, S. R. Jackman, L. Breen, K. Smith, A. Selby, and K. D. Tipton, "Myofibrillar Muscle Protein Synthesis Rates Subsequent to a Meal in Response to Increasing Doses of Whey Protein at Rest and After Resistance Exercise," *American Journal of Clinical Nutrition* 99 (2014): 86–95.

34. A. George, B. M. Holderread, B. S. Lambert, J. D. Harris, and P. C. McCulloch, "Post-Operative Protein Supplementation Following Orthopaedic Surgery: A Systematic Review," *Sports Medicine and Health Science* 6 (2024): 16–24.

35. M. L. Bayer, M. Hoegberget-Kalisz, R. B. Svensson, et al., "Chronic Sequelae After Muscle Strain Injuries: Influence of Heavy Resistance Training on Functional and Structural Characteristics in a Randomized Controlled Trial," *American Journal of Sports Medicine* 49 (2021): 6623.

36. T. A. Järvinen, M. Järvinen, and H. Kalimo, "Regeneration of Injured Skeletal Muscle After the Injury," *Muscles, Ligaments and Tendons Journal* 3 (2013): 337–345.

37. D. Pieters, E. Wezenbeek, J. Schuermans, and E. Witvrouw, "Return to Play After a Hamstring Strain Injury: It Is Time to Consider Natural Healing," *Sports Medicine* 51 (2021): 2067–2077.

38. M. Böl, K. Leichsenring, M. Ernst, C. Wick, R. Blickhan, and T. Siebert, "Novel Microstructural Findings in *M. plantaris* and Their Impact During Active and Passive Loading at the Macro Level," *Journal of the Mechanical Behavior of Biomedical Materials* 51 (2015): 25–39.

39. C. M. Eng and T. J. Roberts, "Aponeurosis Influences the Relationship Between Muscle Gearing and Force," *Journal of Applied Physiology* 125 (2018): 513–519.

40. N. Maniar, A. J. Shield, M. D. Williams, R. G. Timmins, and D. A. Opar, "Hamstring Strength and Flexibility After Hamstring Strain Injury: A Systematic Review and Meta-Analysis," *British Journal of Sports Medicine* 50 (2016): 909–920.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.

16000838, 2025, 4, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/sms.70043 by Universidad Complutense De Madrid, Wiley Online Library on [31/03/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License