Clinical Effectiveness of Protein and Amino Acid Supplementation on Building Muscle Mass in Elderly People: A Meta-Analysis

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Abstract

Objective: A major reason for the loss of mobility in elderly people is the gradual loss of lean body mass known as sarcopenia. Sarcopenia is associated with a lower quality of life and higher healthcare costs. The benefit of strategies that include nutritional intervention, timing of intervention, and physical exercise to improve muscle loss unclear as finding from studies investigating this issue have been inconsistent. We have performed a systematic review and meta-analysis to assess the ability of protein or amino acid supplementation to augment lean body mass or strength of leg muscles in elderly patients.

Methods: Nine studies met the inclusion criteria of being a prospective comparative study or randomized controlled trial (RCT) that compared the efficacy of an amino acid or protein supplement intervention with that of a placebo in elderly people (≥65 years) for the improvement of lean body mass (LBM), leg muscle strength or reduction associated with sarcopenia.

Results: The overall difference in mean change from baseline to the end of study in LBM between the treatment and placebo groups was 0.34 kg which was not significant (P = 0.386). The overall differences in mean change from baseline in double leg press and leg extension were 2.14 kg (P = 0.748) and 2.28 kg (P = 0.265), respectively, between the treatment group and the placebo group.

Conclusions: These results indicate that amino acid/protein supplements did not increase lean body mass gain and muscle strength significantly more than placebo in a diverse elderly population.

Introduction

Sarcopenia is an age related loss of muscle mass and strength, and is associated with a lower quality of life resulting from a reduced ability to perform daily living tasks [1]. Sarcopenia results in increased healthcare costs of approximately $900 per elderly adult which in the USA is approximately $18.5 billion per year [2]. Prevalence of sarcopenia differs by gender, living circumstances, and continent: 13.2% of Chinese men and 4.8% of Chinese women who are ≥70 years of age have sarcopenia, while 45–70% and 7–17.5% of American men and 2%–59% and 4–10% of American women have sarcopenia, respectively [3]. Age-related muscle loss is highly prevalent in nursing homes, with rates being as high as 68% in elderly men and 21% in elderly females [4], whereas community dwelling elderly have lower prevalence rates in males (10%) but higher rates in women (33%) [5].

Inadequate nutrition, oxidative stress, low physical activity levels, inflammation, and reduced hormone concentrations contribute to age related muscle loss [6]. Possible strategies that reliably increase muscle mass and strength in the elderly have been actively investigated, but conclusions on the benefits of different nutritional interventions, timing of administration, and physical exercise from studies have been conflicting [7–20].

Several nutritional interventions such as creatine monohydrate, whey protein, caseinate, and essential amino acids appear to augment protein synthesis in muscles [1,21,22]. Numerous studies have found that these nutritional supplements enhance the magnitude of gain in lean body mass and muscle strength in older adults undergoing exercise training [1,6,15]. Essential amino acid and leucine supplementation have increased protein synthesis in muscles and are thought to be better strategies for offsetting muscle loss than intact protein [7,16,22–24], due in part to their higher absorption [22]. However, several studies that compared the effect of whey protein or amino acid supplementation on skeletal muscle mass, lean body mass, or strength in healthy elderly to that of placebos have not detected a significant difference between the two groups [8,17].

Many of the studies evaluating the impact of protein or amino acid supplementation on sarcopenia have been small and
evaluated different supplements. In order to maximize the biostatistical power of placebo controlled clinical trials, we have performed a meta-analysis to assess the ability of protein or amino acid supplementation to augment lean body mass or strength of leg muscles in elderly patients.

**Experimental Methods**

PubMed, Google Scholar, The Cochrane Library, EMBASE, and ClinicalTrials.gov were searched from inception to 13 Jun 2014 using combinations of the following terms: aging, elder, older, muscle loss or muscular atrophy, protein, amino acid. Inclusion criteria for the meta-analysis required that an article be published in a peer-reviewed reviewed journal that described a prospective study or randomized controlled trial (RCT) which compared the efficacy of an amino acid or protein supplement with placebo in improving lean body mass, leg muscle strength in elderly people (≥65 years of age). Single group uncontrolled studies, cross sectional studies, or retrospective studies were excluded. Studies published as letters, comments, editorials, or case reports were also excluded, as well as studies that included people <65 years of age. We utilized the Delphi list to assess the quality of the included studies [25].

**Data extraction**

Full text articles for the relevant titles were assessed for eligibility which included studies that measured changes in lean body mass (LBM), and may have included evaluation of muscle strength of leg extension and double leg press. Two independent reviewers (coders) extracted the following information from each eligible study: cited reference, type of study, type and duration of interventions, participant number in the intervention and placebo groups, demographics of participants (age, sex, mean body mass index [BMI]), and mean values of the outcome measures (LBM, muscle strength in double leg press, muscle strength in leg extension) at baseline and post intervention. In case of a disagreement, a third reviewer resolved the issue.

To assess coder drift, agreement between coders was calculated by dividing the number of variables coded the same by the total number of variables. Mean agreement of ≥0.90 was considered to be acceptable.

**Biostatistics**

Treatment effectiveness was evaluated by comparison of LBM (primary outcome) and muscle strength of double leg press and leg extension (secondary outcomes) in elderly subjects at baseline and after nutritional intervention for 6 months (24 weeks). For treatment consistency, only studies providing protein supplementation were considered for meta-analysis. The means with standard deviations (SD) for the LBM, mean muscle strength (leg press and leg extension) were calculated for each group at baseline and post study completion. The difference in mean change (from baseline to end of study) with 95% confidence interval (95% CI) was calculated as the mean change of the protein intervention (treatment group) minus mean change of the placebo or non-nutritious supplements (control group) for each outcome.

Heterogeneity was determined by calculating Cochran Q and the I² statistic. The Q statistic indicated statistically significant heterogeneity at P<0.10. The I² statistic reflected the percentage of the observed between-study variability and provided a scale of heterogeneity: 0 to 24% = no heterogeneity; 25 to 49% = moderate heterogeneity; 50 to 74% = large heterogeneity; and 75 to 100% = extreme heterogeneity. If heterogeneity existed between studies (a Q statistic with P<0.1 or an I² statistic >50%), we performed the random-effects model (DerSimonian-Laird method). Otherwise, the fixed-effects model was recommended (Mantel-Haenszel method). Combined difference in mean change from baseline to end of study was calculated and a 2-sided P value <0.05 was considered to indicate statistical significance. Sensitivity analysis was performed using the leave-one-out approach. Publication bias was only assessed for lean body mass by constructing funnel plots and exacerbations rate by Egger’s test. The absence of publication bias is indicated by the data points forming a symmetric funnel-shaped distribution and one-tailed significance level P>0.05 in Egger’s test. All statistical analyses
| Author (Year)     | Was a method of randomization used? | Were the groups similar at baseline regarding the most important prognostic indicators? | Were the eligibility criteria specified? | Was the outcome assessor blinded? | Was the care provider blinded? | Was the patient blinded? | Were point estimate and measures of variability presented for the primary outcome measures? | Did the analysis include an intention-to-treat analysis? |
|-------------------|-------------------------------------|------------------------------------------------------------------------------------------|------------------------------------------|-----------------------------------|-------------------------------|-----------------------------|------------------------------------------------------------------------|--------------------------------------------------|
| Daly et al [27]   | Yes                                 | Yes                                                                                      | Yes                                      | No                                | No                            | Yes                         | Yes                                                                     | Yes                                              |
| Vermeeren et al [28] | Yes                                 | Yes                                                                                      | Yes                                      | Yes                               | Yes                           | Yes                         | Yes                                                                     | No                                               |
| Chale et al [8]   | Yes                                 | Yes                                                                                      | Yes                                      | Yes                               | Yes                           | Yes                         | Yes                                                                     | Yes                                              |
| Alema´n-Mateo et al [29] | Yes                                 | Yes                                                                                      | Yes                                      | Yes                               | No                            | No                          | Yes                                                                     | Yes                                              |
| Tieland et al [20] | Yes                                 | Yes                                                                                      | Yes                                      | Yes                               | Yes                           | Yes                         | Yes                                                                     | Yes                                              |
| Tieland et al [26] | Yes                                 | Yes                                                                                      | Yes                                      | Yes                               | Yes                           | Yes                         | Yes                                                                     | Yes                                              |
| Leenders et al [19] | Yes                                 | Yes                                                                                      | Yes                                      | Yes                               | Yes                           | Yes                         | Yes                                                                     | No                                               |
| Ferrando et al [18] | Yes                                 | Gender different, others similar                                                         | Yes                                      | No                                | No                            | Yes                         | Yes                                                                     | No                                               |
| Verhoeven et al [17] | Yes                                 | Yes                                                                                      | Yes                                      | ND                                | Yes                           | Yes                         | No                                                                      | No                                               |

ND, not described.
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were performed using the statistical software Comprehensive Meta-Analysis, version 2.0 (Biostat, Englewood, NJ, USA).

**Results**

Out of 1840 studies identified by the data base searches, 38 were screened for eligibility, and 29 were excluded for one of the following reasons: no comparison group \((n = 1)\), no placebo \((n = 8)\), cross over design \((n = 1)\) or no value for mean muscle mass or leg muscle strength \((n = 19)\) (Figure 1). Nine prospective studies met the inclusion criteria (Figure 1) \([8,17–20,26–29]\).

All but one of the studies \([18]\) were at least 75% compliant with the Delphi list (Table 1). Eight of the 9 studies were randomized, placebo-controlled clinical trials \([8,17,19,20,26–29]\). Five of the trials included an intention-to-treat analysis \([8,20,26,27,29]\). The 75%–100% compliance levels of 8 of the 9 studies to the Delphi criteria suggest that the studies provided high quality evidence. Coder drift was calculated to be 0.93, indicating satisfactory reliability between coders.

The number of total participants in all 9 studies who had taken the intervention was 267 (range, 10 to 53) and who had received placebo were 244 (range, 11 to 47). Six of the 9 studies provided a protein supplement (whey) to 203 elderly participants and placebo to 191 elderly subjects (controls) \([8,20,26–28]\), 2 studies supplied leucine supplementation to 54 elderly participants and placebo to 42 controls \([17,19]\), and one provided essential amino acids (EAA) to 10 elderly participants and 11 controls \([18]\) (Table 2). The duration of intervention ranged from 10 days to 6 months (Table 2).

**Lean Body Mass**

Among the 6 studies with protein supplementation \([8,20,26–29]\), three reported that nutritional supplementation significantly increased LBM in the elderly compared to placebo \([8,26,27]\). Two studies observed a significantly greater LBM in both the placebo and nutritional intervention groups \([8,26,27]\). Pooling of data from the 6 studies revealed no heterogeneity \((Q = 0.71, df = 5, P = 0.982; I^2 = 0.0%); therefore, a fixed-effects model was used to assess the difference in mean change in LBM from baseline to end of study between the placebo and protein supplementation groups. The difference in mean change of LBM from baseline to end of study between the placebo and protein supplementation groups ranged from \(-0.1\) to \(1.60\) kg. The overall difference in mean change in LBM between treatment intervention and placebo was \(0.34\) kg which was not significant \((95\% CI = -0.42\) to \(1.10\) kg, \(P = 0.386\), Figure 2).

We compared the health status of the participants in the 9 studies to determine whether the health status of the elderly correlated with the greater gain in LBM. No significant gains in LBM compared to the controls were observed in subjects with diabetes \([19]\), chronic obstructive pulmonary disease \([29]\), limited mobility, who were sedentary \([8]\), moderately active \([18]\), or healthy and independent \([17]\) (Table 3).

**Muscle strength: double leg press**

Five of the 9 studies assessed the effect of nutritional intervention on muscle strength be double leg press \([8,17,19,20,26]\). Three of 5 studies reported that the strength of the leg press significantly increased in both placebo and intervention groups during the duration of the study and the mean change was similar in both groups \([8]\). Two studies reported no significant change in the strength of the leg press with respect to treatment time or group \([17,20]\).

Three studies were included in the analysis of the influence of protein supplements on leg strength \([8,20,26]\). No heterogeneity was found among 3 studies \((Q = 0.147, df = 2, P = 0.929; I^2 = 0.0%); and the fixed-effects model revealed no significant difference in mean change in muscle strength by double leg press between the placebo and treatment groups. The difference in mean change from baseline to end of study ranged from \(-1.00\) to \(5\) kg, with the overall difference in mean change being \(2.14\) kg \((95\% CI = -10.92\) to \(15.20\) kg, \(P = 0.748\), Figure 3A).

**Muscle strength: leg extension**

Six studies evaluated the effect of nutritional intervention on muscle strength by comparing leg extension muscle strength between the intervention and placebo groups \([17,19,20,26–28]\). Five of the 6 studies reported that the strength of the leg extension significantly increased in both groups during the duration of the study \([8,19,26–28]\). Two studies reported no significant change in the strength of the leg extension versus treatment time or group \([17,20]\).

Among the 6 studies with protein supplementation, 2 did not provide the mean muscle strength of leg extension for both groups at baseline and at completion of study \([8,17]\), hence the meta-analysis included 4 studies \([20,26,28]\). Since moderate heterogeneity was found among the studies \((Q = 4.52, df = 3, P = 0.360; I^2 = 33.66%); a fixed-effects model was used for the meta-analysis.
| Author                | Study type | Comparison                  | Duration of Intervention | Number of cases | Mean Age (year) | Sex (Male %) | Mean BMI (kg/m²) | Lean body mass (kg) | Muscle strength (kg), double leg press | Muscle strength (kg), leg extension |
|-----------------------|------------|-----------------------------|--------------------------|-----------------|----------------|--------------|------------------|---------------------|----------------------------------------|----------------------------------|
| Daly et al [27]       | RCT        | Protein vs Control          | 4 months                 | 53 vs 47        | 72 vs 74       | 0 v. 0       | 28 vs 28         | 0.6 (0.3, 0.8)* vs 0.1 (-0.4, 1.1)* | NA                                    | NA                                |
| Vermeeren et al [28]  | RCT        | Protein vs Control          | mean 9 days              | 23 vs 24        | 66 vs 65       | 61 vs 75     | 20 vs 21         | Mean change from baseline: – 0.5 ± 2.6 vs –0.4 ± 2.7 | NA                                    | NA                                |
| Chale et al [8]       | RCT        | Protein vs Control          | 6 months                 | 42 vs 38        | 78 vs 77.3     | 40 vs 42     | 27 vs 26.9       | 46.7 ± 8.6 vs 46.4 ± 8.4 vs 46.7 ± 8.4 | 125 ± 39 vs 128 ± 47                  | 151 ± 58 vs 149 ± 54                |
| Aleman-Mateo et al [29]| RCT       | Protein vs Control          | 3 months                 | 20 vs 20        | 75 vs 77       | 40 vs 45     | 27 vs 26         | 37.1 ± 6.3 vs 36.8 ± 6.4 vs 37.9 ± 6.5 vs 37.6 ± 6.4 | NA                                    | NA                                |
| Tieland et al [20]    | RCT        | Protein vs Control          | 24 weeks                 | 34 vs 31        | 78 vs 81       | 41.2 vs 48.9 | 27 vs 26.2       | 45.8 ± 9.9 vs 46.7 ± 9.5 vs 45.8 ± 9.9 vs 46.6 ± 9.5 | 118 ± 47 vs 124 ± 50                  | 136 ± 47 vs 139 ± 50                |
| Tieland et al [26]    | RCT        | Protein vs Control          | 24 weeks                 | 31 vs 31        | 78 vs 79       | 35 vs 32     | 28.7 ± 28.2      | 47.2 ± 9.6 vs 45.7 ± 8.9 vs 48.5 ± 9.4 vs 45.4 ± 8.9 | 124 ± 39 vs 116 ± 36                  | 169 ± 39 vs 162 ± 41                |
| Leenders et al [19]   | RCT        | Leucine vs Control          | 24 weeks                 | 39 vs 28        | 71 vs 71       | 100 vs 100  | 27.4 ± 27.2      | 61.9 ± 6.9 vs 62.2 ± 6.9 vs 62.0 ± 6.2 vs 62.2 ± 6.9 | 202 ± 44 vs 205 ± 37                  | 217 ± 50 vs 218 ± 42                |
| Ferrando et al [18]   | RCT        | Amino acid vs Control       | 10 days                  | 10 vs 11        | 71 vs 68       | 10 vs 50    | NA               | 43.0 ± 0.6 vs 46.8 ± 1.0 vs 42.1 ± 0.6 vs 45.3 ± 1.0 | NA                                    | NA                                |
| Verhoeven et al [17]  | RCT        | Leucine vs Control          | 12 weeks                 | 15 vs 14        | 70 vs 100      | 25.9 ± 26.3  | 54.6 ± 5.8 vs 55.8 ± 3.4 vs 55.0 ± 5.8 vs 56.2 ± 4.1 | 170 ± 8 vs 172 ± 6                    | 85 ± 3 vs 85 ± 3                    |

NA, not available; RCT: randomized controlled trial.

*values are within-group mean absolutes of the change from baseline with 95% confidence intervals in parentheses.
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The difference in mean change from baseline to end of study in the 4 studies ranged from 0 to 18 kg with the overall difference in mean change from baseline to end of study being 2.28 kg (95% CI = 1.73 to 6.29 kg, P = 0.265, Figure 3B). The combined difference in mean change of muscle strength by leg extension from baseline to end of study revealed no significant difference between the control and treatment groups.

Sensitivity analysis
To assess the effect of a single study on the results of the meta-analysis, we removed each study in turn for LBM (Figure 4A), muscle strength by double leg press (Figure 4B), and muscle strength by leg extension (Figure 4C). The removal of any study did not alter the magnitude and direction; taken together, these results indicated that the meta-analysis showed good reliability.

Table 3. Summary of 9 trials included in the systematic review and meta-analysis.

| Author (Year) | Condition of elderly | Supplement given | Significant increased LBM to baseline | Significant increased Leg press to baseline | Significant increased Leg extension to baseline | Significant increased Physical performance |
|---------------|----------------------|------------------|--------------------------------------|--------------------------------------------|-----------------------------------------------|---------------------------------------------|
| Daly et al [27] | Healthy | Max.45 g protein/twice daily | Significant increased in protein group, different between groups | ND | Significant increased in protein group, different between groups | Significant increased in both group, similar between groups |
| Vermeeren et al [28] | COPD | 125 ml/three times daily | Neither group | ND | Neither group | ND |
| Chale et al [8] | Mobility limited | 20 g protein/day twice daily | Both groups improved, and also significant different between groups | Both groups to baseline | Both groups to baseline | Significant for whey group |
| Aleman-Mateo et al [29] | Healthy | 15 g protein/day | Both groups improved, but no significant different between groups | ND | ND | ND |
| Tieland et al [20] | Pre-frail and frail | 15 g protein twice daily | Neither group | Both groups to baseline | Both groups to baseline | Both groups |
| Tieland et al [26] | Pre-frail and frail | 15 g protein twice daily | Significant increased in protein group, different between groups | Neither group | Trend toward significant improvement in protein group vs control | Significant improvement in protein group vs control |
| Leenders et al [19] | Type 2 diabetes | 2.5 g leucine three times daily | None | Increased vs time in both groups, similar between groups | Increased vs time in both groups, similar between groups | ND |
| Ferrando et al [18] | Moderately active | 15 g EAA three times daily | None | ND | ND | Increased vs time in both groups, similar between groups |
| Verhoeven et al [17] | Healthy | 2.5 g leucine three times daily | None vs time or groups | None vs time or groups | None vs time or groups | ND |

COPD, chronic obstructive pulmonary disease; EAA, essential amino acids; LBM, lean body mass; ND, not described.
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The difference in mean change from baseline to end of study in the 4 studies ranged from 0 to 18 kg with the overall difference in mean change from baseline to end of study being 2.28 kg (95% CI = −1.73 to 6.29 kg, P = 0.263, Figure 3B). The combined difference in mean change of muscle strength by leg extension from baseline to end of study revealed no significant difference between the control and treatment groups.

Sensitivity analysis
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Publication Bias
Publication bias (Figure 5) was assessed using the LBM results only as more than 5 studies reported results for this outcome (note: more than five studies are required to detect funnel plot asymmetry [30]). Egger’s test results showed that there was no publication bias in LBM results among studies (Figure 5, t = 0.046, one-tailed P = 0.483).
Figure 3. Forest plot showing results for the meta-analysis of difference in mean change from baseline in (A) muscle strength of double leg press and (B) muscle strength of leg extension after intervention: treatment vs. control. Abbreviation: CI, confidence interval. doi:10.1371/journal.pone.0109141.g003

Figure 4. Results of sensitivity analysis to examine the influence of individual studies on pooled estimates as determined using the leave-one-out approach: (A) lean-body-mass; (B) muscle strength of double leg press. Abbreviation: CI, confidence interval. doi:10.1371/journal.pone.0109141.g004
Protein/Amino Acid Supplementation in Elderly

Discussion

This meta-analysis of 9 placebo-controlled studies assessed protein and amino acid supplementation on improving LBM in elderly subjects. Our analysis detected no significant differences between placebo and treatment groups in mean change from baseline to the end of the studies of LBM or muscle strength as measured by double leg press or leg extension in a mixed elderly population.

Multiple studies, several of which were included in our meta-analysis, found no significant benefit of protein supplementation compared to placebo in improving LBM [8,20,26–29,31]. However, protein supplementation has increased LBM and strength in some studies [32]. This inconsistency raises questions of whether it may be due to differences in study design, difference in efficacy of the supplements tested, or differences among the populations analyzed. Identification of the variables that influence the outcome of high protein intake towards a significant increase in LBM or leg strength would provide important guidance for physicians and for cost effective usage of protein supplementation.

The health and physical status of the patient may influence outcomes. Physical condition may affect response to protein or amino acid supplementation. One study showed that whey supplementation augmented LBM significantly more than placebo in pre-frail and frail elderly subjects receiving resistance training [20] but not in another study of elderly subjects with limited mobility that also received protein supplements and resistance training [8]. These findings suggest that the physical condition of the elderly is not solely responsible for the divergent results. Undernourishment may be another condition that significantly affects the outcome [33]. An earlier meta-analysis showed that protein supplementation induced significant weight gain in undernourished elderly subjects and may reduce mortality [33]. In addition, some elderly subjects may have reduced sensitivity to the amino acid induced anabolic signals and thus have a higher propensity to muscle wasting [21]. Addition of leucine appeared to normalize these anabolic signals [14,32]. The health status or stage of the skeletal muscle (whether the person does or does not have sarcopenia) may also affect their ability to respond to protein or amino acid supplementation.

The provided supplement or its dosage also may impact treatment outcomes since supplementation with essential amino acid was not as efficacious in increasing LBM in elderly subjects as whey protein in a direct comparison [32]. Both whey and caseinate supplementation induced a similar increase in protein synthesis after heavy resistance training in healthy elderly participants [12]. Interestingly, a fortified, hydrolyzed collagen protein supplement added to a relatively low-protein diet maintained LBM to a greater extent than whey protein [34]. In some studies [7,11,13], supplementation with essential amino acids improved LBM or muscle protein synthesis rate in elderly subjects; however, another study did not find any benefit of supplementing with amino acids [14].

Loss of muscle tissue or development of sarcopenia is accelerated by bed rest and lack of physical activity [23]. The elderly in the Tieland et al study [26] performed resistance-type exercise 2 times per week for 24 weeks and had a significant increase in LBM in the supplement group, whereas 5 of the included studies involved participants on bed rest [18], no exercise program [17,20,29], or patients who were hospitalized [28]. All participants in the study reported by Daly et al [27] performed resistance training. Consistent with the findings of Tieland et al [26], Daly et al [27] found that participants in supplement group had a significant increase in LBM compared with participants in the control group. The participants of the Chale et al study [8] also performed resistance training and both treatment and placebo groups had similar increases in LBM and leg muscle strength; although, the whey group showed a significant improvement in physical performance [8]. Similarly, in the study by Leenders et al [19] both treatment and control groups reported a mean of 1.55 h physical exercise daily and both groups had similar but significant increases in mean leg strength (both leg press and extension). The resistance training regimen in the study by Tieland et al [26] included several more types of exercises than that of Chale et al [8], while the training regimen in the study of Daly et al [27] involved progressive resistance training. Hence, the beneficial interaction between resistance training and whey protein supplementation on muscle mass and strength gain may depend to some extent on the type of resistance training regimen used. In support for the benefits of concurrent resistance training, a meta-analysis of six studies of older participants reported that protein supplementation augmented loss of fat free mass [35].

![Funnel Plot of Precision by Difference in means](image-url)

Figure 5. Funnel plot for the assessment of publication bias for studies included in the meta-analysis of the assessment of the mean change from baseline in lean body mass after intervention.
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In conclusion, these results indicate that amino acid or protein supplements did not increase lean body mass gain and muscle strength significantly more than placebo in a diverse elderly population. The ability of protein or amino acid supplementation to augment muscle mass and strength may depend on the nutritional physical status of the participants, or their ability to digest protein and absorb the amino acids, the sensitivity of the anabolic pathways in muscles, and the resistance training regimen itself.

Supporting Information

Figure S1 PRISMA 2009 Flow Diagram. (DOC)

Checklist S1 PRISMA 2009 Checklist. (DOC)

Author Contributions

Conceived and designed the experiments: ZRX YMY. Performed the experiments: QZ. Analyzed the data: QFG. Wrote the paper: QFG.

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