Effects of protein supplements consumed with meals, versus between meals, on resistance training–induced body composition changes in adults: a systematic review

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Context: *The impact of timing the consumption of protein supplements in relation to meals on resistance training–induced changes in body composition has not been evaluated systematically.* ***Objective:*** *The aim of this systematic review was to assess the effect of consuming protein supplements with meals, vs between meals, on resistance training–induced body composition changes in adults.* ***Data Sources:*** *Studies published up to 2017 were identified with the PubMed, Scopus, Cochrane, and CINAHL databases.* ***Data Extraction:*** *Two researchers independently screened 2077 abstracts for eligible randomized controlled trials of parallel design that prescribed a protein supplement and measured changes in body composition for a period of 6 weeks or more.* ***Results:*** *In total, 34 randomized controlled trials with 59 intervention groups were included and qualitatively assessed. Of the intervention groups designated as consuming protein supplements with meals (n = 16) vs between meals (n = 43), 56% vs 72% showed an increase in body mass, 94% vs 90% showed an increase in lean mass, 87% vs 59% showed a reduction in fat mass, and 100% vs 84% showed an increase in the ratio of lean mass to fat mass over time, respectively.* ***Conclusions:*** *Concurrently with resistance training, consuming protein supplements with meals, rather than between meals, may more effectively promote weight control and reduce fat mass without influencing improvements in lean mass.*

INTRODUCTION

It is well established that consuming dietary protein proximate to resistance-type exercise sessions promotes a positive net protein balance during postexercise recovery.[1–4] Two meta-analyses demonstrated that consuming protein supplements concurrently with prolonged resistance exercise training increased lean mass compared with consuming a nonprotein supplement control.[5,6] These reviews did not consider the timing of protein supplementation with respect to meals. The effect of consuming protein supplements with meals, vs between meals, on resistance training–induced changes on body composition has not been reviewed.

Protein supplements are available in ready-to-drink, powdered, and solid form and are marketed to augment different outcomes such as weight gain, weight loss, and weight management. However, for each outcome, the promoted timing of protein intake varies. Protein supplements designed to augment weight gain or support weight stability are promoted for

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consumption between meals.[7–10] For weight loss, protein supplements are often recommended for ingestion either with a meal or as a meal replacement.[11,12] There are scientific rationales that support consuming a protein supplement either with a meal or between meals to differentially influence body composition responses. Consuming a protein supplement between meals may decrease compensatory eating behaviors, thereby increasing energy intakes and body weight.[13] Conversely, consuming a protein supplement twice daily with meals led to complete energetic compensation in adults who performed resistance training, although body composition was not affected.[14] Consequently, the timing of protein supplementation may be of particular importance, depending on the desired body weight and body composition outcome. The aim of this systematic review of literature was to investigate whether the existing research studies support consuming protein supplements between meals, vs with meals, to differentially change body composition in adults who initiate resistance training regimens.

METHODS

The current systematic review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The description of the PICOS (population, intervention, comparison, outcome, and study design) criteria used to define the research question is presented in Table 1.

Table 1 **PICOS criteria for inclusion and exclusion of studies**

Parameter	Inclusion criterion
Population	Apparently healthy adults, mean age of group ≥19 years
Intervention	Groups that consumed protein supplements between meals
Comparison or control	Groups that consumed protein supplements with meals
Outcome	Changes in lean mass
Study design	Studies ≥6 weeks in length
Research question	What is the effect of consuming a protein supplement with meals, vs between meals, on changes in body composition in adults performing resistance training?

Data sources

A systematic search of the literature was conducted in April 2016 using the PubMed, Cochrane Reviews, Scopus, and CINAHL (Cumulative Index of Nursing and Allied Health) databases and is current to May 2017. Search terms, keywords, and phrases were selected to include appropriate articles on protein supplementation, lean mass, and resistance training (see Table S1 in the Supporting Information online).

Inclusion criteria

Inclusion criteria were as follows: randomized controlled trial with parallel design; intervention duration ≥6 weeks; group mean age ≥19 years; male or female participants; pre- or postmenopausal females; apparently healthy humans with no intentional/prescribed diet-induced energy restriction or surplus; concurrent resistance training with or without aerobic training; prescribed a protein supplement while indicating the timing of ingestion; use of an acceptable method of body composition assessment; and English language publication. Protein supplements (whey, casein, soy, bovine colostrum, and rice) were acceptable if they were isolates, concentrates, or hydrolysates consumed alone or in combination with other nutrients (creatine, amino acids, and carbohydrate) and protein sources. Dual-energy X-ray absorptiometry, air-displacement plethysmography, and hydrostatic weighing were deemed acceptable methods for detecting changes in lean mass on the basis of their high reliability and validity.[15–19] Measurement of total body potassium or doubly labeled water was also acceptable; however, none of the vetted articles used these methods. Articles that used skin folds and bioelectrical impedance were excluded because of unreliable estimations of lean mass.[20,21]

Article selection and data extraction

Collectively, database searches yielded 2074 articles (PubMed, 1207; Cochrane, 243; Scopus, 157; CINAHL, 468). After screening abstracts, 264 articles, including 3 other articles identified from other sources, were independently read and reviewed by 2 authors (J.L.H. and R.E.B.). A total of 230 were excluded for the following reasons: full text was not accessible to the authors, article did not report on protein supplement–related research; mean age of intervention group was less than 19 years; participants were in energy restriction; lean mass was not reported or was reported only graphically and numerical data were not accessible; researchers used an unacceptable method of body composition assessment; or participants were characterized as having a chronic disease or having severe injury. Four of 7 authors contacted for additional information responded and provided data included in this systematic review. Thirty-four articles were selected for inclusion in this systematic review (Figure 1).[14,22–54]

The following information was extracted independently by J.L.H. and R.E.B. from the selected articles using an electronic form: first author's last name;

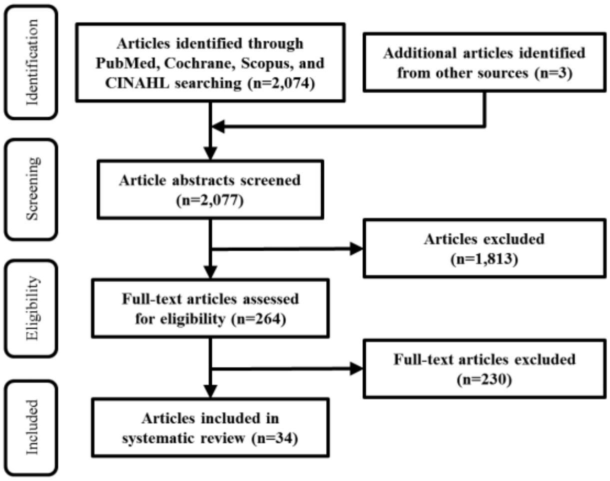

Figure 1 **Flow diagram of the literature search process.**

publication year; sample sizes of each intervention group; sex of participants; mean age of group; duration of intervention; prescribed timing of protein supplement intake; protein source; frequency of resistance training; method of body composition assessment; and pre- and postintervention and net changes in body mass, lean mass, and fat mass. Incongruous information extracted between the 2 authors was reexamined and discussed until concurrence was achieved.

Twenty-nine studies included in this review measured body composition using dual energy X-ray absorptiometry. Two more utilized air displacement plethysmography, and 3 used hydrostatic weighing to measure body composition (see Table S2 in the Supporting Information online). There were some discrepancies in how lean mass was reported, with 21 articles using the term "lean mass," 6 articles using "lean tissue mass," 6 articles using "fat-free mass," and 1 article using "bone-free fat-free mass." For this review, these terms were considered synonymous, and "lean mass" is used consistently. Articles that included bone mineral content within lean mass were included in the analyses because bone mineral content only accounts for approximately 5% of total lean mass[55]; moreover, bone turnover (remodeling) is very slow, requiring a minimum of 4 to 6 months.[56]

Critical appraisal

The risks of selection, performance, and detection biases were evaluated from selected articles using a modified Cochrane tool (see Table S2 in the Supporting Information online).[57] Details of the methods for assessment of dietary control and body composition are also included in Table S2 in the Supporting Information online.

Calculations

With-meal ingestion of protein (PRO-WITH; n = 9 studies and 16 groups[14,22–29]) is defined as consumption of a dietary protein-rich supplement immediately after a meal (n = 4), with a meal (n = 9), or as a high-protein meal replacement (n = 3) (see Table S3 in the Supporting Information online). Between-meal ingestion of protein (PRO-BET; n = 25 studies and 43 groups[30–54]) is defined as consumption of a dietary protein supplement predominantly either proximate to resistance training (n = 31) or during a generic time period (ie, before bed [n = 1], before breakfast and before bed [n = 1], between breakfast and lunch and before bed [n = 1], mid-morning and before bed [n = 3], mid-morning and evening [n = 2], morning and evening [n = 1], or upon waking and before bed [n = 3]) (see Table S3 in the Supporting Information online). Studies that included groups whose prescribed supplement timing fit into both the "with" and "between" categories were classified on the basis of the predominant timing of supplementation (n = 3 studies and 6 groups[24,25,29]). For example, a group consuming a dietary protein supplement with breakfast on non–resistance training days and a dietary protein supplement post resistance training would be placed in the PRO-WITH category if they trained 3 or fewer days per week.

The number of articles that reported changes in body mass, lean mass, and fat mass varied, since some articles did not report results for all parameters. Some articles also did not report changes from baseline. For these articles, the absolute change and the percentage of change were calculated as the difference between pre- and post-intervention values. The results from each group are presented qualitatively as categorical variables that either increased or decreased from baseline.

A modified form of a previously published coding system to classify strength of evidence of associations with physical activity in children and adolescents was used to summarize the effect of consuming protein supplements with meals, vs between meals, on body mass, lean mass, and fat mass (Table 2).[58] The coding system was used to provide discrete cutoff points to indicate whether the totality of the research included in the current review consistently or inconsistently affected the outcomes of interest. If 34% to 66% of groups experienced a change from baseline, the result was categorized as an inconsistent effect (designated as "↔"; Figure 2). When 67% to 100% of the groups experienced a change from baseline, the result was categorized as either a consistent positive (↑, increase from baseline) or a consistent negative (↓, decrease from baseline) effect. By default, if 67% to 100% of groups reported a change from baseline for a specific outcome, 0% to 33% of groups reported a change in the opposite direction. Similarly, if a result was categorized as having an inconsistent effect, by default, the effect was inconsistent in both the positive and the negative directions. Therefore, only the inconsistent and consistent results are reported.

RESULTS

Trial features and participant characteristics

Thirty-four articles that included 59 intervention groups met all inclusion criteria. Descriptions of each article (Trial length and protein supplement timing) and the characteristics of participants (age and sex) are shown in Table S3 in the Supporting Information online. Forty-three of the groups were classified as PRO-BET and 16 were classified as PRO-WITH. This resulted in a total of 608 participants included in the PRO-BET category (age < 50 years, n = 30 groups; age > 50 years, n = 13 groups; mean age, 55 years; median age, 25 years; range, 19–74 years) and 373 participants in the PRO-WITH category (age < 50 years, $n = 3$ groups; age > 50 years, n = 13 groups; mean age, 55 years; median age, 25 years; range, 23–81 years). Twenty-seven groups in the PRO-BET category were less than 12 weeks in duration and 16 were between 12 and 16 weeks in duration. All 16 of the PRO-WITH groups were 12 to 36 weeks in duration, with 7 being 12 to 16 weeks long.

Table 2 **Rules for classifying the strength of evidence for the outcomes assessed**[a]

Percentage of groups in which evidence supported the outcome	Summary code	Meaning of code
34–66	↔	Inconsistent effect
67–100	↑	Consistent positive effect
	↓	Consistent negative effect

[a]Codes represent summary of effect. Inconsistent effect (↔): 34%–66% of groups reported either an increase or a decrease from baseline; consistent positive (increase) (↑) or negative (decrease) (↓) effect: 67%–100% of groups reported a change in that direction from baseline.

Quality of selected articles

Six articles were deemed at low risk of selection bias, since they provided specified methods of randomization and/or allocation concealment in the original articles, while the other selected articles did not clearly report the randomization and allocation concealment methods (see Table S2 in the Supporting Information online). Twenty-seven of the 34 articles included details on

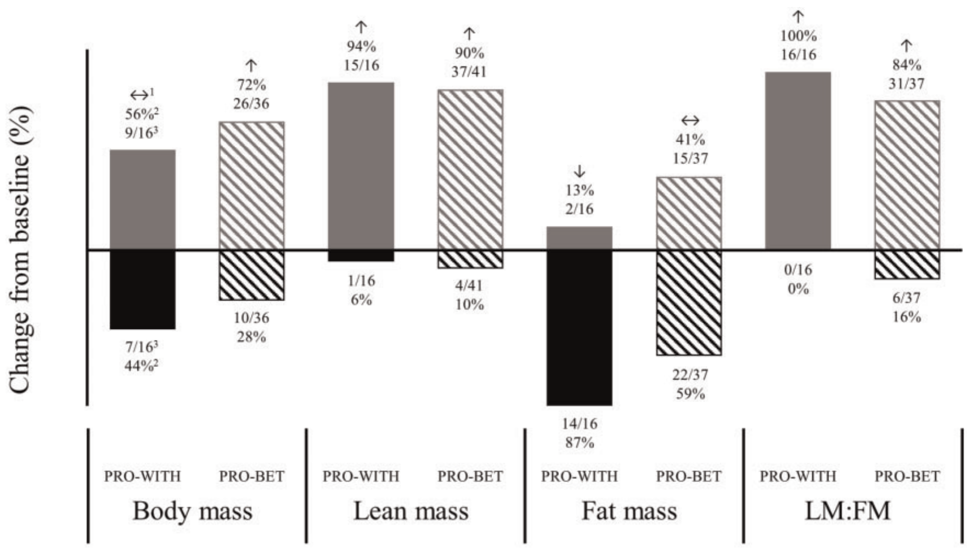

Figure 2 **Changes in body mass, fat mass, lean mass, and ratio of lean mass to fat mass in groups consuming protein supplements with meals vs between meals**. [1]A modified form of a previously published coding system was used to summarize the effects of consuming protein supplements with meals vs between meals.[58] [2]Represents the percentage of groups that reported either an increase or a decrease from baseline. [3]Represents the number of groups that reported either an increase or a decrease from baseline out of the total number of groups assessed for each outcome. *Abbreviations and symbols:* PRO-BET, groups ingesting protein supplements between meals; PRO-WITH, groups ingesting protein supplements with meals; FM, fat mass; LM, lean mass; ↔, inconsistent effect: 34%–66% of groups reported either an increase or decrease from baseline; ↑, consistent positive effect (increase from baseline): 67% to 100% of groups reported a change in that direction from baseline; ↓, consistent negative effect (decrease from baseline): 67% to 100% of groups reported a change in that direction from baseline.

whether participants and investigator(s) were blinded during the intervention or were blinded until data collection was completed. Thirty-one articles indicated that the protein supplements used in the article were provided to the participants.

Results of systematically searched assessment

A quantitative meta-analysis could not be performed because the systematic search of literature did not identify any randomized controlled trial that directly compared the effects of consuming protein supplements with meals, vs between meals, on body composition changes with resistance training. Qualitatively, consuming protein supplements between meals had a consistent effect on increasing body mass (increase in 72% of groups), whereas consuming protein supplements with meals had an inconsistent effect (increase in 56% of groups) (Figure 2).[59] When protein supplements were consumed with meals and between meals, there was a consistent positive effect on lean mass (increase in 90% of PRO-BET and 94% of PRO-WITH groups). Consuming protein supplements between meals had an inconsistent effect on fat mass (decrease in 59% of groups), whereas consuming protein supplements with meals had a consistent negative effect on fat mass (decrease in 87% of groups). With regard to changes in the ratio of lean mass to fat mass, consuming protein supplements between meals and with meals had a consistent positive effect on the ratio (increase in 84% of PRO-BET and 100% of PRO-WITH groups).

A secondary quasi-sensitivity analysis was conducted using results from groups whose interventions were 12 to 16 weeks in duration to better control for any potential temporal effects of the intervention on the outcomes (see Table S4 in the Supporting Information online). The results are comparable to the analyses in which all groups were included. Consuming protein supplements between meals ($n = 16$ groups) had consistent positive effects on body mass, lean mass, and the ratio of lean mass to fat mass; there was an inconsistent effect on fat mass. Consuming protein supplements with meals ($n = 7$ groups) had a consistent negative effect on body mass and fat mass and a consistent positive effect on lean mass and the ratio of lean mass to fat mass.

Further quasi-sensitivity analyses were conducted with younger adults (mean group age, 19–50 years); older adults (mean group age, > 50 years); groups consuming protein supplement doses estimated to achieve maximal muscle protein synthesis (doses of $\geq$0.24 and 0.40 g/kg in younger and middle-aged adults and in older adults, respectively[59]); matching dosing ranges (10–75 g/d); matching total protein intake ranges (0.9–1.6 g/kg/d); matching dosing and total protein intake ranges; and by excluding studies when a protein supplement also contained creatine (see Table S4 in the Supporting Information online). Creatine supplementation was found to increase total body mass and lean mass in older adults concurrently engaged in resistance training in 2 previous meta-analyses[60,61] and was assessed for any mediating effect of the results reported in the current review. The qualitative results from the quasi-sensitivity analyses are comparable with the those from the original analyses, although this cannot be statistically confirmed. The directional changes from baseline are reported here, and specific magnitudes of changes for each outcome are shown in Table S5 of the Supporting Information online.

DISCUSSION

The objective of this systematically searched assessment of literature was to assess whether consuming protein supplements with meals, vs between meals, differentially affected changes in body composition in adults concurrently performing resistance training. Qualitatively, results suggest that consuming protein supplements between meals may promote increases in body mass, and consuming protein supplements with meals may promote reductions in fat mass. Consistent improvements in lean mass and in the ratio of lean mass to fat mass may be achieved when consuming protein supplements either between meals or with meals in combination with resistance training.

Consuming protein supplements between meals consistently increased body mass, whereas consuming protein supplements with meals had an inconsistent result. One inclusion criterion for this systematic review was the absence of a controlled diet aimed at regulating energy intake. Groups were effectively "free-feeding" adults. With this in mind, protein supplements consumed between meals could be considered a snacking occasion. Although the definition of snacking is not clear, it is generally agreed that consuming energy-containing foods or beverages outside a primary eating occasion (ie, breakfast, lunch, dinner) is an acceptable designation.[62] In one 2-week trial, mandatory snacking promoted weight gain in free-living adults.[13] This effect was shown to be exacerbated when the snacks were consumed as beverages,[63,64] the predominant form of protein supplement among the groups included in this review. Consuming protein supplements between meals or as a snack may also increase eating frequency, which may promote higher body weight.[65–67] In contrast, protein supplements consumed with meals or as meal replacements renders them meal components. They may displace some of the energy that otherwise would have been consumed at that meal time. Results from 1 randomized controlled trial showed that participants who consumed an approximately 200-kcal whey protein–rich supplement twice daily (with breakfast and lunch meals) for 36 weeks had complete energetic compensation in the diet and maintained their body weight.[14] Collectively, results from the current systematic review fit within the existing observational and randomized control trial literature, demonstrating that protein supplementation between meals may promote greater increases in body mass than protein supplementation with meals.

Consuming protein supplements either between meals or with meals in combination with resistance exercise training consistently increased lean mass. This finding suggests that resistance training is a more potent anabolic stimulus than the timing of protein supplementation in relation to meals. Consuming protein supplements while concurrently resistance training creates a positive net protein balance.[1–4] Two meta-analyses showed that participants who consumed protein supplements while resistance training had greater lean mass accretion than participants consuming a nonprotein placebo.[5,68] Results from the current study support previous findings that increases in lean mass can be attained through a combination of resistance training and consumption of protein supplements.[5,68]

Consuming protein supplements with meals consistently decreased fat mass, whereas consuming protein supplements between meals had inconsistent effects on fat mass. Consuming protein supplements with meals may lead to partial meal replacement that would displace the energy that would be consumed otherwise. The within-meal effects of protein supplementation are consistent with previous observations that adults may fully compensate for the additional energy from protein supplements that are consumed with meals.[14] The decrease in fat mass fits within the results of this systematic review, which showed a consistent increase in lean mass and an inconsistent change in body mass. Since lean mass consistently increased and body mass change was inconsistent, it follows that fat mass would decrease.

Strengths and limitations

This review is subject to the standard limitations of systematic reviews, such as publication bias and keyword formation that omit publications that would fit within the search parameters. However, in addition to systematically searching PubMed, CINAHL, Cochrane Reviews, and Scopus, 2 authors independently assessed articles within relevant meta-analyses for inclusion in this review to mitigate these limitations. Specific limitations to this study include a disproportionate over-representation of older adults in the PRO-WITH category compared with the PRO-BET category, variations in trial duration, and differences in supplementation quantity and total protein intake. To address these potential confounding factors, quasi-sensitivity analyses were conducted to investigate any potential influence on the outcomes (see Table S4 in the Supporting Information online). There do not appear to be differences in the proportion of groups within each outcome; however, the inability to perform statistical analyses on the subgroups prohibits conclusive statements about their influence.

The inclusion and exclusion criteria for this systematic review were designed to capture studies that adequately documented protein supplementation in relation to meal consumption. Incidentally, more PRO-BET groups consumed protein supplements proximate to resistance training sessions (before or after sessions) than PRO-WITH groups. Protein supplementation around resistance training in order to supply the skeletal muscle with the necessary precursor amino acids to promote skeletal muscle growth has often been a topic of interest. However, the influence of protein supplementation timing could not be adequately reviewed or speculated on here because there may be relevant research not captured during this review process. Four studies included in this review did test the effect of protein supplementation timing proximate to, vs not proximate to, resistance training.[33,35,40,43] Three studies reported that the timing of protein supplementation did not differentially affect changes in lean mass,[33,40,43] while 1 reported that protein supplementation before and after resistance training promoted greater gains in lean mass than when the same protein supplement was consumed in the morning and evening.[35] Supplements containing mixtures of protein and creatine may be another potential limitation.[60,61] A quasi-sensitivity analysis excluding groups that consumed protein supplements containing creatine did not alter the reported results. Collectively, these quasi-sensitivity analyses should be interpreted with caution because of the low number of groups within each category. There is also the possibility that the effects reported in the current review may not be specific to protein supplementation but rather to the energy contents of the supplements. Further research that includes nonprotein supplements is needed.

CONCLUSION

The results from this systematic review provide novel information for individuals who choose to consume a protein supplement as part of their dietary pattern to promote body mass gain or improve body composition through fat mass reduction. Regardless of the timing of protein supplement intake in relation to meals, lean mass is likely to increase in response to resistance training. However, consuming protein supplements with meals, rather than between meals, may be a more effective dietary strategy to improve resistance training–induced changes in body composition by reducing fat mass, which may be relevant for adults looking to improve their health status. Conversely, consuming protein supplements between meals may be more effective at increasing overall body mass.

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Supporting Information

The following Supporting Information is available through the online version of this article at the publisher's website.

Table S1 **Search terms**

Table S2 **Risk-of-bias assessment of randomized controlled trials included in a systematically searched qualitative assessment on the effects of consuming a protein-rich supplement with meals vs between meals on body composition changes in resistance training adults**

Table S3 **Descriptions of the randomized controlled trials included in a systematically searched qualitative assessment on the effects of consuming a protein-rich supplement with meals vs between meals on body composition changes in resistance training adults**

Table S4 **Qualitative assessment on the directional effect of consuming a protein supplement with meals vs between meals on body composition changes in resistance training adults**

Table S5 **Qualitative assessment on the magnitude of effect of consuming a protein supplement with meals vs between meals on body composition changes in resistance training adults**

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