Protein Supplementation and Resistance Training in Childhood Cancer Survivors

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ABSTRACT

KRULL, M. R., C. R. HOWELL, R. E. PARTIN, J. LANCTOT, S. PHIPPS, J. L. KLOSKY, G. CARNEY, D. A. MULROONEY, L. L. ROBISON, M. M. HUDSON, and K. K. NESS. Protein Supplementation and Resistance Training in Childhood Cancer Survivors. *Med. Sci. Sports Exerc.*, Vol. 52, No. 10, pp. 2069–2077, 2020. **Purpose:** Muscle weakness, low lean body mass, and poor physical performance are prevalent among adult survivors of childhood cancer (survivors). We evaluated the feasibility and effects of resistance training with and without protein supplementation on lean body mass and muscle strength among survivors. **Methods:** This double-blind placebo-controlled trial enrolled survivors ≥18 to <45 yr old. Participants were randomized to resistance training with protein supplement (21 g whey protein per day, 90 kcal) (RT + S) or resistance training with placebo (sucrose, 90 kcal) (RT + P). Participants received educational materials, access to a local fitness center, and a tailored resistance training program with tapered supervision. Participant retention and adherence were used to evaluate feasibility. Lean body mass and muscle strength were assessed at baseline and 24 wk, using dual x-ray absorptiometry, and dynamometer testing or one-repetition maximum testing, respectively. Mean changes were compared with two-way ANOVA. **Results:** Of 70 participants randomized, 57 completed the 24-wk intervention (24 in RT + S, 33 in RT + P). The RT + S group completed 74.8% and the RT + P group completed 67.0% of exercise sessions. Mean ± SD age for those who completed was 33.1 ± 7.0 yr, 67% were White and 47% female. There were no differences in change in lean mass (RT + S, 1.05 ± 2.34 kg; RT + P, 0.13 ± 2.19 kg; $P = 0.10$) or strength (grip RT + S, 1.65 ± 4.17 kg; RT + P, 1.63 ± 4.47 kg; $P = 0.98$; mean leg press RT + S, 58.4 ± 78.8 kg; RT + P, 51.0 ± 65.1 kg; $P = 0.68$) between groups. Both lean mass ($P = 0.03$) and strength (grip $P = 0.003$, leg press $P < 0.001$) increased over time. **Conclusions:** Supervised resistance training among survivors with protein supplementation is feasible but not more effective at increasing total lean body mass than resistance training alone. **Key Words:** LEAN BODY MASS, RESISTANCE TRAINING, ONCOLOGY, DIET

Five-year survival rates among children newly diagnosed with cancer exceed 85%; estimates indicate that the number of survivors of childhood cancer living in the United States will surpass 500,000 in 2020 (1,2). However, cure is not without consequences; many survivors experience medical late effects as a result of cancer or its treatment. By age 45 yr, over 95% of childhood cancer survivors have at least one chronic health condition, including 36.5% with obesity, 22.6% with hypertension, and 50.9% with dyslipidemia (3). In addition, nearly 8% of childhood cancer survivors are frail (4), a phenotype characterized by low lean body mass and muscle weakness.

Fortunately, recent evidence indicates that lifestyle factors, including protein intake and resistance training, are associated with greater lean body mass and muscle strength in childhood cancer survivors (5). This suggests that survivors may have the opportunity to influence long-term health outcomes by adopting lifestyles that include a healthy diet and regular exercise. Resistance training with protein supplementation is a proven strategy for increasing muscle mass and strength in healthy populations (6). This strategy has demonstrated efficacy to improve muscle mass and strength in frail populations, including older adults and adults with cancer (7–9). It is possible a resistance training program may be beneficial in young adult survivors of childhood cancer.

The objectives of this study were to evaluate the feasibility and preliminary effectiveness of resistance training with (RT + S) and without protein supplementation (RT + P) on

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lean body mass, muscle strength, walking speed, self-reported exhaustion, and physical activity levels in young adult survivors of childhood cancer with low lean body mass.

METHODS

Participants. Participants were members of the St. Jude Lifetime Cohort, a study designed to characterize health outcomes among childhood cancer survivors as they age (10). The St. Jude Children's Research Hospital Institutional Review Board approved all procedures. Written informed consent was obtained from all participants before study evaluations. For the presented randomized study, eligible survivors were ≥18 and <45 yr of age at enrollment and survived >10 yr after primary cancer diagnosis. Eligible survivors had age- and sex-specific relative lean body mass (lean body mass divided by height in meters squared) *z*-score ≤ −1.0 (11), or, using previously established sex-specific cut points in our cohort (12), total lean body mass less than 75% in males or less than 70% in females. Participants lived in the Greater Memphis, Tennessee, area. Pregnant females and those with contraindications to resistance training or protein supplementation (e.g., renal disease) were not eligible. Participants received clearance to participate by a study physician after providing informed consent. Participants were randomized to receive either a daily medical quality protein supplement powder (Unjury®), which contained 21 g of protein (whey protein isolate and soy lecithin), 55 mg of sodium, 90 mg of potassium, and no sugar (90 calories per serving), to mix with water, or an isoelectric, isocaloric placebo that contained sucrose and no protein. Protein dosing was the same for all participants and based on the overall population averages of protein intake (1 $g \cdot kg^{-1}$ of body weight) and body mass (81.4 kg) seen in previous analysis in the SJLIFE cohort (5). Our goal was to achieve whey protein intake of 1.2–1.4 $g \cdot kg^{-1}$ of body mass (13), but to keep the dose similar to amounts provided in one serving of most commercial products. Twenty-one grams in an individual with body mass 81.4 kg adds approximately 0.3 $g \cdot kg^{-1}$. Zelen's stratified randomization was used to create blocks by sex and age (18–29, 30–<45 yr), assuring relatively equal distribution of participants among the two arms within stratum (14).

Intervention. Individuals in both (RT + S) and (RT + P) groups participated in a supervised individually tailored, progressive resistance training program three times per week for 24 wk. Supervision was tapered, beginning at two times per week for the first 4 wk, one time per week for weeks 5–12, every other week for weeks 13–20, and one time in the last month. Participants completed the remaining sessions each week on their own. Sessions were scheduled to avoid resistance training on two consecutive days. Resistance training consisted of six machine exercises: leg press, leg extension, chest press, horizontal row, and alternating vertical lateral pull and abdominals with biceps and triceps every other session. At the initial session, participants completed a one-repetition maximum (1RM) testing protocol to determine their individual weight limit for each exercise (15). Each training session consisted of 5 min of upper body or cycle ergometer or treadmill warm-up. The first 4 wk included four sets (10–15 repetitions) for lower body exercises and two sets (10–15 repetitions) for upper body exercises at 60% of 1RM, progressing to 75% of 1RM (four sets lower body, two sets upper body, 8–10 repetitions). Beginning at week 5, training was progressed to four sets (8 repetitions) for lower body exercises and three sets (8–10 repetitions) for upper body at 75%–80% of 1RM. The number of sets and repetitions were maintained for the remainder of the study with changes only to the exercise load based on repeated 1RM testing as described above, or at the trainer's discretion. As data support the effects of postexercise protein intake on increases in fat-free mass (16), participants were instructed to consume the supplement or placebo within 60 min after training on exercise days or midmorning on nonexercise days.

OUTCOMES

Feasibility. To examine feasibility, we evaluated participant recruitment and retention, adherence to the intervention, and level of support required to maintain adherence. Recruitment and retention were evaluated by monitoring the number of participants contacted, tested, randomized, and completing treatment. Adherence was assessed by review of participants' log book recordings of exercises performed per session, both when supervised by the exercise physiologist and when exercising independently. Participants also logged supplement consumption and were queried about consumption at the beginning of each training session. Personality type was measured using the Big Five Inventory 2 (BFI-2) (17), a modified version of the original BFI (18). The BFI-2 has 60 brief phrases that assess features of personality in terms of five domains: 1) extraversion, 2) agreeableness, 3) conscientiousness, 4) negative emotionality, or 5) open-mindedness. Scores for each domain range from 1.0 to 5.0. The BFI-2 has good internal validity (test–retest reliability coefficient 0.80) (17).

Lean body mass. After an overnight fast, dual x-ray absorptiometry (DXA) was used to determine lean body mass. Fat-free mass was measured in the total body scanning mode. If a participant was unable to have a DXA scan, skinfold measurements were used to determine lean body mass (19). Relative lean body mass was calculated by dividing lean body mass by height in meters squared (11).

Muscle strength. Approximately 5 to 7 d before the 1RM session, participants completed a familiarization session in which the trainer would teach the participant how to safely perform each warm-up and weight machine exercise, with very light weight to ensure the participants had proper form. At the 1RM session, participants completed a 5-min warm-up on a treadmill, or arm, or leg cycle ergometer before 1RM testing. For each weight exercise, participants performed a progressive warm-up to the perceived 1RM (six repetitions at 50% of perceived 1RM, followed by 3 min of rest, then four repetitions at 70% of perceived 1RM). After 3 min of rest following the machine warm-up, the machine was loaded with 90% of the participant's perceived 1RM and the participant

attempted to lift the weight one time. If the participant completed the lift successfully, weight was added at the trainer's discretion, and the lift was attempted again after 3 min of rest. This process was repeated until the lift was not successfully completed, at which time the previous completed lift was determined to be the 1RM. If the initial 1RM attempt at 90% of the perceived 1RM was not successfully completed, weight was removed at the trainer's discretion, and the lift was attempted again. The 1RM testing has been shown to be safe in untrained middle-age participants (20). Repeat testing for progression (or regression) of exercise load was completed at weeks 4, 8, 12, 16, and 20.

Walking speed. Usual walking speed was evaluated by having participants complete a timed 10-m walk test (21–23). Participants stood at the beginning of a marked location and were asked to walk as quickly as they could past the 10-m mark. An exercise physiologist timed the participant from the initiation of movement to when they crossed the 10-m point. Time was documented to the 10th of the nearest second.

Self-reported exhaustion. Self-reported exhaustion was evaluated with the vitality subscale of the Medical Outcomes Survey Short Form 36, Version 2 (24). This widely used generic health profile is appropriate for adults of all ages, has extensive age- and sex- specific norms for the U.S. population (25), and is valid and reliable in childhood cancer survivors (26).

Physical activity. Participants received an accelerometer with written instructions, programmed to begin recording for 7 d at 12:01 AM, on the day after the baseline assessment.

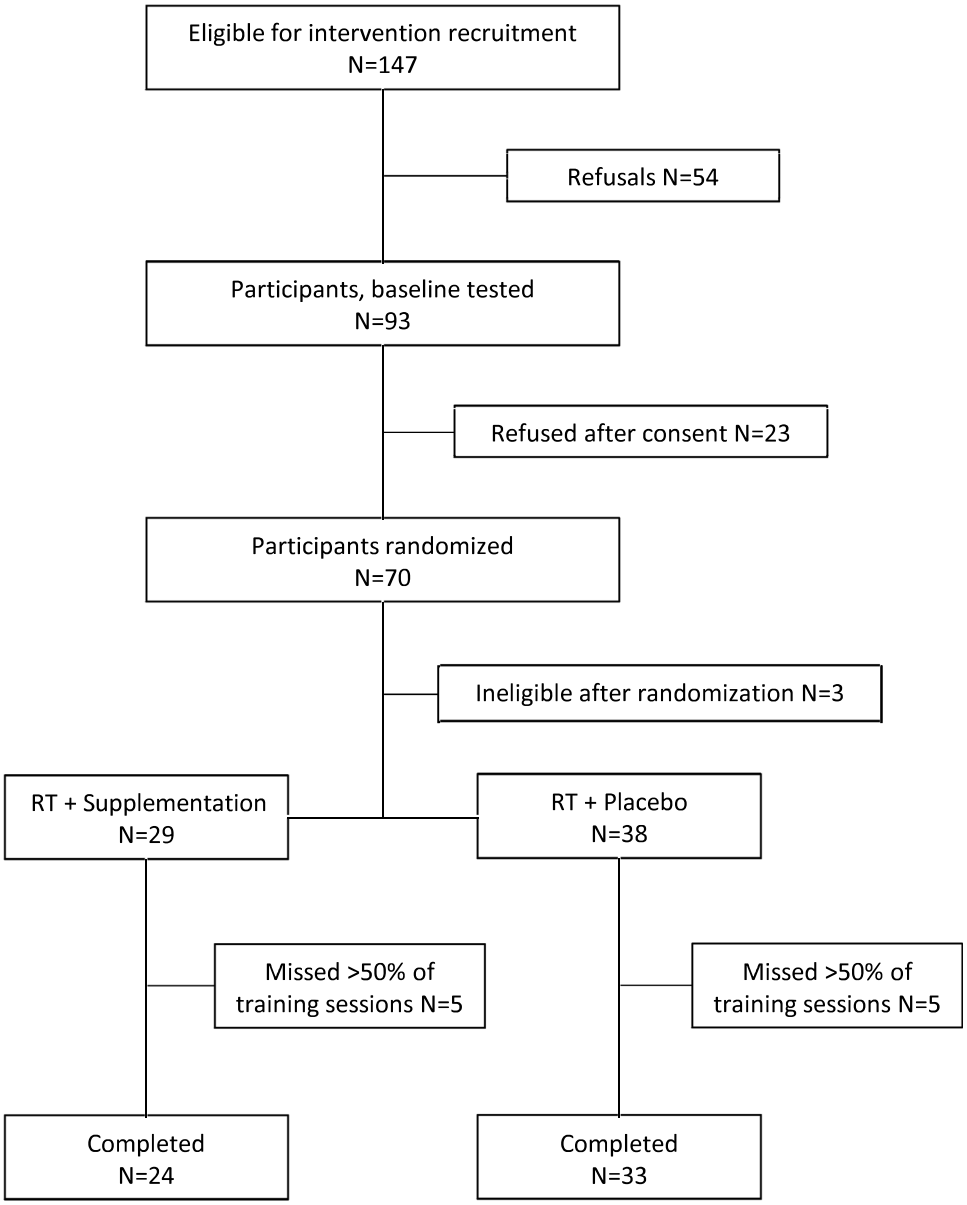

FIGURE 1—Consort diagram outlining recruitment, randomization, and completion of study intervention. Five survivors from the RT + S group completed less than 50% of training sessions. Five survivors from the RT + P group completed less than 50% of training sessions. RT + S, resistance training with protein supplement; RT + P, resistance training with placebo.

Participants received a second accelerometer to being recording for an additional 7 d starting at 12:01 AM on the day after their final training appointment. Wearing instructions were provided verbally, with demonstration. The device was programmed to detect and record magnitude of acceleration or "intensity" of movement. Data are stored in memory as "counts" per time interval. We used a 1-min time interval or "epoch." Minutes per day of moderate and vigorous physical activity were summed for each individual for analysis.

Dietary protein. The 110-item full length Block Food Frequency Questionnaire (27) was used to estimate customary intake of nutrients and food groups over the past year, including dietary protein. The data were processed using a food list from NHANES dietary recalls and a nutrient database from the USDA Food and Nutrient Database. A change in dietary intake, other than the supplement, was not expected. However, because total caloric or protein intake may affect outcomes, it was important to collect this information.

Statistical approach. Descriptive statistics were calculated and compared between those randomized to the RT + S and RT + P in both an intent-to-treat analysis, as well as between those randomized to the RT + S and RT + P who completed the study using *t*-tests, chi-square tests, and Fisher's exact tests where appropriate. Change in lean body mass (and other outcomes of interest described above) was assessed by calculating the difference between baseline and 24-wk follow-up and compared with two-way ANOVA. Multivariable linear regression was used to evaluate associations between adherence to the resistance training program and personality domain scores, irrespective of randomization assignment. Analyses were conducted using SAS version 9.4 (Cary, NC).

RESULTS

Consort schematics. The flow of participant recruitment is described in the consort diagram (Fig. 1). There were 147 survivors eligible for recruitment, 93 completed baseline testing, 70 were randomized to treatment groups, and 57 completed the study. Of the 54 survivors who refused participation, 3 (5.5%) stated they were already exercising, 5 (9.3%) did not want to complete study measures, 3 (5.5%) did not have child care, 5 (9.3%) cited distance or transportation issues (despite being offered no cost transportation services), 24 (44.4%) reported being too busy, 1 (1.9%) did not appear for a baseline appointment, 1 (1.9%) cited a personal health issue, 1 (1.9%) reported a conflicting work schedule, and 11 (20.3%) did not give a specific reason. The overall completion rate was 61.3%.

Body composition and strength gains. The characteristics of the study population are described in Table 1. The median age for the RT + S group (n = 29) was 33.0 (Range: 20.6–44.2), 58.6% were White and 44.8% were female. For the RT + P group (n = 38), the median age was 33.7 (21.1–44.9), 63.2% were White and 50.0% were female. The RT + S and the RT + P groups did not differ at baseline by demographics, treatment, diagnosis, lean body mass, or dietary protein intake.

The intent-to-treat analysis included all participants randomized, regardless of completion rate. Figures 2 and 3 show the comparison of change in lean mass and other outcomes of interest between groups. See Table 2 for two-way ANOVA, and Supplemental Digital Content 1, http://links.lww.com/MSS/B958, for mean changes in lean mass and other outcomes by group (see Table, Supplemental Digital Content 1, Mean change in lean body mass and other outcomes by group from

TABLE 1. Characteristics of the study population by randomization and completion status.

	Randomized			Completed		
	RT + S, n = 29	RT + P, n = 38	P	RT + S, n = 24	RT + P, n = 33	P
Current age, median (range)	33.0 (20.6–44.2)	33.7 (21.1–44.9)	0.63	32.9 (20.6–44.2)	32.8 (21.1–45.0)	0.79
Age at diagnosis, median (range)	7.2 (0.5–18.8)	9.1 (0.0–19.6)	0.68	7.0 (0.5–18.8)	9.5 (0.0–19.6)	0.42
Survival time, median (range)	22.9 (14.2–41.5)	23.7 (10.1–43.8)	0.99	23.2 (14.2–41.5)	22.3 (10.1–42.6)	0.70
Age strata, n (%)						
18–29 yr	8 (40.0%)	21 (44.7%)	0.72	7 (38.9%)	17 (43.6%)	0.74
30–45 yr	12 (60.0%)	26 (55.3%)		11 (61.1%)	22 (56.4%)	
Sex, n (%)						
Female	13 (44.8)	19 (50.0)	0.67	11 (45.8)	16 (48.5)	0.84
Male	16 (55.2)	19 (50.0)		13 (54.2)	17 (51.5)	
Race, n (%)						
Black	10 (34.5)	14 (36.8)	0.34	7 (29.2)	10 (30.3)	0.24
White	17 (58.6)	24 (63.2)		15 (62.5)	23 (69.7)	
Other	2 (6.9)	0 (0.0)		2 (8.3)	0 (0.0)	
Diagnosis, n (%)						
Leukemias	9 (31.0%)	10 (26.3%)	0.96	8 (33.3%)	9 (27.3%)	0.98
Lymphomas	2 (6.9%)	5 (13.2%)		2 (8.3%)	5 (15.2%)	
CNS tumors	6 (20.7%)	9 (23.7%)		5 (20.8%)	8 (24.2%)	
Bone and soft tissue sarcomas	7 (24.1%)	7 (18.4%)		5 (20.8%)	6 (18.2%)	
Wilms' tumor	1 (3.5%)	2 (5.2%)		1 (4.3%)	2 (6.1%)	
Other malignancy	4 (13.8%)	5 (13.2%)		3 (12.5%)	3 (9.1%)	
Treatment, n (%)						
Surgery	29 (100.0)	37 (97.4)	1.00	24 (100.0)	32 (97.0)	1.00
Chemotherapy	21 (72.4)	28 (73.7)	0.91	17 (70.8)	23 (69.7)	0.93
Radiation	14 (48.3)	19 (50.0)	0.89	10 (41.7)	17 (51.5)	0.46
Lean mass, mean ± SD, kg	55.4 (18.4)	60.9 (15.9)	0.19	56.6 (19.7)	61.1 (15.5)	0.34
Relative lean mass, mean ± SD	19.1 (4.1)	21.1 (4.4)	0.06	19.4 (4.4)	21.1 (4.2)	0.14
Dietary protein/total mass, mean ± SD, g·kg^{-1}	0.9 (0.5)	0.8 (0.4)	0.27	1.2 (0.5)	0.8 (0.5)	0.45

Demographic information, including diagnosis and treatment history.
RT + S, resistance training with protein supplement; RT + P, resistance training with placebo; P, paired t-test P value; n, sample size; %, percentage of sample.

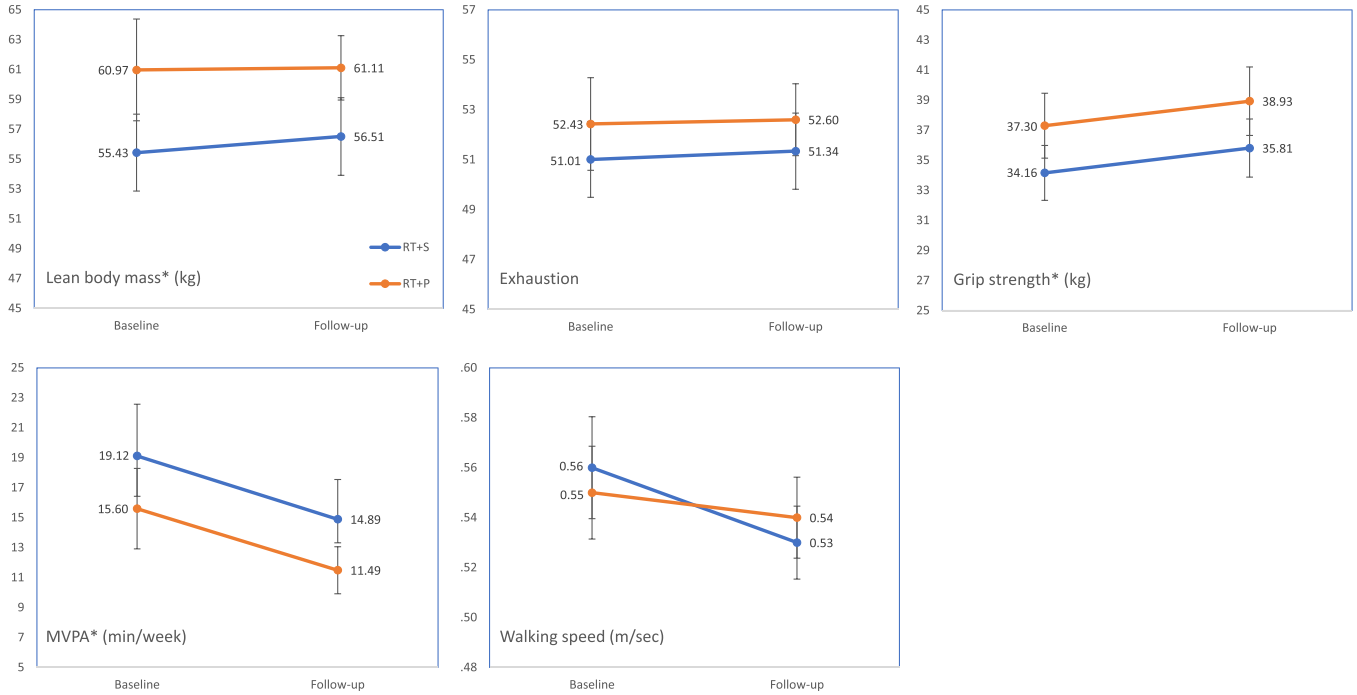

FIGURE 2—Mean change in primary outcomes pre- and postintervention time points, with SE. MVPA, moderate to vigorous physical activity; RT + S, resistance training with protein supplement; RT + *P*, resistance training with placebo. *Outcomes with *P* value ≤0.05 for time effect. Outcomes did not have group–time interactions.

baseline to 24-wk follow-up for all study participants $N = 67$, http://links.lww.com/MSS/B958). There were no differences in change in lean mass (mean ± SD; RT + S, 1.05 ± 2.34 kg; RT + P, 0.13 ± 2.19 kg; $P = 0.10$) or strength (grip RT + S, 1.65 ± 4.17 kg; RT + P, 1.63 ± 4.47 kg; $P = 0.98$; leg press RT + S, 58.4 ± 78.8 kg; RT + P, 51.0 ± 65.1 kg; $P = 0.68$) between groups, although both lean mass ($P = 0.03$) and strength (grip $P = 0.003$, leg press $P < 0.001$) increased over time. An additional analysis was performed on those who had completed the intervention with >50% adherence. Results were similar to the intent-to-treat analysis [see Tables, Supplemental Digital Content 2, Two-way analysis of variance for lean body

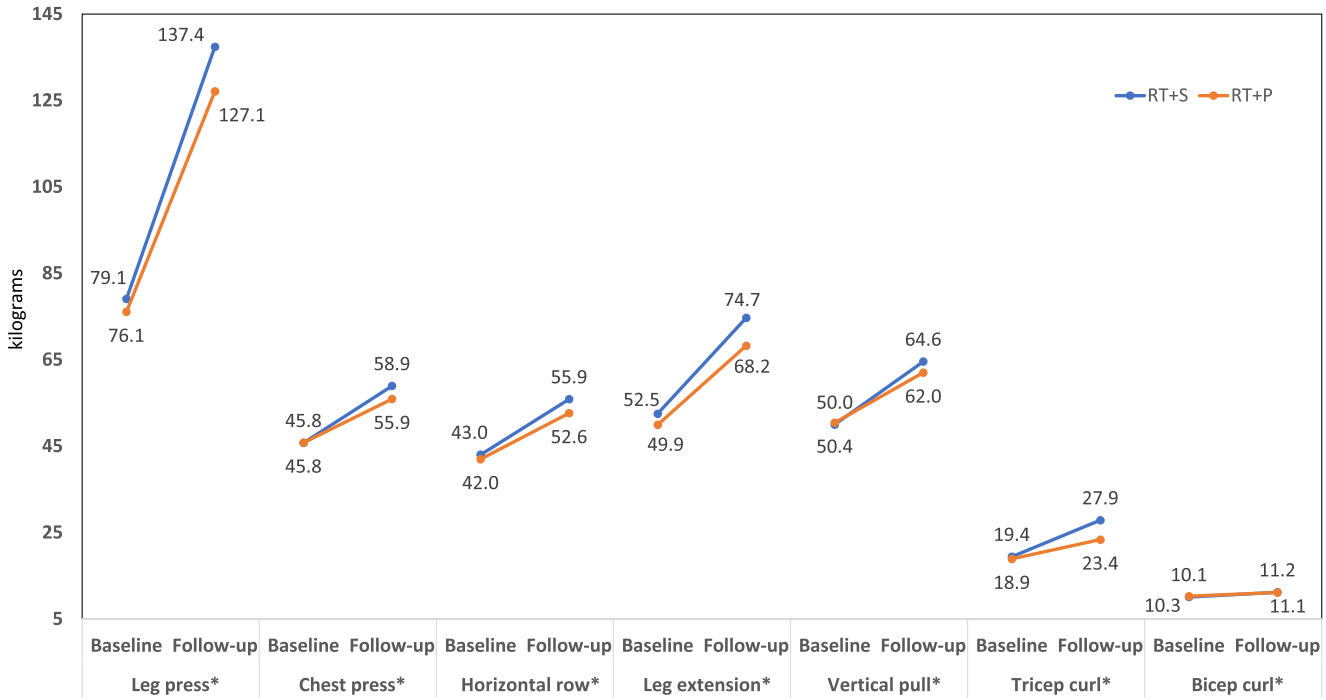

FIGURE 3—Mean change in 1RM at pre- and postintervention time points, with SE. RT + S, resistance training with protein supplement; RT + P, resistance training with placebo. *Outcomes with *P* value ≤0.05 for time effect. Outcomes did not have group–time interactions.

TABLE 2. Two-way ANOVA for primary outcomes and 1RM testing, intention-to-treat analysis, $N = 67$.

Outcome	Variable	df	Sum of Squares	Mean Square	F-Ratio	P
Lean body mass						
	Group	1	842.71	842.71	1.43	0.24
	Time	1	12.22	12.22	4.75	**0.03**
	Group–time	1	7.26	7.26	2.82	0.10
	Error	65	167.30	2.57		
Grip strength						
	Group	1	321.20	321.20	1.20	0.28
	Time	1	88.37	88.37	9.36	**0.003**
	Group–time	1	0.002	0.002	0.00	0.99
	Error	65	613.58	9.44		
Walking speed						
	Group	1	0.0001	0.0001	0.01	0.93
	Time	1	0.01	0.01	1.71	0.20
	Group–time	1	0.001	0.001	0.20	0.65
	Error	65	0.38	0.01		
Exhaustion						
	Group	1	0.07	0.07	0.00	0.99
	Time	1	1.95	1.95	0.06	0.81
	Group–time	1	0.21	0.21	0.01	0.94
	Error	65	2293.36	35.28		
MVPA						
	Group	1	366.15	366.15	1.09	0.30
	Time	1	390.07	390.07	3.93	**0.05**
	Group–time	1	4.48	4.48	0.05	0.83
	Error	65	6455.02	99.31		
Leg press 1RM						
	Group	1	7065.11	7065.11	0.20	0.66
	Time	1	476,235.04	476,235.04	38.72	**<0.001**
	Group–time	1	2135.99	2135.99	0.17	0.68
	Error	65	799,423.10	12,298.82		
Chest press 1RM						
	Group	1	350.57	350.57	0.05	0.82
	Time	1	21,560.40	21,560.40	42.82	**<0.001**
	Group–time	1	372.34	372.34	0.74	0.39
	Error	65	32,726.92	503.49		
Horizontal row 1RM						
	Group	1	731.05	731.05	0.18	0.67
	Time	1	21,978.90	21,978.90	46.98	**<0.001**
	Group–time	1	193.83	193.83	0.41	0.52
	Error	65	30,409.53	467.84		
Knee extension 1RM						
	Group	1	3289.55	3289.55	0.45	0.50
	Time	1	64,971.44	64,971.44	53.04	**<0.001**
	Group–time	1	574.42	574.42	0.47	0.50
	Error	65	79,621.10	124.94		
Vertical pull 1RM						
	Group	1	181.71	181.71	0.04	0.84
	Time	1	27,280.39	27,280.39	49.42	**<0.001**
	Group–time	1	352.03	352.03	0.64	0.43
	Error	65	35,882.67	552.04		
Triceps 1RM						
	Group	1	1001.34	1001.34	0.73	0.40
	Time	1	6621.70	6621.70	37.11	**<0.001**
	Group–time	1	636.38	636.38	3.57	0.06
	Error	65	11,598.68	178.44		
Biceps 1RM						
	Group	1	0.63	0.63	0.00	0.95
	Time	1	152.66	152.66	8.74	**0.004**
	Group–time	1	2.22	2.22	0.13	0.72
	Error	65	1135.31	17.47		

Bold values indicate significant P value ≤0.05.
MVPA, moderate to vigorous activity (min·d^{-1}); n, sample size.

mass and other outcomes among participants that completed (adherence >50%) $N = 57$, http://links.lww.com/MSS/B959; Supplemental Digital Content 3, Mean change in lean body mass and other outcomes by group from baseline to 24-wk follow-up for participants that completed (adherence >50%) $N = 57$, http://links.lww.com/MSS/B960].

Among survivors that completed the intervention, adherence rates for RT + S versus RT + P were 74.8% and 67.0% for resistance training sessions, and 83.8% versus 78.3% for supplement consumption. Of the 57 survivors who completed the intervention, 53 returned the BFI-2. Results of multivariable linear regression examining associations between percent adherence to the resistance training program and personality domain scores are presented in Table 3. Higher negative emotionality domain scores were associated with lower adherence to the resistance training program.

Adverse events. There were eight adverse events potentially related to the study. One was serious (myocardial

TABLE 3. Associations between adherence to the resistance training program and personality domain scores.

Personality Domain	β	SE	P
Agreeableness	−3.35	5.26	0.53
Conscientiousness	−1.18	3.61	0.75
Extraversion	−3.37	3.62	0.36
Negative emotionality	−6.45	3.01	0.04
Open-mindedness	0.83	3.10	0.79

β, beta estimate; P, multivariable linear regression P value.

infarction that did not occur during training); seven were not serious and included knee pain, muscle soreness, nausea, pain, and anxiety. There were four serious adverse events unrelated to the study, which included hypertension, viral infection, and involvement in an automobile accident that required medical care. There were 17 events that were deemed not serious and not related to the study and included pain that did not occur during an exercise session, minor automobile accidents, minor illnesses, and routine medical procedures.

DISCUSSION

This double-blind placebo-controlled trial evaluated the effects of adding 21 g of protein supplementation daily to a 24-wk long progressive resistance strength training program on lean body mass in young adult survivors of childhood cancer. Gains in lean body mass were seen over time but not due to group status, suggesting that the changes were due to the exercise program and not the protein supplement. Thus, adding 21 g of protein daily to a structured progressive resistance strength training program did not result in greater gains in muscle mass than strength training alone. Nevertheless, this study does contribute to the literature and provides a foundation for future study. Delivery of the intervention was feasible in community-based fitness centers, adherence to the intervention was reasonable with tapered supervision, the intervention was safe in this population, and both the intervention group and the control group had significant gains in muscle strength and some gains in lean body mass in response to resistance training.

The failure of a 21-g protein supplement delivered with tailored resistance training to result in a significant change in lean body mass when compared with resistance training alone is likely due to the relatively conservative protein dose, lack of tailoring of dose to body weight or dietary intake, and method of delivery that did not maximize absorption. Lack of a significant change could result from differences in dietary protein intake at enrollment between groups; however, dietary protein did not differ between the groups at baseline. Schoenfeld and Aragon (28) recommend a total daily dose of 1.6–2.2 $g \cdot kg^{-1}$ body weight to produce change and consumption of protein divided into smaller, multiple doses throughout the day to maximize absorption. A systematic review conducted by Morton et al. (29) found that healthy adults engaged in resistance training benefited from 1.6 $g \cdot kg^{-1}$ daily dose of protein, with higher doses not providing additional benefits. These studies are in congruence with the stated position of the International Society of Sports Nutrition (30); individuals participating in exercise programs should consume 1.4 to 2.0 $g \cdot kg^{-1}$ protein daily, with recommendations that those engaged in strength training consume protein at the higher end of this range. Future studies should evaluate if these strategies enhance the effect of protein supplementation and resistance training in building lean body mass in childhood cancer survivors.

Significant increases in muscle strength confirm findings from previous studies that indicate that resistance training is a reliable method for increasing muscle strength, even in vulnerable populations such as adult cancer patients or the frail elderly (8,9). Our results indicate that adult survivors of childhood cancer can gain lean body mass in response to training and that resistance training is safe (31), in a community setting, with tapered supervision. Although we did observe some potentially related adverse events, none that occurred during exercise were serious or beyond what might be expected with routine exercise (i.e., joint pain/muscle soreness).

Adherence to the exercise intervention ranged from 67% to 75% in our study, with a finding that higher negative emotionality personality domain scores were associated with lower adherence to resistance training. It is possible that excluding those with poor adherence from analysis would have resulted in more positive results. However, the finding of an association between personality and adherence provides important information for future study design and clinical care. These data are similar to those reported in a recent meta-analysis, indicating that persons with this personality domain are less likely to engage in physical activity (32). Individuals with higher characteristics of negative emotionality respond disproportionally to stressors and have traits such as anxiety, worry, high vulnerability, self-consciousness, and sensitivity to criticism (33). These individuals have heightened responses to stimuli; physiological responses invoked during exercise may be perceived negatively (32). Screening personality domains before research or clinical intervention would allow investigators and clinicians to target and tailor the support needed to optimize participation among those whose response to exercise may not be initially positive. For instance, mindfulness-based stress reduction approaches (34) help these individuals reduce psychological distress by learning how to regulate emotional responses; using mindfulness-based stress reduction approaches in physical activity interventions may increase adherence.

The resources (paid travel expenses, accessible and multiple local fitness centers, and expert staff) required to complete this study were relatively intense and may be difficult to implement in a broader population of childhood cancer survivors. Because we found that tapering supervision can be successful, future work that uses remote technology for supervision and participant contact after initial training sessions should be considered as this approach would be less labor intensive and costly, and more accessible to persons who do not live near an exercise facility with appropriate expertise. Although reported as less successful than supervised training, home-delivered exercise interventions are better than no specific program delivery at all (35). A remotely accessed home intervention is feasible and might accommodate those who refused intervention because of time constraints, scheduling, child care, and lack of desire to use provided transportation.

Limitations. The results of our study should be considered in the context of several study limitations. First, protein intakes were estimated from Food Frequency Questionnaires. As in all studies done in community dwelling persons where dietary intake is estimated this way, we are not absolutely certain how much protein was consumed. Second, not all exercise sessions were supervised. Although frequency of attendance is likely accurate, dose and intensity of the resistance exercises may have varied from what was prescribed. Finally, although participants were asked to fast before baseline and follow-up testing, DXA estimates of lean mass may be inaccurate if hydration status differed between participants or within participants from baseline to follow-up (36).

CONCLUSION

This study provides strong support that exercise intervention among childhood cancer survivors is feasible, safe, and effective. Although there were changes in lean body mass over time, there was no clear evidence that the addition of protein supplementation had a significant effect in this population. Future research should include new strategies of intervention to reach a larger group of participants, such as an home training program. Tailoring the intervention to meet the needs of specific personality types could reduce dropout and boost adherence.

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The authors have no conflicts of interest, financial or otherwise, to disclose concerning this manuscript. The authors declare that the results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. Results presented here do not constitute endorsement by the American College of Sports Medicine.

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