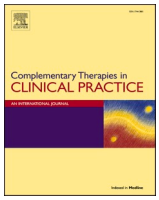
Complementary Therapies in Clinical Practice 48 (2022) 101576

Contents lists available at ScienceDirect

Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctcp



Progressive resistance exercise as complementary therapy improves quality of life and body composition in anorexia nervosa: A randomized controlled trial

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ARTICLE INFO

Keywords:
Anorexia nervosa
Exercise
Physical fitness
Quality of life
Resistance training

ABSTRACT

Background: and purpose: Exercise has not typically been used as an adjunct in treatment of anorexia nervosa (AN). This study aimed to examine the effects of progressive resistance exercise (PREx) on perceived quality of life (QoL) and body composition in adolescents with AN.

Materials and methods: Forty-four adolescents diagnosed with AN were randomly allocated to either PREx or control groups after hospitalization. The PREx group completed twenty-four PREx sessions over two months including three sets of 8–10 repetitions of eight whole-body exercises at a moderate intensity. QoL and body composition were evaluated at baseline and after two months using Health Questionnaire Short-Form 36 (SF-36) and anthropometric measurements.

Results: At completion, forty-one participants (n = 19 PREx, and n = 22 controls) with mean age of 12.78 ± 0.88 years and mean body mass index of 18 ± 2.2 kg/m^2 were analyzed. Significant group x time effects were found on SF-36 role physical (RP) scores. Significant improvements with large effect sizes (d > 0.72) were found in RP, and arm circumferences in the PREx group. Spearman association analyses between percent change in anthropometric variables and change in QoL scores showed positive associations with moderate-to-large effect sizes in the PREx group among the following variables: mid-thigh-circumference, physical functioning (PF) and general health (GH); calf-circumference relaxed and body pain; biceps skinfold and GH scores; triceps-skinfold, and role physical (RP) and vitality (VT); supraspinale-skinfold and RP and VT; mid-thigh-skinfold and calf-skinfold and VT.

Conclusion: PREx after hospitalization enables modest positive changes in QoL associated to anthropometric changes in adolescents with AN without adverse effects on weight recovery.

1. Introduction

Anorexia nervosa (AN) is an eating disorder primarily observed in women [1,2] that over the past decade has shown the greatest prevalence in aged 15–19 years old [3]. Individuals with AN exhibit high levels of psychological distress and anxiety associated with a fear of body fat and weight gain compounded with a pathological desire to achieve extreme thinness [1]. Sadly, AN's mortality rate is one of the highest for all psychiatric disorders with around 5% of all sufferers passing away [1]. Despite best intentions and intensive therapies,

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https://doi.org/10.1016/j.ctcp.2022.101576
Received 29 January 2021; Received in revised form 24 March 2022; Accepted 25 March 2022
Available online 27 March 2022

treatment is successful in no more than 50% of patients, with the relapse rates around 31%, regardless of age [3]. Relapse has long plagued the outcomes of individuals with AN. Along with several other factors such as comorbid illnesses, self-reported lower quality of life (QoL), and engagement in dysfunctional exercise post-acute treatment have all contributed to the rates of relapse and recovery as a whole [3–5].

Quality of life encompasses an individual's perception of their overall wellness and can be reflected in various domains including physical and mental health [6]. Typically, individuals with eating disorders (ED) perceive themselves as having lower QoL. EDs impact QoL through the impairment of mental wellbeing, social skills, sense of self, physical health and relationships [4]. Indeed, previous research investigating QoL in AN found that they have poorer perception of their health-related QoL compared to the general population [5,7–9]. Furthermore, in those with AN, poorer perceptions of QoL were correlated with higher EDs symptom scores [5,7,9], greater incidence of comorbid illnesses (i.e. depression) and poor emotional awareness and low sense of self control [7]. As an indicator of recovery, perception of QoL is understood to trigger or maintain ED symptoms, wherein positive changes in QoL is related to better ED outcomes [4]. Thus, targeting QoL in ED treatment may be an avenue by which treatment trajectories could be improved.

Body weight (BW) and body mass index (BMI) are well known recovery, remission, and relapse markers for AN [10]. BMI is an important marker in the treatment process for AN. Higher BMI and lower rates of weight loss after acute treatment (~1 month) have been associated with successful weight maintenance in these patients [11]. Reports have highlighted that the severity of an ED combined with low BMI are predictors of low QoL [7,12]. However, this association is lost when examining individuals with AN who are admitted to hospital for emergency reasons [5]. Despite research highlighting that body composition, specifically percent body fat and total body fat in weight recovered individuals with AN is not different from controls after weight recovery; abdominal (visceral) fat and intra-muscular fat are disproportionately increased [13–15] while muscle mass is significantly decreased [15]. Individuals with AN have consistently expressed concern about weight gain associated to this abnormal fat redistribution [14,15]. Unlike muscle mass, body fat distribution normalizes after a year of weight maintenance [15,16]. As a consequence, the evaluation of regional changes (i.e. trunk, upper- and lower-extremities) in body composition may be an important influencer of QoL in AN treatment.

Therapeutic exercise interventions are one way in which QoL may be influenced, while facilitating improvements in BMI, BW and anthropometric markers [7,12,17,18]. In fact, exercise in AN—including moderate-to-vigorous intensity exercise—has been associated with improved BMI, anthropometric skinfolds and circumferences percentiles, skeletal muscle mass, fat free mass (FFM) [18–20], ED psychopathology and comorbid symptoms in AN [21–23]. Incorporating exercise into the treatment of EDs, particularly in AN, has been approached with hesitancy and caution [24]. Hesitancy stems in part from the fact that when exercise is engaged in a manner that is physically and psychologically detrimental it becomes a dysfunctional behavior (thus termed dysfunctional exercise) [25]. Dysfunctional exercise is the second highest predictor of relapse in AN [26], and is noted as one of the first presenting and last remaining symptoms of an ED [25,27,28]. Due to the impact of dysfunctional exercise in physical and psychological recovery, exercise has commonly been avoided in treatment [29], thus clinicians have often utilized other strategies such as bed rest and exercise abstinence [24,30]. However, evidence now indicates that these practices can present a harmful risk to both physical and psychological health (i.e. increased feelings of depression, irritability and anxiety, decreased bone density, decreased lean mass, etc.) [31]. The key component of producing beneficial outcomes in exercise interventions in AN has been the implementation of therapeutic exercise programs with nutritional support [17,22,32–35]. Therefore, developing healthier exercise practices seems to be critical to improve psychopathology and reduce relapse risk in AN associated to a dysfunctional behavior [17,25,31,34].

Recent therapeutic exercise interventions in individuals with AN have mainly utilized low-to-moderate intensity activities [21,23,36,37] with only a few studies utilizing moderate-to-high intensity progressive resistance exercise (PREx) [18,22,38]. Overall, moderate-to-high intensity PREx has shown to improve muscle strength, bone health, and BMI when compared to controls [19,22,38] without impacting weight recovery or psychopathologies [17,32,34,39], or increasing reactivity to stress and other triggers of relapse [25]. To the best of our knowledge, only one study analyzed the effects of exercise on QoL in patients with AN. The study included a three-month low-intensity progressive exercise program (i.e. stretching, cardiovascular and isometric exercise) that did not allow improvements in QoL, nor negatively impacted weight or BMI recovery [21]. No other physical fitness-related variables (i.e. strength, cardiovascular fitness, etc.) were assessed. Overall, the results from this study suggest that exercise "dose" (i.e., intensity) may be key for QoL improvement. Given the relationship of QoL with relapse and illness outcomes, the potential benefit of incorporating moderate-to-vigorous resistance exercise calls for additional research. Therefore, the aim of this study was to investigate the effects of PREx on perceived physical and mental health related QoL and body composition in AN after hospitalization. We hypothesized that perceived QoL will improve significantly after two months of PREx compared to the control group and associated with positive changes in body composition without negatively impacting weight gains.

2. Materials and methods

2.1. Design, ethical considerations, and participants

Forty-four young adolescents with AN who previously participated in a study to determine the effects of resistance training on physical fitness [40] were included in this study. Participants were recruited at the hospital's Eating Disorders Treatment Center by convenience sampling. Both parental consent and patients consent forms were obtained before enrollment. The intervention was carried out in accordance with the Declaration of Helsinki. Adolescents with AN were included in the study following the CONSORT guidelines for randomized controlled trials. The study protocol was approved by the *Clinical Research Ethics Committee* (*Comité Ético de Investigación Clínica* – CEIC) at the Hospital Universitario Infantil Niño Jesús de Madrid (ID: R-0034/08–1). The study was registered at www.clinicaltrials.gov (NCT01906320).

In the present study, we utilized a parallel group randomized controlled trial. A total of 44 participants were blocked in a 1:1 ratio based on their BMI at the start of the study and then randomized into PREx (n = 22) and control (n = 22) groups following an allocation concealment process (using sealed/opaque envelopes). To be included in the study participants met the following inclusion criteria: diagnosed with AN based on the Diagnostic and Statistical Manual of Mental Disorder IV [40]; were less than 16 years old; were part of a structured day care program including cognitive behavioral therapy (3 days/week) and diet monitoring; had a BMI >14.0 kg/m^2 [27]; were not currently engaging in dysfunctional exercise and had no contraindications to performing exercise [27]. To continue in the PREx group throughout the course of the study participants had to: not encounter significant losses of weight or BMI attributable to voluntary reduction of dietary intake; not develop dysfunctional exercise behaviors [41,42]. A total of three PREx participants were lost over the course of the study due to: change to treatment center (n = 2) and hospitalization due to voluntary reduction of dietary intake (n = 1). Therefore, 19 participants completed the study in the intervention group (see Fig. 1).

The study was organized in two phases: familiarization phase and intervention phase (see Fig. 2). The familiarization phase included three preparation sessions and physical fitness assessments (i.e. cardiorespiratory fitness (CRF), muscular strength). The intervention phase was preceded and followed by body composition assessments (i.e., weight,

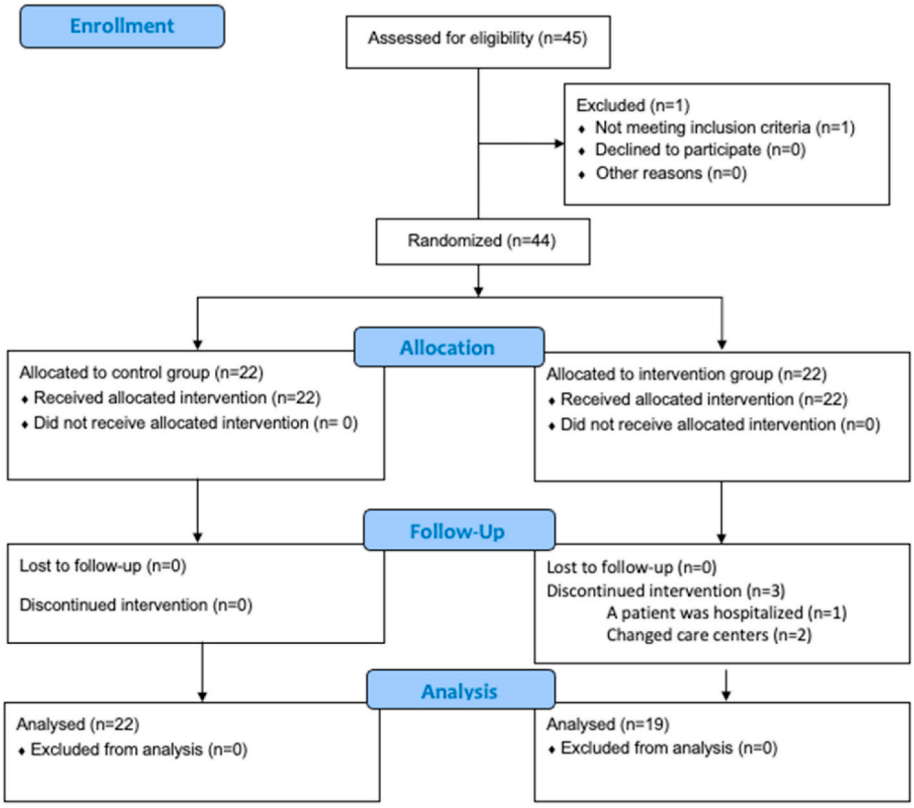

Fig. 1. CONSORT Flow diagram.

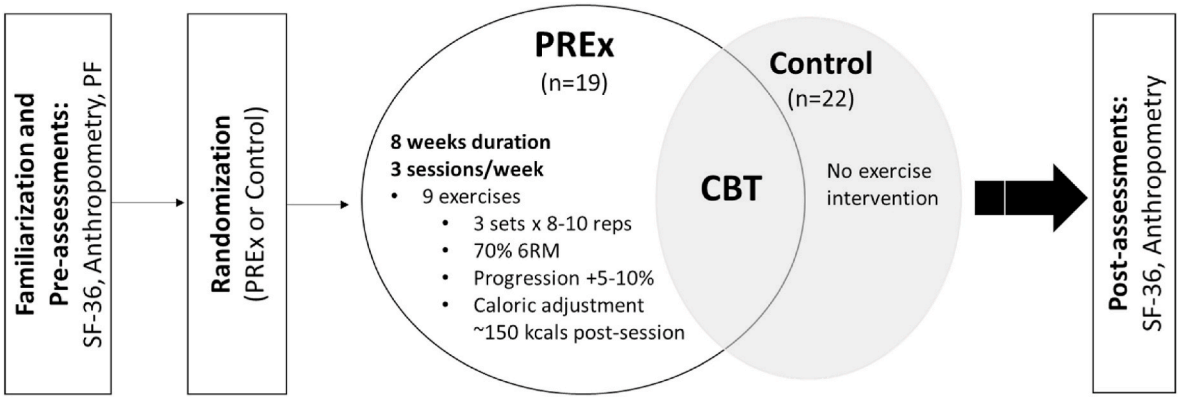

Fig. 2. Schematic of the study design.
SF-36 – health questionnaire short-form 36; PF – physical fitness (including cardiorespiratory and strength testing); PREx – progressive resistance exercise; reps—repetitions; 6RM –six-repetition maximum; kcals—kilocalories; CBT – cognitive behavioral therapy.

height, circumferences and skinfolds) and perceived physical and mental health questionnaire (i.e., SF-36). Clinical exercise professionals who specialized in EDs completed and supervised the assessment and training sessions with the participants. The same group of researchers performed all assessments—except CRF—and supervised the training sessions. All tests were scheduled into two sessions with a day of rest in between, and under similar environmental conditions (20–24 °C, 45–55% relative humidity) and time (10:00 a.m. to 1:00 p.m.). Each patient consumed the same amount of energy each day. Specifically, they consumed a diet of 55% carbohydrate, 30% protein and 15% fat. Additionally, the intervention group increased their calorie intake by consuming a high-protein milkshake (~150 kcals) accounting for the energy expenditure required during the strength training session [35,38,43].

2.2. Familiarization phase

Each participant took part in a familiarization period over the course of one week to minimize the learning effect that could result in technical and neuromuscular improvements on the strength tests [38]. Each individual participated in three 50-min sessions. Each session was preceded and followed by a warm-up and cool-down identical to those performed in the PREx intervention period. Participants completed two to three sets of five to eight repetitions of the exercises that were used to assess strength, and one familiarization session for the treadmill ergometer. The subsequent assessments were performed during the familiarization period to ensure the participants met inclusion criteria and to obtain initial strength values for PREx prescription.

2.2.1. Physical activity levels

To ensure the participants were not dysfunctional exercisers and that both intervention and control groups had similar physical activity levels at the beginning of the study, spontaneous physical activity was assessed. Participants were required to maintain their usual physical activity while wearing a uniaxial accelerometer for ten days (Actigraph MTI, GT1M model, Manufacturing Technology, Fort Walton Beach, FL). A minimum of 10-h registration per day for at least 7 days (Monday–Sunday) was set to count as valid. An average value of three working days and two weekend days was calculated. Additional details on this methodology are provided elsewhere [44].

2.2.2. Cardiorespiratory fitness

To assess CRF, participants completed a graded treadmill test (Technogym Run Race 1400HC; Gambettola, Italy). The test was performed while monitoring heart activity by electrocardiography (BTL-08MT Plus ECG) to ensure that exercise was not contraindicated. The protocol was designed specifically for those with AN and the protocol has been previously used successfully [38,45,46]. The test was terminated when participants experienced volitional fatigue or when a loss of ability to maintain the required workload was shown.

2.2.3. Muscular strength

To determine exercise intensity an upper and lower body muscular strength test was performed. Participants followed a standardized six-repetition maximum (6RM) strength test on the same resistance weight machines (i.e. seated leg press, bench press and lateral row) used during the training sessions. The 6RM "is described as the maximum strength capacity to perform six repetitions until momentary muscular exhaustion" [45]. The assessment included a three-set warm-up (50%, 70%, and 90% of the perceived 6RM) with 1-min resting periods between sets, and 2 min between the last warm-up set and the 100% 6RM attempt. Further details are provided elsewhere [47].

2.3. Assessments and intervention

On assessment day, participants consumed their usual breakfast (fruit juice [~200 mL] and a bowl of cereal [~45 g] with milk [~200 mL]) approximately 3 h before the assessment. The following assessments were completed by both PREx and control groups before and after the intervention period, referred to as pre-assessment and post-assessment, respectively.

2.3.1. Health related quality of life questionnaire short-form 36 (SF-36)

Perceived health was evaluated pre- and post-intervention in both groups using the SF-36 questionnaire. The SF-36 evaluates perceived health-related QoL in two main areas physical health and mental health. There are 36 items that are scored into each domain: physical functioning (PF), role *limitations due to* physical *health* (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role *limitations due to* emotional *problems* (RE) and mental health (MH). The scores from each domain all contribute towards two summary scales: physical component scale (PCS) and mental component scale (MCS). The SF-36 domain scores range from 0 (worst) to 100 (best), with a higher score indicating a better state of health. There are three steps involved in the scoring of each SF-36 domain: recoding of recorded items (i.e. a total of 10 items require reverse scoring), algebraic sum of the items raw scores in the same domain, and transformation of raw scores to 0–100 scores [48]. Summary scales are then computed using general population's mean and standard deviations, calculating z-scores from previously determined domains, and utilizing scoring factor coefficients specific for each scale [49].

2.3.2. Body composition and anthropometry

Weight (kg) and height (m) were collected, and BMI was calculated as kg/m^2. These variables were also recorded weekly by the medical team to ensure the safety of the PREx program and to monitor adverse changes to weight or BMI. Anthropometry data were collected following the International Society for the Advancement of Kinanthropometry (ISAK) standards [50] by the same ISAK Level-3 anthropometrist. Anthropometry measurements included: 6 girths (arm contracted, arm relaxed, upper-thigh, mid-thigh, calf relaxed, and calf contracted) and 7 skinfolds (biceps, triceps, subscapular, abdominal, supra-iliac, mid--thigh and calf).

2.3.3. Intervention

The PREx group engaged in psychotherapy and participated in three 50-min PREx sessions per week for eight weeks (24 sessions total). The exercise session took place between 9:30 and 10:00 a.m. before psychotherapy. To begin the session, the PREx group participated in a dynamic warm-up prior to the PREx session that targeted the major muscle groups. The dynamic warm-up included three sets of 10 repetitions of a total of eight exercises [arm circles, sumo squat with lateral leg rise, lunge walks (with and without knee rise), inch worms, frog walk, walking hamstring stretch with knee rise, leg cross overs (supine), and scorpion (prone)] sequenced in the same order and increasing range of motion each set. The participants then performed three sets of eight exercises (i.e. bench press, leg press, lateral row, leg extension, lateral pull down, abdominal crunch, low back extension and push-ups) and completed 8–10 repetitions. The intensity of leg press, bench press and lateral row exercises was set at 70% of their 6RM. The intensity for the remaining exercises was selected based on the OMNI-Resistance Exercise Scale (OMNI-RES) [51,52]. An OMNI-RES score of 6 was selected to ensure intensity was similar to that used in seated leg press, bench press and lateral row [53]. Rest periods between exercises lasted 1–2 min. The load gradually increased from 5 to 10% after the participant was able to perform the exercise without fatigue for two consecutive sessions [54] coinciding with an OMNI-RES score of <6. Stretching exercises were completed at the end of session. The control group participated in the same psychotherapy as the PREx group every week for eight weeks. However, they did not receive the same exercise program and did not consume the additional protein intake.

2.4. Statistical analyses

All data were checked for normality using the Shapiro-Wilk tests, where normality was assumed if $p > 0.05$. Baseline variables were compared through Student's t-test for independent sample to detect differences between control and PREx groups at baseline. A 2×2 (group x time) repeated measures analysis of variance (ANOVA) model was used to assess PREx effects (control vs. PREx) from pre-to post-intervention on health-related QoL (SF-36 questionnaire), and body composition variables. Bonferroni-corrected pairwise comparisons were performed when appropriate. The eta squared effect sizes (η^2) were classified as 0.01 (small), 0.06 (medium), 0.14 (large) [55]. Likewise, Cohen's effect sizes (*d*) were classified as 0.1 (very small), 0.2 (small), 0.5 (medium), 0.8 (large), 1.2 (very large), and 2.0 (extremely large) [56]. One-sample *t*-test was utilized to compare SF-36 scores with normative values [PF, RP, BP, RE and VT = 100, SF = 90, GH = 75, MH = 70, and MCS and PCS = 50] [57]. Associations between QoL and anthropometric variables were examined by Spearman association analyses. The strength of the relationship was classified as ≤ 0.1 (very small), 0.1–0.29 (small), 0.3–0.49 (moderate), 0.5–0.69 (high), 0.7–0.89 (very high), and 0.9–1 (perfect). All data were summarized as mean ± SD. The level of significance was set at $p < 0.05$. Statistical analyses were performed using the SPSS Statistics for Windows, version 20 (IBM Corporation, Armonk, NY).

3. Results

3.1. Characterization of the sample

A total of 41 participants (mean age = 12.78 ± 0.88 years) diagnosed with AN were analyzed. A description of the sample's baseline measures is included in Table 1. No differences were found for minimum BMI achieved through the course of the treatment, BMI, dietary intake, and moderate-to-vigorous physical activity levels (MVPA) between groups at inclusion in the study.

3.2. Quality of life

Scores from SF-36 broken down into control group and PREx group are included in Table 2. The analysis of QoL variables showed significant group × time interaction effects on RP (F [1,39] = 4.34, p = 0.044, η^2 = 0.1). Pairwise comparisons indicated that the PREx group significantly increased RP scores (t [19] = 6.08; p = 0.018; d = 0.8) and PF scores (t [19] = 5.01; p = 0.031; d = 0.72). Lastly, time interaction effects were found on PCS (F [1,39] = 4.47, p = 0.036; η^2 = 0.11) showing increases in perceived physical health-related QoL for both PREx and control groups.

Results from the comparison between SF-36 domains and scales with normative values are shown in Table 3. Except for PCS, all SF-36-derived scores were significantly different from normative values at baseline in both PREx and control groups. After two months, GH scores were no longer different from healthy cutoffs for any of the groups. Additionally, MH scores were not significantly different from normative scores, and PCS scores were significantly greater in the PREx group after intervention.

3.3. Anthropometry

Table 4 depicts the anthropometric data compared between the control group and PREx group. ANOVA analyses highlighted time interactions for BW (F [1,39] = 12.533; p = 0.001; η^2 = 0.10) with significant improvement pre-to-post in both PREx (F [1,39] = 5.714; p = 0.022; η^2 = 0.13) and control (F [1,39] = 6.930; p = 0.012; η^2 = 0.15) groups. Additionally, the control group presented larger BW (F [1,39] = 5.182; p = 0.028; η^2 = 0.12), mid-thigh circumference (F [1,39] = 4.264; p = 0.046; η^2 = 0.10), relaxed calf circumference (F [1,39] = 5.480; p = 0.024; η^2 = 0.12), contracted calf circumference (F [1,39] = 4.474; p = 0.041; η^2 = 0.10), and mid-thigh skinfold thickness (F [1,39] = 4.225; p = 0.046; η^2 = 0.98) compared to the PREx group at enrollment. Pairwise comparisons revealed significant pre-to-post differences in arm circumference contracted (t [19] = 6.753, p = 0.013; d = 3.18) and arm circumference relaxed (t [19] = 1.402, p = 0.021; d = 0.77) only in the PREx group.

3.4. Association analysis

Spearman association analyses between percent change (% change) of anthropometric variables, and pre-to-post differences in SF-36 scores revealed moderate to high positive associations (rho) in the PREx group between: % change in mid-thigh circumference and pre-to-post difference in PF (rho = 0.60, p = 0.006) and GH scores (rho = 0.49, p = 0.035); % change in calf circumference relaxed and pre-to-post difference in BP scores (rho = 0.50, p = 0.031); % change in biceps skinfold and pre-to-post difference in GH scores (rho = 0.55, p = 0.015); % change in triceps skinfold and pre-to-post difference in RP (rho = 0.53, p = 0.021) and VT scores (rho = 0.56, p = 0.013); % change in suprapinale skinfold and pre-to-post difference in RP (rho = 0.46, p = 0.046) and VT scores (rho = 0.53, p = 0.020); % change in mid-thigh skinfold and pre-to-post difference in VT scores (rho = 0.56, p = 0.0121-β = 0.924); and % change in calf skinfold and pre-to-post difference in VT scores (rho = 0.48, p = 0.036, 1-β = 0.92). Control group association analyses showed a very weak association between % change in abdominal skinfold and pre-to-post difference in SF (rho = 0.43, p = 0.028), and a very small and negative association between % change in mid-thigh circumference and pre-to-post difference in PF (rho = −0.43, p = 0.044).

Table 1
Description of the sample at baseline.

Variables	Control group (n = 22)	PREx group (n = 19)
Minimum BMI (kg/m^2)	16.2 ± 1.8	15.8 ± 1.7
BMI at inclusion (kg/m^2)	18.1 ± 2.1	17.0 ± 2.1
Diet (kcals/day)	2345.4 ± 226.2	2268.42 ± 197.3
MVPA (min/day)	44.6 ± 24.2	42.9 ± 25.6

BMI –body mass index, kcals—kilocalories; MVPA – moderate-to-vigorous physical activity levels; min—minutes; PREx—progressive resistance exercise.

4. Discussion

This is the first study to incorporate a two-month long resistance training program into the treatment of AN after hospital discharge and examine both anthropometric parameters (i.e. circumferences and skinfolds) and QoL. Our results show that the intervention resulted in modest improvements of perceived QoL without negative impact on weight recovery. In addition, this study revealed positive associations between anthropometric measures and QoL improvements. Results from this study suggest that incorporating individualized, supervised and nutritionally supported resistance training into AN treatment offers an avenue by which to improve mental and physical health without hindering treatment progression (i.e. BW or BMI).

This 2-month PREx intervention allowed significant improvements in RP scores in the PREx group compared to controls. Moderate to large effect sizes in RP and PF suggest additional benefits for the exercising group after eight weeks of training. Likewise, moderate effect sizes were found in SF scores for the PREx group only, indicating meaningful improvements in patients' social function QoL domain. At baseline all SF-36-derived scores, except PCS, were significantly lower compared to normative values. After two months, both control and PREx groups showed normalized GH scores, and only patients in the PREx group exhibited normal MH values and PCS values. These findings, together with the significant improvements over time in the PCS scores indicate that despite both AN groups' QoL improvement, those participating in PREx had additional positive effects. Thus, our results highlight the value, for both mental and physical health when incorporating resistance training into AN treatment.

To the best of our knowledge, only one other study examined the effects of exercise on QoL utilizing SF-36 [21]. This study incorporated a graded 3-month exercise intervention [21], and unlike our study, they prescribed a lower intensity training program—including stretching, isometric and strengthening exercises and low impact cardiovascular exercises three times per week—with patients organized into exercise levels based on BW and BMI progress [21]. Contrary to our findings, none of the items nor the SF-36 summary scales changed significantly. However, our 2-month PREx intervention resulted in significant differences in QoL (RP) in the intervention group compared to controls. Consequently, this finding could indicate that intensity and type of exercise could be a key factor in PREx leading to changes in QoL. Specifically higher intensity resistance training may contribute to the improvement of QoL and body composition in AN treatment.

Living with a chronic disease during adolescence seems to lead to a lower QoL and psychosocial impairment. In addition, chronic illnesses such as AN increase the risk for comorbid mental health illnesses [58]. Indeed adolescents with anxiety and depression do benefit from resistance training activities [59,60]. Moreover, high intensity resistance exercise has shown to improve QoL in non-clinical samples of adolescent population without adverse outcomes [61]. This phenomena might be

Table 2
Effects of eight weeks of PREx on perceived physical and mental health related QoL compared to controls.

	Control group (n = 22)								PREx group (n = 19)							
	Pre			Post			Δ		Pre			post			Δ	
	Mean		SD	Mean		SD	Mean	SD	Mean		SD	Mean		SD	Mean	SD
PF	84.24	±	16.35	85.90	±	21.41	1.67	± 15.66	83.42	±	16.83	91.05	±	10.61†	7.63	± 13.88
RP	76.70	±	24.79	74.43	±	31.33	−2.27	± 25.84	62.83	±	24.72	77.63	±	21.68*†	14.80	± 26.53
BP	75.22	±	19.05	72.27	±	24.89	−2.95	± 25.37	69.31	±	25.43	75.63	±	25.17	6.32	± 23.27
GH	62.70	±	20.81	67.63	±	17.91	4.93	± 15.13	61.90	±	18.21	67.84	±	17.24	5.93	± 22.29
VT	58.52	±	26.88	63.06	±	24.69	4.55	± 22.89	54.93	±	24.36	62.50	±	22.34	7.57	± 16.87
SF	69.31	±	32.67	71.02	±	22.94	1.70	± 21.23	61.18	±	26.96	71.05	±	22.45	9.87	± 23.04
RE	73.48	±	25.54	69.69	±	31.02	−3.79	± 24.09	68.86	±	22.87	71.49	±	25.20	2.63	± 21.16
MH	58.22	±	25.60	55.45	±	27.89	−2.77	± 20.56	50.52	±	21.91	58.42	±	27.18	7.89	± 17.02
PCS	50.86	±	8.89	53.22	±	7.47	2.36	± 10.30	50.77	±	7.47	54.52	±	5.84**	3.75	± 7.09
MCS	41.76	±	14.62	40.19	±	14.96	−1.57	± 10.25	37.04	±	12.73	40.51	±	15.12	3.48	± 8.73

SD−standard deviation; **Δ** –pre-to-post change; PF –physical functioning; RP –role limitations due to physical health; BP –bodily pain; GH –general health; VT –vitality; SF –social functioning; RE – role limitations due to emotional problems; MH –mental health; PCS –physical component scale; MCS –mental component scale; PREx—progressive resistance exercise; *Analysis of the variance, time x group effects $p < 0.05$; **Analysis of the variance, time $p < 0.05$; † pairwise comparisons $p < 0.05$.

Table 3
Differences between participants' SF-36 scores at baseline and after intervention compared to normative values broken down by PREx and control groups.

	Control group (n = 22)					PREx group (n = 19)				
		t	df	*p*	Mean diff		t	df	*p*	Mean diff
PF	pre	−4.52	21.00	0.000	−15.76	pre	−4.29	18.00	0.000	−16.58
	post	−3.09	21.00	0.006	−14.09	post	−3.67	18.00	0.002	−8.95
RP	pre	−4.41	21.00	0.000	−23.30	pre	−7.24	18.00	0.000	−37.17
	post	−3.83	21.00	0.001	−25.57	post	−4.50	18.00	0.000	−22.37
BP	pre	−6.10	21.00	0.000	−24.77	pre	−5.26	18.00	0.000	−30.68
	post	−5.22	21.00	0.000	−27.73	post	−4.22	18.00	0.001	−24.37
GH	pre	−2.77	21.00	0.011	−12.30	pre	−3.13	18.00	0.006	−13.09
	post	−1.93	21.00	**0.068**	−7.36	post	−1.81	18.00	**0.087**	−7.16
VT	pre	−7.24	21.00	0.000	−41.48	pre	−8.04	18.00	0.000	−45.07
	post	−7.02	21.00	0.000	−36.93	post	−7.32	18.00	0.000	−37.50
SF	pre	−2.97	21.00	0.007	−20.68	pre	−4.66	18.00	0.000	−28.82
	post	−3.88	21.00	0.001	−18.98	post	−3.68	18.00	0.002	−18.95
RE	pre	−4.87	21.00	0.000	−26.52	pre	−5.93	18.00	0.000	−31.14
	post	−4.58	21.00	0.000	−30.30	post	−4.93	18.00	0.000	−28.51
MH	pre	−2.16	21.00	0.043	−11.77	pre	−3.87	18.00	0.001	−19.47
	post	−2.45	21.00	0.023	−14.55	post	−1.86	18.00	**0.080**	−11.58
PCS	pre	0.45	21.00	**0.654**	0.86	pre	0.51	18.00	**0.618**	0.77
	post	2.03	21.00	0.056	3.23	post	3.37	18.00	0.003[a]	4.52
MCS	pre	−2.64	21.00	0.015	−8.23	pre	−4.44	18.00	0.000	−12.96
	post	−3.07	21.00	0.006	−9.80	post	−2.73	18.00	0.014	−9.48

Δ –pre-to-post change; PF –physical functioning; RP –role limitations due to physical health; BP –bodily pain; GH –general health; VT –vitality; SF –social functioning; RE – role limitations due to emotional problems; MH –mental health; PCS –physical component scale; MCS –mental component scale; PREx—progressive resistance exercise; Non-significant differences are shown in bold; [a] Significantly greater scores compared to the healthy cutoff values.

particularly valuable to AN recovery, as comorbid diagnosis of anxiety or depression is common in AN. Around 20–80% of individuals experience depression [62] and 60% experience comorbid anxiety disorders [63]. Thus, therapeutic exercise used as an adjunct treatment in AN may be an avenue by which to target QoL and subsequently improving comorbid symptoms such as anxiety and depression. In addition, Padierna and colleagues (2002) evaluated the effects on QoL of a two-year psychotherapy intervention in AN using SF-36. Overall, QoL improved in most items – except RE [8]. Conversely, the present study suggests that therapeutic exercise complementary to treatment may have the potential to evoke changes in QoL more rapidly. Thus, not only could PREx be a safe avenue by which comorbid illnesses can be targeted in ED treatment, but by doing so it may be improving QoL more effectively than traditional therapy.

The PREx intervention resulted in improved anthropometric circumferences without negatively impacting skinfolds, BW or BMI. The modest anthropometric findings of this study—the increases in arm circumferences relaxed and contracted in the PREx group—are worth mentioning as they might represent improvements in appendicular muscle mass. This finding indicates that resistance training could be beneficial for muscle mass recovery after hospitalization. When comparing with normative values for age and sex [64,65], ~ 10% of the patients in the control group decreased arm and calf circumference percentiles. However, the AN patients in the PREx group who reached the ≥ 25th percentile increased from ~ 63% to ~ 84% for mid-thigh circumference, from ~ 32% to ~ 48% for triceps skinfold, and from ~ 16% to ~ 21% for subscapular skinfold (with two participants reaching 75th percentile). The improvements in body composition noted here are valuable indicators of health in AN as these patients exhibit not only low levels of fat, but also FFM linked to poor bone health [16,66–68]. Overall, upper extremity force and muscle mass are poor even after significant increase in BMI, body fat percentage, or weight recovery [69]. Therefore, improvements in physical health could be optimized by addressing muscular fitness—muscle mass and strength—in addition to weight regain and nutritional rehabilitation [69]. Further measurement of circumferences as a proxy of muscle content through the course of the disease—together with skinfolds—could help health care professionals understand muscular fitness progress and decide when PREx could be beneficial for patients with AN. Addressing this issue is of great importance, as low muscle mass and decreased physical activity have been reported to determine lower bone mineral density [22,70] and impaired structure in both adults and adolescents with AN [71]. Moreover, more

Table 4
Effects of eight weeks of PREx on body composition and anthropometric variables compared to controls.

	Control group (n = 22)									PREx group (n = 19)								
	Pre			Post			% Δ			Pre			post			% Δ		
	Mean		SD	Mean		SD	Mean		SD	Mean		SD	Mean		SD	Mean		SD
BW (kg)	46.11	±	6.05	47.77	±	5.47†	4.15	±	8.50	41.57	±	7.37	43.19	±	7.38**,***,†	4.10	±	4.91
BMI (kg/m^2)	18.11	±	2.15	20.00	±	7.68	9.57	±	32.14	16.89	±	2.09	17.52	±	2.13	3.83	±	4.71
Circumferences (cm)																		
Arm relaxed	23.19	±	2.18	23.19	±	2.39	0.06	±	4.91	22.04	±	2.39	22.55	±	2.33†	2.40	±	2.79
Arm contracted	24.04	±	1.89	24.02	±	2.29	−0.02	±	5.76	23.00	±	1.98	23.68	±	2.13†	2.98	±	3.15
Upper-Thigh	50.67	±	4.77	50.74	±	5.14	0.17	±	4.64	48.35	±	4.77	49.25	±	4.87	1.93	±	3.60
Mid-Thigh	47.47	±	3.95	47.32	±	4.12	−0.17	±	6.08	44.49	±	3.96	45.27	±	4.25***	1.76	±	3.35
Calf relaxed	32.84	±	2.42	32.68	±	2.25	−0.37	±	4.04	31.49	±	3.15	31.75	±	2.55***	1.56	±	2.76
Calf contracted	33.32	±	2.45	33.34	±	2.35	0.12	±	3.08	31.49	±	3.15	31.75	±	2.55***	1.01	±	3.15
Skinfolds (mm)																		
Biceps	6.54	±	2.33	6.72	±	2.96	1.75	±	23.34	5.28	±	1.41	5.4	±	1.53	2.73	±	15.75
Triceps	12.6	±	3.45	12.88	±	4.53	1.80	±	22.84	10.71	±	2.71	10.76	±	2.74	0.94	±	11.24
Subscapulare	8.93	±	2.76	9.08	±	3.31	1.05	±	16.03	7.48	±	3.00	7.76	±	3.17	4.66	±	15.86
Abdominal	14.85	±	5.86	14.43	±	5.84	−0.88	±	22.05	12.76	±	5.57	12.03	±	5.52	−4.33	±	19.50
Supraspinale	10.27	±	4.19	10.8	±	5.58	4.09	±	28.59	8.58	±	4.00	8.49	±	3.80	−0.03	±	15.11
Mid-Thigh	20.89	±	6.46	21.9	±	8.07	4.08	±	20.06	17.07	±	5.16	17.62	±	5.51***	4.25	±	14.70
Calf	12.75	±	5.30	12.79	±	5.30	0.14	±	16.55	10.38	±	3.21	10.59	±	3.32	2.61	±	10.48

SD−standard deviation; **% Δ** –pre-to-post percent change; BW – body weight; BMI –body mass index; PREx—progressive resistance exercise; **Analysis of the variance, time effects $p < 0.05$; ***Analysis of the variance, group effects $p < 0.05$; † pairwise comparisons $p < 0.05$.

than 38% of recovered patients develop osteoporosis and 92% osteopenia [72]. Therefore, the incorporation of higher intensity PREx shows promise for not only significant improvements in QoL, but also muscle and long-term bone health.

It has long been debated if exercise is safe for adolescents with EDs [34,73]. As noted in our results, no adverse outcomes on AN treatment progression were found. However, the intervention protocol required for participants to nutritionally support their activity throughout the intervention. The addition of nutritional support provides fuel for the body to meet demands of PREx and maintain energy availability [43]. Maintaining a positive energy availability protects against a host of negative outcomes resulting from exercise under insufficient energy availability. Some of the negative effects of exercising under low or negative energy availability includes further hormonal imbalances, increased risk of injury, cardiovascular risk, and additional negative effects on bone health, gastrointestinal health, menstrual function and immunological function, all of which would further aggravate the ED [74,75]. Incorporating exercise supported with nutritional adaptation and the expertise of exercise professionals may support, rather than hinder treatment progression. Although this may require the expansion of the treatment team to include professionals such as athletic trainers or physical therapists, the evidence suggests that PREx was a safe form of complementary treatment that could improve QoL scores and muscle mass.

This study has several strengths with one being that its design was a randomized controlled trial that included a supervised and nutritionally supported exercise intervention. The age of the participants included in the study ranged from 12 to 16 years, reflecting a prominent age of AN onset [76] as opposed to many studies that included more heterogeneous samples (12–45 years) [33–35,42]. Another strength of the study was the novel use of a higher intensity exercise program in AN treatment. Contrary to prior research, this PREx program was able to induce positive changes in perceived QoL and beneficial associations to body composition outcomes. We experienced a low attrition rate (7%), and the participants had a very high level of adherence (88 ± 8.4%) to the program. This study is not without its limitations. A bias may be associated to the convenience sampling method limiting the generalizability of our results to the greater of AN population. Nevertheless, this study was conducted at a nationwide recognized treatment unit, that receives cases from all over the country. This, linked to a very low prevalence rate (<1%) [76] of the disorder would have made population-based recruitment unrealistic and unethical. Low patient numbers have been a common limitation in most studies of exercise in AN [77]. In this study, the sample size allowed for modest improvements in QoL and BW. However, strong associations between QoL scores and anthropometric improvements in the PREx group show promise. Likewise, assessor blinding was not possible in this study, however, the researchers working with patients received anti-bias training consisting of three practical sessions on how to implement the standardized assessment protocols to minimize potential bias. The use of gold standard methods (i.e. dual-energy X-ray absorptiometry, magnetic resonance imaging) to assess body composition would have strengthened our results. However, this technology was not available for our study. In addition, there is lack of equations validated for patients with AN that estimate body components from anthropometry. For this reason, to increase the validity of body composition data and minimize the associated limitations we used anthropometric variables instead of estimation of body components and ensured a professionally trained technician (certified Level 3 anthropometrist) performed all the assessments. Despite these shortcomings, we were able to detect modest changes in QoL and upper body circumferences, and strong associations between QoL scores with body composition changes. Overall, future studies should implement strategies that include assessor blinding, a greater sample size when the primary outcome of the study is QoL (SF-36) or anthropometric variables (include *a priori* sample size calculations) and aim to investigate whether nutritionally supported PREx could impact other outcomes such as ED and comorbid symptomatology, spontaneous physical activity levels, bone health, or overall physical health.

5. Conclusion

In conclusion, the use of nutritionally supported PREx complementary to standard ED treatment resulted in modest improvements in perceived QoL within two months without negatively impacting weight or BMI recovery. Both control and PREx groups increased BW similarly, indicating similar trajectories of weight recovery. In addition, improvements in QoL were associated with positive changes in anthropometry in the PREx group. Our study indicates that PREx is a safe and beneficial exercise protocol for individuals with AN after hospitalization. The findings within this study support the need for more research examining the integration of resistance training exercise into the treatment plan of patients with AN after hospitalization.

Author contributions

Conceptualization, M.F., M.P., E.L.; Data curation, M.F., H.O., E.L.; Formal analysis, M.F., E.L., A.A., H.O.; Investigation, M.F., M.G., M.P.; Methodology, M.F., E.L., M.P.; Project administration, M.F., M.P., M.G.; Resources, M.G., M.P.; Supervision, M.P., M.F.; Validation, E.L., M.F.; Visualization, M.F., E.L., H.O., A.A.; Writing—original draft preparation, A.A., M.F., D.Q., H.O.; Writing—review and editing, M.F., A.A., D. Q., E.L., M.G., M.P., H.O. All authors have read and agreed to the published version of the manuscript.

Declaration of interest statement

The authors declare no competing interests.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

The authors would like to thank the patients and parents from the research unit at the hospital for their support and participation. Additionally, the authors would like to thank JaiLin Allen for her initial contributions to this project.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctcp.2022.101576.

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