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## **Effect of resistive training on gastrointestinal cancer cachexia**

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**Abstract**---Purpose: The current study was conducted to evaluate the therapeutic effect of resistive training in reducing the effect of cancer cachexia. Subjects and Methods: Thirty patients with gastrointestinal cancer cachexia participated in this study. Their ages ranged from 50-70 years. They were recruited from Al Kasr El-Ani hospital outpatient clinic to be treated in the outpatient clinic, Faculty of Physical Therapy, Cairo University and were divided randomly into two equal groups. Group (A) composed of 15 patients who received their ordinary medical treatment in addition to resistive training program 2 times per week for 8 weeks. Group (B) composed of 15 patients who received their ordinary medical treatment. Methods of assesment was measurements of Handgrip strength assessed by handgrip dynamometry, Lower body strength assessed using a 30-second sit to stand test, Lean body mass assessed by bioelectrical impedance analysis. Results: There was a significant increase in both muscle strength and lean body mass in patient who received resistive training. Conclusion: Resistive training can be considered as an effective method in decreasing severity of cancer cachexia in gastrointestinal cancer patient.

**Keywords**---resistive training, cancer, cachexia.

## **Introduction**

Cancer cachexia is a complex skeletal muscle wasting disease that accounts for 20–40% of cancer-related deaths and contributes to patient morbidities (e.g. toxicity, poor chemotherapy adherence, impaired activities of daily living) and mortality (1). Currently, cancer patient survival is negatively affected by a lack of treatment options. The absence of successful therapies for the cachectic condition likely results from the disease's multimodal aetiology and the heterogeneity of cancer pathology amongst patients (2). Skeletal muscle mass is maintained by balancing protein synthesis and breakdown, which fluctuates throughout a 24-hour period (3). The regulation of protein turnover is influenced by circulating hormonal and inflammatory signals as well as varied responses to caloric input and activity level (4).

However, the mechanisms of cancer-induced anabolic resistance are not thoroughly understood. A promising therapeutic option for overcoming anabolic resistance in cancer patients is resistance exercise training, which can increase skeletal muscle mass and metabolic flexibility in a healthy adult. (4). Regular physical activity and exercise provide clear benefits for individuals with chronic diseases (5). Indeed, resistance exercise induces systemic and muscular adaptations, such as antioxidant production (6), hypertrophy, increased oxidative capacity, upregulation of hormetic factors, and turnover of mitochondria (7). The purpose of the study was to evaluate the therapeutic effect of resistive training in reducing the effect of cancer cachexia

## **Methodology**

### **Study design**

A randomized, controlled study with 2 parallel groups was performed between April 2022 and June 2022.

### **Subjects**

A convenient sample of thirty patients (17 males and 13 females) were recruited from Al Kasr El-Ani hospital outpatient clinic to be treated in the outpatient clinic, Faculty of Physical Therapy, Cairo University. They were enrolled and assessed for their eligibility to participate in the study. Included were patients with gastrointestinal cancer cachexia aged maximum value of 60 years and minimum value of 42 years, free from any other illness that might affect the results.

### **Randomization**

The participants were informed about the nature, purpose, and benefits of the study, their right to refuse or withdraw at any time, and the confidentiality of any obtained information. Anonymity was assured through the coding of all data. The subjects with gastrointestinal cancer cachexia were randomly assigned into 2 groups (A and B) by a blinded and independent research assistant who opened sealed envelopes that contained a computer-generated randomization card. No subjects dropped out of the study after randomization.

## **Procedures of the study**

A verbal explanation about the importance of this study procedure, the main aims and conceptual approach was explained to every patient. The exercise intervention was based on standardized but individualized training protocols. All exercises were carried out within the individuals given range of motion and in a dynamic way. The procedure of this study was divided into two main procedures: measurement and therapeutic procedures.

### **Measurement tools**

**Hand Grip Dynamometry:** Eighty percent of occupational therapy schools and clinics in the United States use the Jamar dynamometer as their usual instrument to assess grip strength. The Jamar dynamometer presents good inter-rater reliability and test-retest reliability. The American Society of Hand Therapists (ASHT) has recommended the Jamar dynamometer as the gold standard, leading to its widespread use in clinical practice and research.

**Thirty Minutes Sit to Stand Test:** Standing up from sitting position is a very common and essential activity which enables other vital activities possible, such as walking in daily life. The ability to stand up from a chair is an important component of maintaining independence for elderly people and for individuals with disabilities.

**Bioelectrical Impedance Analysis:** Bioelectrical impedance analysis (BIA) is a noninvasive, inexpensive, and portable method that has been used mainly for body-composition analysis over the past decade. However, BIA does not measure body composition directly. It measures 2 bioelectrical parameters: body resistance and reactance.

### **Measurement procedures**

At the beginning of our study, we assessed: Upper body strength via handgrip strength of the dominant hand by handgrip dynamometry, the average of 3 attempts with 1-minute rest between attempts. Lower body strength will be assessed using a 30-second sit to stand test. The number of times participants can stand from a seated position in 30 seconds will be examined. Lean body mass assessed by bioelectrical impedance analysis.

**Therapeutic tool:** Free weight (sand bag and dumbbells according to 1<sub>RM</sub>) and bodyweight.

**Therapeutic procedures:** According to The American College of Sports Medicine guidelines patient had 2 days/week of Resistive Exercise (RE), focusing on large muscle groups, 60–70% 1<sub>RM</sub>, 1–3 sets of 8–12 repetitions (8). The exercise group had two exercise sessions per week over an 8-week period. Each session lasted 50–60 minutes and included a warm-up (10–15 minutes), active phase with (30 minutes), and stretching/relaxation (10–15 minutes). The exercise program was tailored to the individual patient's level of physical functioning.

Warm-Up : The warm-up session lasted for 10–15 minutes and was aerobic exercise using large muscle groups in an upright or sitting position; alternatively, stationary bicycling was performed.

Active phase: A total body approach of 6–8 exercises per session aimed at stimulating large muscle groups (leg press, leg curl, leg extension, Romanian deadlift, chest press, shoulder press, lat pulldown, seated row) is advocated (9)

Stretching and Relaxation: The last part of the program included stretching of the muscles used during the circuit training and 5 minutes of relaxation to calm muscle. The patients were encouraged to be physically active in their everyday life, but were not given any specific exercises to do at home. Old Patients received professional instruction during two to three initial sessions in the first two weeks.

Statistical procedure: Descriptive statistics and t-test were conducted for comparison of the mean age of both groups. Unpaired t-test was conducted for comparison of upper body strength, lower body strength and lean body mass between both groups. Paired t test was conducted for comparison between pre and post treatment mean values of upper body strength, lower body strength and lean body mass in each group. Chi-square test ( $\chi^2$ ) was used to study comparison between the two groups as regards gender. The level of significance for all statistical tests was set at  $p < 0.05$ . All statistical tests were performed through the statistical package for social sciences (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA).

## Results

Thirty patients of both sexes who had cancer cachexia participated in this study. The participants were randomly distributed into two equal groups.

Group A: Fifteen patients participated on a progressive resistive training program 2 days per week for 2 months beside their ordinary medical treatment. Group B: Fifteen patients who received their ordinary medical treatment.

The mean  $\pm$  SD age of group A was  $52.20 \pm 5.72$  years, with maximum value of 60 years and minimum value of 42 years. The mean  $\pm$  SD age of group B was  $53 \pm 5.62$  years, with maximum value of 60 years and minimum value of 40 years. There was no significant difference between both groups in the mean age values ( $p = 0.702$ ). Table (1)

Table (1) Comparison between patients' groups A and B as regards age

	Group (n = 15)	Group (n = 15)	t	P-value	Sig.
Age (years)			-0.386	0.702	NS
Median (Min. – Max.)	52 (42 –60)	53 (40–60)			
Mean $\pm$ SD.	$52.20 \pm 5.72$	$53 \pm 5.62$			

t: Independent Samples t Test

p: p value for comparing between the studied groups

p value  $>0.05$  is non-significant

NS: non-significant

The mean  $\pm$  SD of lean body mass pretreatment of group A was  $56.60 \pm 3.62$  kg and that post treatment was  $59.07 \pm 3.37$  kg. The mean difference between pre

and post treatment was 2.47 and the percent of change was 4.36%. There was a significant increase in the lean body mass of group A post treatment compared with that pretreatment ( $p < 0.001$ ) (figure 1).

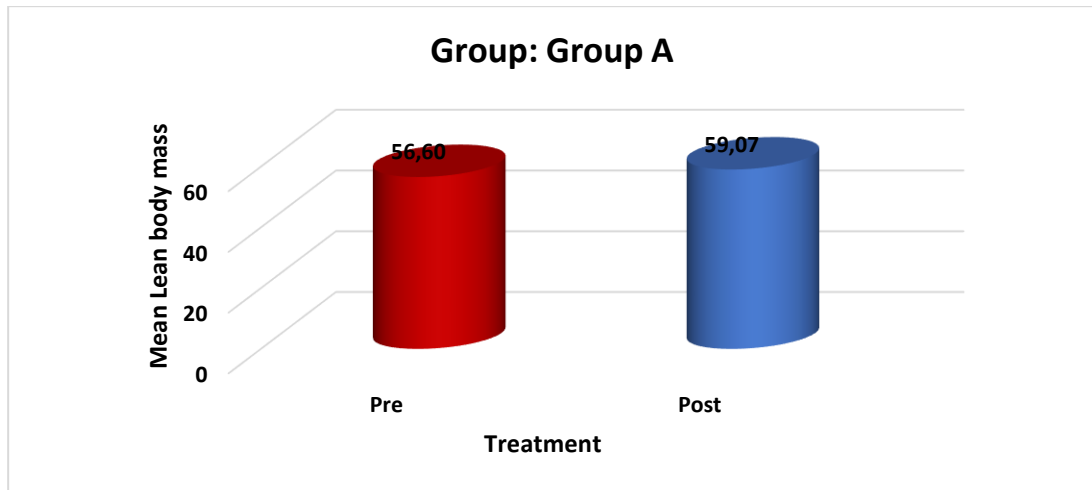


Figure (1) Comparison between Pretreatment and Post treatment lean body mass in group (A)

The mean  $\pm$  SD of lean body mass post treatment of group A was  $59.07 \pm 3.37$  kg and that of group B was  $56.53 \pm 4.45$  kg. The mean difference between both groups was 2.53. There was a significant increase in the lean body mass of group A compared with that of group B post treatment ( $p = 0.041$ ) (Table 2).

Table (2): Comparison between patients' groups A and B as regards Post treatment lean body mass

Post treatment	lean body mass Mean $\pm$ SD			Mean difference	t	p	Sig
Group A	59.07	$\pm$	3.37	2.53	1.757	0.041*	S
Group B	56.53	$\pm$	4.45				

t: Independent Samples t Test

p: p value for comparing between the studied groups

\*: p value  $< 0.05$  is significant

S: significant

The mean  $\pm$  SD of 30 Seconds sit to stand test pretreatment of group A was  $10.93 \pm 2.37$  times and that post treatment was  $12.80 \pm 2.11$  times. The mean difference between pre and post treatment was 1.87 and the percent of change was 17.07%. There was a significant increase in the 30 Seconds sit to stand test of group A post treatment compared with that pretreatment ( $p = 0.001$ ) (figure 2).

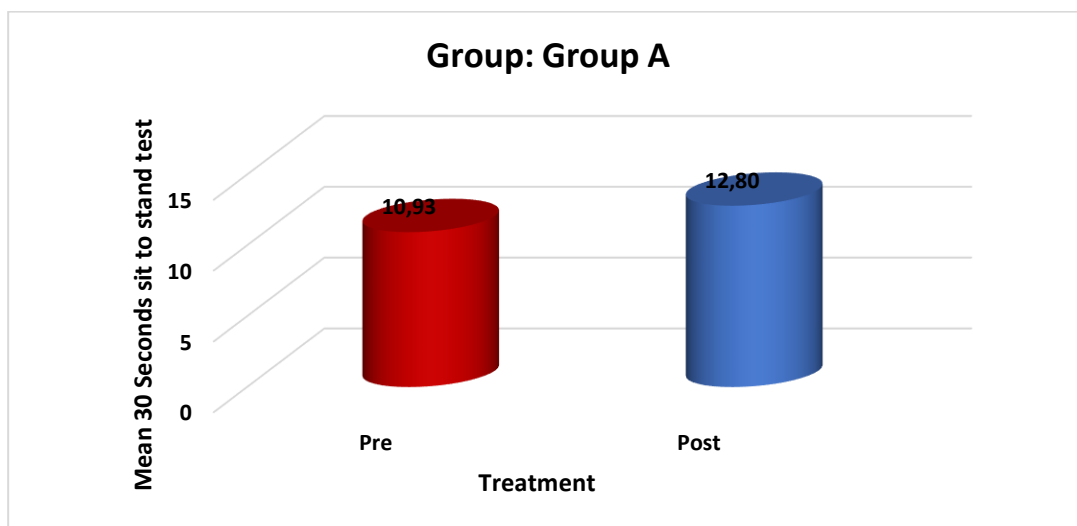


Figure (2) Comparison between Pretreatment and Post treatment 30 Seconds sit to stand test in group (A)

The mean  $\pm$  SD of 30 Seconds sit to stand test pretreatment of group B was  $10.60 \pm 2.29$  times and that post treatment was  $10.80 \pm 1.70$  times. The mean difference between pre and post treatment was 0.20 and the percent of change was 1.89%. There was no significant difference in the 30 Seconds sit to stand test of group B post treatment compared with that pretreatment ( $p = 0.567$ ) (figure 3).

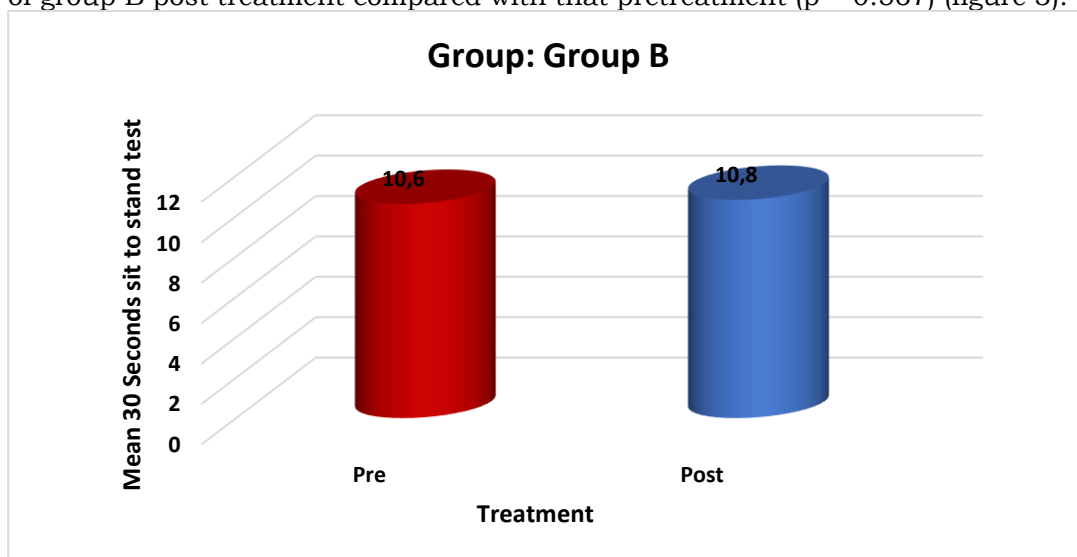


Figure (3) Comparison between Pretreatment and Post treatment 30 Seconds sit to stand test in group (B)

The mean  $\pm$  SD of hand grip force test pretreatment of group A was  $27.13 \pm 5.83$  kg and that post treatment was  $32.80 \pm 4.83$  kg. The mean difference between pre and post treatment was 5.67 and the percent of change was 20.88%. There was a significant increase in the hand grip force test of group A post treatment compared with that pretreatment ( $p < 0.001$ ) (figure 4).

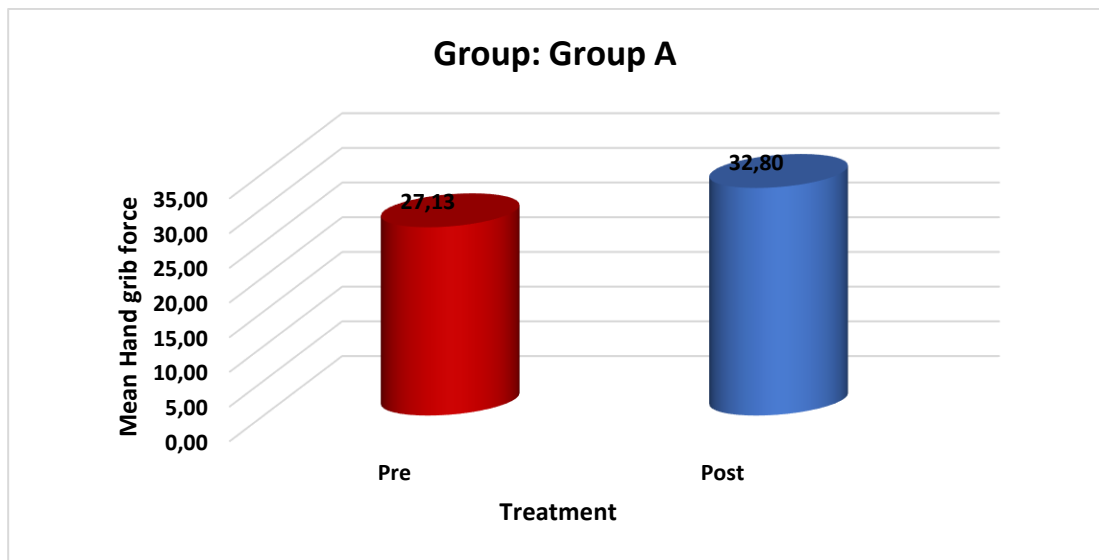


Figure (4) Comparison between Pretreatment and Post treatment hand grip force in group (A)

The mean  $\pm$  SD of hand grip force test pretreatment of group B was  $27.80 \pm 5.07$  kg and that post treatment was  $28.53 \pm 4.87$  kg. The mean difference between pre and post treatment was 0.73 and the percent of change was 2.64%. There was no significant difference in the hand grip force test of group B post treatment compared with that pretreatment ( $p = 0.299$ ) (figure 5).

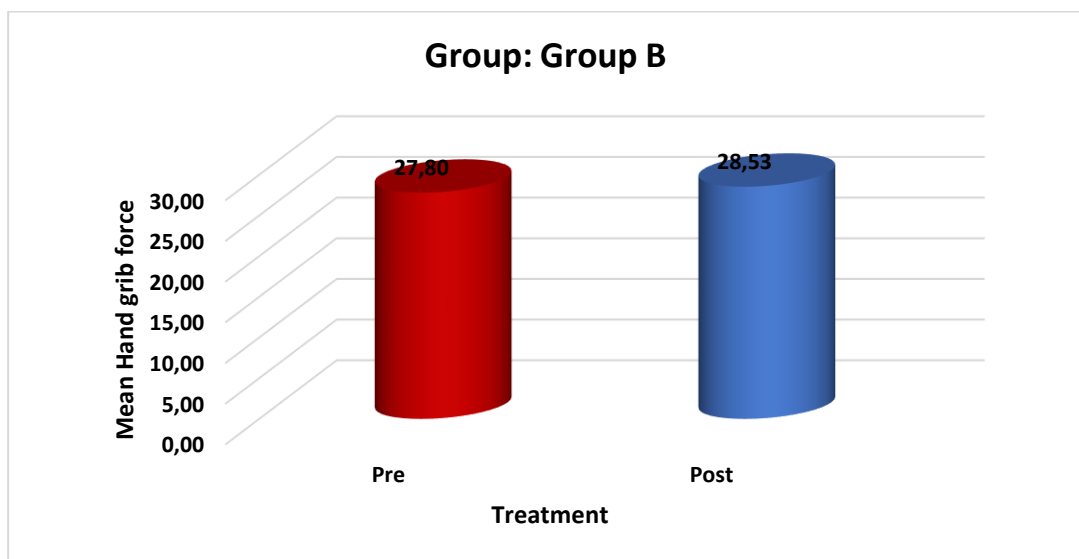


Figure (5) Comparison between Pretreatment and Post treatment hand grip force in group (B)

The mean  $\pm$  SD of hand grip force test post treatment of group A was  $32.80 \pm 4.83$  kg and that of group B was  $28.53 \pm 4.87$ kg. The mean difference between both

groups was 4.27. There was a significant increase in the hand grip force test of group A compared with that of group B post treatment ( $p = 0.023$ ) (Table 3).

Table (3) Comparison between patients' groups A and B as regards Post treatment hand grip force

Post treatment	hand grip force Mean ± SD	Mean difference	t	p	Sig
Group A	32.80 ± 4.83	4.27	27.98	0.023*	S
Group B	28.53 ± 4.87				

t: Independent Samples t Test

p: p value for comparing between the studied groups

\*: p value <0.05 is significant

S: significant

## Discussion

Despite the well-documented capacity of chronic exercise to counteract sustained disease-related inflammation, few studies address the effect of exercise training in cancer cachexia. The aim of the present study was hence to discuss the results of cachexia treatment with resistance training, which is well tolerated by patients, and an effect on body mass and muscle strength may be observed even at low-intensity.

Potential exercise training alterations to the systemic environment during cancer cachexia. Systemic disruptions (eg, inflammation, anemia, hypogonadism) have been identified as therapeutic targets of cancer cachexia. Resistance and aerobic exercise training can positively influence these characteristics, and therefore may be a potential target to increase patient survival (10). The present study was designed to investigate the effect of progressive resistive training on gastrointestinal cancer cachexia.

This study was conducted on thirty patients with gastrointestinal cancer cachexia, their ages ranged from 50-70 years, patients were randomly assigned into two equal groups: group A (control group) received their ordinary medical treatment and group B (resistive training group) received their ordinary medical treatment in addition to resistive training program and the study was conducted for 8 weeks (2times/week). All patients were evaluated before the treatment and after 8 weeks of resistive training program, measuring their lean body mass, Hand Grip Dynamometry and Sit-to-Stand Test.

The results of current study revealed significant increasing in upper body strength, lower body strength and lean body mass in the group of resistive training program (group A) when compared with the control group (group B) as follow where: As regards the mean ± SD of lean body mass post treatment of group A, it was  $59.07 \pm 3.37$  kg and that of group B was  $56.53 \pm 4.45$  kg. The mean difference between both groups was 2.53. There was a significant increase in the lean body mass of group A compared with that of group B post treatment

And the mean ± SD of 30 Seconds sit to stand test post treatment of group A was  $12.80 \pm 2.11$  times and that of group B was  $10.80 \pm 1.70$  times. The mean

difference between both groups was 2.00. There was a significant increase in the 30 Seconds sit to stand test of group A compared with that of group B post treatment. Also, the mean  $\pm$  SD of hand grip force test post treatment of group A was  $32.80 \pm 4.83$  kg and that of group B was  $28.53 \pm 4.87$  kg. The mean difference between both groups was 4.27. There was a significant increase in the hand grip force test of group A compared with that of group B post treatment.

Kamel and others in their study found that found that A 12 weeks resistance training increased the mobility, muscle strength and lean body mass of patients with cachexia due to pancreatic cancer (11). Hardee and others in their study to examine the independent associations of leisure-time aerobic physical activity (PA) and resistance exercise (RE) on all-cause mortality in cancer survivors; they found that PA in cancer survivors was not associated with a lower risk of all-cause mortality. In contrast, RE was associated with a 33% lower risk of all-cause mortality (95% CIs: 0.45–0.99) after adjusting for potential confounders, including PA, so, Individuals who participated in RE during cancer survival had a lower risk for all-cause mortality, and the association was stronger in older individuals. The current findings provide preliminary evidence for benefits of RE during cancer survival (5).

Medical practitioners and clinicians should be aware of these benefits and discuss the importance of PA, particularly RE, during and after cancer treatment (5). In the study of Lønbro and others, they found that progressive resistance training significantly increased lean body mass, maximal muscle strength and functional performance following radiotherapy and it is feasible and effective in rebuilding lean body mass and maximal muscle strength where from pre- to post- PRT, LBM increased significantly by 2.6 kg (12). Also they found that progressive resistance training was feasible in pancreas cancer patients and improved muscle strength with significant results for some muscle groups. Supervised resistance training seemed to be more effective than home-based resistance training. (12).

Where, Gould said that resistance exercise has also been shown to be a potent stimulant for increasing protein synthesis and has been shown to reverse skeletal muscle wasting in other diseases; increasing muscle strength and lean body mass (13). And Oldervoll found that physical performance was clinically and statistically significantly improved after 8 weeks of physical exercise. Physical exercise is an encouraging approach to be applied in future large-scale randomized studies in cancer patients (14).

Where cancer patients were randomized to a physical exercise group or a control usual care group The physical exercise group exercised under supervision 60 minutes twice a week for 8 weeks. Assessments were performed before and after the intervention. The primary outcome was physical fatigue (PF) measured by the Fatigue Questionnaire. Physical performance was a secondary outcome measured by the Shuttle Walk Test (SWT) and hand grip strength (HGS) test (14). On the other hand, the results of this study contradict with Das and Solheim. Patients in the treatment arm had a mean (SD) increase in body weight by 0.91 kg (2.47) whereas those in control arm lost 2.12 kg (2.50). There was no significant difference in physical activity, where grip strength was assessed at follow up and there was no difference between groups (15).

Where Das found that even though RET was ineffective to mitigate cancer-induced skeletal muscle wasting in, the loss of strength capacity was associated with mortality. New studies are still necessary to elucidate the putative therapeutic role of RET in counteracting cancer cachexia during tumor progression (16).

## Conclusion

resistance training and physical activity in general may show promising results in the prognosis of cancer cachexia, and also the mortality rates of cancer patients, but more studies are needed to investigate how to implicate and get the right benefit of trainings.

## Conflict of interest

There is no conflict of interest.

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