

Effect of Resistance Training Exercise Program during Androgen Deprivation Therapy in Prostate Cancer Patients

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Abstract:

Background and Purpose: The purpose of this study is to evaluate the response of muscles to resistance training exercise program during androgen deprivation treatment in prostate cancer patients.

Materials and Methods: Thirty patients suffering from prostate cancer during androgen deprivation therapy participated in this study their ages ranged from 50 to 70 years. They were selected from oncological outpatient clinic of Al-Hussien University Hospital and were divided equally into 2 groups. Group A (Control group): received medical treatment (ADT) and advised not to start strength training and maintain their daily activities. Group B (Study group): received medical treatment (ADT) and resistance training exercise for lower limbs. Assessment of response of muscles and functional performance was done by using Manual muscle test (MMT) and 5X Sit-to-Stand Test (5XSST).

Results: At the end of the treatment course, percentage of improvement in MMT and 5XSST was significantly high in the study group compared to the control group which means that resistance training exercise has beneficial effects in muscle response and function in patients with prostate cancer disease during the treatment with androgen deprivation therapy.

Conclusion: Resistance training exercise program has beneficial effects in increase muscle function and performance in patients suffering from prostate cancer during androgen deprivation therapy.

Key Word: Prostate cancer, Androgen deprivation therapy, Resistance training exercise.

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I. Introduction

One of the most popular cancers among elderly men in the developed countries is Prostate Cancer (PCa).¹ By 2020, 15 million new cases and 10 million new deaths from all cancers are expected worldwide.² In this context, prostate cancer is the sixth most common cancer representing 14.3% of cancers among men in developed countries.³ Prostate Cancer affects about one quarter of a million men in US yearly. There is a significant increase in Five-year survival values during the past twenty years because of the updated treatments including androgen deprivation therapy (ADT).⁴ Androgen deprivation therapy (ADT) is considered a basic treatment for patients with prostate cancer, as it can increase survival rate and reduce disease-related side effects and morbidity.⁵ Obviously, Androgen Deprivation Therapy has negative effects on the function of skeletal muscles by affecting multiple parts, named the neuromuscular junction, androgen receptor, and second messenger systems which include insulin-like growth factor-1. These effects on the skeletal muscles parts lead to wasting with weakness.⁶ There are other common side effects of Androgen Deprivation Therapy including increase of falling risk, fatigue, increased fat mass, loss of bone mass, and a decrease in functional status. Resulting in all of these negative effects, there is a hormonal therapy suggested by evidence, and this treatment might enhance weakness in those people, which in turn is related to negative outcomes including hospitalization, death, and disability.⁷ As a trial to decrease the negative effects of ADT, exercise has been proposed as a treatment.

However the recent meta-analysis has declared the benefit and effects of exercise therapy on the cancer-specific quality of life and fatigue in patients with prostate cancer.⁸ In patients with prostate cancer treated by ADT, multiple studies proved resistance training as an effective way of exercise to increase strength, physical function, lean mass, and quality of life in males with prostate cancer treated by ADT.⁹ Also resistance training exercise might be a good and beneficial way of exercise as it helps in losing fats, controlling body weight, and improving the quality of life.¹⁰ Muscle growth can be stimulated by resistance exercise corresponding to the amount of the force generated in the muscles during the exercise. Moreover, RE that generates eccentric muscle activity can maximize the functional and structural responses of the muscles at the least energetic cost to the individual and produce the greatest forces.¹¹

II. Material And Methods

This study included thirty patients suffering from prostate cancer during androgen deprivation therapy, and their ages ranged from 50 to 70 years. They were selected from oncological outpatient clinic of Al-Hussien University Hospital and were divided equally into 2 groups.

Group A (Control group): received medical treatment (ADT) and advised not to start strength training and maintain their daily activities.

Group B (Study group): received medical treatment (ADT) and resistance training exercise for lower limbs. Assessment of response of muscles and functional performance was done by using Manual muscle test (MMT) and 5X Sit-to-Stand Test (5XSST).

Inclusion criteria:

- Age range between 50-70 years.
- Histologically documented prostate cancer.
- Minimally prior to exposure to ADT longer than 2 months.

Exclusion criteria:

- Severe cardiac disease.
- Uncontrolled hypertension.
- Severe osteoporosis.
- Patients with bone metastatic disease.
- Severe anemia.
- Leg/calf pain.
- Sudden joint pain or that pain not caused by injury.
- Unusual or sudden shortness of breath.
- Irregular heartbeat and Patients who used to do resistance training in the previous 3 months.

Evaluation Process:

All patients were subjected to evaluation of grade of muscle strength according to manual muscle test (MMT)¹². 5X Sit-to-Stand Test (5XSST)¹³ was used for the assessment of the functional performance. All patients were evaluated before starting the study and after 16 weeks of treatment.

Materials for treatment:

Physical therapy equipment's (a multigym, Mechanical resistance training exercise, the band) were used in conducting the resistance training exercise program.

Treatment Plan

The control group received medical treatment (ADT), and it was advised not to start strength training and maintain their daily activities.

The study group received the same exercise program received by the control group in addition to resistance training exercise for lower limbs. Before the start of training of resistance exercise, one familiarization session was designed to habituate participants with different resistance exercises and to familiarize them with performing the 1-RM test (1-RM was defined as the maximum amount of resistance that can be moved through the full range of motion of an exercise for no more than one repetition).

The Designed Exercise Program

The program was directed towards strengthening of weak muscles and improve functional performance.

The first two weeks of the program are supposed to determine the protocol of exercise familiarization for patients with prostate cancer, and undertaken at a load about (40-50% of one repetition maximum (1 RM)) in sets of ten times. Before the strength training session, the patients get around 5 to 10 minutes of warm up exercise including stretching exercises for the involved muscle group and cooling down around 5 to 10 minutes. Moreover, before every training exercise session, the patients achieved a sub maximal set of 10 times as a warming up in squat workout. After passing the 1st two weeks, patients are encouraged to increase the training intensity gradually, to achieve the exercise with the possible greatest load at the end of the sixteenth week.

- Exercise prescription:

- Frequency: 3 sessions per week
- Duration: 30 minutes (5 minutes warm up, 20 minutes of resistive exercise, and 5 minutes cool down).
- Number of sets: 1:3 sets for each exercise per session.
- Number of repetitions: every set contains 6 to 10 repetitions.

- Time of rest between sets: 1:2 minutes.
- Intensity: progress from 6 or 10 repetitions maximum at the end of the sixteenth week.
- Exercise forms: straight leg raising from supine position (SLR), leg press, knee extension, knee flexion , squat.

Statistical analysis :

Illustrative statistics and unmatched t-test were done as a comparison of subject characteristics between the study and control groups. Matched t-test was done to compare 5XSST between pre and post treatment in each group. Unmatched t-test was done as a comparison between the control and study groups regarding the mean values of 5XSST. Muscle strength grades were compared between groups by Mann–Whitney U test and between both groups pre and post treatment by Wilcoxon Signed Ranks. All analysis was done via the statistical package for social studies (SPSS) version 22 for windows (IBM SPSS, Chicago, IL, USA). The significance level for all statistical tests was adjusted at $p < 0.05$.

III. Results

Subject characteristics:

Table (1) shows the characteristics of subjects in both the control group and the study group. There was no obvious change between control and study groups in the mean age and BMI ($p > 0.05$).

Table 1. Comparison of subject characteristics between control group and study group:

	$\bar{x} \pm SD$		M D	t- value	p- value
	Study group	Control group			
Age (years)	62.93 ± 4.54	61.66 ± 5.16	1.2 7	0.71	0.48*
BMI (kg/m ²)	28.86 ± 1.54	28.68 ± 1.67	0.1 8	0.35	0.72*

\bar{x} , Mean; SD, Standard deviation; MD, Mean difference; p value, Probability value*, Non-significant.

Effect of treatment on 5XSST and strength grades:

- Within group comparison:

Compared with that pretreatment ($p < 0.001$), there was an obvious decrease in the study groups in 5XSST post treatment, while there was no significant changes between post and pretreatment in control group ($p > 0.05$). (table 2).

Compared with that pretreatment ($p < 0.001$), there was an obvious increase in hamstring, quadriceps and calf strength grades post treatment in the study groups, while there was no significant changes between post and pretreatment strength grades in control group ($p > 0.05$). (table 3).

- Comparing between groups:

There was no obvious changes between both groups pre-treatment ($p > 0.05$) in 5XSST. Comparing between both groups post treatment showed an obvious decrease in 5XSST of the study group when compared with that of control group ($p < 0.001$). (table 2).

There was no obvious change in strength grades in pre-treatment ($p > 0.05$) between the study and control groups. Comparing between control and study groups post treatment showed an obvious increase in hamstring, quadriceps and calf strength grades of the study group compared with that of the control group ($p < 0.001$). (table 3).

Table 2. Mean 5XSST pre and post treatment of the study and control groups:

5XSST (sec)	Study group	Control group	MD	t- value	p value
	$\bar{x} \pm SD$	$\bar{x} \pm SD$			
Pre treatment	14.88 ± 0.93	15.17 ± 0.79	-0.29	-0.9	0.37*
Post treatment	13.42 ± 0.84	15.19 ± 0.83	-1.77	-5.77	0.001**
MD	1.46	-0.02			
% of change	9.81%	0.13%			

t- value	12.36	-0.61
	<i>p = 0.001**</i>	<i>p = 0.55*</i>

\bar{x} , Mean; SD, standard deviation; p-value, level of significance; *, Non-significant; **, Significant

Table 3. Median values of muscle strength grades post and pretreatment of control and study groups:

Muscle strength grade	Study group	Control group	U- value	p-value
	Median	Median		
Hamstring				
Pre treatment	3	3	105	0.71*
Post treatment	4	3	33	0.001**
Z- value	3.6	0.57		
	<i>p = 0.001**</i>	<i>p = 0.56*</i>		
Quadriceps				
Pre treatment	4	4	96	0.43*
Post treatment	5	4	33	0.001**
Z- value	3.69	1		
	<i>p = 0.001**</i>	<i>p = 0.31*</i>		
Calf				
Pre treatment	4	4	82.5	0.16*
Post treatment	5	4	40.5	0.001**
	3.74	1.73		
	<i>p = 0.001**</i>	<i>p = 0.08*</i>		

U- value, Mann-Whitney test value; Z- value, Wilcoxon signed ranks test value; p-value, level of significance; * Non-significant; ** Significant

IV. Discussion

This study was conducted for patients suffering from prostate cancer during androgen deprivation therapy to examine the efficacy of resistance training exercise on muscle response and function. Assessment of muscle response and functional performance was done by using manual muscle test (MMT) and 5X Sit-to-Stand Test (5XSST).

The results of current study demonstrated that resistance training exercise has positive effects in muscle response and function in prostate cancer patients during androgen deprivation therapy.

The results of this study came in agreement with the results of Galvão et al.,¹⁴ who found that a high-intensity short-term strength training (ST) program improves QoL, physical function, endurance, strength, muscle mass, and power and reduces fatigue in elderly black males with prostate cancer. This assures the positive effects of ST observed previously in PCa patients on ADT and illustrates the effects of high-intensity ST to educe increases in strength, muscle power, and mass that are attached with significant improvements in fatigue, quality of life, and physical function in an understudied population of black elderly males with prostate cancer.

The results of this study came in support with the results stated by Patel et al.,¹⁵ who found that decreased the risk of prostate cancer by 70% for updated ways and in elderly men if they are doing more than 2-3 hrs. of intense exercise weekly. The positive effects of performing the exercise training include maintaining the body fitness, anxiety and stress controlling, maintaining the normal body weight and improving the function of the immune system, which decreases the risk for all cancerous diseases.

The results of this study came in agreement with the results of Segal et al.,¹⁶ who found that the results when they undertook mostly the same resistance exercise protocol later after few years with patients having prostate cancer planned to be treated by radiotherapy, and they have shown great improvements not only in quality of life, muscular strength, and fatigue, but also in percentage of body fat.

The results of this study agreed with the results of Santa Mina et al.,¹⁷ who found that a 6 months long individualized home aerobics exercise to a resistance exercise program undertaken with resistance bands and

stability ball. They concluded that training at home has shown satisfactory results in the IGF axis and adipokine levels. The IGF axis changes might indicate minimizing the risk of prostate cancer.

The results of this study are in accordance with **Buffart et al.**,¹⁸ who found that combining aerobic exercise with resistance training on general and physical health in patients receiving ADT. Authors found that the positive effect in health generally was measured by walking speed and fatigue while the positive effect in physical health was measured by speed of walking and strength of muscle.

The findings of this thesis agreed with the findings of **Holviala et al.**,¹⁹ who discovered that aerobic training and resistance exercise training cause great changes in speed of walking in elderly men. It is found out that AE does not have any effect on walking speed while there is a positive effect of muscle strength on walking speed.

The findings of this study agreed with the results of **Keating et al.**,²⁰ who discovered that the resistance exercise is very important for avoiding the negative side effects of cancer, chronic diseases, such as type 2 diabetes and cardiovascular diseases.

The results of this study came in accordance with the results of **Winters-Stone et al.**,²¹ who concluded promising findings, namely that resistance exercise has a good effect on bone adaptations even in androgen-depleted PCaPs.

V. Conclusion

On the basis of data obtained in present study, resistance training exercise has beneficial effects in muscle response and function in prostate cancer patients during androgen deprivation therapy.

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