LIFESTYLE INTERVENTION FOR PROMOTING PHYSICAL ACTIVITY IN PROSTATE CANCER PATIENTS WITH ANDROGEN DEPRIVATION THERAPY

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ABSTRACT

Background and objective
Despite the awareness of the important roles of physical activity (PA), the majority of cancer survivors fail to meet PA guidelines due to a lack of access to facilities or motivation. The purpose of this study is to examine the effectiveness of lifestyle intervention in prostate cancer (PC) patients receiving androgen deprivation therapy (ADT).

Material and methods
A total of 23 PC patients (aged 75.26 ± 6.9 years) receiving ADT at least 3 months were randomized into an intervention group (n=12) and a control group (n=11). The intervention group received lifestyle intervention in the form of education program. Levels of PA, body composition, physical function, disease-specific quality of life (QoL), and fatigue were assessed before and after the 12-week intervention.

Results
The intervention group showed improvements in the level of PA (step count: p=0.028, moderate to vigorous PA: p=0.013) compared with the control group. Thigh circumference (p=0.002), physical function (grip strength: p=0.034; knee extensor: p=0.004, up and go: p=0.001; 2-min step: p=0.001), QoL (p<0.001),
and fatigue (p=0.001) were also improved compared with the control group. There were no adverse events during the lifestyle intervention period.

**Conclusion**
The 12-week lifestyle intervention program appears to be a promising strategy to increase the PA and mitigate the side effects of ADT for PC patients.

**Keywords:** androgen deprivation therapy; lifestyle intervention; prostate cancer; side effects

**INTRODUCTION**

Prostate cancer (PC) is the second most common cancer and the fifth leading cause of death in men worldwide. However, PC incidence appears to be relatively different by race/ethnicity or geographical factors. For example, PC occurs more often in non-Hispanic whites than Asian, American and Hispanic men. Also, the incidence rates are high as 25-fold more in Australia/New Zealand and Northern America compared with those of Eastern and South-Central Asia. But, recently, an increasing number of new cases of PC have been seen in most Asian countries. According to the International Agency for Research on Cancer data, there was most rapid change seen in annual percentage of PC incidence in South Korea. These results might be an outcome of not only genetic and environmental factors but also western lifestyle and disease early detection.

PC cells are physiologically dependent on androgens to grow, function, and proliferate. These effects can be blocked or reduced through the use of androgen deprivation therapy (ADT), which makes tumors shrink or slows the growth. For these reasons, ADT has been recognized as a mainstay treatment to treat patients with PC by reducing disease-specific mortality. However, this treatment accompanies side effects such as skeletal muscle loss, osteoporosis, depression, and even reduced quality of life (QoL) and physical function. Moreover, recent studies suggest that ADT increases the risk of cardiovascular disease (CVD), metabolic syndrome, and sarcopenia.

In order to eliminate various side effects of ADT, modifiable behaviors such as physical activity (PA) have been heightened. For example, the higher levels of PA that were shown in observational prospective cohort study were found to be associated with the reduced rates of overall mortality and PC-specific mortality. Furthermore, Kenfield et al. reported that men with 3 h per week of vigorous PA had a 61% lower risk of PC death compared with men with less than 1 h per week of vigorous PA. Also, a recent study which conducted systematic review and meta-analysis reported that PA intervention can improve cancer-specific QoL, fatigue, sub-maximal fitness, and lower body strength. Taken these results together, PA is deemed to be safe, feasible, and effective in improving the condition of PC patients receiving ADT.

Many cancer survivors thought that PA had benefits for themselves and they should be more active physically. Despite the awareness of the important roles of PA, the majority of cancer survivors fail to meet PA guidelines due to a lack of access to facilities or motivation. Therefore, it is necessary to study effective intervention that can promote the amount of PA. The aim of this study was to examine the effectiveness of lifestyle intervention in PC patients receiving ADT.

**MATERIALS AND METHODS**

**Participants and Design**

A total of 23 PC patients were screened for participation at Hanyang University Guri Hospital (Gyeonggi-do, South Korea). PC patients were recruited such that they satisfy the eligibility that their PC status was histologically documented while receiving ADT from at least 3 months prior to
their recruitment. Patients with unstable and uncontrolled hypertension, recent myocardial infarction, unstable bone metastases, and neurological or musculoskeletal ailments inhibiting PA were excluded. All participants were randomly allocated at 1:1 ratio into either the intervention group (IG) (n=12) or the control group (CG) (n=11) according to a computer generated PC patient number list (Figure 1). The study was approved by The University of Hanyang Guri Hospital Institutional Review Board (No.2014-06-002), and informed consent was obtained from all the participants.

**Lifestyle Intervention**

The PC patients received a 12-week structured lifestyle intervention in the form of education program. The main purpose of the program was to increase the level of PA of the PC patients. This program was designed by an exercise specialist who adhered to the guidelines for cancer survivors by the American College of Sports Medicine (ACSM).25 The program was individualized in considering the patient’s medical history, initial assessment results, and their PA preference. Brisk walking, stationary biking, or hiking were recommended to the

**FIGURE 1** Flow of participants. PA, physical activity.
patients as of aerobic activities. The PC patients were advised to perform up to 7 days of aerobic PA for at least 150 min of moderate to vigorous intensity. A pedometer was provided to patients to check their daily PA by themselves. Patients were advised to record their daily steps with the help of pedometer. Every morning, text messages were sent to all participants to encourage PA participation and to increase the count of daily steps up to 10,000 if possible.

They were also advised to do muscle-strengthening activity for two or more days a week on the basis of the ACSM’s guidelines for cancer survivors.26 The muscle-strengthening activity included 12 bodyweight and resistance band exercises. The participants were advised to execute two or three sets of 8–12 repetitions at an intensity of 12–15 on the rate of perceived exertion scale. The intensity was increased if a patient performed up to 15 repetitions with ease. To motivate PC patients to engage in muscle-strengthening activity, all patients were provided with a resistance band and a guide book designed to follow 30 min of muscle-strengthening activity targeting large skeletal muscles.

To facilitate compliance and spontaneity of PA program, 60 min of supervised sessions were provided weekly in pursuing the patients to better receive proper instruction and care. In this session, group-based education was provided by a certified exercise specialist. After each session, to motivate the patients, self-monitored records from PA diary and pedometer along with personalized feedback of individualized program were examined, and the goal was continually renewed in accordance with the results. Besides, the program included education that could change their lifestyle patterns such as using stairs, walking over a short distance, taking public transportation and getting off one stop before the destination. The participants in the CG received only two stretching sessions and they were asked to maintain their current PA level as usual and continually checked up by urologists.

**Outcome Measures**

**Anthropometric measurement**

Height, weight, and waist/thigh circumferences (TC) were measured by the research staff at baseline and at the end of 12 weeks. Waist circumference was measured at the midpoint between the lower border of the rib cage and the iliac crest. TC was measured at the midpoint between the iliac crest and the middle of patella. Additionally, body composition was assessed via bioelectrical impedance analysis (BIA) method using InBody (Biospace, South Korea) which is known to offer accurate estimates of a total and appendicular body composition.26

**Physical activity**

To assess PA level, an accelerometer (Actigraph GT3X+, USA) that had been used as a valid and reliable tool among cancer survivors for measuring the level of PA was worn on each patient’s waist for 7 consecutive days at baseline and at the end of the intervention program.27 The intensity of PA level using an accelerometer and its bout cut-off that are used to calculate the time participants spent in activities of daily living (ADL) were determined based on the established criteria.28 A valid-wear-day was set to consist of at least 10 h of wear (non-wear time was defined by 60 consecutive minutes of zero counts) and a valid-wear-period was set at least four of seven days.

**Physical function**

A hand-held dynamometer (Model 01163; Lafayette Instrument Company, USA) and a hand grip dynamometer (TAKEI, Japan) were used for measuring knee extensor and grip strength, respectively.29,30 Assessments were measured twice left and right in turn and the mean value was recorded. In addition, flexibility, agility/dynamic balance, and aerobic endurance were also measured using senior fitness test.31 Prior to the test, all the participants were shown demonstrations of each performance measure and instructed to do their best while not exceeding their physical limit.
**Disease-specific QoL and fatigue**

Disease-specific QoL was measured by the Korean version of Functional Assessment of Cancer Therapy-Prostate (FACT-P) and fatigue was measured by the Korean version of FACT-F. FACT-P included 27 general questions that provide assessments of physical, social or family, emotional, and functional well-being as well as 12 questions specific to PC and its treatment. FACT-F included 13 questions relating to the consequences of fatigue as well as symptom expression. Both questionnaires demonstrated validity and sensitivity and test–retest reliability of 0.93 and 0.90, respectively.\(^{32,33}\)

**Data Analysis**

Data analyses were performed with statistical package for the social sciences (SPSS), windows version 18.0. All data were expressed as mean, standard deviation (SD). Data were assessed for normality, using the Shapiro-Wilk test. The baseline differences between the IG and the CG were assessed by using independent \(t\) test or Mann–Whitney test (not a normal distribution). A repeated-measures analysis of variance (ANOVA) was used to evaluate the treatment effect from baseline to the end of the 12-week period, as well as Group \(\times\) Time interaction. Paired \(t\) test was used for normally distributed variables to compare the baseline and 12-week data within the groups and Wilcoxon test was used for non-normally distributed variables. All tests were two-tailed and the level of significance was set at \(p<0.05\).

**RESULTS**

The participants’ baseline characteristics are shown in (Table 1). There were no significant differences between the groups at baseline (\(p>0.05\)). Of 23 patients, 19 of them completed the 12-week intervention. In the IG, one subject dropped out because of residential movement. The average attendance rate was 88.9% for total supervised sessions. In the CG, three subjects dropped out because of the failure in follow-up. In addition, one subject dropped out due to insufficient wearing time in the

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Baseline Characteristics of Participants.</th>
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<tbody>
<tr>
<td></td>
<td>Control group (n = 8)</td>
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<tr>
<td>Age (year)</td>
<td>73.0 (8.2)</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>65.3 (8.9)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.0 (4.7)</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>24.5 (2.8)</td>
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<tr>
<td>Lean body mass (kg)</td>
<td>25.3 (3.7)</td>
</tr>
<tr>
<td>Body fat mass (kg)</td>
<td>19.0 (5.3)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>89.6 (7.7)</td>
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<tr>
<td>Thigh circumference (cm)</td>
<td>50.3 (4.0)</td>
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<tr>
<td>SBP (mm Hg)</td>
<td>120.3 (14.8)</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>70.7 (9.9)</td>
</tr>
<tr>
<td>ADT duration (year)</td>
<td>3.9 (5.9)</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>3.2 (2.5)</td>
</tr>
<tr>
<td>Gleason score</td>
<td>7.6 (1.0)</td>
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</tbody>
</table>

*Data are shown as mean (standard deviation).*  
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ADT, androgen deprivation therapy; PSA, prostate specific antigen.
objectively measured PA outcome. There were no adverse events that occurred during the 12-week lifestyle intervention period.

**Anthropometric**

There was no significant changes in the anthropometric characteristics found in the 12-week assessment period to baseline (Table 1). However, only TC significantly changed in the IG compared with the CG (p = 0.002).

**Physical Activity**

In the level of PA of the IG, there was a positive change found. Daily steps and moderate to vigorous physical activity (MVPA) were improved compared with those of the CG (Table 2). The differences between the groups in terms of daily steps (p=0.028) and MVPA (p = 0.013) were statistically significant. Yet, there were not any significant changes in light activity (p = 0.779).

**Physical Function**

There were significant improvements in the IG compared with the CG in terms of muscle strength and physical performance (Table 3). The differences between the groups in terms of grip strength (p=0.034) and knee extensor (p=0.004) were statistically significant. In addition, the results from Up and Go test (p=0.001) and 2-min step test (p=0.001) were also improved. In the sit-and-reach test, though there was a significant increase found in the IG, no interaction was found according to time (p=0.127).

**Disease-Specific QoL and Fatigue**

Disease-specific QoL and fatigue were measured in the Korean version of FACT-P, FACT-F (Table 3). There were significant improvements in FACT-P (p<0.001) and FACT-F (p=0.001) of IG when compared with those of the CG. Although all five sub-items of FACT-P were increased in the IG and decreased in the CG, only emotional well-being, functional well-being and additional concerns were statistically, significantly changed.

**DISCUSSION**

To our best knowledge, there are very few studies that evaluate the effects of lifestyle intervention program on level of PA and physical and psychological health outcomes in PC patients with ADT in Asia, particularly in South Korea. In this study, we found that the lifestyle intervention improved the level of PA and physical and psychological health outcomes effectively. Moreover, the program was successfully executed as it was well tolerated and no adverse events were found.

Regular PA participation may help reduce cancer recurrence and cancer-related mortality. Moreover, according to Bonn study, PC patients who were physically active had lower overall mortality and PC-specific mortality. Indeed, following the lifestyle intervention, daily steps were increased by 38% in the IG and decreased by 17% in the CG. MVPA was also significantly increased by 52% in the IG and decreased by 40% in the CG. Such

<table>
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<th>TABLE 2 Effect of Lifestyle Intervention Program on Level of Physical Activity.</th>
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<tr>
<td>Control group (n = 7)</td>
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</tr>
<tr>
<td>Step (count/day)</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Light PA (min/day)</td>
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<tr>
<td>MVPA (min/day)</td>
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</table>

* p<0.05 before vs. after within the group.
results are contrary to Cormie’s study. In Cormie et al., supervised resistance exercise sessions were conducted twice weekly in a clinic and home-based aerobic exercise participation such as walking and stationary cycling were recommended as the sole choice of further exercise for at least 150 min of moderate-intensity each week. As a result, light PA was increased in the IG while it was decreased in the CG and moderate PA was decreased in both groups. Such meaningful differences are considered to be resulted not only from its home-based form of exercise but also from the intervention strategy. In the light of a previous study, written information that emphasized the importance of PA along with an exercise log and a pedometer were provided to each participant in the IG in this study. In addition, text messages were sent to the participants to motivate PA participation. These intervention strategies were expected to make patients highly motivated. According to the previous study, granting short words of encouragement, a provision of pedometer and keeping track of an exercise log were enough to increase the level of PA significantly.

The increased MVPA is considered clinically important because the PC patients who walked 90 min per week at a brisk pace had a 46% lower risk of all-cause mortality compared with that of those who walked at an easy pace. PC patients with ADT significantly gained body fat mass and lost lean body mass (LBM) over 2 years. Several studies supported that exercise could mitigate such side effects of ADT. However, according to a systematic review, the exercise-related changes in body composition were often non-significant and/or of a small magnitude. Similarly, the results from the current study showed that the LBM increased in the IG (+0.3 kg) and decreased in the CG (−0.7 kg), although it was not statistically significant. Meanwhile, TC was

<table>
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<th>TABLE 3 Effect of Lifestyle Intervention Program on Outcome Variables.</th>
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<tr>
<td><strong>Control group (n = 8)</strong></td>
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<tr>
<td><strong>Body mass, kg</strong></td>
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<tr>
<td>körpergewicht, kg</td>
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<td>BMI, kg/m2</td>
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<tr>
<td>Body fat mass, kg</td>
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<td>Lean body mass, kg</td>
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<td>Waist circumference, cm</td>
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<tr>
<td>Thigh circumference, cm</td>
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<tr>
<td>Grip strength, kg</td>
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<tr>
<td>Knee extensor, Nm</td>
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<tr>
<td>Sit and reach, cm</td>
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<tr>
<td>Up and go, sec</td>
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<tr>
<td>2-min step, count</td>
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<tr>
<td>FACT-P</td>
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<td>FACT-F</td>
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Data are shown as mean (standard deviation).

BMI, body mass index; FACT-P, Functional Assessment of Cancer Therapy-Prostate; FACT-F, Functional Assessment of Cancer Therapy-Fatigue.

*p < 0.05 before vs. after within the group.

**p < 0.01 before vs. after within the group.
significantly increased in the IG (+1.2 cm) and decreased in the CG (−0.4 cm). It had a high association with thigh muscle volume which is strongly correlated with physical function in elderly people. Therefore, the increase of the TC seems to be consistent with the result from previous studies which confirmed the increase of muscle mass by MRI or ultrasound. These positive changes in body composition may play an important role in preventing sarcopenia, which can be accelerated by ADT.

ADT affects in aggravating the level of muscle strength and physical function. For example, in Galvao’s study, the upper and the lower muscle strength and physical function of men with ADT were significantly reduced compared with those of age-matched healthy men. In this study, the lifestyle intervention significantly increased muscle strength and physical function in the IG. Grip strength and knee extensor were increased about 7 and 35%, respectively. These improvements of the upper and the lower muscle strength are consistent with the results of previous studies that executed facility-based exercise.

Flexibility, agility/dynamic balance, and aerobic endurance were also significantly improved. In particular, the improved dynamic balance and aerobic endurance could be clinically meaningful as they affect preventing falling and improving ADLs in PC patients. Although body compositions of PC patients measured by BIA were not significantly altered, improved muscle strength, agility/dynamic balance, and endurance appear to be the consequence of positive changes in muscular hypertrophy and/or neuromuscular system.

QoL is crucial for PC patients since it considerably increases their survival rate. However, ADT was associated with greater psychological distresses such as depression, moodiness, irritability, anxiety, and loss of vigor. In this study, the lifestyle intervention significantly improved in FACT-P with 21.1 points and in FACT-F with 6.6 points in the IG. These results are consistent with the previous studies and the changes were considered clinically important from 6 to 10 points in FACT-P and 3 points in FACT-F were reported to be meaningful. Such results are regarded to have positive effects on QoL and fatigue with improvements in physical performance and musculoskeletal benefits.

Even if the most known effective intervention programs appear to be facility-based supervised exercise, visiting a gym to exercise can be a constraint on participation in PA in elderly PC patients. Indeed, the barriers that influenced PA participation in cancer survivors were program accessibility, time, and cost. According to Min’s study, the main barriers that influenced PA participation in South Korean PC survivors were lack of exercise facilities, information, and time. Also, most patients preferred home-based programs over fitness centers or gym. Therefore, the lifestyle intervention program in this study can be an effective strategy that considered exercise preference, accessibility, and motivation. This study does have limitations. The sample size of PC patients was relatively small because many subjects were excluded from participating in the initial study. Also, there was no follow-up on how the positive change in PA was maintained after the intervention. Further studies with larger sample sizes should be followed-up to strengthen this study.

CONCLUSION

This study demonstrated that the 12-week lifestyle intervention program increased the level of PA and mitigated the side effects of ADT. Hence, the lifestyle intervention programs that considered exercise preference, accessibility, and motivation appear to be a promising intervention strategy to mitigate the side effects of ADT in PC patients.

FUNDING

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REFERENCES


