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Original Research

The Clinical Impact of Physical Activity on the Diagnosis of Prostate Cancer and Postprostatectomy Functional Outcomes in the Elderly

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ABSTRACT

Objectives: The effect of physical activity on prostate cancer is controversial. We aimed to investigate the effect of physical activity on prostate cancer detection and functional outcomes after radical prostatectomy.

Methods: Between 2019 and 2020, 166 patients who underwent prostate biopsy were included. The physical activity scores of patients were evaluated by the Physical Activity Scale for the Elderly (PASE) questionnaire before the procedure. PASE scores were compared between the patients with and without prostate cancer and local and metastatic aggressiveness of cancer. Patients who underwent radical prostatectomy were followed up for 12 months to analyze the effect of physical activity on erectile dysfunction (ED) and urinary incontinence (UI).

Results: There was no significant difference between patients with and without prostate cancer in terms of PASE scores (187.7 vs. 195.5, p=0.665). PASE scores were also similar when separated according to D'Amico risk classification and metastatic events. Twenty-seven patients who underwent radical prostatectomy were evaluated in terms of functional outcomes at the first year of surgery. PASE scores of the patients with severe ED were lower than mild-moderate ED, but no statistically significant difference was observed (197.0 vs. 268.5, p=0.267). Patients with persistent UI had a significantly lower PASE score overall than continent patients (128.3 vs. 271.1, p=0.001), and PASE score was the only independent predictor of UI following radical prostatectomy.

Conclusion: The effect of physical activity on prostate cancer development or aggressiveness could not be determined. Physical activity was associated with a reduced risk of UI following radical prostatectomy.

Keywords: Erectile dysfunction, PASE, physical activity, prostate cancer, urinary incontinence

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Prostate cancer treatments and following complications constitute a great burden on the global health system.[1,2] To prevent the development of prostate cancer, many risk factors have been identified. Genetic factors such as germline mutations and family history are the best-known factors associated with prostate cancer. Exogenous factors such as obesity, metabolic syndrome, dietary, and lifestyle factors are also frequently investigated. Nevertheless, any specific risk factor could not be found for the development of prostate cancer.[3,4] Treatments for prostate cancer also have a significant negative impact on quality of life. In a prospective, controlled study, 20.2% of patients had uri-

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nary incontinence (UI) and 74.7% of patients had erectile dysfunction (ED) in the first year following radical prostatectomy.[5] There is no consensus on which patients are more frequently exposed to such complications.

Physical activity may play an important role on preventing cancer. It was shown that regular exercise has an influence on cancer prevention by its anti-inflammatory effects, antioxidant mechanism, and hormonal regulation.[6,7] Previous studies showed that physical activity reduced the incidence of prostate cancer, and also decreased the mortality rates of prostate cancer survivors.[8-11]

In the general population, it is known that physical activity has a positive impact on erectile function and urinary continence.[12,13] ED and UI are two main complications following radical prostatectomy. Physical activity increases nitric oxide levels and also has a positive influence on endothelial function, which regulates testosterone levels.[12] In this way, it can contribute to the preservation of erection after prostatectomy. Moderate physical activity improves all types of UI in older women by potentially strengthening the pelvic floor.[14] Following radical prostatectomy, preserving the pelvic floor muscles represents great importance.

In this study, we evaluated the overall effect of physical activity on prostate cancer in elderly patients. We first investigated the effect of physical activity on the diagnosis of prostate cancer with a validated scoring system, the Physical Activity Scale for the Elderly (PASE), and then evaluated the effect of physical activity on the functional outcomes of patients who underwent radical prostatectomy.

Methods

The local ethics committee approved this study (2020/0520). This study was conducted according to the Declaration of Helsinki standards. Informed consent was obtained from all individual participants included in the study.

Between January 2019 and February 2020, 166 patients aged 65 years or older and who applied to the outpatient clinic with elevated PSA and/or rectal examination finding and underwent transrectal prostate biopsy were included in the study. Patients with previous pelvic radiotherapy, major pelvic surgery, and prostate surgery were excluded from the study. Each patient underwent a 12-core transrectal ultrasound-guided standard prostate biopsy, and informed consent was obtained from each patient. Before the biopsy, a detailed physical examination was done including waist circumference, weight-height, and blood pressure. Questionnaires such as International Prostate Symptom Score (IPSS), International Index of Erectile Function-5 (IIEF-5), Overactive Bladder Version-8 (OAB-V8) were collected by the clinician performing biopsy. PASE was self-reported by the patient in the procedure room, only assisted by the clinician in case of need. Questionnaires were conducted by the clinician blinded to study methodology.

The PASE is a validated questionnaire and used to evaluate the patients' activities during the past 7 days.[15-17] It consists of 12 questions and three parts such as leisure time activity, household activity, and work-related activities. At each part, the duration and frequency of activity are also questioned. Leisure time activities consist of six questions evaluating sitting activities, walking outside the home, light-moderate-strenuous recreational activities, and muscle strength, and endurance exercises. Household activities consist of three questions about light and heavy housework. Work-related activities consist of three questions evaluating the paid work, its hours per week, and the amount of physical activity during work. The frequency of each activity was also questioned. PASE score was calculated by multiplying activity weights by activity frequencies and scored between 0 and 400. Patients who stated that their physical activity in the last week showed a significant difference compared to their general activity were excluded from the study.

Transrectal biopsy results and ISUP scores according to the 2014 consensus, risk classification of prostate cancer patients according to D'Amico risk classification.[18], local and metastatic staging of patients including multiparametric MRI and abdominal CT, bone scan or PSMA-PET/CT, and pathological features of patients who underwent nerve-sparing radical prostatectomy were collected retrospectively. Open retropubic radical prostatectomy (RRP) was performed by a single surgeon with more than 1000 RRP experience. Patients were also followed up prospectively in terms of ED and UI. Functional scores were collected at the 12th month following radical prostatectomy. The severity of ED was assessed by the IIEF-5 questionnaire and categorized as normal when scored between 22-25, mild between 12-21, moderate between 8-11, and severe ED between 5-7. Urinary Incontinence was assessed using a pad test. Continence was defined as no need for pads.

Statistical Analysis

Statistics were performed using SPSS v22.0 (SPSS Inc., Chicago, IL, USA). Independent samples t-test was used for comparing the means. Normal distribution between groups was assessed using Kolmogorov–Smirnov test. Comparing the means between groups of more than two, one-way ANOVA test was used. For the nonparametric *post hoc* analysis of ANOVA, Games–Howell test was used. Chi-square test or Fisher's exact test was used for categorical variables. Logistic regression was performed for multivariate analysis and $p<0.05$ was considered statistically significant.

Data Availability

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

Results

According to the prostate biopsy results of 166 patients, they were divided into two groups, such as patients with and without prostate cancer. Prostate cancer patients were older than the other group (67.6 vs. 68.9, p=0.097), and their waist circumference was larger overall (101.6 vs. 97.4, p=0.049). BMI of prostate cancer patients was higher; however, it was not statistically significant (28.2 vs. 26.9, p=0.063). PSA and PSA density values were significantly higher in prostate cancer patients compared to the other group (43.5 vs. 10.5, p=0.017, 1.29 vs. 0.15, p=0.019, respectively). PASE scores were similar between groups (187.7 vs. 195.5, p=0.665) (Table 1). Patients were divided into groups according to PSA and PSA densities. The PASE scores of those with a PSA level of 10 ng/mL and higher and the PSA lower than 10 were similar in patients with and without prostate cancer. When the PSA density was divided into 0.15 ng/mL^2 or lower and higher, the PASE scores of both the groups were statistically similar (Table 2).

Table 1. Patients' characteristics affecting prostate cancer diagnosis

	No prostate cancer	Prostate cancer	p
Age, years Mean±SD	67.6±4.7	68.9±4.7	0.097 †
BMI, kg/m^2 Mean±SD	26.9±3.72	28.2±4.81	0.063 †
Waist circumference, cm Mean±SD	97.4±13.15	101.6±13.20	0.049 †
Diabetes mellitus			
No	82 (85.4%)	52 (74.3%)	
Yes	14 (14.6%)	18 (25.7%)	0.073 ‡
Hypertension			
No	59 (61.5%)	44 (62.9)	
Yes	37 (38.5%)	26 (37.1%)	0.854 ‡
Mean arterial blood pressure, mmHg Mean±SD	92.1±12.97	95.6±10.58	0.071 †
Family history of prostate cancer			
No	87 (90.6%)	63 (90.0%)	
Yes	9 (9.4%)	7 (10.0%)	0.893 ‡
PSA, ng/mL Mean±SD	10.5±7.66	43.5±133.29	0.017 †
Prostate Volume, mL Mean±SD	76.7±43.62	54.8±30.41	0.001 †
PSA Density, ng/mL^2 Mean±SD	0.15±0.11	1.29±4.64	0.019 †
HDL, mg/dL Mean±SD	44.1±11.79	46.3±10.02	0.225 †
LDL, mg/dL Mean±SD	127.8±33.37	124.5±34.24	0.542 †
Non-HDL, mg/dL Mean±SD	178.5±204.07	154.7±38.71	0.371 †
Total cholesterol, mg/dL Mean±SD	200.8±37.42	202.9±36.99	0.723 †
Triglyceride, mg/dL Mean±SD	172.1±206.68	166.4±81.45	0.835 †
OAB-V8 Mean±SD	9.66±6.25	11.97±11.18	0.100 †
PASE Score Mean±SD	187.7±111.52	195.5±119.2	0.665 †

BMI: Body mass index; CI: Confidence interval; OAB-V8: Overactive bladder-validated 8-question; PASE: The Physical Activity Scale for the Elderly; SD: Standard deviation; ‡: Chi-Square Test; †: Independent samples t-test.

Table 2. PASE scores comparing patients with and without prostate cancer (splitted according to PSA and PSA densities)

	No prostate cancer	Prostate cancer	p
PSA ≤10 ng/mL	193.3±107.1	201.2±114.9	0.727†
PSA >10 ng/mL	174.1±121.3	193.4±127.9	0.541†
PSA Density ≤0.15 ng/mL^2	191.3±105.9	222.6±122.1	0.249†
PSA Density >0.15 ng/mL^2	177.7±120.0	180.3±117.9	0.921†

†: Independent samples t-test.

Table 3. PASE scores according to the D'Amico risk classification

	N	PASE score (Mean±SD)	95% CI	p
No prostate cancer	96	185.5±110.17	163.1–207.9	0.38[§]
Low risk	18	197.3±109.58	142.8–251.8	
Intermediate risk	20	205.8±116.82	151.2–260.5	
High risk	24	165.9±122.61	114.1–217.7	
Locally advanced	8	254.1±130.89	144.7–363.6	
Total	166	189.8±113.82	172.2–207.3	
Metastatic	13	146.46±91.39	91.2–201.7	0.112[†]

CI: Confidence interval; PASE: The Physical Activity Scale for the Elderly;SD: Standard deviation; [§]: One-way ANOVA test; [†]: Independent samples t-test.

Table 4. The effect of PASE score on functional outcomes following radical prostatectomy

	PASE score (Mean±SD)	95% CI	p
Erectile dysfunction (ED)			0.267 [†]
Mild-moderate ED (n=4)	268.5±119.17	-58.08–201.08	
Severe ED (n=23)	197.0±115.73	-106.12–249.12	
Urinary incontinence			0.001 [†]
No (n=15)	271.1±118.25	68.22–217.22	
Yes (n=12)	128.3±45.66	73.18–212.45	
Incontinence severity			0.003 [§]
None (n=15)	271.1±118.25[a]	205.58–336.55	
1 pad/day (n=6)	140.0±25.0[b]	113.76–166.24	
≥2 pads/day (n=6)	116.5±60.24 [b]	53.28–179.72	

CI: Confidence interval; PASE: The Physical Activity Scale for the Elderly; SD: Standard deviation; [§]: One-way ANOVA test; [†]: Independent samples t-test; a-b: Games–Howell *post hoc* test.

To evaluate the effect of physical activity on local and metastatic aggressiveness, PASE scores were compared according to D'Amico risk classification and also metastatic events. PASE scores were similar between risk classification groups. Patients with a metastatic event had lower PASE score overall, but it was statistically nonsignificant (146.5 vs. 189.8, p=0.112) (Table 3).

Among 166 patients, 70 (42.2%) patients' biopsies were malignant, and 27 (38.6%) of them underwent radical prostatectomy. Nine patients had pT2, 14 patients had pT3a, and 4 patients had pT3b stage in RRP pathology. While bilateral nerve-sparing surgery was performed in 21 patients, unilateral nerve-sparing surgery was performed in 6 patients. In the first year of the operation, patients were evaluated in terms of ED and UI, and their data were collected. Mild, moderate, or severe ED persisted in all patients. PASE scores of patients with severe ED were lower; however, it was not statistically significant (197.0 vs. 268.5, p=0.267). The PASE scores of patients whose UI persisted were significantly lower than continent patients (128.3 vs. 271.1, p=0.001). Patients using 2 or more pads per day had the lowest PASE score overall, but there was no statistically significant difference compared to those using 1 pad per day (Table 4). After determining the statistically significant effect of physical activity on 1st-year incontinence, we analyzed the factors, such as BMI, waist circumference, comorbidities, prostate volume, PSA, PASE score, IPSS, IIEF-5, and OAB-V8 questionnaire, affecting postoperative incontinence. While PASE score and prostate volume were found to have a significant effect in univariate analysis, we found that PASE score was the only independent predictor for UI (OR: 0.96, p=0.034) (Supplementary Table 1).

Discussion

In this study, the effect of physical activity on the development of prostate cancer and its contribution to functional outcomes following radical prostatectomy were investigated in elderly patients. We could not detect the effect of physical activity on the development and aggressiveness of prostate cancer. We showed that it has a significant effect on functional recovery following radical prostatectomy. It was determined that patients who were physically active in the preoperative period had higher continence rates in the 1st year following radical prostatectomy.

Since prostate cancer is closely related to inflammation and hormonal factors, the relationship between exercise and prostate cancer has been studied before. Recent studies showed the anti-inflammatory effect of exercise by reducing inflammatory cytokines, adiponectin, and other inflammatory factors such as CRP and interleukins.[19] In addition, some studies have shown that regular exercise reduces sex hormones.[20] Studies evaluating the relationship between prostate cancer and physical activity are controversial. Liu et al.[21] showed a small benefit of occupational and recreational physical activity on prostate cancer in their total meta-analysis cohort, but not for patients older than 65 years old. In our study, we evaluated physical activities such as leisure time activity, household activity, and work-related activities in elderly patients using PASE and compared those with and without prostate cancer, and the physical activity scores between the two groups were similar, and PASE scores were also similar according to local aggressiveness of prostate cancer and the metastatic events. We also divided patients into low-risk and high-risk groups according to their PSA and PSA densities, in order to create homogenous risk groups. Similar PASE scores were found for both groups. In a recent study by De Nunzio et al.[8], physical activity that was assessed by PASE survey decreased the risk of prostate cancer, and also the risk of high-grade prostate cancer. Considering the patient characteristics, PSA values were quite low compared to our study (median: 6.1 ng/mL). In our study, even when patients with PSA levels below 10 ng/mL were evaluated separately, PASE scores were still found to be similar.

We also evaluated the 1st-year functional outcomes of 27 patients who underwent radical prostatectomy. There are some studies reporting the positive effects of regular physical activity on ED and UI. Physical activity increases the secretion of endothelial nitric oxide synthase and provides an increase in endothelial NO levels. As it is known, the increase in NO plays a key role in erection by vasodilation in smooth muscles and corpus cavernosum.[22] In addition, there are studies reporting that physical activity, especially in short-term acute testosterone increases, contributes to erection in this way.[23] Mina et al.[24] showed that patients exercising moderately or vigorously had higher quality of life and erectile function scores. In our study, patients with severe ED had lower PASE scores than the patients with mild-moderate ED, but it was not statistically significant. Since only elderly male patients were included in our study and these patients already had limited physical activity, we may have obtained a closer inter-patient result compared to other studies.

Recent studies showed that regular physical activity improves all types of UI, potentially by strengthening the pelvic floor and regulating the muscle tonus.[14] Mina et al.[24] showed that physically active patients had a 19% reduced risk of incontinence after 6 weeks following radical prostatectomy. Wolin et al.[25] stated that non-obese and physically active patients who underwent radical prostatectomy had a 26% reduced risk of incontinence than others. In our study, we found a lower PASE score as the only independent prognosticator of persistent UI following radical prostatectomy. Patients with UI following radical prostatectomy had significantly lower PASE scores. We also compared UI severity. Overall PASE score of patients with UI of 2 or more pads per day was lower than patients with 1 pad/day UI, although not statistically significant. UI after radical prostatectomy is one of the complications that most impair quality of life. Elderly patients may face difficulties in self-care; therefore; the severity of UI gains importance. The relationship between physical activity and postprostatectomy UI is frequently stated and elderly patients should be informed about this issue.

This is the first study showing that higher preoperative physical activity scores, evaluated by PASE, protect against UI following radical prostatectomy in the elderly. However, there were some limitations of our study. Although the number of patients included was sufficient, the number of patients whose functional outcomes were evaluated after radical prostatectomy was low. Better postoperative recovery phase or early mobilization of physically active patients in the postoperative period may also have contributed to functional results, which were not evaluated. While evaluating functional outcomes, only 1st-year functional results of the patients were analyzed. Their early functional recovery at 3rd and 6th months could have been taken into account.

Conclusion

The effect of physical activity on the development and aggressiveness of prostate cancer is still controversial. In addition, preoperative physical activity has a protective effect against UI after radical prostatectomy.

Disclosures

Supplementary Table 1. https://jag.journalagent.com/sislietfaltip/abs_files/SETB-32549/SETB-32549_(0)_SETB-2022-11-245_supplementary-rvs_(1).pdf

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Ethics Committee Approval: The study was approved by the Ethics Committee of Istanbul Medeniyet University (No: 2020/520, dated 12.08.2020).

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Conflict of Interest: None declared.

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