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Does transrectal prostate biopsy cause sexual dysfunction? Cross-sectional evaluation of 252 patients

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Abstract

Objective: In this study, we aimed to evaluate whether there are negative effects of transrectal prostate biopsy (TPB) on sexual functions (SF).

Methods: This study includes 252 male patients evaluated prospectively who underwent TPB in our clinic between January 2015 and September 2016. Patients with chronic diseases (e.g. diabetes mellitus, hypertension) and the use of drugs (e.g. antihypertensive drugs, antidepressants) that can affect SF were excluded. Patients completed the IIEF-15 forms before TPB, in the first, third, and sixth months after TPB. Patients were evaluated in terms of erectile function (EF), orgasmic functions (OF), sexual desire (SD), intercourse satisfaction (IS), and overall sexual satisfaction (OSS).

Results: The relationship between follow-up time and EF, OF, SD, IS and OSS scores were analyzed. A significant difference was observed in EF scores before TPB and in the first month after TPB (p=0,007). However, in subgroup analyses, it was determined that this significant difference was only in the PCa patients. In BPH-diagnosed patients, there was no significant difference between the ED score and the follow-up times. OF, IS, and OOS scores in the 1st, 3rd, and 6th months decreased significantly according to the initial score (p = 0,001). SD scores showed no significant differences among follow-ups (p=0,191).

Conclusion: Erectile dysfunction (ED) is not likely for all patients who undergo TPB. Our study revealed that PCa patients are short-term sufferers of ED after TPB. But, according to our data, it is not clear whether the cause is TPB or anxiety due to PCa diagnosis.

Keywords: Erectile Dysfunction, Prostate, Prostate-Specific Antigen, Biopsy

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INTRODUCTION

Prostate cancer (PCa) is one of the most important health problems for males. Incidence and mortality rates differ with the race, lifestyle, diet, and geographic features of patients. The main diagnostic tools for PCa are digital rectal examination (DRE), and serum prostate-specific antigen (PSA) levels. Pathological investigation of biopsy material provides a definite diagnosis and verification of the adenoma (1).

Erectile dysfunction (ED) is defined as the inability to maintain a penile erection or maintain adequate penile erection for sexual intercourse for at least six months.

Ejaculation and orgasmic disorders are evaluated in different categories (2).

TPB-related ED was examined in many clinical trials before. But the conclusions of these trials were controversial. According to these trials, TBP-related ED, maybe, based on neurovascular bundle damage during the process and/or negative psychological effects of a possible prostate cancer diagnosis. But we do not clearly document whether TPB causes ED exactly. So, the pathophysiological mechanism could not be documented clearly. In this clinical trial, we aimed to determine if there are negative effects of TPB on sexual functions. And we aimed to document if there is a necessity for treatment in terms of sexual dysfunction after TPB. In the ligt of these aims, we examined and evaluated the long-term effects of TPB on erectile functions in the context of literature.

METHODS

Materials

Patient Population

Study approval for this clinical trial was received from our institution on 11 February 2015 (Session number: 2, decision number: 6). The sample size calculation was performed using G*Power 3.1.9.2 program. It was calculated according to the previous article (5). After considering the alpha level, 0.05, beta error, 0.20, and the effect size, 0.7, the total required sample size was calculated as 121. Then, 252 male patients undergoing transrectal ultrasonography-guided prostate biopsy in our clinic between January 2015 and September 2016 were evaluated in this cross-sectional study. The selection of the study population is summarized in the following diagram (Figure 1).

Written informed consent from all patients who agreed to participate in the study was obtained. Prostate biopsies were performed in each patient with transrectal ultrasonography, and twelve cores of prostate tissue were sampled for pathological investigation. Biopsy decision criteria were determined as abnormal digital finger examination findings and/or PSA levels > 4 ng / mL. All patients' biopsies were performed by the same clinician. Controls were

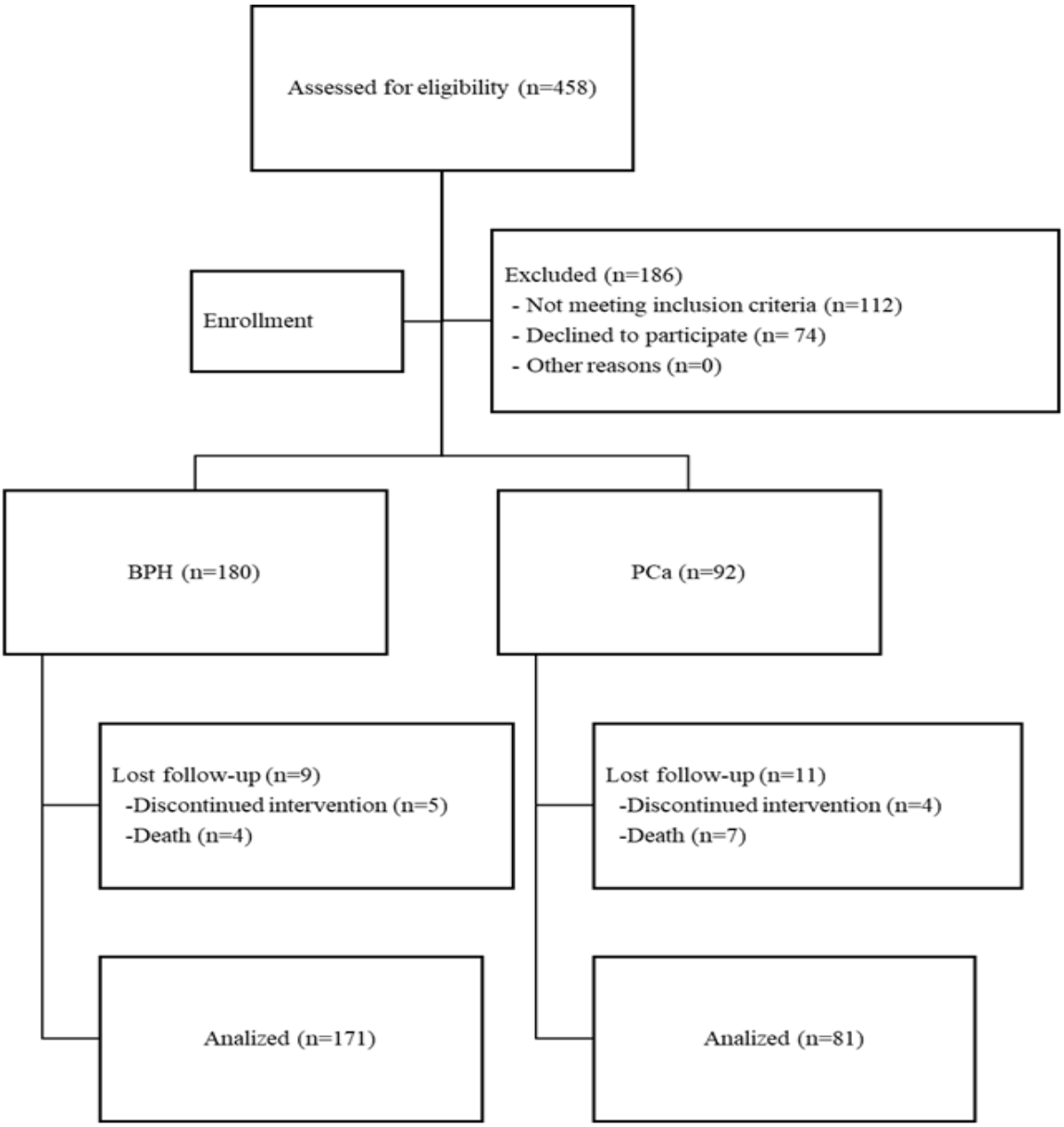

Figure 1. Selection of the study population

made in the urology clinic to assess the ED complaints of the patients and to identify possible ED-related pathologies. A detailed medical and sexual history of all cases was taken and the age of the patients, the presence of a complaint of erectile dysfunction was questioned. All patients with hypertension, diabetes mellitus, presence of malignancy, endocrinologic pathologies which requires hormonotherapy, receiving medical treatment

for psychotic disorders, ED predisposing drug use (e.g., antihypertensive, antidepressant drugs), ED-related surgical trauma, all patients with surgical and/or pelvic trauma history that could be associated with ED were excluded. Also, patients with suspected biopsy results

such as atypical small acinar proliferation (ASAP), low-grade prostatic intraepithelial neoplasia (LGPIN), and high-grade prostatic intraepithelial neoplasia (HGPIN) were excluded. International Erectile Function Index 15 (IIEF-15), consisting of 15 standard questions, was filled out for each of the 252 eligible patients selected for the study. IIEF-15 includes fifteen items referring to EF, OF, SD, IS, and OSS. Questions 1-5 and 15 evaluate EF, with a score range of 0-5 for each question and a maximum score of 30. The ninth and tenth questions evaluate OF, with a score range of 0-5 for each question and a maximum score of 10. The eleventh and twelfth questions evaluate SD with a score range of 1-5 for each question and a maximum score of 10. Questions 6-8 evaluate IS, with a score range of 0-5 for each question and a maximum score of 15. The thirteenth and fourteenth questions evaluate OSS with a score range of 1-5 for each question and a maximum score of 10. Patients were asked 15 questions by their physicians and their answers were recorded.

Biopsy Procedure:

All of the patients were informed by the same clinician doctor about the procedure. And the same clinician performed all of the TPB procedures. Patients were questioned for implants, heart valve disease, anticoagulant / antiaggregant use, allergic diseases, and history of previous allergic reactions. In the presence of active urological infective pathologies, prostate biopsy procedures of patients were delayed after treatment. About 2 hours before the procedure for bowel cleansing, they were told to apply one laxative-purpose sorbitol and glycerin-containing enema to the rectum. Ciprofloxacin 500 mg tablet was given orally 1 day before the procedure and on the morning of the biopsy. Biopsy was performed with an 18-gauge biopsy needle and automatic biopsy gun (GEOTEK Estacore, Daventry, UK) under standard gray-scale ultrasonography and a 7.5 MHz frequency rectal probe (Mindray M5, Shenzen, PRChina). Twelve cores of biopsy specimens from each patient were taken and all the specimens were sent for pathological examination in individually numbered tubes. When the patients came to control with the results of pathology on the 30th day after the biopsy the IIEF-15 form was filled. Then, they were recalled in 3rd and 6th months after the biopsy and the IIEF-15 form was filled again.

Statistical Analysis

The statistical package for the Social Sciences version 22 (SPSS Inc, Chicago, USA) was used for the statistical analysis of the study. The Shapiro-Wilk test was used to assess whether the data were fit to normal distribution. The use of non-parametric tests seemed appropriate as the distribution of data did not fit the normal distribution. Median and interquartile range values were used to represent distribution ranges. The Friedman test was used to assess excess repeat measures, and the Wilcoxon test

was used to evaluate pairwise post hoc comparison. The Mann-Whitney U test was used for the comparison of binary groups. In all statistical analyzes of the study
p <0.05 was considered statistically significant.

RESULTS

The study included 252 men with no risk factors for ED, no chronic disease that could lead to ED, no drug use that could lead to ED, no surgical and/or trauma that could lead to ED. The demographic data of the cases are summarized in Table 1.

When the relationship between the follow-up times of the patients and erectile function scores was examined, the erectile function score at 1st month decreased significantly compared to the baseline score (p = 0.007). There was no significant difference between baseline and 3rd and 6th-month scores. According to biopsy pathology results, patients were divided into 2 groups (BPH and PCa) and the changes in erectile function scores during follow-up were examined (Table 2).

The ED scores of patients who were diagnosed with PCa decreased over time and the difference between the baseline and first-month, third-month, and sixth-month scores were statistically significant (p = 0.0001). In BPH-diagnosed patients, there was no significant difference between the ED score and the follow-up times (Table 2).

When the IIEF subgroups were examined, the orgasmic function scores at the 1st, 3rd, and 6th months decreased significantly according to the initial score (p = 0,001). There was no significant difference between the sexual desire points of the patients (p = 0,191).

It was found that the sexual satisfaction scores of the first month, third month, and sixth month of the cases were significantly lower than the initial score (p = 0.001).

Patients' overall satisfaction scores at 1 month, 3 months, and 6 months were found to be significantly lower than the baseline score (p = 0,045).

Comparisons of IIEF-15 scores according to pathology results of the prostate biopsy were also made in 252 cases evaluated in the study. All IIEF-15 subscale scores other than sexual desire were significantly lower in patients with pathologically proven prostate cancer (PCa) than those with benign prostatic hyperplasia (BPH) (p <0,05) (Table 3).

Table 1. The demographic data of the cases

Features	Median	(Interquartile Range)
Age (years)	63	59 – 67.7
BMI (Body Mass Index) kg/m^2	22	20 – 24
Total PSA (ng/ml)	7.01	4.9 – 10.9
Free PSA (ng/ml)	2.04	1.2 – 3.6
Prostate Volume (ml)	48.15	38.2 – 70
IPSS	14.00	9 – 20.7

Table 2. Change of ED scores during follow-up in BPH, PCa and in all patients

IIEF (International Index of Erectile Function) (ED)	n	Baseline (Interquartile Range)	1th Month (Interquartile Range)	3rd Mont (Interquartile Range)	6th Month (Interquartile Range)	P*
Pca	81 (%32.1)	8 (1-23)[a]	3 (1-19.5)[b]	2 (1-18.5)[b]	1 (1-11.5)[b]	0,0001
BPH	171 (%67.9)	18.0(6-24)	17. (3-24)	18 (6-24)	18 (6-24)	0,0820
Total	252	15.5 (2-24)	13 (1-24)	13.5(1-24)	12 (2-24)	0,0075

*=Friedman test, Groups with different letters are different from each other (Wilcoxon test).

Table 3. Evaluation of the research group according to pathology results

Variables	AdenoCa	BPH	
	Mean (Interquartile Range)	Mean (Interquartile Range)	p
Age (years)	65 (62 – 70.5)	61 (59 – 66)	<0.001
Erectile Function	8 (1 – 23)	18 (6 – 24)	0,014
Orgasmic Function	2 (0 – 8)	6 (2 – 8)	0,003
Sexual Desire	6 (2 – 8)	6 (4 – 8)	0,119
Sexual Satisfaction	4 (0 – 10)	7 (3 – 10)	0,011

DISCUSSION

Prostate cancer (PCa) is one of the most important health problems seen in men. Incidence and mortality rates differ with the race, lifestyle, diet, and geographic features of patients. The main diagnostic tools for PCa are digital rectal examination (DRE), and serum prostate-specific antigen (PSA) levels. Pathological investigation of biopsy material provides a definite diagnosis and verification of the adenoma (1).

Transrectal ultrasound-guided prostate biopsies are thought to lead to erectile dysfunction because of direct damage of the periprostatic neurovascular bundle, nerve damage due to compression of the neurovascular bundle while periprostatic blockade and secondary to compression due to periprostatic neurovascular bundle edema and/or hematomas (3). When we look at studies examining ED marrow with TPB, Zisman et al. (4), it has been reported that TPB may make acute ED in the early post-biopsy period (days 7 - 30) and this condition should be shared with patients before the procedure. Christofos et al. (5) reported that no significant difference was found between IIEF-5 scores before TPB and IIEF-5 scores at 1 month and 3 months after TPB (up to 3 months after biopsy). In the studies of Aktöz et al. (6), the mean IIEF-5 scores in the first month after TPB showed a significant decrease compared to the baseline mean IIEF-5 scores, but when the mean IIEF-5 scores in the third month after TPB were taken into consideration, no significant decrease was determined. In another study, a significant decrease was detected in the IIEF-5 scores in the first week after TPB compared to the before biopsy and it was reported that this significant decrease continued at 4 weeks after TPB and at 12 weeks after TPB (7). Another study reported a decrease in post-TPB IIEF-5 scores and that ED was a short-lived and transient condition,

and that the post-TPB erectile function correction after the biopsy was initiated from the first lunar month and that total healing was achieved in approximately six months (8).

In our study, the relationship between follow-up time and EF, OF, SD, IS and OSS scores were analyzed. A significant difference was observed in EF scores before TPB and in the first month after TPB (p=0,007). However, in subgroup analyses, this significant difference was only determined in the PCa patients. In BPH-diagnosed patients, there was no significant difference between the ED score and the follow-up times. OF, IS, and OOS scores in 1st, 3rd and 6th months decreased significantly according to the initial score (p = 0,001). SD scores showed no significant differences among follow-ups (p=0,191).

In our study, similar to the studies of Linden-Castro et al. (8) and Aktöz et al. (6), a statistically significant decrease in IIEF-15 scores occurred in the early post-TPB period (at 1-month post-TPB). However, the IIEF-15 score decrease in the long term after TPB (3 months after TPB and 6 months) is statistically insignificant. Additionally, IIEF-15 subgroups were also evaluated. 252 patients were evaluated prospectively in terms of orgasmic function, sexual desire level, relationship satisfaction, and overall satisfaction scores during the follow-up period. Statistically significant decreases in orgasmic function scores at 1 month, 3 months, and 6 months after TPB compared to baseline scores were found. There was no statistically significant decrease in sexual desire level scores according to baseline scores at 1 month, 3 months, and 6 months after TPB. Sexual satisfaction of the patients at the 1st, 3rd, and 6th months after TPB and overall satisfaction scores were found to be statistically lower than the baseline scores.

There are many studies in the literature, including our study, that examines the relationship between TPB and ED, and there is no consensus on the relationship between TPB and ED in these studies. In the year 2016, Murray et al. (7), reported different opinions on the relationship between TPB and ED. According to some studies, TPB - related ED development was reported (9, 10). A few studies have also been cited in the article indicating that there is no significant relationship between TPB and ED development (11, 12). Murray et al. (7), reported that a significant decrease in IIEF-5 scores at 1-, 4-, and 12 weeks post-TPB was found in their study.

When studies are evaluated in terms of the relationship between TPB and ED, it is revealed that anxiety is an important factor thought to be an effect on the development of ED after TPB. Since Zisman et al. (3), investigated the relationship between anxiety with TPB and ED for the first time, many other investigators have investigated the relationship between PCa diagnosis and anxiety (13-17). Some of them

found a positive correlation between PCa diagnosis-based anxiety and ED (14). Conversely, some of them didn't (17). In a recent study, Turgut et al. (18), evaluated the sexual function in patients who underwent a transrectal ultrasonography-guided prostate needle biopsy (TRUS-Bx) using 16G and 18G needles. They found no difference in terms of erectile functions.

In our study, no validated forms were used to document procedure-related anxiety.

However, in order to minimize the effect of TPB - related anxiety on erectile function, patients' initial post-biopsy evaluations were made after four weeks with benign pathology results. To determine the effect of PCa diagnosis on ED, the patients with BPH were assessed between themselves, and the patients with PCa were assessed between themselves separately for a six-month follow-up. PCa patients' IIEF -15 scores were significantly lower than the BPH group at baseline and at the six-month follow-up. These results may be related to low initial IIEF-15 scores of PCa patients and/or cancer-related anxiety as mentioned above. Lack of anxiety and or depression assessment via validated questionnaires is an important limitation of our study. Similarly, it is known that some infectious/inflammatory diseases occur in a hidden/silent manner in males, especially at older ages. We didn't perform the MAGI score (Male Accessory Gland Infection /inflammation) score of the patients before undergoing TPB and that's an important limitation for our study, too. Additionally, we didn't evaluate hormone profiles, e.g., total testosterone measurement and free testosterone calculation in our cohort. So, no patient had been excluded for subtle etiologies of ED, e.g., hypogonadism late-onset or testosterone levels in a gray zone. That's an additional limitation of our study.

When all this literature information is taken into account, it is clear that the design of studies dealing with the change in erectile function of patients with TPB can be achieved by establishing patient/case populations excluding all other factors affecting erectile function. It is also evident that, although all factors affecting erectile function are tried to be excluded, it can be stated that TPB procedure-related and pathology-related (BPH / PCa) anxiety can cause ED.

In order to clarify the relationship between TPB and ED, there is a need for comprehensive studies with several homogeneous patient populations, several different erectile function surveys, and patients' health-related quality-of-life assessments.

In conclusion, our study showed that after TPB, erectile function was significantly decreased at 1 month after TPB but not at 3 and 6 months after TPB. Transrectal prostate biopsy, which is the gold standard in the diagnosis of PCa and which is used frequently,

may have various negative effects on sexual functions, especially in the short term. But our data analyses are not sufficient to determine whether ED is related to the TPB procedure or PCa. Therefore, it is not mandatory to inform all patients who will undergo TPB about the biopsy-related ED.

The main points of our study are:

1-Erectile dysfunction (ED) is possible after transrectal prostate biopsy (TPB) but only in PCa patients.

2-We cannot say that patients must be informed about TPB-related ED.

After pathology results, PCa patients can be informed about TPB-related short-term

ED. But it is not clear that ED is related to TPB or anxiety due to PCa diagnosis.

Ethics Committee Approval: Study approval for this clinical trial was received from Samsun Training and Research Hospital Educational Planning Board on 11 February 2015 (Session number: 2, desicion number: 6).
Peer-review: Externally peer-reviewed.
Author Contributions: Concept - MA; Design – MK; Süpervision – MKAT; Data Collection – MK, EA; Analysis and Interpretation – Lİ; Literature search – AB, MK; Writing Manuscript – MK; Critical Review – Mustafa KA, MA.
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