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The impact of prostate biopsy on erectile and ejaculatory function: A prospective study

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Summary *Objective: To evaluate the impact on erectile and ejaculatory function following transrectal ultrasound-guided biopsies of the prostate (TRUS-Bx) in sexually active men.*

Methods: Monocentric prospective study from May 2021 to January 2022 of consecutive patients with suspected prostate cancer [elevated prostate specific antigen (PSA) level and/or abnormal digital rectal examination] undergoing TRUS-Bx. The 15-item version of the International Index of Erectile Function (IIEF-15), Premature Ejaculation Diagnostic Tool (PDET) and short form of Male Sexual Health Questionnaire (MSHQ-EjD Short Form) were assessed before, one and three months after TRUS-Bx. The primary endpoint was to evaluate the risk of temporary post-biopsy erectile and/or ejaculatory dysfunctions. The statistical significance was set as p value < 0.05.

Results: A total of 276 consecutive patients were included in the study. The median age, PSA and biopsy cores were 65 years (IQR 59-69), 7 ng/ml (IQR 5-9.7) and 16 (IQR 12-16), respectively. We compared the IIEF subdomains before TRUS-Bx vs. one or three months: the erectile function (EF) decreased after one month (p<0.001) but recovered after three months (p=0.833); the Orgasmic Function (OF), the Sexual Desire (SD), the Intercourse Satisfaction (IS), the Overall Satisfaction (OS), and Total IIEF decreased significantly after both one and three months compared to pre-biopsy values (p < 0.05). As for ejaculatory function (EjF), PDET, MSHQ-EjD Short Form 1, 2, 3 and MSHQ-EjD Short Form 4 scores decreased significantly after one month (p < 0.001), but they returned to pre-biopsy values after 3 months: p = 0.538, p = 0.071 and p = 0.098, respectively.

Conclusions: Our study proved that EF, assessed through IIEF-15, and ejaculatory function, assessed through PDET and MSHQ-EjD Short Form, were negatively affected by TRUS-Bx one month after the procedure and recovered after three months. Interestingly, the other IIEF-15 subdomains (OF, SD, IS, OS and Total) resulted as significantly reduced also after 3 months: this issue highlights the importance of carefully considering the indication to TRUS-Bx.

KEY WORDS: *Prostate cancer; Prostate needle biopsy; Erectile dysfunction; Ejaculatory dysfunction.*

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INTRODUCTION

Prostate cancer (PCa) is the second most common cause of cancer death among men (1). *Transrectal ultrasound-guided* biopsies of the prostate (TRUS-Bx), is a well-known diagnostic tool for prostate cancer, with over 2 million/procedures per year in *Europe* and *North America* combined (2).

Despite recent evidence that suggests reduced infection risk with the transperineal route (3), TRUS-Bx is still routinely performed all over the world and is considered a relatively safe procedure with low risk of serious adverse events. Nevertheless, minor complication such as transient *erectile dysfunction* (ED) or *ejaculatory dysfunctions* (EjD) are rare though possible complication after TRUS-Bx with complete recovery after 1-3 mos (4). Notably, data on ED following TRUS-Bx are heterogeneous as a consequence of varied patient populations and ED classifications. Moreover, *Mehta et al.* (5) showed the lack of outcome measurement through validated questionnaires, with only three studies that included the *International Index of Erectile Function-15* (IIEF-15) and just one the *Male Sexual Health Questionnaire* (MSHQ-EjD).

Thus, the aim of our study was to prospectively evaluate, through validated questionnaires, the likelihood of a short-term post-TRUS-Bx erectile and/or ejaculatory dysfunctions in sexually active men.

MATERIALS AND METHODS

Study population and data collection

The study was conducted in accordance with the Declaration of Helsinki. We prospectively included all male patients, suspected of prostate cancer, undergoing TRUS-BX in the department of *Urology, Federico II University, Naples, Italy*, between May 2021 and January 2022. The indications for biopsy were the following: elevated *prostate specific antigen* (PSA) level, PSA between 4-10 ng/mL with PSA density ≥ 0.15 ng/mL/cm^3 , PSA > 10 ng/mL and/or abnormal *digital rectal examination* (DRE).

No conflict of interest declared.

The validated questionnaires were administered by the urologist who conducted the study via e-mail. Baseline parameters were recorded and included: Patients age, *Body Mass Index* (BMI), Charlson score, Diabetes, Hypertension, Anticoagulant therapy, Antiaggregant therapy, Angiotensin receptor blockers therapy, 5-alpha reductase inhibitors therapy, PSA values and number of biopsy cores.

Sexual function questionnaires

The participants were asked to answer the validated questionnaires (translated in Italian) via e-mail: 15- items IIEF-15 (6), *Premature Ejaculation Diagnostic Tool* (PDET) (7) and a short form of *Male Sexual Health Questionnaire* (MSHQ-EjD Short Form) (8). Patients were followed with IIEF-15, PDET and MSHQ-EjD Short Form during the study period divided in before (T1) and at 1 (T2) and 3 (T3) months after TRUS-Bx. Only the complete questionnaires were recorded in the analysis.

The IIEF-15 score included 5 categories: erectile function (EF), orgasmic function (OF), sexual desire (SD), intercourse satisfaction (IS) and overall satisfaction (OS). Response options ranged from 0 (no sexual intercourse) to 5 (normal sexual activity). A Total IIEF-15 score ranging from 5 to 25 was then calculated.

The PDET score was categorized from 0 (no problem at all) to 4 (always), with higher scores indicating difficulty with premature ejaculation.

The MSHQ-EjD Short Form, comprised the four-item ejaculatory function domain assessing frequency of ejaculation, strength of ejaculation, volume of ejaculation and satisfaction.

Biopsy procedure

Antibioprophylaxis was started 1 day before the procedure with Ciprofloxacin 500 mg (2 tablets per day). TRUS-Bx was performed by senior urologists (> 100 procedures) under local anesthesia (10 mL of 2% lidocaine), with automated tru-cut 18-gauge needle (*Bard; Covington, GA*). We performed sextant biopsies (with six cores each lobe) and additional cores from suspected areas.

The primary endpoint was to determine early post TRUS-Bx erectile and/or ejaculatory dysfunctions through validated questionnaires in men suspected for PCa.

Table 1.
Baseline and patients characteristics.

	Overall cohort (n = 276)
Median (IQR) age, years	65 (59-69)
Median (IQR) Body Mass Index	26 (24-29)
Median (IQR) Charlson score	4 (2-6)
Diabetes, n (%)	37(14.4)
Hypertension, n (%)	29 (10.5)
Anticoagulant therapy, n (%)	8 (2.9)
Antiaggregant therapy, n (%)	39 (14.1)
Angiotensin receptor blockers therapy, n (%)	72 (26)
5-alpha reductase inhibitors therapy, n (%)	42 (15.2)
Median (IQR) PSA antigen	7 (5 -9.7)
Median (IQR) biopsy cores	16 (12 -16)

IQR: Interquartile range; PSA: Prostate-specific antigen.

Data analysis

Descriptive statistics included frequencies and proportions for categorical variables. Mean, medians and *interquartile ranges* (IQR) were reported for continuously coded variables. The categorical variables between the groups were analyzed using the chi-squared and Fisher's exact tests, while the continuous variables between groups were analyzed using the Mann-Whitney U test. Wilcoxon sign rank test for paired sample was used to compare continuous non-parametric variables. In all statistical analyses, *Statistical Package for Social Science* (SPSS), Version 20 (*IBM Corporation, Armonk, NY, USA*) was used. All tests were two-sided with a level of significance set at $p < 0.05$.

Results

Study population

A total of 276 male patients that underwent TRUS-Bx between May 2021 and January 2022 met the inclusion criteria: elevated *prostate specific antigen* (PSA) level, PSA between 4-10 ng/mL with PSA density ≥ 0.15 ng/mL/cm^3, PSA > 10 ng/mL and/or abnormal *digital rectal examination* (DRE).

The baseline characteristics are summarized in Table 1. In the overall cohort, the median age, BMI and Charlson Comorbidity score were 65 (IQR 59-69) years, 26 (IQR 24-29) and 4 (IQR 2-6), respectively. The median PSA was 7 (IQR 5-9.7) and a median of 16 (IQR 12-16) biopsy cores were taken during the TRUS-Bx procedure.

IIIEF-15 Questionnaire

From T1 to T2, the IIEF-EF score decreased significantly (21 (IQR 3.0-25.0) vs 19 (IQR 2.0-22.5), $p < 0.001$) and from T1 to T3, no statistically significant difference was recorded ($p = 0.833$) (Table 2).

Finally, in the other subdomains (OF, SD, IS, OS) and Total, from T1 to both T2 and T3, the IIEF score decreased significantly ($p < 0.05$), the changes of specific domains are shown in Table 2.

Table 2.
International Index of Erectile Function (IIEF) Questionnaire administrated to 276 patients before prostate biopsy (Time 1), 1 month after (Time 2) and 3 mos after (Time 3).

					Wilcoxon sign rank test p-value	
		Time 1	Time 2	Time 3	Time 1 vs time 2	Time 1 vs time 3
IIEF-EF	Median IQR	21 3.0-25.0	19 2.0-22.5	21 3.0-25.0	< 0.001	0.833
IIEF-OF	Median IQR	7.5 0-9.8	6.5 0-7.5	7 0-8.0	< 0.015	< 0.001
IIEF-SD	Median IQR	6 5.0-7.0	5 4.5-6	6 5.0-7.0	< 0.02	< 0.023
IIEF-IS	Median IQR	10 0-12.0	9 0-11.0	9.5 0-12.0	< 0.015	< 0.001
IIEF-OS	Median IQR	7 4.0-8.0	6 2.0-8.0	7 4.0-8.0	< 0.001	< 0.001
IIEF-TOT	Median IQR	53 12.0-61.0	49 7.0-58	51 12.0-60.0	< 0.001	< 0.001

EF: Erectile Function; IS: Intercourse Satisfaction; OF: Orgasmic Function: OS: Overall Satisfaction; SD: Sexual Desire.

Table 3.
Ejaculatory function questionnaires administrated to 276 patients before prostate biopsy (Time 1), 1 month after (Time 2) and 3 mos after (Time 3).

					Wilcoxon sign rank test p-value	
		Time 1	Time 2	Time 3	Time 1 vs time 2	Time 1 vs time 3
MSHQ-EjD 1, 2, 3	Median IQR	12 5.0-14.0	11 6.3-14.0	12 5-14.5	< 0.001	0.538
MSHQ-EjD 4	Median IQR	5 3.0-5.0	4 4.0-5.0	5 3.0-5.0	< 0.001	0.071
PDET	Median IQR	2 0-4.0	2 0-4.0	2 0-4.0	< 0.001	0.098

PEDT: Premature Ejaculation Diagnostic Tool; MSHQ-EjD: Male Sexual Health-Ejaculatory Dysfunction Questionnaire-Ejaculatory Dysfunction.

PDET Questionnaire

From T1 to T2, the PDET score decreased significantly (2 (IQR 0-4.0) *vs* 2 (IQR 0-4.0), $p < 0.001$) and from T1 to T3, no statistically significant difference was observed ($p = 0.098$) (Table 3).

MSHQ-EjD Short Form Questionnaire

From T1 to T2, the MSHQ-EjD Short Form score (1,2,3) decreased significantly (12 (IQR 5.0-14.0) *vs* 11 (IQR 6.3-14.0), $p < 0.001$) and from T1 to T3, no statistically significant difference was observed ($p = 0.538$) (Table 3). Similarly, From T1 to T2, the MSHQ-EjD Short Form score (4) decreased significantly (5 (IQR 3.0-5.0) *vs* 4 (IQR 4.0-5.0), $p < 0.001$) and from T1 to T3, no statistically significant difference was observed ($p = 0.071$) (Table 3).

A univariate analysis failed to identify the independent predictive factors of erectile and sexual disfunction (results not shown).

Discussion

The study showed a rapid decrease in erectile and ejaculatory function at one month but a promising return to pre TRUS-Bx values was observed.

Aetiology of ED after TRUS-Bx is likely multifactorial. As suggested by *Zisman et al.* (9), trauma caused by compression associated with haematoma or oedema in the neurovascular bundle are considered the main reasons. Moreover, *Tuncel et al.* (10) described multiple radiological changes in prostate parenchyma and bundle in post biopsy men with ED, indeed this could be explained by the fact that the most common form of analgesia used for this *procedure is periprostatic nerve block* (PPNB) and it is likely to be responsible for damage in neurovascular bundle area, leading to a possible cause of transient ED (11). Despite many studies have been correlating ED and prostate biopsy, only limited and controversial results are shown in literature, ranging from no meaningful effect to significant linking with ED in short- and long-term post TRUS-Bx. *Chrisofos et al.* (12), prospectively evaluated 46 men after TRUS-Bx; post biopsy ED were reported in just 6.5% and 4.3% of patients at one and three months, meaning that TRUS-Bx did not induce ED in a statistically significant manner. On the other hand,

Kamali et al. (13) showed that TRUS-Bx was linked to ED, and by the passage of time (6 months later); the degree of dysfunction significantly worsened (IIEF-5 mean scores 1 month after biopsy: 18 (6-25); 3 months after: 17 (5-25); 6 months after: 14.5 (5-25)). Herein, we assessed the decrease in EF through IIEF-EF in sexually active men one month after TRUS-Bx and recovering after three months. Notably, the other IIEF subdomains (OF, SD, IS, OS and Total) resulted significantly reduced also after 3 months. There are several explanations to this discrepancy of results. First, despite the use of validated questionnaires, the patients may not have sufficient cognition to understand the different subdomains of IIEF-15. Second, in the multifactorial nature of ED, a prevalent issue on psychological condition in our study was observed (IS, OF, OS, SD). Deep effect on increased anxiety in patients who undergo TRUS-Bx may be related to the acute healing phase after the procedure and presence of a potentially lethal cancer specific disease (9, 12, 14). Moreover, an important aspect of our study, comparable to the current literature (15, 16) was that Ejaculation function, assessed through PDET and MSHQ-EjD short form, didn't show any change between pre and post TRUS-Bx values.

The limitations of the present study should also be acknowledged. First, the absence of a complete psychologic and mental health assessment in our study population considering that the main statistic differences at 3 months were IS, OF, OS and SD. Another limitation was the lack of a control group; we were unable to determine the relative short term erectile and ejaculatory disfunction of TRUS-Bx compared to the transperineal approach.

However, our study also has several strengths which lies on his methodology. This study is a longitudinal study in which participants were evaluated before, 1 month after and 3 months after TRUS-Bx to avoid possible memory bias. Additionally, all subdomains of the international validated scales for examining sexual functions, such as IIEF, PDET and MSHQ-EjD short form, were evaluated.

Conclusions

The discrepancy of results existing in literature and the issue in our study highlights the importance of carefully considering the indication to TRUS-Bx. Magnetic resonance imaging and other tools (e.g., PSA-density/velocity, biomarkers) are warranted to determine the real need for TRUS-Bx, which may negatively affect important domains of male sexual life.

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