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ORIGINAL ARTICLE

Impact of transrectal prostate needle biopsy on erectile function: Results of power Doppler ultrasonography of the prostate

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Abstract We evaluated the impact of transrectal prostate needle biopsy (TPNB) on erectile function and on the prostate and bilateral neurovascular bundles using power Doppler ultrasonography imaging of the prostate. The study consisted of 42 patients who had undergone TPNB. Erectile function was evaluated prior to the biopsy, and in the 3rd month after the biopsy using the first five-item version of the International Index of Erectile Function (IIEF-5). Prior to and 3 months after the biopsy, the resistivity index of the prostate parenchyma and both neurovascular bundles was measured. The mean age of the men was 64.2 (47–78) years. Prior to TPNB, 10 (23.8%) patients did not have erectile dysfunction (ED) and 32 (76.2%) patients had ED. The mean IIEF-5 score was 20.8 (range: 2–25) prior to the biopsies, and the mean IIEF-5 score was 17.4 (range: 5–25; $p < 0.001$) after 3 months. For patients who were previously potent in the pre-biopsy period, the ED rate was 40% ($n = 4/10$) at the 3rd month evaluation. In these patients, all the resistivity index values were significantly decreased. Our results showed that TPNB may lead to an increased risk of ED. The presence of ED in men after TPNB might have an organic basis.

Conflicts of interest: All authors declare no conflicts of interest.

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Introduction

Transrectal prostate needle biopsy (TPNB) has been the standard urological procedure to detect prostate cancer since it was introduced by Hodge et al. [1]. It is considered a safe and common practice with few major complications but there can be frequent minor complications such as hematospermia, hematuria, and rectal bleeding [2,3]. In the international literature, studies have investigated the effect of TPNB on erectile dysfunction (ED). Most have demonstrated that these post-biopsy effects occur over a short period of time and are transient [4–8]. However, our previous published study reported that some men could still have ED at 6 months after TPNB [9]. In the international studies, the patients' erectile function was only assessed on the basis of the scores from a validated evaluation scale. To the best of our knowledge, no study has investigated radiological alterations in prostate and neurovascular bundles in patients with or without ED after TPNB.

In the current study, we prospectively investigated the impact of TPNB on erectile function and on prostate and bilateral neurovascular bundles using power Doppler ultrasonography imaging of the prostate.

Methods

This study was approved by the Institutional Review Board (ANEAH:09/86) and written informed consent was obtained for each patient. A total of 42 patients who underwent TPNB due to both or either abnormal digital rectal examination findings and/or elevated blood serum prostate-specific antigen levels ($\geq$2.5 ng/mL) were included in this study. All the men were either married or had been in a stable relationship with a female sexual partner for at least 12 months. History of previous prostatic biopsy or prostatic surgery, active urinary tract infection, any urological malignancy, bleeding diathesis, use of 5-α reductase inhibitors, and/or α blockers, and previous history of diabetes mellitus and hypertension were exclusion criteria. According to histopathological examination, patients who had prostate cancer were not included. All the patients' histopathological examination results were consistent with benign prostatic enlargement.

One hour prior to TPNB, the patients underwent a transrectal prostatic power Doppler ultrasonography examination in our radiology department. This procedure was performed by our radiologist (U.T.). Then, the biopsy procedure was performed with the patients in the left decubital position, using a Shimadzu SDU 450 scanner (Schimadzu Corporation, Kyoto, Japan) with a 7.5-MHz biplanar probe attached. A standard of 10 cores of prostatic tissue were obtained using an 18-gauge (1.2-mm diameter) biopsy needle and a biopsy gun. Transrectal ultrasound and prostatic biopsy were performed by one of the authors (A.T.). The patients received 500 mg ciprofloxacin orally twice daily at the beginning of the day prior to the biopsy and continued for 5 days. The radiological examination was repeated at 3 months after the biopsy.

Radiological examination

The study was undertaken using a GE Logiq 7 scanner (GE Medical Systems, Milwaukee, WI, USA) with 7.5-MHz multifrequency biplanar transducers. We chose power Doppler ultrasonography because it is easily applied, inexpensive, and readily available. The most well-vascularized area of the prostate parenchyma was found approximately at the midpoint of the gland with an axial scan. The two-dimensional power Doppler images of the vascularization were recorded without artifacts as far as possible. Then, the mean values of the resistivity index (RI) obtained from three spectral waves of the prostate parenchyma and from both the neurovascular bundles were recorded. The RI was calculated using the following formula:

$$\text{Peak systolic velocity} - \text{end diastolic velocity}/\text{peak systolic velocity}$$

Thus, the right and left neurovascular bundle and prostate parenchyma RI values and prostate parenchyma vascularization images were obtained. After 3 months, the same parameters were recorded using transrectal power Doppler ultrasonography.

Digital image analysis

The digital image processing software developed by one of the authors (Y.A.) in April 2011 using the MATLAB computing language (MATLAB R2008a; Mathworks, Natick, MA, USA) was used for analysis of ultrasound images. This software and algorithm, based on the differences between the color channels of images, was developed uniquely for this research.

The jpeg images obtained from ultrasound imaging consisted of three color channels: red, green, and blue. Each channel had a different value for each pixel in the image and these values determined the color and brightness of the pixel. To identify the vascular regions, which appeared yellow and red in the ultrasound data, the differences between these three color channels were used. In the red pixels, the red channel had higher values whereas the other two channels had lower values. In the yellow pixels, the red and green channels had higher values whereas the blue channel had lower values. Considering that the red channel had higher values and the blue channel had lower values in the relevant regions, the difference between these two channels can be computed and an image map consisting of the candidate vascular regions was created (Fig. 1A–C). With this technique, the gray areas in the image were eliminated. After thresholding to eliminate the noise resulting from the image and compression, the area of the vascular regions was calculated.

Prior to the current study, a pilot study was performed to determine the optimal selection of the best-vascularized area. Two power Doppler ultrasonography images were obtained from each person in order to compare the amount of vascularization similarity. There were no significant differences between the vascularization of the two images, thus, the method was accepted as reliable (Fig. 1D and E).

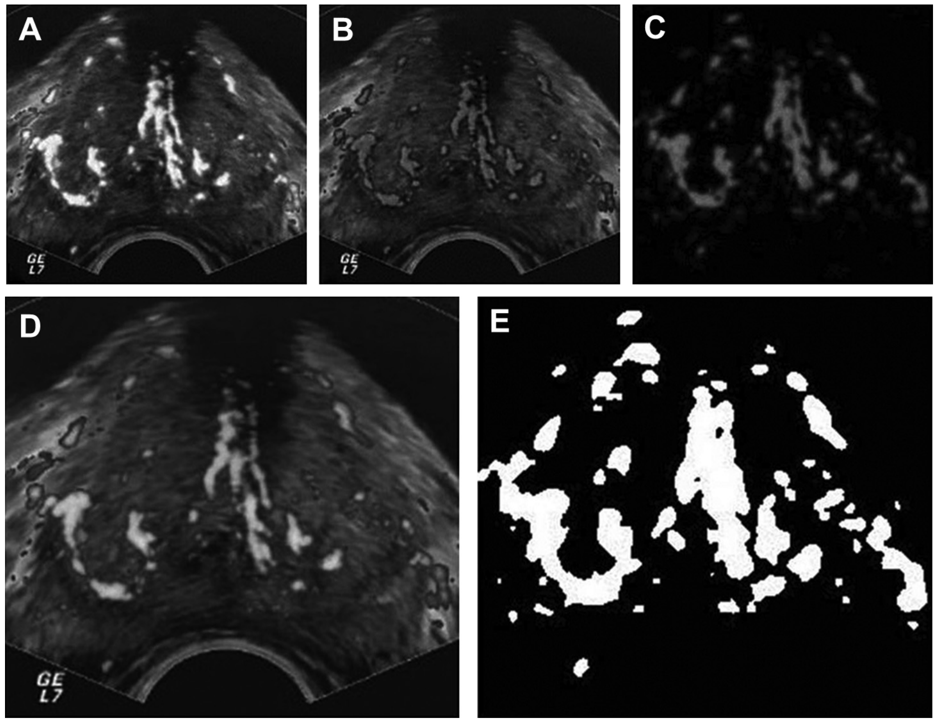

Figure 1. (A—C) The differences between the red, blue, and both channels respectively, in the digital image analysis. (D,E) The original power Doppler image and an image showing the vascularization areas obtained after analysis.

Assessment of erectile function

All the men completed the five-item version of the International Index of Erectile Function (IIEF-5) [10] on the day of the biopsy and after 3 months. An IIEF-5 score of <22 was considered to indicate that the patient had ED.

Statistical analysis

The statistical analysis was performed using SPSS for Windows version 13.0 (SPSS Inc., Chicago, IL, USA). A Student *t* test was used to compare the demographic data. The comparison of RI values was performed with a Mann—Whitney test. The pre- and post-biopsy image analysis value comparison was made using repeated measures analysis of variance. A p value <0.05 was considered significant.

Results

The mean age of the men was 64.2 ± 6.4 (47—78) years. Prior to TPNB, 32 (76.2%) patients had ED (Group 1) and 10 (23.8%) patients did not have ED (Group 2). The mean age of the patients with and without ED was 62 ± 6.7 (56—78) years and 59 ± 5.8 (47—69) years, respectively ($p = 0.217$). The mean IIEF-5 score was 20.8 ± 3.7 (range: 2—25) prior to TPNB, whereas, the mean IIEF-5 score was 17.4 ± 5.5 (range: 5—25) 3 months after TPNB. We found significant differences between the pre-biopsy IIEF-5 score and the post-biopsy 3-month IIEF-5 score ($p < 0.001$).

Prior to the biopsy, we found similar RI values for the parenchymal and bilateral neurovascular bundles, and prostatic blood flow in both groups. After the biopsy, all the RI values significantly decreased in Group 2. Conversely, we did not find significant alteration in prostatic blood flow in either group. Also, we did not find a significant alteration in terms of the RI and prostatic blood flow in Group 1 (Table 1). Three months after TPNB, four of the 10 previously potent patients in Group 2 reported ED. In those four patients, the post-biopsy prostate blood supply was significantly increased, and all the RI values were significantly

Table 1 Pre- and post-biopsy power Doppler ultrasonography findings for the two groups.

Parameters	Group 1 ($n = 32$)	Group 2 ($n = 10$)	p
Right neurovascular bundle RI			
Pre-biopsy	0.86 ± 0.13	0.87 ± 0.12	0.154
Post-biopsy	0.86 ± 0.10	0.73 ± 0.10	0.001
p	0.988	0.003	
Left neurovascular bundle RI			
Pre-biopsy	0.87 ± 0.10	0.86 ± 0.10	0.116
Post-biopsy	0.79 ± 0.14	0.77 ± 0.51	0.021
p	0.873	0.004	
Prostate parenchyma RI			
Pre-biopsy	0.80 ± 0.14	0.76 ± 0.13	0.216
Post-biopsy	0.86 ± 0.10	0.80 ± 0.67	0.173
p	0.406	0.010	
Image analysis outcomes			
Pre-biopsy	5645 ± 2962	4848 ± 2147	0.153
Post-biopsy	5415 ± 2758	7346 ± 2401	0.090
p	0.437	0.054	

RI = Resistivity Index.

Table 2 Power Doppler ultrasonography data of the four patients who had post-biopsy erectile dysfunction.

Parameters	Prior to biopsy	After biopsy	p
Right neurovascular bundle RI	0.86 ± 0.50	0.67 ± 0.07	0.009
Left neurovascular bundle RI	0.86 ± 0.07	0.69 ± 0.53	0.071
Prostate parenchyma RI	0.79 ± 0.05	0.65 ± 0.11	0.024
Image analysis outcomes	3960 ± 2112	7470 ± 2672	0.032

RI = Resistivity Index.

decreased (Table 2). In the remaining six patients, we did not find any significant alterations in all the parameters.

Discussion

Prostate cancer is now recognized as one of the important urological problems and TPNB is one of the procedures used for its diagnosis. TPNB is a commonly performed and relatively safe procedure with an acceptably low risk of serious complications. Minor complications including hematospermia, hematuria, and rectal bleeding are relatively common but are always self-limited [2,3]. However, ED has been generally neglected as a complication following TPNB. In the international literature, there are few studies that have investigated the relationship between TPNB and ED, and the limited data that do exist are conflicting.

In 2001, 218 ultrasound-guided prostate biopsies were performed in a questionnaire-based survey that focused on pain, anxiety, and erectile function [4]. The questionnaires were administered prior to, immediately after 1 week, and 30 days after TPNB. The authors reported that ED attributed to anxiety in anticipation of the biopsy was found in 7% of cases. Moreover, 30 days after TPNB, 15% of the previously potent patients reported ED. In 2006, Chrisofos and co-workers [5] investigated ED after TPNB. In that study, 46 men underwent TPNB and completed the IIEF-5 questionnaire on the day of the biopsy, and 1 month and 3 months later. No significant difference in erectile function was found in the 1st month and 3rd month after TPNB. In the previously potent men, 9% reported persistent ED at 3 months after the biopsy. Akbal and associates [6] performed saturation prostate biopsy on 150 patients. Patients were evaluated using the IIEF-5 and the IIEF-Erectile Function domain scoring at 1 month and 6 months after the saturation biopsy. According to the IIEF-5 score for patients who were previously potent and found to be free of prostate cancer, the ED rate was 11.6% at the 1st month, and no ED was reported at the 6th month of evaluation. The IIEF-5 and IIEF-Erectile Function domain scores displayed a significant difference between the baseline and 1-month scores, but not between baseline and 6-month scores, which returned to baseline values. In 2008, we published our study investigating the association between TPNB and ED [9]. In our study, 97 men underwent a 10-core TPNB and we found that 41% of men who had performed previously without ED experienced ED 1 month after TPNB. By 6 months, 15% still had ED. In this study, we also evaluated the impact on female sexual function and detected a significant impact even after 6 months. In a study by Fujita et al. [7], 231 men with prostate cancer on an active surveillance protocol completed the five-item Sexual Health Inventory for Men (SHIM) and International Prostate Symptom Score questionnaire upon entry to the protocol, and at a cross-sectional point. All the men had at least one 10–12-core TPNB at protocol entry and yearly surveillance biopsies thereafter were recommended. According to their results, correlations were found between the number of biopsies and ED, with an increasing number of biopsies being associated with a decrease in the SHIM. When men were stratified by a baseline SHIM, those without pre-existing ED trended toward steeper decreases in the SHIM score after three or more biopsies. They concluded that serial prostate biopsies appear to have an adverse effect on erectile function in men with prostate cancer under active surveillance. However, there is a significant difference between the Fujita study and previous publications. Only patients with prostate cancer were enrolled in this study, whereas prior research also included patients without prostate cancer. We believe that the presence of prostate cancer itself might have a negative impact on erectile function. Also, in Fujita's study, the anxiety level of patients prior to and after TPNB was not mentioned. In 2010, Klein et al. [8] evaluated the effect of multiple-core TPNB and a periprostatic nerve block on erectile function and voiding. In that study, 198 men underwent 10-core TPNB with (n = 71) or without (n = 74) a periprostatic nerve block. They reported that the IIEF scores decreased significantly in all groups in the 1st week. The decrease persisted to the 1st month and resolved at 3 months in all groups. The authors concluded that erectile function is transiently impaired after TPNB.

No exact cause of ED has been found in the population that undergoes TPNB, especially in those patients without ED. Zisman et al. [4] claimed that prostate-biopsy-attributed ED may occur by direct neurovascular bundle damage or secondary trauma such as nerve compression caused by a hematoma and/or edema. Some authors have speculated that ED associated with TPNB may be related to a direct injury to the neurovascular bundles, inflammation, and/or scarring related to the laterally directed biopsies [5,7,8]. However, as mentioned above, these suppositions have not yet been confirmed with radiological studies. To the best of our knowledge, our pilot study is the first to evaluate the impact of TPNB on the neurovascular bundles and prostate blood flow in patients who have undergone TPNB. According to our results, at 3 months after TPNB, 40% (4/10) of previously potent patients reported ED. In these four patients, the power Doppler ultrasonography findings showed inflammation of the prostate parenchyma and the surrounding area of the neurovascular bundle. As mentioned above, this result in relation to the development of ED after TPNB supports the theory speculated on in the previous studies that this development was caused by neurovascular bundle injury originating from as hematoma and/or edema compression, inflammation, and/or scarring. In the remaining six patients, there was no significant change in the power Doppler ultrasonography findings. In the present study, the RI values of the right and left neurovascular bundles significantly decreased in Group 2. However, we did not find a significant change in terms of all the RI values in Group 1. Although we do not have precise answer to this situation, we can speculate that each neurovascular bundle could be affected by tissue reaction at different levels.

The use of quantitative analysis methods in Doppler imaging began in the early 2000s with the use of semiquantitative methods [11—14]. The method used in the present study was also semiquantitative. Nowadays, although the three-dimensional analysis has been found to be more successful in terms of intra-observer accordance, both two-dimensional analysis and three-dimensional analysis methods are considered reliable [15—18]. Imaging analysis studies concerning the prostate have been used for cancer scanning [12,13], but have never been used for the purpose used in the present study. Three months after TPNB, four of 10 (40%) patients who were previously potent had ED. The findings from the patients' power Doppler ultrasonography showed decreased RI values of the prostate parenchyma and neurovascular bundles. The image analysis revealed an increased vascularization of the parenchyma. Both the parameters showed that the vascular dilatation of the parenchyma was an inflammatory response. We think that the durability of these radiological parameters should be re-evaluated in the long-term follow-up. Inflammation and edema are the basic pathological and histological responses to trauma. Undoubtedly, every biopsy does greater or lesser damage to the tissue. The damage may be seen through imaging methods (magnetic resonance imaging, computerized tomography, and power Doppler ultrasonography) as tissue hemorrhage with increasing density and/or intensity. However, it is morphologically impossible to detect this in every case [19,20]. The post-traumatic damage of the neurovascular bundle of the prostate is similar to that of other tissues. The power Doppler ultrasonography examination revealed post-biopsy inflammation (increased blood supply to the prostate parenchyma, decreased prostatic and neurovascular RI, in only 4 of 10 patients in Group 2). Undoubtedly, there was also tissue damage in other patients, however, this was probably not so obvious as to be detected on power Doppler ultrasonography or could not be detected radiologically.

The major limitations of our study were that there were a small number of patients and the duration of our follow-up was not yet long enough to report on the long-term erectile function status of our patients and durability of the radiological parameters.

Finally, our short-term study shows that TPNB may have a negative impact on erectile function. In the present study, the findings from the power Doppler ultrasonography showed inflammation of the prostate parenchyma and surrounding neurovascular bundle in patients suffering from ED after TPNB. Our findings show that the presence of ED after TPNB might have an organic basis. We believe that the findings of our study could be a good starting point for understanding the development mechanism of ED after TPNB. We believe that further long-term studies, possibly with more patients, are needed to clarify the issue.

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