Association Between Prostate Zonal Volume and Erectile Dysfunction in Patients With Benign Prostatic Hyperplasia

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ABSTRACT

Introduction: The impact of prostate zonal volume on erectile function and penile Doppler parameters is not yet settled.

Aim: To assess the association between prostate zonal volume and erectile dysfunction in patients with benign prostatic hyperplasia.

Methods: This cross-sectional analytical study included 70 men (aged ≥ 40 years). Of them, 60 patients were assigned to 3 study groups (n = 20 each): group (A) patients who had lower urinary tract symptoms (LUTSs) and erectile dysfunction (ED), group (B) patients who had LUTSs with no ED, group (C) patients who had ED with no LUTS, and other 10 age-matched patients who had no LUTS or ED acted as a control group (D). All patients were subjected to detailed medical and sexual history. International prostate symptom score (IPSS) was used to assess LUTSs, and international index of erectile function (IIEF) was used to assess ED.

Main Outcome Measure: Transrectal ultrasound and penile Doppler ultrasound were used to assess zonal anatomy of the prostate and the vascular pattern of erection.

Results: There was a significant difference in IPSS between group A (26) and B (19) (P < .05). Each of groups A and C had significant lower peak systolic velocity (PSV) than each of groups B and D (P < .001/each). There was a significant positive correlation between transitional zone index (TZI) and IPSS (r = 0.71, P < .01), and significant negative correlation between TZI and both of IIEF (r = -0.48, P < .05) and PSV (r = -0.606, P < .05).

Conclusion: This study clearly demonstrated that there were significant correlations between increased transitional zone volume, TZI, and decreased both of IIEF score and PSV. Qalawena MM, Al-Shatouri MA, Motawaa MA, et al. Association Between Prostate Zonal Volume and Erectile Dysfunction in Patients With Benign Prostatic Hyperplasia. Sex Med 2020;8:205-213.

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Key Words: Prostate; Zonal Volume; Erectile Function; BPH

INTRODUCTION

Benign prostatic hyperplasia (BPH) and erectile dysfunction (ED) are common conditions in aging men. The prevalence of ED in men aged more than 40 years is more than 50%. About 75% of men complain of obstructive urinary symptoms sometimes during their life. ED correlates with age, diabetes, cardiovascular diseases, and some medication use. ED is more likely to be present in men with lower urinary symptoms (LUTSs). Furthermore, LUTSs were reported to have negative effect on men’s sexual life. The clinical application of transrectal ultrasonography (TRUS) had provided an accurate revenue of assessing prostate volume and delineating the zonal anatomy of the prostate. Prostatic anatomical factors, such as transitional zone volume (TZV), transitional zone index (TZI), peripheral zonal volume (PZV), presumed circle area ratio, intravesical prostatic protrusion, and prostatic urethral angulation, were reported to have association with urinary symptom scores, maximum urinary flow rate, and urodynamically confirmed obstruction than total prostate volume (TPV).

Previous study using TRUS had identified the TZI as a potential predictor for bladder outlet obstruction. Another study had demonstrated a significant correlation between the TZI and both the international prostate symptom score (IPSS) and peak
flow rate, and concluded that the TZI was the better indicator for bladder outlet obstruction and obstructive symptoms. TPV was reported to independently correlate with international index of erectile function (IIEF) but not with premature ejaculation.

Furthermore, although few studies have shown the association between change in prostate zonal volume and ED severity and duration, however, the impact of prostate zonal volume on erectile function and penile Doppler parameters including peak systolic velocity (PSV), end diastolic velocity (EDV), and resistive index (RI) in patients with BPH/LUTS has not yet been settled. This prompted us to investigate the impact of prostate zonal volume on IIEF and penile Doppler parameters including peak systolic velocity (PSV), end diastolic velocity (EDV), and resistive index (RI) in patients with BPH/LUTS.

**MATERIALS AND METHODS**

This cross-sectional analytical study included 70 men (aged ≥ 40 years). Of them, 60 patients who attended to the urology clinic at Suez Canal University Hospital with LUTS and/or ED from July 2017 throughout June 2018 were assigned to 3 study groups (n = 20/each): group (A) patients who had LUTS and ED, group (B) patients who had LUTS with no ED, group (C) patients who had ED with no LUTS. Other 10 age-matched patients who attended to the urology clinic with complaints other than LUTS or ED acted as a control group (D). Patients with bladder or prostate malignancy, a history of lower urinary tract surgery, history of catheterization, urinary retention, urinary tract infection, stone disease, any neurological disease, or medications that affect bladder outlet function were excluded from the study. Patients with high PSA and/or suspicious hard prostatic nodule at digital rectal examination were excluded from study. IPSS was used to assess LUTS. This validated 7-item scale is based on questions that include incomplete emptying, urinary frequency, intermittency, urgency, weak stream, straining, and nocturia. This scale has an ordered categorical response frame that can be scored from 0 to 5, for an overall composite score of 0–35. Symptoms were classified as absent (IPSS = 0), mild (IPSS = 1–7), moderate (IPSS = 8–19), or severe (IPSS = 20–35). International index of erectile function (IIEF-5) was used to assess ED. The erectile function domain consists of questions 1–5 and question 15 for assessing the global erectile function. Scoring the IIEF domain of erectile function allowed the classification of each patient as having no (26–30), mild (17–25), moderate (11–16), or severe (0–10) ED.

All patients in group A underwent TRUS and penile color Doppler ultrasound (CDU). In groups B, C, and D, patients were offered to undergo TRUS and CDU to assess the zonal anatomy of the prostate and the vascular pattern of erection. The patients who agreed were included in this study.

**Baseline Assessment**

All patients were subjected to detailed medical, sexual history, complete physical examination, and laboratory investigations including plasma PSA assessment. Patients with high PSA and/or suspicious hard prostatic nodule at digital rectal examination were excluded from study. TPV was calculated by the formula: 

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\text{TPV} = \frac{\pi}{6} \times \text{AP diameter} \times \text{transverse diameter} \times \text{longitudinal diameter}
\]

The PZV was measured from image plains with maximal TZV.

**Color Doppler Ultrasound**

Assessment of the penile vasculature was achieved by using color Doppler ultrasonography with 7.5 MHz probe (Siemens,
Doppler angle of 60° was performed along an arterial segment corresponding to a stimulation. Then, CDU recording of the cavernous arteries taglandin E1, patients were allowed 5 minutes for manual self-stimulation. Sex Med 2020;8:205

### Table 2. Comparison of clinical, laboratory, and radiological variables among study groups (n = 70)

| Variables | Group A (n = 20) Median (IQR) | Group B (n = 20) Median (IQR) | Group C (n = 20) Median (IQR) | Group D (n = 10) Median (IQR) | P-value |
|-----------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|---------|
| IPSS      | 26 (22–30)                    | 19 (16–22)                    | 0                             | 0                             | .048    |
| IIEF      | 10 (9–11)                     | 26 (25–27)                    | 15 (13–17)                    | 28 (27–29)                    | <.001   |
| PSA, ng/ml| 3.3 (1.28–4)                  | 2.8 (1.73–3.28)               | 2.05 (1.1–3.28)               | 1.3 (1.9–2.7)                 | .91     |
| Creatinine, mg/dl | 0.72 (0.6–.95) | 1.05 (0.8–1.18) | 0.82 (0.73–.95) | 0.65 (0.6–.75) | .84     |
| Prostate measurements |                               |                               |                               |                               |         |
| TPV (ml)  | 41.5 (37–48)                  | 37.6 (36–47.3)                | 23.5 (20–27.8)                | 20.5 (18–28.8)                | <.001   |
| PZV (ml)  | 8 (6.3–11.8)                  | 10 (7.3–12)                   | 14 (13–15)                    | 16 (15–17)                    | <.001   |
| TZV (ml)  | 20.2 (18–21.8)                | 16.7 (15–20.9)                | 8 (7–13)                      | 5 (4–6.8)                     | <.001   |
| TIZ %     | 48.6 (45–60)                  | 44.4 (36.3–58)                | 34 (32.3–49)                  | 25 (18.3–30.3)                | <.001   |
| CZV (ml)  | 16.2 (12.5–23)                | 13.5 (11–26.8)                | 7 (5–10)                      | 4 (3–6)                       | <.001   |
| Doppler measurements |                               |                               |                               |                               |         |
| PSV       | 20 (18–28)                    | 40 (25–45)                    | 22 (16–23)                    | 42 (34–44)                    | <.001   |
| EDV       | 5 (3–6)                       | 4 (1–5)                       | 8 (5–12)                      | 3 (0–4)                       | <.01    |
| RI        | 0.72                          | 1.1                            | 0.81                          | 1.3                           | <.01    |

IQR = interquartile range; IPSS = international prostate symptom score; IIEF = international index of erectile function; PZV = peripheral zonal volume; TIZ = transitional zonal index; TZV = transitional zonal volume; TPV = total prostate volume; PSV = peak systolic velocity; EDV = end diastolic velocity; RI = resistive index.

P-values are based on Kruskal-Wallis H test. Statistical significance at P < .05. Bold indicates statistically significant difference.

### Bivariate group analysis among the studied variables

| P-value | IPSS | IIEF | PSA | S. Creatinine | TPV | PZV | TZV | CZV | PSV | EDV | RI |
|---------|------|------|-----|--------------|-----|-----|-----|-----|-----|-----|----|
| Group A vs B | **.048** | .002 | .88 | .98          | .45 | .71 | .76 | .61 | .001 | .55 | .01|
| Group A vs C | .001 | .22  | .78 | .75          | .001| .001| .001| .001| .001 | .56 | .15 |
| Group A vs D | .001 | .001 | .99 | .77          | .001| .001| .001| .001| .001 | .38 | .01|

P-values are based on Mann–Whitney U test. Statistical significance at P < .05. Bold indicates statistically significant difference.

GM-6600A2E00). After intracorporeal injection of 10 μg prosta
glandin E1, patients were allowed 5 minutes for manual self-
stimulation. Then, CDU recording of the cavernous arteries was performed along an arterial segment corresponding to a Doppler angle of 60° and sample volume of 2 mm in all patients to obtain comparable data among them. The Doppler parameters include PSV, EDV, and RI. Arteriogenic ED was diagnosed when PSV is lower than 35 cm/sec. Veno-occlusive ED was diagnosed when EDV is higher than 5 cm/sec and RI is lower than 0.9. Mixed arteriogenic-veno-occlusive ED was diagnosed when PSV is lower than 35 cm/s and in concomitant with EDV is higher than 5 cm/sec.

The institutional research and ethical committee (Institution Review Board) had reviewed and approved the study. Each patient had provided an informed consent.

### Data Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS© ver. 21.0) software program (SPSS, Inc, Chicago, IL, USA). Chi-square test was used to compare categorical variables. Kruskal–Wallis H test was used to compare median of age, IPSS, IIEF, and Doppler parameters and prostate measurements. Mann-Whitney U test was used for bivariate analysis of non-normal distribution variables. ANOVA was used to compare means of more than 2 variables of normally distributed parameters. Spearman’s correlation coefficient was used to assess correlation between variables. A P value < .05 was considered statistically significant.

### RESULTS

#### Sociodemographic Data

70 patients were recruited to this study. The median age (years), interquartile range (IQR) of the studied groups A, B, C, D were 58 (50–66), 56 (45–69), 54 (47–63), 50 (45–55), respectively, with no statistically significant difference among groups (P > .05). Of the studied population, more than 50% had risk factors and chronic illnesses that included smoking, hypertension, diabetes, and dyslipidemia with no statistically significant difference among groups (P > .05) Table 1.
Figure 1. 1-I: TRUS of the patient in group A showed a) TPV = 97.6 ml, b) CZV = 40 ml, c) PZV = 6.8 ml, and d) TZV = 50.8 ml. 1-II: TRUS of patient in group B showed a) TPV = 64.2 ml, b) CZV = 29 ml, c) PZV = 10.4 ml, and d) TZV = 23.8 ml. 1-III: TRUS of a patient in group C showed a) TPV = 33.9 ml, b) CZV = 16 ml, c) PZV = 12.6 ml, and d) TZV = 4.4 ml. 1-IV: TRUS of the patient in group D showed a) TPV = 28.3 ml, b) CZV = 10 ml, c) PZV = 13 ml, and d) TZV = 5.3 ml. CZV = central zonal volume; PZV = peripheral zonal volume; TRUS = transrectal ultrasonography; TPV = total prostate volume; TZV = transitional zone volume.
Correlation analysis between radiological prostate measurements and IPSS, IIEF, and Doppler parameters among different study groups

| Variables | TPV  | PZV  | TZV  | TZI  | CZV  |
|-----------|------|------|------|------|------|
|           | r    | P-value | r    | P-value | r   | P-value | r   | P-value |
| Group A   |      |        |      |        |      |         |      |         |
| IPSS      | 0.18 | .34   | -0.83 | .001* | 0.78 | .028    | 0.71 | .014    | 0.16 | .51    |
| IIEF      | -0.154 | .221 | 0.876 | .001* | -0.66 | .038 | -0.48 | .03*    | 0.006 | .97    |
| Doppler parameters |      |        |      |        |      |         |      |         |
| PSV       | -0.239 | .331 | 0.742 | .001  | -0.61 | .01   | -0.62 | .04     | 0.112 | .63    |
| EDV       | 0.336 | .148 | 0.136 | .568  | 0.193 | .416  | 0.05  | .833    | 0.16  | .51    |
| RI        | 0.325 | .162 | 0.046 | .848  | 0.392 | .087  | 0.043 | .856    | 0.29  | .22    |
| Group B   |      |        |      |        |      |         |      |         |
| IPSS      | 0.18 | .445  | -0.93 | .001  | 0.56  | .02    | 0.491 | .03     | 0.028 | .625   |
| IIEF      | 0.044 | .722  | 0.11  | .638  | -0.26 | .274  | -0.065 | .786    | -0.29 | .72    |
| Doppler parameters |      |        |      |        |      |         |      |         |
| PSV       | -0.17 | .467  | 0.11  | .656  | 0.005 | .982  | 0.035 | .872    | 0.136 | .569   |
| EDV       | 0.07  | .762  | 0.354 | .126  | 0.3   | .198  | 0.27  | .247    | 0.41  | .176   |
| RI        | 0.148 | .533  | 0.284 | .226  | 0.04  | .884  | 0.05  | .821    | 0.43  | .159   |
| Group C   |      |        |      |        |      |         |      |         |
| IPSS      | -0.18 | .438  | .034  | .11   | -0.16 | .411  | 0.05* | .821    | -0.17 | .471   |
| IIEF      | -      | -      | -      | -      | -      | -      | -      | -       |
| Doppler parameters |      |        |      |        |      |         |      |         |
| PSV       | -0.145 | .484  | 0.19  | .032  | 0.045 | .762  | 0.012 | .822    | 0.036 | .769   |
| EDV       | 0.08  | .962  | 0.021 | .826  | 0.23  | .212  | 0.27  | .247    | 0.11  | .77    |
| RI        | 0.167 | .542  | 0.264 | .626  | 0.06  | .814  | 0.05  | .821    | 0.21  | .159   |
| Group D   |      |        |      |        |      |         |      |         |
| IPSS      | -0.09 | .701  | 0.031 | .898  | 0.092 | .699  | 0.11  | .09     | 0.701 | .031   |
| IIEF      | -      | -      | -      | -      | -      | -      | -      | -       |
| Doppler parameters |      |        |      |        |      |         |      |         |
| PSV       | -0.13 | .435  | 0.22  | .234  | 0.012 | .982  | 0.035 | .872    | 0.127 | .523   |
| EDV       | 0.09  | .548  | 0.354 | .213  | 0.147 | .623  | -0.21 | .247    | 0.41  | .145   |
| RI        | 0.127 | .234  | 0.284 | .226  | 0.145 | .314  | 0.08  | .821    | 0.43  | .112   |

CZV = central zonal volume; EDV = end diastolic velocity; IIEF = international index of erectile function; IPSS = international prostate symptom score; PSV = peak systolic velocity; PZV = peripheral zonal volume; r = correlation coefficient; RI = resistive index; TPV = total prostate volume; TZI = transitional zonal index; TZV = transitional zonal volume. Bold indicates statistically significant difference. *P values are based on Spearman’s correlation coefficient. Statistical significance at P < .05.

Clinical, Laboratory, and Radiological Findings Among Study Groups

The median (IQR) of IPSS in groups A and B were 26 (22–30), 19 (16–22). There was a statistically significant difference between groups A and B (P < .05) Table 2. The median (IQR) of IIEF in the studied groups were 10 (9–11), 26 (25–27), 15 (13–17), 28 (27–29). There was a statistically significant difference among the study groups (P < .001) Table 2. There was no statistically significant difference in PSA among study groups (Table 2).

The median (IQR) of PZV in groups A, B, C, and D were 8 (6.3–11.8), 10 (7.3–12), 14 (13–15), and 16 (15–17), respectively. Groups C and D had significantly higher PZV than groups A and B (P < .001) Table 2, Figure 1(1-I & 1-II). The median (IQR) of TZV in groups A, B, C, and D were 20.2 (18–21.8), 16.7 (15–20.9), 8 (7–13), 5 (4–6.8). Groups A and B had significantly higher TZV than groups C and D (P < .001 for each) Table 2.
Association Between Prostate Measurements and IPSS, IIEF, and Doppler Parameters Among Study Groups

In group A, there was a significant negative correlation between PZV and IPSS ($r = -0.83$, $P < .001$) (Table 3 and Figure 2A). PZV has a significant positive correlation with IIEF ($r = 0.876$, $P < .001$) (Table 3 & Figure 2B), and PSV ($r = 0.742$, $P < .01$) (Table 3 & Figure 2C). There was a significant positive correlation between TZV and IPSS ($r = 0.78$, $P < .05$) (Table 3 & Figure 2D). TZV has a significant negative correlation with IIEF ($r = -0.66$, $P < .05$) (Table 3 and Figure 2E), and PSV ($r = -0.61$, $P < .05$) (Table 3 and Figure 2F). There was a significant positive correlation between TZI and IPSS ($r = 0.71$, $P < .05$), and a significant negative correlation with IIEF ($r = -0.48$, $P < .05$) and PSV ($r = -0.62$, $P < .05$) (Table 3). In group B, there was a significant negative correlation between IPSS and PZV ($r = -0.931$, $P < .01$). IPSS has a significant positive correlation with TZV ($r = 0.56$, $P < .05$), and TZI ($r = 0.491$, $P < .05$) (Table 3). Among group C and group D, there was no significant correlation between IIEF or penile Doppler parameters and prostate measurements ($P > .05$ for each) (Table 3).

**DISCUSSION**

BPH and ED commonly evolve as age-related phenomena in most men, initiating at approximately 40 years of age. Many hypotheses have been proposed to explain the association between ED and BPH/LUTS. Although relationship between prostate zonal volume and ED is not well understood, the pathophysiologic mechanisms of ED in men with BPH/LUTS are relatively well defined (autonomic hyperactivity, pelvic ischemia, rho-kinase pathway activation, etc.). The main objective in the present study was to evaluate the association between prostate zonal volume and erectile function in patients with BPH/LUTS independent of medical comorbidities and vascular risk factors.

Hence, BPH was suggested as a component of the metabolic syndrome and that the underlying cause of BPH might be systemic rather than local. In the present study, there was an association between ED and/or BPH/LUTS and having chronic illnesses such as hypertension, diabetes mellitus, and ischemic heart disease.

Prostatic anatomical factors rather than TPV were the focus of interest of several previous studies to investigate their effect on BPH/LUTS, symptom severity, and maximum flow rate. Previous studies have indicated that the correlation between TPV and LUTS severity is relatively modest. Therefore, researchers have searched for other prostatic anatomical factors, such as TZV, TZI, intravesical prostatic protrusion, and prostatic urethral angulation, which may be more associated with dynamically confirmed obstruction than TPV.

It is well known that BPH develops in the transitional zone of the prostate. Thus, several studies have focused on the TZV and TZI and indicate that the TZV may be more strongly associated with LUTS and the response to therapy than the TPV. However, these findings were not consistent throughout the literature. Kaplan et al reported that the TZI is highly correlated with both clinical symptoms and objective parameters such as uroflowmetry parameters and bladder function regardless of the TPV or TZV. In reverse to that result, a more recent study had demonstrated that TZI could not be directly correlated with any of the different parameters in patients with obstruction and retention, rendering the clinical value of such an index questionable.

In the present study, mean TPV in patients with BPH/ED was 41.5 which was positively correlated with mean IPSS and was negatively correlated with IIEF-5. Patients in groups C and D had no storage or voiding symptoms; thus, their IPSS was considered zero. Previous study reported that the IIEF-5 score was inversely proportional to the TPV. However, that study had not assessed the effect of the zonal anatomy of prostate on penile vascular parameters or ED severity. Another study had shown that whole prostate, central gland, and PZV were correlated with age, IPSS, and sexual health inventory for men scores. That study was relied upon magnetic resonance imaging, which may be more accurate to make the measurements of the prostate than TRUS. Furthermore, another study had demonstrated that there was a significant association between presence of LUTS and arteriogenic and neurogenic causes of ED, poor response to intracorporeal injection, poor rigidity in the rigidometer, and low PSV.

In the present study, mean PZV was 8 mm and mean IPSS was 26 in patients with BPH and ED. Mean PZV was 10 mm and mean IPSS was 19 in patients with BPH only. Furthermore, when the means of TZV and TZI were increased, the mean IPSS was also increased while the means of IIEF and PSV were decreased. The mean PZV had a negative correlation with IPSS and a positive correlation with IIEF. Of patients with BPH and ED, most of the patients had PZV less than 8 ml, TZV more than 20 ml, and TZI more than 40%. This means that enlargement of the TZV may negatively affect PSV and erectile function while the increase in PZV does not have this negative effect. The difference in IPSS between group A and group B may also be explained by adding the negative effect of ED in BPH patients. However, in groups A and B, the difference in TZV and PZV was not significant and cannot be clearly correlated with IIEF score.

As an explanation of the effect of zonal anatomy changes in BPH and its reflection on erectile function, several basic researches had shown that BPH begins in the submucosal layer of the TZ around the proximal urethra. Consequently, proliferation of epithelial cells of the acini, ductules, smooth muscle, and stromal fibroblasts occur, so TZV will increase. As a result of TZV enlargement, the central prostate is causing compression of the peripheral zone resulting in decrease in PZV. Ultimately,
increased urethral resistance results in compensatory changes in bladder function. These anatomic factors that can occur with alteration in zonal volume of the prostate could impinge on local nerves or blood supply to the erectile tissue.

In consistent with our results, a recent study had shown that, as the PZV became smaller, all urinary symptom scores including IPSS, quality of life, and over active bladder symptoms score were significantly increased. In the present study, we used a prospective study design and standardized diagnostic tools performed by one operator for assessment of prostatic zonal anatomy and penile vasculature of erection to minimize the bias and to enhance the reliability of the study results.

Our aim was to find out if there was an association between BPH/LUTS and ED and ultimately to determine the impact of zonal anatomy on the pathophysiology of both conditions. A potential limitation of the present study was the relatively small number of patients in each subgroup. Although the causality relation in this study was not approved, however, the present study may denote a base for future prospective large-scale studies to address the impact of prostate zonal

Figure 2. Scatterplot for correlation between prostate zonal volume and IPSS, IIEF, and PSV. IPSS = international prostate symptom score; PSV = peak systolic velocity; PZV = peripheral zonal volume; TZV = transitional zonal volume.
volume on vascular impairment of erection in patients with BPH/LUTS.

CONCLUSION
This study clearly demonstrated that there were significant correlations between increased TZV, TZI, and decreased both of IIEF score and PSV. There was a negative impact of alteration in zonal anatomy of the prostate on erectile function in patients with BPH/LUTS-associated ED.

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