Original Article

Relation of baseline prostate volume to improvement of lower urinary tract symptoms due to tamsulosin monotherapy in benign prostatic hyperplasia: An exploratory, multicenter, prospective study

Mahmoud Shoukry El-Adawy, Ahmed Yehia Abdelaziz[1], Ahmed Salem[1], Waseem Aboul Ela[1], Ayman Salah Moussa[2], Rabee Ibrahim[2], Fouad Zanaty[3], Mohamed H. Abdelhamid[1], Hussien Aldaqadossi, Ahmed M Ragheb[2], Hossam A. Shaker, Sameh Kotb[1]

Department of Urology, Fayoum University, Fayoum, [1]Department of Urology, Cairo University, Cairo, [2]Department of Urology, Beni-Suef University, Beni-Suef, [3]Department of Urology, Menoufia University, Menoufia, Egypt

Abstract

Aims: The aim of the study was to investigate the relation between baseline prostate volume (PV) and the improvement of lower urinary tract symptoms (LUTS) induced by tamsulosin monotherapy after 2-year follow-up in Egyptian benign prostatic hyperplasia (BPH) patients.

Settings and Design: This was a prospective comparative multicenter study.

Subjects and Methods: Three hundred and eighty-one BPH patients were included in the study from January 2014 to January 2017. The patients were divided according to their PV into two groups. Group A included patients with small-sized prostate (≤40 ml) and Group B included those with PV larger than 40 ml. Full evaluation was done at presentation. The patients are followed up at 6, 12, and 24 months of continued medical treatment with tamsulosin 0.4 mg once daily.

Statistical Analysis Used: Data were coded and entered using the Statistical Package for the Social Sciences version 24. Data were summarized using mean and standard deviation in quantitative data. Comparisons between quantitative variables were done using unpaired *t*-test or the nonparametric Mann–Whitney test. A comparison between paired measurements in the same person was done using paired *t*-test (Chan, 2003). $P < 0.05$ was considered as statistically significant.

Results: The mean age was 60.1 ± 7.2 years. The mean value of the International Prostate Symptom Score (IPSS) was recorded for the 381 patients at presentation. In Group A, the mean value of IPSS was 20.44 ± 3.18, whereas in Group B, the mean value of IPSS was 21.23 ± 3.5. There was a significant improvement in symptoms (Q_{max}-IPSS) in both groups, but we found that this improvement was significantly better in Group A ($P = 0.017$).

Conclusions: PV is an important prognostic factor affecting the improvement of the LUTS by α1-blocker monotherapy. Tamsulosin monotherapy may not be enough for large prostate (>40 mg) to maintain adequate symptom relief, and it is better to start with other medical options such as combined therapy

Address for correspondence: Dr. Sameh Kotb, Department of Urology, Cairo University, Cairo, Egypt.
E-mail: dr_samehkotb@kasralainy.edu.eg

Received: 15.06.2019, **Accepted:** 20.01.2020, **Published:** 17.07.2020

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/UA.UA_91_19

How to cite this article: El-Adawy MS, Abdelaziz AY, Salem A, Ela WA, Moussa AS, Ibrahim R,*et al*. Relation of baseline prostate volume to improvement of lower urinary tract symptoms due to tamsulosin monotherapy in benign prostatic hyperplasia: An exploratory, multicenter, prospective study. Urol Ann 2020;12:271-5.

or early nonmedical therapy. Starting α1-blocker monotherapy in smaller prostates may be of benefit in symptomatic patients without considering watchful waiting.

Keywords: Benign prostatic hyperplasia, lower urinary tract symptoms, prostate volume, tamsulosin monotherapy

INTRODUCTION

In old men, benign prostatic hyperplasia (BPH) is the most common disease. It is associated with lower urinary tract symptoms (LUTS) that may interfere with everyday activities.[1] Moreover, long-term consequences may happen including urinary tract infections, deterioration of bladder function, acute urinary retention (AUR), and the need for surgical intervention.[2]

Pharmacological therapy for BPH includes α1-blockers and 5 alpha reductase inhibitors. α1-blockers are well established for the management of LUTS in elderly men with BPH. Tamsulosin is the most widely used α1-blocker in Egypt. Some studies show that α1-blockers can decrease the International Prostate Symptom Score (IPSS) by approximately 30%–40% and increase Q_{max} by approximately 20%–25%.[3,4]

The relation of prostate volume (PV) to BPH/LUTS complex has been always an interesting field to explore. Some studies suggested that improvement of LUTS by α1-blockers in BPH patients may seem to be better with smaller prostates (<40 mL) in longer term studies, whereas larger prostates (>40 ml) may have not the same good improvement.[5-9] Tamsulosin monotherapy is offered to small prostates patients and also can be offered to larger prostates, but it is enough in larger prostates. Our aim was to study the relation between baseline PV and the improvement of LUTS on α1-blocker monotherapy after long period (2 years) follow-up in both small and large prostates. We believe that this may be beneficial in better planning of medical treatment of BPH patients according to PV at presentation.

SUBJECTS AND METHODS

This prospective comparative study was done at four different medical centers between January 2014 and January 2017.

Informed consent

Informed consent was signed in each case after explaining the nature of the disease, the risks, and potential benefits of the study.

All patients were subjected to full history taking including IPSS, physical examination including digital rectal examination, laboratory investigations in the form of total and free prostate-specific antigen (PSA), urine analysis, urine culture, and renal function tests (urea and creatinine) and radiological investigations in the form of abdominopelvic ultrasound, transrectal ultrasound, and uroflowmetry.

Patients were divided according to their PV into two groups. Group A (210 patients) included patients with small-sized prostate (≤40 ml) and Group B (171 patients) included those with PV larger than 40 ml. The evaluation is repeated after 6, 12, and 24 months of continued medical treatment with tamsulosin 0.4 mg once daily. Results at 24 months are recorded and statistically analyzed.

Patients aged <50 years, serum PSA level above 4 ng/dl, good uroflow with Q_{max} above 15 ml/s, or accompanying lower urinary tract disease (e.g., Infections, calculi, and tumors) were excluded from the study.

Statistical analysis was done using data which were coded and entered using the Statistical Package for the Social Sciences version 24 (IBM corp., Armonk, NY, USA). Data were summarized using mean and standard deviation in quantitative data. Comparisons between quantitative variables were done using unpaired *t*-test or the nonparametric Mann–Whitney test.

A comparison between paired measurements in the same person was done using paired *t*-test (Chan, 2003). $P < 0.05$ was considered as statistically significant.

Ethical committee approval

This study was approved by the local ethical committee.

RESULTS

This study included 501 patients, but 21 patients were excluded as they developed AUR during the 2-year follow-up period, although of their medical treatment. Another 99 patients were lost during follow-up.

Three hundred and eighty-one Egyptian male BPH patients with a mean age of 60.1 ± 7.2 years completed the 2

years follow up period. The mean size of the prostate was 47.84 ± 16.2 g. The mean value of IPSS was recorded for the 381 patients at presentation. In Group A, the mean value of IPSS was 20.44 ± 3.18, whereas in Group B, the mean value of IPSS was 21.23 ± 3.5. This shows statistically significant higher baseline IPSS values in Group B compared to Group A ($P = 0.022$). After 2 years of medical treatment, IPSS was recorded again, and the mean value of IPSS in Group A was 11.98 ± 2.88, whereas in Group B, the mean value of IPSS was 13.5 ± 3.32. Again, this was statistically significant higher (worse) IPSS values in Group B compared to those of Group A ($P < 0.001$) after 2 years of therapy. Uroflowmetry was done for the 381 patients at presentation. In Group A, the value of Q_{max} varied from 5 to 14.2 ml/s with the mean value of 9.54 ± 2.0 ml/s, whereas in Group B, Q_{max} varied from 5 to 14.5 ml/s with the mean value of 9.71 ± 2.21 ml/s. There was no statistically significant difference between baseline Q_{max} values in both groups ($P = 0.41$). After 2 years of medical treatment, uroflowmetry was done again, and the value of Q_{max} in Group A varied from 7.5 to 21 ml/s with the mean value of 15.57 ± 2.58 ml/s, whereas in Group B, the value of Q_{max} varied from 7.5 to 22 ml/s with the mean value of 15.12 ± 3.17 ml/s.

Again, there was no statistically significant difference Q_{max} values after 2 years of treatment in both groups ($P = 0.41$) [Table 1].

Finally, improvement in IPSS values after 2-year follow-up was calculated in each group of patients. In Group A, the mean value of improvement was 8.46 ± 4.05, whereas in Group B, the mean value of improvement was 7.74 ± 3.88. By comparing the improvement of both groups statistically, it showed better improvement in IPSS in Group A ($P = 0.017$).

Improvement in Q_{max} values after 2-year follow-up was calculated in each group of patients. In Group A, the mean value of improvement was 6.03 ± 3.04 ml/s, whereas in Group B, the mean value of improvement was 5.40 ± 3.19 ml/s. This was statistically significant when comparing both groups in favor of Group A ($P = 0.010$) [Table 2].

DISCUSSION

Many studies were done to investigate the importance of prostate size as a prognostic factor in determining the outcome in patients with prostatic obstruction in BPH disease complex. Its relation to several factors as prostate growth, volume, symptoms, or complications of the BPH disease was studied several times.[5-9] It is important to investigate baseline factors that influence outcomes for men with BPH on medical therapy; this may help to improve outcomes and cost-effectiveness and may be beneficial for the prevention of future adverse outcomes such as AUR and urosepsis.

While it has been shown that increased PV is a predictor of LUTS/BPH progression in symptomatic men,[10-12] it has yet to be determined whether prostate size predicts improvement of LUTS symptoms and flowmetry in men with BPH symptoms on medical treatment.

We performed this study to predict the effect of prostate size on improvement of urinary symptoms on the long run after 2 years of treatment with α1-blockers so that we can alter medical treatment according to initial PV and predict patients who may need surgical intervention due to failed medical treatment.

Overall, among men treated with α1-blockers, decreased PV was associated with a better improvement of IPSS and urine flowmetry after 2 years. This was evident in men with a smaller prostate size (≤40 ml). These findings suggest that PV may predict the result of medical treatment (alpha-blocker in BPH).

Prior studies have shown conflicting results when correlating total PV to LUTS severity, with some studies showing no correlation and others showing very weak correlation.[13,14] Yet, these studies were concerned mainly in relation between baseline PV and baseline LUTS,

Table 1: Summarized results of both groups

	Mean±SD		*P*
	Group A (prostate size <40)	Group B (prostate size >40)	
Total PSA at presentation	1.51±0.76	1.59±0.82	0.507
Symptom score at presentation	20.44±3.18	21.23±3.50	0.022
Ultrasound prostate size at presentation	33.73±4.48	61.41±16.38	<0.001
Uroflow Q_{max} at presentation (ml/s)	9.54±2.00	9.71±2.21	0.410
Symptom Score after 2 years	11.98±2.88	13.50±3.32	<0.001
Ultrasound prostate size after 2 years	40.81±9.62	62.94±17.14	<0.001
Uroflow Q_{max} after 2 years (ml/s)	15.57±2.58	15.12±3.17	0.128

PSA: Prostate-specific antigen, SD: Standard deviation

Table 2: Improvement in International Prostate Symptom Score and urine flow in both groups

	Mean±SD		*P*
	Group A (prostate size <40)	Group B (prostate size >40)	
Improvement in symptoms score	8.46±4.05	7.74±3.88	0.017
Improvement in urine flow (ml/s)	6.03±3.04	5.40±3.19	0.010

SD: Standard deviation

whereas our study is concerned with relation of baseline PV and improvement of LUTS due to treatment. In a cohort selected from the Olmsted County study of urinary symptoms and health status among men, even increasing central-zone PV was only weakly correlated with IPSS and peak urinary flow rate.[13]

While this lack of correlation between PV and LUTS severity argues against the effect of a growing prostate leading to urinary complications, several studies have highlighted the relationship between increased PV and LUTS/BPH progression in symptomatic individuals.[10-12,15] Of note, in the Olmsted County study of urinary symptoms and health status among men, those with a PV >30 ml were more than twice as likely to receive treatment for BPH.[12]

A secondary analysis of the placebo arm of three randomized finasteride trials demonstrated that men with a prostate size ≥40 ml were twice as likely to develop AUR at 2 years compared to men with prostate size <40 ml.[11] In addition, a secondary analysis of the Medical Therapy of Prostatic Symptoms trial, which limited enrollment to men with IPSS ≥8, demonstrated that in the placebo arm, prostate size of ≥31 ml was a significant predictor of clinical BPH progression, defined as an increase in IPSS of ≥4, AUR, urinary incontinence, renal insufficiency, or recurrent urinary tract infection.[10]

In the literature on the role of prostate size in predicting IPSS progression (one occurrence of IPSS >7 in men with IPSS ≤7 in the previous round) in men with mild to no symptoms, the Krimpen study found that prostate size was a predictor of incident IPSS progression in univariable analysis, but not multivariable analysis.[16] However, the study revealed that variables such as PSA are predictive of IPSS progression. Furthermore, while there is a correlation between prostate size and PSA, PSA is also a marker for inflammation and is not a pure surrogate for PV.[17]

Our findings suggest that the question of whether or not there is clinical utility in being able to predict symptomatic improvement after α1-blockers in a man with BPH must be discussed. First, and most importantly, such a prediction could potentially allow for closer follow-up in a man who perhaps would not normally be followed for LUTS/BPH because of few current symptoms.

Our study aimed to examine baseline PV as a prognostic factor affecting the efficiency of tamsulosin monotherapy to improve LUTS with long follow-up. Our results showed that after 2 years of medical treatment for BPH, patients with smaller prostates at presentation had better-maintained improvement in IPSS and urine flow on tamsulosin compared to larger prostates.

This may justify offering larger prostates cases altered medical treatment from the start, for example, offer routine combined therapy or encouragement of early intervention. Moreover, this may justify starting a-blockers as early as possible with smaller prostate at presentation without considering conservative therapy.

Regarding limitations of our study, while it is possible that the increase in LUTS is attributed to BPH, we cannot rule other factors, such as bladder dysfunction, as the cause of the observed increase in IPSS. We also could not exclude all cofounders of incident LUTS such as baseline peripheral or central nervous system abnormalities, or detrusor instability, which was not measured in this study.

Another limitation of our study is the prostate shape and specifically the presence of an intravesical protrusion or middle lobe may accelerate symptom severity. We have no data to support or refute these hypotheses as the shape was not recorded.[18,19]

Despite these limitations, our study has a key strength that prior studies did not stress on investigating symptomatic improvement with tamsulosin alone; they usually studied combinations with 5 alpha reductases or 5 alpha reductases alone.

CONCLUSIONS

PV is an important prognostic factor affecting the improvement of the LUTS by α1-blocker monotherapy. Tamsulosin monotherapy may not be enough for large prostate (>40 mg) to maintain adequate symptom relief, and it is better to start with other medical options such as combined therapy or early nonmedical therapy. Starting α1-blocker monotherapy in smaller prostates may be of benefit in symptomatic patients without considering watchful waiting.

Financial support and sponsorship
Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Girman CJ, Epstein RS, Jacobsen SJ, Guess HA, Panser LA, Oesterling JE, *et al*. Natural history of prostatism: Impact of urinary symptoms on quality of life in 2115 randomly selected community men. Urology 1994;44:825-31.
2. Barry MJ, Fowler FJ Jr, Bin L, Pitts JC 3rd, Harris CJ, Mulley AG Jr. The natural history of patients with benign prostatic hyperplasia as diagnosed by North American urologists. J Urol 1997;157:10-4.
3. Djavan B, Fong YK, Harik M, Milani S, Reissigl A, Chaudry A, *et al*. Longitudinal study of men with mild symptoms of bladder outlet obstruction treated with watchful waiting for four years. Urology 2004;64:1144-8.
4. Michel MC, Mehlburger L, Bressel HU, Goepel M. Comparison of tamsulosin efficacy in subgroups of patients with lower urinary tract symptoms. Prostate Cancer Prostatic Dis 1998;1:332-5.
5. McConnell JD, Roehrborn CG, Bautista OM, Andriole GL Jr., Dixon CM, Kusek JW, *et al*. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003;349:2387-98.
6. Boyle P, Robertson C, Manski R, Padley RJ, Roehrborn CG. Meta-analysis of randomized trials of terazosin in the treatment of benign prostatic hyperplasia. Urology 2001;58:717-22.
7. Roehrborn CG. Three months' treatment with the alpha1-blocker alfuzosin does not affect total or transition zone volume of the prostate. Prostate Cancer Prostatic Dis 2006;9:121-5.
8. Roehrborn CG, Siami P, Barkin J, Damião R, Major-Walker K, Morrill B, *et al*. The effects of dutasteride, tamsulosin and combination therapy on lower urinary tract symptoms in men with benign prostatic hyperplasia and prostatic enlargement: 2-year results from the CombAT study. J Urol 2008;179:616-21.
9. Roehrborn CG, Siami P, Barkin J, Damião R, Major-Walker K, Nandy I, *et al*. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. Eur Urol 2010;57:123-31.
10. Crawford ED, Wilson SS, McConnell JD, Slawin KM, Lieber MC, Smith JA, *et al*. Baseline factors as predictors of clinical progression of benign prostatic hyperplasia in men treated with placebo. J Urol 2006;175:1422-6.
11. Marberger MJ, Andersen JT, Nickel JC, Malice MP, Gabriel M, Pappas F, *et al*. Prostate volume and serum prostate-specific antigen as predictors of acute urinary retention. Combined experience from three large multinational placebo-controlled trials. Eur Urol 2000;38:563-8.
12. Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, *et al*. Treatment for benign prostatic hyperplasia among community dwelling men: The Olmsted County study of urinary symptoms and health status. J Urol 1999;162:1301-6.
13. Corica FA, Jacobsen SJ, King BF, Bostwick DG, Jacobson DJ, Girman CJ, *et al*. Prostatic central zone volume, lower urinary tract symptom severity and peak urinary flow rates in community dwelling men. J Urol 1999;161:831-4.
14. Barry MJ, Cockett AT, Holtgrewe HL, McConnell JD, Sihelnik SA, Winfield HN. Relationship of symptoms of prostatism to commonly used physiological and anatomical measures of the severity of benign prostatic hyperplasia. J Urol 1993;150:351-8.
15. Emberton M, Andriole GL, de la Rosette J, Djavan B, Hoefner K, Vela Navarrete R, *et al*. Benign prostatic hyperplasia: A progressive disease of aging men. Urology 2003;61:267-73.
16. Kok ET, Schouten BW, Bohnen AM, Groeneveld FP, Thomas S, Bosch JL. Risk factors for lower urinary tract symptoms suggestive of benign prostatic hyperplasia in a community based population of healthy aging men: The Krimpen Study. J Urol 2009;181:710-6.
17. Jung K, Meyer A, Lein M, Rudolph B, Schnorr D, Loening SA. Ratio of free-to-total prostate specific antigen in serum cannot distinguish patients with prostate cancer from those with chronic inflammation of the prostate. J Urol 1998;159:1595-8.
18. Lee LS, Sim HG, Lim KB, Wang D, Foo KT. Intravesical prostatic protrusion predicts clinical progression of benign prostatic enlargement in patients receiving medical treatment. Int J Urol 2010;17:69-74.
19. Wang D, Huang H, Law YM, Foo KT. Relationships between prostatic volume and intravesical prostatic protrusion on transabdominal ultrasound and benign prostatic obstruction in patients with lower urinary tract symptoms. Ann Acad Med Singapore 2015;44:60-5.