Profile of Prostatectomy Cases

Prostatektomi Yapılan Olguların Profili

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ABSTRACT Objective: To define the clinical and demographic features of the patients who underwent prostatectomy and find out current trends in treatment of lower urinary tract symptoms (LUTS) before prostatectomy. **Material and Methods:** Data were collected using questionnaires filled by hospitalized patients and urologists. Data of 102 primary cases were analyzed and presented in this study. **Results:** Median age of the patients was 68 (46-90) years. Among all, 49% of the patients underwent surgery in the first 4 years after the beginning of LUTS. Acute urinary retention (AUR) was the indication for surgery in 34.3% of the cases, and the rest were operated due to high International Prostate Symptom Score (IPSS). Preoperatively, nocturia (34.3%) was the most bothersome symptom followed by frequency (29.4%). Although 58.8% of the cases had a preoperative prostate specific antigen (PSA) value above 2.5 ng/mL, only 27.3% of the patients had a biopsy. Prescription history of α-blockers, 5α-reductase inhibitors (5ARI) and combination of them at any time before surgery were 74.6%, 12.8% and 4.9%, respectively. In the statistical analysis; AUR was found to be correlated with a large prostate volume (Vp), high PSA, and combination of prostatic inflammation with benign prostatic hyperplasia in the prostatectomy pathology report ($p<0.05$). According to the International Index of Erectile Function (IIEF-5) questionnaire, only 15.6% of the cases had no erectile disfunction (ED) (score 22-25) preoperatively. Age had a negative correlation with IIEF-5 scores ($p<0.05$). **Conclusion:** The leading indication for prostatectomy was high IPSS. Most bothersome symptom was nocturia. Preoperative rates for biopsy, prescription of 5ARI, and combination treatments was lower than expected. ED was common, and increased with age. Large Vp, high PSA, and prostatic inflammation were related with AUR.

Key Words: Lower urinary tract symptoms; prostatectomy; therapy

ÖZET Amaç: Alt üriner sistem semptomları nedeniyle prostatektomi yapılan olguların klinik ve demografik özelliklerini ve prostatektomi öncesi bu olguların tedavisindeki güncel yaklaşımları saptamak. **Gereç ve Yöntemler:** Hastalar ve servis doktorları tarafından doldurulan formlar aracılığı ile veri toplanmıştır. Bu çalışmada 102 primer olgunun verileri analiz edilmiştir. **Bulgular:** Olguların median yaşları 68 (46-90) yıldır. Olguların %70'inin yakınmalar başladıktan sonra ilk dört yıl içinde opere edildiği gözlenmiştir. Olguların %34,3'ünün tekrarlayan akut üriner retansiyon, diğerlerinin ise yüksek Uluslararası Prostat Semptom Skoru (IPSS) nedeni ile opere edildiği görülmüştür. En çok yakınılan semptomlar %34,3 ile noktüri ve %29,4 ile pollaküridir. Preoperatif 2,5 ng/mL üzerinde prostat spesifik antijen (PSA) değeri olan olgu oranı %58,83 iken, preoperatif biyopsi yapılan olgu oranı %27,3'te kalmıştır. Özgeçmişinde sırası ile α-bloker, 5α redüktaz inhibitörü ve kombine tedavi kullanımı öyküsü olan olgu oranı sırasıyla %74,6, %12,8 ve %4,9 olarak bulunmuştur. Yapılan istatistiksel analizde, AUR; büyük prostat hacmi, yüksek PSA ve patolojik incelemede benigh prostat hiperplazisi ve inflamasyonun birlikteliği ile ilişkili bulunmuştur ($p<0,05$). Preoperatif değerlendirmede, Uluslararası Erektil Fonksiyon İndeksine (IIEF-5) göre olguların sadece %15,6'sının erektil disfonksiyonu (ED) yoktur. Yaş ile IIEF-5 skoru arasında negatif korelasyon saptanmıştır ($p<0,05$). **Sonuç:** Önde gelen prostatektomi endikasyonu yüksek IPSS skorudur. En çok yakınılan semptom noktüridir. Preoperatif biopsi oranı, 5α redüktaz inhibitörü ve kombine tedavi kullanım oranı beklenenden düşüktür. ED bu hasta grubunda yaygındır ve yaşla artmaktadır. Büyük prostat, yüksek PSA ve prostatik inflamasyon, AUR ile ilişkilidir.

Anahtar Kelimeler: Alt üriner sistem semptomları; prostatektomi; tedavi

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Lower urinary tract symptoms (LUTS) are common in aging men. Benign prostatic hyperplasia (BPH) is one of the factors that contribute to LUTS. Currently, treatment of LUTS suggestive of BPH is almost uniquely defined, and recommendations by several guidelines have only minor differences.[1-3] Treatment indications and options are mostly recommended according to trials and/or studies on LUTS, rather than traditional practices.[1-3] On the other hand, the data from real life practice are limited, and the effect of geographical and cultural differences on treatment practices and guideline compliances are not clearly known.[4,5] In addition, symptoms and degree of suffering from LUTS may vary considerably between cultures and countries.[6-8]

The aim of this study was to define the clinical and demographic features of the patients who underwent prostatectomy, and to find out current trends in treatment of LUTS before prostatectomy by examining the data of a referral center of a Turkish university hospital.

MATERIAL AND METHODS

The study group consisted of 102 consecutive patients hospitalized for prostatectomy in Gazi University hospital due to LUTS, suggestive of BPH. Only primary cases were included to the study.

Data were collected by questionnaires filled by hospitalized patients, under the supervision of urologists and nurses in the related departments. Along with International Prostate Symptom Score (IPSS) and International Index of Erectile Function (IIEF-5) questionnaires, a standard form created for this study was used to record history, symptoms, physical examination, laboratory and radiological findings, comorbidities, previous drugs used for LUTS, and most distressing symptom as stated by the patients.[9,10] Only preoperative data was presented in this study.

Ten urologists treated these patients.

As there were some missing data due to unanswered questions and unrecorded parameters, percentages were used for presenting the data. The numbers in the brackets are the actual number of the events that are used in calculations.

Descriptive statistics were presented by frequencies, percent and median (minimum, maximum) values. Categorical data were compared using Pearson Chi-square test. Continuous data were tested for normality using histograms, p-p plots, and Kolmogorov Smirnov test. Since the variables were not normally distributed, the continuous variables were compared between two groups using Mann Whitney U test. Spearman's Correlation (Rho) Test was used for evaluating the correlation of continuous variables. All comparisons were made for a two-tailed significance level of 0.05.

This study complies with Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects.

RESULTS

AGE

The median age was 68 (46-90) years. Of the patients, 89.3% (n=86) cumulated between 55-84 years of age, and 65-74 age group was the most crowded (39.3%, n=37) group. Age distribution is shown in Figure 1.

Aging was negatively correlated with IIEF-5 score (r=-0.638, p=0.001). Aging also had a positive correlation with preoperative creatinine level (r=0.22, p=0.030). There was no correlation between aging and total IPSS score, prostate volume (Vp), preoperative prostate specific antigen (PSA) value, postvoiding residual urine volume (PVR), preoperative maximum flow rate (Qmax) and acute urinary retention (AUR).

LUTS

Median timespan between beginning of LUTS and prostatectomy was 2 (0.1-15) years. Among all, 49% (n=50) of the cases were operated in the first 4 years, and 90.2% (n=92) were operated in the 7 years after beginning of LUTS. LUTS duration was not found to be related with IPSS score, PVR, PSA, Vp or IIEF-5 score (p>0.05). In addition, there was no statistically significant relation between LUTS duration and AUR (p>0.05).

The most distressing symptom was nocturia. Nocturia frequency of patients is shown in Figure

2. Nocturia was selected as the most distressing symptom by 34.3% (n=35) of the cases, and it was followed by frequency (29.4%, n=30), urgency (7.8%, n=8), dysuria (5.9%, n=6), and a sense of incomplete emptying (4.9%, n=5).

Nocturia had a correlation with preoperative PVR (r=0.27 p=0.034), but with no other clinical or laboratory parameters.

According to IPSS, most of the cases were either moderately (36.8%, n=35) or severely (57.9%, n=55) symptomatic (Figure 3).

PREVIOUS LUTS-RELATED DRUG TREATMENTS

Prescription history of α-blockers, 5α-reductase inhibitors (5ARI) and combination of them previously, before surgery were 74.6% (n=52), 12.8% (n=9), and 4.9% (n=5), respectively (Figure 4). Tamsulosin, doxazosin, alfuzosin and terazosin were used by 31.3% (n=32), 9.8% (n=10), 8.8% (n=9), and 0.9% (n=1) of the cases, respectively. Other α-blockers were on market in Turkey during the study period. The only drug combination used by the patients was tamsulosin and dutasteride combination. Anticholinergics and phytothrapeutic drugs were not used by any of the patients.

LABORATORY AND CLINICAL FINDINGS

Most of the patients (88.2%, n=90) had normal serum creatinine levels (0.6-1.2 mg/dL). Serum creatinine levels were 1.2-2.0 mg/dL in 8.8% (n=9) of them, and the remaining 2.9% (n=3) had higher levels. As stated above, preoperative creatinine level had a positive correlation with aging (r=0.22, p=0.030).

Median preoperative PSA value was 3.6 (0,13-24) ng/mL. Among all, 58.8% (n=60) of the cases had PSA values over 2.5 ng/mL, 45.1% (n=46) had values over 4 ng/mL, and 18.6% (n=19) had values over 10 ng/mL. Preoperative PSA value was highly correlated with Vp (r=0.74, p=0.001).

Median Vp based on transrectal ultrasonography was 56 (15-290) mL. In 72.4% (n=71) of the cases, Vp was above 40 mL.

Preoperatively, 69.2%(n=45) of the patients had Qmax values lower than 10 mL/sec. Qmax was not correlated with age, preoperative PVR, PSA, Vp or IPSS.

Median preoperative PVR was 167.5 (0-1400) mL.

Preoperative transrectal ultrasound-guided prostate needle biopsy rate was 27.3% (n=27). Biop-

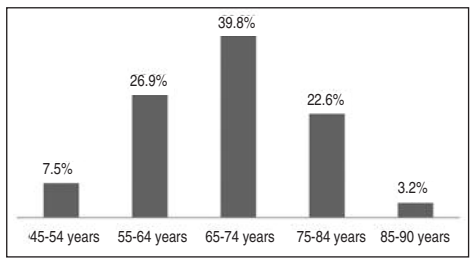

FIGURE 1: The age distribution of the patients.

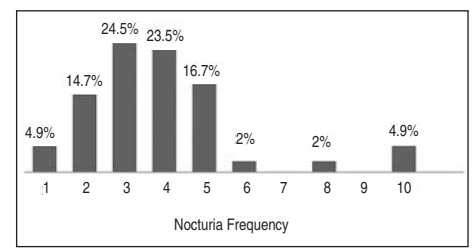

FIGURE 2: Frequency of nocturia.

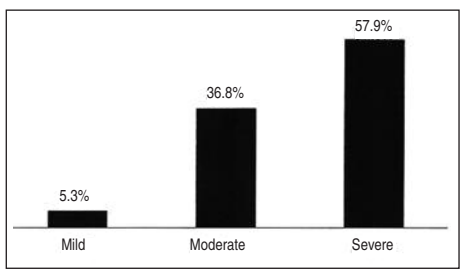

FIGURE 3: International Prostate Symptom Scores of the patients (1-7 mild, 8-19 moderate, 20-35 severe).

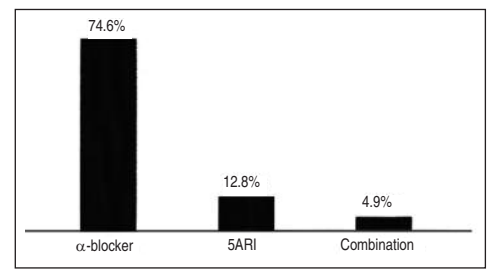

FIGURE 4: Previous lower urinary tract symptom-related medical therapies. 5ARI: 5α-reductase inhibitors.

sies revealed BPH in 92.5% (n=25), BPH with inflammation in 3.7% (n=1), and atypical small acinar proliferation in 3.7%(n=1) of the cases.

Only 15.6% (n=12) of the cases had IIEF-5 scores between 22-25 [no erectile dysfunction (ED)]. As stated before, age had a strong negative correlation with IIEF-5 score (r= -0.638, p=0.001).

Prostatectomy indication was recurrent AUR in 34.3% (n=35) of the patients. The rest of the cases were operated for high IPSS. None of the patients were recorded to have other absolute indications of prostatectomy (bladder stones, recurrent urinary tract infections, recurrent hematuria and dilatation of upper urinary tract due to BPH).

Monopolar transurethral prostatectomy (TURP) was the most frequent operation. While 75.5% (n=77) of the cases had TURP, 19.6% (n=20) had open prostatectomy and 1% (n=1) had transurethral prostatic incision. Of the cases, 3.9% (n=4) were not operated and discharged because of comorbidities. Postoperative pathologic examinations of the patients revealed BPH in 73.2% (n=71), BPH with inflammation in 24.7% (n=24), and BPH with prostatic adenocarcinoma in 2.1% (n=2) of the patients. Among patients who experienced AUR, 25.4% (n=18) had only BPH, and 50% (n=12) had BPH with prostatic inflammation. The difference was found to be statistically significant between these groups (p=0.025). It seems that prostatic inflammation may trigger AUR.

PSA levels were higher in the cases with AUR. Median PSA was 5.8 (0.1-24) ng/mL in the ones with AUR, while it was 2.9 (0.2-18) in the ones without AUR. Again, it was statistically significant (p=0.017).

In addition, the cases who experienced AUR had larger prostate volumes. Median Vp was 74 (16-280) mL in those with AUR while it was 52 (15-180) mL in those without AUR. The difference was statistically significant (p=0.028).

DISCUSSION

The results of this study gives us a chance to overview the spectrum of LUTS/BPH treatment in our country. To our knowledge, it is the first study on this context in our country. As prostatectomy is the final treatment option in LUTS due to BPH, we had an opportunity to observe all previous treatment modalities. One must keep in mind that, patients were operated in this single center, but previous treatments were administered by different urologists and even practitioners. Data collection is easier, better and more reliable in hospitalized patients. This gave us the chance to define the LUTS symptomatology leading to prostatectomy, and patient profile of prostatectomy cases in Turkey along with current local treatment practices.

When patient demographics are considered, the median age (68 years) of prostatectomy in this group of patients was not different from those reported elsewhere. In a recent database search of contemporary TURP series, the mean patient age was 67 years.[11] Older studies by Borboroglu et al. and Mebust et al. reported similar findings for the mean patient age.[12,13] This finding implies the fact that age distribution of patients who undergo prostatectomy for LUTS is more or less the same in different countries. In contrast to current literature, aging did not correlate with PSA levels in our study. It may be speculated that, young patients with big prostates (in 72.4% of the cases Vp was above 40 mL) is the reason for this finding.

Most bothering symptom was nocturia followed by daytime frequency in this group of patients who were hospitalized for prostatectomy. This was not surprising as a previous community-based study about prevalence of LUTS in Turkey had already found nocturia as the most prevalent symptom, followed by frequency.[8] It seems that, from the beginning of LUTS, nocturia is the most bothering symptom in Turkish patients. Actually, this finding is not different from other regions of the world. Studies from Japan, India, England and Austria, point to nocturia and frequency as the most common and most bothering symptoms of LUTS.[6,7,14,15] Nocturia, as a systemic disorder, is not a prostatectomy indication and has a different workup. Despite this, it seems that while operating for high IPSS score and failed medical treatment, prostatectomy may become an unintended treatment for nocturia in some patients.

Larger Vp may be the main difference of Turkish prostatectomy patients as the median Vp (56 mL) of the patients in this study was definitely larger than those reported in other series. In a recent analysis of 67 randomized controlled trials on TURP, the mean Vp was 47.6 mL and Borboroglu et al. reported mean Vp as 37.1 mL.[11,12] In TURP study of Mebust et al., 85% patients had prostates smaller than 45 mL.[13] Interestingly, Indian, Chinese, Japanese and American men were reported to have smaller prostates than the patients of this study.[6,16,17] There may be ethnic, genetic, behavioral and environmental reasons for Turkish men to have bigger adenomas than the others in the world. If this finding is confirmed by other studies with bigger scales, it may effect the treatment policies of LUTS in Turkey.

Most of our study group had some degree of ED. Not surprisingly, ED severity was increasing with aging. This finding correlates well with a previous Turkish ED prevalence study. Akkuş et al. reported the age-adjusted overall prevalence of ED in Turkey was 69.2%, and concluded that the frequency was increasing with age.[18] The underlying complex pathogenetic mechanisms linking BPH/LUTS to ED have been elegantly reviewed by Gacci et al., and the effect of age is stressed in article this as well.[19]

There was a rather low preoperative transrectal ultrasound-guided prostate needle biopsy rate in our patients. Currently, there is no universally accepted threshold to trigger a biopsy, but there is tendency to lower PSA threshold from classical 4 ng/mL to 2.5 ng/mL, especially in patients younger than 60 years of age.[20] When we look at the trend of our colleagues from this point of view, there was lower than expected biopsy rate, as 58.83% of the cases had PSA values over 2.5 ng/mL. There may be two explanations for this attitude. First is the larger Vp in these patients as stated above, and the second may be the percentage of patients over 65 years of age. Slightly more than 65% of the patients were 65 years old or older. It is known that there is a general tendency toward allowing older men (70 years or older) to have slightly higher "normal" PSAs, in the range of 5.5 to 6.5 ng/mL, although this is not universally accepted.[20]

Previous LUTS related treatments were another point of interest in this study. As stated before, these medical therapies were not necessarily given in the study clinic (i.e. Gazi University Hospital), therefore they represent a rather general opinion of our colleagues. Prescription history of α-blockers, 5ARI and combination of them at any time previously, before surgery were 74.6%, 12.8% and 4.9%, respectively. In a prospective, cross-sectional, observational survey in six European countries, α-blockers were prescribed in 57%, and finasteride was prescribed in 11% of the patients at any moment during the follow-up (including switches and combination of treatment).[4] Prescription rates are not similar, but close to each other, and especially 5ARI prescription trends resemble to each other. When our study group with larger Vps was considered, more 5ARI prescription was expected, but this was not seen in practice. MTOPS and CombAT studies have clearly shown the superiority of combination treatment, but in practice, the recommendations derived from these studies were not taken into consideration, as expected.[21,22] This was the case in other countries as well. Strope et al. stated that wide variations in evaluation and treatment were observed in practice in US Medicare population, and guideline compliance was not as expected.[23] This article discussed factors as awareness of the guideline, familiarity with the guideline recommendations, lack of agreement with the recommendations, poor self-efficacy for implementing guideline recommendations, inertia of previous practice, and a belief that the guideline would not improve patient outcomes; but in our case with drug use, more must be taken into consideration.[24] The side effects of 5ARI, like ED and ejaculation disorders, which are not easily accepted by younger patients may be important reasons.[25]

Prostatectomy indication was recurrent AUR in 34.3% (n=35) of the patients. The rest of the cases were operated for high IPSS. According to EAU guidelines on LUTS/BPH, severe symptoms is a relative indication for surgery, but EAU and AUA guidelines accept surgery as an option even in patients with moderate symptoms.[1,2] AUA guidelines

do not consider medical therapy as a requirement in all patients, and state that some patients may wish to pursue the most effective therapy as a primary treatment if their symptoms are particularly bothersome. Anyhow, it may be speculated that surgery is used more liberally used by our colleagues as relative indications dominated in prostatectomy decision of our cases.

Another point that must be stressed in this study is the relation of AUR with prostatic inflammation in prostatectomy specimens. It seems that prostatic inflammation triggers AUR, and patients with prostatic inflammation carry a higher risk for prostatectomy. This finding can be supported by several studies. A subanalysis of the MTOPS study suggested that inflammation detected in baseline prostatic biopsies was highly predictive of progression of BPH to AUR, and the need for more invasive therapy.[26] In addition, Mishra et al. and Asgari and Mohammadi pointed to the highly possible relation of prostatic inflammation with AUR.[27,28] The authors of this study aim to conduct a detailed pathological study of prostatectomy specimens for quantification of inflammation and its relation with severity of LUTS.

CONCLUSIONS

This study has given us a chance to overview the LUTS symptomatology and patient profile of prostatectomy cases in a Turkish University hospital,along with current local treatment practices. The leading indication for prostatectomy was high IPSS. The most bothersome symptom was nocturia. The rate s of preoperative biopsy, prescription of 5ARI, and combination treatments were lower than expected. ED was common in these cases and it was increasing with age. Large Vp, high PSA, and prostatic inflammation were related with AUR.

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