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ORIGINAL PAPER

Analysis of benign prostatic obstruction surgery: A long-term evaluation in a real-life context

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Summary

Objective: *Surgery is the treatment for male lower urinary tract symptoms (LUTS) related to benign prostatic obstruction (BPO) refractory to pharmacological treatment or with complications. This study aimed to assess factors associated with the need for surgical reintervention and/or continuation of pharmacological treatment.*
Materials and methods: *A retrospective analysis of patients who underwent prostatic surgery for male LUTS associated with BPO between 1 May 2015 and 1 May 2016, with a minimum follow-up of five years, in an academic tertiary hospital.*
The type of surgery, preoperative, postoperative and follow-up analysis were collected in a database.
Results: *A total of 212 patients were included with a mean age of 70 ± 8.66 years at five years follow-up. At 5 years, a total of 86.9% of patients do not need pharmacological treatment and 12% required surgical reintervention. Of the preoperative parameters, it was found a relationship between prior prostatitis and the need for second surgery with an odds ratio of 4.6.*
Conclusions: *Patients should be informed of the potential need for pharmacological treatment following surgery, or even of the need for reintervention. History of prostatitis seems to be a risk factor for reintervention.*

KEY WORDS: *Prostatic Hyperplasia; Quality of life; Transurethral resection of prostate; Prostatectomy.*

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INTRODUCTION

Male lower urinary tract symptoms, commonly known as male LUTS, are one of the most frequent reasons for contact with healthcare, namely with the urologist. Presence of LUTS has a negative impact on patients' quality of life (1). LUTS have historically been linked to *bladder outlet obstruction* (BOO) and the most frequent cause in males is *benign prostatic hyperplasia* (BPH). This occurs when BPH advances from *benign prostatic enlargement* (BPE) to *benign prostatic obstruction* (BPO) (2).
Currently, the treatment is organized on a therapeutic ladder, starting with lifestyle measures, followed by pharmacological treatments. Surgical interventions are most often reserved for patients with bothersome LUTS refractory to medical therapy. Although this ladder is effective for the majority of patients, in real-life clinical practice, surgery is not always successful and reintervention or the need to restart or continue pharmacological treatment may be needed in some patients (3). Risk factors for surgical reintervention are not well defined but some authors showed that higher prostatic volume and history of urinary retention with urethral catheterization could be associated with a higher need for reintervention (4).
This study aimed to assess factors associated with the need for surgical reintervention and/or continuation of pharmacological treatment.

MATERIALS AND METHODS

After ethical committee approval (Protocol number 339/21) and informed consent of the patients, it was performed a retrospective analysis of all consecutive patients who underwent prostatic surgery for male LUTS associated with BPO in an academic tertiary hospital between 1 May 2015 and 1 May 2016, with a minimum follow-up of five years.
The type of surgery, preoperative, postoperative and follow-up analysis were collected in a database. The following preoperative parameters were evaluated: *prostate-specific antigen* (PSA), prostate volume, *post-void residual volume* (PVR), the pattern of complaints (predominance of storage or emptying), need for previous catheterization, previous episode of acute bacterial prostatitis, duration of pharmacological treatment before surgery and type of drugs used. Prostatic volume was measured by transrectal or suprapubic ultrasound. For those taking *5-α reductase inhibitors* (5ARIs) for more than 6 months, tPSA value was adjusted to double. Acute bacterial prostatitis was clinically defined as an episode of febrile LUTS with swollen and tender prostate on digital rectal examination and positive urine culture.
In terms of surgical procedures, patients were classified as being submitted to *transurethral resection* (TURP), open/laparoscopic *transvesical prostatectomy* (TVP) or open/laparoscopic *retropubic prostatectomy* (RP) according to the surgical report.
Patients with the following conditions were excluded: history of chronic prostatitis or chronic pelvic pain, previous surgery in the context of prostatic cancer and patients with post-surgical histology of the specimen showing malignancy. Prostatic tissue resected was measured and a ratio (Percent of Resected Tissue) was calcu-

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lated dividing by the preoperative prostate volume.
Concerning post-surgery parameters, we considered the medication prescribed when the surgery was not effective, the need for a reintervention and the type of surgical technique used. All medications were verified by accessing the patient's clinical file and by asking the patient himself. We grouped the drugs in *alpha-blockers* (AB), 5ARI, *anticholinergic* (AC) and *β3-agonist* (B3A). Drugs were prescribed by urologists or primary health care physicians. It was confirmed that the medication was not being taken for other purposes (eg, 5ARI for androgenetic alopecia). Surgical reintervention was verified by the patient's clinical file and only surgeries performed in the national health service were considered.
Overall patients characteristics like age, main comorbidities and renal function were also collected.
The need for maintenance of pharmacological treatment as well as the need for surgical re-intervention at 5 years was assessed and its association with preoperative parameters was explored.

Statistical analyses

The data were collected and analysed using SPSS (v. 27 IBM, USA). The Shapiro-Wilk test was used to test parameter distribution. Continuous variables with normal distribution were expressed as the mean ± the standard deviation, non-normally distributed variables were expressed as the median (25^{th}-75^{th} quartiles), and nominal variables were expressed in relative frequencies. For continuous variables, the differences between the groups were evaluated using the ANOVA test if a normal distribution was assumed; otherwise, the Kruskal-Wallis test was used. Categorical variables were compared using the chi-square test. The p significance was set at < 0.05.

RESULTS

A total of 212 patients were included. The patient's mean age at five years follow-up was 70 ± 8.66 years old. Overall patient characteristics and perioperative data are depicted in Tables 1, 2.
Regarding the medication taken before surgery, 33.0% were under AB; 13.7% were taking only 5ARI; 34% had a combination of AB and 5ARI; 5.7% took another combination (mainly AB plus AC). Only 13.7% were not under any medication before surgery. Regarding the initial surgery performed, 65.6% underwent TURP; 24.1% underwent TVP and 10.4% underwent RP.
A total of 86.9% of patients did not need pharmacological treatment 5 years after surgery. Of those who required pharmacological treatment after surgery, 24.5% were taking AB, 12.2% were taking 5ARI, 20.0% were taking a combination of both, 18.4% were taking AC, 12.2% were taking a combination of AB and AC, and 10% took B3A.
Twelve per cent required surgical reintervention and it was performed in the first 2 years in 57.7% men and between the second and third years in the 34%. Only 8% underwent surgery after more than 3 years. Of the patients who underwent initial TURP, TVP and RP, 84.9%, 98% and 95.5% did not need a surgical reintervention, respectively.
The surgical modality chosen for reintervention was re-TURP in 73,1%, internal urethrotomy in 15.4%, bladder-neck resection in 7.7% and TVP in 3.8%.
There seems to be a statistical association between the presence of a previous episode of prostatitis and the greater need for surgical reintervention ($p = 0.004$). The relationship between prior prostatitis and the need for a second surgery has an odds ratio of 4.6 (95%, CI 1,71-12,32). Of those with a previous episode of prostatitis, 28.6% required surgical reintervention. Of all patients who required a surgical reintervention, 36.4% had previous prostatitis. The other data were not statistically related to the need for resume pharmacological treatment or of surgical reintervention (Table 3).

Table 1.
Demographic characteristics.

Age [1]	70 ± 8.66
Serum creatinine [2]	0.98 (0.80-1.12)
Obesity	34% (74)
Hypertension	27% (57)
Diabetes	18% (40)
Depression	12% (25)
Parkinson disease	2.5% (5)
Chronic kidney disease	1,8% (4)
Hypogonadism	0.4% (1)

[1] Mean ± standard error; [2] Median (25^{th}-75^{th} quartile).

Table 2.
Perioperative data.

PSA [1]	2.4 ng/dl (1.20-4.53)
Preoperative prostate volume [1]	60.00 cm^3 (44.25-85.00)
PVR [2]	69.00 ml (± 22.12)
Predominance of symptoms	75% voiding; 25% storage
Presence of nocturia	53.8%
Urethral catheter for urinary retention	30%
Percent of resected tissue [1]	22.22% (8.62-35.80) ≤ 30%-68.90% 30-50%-12.76% ≥ 50%-18.34%

[1] Median (25^{th}-75^{th} quartile); [2] Mean ± standard error; PSA: Prostate-specific antigen; PVR: Post-void residual volume.

Table 3.
Association between preoperative parameters and medication continuation or surgical reintervention; results shown in p-values.

Variables	Medication continuation	Surgical reintervention
Symptoms pattern [1]	0.785	0.840
Prostatitis [1]	0.073	0.004
Urethral catheter for urinary retention [1]	0.611	0.635
Prostatic volume [2]	0.262	0.069
PSA [2]	0.444	0.903
PVR [2]	0.230	0.113
Duration medical treatment [1]	0.088	0.022
Percent of Resected Tissue [2]	0.643	0.138

[1] Chi-square test; [2] Kruskal-Wallis test; PSA: prostate-specific antigen; PVR: post-void residual volume.

Discussion

Between our patients, 68.9% of them have PSA > 1.4 ng/ml (median PSA of 2.4 ng/dl), corroborating the potential relationship between higher PSA and the need for intervention. Previous studies, like the PLESS trial, Olmsted County Study and MTOPS, have shown that patients with this cut-off of PSA are at higher risk of needing surgical treatment (5-7). Thirty percent of our patients were catheterized which is similar to other studies (4, 8). We did not find a relationship between the presence of a catheterization (due to urinary retention), higher prostatic volumes, and the need for surgical reintervention, differently to the findings by other authors (4). Concerning baseline PVR values, it is known that has little prognostic value for the risk of surgery in patients on medical treatment (namely, AB) (9).

Three-quarters of patients took medication for less than a year before being submitted for surgery. The duration of medical treatment had no impact on the need for reintervention or the need to return to medication.

The predominance of voiding or storage symptoms before first surgery was not associated with the need for post-surgery medication. This finding diverges from *Han et al.*, which showed that storage symptoms and use of antimuscarinics were significantly associated with symptom persistence and the need to continue medical therapy after surgery (10). Moreover, this group also showed that any previous LUTS/BPO medication use was significantly associated with symptom persistency and continuing medical therapy, a fact that was not corroborated by our sample.

The epidemiological relationship between prostatitis and benign prostatic hyperplasia was shown in case-control studies and a cohort study (11). However, that association is not broadly accepted. In our study, a history of acute prostatitis is significantly associated with the need for a surgical reintervention, resulting in a 4.6 times higher risk of a second procedure, which means a probability of 82% of needing reintervention. This data gives strength to the finding of *Sauver et al.* with an odds ratio of 1.69 and a probability of 70% (12). The baseline degree of LUTS, even after surgery, in patients with a history of prostatitis may induce a false sense in the urologist of the need for intervention, lowering the threshold for reintervention. The true benefit and consequences of surgery in these patients remain to be seen, and further studies are needed.

In this study, a higher ratio of prostatic tissue resected was not associated with less medical continuation or less surgical reintervention. Some studies show that there is a poor correlation between the residual prostate weight and symptoms and these are affected by several other confounding factors (13-18). Some authors even claim that resection of less than 30% of prostatic tissue seems to be sufficient to alleviate lower urinary tract symptoms related to benign prostate hyperplasia (13). A recent study shows that less profound prostate resections may be sufficient, depending on maximum flow rate (19). In our study, more than two-thirds of our patients have less than 30% of prostatic tissue resected and it was not associated with poorer outcomes. Despite that, this is a controversial subject, and some authors postulate the opposite.

Although nowadays the choice of surgical interventions includes less invasive techniques, our patients were submitted to the "*classic*" techniques of TURP, TVP and RP. In our study, TVP and RP have shown a low rate of need for re-intervention, while TURP, although effective, has a higher risk for reintervention.

A total of 25 patients (12%) required surgical reintervention. This number is supported by *Rassweiler et al.*, who showed similar values, between 3 to 14.5% (3). The reinterventions are mainly performed in the first 3 years (92,0%). The follow-up of patients after surgical reintervention is not well defined and should be evaluated in further studies. However, given these data, we believe that these patients need to be followed for at least 3 years, although not necessarily by a urologist. In the majority of cases, the modality chosen for reintervention was TURP (73% of these 25 patients). In 1.9% and 0.9% of all the 212 patients, the reintervention was an internal urethrotomy for urethral stricture and loop resection of bladder neck for *bladder neck contracture* (BNC), respectively. Both complications are more common after TURP (20). All our patients who needed urethrotomy or resection of BNC had previously undergone TURP. Our urethrotomy incidence is similar to the study of *Sucki et al.* (21) and is within the lower range of the 1.4-19% referred in literature (3, 20). Our BNC is relatively lower than the 1.7-9.7% mentioned in other studies (20, 22, 23).

We only considered surgical reintervention made in our centre or another one of the *Portuguese National Health Service*, therefore, there is a chance that some patients who have had surgical reintervention in private clinical setting could be missed. It would be interesting to compare the rate of reinterventions and complications of both "*classic*" and modern techniques being performed nowadays in a real-life context as a tertiary hospital - where both residents and consultants perform surgeries.

Twenty-three percent of our patients still needed to use male LUTS medication after surgery and this factor was independent of the type of surgery. Some studies show rates of patients needing medication ranging between 15 and 55%. A previous study with longer follow-up (3 years) showed an estimated rate of use of medication of 22% (24), so data of our cohort is in line with other centres. Compared with 86.3% of patients who were medicated for BPO before surgery, we have an important decrease in the relative number of patients who need medication after surgery. Lifelong medications are cost-burden and are associated with consequences given by adverse effects and associated with drug interactions. So, medication discontinuation could be an indicator of the success of the procedure, and is important to include it as an effective measure when comparing surgical options, since a large proportion of patients are motivated to undergo surgery in order to discontinuing medication for male LUTS (25). Despite this, we should keep in mind that sometimes the need for medication does not result from a failure in the surgical technique but rather from the LUTS physiopathological pleiotropism, namely the coexistence of other causes for bladder outlet obstruction (as an anatomical abnormality), the presence of underactive or overactive bladder and of chronic prostatitis (of any type) (10).

Only 4.2% and 2.4% of our patients are using AC and B3A, respectively. This is lower than 5.7% and 4.7% of the use of AB and its combination with 5ARI.
In a study by *Campbell et al.*, it was shown that ABs are used in about 9%, being the most commonly used drug class (25). Because AB's mechanism of action is mainly on receptors located in the bladder neck and prostatic smooth muscle, AB utility following a thorough surgery should be minimal, these Authors stated that use of AB is a indicator of quality of surgery (25). Given the bladder remodelling and the prevalence of storage symptoms after surgery, they felt that AC and B3A would be commonly used. Also, *Campbell et al.* showed that use of AB, 5ARIs, AC/B3A within the first 5 years after surgery is roughly 25%, 20%, and 15%, respectively (26).
A non-negligible portion of the patients (13%) was submitted to surgery without taking any medication previously but our numbers are inferior to those of some literature, referring values around 50% (24).
In our series, these were patients referred by primary care physicians with end-term BPO (most commonly with a urethral catheter) or with contraindications to male LUTS medication and were quickly scheduled for surgery. These data may indicate that primary health care has a more conservative approach to LUTS, namely through watchful waiting. These data make us believe that education programs targeted to primary care physicians and medical literacy campaigns for the general population should be encouraged.
Our study has some limitations. It is a retrospective study with possible selection bias. New surgical techniques are the main hot topic nowadays in male LUTS treatment, and most of their benefits are very well expressed (27-30). During the last years, laser enucleation of prostate, namely with Holmium laser (HoLEP), has replaced TURP as the gold standard surgical treatment for BPH (31). On the other hand our study focused on the outcomes of our centre that did not have other newer surgical modalities of BPO treatment. Furthermore, the results are from a single tertiary centre where multiple surgeons performed the procedures, including both residents and graduated urologists.
This is a reality present in most university hospitals and it's one of the reasons for considering this study a real-life-based one. A limited number of patients were enrolled, although it is quite an elevated number for 1 year in a single centre. Medication compliance is an identified problem in BPO therapy, and we could not evaluate it. We lack data about the time before the beginning of medical treatment and the first surgery such as IPSS, Q_{max} and sexual function, which is why we chose not to use data related to these variables collected in the post-operative period given the impossibility of a comparison.

Conclusions

Patients should be informed of the potential need for pharmacological treatment following surgery, or even of the need for reintervention.
History of prostatitis seems to be a risk factor for reintervention in patients submitted to prostatic surgery for benign obstruction.

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