



Evaluation of Prostatic Artery Embolization Efficiency in Benign Prostatic Hyperplasia Patients with High Comorbidity

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Abstract

Objective: The purpose of this study was to evaluate efficacy outcomes following prostate artery embolization (PAE) for the treatment of benign prostatic hyperplasia (BPH) patients with high comorbidity.

Materials and Methods: This retrospective study included 22 patients treated with PAE from May 2015 to June 2017. Patients with Charlson comorbidity index ≥ 2 , International Prostate Symptom Score (IPSS) >12 , prostate specific antigen (PSA) levels <4 ng/mL or between 4 and 10 ng/mL with negative prostate biopsy and total prostate volume (TPV) >90 cm³ were included. Total PSA, maximum flow rate (Q_{max}), TPV, IPSS, post-voiding residual (PVR) values were recorded in all patients in the urology clinic before PAE and at 3 and 6 months after PAE.

Results: The average patient age was 73.86 ± 6.25 years and operative time was 80 minutes (range, 60-120 min). Pre-PAE and 6-month post-PAE values were: IPSS: 25.18 ± 6.75 and 11.27 ± 3.29 ($p < 0.05$), Q_{max} : 8.31 ± 3.12 and 17.22 ± 3.23 ($p < 0.05$), PVR: 87.9 ± 19.25 and 25.86 ± 7.72 ($p < 0.05$), TPV: 134.45 ± 57.56 and 86 ± 15.4 ($p < 0.05$), and PSA: 3.89 ± 1.26 and 2.11 ± 1.06 ($p < 0.05$). Embolization was performed unilaterally due to atherosclerosis and strictures in the internal iliac artery branches in 2 patients. After the procedure, 2 patients experienced transient hematuria which did not require bladder irrigation, 1 patient had acute urinary retention due to dysuria, and 1 patient had transient hematospermia.

Conclusion: PAE may be an alternative treatment method in BPH patients with high comorbidity.

Keywords: High comorbidity, benign prostatic hyperplasia, prostate artery embolization

Introduction

The prostate gland, unlike other organs, grows in volume with age. Cell proliferation in the periurethral and transitional zone is called benign prostatic hypertrophy (BPH), and occurs in over 50% of men over 60 years old (1).

This enlargement of the prostate gland causes lower urinary tract symptoms such as irritative and obstructive symptoms, which substantially impact quality of life. The primary aim of BPH treatment is to maximally improve quality of life by reducing urinary incontinence and retention. Medical treatment is beneficial in most cases; however, there are also minimally

invasive and surgical options for patients who do not respond to medical treatment. In particular, transurethral resection (TUR) is considered the gold standard for the treatment of BPH.

Prostate volume is important in the TUR procedure, which is most effective in prostates of 30-80 cm³. For larger prostate volumes, open prostatectomy is considered the gold standard. However, open prostatectomy requires longer hospital stays and, when compared to TUR, has more potential for complications and carries serious risks in patients with comorbidities (2).

Many recent studies on the treatment of BPH have focused on reducing prostate volume and eliminating lower urinary tract symptoms via prostate artery embolization (PAE). It was

emphasized in these studies that PAE significantly decreased prostate volume and lower urinary tract symptoms, leading to an increase in quality of life (3,4,5,6,7,8).

This study evaluated the effects of PAE in patients with high prostate volume and comorbidities, and in patients with lower urinary tract symptoms despite previous TUR surgery.

Materials and Methods

Twenty-two BPH patients who had lower urinary tract symptoms and were under alpha-blocker treatment for 6-24 months (mean 7.5 months) underwent superselective PAE between May 2015 and July 2017. Written informed consent was obtained from all patients. Patients who met the following criteria were included in this study: Charlson comorbidity index ≥ 2 and International Prostate Symptom Score (IPSS) >12 , prostate specific antigen (PSA) value <4 ng/mL, and total prostate volume (TPV) >90 cm³. Patients with repeated uroflowmetry volumes below 150 mL and post-voiding residual (PVR) volumes over 300 mL were excluded from the study due to the possibility of neurogenic bladder and sphincter decompensation. Patients with high creatinine levels and coagulation disorders were also excluded. Total PSA, maximum flow rate (Q_{max}), TPV, IPSS, and PVR volume was recorded for all patients. TPV was calculated using transabdominal measurements (taken with full bladder) of craniocaudal, anteroposterior, and transversal dimensions in the formula $0.52 \times a \times b \times c$.

The PAE procedures were performed by interventional radiologists with 5-20 years of experience. All procedures were performed under local anesthesia and all patients received 400 mg intravenous ciprofloxacin prior to the procedure. A Foley catheter was inserted and the balloon was filled 50% with iodinated contrast medium and saline, then positioned at the base of the urinary bladder. This facilitates identification of the prostate artery among the complex internal iliac artery anatomy during angiography. Access was through the right femoral artery in all patients. The left main internal iliac artery was catheterized using a 5F Cobra vertebral catheter and a 0.035 guidewire. Selective catheterization of the anterior branch iliac artery was performed with angiograms in the ipsilateral oblique view. Because the internal iliac artery anatomy is very complex in angiography, some difficulties may arise when identifying the prostate artery. In our experience, the gonadal prostatic branch usually originates from the inferior vesicular artery. However, in this study we superselectively catheterized branches of the anterior internal iliac artery using microcatheter (Progreat 2.8, Terumo, Japan) and microwire manipulation in ambiguous cases. Embolization was initiated after detection of typical parenchymal staining of the prostate gland in angiography assisted by contrast-filled catheter balloons positioned at the bladder base. Distal embolization of the prostate artery was performed using 300-500 micron microspheres (Biosphere Medical, Roissy, France). Embolization was continued until no parenchymal enhancement was visible in angiography. For embolization of the left prostate artery, the left main internal iliac artery was catheterized using Simmons I or II catheters (Merit Medical Systems, Inc., USA) and similar techniques were also used for right PAE (Figure 1). The duration of the

PAE procedure was approximately 60-120 minutes. After the procedure, all patients were examined for inguinal hemorrhage in the urology unit. The Foley catheters were removed 4 hours later. Although PAE is not a painful procedure, some patients were given nonsteroidal anti-inflammatory drugs if needed. After the procedure, all patients received 500 mg of ciprofloxacin (oral, twice a day) for 7 days. Patients with dysuria or difficulties urinating were given alpha blockers for 1 week. All patients were discharged in 1-3 days.

Statistical Analysis

Statistical evaluations were performed using SPSS 15 (Statistical Package for Social Sciences) program. In addition to descriptive statistical methods (mean, standard deviation), Student's t-test was used to evaluate the quantitative data. The results were evaluated within a 95% confidence interval and p value <0.05 was considered statistically significant.

Results

Twenty-two patients underwent PAE. Four of these patients had history of previous TUR. The mean age of the patients was 73.86 ± 6.25 years. The mean of Charlson comorbidity index score was 3 (2,3,4). Pre-PAE and post-PAE values at 3 and 6 months for the studied variables were as follows: IPSS: 25.18 ± 6.75 , 13.13 ± 4.85 , 11.27 ± 3.29 ($p < 0.05$); Q_{max} : 8.31 ± 3.12 , 16.13 ± 2.93 , 17.22 ± 3.23 ($p < 0.05$); PVR: 87.9 ± 19.25 , 30.5 ± 8.5 , 25.86 ± 7.72 ($p < 0.05$); TPV: 134.45 ± 57.56 , 92.18 ± 18.32 , 86 ± 15.4 ($p < 0.05$); PSA: 3.89 ± 1.26 , 2.68 ± 1.14 , 2.11 ± 1.06 ($p < 0.05$). All values are shown in Table 1. The average surgery time was 80 minutes (range, 60-120 minutes). Embolization was performed unilaterally in 2 patients due to diffuse atherosclerosis and stenosis in the internal iliac artery. Following the procedure, 2 patients had transient hematuria that did not require bladder irrigation, 1 patient had transient hematospermia, and 1 patient had acute urinary retention secondary to dysuria.

Table 1. International Prostate Symptom Score, uroflowmetry and prostate specific antigen values of before prostate arterial embolization and 3rd and 6th months after prostate arterial embolization

	Pre-PAE	Post-PAE 3 months	Post-PAE 6 months	p value
IPSS ± SD	25.18±6.75	13.13±4.85	11.27±3.29	p<0.05
Q_{max} mL/s ± SD	8.31±3.12	16.13±2.93	17.22±3.23	p<0.05
PVR, mL ± SD	87.90±19.25	30.5±8.5	25.86±7.72	p<0.05
TPV, mL ± SD	134.45±57.56	92.18±18.32	86±15.4	p<0.05
PSA, ng/dL ± SD	3.89±1.26	2.68±1.14	2.11±1.06	p<0.05

IPSS: International Prostate Symptom Score, Q_{max} : Maximum flow rate, PVR: Postvoid residue, TPV: Total prostate volume, PSA: Prostate specific antigen, SD: Standard deviation, PAE: Prostate artery embolization

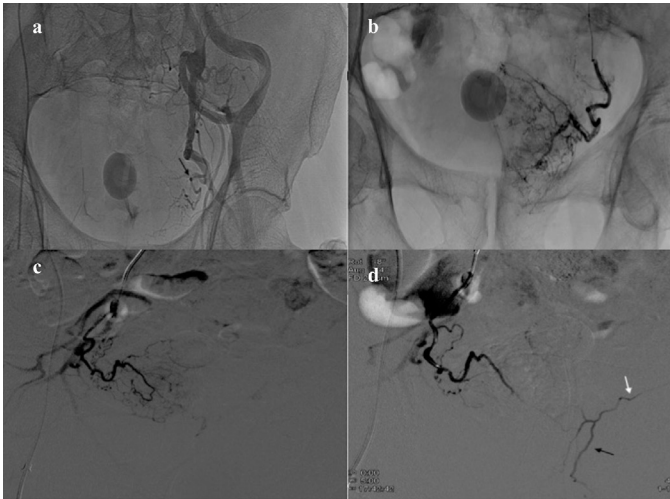


Figure 1. a) Internal iliac arteriogram of a 78-year-old male patient shows the complex internal anatomy of left main iliac artery. Filling the Foley catheter with contrast medium assists in locating the prostate gland and identifying the feeding prostate artery (black arrow). b, c) Superselective prostate artery arteriograms show typical staining of the left and right prostate gland. d) Typical staining in the right prostate artery disappears after embolization, but the collateral arterial structure feeding the left lobe of the prostate is visible during embolization (white arrow). Nevertheless, the embolization was discontinued due to the formation of a shunt to the dorsal penile artery (black arrow)

Discussion

TUR and open prostatectomy have long been considered the gold standard in surgical treatment of BPH. Open prostatectomy is recommended for patients with prostate volume greater than 80 cm³. However, open prostatectomy carries serious risks for many patients with high comorbidity. Furthermore, it is still unclear which patient groups should be included or excluded for PAE. The utility of PAE as an alternative to open prostatectomy is a currently active area of research. In a study comparing TUR and PAE results, Gao et al. (5) emphasized that there was a greater improvement in IPSS, the quality of life (QOL) scores, Q_{max} , and PVR values in the first 3 months with TUR compared to PAE. They also emphasized that PSA and PV values were lower in the TUR group at 24 months compared to the PAE group, and more side effects and complications were observed in the PAE group.

In a similar study, Carnevale et al. (9) reported comparable reductions in IPSS in the PAE and TUR groups, whereas TUR had a greater effect on Q_{max} values, and PV decreased more in the PAE group.

Russo et al. (10) compared open prostatectomy patients with PAE patients and noted greater improvement in IPSS, QOL scores, Q_{max} , PVR, and PSA values at 1 year in the open prostatectomy group. However, they reported better results for International Index of Erectile Function scores, postoperative complications, and length of hospital stay in the PAE group.

While TUR can be performed effectively in many centers, potential complications include hemorrhage requiring transfusion,

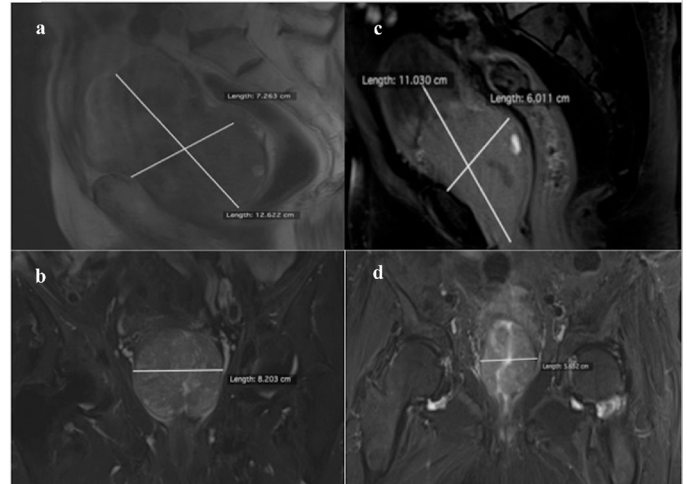


Figure 2. a, b) The largest prostate in our study was measured as 386 cm³ in an 80-year-old male. c, d) At 6 months post-prostate artery embolization, prostate volume was decreased to 192 cm³

TUR syndrome, urethral stricture, urinary incontinence, and retrograde ejaculation (11). Although PAE is still being investigated as an alternative to open prostatectomy and TUR, numerous studies have reported that the procedure relieves lower urinary tract symptoms in BPH patients (3,4,5,6,7,8,9,10). However, it remains unclear which patients should be selected for PAE. Therefore, in the present study we included patients with high comorbidity, those with lower urinary tract symptoms despite undergoing TUR previously, and patients considered high-risk for open prostatectomy. Both patient groups also had prostate volume over 90 cm³. Our results showed statistically significant improvements in total PSA, Q_{max} , TPV, IPSS, and TPV values in all patients (Figure 2). Although the superiority of PAE over TUR or open prostatectomy has not been clearly established in the literature, PAE yielded favorable outcomes for IPSS and other parameters in patients with high comorbidity, suggesting that PAE may be beneficial in this patient group. PAE provided marked benefits at 3 months in all patients, but there was less improvement in values measured between 3 and 6 months.

Study Limitations

The long-term results of this study remain uncertain. Further research is required to investigate the effect of the prostate gland on post-PAE collateralization and the long-term outcomes of PAE. To our knowledge, there has been no study investigating the long-term outcomes in a large patient group. Prospective studies utilizing perfusion imaging methods are needed to investigate prostate gland vascularity following PAE. Another limitation of our study is that we had to use ultrasonography (USG) instead of magnetic resonance imaging (MRI) for prostate volume measurements. USG is a user-dependent modality and is less sensitive than MRI for measuring prostate gland volume. Another limitation of the study is that there are few centers in Turkey that perform the PAE and awareness of the procedure is generally low. In addition, clinics approach PAE with caution due to the paucity of data regarding its long-term efficacy. Thus, the study included a small number of patients.

Conclusion

Although the indications for PAE are not yet clearly defined, PAE may be an alternative treatment option for BPH patients who have high comorbidity and for whom TUR and open prostatectomy are risky.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.O.Y., E.D., A.F., K.S., Concept: E.D., Design: A.F., Data Collection or Processing: İ.O.Y., H.Ç., Analysis or Interpretation: İ.O.Y., E.D., Literature Search: A.F., H.Ç., Writing: İ.O.Y.

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References

1. Berry SJ, Coffey DS, Walsh PC, Ewing LL. The development of human benign prostatic hyperplasia with age. *J Urol* 1984;132:474-479.
2. Oelke M, Bachmann A, Descazeaud A, et al. EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *Eur Urol* 2013;64:118-140.
3. Carnevale FC, da Motta-Leal-Filho JM, Antunes AA, et al. Quality of life and clinical symptom improvement support prostatic artery embolization for patients with acute urinary retention caused by benign prostatic hyperplasia. *J Vasc Interv Radiol* 2013;24:535-542.
4. Pisco JM, Pinheiro LC, Bilhim T, et al. Prostatic arterial embolization to treat benign prostatic hyperplasia. *J Vasc Interv Radiol* 2011;22:11-19.
5. Gao YA, Huang Y, Zhang R, et al. Benign prostatic hyperplasia: prostatic arterial embolization versus transurethral resection of the prostate: a prospective, randomized, and controlled clinical trial. *Radiology* 2014;270:920-928.
6. Wang MQ, Guo LP, Zhang GD, et al. Prostatic arterial embolization for the treatment of lower urinary tract symptoms due to large (>80 mL) benign prostatic hyperplasia: results of midterm follow-up from Chinese population. *BMC Urol* 2015;15:33.
7. Bagla S, Martin CP, van Breda A, et al. Early results from a United States trial of prostatic artery embolization in the treatment of benign prostatic hyperplasia. *J Vasc Interv Radiol* 2014;25:47-52.
8. Pisco JM, Rio Tinto H, Campos Pinheiro L, et al. Embolisation of prostatic arteries as treatment of moderate to severe lower urinary symptoms (LUTS) secondary to benign hyperplasia: results of short- and mid-term follow-up. *Eur Radiol* 2013;23:2561-2572.
9. Carnevale FC, Iscaife A, Yoshinaga EM, et al. Transurethral resection of the prostate (TURP) versus original and PERFECTED prostatic artery embolization (PAE) due to benign prostatic hyperplasia (BPH): preliminary results of a single center, prospective, urodynamic-controlled analysis. *Cardiovasc Intervent Radiol* 2016;39:44-52.
10. Russo GI, Kurbatov D, Sansalone S, et al. Prostatic arterial embolization vs open prostatectomy: a 1-year matched-pair analysis of functional outcomes and morbidities. *Urology* 2015;86:343-348.
11. Rassweiler J, Teber D, Kuntz R, Hofmann R. Complications of transurethral resection of the prostate (TURP)-incidence, management, and prevention. *Eur Urol* 2006;50:969-979.