Prostatic Artery Embolization: A Promising Technique in the Treatment of High-Risk Patients with Benign Prostatic Hyperplasia

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Key Words
Prostate · Hyperplasia · Embolization · High-risk

Introduction
Lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH) affect old aged men and create a lot of discomfort in them [1]. The severity of symptoms and its effect on the quality of life (QoL) are important factors for deciding the treatment option. The International Prostate Symptom Score (IPSS) is used to...
access the severity of symptoms through a questionnaire consisting of 7 questions yielding a score from 0 to 35. Patients with score of 0–7 is mildly symptomatic, 8–19 moderately symptomatic and 20–35 severely symptomatic. The IPSS is effective in helping to determine treatment methods for LUTS/BPH patients [2]. Patients with mild-to-moderate symptoms can be managed with medical therapy, which includes alpha-blockers and 5-alpha-reductase inhibitors [3]. Patients who have severe symptoms and those in whom medical therapy is ineffective or inappropriate are ideal candidates for surgical intervention.

Transurethral resection of the prostate (TURP) is the gold standard therapy for LUTS/BPH and, for many years, has been considered the surgical treatment of choice and the standard of care when other treatment methods fail [4]. Although minimally invasive therapies were developed to overcome TURP-related complications, they were not proved to be completely superior [5]. Because of the high morbidity rate associated with BPH surgical treatment, there has been a continuous search for other alternatives, especially in high-risk patients. Recently, prostatic artery embolization (PAE) has emerged as a promising innovative technology that could be an alternative to various BPH treatment options [4, 6].

The aim of our study was to evaluate the safety and efficacy of PAE in BPH patients who are at high risk for surgery and/or anesthesia.

Patients and Methods

Between June 2013 and February 2015, patients over 50 years of age with LUTS/BPH refractory to BPH-related medical therapy or had an indwelling urethral catheter due to refractory urine retention were prospectively enrolled in the study. All patients were ineligible to standard BPH surgical treatment due to the high risk of surgery/anesthesia because of associated comorbidities. All included patients had an American Society of Anesthesiologists score of 3. The possible side effects and outcome of standard prostatic surgeries, alternative minimally invasive surgeries and PAE procedure were explained in detail to each patient before inclusion in the study. The selection of PAE procedure was achieved in a multidisciplinary manner in conjunction with the patient, anesthesiologist, interventional radiologist and urologist. The local institutional review board approved the study and all patients provided written informed consent before study participation.

Before intervention and 1, 3, 9 months post intervention, all patients were evaluated by considering their medical history including IPSS and International Index of Erectile Function (IIEF-5) questionnaire, physical examination comprising digital rectal examination (DRE), laboratory tests in the form of urine analysis, urine culture and sensitivity, complete blood cell count, serum creatinine, coagulation profile and serum prostate-specific antigen (PSA), uroflowmetry, and abdominal and transrectal ultrasonography (TRUS). Prostate volume was assessed by TRUS using the following formula: \( \pi/6 \times \text{transverse diameter} \times \text{anteroposterior diameter} \times \text{superoinferior diameter} \).

Patients with IPSS <8, prostate size <60 g, suspicious cancer prostate by DRE, ultrasound finding or elevated serum PSA, previous lower urinary tract surgery, history of stricture urethra, stone bladder, neurogenic bladder, large bladder diverticulum, and other urethral/bladder abnormalities affecting the LUTS/BPH treatment, as well as those with medical condition that impede the usage of iodine contrast media were excluded from the study.

Prior to PAE, CT angiography was performed to evaluate the conditions of the distal abdominal aorta and ilio-femoral arteries. Patients with advanced atherosclerosis and tortuosity either in the aortic bifurcation or internal iliac arteries and those with advanced atherosclerosis of prostatic arteries were also excluded. Protocol, using 64 multi-detector CT machine, entailed usage of 100 ml non-ionic contrast media with injection flow rate of 4 ml/s with ROI at the infra-renal aorta, followed by post processing image reconstruction, using maximum intensity projection, at the workstation.

Technique of Prostate Artery Embolization

All patients discontinued the BPH medication(s) 1 week before embolization. Patients were admitted to the hospital on the day of the procedure. On arrival of the patients to the theater suite and after routine monitoring of vital signs, peripheral i.v. cannula was inserted and patients were premedicated with midazolam 0.05 mg/kg, ketorolac tromethamine 30 mg and cefotaxime 1 g injection.

The technique was selective embolization of prostatic artery and right femoral access with retrograde approach was used for both ipsilateral and contralateral sides. After complete sterilization, a urethral catheter was inserted and 10 ml of xylocaine 2% was infiltrated around the puncture site. Right femoral puncture was done through a 2-mm incision, and a 5-Fr sidearm sheath was introduced and passed over a gently curved J guide wire. The sidearm sheath allowed interim contrast injection. Once the sheath is localized in the desired vessel, the patient is systemically heparinized with 5,000 IU of heparin. Under fluoroscopic guidance, the cross-over technique was employed by using 5 Fr Cobra or Simmons catheters over a 0.35-inch Terumo guide wire. Then catheterization of the contralateral common iliac artery was done.

We did diagnostic angiogram, with catheter-tip just distal to the aortic bifurcation, to determine the origin of the internal iliac artery to be catheterized, followed by angiogram to locate the anterior division of the internal iliac artery. After selection of the anterior division of the internal iliac artery, diagnostic angiograms were done in antero-posterior, right and left oblique projections to localize the prostatic artery and other pelvic branches. Using micro-catheter (Renegade 2.8 Fr of Boston scientific over 0.18 inch guide wire) super selective catheterization of the inferior vesical and prostatic arteries were done, followed by diagnostic angiogram to be sure of the super selection and positioning of the micro-catheter.

Biosphere 300–500 μm particles were used for embolization. The ampule 2 ml biosphere is diluted in 1:1 concentration with contrast agent divided in 2 equal volumes for each side. The end-
point chosen for embolization was slow flow or near-stasis in the prostatic vessels with interruption of the arterial flow and prostatic gland opacification.

After embolization of the left prostatic arteries, the Waltman loop technique was used to select the ipsilateral internal iliac artery first and then its anterior division. Using the microcatheter, the right inferior vesical and prostatic arteries were embolized in the same way.

Final arteriogram was done to assess the final results. The sheath was removed at the completion of the procedure over the guide wire, and hemostasis was achieved by using the closure device.

Patients remained in the hospital for 12–24 h after completion of the procedure. The urethral catheter was left in place for 5–10 days.

Data Collection and Statistical Analysis
The evaluated procedure-related parameters were operative time, fluoroscopy time, hospitalization time, duration of urethral catheterization and complication rate. The changes in IPSS, IIEF-5, PSA level, maximum urinary flow rate (Qmax), prostate size and post-void residual (PVR) urine volume were measured at each follow-up time point and compared with the baseline data, by using the paired sample t test or Wilcoxon signed-rank test, to evaluate the efficacy in all cases. Data analysis was performed using software SPSS version 20 for Window 7 and p value <0.05 was considered significant.

Results
During the recruitment of patients, 27 met the inclusion criteria. Of those, 5 were excluded because of advanced atherosclerosis of prostatic arteries. Therefore, we left with 22 patients with a mean age of 72.50 ± 10.92 (range 53–86) years and a mean prostate volume of 77.30 ± 14.89 (range 60–105) cm³. The mean procedure time was 76.00 ± 20.36 (range 45–110) min and the mean fluoroscopy time was 20.60 ± 8.21 (range 10–35) min. The procedure was technically successful in all patients with a mean procedure time of 76.00 ± 20.36 min. No procedure-related complications were recorded in any patient.

All patients were able to urinate successfully after the removal of the urethral catheter. To evaluate the clinical success of PAE, we compared the baseline clinical parameters with those recorded at follow-up and found that IPSS, QOL, and Qmax were significantly improved starting from the first follow-up visit till the end of study (p value <0.001). Also, there was a significant reduction in serum PSA level, PVR urine volume and prostate volume (p value <0.001).

The mean value and percent change of the evaluated parameters at different follow-up time points are shown in table 1.

In the first month of follow-up, 15 patients developed urinary tract infection and all responded to suitable antibiotics.

An example of bilateral prostatic arteries embolization is shown in figure 1.

Discussion
This prospective study was conducted on high-risk BPH patients who did not experience clinical improvement after medical treatment. Because the procedure is considered a new therapeutic technique, which has not yet universally approved or documented in guidelines, we preferred to limit its use to high-risk patients who are not able to undergo operation because of surgical or anesthetic risks. The results showed that PAE is a safe and effective procedure that could be viewed as an alternative to surgery.

Table 1. Mean value and % change of the evaluated parameters at different follow-up time points

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline, mean ± SD</th>
<th>At 1-month follow-up</th>
<th>At 3-month follow-up</th>
<th>At 9-month follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean ± SD</td>
<td>% change</td>
<td>p value</td>
<td>mean ± SD</td>
</tr>
<tr>
<td>IPSS</td>
<td>22.38±4.87</td>
<td>12.88±6.74</td>
<td>−42.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QoL</td>
<td>4.20±1.00</td>
<td>2.80±1.58</td>
<td>−33.33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IIEF-5 score</td>
<td>15.80±6.79</td>
<td>16.50±6.14</td>
<td>4.43</td>
<td>0.135</td>
</tr>
<tr>
<td>Serum PSA, ng/ml</td>
<td>4.98±3.04</td>
<td>3.52±1.82</td>
<td>−29.31</td>
<td>0.003</td>
</tr>
<tr>
<td>Prostate volume, cm³</td>
<td>77.30±14.89</td>
<td>56.80±15.77</td>
<td>−26.52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PVR urine volume, ml</td>
<td>111.62±38.27</td>
<td>47.50±25.43</td>
<td>−57.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Qmax, ml/s</td>
<td>8.06±2.95</td>
<td>14.31±5.73</td>
<td>77.54</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
The first report of a successful intervention for prostatic hemorrhage using embolization of prostatic artery was reported in 2000 by Demeritt et al. [7]. However, it was not until 2010 when Carnevale et al. [4] published their work on managing 2 patients with BPH through prostatic embolization. The experimental studies have shown that the desired effect for PAE is mostly due to cell necrosis secondary to the resultant ischemia [8, 9].

We routinely performed preprocedural CT angiography as an essential step for the selection process and to be able to detect the presence of normal vasculature aiming at decreasing the procedure time. Although looking relatively long, we had a comparable procedure time to what reported in other studies. The mean procedural time in our study was 76 min, compared to 69 and 197.5 min in the studies of Grosso et al. [2] and Carnevale et al. [10], respectively.

Compared to other minimally invasive procedures (e.g. transurethral microwave thermotherapy) [11, 12], clinical changes of IPSS in our study are similar. However, our results were better when compared with the outcomes of medical treatment [13–15].

Fig. 1. Bilateral prostatic arteries embolization. a CT angiography of the pelvis shows both sides prostatic arteries. b Right side, pre-embolization angiogram. c Left side pre-embolization angiogram. d Right side, post-embolization angiogram. e Left side post-embolization angiogram.
We did not encounter any of the complications that might be associated with TURP including TUR syndrome, need for blood transfusion, urethral stricture, bladder neck contracture, urinary incontinence or impotence. The sexual function might even be improved in a number of patients, which may be attributed to cessation of prostate medications and improvement of QoL.

Our study has some limitations. It is not controlled or randomized. In addition, the follow-up period was relatively shorter with lack of MRI at follow-up. Patients should be followed for longer periods with prostatic MRI to justify continuous improvements.

Conclusions

Our results show that BPH patients with failed medical treatment who are at high risk for surgery and/or anesthesia could be treated safely and effectively through PAE. However, larger cohort prospective randomized studies with longer periods of follow-up are needed to validate results.

Disclosure Statement

None.

References