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Role of Prostatic Artery Embolization in Management of Benign Prostatic Hyperplasia

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ABSTRACT

Background: Prostatic artery embolization is one of the most recent emerging and sophisticated interventional radiology procedures. Prostatic artery embolization is a minimally invasive procedure in management of lower urinary tract symptoms due to benign prostatic hyperplasia after failure of medical management. It represents a safer choice as compared to the usual surgical procedures used in this case. Under local anesthesia via femoral artery puncture catheter navigation is performed under fluoroscopy guidance to catheterize prostatic arteries followed by embolization of the prostatic bed aiming to reduction of the prostatic size and thus reliving the lower urinary tract symptoms. The aim of this study is to evaluate efficacy of prostate artery embolization in managing benign prostatic hyperplasia presented with clinically significant lower urinary tract symptoms. In our study prostatic artery embolization was performed on 20 benign prostatic hyperplasia patients, (mean age, 65.3 years; range, 59 – 77 years). The mean prostatic volume measured were 95.95 ml, (range 52-180 ml). The mean scoring of LUTS were (IPSS =19.35) and (QOL =4.35), with range of (IPSS 7-31) and (QOL 3- 5). Four of them complained of urinary retention and were already catheterized during procedure

Results: There are statistically significant differences (P values < 0.05) between (International prostatic scoring system, quality of life, Prostate volume and post-voiding urine volume) of the same patient before and after Prostatic artery embolization.

Conclusion: Prostatic artery embolization is efficient procedure in management of benign prostatic hyperplasia, significantly reducing the prostatic volume, post-voiding residual urine volume and patient's lower urinary tract symptoms.

Keywords: Lower urinary tract symptoms, Interventional radiology, Benign prostatic hyperplasia, Prostatic artery embolization

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BACKGROUND

Benign prostatic hyperplasia, Pathologically, is proliferation of the transitional zone of the prostate, enlarging the gland and resulting in lower urinary tract symptoms (LUTS). (Priest R et al, 2012). Benign prostatic clinically manifests with lower urinary tract symptoms, including frequency, urgency, nocturia, hesitancy, weak and interrupted stream, and incomplete emptying of urine. All these symptoms have a significant impact on quality of life and sleep pattern. (Pisco JM et al, 2016). Lower urinary tract symptoms are not sufficient to diagnose benign prostatic hyperplasia. Differential diagnosis includes carcinoma of the prostate, prostatitis, urethral stricture, urinary tract infection and neurogenic bladder. (Priest R et al, 2012). Benign prostatic hyperplasia affects 50% of males over 60 years of age, 75% of men over the age of 70 and 90% of men over age of 85 years age. (Patel AK et al,2006).

The treatment of BPH became a burden to the health care system. The expenses annually could be attributed to treatment of BPH and its associated symptoms are estimated at $4 billion. (Priest R et al, 2012). Because BPH is not a mortal disorder, treatment decisions are based on morbidity and Quality of Life issues and the patient's perception of bother has a central role in decision-making. If symptoms do not negatively affect morbidity or Quality of Life, treatment is not required. When symptoms start to interfere with daily activities, patients should undergo medical therapy before any form of surgical intervention. (A Pereira J et al,2012). The gold standard treatment of clinically significant benign prostatic hyperplasia not tolerating medical treatment was for many years' transurethral resection of the prostate. The significant associated morbidity has led to the development of new minimally invasive techniques. The least invasive of which is Percutaneous embolization, performed under local anesthesia with no surgical incision. (Priest R et al, 2012)

METHODS

Type of Study: Prospective interventional study conducted from the period of August 2018 to April 2020

Study Population:

Inclusion criteria:

- Male patients, age >40 years.
- Prostate volume > 30 cm3.
- BPH with moderate to severe LUTS, refractory to medical treatment for at least 6 months
- (IPSS > 18, or QoL > 3, or both)

Exclusion Criteria:

- Malignancy (based on TRUS examinations and PSA measurements with positive biopsy).
- large bladder diverticula and large bladder stones.
- Active urinary tract infection
- Unregulated coagulation Profile.
- Renal impairment

Ethical Considerations:

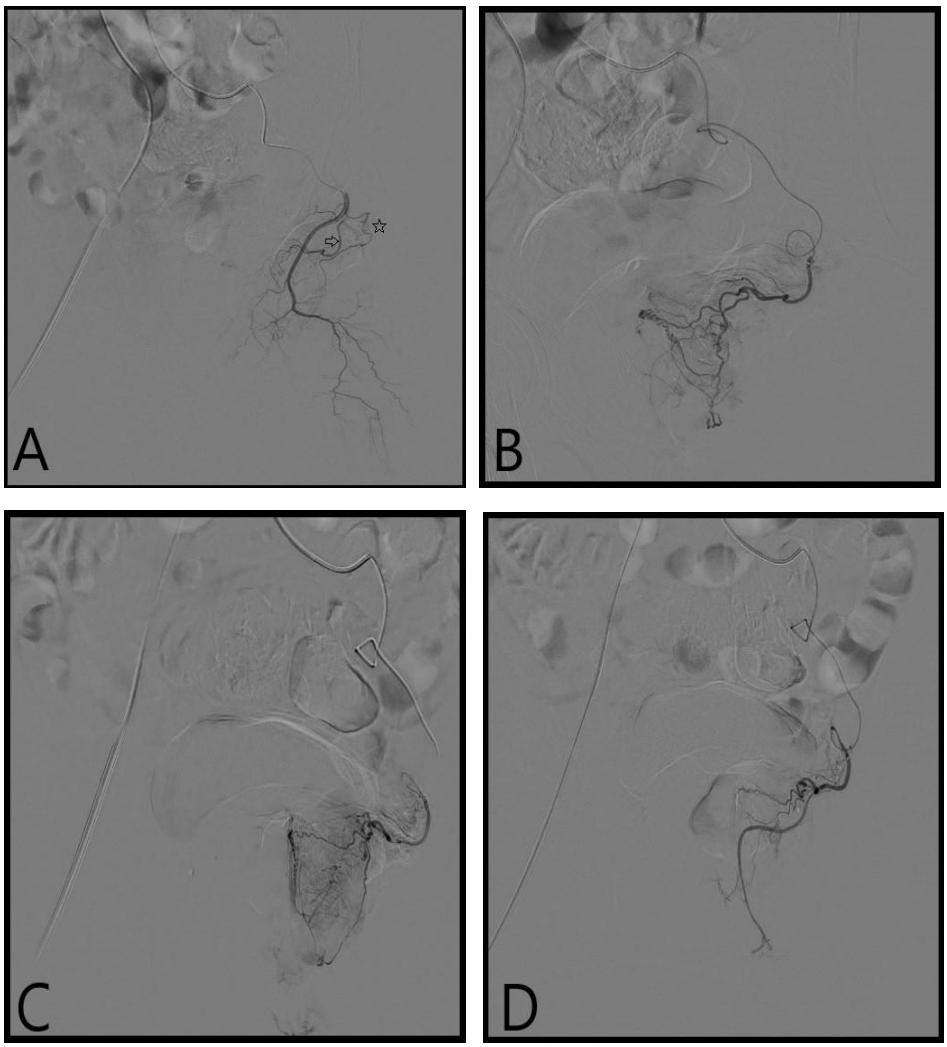
Informed consents were obtained from all patients or their guardian prior to inclusion in the study.

The study conducted according to the stipulations of the ASU ethical and scientific committee.

Procedure

Twenty procedures were performed by at least two interventional radiologists at least one of them is consultant with at least 20 years' experience. Right femoral artery access was obtained under local anesthesia. The left internal iliac artery and then its anterior division was selectively catheterized using a 5 F Cobra head catheter (Tempo, Cordis) mounted over a 0.035" hydrophilic guidewire (Radiofocus, Terumo). Digital subtraction angiography (DSA) was obtained in left anterior oblique projection (35 degree) and caudal-cranial angulation (10 degree) to visualize the anatomy of prostatic arteries. Microcatheters (Progreat 2.7, Terumo) and micro guidewires (Progreat 2.7, Terumo) were used for selective prostatic artery catheterization. Manual angiography is performed in frontal and same-side anterior oblique projection (35 degree) and caudal-cranial angulation (10 degree) to confirm the position of the catheter in the ostium of the prostatic artery and to visualize the prostate vascularity and exclude significant anastomosis with nontarget vasculature. In our cases we noticed anastomosis with non-target vasculature distal navigation of the catheter to bypass the anastomosis was done, not a single case needed coiling of the anastomosis. Embolization was performed using Embosphere (300–500 mm; Merit Medical) till near stasis then the microcatheter was advanced distally into the PA followed by further delivery of embolizing agent (according to the Proximal Embolization First, Then Embolize Distal technique) , PErFecTED technique.

The same procedure was done for the right side, a Waltman loop is formed and used to select the right iliac artery. Angiography is then performed with the catheter in the artery origin in ipsilateral anterior oblique (35 degree) and with caudal-cranial angulation (10 degree) and in frontal view. Followed by the same procedural details of the opposite site to catheterize the right prostatic artery via Microcatheters (Progreat 2.7, Terumo) and micro guidewires (Progreat 2.7, Terumo). Embolization is performed slowly with a 3-mL syringe, and postembolization angiography was obtained. In one case with markedly tortious atherosclerotic vessels, Waltman loop is formed in the renal artery then used to catheterize both right and left internal iliac arteries. The PErFecTED technique done in almost all cases except for 7 arteries out of 39 totally embolized prostatic artery of 20 BPH patients in our study, the technique could not be done due to proximal prostatic artery atherosclerotic plaques preventing further distal navigation of the microcatheter. Manual compression of the puncture site for 10 minutes was performed to achieve hemostasis followed by immobilization for 6 hours.



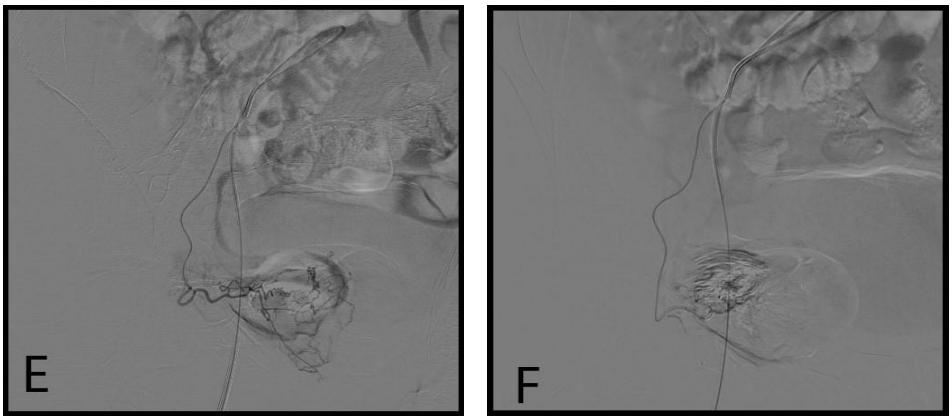
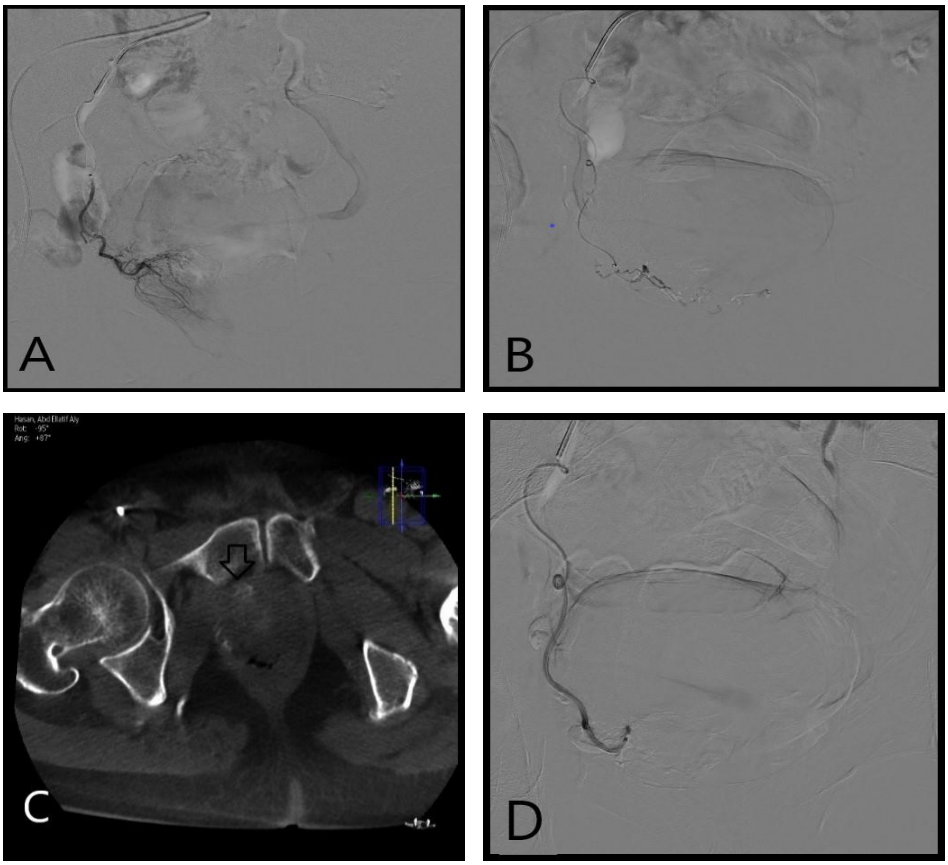


Figure 1: (A)Digital subtraction angiography of the anterior division of the left IIA revealing common origin of the prostatic artery (arrow) and vesical artery (star). Type I. Selective catheterization of the left prostatic artery in Left oblique view **(B)** and AP view **(C)** revealing the prostatic tissue vascularity. **(D)** Post-embolization of the left prostatic artery, notice disappearance of the prostatic vasculature. **(E)** Selective catheterization of the right prostatic artery in right oblique view revealing the prostatic tissue vascularity. **(F)** Post-embolization of the right prostatic artery, notice disappearance of the prostatic vasculature.



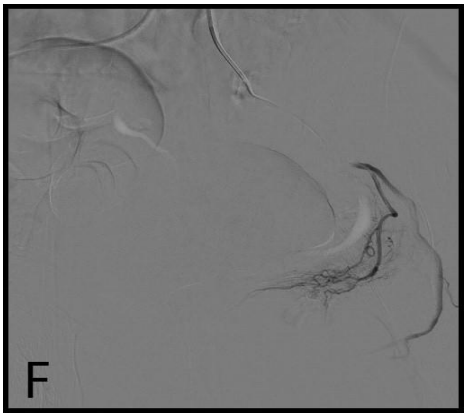


Figure 2: (A) Selective catheterization of the right prostatic artery in right oblique view revealing the prostatic tissue vascularity. **(B)** Further distal propagation of the microcatheter after more distal embolization.The PErFecTED (Proximal Embolization First, Then Embolize Distal) technique. (C) Cone beam CT after selective prostatic artery catheterization Revealing prostatic tissue enhancement. (D) Post-embolization of the right prostatic artery, notice disappearance of the prostatic vasculature. (E) Digital subtraction angiography of the anterior division of the left IIA revealing Origin of the prostatic artery from the upper third of IPA. Type IV. (F) Selective catheterization of the left prostatic artery in Left oblique view.

RESULTS

PAE was performed on 20 benign prostatic hyperplasia patients, (mean age, 65.3 years; range, 59 – 77 years).

The mean prostatic volume measured were 95.95 ml, (range 52-180 ml). The mean scoring of LUTS were (IPSS =19.35) and (QOL =4.35), with range of (IPSS 7-31) and (QOL 3- 5). Four of them complained of urinary retention and were already catheterized during procedure. **(Table 1)**

All patients were on medical treatment for at least 6 months with little or no response.

Technical success is considered when selective prostatic arterial catheterization and embolization is achieved at least on 1 pelvic side. Out of the 20 cases, in 19 cases bilateral embolization was done, while unilateral embolization was done in only 1 case, with technical success rate 100%.

By recording the anatomical variants of the origin of prostatic artery in our cases, out of 39 embolized prostatic arteries (of 20 patients), 19 prostatic arteries were originated from a common origin together with superior vesical artery (Type I). 8 arteries were originated from the anterior division of the IIA independently (Type II). Another 8 arteries were originated obturator artery (Type III), while 6 arteries originated from the internal pudendal artery (Type IV).

All the procedures were performed on outpatient basis and were discharged on the same day of the procedure after being kept under observation, in the supine position, for 6 hours. Patients were prescribed prophylactic antibiotics to guard against urinary tract infections and prostatitis, analgesics, antiflammatory drugs and antacid as discharge medications. Patients were advised to continue for their medical treatment for another two weeks then were asked to stop gradually in patients with more than drug stopped one by one. As regard the four patients with indwelling urinary catheters, trial of removal of catheter was done successfully after 2 to 3 weeks. Only one of them with prolonged catheterization (> 6 months), needed re-catheterization two months later.

There was minor adverse event for two patients, complained of symptoms of prostatitis managed conservatively for 2 weeks by prolonged course of antibiotics and anti-inflammatory drugs. One patient complained of small groin subcutaneous tissue stable hematoma and skin ecchymosis at the site of femoral puncture managed conservatively by hot fomentations and follow up. There were no major adverse events.

Follow up was done after 1 month by IPSS and QOL scoring calculation. Together with Ultrasound calculation of prostatic volume and post voiding residual urine volume. **(Table 1)**

Statistical Data

Statistical analyses were performed using SPSS version 22 (IBM© Corp., Armonk, NY). Quantitative data are expressed as mean and standard deviation. Paired-samples T test was used to compare continuous variables of the same patient pre and post intervention including (IPSS, QOL, Prostate volume and post-voiding urine volume). Look at **(Graph 1)**

P values < 0.05 were considered statistically significant.

There are statistically significant differences between (IPSS, QOL, Prostate volume urine volume) of the same patient before and after the intervention. **(Table 1)** and **(Table 2).**

Table 1: List of Patient's variables pre and post intervention and their means and standard deviations.

Paired sample t-test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	IPSS (pre) - IPSS (post)	9.0000	5.9687	1.4476	5.9312	12.0688	6.217	16	.000
Pair 2	QOL (pre) - QOL (post)	2.7000	1.4903	.3332	2.0025	3.3975	8.102	19	.000
Pair 3	PVRU (pre) – PVRU (post)	46.3125	73.1380	18.2845	7.3400	85.2850	2.533	15	.023

Table 2: Paired sample t-test to determine if there is statistical difference between the mean of our variables (IPSS, QOL and PVRU) pre and post intervention.

	Minimum	Maximum	Mean	Standard Deviation
Age	59	77	65.30	5.131
IPSS (preintervention)	7	31	19.35	6.661

IPSS (postintervention)	3	23	11.050	5.0103
QOL (preintervention)	3	5	4.350	0.7452
QOL (postintervention)	0	5	1.65	1.3485
Prostatic volume (preintervention)	52	180	95.95	36.1539
Prostatic volume (postintervention)	30	111	62.9	24.7469
PVRU (preintervention)	0	235	64.81	69.11
PVRU (postintervention)	0	150	25.15	36.4696

DISCUSSION

For decades Prostatic artery embolization has been performed by interventional radiologists in management of bleeding from different prostatic causes. DeMeritt et al. (2000) first reported prostatic artery embolization for the treatment of benign prostatic hyperplasia as consequence of the treatment of refractory hematuria in 2000. In 2008, Carnevale et al (2010) performed the first intentional treatment of lower urinary tract symptoms due to benign prostatic hyperplasia using prostatic artery embolization as a successful minimally invasive. The Society of Interventional Radiology (SIR) published in 2014 an initial statement on prostatic artery embolization for benign prostatic hyperplasia, concluding PAE as a safe and effective procedure for BPH and recommending further clinical investigation. (McWilliams JP et al., 2014).

Our study demonstrated several important findings. Firstly, prostatic artery embolization is a safe procedure. Among the 20 performed procedures, 3 minor complications were observed, managed conservatively with no need for hospitalization and no lone term morbidity. No major adverse events were noted. No reports of sexual dysfunction, incontinence, or infection.

Also, the study was conducted entirely in an interventional radiology unit on outpatient basis. No patients had to be admitted longer than 6 hours. This is a great advantage in providing a minimally invasive method for management. The total procedural time (starting from femoral puncture till sheath removal) was of mean 103 minutes (ranging from 60 up to 152 minutes) , which is average procedural time compared to mean of 116 minutes according to (Yu SC et al., 2017).

The radiation exposure was measured in only 11 patients out of 20 due to technical limitations , the mean total dose–area product (DAP) measured among the 11 patients was 260 Gy.cm2 per procedure (range, 124–653 Gy·cm 2) compared to 450.7 Gy·cm 2 (range, 248.3–791.73 Gy·cm 2) per procedure according to (G. Andrade et. al., 2017). The relatively low radiation exposure of our study may be due to the lack of cone beam CT of 4 cases of them and due to the small sample size (11 patients).

In our study we evaluated the patient's response to treatment by not only radiological data (the prostatic volume and post-voiding residual urine) but mainly by the patient symptoms (IPSS and QOL calculation). One patient shows a significant reduction in the prostatic volume yet worsening of his symptoms were considered a technical success yet a clinical failure.

Prostatic artery embolization resulted in an average reduction of prostate volume of 34.4% and improved International Prostate Symptom Score and quality-of-life score by a mean of 8.33 points and 2.7 points, respectively. Four patients were having an indwelling catheter for a variable period of time, three of them were inserted within three months preoperatively while the fourth patient was having it for more than six months. All patient their catheters were removed successfully after two weeks. The patient with prolonged indwelling catheter needed recanalization latter with worsening of his symptoms after two months, patient was sent for physiotherapy. The other 16 patients with no indwelling catheters, there was no need for inserting a urinary catheter during the procedure (identification of prostatic artery done without the need of catheter ballon as reference for the prostate size) or after the procedure (neither of them needed cathetrization during the prostatic edema phase post embolization). Also, out of the 20 procedures performed, not a single case done preoperative CT angiography due to funds limitations, with a technical success 100%. Suggesting that preoperative CTA is not mandatory, and that PAE is doable without it.

LITERATURE REVIEW

In 2014 Gao YA et al. (2014) published the first randomized controlled trial comparing prostatic artery embolization with transurethral resection of the prostate. Randomized trial done on 114 patients with moderate to severe LUTS and prostate volume < 100 cm3 to undergo PAE or TURP and followed for 2 years. At 1 month and 3 months follow up TURP was associated with better outcomes yet at 1 year and 2 years follow up all outcomes including IPSS, QOL, and postvoid residual volume (PVR), were equivalent between the two groups. With longer hospital stay, more likely to require catheterization of the bladder in the TURP group. Major complications were seen only in the group underwent TURP.

Another randomized controlled trial done by Abt D et al. (2018) compared 48 patients underwent prostatic artery embolization and 51 patients underwent transurethral resection of prostate (TURP). Average volume of prostate volume was 25–80 cm3, minimum IPSS of 8, QOL higher than 2. At 3 months post-interventional follow up, the mean IPSS improvement was not significantly different between the 2 groups (9.2 points for PAE and 10.8 points for TURP). TURP was associated with twice as many adverse events as PAE, including more than 3 times as many severe adverse events. Blood loss, duration of hospitalization, and bladder catheterization time were higher for TURP than for PAE.

The minimally invasive therapies for BPH treatments are rapidly evolving especially with mild side-effect as compared to surgery. The least invasive is by far PAE as it

avoids transurethral access, anesthesia, and hospitalization. At the same time, prostatic artery embolization outcomes by reviewing published data for more than 2,000 benign prostatic hyperplasia patients complaining of lower urinary tract symptoms, Prostatic artery embolization proven to be effective, reducing mean IPSS by 10.8 to 18.0 points, and safe, less than 0.5% of patients experiencing major complications.

LIMITATIONS

Lack of long term follow up data for all the patient's is the major limitation in this study. However, the available intermediate term follows up data are promising. Baseline IPSS and post-voiding residual urine couldn't be assessed for patients with indwelling catheters. Out of 20 cases only one case was done as unilateral embolization of the prostatic artery, with promising post-intervention clinical data, yet one case is not statistically significant to assess the efficacy of unilateral embolization. A separate study in the future for the efficacy of unilateral embolization is advised. Few procedures (about 5 patients) were carried out without cone-beam CT due to technical problems of the machine or unavailability in some institutes. As we mentioned before, the lack of preoperative CTA for all the patients may made the procedures more difficult and longer procedural time. Yet technical success was obtained in all cases with average procedural time.

CONCLUSION

Prostatic artery embolization is efficient procedure in management of benign prostatic hyperplasia, significantly reducing the prostatic volume, post-voiding residual urine volume and patient's lower urinary tract symptoms (measured by IPSS and QOL calculation).

List of abbreviations

Prostatic artery embolization (PAE), Benign prostatic Hyperplasia (BPH), International prostatic scoring system (IPSS), Quality of life (QOL).

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