

# PROSTATIC ARTERY EMBOLIZATION AS A NEW OPTION IN THE TREATMENT OF LOWER URINARY TRACT SYMPTOMS IN BENIGN PROSTATIC HYPERPLASIA – CURRENT EVIDENCE

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**SUMMARY** – Prostatic artery embolization is a minimally invasive endovascular treatment that improves lower urinary tract symptoms in men with benign prostatic hyperplasia. Although further randomized studies and long-term evidence is still needed for this method to be fully incorporated into treatment guidelines for benign prostatic hyperplasia, current studies show that this method can be an effective and safe alternative in patients with a significantly enlarged prostate gland who are not good surgical candidates. Therefore, we present the theory, technical details and potential benefits of this method as we review the current evidence on prostatic artery embolization.

**Keywords:** *Benign prostatic hyperplasia; Arterial embolization; Endovascular treatment; Interventional radiology; Lower urinary tract symptoms*

## Introduction

Benign prostate hyperplasia (BPH) is a disease with a prevalence that reaches 50% to 60% for men aged 60-70, and 80% to 90% for men aged 70-90<sup>1</sup>. Histologically characterized by smooth muscle proliferation, BPH, when symptomatic, is most often associated with lower urinary tract symptoms (LUTS) consisting of obstructive and irritative symptoms. Obstructive symptoms include hesitancy, weak flow, prolonged voiding, urinary retention and overflow incontinence, while irritative symptoms include urgency, frequency, nocturia and painful urination. Patients are evaluated based on a quantitative symptom score, most commonly the International Prostate Symptom Score

(IPSS), a 7-item questionnaire addressing the most common LUTS symptoms<sup>2</sup>. The indication for treatment depends on the severity and bother of urinary symptoms. Patients with mild symptoms first undergo watchful waiting or medical therapy that includes alpha-blockers and 5-alpha-reductase inhibitors as the first line option. When moderate to severe symptoms occur, the only remaining option often involves surgical treatment. Traditional surgical solutions include open prostatectomy, which usually requires long hospitalisation and has high morbidity rates, and transurethral resection of the prostate (TURP), which is currently the gold standard definitive treatment for BPH. However, this procedure is accompanied by significant risks, including bleeding and nerve damage potentially leading to impotence<sup>3</sup>. In addition, patients with LUTS due to BPH are often elderly and with serious comorbidities. Because of high operative risk of undergoing TURP or open surgery, especially with an enlarged prostate gland with a volume of more than

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80 mL<sup>4</sup>, non-surgical treatment alternatives have been explored. There is a list of minimally invasive therapies that have been developed for the treatment of BPH, such as transurethral microwave thermotherapy (TUMT), transurethral needle ablation (TUNA), the placement of a urethral stent, electrovaporization of the prostate, transurethral laser vaporization or coagulation, transurethral Holmium laser resection or enucleation. However, these have not proven to be more efficient in the long term when compared to TURP<sup>5</sup>. In the last decade, a new interventional radiology endovascular procedure called prostatic artery embolization (PAE) has been introduced for the treatment of lower urinary tract symptoms related to BPH. It has shown to cause a decrease in prostate volume and possibly present a safe and effective alternative to both TURP, and minimally invasive therapies. Even though there is growing evidence supporting this method, it has not been widely accepted or incorporated into urologic society guidelines as yet. This article presents the development, technical aspects, the theory behind the method and results through a review of currently available evidence.

### PAE development and evidence

The first case of successful PAE was recorded in a patient with severe gross hematuria, who was subjected to embolization with polyvinyl alcohol particles, as published by DeMeritt in 2000<sup>6</sup>. The patient stopped bleeding after embolization, but it was also observed that the size of the prostate was reduced by 50–60%. Although embolization of internal iliac arteries had been previously used in the treatment of pelvic haemorrhage, an idea was born at the time that ischaemic infarction occurring after the occlusion of distal arterial branches supplying the prostatic tissue would partially reduce the volume of the gland with LUTS reduction without the need for further surgery<sup>7</sup>. A similar effect had been observed earlier and used in the treatment of symptomatic uterine fibroids by uterine artery embolization<sup>8</sup>. Following studies on animals, Carnevale was the first to perform, and publish the results of, PAE in two BPH patients in 2010<sup>9</sup>. Shortly thereafter, the first large prospective study with the longest follow-up period was published by Pisco *et al.*<sup>10</sup>, who treated 255 patients with BPH refractory to medical treatment and moderate to severe LUTS between 2009 and 2012. The procedure was deemed

technically and clinically successful, showing good results (IPSS reduction of at least 25 % and QoL improvement of >1) at 1 and 36 months after the procedure (82% and 72%, respectively). This study, as well as other randomized and non-randomized studies performed using different embolization particle sizes and involving patients with different initial sizes of the prostate gland all showed benefits of PAE with very rare serious complications. Over 700 patients were treated and all studies demonstrated statistically significant reduction in IPSS, ranging from 12 to 21, and an improvement in quality of life. In our search of databases we have found 11 studies published in the last 17 years, most of them non-randomized. Main study characteristics and results are presented in Table 1.

Lately, PAE has been particularly recommended for and examined in a subgroup of BPH patients with larger prostate glands (>80mL). This is due to the fact that these patients show worse results after TURP treatment, while open prostatectomy remains the last treatment option due to its invasiveness and potential complications. 3 studies have reported good results with significant IPSS and QoL improvement, 12–15 points and 2–4, respectively. They did not show any major complications occurring in these patients<sup>11</sup>. Wang *et al.*<sup>12</sup> performed a comparative study of PAE treatment of large (>80 mL) and medium-sized prostate glands (50–80 mL) to determine whether size affects the outcome of PAE. They concluded that clinical and imaging outcomes of PAE were better in patients with larger prostate glands than medium-sized ones.

### Technical aspects

Although transarterial selective catheter embolization has been widely used by interventional radiologists in a variety of locations and indications that can sometimes be challenging, such as liver chemoembolization, uterine fibroid embolization or upper and lower gastrointestinal bleeding embolization, PAE is technically one of the most difficult procedures to perform. This is due to the fact that prostatic arterial supply is variable and closely related to the rectal and urinary bladder arterial branches, which can potentially lead to non-target embolization and complications like bladder ischaemia<sup>10</sup>. Therefore, detailed knowledge of pelvic arterial anatomy and advanced microcatheter skills are obligatory for performing this procedure. Furthermore, due to progressive atherosclerotic arte-

*Table 1. Characteristics and results of published studies investigating prostatic artery embolization*

Authors	Study type	Mean prostate volume (mL)	Embolic type and particle size (mm)		Number of patients	1 year IPSS reduction	Technical success	1 y QoL score change
Antunes (20)	Prospective, single centre	69.7	Embospheres	300-500	11	N/A	N/A	N/A
Pisco (10)	Prospective, single centre	83.5	PVA	100-200	255	13.7	82%	2.4
Bagla (21)	Retrospect single centre	93.9	Embozene	100-400	78	12.2 at 6 mo	96%	2.7 at 6 mo
Kurbatov (17)	Prospective single centre	129.3	Embospheres	300-500	88	13.6	100%	2.9
Grosso (16)	Retrospect single centre	N/A	Embospheres	300-500	13	17.1	75%	2.6
Somani (22)	Prospective, single centre	94.9	PVA	N/A	35	12	90%	2.9
Assis (23)	Prospective single centre	135.1	Embospheres	300-500	35	15.6 at 3 mo	94%	3.9 at 3 mo
Wang (12)	Prospective single centre	96.5	PVA	100	115	12.9	95%	2.9
Gao (18)	Prospective single centr randomized (vrs TURP)	64.7	PVA	355-500	57	11.9	84%	2.9
Carnevale (19)	Prospective, single centre Randomized (vrs TURP)	64.6	Embospheres	300-500	30	21.0	93%	3.1
Li (24)	Prospective single centre	110.0	Embospheres	50-100	24	19.5	86%	2.5

PVA - polyvinyl alcohol

rial changes bilateral selective catheterisation is sometimes difficult, which can lead to lower clinical success, reportedly around 50%<sup>13</sup>.

Even though serious adverse events that required surgical intervention or treatment were very rare in the published studies and involved cases of proctitis<sup>14</sup> and bladder necrosis<sup>10</sup> with a variety of minor side effects like dysuria hematospermia, haematuria and diarrhoea, this is still an area of concern. Non-target embolization risks are potentially greater if the embolization material-particles are smaller in size, due to their ability to penetrate deeper and cause micro vessel occlusion and tissue necrosis. For this reason and for reasons of prostatic gland and LUTS reduction effect, different particle sizes have been tested in reported studies. Non-spherical PVA particles, as well as spherical par-

ticles have been used with success and different sizes ranging from 50 to 500  $\mu$ m. Even though all have shown to have success, there was a theoretical advantage leaning toward smaller particles due to better penetration and prevention of revascularization and recurrent growth. However, a study by Bilhim<sup>15</sup> comparing 100 and 200  $\mu$ m particles did not show any significant difference in complications or pain. Clinical outcome was slightly better with larger particles, while greater volume reduction of the prostate was achieved with smaller particles.

### Potential and limitations of PAE

Like other interventional radiologic procedures, PAE has certain advantages it can offer to patients

with LUTS due to BPH. It is performed under conscious sedation through a femoral or radial artery puncture, which allows it to be performed as a one day procedure, eliminating the need for prolonged recovery. Even though it is technically demanding, the published data shows it to be highly successful, with results ranging from 75 to 100%<sup>16,17</sup>. Medication treatment is usually abandoned soon after the procedure, and Foley catheterisation is not required in most cases after PAE. There have been two studies that randomized patients and compared PAE to the gold standard therapy, the TURP<sup>18,19</sup>, with additional larger studies scheduled to be published soon. Both of these published studies showed promising results. Urinary flow was similar after both procedures in the larger study, and while there was a higher incidence of technical failure and clinical failure with PAE (9, 4%) compared to TURP (3, 9%), complications (bleeding) occurred only after TURP, which required longer hospital stay and more frequent catheterisation. In the second study there was no significant difference in IPSS after TURP and PAE, but urinary flow was significantly higher after TURP. Also here, adverse events were more frequent and more serious after TURP.

These results are still insufficient to establish PAE as a procedure equal to standard surgical methods and there is still a lack of randomized prospective evidence, but initial results are promising and can lead to a certain number of patients for whom medical therapy was ineffective and who either refuse surgery or are poor surgical candidates to be referred to interventional radiology in centres with experienced endovascular specialists. Most promising results can be expected in a subgroup of patients with prostate volume larger than 80 mL in which TURP has shown to have higher complication rates, while PAE so far has not shown to have an upper limit of prostate volume that can be effectively treated<sup>17</sup>.

## Conclusion

In the search of minimally invasive alternatives for the standard surgical methods of TURP and open prostatectomy, PAE has emerged as a safe and effective endovascular treatment with low morbidity, that could be offered to patients refractory to medical treatment of BHP who are the same time at risk if subjected to surgery or who refuse it. Even though studies published so far have all shown promising results that can

be clinically compared with TURP in the reduction of symptoms, with fewer reported complications and shorter hospital stay and recovery time, additional prospective and randomized studies are required, with long term follow-up. For now, PAE can be recommended for a selected group of patients, with large volume prostate glands who are poor surgical candidates, in centres with experienced interventional radiologists.

## References

1. Roehrborn C, McConnell J. Etiology, pathophysiology, epidemiology and natural history of benign prostatic hyperplasia. In: Walsh P, Retik A, Vaughan E, Wein A, editors. *Campbell's Urology*. 8th ed. Philadelphia: Saunders; 2002. pp. 1297–1336.
2. Barry MJ, Fowler FJ, Jr, O'Leary MP, *et al.* The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol*. 1992;148:1549–1557. doi: 10.1016/S0022-5347(17)36966-5.
3. Mebust WK, Holtgrewe HL, Cockett AT, Peters PC. Transurethral prostatectomy: immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3,885 patients. *J Urol*. 2002;167:999–1003. doi: 10.1016/S0022-5347(02)80323-8.
4. Geavlete B, Stanescu F, Iacoboaie C, Geavlete P. Bipolar plasma enucleation of the prostate vs open prostatectomy in large benign prostatic hyperplasia cases - a medium term, prospective, randomized comparison. *BJU Int*. 2013;111:793–803. doi: 10.1111/j.1464-410X.2012.11730.
5. American Urological Association Practice Guidelines Committee. AUA guidelines on management of benign prostatic hyperplasia (2003). Chapter 1: diagnosis and treatment recommendations. *J Urol*. 2003;170:530–547. doi:10.1097/01.ju.0000078083.38675.79.
6. DeMeritt JS, Elmasri FF, Esposito MP, Rosenberg GS. Relief of benign prostatic hyperplasia-related bladder outlet obstruction after transarterial polyvinyl alcohol prostate embolization. *J Vasc Interv Radiol*. 2000;11:767–70. doi:10.1016/S1051-0443(07)61638-8.
7. Camara-Lopes G, Mattedi R, Antunes AA, *et al.* The histology of prostate tissue following prostatic artery embolization for the treatment of benign prostatic hyperplasia. *Int Braz J Urol*. 2013;39:222–7. doi: 10.1590/S1677-5538.IBJU.2013.02.11.
8. Goodwin SC, Vedantham S, McLucas B, Forno AE, Perrella R. Preliminary experience with uterine artery embolization for uterine fibroids. *J Vasc Interv Radiol*. 1997;8(4):517–526. doi: 10.1016/S1051-0443(97)70603-1.
9. Carnevale FC, Antunes AA, da Motta Leal Filho JM, *et al.* Prostatic artery embolization as a primary treatment for benign prostatic hyperplasia: preliminary results in two patients. *Cardiovasc Intervent Radiol*. 2010;33:355–61. doi: 10.1007/s00270-009-9727-z.
10. Pisco JM, Tinto HR, Pinheiro LC, *et al.* Embolisation of prostatic arteries as treatment of moderate to severe lower urinary

- symptoms (LUTS) secondary to benign hyperplasia: results of short- and midterm follow up. *EurRadiol.* 2013;23:2561-72. doi: 10.1007/s00330-012-2714-9.
11. Wang M. Q., Guo L. P., Zhang G. D., *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 Urology.* 2015;15:p33. doi: 10.1186/s12894-015-0026-5.
  12. Wang M, Guo L, Duan F, *et al.* Prostatic arterial embolization for the treatment of lower urinary tract symptoms caused by benign prostatic hyperplasia: a comparative study of medium- and large-volume prostates. *BJU Int.* 2016 Jan;117(1):155-64. doi: 10.1111/bju.13147.
  13. Bilhim T, Pisco JM, Rio Tinto H, *et al.* Unilateral versus bilateral prostatic arterial embolization for lower urinary tract symptoms in patients with prostate enlargement. *Cardiovasc Intervent Radiol.* 2013;36:403-11. doi: 10.1007/s00270-012-0528-4.
  14. Moreira AM, Marques CF, Antunes AA, *et al.* Transient ischemic rectitis as a potential complication after prostatic artery embolization: case report and review of the literature. *Cardiovasc Intervent Radiol.* 2013;36:1690-4. doi: 10.1007/s00270-013-0739-3.
  15. Bilhim T, Pisco JM, Campos Pinheiro L, *et al.* Does polyvinyl alcohol particle size change the outcome of prostatic arterial embolization for benign prostatic hyperplasia? Results from a single-center randomized prospective study. *J Vasc Interv Radiol.* 2013;24:1595-602. doi: 10.1016/j.jvir.2013.06.003.
  16. Grosso M, Balderi A, Arno M, *et al.* Prostatic artery embolization in benign prostatic hyperplasia: preliminary results in 13 patients. *Radiol Med.* 2015;120:361-8. doi: 10.1007/s11547-014-0447-3.
  17. Kurbatov D, Russo GI, Lepetukhin A, *et al.* Prostatic artery embolization for prostate volume greater than 80 cm<sup>3</sup>: results from a single center prospective study. *Urology.* 2014;84:400-4. doi: 10.1016/j.urology.2014.04.028.
  18. 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;270:920-8. doi: 10.1148/radiol.13122803.
  19. Carnevale FC, Iscaife A, Yoshinaga EM, Moreira AM, Antunes AA, Srougi M. Transurethral Resection of the Prostate (TURP) Versus Original and PERFeCTED Prostate 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. doi: 10.1007/s00270-015-1202-4.
  20. Antunes AA, Carnevale FC, da Motta-Leal-Filho JM, *et al.* Clinical, laboratorial and urodynamic findings of prostatic artery embolization for the treatment of urinary retention related to benign prostatic hyperplasia: a prospective single center pilot study. *Cardiovasc Intervent Radiol.* 2013;36:978-86. doi: 10.1007/s00270-013-0611-5.
  21. 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. doi: 10.1016/j.jvir.2013.09.010.
  22. Somani BK, Hacking N, Bryant T, *et al.* Prostate artery embolization (PAE) for benign prostatic hyperplasia (BPH). *BJU Int.* 2014;114:639-40. doi: 10.1111/bju.12672.
  23. Assis A, Moreira AM, De Paula Rodrigues VC, *et al.* Prostatic artery embolization for treatment of benign prostatic hyperplasia in patients with prostates > 90 g: a prospective single-center study. *J Vasc Interv Radiol.* 2015;26:87-93. doi: 10.1016/j.jvir.2014.10.012.
  24. Li Q, Duan F, Wang MQ, Zhang GD, Yuan K. Prostatic arterial embolization with small sized particles for the treatment of lower urinary tract symptoms due to large benign prostatic hyperplasia: preliminary results. *Chin Med J (Engl).* 2015;128:2072-7. doi: 10.4103/0366-6999.161370.

## Sažetak

EMBOlizacija PROSTATE  
– NOVA TERAPIJSKA MOGUĆNOST LIJEČENJA SIMPTOMA DONJEG URINARNOG TRAKTA  
KOD MUŠKARACA S BENIGNOM HIPERPLAZIJOM PROSTATE

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Embolizacija prostate je minimalno invazivna endovaskularna metoda liječenja koja se koristi za liječenje simptoma donjeg urinarnog trakta kod muškaraca s benignom hiperplazijom prostate. Iako su potrebne dodatne randomizirane studije s dugoročnim praćenjem i rezultatima kako bi ova metoda bila uključena u smjernice liječenja benigne hiperplazije prostate, dosadašnje studije ukazuju da ova metoda može predstavljati učinkovitu i sigurnu alternativu kod pacijenata s uvećanom prostatom koji nisu dobri kirurški kandidati. Stoga prikazujemo teoriju, tehničke detalje i moguće prednosti ovog zahvata kroz analizu dosadašnjih studija o embolizaciji prostate.

Ključne riječi: *Prostata; Embolizacija; Simptomi donjeg urinarnog trakta; Benigna prostaticna hiperplazija*