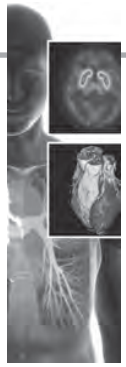

Prostate artery embolization for benign prostatic hyperplasia

Prostate artery embolization (PAE) has emerged as a promising treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia (BPH). We aim to provide an up-to-date review of this minimally invasive technique, including discussion of potential benefits and technical challenges. Current evidence suggests it is a promising and effective option for patients with large prostate volumes, multiple comorbidities, and suboptimal results from pharmacotherapy. Larger, randomized studies with long-term follow-up data are needed for this technique to be formally established in the treatment paradigm for BPH. .

KEYWORDS: Prostatic hyperplasia; lower urinary tract symptoms; embolization; transurethral resection of prostate; interventional radiology

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Prostate artery embolization (PAE) is becoming an increasingly well recognized therapeutic modality in the management of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH). Although the procedure has not yet been widely adopted, a growing body of evidence suggests it represents an innovative, effective, and safe alternative to transurethral resection of the prostate (TURP) and open prostatectomy as well as minimally invasive surgical therapies such as holmium laser enucleation of the prostate (HoLEP) and photoselective vaporization of the prostate (PVP). Thus, it has garnered much interest in both the interventional radiologic and urologic communities. This article provides an up-to-date review of PAE in the treatment of LUTS secondary to BPH.

Background

LUTS typically include incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. BPH represents the most common cause of LUTS, with more than 50% of men aged 60–69 years and as many as 90% aged 70–89 years experiencing such symptoms [1]. BPH symptoms are quantified by the International Prostate Symptom Score (IPSS), which assigns a severity score of 0 to 5 to each of the seven LUTS symptoms. A total score of 0–7 is considered mild, 8–19 is moderate, and 20–35 is severe [2]. An eighth question pertains to the patient-perceived quality of life related to LUTS, ranging from 0 (delighted) to 6 (terrible).

Existing treatment paradigm

The goal of treatment is to facilitate quality of life and to avoid the potential sequelae of bladder outflow obstruction, including acute urinary retention and recurrent urinary tract infection. Pharmacotherapy with alpha-blockers and/or 5- alpha-reductase inhibitors is usually the first line option for symptomatic patients. Patients who cannot tolerate pharmacotherapy, who develop complications of BPH, or whose disease is severe and/or refractory to treatment are considered for surgical intervention. Transurethral resection of the prostate (TURP) remains the gold standard surgical therapy for BPH, with reported IPSS reduction up to 70% [3,4]. However, as many as 20% of patients have significant complications including sexual dysfunction, perioperative bleeding requiring blood transfusion, and incontinence [3,4]. Open prostatectomy is the gold standard treatment for prostates larger than 80–100 cm^3, but it is an invasive surgical procedure with concomitant morbidity and extended hospitalization. Several other less invasive techniques have been popularized in the past two decades, including intraprostatic stents, transurethral needle ablation, transurethral microwave therapy, HoLEP and PVP. However, none of these newer techniques have been shown to be superior to TURP from a costversus- benefit standpoint, and none of them have supportive long term efficacy data [5,6].

PAE

■ History and expanding research

Embolization of internal iliac artery branches has been successfully used to manage severe prostatic hemorrhage secondary to prostate

cancer or BPH for over 30 years [7-10]. However, it was not until 2000 when the first case documenting therapeutic effect of PAE on BPH was published [9]. The premise behind PAE is simple therapeutic occlusion of the arteries supplying the prostate results in ischemic necrosis and reduction in gland volume [11]. The resultant effect is improvement in the objective and subjective parameters of voiding. PAE has only recently started to be used for primary control of LUTS related to BPH after feasibility and safety from trials in dogs and pigs were established [12-14]. The first intentional treatment of BPH with PAE in humans was done by Carnevale *et al* [15] in June 2008 and published in 2010. They performed PAE for 2 patients with acute urinary retention due to BPH who were waiting for surgery. After 6 months, magnetic resonance imaging (MRI) revealed a relative prostate volume reduction of 47.8% and 27.8% in these patients who had undergone bilateral and unilateral PAE, respectively. Early in 2013, through a pilot study of 11 patients, Antunes *et al* [16] further affirmed PAE' s potential role in the management of urinary retention as clinical success was reported in 91% of their patients with a decrease in mean detrusor pressure from 87.5 to 51.5 cm H2O (p=0.007). With a mean follow-up of 22.3 months, at 1 year the mean IPSS was 2, prostate volume had decreased by 30%, there was no erectile dysfunction, and no major complications were observed. Later in 2013, Pisco *et al* [17] reported findings from a prospective single-center study in Lisbon, the largest to date, in which 255 patients with a history of symptomatic BPH, refractory to pharmacologic treatment for at least 6 months, underwent PAE as an alternative treatment. The average procedure time was 73 minutes, and technical success was achieved in 98% of cases. Clinical success was achieved in 81.9% of patients at 1 month, 75.2% at 1 year, and 72.0% at 2 and 3 years and there were no reported cases of sexual impotence [17]. In 2014, Bagla *et al* [18] reported successful bilateral PAE in 18 of 19 patients in their American cohort. At 1 month, the average American Urological Association (AUA) symptom score improvement was 10.8 points (p<0.0001). At 6 months, prostate volume had decreased by 18% and quality of life had improved 2.6 points (p=0.007). Subsequently, results from another nonrandomized prospective study were published where PAE was performed on 88 patients with prostate volume >80 mL, affected by benign prostatic obstruction with severe symptoms. [19] This study showed significant improvements in mean IPSS (10.40 vs. 23.98; p<0.05). In late 2014, early findings were released from a study by Somani *et al* [20] in the United Kingdom, carried out on a population of 35 severely symptomatic patients (mean IPSS of 24 and mean prostate volume of 94.9 mL). Even though bilateral embolization could not be performed in all patients, a prostate volume reduction of 42% was achieved. At the beginning of 2015, the Carnevale group out of Sao Paulo published findings from a single-arm study conducted in 35 patients with prostates >90 g.21 At 3-month follow-up, mean quality of life and IPSS had improved from 4.8 to 0.9 and 18.3 to 2.7, respectively (p<0.001). Most recently, Wang *et al* [21,22] published findings comparing outcomes of PAE in the treatment of large sized prostates (>80 mL) vs. medium-sized prostates (50-80 mL). Their results revealed a significantly greater improvement in IPSS, post void residual and prostate volume in the group with large-sized prostates.

Randomized controlled trials (RCTs)

To date, only one RCT has been published evaluating PAE. In 2014, a group out of China, assigning 57 patients each to PAE and TURP, respectively, found all parameters to be improved by both treatment modalities [20]. Technical failures (5.3% vs. 0%) and clinical failures (9.4% vs. 3.9%) were more common with PAE, whereas substantial bleeding (3.8%) and transurethral resection syndrome (1.9%) occurred only with TURP. PAE recipients were less likely to require urethral catheterization and required a shorter hospital stay. A few randomized controlled trials are underway in the United States and elsewhere around the world. Pisco and colleagues are lead investigators in a randomized trial assessing PAE, scheduled to release early results in 2016, according to clinicaltrials.gov. An industry-sponsored prospective multisite clinical trial comparing PAE and TURP, under the direction of Carnevale *et al*, is enrolling candidates to reach its target of 186 patients, according to clinicaltrials.gov. The primary endpoint will be improvement of LUTS evaluated using the IPSS at 12 months post procedure [23,24].

Making the case for PAE

PAE has several advantages over traditional surgical therapies. First, it is minimally invasive, usually performed via a single femoral artery puncture under conscious sedation rather than general anesthesia. In contrast to more invasive

procedures, PAE can be done under local anesthesia and in the outpatient setting, enabling the patient to go home the same day. Technical success, defined as bilateral embolization, is achieved in 75-94% of patients [18,25]. Prolonged Foley catheterization is not needed after PAE, and pharmacologic BPH treatments are usually discontinued in the weeks after the procedure. Unlike TURP, where the complication rate is higher with increased gland size (>80 cc), there does not appear to be an upper limit of prostate size that can be effectively treated with PAE [26]. Evidence from short and intermediate-term data on PAE suggests that this evolving technology can be used for large prostates with no additional risk of adverse events.[19,21,22]

Current limitations and challenges

Although PAE promises to be a viable therapeutic alternative for BPH, current evidence remains limited, and PAE for the treatment of BPH should, at present, be considered only in patients who have failed medical therapy and either refuses surgery or is contraindicated for surgery. It is also important to recognize that LUTS has a multitude of causes apart from BPH, including neurogenic bladder and interstitial cystitis, for which PAE is not likely to be effective [26,27]. Further research is needed to establish clear indications and contraindications for PAE. We expect that the on-going prospective, multicenter, randomized, controlled trials will address these issues and allow for objective comparison of post-intervention outcomes. PAE is a technically challenging procedure, requiring detailed knowledge of pelvic arterial anatomy and advanced microcatheter skills. Occasionally, PAE cannot be achieved on at least one side, usually as a result of atherosclerosis, small artery size or tortuous anatomy. Clinical success may only be achieved in 50% of patients in whom only unilateral embolization is possible. Even if technically successful (bilateral), PAE does not guarantee that the patient will experience significant clinical improvement. As many as 25% of patients may not show a significant reduction in IPSS [25]. The prostatic arterial supply is closely related to that of the bladder and rectum, thus, there is potential for complications with non-target embolization. Non-target embolization may occur even if not detected during the procedure, as manifested by minor side effects that have been reported following PAE. These include dysuria, hematuria, hematochezia, hematospermia, and diarrhea and are almost always self-limited [14,28]. As outlined in the Society of Interventional Radiology position (SIR) statement on PAE, radiation exposure during the procedure must be carefully monitored with patients at risk for skin burns in cases with prolonged fluoroscopy times [28]. Iodinated contrast material utilized during the procedure can cause allergic reaction or nephropathy.

Conclusion

PAE for BPH is a novel and promising therapy with positive short and intermediate term outcomes data. Long-term data on PAE is not available, and there is a paucity of RCT data. On-going trials comparing PAE with TURP will shed more light on how PAE should be incorporated into the treatment paradigm for BPH refractory to medical therapy.

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