Review Article on Interventional Radiology in Glands

State of the art of prostatic arterial embolization for benign prostatic hyperplasia

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Abstract: Prostatectomy via open surgery or transurethral resection of the prostate (TURP) is the standard treatment for benign prostatic hyperplasia (BPH). Several patients present contraindication for standard approach, individuals older than 60 years with urinary tract infection, strictures, post-operative pain, incontinence or urinary retention, sexual dysfunction, and blood loss are not good candidates for surgery. Prostatic artery embolization (PAE) is emerging as a viable method for patients unsuitable for surgery. In this article, we report results about technical and clinical success and safety of the procedure to define the current status.

Keywords: Prostate gland; interventional radiology; embolization; review

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Introduction

Benign prostatic hyperplasia (BPH) is histologically characterized by proliferation of prostatic cellular elements. Chronic bladder outlet obstruction (BOO) may be a consequence; it leads to urinary retention, urinary infections, hematuria, bladder calculi and renal insufficiency. In male, BPH represents one of the most common reason causing lower urinary tract symptoms (LUTS) (1). In clinical practice, urinary tract infections secondary to BPH are most common causes for urologic consultation.

In presumed BPH diagnosis the first step is still based on digital rectal examination (DRE) to evaluate prostate size and contour. Urinalysis are usually performed to assess the presence of blood, leukocytes, bacteria, protein, or glucose. Prostate-specific antigen (PSA), even if BPH does not cause prostate cancer (PCa) should be screened (2). Moreover, renal function must be investigated in those patients who have elevate post-void residual (PVR) urine volumes (3).

Symptomatology alone is insufficient for diagnosis (4) and patients with suspected large PVR should undergo a bladder ultrasound (US) to determine urine volume and assess for BOO. Trans-rectal US (TRUS) is useful only in selected patients, to determine prostate gland dimensions and volume over the anatomical characteristics of the gland to improve success of minimally invasive treatments or following biopsies on areas incidentally found as suspect for PCa (3,5,6).

During the past years, BPH was considered a surgical disease and patients with moderate or severe LUTS and an abundant PVR with gross hematuria or recurrent urinary tract infection were addressed to radical prostatectomy (RP) or transurethral resection of the prostate (TURP) to reduce symptoms (3). Currently, the wait and watch strategy is recommended for patients referred with mild BPH symptoms [International Prostate Symptom Score (IPSS) ≤7] and for those with moderate/severe (IPSS ≥8) without complications of BPH. Those patients are managed with medical therapy.

Although the TURP is still considered the gold standard for BPH surgical treatment, a morbidity of 20% and several complications are still reported in literature such as ejaculatory dysfunction, erectile dysfunction, urethral strictures, urinary tract infection and post-operative bleeding in same cases requiring transfusion, with an overall retreatment rate of 6% (7).

Moreover, some patients are unfit for surgery based on their comorbidities (8).

For this class of patients and for patients that refuse surgery, novel minimally invasive procedures have been developed, pointing to a safer profile that is fundamental for QoL after treatment and equally effective to surgical techniques, sparing costs with a durable relief of symptoms (9). Among the available minimally invasive procedures (such as intraprostatic injectables, medical devices, and approaches based on tissue ablation) the prostatic artery embolization (PAE) can be considered an emerging technique performed under radiological guidance by interventional radiologists through selective prostatic arteries embolization.

In 2000, the first case of PAE was reported (10). With the goal to reduce recurrent episodes of acute urinary retention (AUR) and persistent gross hematuria in a patient unsuitable for surgery due to its relevant comorbidities PAE was performed. Over the successful management of prostatic bleeding, a great relief in BPH symptoms, including urinary retention, was registered: an unexpected useful side effect (10). Currently, the increased experience with PAE and a conspicuous available literature, have led to more interesting results showing acceptable outcomes in terms of reduced failure rates with some studies that show acceptable IPSS/AUA-SI score at 24 and 36 months post-intervention (11,12). Extensive improvement in technology concerning interventional devices, angiographic suites and guidance software, have reduced complications rate and risk of inadvertent and untargeted embolization that heavily compromise patient outcomes (12-14). These developments have renewed the interest in PAE.

The aim of this review is to define current evidence on feasibility, effectiveness and safety of PAE according with clinical experiences available in literature.

Methods

A systematic literature search was performed on Medline, Scopus and Google Scholar using the syntax "benign prostatic hyperplasia" and "embolization" or embolic agents" and "results" or "indications" or "complications" or "technical success" or "effectiveness and clinical success" for studies published in English from January 2005 to December 2017. All titles and abstracts of studies found in the initial search were then selected to individuate those evaluating patients with BPH that were unsuitable for any other treatment (medical therapy or surgery) and underwent prostatic arterial embolization. Two reviewers (AMI and MP) included all relevant studies. Based on titles and related abstract, duplicated studies, nonhuman studies, studies not concerning prostatic hyperplasia, comments, letters, case reports (<5 patients) and conference abstracts were all excluded. Remaining studies were considered relevant.

Data extraction was performed by two authors (FP and FP) and extracted data were included. A third external reviewer performed final consensus (SAA).

The primary endpoint was to evaluate technical and clinical success and safety of prostatic arterial embolization. The secondary endpoint was the evaluation of the quality of life in terms of symptoms control and erectile function.

The following parameters were extracted, where available, from the included papers: inclusion criteria, embolic agent, technical success, follow up (FU) time points, complications, prostate volume (PV), PSA, PVR, maximal flow rate (Qmax), IPSS, QoL and International Index of Erectile Function (IIEF).

Indications

Preliminary evidence shown has that PAE may be an effective therapy for the relief of LUTS in patients with BPH, representing a minimally invasive treatment that can replace TURP when not feasible (8).

However, to date, indications and contraindications to PAE have not been fully clarified (15,16). According to most recent guidelines (15), PAE should be contemplated only for highly symptomatic patients with BPH who are not responsive to medical treatment and are unsuitable for surgery or refuse surgery (3,15). In contrast, PAE should be excluded in all other causes of LUTS, such as PCa, prostatitis or urethral strictures, because its efficacy has never been demonstrated (15,17,18).

One of the main limit in defining indications and contraindications of PAE is the lack of evidence from randomized trials, since as of today, PAE has been prospectively evaluated only by single cohort studies (19).

Tables 1-3 reports the studies that we selected from literature and their inclusion criteria.

All studies included only symptomatic patients presenting moderate or severe LUTS (12,20-24). Some of them (12,21,23,24), also specified the required grade of LUTS in terms of IPSS: Li defined a threshold score of 12 (23), while Bilhim, Pisco and Wang demanded an IPSS higher than 18, therefore involving only patients with severe LUTS (12,21,24). In addition, most of these studies were designed to comprise only patients who were not responsive to medical treatment for at least 6 months (12,21,22). Further criteria of eligibility were: QoL score >3 (12,21,22) Qmax ≤12 or <15 mL/s (23), PSA <4 ng/mL (23) and sexual dysfunction (12). Notably, no age restrictions were mentioned in any of the published studies (12,20-24).

Thus, despite some heterogeneity, altogether these data underline the agreement between the investigators to consider PAE as a surrogate to TURP for treatment of BPH not amendable to medical therapy.

Procedure technique

Anatomical aspects

The fact that there are no specific anatomical patterns associated with pelvic and prostatic vascular anatomy make the identification and navigation of the prostatic arteries one of the major challenges related to PAE.

However, a few patterns are more generally seen (25).

The main artery that supplies the pelvis is the internal iliac artery (IIA) that supply most of the pelvic viscera, the pelvic walls, the perineum, and the gluteal region (26); the main trunk bifurcates after 3–4 cm in two large branches, one anterior and the other one posterior. Superior gluteal, iliolumbar and lateral sacral arteries generally arise from the posterior branch; superior (SVA) and inferior vesical arteries (IVA), obturator, middle rectal, inferior gluteal, and internal pudendal arteries (IPA) from the anterior. Carnevale *et al.* (27) created an acronym, PROVISO (Pudendal, Rectal, Obturator, Vesical Inferior and Superior) which can help to memorize the arteries related to prostate vascularization under the ipsilateral Oblique view (last letter of PROVISO) listed in a caudo-cranial sense.

The prostate arteries (PAs) can have multiple origins from the arteries described above but frequently arise as a common trunk and it divides right away in two main branches: the anteromedial for the central gland including the median lobe, and the posterolateral for the peripheral zone and the apex (28,29).

Despite BPH occurs in the central gland, embolization of the anteromedial prostate branch alone is not enough because the deep interconnection between the two branches lead to the necessity to embolize all the ramifications to avoid later revascularization of the central gland (27).

de Assis *et al.* (29) proposed a vascular anatomical classification of the prostatic arteries into five types.

A knowledge of the normal prostate vascularization and its main variations is mandatory to approach the embolization procedure, and to avoid non-target embolization and cause ischemia to the penis, bladder and rectum. Moreover this assumption is important to avoid loss-time and injury to other vessels due to excessive handling of catheters and wires, more frequent in patients with severe atherosclerosis (27).

Access

PAE procedures are generally performed via transfemoral access (TFA) (12,30,31).

A trans radial approach (TRA), originally developed for percutaneous coronary interventions, has gained interest in recent years (32). Advantages of this approach are reduced bleeding risk, early discharge, patient preference, low cost, and lower risk of morbidity and mortality (32). This method would also allow patients to ambulate immediately post-PAE, which could facilitate urination.

In 2016, Bhatia *et al.* (33) conducted a retrospective analysis on a total of 64 procedures with the aim to compare safety and feasibility of PAE via TRA and TFA. TRA represented a safe and feasible method to perform PAE; the learning curve of the operator is important.

Technique

Bilateral PAE is generally accepted as the best choice in terms of clinical results compared to unilateral embolization, due to the deep connections that exist between the PAs. This clinical suspicion has been investigated by Bilhim *et al.* (8) in a retrospective analysis: poor outcomes were observed in the unilateral group compared to the bilateral one, even if no statistical significance was seen between the two groups.

Table 1 Data summary of the main studies

Author	Number of patients (n)	Mean age (years old)	Study type	Data collection	Inclusion criteria	Embolic agent	Technical success	Outcome measures	Follow-up (months)	Complications
Bagla *et al.* (20)	78	65.2	Single cohort	Retrospective	BPH patients with moderate or severe grade LUTS	100–400 µm PVA particles	96%	IPPS, QoL, IIEF-5	1, 3, 6	Major: 0%; minor: mild urinary tract infection (1.3%), inguinal hematoma (1.3%)
Bilhim *et al.* (21)	186	65.5	Double cohort	Retrospective	BPH patients with LUTS, IPSS >18 and QoL scores ≥3, refractory to medical treatment for at least 6 months, Qmax ≤12 mL/s	100–300 µm PVA particles	98%	IPPS, QoL, IIEF-5	1, 6, 12, 18, 24	Major: 0%; minor: urinary frequency more severe than before PAE (51.1%), dysuria (42.5%), hematospermia (8.1%), hematuria (7.5%), rectal bleeding (5.4%), inguinal hematoma (3.2%)
Gabr *et al.* (22)	22	72.5	Single cohort	Retrospective	BPH patients with LUTS refractory to medical treatment for at least 6 months	300–500 µm embosphere	100%	IPPS, QoL, IIEF-5	1, 3, 9	Major: 0%; minor: N/A
Li *et al.* (23)	22	74.5	Single cohort	Prospective	BPH patients with LUTS, IPSS >12, Qmax <15 mL/s and PSA <4 ng/mL	50–100 µm PVA particles	92%	IPPS, QoL, IIEF-5	1, 3, 6, 12	Major: 0%; minor: hematuria (14%), hematospermia (9%), rectal bleeding (14%), acute urinary retention (32%)
Pisco *et al.* (12)	250	65.5	Single cohort	Prospective	BPH patients with LUTS, IPSS >18 and QoL scores ≥3, refractory to medical treatment for at least 6 months, Qmax ≤12 mL/s, sexual dysfunction	100–200 µm PVA particles	97.9%	IPPS, QoL, IIEF-5	1, 3, 6, 12, 24	Major: bladder ischaemia (0.4%); minor: urinary tract infections (7.6 %), haematuria (5.6 %), haematospermia (0.4 %), rectal bleeding (2.4 %), balanitis (1.6 %), acute urinary retention (2.4%)
Wang *et al.* (24)	109	71.5	Single cohort	Prospective	BPH patients with LUTS, IPSS >18 and QoL scores >3, refractory to medical treatment for at least 6 months, Qmax ≤12 mL/s	50–100 µm PVA particles	93.2%	IPPS, QoL, IIEF-5	1, 3, 6, 12, 24	Major: 0%; minor: hematuria (10.9%), hematospermia (8.1%), rectal bleeding (7.3%), inguinal hematoma (2.8%), acute urinary retention (28.4%)

PVA, polyvinyl alcohol; IPSS, International Prostate Symptom Score; QoL, quality of life; IEEF, International Index of Erectile Function; LUTS, lower urinary tract symptoms (LUTS); BPH, benign prostatic hyperplasia; Qmax, maximal flow rate; PAE, prostate artery embolization; N/A, not available.

Table 2 Baseline parameters

Author	Mean PV (mL)	Mean PSA (ng/mL)	Mean PVR (mL)	Mean Qmax (mL/s)
Bagla *et al.* (20)	<50	4.7	N/A	7.11
Bagla *et al.* (20)	50–80	4.7	N/A	7.11
Bagla *et al.* (20)	>80	4.7	N/A	7.11
Bilhim *et al.* (21)	>30	4.5	91.9	10.3
Gabr *et al.* (22)	>70	4.9	111.6	8.6
Li *et al.* (23)	>80	3.8	140	6
Pisco *et al.* (12)	>80	5.68	102.9	9.2
Wang *et al.* (24)	>80	4	125	8.5

PV, prostate volume; PSA, prostate-specific antigen; PVR, post-void residual; Qmax, maximal flow rate; N/A, not available.

Bilateral PAE is feasible from a single-sided approach, due to intraprostatic anastomoses and the possibility to cross from one side to the other one (34). This technique may be considered in patients with occluded internal iliac artery on one side.

PAE is generally performed as an inpatient procedure; intravenous ciprofloxacin 400 mg should be administered within 1 hour before the procedure and continued for 7 days with 500 mg twice a day orally (30).

Pre-procedural medication may include oral diclofenac 100 mg/d and famotidine 20 mg twice daily for 2 days before the procedure and the morning of the procedure (35).

The PErFecTED technique

The "PErFecTED technique", as described by Carnevale *et al.* (36), led to clinical success as demonstrated with an improvement of lower urinary symptoms and lower recurrence rates.

To the best of our knowledge, the PErFecTED technique has been compared to original PAE in two studies so far. Authors found a superiority in IPSS reduction and Qmax improvement during a FU of 12 months (37).

A second study consisted in retrospectively analysis on 105 consecutive patients who underwent PAE with the two different techniques (38). Of these patients, clinical recurrence at 12 months was statistically higher in the group treated with the original PAE technique.

A Foley catheter is introduced into the bladder and filled with a mixture of iodinated contrast medium (20–30%) and saline solution (36). Vascular access is achieved by the femoral artery. A preliminary internal iliac angiography is performed to evaluate the PAs. Then, an internal vesical artery (IVA) catheterization with an ipsilateral 25–55° oblique view, is obtained. Nitroglycerine or isosorbide mononitrate are vasodilator used to prevent vasospasm and to increase artery size to facilitate microcatheter navigation and distal positioning. When the microcatheter is advanced beyond the collateral branches, the embolization can start. It is preferred to start from the peripheral part of the gland. The recommendation is to embolize with gelatin microspheres slowly (36).

When reached the stasis, the microcatheter should be advanced into the prostatic parenchyma branches for an intraprostatic embolization. The periurethral region of the prostate must be embolized because strictures start from this part of the gland (36).

Cone-beam computed tomography (CBCT)

Digital subtraction angiography (DSA) provides excellent visualization of pelvic vessels, but its low sensitivity for soft-tissue contrast and two-dimensional projection makes it difficult to evaluate complex prostatic vascular anatomy and identify the prostatic arterial supply. CBCT consists in an angiographic unit equipped with a flat-panel detector that can provide volumetric tomographic images. Many authors proved that CBCT can be helpful in endovascular procedures (39-41). In vascular procedures, CBCT permits the assessment of complex vascular anatomy after a single injection of contrast medium in a targeted artery (38).

During PAE, CBCT can be used to localize the prostate, identify PAs and their anatomic variants, improving safety and feasibility of selective embolization (42). For this reason, CBCT must be performed with the catheter into the IIA to evaluate the origin of the PAs. A new CBCT can

Table 3 Outcomes

Author	Mean IPSS						Mean QoL						Mean IIEF					
	B	1 mos	3 mos	6 mos	12 mos	24 mos	B	1 mos	3 mos	6 mos	12 mos	24 mos	B	1 mos	3 mos	6 mos	12 mos	24 mos
Bagla *et al.* (20)	27.2	14	11.9	15.9	N/A	N/A	5.0	3.2	3.1	3.1	N/A	N/A	15	14.7	N/A	17.5	N/A	N/A
Bagla *et al.* (20)	25.6	17.2	16.3	13.5	N/A	N/A	4.9	3.2	3	2.1	N/A	N/A	14.8	14.4	N/A	16.9	N/A	N/A
Bagla *et al.* (20)	26.5	15.6	12.5	13,6	N/A	N/A	4.7	2	1.8	1.7	N/A	N/A	13.2	13.2	N/A	16.4	N/A	N/A
Bilhim *et al.* (21)	22.4	11.8	N/A	10.9	10.2	8.1	4.2	2.5	N/A	2.4	2.3	2.4	16.6	16.8	N/A	18.1	18.4	18.8
Gabr *et al.* (22)	22.3	12.9	11.6	11.5	N/A	N/A	4.2	2.8	2.9	2.9	N/A	N/A	15.8	16.5	16.6	16.6	N/A	N/A
Li *et al.* (23)	27	12	7	8	7.5	N/A	4.5	2.5	2	2	2	N/A	20	18	19	18	17	N/A
Pisco *et al.* (12)	24	12.2	11	11.5	10.4	9	4.4	2.5	2.3	2.2	1.9	1.8	18.9	20.6	20.9	20.5	20.1	18.7
Wang *et al.* (24)	26	9.5	8.5	7.5	8	9	5	2.5	3	3	2.5	3	11	11	10	12	13	10

B, baseline; mos, months; IPSS, International Prostate Symptom Score; QoL, quality of life; IIEF, International Index of Erectile Function; N/A, not available.

be performed with the microcatheter in the PA, to avoid non-target embolization (38).

As far as we know, studies have evaluated the usefulness of CBCT. Bagla *et al.* (43,44) found that CBCT provided information that could probably save the patient from complications or recurrence in 46% of cases.

Wang *et al.* (38) discovered that CBCT provided more informations than DSA in 64.2% of cases.

The third study by Chiaradia *et al.* (42) had the goal to evaluate the automatic three-dimensional detection of PAs with the use of CBCT imaging and vessel-tracking software. In all six patients considered in this study, CBCT was useful in the detection of the PAs.

Embolization particles

Dimension of the particles used during PAE vary in the published experience from 50 to 300 to 500 μm (11,23,45,46).

Bilhim *et al.* (47), performed a comparison between different PVA sizes (80 to 180, 180 to 300 μm). They found out that the larger particles cohort led to a greater reduction in IPSS during the first 6 months, with a nearly statistically significant result.

Goncalves *et al.* (45) found minor adverse events in patients treated with smaller microspheres. From 3 to 12 months, the smaller particles size revealed a lower regrowth rate in prostate size.

In conclusion, both studies (45,47) have suggested that larger particles tend to perform slightly better, but studies are heterogeneous, and data are yet not enough.

Microcoils

As intraprostatic anastomosis with extraprostatic arteries represents a known cause of nontarget embolization and subsequent ischemic complication of PAE (48), a recent study by Bhatia *et al.* (49) tried to determine if microcoils during PAE could be a safe adjunctive measure to prevent this complication; in particular, coils were deployed when there was significant reflux or direct filling of distal communications branch arteries between PA and penile, rectal or bladder vasculature. For this reason, the microcatheter need to be advanced or positioned distally enough from these anastomoses. However, given the end-vessel nature of bladder and penile vasculature, there is a risk of ischemia from coil embolization itself and given the small caliber and great tortuosity of this vessel, this method could lead to an increase in procedure and fluoroscopy times.

Complications

Complications of PAE are divided in two categories: minor complications that include all the events that don't require any therapy up to the admission for observation only, and major complications that include therapies requiring hospitalisation up to permanent adverse sequelae and death (50).

Major complications rate is less than 1% (51). The broad range of post-procedural minor events—such as a higher urinary frequency, hematospermia, urinary tract infections and balanitis, haematuria, dysuria, rectal bleeding, AUR, inguinal hematoma, etc.—more often includes self-limiting diseases, with the advantage of restricting transurethral procedure-related complications as bleeding, sexual dysfunction and dilutional hyponatremia (43). The overall incidence is estimated to be around 30% (51).

Mild urethral or perineal pain may occur as post-embolization syndrome and this is not related with PVA particles size using during PEA (47). Patients can experience moderate/severe LUTS after the procedure. The great number of them continues medical therapy, while others undergo to prostatic surgery. Some non-responder patients could repeat PAE 12 months after the first one, but it's seen that the development of collateral circulation limited the procedural success (21).

The bladder ischemia, rarely described as a post-procedural event, is the main major complication reported until now (51). It is a necrosis and desquamation of the bladder wall that, when localised, requires surgical cystoscopy removal 1 month after PAE without need for bladder reconstruction. It is potentially caused by no-target embolization and emphasize the importance of a correct pre-procedural planning (52). The only other major complication described in the literature is the persistent urinary tract infection requiring hospitalisation for intravenous antibiotics and it seems to be related to the urodynamic study (28)

Complications most frequent observed after PAE are described in *Table 1*.

Results

PAE is typically evaluated with respect to technical and clinical success. According to Gao *et al.* (11), a PAE procedure is technically successful when selective prostatic arterial catheterization and embolization on at least one side of the pelvis are achieved. Technical success rates of 92% (22/24 patients) and 1.9% (12/630 patients) are reported by Li and Pisco, respectively (23,53). Cases of failure are mainly related to intra-operative evidence of high tortuosity and atherosclerotic changes of the iliac arteries and may be treated surgically. For the same reason, sometimes PAE can be performed only unilaterally. Pisco *et al.* have recently suggested a very angled origin of the prostatic artery as another possible cause (53). Anatomic and degenerative vessel-related features are the only reported causes of technical failure.

The clinical outcome of a technically successful PAE procedure describes the perceived or measured improvement of the patient's clinical conditions. According to Pisco *et al.* (53), clinical success is achieved when all the three following requirements are met:

(I) IPSS ≤15 points with a decrease of at least 25% from the baseline score;
(II) QoL score ≤3 points or a decrease of at least 1 point from baseline;
(III) No need of any additional medical or surgical therapy after PAE.

In addition to IPSS and QoL, clinical success of PAE is also quantified in terms of Qmax, PV, PVR and IIEF. As the aim of PAE is to cause ischemic necrosis and shrinkage of the prostate gland (54), it is reasonable to assume that clinical improvement goes together with PV reduction and long-term PSA value decrease, in proportion with the extension of infarction area.

In the studies reviewed (*Tables 1-3*), patients have been evaluated periodically after PAE presenting promising results. Wang *et al.* (24) reported data of 105 patients observed for a mean of 24 months. They showed a cumulative rate of clinical success at during 24 months FU. In the same study, 84 patients observed for 24 months, have shown a significative decrease of PV, a consistent and stable increment of Qmax and decrement of PVR (24) . In a wide systematic review by Kuang *et al.* (18), all data by relative recent studies have been compared to demonstrate a significant improvement of Qmax, IPSS and QoL associated with reduced PV and PVR in a maximum FU of 24 months. Consistent results emerge also from large prostates trials: Bagla *et al.* (20) have tested PAE effectiveness in three group with increasing prostate size (mean volumes: 37.5, 65.7, 139.4 cm^2) during a maximum FU term of 6 months and have demonstrated high and stable rate of clinical success with significant QoL improvement in small prostates as in the larger ones.

Concerning PSA value, several authors (21,23,24) reported a consistent increment at 24 hours after PAE, and then a drop to a significantly lower level than the baseline in the following months almost sustained over time (23,24). Also, Bilhim *et al.* (21) have found a statistically significant association between higher levels of early PSA and lower IPSS over time, suggesting a potential prognostic role of early PSA value.

Finally, just a minority part of studies includes complete data on IIEF score and no significant difference in erectile function at 1, 3 or 6 months after PAE is shown (51). However, in a recent study by Pisco *et al.* IIEF score improved in 21.9% of patients, probably due to the discontinuation of medication for BPH that may affect sexual function (53).

Clinical failure affects a minor number of patients. Pisco *et al.* have reported different results: they have registered clinical failure in 43 patients of 238 (18.1%) during the first month after PAE (unilateral PAE in 12 patients, bilateral PAE in 25 patients, incomplete PAE in 6 patients) without recognizing technical reason for failure or a direct relationship with PV reduction (52). Bilhim *et al.* (8) have studied the difference between patients treated unilaterally or bilaterally showing a better but not statistically significative outcome in case of bilateral treatment. Finally, Gao *et al.* (11) have presented 5 cases of failure of 54 patients (9.3%), 4 bilaterally and 1 unilaterally treated.

Some authors finding PAE as a possible solution to manage BPH in poor surgical candidates at substantial risk. Recently, Rampoldi *et al.* (30) selected a court of 43 patients unsuitable for surgery. PAE have been performed in 41 patients and a significant improvement of the QoL was assessed for 33 of them (80%). Bhatia *et al.* (55) selected a population of 30 catheter-dependent patients with large PV. PAE allowed to 26 patients (86.7%) to remove catheter at a mean time of 18.2 days and these results have been confirmed at 6 and 12 months of FU. All these patients have continued to void independently and have not required reintroduction of a urethral catheter with a net improvement of QoL. Finally, consistent results have been reported by Carnevale *et al.* (56) performing PAE on an analogous court of 11 patients: 10 patients removed catheter at a mean of 12.1 days and have shown a consequent improvement in terms of QoL.

Discussion

Regarding the results published, PAE represents an emerging as a viable non-surgical treatment for LUTS caused by BPH.

On the basis of the data published, IPSS as well as QoL improve in the first 12 months of FU.

In literature, the only randomized controlled trial published comparing PAE and TURP (11), concluded that both procedures led to significant clinical improvements. However, the advantages of the PAE procedure must be evaluated against the potential for technical and clinical failures in a minority of patients surgically treated. PAE was associated with shorter hospital stays compared with TURP.

Knowledge of the arterial anatomy is essential for an effective and a safe embolization, avoiding complications related to no-target embolization to surrounding organs (bladder, rectum, and penis). Prostatic arterial anatomy is highly variable; in most cases PAs arise from the internal pudendal artery or they present a common origin with the SVA or from the common anterior gluteal-pudendal trunk. But in other cases, PAs arise from different arteries (branches of the internal iliac artery) (25-29).

Rotational angiography and CBCT represent a valid help for identifying the PAs and its origin (38,43,44).

The concept that smaller-sized particles may penetrate more distal inducing greater ischemia is well known. BPH develops primarily in the peri-urethral region, therefore embolization of this area leads to improvement of symptoms and clinical success (24,47).

Bilateral PAE produces better results than that unilateral (24).

On the basis of the results analyzed, PAE may be considered effective for the treatment of LUTS secondary to BPH. In *Tables 2* and *3* objective results (PV and PVR) and symptoms like Qmax, IPSS, and QoL are reported (*Tables 2,3*) (12,20-24).

No major complications were observed in most published series; Pisco *et al.* (12) reported bladder ischemia in 0.4% of cases. The incidence of minor complications (i.e., transient hematuria, hematospermia, and rectal bleeding) after PAE is acceptable (12,20-24). The AUR after PAE was described; it was attributed to the edema in the periurethral area after embolization. AUR was managed conservatively with a bladder catheter and antibiotics for about 1 week (12).

Limitations of this review include a lack of direct comparison of clinical outcomes and complications to TURP. As reported above, only one was a randomized control trial that compared PAE to TURP (11). The outcomes in the remaining articles could not be directly compared to TURP.

In most studies, the lack of standardized methods of reporting complications represent another limitation. The risk should be an overlap of data between studies from the same researchers.

Another limitation is the lack of long-term FU; patient outcomes demonstrated an improvement in the short term; at the moment, no data about the recurrence rate of the symptomatology are available.

Conclusions

With the data available to date, PAE is an effective treatment for BPH in short-to-intermediate FU period.

Prospective controlled multicenter trials with longer FU periods will be required for validation of PAE. Moreover, larger randomized control trials with comparison to TURP are required.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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