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Prostate artery embolisation: an all-comers, single-operator experience in 159 patients with lower urinary tract symptoms, urinary retention, or haematuria with medium-term follow-up

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AIM: To describe the authors' experience with prostate artery embolisation (PAE) to treat lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) or refractory haematuria of prostatic origin (RHOPA).

MATERIALS AND METHODS: PAE was attempted in 159 patients. Procedural details, pre/post-PAE symptom scores, and pre/post-PAE magnetic resonance imaging (MRI) data were recorded. Statistical analysis was performed to determine clinical outcomes and factors predicting clinical success.

RESULTS: Technical success was achieved in 156 patients. In patients with LUTS, the International Prostate Symptom Score (IPSS) improved from a mean of 22 at baseline to 9.5 at 6-months post-PAE, then to 10.7, 10, 11.3, and 11 at 1, 2, 3, and 4 years. The quality of life (QoL) score improved from 4.6 at baseline to 2, 2.2, 2.4, 3.1, and 2.5 at the same time points. The International Index of Erectile Function (IIEF-5) scores remained stable. There was no significant difference in IPSS between bilateral or unilateral embolisation to 2 years, or between BPH alone or BPH with biopsy-proven prostate cancer to 3 years post-PAE. Percentage improvement in IPSS at 1 year correlated with percentage reduction in prostate volume on first post-PAE MRI. Percentage improvement in IPSS at 3 years correlated with initial IPSS. PAE facilitated urinary catheter removal in 13/24 patients in retention. PAE controlled bleeding in 12/12 patients with RHOPA.

CONCLUSION: PAE is safe and effective in the management of symptomatic BPH. Patients with the highest baseline IPSS and reduction in prostate volume on first post-PAE MRI are likely to derive most benefit from embolisation.

Introduction

Benign prostatic hyperplasia (BPH) causing lower urinary tract symptoms (LUTS) is a common condition in males resulting in bladder storage and voiding symptoms due to

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outflow obstruction. The estimated global prevalence of BPH is 26% and increases with age, particularly in those over 60 years.[1,2] Previously used only in the management of refractory haematuria of prostatic origin (RHOPA),[3] prostate artery embolisation (PAE) is an emerging minimally invasive image-guided technique that has shown promising technical and clinical success in relieving symptoms of BPH, along with a reassuring safety profile.[4–6] The aim of the present study was to describe a single-operator experience of PAE for the management of BPH (causing LUTS or requiring urethral catheterisation) and RHOPA in the UK, with medium-term clinical outcomes and an assessment of predictors of clinical success to complement recently published data in this area.

Materials and methods

Patients were reviewed by a consultant urologist prior to PAE. All elective embolisation cases were worked-up with a computed tomography (CT) arteriogram of the pelvis and discussed in a multidisciplinary team meeting. Patients were excluded if their CT arteriogram demonstrated bilateral internal iliac artery occlusion or if they had organ-confined prostate cancer and were eligible for curative resection. There were no other specific exclusion criteria; patients with metastatic prostate cancer, unilateral internal iliac artery occlusion, or those on anticoagulation were considered candidates for PAE. Based on the pre-procedural CT examination, a schematic diagram of the internal iliac artery branch anatomy was produced and used as a reference during embolisation. All procedures were performed by a single consultant interventional radiologist (TS). Approval for performing the PAE procedure was granted by the local governance committee, and this study was performed in accordance with the principles detailed in the Declaration of Helsinki (7th revision, 2013).

Elective PAE for LUTS was generally performed as a day-case procedure under local anaesthetic, although selected patients received conscious sedation with intravenous fentanyl and midazolam and one patient required general anaesthesia due to moderately advanced Alzheimer's disease. Pre-medications consisted of 750 mg cefuroxime intravenously and 100 mg diclofenac per rectum. Bilateral common femoral arterial access was used if both internal iliac arteries could not be stably cannulated from a single groin puncture. Four French sheaths and catheters (both Cordis, High Wycombe, UK) were employed to access the internal iliac arteries, upsized to a 6 F 45 cm crossover sheath (Flexor Balkin, Cook Medical, Limerick, Eire, Ireland) if a stable position in the contralateral internal iliac artery could not be obtained with a 4 F catheter alone. A 2 F ProGreat microcatheter (Terumo UK, Bagshot, UK) and 0.014″ Fathom wire (Boston Scientific, Hemel Hempstead, UK) were used to cannulate the prostate arteries (PAs) bilaterally. The PAs were then embolised to stasis with a combination of 100 and 200 μm polyvinyl alcohol particles (Cook Medical, Limerick, Eire, Ireland). In procedures performed after January 2016, the PErFecTED technique was employed where technically possible. Briefly, the PErFecTED technique (Proximal Embolisation First Then Embolise Distally) involves initially injecting embolic material from just proximal to the division of the PA into central and peripheral branches, and then after achieving stasis of flow, advancing the microcatheter deeper into the intraprostatic vessels to inject further embolic material until stasis occurs again. The first injection is a flow-directed embolisation, which distributes embolic particles equally between all PA branches, while the more distal injection ensures complete occlusion of the intraparenchymal microcirculation and results in a more complete infarction of the central zone of the prostate, as reported by Carnevale *et al.*[7] Non-prostatic branches of the PA were protected by coil embolisation (Fig 1a and b) or by advancing the microcatheter well beyond their origin before injection of embolic material (Fig 1c–f). Cone-beam CT was not used, and apart from the initial internal iliac digital subtraction angiography (DSA) run performed at 3 frames-per-second (FPS), all subsequent DSA runs and fluoroscopy were performed at one frame or one pulse per second to minimise patient and operator radiation exposure. Day-case patients were discharged home following 4 hours of observation. A course of 500 mg ciprofloxacin orally twice daily and 400 mg ibuprofen three times daily for 1 week was prescribed.

Baseline measurements of the International Prostate Symptom Score (IPSS) and Quality of Life (QoL) score were obtained from those patients with LUTS, and each patient was invited to fill out the International Index of Erectile Function (IEFF) five-point questionnaire. A magnetic resonance imaging (MRI) scan was also performed in all patients with LUTS, and the prostate volume calculated from the axial and sagittal T2 sequences using the formula

$$volume = length \times width \times height \times 0.52.$$

Measurements of the post-void residual volume (PVR) and peak urinary flow (Qmax) were also recorded.

Clinical follow-up was sought at 6, 12, 24, 36, and 48 months post-PAE, at which points IPSS-QoL and IIEF scores were obtained and recorded in a prospectively maintained database. The mean clinical follow-up period was 1,024 days (range 363–1,623 days). All patients had an MRI examination booked for 3 months post-PAE, and where possible a further MRI 12-months post-PAE was performed. Any further MRI examinations performed beyond this were also included in the analysis. For the purposes of statistical analysis, follow-up MRI examinations were allocated to three groups: first post-procedure scan being within 6 months of PAE (112 patients, mean 3.4 months, range 2–6 months), second post-procedure scan being 7–19 months post-PAE (73 patients, mean 12.6 months, range 7–19 months), and third post-procedure scan being 20 or more months post-PAE (19 patients, mean 25.7 months, range 20–36 months).

Data collection was performed using Excel (Microsoft, Reading, UK) and statistical analysis using Excel and GraphPad QuickCalcs (Graphpad Software, CA, USA). Mean, range, and standard deviation were calculated for all

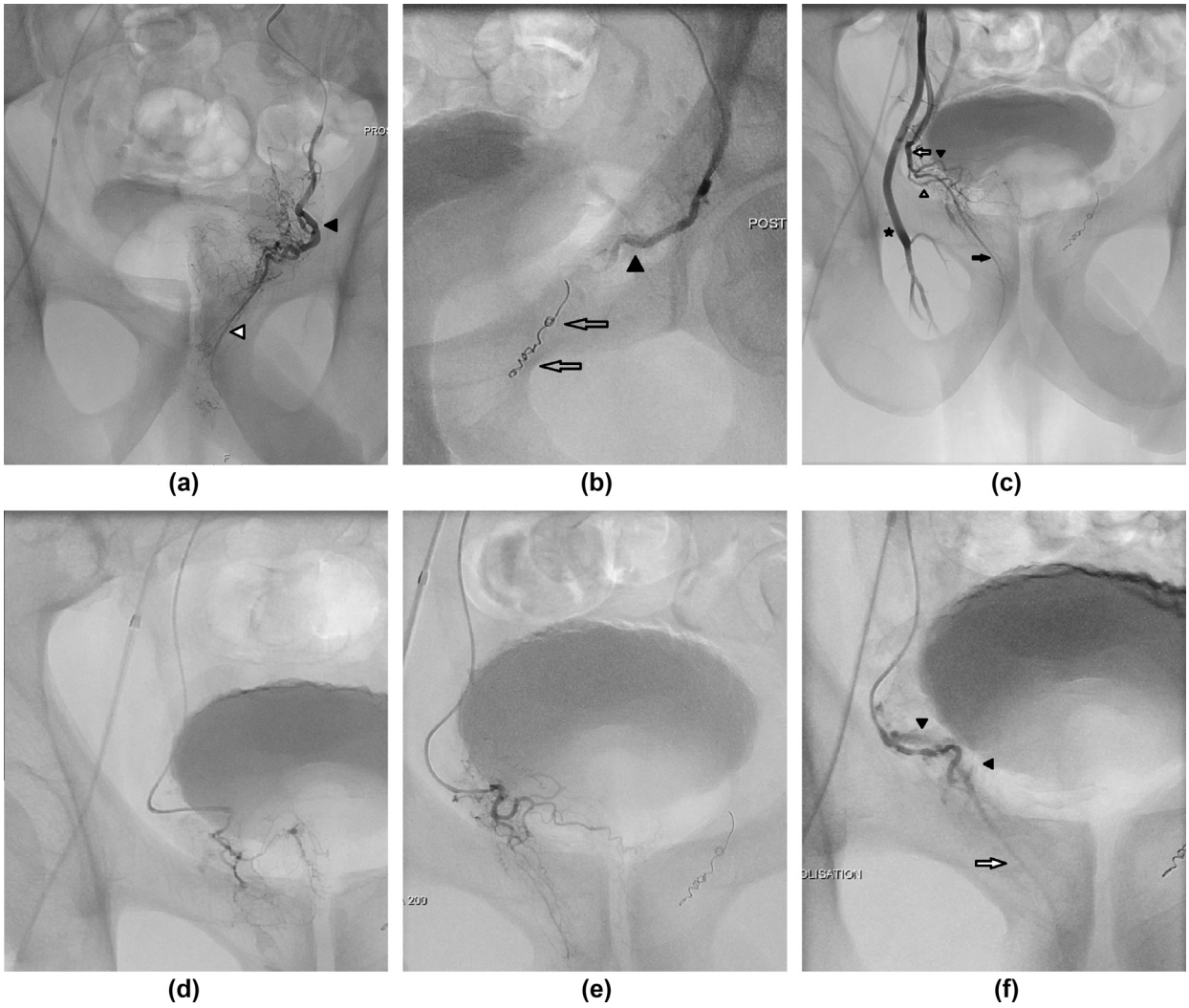

Figure 1 PAE in a patient with bilateral penile branches arising from the PA. (a) Selective DSA demonstrating the left PA (solid black arrowhead) with a prominent penile branch coursing inferiorly (open black arrowhead). (b) Two microcoils (open black arrows) have been deployed to protect the penile branch, and the left PA then embolised with PVA particles until flow stasis is seen (solid black arrowhead). (c) Selective DSA demonstrating the right PA (open black arrow), again with a prominent penile branch coursing inferiorly (solid black arrow). The penile branch arises from a superior PA branch (solid black arrowhead), and a discrete inferior PA branch is also seen (open black arrowhead). Some reflux into other branches of the anterior division of the internal iliac artery is also evident, most obviously the obturator artery (black star). (d) The inferior PA branch was super-selectively catheterised and embolised with PVA particles from this position. (e) The superior branch was super-selectively catheterised and embolised with PVA particles from this position. (f) Post-embolisation angiography shows ablation of the previously seen right-sided prostatic branches (solid black arrowheads), but preserved flow in the penile branch (open black arrow).

variables. The mean symptom scores between baseline and follow-up time points and between the subgroups of patients with LUTS were compared using unpaired *t*-tests. The percentage change in IPSS from baseline (%ΔIPSS) was calculated at 1, 2, and 3 years post-PAE. Percentage change in prostate volume at each of the follow-up MRI examinations was also calculated. Pearson's correlation coefficient was calculated for the %ΔIPSS values against each of the measured pre-procedure variables as well as change in prostate volume seen on the first post-PAE MRI examination. In all comparative statistics, a p-value of <0.05 was considered significant.

Results

Technical outcomes, dose analysis, and complications

PAE was attempted in 159 consecutive patients between January 2014 and June 2017, comprising 123 with LUTS, 24 catheterised due to urinary retention, and 12 patients with haematuria. Mean patient age at PAE was 70 years (range 49–98, standard deviation 10 years). Technical success (unilateral or bilateral embolisation) was achieved in 120 out of 123 patients with LUTS, and all 24 patients with

indwelling catheter and 12 with haematuria. Of the 120 technical successes in patients with LUTS, five patients did not have an IPSS recorded pre-procedure and were excluded from the analysis. Of the remaining 115 patients, bilateral embolisation was achieved in 100 whereas the remainder had unilateral embolisation only (due to extreme tortuosity or excessive steno-occlusive atheromatous disease of the internal iliac artery branches).

Mean fluoroscopy time was 36.14 minutes (range 10.23–170.05 minutes), with a mean dose–area product (DAP) of 10,314 μGy·m^2 (range 901–39,971 μGy·m^2) and mean skin dose of 916 mGy (range 81–3300 mGy).

Eleven patients experienced minor complications (seven with transient haematuria or haematospermia; two with urinary tract infections, which resolved with an extended course of oral antibiotics; and one with transient faecal incontinence secondary to non-target embolisation of the middle rectal artery). There were no major complications.

Symptomatic improvement with subgroup comparison

In all patients with LUTS included in the analysis, mean IPSS improved from 22 (range 2–36) at baseline to 9.5 (range 1–32) at 6 months, 10.7 (range 0–34) at 1 year, 10 (range 0–28) at 2 years, 11.3 (range 3–26) at 3 years, and 11 (range 3–20) at 4 years post-PAE. Mean QoL score improved from 4.6 (range 1–6) at baseline to 2 (range 0–6) at 6 months, 2.2 (range 0–6) at 1 year, 2.4 (range 0–6) at 2 years, 3.1 (range 0–6) at 3 years and 2.5 (range 0–5) at 4 years post-PAE. Mean IEFF scores demonstrated a modest increase, from 14.8 (range 1–25) at baseline to 16.3 (range 3–25) at 1 year, 19 (range 4–25) at 2 years, 18.2 (range 5–25) at 3 years and 15 (range 5–25) at 4 years post-PAE, although this only reached significance at 2 years post-PAE. Symptom score progression for all patients with LUTS in whom PAE was technically successful are shown in Table 1.

Patients in whom bilateral PAE was achieved had an increased mean %ΔIPSS compared to those who underwent unilateral PAE at both 1 year (52% versus 41.5%) and 2 years (55% versus 47.8%) post-embolisation, but this did not reach statistical significance (p=0.12). There was also no statistically significant difference in mean %ΔIPSS between patients with LUTS alone and those with LUTS along with biopsy-proven prostate cancer at 1, 2, 3, or 4 years post-PAE (p=0.26). There was no mortality in the cancer group during the follow-up period. These subgroup comparisons are demonstrated in Figs 2 and 3, respectively.

Mean %ΔIPSS from baseline at 1, 2, and 3 years was compared between patients with mild to moderate LUTS (IPSS ≤20) and those with severe LUTS (IPSS >20). Although the mean %ΔIPSS in patients with severe LUTS was greater at 1, 2, and 3 years post-PAE than that of patients with mild to moderate LUTS, this did not reach significance at any time point. Comparison of mean %ΔIPSS between these two groups along with p-values is demonstrated in Table 2. Although the association between severity of symptoms at baseline and %ΔIPSS was weak, this was considered grounds to assess for potential correlation between these two variables.

Twenty-one patients went on to have an endo-urological procedure due to clinical failure of PAE or a return of symptoms following initially successful embolisation, of whom 17 had holmium laser enucleation of the prostate (HoLEP) and four had a trans-urethral resection of the prostate (TURP).

Prostate volume changes

Prostate volume measured within the first 6 months post-PAE (mean 3.4 months, range 2–6 months) decreased from a mean of 129 ml (range 40–630 ml, SD 94.8) to 99.9 ml (range 30–565 ml, SD 69), representing a mean volume decrease of 15.6% (p<0.0001). Prostate volume measured between 7 and 19 months post-PAE (mean 12.6 months,

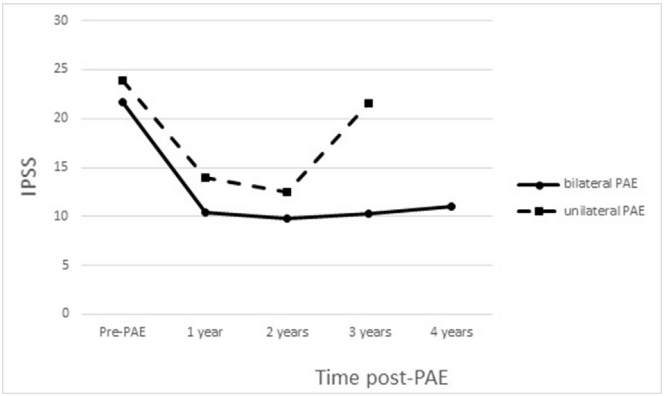

Figure 2 Improvement in IPSS in patients in whom bilateral embolisation was performed compared to those in whom only unilateral embolisation achieved.

Table 1
Pre and post-embolisation International Prostate Symptom Score (IPSS), quality of life (QoL), and International Index of Erectile Function (IIEF) scores in all patients with lower urinary tract symptoms (LUTS) and technically successful prostate artery embolisation (PAE).

Parameter	Time point					
	Baseline	6 months	1 year	2 years	3 years	4 years
IPSS	22±7.3 (115)	9.5±7 (58) p<0.0001	10.7±7.5 (64) p<0.0001	10±7 (46) p<0.0001	11.3±6.8 (23) p<0.0001	11±6.3 (4) p<0.01
QoL	4.6±1.3 (96)	2±1.6 (43) p<0.0001	2.2±1.6 (45) p<0.0001	2.4±1.8 (32) p<0.0001	3.1±1.7 (19) p<0.0001	2.5±2.5 (2) p=0.03
IIEF	14.8±7.4 (58)	14.4±7.8 (29) p=0.82	16.3 ± 6.9 (27) p=0.38	19±6.5 (20) p=0.03	18.2±6.4 (16) p=0.10	15±10 (2) p=0.97

Data are mean±SD (n).

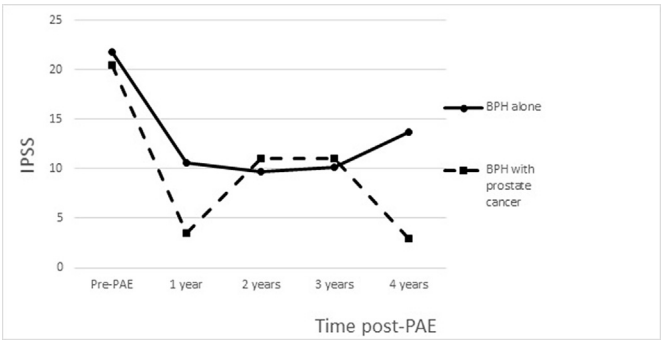

Figure 3 Improvement in IPSS in patients with BPH alone compared to those with BPH and biopsy-proven prostate cancer.

Table 2
Comparison of mean percent change International Prostate Symptom Score (IPSS) between patients with mild to moderate lower urinary tract symptoms (LUTS) (IPSS <=20) and those with severe LUTS (IPSS > 20).

Time post-PAE	Baseline IPSS ≤20 mean %ΔIPSS±SD (*n*)	Baseline IPSS >20 mean %ΔIPSS±SD (*n*)	*p*-Value
1 year	41±32.6 (34)	54.6±28.9 (31)	0.08
2 years	43.2±36.1 (24)	56.1±28.4 (22)	0.19
3 years	24.7±20.4 (11)	54.6±24.2 (12)	0.17

range 7–19 months) maintained a significant decrease to 100.5 ml (range 31–248 ml, SD 54.8), a mean volume decrease of 7.9% (p=0.007) compared to baseline; however, there was a rebound in prostate volume measured 20+ months post-PAE (mean 25.7 months, range 20–36 months), with mean volume increasing to 147.9 ml (range 50–290 ml, SD 73.9), a mean volume increase of 3.1% compared to baseline (p=0.65).

Predictive factor analysis

Calculation of Pearson's correlation coefficient was performed for %ΔIPSS at 1 year against baseline prostate volume, Qmax, and post-void residual, along with percentage change in prostate volume at first post-embolisation (within 6 months) MRI examination. Only percentage change in prostate volume at first post-embolisation MRI was found to demonstrate a significant bivariate association (r=−0.033, p=0.01). Pearson's correlation coefficient was then calculated for %ΔIPSS at 1, 2, and 3 years post-embolisation against baseline IPSS. No association was found at 1 or 2 years; however, there was a significant association between baseline IPSS and percentage improvement in IPSS at 3 years (r=0.43, p=0.04). Pearson's correlation coefficient and significance for each pair of variables are shown in Table 3.

PAE for other indications

Of 24 patients with urinary retention and indwelling urethral catheter who underwent PAE, 13 (54.2%) had subsequent successful trial without catheter (TWOC) within the first 3 months post-PAE. One patient required re-catheterisation due to acute urinary retention 6 months post-PAE and passed away 6 months later, and one further patient went onto have HoLEP 2-years post-TWOC due to worsening LUTS. Of the 11 patients who did not achieve freedom from catheter post-PAE, seven underwent subsequent HoLEP with all undergoing successful TWOC after surgery. One patient passed away 3-years post-PAE and the remaining three were lost to follow-up.

PAE was successful at controlling haematuria in all 12 patients. Four patients passed away within the first 6 months following PAE, of whom three had biopsy-proven and metastatic prostate cancer.

Table 3
Pearson correlation coefficients (r) for all assessed parameters.

Parameters	% change (%Δ) in IPSS at 1 year	%ΔIPSS at 2 years	%ΔIPSS at 3 years
Baseline IPSS	r=0.037	r=0.127	***r*=0.431**
	p=0.77	p=0.40	***p*=0.04**
% change in prostate volume at <6 months	***r*=−0.328**		
	***p*=0.01**		
Baseline PVR	r=0.037		
	p=0.83		
Baseline Qmax	r=0.027		
	p=0.88		
Baseline prostate volume	r=0.054		
	p=0.68		

Significant values in bold.
IPSS, International Prostate Symptom Score; PVR, post-void residual volume; Qmax, peak urinary flow.

Discussion

Symptomatic improvement

The present data demonstrate that PAE is a safe and effective treatment option for patients with LUTS due to BPH, and that efficacy of embolisation (as measured by IPSS and QoL scores) can be sustained to 4 years post-procedure. The improvement in IPSS in the present series is similar to that reported in previous reports.[6,8–11] IIEF scores remained essentially stable following PAE, and the small, but mostly not statistically significant, increase in IIEF seen is likely due to successful discontinuation of 5-alpha-reductase medication after successful embolisation. There are many patients living with localised prostate cancer for decades, and therefore, at risk of developing LUTS due to non-cancerous prostatic enlargement. Mordasini *et al.* demonstrated histologically that PAE induces partial necrosis in prostate cancer,[12] but the present data confirm that PAE is also safe and effective in patients with cancer and BPH and can be offered for symptom relief irrespective of the presence of underlying cancer.

Technical considerations

The present study demonstrated a markedly lower patient radiation dose than other series,[13] likely due to not using cone-beam CT and minimising DSA/fluoroscopy frame/pulse rates where possible. These data can be used to reassure patients that PAE can be performed effectively

without conferring a high radiation dose, which anecdotally is a concern several of patients raised when being considered for embolisation. The use of cone-beam CT is a trade-off between increased radiation dose and procedure time against definitive demonstration of successful prostate artery cannulation along with confirmation that no non-prostatic branches arise distal to the microcatheter tip. Although cone-beam CT may have a role in reassuring the operator earlier in the PAE learning curve, the incidence of only one complication (transient faecal incontinence, Clavien–Dindo grade I) potentially attributable to non-target embolisation in the present series of 159 patients suggests that with increased operator experience, planar imaging alone can be sufficient to confirm safe micro-catheter position prior to embolisation.

Bilhim *et al.* suggested that bilateral PAE offers an outcome advantage over unilateral[14]; however, this improvement did not reach significance to 2 years in the present series. This is due to the rich crossover anastomoses within the prostate, meaning that even if particles are only injected from one side, a significant quantity still reach both sides of the central gland; however, a return in symptoms was noted in the unilateral embolisation group at 3 years, and it may be that continued flow within the non-embolised side aids recanalisation/revascularisation of the central gland.

Predicting factors for clinical success

The present patients had relatively larger baseline prostate volumes (mean 129±94.1 ml) than those reported in some previous series[6,10,11]; however, in concordance with Bagla *et al.*,[15] baseline prostate volume did not correlate with percentage change in IPSS at 1 year post-PAE in the present series, reaffirming embolisation as a viable option in those patients with very large prostates and thus deemed to be poor candidates for surgical treatment (considering the increased operative times and associated bleeding and anaesthetic risks). The present finding of percentage change in prostate volume at first post-embolisation MRI correlating with symptom improvement at 1 year is in line with recently published data from Maclean *et al.*[13] Although this does not aid in identifying patients in whom PAE is likely to be more successful, it is of use for early prognostication to allow planning of alternative surgical treatment, should this be necessary. More useful to patient selection, however, was the correlation observed between pre-embolisation IPSS and percentage improvement in IPSS at 3 years, confirming that patients with even the severest LUTS can achieve a lasting clinical benefit from PAE.

The role of OAB in suboptimal clinical outcomes

Although the aim of PAE was to remove the patient's dependence on alpha-blocker or 5-alpha-reductase medication, some patients continued to experience bothersome LUTS despite technically successful PAE and a favourable reduction in prostate volume. On more detailed breakdown of their LUTS post-PAE, several of this cohort demonstrated a strong predominance of storage symptoms (urgency, frequency, nocturia, urge incontinence) over voiding symptoms (hesitancy, weak or intermittent urine flow, terminal dribbling, incomplete emptying). As this was likely due to a degree of overactive bladder (OAB), these patients were trialled on solifenacin succinate 5 mg orally once daily (VesiCare, Astellas Pharma, Chertsey, UK), usually with excellent results. Although some physicians are cautious in prescribing anti-muscarinic agents such as solifenacin in patients with BPH, the reduction in bladder outflow obstruction (BOO) following PAE means anti-muscarinics can be used with more confidence that they will not cause an increase in Post-Voiding Residual (PVR) or lead to Acute Urinary Retention (AUR). Indeed, the 2013 European Association of Urology guidelines do include a recommendation to consider the use of anti-muscarinics in BPH patients with predominant bladder storage symptoms.[16] Further focused research in this area is required to determine if the presence of underlying OAB can be predicted at initial screening, allowing anti-muscarinic therapy to be initiated immediately following PAE to accelerate the clinical improvement following reduction in BOO.

PAE for other indications

In the present series, only 54.2% of catheterised patients who underwent PAE were able to have successful trial without catheter, which compares unfavourably with previous data from Yu *et al.*[17] and Rampoldi *et al.*[18] who were able to achieve successful TWOC in 87.5% and 80.5% of patients, respectively; however, it should be noted that the mean catheterisation durations in these series were 69.5 days and 7.1 months, respectively, whereas the majority of the present patients had a catheter *in situ* for several months (and in some cases years) before PAE. The implication is that if a urethral catheter has been *in situ* on free drainage sufficient time for the bladder to lose tone, then despite PAE improving BOO, the patient will still not be able to void voluntarily. To mitigate this, Flip-Flo catheter valves (Bard Medical, Crawley, UK) were fitted to patient's catheters as soon as the decision to undergo PAE was made, or if this was not possible, the patient's urethral catheter was replaced with a spigotted supra-pubic catheter at the time of PAE so that the patient could immediately begin bladder training to aid voluntary transurethral voiding.

Although the earliest report for selective PAE was in patients with haematuria,[19] the overwhelming published experience with PAE is now in the setting of BPH; however, the experience gained in selective PAE for BPH will no doubt increase the availability of practitioners who can perform the procedure, and at Guy's & St Thomas' NHS Foundation Trust an endovascular approach to managing intractable haematuria is now well-established, especially in patients who are on anticoagulation.

Areas of future development

Future efforts to identify the most accurate predictors of clinical success and hone the technical aspects of PAE should leverage increased understanding of the mechanism

of action of PAE in improving LUTS. Although the study sample was small, Little *et al.* demonstrated increased clinical success of PAE in patients with adenomatous-dominant BPH (AdBPH) compared to age-matched controls, noting that central gland necrosis was seen in all AdBPH patients.[20] Pre- and post-embolisation MRI images of a patient from the present series with AdBPH are demonstrated in Fig 4. Prostate gland ischaemia seen on MRI 30 days post-PAE has separately been shown to predict clinical success in patients with AUR secondary to BPH.[21] Lin *et al.* analysed the degree of volume reduction in the difference zones of the prostate following PAE and found that patients with significant central gland infarction had the greatest reduction in whole-prostate volume.[22] Therefore, using MRI during the work-up to identify patients that will benefit most and then focusing embolisation technique (e.g., using the PErFecTED method) to achieve maximal and durable prostate infarction[23] will likely increase the proportion of patients who gain lasting clinical success from PAE. Larger comparative studies with optimal PAE technique and detailed analysis of pre- and post-embolisation MRI are needed to demonstrate how best to achieve the eventual aim of using pre-embolisation MRI findings and detailed symptom score analysis as a tool to provide the patient with an accurate estimate of how successful PAE is likely to be, in order to empower those in whom PAE might be less successful to make an informed choice as to whether to seek embolisation or a surgical alternative as first-line treatment.

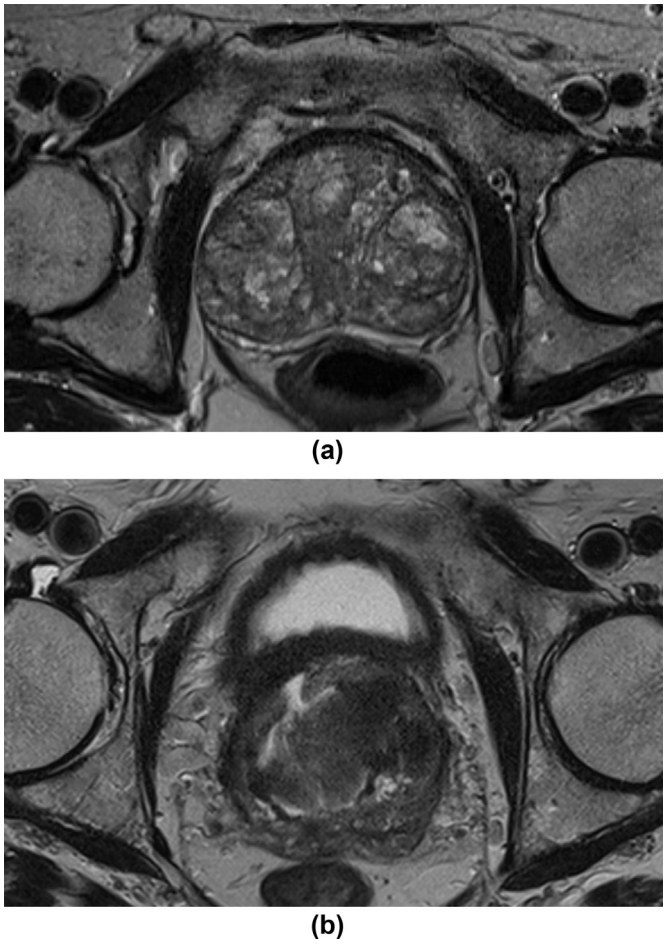

Figure 4 T2-weighted axial MRI images through the prostate gland. (a) Pre-PAE study demonstrates multiple T2 hyperintense areas consistent with adenomatous-dominant BPH. The measured prostate volume was 282 ml. (b) Post-PAE study demonstrates a marked loss of T2 signal in central gland areas in keeping with necrosis, and measured prostate volume reduced to 110 ml.

An anti-hormonal mechanism of action has also been postulated in PAE, with Sun *et al.* proposing a reduction in the number of alpha-1-adrenergic receptors in the prostate due to the direct effects of cell necrosis[24] and Frenk *et al.* suggesting that reduced testosterone entry to the prostate due to vascular occlusion would inhibit growth of new prostatic tissue, including alpha-1-adrenergic receptors.[25] These mechanisms together might reduce the smooth muscle tone within the peri-urethral prostate, thus reducing urethral compression. Direct targeting of alpha-1-adrenergic receptors using embolic material as a vector could represent a way of increasing the effectiveness of the current PAE procedure.

Finally, the effectiveness of PAE will always be compared to existing endo-urology therapies such as TURP, HoLEP, and greenlight-laser photovaporisation (PVP). Although the UK Registry of Prostate Embolisation (UK-ROPE) trial demonstrated non-inferiority of PAE to TURP at 12 months,[11] further large-scale randomised controlled trials with longer follow-up will be required for PAE to gain acceptance among the wider urology community, and to convince healthcare commissioners to support embolisation, as the National Institute for Health and Clinical Excellence (NICE) has recommended in the UK.[26] At present, the longest published follow-up period for PAE is 6.5 years,[6] although it must be noted that the proportion of patients who had reached that milestone in this cohort was relatively small. Therefore, it is imperative that previously published PAE patient cohorts continue to be followed-up in order that data regarding the long-term durability of PAE can be generated and directly compared with existing long-term outcomes for TURP, HoLEP, and PVP. It has been suggested that given the minimally invasive nature of PAE, it would be more appropriate to compare it to medical therapy in early BPH[27]; however, recent years have seen the advent of several day-case urologist-performed BPH treatments, which are less invasive than TURP, such as transurethral needle ablation of the prostate (TUNA), Rezūm steam ablation, and prostatic stenting, and it may be that PAE's eventual place is amongst these as a middle ground between medication and traditional surgical techniques.

Conflict of interest

The authors declare no conflict of interest.

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References

1. Berry SJ, Coffey DS, Walsh PC, *et al*. The development of human benign prostatic hyperplasia with age. *J Urol* 1984;**132**(3):474–9.
2. Lee SWH, Chan EMC, Lai YK. The global burden of lower urinary tract symptoms suggestive of benign prostatic hyperplasia: a systematic review and meta-analysis. *Sci Rep* 2017;**7**(1):7984.
3. Rastinehad AR, Caplin DM, Ost MC, *et al*. Selective arterial prostatic embolization (SAPE) for refractory haematuria of prostatic origin. *Urology* 2008 Feb;**71**(2):181–4.
4. DeMeritt JS, Elmasri FF, Esposito MP, *et al*. Relief of benign prostatic hyperplasia-related bladder outlet obstruction after transarterial polyvinyl alcohol prostate embolization. *J Vasc Interv Radiol* 2000;**11**(6):767–70.
5. Carnevale FC, da Motta-Leal-Filho JM, Antunes AA, *et al*. Midterm follow-up after prostate embolization in two patients with benign prostatic hyperplasia. *Cardiovasc Interv Radiol* 2011;**34**(6):1330–3.
6. Pisco JM, Bilhim T, Pinheiro LC, *et al*. Medium- and long-term outcome of prostate artery embolization for patients with benign prostatic hyperplasia: results in 630 patients. *J Vasc Interv Radiol* 2016;**27**(8):1115–22.
7. Carnevale FC, Moreira AM, Antunes AA. The "PErFecTED technique": proximal embolization first, then embolize distal for benign prostatic hyperplasia. *Cardiovasc Interv Radiol* 2014 Dec;**37**(6):1602–5.
8. Wang MQ, Guo LP, Zhang GD, *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 Urol* 2015 Apr 16:15–33.
9. Bhatia S, Sinha VK, Harward S, *et al*. Prostate artery embolization in patients with prostate volumes of 80 ml or more: a single-institution retrospective experience of 93 patients. *J Vasc Interv Radiol* 2018 Sep 11;(18):31210–7. pii: S1051-0443.
10. Abt D, Hechelhammer L, Müllhaupt G, *et al*. Comparison of prostatic artery embolisation (PAE) versus transurethral resection of the prostate (TURP) for benign prostatic hyperplasia: randomised, open label, non-inferiority trial. *BMJ* 2018 Jun 19;**361**:k2338.
11. Ray AF, Powell J, Speakman MJ, *et al*. Efficacy and safety of prostate artery embolization for benign prostatic hyperplasia: an observational study and propensity-matched comparison with transurethral resection of the prostate (the UK-ROPE study). *BJU Int* 2018 Aug;**122**(2):270–82.
12. Mordasini L, Hechelhammer L, Diener PA, *et al*. Prostatic artery embolization in the treatment of localized prostate cancer: a bicentric prospective proof-of-concept study of 12 patients. *J Vasc Interv Radiol* 2018 May;**29**(5):589–97.
13. Maclean D, Harris M, Drake T, *et al*. Factors predicting a good symptomatic outcome after prostate artery embolisation (PAE). *Cardiovasc Interv Radiol* 2018 Aug;**41**(8):1152–9.
14. Bilhim T, Pisco J, Rio Tinto H, *et al*. Unilateral versus bilateral prostatic arterial embolization for lower urinary tract symptoms in patients with prostate enlargement. *Cardiovasc Interv Radiol* 2013 Apr;**36**(2):403–11.
15. Bagla S, Smirniotopoulos JB, Orlando JC, *et al*. Comparative analysis of prostate volume as a predictor of outcome in prostate artery embolization. *J Vasc Interv Radiol* 2015;**26**(12):1832–8.
16. Oelke M, Bachman A, Descazeaud A, *et al*. European Association of Urology guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *Eur Urol* 2013 Jul;**64**(1):118–40.
17. Yu SC, Cho CC, Hung EH, *et al*. Prostate artery embolization for complete urinary outflow obstruction due to benign prostatic hypertrophy. *Cardiovasc Interv Radiol* 2017 Jan;**40**(1):33–40.
18. Rampoldi A, Barbosa F, Secco S, *et al*. Prostatic artery embolization as an alternative to indwelling bladder catheterization to manage benign prostatic hyperplasia in poor surgical candidates. *Cardiovasc Interv Radiol* 2017 Apr;**40**(4):530–6.
19. Küss R, Merland JJ, Le Guillou M, *et al*. Embolization of prostatic arteries, a rescue approach in uncontrolled hemorrhage after adenomectomy (proceedings). *J Urol Nephrol (Paris)* 1978 Jun;**84**(6):476–80.
20. Little MW, Boardman P, Macdonald AC, *et al*. Adenomatous-dominant benign prostatic hyperplasia (AdBPH) as a predictor for clinical success following prostate artery embolization: an age-matched case–control study. *Cardiovasc Interv Radiol* 2017 May;**40**(5):682–9.
21. Kisilevzky N, Faintuch S. MRI assessment of prostatic ischaemia: best predictor of clinical success after prostatic artery embolisation for benign prostatic hyperplasia. *Clin Radiol* 2016 Sep;**71**(9):876–82.
22. Lin YT, Amouyal G, Correas JM, *et al*. Can prostatic arterial embolisation (PAE) reduce the volume of the peripheral zone? MRI evaluation of zonal anatomy and infarction after PAE. *Eur Radiol* 2016 Oct;**26**(10):3466–73.
23. Carnevale FC, Moreira AM, Harward SH, *et al*. Recurrence of lower urinary tract symptoms following prostate artery embolization for benign hyperplasia: single center experience comparing two techniques. *Cardiovasc Interv Radiol* 2017 Mar;**40**(3):366–74.
24. Sun F, Sánchez FM, Crisóstomo V, *et al*. Benign prostatic hyperplasia: transcatheter arterial embolization as potential treatment—preliminary study in pigs. *Radiology* 2008 Mar;**246**(3):783–9.
25. Frenk NE, Baroni RH, Carnevale FC, *et al*. MRI findings after prostatic artery embolization for treatment of benign hyperplasia. *AJR Am J Roentgenol* 2014 Oct;**203**(4):813–21.
26. National Institute for Health and Care Excellence. Prostate artery embolisation for lower urinary tract symptoms caused by benign prostatic hyperplasia. Interventional procedures guidance [IPG611], published 24th April 2018. Available at: https://www.nice.org.uk/guidance/ipg611. Accessed.
27. Sabharwal T, Popert R. Prostate artery embolization. *BJU Int* 2018 Aug;**122**(2):167–8.