
ORIGINAL ARTICLE

Prostatic Arterial Embolisation in Men with Benign Prostatic Enlargement and Refractory Retention Considered High-risk Surgical Candidates

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ABSTRACT

Introduction: Prostatic arterial embolisation (PAE) is increasingly used for treatment of benign prostatic enlargement. We investigated the use of PAE for patients with refractory urinary retention resistant to alpha blockers, who were high-risk for conventional transurethral surgery.

Methods: This was a prospective cohort study of American Society of Anesthesiology (ASA) Class 3/4 patients. Computed tomographic angiography of the pelvis was used to screen for feasibility of PAE. PAE was performed using a standardised technique with tris-acryl microspheres. The primary outcome was the ability to void within 12 weeks after PAE. Secondary outcomes included complications, change in prostate size, and change in serum prostate-specific antigen (PSA).

Results: Twenty one men were recruited. Mean (\pm standard deviation) age was 83 ± 5 years, prostate size was 124 ± 63.4 mL, and serum PSA level was 18.4 ± 10.5 ng/mL. Fourteen patients (66.7%) were judged to be candidates for PAE; PAE was performed in 13 patients. Median follow-up was 10 weeks (range, 4-30 weeks). Nine (69.2%) patients had successful voiding trials with seven of them able to void within 2 weeks after PAE. At 6 months after PAE, PSA was decreased by $46.7\%\pm 20.9\%$ and prostate size was reduced by $58.6\%\pm 22.5\%$. Larger prostate size was significantly correlated with larger percentage reduction of prostate volume ($p = 0.036$). One patient developed haematuria requiring readmission on day 5 after PAE; it resolved spontaneously.

Conclusion: PAE was effective and safe for high-risk patients with benign prostate enlargement and refractory urinary retention.

Key Words: Angiography; Embolization, therapeutic; Haematuria; Prostate-specific antigen; Prostatic hyperplasia; Tomography, X-ray computed

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Submitted: 29 Apr 2018; Accepted: 25 Jul 2018.

Contributors: KCC, WYW and SMY designed the study. KCC, HCC and KKL acquired the data. KCC analysed the data and drafted the manuscript. KCC, WYW, HSS and CSC critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics Approval: This study was approved by the Kowloon Central/Kowloon East Research Ethics Committee (Ref REC (KC/KE)-18-0142/FR-3).

中文摘要

前列腺栓塞術治療高手術風險尿瀰留患者

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引言：利用前列腺栓塞術（PAE）治療良性前列腺肥大愈發普及。我們研究使用PAE，治療高手術風險而不適合傳統經尿道手術的尿瀰留患者。

方法：這是一個前瞻性研究，對象是美國麻醉學會分級為3或4病人。經過盆腔電腦斷層血管掃描證實PAE技術可行後，病人會接受以微球進行的血管栓塞術。首要結果是量度術後十二週內自行排尿的成功率。次要結果是量度術後的併發症，前列腺體積及血清前列腺抗原（PSA）的改變。

結果：共有21位病人參與研究。平均年齡（標準差）為 83 ± 5 歲，前列腺體積為 124 ± 63.4 mL，PSA為 18.4 ± 10.5 ng/mL。14位病人（66.7%）經掃描評估後確認為PAE技術上可行。最終13位病人接受PAE治療。隨訪中位數為10周（範圍，4-30周）。9位病人（69.2%）術後成功排尿，其中7位術後2周已能排尿。術後6個月，PSA下降 $46.7\% \pm 20.9\%$ ，前列腺體積縮減了 $58.6\% \pm 22.5\%$ 。體積較大的腺體術後縮減較多（ $p=0.036$ ）。一位病人術後5天出現血尿須住院觀察，其後血尿自行消退。

結論：PAE為高手術風險的前列腺肥大併發尿瀰留患者提供有效及安全的治療。

INTRODUCTION

Acute urinary retention is a well-known complication in the development of benign prostatic enlargement (BPE).¹ In patients that have failed voiding trials or presented with obstructive uropathy, transurethral prostate surgery is the standard treatment. Transurethral prostate surgery, despite its minimally invasive nature, has associated morbidities.² These are of great concern in patients with poor general health that puts them at high surgical risk.

Prostatic arterial embolisation (PAE) is an alternative treatment for BPE, which can result in a significant reduction in prostate volume, improvement in flow rate and residual urine volume, and reduction in symptom score.³ However, there have been limited publications on the use of PAE in patients with refractory retention. We investigated the use of PAE for patients who were at high surgical risks and had refractory retention, and studied the post-PAE voiding outcomes.

METHODS

We conducted a prospective single-arm cohort study from April 2017 to March 2018. All emergency admissions to urology wards were screened by urologists for study eligibility. Principles outlined in the Declaration of Helsinki were followed. Informed consent was obtained, and factsheets were given to patients. Inclusion and

exclusion criteria are shown in Table 1. Refractory retention was defined as emergency admissions for acute urinary retention, and failed voiding trials within 2 weeks after given daily doses of alpha blockers. Medical history was evaluated and an American Society of Anesthesiologists (ASA) score was assigned to patients. Prostate size was measured by transrectal ultrasound by urologists using the ellipsoid formula. Prostate size was divided into moderate enlargement (≤ 80 mL) and severe enlargement (>80 mL) to assess the effect of PAE on these two groups.

Once patients were recruited, alpha-adrenergic blockers were discontinued. Pre-PAE uroflowmetry was not possible as patients had indwelling catheters. Computed tomography angiography (CTA) of the pelvis was performed with a 64-slice multidetector CT (General Electric Healthcare, Milwaukee [WI], US) to screen for vascular abnormalities that might preclude PAE and to look for any potential variant origins of the prostatic arteries. An injection of 120 mL of iodinated contrast (Omnipaque 350; GE Healthcare [Shanghai] Co., Ltd. Shanghai, China) at 3.5 to 4 mL/s, depending on the size of the angiocatheter, was administered. A pre-contrast scan of the pelvis preceded the contrast-enhanced acquisition. A sublingual vasodilator (0.5 mg nitroglycerine) was given before imaging of the arterial phase to help

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
1. Emergency admissions for acute urinary retention, and failed voiding trials within 2 weeks after given daily doses of alpha blockers	1. Biopsy-proven prostate malignancy
2. History of lower urinary tract symptoms	2. Hypocontractile or acontractile bladder proven by cystometrography
3. ASA 3/4	3. Neurogenic bladder
4. Age \geq 50 y	4. Bladder diverticulum or stones
5. Prostate size \geq 50 cc on transrectal ultrasound	5. Urethral stenosis
6. Serum PSA level \leq 4 ng/mL and no clinical suspicion of malignancy on digital rectal examination	6. Active urinary tract infection
7. Serum PSA level $>$ 4 ng/mL or clinical suspicion of malignancy on digital rectal examination, with cancer excluded by biopsy, unless biopsy is refused by patient	7. Previous prostatic surgery including transurethral resection of prostate, needle ablation, stent implantation, or any other invasive treatment of the prostate
8. Erectile dysfunction, or sexual function is not a concern	8. Chronic kidney disease with baseline serum creatinine level $>$ 150 μ mol/L
	9. History of pelvic irradiation or radical pelvic surgery, or known major iliac arterial occlusive disease
	10. Vascular occlusion or severe stenosis along the relevant vascular access path leading to the prostate artery

Abbreviations: ASA = American Society of Anesthesiologists; PSA = prostate-specific antigen.

identify small arteries. Arterial phase imaging was then performed with bolus triggering in the abdominal aorta plus a 10 s delay. Afterwards, the venous phase was acquired with a mean time of 70 to 80 s from the time of injection. A designated radiologist with 5 years of endovascular intervention experience reviewed the CTA images and decided upon the feasibility of PAE. If there was any doubt about the feasibility, the first radiologist would seek a second opinion from a radiologist with 30 years' experience. Catheterised urine was saved for culture and indwelling urinary catheters were not removed until PAE.

PAE was performed as an inpatient procedure with patients admitted one day prior to the procedure. Baseline pre-PAE blood tests included serum prostate-specific antigen (PSA). All antiplatelet and anticoagulation medications were withheld perioperatively according to physicians' advice. Patients fasted for 6 hours before PAE. Premedication including oral diclofenac extended-release tablet 100 mg, oral pantoprazole 40 mg, and a bisacodyl 10 mg suppository, administered on the day before embolisation. Intravenous levofloxacin 500 mg was used for antibiotic prophylaxis on-call to the radiology suite.

PAE was performed with a standardised technique for all recruited patients. All procedures were performed by the two interventional radiologists. A Siemens Artis Zee ceiling-mounted fluoroscopy unit (Siemens Medical Solutions, Forchheim, Germany) was used for all procedures. The procedures were performed under local anaesthesia using 5 mL 1% lidocaine. The right femoral

artery was cannulated with a 5-Fr vascular sheath. Bilateral internal iliac angiograms were performed using tube rotation at ipsilateral 35° and craniocaudal angulation at 10°. The choice of angiographic catheters for internal iliac artery angiograms (4-Fr Cobra 1, Cordis, Bridgewater [NJ], US; 4-Fr Simmons Sidewinder 1 Terumo, Inc., Tokyo, Japan; 5-Fr RIM, Cook, Bloomington [IN], US) depended on the CTA findings and operators' preference. In case of difficult anatomy making cannulation of the right prostatic artery impossible via a right femoral approach, a left femoral approach was used.

Using the CTA for reference, the arterial supply to the prostate was identified and one or both prostatic arteries were cannulated using a microcatheter (Merit Maestro 2.4 Fr; Merit Medical Systems Inc. South Jordan [UT], US) with or without the use of a microguidewire. Either a Tenor steerable guidewire 0.014 in (Merit Medical) or a Transcend 0.014 in steerable guidewire (Boston Scientific, Inc., Natick [MA], US) were used. When the position of a catheter was in doubt, cone beam CT was used for further delineation.

After successful cannulation of one or both prostatic arteries, selective angiograms were performed before embolisation to ensure the position of microcatheter inside the prostatic artery, to confirm the arterial supply to that side of the prostate, and to exclude other arterial supply from the prostatic artery to areas other than the prostate. Embolisation was performed using tris-acryl microspheres (Embosphere microspheres, Merit Medical) of diameter 300 to 500 μ m. Nitroglycerine

100 µg was injected intra-arterially before embolisation to prevent vasospasm, facilitate delivery of particles, and minimise reflux of particles and non-target embolisation. In order to avoid non-target embolisation, the Embosphere particles (2 mL) were suspended in a 22-mL solution (a mixture of 8 mL normal saline and 14 mL Omnipaque 350), which was slowly injected using a 2-mL syringe under fluoroscopic guidance until there was contrast stasis in the prostatic artery. Angiograms were performed after PAE to confirm obliteration of the prostatic arteries. Technical success was defined as successful embolisation of one or both prostatic arteries.

After PAE, patients were kept on complete bed rest for 24 h. Any complications were managed and recorded according to the Society of Interventional Radiology Classification System. Diclofenac extended-release tablets, pantoprazole, and levofloxacin were continued for 1 week following the procedure. Patients were discharged with an indwelling urinary catheter. Outpatient voiding trials were scheduled for 1, 2, 4, and 12 weeks after PAE. Clinical follow-up was arranged 3 months after PAE. Clinical assessment of lower urinary tract symptoms, uroflowmetry, post-void residual urine volume, serum PSA, transrectal ultrasound scans, and validated questionnaires with International Prostate Symptoms Score and Quality of Life (IPSS/QoL) was conducted.

Primary outcome measure was successful voiding within 12 weeks after PAE. Successful voiding was defined as a residual <350 mL and no evidence of painful retention. Other outcomes included complications of PAE, reduction in prostate size, and changes in serum PSA level.

Statistical calculations were conducted using SPSS (Windows version 22.0; IBM Corp, Armonk [NY], US). Descriptive statistics was used to calculate the primary and secondary outcomes. Serum PSA levels and prostate volumes before and after PAE were compared with the Wilcoxon signed rank test. Correlation between prostate size and prostate size percentage reduction were tested with Spearman's correlation. The Mann-Whitney *U* test was performed to test any difference in percentage reduction in prostate volume between moderately and severely enlarged glands. Statistical significance was taken as *p* < 0.05.

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were

used in reporting of the study results.⁴

RESULTS

Twenty-one men were recruited into the study. The mean (±standard deviation) age was 83±5 years. Eighteen patients belonged to ASA class 3 (attributable to chronic obstructive pulmonary disease [*n* = 5], congestive heart failure [*n* = 3], coronary artery disease [*n* = 5], and poorly controlled hypertension [*n* = 5]). Four patients belonged to ASA class 4 (attributable to chronic obstructive pulmonary disease [*n* = 2] and congestive heart failure [*n* = 2]). The mean PSA was 18.4±10.5 ng/mL and the mean prostate size was 124±63.4 mL. Fourteen (66.7%) patients were deemed feasible for PAE after CTA assessment and seven patients were excluded after CTA (severe atherosclerosis [*n* = 4], small prostate size [*n* = 2], metastatic prostate cancer [*n* = 1]) [Table 2].

One patient died of pneumonia before PAE. Thirteen patients proceeded to PAE with 16 total embolisations. The technical success rate was 100%. Bilateral embolisations were successful in nine patients (Figures 1 to 4). Three patients had only unilateral embolisation performed on the first attempt due to prolonged procedure time reaching the peak dose of contrast. Embolisations of the contralateral prostatic artery were performed in these cases 2 months after the first embolisations. One patient had one-sided PAE performed only, as the preprocedural angiogram showed the entire prostate to be supplied by the right prostatic artery (Figures 5 to 7). The mean dose area product was 14,489.5 µGy·m² (range, 5230.2-24212.3 µGy·m²). All 13 patients attended follow-up and were analysed.

Table 2. Patient demographics and CTA findings (*n* = 21).*

	Value
Age (years)	83 ± 5
ASA grade	
3	18 (86%)
4	3 (14%)
Serum PSA level (ng/mL)	18.4 ± 10
Prostate size (cc)	124 ± 61
CTA findings	
Normal / feasible for PAE	14 (67%)
Severe atherosclerosis	4 (19%)
Small prostate size	2 (10%)
Metastatic disease	1 (5%)

Abbreviations: ASA = American Society of Anesthesiologists; CTA = computed tomography angiography; PSA = prostate-specific antigen; PAE = prostatic arterial embolisation.

* Data are presented as mean ± standard deviation or No. (%) of patients.

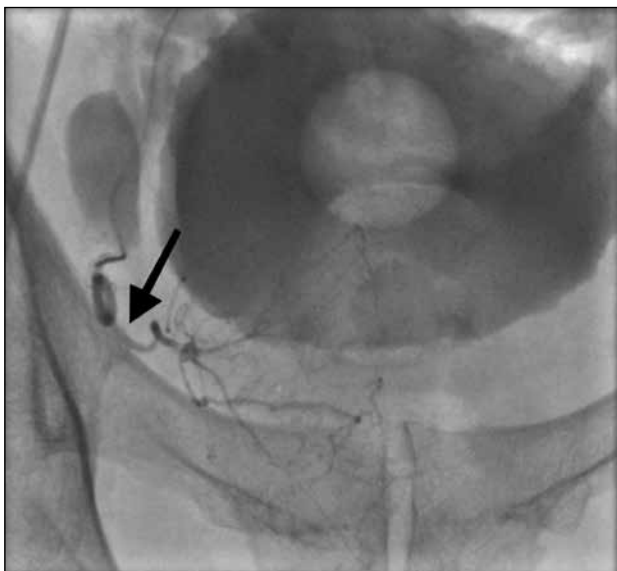


Figure 1. Right prostatic artery (arrow) before embolisation (case 1).



Figure 3. Right prostatic artery (arrow) before embolisation (case 2).



Figure 2. Post-embolisation showing stasis of contrast in right prostatic artery (arrow) [case 1].



Figure 4. Post-embolisation showing stasis of contrast in right prostatic artery (arrow) [case 2].

Nine patients (69.2%) had successful voiding trials with seven of them able to void within 2 weeks after PAE (Table 3). Despite the poor results of voiding trials, there were reductions in PSA and prostate size. Serum PSA levels were decreased by $46.7\% \pm 20.9\%$ ($p = 0.041$) and prostate size was reduced by $58.6\% \pm 22.5\%$ ($p = 0.028$). Larger prostate size was significantly correlated with larger percentage reduction of prostate volume after PAE ($p = 0.036$). Prostate volume percentage reduction was 19.4% for moderately enlarged prostates and 43.6% for severely enlarged prostates.

One patient developed haematuria requiring readmission on day 5 after PAE. The haematuria subsided spontaneously on observation (Society of Interventional Radiology Classification Class B). No other adverse events were recorded.



Figure 5. Right prostatic artery (arrow) supplying both right and left prostatic lobes (case 3).



Figure 6. Superselective right prostatic arterial angiogram showing supply to both right and left lobes (case 3).

DISCUSSION

Refractory retention in men with evidence of BPE is one of the indications for transurethral prostate surgery. When successful, the surgery provides patients with



Figure 7. Post-embolisation showing stasis of contrast in right prostatic artery (arrow) [oblique projection] (case 3).

Table 3. Outcomes of patients received PAE (n = 13).*

	Value
Follow-up (weeks)	10 (4-30)
Successful voiding	9 (69.2%)
3-month IPSS / QoL	12.5 ± 6.9 / 2.9 ± 1.3
3-month peak flow rate (mL/s)	10.2 ± 3.4
3-month residual urine (mL)	84 ± 49
6-month PSA (ng/mL)	9.8 ± 6.2
6-month prostate size (mL)	69 ± 17
Reduction of PSA (%)	46.7% ± 20.9%
Reduction of prostate size (%)	58.6% ± 22.5%

Abbreviations: IPSS = International Prostate Symptoms Score; QoL = quality of Life; PSA = prostate-specific antigen; PAE = prostatic arterial embolisation.

* Data are presented as median (range), mean ± standard deviation, or No. (%) of patients.

the opportunity to live without an indwelling urinary catheter. However, some men of advanced age have co-morbidities, especially cardiorespiratory diseases, which might preclude surgery. In these cases, long-term indwelling urinary catheters, intermittent catheterisation, or prostate stent insertion under local anaesthesia are possible considerations. Prostate stent insertion is a self-financed item in our district; thus, men with co-morbidities and financial constraints would have to deal with urinary catheters for the rest of their lives.

PAE is increasingly used for treatment of BPE. In the

study by Pisco et al,³ PAE was successful in 97% of cases with a significant reduction in IPSS/QoL score and improvement in peak flow rate. Recent meta-analyses^{5,6} also showed a significant improvement in peak flow rate and IPSS/QoL scores at 12 months after PAE. The majority of published studies, however, are small and single-site studies. The indications were heterogeneous and few had reported the clinical success of PAE in patients with co-morbidities.⁷⁻⁹ A local study had reported successful PAE outcomes in weaning catheters in patients with retention of urine due to BPE.¹⁰ In our study we utilised PAE for high-surgical-risk patients with indwelling catheters due to refractory retention. The ultimate goal was to achieve spontaneous voiding without exposure to the risk of anaesthesia and surgery.

Our pilot study showed a promising result in these high-risk patients. The technical success rate was 100%, although in some cases only unilateral embolisations were possible in the first session. Conventional angiograms had already confirmed the position of the microcatheter and of the prostate arterial supply; thus, cone beam CT was avoided in most cases. Nearly 70% of patients in our cohort had successful voiding trials after PAE, with the majority of them able to void within 2 weeks after PAE. This fast-acting clinical success of PAE was accompanied by substantial early reduction in prostate volume at 1 month after PAE and sustained reduction 6 months after PAE (Figure 1). Serum PSA levels also reduced substantially.

To the best of our knowledge, this is the first local study to report PAE outcomes in men with refractory retention and high surgical or anaesthetic risks. Yu et al¹⁰ had reported the excellent local results of PAE in patients with complete urinary outflow obstruction. Their group reported a higher success rate of voiding trials (87.5% vs. 69.2%) than ours. The difference could be explained by the younger mean age (66 vs. 83 years) and smaller prostate size (77 [study group]/65.6 [control group] vs. 124 mL) in their cohort. The chance of underactive bladder increased when patients are older or when there is prolonged bladder outlet obstruction.¹¹ Our lower rate of clinical success could be related to the poorer bladder function in our older group of patients with larger prostates. To address this issue, we could investigate all cases with cystometrography before and after PAE in future. Their study, however, did not show any data on the anaesthetic risks and co-morbidities. Our early results could potentially broaden the utilisation of PAE in patients with high cardiorespiratory risks.

More studies are needed to establish the role of PAE in these high-risk patients and to validate our results.

The 80 mL was used in our study as a cut-off to differentiate moderately and severely enlarged prostate glands. This is based on the European Association of Urology guidelines, which recommend different treatment options for glands using the 80 mL cut-off.¹² Conventional transurethral prostatectomy was not recommended for prostates >80 mL, as it was considered ineffective to resect such a large gland and possessed high surgical risk. Instead, techniques such as holmium laser enucleation of prostate or more invasive techniques, such as open enucleation, were recommended.¹² However, the clinical success of PAE had been shown to be independent of the prostate size and even had better result in larger prostate glands. Kurbatov et al¹³ reported the efficacy and safety of PAE for prostate volumes >80 mL. Wang et al¹⁴ had compared the PAE results of different prostate sizes with cut-off of 80 mL. They found the improvement in IPSS/QoL, peak flow rate, post-void residual, and prostate volume reduction were all significantly better in prostate sizes >80 mL.¹⁴ These agree with our findings, which showed the prostate volume reduction was much greater in larger prostates. The reason is still uncertain. It was hypothesised that the hypervascularity and larger prostate size in large glands might facilitate embolisation and result in a larger volume of infarction.¹⁴ It makes PAE even more appealing to those high-surgical-risk patients with large prostates, as they could avoid more invasive procedures such as open enucleation.

PAE was in general well tolerated and the majority of studies reported few minor complications.^{3,5,10} Commonly reported complications were urinary tract infections (2%-19%), transient haematuria (10%), transient haemospermia (7%), inguinal haematoma (7%), urinary retention (8%-26%), and pelvic pain (2%-9%).^{3,5,15} In our cohort, only one patient had haematuria requiring readmission, which resolved spontaneously.

Our results were limited by the single-centre design with small sample size. Moreover, approximately one-third of patients were excluded owing to unfavourable vascular anatomy or diffuse atherosclerotic disease. These exclusions were higher than previously reported (inclusion rate, 89.9%-100%).^{3,10,15} Compared with other studies, our patients were much older, with multiple co-morbidities. After considering technical factors and anatomical difficulties, more patients were inevitably

excluded due to poor vascular status. Three patients had unilateral PAE performed only in the first embolisation attempt. These could be explained by the learning curve of radiologists, as all these cases were done in the early phase of the study. With more experiences in catheterisation of the prostatic artery and in interpreting the CTA, bilateral embolisations were achievable in single session in later cases. Due to limited resources, magnetic resonance imaging was not performed to assess the percentage of prostate infarction. We were also unable to show the changes in urodynamics and IPSS/QoL results as all patients were on indwelling catheters before PAE.

CONCLUSION

PAE was an efficacious and safe option for high-surgical-risk patients with benign prostate enlargement in refractory retention. With this encouraging preliminary result, we could further develop and establish the role of PAE among the different treatment modalities for BPE in our centre.

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