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Original Article

The 'Prostate Embolisation AS first-line therapY compAred to meDication in treatment naïVe men with prostAte eNlargement, a randomised ControllEd trial' (P-EASY ADVANCE): a randomised controlled trial of prostate embolisation vs medication for BPH

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Objective

To compare prostate artery embolisation (PAE) to the combination of tamsulosin and dutasteride therapy as a potential first-line therapy for obstructive benign prostatic hyperplasia (BPH) in treatment-naïve patients in the 'Prostate Embolisation AS first-line therapY compAred to meDication in treatment naïVe men with prostAte eNlargement, a randomised ControllEd trial' (P-EASY ADVANCE).

Patients and Methods

A total of 39 men with enlarged prostates, moderate–severe lower urinary tract symptoms (LUTS) and obstructed/equivocal urodynamic studies (UDS), and who had no prior treatment for BPH, were randomised to receive either combined medical therapy with tamsulosin and dutasteride (medication) or PAE. Follow-up UDS, International Prostate Symptom Score (IPSS), uroflowmetry and ultrasound were performed at short- to medium-term intervals following interventions and compared to baseline.

Results

The medication and PAE treatment groups had similar baseline characteristics, including prostate volumes (87.8 and 85.4 mL respectively), maximum urinary flow rate (Q_{max}; 6.5 and 6.6 mL/s, respectively), IPSS (19.5 and 21, respectively) and obstructed UDS (79% and 74%, respectively). Both interventions improved voiding and bladder outflow obstruction from baseline, with more patients unobstructed after PAE (63%) compared to medication (28%) ($P = 0.03$). PAE patients had significantly greater reductions in prostate size ($P < 0.001$), incomplete emptying ($P = 0.002$), total IPSS ($P = 0.032$), Q_{max} ($P = 0.006$) and quality of life ($P = 0.001$). Altered ejaculation, erectile dysfunction and nausea were more common in the medication group.

Conclusion

Prostate artery embolisation was more effective than combined medical therapy at reducing urinary obstruction, decreasing prostate volume and improving LUTS in patients with BPH who had not previously been treated. This is the first randomised control study to compare PAE and combined medical therapy in exclusively treatment-naïve patients and raises the potential of PAE as an alternative early treatment option for BPH. Further randomised comparative trials are planned to further validate the role of PAE in mitigating obstructive BPH.

Keywords

benign prostatic hyperplasia, embolisation, medical therapy, urinary tract symptoms, urodynamics

Introduction

Benign prostatic hyperplasia (BPH) is a common cause of LUTS [1,2]. Options for management include α-blockers, 5α-reductase inhibitors (and combined therapies) [3], minimally invasive procedures (UroLift®, Rezum®) and surgical interventions (TURP, Greenlight laser vaporisation, holmium laser enucleation). These treatments all have different efficacy, safety and side-effect profiles. The specific side-effects of combined medical therapy with dutasteride and tamsulosin include: postural hypotension, syncope, dizziness, insomnia, floppy iris syndrome, vision impairment, ejaculation disorders, fatigue, gynecomastia, and cardiac arrhythmia.

Prostate artery embolisation (PAE) is a non-surgical, minimally invasive interventional radiology treatment for obstructive BPH. There are increasing clinical data to support its use as a medium- to long-term management option to relieve obstructive LUTS and improve quality of life (QoL) [4–6]. Since 2014 [7–10] there have been several randomised controlled trials (RCTs) comparing the safety and efficacy of PAE to TURP in patients with moderate–severe symptoms refractory to medical therapy. PAE's low impact on sexual function and urinary continence makes it a potential treatment option in the earlier stages of BPH. The use of PAE as a first-line non-surgical alternative to long-term medical therapy for BPH may delay clinical progression to surgical intervention [10].

A recent RCT evaluated the efficiency of PAE against Duodart® (GlaxoSmithKline [GSK], London, UK; active ingredients dutasteride and tamsulosin hydrochloride) in patients previously refractory to α-blockers [11]. However, the present study is the first known RCT to compare the efficacy, safety and tolerability of PAE and combined medical therapy with dutasteride and tamsulosin in treatment-naïve patients.

Patients and Methods

Trial Design and Participants

This trial (P-EASY ADVANCE: Prostate Embolisation AS first-line therapY compAred to meDication in treatment naïVe men with prostAte eNlargement, a randomised ControllEd trial) was a collaboration between interventional radiologists and urologists at The Wesley Hospital, Brisbane, Australia between 2020 and 2022. The study was approved by the Uniting Care Health Human Research Ethics Committee (reference number: 1735) and registered with the Australian New Zealand Clinical Trial Registry (ID: ACTRN12617001199303). All participants provided written informed consent.

Patients with treatment-naïve clinical BOO secondary to BPH were recruited to this trial after urological and interventional radiologist consultations. All patients completed baseline IPSS, ultrasound renal tracts, uroflowmetry, and urodynamic studies (UDS). Exclusion and inclusion criteria are outlined in Fig. 1. Patients with obstruction or equivocal for obstruction on UDS were eligible for inclusion. The first follow-up investigations were performed in all patients, on average, between 7.4 and 12.3 months post-intervention with repeat uroflowmetry and UDS, IPSS, and ultrasound to assess clinical progress. All patients could elect to cross-over to the alternative intervention after the first follow-up time point if the effects were considered by the patient to be unsatisfactory. According to the power calculations, it was estimated that a minimum of 15 patients in each treatment group would provide sufficient statistical power to detect significant differences, assuming a two-sided alpha level of 5% and a power of 90%. To mitigate the potential impact of discontinuations or loss to follow-up, we aimed to screen and recruit at least 20% more participants than the calculated minimum. In total, 54 patients were screened, and 39 eligible patients were randomised into the medication (17 patients) and PAE (22 patients) groups.

Fig. 1 Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Age >50–80 years	Prostate malignancy
BPH with prostate volume > 50 mL	Neurogenic bladder
Moderate-Severe LUTS (IPSS > 8)	Renal failure eGFR <35 mL/min
Peak urinary flow <15 mL/s	Severe peripheral vascular disease
Obstructive urodynamics	Urethral or bladder pathology
Treatment-naïve, i.e. no previous treatment for BPH	History of prior treatment for BPH

IPSS: International Prostate Symptom Score; **BPH:** Benign prostatic hyperplasia; **eGFR:** Estimated Glomerular Filtration Rate

Interventions

Medical Therapy

A total of 17 men were randomised to combined medical therapy with dutasteride 500 μg and tamsulosin 400 μg (medication; Duodart, GSK) and commenced treatment. Following the first follow-up investigation and UDS, patients who elected to cross over into the PAE treatment arm completed another IPSS questionnaire at a second follow-up but were not subjected to further invasive UDS.

The PAE Procedure

A total of 22 patients underwent PAE, performed by experienced interventional radiologists (N.B., D.W.) according to the previously described techniques [12]. In summary, selective catheterisation of prostate arteries was performed via radial artery approach using a 135-cm Bern-tip 4-F Navicross® catheter (Terumo, Tokyo, Japan) with coaxial 1.3-F 168-cm Headway Duo® microcatheter (Microvention, Aliso Viejo, CA, USA), 0.041 cm/0.016 inch Radifocus Guidewire GT® (Terumo) or 0.036 cm/0.014 inch Chikai® wire (Asahi, Tokyo, Japan). Embozene® microspheres 250 μm (Varian, Palo Alto, CA, USA) were used for embolisation of the selected arteries, followed by a small volume of intra-arterial gelfoam (Pfizer, New York, NY, USA) or Spongostan® (Ethicon Inc., Somerville, NJ, USA) slurry to further reduce arterial flow.

Urodynamic Assessments

Patients underwent UDS at baseline and first follow-up. BOO was classified according to the calculated BOO index (BOOI = detrusor pressure at maximum urinary flow ($PdetQ_{max}$) − $2Q_{max}$) and their contractility status was determined using the bladder contractility index (BCI = $PdetQ_{max}$ + $5Q_{max}$) criteria [13].

Outcomes

Primary outcomes were the change in prostate size, UDS parameters, IPSS findings, and QoL scores at the first follow-up point compared to baseline. Secondary outcomes comprised changes in the urinary symptoms (IPSS) and QoL scores at the second follow-up point in patients who crossed over to the other treatment arm. Sexual function was assessed by patient self-reporting answers to change in erectile function, change in ejaculate, or loss of ability to penetrate (erectile dysfunction [ED]).

Statistical Analysis

The sample size calculation was completed using Power Analysis and Sample Size (PASS) (Version 13.0.14; National Council for the Social Studies [NCSS] Statistical Software, Kaysville, UT, USA) based on a two-sample *t*-test assuming equal variance. The statistical analyses were conducted using Stata statistical software, version 13.1 (StataCorp, College Station, TX, USA). Descriptive data are summarised as mean (SD, range) for continuous variables and frequency (percentage) for categorical variables. Continuous outcome variables summarising associations between exposure and outcome variables used linear regression and effect estimates were reported as mean difference with 95% CIs; *P* values. Categorical outcome variables summarising associations between exposure and outcome variables used multinomial logistic regression and effect estimates were reported as odds ratios with 95% CIs; *P* values. Linear regression models were conducted as a regression of the difference between timepoints. Logistic regression models were adjusted for baseline scores. In all models, the treatment group was included as a fixed effect.

Results

A flow diagram of participant recruitment, randomisation, interventions and assessments is presented in Fig. 2. From the 54 patients initially screened for this study, 15 were excluded prior to randomisation as they did not meet the inclusion criteria (six), declined to proceed (eight), or were lost to follow-up (three). The remaining 39 men were randomised to the medication (17) or PAE (22) groups. In all, 21 patients in the PAE arm and 15 in the medication arm completed their first follow-up assessments. Two patients in the PAE arm and one in the medication arm declined to undergo follow-up UDS.

At the end of the first follow-up time point, 13 of 15 patients initially randomised to the medication group crossed-over to the PAE procedure. None of the patients in the PAE group elected to cross over to the medication arm.

Demographics and the pre-intervention parameters for each study group are presented in Table 1. PAE procedural details are presented in Table S1. PAE was technically successful in all patients, with 17 bilateral and four unilateral PAEs. Overall initial follow-ups with ultrasound, IPSS and QoL evaluations were completed at a mean (SD, range) of 10.4 (5.2, 4.8–27.2) months for the medication group and 12.3 (5.5, 6.6–28.2) months for the PAE group, with a mean difference of 1.9 months between the two groups (95% CI −5.6, 1.8; $P = 0.30$). However, follow-up UDS were performed earlier in the medication group, at a mean (range) of 7.4 (5.6–10.1) months compared to 9.7 (6.5–17.9) months in the PAE group, for a mean difference of 2.3 months (95% CI −3.9, −0.7; $P = 0.005$). The variability in follow-up was due largely to operational

Fig. 2 Flow diagram of participant recruitment, randomisation, and subsequent tests.

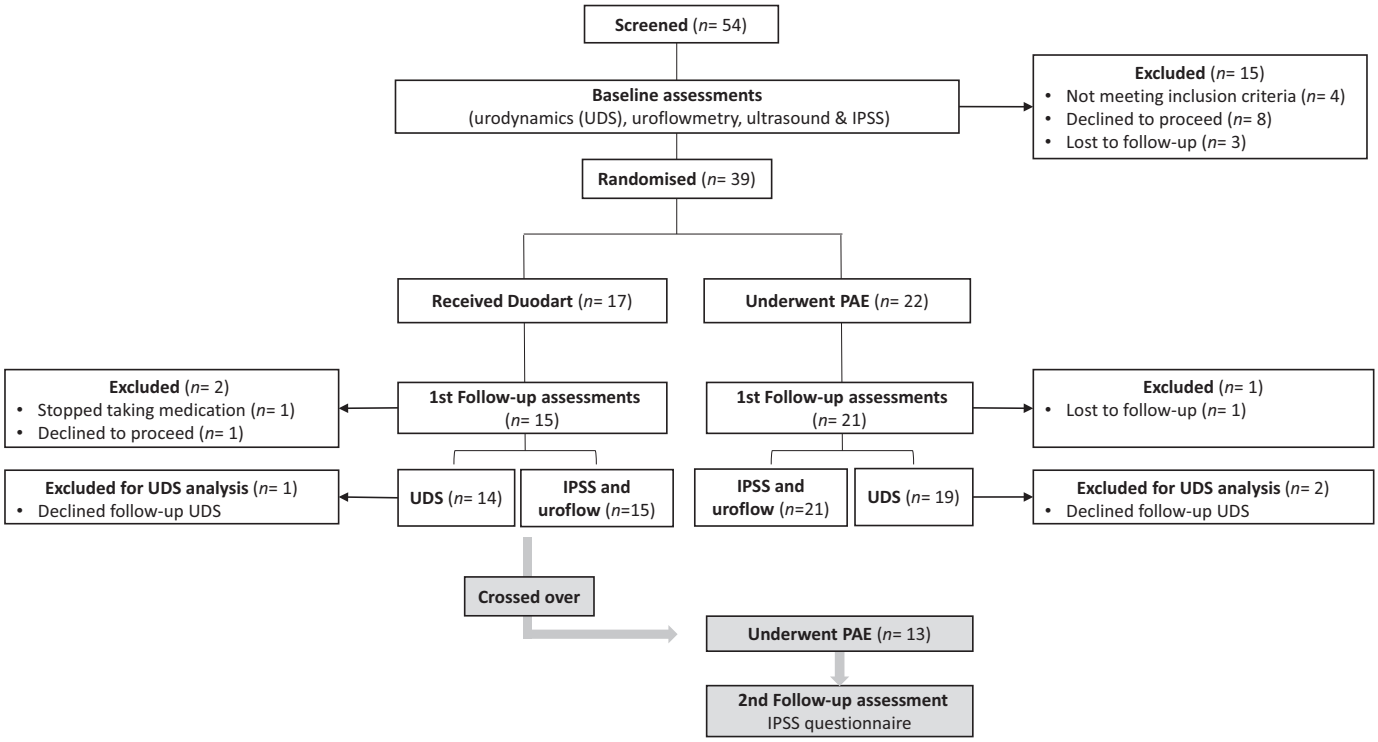


Table 1 Pre-intervention baseline clinical and urodynamic characteristics.

Variable	Duodart (*n* = 15)	PAE (*n* = 21)
Age, years, mean (SD, range)	68.00 (7.3, 55.0–80.0)	66.76 (5.3, 57.0–75.0)
Urodynamic		
Q_{max}, mL/s*,† , mean (SD, range)	6.50 (2.8, 2.0–13.0)	6.63 (2.7, 2.0–14.0)
PVR, mL†,‡, mean (SD, range)	156.15 (107.4, 25.0–400.0)	166.58 (140.1, 25.0–500.0)
PdetQ_{max}, cmH_2O†,‡, mean (SD, range)	78.38 (40.9, 48–177)	69.42 (21.9, 34–120)
Ultrasound		
Prostate size, mL, mean (SD, range)	87.79 (35.2, 47.0–150.0)	85.42 (41.9, 41.0–217.0)
IPSS, mean (SD, range)		
Incomplete emptying	2.33 (1.4, 1.0–4.0)	3.05 (1.8, 0.0–5.0)
Frequency	3.40 (1.3, 1.0–5.0)	3.81 (1.2, 1.0–5.0)
Intermittency	2.80 (1.7, 1.0–5.0)	3.14 (1.4, 0.0–5.0)
Urgency	3.27 (1.3, 1.0–5.0)	3.38 (1.5, 0.0–5.0)
Weak stream	3.27 (1.4, 1.0–5.0)	3.76 (1.1, 2.0–5.0)
Straining	1.87 (1.8, 0.0–5.0)	1.86 (1.6, 0.0–5.0)
Nocturia	2.53 (1.1, 1.0–4.0)	2.24 (1.3, 1.0–5.0)
Total IPSS	19.47 (6.5, 11.0–30.0)	21.05 (6.0, 11.0–30.0)
QoL* score, mean (SD, range)	4.07 (0.7, 3.0–5.0)	3.95 (1.1, 2.0–6.0)
BOOI*,†, *n* (%)		
Unobstructed (BOOI ≤20)	0 (0)	0 (0)
Equivocal (BOOI 20–40)	3 (21)	5 (26)
Obstructed (BOOI ≥40)	11 (79)	14 (74)
BCI†,‡, *n* (%)		
Weak (BCI <100)	7 (54)	10 (53)
Normal (BCI 100–150)	4 (31)	7 (37)
Strong (BCI >150)	2 (15)	2 (11)

**One missing value in the Duodart group. †Two missing values in the PAE group. ‡Two missing values in the Duodart group.*

restrictions and travel limitations imposed by the COVID-19 pandemic. In addition, as the majority of patients in the medication group expressed interest in crossing over to the PAE group, this may explain the shorter average follow-up period post-intervention in the medication group compared to the PAE group.

Table 2 Clinical and urodynamic characteristics at baseline and follow-up 1.

Variable	Duodart (*n* = 15)		PAE (*n* = 21)		PAE vs Duodart
	Change from baseline		Change from baseline		Follow-up 1†
	Mean difference (95% CI); *P*	% Change	Mean difference (95% CI); *P*	% Change	Mean difference (95% CI); *P*
Ultrasound					
Prostate size, mL	−6.5 (−15.8; 2.8); 0.153	−7.70	−32.2 (−45.8; −18.6); <0.001*	−47.3	−26.7 (−39.8; −13.6); <0.001*
IPSS					
Incomplete emptying	−0.1 (−1.2;0.9); 0.784	−5.7	−2.2 (−3.1; −1.4); <0.001*	−132.6	−1.5 (−2.4; −0.6); 0.002*
Frequency	−0.9 (−2.0; 0.3); 0.115	−29.6	−2.1 (−2.8; 1.4); <0.001*	−80.1	−0.9 (−1.9; 0.1); 0.083
Intermittency	−1.1 (2.4; 0.1); 0.066	−51.7	−1.9 (−2.7; −1.1); <0.001*	−92.9	−0.5 (−1.5; 0.6); 0.358
Urgency	−1.3 (−2.4; −0.3); 0.014*	−52.7	−2.1 (−3.1; −1.1); <0.001*	−96.3	−0.6 (−1.6; 0.3); 0.182
Weak stream	−1.3 (−2.4; −0.1); 0.031*	−49.2	−2.7 (−3.4; −1.9); <0.001*	−122.9	−1.0 (−2.1; 0.1); 0.067
Straining	−1.1 (−2.0; −0.1); 0.030*	−84.9	−1.3 (−2.1; −0.6); 0.001*	−127.5	−0.3 (−0.9; 0.4); 0.404
Nocturia	−0.7 (−1.2; −0.2); 0.012*	−30.2	−0.9 (−1.5; −0.2); 0.016*	−48.4	−0.4 (−1.1; −0.3); 0.297
Total IPSS	−6.5 (−11.4; −1.5); 0.014*	−40.4	−13.0 (−16.8; −9.2); <0.001*	−96.1	−5.2 (−9.9; −0.5); 0.032*
QoL‡	−1.4 (−2.3; −0.6); 0.003*	−43.3	−2.9 (−3.6; −2.1); <0.001*	−127.8	−1.5 (−2.5; −0.6); 0.001*
Urodynamic (bladder function test)					
Q_{max}, mL/s	2.1 (0.3; 3.9); 0.023*	28.50	6.9 (4.3; 9.4); <0.001*	71.10	4.7 (1.4; 8.0); 0.006*
PVR, mL	−56.9 (−134.6; −1.7); 0.055	−45.3	−66.5 (−134.6; 1.7); 0.055	−50.9	−4.7 (−85.9; 76.4); 0.906
PdetQ_{max}, cmH_2O	−21.7 (−39.0; −4.4); 0.018*	−36.5	−29.4 (−40.4; −18.3); <0.001*	−55.0	−12.1 (−27.4; 3.1); 0.115

Variable	Duodart		PAE		PAE vs Duodart
	Baseline	Follow-up 1	Baseline	Follow-up 1	Follow-up 1
BOOI – categorical	Number of participants (%)				
Unobstructed (BOOI ≤20)	0 (0)	4 (28)	0 (0)	12 (63)	
Equivocal (BOOI 20–40)	3 (21)	5 (36)	5 (26)	3 (16)	
Obstructed (BOOI ≥40)	11 (79)	5 (36)	14 (74)	4 (21)	
BCI – categorical	Number of participants (%)				
Weak (BCI <100)	7 (54)	8 (57)	10 (53)	10 (53)	
Normal (BCI 100–150)	4 (31)	5 (36)	7 (37)	6 (32)	
Strong (BCI >150)	2 (15)	1 (7)	2 (11)	3 (16)	
	Mean difference from baseline (95% CI); *P*		Mean difference from baseline (95% CI); *P*		Mean difference (95% CI); *P*
BOOI – numerical	−26.3 (−44.5; −8.1); 0.008*		−43.1 (−56.7; −29.5); <0.001*		−21.1 (−40.0; −2.2); 0.030*
BCI – numerical‡	−10.2 (−29.0; 8.7); 0.263		5.0 (−8.7; 18.7); 0.456		11.4 (−8.0; 30.8); 0.239

*$P \leq 0.05$. †Adjusted for baseline values. ‡One value missing in the medication group.

Post-Intervention Outcomes: Baseline vs First Follow-Up

Overall, both interventions improved voiding and BOO outcomes compared to the baseline measurements (Table 2). Improvements from baseline were statistically significant across all parameters in the PAE group, except for the post-void residual (PVR) urine volume, whereas in the medication group statistical significance was not observed for PVR, prostate size, and scores related to incomplete emptying, frequency, and intermittency (Table 2).

Post-Intervention Outcomes: Medication vs PAE at the First Follow-Up Point

With PAE there was a statistically significantly greater reduction in prostate size ($P < 0.001$), incomplete emptying ($P = 0.002$) and total IPSS ($P = 0.032$) compared to medication (Table 2). In addition, PAE significantly increased Q_{max} by 4.7 mL/s ($P = 0.006$) and improved patients' QoL by 1.5 points ($P = 0.001$) more than medication (Table 2).

At baseline participants in both groups had either obstructed (medication: 79%; PAE: 74%) or equivocal (medication: 21%; PAE: 26%) UDS findings (Table 2). Following PAE, 63% of the participants were unobstructed, 16% were equivocal and 21% were obstructed. In comparison, only 28% of those who had received medication were unobstructed at the first follow-up point, with the majority remaining either equivocal (36%) or obstructed (36%) ($P = 0.030$, Table 2). At baseline, nearly half of the patients in both study arms had hypocontractile bladders and the proportions did not significantly change post-intervention for either of the groups (BCI <100: medication 57%, PAE 53%, Table 2).

Adverse Effects

The observed and reported post-intervention adverse effects in the first 4 weeks after treatment are presented in Table 3.

Table 3 Interventions' adverse effects.

Adverse effects (1–4 weeks post intervention)	Duodart group (*n* = 15) Number (%)	PAE group (*n* = 21) Number (%)
Altered ejaculation	3 (20)	1 (5)
Impotence/erectile dysfunction	2 (13)	0 (0)
Nausea/dizziness	2 (13)	1 (5)
Increased frequency	0 (0)	20 (95)
Painful urination	0 (0)	19 (90)
Prostate/perineal pain	0 (0)	16 (76)
Pain in rectal area	0 (0)	5 (24)
Pain in penile tip	0 (0)	5 (24)
Blood in urine	0 (0)	3 (14)
Blood in semen	0 (0)	2 (10)
Fever	0 (0)	1 (5)
		Average + SD, range
Pain/discomfort scale (1–10) following PAE		6.8 (2.6); 0–10
No. of days pain experienced post-PAE		5.9 days (3.7); 0–14

Altered ejaculation, ED and nausea/dizziness were more common in the medication group. Additionally, six of the 15 men (40%) in the medication group reported reduced libido. Only one man (5%) in the PAE group reported altered ejaculation. The most reported adverse effects after PAE were transient increased frequency (95%) and painful urination (90%), both of which resolved completely within 1-month post-procedure.

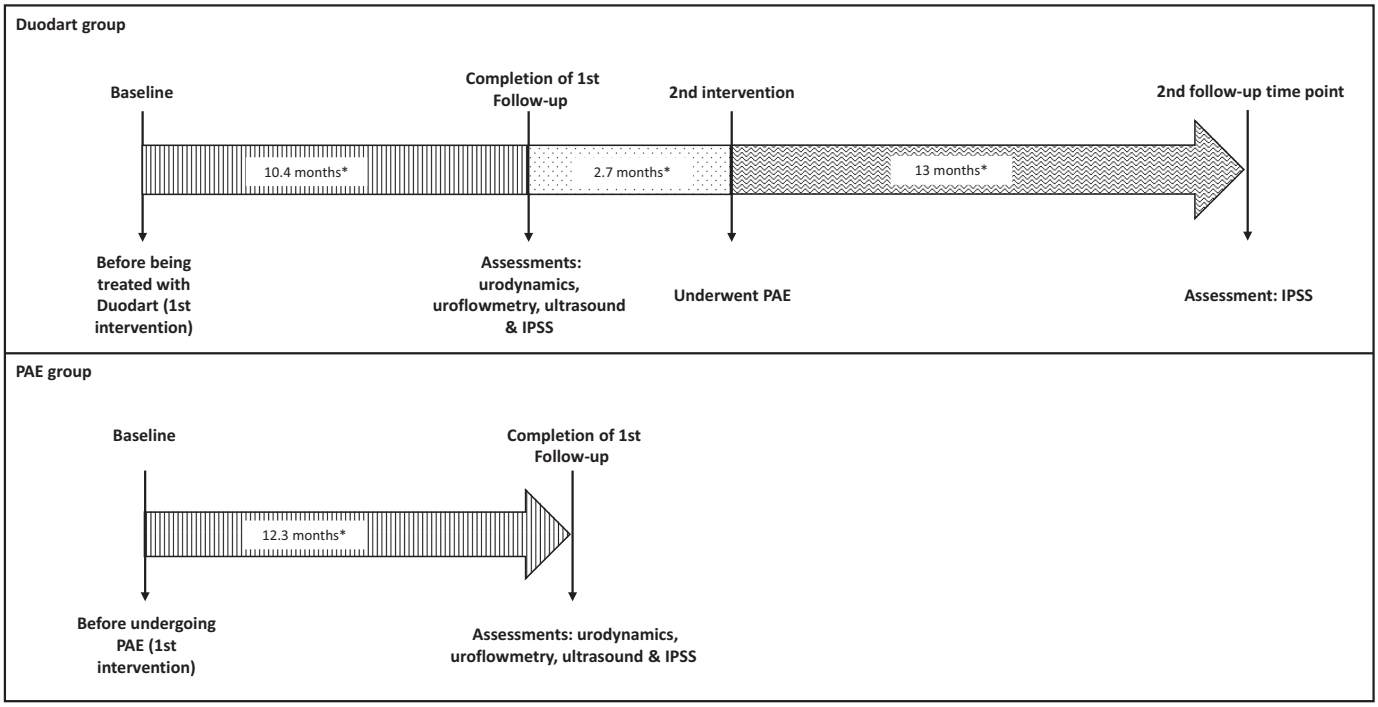
Cross-over of Patients

No patients in the PAE group elected to commence medical therapy, whereas 87% (13/15) of patients in the medication group reported unsatisfactory benefits and requested to undergo a PAE procedure. These patients completed a further IPSS questionnaire at a mean (range) of 13.0 (2.8–29.9) months after their PAE procedure (Fig. 3). At the second follow-up all cross-over PAE patients experienced statistically significant improvements in their IPSS and QoL scores compared to baseline (Table S2). Compared with their results from the first follow-up point (after completing medical therapy), these patients had significantly reduced incomplete emptying (difference of −1.3 points; $P = 0.015$) and urinary frequency (difference of −1.0 point; $P = 0.042$) scores after PAE (Table S2). The total IPSS reduced on average a further 4.2 points and QoL improved an extra 1 point, although these were not statistically significant.

Discussion

Lower urinary tract symptoms from BPH are progressive, affecting 50–75% of men aged >50 years, reaching 80% among those aged >70 years [14]. Men with symptomatic BPH often delay treatment until LUTS have become severe. Escalation from medical management usually occurs due to medication side-effects or limited symptomatic improvement

Fig. 3 The intervention and follow-up timeline of the patients that were initially treated with Duodart (GSK) and crossed over to the PAE group at the end of the first follow-up time point.



*: average number of months; **IPSS**: International prostate symptom score; **PAE**: prostate artery embolisation

[15,16]. PAE has emerged as a second-line option for patients with BPH who are refractory to medical therapy and are unsuitable for, or unwilling to undergo, more invasive surgery with a TURP [17]. Studies investigating PAE have focused on comparisons with the surgical 'gold standard' TURP. However, considering its proven efficacy, favourable side-effect profile, short recovery time and ability to be performed as a day case under conscious sedation, there may be benefits to PAE as an alternative first-line treatment for patients with BPH. To date, only one RCT directly comparing PAE to medical therapy has been performed, but in men refractory to medical therapy with α-blockers [11]. This present study compared the results of PAE to combined medical therapy (Duodart, GSK) in symptomatic, treatment-naïve patients.

Compared to baseline measurements both combined medical therapy and PAE significantly improved Q_{max}, urgency, weak stream, straining, nocturia, total IPSS and QoL. However, only PAE significantly reduced prostate volume, incomplete emptying, frequency and intermittency scores when compared to their baseline levels. When the two groups were compared with each other, Q_{max}, prostate size, incomplete emptying, total IPSS and QoL were all significantly superior in the PAE group.

The overall improvement of IPSS in the PAE group (–13.0 points) was similar to a prospective clinical trial comparing PAE to TURP, in which patients experienced an average of 13.4 points reduction in their total IPSS after 12 months [9]. In the present study, the positive effect of PAE on the reported QoL score derived from the IPSS ('mostly-dissatisfied' to 'pleased') is also consistent with the outcomes of a large long-term (10 years) retrospective study [18].

The association between pre-procedure prostate size and clinical outcomes of PAE remains controversial [19,20]. In our study, patients in both groups had >80 mL average prostate size at baseline (medication = 87.79 mL, PAE = 85.42 mL). PAE resulted in a statistically significantly greater reduction in the mean prostate size (medication = 81.29 mL; PAE = 53.21 mL), which may explain some of the improved QoL outcomes with PAE.

To date, only a few studies have evaluated post-PAE UDS findings. In a small prospective study by Carnevale et al. [8], the authors suggested that introducing PAE earlier in the BPH treatment paradigm could increase the number of patients with unobstructed bladders. This may reduce future decline of bladder function and detrusor over-activity from long-term BOO [21,22]. Aside from the beneficial symptomatic improvement of PAE on LUTS, our UDS showed PAE improves bladder function and significantly decreases urodynamic obstruction above combined medical therapy. The higher unobstructed rates of UDS after PAE further support the concept of early PAE intervention for symptomatic BPH as an alternative to first-line, long-term medical therapy. Although the time to completion of overall follow-up at the first time point was not significantly different between groups, the average follow-up for UDS after baseline in the medication group was 7.4 months, which was 2.3 months earlier than the PAE group. The earlier UDS results for the medication group may have been driven by the need for these patients to have completed their follow-up before being able to cross-over and receive PAE treatment. This difference may represent a confounder for the UDS results that exacerbated the differences between the two groups. However, non-invasive follow-up testing for both groups completed at similar time points reflected similar results and confirmed a trend that confirmed the UDS findings.

The higher residual IPSS, incidence of sexual adverse effects and persistent obstructed BOOI rates observed in the medication group may explain why 87% of these patients decided to cross-over to the PAE procedure at the end of the first follow-up point. These patients subsequently ceased medication and underwent PAE within an average of 2.7 months. A final evaluation of the IPSS and QoL scores was conducted at a mean (range) of 13 (2.8–29.9) months after the PAE procedure in the cross-over cohort, for a combined mean (range) follow-up of 26 (14–41) months since initial baseline assessment. Compared to the first follow-up point since ceasing medical therapy, these patients experienced further significant improvements in their symptoms, including incomplete emptying ($P = 0.015$) and frequency scores ($P = 0.042$) (Table S2).

Sexual side-effects are a potential consequence following treatment for BPH, including medical therapy [23]. In a large multicentre observational clinical trial (UK-ROPE; ClinicalTrials.gov identifier: NCT02434575) comparing PAE to TURP, retrograde ejaculation was almost double in the TURP group [24]. In the present study, the most reported side-effect by patients in the medication group was decreased libido (40%), followed by altered ejaculation (20%). In contrast, only 5% of men in our PAE group experienced altered ejaculation. Transient frequency (95%) and dysuria (90%) reported post-PAE resolved within 1 month of the procedure.

An important consideration in utilising PAE as a potential first-line alternative to medical therapy for symptomatic BPH is the radiation dose involved in performing the procedure. A recent systemic review [25] modelled the increased risk of cancer death from PAE radiation exposure, in a 66-year-old patient exposed to 200 Gy cm^2 as 0.117%, or one in 850. In our study the average patient age was 67 years, and the average dose-area product was 208.5 Gy cm^2. This compares favourably to the estimated increased risk of fatal cancer from a multiphase CT IVU (effective dose of 15–20 mSv) of one in 1000. The risks of death from radiation exposure are very low,

and compares favourably to other invasive interventions, such as postoperative mortality following BPH laser procedures or TURP of between 0.59% and 1.16% [26]. There is a reported small risk of death within 6 months of commencing tamsulosin, but the long-term mortality risk directly related to combined medical therapy is unknown [27].

The impact of unilateral PAEs in a small study will always be amplified; however, the rate of 19% in this study was higher than the original 'Prostate artery Embolisation Assessment of Safety and feasibilitY' (P-EASY) study [12] that had a unilateral rate of 7.8% in a cohort of 51 men. With greater experience and more technologically advanced materials, such as smaller microcatheters and specialised microwires, the rate of unilateral PAE will likely be lower in future studies.

Other limitations of this study include the small population in each arm, the significant time differences in completing first follow-up UDS between the two groups. Previous experiences with the International Index of Erectile Function resulted in poor compliance rates, so qualitative patient self-reported sexual questionnaires of erectile and ejaculate change were instead used for this study to record outcomes. This study only performed invasive UDS after the first follow-up point and not in the crossed-over group at the second follow-up, due in part to patients being unwilling to subject themselves to further invasive testing. Future comparative studies are planned in larger populations and multicentre settings, and validated questionnaires will be utilised for these.

Conclusion

Prostate artery embolisation was significantly more effective than combined dutasteride and tamsulosin in reducing prostate size, incomplete emptying, total IPSS, relieving urodynamic obstruction and improving QoL. Although more studies are needed, our results suggest that PAE could be a suitable first-line or early intervention for treatment-naïve men with moderate–severe LUTS due to BPH and may be better tolerated with fewer adverse effects compared to combined medical therapy.

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Disclosure of Interests

The authors declare no conflicts of interest.

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Abbreviations: BCI, bladder contractility index; BOOI, BOO index; Duodart, dutasteride 500 μg and tamsulosin 400 μg; ED, erectile dysfunction; GSK, GlaxoSmithKline; PAE, prostate artery embolisation; $PdetQ_{max}$, detrusor pressure at maximum flow rate; PVR, post-void residual urine volume; P-EASY ADVANCE, Prostate Embolisation AS first-line therapY compAred to meDication in treatment naïVe men with prostAte eNlargement, a randomised ControllEd trial; Q_{max}, maximum urinary flow rate; QoL, quality of life; RCT, randomised controlled trial; UDS, urodynamic studies.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. The PAE procedural details of the PAE group.

Table S2. Outcomes of cross-over patients at the second follow-up timepoint.

