

PROSTATIC ARTERY EMBOLIZATION FOR THE TREATMENT OF BENIGN PROSTATIC OBSTRUCTION – A RETROSPECTIVE REVIEW OF THE NOVEL EXPERIENCE OF 2 TERTIARY UROLOGY CENTERS

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ABSTRACT:

Background: Benign Prostatic Hyperplasia (BPH) is common in aging men with worldwide prevalence at 20-62%, while Malaysian prevalence was 39.3% (2001) and increased at 8% per decade. In surgical treatment of BPH, Trans-Urethral Resection of Prostate (TURP) remains the gold standard. Other surgical options would mostly also require general anesthesia (GA). Therefore, more Local-Anaesthesia (LA) based options should be made available for patients who are not fit or unwilling to be under GA. Those currently available LA-based procedure has shown promising results including prostatic stents and trans-urethral lifts, but have drawbacks due to being expensive, not widely available, less suitable in median lobe enlargement or may cause complications including migration, overgrowth of prostatic tissue or foreign-body related complications which may require GA for their treatment. Prostatic Artery Embolization (PAE), initially an LA-based emergency treatment option for persistent life-threatening hematuria from a bleeding BPH, now has been proven to be a safe elective treatment. In Malaysia this novel technique was first reported in 2017 for treatment of post TURP intractable hematuria.

Methods and Material: We retrospectively evaluated all 13 catheter-dependent BPH patients in two tertiary urology centres treated with PAE from April 2019 until December 2021 to assess post-treatment efficacy.

Results: One patient failed removal of catheter within 3 months post-procedure but 12 out of 13 patients safely got their catheter removed within 1-3 months and resulted in significant IPSS improvement.

Conclusion: PAE is a safe and effective treatment option for BPH patients of the Malaysian population but needs prospective evaluation.

Keywords: Benign prostatic hyperplasia, prostate, embolization.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition in ageing men, the prevalence of which increases with age. It is caused by the proliferation of smooth muscle and epithelial cells in the prostatic transition zone [1,2]. The worldwide prevalence of symptomatic BPH is estimated to be 20-62%, with prevalence increasing after age 50 years [2]. In Malaysia, a prevalence study conducted in 2022 showed that the prevalence of symptomatic BPH in men aged 40 years and above was 16.3%, while the prevalence in men aged 60 years and above was 23.9%.³ The prevalence is increasing at a rate of 8% per decade and given the increasing life expectancy of men in Malaysia, which is currently 73.2 years, the number of patients with this condition is also likely to increase and will certainly burden our healthcare system if more treatment options are not made available [4].

Drug therapy is usually the first option offered to patients with BPH. Surgical options may be offered depending on the patient's response to treatment, tolerance to potential side effects, reluctance to take long-term medication, or the extent of obstruction. Although there are several surgical options, the main issue for BPH patients is their age, as they are usually 50 years or older and therefore at higher risk for surgery. The surgical gold standard for BPH treatment is transurethral resection of the prostate (TURP), although open prostatectomy may be preferred for larger prostates and less invasive enucleation of the prostate is also a viable option. However, these

procedures require general anaesthesia, which may not be suitable for all patients [4,5].

In view of this problem, several minimally invasive treatment methods have been developed that do not necessarily require general anaesthesia and have shown promising results. These include prostate stents and transurethral lifts. However, these treatments insert a foreign body into the urethral lumen and can lead to long-term complications, such as migration or ingrowth of prostate tissue [5-10]. Treatment of these complications usually involves general anaesthesia. Therefore, the method of prostatic artery embolization (PAE) was introduced to avoid all the above complications and to achieve a more permanent result [10,11]. Initially, the development of PAE was simply a non-invasive method of controlling severe life-threatening bleeding. Mitchell ME et al. first reported on transcatheter embolization in 1976 for the control of severe haematuria [12]. PAE started as nonselective embolization of internal iliac arteries, then gradually embolization became more selective [13,14].

The use of prostate artery embolization (PAE) for the treatment of BPH began with an animal study conducted by Darewicz J et al in 1984 [15]. The study involved angio-embolization of 5 dogs with clinically enlarged prostates, which resulted in improvement of the clinical symptoms. This approach was later tested on a human patient, when DeMeritt et al noticed an improvement in the International Prostate Symptom Score (IPSS) after performing PAE on a patient with unilateral inferior vesical artery to control intractable

hematuria in 2000 [16]. Not only did the treatment stop the hematuria, but it also improved the patient's LUT symptoms. In 2010, Carnevale et al performed PAE to treat acute urinary retention (AUR) in 2 patients and noted a gradual improvement in their LUT symptoms over a follow-up period of up to 1 year [17]. The trial became larger as Pisco et al treated 14 out of 15 LUTS patients in 2011, and 89 patients in 2013, with promising long-term outcomes over a period of up to 1 year [18]. Subsequently, an attempt was made to compare PAE against the gold standard of TURP. An RCT by Gao et al in 2014 demonstrated that PAE and TURP had comparable outcomes over a period of 2 years [19].

PAE involves cannulation of a peripheral artery either in the femoral or radial and an angiocatheter is introduced and advanced all the way into the internal iliac artery. A micro catheter is then advanced to enter the inferior vesical artery and careful selection of the prostatic vessels is performed, and microbeads are then delivered to occlude the said vessels, permanently severing arterial blood supply to the prostatic gland and inducing ischemia. In summary, from first being reported as a method to control persistent life-threatening hematuria from a bleeding BPH, it was subsequently refined by invention of microcatheters and finer embolic agents to become more and more selective: from angio-embolizing the internal iliac arteries then the inferior vesical arteries and finally super-selectively the prostatic arteries. This advancement reduces the complications of the procedure and increases confidence in its ability to safely induce ischemia and apoptosis of the prostate gland, reducing its size and severity of the lower urinary tract symptoms (LUTS). A few clinical trials have already proven its safety and efficacy since its inception [20-22].

This technique, however, remains relatively novel in the local context. The first Malaysian case locally reported in 2017 was to control hemostasis from a delayed intractable hematuria post TURP [23]. This paper attempts to retrospectively review the efficacy and safety of

PAE in treating catheter dependent BPH patients in the Malaysian population, but in a larger sample and up to a short 3 months evaluation. The Urology Clinic at Hospital Serdang and Hospital Pengajar Universiti Putra Malaysia (HPUPM) provided data on patients who underwent PAE treatment at a designated Interventional Radiology (IR) centre of National Cancer Institute (Malaysia) (NCIM) and HPUPM. Both centres have been offering PAE services since 2019 and 2020, respectively. After counselling on all available options, patients who were deemed high risk or preferred not to undergo general anesthesia were offered PAE. A total of 55 BPH patients were planned for PAE, mostly elderly patients who were high risk for GA, but only 12 were managed to undergo this procedure as 32 of them passed away mostly due to the COVID-19 Pandemic, and the remaining 10 are still waiting for their elective dates as the country's healthcare system is still recovering from the after-effects of COVID-19 Pandemic. The patients who were prioritized were catheter-dependent patients, and all 13 patients belong to this category.

We present a retrospective evaluation of these 13 patients for the safety and effectiveness of PAE in treating their BPH.

MATERIALS AND METHODS

This is a retrospective study. All BPH patients who were treated at Urology Clinic of Hospital Serdang and HPUPM from January 2019 until December 2021 who were of high risk to receive GA but were indicated to receive surgical treatment.

Exclusion criterion:

PAE offered as secondary or adjunctive surgical treatment for BPH, LUTS diagnosed with causes other than BPH, and other prostate diagnoses discovered in the course of treatment besides BPH.

DATA COLLECTION

The data of all these patients were retrieved electronically from the patient registers of the urology clinic of Serdang Hospital and HPUPM and the following data were included.

1. Baseline demographic data, physical status classification according to the American Society of Anesthesiology (ASA), sexual activity and reasons for PAE
2. BPH-related clinical parameters: Duration of drug therapy before PAE, International Prostate Symptom Score (IPSS) and Quality of Life (QoL) before catheterisation, serial IPSS and QoL values after PAE, uroflowmetry values for maximal micturition velocity (Qmax).
3. Post voiding residual volume (PVR), prostate size before and after the procedure (estimated by ultrasound) and any documented intra- or postoperative complications.

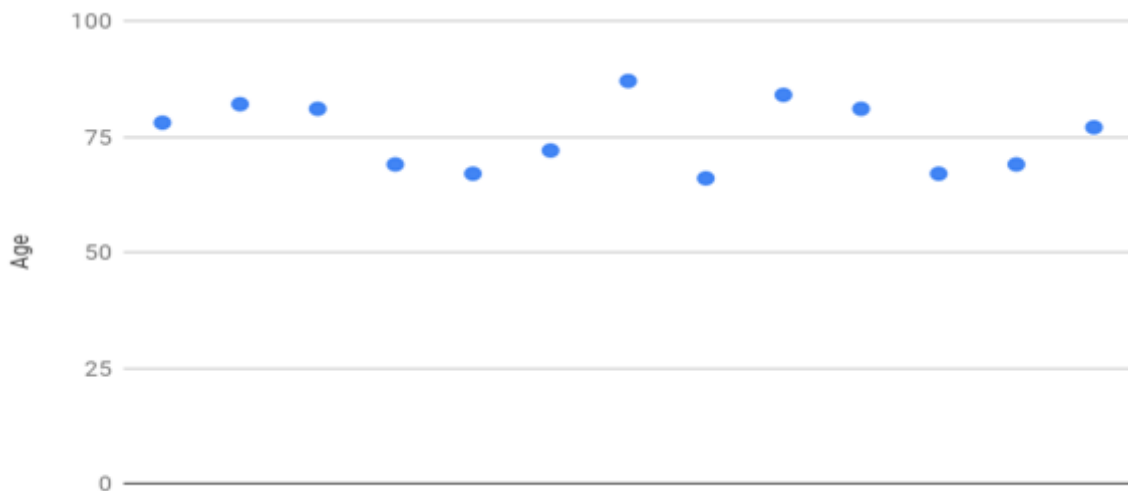
Follow-up documentation of these patients 2 weeks, 1 month and 3 months after PAE was reviewed, considering the success of the trial

without catheter (TWOC) performed at these intervals as standard practice in these institutions.

RESULTS

Regarding age, the patients were men aged 66 to 87 years with an average age of 75.4 years. All patients belonged to the elderly group, which is to be expected in BPH patients with high risk of surgery, as BPH only occurs after the age of 50 and advanced age is usually associated with more concomitant diseases. As Malaysia is a multicultural country, the patients were composed of men from the 4 main ethnic groups: 7 Malays (53.8%), 3 Indians (23.1%), 2 Chinese (15.4%) and 1 Punjabi (7.7%).

As expected, all patients had a higher risk of getting GA, with 9 falling in the ASA 4 category and 4 in the ASA 3 category. All of them opted for PAE after counselling for this reason. All of them also admitted that they were not sexually active.



Graph 1: Age distribution of BPH patients who underwent PAE from January 2019 to December 2021 in both IR centers (66-87, mean=75.4)

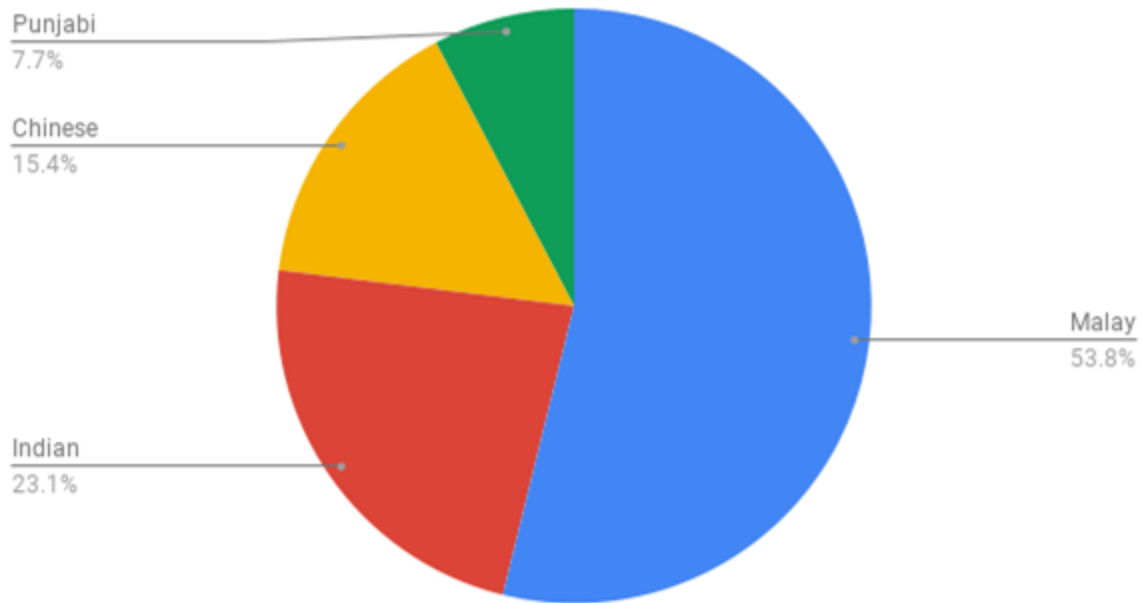


Chart 1: Ethnic distribution of BPH patients who underwent PAE from January 2019 to December 2021 at both IR centers.

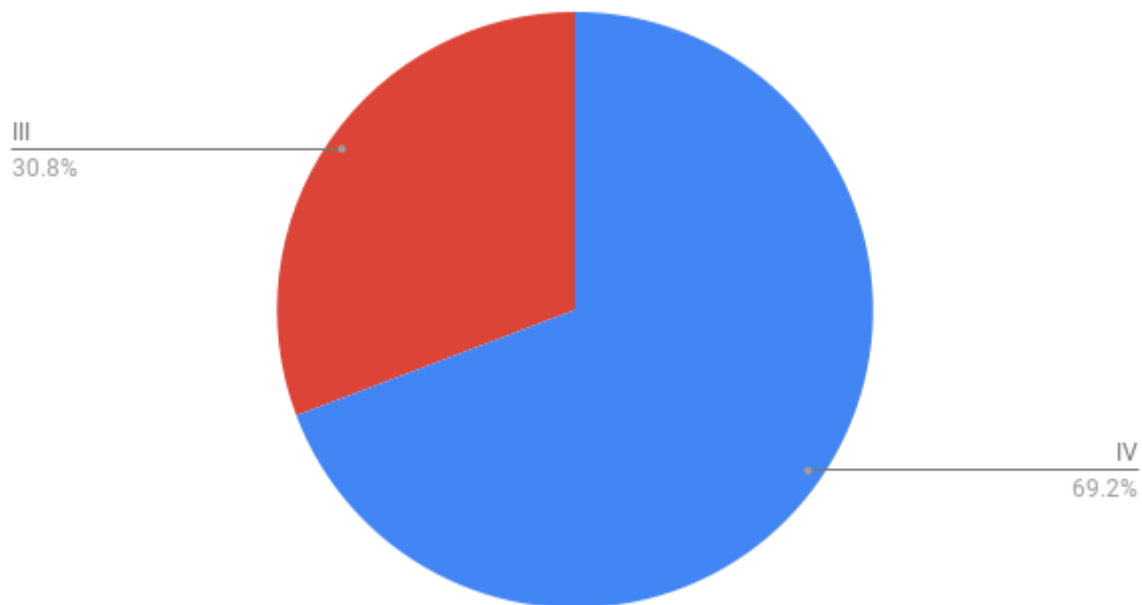


Chart 2: ASA Physical Status Classification Class distribution of BPH patients who underwent PAE from January 2019 to December 2021 in both IR centers.

Duration of Medical Therapy pre PAE

All 13 patients received medical therapy from 1 to 18 months but were treated for an average of 6.2

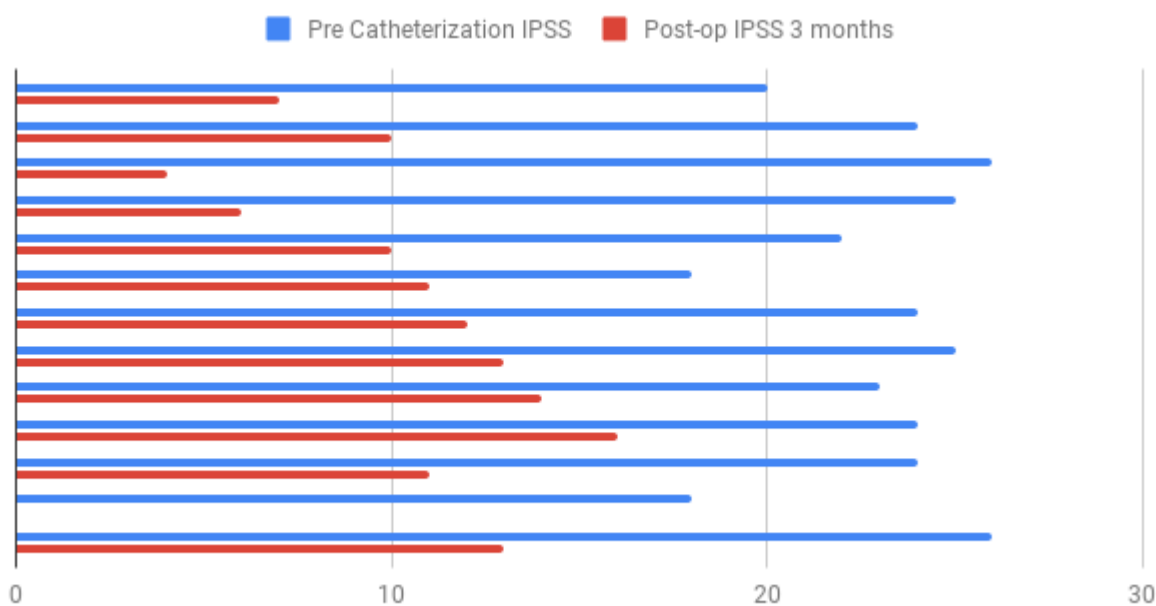
months. All have received combination therapy of alpha blockers with 5-alpha reductase inhibitors (5ARI). After catheterisation and failed episodes

of TWOC, all these patients were treated with 5ARIs only and the alpha blockers were discontinued.

Pre-Catherization IPSS and QoL versus Post PAE IPSS and QoL

All 13 patients were catheterised and the IPSS documented before catheterisation showed moderate to severe IPSS with a score of 18 - 26 (mean 23). We could not determine the IPSS score when the patients were catheterised as the assessment would have been invalid. The QoL

score also indicated that they were troubled by symptoms, with a score of 4-5 (mean 5.2). In 12 of 13 patients in whom the catheter was successfully and safely removed 3 months after PAE, the IPSS decreased significantly to 4-16 (mean 11). This reduction in IPSS was analysed with a paired t-test and the two-sided P-value is less than 0.0001. The same applies to quality of life before and after PAE, where quality of life after PAE had a score of 1-6 (mean 1.8) and the difference in comparison is also statistically significant (two-sided P-value is less than 0.0001).

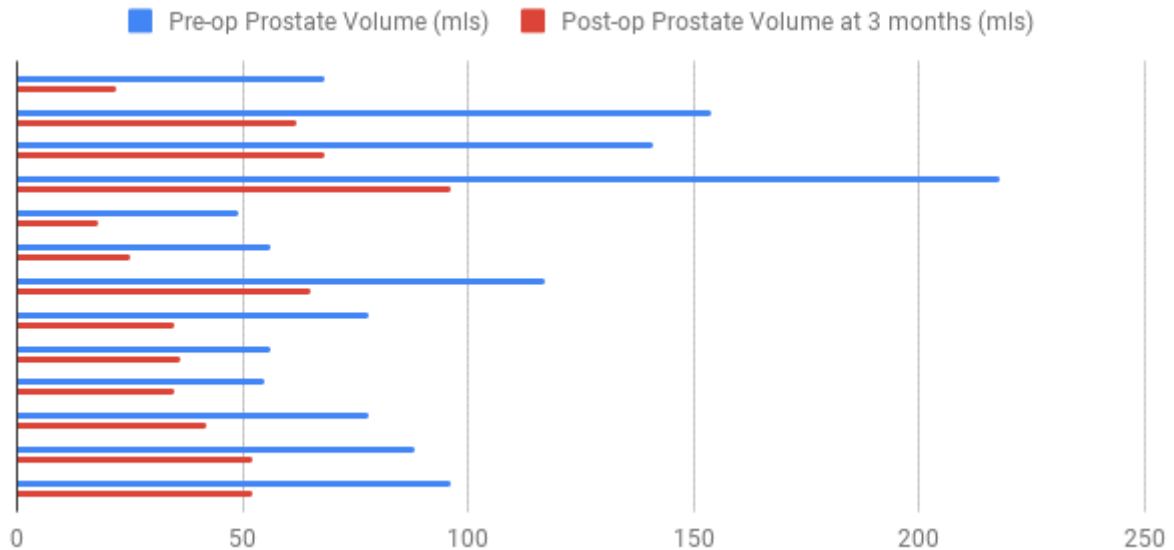


Graph 2: Comparison of IPSS Score Pre-Catheterization (Pre PAE) and Post TWOC (Post PAE) of BPH patients who underwent PAE from January 2019 to December 2021 at both IR centers

Pre and Post PAE Prostate Volume

Prostate volume before PAE ranges from 49.2 - 218 (mean 96.48) and after PAE the volume is reduced to a range of 18 - 96 (mean 46.77). The reduction is again calculated by a paired t-test,

which gives a two-tailed P-value of less than 0.0001. This reduction occurs regardless of the fact that one patient failed the TWOC test. This patient also had a reduction in prostate volume after PAE from 88 ml to 52 ml.



Graph 3: Comparison of Prostate Volume in mls before and after (at 3 months) PAE by Trans-Abdominal Ultrasound Estimation.

Post PAE TWOC, Qmax and PVR at 3 months

The most important result of the PAE is that in 12 out of 13 patients the catheter could be safely removed (acceptable Qmax of more than 10 and PVR of less than 100 according to TWOC) and this parameter itself was statistically significant (the two-sided P-value is less than 0.0001).

Qmax 3 months after PAE in all 12 patients with successful TWOC ranged from 10.7 to 16.3 (mean 12.5) and PVR 3 months after PAE ranged from 0 to 87 ml (mean 29.8 ml). As all patients were catheterised, Qmax and PVR values before PAE are not available (values before catheterisation are considered irrelevant for comparison in this review). Regarding adverse events or complications, none were documented in all 13 patients.

DISCUSSION

BPH is closely related to the ageing process in men and can cause significant morbidity due to LUTS and associated complications. Studies have shown that the prevalence of BPH increases with age, with a prevalence rate of approximately 8% in the 4th decade of life and 80% in the 9th decade of life [2,4]. In Malaysia, the prevalence of BPH was found to be 41.7% in men in their 50s and 65.4%

in those over 70 years of age. The prevalence of BPO in this study was 15.8% and the cohort of 13 patients was between 66-87 years old [3,24].

PAE is a relatively new treatment for BPH but has been shown to be effective internationally. Although relatively safe and effective, the gold standard TURP is still superior. Recent studies comparing PAE and TURP have shown that TURP produces better and faster results. The only advantage of PAE over TURP is the preservation of sexual function, which may not be relevant for patients who are not sexually active [19, 25, 26]. However, the main advantage of PAE is its suitability for patients who are at high risk for GA. This retrospective evaluation showed that PAE successfully led to TWOC in 12 of 13 patients, and even in the patient with an unsuccessful TWOC, a significantly reduced prostate size may indicate that a subsequent TWOC attempt could be successful.

Another aspect of the discussion on PAE is that it requires a relatively steep learning curve for interventional radiologists. PAE requires formal training in high volume centres to minimise the possibility of non-target embolization [27]. This study aims to stimulate a prospective evaluation of PAE with a larger sample size to better represent

the niche of BPH patients who do not have GA - based surgical options due to their underlying comorbidities. A better conducted prospective study will not only provide insight into the Malaysian population's response to PAE, but also assess the ability of the healthcare system, urology, and interventional radiologists to deliver this novel service safely and effectively.

CONCLUSION

PAE is a promising, safe, and effective treatment option, especially for patients who are at high risk for GA surgical treatment options. However, further prospective studies are needed to evaluate this in the context of patients from the Malaysian population.

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