Urology : Research And Therapeutics Journal

SCIENTIFIC LITERATURE

Research Article

Impact of Prostate Artery Embolization on Irritative Lower Urinary Tract Storage Symptoms: A Retrospective Analysis in 176 Men

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ARTICLE INFO

Received Date: June 10, 2022
Accepted Date: July 01, 2022
Published Date: July 04, 2022

KEYWORDS

Lower urinary tract symptoms
Prostate volume
Intravesical prostate protrusion
Prostatic urethral angle
Prostatic artery embolization
International prostate symptom score

Citation for this article: Bernard P, Bischoff P, Schafer A, Yu W, Hanitzsch H, El-Mansouri A, Panagiotopoulos N and Kovacs A. Impact of Prostate Artery Embolization on Irritative Lower Urinary Tract Storage Symptoms: A Retrospective Analysis in 176 Men. Urology : Research And Therapeutics Journal. 2022; 3(2):132

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ABSTRACT

Purpose: Urge incontinence, nocturia and the sense of residual urine have been identified as the three most bothering Lower Urinary Tract Symptoms (LUTS) at all. Prostate Volume (PV), Intravesical Prostate Protrusion (IPP) and Prostatic Urethral Angle (PUA) are the three parameters of prostate architecture determining LUTS. The aim of the study was to evaluate the effectiveness of Prostatic Artery Embolization (PAE) on the morphology of the prostate and the three clinical symptoms mentioned above.

Materials and Methods: 176 consecutive men treated with PAE were assessed prior PAE, 48 hours after and one to two months after PAE. In MRI the following morphological parameters were recorded: PV, IPP, and PUA. The clinical symptoms nocturia, urge incontinence and residual urine sensation were investigated using the established International Prostate Symptom Score (IPSS) questionnaire.

Results: Over the course of one to two months clinical symptoms (urge incontinence, nocturia, and residual urine sensation improve by 26%, 24%, and 43% respectively) improve better compared to the morphological changes in the prostate after PAE (PV, IPP, and PUA are reduced by 19%, 15%, and 10% respectively). 14% of the patients experienced temporary post embolization syndrome, in all cases successfully treated with antipyretics and analgesics.

Conclusions: PAE is a suitable alternative to significantly improve the three most bothersome irritative LUT complaints, urge incontinence, nocturia and residual urinary sensation without relevant side effects.

INTRODUCTION

Lower Urinary Tract Symptoms (LUTS) are most frequently caused by Benign Prostatic Hyperplasia (BPH). Whereby the sole increase in volume correlates only to a limited extent with the complexity of LUT-symptoms [1]. Three parameters of prostate architecture have been identified as determining for LUTS - the Prostate Volume (PV), the Intravesical Prostate Protrusion (IPP) and the Prostatic Urethral Angle (PUA) [2]. Furthermore, the individual LUT-symptoms are not equally bothering for the patients [3]. LUTS are broadly grouped into irritative storage symptoms, obstructive voiding symptoms, and post-micturition symptoms. Although in general thinking the weak urinary stream is often equated with prostate problems, the Benign Prostatic Syndrome (BPS) contains not only voiding but also storage symptoms. Irritative storage symptoms are even twice as common and more bothersome as voiding symptoms. Urge incontinence, nocturia and the sense of residual urine have been identified as the

three most bothering symptoms of all [4]. Prostatic Artery Embolization (PAE) is an emerging minimal-invasive therapy of BPH, able to reduce the PV, the IPP, as well as the PUA [5,6]. Our current study analyses the effect of PAE on the determining morphological parameters of the prostate (PV, IPP and PUA) as well as on the three most disturbing lower urinary tract symptoms as stated above.

MATERIAL AND METHODS

From April 14th 2015 to November 28th 2018 a retrospective analysis of 176 men treated with PAE was done at the MediClin Robert Janker Clinic in Bonn/ Germany. All interventions were carried out under local anesthesia via femoral puncture from the right side.

Exclusion criteria were: Patients with any kind of urologic tumors, patients with a neurogenic bladder and patients with any kind of urinary tract infection or bladder stones that could affect voiding. MR-imaging, assessing the morphological parameters PV, IPP and PUA, was performed before PAE, 48 hours post PAE and one to two months post PAE in every patient. For the IPP the shortest perpendicular distance between the bladder base on the bladder neck and the protruded end of the prostate was measured in midsagittal plane in T2- weighted MR-images. For the PUA the angle between the prostatic and the membranous urethra was measured, again in midsagittal plane in T2- weighted MR-images. The definitions of IPP and PUA used here are adopted from the scientific literature for better comparability with other studies [7,8]. Furthermore, the patients answered to the validated German International Prostate Symptom Score Questionnaire (IPSS) pre PAE, 48 hours post PAE and one to two months post PAE. In this study a special attention is given to the three most bothering irritative storage symptoms: nocturia, residual urine sensation, urge incontinence. In detail, using the IPSS questionnaire nocturia, urge incontinence and residual urine sensation were analysed for this study. For all PAE, calibrated spheric embolics with a diameter of 100-300µm (Merit Embosphere®) were used. For the statistic analysis IBM SPSS Statistics for Windows, version 26, was used. Considered statistically significant were p-values of <0.05. Approval of the ethics committee was obtained for the retrospective data analysis.

RESULTS

The mean age was 62.5±6.9 years. Selective cannulation of the prostatic arteries was 100% technically successful. Only 14% of the patients experienced minor side effects (adverse events Clavien-Dindo I), mostly temporary post embolization syndrome for 1-3 days, in all cases successfully treated with antipyretics and analgetics. Hematoma of the groin as well as serious Side Adverse Events (SAE) have been reported in 0%, each. Procedural time and fluoroscopy time were 70.3 ± 25.7 min and 23.2 ± 8.2 min. Median dose-area product was 7449µGym2.

Changes in morphological parameters

The PV could be reduced from 78±45.89 ml pre PAE to 71.6±40.63 ml 48 hours post PAE (p<0.000). After 1-2 months post PAE the results improved further to a mean volume of 63,91±37,62ml (p<0.000). The mean IPP amounted pre PAE 12.72±6.35mm a decreased to 12.06±6.11mm after 48 hours (p<0.000). After 1-2 months the IPP was again reduced to 10.86±5.89mm (p<0.000). During the first 48 hours the mean PUA could be reduced from 71.17±15.3° to 67.88±14.66° (p<0.000) and 1-2 months after PAE the mean PUA decreased further to 64.08±14.82° (p<0.000).

Changes in clinical symptoms

The three urge symptoms assessed in our study could be significantly improved by PAE. Nocturia improved from 2.98±1.47 to 2.73±1.51 points (p<0.623) during the first 48 hours. After 1-2 months the score decreased to 2.29±1.29 points (p<0.012). Therefore, the overall improvement was significant with p<0.006. Urge incontinence symptoms were reduced from 3.15±1.64 points pre PAE to 2.6±1.65 points 48 hours post PAE (p<0.990). At 1-2 months post PAE the score improved to 2.34±1.6 points (p<0.030). The overall improvement was significant due to p<0.009. The residual urine sensation score decreased from 3.03±1.76 points pre PAE to 2.27±1.57 points 48 hours post PAE (p<0.003). 1-2 months after PAE the score decreased to 1.71±1.45 points (p<0.003). The overall improvement was also significant with p<0.000 (Figure 1).

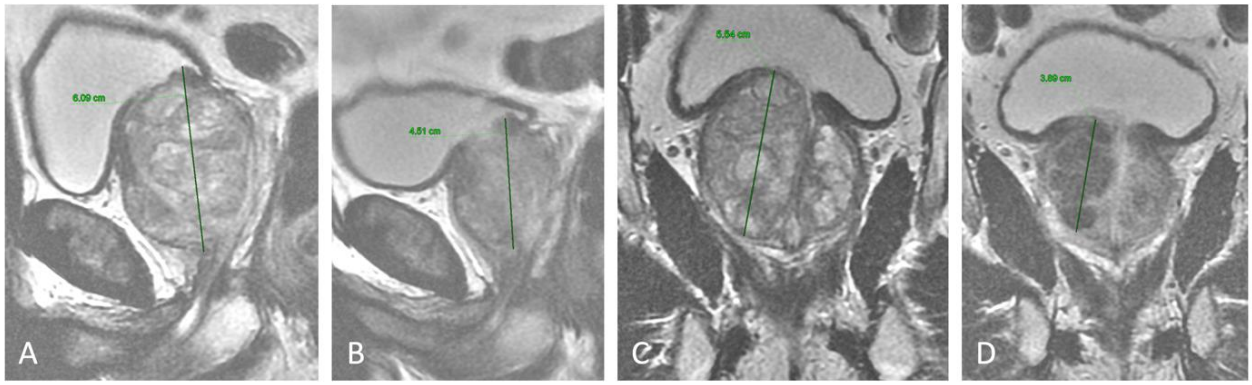

Figure 1: Morphological parameters of prostate before and 2 months after PAE. A. Maximum cranio-caudal diameter of the prostate is 6.09cm before therapy. B. This diameter shrinks to 4.51 cm after two months. The IPP has almost completely disappeared. C. The cranio-caudal diameter of the right lateral lobe protruding into the bladder is 5.54cm before therapy. D. After two months this diameter shrinks to 3.89cm. The numerous adenoma nodules (bright zones) before therapy (A, B) have completely disappeared after two months (C, D).

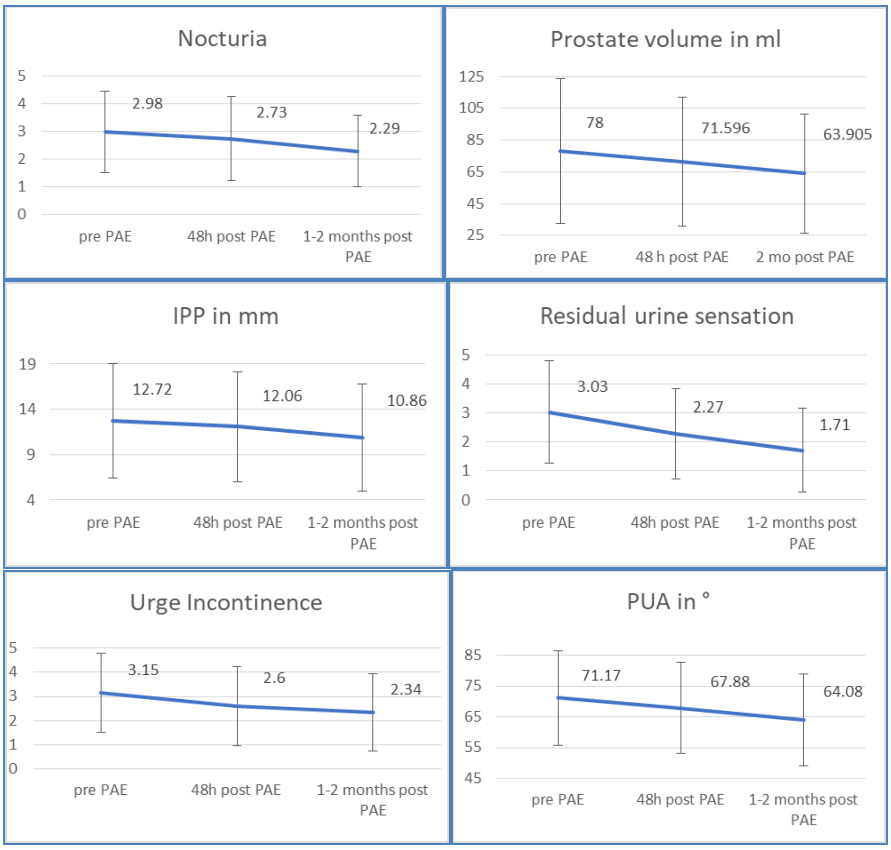

Diagram1: One to two months after PAE the clinical symptoms and the prostate morphology improved significantly. The PV lowers significantly from 78 ± 45.89 ml to 63.91± 37.62 ml ($p<0.000$). The IPP improves significantly from a mean score of 12.72± 6.35mm to 10.86± 5.89mm ($p<0.000$). The PUA straightens up from 71.17± 15.3° to 64.08± 14.82° ($p<0.000$). The nocturia symptoms improve from an average score of 2.98± 1.47 to 2.29± 1.29 ($p<0.006$). The urge incontinence score decreases from a mean score of 3.15± 1.64 to 2.34± 1.6 ($p<0.009$). The residual urine sensation improves from an average score of 3.03± 1.76 to 1.71± 1.45 ($p<0.000$).

DISCUSSION

The results of our study show a disproportionate improvement in favour of clinical symptoms over the course of one to two months compared to the morphological changes in the prostate after PAE. While PV, IPP, and PUA are reduced by 19%, 15%, and 10% respectively, urge incontinence, nocturia, and residual urine sensation improve by 26%, 24%, and 43% respectively. These results suggest that the effect of PAE goes beyond volume reduction alone. The reason lies in the variety of therapeutic effects of the PAE and their synergistic effects: 1. shrinkage of the enlarged prostate gland as a result of ischemic infarction, 2. relaxation of the increased prostatic smooth muscle tone by reducing the prostate stroma and additionally α-adrenergic denervation, 3. the softening effect of nitric oxide pathway, 4. blockage of androgen circulation into the prostate, and 5. ischemia-induced apoptosis [9].

Our study is one of the first to evaluate changes in prostate morphology and irritative storage symptoms following PAE. The IPS-score correlate only partially with prostate enlargement, bladder outlet obstruction and LUTS [10]. Further, there is no fixed correlation between PV, degree of compression of the prostatic urethra and Bladder Outlet Obstruction (BOO) [11]. It is already generally known and scientifically proven that patients with LUTS primarily suffer from storage symptoms, particularly urge incontinence and nocturia [4,12,13]. An indication that after PAE the clinical symptoms improve more than the morphological ones suggests a study of Carnevale and co-workers. Carnevale et al. found that TURP and PAE yield similar symptom improvements after 1 year, but TURP was associated with both better urodynamic results and more adverse events [14]. Our findings show a comparable trend, that PAE better improves clinical symptoms than morphological parameters.

Current evidence suggests that, e.g., PAE, has a proportionally greater effect on storage symptoms, including nocturia, than surgical therapies [15, 16]. In their study, Abt et al. found that nocturia decreased more after PAE than after TURP (by 0.35 versus 0.21 in favor of PAE, $p = 0.68$), and assumed that irritative storage symptoms, which are usually more bothersome to patients, improve less than voiding symptoms after conventional surgery [4,17]. Our results also confirm these findings that PAE is very effective in improving nocturia, urge incontinence and residual urine sensation.

Nocturia has a special position among the LUTS, not least because it is the only symptom proven to be associated with enormous socioeconomic losses. It is a common and bothersome condition, with two voids per night as a critical threshold. Nocturia is associated with higher levels of sleep disturbance and daytime fatigue, as well as lower life satisfaction, work engagement, and productivity. A recent economic analysis found that nocturia is associated with $79 billion lost economic output per year across six countries (US, Japan, Germany, UK, Spain, and Australia), indicating that nocturia is an important concern that requires intervention [18]. An analysis in the EU-15 countries estimated the total annual costs of hospitalization for hip fracture due to severe nocturia to be approximately one billion Euro [19].

The increasing prevalence of BPH seen in recent decades has been met with a growth of treatment options. According to the current EAU recommendations from 2019, the choice of treatment depends on the findings of patient assessment, the ability of the treatment to change the respective bothering symptoms (instead of “one therapy fits all”), the individual patient’s treatment preferences, and the expectations to be met in terms of speed of onset, efficacy, side effects, QoL, and disease progression [20]. Minimal-invasive therapies are rapidly evolving treatment options for LUTS associated with BPH, with encouraging mid-term functional outcomes, improved health- related QoL, and a better preservation of ejaculation [21].

Especially in the context of modern, low side effects and individualized therapy of LUTS, the knowledge, that PAE can effectively reduce three of the most bothersome complaints is an important scientific finding. The major asset of PAE is the high degree of satisfaction reported by the majority of the patients attributable to its safety and low side effects rate, without the concern of incontinence, impotence and retrograde ejaculation [5,6,22].

Special advantages of PAE are the absence of general anesthesia risk, the favourable complication profile without blood loss, the preservation of erectile function, and the absence of retrograde ejaculation. Furthermore, PAE does not exclude a subsequent surgical intervention in case of disease

progression, which is why it should also be seen as a supplement to established therapeutic strategies. PAE is not a substitute for established surgical procedures for severe obstructions, but rather a bridge between exhausted drug-based treatment options and surgery in patients with moderate to severe storage-dominant symptoms [5,6].

Although the PAE has many advantages, it also has some disadvantages. A method inherent limitation of the PAE is the applied radiation exposure. This equates to 19 mSv with a 0.07% additional lifetime cancer risk in a 60- year old man. The duration of the radiation depends on the complexity of the pelvic and prostatic vascular anatomy and the degree of atherosclerosis. The reduction of radiation exposure is an essential objective of the further development of the PAE. Furthermore PAE is technically limited in patients suffering from severe Atherosclerosis (AS), why in case of AS a pre interventional non-invasive assessment of the pelvic vasculature, e.g., with CT- or MR-angiography is advised [22]. A limitation of the study presented herein are the missing long-term results.

CONCLUSION

The PAE is able to improve the three most bothersome irritative LUT-complaints, urge incontinence, nocturia and residual urinary sensation relatively quickly and with very few side effects. PAE should be considered as a therapeutic alternative, at least as a transitional solution for patients with predominantly irritative storage symptoms.

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