PROSTATIC ARTERY EMBOLIZATION AS A NEW OPTION IN THE TREATMENT OF LOWER URINARY TRACT SYMPTOMS IN BENIGN PROSTATIC HYPERPLASIA – CURRENT EVIDENCE

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SUMMARY – Prostatic artery embolization is a minimally invasive endovascular treatment that improves lower urinary tract symptoms in men with benign prostatic hyperplasia. Although further randomized studies and long-term evidence is still needed for this method to be fully incorporated into treatment guidelines for benign prostatic hyperplasia, current studies show that this method can be an effective and safe alternative in patients with a significantly enlarged prostate gland who are not good surgical candidates. Therefore, we present the theory, technical details and potential benefits of this method as we review the current evidence on prostatic artery embolization.

Keywords: Benign prostatic hyperplasia; Arterial embolization; Endovascular treatment; Interventional radiology; Lower urinary tract symptoms

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Introduction

Benign prostate hyperplasia (BPH) is a disease with a prevalence that reaches 50% to 60% for men aged 60-70, and 80% to 90% for men aged 70-901. Histologically characterized by smooth muscle proliferation, BPH, when symptomatic, is most often associated with lower urinary tract symptoms (LUTS) consisting of obstructive and irritative symptoms. Obstructive symptoms include hesitancy, weak flow, prolonged voiding, urinary retention and overflow incontinence, while irritative symptoms include urgency, frequency, nocturia and painful urination. Patients are evaluated based on a quantitative symptom score, most commonly the International Prostate Symptom Score (IPSS), a 7-item questionnaire addressing the most common LUTS symptoms2. The indication for treatment depends on the severity and bother of urinary symptoms. Patients with mild symptoms first undergo watchful waiting or medical therapy that includes alpha-blockers and 5-alpha-reductase inhibitors as the first line option. When moderate to severe symptoms occur, the only remaining option often involves surgical treatment. Traditional surgical solutions include open prostatectomy, which usually requires long hospitalisation and has high morbidity rates, and transurethral resection of the prostate (TURP), which is currently the gold standard definitive treatment for BPH. However, this procedure is accompanied by significant risks, including bleeding and nerve damage potentially leading to impotence1. In addition, patients with LUTS due to BPH are often elderly and with serious comorbidities. Because of high operative risk of undergoing TURP or open surgery, especially with an enlarged prostate gland with a volume of more than
80 mL\(^4\), non-surgical treatment alternatives have been explored. There is a list of minimally invasive therapies that have been developed for the treatment of BPH, such as transurethral microwave thermotherapy (TUMT), transurethral needle ablation (TUNA), the placement of a urethral stent, electrovaporization of the prostate, transurethreal laser vaporization or coagulation, transurethreal Holmium laser resection or enucleation. However, these have not proven to be more efficient in the long term when compared to TURP\(^5\).

In the last decade, a new interventional radiology endovascular procedure called prostatic artery embolization (PAE) has been introduced for the treatment of lower urinary tract symptoms related to BPH. It has shown to cause a decrease in prostate volume and possibly present a safe and effective alternative to both TURP and minimally invasive therapies. Even though there is growing evidence supporting this method, it has not been widely accepted or incorporated into urologic society guidelines as yet. This article presents the development, technical aspects, the theory behind the method and results through a review of currently available evidence.

**PAE development and evidence**

The first case of successful PAE was recorded in a patient with severe gross hematuria, who was subjected to embolization with polyvinyl alcohol particles, as published by DeMeritt in 2000\(^6\). The patient stopped bleeding after embolization, but it was also observed that the size of the prostate was reduced by 50-60%.

Although embolization of internal iliac arteries had been previously used in the treatment of pelvic hemorrhage, an idea was born at the time that ischemic infarction occurring after the occlusion of distal arterial branches supplying the prostatic tissue would partially reduce the volume of the gland with LUTS reduction without the need for further surgery\(^7\). A similar effect had been observed earlier and used in the treatment of symptomatic uterine fibroids by uterine artery embolization\(^8\). Following studies on animals, Carnevale was the first to perform, and publish the results of, PAE in two BPH patients in 2010\(^9\). Shortly thereafter, the first large prospective study with the longest follow-up period was published by Pisco et al.\(^10\), who treated 255 patients with BPH refractory to medical treatment and moderate to severe LUTS between 2009 and 2012. The procedure was deemed technically and clinically successful, showing good results (IPSS reduction of at least 25 % and QoL improvement of >1) at 1 and 36 months after the procedure (82% and 72%, respectively). This study, as well as other randomized and non-randomized studies performed using different embolization particle sizes and involving patients with different initial sizes of the prostate gland all showed benefits of PAE with very rare serious complications. Over 700 patients were treated and all studies demonstrated statistically significant reduction in IPSS, ranging from 12 to 21, and an improvement in quality of life. In our search of databases we have found 11 studies published in the last 17 years, most of them non-randomized. Main study characteristics and results are presented in Table 1.

Lately, PAE has been particularly recommended for and examined in a subgroup of BPH patients with larger prostate glands (>80mL). This is due to the fact that these patients show worse results after TURP treatment, while open prostatectomy remains the last treatment option due to its invasiveness and potential complications. 3 studies have reported good results with significant IPSS and QoL improvement, 12-15 points and 2-4, respectively. They did not show any major complications occurring in these patients\(^11\). Wang et al.\(^12\) performed a comparative study of PAE treatment of large (>80 mL) and medium-sized prostate glands (50-80 mL) to determine whether size affects the outcome of PAE. They concluded that clinical and imaging outcomes of PAE were better in patients with larger prostate glands than medium-sized ones.

**Technical aspects**

Although transarterial selective catheter embolization has been widely used by interventional radiologists in a variety of locations and indications that can sometimes be challenging, such as liver chemoembolization, uterine fibroid embolization or upper and lower gastrointestinal bleeding embolization, PAE is technically one of the most difficult procedures to perform. This is due to the fact that prostatic arterial supply is variable and closely related to the rectal and urinary bladder arterial branches, which can potentially lead to non-target embolization and complications like bladder ischaemia\(^13\). Therefore, detailed knowledge of pelvic arterial anatomy and advanced microcatheter skills are obligatory for performing this procedure. Furthermore, due to progressive atherosclerotic arte-
rial changes bilateral selective catheterisation is sometimes difficult, which can lead to lower clinical success, reportedly around 50%\textsuperscript{13}.

Even though serious adverse events that required surgical intervention or treatment were very rare in the published studies and involved cases of proctitis\textsuperscript{14} and bladder necrosis\textsuperscript{10} with a variety of minor side effects like dysuria, hematospermia, haematuria and diarrhoea, this is still an area of concern. Non-target embolization risks are potentially greater if the embolization material-particles are smaller in size, due to their ability to penetrate deeper and cause micro vessel occlusion and tissue necrosis. For this reason and for reasons of prostatic gland and LUTS reduction effect, different particle sizes have been tested in reported studies. Non-spherical PVA particles, as well as spherical particles have been used with success and different sizes ranging from 50 to 500 um. Even though all have shown to have success, there was a theoretical advantage leaning toward smaller particles due to better penetration and prevention of revascularization and recurrent growth. However, a study by Bilhim\textsuperscript{15} comparing 100 and 200 um particles did not show any significant difference in complications or pain. Clinical outcome was slightly better with larger particles, while greater volume reduction of the prostate was achieved with smaller particles.

**Potential and limitations of PAE**

Like other interventional radiologic procedures, PAE has certain advantages it can offer to patients

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study type</th>
<th>Mean prostate volume (mL)</th>
<th>Embolic type and particle size (mm)</th>
<th>Number of patients</th>
<th>1 year IPSS reduction</th>
<th>Technical success</th>
<th>1 y QoL score change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antunes (20)</td>
<td>Prospective, single centre</td>
<td>69.7</td>
<td>Embospheres 300–500</td>
<td>11</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Pisco (10)</td>
<td>Prospective, single centre</td>
<td>83.5</td>
<td>PVA 100–200</td>
<td>255</td>
<td>13.7</td>
<td>82%</td>
<td>2.4</td>
</tr>
<tr>
<td>Bagla (21)</td>
<td>Retrospect single centre</td>
<td>93.9</td>
<td>Embozene 100–400</td>
<td>78</td>
<td>12.2 at 6 mo</td>
<td>96%</td>
<td>2.7 at 6 mo</td>
</tr>
<tr>
<td>Kurbatov (17)</td>
<td>Prospective single centre</td>
<td>129.3</td>
<td>Embospheres 300–500</td>
<td>88</td>
<td>13.6</td>
<td>100%</td>
<td>2.9</td>
</tr>
<tr>
<td>Grosso (16)</td>
<td>Retrospect single centre</td>
<td>N/A</td>
<td>Embospheres 300–500</td>
<td>13</td>
<td>17.1</td>
<td>75%</td>
<td>2.6</td>
</tr>
<tr>
<td>Somani (22)</td>
<td>Prospective, single centre</td>
<td>94.9</td>
<td>PVA N/A</td>
<td>35</td>
<td>12</td>
<td>90%</td>
<td>2.9</td>
</tr>
<tr>
<td>Assis (23)</td>
<td>Prospective single centre</td>
<td>135.1</td>
<td>Embospheres 300–500</td>
<td>35</td>
<td>15.6 at 3 mo</td>
<td>94%</td>
<td>3.9 at 3 mo</td>
</tr>
<tr>
<td>Wang (12)</td>
<td>Prospective single centre</td>
<td>96.5</td>
<td>PVA 100</td>
<td>115</td>
<td>12.9</td>
<td>95%</td>
<td>2.9</td>
</tr>
<tr>
<td>Gao (18)</td>
<td>Prospective single centre</td>
<td>64.7</td>
<td>PVA 355–500</td>
<td>57</td>
<td>11.9</td>
<td>84%</td>
<td>2.9</td>
</tr>
<tr>
<td>Carnevale (19)</td>
<td>Prospective, single centre Randomized (vrs TURP)</td>
<td>64.6</td>
<td>Embospheres 300–500</td>
<td>30</td>
<td>21.0</td>
<td>93%</td>
<td>3.1</td>
</tr>
<tr>
<td>Li (24)</td>
<td>Prospective single centre</td>
<td>110.0</td>
<td>Embospheres 50–100</td>
<td>24</td>
<td>19.5</td>
<td>86%</td>
<td>2.5</td>
</tr>
</tbody>
</table>

PVA - polyvinyl alcohol
with LUTS due to BPH. It is performed under conscious sedation through a femoral or radial artery puncture, which allows it to be performed as a one day procedure, eliminating the need for prolonged recovery. Even though it is technically demanding, the published data shows it to be highly successful, with results ranging from 75 to 100%\textsuperscript{16,17}. Medication treatment is usually abandoned soon after the procedure, and Foley catheterisation is not required in most cases after PAE. There have been two studies that randomized patients and compared PAE to the gold standard therapy, the TURP\textsuperscript{18,19}, with additional larger studies scheduled to be published soon. Both of these published studies showed promising results. Urinary flow was similar after both procedures in the larger study, and while there was a higher incidence of technical failure and clinical failure with PAE (9.4%) compared to TURP (3.9%), complications (bleeding) occurred only after TURP, which required longer hospital stay and more frequent catheterisation. In the second study there was no significant difference in IPSS after TURP and PAE, but urinary flow was significantly higher after TURP. Also here, adverse events were more frequent and more serious after TURP.

These results are still insufficient to establish PAE as a procedure equal to standard surgical methods and there is still a lack of randomized prospective evidence, but initial results are promising and can lead to a certain number of patients for whom medical therapy was ineffective and who either refuse surgery or are poor surgical candidates to be referred to interventional radiology in centres with experienced endovascular specialists. Most promising results can be expected in a subgroup of patients with prostate volume larger than 80 mL in which TURP has shown to have higher complication rates, while PAE so far has not shown to have an upper limit of prostate volume that can be effectively treated\textsuperscript{17}.

Conclusion

In the search of minimally invasive alternatives for the standard surgical methods of TURP and open prostatectomy, PAE has emerged as a safe and effective endovascular treatment with low morbidity, that could be offered to patients refractory to medical treatment of BPH who are the same time at risk if subjected to surgery or who refuse it. Even though studies published so far have all shown promising results that can be clinically compared with TURP in the reduction of symptoms, with fewer reported complications and shorter hospital stay and recovery time, additional prospective and randomized studies are required, with long term follow-up. For now, PAE can be recommended for a selected group of patients, with large volume prostate glands who are poor surgical candidates, in centres with experienced interventional radiologists.

References


Sažetak

EMBOLIZACIJA PROSTATE
– NOVA TERAPIJSKA MOGUĆNOST LIJEČENJA SIMPTOMA DONJEG URINARNOG TRAKTA KOD MUŠKARACA S BENIGNOM HIPERPLAZIJOM PROSTATE

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Emboliacija prostate je minimalno invazivna endovaskularna metoda liječenja koja se koristi za liječenja simptoma donjeg urinarnog trakta kod muškaraca s benignom hiperplazijom prostate. Iako su potrebne dodatne randomizirane studije s dugoročnim praćenjem i rezultatima kako bi ova metoda bila uključena u smjernice liječenja benigna hiperplazije prostate, dosadašnje studije ukazuju da ova metoda može predstavljati učinkovitu i sigurnu alternativu kod pacijenata s uvećanom prostate koji nisu dobri kirurški kandidati. Stoga prikazujemo teoriju, tehničke detalje i moguće prednosti ovog zahvata kroz analizu dosadašnjih studija o emboliaciji prostate.

Ključne riječi: Prostata; Emboliacija; Simptomi donjeg urinarnog trakta; Benigna prostaticna hiperplazija