REVIEW PAPER

FUNCTIONAL UROLOGY

The application of prostate artery embolization in the management of intractable prostate bleeding

Agata Stężewska[1], Magdalena Stężewska[1], Bartosz Żabicki[2], Maciej Salagierski[1]

[1]Department of Urology, Collegium Medicum, University of Zielona Góra, Zielona Góra, Poland
[2]Department of Radiology, Collegium Medicum, University of Zielona Góra, Zielona Góra, Poland

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Corresponding author
Maciej Salagierski
Faculty of Medicine and Health Science
Department of Urology
26 Zyty Street
65-046 Zielona Góra, Poland
m.salagierski@wlnz.uz.zgora.pl

Introduction Prostate cancer is one of the most common malignancies affecting European men. Sequelae of the advanced malignancy require invasive procedures which may not be eligible especially for old, debilitated patients. The aim of this manuscript is to review the outcomes of prostate artery embolization in the management of refractory bleeding.

Material and methods A PubMed database search was done for all English language articles on prostate artery embolization in prostate cancer, published between 2003 and 2019. For current review, information related to number, age of the patients, aetiology of the hematuria, bilateral or unilateral procedure, type of embolic material, technical and clinical success, complications, recurrent hematuria, hematocrit and hemoglobin levels were analyzed.

Results A total of 10 original full-text comparative and non-comparative (case series) studies were reviewed. Minor complications described in the literature ranged from 10–50%. After prostate artery embolization, the recurrence of the haematuria occurred in 10–57% of the patients. Moreover, prostate artery embolization successfully treated lower urinary tract symptoms and urinary retention in prostate cancer patients.

Conclusions The procedure appears safe, burdened with low risk of complications and accomplishes technical and clinical success. It is a promising option for patients with hemorrhage, but due to the scarcity of data further investigations are needed.

Key Words: prostate cancer ‹› haematuria ‹› prostate artery embolization

INTRODUCTION

Prostate cancer is one of the most common malignancies and, it is estimated, that excluding non-melanoma skin cancer, over 20% of cancers affecting European men are related to the prostate [1]. Personalized medical care, with the consideration of the current health status of the patients is required, for the aging population [2]. Locally advanced, aggressive, or untreated prostate cancer might lead to the invasion of urethras, ureters, bladder, or rectum. Whereas, hematuria, urinary obstruction, and severe pelvic pain are sequelae of the advanced malignancy and previous therapies [3]. Gross hematuria especially in elderly, unfit patients may necessitate various managements including bladder irrigation using a three-way catheter in case of clots evacuation. Medical treatments such us alum or formalin irrigation, hydrostatic pressure, and hyperbaric oxygen are used as a conservative approach [4]. Debilitated patients may require blood transfusion, hospitalization or even intensive care admission declining the quality of life. Repeated catheterization and other procedures increase the risk of lower urinary tract infections [5]. When conservative treatment is not sufficient, more invasive procedures might become necessary [6]. Unfortunately, some of the patients, especially those with an advanced prostate cancer, bladder invasion or radiation cystitis might not be eligible for the surgical procedures due to the high risk of mortality.

Pisco et al. [7] in a large retrospective cohort study, demonstrated a high success rate of prostate artery embolization (PAE) in benign prostatic hyperplasia (BPH) patients with moderate to severe lower urinary tract symptoms (LUTS). Importantly, PAE showed very promising results in the management of hematuria in patients with BPH [8], but the data on its potential application in prostate cancer remain scarce. Therefore, the aim of this manuscript is to review the outcomes of prostate artery embolization in the management of refractory bleeding from the lower urinary tract.

MATERIAL AND METHODS

A comprehensive search was performed in the PubMed/MEDLINE database. Articles published between 2003 and 2019 in English language were considered. The search terms used for extraction included: prostate artery embolization in prostate cancer, transcatheter arterial embolization, prostate haemorrhage. The aforementioned were used with Boolean operators (AND, OR). One additional relevant article was selected from manuscript bibliographies. We selected 10 original trials and case series for the summation of the efficacy of arterial embolization performed due to intractable hematuria (Table 1). With one exception, all selected articles were of retrospective nature. Contemporary literature does not contain sufficiently eligible studies involving prostate artery embolization in the management of refractory hematuria as a sequalae of prostate cancer. Therefore, data reporting transcatheter arterial embolization for control of hematuria in non-prostate aetiology were included. For that matter, we did not exclude the article describing embolization as a treatment for lower urinary tract symptoms or urinary retention in men with prostate cancer. For current review, we analyzed information related to number, age of the patients, aetiology of the hematuria, bilateral or unilateral procedure, type of embolic material, technical and clinical success, complications, recurrent hematuria, hematocrit and hemoglobin levels.

Prostate artery embolization

1. Prostate artery embolization background

The history of this non-invasive method has a beginning in 1970s, when Margolies et al. [9] report-

Table 1. *Prostate artery embolization in the management of intractable hematuria (reported cases in the literature)*

Ref.	Authors	Year	No. of patients	Mean age	Aetiology of the hematuria
[33]	Nabi et al.	2003	6	80	Bladder cancer n = 3 Prostate cancer n = 3
[6]	Rastinhead et al.	2008	8	78	Prostate cancer n = 6 BPH n = 2
[24]	Prasad et al.	2009	11	76	TCC of the bladder n = 4 TCC of the bladder + prostate cancer n = 3 Prostate cancer n = 1 Radiation cystitis n = 1 Adenocarcinoma of the colon n = 1 Endometrial carcinoma n = 1
[39]	Liguori et al.	2010	44	79	Prostate cancer n = 12 Other n = 32
[25]	Delgal et al.	2010	20	73	Bladder cancer n = 11 Radiation cystitis n = 3 Cyclophosphamide induced cystitis n = 1 Prostate cancer n = 2 TURP in BPH n = 3
[34]	Korkmaz et al.	2016	18	67	Prostate cancer n = 6 Bladder cancer n = 6 Cervical cancer n = 2 Endometrial cancer n = 1 Radiation cystitis n = 2 Hemorrhagic cystitis n = 1
[23]	Chen et al.	2017	9	72	Prostate cancer n = 9
[40]	Bonne et al.	2017	10	62	Post RA radical prostatectomy- cancer
[35]	Tapping et al.	2019	4	69	Prostate cancer n = 4
[38]	Malling et al.	2019	15	74	

No. – number, RA – robot-assisted, ref. – reference; BPH – benign prostatic hyperplasia; TCC – transitional cell carcinoma; TURP – transurethral resection of prostate

ed three cases of massive hemorrhage from pelvic fractures and the embolization as a method to impede flow in a bleeding vessel. Thereafter, Hald and Mygind [10] tested the effect of hypogastric embolization in the management of haemorrhage caused by radiation cystitis. They needed more effective, non-invasive treatment as opposed to a procedure that used pressure in the bladder. They stopped the bleeding by performing the embolization of hypogastric artery [10]. Equally, Mitchell et al. [11] reported bilateral transcatheter embolization in the management of hemorrhage of prostatic origin in four cases. Authors propitiously introduced the above method as an eligible solution to mitigate the amount of complications and death rate [11]. Several years later was published the first animal study relating to the outcomes of embolotherapy in postprostatectomy hemorrhage. The purpose of this investigation was to explore the changes in prostate gland tissue after embolization of the internal iliac arteries and justify its property in clinical practice [12, 13]. Other two animal studies reported prostate volume reduction in response to transcatheter arterial embolization [14, 15, 16]. Meanwhile, Carnevale et al. [17] primarily performed prostate artery embolization in two cases of acute urinary retention, secondary to benign prostatic hyperplasia after ineffective therapy with selective α-blockers and urethral catheterization. Authors reported prostate volume reduction after 1 and 6-month follow-up control imaging with US and MRI. For the patient who had undergone the bilateral procedure, prostate shrinkage was more effective than for the patient with unilateral treatment [16, 17]. With steadily published case reports and review papers, the embolization was improved and its reliability was strengthened. Thereby, the technique was continuously developed and the use of interventional radiology expanded [18, 19].

Prior to prostate artery embolization (PAE) procedure, patient is referred for computed tomography angiography (CTA), to verify pelvic and prostatic arterial anatomy and identify collateral vessels [20–23]. Detection of active bleeding is not an obligatory finding to proceed with PAE in patients with refractory cancer hemorrhage [5, 24, 25]. Because vascularity in this area is highly diversified, it is particularly important to become familiarized with possible disparities and anastomoses. That enables to perform selective catheterization avoiding untargeted occlusion which yield undesirable ischemia [19, 22]. According to current findings, the probability of the occurrence of single prostate artery from each pelvic side is 57% and double independent arteries arise from both sidewall occur in 43% of patients [26]. One patient on both sides can present different amount of the arteries.

Figure 1. *Selective angiography of the left inferior epigastric artery (IEA). In this less common pattern left prostate artery (PA) originates from obturator artery (OA) which is a branch of IEA in this case. CFA – common femoral artery; EIA – external iliac artery.*

Prostate artery is usually a continuity of the inferior vesical artery (IVA) and its most common origin is the internal pudendal artery. It frequently originates from the obturator artery and the anterior division of internal iliac artery (IIA) either in common trunk with the superior vesical artery or separately or inferiorly to it. Prostate arteries in their courses divide into two branches: anterior-lateral pedicle and posterior-lateral pedicle [19, 26, 27, 28]. Knowledge of presented variants and some other rare patterns is very essential to complete the procedure successfully without non-target embolization complications (Figure 1).

2. Prostate artery embolization technique

Prostate artery embolization is performed under local anesthesia, most often from common femoral artery approach [16]. Lately radial artery approach has been explored with satisfactory results. 4Fr or 5Fr diagnostic catheter is navigated to the IIA and its anterior division. Angiography is utilized to recognize pelvic vascular anatomy, especially IVAs and prostate arteries. Embolization for bleeding control might be achieved at different levels of pelvic blood supply, but superselective embolization of the prostate arteries or targeted embolization of visible extravasation seems to be the goal of the procedure. Coils, particles, gelfoam or liquid embolics can be

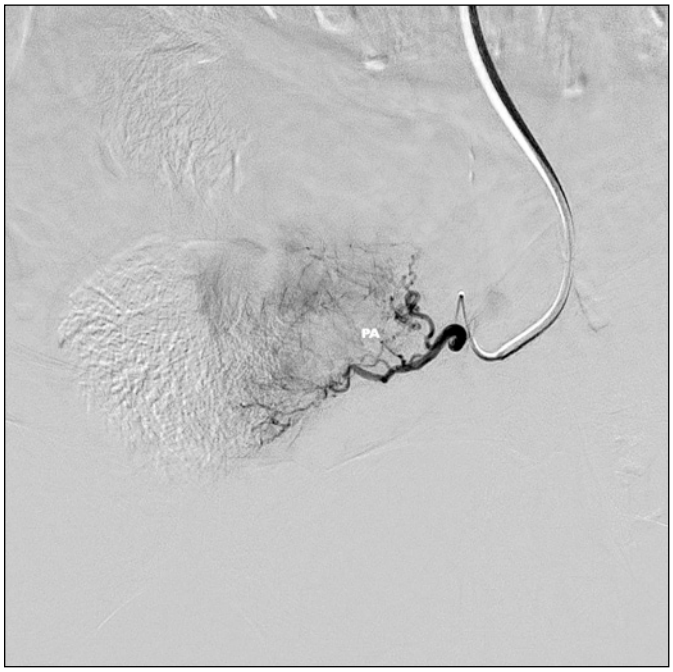

Figure 2A. *Superselective catherization of PA with a coaxial microcatheter.*

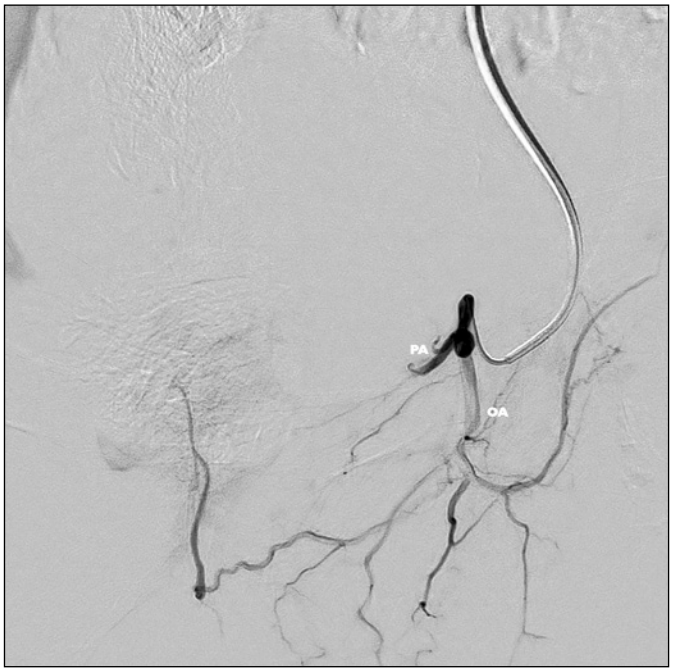

Figure 2B. *Complete embolization of the PA using 400 µm Embozene particles (prev. Boston Scientfic, currently Varian).*

used. Proximal embolization with various types of 0,035" coils, poorly calibrated particles. Gelfoam can be used to block proximal vessels to achieve hemostasis, especially in emergency cases when distal catheterization is impossible or time-consuming. Superselective approach to occlude normal vascularity, hypervascularity and extravasation requires coaxial microcatheter and properly selected microspheres (Figure 2A and Figure 2B). Microcoils may be utilized to protect vital branches from non-target embolization with microspheres [25, 27]. Cone-beam CT should be performed to confirm the proper position of the microcatheter prior to injection of the particles (Figure 3). Compression dressing or closure device is applied to the vascular access site after the procedure has been completed [5, 27, 29, 30].

3. Prostate artery embolization complications

According to the Society of Interventional Radiology [31], PAE might lead to minor and major complications. Cizman et al. [32] reported side effects of embolization i.e. pain, hematuria, hematospermia, urethral burning, rectal bleeding, urinary tract infection, balanitis, hematoma, diarrhoea, dissection, acute urinary retention, non-target embolization. Non-target embolization can also be sometimes categorised as a major complications. It depends on necessity of the therapy, overnight admission, or prolonged hospitalization [19, 31, 32].

RESULTS

We identified 75 records through literature search. After screening the titles and abstracts, 65 non-English, non-original and no full-text articles had been excluded. There were 145 patients (total number from 10 studies) with a mean age of 73 years. The aim of the manuscript was to review prostate artery embolization in patients with prostate cancer. However, construction of the studies did not allow to exclude other aetiologies of the hematuria in study groups. Nabi et al. [33], Korkmaz et al. [34] and Tapping et al. [35] conducted bilateral TAE in all patients. Because the collateral vascularity of the ligated internal iliac artery (i.e inferior mesenteric, external iliac, femoral, and opposite internal iliac artery) may still provide a blood supply, Pisco et al. [36] emphasized the necessity of the both sides embolization. Even though there was no bleeding revealed on the medical imaging, there was a need to perform both-sided embolization [37]. Prasad et al. [24] in their study of 11 cases reported recurrence of haematuria in a patient with transitional cell carcinoma (TCC) of the bladder and prostate cancer after 11 days. Unsuccessful embolization was assumed to be a result of the unilateral procedure. Malling et al. [38] in their study established technical success only when the bilateral PAE had been performed. In some cases there was a need to repeat TAE. Nabi et al. [33] in their study reported a control of bleed-

Figure 3. *Coronal reconstruction of the Cone Beam CT during the procedure. Contrast injection through the microcatheter in the prostatic artery depicts the enhancement of the left prostate (P) lobe. No enhancement of the adjacent structures confirms the minimal risk of non-target embolization.*

ing in one patient exclusively at a second attempt. Liguori et al. [39] and Delgal et al. [25] performed repeat successful procedure in 5 (11%) and 3 (16,7%) patients, respectively. Clinical success was defined as a cessation of hematuria except for Malling et al. [38] study. The authors reported no major complications related to PAE. Minor complications revealed in the literature ranged from 10–50%. Postembolization syndrome (i.e gluteal pain, fever, nausea, emesis) [25, 33, 34, 38, 39] was managed with symptomatic treatment approach only, with its resolution within few days. Embolization of the main trunk or whole anterior or posterior divisions of the internal iliac artery, compared to superselective embolization as distal as possible, increased a chance of ischemic complications. When the gluteal artery was not protected buttocks and upper tights pain could occur as a complication [39, 40]. Rastinhead et al. [6] reported an individual case with rectovesical fistula one month after embolization. The complication was related to prior advanced cancer status with rectum invasion. One microcoil migration from the anterior division of the internal iliac artery [25] and singular case with a pseudoaneurysm of the common femoral artery [40] had been described in the studies. Malling et al. [38] used CIRSE classification system for complications to reveal post-embolization difficulties. Groin hematoma and balanitis were considered as grade 1 complications which occurred in two patients, and grade 3 manifested in urinary tract infection and pelvic pain was described in two cases.

After analysis of the published studies we revealed recurrence of the hematuria which ranged 10–57% [6, 23, 24, 25, 34, 35, 39, 40]. Nabi et al. [33] reported no situation with re-bleeding in all six patients. One out of three patients with prostate cancer needed a second attempt of the procedure to obtain initial bleeding control. Liguori et al. [39] described recurrent bleeding in 57% of the patients. Because of the various aetiology of the enrolled group, it is not clear how many patients with prostate cancer after embolization obtained permanent control of the bleeding. Rastinhead et al. [6] reported only one out of eight cases with recurrence developed 14 months after embolization. It was related to bladder tumor recurrence. Two of four patients with prostate cancer in the Prasad et al. [24] study had recurrence (at 11 and 84 days after embolization). The first one had unilateral procedure performed, which was perceived as the reason of the re-bleeding. Delgal et al. [25] reported four late bleeding recurrences. Two of them had a prostate cancer. The 22% of Chen et al. [41] study group (all with prostate aetiology) had a recurred hematuria successfully treated by supportive treatment. Two recent studies focusing on the hematuria in prostate cancer had only one patient each with recurrence [8, 42]. Nevertheless, we have to admit that study groups were small. In our review two studies described significant improvement of hematocrit and hemoglobin level [34, 39]. The mean hematocrit levels before and after embolization increased from: 27 to 31% ($P < 0001$) [39] and 26.95 to 30.11% ($P = 0.003$) [34], whereas hemoglobin levels changed: 8.7 to 10.3 g/dL ($P < 0001$) and 8.95 to 10.25 g/dL ($P = 0.005$), respectively. Liguori et al. [39] reported a requirement of blood transfusion in 24 patients before transarterial embolization and only in 13 patients after the procedure.

The present systematic review collected the available data attributable to prostate arterial embolization in patients with prostate cancer. We analyzed and assessed comparative and non-comparative (case series) publications. Not all focused only on the patients with prostate cancer. Nevertheless, the heterogeneity of the population showed the wide range of the indications and effectiveness of this method (Table 2). Malling et al. [38] in their study proved that PAE can successfully treat urinary retention and LUTS not only in BPH but as well in prostate cancer patients. Because they also observed pain relief in one patient and a 2-point improvement

Table 2. *Summary of selected publications – prostatic artery embolization in different clinical management*

Authors	Bilateral embolization (%)	Type of embolic material	Months (follow-up)	Technical success (%)	Clinical success (%)	Complications (%)	Recurred hematuria (%)
Nabi et al.	100	coils n = 6	22	100	83	50	0
Rastinhead et al.	Not said	coils (0.018–0.035 inch) n = 2 PVA or TGM (100–500 µm) n = 6	20	100	100	12.5	12.5
Prasad et al.	91	PVA (500–1000 µm) n = 7 PVA+coils n = 3 PVA+ GS n = 2 TGM (700–900 µm) n = 2 GS+coils n = 2 coils n = 1	2	100	100	0	27
Liguori et al.	59	PVA (150–700 µm)	10.5	100	82	27	57
Delgal et al.	72	PVA or TGM (300–500 µm, 500–700 µm) n = 7 coils (0.018–0.035) inch. n = 2 PVA or TGM + coils n= 3 GS n = 2 glue embolization n = 2 coil blockade n = 2	16	90	83	12.5	28.6
Korkmaz et al	100	PVA (300–500 µm, 500–700 µm) n = 11 coils n = 2 PVA + coils n = 2 coil blockade n = 1	18	88	100	31	18.75
Chen et al.	89	PVA (45–150 µm) n = 2 PVA (355–500 µm) n = 3 GS n = 2 PVA+coils n = 1 PVA, GS n = 1	3	89	67	0	22
Bonne et al.	40	PVA (500–700 µm) n = 1 PVA (300–500 µm) + coils n = 3, nester macrocoils n = 1 GS n = 1 NBCA n = 1 contour PVA n = 1, SGP n = 1	45	100	90	10	10
Tapping et al.	100	PVA (300–500 µm)	18	100	100	0	25
Malling et al.	67	TGM (300–500 µm)	6	67	54.5	27	

PVA – polyvinyl alcohol; TGM – tris-acryl gelatin microspheres; GS – gelatin sponge; NBCA – n-butyl-2-cyanoacrylate; SGP – stent graft placement

in International Prostate Symptom Score-Quality of Life (IPSS-Qol), new indications for the treatment should be considered in the future studies. The necessity to further investigate LUTS in patients with prostate cancer had been also quite rightly observed 2 years before by Chen et al. [23]. They reported 2 patients with voiding difficulties regained ability to spontaneous urination after PAE procedure.

CONCLUSIONS

Since prostate artery embolization for prostatic origin bleeding is steadily undertaken, it is worth assessing the results enabling to establish the urological practice for this method. The studies prove the procedure is safe, burdened with low risk of complications and accomplishes technical and clinical success. In selecting the optimal treatment method in poor surgical patients, the minimally invasive method has to be considered. Thereby, prostate artery embolization is a promising option. This review contributes that prostate artery embolization is becoming a part of the standard-of-care treatment algorithm for patients with hemorrhage and other sequelae secondary to prostate cancer. However, further investigations are necessary to confirm the clinical application of this intervention.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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