



(RESEARCH ARTICLE)



The Efficacy of Prostatic Artery Embolization (PAE) as Palliative Therapy in Prostate Cancer

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World Journal of Advanced Research and Reviews, 2024, 21(01), 1630–1637

Publication history: Received on 10 December 2023; revised on 17 January 2024; accepted on 19 January 2024

Article DOI: <https://doi.org/10.30574/wjarr.2024.21.1.0250>

Abstract

Introduction: Prostate cancer, the primary contributor to cancer-related fatalities in Western countries, predominantly impacts individuals between the ages of 45 and 60. The World Health Organization (WHO) has documented 1,414,259 new cases worldwide. Diagnosis methods include prostate biopsy, PSA testing, and MRI, with risk factors such as age, weight, race, and family history contributing to the varied epidemiology of the disease. Treatment alternatives such as surgery and radiation therapy come with notable side effects, prompting ongoing research into alternatives like prostate artery embolization (PAE) for benign prostatic obstruction. However, the role of PAE in patients with prostate cancer remains uncertain.

Aim: The purpose of this systematic review is to determine the efficacy of Prostatic Artery Embolization as one of the palliative management strategies for clinical outcomes in prostate cancer.

Method: We searched for English-language full-text literature from Pubmed, Cochrane, Wiley Library, Proquest, SpringerLink, and ScienceDirect databases from January 2013 to Desember 2023. Based on the 1442 journals identified in this study, the number of evaluated articles is 6.

Results: In six studies, PAE induces tissue ischemia through femoral artery embolization, offering promise for localized prostate cancer treatment. Administered under local anesthesia, PAE has shorter hospital stays and is well-tolerated compared to TURP. After PAE treatment, significant IPSS reduction occurred, with improved outcomes reported at 1 and 6 months. Histopathology showed necrotic zones, but viable cancer cells persisted. PAE is a valuable adjunctive therapy for reducing organ-at-risk doses in exclusive prostate radiation therapy.

Conclusion: PAE is a minimally invasive treatment for LUTS related to BPH and its potential in managing PCa. PAE, utilizing femoral artery occlusion, shows significant short and medium-term reductions in IPSS. While there's notable success in PCa management and reduced radiation doses, further research is essential for a comprehensive understanding of PAE's efficacy in localized PCa treatment.

Keywords: Prostate Neoplasm; Prostate carcinoma; Prostate artery embolization; Meta-analysis

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1. Introduction

Prostate cancer stands as the foremost reason for cancer-related deaths in Western nations, impacting predominantly middle-aged men, particularly those aged between 45 and 60¹. As per World Health Organization (WHO) data, prostate cancer ranks as the second most widespread disease globally, with 1,414,259 new cases reported worldwide. In the realm of male cancer-related mortality, it holds the fifth position. The Global Cancer Statistics for 2020 provide additional insights into the consequences of prostate cancer, indicating that it resulted in 375,304 deaths among men across diverse age groups². Statistics on the incidence of prostate cancer in Indonesia are currently unavailable. However, data from the last eight years, spanning from 2004 to 2011, indicate that three urological education centers collectively recorded 761 cases during that period³.

The diagnosis of prostate cancer in males typically involves procedures such as prostate biopsy and analysis, PSA testing, digital rectal examination, magnetic resonance imaging (MRI), or health screening. Risk factors for prostate cancer include age, weight, race, family history, and various environmental factors. Prostate cancer is a heterogeneous disorder with respect to geography and genetics. Because of the interplay of genetics, environment, and social effects, there are differences in the prostate cancer epidemiology of different countries, which reduces estimates of the prostate cancer survival rate particular to a given race⁴. Extensive research has consistently demonstrated a genetic link to prostate cancer. Investigating the genetic predisposition and hereditary aspects of prostate cancer has been a focus of research for many years. Family inheritance emerges as a significant genetic risk factor for prostate cancer, as indicated by both studies and epidemiological research, underscoring the importance of hereditary factors in this condition⁵. Several studies have looked into how genetic variety may affect androgen production, metabolism, and function^{6,7}. Genomic research has connected a number of biological mechanisms, including chromosome rearrangements, to the emergence of some malignancies⁴.

Androgen sensitivity and androgen insensitivity in prostate cancer refer to the degree of testosterone stimulation and the potential therapeutic options⁸. Prostate cancer can be addressed through diverse methods, including surgery, hormonal therapy, radiation therapy, active surveillance, and cryotherapy. The selection of therapy for patients depends on factors such as tumor type, PSA level, grade and stage, and the probability of recurrence. For instance, radiation therapy is often employed in conjunction with radical prostatectomy, a surgical procedure involving the removal of the prostate and surrounding tissues, to treat low-risk prostate cancer⁹. Treatment recommendations for cancers that have resurfaced and spread outside of the prostate include hormonal therapy, also referred to as androgen-deprivation therapy¹. All treatment approaches come with potential adverse effects, including toxicity and reductions in white and red blood cell counts. Fatigue, hair loss, peripheral neuropathy, erectile dysfunction, and incontinence are among the possible outcomes. Additionally, treatments may lead to metastasis, and over time, the development of treatment resistance can occur. Notably, existing treatments are costly and carry detrimental side effects¹⁰.

Prostate artery embolization, abbreviated as PAE, is a therapeutic approach for alleviating lower urinary tract symptoms (LUTS) caused by benign prostatic obstruction (BPO) and is gaining increasing popularity worldwide. Nevertheless, the specific role of PAE in patients with prostate cancer (PCa) remains unclear¹¹. Definitive radiation (RT) remains a crucial treatment option for localized PCa. Radiation therapy can be administered through various modalities, including brachytherapy (BT), stereotactic body radiation therapy (SBRT), and external beam radiation therapy (EBRT). Prostate size, PCa features, and patient demographics all have an impact on the treatment technique selection. It is noteworthy that up to 33% of men having RT may experience both short-term and long-term genitourinary (GU) problems, which pose significant management challenges. Furthermore, those exposed to excessive dosages in the central urethral area are more likely to experience long-term symptoms, and those with larger prostates are more likely to experience persistent GU issues¹².

PAE, or prostate artery embolization, is a minimally invasive procedure wherein proficient interventional radiologists block the prostatic arteries under the guidance of fluoroscopic images¹³. Among the most dependable and helpful options for men experiencing severe pain and bleeding due to advanced prostate cancer appears to be PAE¹¹. It can be finished in an outpatient environment and usually results in an IPSS drop of 10–12 points after six months in benign hyperplastic prostate (BPH)¹³. PAE intervention as curative or palliative are not studied entirely. The objective of this systematic review is to assess the efficacy of Prostatic Artery Embolization (PAE) as a palliative therapy method in influencing clinical outcomes for individuals with prostate cancer.

2. Material and methods

2.1. Search Strategy and methodology

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) criteria were followed in our systematic review, guaranteeing a consistent framework for methodical conduct and clear reporting of our research.¹⁴

We conducted a systematic search of English-language literature in PubMed, Cochrane, Wiley Library, Proquest, SpringerLink, and ScienceDirect databases, spanning from December 2013 to December 2023. We identified relevant articles by utilizing the following terms: “Prostate Carcinoma” or “Prostate Neoplasm” or “Prostate Cancer” and “Prostate artery embolization” or “Prostatic artery embolization” not “Hyperplasia”. We added to this search by manually looking through a reference list of pertinent papers.

2.2. Eligibility Criteria

Five reviewers (Y.L.I., E.N., B.A.T., W.A.P., and M.P.W.) independently evaluated each paper that was retrieved for consideration; differences were settled by consensus. The following inclusion criteria were set:

- Adults undergoing embolisation of the prostate artery.
- Including Randomised Controlled Trials (RCTs) and prospective and retrospective observational research
- Full-text versions are accessible. Research carried out using the English language only.
- Research works released from January 2013 to December 2023.

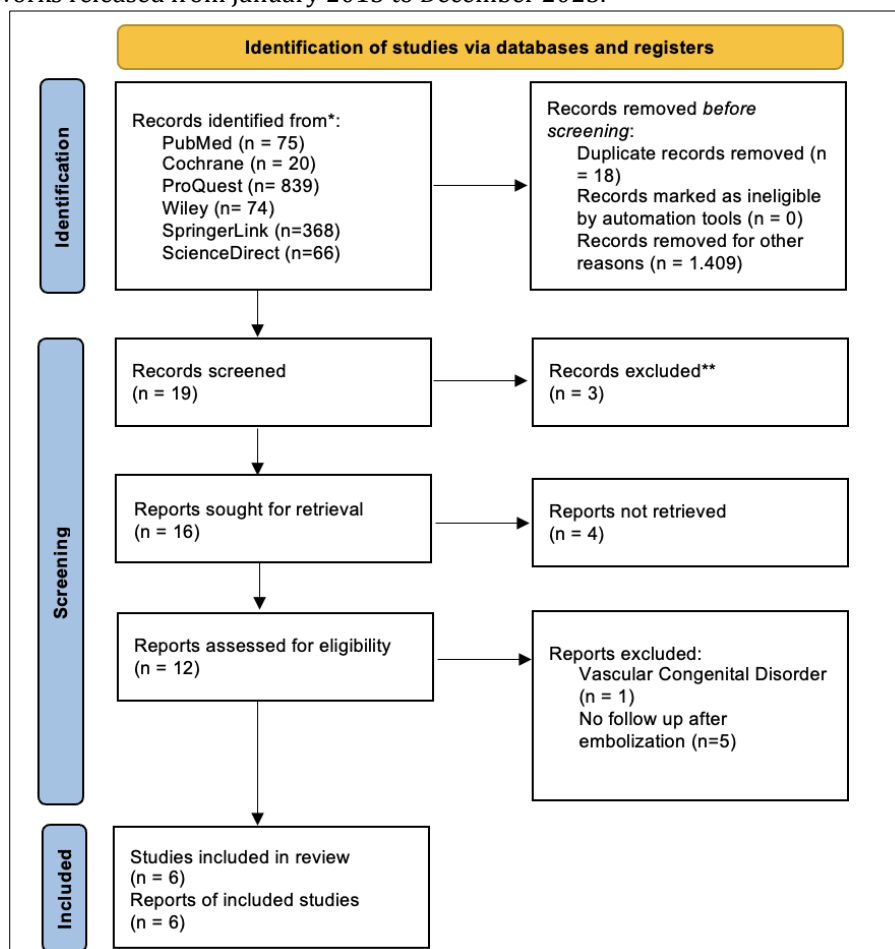


Figure 1 PRISMA flow chart

Using a standardised data collecting form, five investigators (Y.L.I., E.N., B.A.T., W.A.P., and M.P.W.) carried out the data extraction process independently. Each study’s author, publication year, study design, patient count, age, embolisation method, follow-up period and follow-up time after embolisation, IPSS score, prostate volume, PSA ratio, and

histopathology results were among the data that were extracted. Every one of these objects was assessed for chemoembolization as well as embolization

2.3. Description of studies based on criteria

Based on 1442 identified journal articles, 1427 articles were excluded before screening. Out of a total of 19 journals, 3 articles were excluded, and 4 journals were not included. Eligibility evaluation revealed 12 journals, with a total of 6 journals being excluded. Therefore, this study encompasses 6 discussed studies.

2.4. Quality Assessment and risk of bias assessment

Two authors (W.A.P and M.P.W) evaluated the possibility of bias in cohort studies using the modified Newcastle-Ottawa Scale (NOS). The results are shown graphically in Table 1. Consensus was used to settle disagreements. Six reviewed studies¹⁵⁻²⁰ were found to have achieved seven or more stars using the modified NOS star system, which has a range of 0-9 stars. As a result, these studies were classified as good quality studies.

Table 1 Risk of Bias Assessment

Study (cohort)	Selection (Maximum 4 stars)				Comparability (Maximum 2 stars)	Outcome (Maximum 3 stars)			Total	
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not	Comparability of cohorts on the basis of the design or analysis controlled for confounders	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total	
Pisco et al., 2018	*	-	*	*	**	*	*	*	8	Good quality
Mordasini et al., 2018	*	-	*	*	*	*	*	-	7	Good quality
Wang et al., 2022	*	-	*	*	**	*	*	-	7	Good quality
Peacock et al., 2020	*	-	*	*	**	*	*	*	8	Good quality
Malling et al., 2019.	*	-	*	*	**	*	*	-	8	Good quality
Frandon et al., 2021	*	-	*	*	**	*	*	-	7	Good quality

3. Results

Lower urinary tract symptoms (LUTS) are commonly addressed through the palliative method of transurethral resection of the prostate (TURP). However, prostatic artery embolization (PAE) is emerging as a viable alternative for treating LUTS in cases of benign prostatic hyperplasia (BPH). PAE induces tissue ischemia through femoral artery embolization. In the context of localized prostate cancer (PCa), chemoembolization using epirubicin and docetaxel demonstrates promise. Administered under local anesthesia, PAE is reported to be more tolerable than TURP, leading to shorter hospital stays. Various investigations have examined improvements in the International Prostate Symptom Score (IPSS), reduced prostate volume, changes in biochemical markers, and histologic alterations associated with PAE.

Table 2 Studies Characteristics

Study (year)	Country	Design	PAE							Follow-up (months)
			Patients (n)	Age (mean \pm SD)	IPSS post PAE (n \pm SD)	Prostate volume post PAE (cm ³ \pm SD)	PSA post PAE (μ g/ml)	Negative biopsies (%)	RT dose difference (%)	
Frandon et al. (2021)	France	Retrospective cohort	10	72 (no SD data)	-	-	-	30 (no SD data)	Not available	6 and 12
Malling et al. (2019)	Denmark	Prospective cohort	15	73.8 \pm 9.5	14 and 1.8 (no SD data)	1.01 and 9.86 (no SD data)	0.78 and 16.42 (no SD data)	-	-	1 and 6
Mordasini et al. (2018)	Switzerland	Prospective cohort	12	-	4.5 (no SD data)	-	1.84	0	-	1.5
Peacock et al. (2020)	United States	Retrospective cohort	9	67.2 \pm 9.95	3.6 \pm 1.85	23.14 \pm 14.05	2.52 \pm 2.6	-	28.63	18
Pisco et al. (2018)	Portugal	Retrospective cohort	20	8.78 \pm 4.49	8.78 \pm 4.49	54.4 \pm 40.6	1.2 \pm 0.9	-	-	12 for 2 patients and 18 for 18 months
Wang. (2022)	China	Retrospective cohort	32	72.5 range 60-89	-	55%	-	84.2	-	Mean 27

IPSS significantly reduced post-PAE, with Malling et al.¹⁶ reporting improvements at 1 and 6 months. Wang et al.²⁰ noted bleeding control within 5 days, with spontaneous urination recovery in 17 patients during 30 months. Chronic catheter dependency may impact urination recovery in PCa patients. Prostate volume and PSA changes varied among studies, with Malling et al.¹⁶ observing an increase after 6 months. Biochemical success, assessed through PSA, ranged from 62.5% at 18 months post-PAE.

Necrotic tissue zones were found in PCa patients' histopathological examinations, yet live cancer cells continued to exist. PAE prior to radiation therapy reduced toxicity and allowed lower radiation doses. PAE effectively treated LUTS, hemorrhage, and urinary retention in PCa, but more research on its effectiveness in localized PCa, considering biochemical response and histopathology, is crucial. PAE is a valuable adjunctive therapy for reducing organ-at-risk doses in exclusive prostate radiation therapy.

4. Discussion

Despite being recognized as a minimal invasive technique and a novel treatment for LUTS associated with benign prostatic hyperplasia (BPH), palliative transurethral resection of the prostate (TURP) remains the standard approach for managing LUTS. Through the introduction of embolic particles into the femoral artery, PAE causes tissue ischemia by obstructing blood flow to the targeted tissue. Chemoembolization with docetaxel and epirubicin presents a promising approach for treating localized PCa. Conducted under local anesthesia, this method is well-tolerated, making it suitable for individuals with comorbidities or elderly males who may not be ideal surgical candidates. Furthermore, PAE has demonstrated comparable clinical outcomes to TURP, accompanied by a reduction in hospital stay duration¹⁶. In this systematic study, various metrics such as the IPSS reduction in prostate volume, changes in biochemical indicators, and histopathological findings were systematically compared before and after PAE.

IPSS < 19 and an increase of ≥ 3 points in individuals without urinary retention and without the capacity to release urine through a catheter were considered substantial reductions in IPSS. Malling et al. reported IPSS improvements of 9.6 and 12.2 after PAE within a 1- and 6-month follow-up, respectively¹⁶. Pisco et al. (2018) found a similar result, demonstrating an improvement of 3.32 in the IPSS in just 18 months. Frandon et al. also discovered a mean IPSS improvement of 2¹⁷.

In a recent study, Wang et al.²⁰ found that all 32 patients experienced spontaneous bleeding control within 5 days of PAE, and that during the average 30-month follow-up, 17 patients experienced spontaneous urination again. Men diagnosed with prostate cancer often exhibit advanced age, and they commonly experience a higher incidence of detrusor underactivity due to prolonged reliance on pre-procedural catheters. This condition is frequently compounded by persistent urine retention and detrusor overactivity. Additionally, a recent study suggests that catheter reliance for longer than three months reduces the likelihood of spontaneous urination after PAE. 22 patients had a 55.5% reduction in prostate volume at the last follow-up. Nonetheless, Malling et al.¹⁶ showed that after six months, there was an increase in prostatic volume. During the same time span, PSA measurements increased in tandem with this.

A recent study measured PSA or biochemical success, which Pisco et al.¹⁹ defined as PSA decreasing to less than 2 ng/mL and then increasing to more than 2 ng/mL within a month of success. Of 16 patients who underwent effective embolisation within the 18-month timeframe, 62.5% were classified as biochemically successful. Another indicator that could be used in PCa treatment after PAE was the histopathological finding. Histological analysis by Mordasini et al. revealed centrally positioned, well defined necrotic tissue zones. Two of the twelve patients had full necrosis, while five of them had partial necrosis within the lesion. All twelve patients still had detectable cancer cells¹⁸.

Frandon et al. achieved comparable outcomes in their study involving 10 males with low-risk prostate cancer (PCA). At the 6-month mark, four patients exhibited negative results in both targeted and systematic biopsies. It is noteworthy that three individuals showed no lesions on MR imaging, while one patient experienced progression in the target lesion, leading to curative radiation treatment instead¹⁷.

Peacock et al.¹⁵ also identified a second application PAE, which involves its use before radiation therapy. Of the five patients included in the trial, two chose to get a lower RT dose after PAE, and none of them experienced grade 3 or greater toxicity. Because the other three patients did not experience significant dose changes as a result of the full pelvic nodal coverage, prostate volume reduction using PAE is the most advantageous method for lowering the dose of prostate radiation alone.

The findings of this study endorse the efficacy of PAE as a viable therapeutic choice for addressing LUTS, bleeding, and urine retention—commonly associated with PCa. Further investigations are essential to assess its feasibility as a

treatment option for localized PCa, considering factors such as biochemical response (mentioned earlier) and histological data. In the context of exclusive prostate radiation therapy, PAE stands out as a noteworthy complementary treatment for reducing the dose to the organ at risk.

4.1. Strength and Limitation

This is the first meta-analysis that, to the best of our knowledge, details the effectiveness of prostate artery embolisation as a palliative therapy for patients with malignant prostate cancer. The limitations of this study include its status as the first investigation addressing prostate artery embolization, which is itself one of the recent interventions applied to patients with prostate cancer. Consequently, the recruited sample size for each study remains limited, despite its spread across several countries.

5. Conclusion

PAE serves as a minimally invasive treatment for addressing LUTS associated with BPH. Additionally, its potential role in managing prostate cancer (PCa) is being explored. PAE, through femoral artery occlusion, proves well-tolerated for elderly and medically compromised individuals. Significant short and medium-term reductions in International Prostate Symptom Score (IPSS) post-PAE were observed. PCa patients undergoing PAE showed improved urination and spontaneous bleeding control, influenced by pre-procedural catheter dependency duration. While biochemical success was notable, histopathological examinations revealed variable necrosis levels. PAE's potential as a pre-treatment modality before radiation therapy holds promise in reducing prostate radiation doses. Overall, PAE effectively addresses LUTS and shows promise in PCa management, but further research is needed for its efficacy in treating localized PCa.

Compliance with ethical standards

Disclosure of conflict of interest

The writers claim to have no conflicting agendas.

Data and Materials' Availability

This study was a systematic review and the information of study are described in the table 1.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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