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Transcatheter Arterial Embolization for Chronic Prostatitis/Chronic Pelvic Pain Syndrome: A Retrospective Study of 44 Patients

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Abstract

Purpose To investigate the preliminary treatment outcomes of transcatheter arterial embolization (TAE) for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).

Materials and Methods This retrospective study included patients with refractory CP/CPPS who underwent TAE between April 2022 and February 2023. All patients had persistent pelvic pain for at least 3 months, a total score of at least 15 on the NIH-Chronic Prostatitis Symptom Index (NIH-CPSI), and lacked evidence of infection. All procedures were performed by injecting imipenem/cilastatin sodium (IPM/CS) from bilateral prostatic arteries ± internal pudendal arteries. NIH-CPSI, pain numeric rating scale (NRS), and complications were evaluated at 1, 3, and 6 months after the initial TAE and at the final follow-up.

Results Out of 48 patients, 44 were included in this study, with four excluded because of loss of follow-up. No severe procedure-related complications were observed. Pretreatment and post-treatment evaluations at 1, 3, and 6 months after the initial TAE and at the final follow-up (mean 16.6 months) revealed a decrease in the mean NIH-CPSI scores from 27 ± 6 to 21 ± 8, 20 ± 9, 17 ± 9, and 18 ± 9, respectively (all $P < 0.001$). Pain NRS scores were also decreased from 7.0 ± 1.6 to 4.8 ± 2.5, 4.1 ± 2.6, 3.7 ± 2.4, and 3.4 ± 2.3, respectively (all $P < 0.001$). The proportions of clinical success, defined as a reduction of at least 6 points from baseline in the NIH-CPSI, at 6 months after TAE and at the final follow-up were 70 and 64%, respectively.

Conclusions This study provides evidence of the feasibility of TAE using IPM/CS for CP/CPPS, suggesting both symptomatic improvement and safety.

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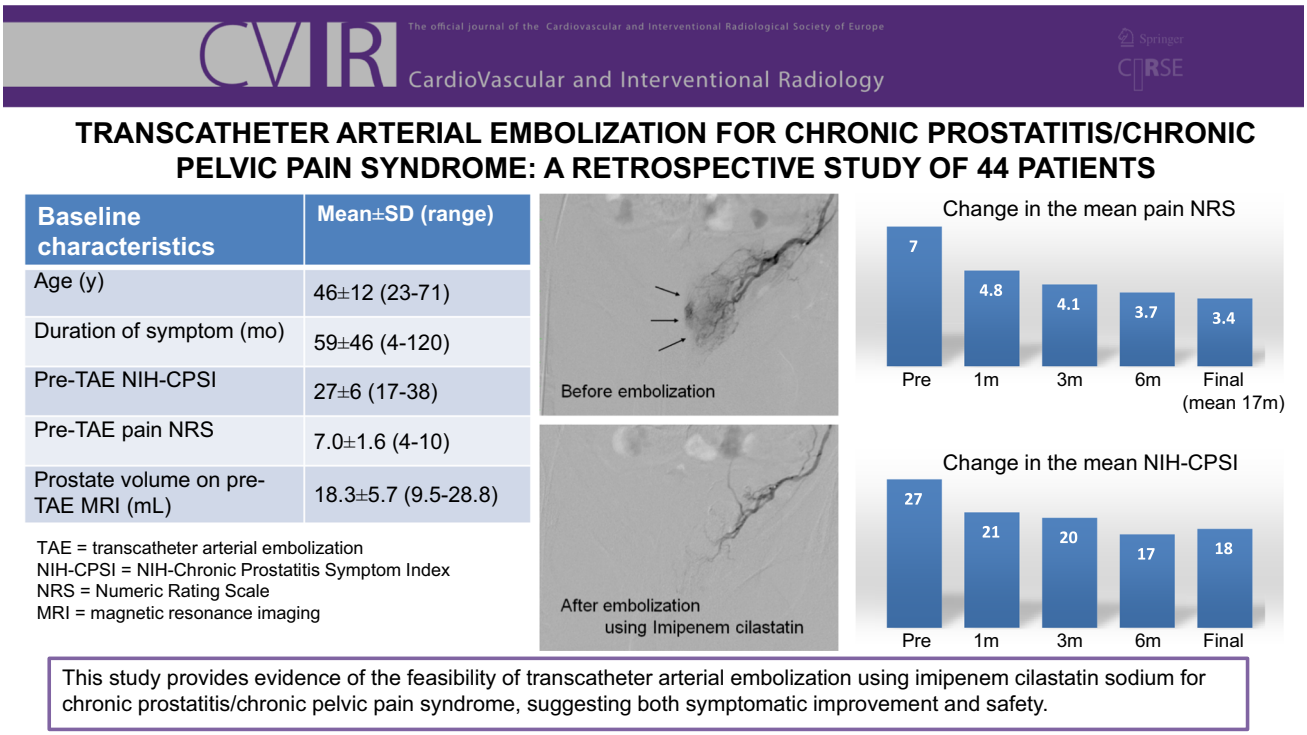
Graphical Abstract



Keywords Chronic prostatitis/chronic pelvic pain syndrome · Pelvic pain · Transcatheter arterial embolization

Introduction

Prostatitis is a common disease in men, and the National Institutes of Health (NIH) Consensus Classification System for Prostatitis categorizes symptomatic, nonbacterial prostatitis as chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) [1]. CP/CPPS is a prevalent condition associated with symptoms such as genitourinary pain and lower urinary tract symptoms [2] and more than 90% of all symptomatic prostatitis [1] and affects 10–15% of the male population [3]. The negative impact of CP/CPPS on the quality of life is similar to that of myocardial infarction, angina, or Crohn's disease [4]. The etiology and pathophysiology of CP/CPPS are still unclear, but may involve a combination of neuropsychological factors such as inflammation, anxiety and depression, and dyssynergia voiding [5–7]. Empiric antibiotics, alpha-blockers, and anti-inflammatory drugs are predominantly used in clinical practice; however, they have not shown beneficial effects when compared to placebos [8–10].

Recently, the therapeutic benefits of transcatheter arterial embolization (TAE) in addressing inflammation and pain by occluding aberrant blood vessels that proliferate in chronic inflammatory tissues have been recognized. This efficacy has been reported for conditions such as frozen shoulder [11, 12] and knee osteoarthritis [13]. The mechanism is believed to involve occlusion of neovascularization resulting from inflammation, leading to a reduction in the number of inflammation-induced microvessels, infiltration of inflammatory cells, and alleviation of the severity of inflammation [12, 14, 15]. In the context of CP/CPPS, inflammation is thought to be one of the causes of symptoms, similar to other chronic inflammatory conditions; there is potential symptom improvement through TAE. However, such reports have not been observed thus far.

The aim of the present study was to evaluate the mid-term results of TAE in patients with CP/CPPS that were refractory to traditional non-surgical management.

Material and Methods

This retrospective, single-arm study was performed by reviewing the medical records of the patients. Written informed consent was obtained from all patients prior to the procedure, and an opt-out method was used to secure the opportunities for referral from the patients. Our

institutional review board approved this retrospective study (OC 2024-007).

Patients

We identified patients with CP/CPPS who received initial TAE between April 2022 and February 2023. The diagnosis of CP/CPPS was defined as persistent pelvic pain for at least three months within the previous six months, without evidence of infection [2]. Lack of infection was demonstrated by a 2-glass test [16]. We included patients who had moderate-to-severe symptoms defined as a total score of at least 15 on the NIH-Chronic Prostatitis Symptom Index (NIH-CPSI) [17]. The NIH-CPSI is a universally accepted, reliable, and valid instrument recommended by consensus guidelines for clinical evaluation of and research on CP/CPPS [2, 18]. It measures pain, urinary function, and effect on quality of life, with a total score ranging from 0 to 43 and higher scores indicating worse conditions [18]. Patients with a history of prostate surgery and prostate cancer were excluded.

Multi-parametric magnetic resonance imaging (MRI) consisting of T2-weighted, T1-weighted, diffusion-weighted, and dynamic contrast-enhanced imaging was performed before TAE to assess Prostate Imaging Reporting and Data System version 2.1 (PI-RADS v2.1) [19] and prostate volume. Prostate volume was calculated using the prolate ellipsoid formula (length × width × height × π/6). In the case of gadolinium allergy, dynamic contrast-enhanced imaging was skipped.

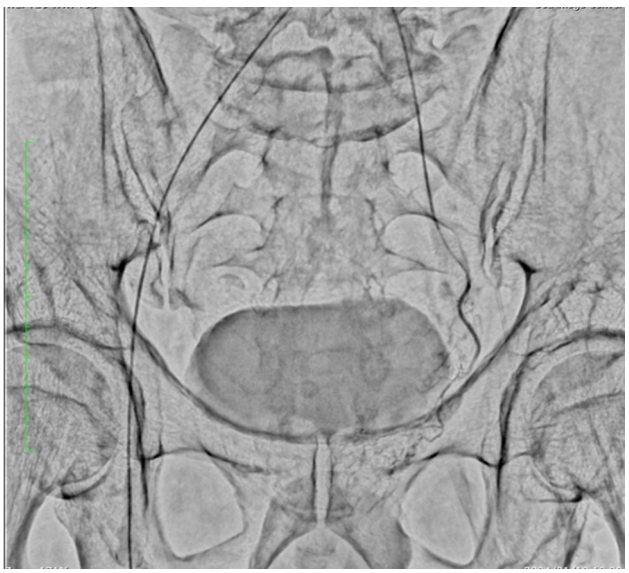


Fig. 1 Fluoroscopic image during embolization for chronic prostatitis. The tip of the catheter inserted from the right femoral artery is positioned in the left prostatic artery (white arrow)

Procedure

Treatment was performed as an outpatient procedure under local anesthesia without sedation in all patients. A 3.3-Fr sheath (Super Cath, Medikit, Japan) was inserted through the femoral artery, and a 3-Fr angiographic catheter (Jadkins Right 2.5, Medikit, Japan) was advanced into the internal iliac artery. A 1.7-Fr microcatheter (Veloute; Asahi Intec Co., Inc., Japan) was inserted coaxially through a 3-Fr catheter and advanced into the target arteries (Fig. 1).

We selected bilateral prostatic arteries and internal pudendal arteries (IPAs) as candidate vessels for treatment, and the vessels that were positive for evoked pain were chosen as target vessels. Positive evoked pain was defined as pain or discomfort in the area where the patient usually felt pain or discomfort when contrast medium was injected manually and selectively from the vessel [20]. If no pain or discomfort occurred, or if pain or discomfort occurred but at a different site from the patient's usual site, the vessel was considered to be evoked pain negative, and no treatment was performed from the vessel. Angiographic findings were not used to select the vessel for treatment.

IPM/CS (Primaxin; Merck & Co., Inc., Whitehouse Station, NJ, USA) was used as temporary embolic material. A suspension of 1 g IPM/CS (i.e., imipenem [0.5 g] in 10 mL of contrast agent) was prepared by pumping syringes for 10 s and then injected in 0.5 mL increments. IPM/CS was injected from the proximal portion of the main trunk of the target vessel until blood flow was completely stagnant. Figures 2, 3, and 4 show examples of digital subtraction angiography images. After IPM/CS injection, the catheter and sheath were removed, and manual compression was performed for 10 min. The patients were discharged 1 h after treatment, provided that they remained at rest.

During follow-up, additional sessions of TAE were performed within 6 months of the initial TAE if the NIH-CPSI score was greater than 15 points after 2 months of initial TAE and the patient requested additional treatment. Patients were allowed to continue with previous conservative therapies, and the use of these conservative therapies was recorded at follow-up visit.

Assessment

Technical success was defined as selective administration of IPM/CS to target arteries. NIH-CPSI, pain numeric rating scale (NRS), and complications were obtained at 1, 3, and 6 months after the initial treatment and at final follow-up performed 12 months after initial treatment or later. Clinical success was defined as a reduction of at least 6 points from baseline in the NIH-CPSI because 6-point

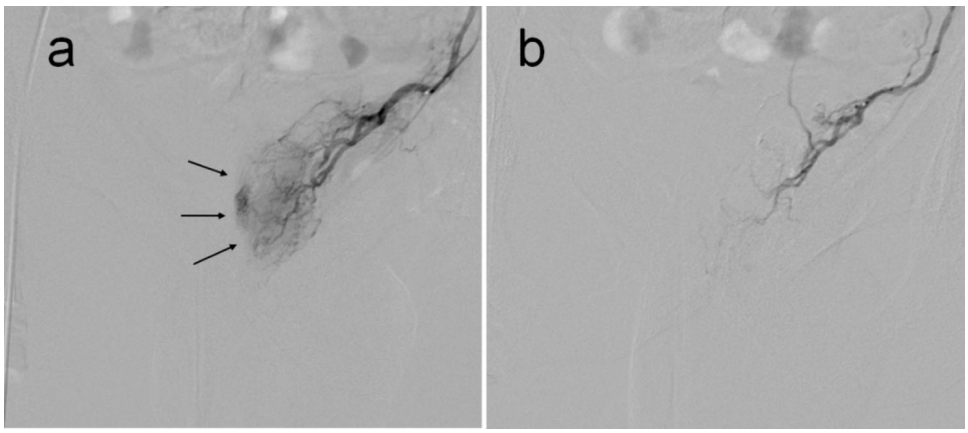


Fig. 2 Angiographic findings before **a** and after **b** transcatheter arterial embolization in a 45-year-old patient with chronic prostatitis. Angiography from the left prostate artery before embolization **a** shows vessels in the prostate (black arrowheads); embolic material is administered until blood flow is completely stagnant

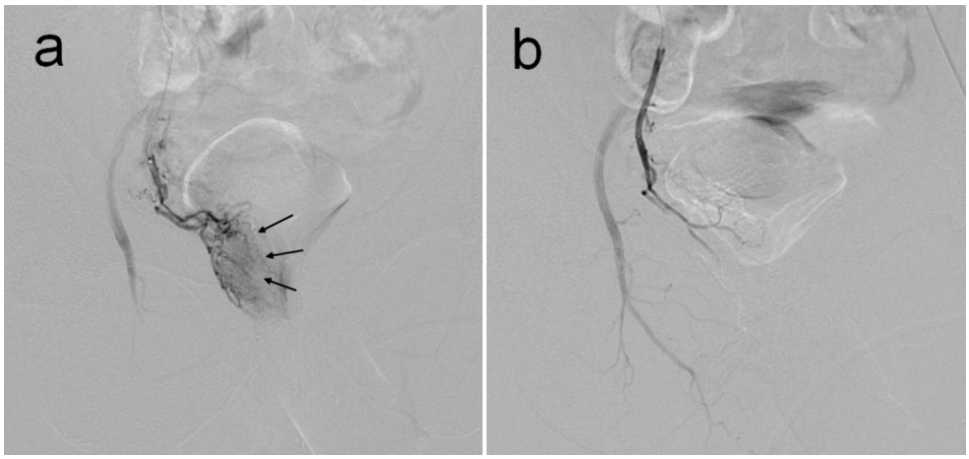


Fig. 3 Angiographic findings before and after transcatheter arterial embolization (TAE) in a 35-year-old patient with chronic prostatitis. **a** Digital subtraction angiography of the right prostate artery before and **b** after TAE. Angiography before embolization shows vessels in the prostate (black arrowheads); it is difficult to identify abnormal hypervascularity, but embolic material is administered because of the presence of evoked pain. The endpoint of embolization is until blood flow is completely stagnant

decrease in the NIH-CPSI was reported as the optimal threshold to predict treatment response [17].

Statistical Analysis

Patient characteristics and outcomes were summarized. Comparisons of NIH-CPSI and pain NRS scores at every period were analyzed using Dunnett's test. All P values were two-tailed, and $P < 0.05$ was considered a statistically significant difference. Statistical analyses were performed with R version 4.1.2.

Results

A total of 48 patients of CP/CPPS who had moderate to severe symptoms were treated with TAE between April 2022 and February 2023. Four patients were excluded because of loss of follow-up, and 44 patients were enrolled in this study. The mean follow-up period was 16.6 ± 3.1 months (range 12–22 months).

Patient characteristics are summarized in Table 1. The mean age was 46 ± 12 years, and the mean duration of symptoms was 59 ± 46 months. The mean NIH-CPSI and NRS score before TAE was 27 ± 6 and 7.0 ± 1.6, respectively. On pre-TAE MRI, the mean prostate volume was 18.3 ± 5.7 mL (range 9.5–28.8), and PI-RADS scores were category 1 in all cases.

Technical Outcomes

Evoked pain from the prostate arteries was positive in all cases. Additionally, 31 patients (70%) were positive for evoked pain from the IPAs. The technical success was obtained in 42 patients (95%). Only unilateral prostate arteries could be embolized in the two patients with technical failures. TAE was performed once in 17 patients, twice in 22 patients, and three times in five patients for a

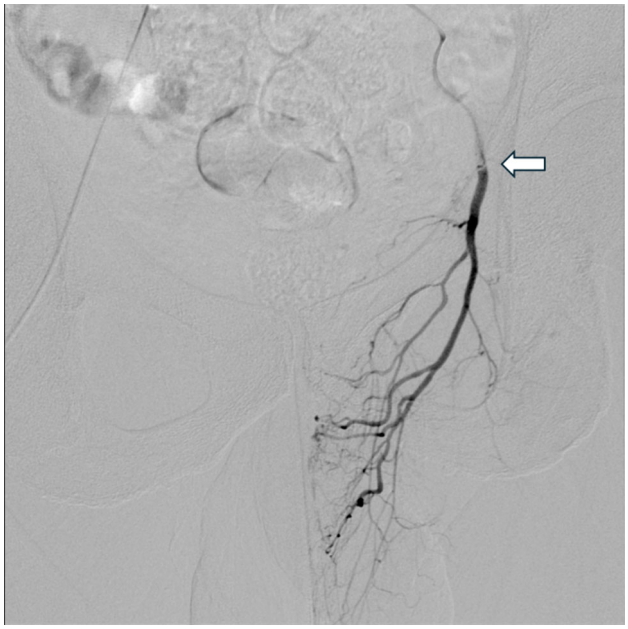


Fig. 4 Angiographic findings from left internal pudendal artery before transcatheter arterial embolization (TAE) in a 52-year-old patient with chronic prostatitis. The tip of the microcatheter (white arrow) is located in the proximal portion of the main trunk of the internal pudendal artery and embolic material is administered from the same location

Table 1 Patient characteristic

Parameter	
Age (y)	46 ± 12 (23–71)
Duration of symptom (mo)	59 ± 46 (4–120)
Last follow-up from initial TAE (mo)	17 ± 3 (12–22)
Pre-TAE NIH-CPSI	27 ± 6 (17–38)
Pre-TAE pain NRS	7.0 ± 1.6 (4–10)
Prostate volume on pre-TAE MRI (mL)	18.3 ± 5.7 (9.5–28.8)
PI-RADS score on pre-TAE MRI*	
1	44 (100)
> 1	0 (0)

Except where indicated, data are means ± standard deviations, with range in parentheses

TAE = transcatheter arterial embolization, NIH-CPSI = NIH-chronic prostatitis symptom index, NRS = Numeric rating scale, MRI = Magnetic resonance imaging, PI-RADS = Prostate imaging reporting and data system

*Data are numbers of patients, with percentages in parentheses

total of 76 sessions. The mean procedural time, from local anesthesia to catheter removal, was 56 ± 21 min (range, 15–113 min). The mean IPM/CS volume in each procedure was 402 ± 127 mg (range, 100–800 mg).

Table 2 Conservative treatment before TAE and at final follow-up

	Before TAE	At final follow-up
Oral treatments		
Antibiotics	44 (100)	2 (5)
Cernilton	36 (82)	14 (32)
Alpha blocker	17 (39)	8 (18)
Analgesics	28 (64)	6 (14)
Antidepressants	17 (39)	2 (5)
Herbal medicine	29 (66)	9 (20)
Tadalafil	3 (7)	3 (7)
Other treatments		
Prostate massage	14 (32)	5 (11)
Acupuncture	5 (11)	1 (2)
ESWT	1 (2)	0 (0)

Data are Numbers of patients, with percentages in parentheses

TAE = transcatheter arterial embolization, ESWT = extracorporeal shock wave therapy

Clinical Outcomes

The mean NIH-CPSI scores before treatment and at 1-, 3- and 6-month post-treatment, and at final follow-up (mean 16.6 months after an initial TAE) were 27 ± 6, 21 ± 8, 20 ± 9, 17 ± 9 and 18 ± 9, respectively. The pain NRS scores changed from 7.0 ± 1.6 to 4.8 ± 2.5, 4.1 ± 2.6, 3.7 ± 2.4 and 3.4 ± 2.3 at the corresponding time points. The NIH-CPSI and pain NRS score at every period after the initial procedure significantly improved compared to pretreatment (all $P < 0.001$).

The proportions of clinical success at 6 months after initial TAE and final follow-up were 70 and 64%, respectively. 90% of clinically successful patients at 6 months after initial TAE maintained response at final follow-up.

Table 2 summarizes the number of patients who used other conservative treatments before initial TAE and at final follow-up. The number of patients receiving one or more conservative therapies decreased from 100% before treatment to 50% at the final follow-up.

Adverse Events

There were some minor complications, including subcutaneous hematoma at the puncture site in six patients, pain at the puncture site in three patients, and hives in one patient, all resolved spontaneously within one week of follow-up. No severe procedure-related complications were recorded.

Discussion

This study retrospectively analyzed 44 patients who underwent TAE for CP/CPPS. The present study observed a significant reduction (≥ 6 points) in the NIH-CPSI scores in 70% at 6-month post-TAE without severe complications. The effect was maintained in 64% for more than 12 months, suggesting TAE used temporary embolic material as a potential alternative therapy for CP/CPPS.

In this study, selective embolization of target arteries was achieved in 95% of patients, and in all cases, selective embolization of at least unilateral prostate artery was achieved. According to a systematic review of prostatic artery embolization (PAE) for benign prostatic hyperplasia (BPH), the success rate of both bilateral and unilateral prostate artery embolization has been reported to be between 76.7–100% [21]. Therefore, TAE for CP/CPPS is considered technically feasible because of its high technical success rate, which is as high as that of PAE for BPH, which is widely performed. Empiric antibiotics, alpha-blockers, and anti-inflammatory drugs are mainly used for CP/CPPS in clinical practice, but they have not demonstrated significant beneficial effects when compared to placebo [8–10]. Recently, a multicenter randomized controlled trial comparing acupuncture with sham treatment for CP/CPPS was reported from China, demonstrating the efficacy of acupuncture [22]. Although acupuncture may be an effective treatment for CP/CPPS, the above study involved 20 acupuncture sessions over 8 weeks, and it may not be feasible to perform similar treatments in all countries. Conversely, TAE for CP/CPPS is a technically feasible procedure for interventional radiologists, as mentioned above, and may be an alternative therapy.

Although the mechanisms underlying the therapeutic effect of arterial embolization on abnormal neovessels using temporary embolization materials has not been fully elucidated, several basic studies have been reported. Kamisako et al. demonstrated a reduction in abnormal neovascularization in a pig model of knee arthritis following intra-arterial administration of IPM/CS [14]. Using a rat frozen shoulder model, Taguchi et al. reported that intra-arterial administration of IPM/CS reduced abnormal neovascularization and inflammatory cells in the synovial membrane of the joint capsule and improved physical activity [15]. Shintaku et al. performed TAE using IPM/CS as an embolizing agent in patients with idiopathic frozen shoulder, reporting reduced FDG-PET accumulation, known to be taken up by inflammatory cells, after TAE when compared with baseline values [12].

There are various theories about the etiology of CP/CPPS. One of the prevailing theories is that inflammation is caused by immune abnormalities or neurogenesis [5, 23, 24]. In addition, in chronic prostatitis, blood vessels proliferate along with fibrous connective tissue, resulting in increased blood supply [25] and a significantly higher blood flow than normal prostate tissue [26]. One possible hypothesis for the decreased symptoms of CP/CPPS in the present study is that embolization of angiogenesis blocks the inflow of proinflammatory cells and reduces inflammation. However, in this study, we selected the treatment vessel based on evoked pain because qualitative evaluation of abnormal neovessels was difficult on angiography. In TAE for pain relief in the musculoskeletal areas, evoked pain is known to be useful in identifying abnormal neovessels [20]. In this study, the prostatic artery was positive for evoked pain in all patients, suggesting that abnormal neovessels may occur at least in the zone dominated by the prostatic artery. Further studies are needed to test these hypotheses, including quantitative dynamic contrast-enhanced MRI evaluation before and after treatment.

Another critical component of CP/CPPS is pelvic floor muscle dysfunction, or increased muscle spasm or tenderness [27]. Therefore, in this study, not only the prostatic arteries, but also the IPAs, the main dominant vessel of the pelvic floor muscles, were considered candidates for treatment. Indeed, in 70% of patients, evoked pain of IPA was positive, and embolization was performed. However, since this was a single-arm, retrospective study, it is unclear whether IPA embolization contributed to the therapeutic effect, and further research is needed to determine the necessity of IPA embolization. In addition, although no severe ischemic complications occurred in the IPA-embolized patients in this study, IPA embolization may cause erectile dysfunction and penile necrosis [28]. From a complication perspective, a short-dissolving temporary embolization material such as IPM/CS should be used when embolizing IPA.

PAE for BPH is widely performed and aims to decrease prostate volume to improve symptoms [21]. Therefore, microspheres, a permanent embolic material, are mainly used in PAE for BPH [21]. In contrast, embolization for CP/CPPS performed in this study aimed to reduce inflammation, and therefore, IPM/CS, a temporary embolic material, was used. All patients in this study had a prostate volume of less than 30 mL, which was different from that in the disease group of BPH, indicating that this treatment was based on a completely different concept from that used in PAE for BPH. Therefore, the embolization procedure in this study should not be adapted to PAE for BPH.

This study has some limitations. First, it was a retrospective study including small number of patients, which could introduce a selection bias, and the nature of a retrospective study makes background generalization difficult. Second, the pure TAE treatment effect may not have

been evaluated because there was no restriction on comorbid treatment and no washout period from the previous treatment. Third, dynamic contrast-enhanced MRI with unified protocol was not evaluated before and after treatment, and it is unclear whether the inflammation improved after TAE. Fourth, because computed tomography or cone beam computed tomography arteriography was not performed, it may have missed some variant vessels that supply the prostate area. Future studies are needed to refine patient selection criteria, investigate underlying mechanisms, and conduct prospective randomized controlled trials, including sham interventions.

Conclusion

TAE with IPM/CS for CP/CPPS demonstrated technical success, safety, and therapeutic efficacy in this retrospective study. The sustained improvement in symptoms over the 12-month follow-up period suggests that TAE is a viable treatment option for refractory CP/CPPS.

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Declarations

Conflict of interest Yuji Okuno has received consulting fee from Asahi Intecc, lecture fee from Terumo, and Daiichi Sankyo outside the submitted work. The rest of the authors declare that they have no conflict of interest.

Consent for Publication Consent for publication was obtained from every individual whose data are included in the study.

Ethics Approval The Institutional Review Board of Okuno Clinic approved this study (Approval Number: OC 2024–007).

Informed Consent Written informed consent was obtained from all patients prior to the procedure, and an opt-out method was used to secure the opportunities for referral from the patients.

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