Original Article

Retrospective observation of the early efficacy and safety of temperature-sensitive liquid embolic agent combined with polyvinyl alcohol microspheres for prostatic artery embolization in the treatment of lower urinary tract symptoms caused by benign prostatic hyperplasia

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Background: In recent years, prostatic artery embolization (PAE) has gradually become a hot topic in the treatment of symptomatic benign prostatic hyperplasia (BPH). However, there is an ongoing debate regarding the best embolization material for PAE. This study aimed to compare the safety and efficacy of the temperature-sensitive liquid embolic agent (TempSLE) combined with polyvinyl alcohol (PVA) microspheres and simple PVA microspheres for PAE in treating lower urinary tract symptoms (LUTS) caused by BPH.

Methods: The clinical data of 39 patients with LUTS caused by BPH were included in this study, including 21 cases of PVA microspheres group and 18 cases of PVA microspheres + TempSLE group. The changes in various subjective and objective indexes were compared between the two groups before PAE, 1 and 3 months after operation.

Results: Three months after operation, the improvement in prostatic volume (PV), post-void residual volume (PVR), peak urinary flow rate (Q_{max}), international prostate symptom score (IPSS), quality of life (QoL) and total prostate-specific antigen (T-PSA) in both groups were significantly improved compared with those before operation ($P<0.05$). And the above clinical improvement indicators at the 3-month mark demonstrated a statistically significant difference between the two groups ($P<0.05$). Compared with the PVA microspheres group, the prostate necrosis rate of the PVA microspheres + TempSLE was higher at 1 and 3 months after operation ($P<0.05$). Moreover, the PVA microspheres + TempSLE group had no significant complications, with the exception of a single case of transient gross hematuria during the perioperative period.

Conclusions: The combination of PVA microspheres and TempSLE for PAE appears to be safe and

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effective in the treatment of symptomatic BPH patients, with a higher degree of damage to hyperplastic prostate tissue compared to simple PVA microspheres embolization.

Keywords: Benign prostatic hyperplasia (BPH); lower urinary tract symptoms (LUTS); prostatic artery embolization (PAE); temperature-sensitive liquid embolic agent (TempSLE); clinical efficacy

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Introduction

Benign prostatic hyperplasia (BPH) is one of the most common benign diseases in middle-aged and elderly men, often accompanied by lower urinary tract symptoms (LUTS) (1). In recent years, prostatic artery embolization (PAE) has gradually become a hot topic in the treatment of symptomatic BPH. The study demonstrated that the clinical efficacy of PAE in the treatment of symptomatic BPH was comparable to that of transurethral resection of the prostate (2). The commonly used embolic agents for PAE are polyvinyl alcohol (PVA) microspheres (3), triacrylic acid gel microspheres (4,5), polyethylene glycol microspheres (6), and n-butyl cyanoacrylate (NBCA) (7).

The temperature-sensitive liquid embolic agent (TempSLE) (8) (Beijing Guanhe Medical Technology Co. Ltd., Beijing, China) is a new type of embolic agent, which is prepared by poly(N-isopropylacrylamide) (PNIPAAm) and iohexol in a certain proportion and dissolved in normal saline. TempSLE is primarily utilized for pre-operative embolization of tumors with abundant blood flow to occlude tumor blood supply arteries, induce tumor tissue ischemia, hypoxia, and necrosis. As a temperature-sensitive hydrogel, PNIPAAm stays in a liquid solution state at low temperatures and undergoes rapid dehydration at temperatures above 30 ℃, followed by the aggregation and contraction of macromolecular chains to form a gel state (9). Due to its non-toxicity, absence of adhesion, biocompatibility and ease of administration, PNIPAAm has been extensively applied in the biomedical and pharmaceutical domains (10-12). Notably, the incorporation of various crosslinkers or natural polymers, such as polysaccharides (13) and proteins (14), along with synthetic polymers like polyethylene glycol (15), has significantly broadened the utilization of PNIPAAm in clinical medicine. However, the safety and efficacy of TempSLE in the treatment of PAE still need to be proved by clinical practice. In this study, the clinical data of patients with BPH treated with different embolic agents were retrospectively analyzed. We initially assessed the safety of TempSLE combined with PVA microspheres by monitoring post-procedural complications in PAE. Subsequently, we calculated indicators, including prostate volume (PV), post-void residual volume (PVR), peak urinary flow rate (Qmax), international prostate symptom score (IPSS), quality of life (QoL), and the rate of embolized tissue necrosis at 1 and 3 months. We present this article in accordance with

Highlight box

Key findings

- Three months after prostatic artery embolization (PAE), the improvement in prostate volume, post-void residual volume, peak urinary flow rate, quality of life, international prostate symptom score and total prostate-specific antigen in the polyvinyl alcohol (PVA) microspheres + temperature-sensitive liquid embolic agent (TempSLE) group were significantly higher than those in the PVA microspheres group.
- Three months after PAE, the prostate necrosis rate was 60.24% with the PVA microspheres + TempSLE group and 37.30% with simple PVA microspheres group.

What is known and what is new?

- In recent years, the application of PAE in the treatment of benign prostatic hyperplasia (BPH) has garnered increasing attention.
- To explore the optimal embolization material for PAE, we retrospectively evaluated the efficacy and safety of PVA microspheres combined with TempSLE versus PVA microspheres alone in the treatment of BPH.
- The efficacy of PVA microspheres combined with TempSLE appears to surpass that of PVA microspheres alone.

What is the implication, and what should change now?

- The combination of PVA microspheres and TempSLE for PAE was safe and effective in the treatment of symptomatic BPH patients, and its degree of damage to hyperplastic prostate tissue was higher than that of simple PVA microspheres embolization.
- These data may assist the interventional radiologist in developing a more comprehensive treatment plan.

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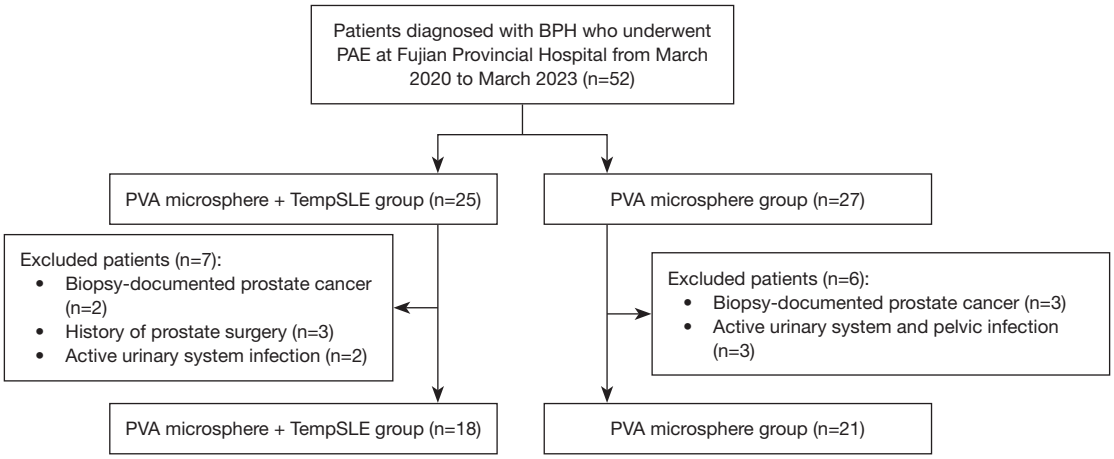

Figure 1 Study flow chart. BPH, benign prostatic hyperplasia; PAE, prostate artery embolization; PVA, polyvinyl alcohol; TempSLE, temperature-sensitive liquid embolic agent.

the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-24-215/rc).

Methods

Patient information

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Medical Ethics Committee of Fujian Provincial Hospital (China) (No. K2023-12-015). The informed consent was waived by the Medical Ethics Committee of Fujian Provincial Hospital due to the retrospective nature of this study.

A total of 39 patients diagnosed with BPH in Fujian Provincial Hospital from March 2020 to March 2023 were included, including 21 patients in PVA microsphere group (group A) and 18 patients in PVA microsphere + TempSLE group (group B) (*Figure 1*).

The inclusion criteria were as follows (16-18): (I) patients diagnosed with BPH complicated with moderate or severe LUTS and showed no obvious effect after 24 months of drug treatment (such as α receptor blockers, 5α reductase inhibitors, etc.), that is, IPSS >20 points, QoL score >3 points; (II) patients with acute urinary retention and cannot or refuse surgery, or unable to remove the catheter after drug treatment; (III) uroflowmetry showed Q_{max} <10 mL/s, and PVR ≥60 mL; (IV) PV >80 cm^3 [PV (cm^3) = 0.52 × anteroposterior diameter (cm) × left and right diameter (cm) × upper and lower diameter (cm)].

The exclusion criteria were as follows (16-18): (I) malignant tumor, prostate-specific antigen (PSA) ≥4.0 ng/mL and (or) imaging examination showed occupying lesions and (or) digital rectal exploration detected occupying lesions, but transrectal biopsy was performed to rule out prostate malignancy; (II) bladder lesions: bladder diverticulum, bladder stones; (III) allergic to iodine contrast medium; (IV) active urinary system and (or) pelvic infection, (V) history of bladder and prostate surgery, history of bilateral internal iliac artery embolization or severe stenosis of internal iliac artery or prostatic artery (PA) orifice, severe atherosclerosis and tortuosity of the internal iliac artery.

Interventional embolization method

PAE was performed by the same group of interventional radiologists in both groups: Seldinger technique was used to puncture the right or left femoral artery under local anesthesia (for patients with severe tortuosity and difficulty in superselective catheterization on the ipsilateral side, catheterization from the other femoral artery can be selected). A 5 F Cobra catheter (Cook, USA) or hepatic artery catheter (Terumo, Japan) was used in ipsilateral 37° oblique position, and left and right internal iliac artery angiography was performed at cephalic 15° oblique position, with a contrast medium flow rate of 3 mL/s, 8 mL total volume, and injection pressure at 400 psi (1 psi = 6.895 kPa). PA was identified by the results of internal iliac artery angiography. Under the guidance of roadmap, 2.2 or 2.6 F microcatheter (Jiangsu Hengrui Medicine Co., Ltd., Jiangsu, China) was super selectively inserted into PA, and anteroposterior PA angiography was performed.

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The contrast medium flow rate was set to 0.5 mL/s, the total amount was 2–3 mL, and the injection pressure was 400 psi. Simple PVA microspheres group (Figure S1): when the 100–300 μm embolic microspheres (Jiangsu Hengrui Medicine Co., Ltd.) was filled to the proximal end of PA, it was necessary to stay at 4–5 min to redistribute and fill the embolic particles in the blood vessels, and then continue to push slowly until they were retained in the blood vessels. The appearance of PA casting indicated the completion of embolization. PVA microspheres + TempSLE group (Figure S2): when PVA microspheres were injected into PA and blood flow was significantly slowed, the prostate tissue was slightly stained during parenchymal phase of repeated angiography, and TempSLE were slowly injected to the proximal end of PA to stay 4–5 min. The microcatheter was withdrawn and angiography was performed to evaluate the degree of embolism and determine the presence of other collateral blood supply. At the end of the operation, the right or left lower limbs were immobilized for 24 hours. Following embolization, the patients continued to receive 5α-reductase inhibitors.

Collection of clinical data

- Perioperative data: operation time (OT), hospital stay time (HST), fluoroscopy exposure time, and dose-area product (DAP) were recorded.
- Laboratory examination: total prostate-specific antigen (T-PSA) and free prostate-specific antigen (F-PSA) were measured by Roche electrochemical method before the operation and at 1 and 3 months after the operation in simple PVA microspheres group and combined embolization group.
- Imaging examination: the PV and postoperative necrosis rate of simple embolization group and combined PVA microspheres + TempSLE group before, 1 and 3 months after embolization were calculated by prostate magnetic resonance imaging (MRI).
- The PVR, Q_{max}, prostate necrosis rate, IPSS, and QoL were measured before embolization, and at 1 and 3 months after embolization. Additionally, the ratios of IPSS, obstruction scores and irritation scores between the postoperative at 3 months and the preoperative condition were measured in two groups.
- Safety assessment: intraoperative or postoperative complications such as hematuria, urinary infection, urethral stricture, urinary incontinence and epididymitis were observed to evaluate the safety of TempSLE combined with PVA microspheres.
- Necrosis rate after embolization: three-dimensionally (3D)-Slicer software (version 5.6.1) was used to compute the volume of prostate necrosis following embolization in two groups. Contrast-enhanced magnetic resonance imaging (CEMRI) images of the prostate at 1 and 3 months after PAE were exported in DICOM format and then uploaded to 3D-Slicer software. Two professional interventional physicians utilized 3D-Slicer software for the 3D reconstruction of both the ischemic necrosis area and the entire prostate region after embolization based on prostate MRI. Following the acquisition of the 3D image of the region of interest, the software automatically measured the volume of the image (*Figure 2*). Percentage of prostate necrosis (named prostate necrosis rate) = volume of prostate ischemic necrosis after embolization/total prostate volume after embolization.

Evaluation of curative effect

Clinical efficacy: the main criterion was that the IPSS score ratio was ≤75%, and Q_{max} increased by at least 3 mL/s (19). According to different ratios, the efficacy was divided into four levels: ≤25% was "good"; 25–50% was "preferably", 50–75% and >75% were "average" and "poor". Similarly, the ratio of obstructive and irritating symptoms was evaluated according to the above grading criteria.

Clinical inefficacy: unable to remove the catheter or cystostomy tube, additional adjuvant treatment was needed to improve symptoms, or IPSS score ratio >75%, Q_{max} increase <3 mL/s.

Statistical analysis

Statistical analysis was carried out using SPSS22.0 statistical software (IBM Corp., Armonk, NY, USA). Shapiro-Wilk test was used to analyze the normality of the measurement data. The measurement data that conformed to a normal distribution were expressed as mean ± standard deviation, while those that did not conform to a normal distribution were described as median (upper and lower quartile) [M (P_{25}–P_{75})]. Independent sample *t*-test was used for measurement data conforming to a normal distribution, and Mann-Whitney *U* rank sum test was used for measurement data not conforming to a normal distribution. Fisher exact

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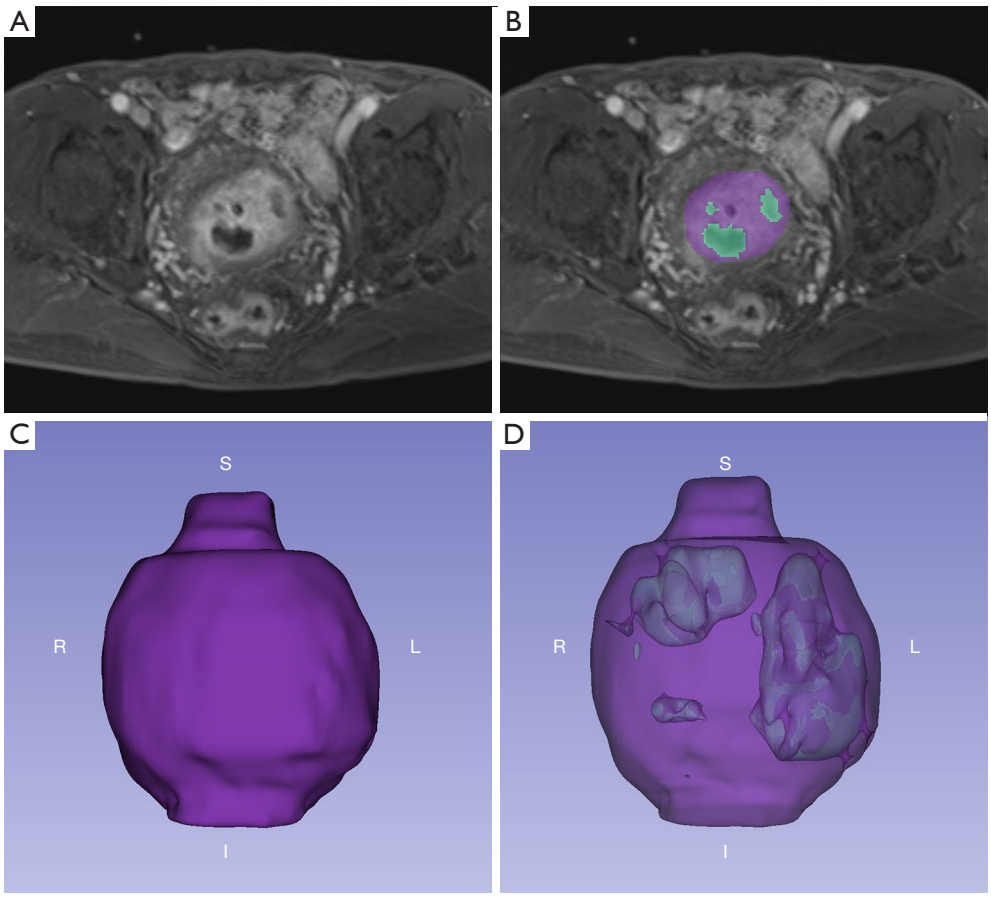

Figure 2 3D-Slicer software was used to 3D reconstruct the entire prostate area after 3 months of PAE and the area of prostate ischemic necrosis after 3 months of PAE. (A) Magnetic resonance images of the prostate after 3 months of PAE; (B) delineated areas of interest; (C,D) constructed 3D stereoscopic images. The purple indicates the entire prostate area, and the green indicates the ischemic necrosis area of the prostate. R, right; L, left; S, superior; I, inferior; 3D, three-dimensionally; PAE, prostate artery embolization.

probability method was used for the counting data that did not meet the relevant conditions of chi-square test. Mann-Whitney *U* rank sum test was used for one-way ordered rank data. PV, IPSS, QoL, PVR, PSA, and Q_{max} assessment at different times were compared by repeated measurement analysis of variance and custom contrast. P<0.05 was considered statistically significant.

Results

Perioperative and postoperative data

Simple PVA microspheres group (group A): there were 21 patients, IPSS 29.57±3.63, PV 119.75 ±30.97 mL, Q_{max} 6.55±1.22 mL/s, 10 patients with urinary retention, and the average duration of indwelling bladder catheterization was 30.00±37.80 days (range, 2–150 days). PVA microspheres + TempSLE group (group B): there were 18 patients, IPSS 30.50±3.87, PV 120.16±32.19 mL, Q_{max} 7.37±1.44 mL/s, 7 cases had catheter because of urinary retention, and the average duration of indwelling bladder catheterization was 30.79±38.12 days (range, 2–160 days). There was no significant difference in baseline data between the two groups (P>0.05) (Table S1). Although OT, fluoroscopy exposure time and HST in the PVA microspheres + TempSLE group were lower than those in the PVA microspheres group, there was no significant difference between the two groups (P>0.05) (*Table 1*).

Comparison of clinical follow-up indexes

At 1 and 3 months after operation, the scores of PV, PVR,

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Table 1 Comparison of procedural details between group A and group B in patients with benign prostatic hyperplasia

Item	Group A	Group B	*T* value or Z value	P value
Procedure time (min)	90.67±5.74	86.28±8.01	1.988†	0.054
Fluoroscopy exposure time (min)	21 (19–24)	19.50 (17.75–22)	–1.235‡	0.22
DAP (mGy·cm^2)	44,331.86±1,047.98	44,526.06±1,117.54	–0.560†	0.58
Hospital stay time (d)	5 (4–5)	4 (4–5)	–0.900‡	0.37

Data are presented as means ± standard deviations or as medians with interquartile ranges in parentheses. Group A: PVA microspheres group. Group B: TempSLE + PVA microspheres group. †, Student *t*-test; ‡, Mann-Whitney *U* test. DAP, dose-area product; PVA, polyvinyl alcohol; TempSLE, temperature-sensitive liquid embolic agent.

Table 2 Comparison of curative effect evaluation indexes at different time points before and after PAE between group A and group B in patients with benign prostatic hyperplasia

Item	Treatment mode (group)	Before operation	1 month after operation	3 months after operation	Statistics of intra-group factor test	Inter-group and intra-group interaction factors (inter-group × intra-group)
PV (mL)	Group A	119.75±30.97	96.61±31.18	76.18±27.32	F =105.154	F =4.028
	Group B	120.16±32.19	92.67±31.07	58.38±25.91*	P<0.001	P=0.03
QoL (points)	Group A	4.95±0.74	2.71±1.15	1.95±0.97	F =275.390	F =7.527
	Group B	4.94±0.80	2.78±0.94	1.22±0.65*	P<0.001	P=0.002
Q_{max} (mL/s)	Group A	6.55±1.22	9.72±2.84	12.24±2.62	F =375.575	F =30.717
	Group B	7.37±1.44	10.64±2.43	16.89±2.79***	P<0.001	P<0.001
PVR (mL)	Group A	187.52±61.29	73.57±26.76	53.14±25.86	F =171.501	F =3.555
	Group B	189.94±64.41	65.00±23.11	30.67±25.09**	P<0.001	P=0.04
IPSS (points)	Group A	29.57±3.63	15.19±6.13	9.81±5.52	F =403.300	F =5.117
	Group B	30.50±3.87	12.89±5.65	5.61±4.41*	P<0.001	P=0.008

Data are presented as means ± standard deviations. Group A: PVA microspheres group. Group B: TempSLE + PVA microspheres group. The comparison between PVA microspheres group and TempSLE + PVA microspheres group was as follows: ***, P<0.001; **, P<0.01; *, P<0.05. The preoperative PV, QoL, Q_{max}, PVR, IPSS between the two groups were comparable (P>0.10). PAE, prostatic artery embolization; PV, prostatic volume; QoL, quality of life; Q_{max}, peak urinary flow rate; PVR, post-void residual volume; IPSS, international prostate symptom score; PVA, polyvinyl alcohol; TempSLE, temperature-sensitive liquid embolic agent.

Q_{max}, IPSS and QoL in both groups were significantly improved compared with those before operation (P<0.05) (*Table 2*). The aforementioned clinical improvement indicators at the 3-month mark demonstrated a statistically significant difference between the two groups (P<0.05 for all) (*Table 2*). Among them, the PV average at 3 months after operation in the simple embolization group decreased by 36.38% compared to before intervention, while in the TempSLE + PVA microspheres group, it decreased by 51.41%. At 1 month after operation, the average values of T-PSA and F-PSA in both groups were higher than those before operation, but decreased at 3 months after operation compared to before intervention (P<0.05) (*Table 3*). Compared with the PVA microspheres group, the improvement of T-PSA in the TempSLE + PVA microspheres group at 3 months after operation was more significant (P<0.05) (*Table 3*). Three months after PAE, the IPSS ratio of the two groups were 33.33% and 66.67%, respectively. The improvement of obstruction and irritation symptoms in the TempSLE + PVA microspheres group was better than that in the PVA microspheres group (P<0.05) (*Table 4*). The prostate necrosis rate at 1 and 3 months after operation in the TempSLE + PVA microspheres group was higher than that in the PVA microspheres group (*Table 5*).

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Table 3 Comparison of PSA results at different time points before and after PAE between group A and group B in patients with benign prostatic hyperplasia

Item	Treatment mode (group)	Before PAE	1 month after PAE	3 months after PAE	Statistics of intra-group factor test	Inter-group and intra-group interaction factors (inter-group × intra-group)
T-PSA (ng/mL)	Group A	5.59±1.51	6.83±1.17	4.00±0.84	F =628.431	F =21.111
	Group B	5.28±1.27	6.98±0.71	2.80±1.02***	P<0.001	P<0.001
F-PSA (ng/mL)	Group A	2.42±1.24	3.43±1.25	2.35±1.10	F =54.986	F =0.411
	Group B	2.28±1.28	3.32±1.62	2.05±1.16	P<0.001	P=0.67

Data are presented as means ± standard deviations. Group A: PVA microspheres group. Group B: TempSLE + PVA microspheres group. The comparison between PVA microspheres group and TempSLE + PVA microspheres group was as follows: ***, P<0.001. The preoperative T-PSA and F-PSA between the two groups were comparable (P>0.10). PSA, prostate-specific antigen; PAE, prostatic artery embolization; T-PSA, total prostate-specific antigen; F-PSA, free prostate-specific antigen; PVA, polyvinyl alcohol; TempSLE, temperature-sensitive liquid embolic agent.

Postoperative complication

According to Clavien (20), the complications were divided into 5 grades. Both PVA microspheres group and TempSLE + PVA microspheres group experienced one case of transient gross hematuria during the perioperative period, and the catheter was removed successfully after embolization. There were no Clavien grade II, III, IV, V complications in both groups.

Discussion

The commonly used embolic agents in clinical practice include particles, microspheres and liquid embolic agents (21). Liquid embolic agents can be divided into two categories: adhesive and non-adhesive. Salet *et al.* suggested that the safety and efficacy of NBCA as an adhesive embolic agent for PAE were comparable to those of microspheres, but with reduced interventional procedure duration and X-ray radiation exposure (22). However, NBCA is absorbed slowly, and vascular remodeling and recanalization occur occasionally (23,24). Additionally, NBCA exhibits strong adhesion, making it prone for the catheter to adhere to the vascular wall during the embolization process. During intravascular polymerization, NBCA can penetrate the vascular endothelium into the interstitial tissue (21), potentially causing damage to the surrounding perivascular tissues. TempSLE (8) is a novel temperature-sensitive embolic agent that falls under the category of non-adhesive embolic agent. Compared to NBCA, TempSLE is absorbed more rapidly. It consists of thermosensitive PNIPAAM hydrogels, iohexol and normal saline. Matsumaru *et al.* were the first to report the use of PNIPAAM as an embolic agent for renal embolization in rabbits in 1996 (25). However, it is worth noting that the embolization material utilized in their study was nonradiopaque. Due to the inclusion of iohexol, TempSLE can be visualized under fluoroscopy, facilitating the monitoring and evaluation of embolism (10). This enables clear observation of the initiation and completion of the embolization process. More importantly, the addition of iohexol can alter both the sol-gel phase transition time and the lower critical solution temperature (LCST) of the copolymer solution (26). The LCST of TempSLE is 30–35 ℃. When the temperature drops below 30 ℃, the material swells in water, and the macromolecular chain expands to form a liquid sol due to hydration; when the temperature reaches 30–35 ℃, the material undergoes rapid dehydration, causing the aggregation and contraction of macromolecular chains, resulting in the formation of gel-like substances. This gel-like state plays a critical role in the process of embolism.

In this study, the PA was embolized for the first time using TempSLE in combination with 100–300 μm PVA microspheres. Due to the spherical shape of PVA, there were still certain gaps between the microspheres after injection into the PA and redistribution. Liquid embolization could effectively fill these gaps and enter the terminal vascular, thereby enhancing the effectiveness of embolization. The liquid nature of TempSLE allows it to diffuse into vascular lumens with a diameter of 100–200 μm or be directly injected into microvessels through slender microcatheters. The sol-gel phase transition of TempSLE occurred within 11 s, and the optimal injection speed is approximately 0.27 mL/s. Therefore, after being released from the microcatheter for 11 s, TempSLE transforms

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Table 4 Efficacy evaluation of patients with benign prostatic hyperplasia in group A and group B 3 months after PAE

Item	Treatment mode (group)	Efficacy level	Number of cases	Percentage (%)	Z value	P value
IPSS score ratio	Group A	Very good	7	33.33	–2.051	0.04
		Good	8	38.10		
		General	6	28.57		
		Poor	0	0.00		
	Group B	Very good	12	66.67		
		Good	4	22.22		
		General	2	11.11		
		Poor	0	0.00		
Obstruction symptom score ratio	Group A	Very good	8	38.10	–2.480	0.01
		Good	8	38.10		
		General	5	23.80		
		Poor	0	0.00		
	Group B	Very good	14	77.78		
		Good	3	16.67		
		General	1	5.56		
		Poor	0	0.00		
Stimulus symptom score ratio	Group A	Very good	8	38.10	–2.135	0.03
		Good	9	42.85		
		General	4	19.05		
		Poor	0	0.00		
	Group B	Very good	13	72.22		
		Good	4	22.22		
		General	1	5.56		
		Poor	0	0.00		

Group A: PVA microspheres group. Group B: TempSLE + PVA microspheres group. IPSS score ratio: IPSS score at 3 months after PAE/preoperative IPSS. Obstruction symptom score ratio: obstruction symptom score at 3 months after PAE surgery/preoperative obstruction symptom score. Stimulus symptom score ratio: stimulus symptom score at 3 months after PAE surgery/preoperative stimulus symptom score. PAE, prostatic artery embolization; IPSS, international prostate symptom score; PVA, polyvinyl alcohol; TempSLE, temperature-sensitive liquid embolic agent.

Table 5 Comparison of prostatic necrosis rates in patients with benign prostatic hyperplasia between group A and group B 1 and 3 months after PAE

Treatment mode (group)	1 month after PAE	3 months after PAE	*T* value	P value
Group A	39.24%±0.98%	37.30%±1.05%	59.935†	<0.001
Group B	61.96%±3.54%	60.24%±3.53%	35.148†	<0.001
T value	–26.363‡	–26.611‡	–	–
P value	<0.001	<0.001	–	–

Data are presented as means ± standard deviations. Group A: PVA microspheres group. Group B: TempSLE + PVA microspheres group. †, paired samples *t*-test; ‡, independent samples *t*-test. PAE, prostatic artery embolization; PVA, polyvinyl alcohol; TempSLE, temperature-sensitive liquid embolic agent.

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into a gelatinous flocculent substance. This transformation makes it difficult for TempSLE to enter the arteries of non-target organs through distal collateral vessels, effectively preventing ectopic embolism.

The correct selection of the diameter of embolic particles is a critical factor influencing the efficacy of PAE. Jeon *et al.* (27) suggested that the smaller the diameter of PVA particles, the more they penetrate into the periphery, and the more effective the PAE is. However, due to the abundant collateral vessels of the PA, the PVA particles with smaller diameter are more likely to cause non-target embolism (28). Brook *et al.* (29) suggested that 500–700 μm particles were the first choice for PAE in a canine model, but the volume and rate of prostate necrotic in the 100–300 μm particle groups were significantly higher than those in the larger particle groups. Garcia-Monaco and colleagues measured the diameter of intraprostatic vessels in 18 White men and found that the diameter of internodal (IT), perinodal (PN) and intranodal (IN) arteries were 155–555, 59–266 and 24–104 μm, respectively, and the diameter of internal prostate artery was not related to PV (30). Hence, particles with a diameter of 300–500 μm may not be able to enter the PN and IN vessels.

Between the first and third months after PAE, both subjective and objective parameters improved in two groups, with the exception of PSA. This observation confirms that PAE can rapidly alleviate LUTS in BPH patients (18). In addition, both subjective and objective parameters at the 3-month mark revealed a statistically significant difference between the two groups ($P<0.05$). This suggested that PAE using TempSLE in combination with PVA microspheres yields a more satisfactory effect in the treatment of patients with BPH.

Sun *et al.* (31) suggested that PAE disrupts the blood supply to enlarged prostate tissue, causing ischemic necrosis or infarction of the prostate tissue and inducing cellular apoptosis. This process leads to prostate atrophy and alleviate LUTS. Ischemia or infarction of prostate tissue after embolization is considered to be a potential predictor of clinical outcomes and reflects the efficacy of embolization to some extent (32,33). Performing CEMRI and utilizing random-effects regression models 2–4 weeks after PAE to examine the predictive role of prostate ischemia, the authors discovered that a lower IPSS during follow-up correlated with a higher percentage of tissue ischemia (32). A recent study utilized contrast-enhanced ultrasound instead of CEMRI to assess the ischemic effect of PAE in treating BPH (34). It revealed that unilateral PAE resulted in lower levels of tissue ischemia and clinical success rates compared to bilateral PAE. The aforementioned observations suggest an association between prostate tissue ischemia and clinical outcomes. In this study, we measured the prostate necrosis rate at 1 and 3 months after PAE by importing the images of CEMRI into 3D-Slicer software. We observed that the improvement in both subjective parameters (QoL, IPSS, obstruction symptom score ratio, stimulus symptom score ratio) and objective parameters (Q_{max}, PVR, PV, prostate necrosis rate) correlated with a higher prostate necrosis rate. Furthermore, the rate of prostate necrosis in the TempSLE + PVA microspheres group was higher than that in the PVA microspheres group at 1 and 3 months post-operation. It suggested that the utilization of TempSLE in conjunction with PVA microspheres can enhance the degree of damage to hyperplastic prostate tissue during PAE and improve the therapeutic efficacy of PAE. We speculate that this is related to the properties of TempSLE. The gelatinous TempSLE entraps a significant number of PVA microspheres, forming a cast within the arteries that supply the prostate, leading to sustained ischemia and necrosis of prostate tissue, thereby increasing the necrosis rate.

T-PSA and F-PSA increased at 1 month after PAE, and gradually decreased to below preoperative levels at 3 months of follow-up. PSA serves as a crucial predictor of the risk of clinical progression (acute urinary retention, urinary tract infection) and the necessity for surgery for BPH in patients (35). The early elevation of PSA may be related to the inflammatory effects of prostatic ischemia induced by PAE (31), and its level can reflect the extent of prostate ischemic lesions after PAE to some extent (3). Comparing the change trends in T-PSA between the two groups, the PVA microspheres + TempSLE group exhibited higher fluctuation amplitude and peak values of T-PSA at 1 month after embolization compared to the PVA microspheres group. Furthermore, the elevated T-PSA level 1 month after embolization was correlated with the improvement in IPSS and Q_{max}. It can be seen from the above that the serum PSA level after PAE appears to be associated with the efficacy of embolization. Nevertheless, Abt *et al.* conducted Spearman rank correlation analysis on 48 patients and failed to find statistically significant correlations between PSA levels after PAE and changes in IPSS ($P=0.48$, $r=-0.10$) and Q_{max} ($P=0.44$, $r=0.12$) (36). In this study, owing to the limited follow-up time for patients, further investigation is required to determine whether the PSA peak can predict the treatment effect of PAE.

In this study, patients were hospitalized for monitoring

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potential complications of ectopic embolism following PAE. The PVA microspheres + TempSLE group was found to have no significant complications, including ectopic embolism, which is consistent with the literature (37,38). The incidence of complications related to PAE is relatively low, primarily attributed to the entry of embolic materials into the blood vessels of adjacent organs, resulting in ischemia of the penis, bladder wall, and rectum (39,40). Generally, with prompt intervention, these complications can be effectively addressed.

The current work is associated with several limitations: this study employed a retrospective design, potentially lacking the adequate power to detect robust differences between the two methods. Additionally, due to the small sample size and short follow-up time of this study, the clinical data obtained cannot fully reflect the true efficacy of TempSLE combined with PVA microspheres.

Conclusions

Using TempSLE embolic agent for PAE seems to be safe and effective. TempSLE combined with PVA microspheres enriches the means of PAE, further improving the degree of damage of embolic microspheres to prostate hyperplasia tissue.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Medical Ethics Committee of Fujian Provincial Hospital (China) (No. K2023-12-015). The informed consent was waived by the Medical Ethics Committee of Fujian Provincial Hospital due to the retrospective nature of this study.

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