Original Article

# Epirubicin-loaded beads transarterial prostatic arterial chemoembolization is a promising treatment for advanced prostate cancer with lower urinary tract obstruction or hematuria—a case series report

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**Background:** Prostatic arterial embolization (PAE) is an effective minimally invasive treatment for lower urinary tract obstruction and hematuria in patients with benign prostatic hyperplasia (BPH). This study was aim to evaluate the safety and short-term efficacy of drug epirubicin-loaded beads transarterial prostatic arterial chemoembolization (DEB-PACE) for the treatment of advanced prostate cancer (PC) with lower urinary tract obstruction or hematuria.

**Methods:** A total of 8 patients with advanced PC undergoing DEB-PACE from August 2020 to February 2022 were retrospectively enrolled. The patients were followed up at 1 week, 1, 3, 6 and 12 months after DEB-PACE. The origin of prostatic arteries, technical success, clinical success rate, duration of the indwelling urinary catheter, International Prostate Symptom Score (IPSS), QoL score (quality of life), prostate volume (PV), prostate-specific antigen (PSA) level and complications were recorded. The short-term efficacy (changes in IPSS, PV and QoL value from baseline to 3 months) were analysed.

**Results:** There were 17 prostatic arteries in 8 patients, which mainly originated from internal pudendal artery (11/17, 64.7%), the technical success rate is 100%. After treatment, the symptoms of lower urethral obstruction in 8 patients were significantly improved that PSA, PV, IPSS and QoL level were significantly reduced. The catheter was successfully removed within 1 week on average, and 2 patients with hematuria disappeared within 5 days. The clinical success rate is 100%. At 1 month postoperatively, mean PV reduction was 30.28±6.963 $cm^3$ (P=0.0457), mean IPSS reduction was 21.13±2.887 points (P=0.0042), mean QoL reduction was 3.75±0.366 points (P=0.006). At 3 months postoperatively, mean PV reduction was 46.14±8.906 $cm^3$ (P=0.0112), mean IPSS reduction was 24.5±2.398 points (P=0.0003), mean QoL reduction was 4.25±0.25 points (P=0.0003). There were no serious complications occurred in all patients.

**Conclusions:** DEB-PACE is a promising treatment for advanced PC with lower urinary tract obstruction or hematuria. However, the efficacy and safety of DEB-PACE for advanced PC is needed to validated by

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prospective large sample randomized controlled study.

**Keywords:** Drug epirubicin-loaded beads; epirubicin; prostatic arterial embolization (PAE); advanced prostate cancer

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## Introduction

Prostate cancer (PC) is an epithelial malignancy that occurs in the prostate and ranks sixth in incidence among malignant tumors and ninth in mortality among men (1,2). Generally, most patients have no obvious clinical symptoms in the early stage of PC and are diagnosed at an advanced stage, losing the best opportunity for treatment. Palliative transurethral prostatectomy (pTURP) is an effective treatment which could improve the symptom of bladder outlet obstruction for advanced PC. However, pTURP could increase the risk of tumor progression, delayed urination after surgery and a high rate of secondary surgery. In addition, many patients have to have long-term indwelling urinary catheters or cystostomy after pTURP, with very poor quality of life (QoL) (3). Prostatic arterial embolization (PAE) is an effective minimally invasive treatment for lower urinary tract obstruction and hematuria in patients with benign prostatic hyperplasia (BPH) or PC (4-6). PAE and TURP obtained statistically significant improvements on International Prostate Symptom Score (IPSS), QoL and prostate volume (PV), in patients with BPH, and PAE had a lower rate of complications than TURP (4,5). A single-center prospective study enrolled 20 patients with PC undergoing PAE [embolized with Docetaxel and 150–300 µm Embosphere microspheres Embolization (Merit Medical Systems, Inc., South Jordan, Utah)] revealed that PAE could significantly reduce the level of prostate-specific antigen (PSA) and PV at 18 months (6). CalliSpheres microsphere is a kind of drug-loaded embolization microsphere, which can embolize the tumor supply vessel and maintain high concentration of anticancer drug in target tumor, resulting in tumor necrosis. It has shown good efficacy and safety in hepatocellular carcinoma patients (7,8). This study was aim to evaluate the safety and short-term efficacy of drug epirubicin-loaded beads transarterial prostatic arterial chemoembolization (DEB-PACE) for the treatment of advanced PC with lower urinary tract obstruction or hematuria. We present the following article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-22-189/rc).

## Methods

### *Participants*

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Meizhou People's Hospital (No. 2020-C-78) and informed consent was taken from all the patients. This is a case series report. Patients with advanced PC complicated with lower urinary tract obstruction or hematuria who treated with DEB-PACE in Meizhou People's Hospital between August 2020 and February 2022 were enrolled. Epirubicin was loaded into CalliSpheres® beads (CB, Hengrui Callisyn Biomedical Technology Co., Ltd., Suzhou, China).

The inclusion criteria were as follows: (I) The patient was diagnosed as PC with pathology; (II) Stage III~IV according to American Joint Committee on Cancer [AJCC, 8th Edition)]; (III) complicated with significant lower urinary tract obstruction or hematuria; (IV) refused to accept surgery and local radiotherapy; (V) the conditions of bilateral iliac vessels could meet the requirements of operation.

The exclusion criteria were as follows: (I) patients who had received radiotherapy or systemic chemotherapy 3 months before DEB-PACE; (II) Karnofsky performance scale (KPS) score less than 60 points; (III) heart, liver and kidney insufficiency (cardiac function grade III and above; aminotransferase (AST) and/or alanine aminotransferase (ALT) >4 times the upper limit of the normal value; and creatinine >2 mg/L); (IV) patients with neurological dysfunction or cognitive impairment; and (V) patients with active infections; (VI) patients with contraindications for PACE and Epi treatment. According to the above inclusion and exclusion criteria, there were 12 patients with advanced PC undergoing DEB-PACE treatment, among which 4 patients had missing data, and 8 patients were included in this study. All 8 patients were complicated with lower urinary tract obstruction and had complete urinary retention before admission, with the need for an indwelling urinary catheter. Two patients were also complicated with hematuria.

### *Chemoembolization*

#### Preoperative preparation

All patients completed the following preoperative examinations:

- (I) Laboratory tests: routine blood, routine urine, coagulation function, liver and kidney function and PSA;
- (II) Imaging examinations: enhanced magnetic resonance (MR) or computed tomography (CT) of the lower abdomen, chest CT, ultrasound of the liver, gallbladder, pancreas, spleen, and urinary system, electrocardiogram, whole body bone scan, etc.
- (III) Antacid (omeprazole 20 mg: Harbin Pharmaceutical Group Bioengineering Co., Ltd., No. 99, Zhuhai Road, Limin Development Zone, Hulan District, Harbin, China) once daily beginning 3 days before surgery and 500 mg of levofloxacin (Daiichi Sankyo Pharmaceutical (Beijing) Co., Ltd., No. 5, Yongchang Middle Road, Beijing Economic and Technological Development Zone, Beijing, China) twice a day on the day before surgery.

#### Operation al procedures

- (I) Instruments and equipment: an Innova IGS 530 system with the function of processing C-arm cone beam CT (CBCT) images and a AW4.6 (Advantage Workstation) postprocessing workstation manufactured by GE (USA) were used.
- (II) Surgical drugs and materials:
  - (i) Chemotherapy drugs: Epi (Pfizer Pharmaceutical Wuxi Co., Ltd., GYZZ H20000496, Mashan No. 7 Bridge, Binhu District, Wuxi, Jiangsu Province, China), 80 mg;
  - (ii) Embolization materials: CalliSpheres beads (CB) (Drug-loaded embolization beads70–150 μm) (Hengrui Callisyn Biomedical Technology Co., Ltd., south building of Building No. 9, 8 Jinfeng Road, Science and Technology City, Suzhou High-tech Zone, product code: CS30) and 8Spheres (PVA embolization beads 100–300 μm) (Hengrui Callisyn Biomedical Technology Co., Ltd., south building of Building No. 9, 8 Jinfeng Road, Science and Technology City, Suzhou High-tech Zone, product code: CS31);
  - (iii) 5F angiographic catheters (Terumo (China) Investment Co., Ltd., Room 805-A, Building 2, Jianguomenwai Street, Chaoyang District, Beijing, CFDA Approval: 20153032356), 0.014'' microguidewire (Terumo (China) Investment Co., Ltd., Room 805-A, Building 2, Jianguomenwai Street, Chaoyang District, Beijing, CFDA Approval: 20173030337), and 2.4F microcatheters (Merit Medical systems, USA, 1600 West Merit Parkway, South Jofdan, Utah84095 USA, batch number: H2130713).
- (III) Operation:
  - (i) Arteriography: with the patient was under local anesthesia, catheter was placed in the common femoral artery, then placed the internal iliac artery, and angiography was performed. During the angiography, the anatomical structure of the prostate artery was closely observed and compared with the preoperative CTA or MRA angiography of the prostate. The prostate supplying arteries should be identified by sagittal, coronal and lateral position observation. Sagittal, coronal and lateral positions were used to identify the prostate supplying arteries, and the collateral supplying arteries of the tumor should be searched to identify all the blood supplying arteries of the tumor. Meanwhile, attention should be paid to looking for collateral supplying arteries of tumors to find all blood supply artery. The results were evaluated by two interventional radiologists with more than 10 years of experience and a senior interventional radiologists including the number and origin of prostatic arteries and anastomotic branches with adjacent arteries.
  - (ii) DEB-PACE: a 2.4F-microcatheter was introduced to selectively catheterize the bilateral PA. Embolization was performed with 70–150 μm CB 1 mL loaded with Epi (60 mg) mixed with nonionic contrast medium at a

ratio of 1:1 under fluoroscopy (CBCT). For patients with PAs >1.2 mm, PVA embolization beads (100–300 µm) were added to supplement the embolization. The end point of embolization was defined as no staining of the prostate and stagnation of blood flow in the peripheral vessels of the tumor-feeding arteries, which had a withered tree branch appearance. Angiography was performed 5 minutes after the chemoembolization procedure.

#### Postoperative treatment

All patients were given analgesics and treatment to protect the stomach and protect against infection for 72 hours. For patients complicated with hematuria, intravenous hemostatic drugs were required, and continuous bladder irrigation was performed using a triple-lumen catheter until the urine was clear. One week after the operation, enhanced MRI of the prostate was performed to evaluate the PV and tumor necrosis. At 5–10 days after the operation, catheter removal was attempted. Adjuvant therapy with a goserelin acetate sustained-release implant and anti-androgen therapy with oral bicalutamide or abiraterone were started on the third postoperative day for all patients.

#### Follow-up

Follow-up was performed at 1 week, 1, 3, 6 and 12 months after the operation, and IPSS, QoL, TPSA, PV, hematuria clearance, duration of the indwelling catheter and complications were recorded. Both the IPSS and QoL were assessed and recorded by the same senior attending interventionalist to control for bias.

### *Efficacy evaluation*

#### Technical success

Chemoembolization of the bilateral PAs was defined according to the criteria reported in previous publications (9-11); otherwise, the procedure was considered a technical failure.

#### Clinical success

(I) Clinical success in patients with lower urethral obstruction was defined as significant improvement in lower urethral obstruction symptoms after embolization, improved QoL, and no serious complications. (II) Recent hemostatic success in patients with hematuria was defined as no further active bleeding 1 month after the intervention or significantly reduced bleeding volume and no need for blood transfusions. Delayed recurrent bleeding was defined as the reappearance of active bleeding 1 month after the operation, requiring a blood transfusion, reintervention, or another interventional therapy (12).

Short-term efficacy (PV as assessed by MRI, serum TPSA, IPSS score [to assess the relief of lower urinary tract symptoms), and QoL score] and adverse reactions (embolism syndrome, gastrointestinal reactions, impaired liver and kidney function, ectopic embolism, etc.) within 12 months after treatment were evaluated.

### *Outcome measures*

Preoperative and postoperative IPSS and QoL scores, serum TPSA, PV assessed by enhanced MRI, disappearance time of hematuria, and duration of the indwelling catheter, perioperative embolization complications including ischemic bladder necrosis, penile necrosis, ischemic necrosis of buttock and perineal skin, nerve injury, and postembolization syndrome were recorded in detail.

### *Statistical analysis*

SPSS 22 software was used for the statistical analysis of the data. Measurement data are expressed as the mean ± SD, and count data are expressed as frequencies and percentages. For IPSS and QoL, within-group differences between baseline, 1-week, 1-month and 3-month evaluations were compared using nonparametric test (Friedman test). For PV, within-group differences between baseline, 1-week, 1-month and 3-month evaluations were compared using mixed-effects analysis of variance models. All tests are 2-tailed, $P<0.05$ was considered statistically significant.

## Results

### *Baseline characteristics of the patients*

A total of 12 patients with advanced PC complicated with lower urinary tract obstruction or hematuria were treated with DEB-PACE in our hospital from August 2020 to February 2022, among whom 4 patients had irregular reexaminations; therefore, 8 cases with advanced PC were included in this case series report. The age of the 8 patients ranged from 68 to 90 years, with a mean age of 77.63±

8.314 years; the Gleason score ranged from 7 to 10, with a mean of 8.50±0.9258; the PV of the patients ranged from 34.944 to 146.39 cm³, with a mean of 86.20±37.70 cm³; the PSA level of the patients ranged from 30.99 to 1,000 ng/mL, with a mean of 326.3±418.8 ng/mL; the IPSS score ranged from 20 to 35, with a mean of 31.63±5.655; and the QoL score ranged from 5 to 6, with a mean of 5.625±0.5175 (*Table 1*).

### *PA origin*

Intraoperative angiography revealed a total of 17 PAs in 8 patients. There were 9 left PAs, of which 6 originated from the internal pudendal artery (66.67%, 6/9), 1 originated from the superior vesical artery (11.11%, 1/9), 1 originated from the inferior vesical artery (11.11%, 1/9), and 1 originated from the inferior gluteal artery (11.11%, 1/9). There were 8 right PAs, of which 4 originated from the internal pudendal artery (50.00%, 4/8), 1 originated from the inferior vesical artery (12.25%, 1/8), 1 originated from the inferior gluteal artery (12.25%, 1/8), and 2 originated from the anterior branch of the internal iliac artery (25.00%, 2/8) (*Table 2*).

**Table 1** Baseline characteristics of the patients

| Variable | Mean | SD | Range |
|---|---|---|---|
| Age (years old) | 77.63 | 8.314 | 68–90 |
| Gleason score | 8.5 | 0.9258 | 7–10 |
| PV ($cm^3$) | 86.20 | 37.70 | 34.944–146.39 |
| PSA (ng/mL) | 326.3 | 418.8 | 30.99–1,000 |
| IPSS | 31.63 | 5.655 | 20–35 |
| QoL | 5.625 | 0.5175 | 5–6 |

IPSS, International Prostate Symptom Score; PSA, prostate-specific antigen; PV, prostate volume; QoL, quality of life; SD, standard deviation.

### *Short-term efficacy*

The average follow-up time for the 8 patients was 6.75 months (3–12 months). Lower urinary tract obstruction significantly improved in all 8 patients after the operation. The catheter was successfully removed on average at 1 week after the operation. The urine of the 2 patients with hematuria turned clear 3 days after the operation, and gross hematuria disappeared 5 days after the operation. One week after the operation, the urine test was negative for red blood cells, and there was no gross hematuria during the follow-up period. The clinical success rate was 100%.

#### PSA level

The normal PSA level is generally smaller than 4 ng/mL. In PC, PSA levels can increase to greater than 10 ng/mL which can significantly assist clinical diagnosis. Preoperatively, the PSA levels of all 8 patients were much greater than 10 ng/mL (the mean was 326.3±418.8 ng/mL), and after D-PACE, the PSA levels of the patients decreased significantly. One month after D-PACE, the PSA levels in 2 patients decreased to the normal range (28.57%, 2/7), and 3 months after D-PACE, the PSA levels in 5 patients decreased to the normal range (62.5%, 5/8). Six months after D-PACE, one patient had a slight increase in PSA, but the level remained below 10 ng/mL. Twelve months after the surgery, the PSA level in 2 patients decreased to the normal range (*Table 3*).

#### Lower urinary tract obstruction symptoms

PC can lead to the continuous enlargement of the prostate gland, which in turn compresses the urethra, making the urethra narrow and thus resulting in progressive dysuria and seriously affecting the QoL of patients. Therefore, changes in prostate symptoms are also an important factor when investigating the efficacy of PC treatment. In this paper, the IPSS [which ranges from 0 to 35 points, i.e., asymptomatic to severe symptoms, divided into 3 grades (mild, moderate,

**Table 2** The origin of prostatic arteries in patients

| Prostatic artery | Number | The origin of the prostatic arteries (n, %) | | | | |
|---|---|---|---|---|---|---|
| | | Internal pudendal artery | Superior vesical artery | Inferior vesical artery | Inferior gluteal artery | Anterior trunk of internal iliac artery |
| Left | 9 | 6 (66.67) | 1 (11.11) | 1 (11.11) | 1 (11.11) | 0 |
| Right | 8 | 4 (50.00) | 0 | 1 (12.50) | 1 (12.50) | 2 (25.00) |

 

**Table 3** The changes in PSA level after chemoembolization

| Patient | D-PACE date | TNM | Gleason | Before | PSA after treatment (ng/mL) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 week | 1 month | 3 months | 6 months | 12 months |
| 1 | 2020/8/24 | T4N1M1c | 8 | 145.471 | 243.68 | 22.863 | 6.09 | 3.35 | 0.038 |
| 2 | 2020/11/5 | T3N2M0 | 7 | 30.992 | 11.93 | 1.79 | 0.04 | 0.018 | 0.009 |
| 3 | 2021/4/7 | T4N1M1a | 8 | 39.12 | – | – | 0.21 | 0.11 | – |
| 4 | 2021/5/31 | T3N1M1 | 9 | 155.638 | 215.68 | 88.814 | 2.55 | 7.48 | – |
| 5 | 2021/6/18 | T4NxMx2 | 10 | 1,000 | 1,000 | 742.14 | 165.823 | 43.48 | – |
| 6 | 2021/8/2 | T4N1Mib | 8 | 156.658 | 21.516 | 0.887 | 0.022 | – | – |
| 7 | 2021/8/9 | T4NxMx | 9 | 82.236 | 40.398 | 53.361 | 272.625 | – | – |
| 8 | 2021/8/11 | T4N1M0 | 9 | 1,000 | 1,000 | 159.124 | 2.23 | – | – |

PSA, prostate-specific antigen; TNM, tumor, lymph node, metastasis.

**Table 4** PV in 8 patients after chemoembolization

| Patient | Before | PV after treatment ($cm^3$) | | | | |
|---|---|---|---|---|---|---|
| | | 1 week | 1 month | 3 months | 6 months | 12 months |
| 1 | 74.614 | 79.523 | 26.832 | 22.471 | 17.662 | 7.032 |
| 2 | 114.065 | 108.165 | 76.424 | 61.002 | 45.864 | 35.568 |
| 3 | 107.848 | – | – | 43.680 | 20.966 | – |
| 4 | 34.944 | 34.944 | 34.944 | 22.277 | – | – |
| 5 | 49.889 | 29.336 | 22.131 | 14.669 | 10.616 | – |
| 6 | 102.703 | 83.398 | 47.902 | 21.622 | – | – |
| 7 | 59.165 | 59.585 | 39.836 | – | – | – |
| 8 | 146.390 | 121.738 | 36.000 | 41.787 | – | – |

PV, prostate volume.

and severe), i.e., 1–7 points, mild; 8–19 points, moderate; and 20–35 points, severe], QoL score (which ranges from 0 to 6 points; the higher is the score, the lower the QoL) and PV were used to assess the prostate function of the patients.

The normal PV is 4*3*2 cm (12.48 $cm^3$). Preoperatively, the PV level of all 8 patients were larger than 12.48 $cm^3$, and that of 4 patients exceeded 100 $cm^3$. As shown in *Table 4*, mean PV reduction was 9.297±4.517 $cm^3$ (10.79%) at 1 week, mean PV reduction was 30.28±6.963 $cm^3$ (35.13%) at 1 month, mean PV reduction was 46.14±8.906 $cm^3$ (53.53%) at 3 month. In two of the four patients followed, PV decreased to normal level at 6 and 12 months postoperatively, respectively.

Preoperatively, all 8 patients had severe dysuria symptoms (mean 31.63±5.655 points), with a very poor QoL (5.625±0.5175 points). And all patients showed significant improvement in lower urinary tract obstruction symptoms and quality of life after treatment. At 1 week postoperatively, the prostate symptoms of 5 patients changed from severe to moderate, mean IPSS reduction was 10.13±3.367 points (32.03%); at 1 month postoperatively, the prostate symptoms of 2 patients have turned to moderate and 6 patients to mild, mean IPSS reduction was 21.13±2.887 points (66.80%); at 3-month postoperatively, the prostate symptoms of 6 patients have turned to moderate and 2 patients to mild, mean IPSS reduction was 24.5±2.398 points (77.46%). And the prostate symptoms have turned to mild in 6 patients followed at 6 and 12 months postoperatively (*Table 5*).

At 1 week postoperatively, 6 patients had a slight

 

**Table 5** IPSS for 8 patients after chemoembolization

| Patient | Before | IPSS after treatment | | | | |
|---|---|---|---|---|---|---|
| | | 1 week | 1 month | 3 months | 6 months | 12 months |
| 1 | 26 | 18 | 9 | 5 | 5 | 5 |
| 2 | 35 | 28 | 13 | 7 | 6 | 7 |
| 3 | 35 | 35 | 5 | 5 | 3 | – |
| 4 | 20 | 19 | 17 | 10 | 5 | – |
| 5 | 32 | 30 | 7 | 7 | 5 | – |
| 6 | 35 | 17 | 11 | 7 | 6 | – |
| 7 | 35 | 12 | 10 | 12 | – | – |
| 8 | 35 | 13 | 12 | 4 | – | – |

IPSS, International Prostate Symptom Score.

**Table 6** QoL score for 8 patients after chemoembolization

| Patient | Before | QoL score after treatment | | | | |
|---|---|---|---|---|---|---|
| | | 1 week | 1 month | 3 months | 6 months | 12 months |
| 1 | 5 | 4 | 2 | 1 | 1 | 1 |
| 2 | 5 | 3 | 2 | 1 | 1 | 1 |
| 3 | 6 | 6 | 1 | 1 | 1 | – |
| 4 | 5 | 4 | 3 | 2 | 1 | – |
| 5 | 6 | 6 | 1 | 2 | 1 | – |
| 6 | 6 | 3 | 2 | 1 | 1 | – |
| 7 | 6 | 3 | 2 | 2 | – | – |
| 8 | 6 | 3 | 2 | 1 | – | – |

QoL, quality of life.

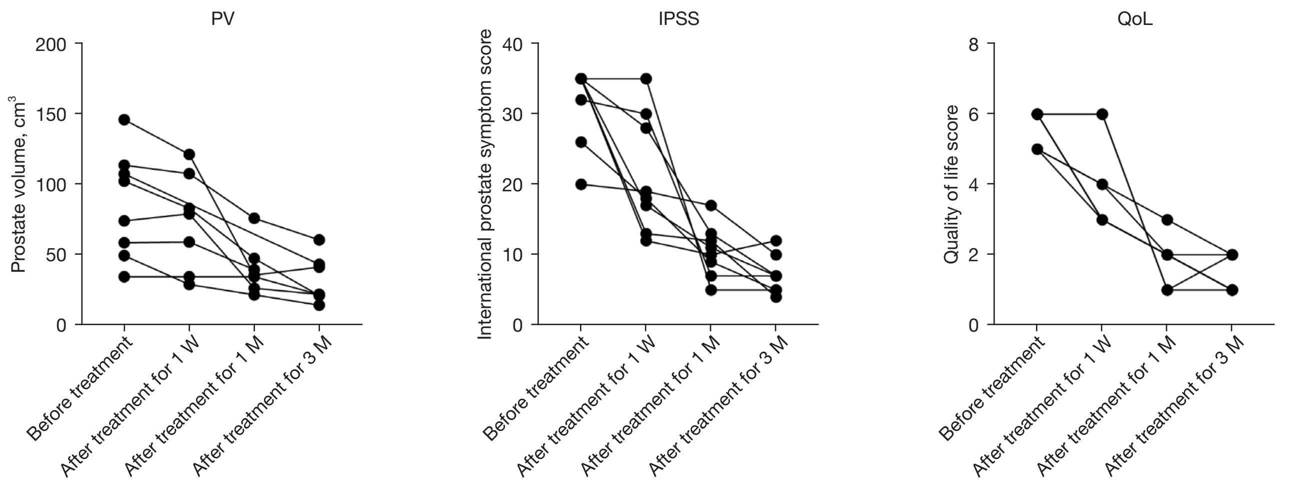


**Figure 1** Change in biochemical parameters and scale scores in 8 patients. PV, prostate volume; IPSS, International Prostate Symptom Score; QoL, quality of life.

improvement in QoL, mean QoL reduction was 1.625±0.4606 points (28.89%); at 1 month postoperatively, 7 patients had a slight improvement in QoL, mean QoL reduction was 3.75±0.366 points (66.67%); at 3 month postoperatively, 7 patients had a slight improvement in QoL, mean QoL reduction was 4.25±0.25 points (75.56%); and the QoL score have decreased to 1 point, which indicated that patients feel good about their current quality of life, in 6 patients followed at 6 and 12 months postoperatively (*Table 6*).

In addition, we assessed the short-term efficacy (1 week, 1 month and 3 months after treatment) (*Figure 1*). Most of the improvement is observed during the first 1 months. At 1 month postoperatively, mean PV reduction was 30.28±6.963 $cm^3$ (86.20±37.70 *vs.* 40.58±17.89 $cm^3$, P=0.0457), mean IPSS reduction was 21.13±2.887 points (31.63±5.655 *vs.* 10.50±3.703, P=0.0042), mean QoL reduction was 3.75±0.366 points (5.625±0.518 *vs.* 1.857±0.641, P=0.0060). At 3 months postoperatively, mean PV reduction was 46.14±8.906 $cm^3$ (86.20±37.70 *vs.* 32.50±16.66 $cm^3$, P=0.0112), mean IPSS reduction was 24.5±2.398 points (31.63±5.655 *vs.* 7.125±2.696, P=0.0003), mean QoL reduction was 4.25±0.25 points (5.625±0.518 *vs.* 1.375±0.518, P=0.0003) (*Tables 7,8*).

In summary, the PV, IPSS and QoL scores for patients significantly decreased after D-PACE compared with those

**Table 7** Mean values before treatment and after treatment (*Figure 1*)

| Variable | Before treatment | After treatment for 1 week | After treatment for 1 month | After treatment for 3 months |
|---|---|---|---|---|
| PV ($cm^3$), mean ± SD | 86.20±37.70 | 73.81±34.86 | 40.58±17.89 | 32.50±16.66 |
| IPSS, mean ± SD | 31.63±5.655 | 21.50±8.435 | 10.50±3.703 | 7.125±2.696 |
| QoL, mean ± SD | 5.625±0.518 | 4.000±1.309 | 1.857±0.641 | 1.375±0.518 |

IPSS, International Prostate Symptom Score; PV, prostate volume; QoL, quality of life; SD, standard deviation.

**Table 8** P values before treatment and after treatment (*Figure 1*)

| Comparison time period | P value | | |
|---|---|---|---|
| | PV | IPSS | QoL |
| Before treatment *vs.* after treatment (1 week) | 0.1192 | 0.8784 | >0.9999 |
| Before treatment *vs.* after treatment (1 month) | 0.0457 | 0.0042 | 0.0060 |
| Before treatment *vs.* after treatment (3 months) | 0.0112 | 0.0003 | 0.0003 |
| After treatment (1 week) *vs.* after treatment (1 month) | 0.0846 | 0.3168 | 0.1990 |
| After treatment (1 week) *vs.* after treatment (3 months) | 0.0368 | 0.0537 | 0.0221 |
| After treatment (1 month) *vs.* after treatment (3 months) | 0.3234 | >0.9999 | >0.9999 |

PV, prostate volume; IPSS, International Prostate Symptom Score; QoL, quality of life.

before D-PACE, and D-PACE significantly improves the symptoms of lower urinary tract obstruction and hematuria in patients with advanced PC.

### *Typical case (the No. 1 patient)*

An 81-year-old male patient was admitted to the hospital due to progressive dysuria for more than 1 year, with acute urinary retention and catheter indwelling. Preoperatively, the patient's PV was 89.86 $cm^3$ (6.0 cm × 4.5 cm × 6.4 cm), with multiple organ metastases in bone, liver and lung, which indicated that he was in advanced stage of PC. Pathological examination of prostate biopsy showed Gleason score of 8 point (4+4) (*Figure 2*). In addition, the PSA level was abnormally increased with a concentration of 145.471 ng/mL, and the patient had severe dysuria (IPSS score was 26 points) and poor quality of life (QoL score was 5 points).

As shown in *Figure 3*, DSA angiography showed that one prostatic artery on the left and one on the right originated from the internal pudendal artery, which was confirmed by multidimensional observation and reconstruction of CBCT. Embolization was performed with 70–150 μm microspheres loaded with 60 mg epirubicin until the blood flow stopped in the prostatic artery. Two prostatic arteries have reached the end point of embolization. After embolization, the patient had no serious adverse reactions, but mild perineal pain lasting about 1 week, which could be relieved by taking tramadol sustained release tablets without affecting daily life. And punctured skin damage in perianal and perineal areas, which healed after 1 week.

After DEB-PACE treatment, the symptoms of lower urinary tract obstruction and the quality of life were significantly improved in the patient. At 1 week postoperatively, the catheter was successfully removed and the patient was able to self-relieve urine with smooth urination. As shown in *Figures 4*-7 and *Figure 8A*, the PV of the patient also gradually decreased after surgery, and was reduced to the normal size of 7.03 $cm^3$ at 12 months. As shown in *Figure 8B*, the patient's PSA level increased 1 week after surgery, but gradually decreased 1 month later, decreasing to the normal level of 3.35 ng/mL at 6 months. In addition, IPSS and QoL scores decreased gradually with time (*Figure 8C,8D*). At 3 months, the patient had only mild dysuria (IPSS score was 5 point) and was satisfied with his current quality of life (QoL score was 1 point). No recurrence was found during the 12-month follow-up in the patient.

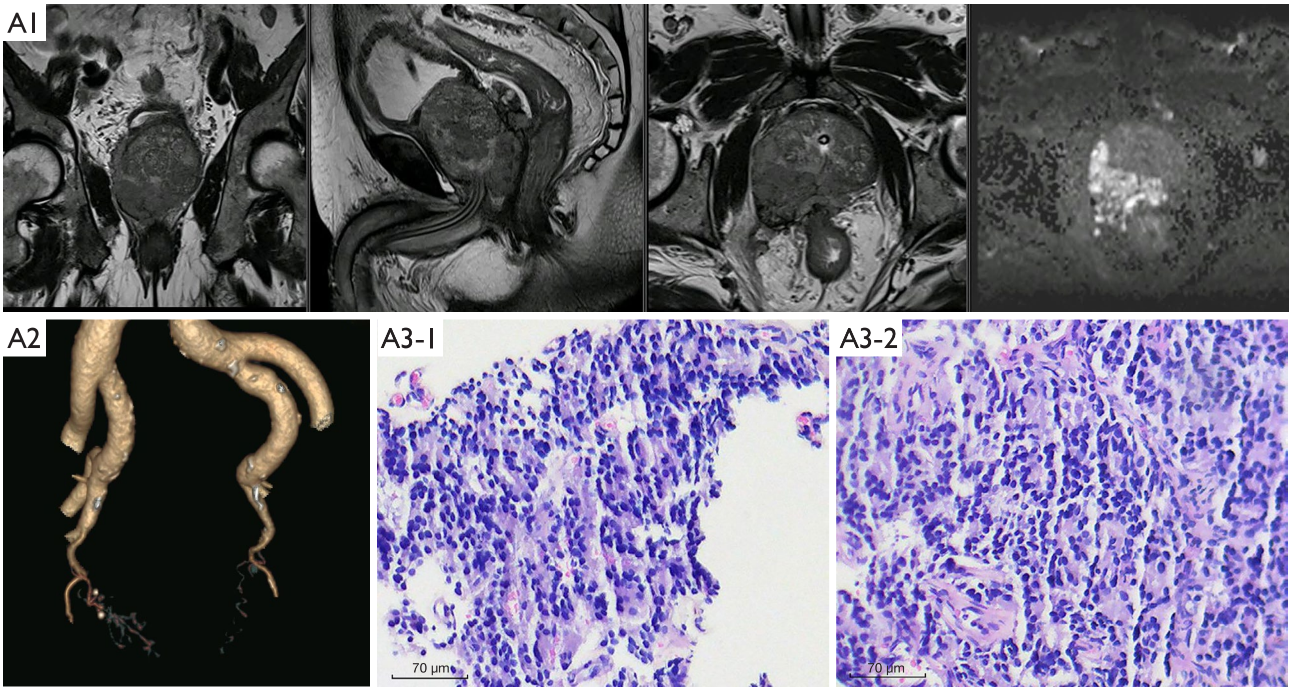


**Figure 2** Preoperative MRI findings: A1: PV approximately 6.0 cm × 4.5 cm × 6.4 cm, irregular soft tissue mass shadow observed on the right side of the central gland-right peripheral zone, and DWI sequence showed high signal intensity. A2: CTA of the bilateral prostate arteries (VR). A3: prostate biopsy pathology (Hematoxylin eosin staining; 200×): tumor cell nuclei were enlarged, with some showing nucleoli and abundant cytoplasm; the cells were arranged in cribriform and solid structures, and glandular lumen formation was still visible, with a Gleason score of 4 + 4 = 8 points and a WHO/ISoP grade of 4. MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; CTA, computed tomography angiography; PV, prostate volume.

### *Complications*

After the operation, 1 patient had a perineal punctate skin defect, and 1 patient had an ischemic area, approximately 0.5 cm × 0.5 cm, on the left side of the penile urethral orifice; both were cured by symptomatic treatment within 2 weeks. One patient had anterior rectal wall ischemia, as determined by MRI on the 6th day after the operation; however, there were no clinical manifestations of rectal necrosis, and no rectal fistulas or rectal perforations were observed after close follow-up for 1 month. None of the patients had disabling or fatal complications.

## Discussion

PAE was first applied in refractory BPH patients with bleeding (13). After PAE treatment, the bleeding symptom of BPH patients disappeared, and the symptoms associated with lower urinary tract obstruction were significantly relieved, without serious complications and sexual dysfunction. The prostate shrank by nearly 40% at 12 months follow-up. The principle of PAE is similar to the treatment of uterine artery embolization, which is mainly to embolize the blood supplying artery of the prostate, leading to local ischemic necrosis of the prostate, and gradually reduce its volume (14).

The accurate identification of PAs is key to the success of PAE for its fine diameter and great variation in anatomical origin. Studies (15,16) have shown that PAs vary greatly, with a maximum of 4 branches on one side, mainly originating from the internal pudendal artery, superior vesical artery, and gluteal-pudendal artery trunk, which were consistent with this study. Bilhim *et al.* (15) used a combination of DSA and CTA to determine the origin of PAs. In this study, a complete preoperative CTA/MRA evaluation was combined with intraoperative CBCT, and the results were interpreted by 2 interventional surgeons with more than 10 years of experience. It was found that PAs tend to have anastomotic branches with adjacent organs, such as the bladder, penis, and rectum; therefore,

 

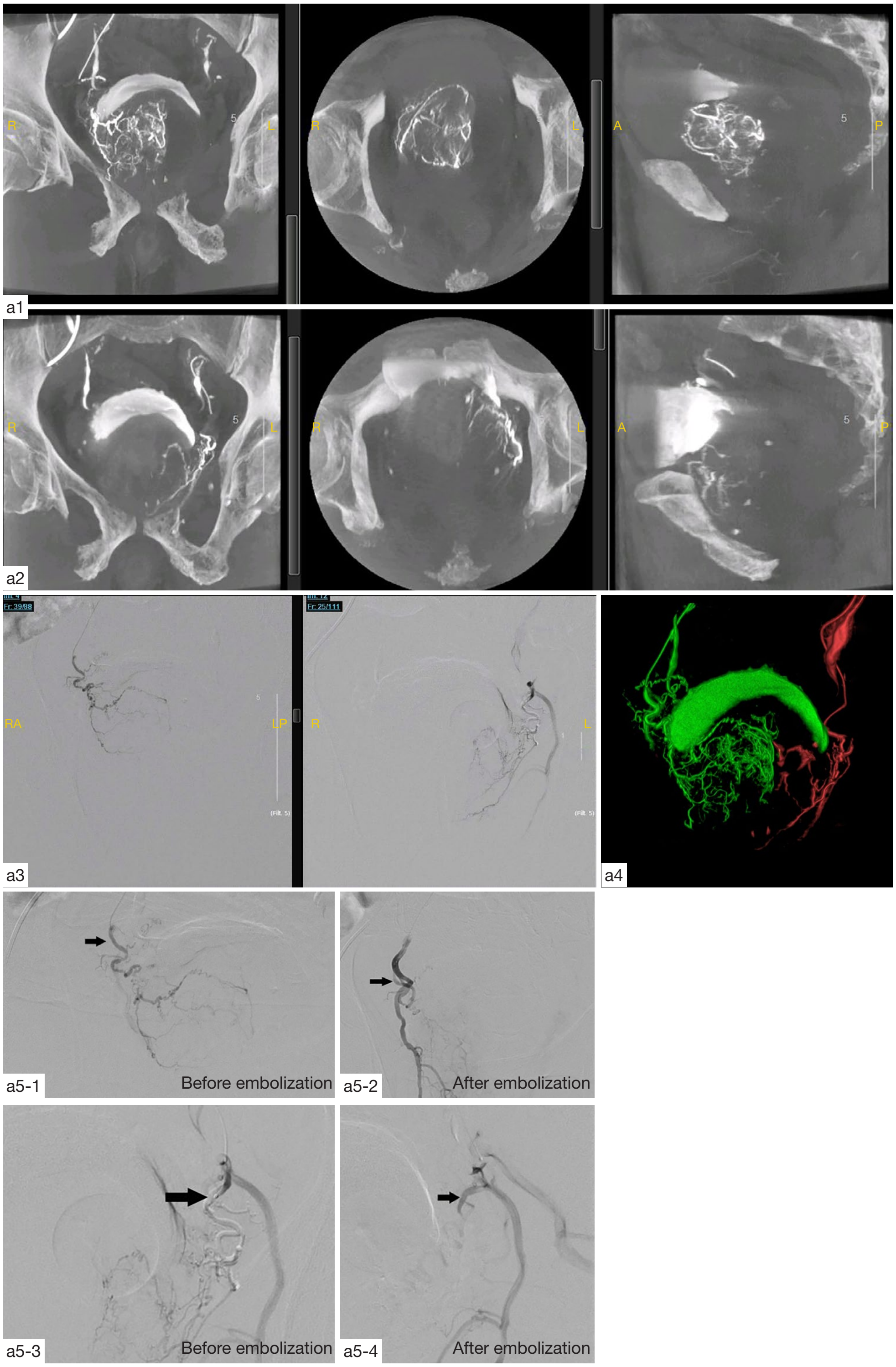


**Figure 3** Intraoperative DSA and C-arm CT images, a1: C-arm CT of the right PA in the coronal, transverse and sagittal planes; a2: C-arm CT of the left PA in the coronal, transverse and sagittal planes; a3: bilateral PAs; a4: CBCT of the bilateral PAs (VR); a5-1-2: DSA images of the right PA before and after embolization; a5-3-4: DSA images of the left PA before and after embolization; the black arrows indicate the prostate artery. PA, prostate arteries; DSA, digital subtraction angiography; CBCT, C-arm Bundle Computed Tomography; A, ahead; P, post; R, right; L, left; RA, right ahead; LP, left post.

 

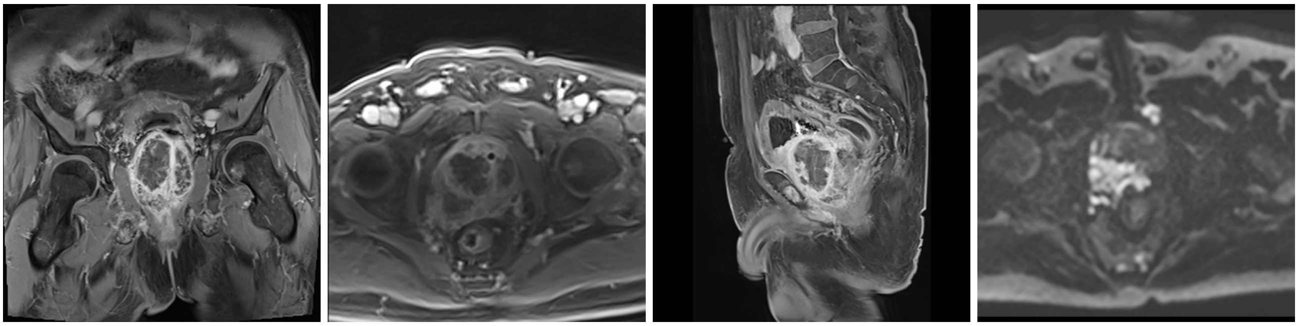

**Figure 4** MRI findings at 1 week after the operation: PV was approximately 5.4 cm × 4.8 cm × 5.9 cm, the soft tissue mass shadow was slightly smaller than that in previous MRI findings, the high signal intensity of the DWI sequence was weaker than that in previous MRI findings, and the range was smaller than that in previous MRI findings. MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; PV, prostate volume.

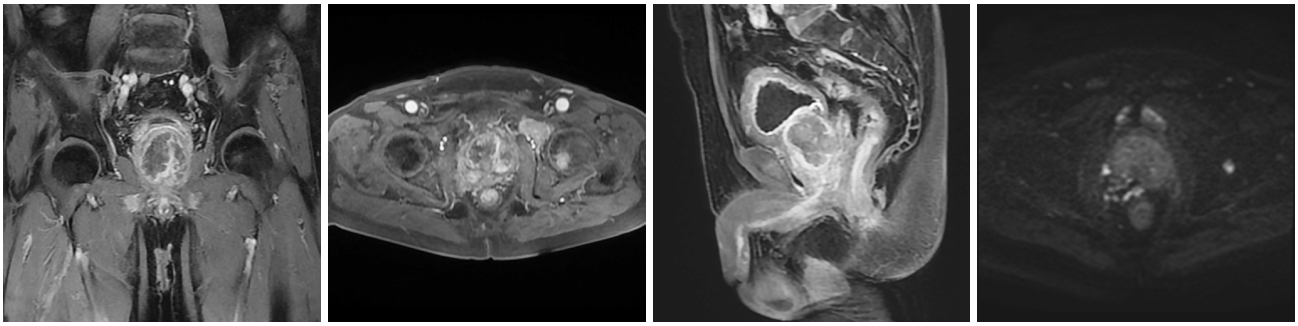

**Figure 5** MRI findings at 1 month after the operation: the PV was approximately 4.3 cm × 3.0 cm × 4.0 cm at 1 month after the operation, the soft tissue mass shadow was smaller than that in previous MRI findings, and the range of the DWI sequence with high signal intensity continued to decrease. MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; PV, prostate volume.

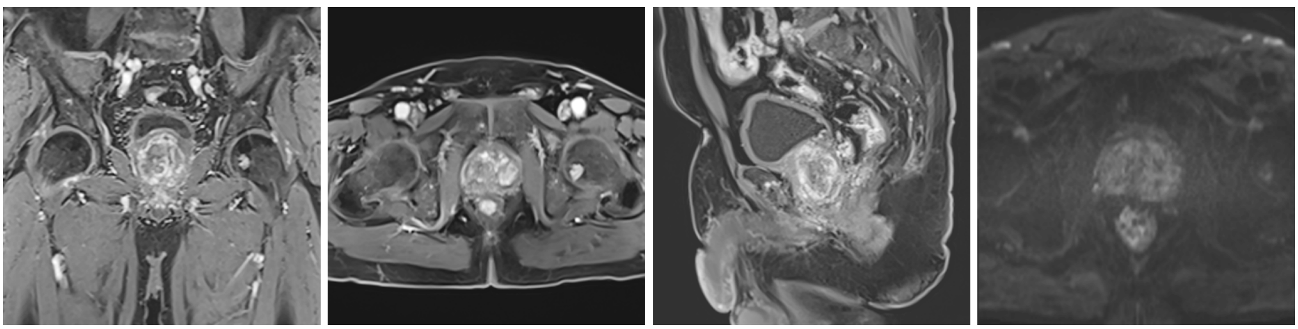

**Figure 6** MRI findings at 3 months after the operation: the PV was approximately 3.4 cm × 3.1 cm × 4.1 cm, the soft tissue mass shadow was further reduced than before, the region with high signal intensity of DWI sequence almost disappeared. MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; PV, prostate volume.

extra attention should be paid to avoiding the ischemic necrosis of adjacent organs caused by ectopic embolisms. The technical success was 100% in this study.

The selection of embolization materials is critical to the efficacy of prostatic arterial chemoembolization (PACE). Currently, the embolization materials include PVA

 

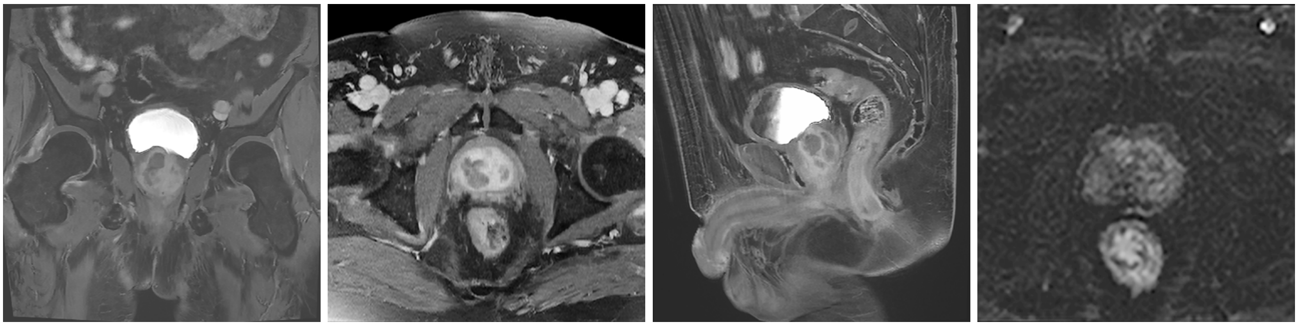

**Figure 7** MRI findings one year after the surgery: PV was approximately 2.8 cm × 2.3 cm × 2.1 cm, soft tissue mass shadow was not obvious anymore, and the region with high signal intensity (DWI) disappeared. MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; PV, prostate volume.

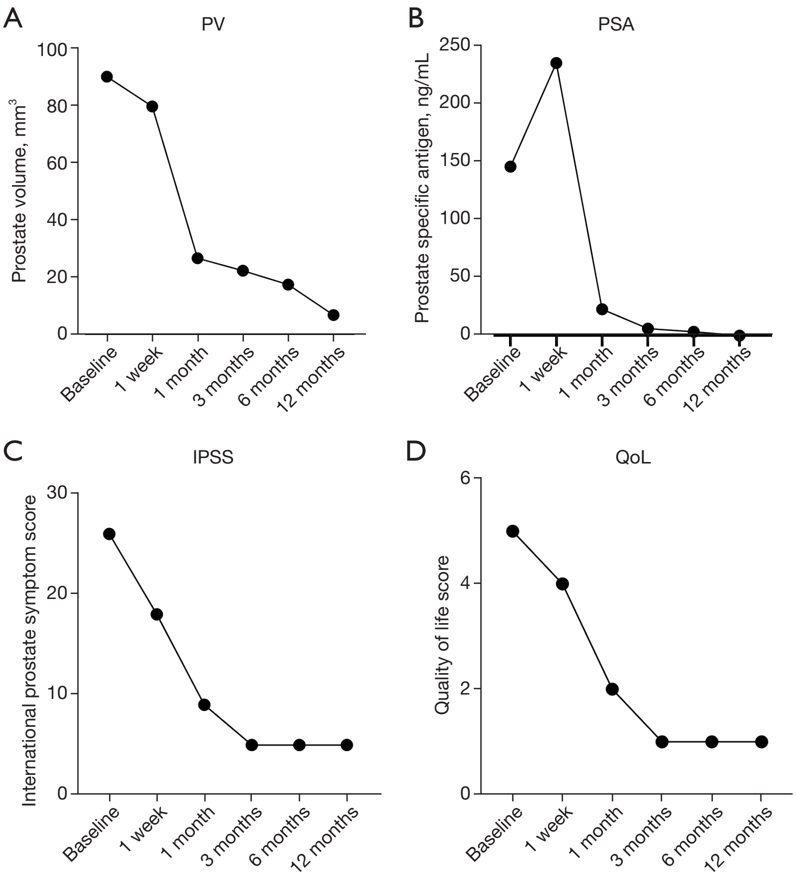


**Figure 8** Changes in biochemical parameters and scale scores in No. 1 patient. (A) PV; (B) PSA; (C) IPSS; (D) QoL. PSA, prostate specific antigen; PV, prostate volume; IPSS, International Prostate Symptom Score; QoL, quality of life.

particles, gelatin sponge beads, and polypropylene beads, with diameters ranging from 100 to 500 µm (17). Iodized oil conventional transarterial chemoembolization (c-TACE) employs mixtures of lipiodol and chemotherapeutics as suspensions for injection. Although c-TACE could improve the drug concentration in local tissues, uncontrollable drug release reduces local efficacy. Furthermore, the particle sizes in lipiodol suspensions are difficult to control, potentially causing serious complications for ectopic embolization. Drug-eluting bead transarterial chemoembolization (DEB-TACE) can deliver high concentrations of chemotherapy drugs to targeted lesions and release them slowly locally, thereby reducing systemic adverse reactions. In addition, tumor blood supply artery was blocked by beads, resulting in tumor necrosis for ischemia, hypoxia (18). DEB-TACE has been applied in the treatment of hepatocellular carcinoma patients and showed a good long-term efficacy (8,9). CB is a polymerized sulfonic group-modified PVA hydrogel bead that is routinely stored in NaCl solution. CB contains negatively charged organic small molecule groups, which can adsorb positively charged anticancer drugs such as adriamycin, epirubicin, pirubicin, arsenic trioxide and irinotecan by using positive ion exchange mechanism. The 2019 EAU-EANM-ESTRO-ESUR-SIOG guidelines recommend Epi as a selective treatment for advanced PC. Epi-loaded CBs contain a large amount of adsorbed drug and can release the drug for up to 1 month (19). CBs have been widely used in the treatment of primary liver cancer, but there is no relevant study on the use of Epi-loaded CBs in the treatment of PC.

There are few effective treatments for patients with advanced PC complicated with lower urinary tract obstruction or hematuria. pTURP is an effective treatment which could improve the symptom of bladder outlet obstruction for advanced PC. However, pTURP could increase the risk of tumor progression, delayed urination after surgery and a high rate of secondary surgery. In addition, many patients have to have long-term indwelling urinary catheters or cystostomy after pTURP, with very poor quality of life (QoL) (3). Zhou *et al.* (20) used pTURP combined with endocrine therapy to treat advanced PC complicated with bladder outlet obstruction, leading to significant improvement in the prostate function and clinical symptoms in a short period of time. However, there occurred serious postoperative complications such as electro resection syndrome, bleeding, and urethral stricture. And there was no significant difference in the long-term survival of patients compared with that of patients who received endocrine therapy alone. Many patients had to have a long-term indwelling catheter or cystostomy, resulting in a poor QoL. Xie *et al.* (21) used 100~300 μm PVA microspheres (Merit Medical Systems, USA) for PACE treatment in 32 PC patients. The PV of patients decreased by 47.82% on average at 8 weeks after treatment. In a single-center prospective study, docetaxel combined with PVA microspheres chemoembolization was used for the treatment of PC, Pisco *et al.* (6) reported that the technical success rate was 80.0% and that 31.3% of patients experienced adverse events. The study suggested that PACE might be an effective and safe treatment for patients with localized PC. In this study, DEB-PACE treatment was used in advanced PC patients complicated with lower urinary tract obstruction or hematuria. The clinical success rate was 100%. The PV of patients decreased by 53.53% on average at 3 months after treatment. And the symptoms of lower urinary tract obstruction and hematuria significantly improved in all 8 patients after treatment. The catheter was successfully removed on average at 1 week. However, there are some limitations in this study. Firstly, this study is a retrospective study. Secondly, the sample size of this study is limited and without a control group. Thirdly, the follow-up time is short. Therefore, a large sample, prospective randomized controlled trial with long-term follow-up is need to be confirmed the effect and safety of this method in the future.

In summary, DEB-PACE treatment with CBs (70–150 μm) loaded with Epi for advanced PC patients showed good short-term efficacy and no serious complications. It was indicated that DEB-PACE might be a selective treatment for advanced PC patients in the future. But the results need to be confirmed in large sample, prospective randomized controlled trials.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://tau.

 

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*Data Sharing Statement:* Available at https://tau.amegroups.com/article/view/10.21037/tau-22-189/dss

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-22-189/coif). The authors have no conflicts of interest to declare.

*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 Ethics Committee of Meizhou People's Hospital (No. 2020-C-78) and informed consent was taken from all the patients.



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