Large inoperable leiomyosarcoma of the prostate: treated by transcatheter arterial chemoembolization with drug-eluting microspheres

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Abstract

Background: Prostatic leiomyosarcoma (LMS) has a poor prognosis with a median overall survival (OS) of 15–18 months. For patients with metastatic disease, radical surgical resection, with or without adjuvant systemic chemotherapy and radiation therapy, unfortunately provides limited therapeutic benefit. Novel approaches for this lethal disease are urgently needed.

Objectives: To evaluate the feasibility and efficacy of transarterial chemoembolization (TACE) with doxorubicin-eluting HepaSpheres (HS) for inoperable LMS of the prostate.

Methods: This case series included 12 patients (median age 57 years, range 32–74) with inoperable LMS of the prostate who were treated with TACE using doxorubicin-eluting HS. All patients were pathologically proved by fine-needle biopsy. Symptomatic relief, complications, OS, and local disease control based on modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria were evaluated.

Results: Symptomatic relief, including control of the gross hematuria, removal of indwelling catheters, improvement of constipation and perineal pain, were obtained in 100%, 75%, 100%, and 86%, respectively after TACE, without any major complications. At the last follow-up after TACE, the percentage of the tumor necrosis and volume reduction were present with a median value of 90% and 84%, respectively. TACE after two to four sessions allowed subsequent surgical resection in five (41.7%) patients. The median follow-up time was 29 months; the survival rate at 1, 2, and 3 years was 91.7%, 83.3%, and 41.7%, respectively, and the median OS was 29 months [range 9–49 months].

Conclusions: TACE of inoperable LMS of the prostate appears to be safe and effective in providing tumor necrosis, shrinkage, and symptom relief; that could improve the quality of life and the survival rate of these patients.

Keywords: digital subtraction angiography (DSA), leiomyosarcoma, lower urinary tract symptoms, prostate

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Introduction

Leiomyosarcoma (LMS) of the prostate is a rare primary malignant neoplasm of prostatic smooth muscle that accounts for less than 0.1% of all prostate malignancies and typically follows an aggressive clinical course. It is the most common primary sarcoma of the prostate in adults, accounting for 38% to 52% of primary prostatic sarcomas. The majority of the prostatic LMSs are high-grade hypercellular lesions composed of intersecting bundles of eosinophilic spindle-shaped cells with increased mitotic activity and moderate to severe nuclear atypia. High-grade prostatic LMSs typically exhibit prominent necrosis and cystic degeneration. Unlike stromal sarcomas, which often contain scattered normal prostatic...
glands, the high grade prostatic LMSs are devoid of prostatic glands except at the interface between tumor and normal adjacent prostatic tissue.3,4 Low grade prostatic LMSs can be distinguished from LMS by the presence of distinct nuclear atypia, mitotic activity, increased cellularity and focal infiltration of normal prostatic parenchyma.1,4 Stromal tumor of uncertain malignant potential (STUMP) of the prostate, an extremely rare prostate specific stromal tumor, is marked by epithelial hyperplasia, without atypia, mitoses, and no necrosis.5

Clinically, the lack of early specific symptoms results in more advanced disease at presentation. Multimodality treatment combinations including surgery, pre or postoperative radiation therapy, and neoadjuvant or adjuvant chemotherapy have been used in the management of prostatic LMS, but there are no standard treatment recommendations.1,6,7 For patients with regional or distant metastatic disease, radical surgical resection, with or without adjuvant systemic chemotherapy and radiation therapy, unfortunately provides limited therapeutic benefit.1,7 In a study by Sexton et al.,1 six patients received surgery after preoperative neoadjuvant treatment, only three patients (50%) had appreciable downsizing of the primary tumor.1 Therefore, novel approaches for this lethal disease are urgently needed.

Transarterial chemoembolization (TACE) has been widely used for the treatment of solid tumors, especially in hypervascular tumors.8–10 However, there is no report on the efficacy of TACE therapy for LMS of the prostate. Because LMS of the prostate is a hypervascular and rapidly progressive tumor, and usually presents with a large prostatic mass and obstructive urinary symptoms,1–4 TACE through the feeding arteries can be hypothesized to be an effective palliative treatment. The purpose of this study was to evaluate the effectiveness and safety of TACE with doxorubicin-eluting HepaSpheres (HS) for the treatment of symptomatic inoperable LMS of the prostate, especially in palliation.

Patients
This case series included 12 patients (median age 57 years, range 32–74) with inoperable LMS of the prostate who were treated with TACE using doxorubicin-eluting HS. Between January 2014 and May 2018, patients meeting the following criteria were included in the study: presence of a symptomatic histologically confirmed LMS of the prostate; no evidence of distant metastases at initial presentation; en-bloc resection not possible; refractory gross hematuria; recurrence or relapse of symptoms after radiation therapy and/or resistance to systemic chemotherapy and/or radiation therapy. TACE was approved in a multidisciplinary team (MDT) meeting, consisting of a urologist, medical oncologist, radiation oncologist, and interventional radiologist. The exclusion criteria were: patient with cachexia status with expected survival <3 months, chronic renal failure (serum creatinine >1.2 mg/dL), active urinary tract infection [>= Common Terminology Criteria for AE (CTCAE) grade 2], unregulated coagulation parameters (>= CTCAE grade 2), and allergic to iodized contrast media (>= CTCAE grade 2).

All patients had clinical and laboratory evaluation as well as cross-sectional imaging with contrast enhanced computed tomography (CT) or magnetic resonance imaging (MRI) of the pelvis prior to and following the procedure to assess for tumor response. The radiotherapy and chemotherapy were ineffective for the 12 patients having progressive disease after neoadjuvant radiation and chemotherapy. Prior to TACE, all patients received neoadjuvant radiation with goals of tumor shrinkage and improved resectability in 1.8–2 Gy/day fractionated doses to a total of 50–56.4 Gy. Concurrent chemotherapy was given in 10 patients for three to six cycles, with doxorubicin, ifosfamide, vincristine or platinum based combination, as suggested by other authors.1–4 Chemotherapy was not used in two because of patient preference.

Patients and methods

Ethics statement
This case series study was approved by the hospital review boards of Chinese Peoples Liberation Army General Hospital (approval number: S2019-313-01; Clinical trial registration number: ChiCTR1900028819), and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all the patients for the study, including properly explaining the aims, methods, anticipated benefits and potential hazards of the procedure. All patients agreed to complete the clinical, laboratory, and imaging follow-up, according to the study protocol.
Pathological evaluation

Transrectal ultrasound-guided needle biopsy was performed in the 12 patients. The diagnosis of LMS of the prostate was made by histological and immunohistochemical examinations in all the patients. Eight tumors were high grade, typically exhibiting high-grade hypercellular lesions, intersecting bundles of eosinophilic spindle-shaped cells and moderate to severe nuclear atypia; four tumors were low grade, exhibiting distinct nuclear atypia, scattered mitoses, mitotic activity, increased cellularity, and focal infiltration of normal prostatic parenchyma.

Embolication technique

Preparation of doxorubicin-eluting HS was performed as suggested by the manufacturer. One vial of 25 mg of dry HS 50–100μm (HS; BioSphere Medical, Roissy-en-France, France) was prehydrated with 10 mL of normal saline (N/S, 0.9% NaCl) for 10 minutes. Each vial of HS was loaded with 50–90 mg of doxorubicin (Pfizer Pharmaceuticals Ltd., Wuxi, China), calculated on the basis of body surface area (75 mg/m²). The vial was agitated every 10–15 minutes for 60 minutes to complete the ionic bonding of doxorubicin. After the loading period, all the supernatant was extracted, and an equal quantity of nonionic contrast (Visipaque 320 mg/mL; GE Healthcare, Co., Cork, Ireland) diluted with saline (1:1) was added to form the final suspension for injection. The protocol used in this study provided for the administration of up to two bottles of doxorubicin-eluting HS per treatment, for the maximum allowable dose of 100 mg doxorubicin.

TACE was performed by an interventional radiologist (MQW), with 25 years’ interventional radiology experience, using a digital subtraction angiography unit (INNOVA 4100 IQ; GE Healthcare, Milwaukee, WI, USA) and the non-ionic contrast medium. Under local anesthesia with 5 mL 2% lidocaine, a 4-Fr vascular sheath (Terumo, Tokyo, Japan) was inserted into the right femoral artery with the Seldinger technique. Pelvic digital subtraction angiography (DSA) was performed using a 4-Fr pigtail-type catheter (Cordis, Miami Lakes, FL, USA) to evaluate the iliac vessels. Next, DSA was performed using a 4-Fr Simmons I catheter (Cordis) at the anterior division of the iliac artery with the purpose of identifying feeder arteries. In patients with identification of tumor feeder vessels that were challenging, cone-beam computed tomography (CB-CT) was performed, using a coaxial 2.6-Fr microcatheter (Progreat; Terumo, Tokyo, Japan).

The doxorubicin-eluting HS particles were slowly injected under fluoroscopic guidance. The embolization endpoint was determined by obliteration of tumor blush and sluggish flow through the feeding arteries. If there was still flow after using up two bottles of the eluting HS particles, the polyvinyl alcohol (PVA) particles 300–500μm (PVA foam embolization particles; Cook Inc., Bloomington, IN, USA) were injected to achieve complete stasis of the feeding arteries. When the multiple feeding arteries were identified, the doxorubicin-eluting HS were injected into the main feeders, and the other arterial branches were embolized with PVA 300–500μm.

Follow-up

Clinical and imaging follow-up for 6 months was planned for all patients but collection of imaging and clinical follow-up continued until the end of May 2018 depending on the symptoms for all patients. A physician (XM) from the department of urology in our hospital was responsible for the clinical outcome assessment after TACE. All patients received imaging follow-up using MRI with contrast injection. The first MRI follow-up was performed at 1 month after TACE for evaluation of the primary effectiveness and detection of complications, then subsequently MRIs were obtained at 2–3 months and thereafter depending on clinical follow-up, to assess the local efficacy and the absence of local tumor progression.

Patients with residual lesions underwent retreatment approximately 6–8 weeks after the preceding procedure until a radiological complete response was observed. Patients who achieved a complete response were then followed by means of 3-monthly laboratory and MRI investigations. TACE was discontinued in patients who exhibited disease progression (local or extra-pelvic) or
treatment intolerance, those who translated from unresectable to resectable tumors, and those who refused to continue the study.

**Outcome measures**

**Safety evaluation.** Technical success was defined as successful embolization of all angiographically identifiable arterial supply to the tumor. Adverse events (AEs) of TACE were graded according to National Cancer Institute Common Terminology Criteria for AE (NCI CTCAE), version 4.03 (CTCAE v4.03). Renal function was monitored by serum electrolytes, urea, creatinine, and creatinine clearance; liver function was monitored by glutamicoxaloacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), alkaline phosphatase, and bilirubin; and cardiac function was monitored by electrocardiograms, Doppler echocardiograms, and myocardial enzyme levels. Significant or major AEs were defined as ≥CTCAE grade 2, with higher than the upper limit of normal values. The index of Erectile Function short form (IIEF-5) was used to evaluate the erectile function. A total IIEF-5 score ranges from 5 to 25. Severity of erectile dysfunction (ED) can be classified into the following five categories: no ED (22–25), mild (17–21), mild-to-moderate (12–16), moderate (8–11), and severe (5–7).

**Efficacy evaluation.** Clinical success was defined as cessation of gross hematuria within 1 week after TACE, significant pain relief and constipation, and improvement of the urinary obstruction symptoms with removal of indwelling catheters. For the perineal pain evaluation, patients were asked to rate their pain severity from 0 to 10 (0 = no pain, 1–2 = light pain, 3–5 = moderate pain, 6–7 = severe pain, 8–10 = very severe pain), prior to TACE. Constipation was grading as mild: (a) feces cold be removed by forced defecation without impact on daily life; (b) moderate: defecation difficulty with impact on daily life, needed medicine to defecate; and (c) severe: dependence of defecation on cathartic or defecated by enema. The outcome measures were TACE response, disease status at last follow-up, and overall survival (OS). Tumor response of target lesions in each patient after treatment was assessed by dynamic contrast-enhanced MRI, based on the modified Response Evaluation Criteria in Solid Tumors (mRECIST). Complete response (CR) was defined as the absence of any enhanced tumor. Measurements of ischemic volume, total tumor volume (volume = length × depth × width × 0.5233), and ratio of ischemic volume to total tumor volume were calculated, by using segmented manual measurements on each axial section, performed by two diagnostic radiologist (HYY and YGS) with 20 and 12 years of experience in interpreting body MRI, respectively, in consensus reading.

**Statistical analysis**

Overall survival (OS) was determined from the date of diagnosis until the date of death from prostate sarcoma. Median follow-up time was determined by using the reverse Kaplan–Meier method.

**Results**

**Patient characteristics**

A total of 12 patients were included and the characteristics are summarized in Table 1. The median age at presentation was 57 years (range 32–74; mean ±20 years). The presenting symptoms were urinary obstruction in 12 patients (100%). Perineal pain was present in seven patients: moderate in five and severe pain in two patients. Constipation was present in seven patients: moderate in five and severe in two patients. The median interval from the onset of clinical symptoms to admission to our hospital was 2.5 months (range 0.5–5 months). The median serum prostate-specific antigen (PSA) level was 1.39 ng/mL (range 0.39–2.5 ng/mL; normal range <4 ng/mL).

The median maximum diameter of the tumor was 11.5 cm (range 9–18 cm) with median volume of 720 mL ± 160 (range 410–890 mL) measured by MRI. The diagnosis of LMS of the prostate was made using transrectal ultrasound-guided needle biopsy in all patients. At diagnosis, three patients were diagnosed with stage II (local lesion with the pelvic lymph node metastasis) and nine patients were diagnosed with stage III (local lesion with bladder or/and rectal invasion). Metastatic work-up, including chest/abdomen CT scan and bone scan, did not reveal any evidence of distant metastasis. Blood tests showed normal liver and kidney function. No abnormality was found in cardiac examination. No ED had been reported pre-TACE in six patients, moderate ED in three, and severe in three patients.

**Technical outcomes**

TACE was repeated on an as-needed basis, and a total of 29 TACE sessions were performed (one...
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A second or more sessions of TACE were performed due to the establishment of collateral supply to the tumor after the first TACE. One of the 12 patients underwent TACE once, six patients underwent two sessions, four patients underwent three sessions, and one patient underwent four sessions.

The arterial supply to the tumors identified by DSA and CB-CT included from the prostatic arteries \( (n = 28) \), the superior vesical arteries \( (n = 7) \), the branches of the internal pudendal arteries \( (n = 4) \), the middle rectal arteries \( (n = 4) \), the inferior epigastric artery \( (n = 4) \), the obturator artery \( (n = 3) \), the middle sacral arteries \( (n = 3) \), the iliolumbar artery \( (n = 2) \), and the inferior mesenteric arteries \( (n = 2) \). Seven patients (58.3%) presented with multiple feeders supplying and five (41.7%) patients had only PAs feeding arteries. Representative cases are shown in Figures 1–4.

The detailed information for TACE-related adverse events (CTCAE v4.03) is summarized in Table 2. No major complications (CTCAE v4.03 > grade II) were noted. The low grade fever, urethral burning, and perineal pain were treated with non-opioid analgesic and non-steroidal anti-inflammatory drugs and disappeared before discharge. The other minor adverse events (CTCAE v4.03, grade I), including nausea, poor appetite,
frequency, and a small amount of rectal bleeding, were self-limiting and disappeared during the first 1 week. There was no marked chemotherapeutic agent-induced toxicity noted during TACE. Normal sexual function had been reported pre-TACE in six patients and no erectile dysfunction or ejaculatory disorders occurred post-TACE in these patients; there was no improvement or deterioration of sexual function in these patients with ED prior to TACE.

**Clinical outcomes**

After a median follow-up of 29 months (range 9–52), five patients (41.7%) had died of their disease progression systemically, with a median survival of 26 months (range 9–37 months, 26.6 months ± 10); seven patients (58.3%) were alive at last follow-up with a median survival of 29 months (range 19–49 months, 32 months ± 10): five patients were disease free (three treated with TACE alone and two treated with TACE plus...
surgery) and two patients were alive with disease (one treated with TACE alone and one treated with TACE plus surgery), confirmed by MRI. Overall, the survival rate at 1, 2, and 3 years was 91.7%, 83.3%, and 57.1%, respectively, and the median OS was 29 months (range 9–49 months, 29.8 months ± 18).

TACE allowed subsequent surgical resection in five cases (41.7%): two cases underwent radical prostatectomy (RP) and three cases underwent radical cystoprostatectomy (RCP) with urinary reconstruction. Pathological examination showed complete necrosis in the excisional specimens in three patients. The remaining two patients had 90% and 95% of the necrotic area within the tumors, respectively (Table 3). Surgical margins were microscopically positive in one patient (20%) and the margins were negative in the remaining four (80%) patients. The

Figure 2 (Case 2). The tumor blood supply originated from the multiple feeders. A 47-year-old man presented with progressive obstructive voiding symptoms and repeated episodes of gross hematuria for the past 2 months. For relief of his urinary retention, a transurethral catheter was inserted. Pathological examination of the prostate needle biopsy indicated leiomyosarcoma confirmed with immunohistochemical staining. [A] Digital subtraction angiography (DSA) of the pelvic arteries shows a large hypervascular mass (asterisk) supplied from the branches of the internal iliac arteries (white straight arrow); [B] DSA of the inferior mesenteric artery (white straight arrow) shows the contrast tumor staining (asterisk); [C] DSA of the middle sacral artery (white straight arrow) shows the contrast staining in the lower part of the tumor (asterisk); [D] Axial contrast-enhanced T1-weighted magnetic resonance image (MRI) obtained before transcatheter arterial chemoembolization (TACE) shows a large hypervascular tumor arising from the prostate gland (asterisk) with infiltrating the bladder. Noted the indwelling catheter (white straight arrow); and [E] Axial contrast-enhanced T1-weighted MRI obtained at 18 months after four sessions of TACE shows almost complete necrosis of the prostatic tumor (asterisks). Subsequent radical prostatectomy was performed and pathological examination showed complete necrosis in the excisional specimen with negative margins. No further treatments were performed and he is alive asymptomatic with imaging disease free during his 42 months of follow-up.
Figure 3 (Case 6). A 62-year-old man with prostatic leiomyosarcoma presented with progressive obstructive voiding symptoms for 4 months. (A) Digital subtraction angiography (DSA) of the right prostatic artery (PA) [white straight arrow] shows a large hypervascular mass [asterisk] in the right lobe of the prostate; (B) DSA of the left PA [white straight arrow] shows the large hypervascular mass [asterisk] in the left lobe of the prostate; (C) Pelvic cone-beam computed tomography (CB-CT) with coronal MIP reformat after selective catheterization of the right PA [white straight arrow] shows the large hypervascular tumor [asterisk]; (D) Pelvic CB-CT with coronal MIP reformat after selective catheterization of the left PA [white straight arrow] shows the large hypervascular tumor in the left lobe of the prostate [asterisk]; (E) Axial contrast-enhanced T1-weighted magnetic resonance image (MRI) obtained before transcatheter arterial chemoembolization (TACE) shows a large hypervascular tumor arising from the prostate gland [asterisk]. Noted the indwelling catheter [white straight arrow]; (F) Axial contrast-enhanced T1-weighted MRI obtained at 1 month after TACE shows complete necrosis of the prostatic tumor [asterisks]; and (G) Axial contrast-enhanced T1-weighted MRI obtained at 36 months after two sessions of TACE shows complete shrinkage of the prostatic tumor with residual scar [asterisk]. Transrectal biopsy of the prostate at 24 months after TACE revealed no malignant cells. No further treatments were performed and he is alive asymptomatic with imaging disease free during his 38 months of follow-up. The patient was able to remove the bladder catheter at 2 weeks after PAE and was catheter-free at his last follow-up.

MIP, maximum intensity projection.
median OS for those with TACE plus surgery was 36 months and median OS for those with TACE alone was 26 months (Table 3; \( p = 0.03 \)).

After TACE, the gross hematuria was completely stopped in all 10 patients within 24, 48, and 72 hours in four, three, and three patients, respectively, translating to a 100% clinical success rate in control of the bleeding. During a median follow-up of 25 months (range 6–37 months), six of the 10 patients exhibited good bleeding control and did not require further emergency admission to treat hematuria. In the remaining four patients, hematuria recurred after 2–3 months and was controlled medically.

After TACE, nine of the 12 patients recovered spontaneous urination within 1 week (\( n = 2 \)), 2 weeks (\( n = 3 \)), and 4 weeks (\( n = 4 \)), respectively. During follow-up, five patients underwent surgical treatment (RP = 2, RCP = 3) after TACE with no need for a catheter; four patients were catheter-free at their last follow-up. Three patients had persistent difficulty voiding after TACE and they continued to receive catheterization therapy. At the first month after TACE, constipation was
Improved in 100% (7/7) from ≥moderate to mild constipation (n = 4) or normal defecation (n = 3); perineal pain was improved significantly in 85.7% (6/7) from ≥moderate to light (n = 5) or no pain (n = 1).

MRI follow-up
All tumors demonstrated a marked response to TACE (Table 3). After the last TACE, the percentage of necrotic area within the tumor ranged from 65% to 100%, with a median value of 90% (mean 90% ± 10; Figures 1–4). Tumor volumes were reduced by 35%–100% (median 83.6%; interquartile range (IQR) 91.6–42.3%; mean, 71.4% ± 25) after their last TACE. According to the mRECIST criteria, the objective response [complete response/necrosis (CR) + partial response (PR)] and disease control after TACE were presented with 100% [CR in three (25%) and PR in nine patients (75%)].

Discussion
In the present series, all 12 patients with prostatic LMS had inoperable non-metastatic disease at the initial diagnosis, the tumors also had non-response to neoadjuvant chemotherapy plus radiotherapy chemotherapy or radiotherapy alone. For the purpose of control of the bleeding and relief of the bulk-related symptoms, TACE using doxorubicin-eluting HS was performed and all patients were well tolerated for the procedure without major complications. The benefits of TACE in the present study appear to be extensive tumor necrosis evaluated by MRI with a median value of 90% and significant volume reduction with a median value 84% at the last follow-up after TACE and rapid resolution of gross hematuria, urinary retention, constipation, and perineal pain, apparently attributed to bulky tumors and rapid tumor progression. In addition, the median OS in the present study was much longer (29 months, mean 30 months) than the median OS of 15–18 months (mean 24 months) in patients with non-resectable non-metastatic LMS reported by others.1–3,14–16 The actuarial survival rate at 1, 2, and 3 years were 91.7%, 83.3%, and 41.7%, respectively, and longer than those reported by Vandoros et al.16 with the 1 and 3-year survival rates of 68% and 34%, respectively; and also longer than the reported by Wang et al.17 with the 1, 2, 3-year survival rates of 80.0%, 47.4%, and 22.6%, respectively.

Patients with large prostatic LMSs involving surrounding structures should be considered for neoadjuvant radiotherapy with or without chemotherapy to improve the probability of a complete resection. However, only a few patients could be converted from an unresectable tumor to a resectable tumor after these treatments.1–3 Wang et al. reported outcomes of 25 patients with inoperable prostate sarcoma and they concluded that neither chemotherapy nor radiotherapy improved survival in that series.17 In the present series, TACE allowed surgical resection in five (41.7%) patients after two to four sessions; a negative surgical margin was present in four of the five patients. TACE may thus be considered the initial preoperative treatment instead of systemic chemotherapy, especially for patients without distant metastasis, and it may be repeated until the tumor becomes resectable.

LMSs of the prostate are typically large hypervascular lesions.1–4 For this reason, intravascular locoregional therapy may represent an effective therapeutic approach for inoperable LMS of the prostate, in particular, in the case of high tumor mass with obstructive urinary symptoms. TACE

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**Table 2. TACE-related adverse events (CTCAE v. 4.03).**

| Symptoms          | Grades | Incidence |
|-------------------|--------|-----------|
| Low-grade fever   | 0      | 0         |
|                   | I      | 12 [100%] |
| Nausea            | 0      | 0         |
|                   | I      | 12 [100%] |
| Poor appetite     | 0      | 0         |
|                   | I      | 12 [100%] |
| Urethral burning  | 0      | 6 (50%)   |
|                   | I      | 6 (50%)   |
| Perineal pain     | 0      | 6 (50%)   |
|                   | I      | 6 (50%)   |
| Frequency         | 0      | 7 (58.3%) |
|                   | I      | 5 (41.7%) |
| Rectal bleeding   | 0      | 9 (75%)   |
|                   | I      | 3 (25%)   |

CTCAE, common toxicity criteria for adverse events; TACE, transcatheter arterial chemoembolization.
using drug-eluting microspheres (DEMs) has recently been performed for the treatment for several different types of malignant liver tumors, including hepatocellular carcinoma (HCC).\(^8,18\)

The advent of DEM represents an advancement, as these delivery systems slowly release chemotherapy into tumor tissues, consequently improving treatment efficacy and tolerability as compared with conventional TACE.\(^8,19\)

In the present study, TACE using doxorubicin-eluting HS for the treatment of prostatic LMS has been shown to be safe and well tolerated. There was no marked chemotherapeutic agent-induced toxicity noted. One of the reasons for this may be that the maximum dose of doxorubicin used was relatively low (75 mg/m\(^2\)). Another reason may be that doxorubicin, which was used in the DEM, entered the systemic circulation at a relatively slow rate, causing little damage to the bone marrow and cardiac system.

In patients with large aggressive LMSs of the prostate, complete local control of the lesion was difficult to achieve with a single session of TACE, repeat TACE thus usually needed. Although the blood supply of most prostate tumors is provided by the prostatic arteries, it is well known that some large lesions have multiple feeding arteries.\(^20,21\)

In the present series, multiple feeding arteries supplying the tumors, including the prostatic arteries, superior vesical arteries, internal pudendal arteries, middle rectal arteries, obturator arteries, were detected in seven (58.3%) of 12 patients. After embolization of the main feeders, establishment of collaterals from unusual blood supply may occur. Therefore, a careful search for feeding arteries is required.

There are several limitations to this study. First, the number of cases is small from a single institute. Second, it is difficult to compare our results with those of other therapies. Third, because subsequent surgical resection was performed in five (41.7%) of the 12 patients, which may overestimate the OS of TACE alone. In addition, only doxorubicin was used as a chemotherapeutic agent. Theoretically, combination of other chemotherapeutic drugs may be more effective. Nonetheless, rapid resolution of gross hematuria, urinary retention, constipation, perineal pain, and the relatively longer median OS, were achieved by TACE. In addition, MRI revealed the efficacy of TACE as necrotic change and volume reduction in the tumor. Thus, it is expected

**Table 3. Outcomes in patients with prostatic leiomyosarcoma treated by TACE (n = 12).**

| Patient | No. of TACEs | Tumor size (mL) pre-TACE | Tumor size (mL) post-TACE (last time) | MRI-Tumor necrosis (%) | Post-TACE treatment | Pathology necrosis (%) | Current status | Survival (months) |
|---------|--------------|-------------------------|--------------------------------------|------------------------|---------------------|-----------------------|----------------|------------------|
| 1       | 3            | 810                     | 0†                                   | 100                    | NO                  | –                     | ADF            | 49               |
| 2       | 4            | 410                     | 110                                  | 100                    | RP                  | 100                   | ADF            | 42               |
| 3       | 2            | 870                     | 560                                  | 75                     | NO                  | –                     | Died           | 26               |
| 4       | 1            | 790                     | 510                                  | 65                     | NO                  | –                     | Died           | 9                |
| 5       | 3            | 720                     | 180                                  | 95                     | RP                  | 95                    | ADF            | 27               |
| 6       | 2            | 690                     | 0†                                   | 100                    | NO                  | –                     | ADF            | 38               |
| 7       | 2            | 640                     | 70                                   | 95                     | RCP                 | 100                   | Died           | 37               |
| 8       | 3            | 670                     | 110                                  | 90                     | RCP                 | 90                    | AWD            | 28               |
| 9       | 2            | 570                     | 80                                   | 95                     | RCP                 | 100                   | Died           | 36               |
| 10      | 2            | 830                     | 70                                   | 95                     | NO                  | –                     | ADF            | 19               |
| 11      | 2            | 890                     | 360                                  | 80                     | NO                  | –                     | Died           | 25               |
| 12      | 3            | 710                     | 410                                  | 95                     | NO                  | –                     | AWD            | 30               |

ADF, alive with disease free; AWD, alive with disease; CT, chemotherapy; MRI, magnetic resonance imaging; NO, no other treatment; RCP, radical cystoprostatectomy; RP, radical prostatectomy; RT, radiotherapy, TACE, transcatheter arterial chemoembolization.

†Invisible tumor.
that TACE is effective for symptomatic relief and the local control of the lesion.

In conclusion, TACE of inoperable LMS of the prostate appears to be safe and effective in providing tumor devascularization, shrinkage, and symptom relief. TACE may play an important role in reducing tumor size and converts an unresectable tumor to a resectable tumor, thus improving prognosis. Our patients treated with TACE alone or TACE subsequent to surgical resection, had favorable OS compared with historic series.

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Conflict of interest
The authors declare that there is no conflict of interest.

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