CLINICAL STUDY

Safety and Efficacy of Prostatic Artery Chemoembolization for Prostate Cancer—Initial Experience

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ABSTRACT

Purpose: To evaluate outcome of prostatic artery chemoembolization for patients with prostate cancer (PCa).

Materials and Methods: This single-center prospective cohort study was conducted between August 2013 and July 2016 in 20 patients with PCa who underwent chemoembolization. Mean patient age was 67.5 years ± 6.4. Gleason score was 6–10, and staging was T2N0M0. Fifteen patients refused prostatectomy and 5 wanted to stop hormonal therapy because of side effects. For chemoembolization, *Chelidonium majus* mother tincture 1 mL was slowly injected into the prostatic arteries. Docetaxel 1 mL and 150–300 μm Embosphere (Merit Medical Systems, Inc, South Jordan, Utah) microspheres 0.5 mL were thoroughly mixed, and the mixture was slowly injected by the same route. Embolization of prostatic arteries was finished with 150–300 μm Embosphere microspheres. Technical success was defined as bilateral prostatic artery embolization. Biochemical failure was defined as prostate specific antigen (PSA) decrease to < 2 ng/mL followed by recurrence when PSA increased to > 2 ng/mL within 1 month after success.

Results: Technical success was 80.0% (16/20 patients). Biochemical failure was 18.7% (3/16 patients). There was 1 short-term biochemical recurrence at 4 months and 2 midterm recurrences (12–18 months). Biochemical success at 12–18 months was 62.5% (10/16 patients). Adverse events (31.3%) included a small area (2 cm^2) of bladder wall ischemia, which was removed by surgery (n = 1); transient acute urinary retention (n = 1) and urinary urgency (n = 1) for 1 week; sexual dysfunction (n = 2), which completely recovered after 10 and 12 months, respectively.

Conclusions: Prostatic artery chemoembolization allowed a biochemical response in patients with localized PCa and is a promising treatment.

ABBREVIATIONS

BF = biochemical failure, BR = biochemical recurrence, BS = biochemical success, CI = confidence interval, EBRT = external-beam radiotherapy, IPSS = International Prostate Symptom Score, PAE = prostatic artery embolization, PCa = prostate cancer, PSA = prostate specific antigen, RP = radical prostatectomy

Prostate cancer (PCa) is the most frequent cancer in Europe in men > 70 years old and the most commonly diagnosed nonskin cancer in men in the United States, second only to lung cancer in annual fatality rate, with a lifelong risk for diagnosis currently estimated at 15.9% (1,2). Each year, > 200,000 new cases are diagnosed with approximately 1 in every 6 US men affected by the disease. Histology studies from autopsy series show that approximately 33% of men 40–60 years old have PCa (3). The incidence of PCa increases with age and reaches 75% in men > 85 years old (4).

Radical prostatectomy (RP) is a curative treatment for localized PCa. Other curative treatments are external-beam radiotherapy (EBRT) and brachytherapy. Alternative options to RP include hormonal therapy, watchful waiting, and active surveillance (5–7). Prostatic artery embolization (PAE) in patients with benign prostatic hyperplasia has shown good results at short-term, midterm, and long-term follow-up (8–17). These results led us to consider treating PCa by prostatic artery chemoembolization.

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EDITORS' RESEARCH HIGHLIGHTS

- This retrospective study reports prostatic artery chemoembolization in 20 patients with prostate cancer with Gleason 6–10, stage T2N0M0 disease who refused surgery or wished to cease hormonal therapy. Embolization with *Chelidonium majus* mother tincture, Lipiodol, and bland microspheres was possible in 16 of 20 patients.
- Midterm biochemical success (prostate specific antigen < 2 ng/mL) was achieved in 10 patients (62.5%), and gland volume reduction was seen in most cases.
- Adverse events included transient sexual dysfunction, urinary retention and urgency, and 1 case of surgically managed bladder wall ischemia.
- Patients with prostate cancer who may wish to avoid surgery or may be unsuitable surgical candidates may benefit from cytoreductive therapies. This study demonstrates feasibility and early success supporting a potential role for embolotherapy. Prostate cancer embolization bears further study under prospective structured protocols.

Chelidonium majus is a plant extract that was approved by the German Commission E Monographs for use in humans; it is devoid of significant side effects on normal cells but is cytotoxic to cancer cells and has been used experimentally in Austria with success for a vast array of cancers (18–20). Docetaxel, a chemotherapy agent currently used for prostatic cancer, is also made of a plant extract that is submitted to a small chemical transformation that turns it into a semisynthetic agent (21). Therefore, a treatment protocol was designed based on prostatic artery chemoembolization and using *Chelidonium majus* plus docetaxel mixed with Embosphere (Merit Medical Systems, Inc, South Jordan, Utah) microspheres for patients with PCa without extracapsular invasion who refused or discontinued conventional treatments. In this study, the preliminary results and initial efficacy of a new, highly conservative treatment for PCa with chemoembolization using a combination of *Chelidonium majus* plus docetaxel mixed with Embosphere microspheres are reported.

MATERIALS AND METHODS

This single-center prospective study was conducted from August 2013 to July 2016 with approval by the institutional review board and written informed consent obtained from every patient. The study included men $\geq$ 50 years with biopsy-proven diagnosis of stage T2N0M0PCa without extracapsular extension who refused other treatment or who were intolerant to the side effects of hormonal therapy and wanted to discontinue it and who had sexual dysfunction or accepted the risk of developing sexual dysfunction after treatment. Patients with advanced atherosclerosis or tortuosity of the iliac and prostatic arteries on computed tomography (CT) angiography that could prevent selective catheterization of both prostatic arteries or secondary renal insufficiency owing to prostate enlargement or active prostatitis were excluded. If prostatitis was present, antibiotics were given, and biopsy was performed after only cure of prostatitis. All patients were informed of the procedure and the experimental nature of it; the possible benefits and risks of the available treatment options; their option to freely change to other therapies at any time; and the possibility that the treatment might cause bowel and urinary problems, sexual dysfunction, and infertility.

Prostate specific antigen (PSA) levels were evaluated before chemoembolization and then monthly for 6 months after chemoembolization, then every 3 months for 2 years, and then every 6 months thereafter. At each evaluation, if there was no decrease in serum PSA level to < 2 ng/mL at 1 month after prostatic artery chemoembolization, if there was recurrence of PSA > 2 ng/mL, or if there was an increase of PSA $\geq$ 2mg/mL above the nadir PSA, the patients would be advised to change to 1 of the standard therapies. The following parameters were evaluated before chemoembolization and every 6 months after the procedure: International Prostate Symptom Score (IPSS), quality-of-life question from the IPSS, International Index for Erectile Function, prostate volume by transrectal ultrasound, and peak urinary flow rate and postvoid residual volume assessed by uroflowmetry (13). CT angiography of prostatic arteries was performed before every chemoembolization, whereas nuclear medicine bone scan (scintigraphy) was performed in patients with PSA $>$ 10 ng/mL. Multiparametric magnetic resonance (MR) imaging using T2-weighted, diffusion-weighted, and perfusion imaging was performed before and 6–12 months after chemoembolization. Multiparametric MR imaging has been used for detecting locally recurrent PCa after EBRT (21). Suspicious nodules were marked and followed before and after chemoembolization (**Figs 1a–d**, **2a–d**).

Chemoembolization

Patients were started on an acid-suppressing drug once daily (omeprazole 20 mg [Bluepharma, Coimbra, Portugal]), a nonsteroidal anti-inflammatory drug twice daily (naproxen 1,000 mg [Naprosyn; Roche, Basel, Switzerland]), and an antibiotic twice daily (levofloxacin 500 mg [Ciprofloxacin; Jaba, Santiago de Besteiros, Portugal]) 1 day before the procedure and continued for 1 week after chemoembolization (9–11). The patients were admitted to the hospital 2 hours before the procedure. Before chemoembolization, nitroglycerin 150 μg was injected into the prostatic arteries. During embolization, an analgesic (metamizole 2 g [Nolotil; Boehringer Ingelheim, Ingelheim, Germany]) and an anti-inflammatory (ketorolac trometh-amine 30 mg [Toradol; Roche) were administered intravenously. Pethidine (meperidine 0.5 mg [Labesfal, Campo de Besteiros, Portugal]) was given subcutaneously. Chemoembolization was performed by interventional radiologists