CLINICAL STUDY

Prostatic Artery Embolization in the Treatment of Localized Prostate Cancer: A Bicentric Prospective Proof-of-Concept Study of 12 Patients

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ABSTRACT

Purpose: To provide initial data on tumoricidal efficacy of embolization on prostate cancer via histopathologic examination of prostatectomy specimens after embolization.

Materials and Methods: In this bicentric prospective trial, 12 men with localized prostate cancer underwent radical prostatectomy 6 weeks after prostatic artery embolization (PAE) from October 2016 to May 2017. PAE was performed with the use of 100-μm Embozene microspheres (Boston Scientific, Natick, Massachusetts). Response of prostate cancer tissue to PAE was assessed according to tumor regression grades. The major outcome measure was complete histopathologic absence of viable cancer cells, including secondary foci, in the prostatectomy specimens.

Results: Complete necrosis of the index lesion was found in 2 patients and partial necrosis in 5. Considering secondary cancerous foci, viable cancer cells were found in all 12 patients. Pathologic specimens were characterized by demarcated zones of necrotic tissue predominantly located in the central gland. Two patients required additional surgery to remove necrotic bladder tissue caused by PAE.

Conclusions: PAE with the use of 100-μm microspheres failed to achieve complete elimination of tumor cells. Extensive tumor regression was induced in some lesions, highlighting the need for further assessment of PAE as a potential treatment option for prostate cancer.

ABBREVIATION

PAE = prostatic artery embolization

Prostate-specific antigen (PSA) screening has led to a shift toward the detection of lower-stage prostate tumors, and overtreatment of prostate cancer represents a fundamental problem (1). Men are younger at the time of diagnosis and more interested in preserving not only continence but also sexual function (2). Robotic-assisted radical prostatectomy (RARP) has advanced technically but is still associated with substantial functional losses and other complications (3,4). Well tolerated and efficient treatment alternatives to optimize functional and oncologic outcomes are therefore highly warranted. Currently, focal therapies, such as high-intensity focused ultrasound (HIFU) and irreversible electroporation (IRE), are being investigated as minimally invasive techniques to ablate prostate cancer tissue. A limitation of these methods, however, is the substantial rate of metachronous tumor recurrence in the remaining prostatic tissue (5).

The challenge of oncologic surgery is to achieve optimal local tumor control while preserving urinary continence and sexual function. Improvement of erectile function can be achieved by preservation of the neurovascular bundles (6), but nerve-sparing surgery might be associated with an

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EDITORS' RESEARCH HIGHLIGHTS

- Prostate artery embolization before robotic-assisted radical prostatectomy was performed in 12 patients with biopsy-proven prostate cancer; bilateral embolization with the use of 100 μm Embozene microspheres (Boston Scientific, Natick, Massachusetts) was started in the proximal prostatic arteries and finished distally in all patients.
- Two patients (17%) developed partial bladder wall necrosis requiring surgery. Histology of the 12 specimens showed microspheres and ischemia with fibrosis, mainly in the central gland and around the prostatic urethra, but also in the seminal glands.
- All patients had residual viable tumor in the resected prostate specimens.
- PAE with small-sized microspheres and this embolization approach led to some severe nontarget ischemic complications without clear evidence of complete tumor control.

increased risk of positive surgical margins (7). Positive surgical margins are associated with a twofold increased hazard of biochemical relapse (8,9) and are often associated with additional therapies and anxiety among affected patients (10).

Prostatic artery embolization (PAE) is increasingly used in the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia (BPH) (11). Technical performance of PAE has been refined through recent years and is now well established (12,13). PAE has been shown to be a safe procedure with low morbidity in carefully selected patients, and no adverse effects on erectile function and urinary continence have been reported so far (11). A substantial decline of PSA and complete absence of prostatic vascularization in post-PAE multiparametric magnetic resonance (mpMR) imaging was reported after bilateral PAE (11).

The present trial intended to elucidate the role of PAE as a treatment modality of prostate cancer. We hypothesized that metachronous tumor recurrence might be more infrequent after PAE compared with focal therapies, because all prostatic tissue is expected to be exposed to ischemia. Furthermore, PAE could also be taken into consideration as a neoadjuvant treatment option to reduce positive surgical margins after RARP.

MATERIALS AND METHODS

The trial was conducted as a bicentric study at 2 tertiary referral centers. Approval from the local ethical committee was obtained (BASEC PB_2016-02294), prior to commencement of the study and the trial was registered at clinicaltrials.gov (NCT02917161). All potential study participants were thoroughly informed about the nature and conduct of the study and were included in the trial after they provided written informed consent. Inclusion criteria were: (*i*) patient age 45–75 years; (*ii*) RARP indicated because of biopsy-proven adenocarcinoma of the prostate; and (*iii*) localized disease according to digital rectal examination and mpMR imaging were considered for study inclusion. Patients with (*i*) history of pelvic irradiation, (*ii*) radical pelvic surgery, (*iii*) severe atherosclerosis, (*iv*) allergy to intravenous contrast media, (*v*) contraindications for MR imaging imaging, or (*vi*) renal failure (glomerular filtration rate <60 mL/min) were excluded.

The trial was designed as a bicentric open-labeled prospective proof-of-concept trial. PAE was performed 6 weeks before RARP. The primary outcome measure was histologic assessment of the excised prostate to determine whether pathologic complete response was achieved, defined as complete absence of viable cancer cells. Secondary outcome measures included tumor regression grades, surgical margins, functional outcomes, intraoperative details, and assessment of complications and adverse events according to the Clavien-Dindo classification and the National Institutes of Health Common Terminology Criteria for Adverse Events (CTCAE, version 4.03.)

Study Population

From October 2016 to May 2017, a total of 12 patients with a median age of 65 (range 54–72) years were included in the study. Baseline patient and tumor characteristics of prostate biopsies are reported in **Tables 1** and **2**.

Prostatic Artery Embolization

PAE was performed by 1 experienced interventional radiologist familiar with the procedure (10 years of interventional radiology, 4 years of PAE experience) in an outpatient setting with the use of local anesthesia. A unilateral femoral sheath was placed in the right common femoral artery. Prostatic arterial supply was identified by means of selective internal iliac arteriography with the use of a 5-F uterine artery catheter (Merit Medical, South Jordan, Utah). The prostatic vessels were selectively catheterized with the use of a 1.9-F microcatheter (Parkway soft; Asahi Intecc, Nagoya, Japan) and subsequently embolized with the use of 100-μm Embozene microspheres (Boston Scientific). The microspheres delivered in 20-mL syringes containing 2 mL of microspheres, and 5 mL NaCl was diluted with 2 mL Visipaque 320 (GE Healthcare, Little Chalfont, United Kingdom) according the manufacturer's instructions. Cone-beam computerized tomography (CT) was applied to identify tumor-feeding arteries and independent prostatic arteries, as well as to exclude nontarget embolization if deemed to be necessary by the interventionalist in challenging cases (14). Special attention was paid to embolize tumor-feeding arteries in concordance with the localization of the tumor according to the pre-PAE mpMR imaging. Embolization was performed starting proximally and then finishing distally in the prostate artery (12) and was considered to be successful in the absence of the normal blush of the prostate and complete stasis of flow in the prostate arteries on post-embolization angiography. The procedure was performed on both sides.