Urological Science 27 (2016) 226–229

Contents lists available at ScienceDirect

Urological Science

journal homepage: www.urol-sci.com

Original article

Single session of high-intensity focused ultrasound therapy for the management of organ-confined prostate cancer: A single-institute experience

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ARTICLE INFO

Article history:
Received 20 April 2016
Received in revised form
4 July 2016
Accepted 3 September 2016
Available online 28 September 2016

Keywords:
high-intensity focused ultrasound
localized
nadir
prostate cancer
prostate-specific antigen

ABSTRACT

Objective: The aim of this study was to evaluate the therapeutic response and complications of high-intensity focused ultrasound for patients with localized prostate cancer.
Materials and Methods: We evaluated the clinical outcomes of 29 patients who received high-intensity focused ultrasound as first-line treatment for localized prostate cancer at our hospital from October 2010 to March 2016. Biochemical recurrence was defined, according to the Stuttgart definition of biochemical failure, as the prostate-specific antigen nadir plus 1.2 ng/mL. Prostate-specific antigen levels and complications were recorded during regular follow-up.
Results: The mean follow-up period was 24.6 months. Six patients experienced biochemical recurrence (20.68%). Disease progression was noted in six patients (20.68%), and salvage therapy was performed in these patients. The 24.6-month cancer-specific survival rate was 100%. No severe complications were reported.
Conclusion: High-intensity focused ultrasound is an alternative therapy for patients with localized prostate cancer. In combination with preceding transurethral resection of the prostate, this treatment shows promise in disease control with a low complication rate in short-term follow-up.

1. Introduction

Prostate cancer was among the most frequently diagnosed tumors among men in the United States in 2014.[1] For patients with localized disease, radical surgery including radical prostatectomy, laparoscopic prostatectomy, or robotic-assisted radical prostatectomy should be considered. Brachytherapy and external beam radiation therapy are regarded as equally effective against localized disease.[2] However, these therapeutic approaches can result in complications that can affect the quality of life.[3] Patients with multiple comorbidities are at high risk when undergoing radical surgery. Consequently, the need for minimally invasive treatments for localized prostate cancer, such as high-intensity focused ultrasound (HIFU) and cryotherapy, has increased in recent years.

Hyperthermia and cavitation are the two major mechanisms by which HIFU can be used to treat localized prostate cancer.[4] The therapeutic effect of HIFU on human prostate cancer *in vivo* was first described in 1995.[5] Study results showed that HIFU was an effective, minimally invasive treatment for prostate cancer. Over time, as technology improved, HIFU became a more accessible therapeutic option for patients with localized prostate cancer. Nonetheless, HIFU is not routinely recommended owing to a lack of prospective, randomized, and controlled clinical trials with sufficient follow-up in the medical literature.[6,7]

Here, we present a single-center experience of 29 patients with localized prostate cancer treated with HIFU between October 2010 and March 2016. Oncological outcomes and complications are also discussed in relation to the literature.

2. Materials and methods

This study involved 29 patients with localized prostate cancer who received HIFU as first-line therapy at Tri-Service General

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http://dx.doi.org/10.1016/j.urols.2016.09.002

Hospital, Taipei, Taiwan, between October 2010 and March 2016. General characteristics, prostate-specific antigen (PSA) levels, and clinical staging data were collected prospectively from patient medical records. We established the following inclusion criteria: localized prostate cancer, clinical stages T1N0M0–T2N0M0, no previous hormone therapy (HT) or radiation therapy, and lack of suitability for radical prostatectomy due to multiple comorbidities or high risk for surgical complications. Our exclusion criteria included locally advanced disease, metastatic disease, and rectal wall disease. The diagnosis of prostate cancer was established by transrectal ultrasound (TRUS)-guided needle biopsy of the prostate. Clinical staging was determined on the basis of magnetic resonance imaging of the pelvis and a whole-body bone scan. According to the results of clinical stage, Gleason score, and PSA levels, patients were classified into risk groups according to the National Comprehensive Cancer Network recurrence risk stratification guidelines. Patients first underwent transurethral resection of the prostate (TURP), and then returned 4 weeks later to receive HIFU therapy.

The Ablatherm HIFU device (EDAP TMS, Vaulx-en-Velin, France) is composed of a treatment module, a control module, and a probe with both image and treatment transducers. After the administration of general or spinal anesthesia, the patient is transferred to the treatment module and placed in the right lateral decubitus position. The probe is then introduced into the rectum for a pretreatment evaluation using an ultrasound image. The prostate cancer will be observed as a hypoechoic lesion under the image transducer before treatment. Depending on the tumor location and volume, a personalized therapeutic strategy is designed by adjusting the parameters of the control module. Using the HIFU system, the treatment process may be performed automatically. During HIFU therapy, a hypoechoic lesion will change to a hyperechoic lesion in which we can evaluate the degree of destruction in real time.[8]

Following whole-gland ablation with HIFU, suprapubic cystostomy was performed in the study patients. Two days later, the Foley catheter was removed, and patients were discharged. Follow-up was arranged by our outpatient department. The suprapubic cystostomy tube was removed 1 week after discharge during the first outpatient department visit. Patients were subsequently seen every month, and their PSA levels were checked every other month. The PSA nadir was defined as the lowest level during follow-up. Oncological outcomes were assessed on the basis of biochemical failure and cancer-specific survival rate. The Stuttgart definition of biochemical failure was used to define biochemical recurrence (PSA nadir plus 1.2 ng/mL).[9] Repeated TRUS-guided needle biopsy was recommended if biochemical failure developed. Salvage therapy would be arranged in the event of biochemical recurrence even if the result of TRUS-guided needle biopsy of the prostate was negative. HIFU-related complications were also recorded during outpatient department follow-up.

3. Results

3.1. Patients

This study included 29 patients diagnosed with localized prostate cancer who received HIFU therapy at Tri-Service General Hospital between October 2010 and March 2016. Characteristics of the 29 patients with localized prostate are shown in Table 1. The mean age was 68.1 years, and the mean follow-up duration was 24.6 months. The mean PSA level was 10.3 ng/mL. The predominant clinical stages were T1cN0M0 (19 patients, 65.5%) and T2cN0M0 (4 patients, 13.79%). Almost all patients underwent TURP (27 patients, 93.1%) before HIFU therapy. According to National Comprehensive Cancer Network guidelines, the majority of patients were classified to be at intermediate risk (14 patients, 48.27%). However, four patients were lost to follow-up due to relocation.

Table 1
Characteristics of 29 patients with localized prostate.

Age (y)	68.1 (59–82)
PSA (ng/mL)	10.3 (0.5–31.5)
Clinical stage	
cT1a	1 (3.44)
cT1b	3 (10.34)
cT1c	19 (65.5)
cT2a	1 (3.44)
cT2b	1 (3.44)
cT2c	4 (13.79)
TURP before HIFU	
No	2 (6.89)
Yes	27 (93.1)
Gleason score	
≤6	16 (55.17)
7	12 (41.37)
>7	1 (3.44)
NCCN risk groups	
Low risk	11 (37.93)
Intermediate risk	14 (48.27)
High risk	4 (13.79)
Median prostate volume (mL)	27.15 (9.32–59.6)

Data are presented as *n* (%) or mean (range), unless otherwise indicated.
HIFU = high-intensity focused ultrasound; NCCN = national comprehensive cancer network; PSA = prostate-specific antigen; TURP = transurethral resection of the prostate.

3.2. Treatment

Patients were treated with the Ablatherm HIFU device (EDAP TMS) between October 2010 and March 2016. Most patients underwent a single HIFU session, although three patients (10.34%) underwent a second HIFU session due to biochemical failure or biopsy-proven malignancy.

3.3. Oncological outcomes

Postoperative outcomes and complications are shown in Table 2. The mean PSA nadir was 0.21 ng/mL and was achieved within a mean of 1.9 months after HIFU therapy. Undetectable PSA levels were noted in 16 patients. Only three patients had PSA nadir levels greater than 1 ng/mL. One of these patients displayed biochemical recurrence 6 months later and underwent TRUS-guided needle biopsy that revealed adenocarcinoma of the prostate. Secondary HIFU was arranged immediately for disease control, but owing to progression of the PSA level, salvage radiation therapy was performed. The second patient with a PSA nadir of > 1 ng/mL

Table 2
Postoperative outcomes and complications.

Mean time to PSA nadir (d)	57.96
PSA nadir (ng/mL)	0.2116
Undetectable (<0.04 ng/mL)	16
Detectable (ng/mL)	13
<1	10
>1	3
Secondary biopsy	5
Complications	
Urinary tract infection	6 (20.6)
Urethral stricture	8 (27.58)
Erectile dysfunction	7 (24.13)
Bladder neck contracture	7(24.13)

Data are presented as *n* or *n* (%).
PSA = prostate-specific antigen.