Pathological, Oncologic and Functional Outcomes of a Prospective Registry of Salvage High Intensity Focused Ultrasound Ablation for Radiorecurrent Prostate Cancer

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Purpose: In this prospective registry we prospectively assessed the oncologic, functional and safety outcomes of salvage high intensity focused ultrasound for radiorecurrent prostate cancer.

Materials and Methods: A total of 81 men were prospectively recruited and evaluated at regular scheduled study visits to 6 months after high intensity focused ultrasound and thereafter as per standard of care. Transrectal ultrasound guided biopsy was performed at 6 months. The primary end point was absence or histological persistence of disease at 6-month biopsy. Secondary end points included quality of life, biochemical recurrence-free survival, overall survival, cancer specific survival and progression to androgen deprivation therapy. Survival analysis was performed according to the Kaplan-Meier method and multivariate analysis was performed using the log rank (Mantel-Cox) test.

Results: Mean ± SD prostate specific antigen before high intensity focused ultrasound was 4.06 ± 2.88 ng/ml. At 6 months 63 men underwent biopsy, of whom 22 (35%) had residual disease. At a mean followup of 53.5 ± 31.6 months median biochemical recurrence-free survival was 63 months. The 5-year overall and cancer specific survival rates were 88% and 94.4%, respectively. Nadir prostate specific antigen less than 0.5 ng/ml was a significant predictor of biochemical recurrence-free survival (p=0.014, 95% CI 1.22–5.87). I-PSS significantly increased (p <0.001) while IIEF-5 scores decreased and the SF-36 score did not change significantly. The rate of rectal fistulization and severe incontinence was 3.7% each. A total of 223 complications were recorded in the 180 days after high intensity focused ultrasound (Clavien-Dindo grade 1—195, grade II—20, grade III—7, grade IVa—1).

Abbreviations and Acronyms

ADT = androgen deprivation therapy
BRFS = biochemical recurrence-free survival
CSS = cancer specific survival
EBRT = external beam radiotherapy
HIFU = high intensity focused ultrasound
IIEF = International Index of Erectile Function
I-PSS = International Prostate Symptom Score
OS = overall survival
PSA = prostate specific antigen
QoL = quality of life
rr-PCa = radiorecurrent prostate cancer
SF-36™ = RAND 36-Item Health Survey
s-HIFU = salvage HIFU
SP = salvage prostatectomy
UTI = urinary tract infection

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Conclusions: Salvage high intensity focused ultrasound appears to be a viable treatment option for radiorecurrent prostate cancer, with acceptable morbidity.

Key Words: prostatic neoplasms, radiotherapy, recurrence, salvage therapy, high-intensity focused ultrasound ablation

THE CaPSURE™ (Cancer of the Prostate Strategic Urologic Research Endeavor) database reports a 63% recurrence rate after EBRT.[1] The majority (80%) of these patients is older than 65 years and during the course of disease are likely to have metastases and eventually die of prostate cancer. Only a small proportion (0.9%) of the patients undergo salvage prostatectomy, underscoring the fact that these men are not offered the surgical option due to their comorbidities and poor surgical candidacy, or due to the inordinate risks and complexity of the procedure.[1] Alternatively, some patients do not opt for salvage prostatectomy because they perceive the potential complications as prohibitive and unacceptable. Energy based ablative treatments are minimally invasive options which reportedly can provide durable oncologic control with acceptable morbidity.[2] HIFU is one such modality which has been in use in Europe for more than 2 decades, mostly as primary therapy,[3] and which has recently been approved by the FDA (Food and Drug Administration) in the United States for prostate tissue ablation. The objective of this prospective registry is to assess oncologic, functional and safety outcomes of HIFU in the salvage setting of radiorecurrent prostate cancer, and in this article we report the intermediate term salvage HIFU results.

MATERIALS AND METHODS

A total of 81 men were accrued to this phase II study at London Health Sciences Centre, an academic tertiary care hospital in London, Ontario, Canada, between January 2004 and December 2015. Ethics review board approval was obtained (REB #100955). We excluded patients with less than 6 months of followup and those who were enrolled in an FDA sponsored trial and whose data are still quarantined. All patients had biopsy proven rr-PCa, cT1c-T2 cancer. All patients underwent radionuclide bone scan and computerized tomography of the abdomen and pelvis to confirm the localized nature of the disease. Preoperative clinical data included age, PSA, Gleason score from the pre-HIFU biopsy, Charlson comorbidity score, previous treatment history, baseline IIEF-5 score, I-PSS and SF-36 score for assessment of QoL.[4] The patients also underwent anoscopy and transrectal prostate ultrasonography as part of the screening assessment. Exclusion criteria for the study were metastatic prostate cancer, radiation proctitis, ECOG performance status score greater than 1, prostatic volume greater than 40 ml, intraprostatic calcifications greater than 10 mm, urethral stricture/bladder neck stenosis, active untreated UTI, history of bleeding disorders, American Society of Anesthesiologists® score greater than 3, other malignancies and inflammatory bowel disease.

HIFU treatment was performed using the Sonablate® 500 with the patient under general anesthesia. Flexible cystoscopy and percutaneous suprapubic cystostomy were performed. Treatment planning was based on whole gland ablation with a nonnerve sparing approach under transrectal ultrasound guidance. The protocol involved side to side ablation, divided into 2 or 3 zones depending on prostate size, with a standard power setting of 36 to 38 W for the anterior and mid zones (using the 4 cm focal length probe), and 20 to 24 W for the posterior zone (using the 3 cm probe). Continuous real-time transrectal monitoring of the thermal effects was performed by visualization of the intraprostatic acoustic pattern changes including any popcorn effect (caused by collapse of gas bubbles). Special attention was paid to Denonvilliers fascia, the rectal wall and external sphincter areas. The built-in SonaChill® device was used for rectal cooling. Rectal temperature was continuously monitored and based on the reflective index. Treatment was automatically suspended if the rectal wall temperature became excessive. All procedures were performed by a single surgeon with extensive expertise in HIFU treatments (JLC). All patients were discharged home on the first postoperative day with the suprapubic catheter in place, which was removed after a successful trial of voiding at 3 weeks after HIFU.

Postoperative study visits were scheduled at 45, 90 and 180 days after HIFU, when morbidity data were collected along with completion of the IIEF, I-PSS and SF-36 questionnaires. Further followup was scheduled as per standard of care. Transrectal ultrasound guided biopsy was performed at 6 months. Complications were graded according to the Clavien-Dindo classification system. Incontinence was defined as mild to moderate if the patient required 0 to1 pad only and as severe if 2 or more pads were needed. Incontinence requiring surgery was defined as incontinence requiring any form of surgical intervention. Gross hematuria and perineal pain were classified under self-reported complications. Bladder neck contracture, urinary retention, UTI and fistula were all physician recorded variables logged at scheduled followup appointments, and/or extracted from hospital records.

The primary end point was absence or persistence of disease at 6-month biopsy. Secondary end points included QoL, BRFS, OS, CSS and time to progression to ADT. Treatment failure was identified by biopsy positive for prostate cancer and/or biochemical failure as per the Phoenix criterion and/or detection of metastasis.