Salvage Radical Prostatectomy Following Primary High Intensity Focused Ultrasound for Treatment of Prostate Cancer

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Abbreviations and Acronyms

ADT = androgen deprivation therapy

HIFU = high intensity focused ultrasound

IIEF = International Index of Erectile Function

I-PSS = International Prostate Symptom Score

MSKCC = Memorial Sloan-Kettering Cancer Center

PC = prostate cancer

PSA = prostate specific antigen

RP = radical prostatectomy

TURP = transurethral prostate resection

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Purpose: High intensity focused ultrasound for the treatment of primary prostate cancer is increasing in a subset of men seeking definitive treatment with reduced morbidity. We review outcomes in men undergoing salvage radical prostatectomy after failed whole gland high intensity focused ultrasound.

Materials and Methods: Prospective data were collected for men presenting with an increasing prostate specific antigen and biopsy proven prostate cancer after high intensity focused ultrasound from 2007 to 2010 who underwent salvage open radical prostatectomy with a 22-month median followup, including prostate specific antigen, prostate volume, pathology results, continence and erectile function.

Results: Data for 15 men were available, including median age 64 years (IQR 55–69), Gleason score before high intensity focused ultrasound of 6 (8), Gleason score 7 (7), median cores positive 39% (IQR 17%–63%) and median prostate specific antigen 7 ng/ml (IQR 5–8). Whole gland high intensity focused ultrasound achieved median nadir prostate specific antigen 1.1 ng/ml (IQR 0.5–3.1). Biopsy after high intensity focused ultrasound demonstrated Gleason score 6 (in 3 patients), 7 (9) and 8/9 (3), and 42% (IQR 25%–50%) cores positive and a median time from high intensity focused ultrasound to radical prostatectomy of 22 months (IQR 7–26). Perioperative morbidity was limited to 1 transfusion in a patient with a rectal injury. Pathologically extensive periprostatic fibrosis was found with persistent prostate cancer, as pT3 disease (in 9 of 14), Gleason scores 6 (2), 7 (9) and 8 of 9 (4), with focally positive margins in 3 of 11 (pT3a). Postoperative prostate specific antigen was unrecordable in 14 of 15 patients with further treatment in 2. Postoperative continence (more than 12 months of followup) yielded no pad use in 6 of 10 men with universally poor erectile function.

Conclusions: Radical prostatectomy as salvage is feasible for men in whom high intensity focused ultrasound failed, but with a higher morbidity than for primary surgery. Pathology results are alarming given the number of cases with extraprostatic extension yet early followup data suggest acceptable oncologic control. These results should be factored in when counseling men who wish to undergo primary high intensity focused ultrasound.

Key Words: prostatic neoplasms, prostatectomy, treatment outcome, pathology, ultrasonography

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PROSTATE cancer remains the most common malignancy in men yet it is not the most common cause of cancer related mortality.[1] In essence the PSA era has ushered in a period where over detection of clinically insignificant PC must be balanced against the over treatment of clinically insignificant disease with radical therapies given their effect on quality of life. Furthermore, with diagnosis in younger men[2] and the occurrence of stage migration,[3] there has been a shift toward minimally invasive treatments with potentially reduced morbidity compared to traditional radical therapies. Thus, while active surveillance has arisen as a management option for low risk PC, clinicians are still striving for a middle ground with a modality that has minimal morbidity but definitively gains oncologic control.[4]

High intensity focused ultrasound has emerged as one such option.[5] HIFU began as a modality to treat cases of radiotherapy failure but has now become a modality for primary treatment of PC, usually treating the whole gland.[6] In the development of whole gland treatments various nomenclatures have emerged for minimally invasive focal PC therapies such as lesion targeted therapy, hemiablative therapy or subtotal gland therapy, sparing at least 1 neurovascular bundle.[7] Several energy modalities exist for such therapies including HIFU, laser and cryotherapy.[8–10] However, moving to more focal-type approaches is relatively new and under investigation, and in Europe and other parts of the world HIFU has been practiced as a whole gland modality. Thus, we are now confronted with cases of HIFU treatment failure and urologists need to be aware of options for the management of such cases, which include further HIFU treatments, salvage radical prostatectomy or salvage radiation.[8,11]

Salvage RP after failed radiation treatment has been well documented with increased operative length and morbidity. However, few reports exist on salvage RP after primary HIFU treatment of PC. In this study we review the outcome of salvage RP in a series of men in whom whole gland HIFU failed as primary treatment of PC.

PATIENTS AND METHODS

In this multi-institutional study (5 centers with 7 surgeons), with informed consent and ethical standards at each center, all data were prospectively collected as part of RP databases. No patient had HIFU at the participating centers. The database and records were retrospectively reviewed for men presenting with an increasing PSA and biopsy proven PC who underwent salvage RP after primary PC therapy with HIFU (using Ablatherm® or Sonablate®). All men were offered surgery or radiation, and those selected chose surgery. IIEF and I-PSS data were available. Cases were staged initially or restaged with a bone scan and computerized tomography where D'Amico high risk parameters existed.

RP was performed in a standard retrograde open fashion, in a nonnerve sparing fashion taking tissue wide of the neurovascular bundles with extended lymphadenectomy where appropriate for Gleason 8/9 disease and where possible (2 patients could not undergo lymphadenectomy due to dense fibrosis over the pelvic vessels).[12] Antegrade dissection was performed in 2 cases due to excessive fibrosis. Pathological examination of biopsy and RP specimens was performed by experienced uropathologists after standard processing, with a positive margin defined as PC at the inked edge. Clinical history, complications, PSA, prostate volume, pathology results, continence and erectile function data were all available before and after HIFU, and after surgery.

Followup with clinical examination and PSA was consistent across institutions. A strict definition of continence was to be pad-free or the number of pads used reported.[13] The use of adjuvant treatment was not set by protocol, allowing individualization and institutional preference to prevail. The MSKCC Kattan pretreatment nomogram (http://www.mskcc.org) was used before HIFU and RP.

RESULTS

Study Population

A total of 15 men fulfilled the criteria of recurrent PC after HIFU undergoing RP, with HIFU performed using the Ablatherm (7) or Sonablate (8) devices (tables 1 and 2). The clinical characteristics of the patients at the initial diagnosis of prostate cancer were median age 64 years (range 48 to 74), pre-HIFU Gleason score 6 (8) and Gleason score 7 (7) with median 39% (range 17% to 83%) cores positive (minimum 10 cores) and median PSA 7 ng/ml (range 3 to 12). All men underwent whole gland HIFU for initial PC treatment, with 3 men undergoing additional whole gland HIFU treatments due to biochemical failure with a median PSA nadir of 1.0 ng/ml (range 0.2 to 5.6). Median PSA before RP was 3.8 ng/ml (range 0.7 to 8.84) while median time from last HIFU treatment to RP was 22 months (range 6 to 31). Repeat biopsy diagnosing recurrent cancer after HIFU demonstrated Gleason scores 6 (3), 7 (9) and 8/9 (3) with a median of 42% (range 8% to 69%) cores positive. No patients with high risk features had a positive bone scan or computerized tomgraphy in this study.

HIFU and Any Prior or Adjuvant Treatments

HIFU was given as 1 treatment except in 4 patients (numbers 9, 12, 14 and 15) who received 2 whole gland HIFU treatments due to presumed failure and biochemical recurrence (biopsy proven in only 1). Patient number 12 also had ADT with a single depot dose of luteinizing hormone-releasing hormone just before initial HIFU as did 1 further patient who only had 1 HIFU treatment. Some patients underwent