Partial Gland Treatment of Prostate Cancer Using High-Intensity Focused Ultrasound in the Primary and Salvage Settings: A Systematic Review

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Abbreviations and Acronyms

ADT = androgen deprivation therapy
AUR = acute urinary retention
BCR = biochemical recurrence
ED = erectile dysfunction
EORTC = European Organization for Research and Treatment of Cancer
EPE = extraprostatic extension
EPIC = Expanded Prostate Cancer Index Composite
FACT-G = Functional Assessment of Cancer Therapy-General
FACT-P = Functional Assessment of Cancer Therapy-Prostate
HIFU = high-intensity focused ultrasound ablation
HRQOL = health related quality of life
ICS = International Continence Society
IIEF-5 = International Index of Erectile Function 5-item questionnaire
IIEF-15 = International Index of Erectile Function 15-item questionnaire
IPSS = International Prostate Symptom Score
mp = multiparametric
MRI = magnetic resonance imaging
PCI = Prostate Cancer Index
PGA = partial gland ablation
PSA = prostate specific antigen
QOL = quality of life
RP = radical prostatectomy
RT = radiation therapy
RUF = rectourethral fistula
TPM = template prostate mapping
TRUS = transrectal ultrasound
TURP = transurethral prostatectomy
UCLA = University of California-Los Angeles
UI = urinary incontinence
UTI = urinary tract infection

Purpose: Advances in prostate imaging, biopsy and ablative technologies have been accompanied by growing enthusiasm for partial gland ablation, particularly using high-intensity focused ultrasound, to treat prostate cancer. Preserving noncancerous prostate tissue and minimizing damage to the neurovascular bundles and external urethral sphincter may improve functional outcomes.

Materials and Methods: A systematic review was performed following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines using a combination of MeSH® terms, free text search and examination of relevant bibliographies using MEDLINE® and Embase® from the inception of each database through October 10, 2016. We excluded studies describing exclusively whole gland ablation, case reports and series where treatment was followed by immediate resection.

Results: A total of 13 studies that enrolled 543 patients were included. Of the studies 11 were performed in the primary setting and 2 in the salvage setting. Median followup ranged from 6 months to 10.6 years. Rates of posttreatment erectile dysfunction and urinary incontinence ranged from 0% to 48% and 0% to 50%, respectively, with definitions varying by study. Overall there were 254 reported complications. Marked heterogeneity between studies limited the ability to pool results regarding functional and oncologic outcomes. A total of 76 patients (14%) subsequently received further oncologic treatment.

Conclusions: Early evidence suggests that partial gland ablation is a safe treatment option for men with localized disease. Longer term data are needed to evaluate oncologic efficacy and functional outcomes, and will aid in identifying the optimal candidates for therapy. Standardization of outcomes definitions will allow for better comparison between studies and among treatment modalities.

Key Words: ablation techniques, high-intensity focused ultrasound ablation, prostatic neoplasms

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In the era of prostate specific antigen screening survival in men with prostate cancer has improved as more disease is detected and treated earlier, although there is concern regarding increased treatment in those with insignificant disease.[1] Therapeutic options for localized prostate cancer include radiotherapy, radical prostatectomy and active surveillance, depending on disease stage and patient preference. However, definitive approaches such as radical prostatectomy and radiotherapy are associated with significant side effects, including erectile dysfunction, urinary incontinence and rectal bother.[2]

PGA has gained momentum among patients and providers seeking to treat localized disease while preserving HRQOL.[3] Active surveillance similarly preserves these desired functions but may be associated with increased anxiety due to the presence of untreated disease as well as the risk of undertreatment of potentially missed disease.[4,5] Since mp MRI has improved the detection of clinically significant (Gleason score 7 or higher) prostate cancer, coupled with magnetic resonance fusion and template mapping techniques to biopsy areas of suspicion, clinicians are better able to identify and stage the extent of disease. In the last decade HIFU has emerged as a PGA modality due to its noninvasive transrectal delivery under image guidance, with a predictable and consistent pattern of ablation.[6,7] The prostate tissue is selectively ablated by a combination of thermal and mechanical effects, with minimal damage to the rectal wall and prostate uninvolved by cancer.[6–8] Since the U.S. Food and Drug Administration approval of HIFU in late 2015 for ablation of prostate tissue, there has been an increased interest in this modality for treating prostate cancer.[9,10]

Whole gland therapy for treatment of prostate cancer is the most commonly performed HIFU schema published in the literature, and the longer term functional and oncologic outcomes are promising.[11–13] As imaging and ablative technology continues to improve, there has been a shift toward subtotal or partial gland prostate ablation such that urinary and sexual function may be better preserved by allowing for margins excluding the neurovascular bundles, urethra and external urinary sphincter. We systematically reviewed the oncologic and functional outcomes of partial gland HIFU in the treatment of prostate cancer.

METHODS

We systematically reviewed studies reporting the functional and oncologic outcomes, as well as safety profile, of partial gland HIFU performed in either the primary or salvage setting. The review was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[14] MEDLINE (through PubMed®) was searched for relevant articles from the inception of the database until October 10, 2016. Systematic searches included the MeSH or free text phrases, "prostatic neoplasms" OR "prostate cancer" AND "HIFU" OR "high-intensity focused ultrasound" OR "high-intensity focused ultrasound ablation." All results were limited to English language abstracts with human adult male participants. Additionally a systematic search of Embase (through Ovid®) as well as a manual search of relevant bibliographies was performed to identify studies that may have been missed by the search strategies.

Study Selection

After removal of duplicates, 2 authors (RG, ANB) screened all titles and abstracts independently to identify potentially relevant articles. Full text articles were evaluated when there was inadequate information within the title or abstract. When discrepancies arose, the senior authors arbitrated. We included randomized controlled trials, case series, prospective development studies and retrospective series of partial gland ablation in either the primary or salvage treatment setting. Single patient case reports, review articles, conference or poster presentations and editorial or descriptive commentaries were excluded. On quality review studies were excluded if they involved solely whole gland ablation, lacked followup information beyond 4 weeks or included overlapping patient cohorts. Proof of concept studies demonstrating feasibility of ablative therapy were excluded so that functional and oncologic outcomes could be adequately evaluated.

Data Extraction and Analysis

Three authors (RG, ANB, TDM) independently reviewed all studies and extracted relevant data, which were then compared for accuracy. Again, discrepancies were resolved by the senior authors. Within each study we evaluated 1) study design; 2) device; 3) field of ablation; 4) primary or salvage treatment; 5) inclusion and exclusion criteria; 6) patient and treatment related factors including number of subjects, age, prostate volume, pretreatment biopsy, type of biopsy performed, pretreatment PSA, prior ADT, prior TURP, duration of followup and length of stay; 7) oncologic outcomes including posttreatment PSA, indications for repeat biopsy, numbers with positive biopsy or clinically significant disease and repeat treatment, overall survival, disease specific survival, metastasis-free survival and biochemical failure rates, and their associated definitions; 8) functional outcomes including the surveys used for measuring patient reported outcomes; and 9) complications including Clavien-Dindo classification,[15] urinary retention, stricture, RUF, UI and ED. Since the raw study data were often unavailable, we report the aforementioned items when available and as presented by the study authors.

Continuous and categorical variables were reported as presented within the study. For baseline demographics the denominator was the total number of subjects undergoing subtotal HIFU. When reporting positive biopsies following treatment, the denominator was the number of men who underwent prostate biopsy. The definition of