Prostate Ablation Using High Intensity Focused Ultrasound: The Potential Role for Patient Preference Information—A Literature Review

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Purpose: The FDA (Food and Drug Administration) recently allowed the marketing of 2 high intensity focused ultrasound devices for prostate tissue ablation indications after previous rejections for a prostate cancer indication due to insufficient data on clinical effectiveness or direct patient benefit. We reviewed the safety and effectiveness of high intensity focused ultrasound and knowledge regarding patient preferences, such as tolerance for adverse events associated with high intensity focused ultrasound ablation of tissue, in men with prostate cancer. This may inform decision making for device developers and the FDA.

Materials and Methods: We searched PubMed® and gray literature, including FDA reports for relevant data on 1) the safety and effectiveness of primary and salvage high intensity focused ultrasound of localized prostate cancer in studies performed in or outside the United States and 2) patient preference information on high intensity focused ultrasound related safety and effectiveness outcomes.

Results: We found no high intensity focused ultrasound effectiveness data relevant to clinical decision making, such as overall or prostate cancer specific survival, in the United States. Long-term effectiveness data from outside the United States were sparse and outcomes varied. We also found no patient preference data on high intensity focused ultrasound treatment in men with prostate cancer.

Conclusions: The lack of long-term high intensity focused ultrasound oncological data in an American population has brought new challenges to prostate cancer stakeholders, including clinicians, patients and the FDA. Patient preference information from future patient studies on high intensity focused ultrasound could provide additional information to patients, clinicians, and current and prospective device developers. In addition, it can be used by regulators in risk-benefit evaluations of this class of treatment devices.

Abbreviations and Acronyms

AS = active surveillance
BOO = bladder outlet obstruction
FDA = Food and Drug Administration
HIFU = high intensity focused ultrasound
IIEF = International Index of Erectile Function
OUS = outside United States
pHIFU = primary HIFU
PPI = patient preference information
PSA = prostate specific antigen
QALY = quality adjusted life-year
QoL = quality of life
RP = radical prostatectomy
SG = standard gamble
sHIFU = salvage HIFU
TTO = time trade-off
UI = urinary incontinence
UTI = urinary tract infection

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PROSTATE cancer is the most common malignancy and the third leading cause of cancer related death in men in the United States and Europe.[1] Current standard treatment options for localized prostate cancer range from AS to definitive interventions, including RP or radiation therapy. AS carries a significant mental burden and delayed treatment could lead to disease progression.[2] While there may be excellent long-term oncologic outcomes, RP and external beam radiation therapy are often associated with significant morbidity that negatively affects patient QoL.[3] HIFU is a minimally invasive technology which offers an alternative to traditional therapies, especially in the low and intermediate risks groups in primary and salvage settings in OUS and American studies.[4–7]

The FDA recently allowed 2 HIFU devices to be marketed as tools for prostate tissue ablation. This came after rejecting prior premarket applications with prostate cancer indications, which failed to demonstrate appropriate clinical effectiveness or direct patient benefit[8] with respect to prostate cancer treatment. Although clinical outcome data such as disease-free survival is unavailable in the United States, evidence of tissue ablation is known, including posttreatment biopsy data and the adverse event profile of HIFU. Since the translatability of posttreatment prostate biopsy information to disease-free survival is unclear, patients and other stakeholders must currently make a decision regarding HIFU treatment in the absence of relevant clinical outcome data but in light of known potential adverse events and tissue ablation effectiveness.

As more devices for and treatment methods of prostate tissue ablation become available, patient perspectives about health outcomes offer valuable information that may not be captured by clinical outcomes. Preferences assign values to different events and can shed light on the safety and effectiveness trade-offs that patients are willing to make when undergoing treatment. PPI, such as tolerance for adverse events associated with HIFU ablation of tissue in men with prostate cancer, could inform decision making by patients, clinicians, device sponsors and the FDA.

This article provides a literature review of what is currently known about the results of HIFU for prostate tissue ablation in patients with prostate cancer as well as PPI on HIFU related outcomes. It identifies current gaps in the literature while suggesting that PPI might prove useful to multiple stakeholders to assess the role of these devices in men with prostate malignancy.

METHODS

We performed 2 literature searches. 1) We searched the literature to review the outcomes of primary and salvage HIFU in men with localized prostate cancer in studies OUS and in the United States. Publications were sourced primarily using the PubMed® database as well as the gray literature, including FDA reports. The search was performed using combinations of the key words HIFU, high intensity focused ultrasound and prostate cancer. Articles were included if they were published in peer reviewed journals. Studies with the same patient series, review articles and abstracts not reported in English were excluded from analysis.

Abstracts resulting from this search were reviewed for relevant clinical information. Full manuscripts were retrieved for clinical effectiveness data and rates of adverse events following HIFU. Reference lists of manuscripts were also checked for additional relevant studies.

2) We also reviewed patient preference studies using patient preference, prostate cancer, stated preference and quality of life as key words in the title and the abstract to find peer reviewed publications in the PubMed® and the gray literature. Studies on cancer screening, clinical research, explorations of novel treatment methods and method guidelines were excluded from analysis.

RESULTS

Our literature search included 20 OUS studies and 2 performed only in subjects in the United States and Canada with the majority from the United States. We noted differences in inclusion and exclusion criteria, and the study design, which made direct comparisons of outcome and safety data difficult. These differences included varying definitions of biochemical failure based on the Phoenix, ASTRO (American Society for Radiation Oncology) and Stuttgart definitions, inclusion of retreatments (multiple HIFU sessions) in effectiveness metrics, differences in patient population, differences in outcome definitions, heterogeneity in risk stratification, differences in followup, differences in ablation extent and differences in definitions of complications.

Primary and Salvage Treatment Effectiveness and Safety

To our knowledge no randomized controlled trials have been done to compare the effectiveness of primary or salvage HIFU in men with localized prostate cancer with that of other conventional management