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Review article

Maximizing resources in the local treatment of prostate cancer: A summary of cost-effectiveness studies

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Abstract

Objectives: Prostate cancer is a common diagnosis with several treatment options for the newly diagnosed patient, including radiation, surgery, active surveillance, and watchful waiting. Although tailoring of treatment to individual patient needs is an important goal, the recent passage of the Affordable Care Act has placed renewed interest in cost containment and cost-effectiveness. We sought to conduct a literature review of recent US-based studies to analyze the cost-effectiveness of initial local treatments for localized prostate cancer.

Methods: We conducted a systematic literature search through PubMed, the Cost-Effectiveness Analysis Registry, and manual cross-referencing of articles. We identified US-based studies with cost analyses starting in 2005 that studied the cost-effectiveness of initial local treatments for localized prostate cancer (surgery, radiation, or observation).

Results: There were eight studies that met our inclusion and exclusion criteria. Most studies took the cost perspective of Medicare, and two studies also considered the societal cost in terms of lost patient time. Most studies also used a Markov model with inputs based on the available literature for the effectiveness and toxicity of the different treatment options. The radiation-focused studies tended to find brachytherapy (BT) or stereotactic body radiation therapy (SBRT) to be more cost-effective than intensity-modulated radiation therapy or proton beam therapy. These findings were primarily based on the lower cost of SBRT or BT with roughly equal efficacy and toxicity. The two studies focused on surgery found surgery to be more cost effective than intensity-modulated radiation therapy, at least for low-risk disease, and one study found BT to be more cost-effective than surgery, and watchful waiting to be the most cost-effective option overall.

Conclusion: Cost-effectiveness analysis is important because it helps patients, physicians, and policymakers make quantitatively-based decisions, which balance treatment efficacy, toxicity, and costs. Significant methodological heterogeneity in the studies we found limit the ability to compare their results directly, but most found that for favorable-risk prostate cancer, shorter or simpler treatments tended to be more cost-effective, including no treatment (watchful waiting) in one study.

Keywords: Cost-effectiveness; Prostate cancer; Local therapy; Surgery; Radiation; Active surveillance; Watchful waiting

1. Introduction

In 2016, it is estimated that 180,890 new cases of prostate cancer will be diagnosed in the United States, with an estimated number of 26,120 deaths due to prostate cancer [1]. The prognosis of localized (T1-T3aN0M0) prostate cancer is related to its National Comprehensive Cancer Network risk group classification: low-risk (defined as prostate-specific antigen [PSA] < 10 ng/ml, Gleason 6, and T1c-T2a), intermediate-risk (PSA = 10–20 ng/ml, Gleason 7, or T2b-T2c), and high-risk disease (PSA > 20 ng/ml, Gleason 8–10, or T3a) [2]. Across all risk groups and stages (including patients with nonlocalized disease), spending in 2012 for prostate cancer was $1.3 billion [3]. Although PSA screening remains controversial and decreased screening may reduce the number of diagnoses [4], the aging US population may lead to a higher or at least stable number of prostate cancer diagnoses in the coming decades [5]. Given this considerable burden of prostate cancer in the United States, an important question remains what treatments are most cost-effective for prostate cancer. Furthermore, the Patient Protection and Affordable Care Act of 2010 will likely increase the importance of cost containment within the US health care system,

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especially within the context of Accountable Care Organizations [6].

This review aims to identify and summarize peer-reviewed studies based in the United States that performed a cost-effectiveness analysis for initial locoregional treatment (or observation) of localized prostate cancer. We focused on US-based studies only because of the unique health care economics present in the US, and due to uncertainty as to whether differences in cost-effectiveness found in other contexts would translate to inform the choice among treatment options within the United States. As opposed to including studies analyzing comparative effectiveness, which is the design most often chosen by randomized trials and retrospective studies, we only included articles that considered the costs of treatments relative to their effectiveness.

Many cost-effectiveness studies report the cost of each treatment per quality-adjusted life year (QALY) achieved [7]. The QALY measurement combines both the length and quality of life, and is calculated by multiplying (or integrating) the quality of life spent in a given health state with the duration of time spent in that health state. For example, if a patient has a predicted 10-year life expectancy with mild urinary incontinence, which might be assigned a utility value of 0.9, their QALY estimate would be $0.9 \times 10 = 9$ QALYs. The incremental cost-effectiveness ratio (ICER) is the ratio of the incremental cost between two treatments and the incremental effectiveness between them (usually measured in QALYs). Therefore, if a treatment provides an additional 0.5 QALYs compared with another treatment, but costs an additional $10,000, the calculated ICER would be $10,000/0.5 QALY = $20,000 per QALY. A common threshold at which an intervention is considered to be cost-effective compared with another intervention (including no intervention) is at the willingness-to-pay (WTP) threshold of $50,000 per QALY [8,9].

2. Methods

2.1. Search strategy

A complex search strategy was used. First, the PubMed database was searched using the key search terms: *prostate cancer AND* ([*cost effectiveness*] OR [*cost utility*]) Then, we searched the Cost-Effectiveness Analysis Registry (https://research.tufts-nemc.org/cear4/), which compiles and assesses cost-effectiveness studies, using the key term *prostate*. No limits were placed on dates of publication. Following the initial selection of studies to be included, manual cross-referencing of reference lists from these studies was used to find additional studies of interest. Similarly, we cross-referenced recent review articles on the cost-effectiveness of local therapies for prostate cancer to search for additional studies.

2.2. Study selection

Studies were included in this review if they performed a cost-effectiveness analysis for primary treatment of prostate adenocarcinoma and if they were published in a peer-reviewed journal. Studies were not included if they analyzed cost alone or comparative effectiveness alone. Only US-based studies were included and studies must have been written in English. The modalities considered included radiotherapy (2-dimensional [2D]-conformal radiation therapy [CRT], 3D-CRT, intensity-modulated radiation therapy [IMRT], brachytherapy [BT], proton beam therapy [PBT], stereotactic body radiation therapy [SBRT]), surgery (open radical prostatectomy [ORP], robot-assisted radical prostatectomy [RARP], laparoscopic radical prostatectomy [LRP]), and no local therapy (active surveillance [AS], watchful waiting [WW]). Only studies with cost analyses conducted starting in 2005 were included to ensure relevance to current practice. Studies were excluded if they evaluated the cost-effectiveness of only systemic therapy (e.g., hormonal therapy and chemotherapy) or if they evaluated the cost-effectiveness of only recurrent or metastatic disease. In addition, we excluded studies that analyzed the cost-effectiveness of adjuvant or salvage radiotherapy following prostatectomy. Data from these studies were extracted by the first author and verified by the second author. We used the Philips checklist [10] to guide our critical appraisal of studies.

3. Results

3.1. Characteristics of studies

The initial database search yielded 861 published articles from the database search and 87 articles from the CEAR. After reading the titles and/or abstracts of these publications, 32 candidate studies were identified. Of these studies, 11 were excluded because they were not based in the United States, five were excluded because of being a cost analysis only, two were excluded because they only studied systemic therapy, two were excluded as they were actually meta-analyses of prior studies, two were excluded because the cost analysis took place prior to 2005, and two were duplicate articles. This left a remaining eight studies for inclusion in this review. Manual cross-referencing of these studies and prior reviews on this topic did not reveal any additional studies that met our inclusion and exclusion criteria (we did identify one study using this method, which the initial search had not identified, but it was not published in a peer-reviewed journal). Fig. summarizes our study selection process.

The included studies generally considered men with low- or intermediate-risk prostate cancer. Most articles focused on comparing different radiation techniques, including external beam radiation therapy, IMRT, low-dose-rate (LDR) BT, high-dose-rate (HDR) BT, SBRT, and PBT. Two studies considered no local treatment, including WW or AS, or surgical treatments, including ORP, LRP, or RARP. One study considered different image-guidance