



Platinum Priority – Review – Prostate Cancer

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Surgery Versus Radiotherapy for Clinically-localized Prostate Cancer: A Systematic Review and Meta-analysis

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Abstract

Context: To date, there is no Level 1 evidence comparing the efficacy of radical prostatectomy and radiotherapy for patients with clinically-localized prostate cancer. **Objective:** To conduct a meta-analysis assessing the overall and prostate cancer-specific mortality among patients treated with radical prostatectomy or radiotherapy for clinically-localized prostate cancer.

Evidence acquisition: We searched Medline, EMBASE, and the Cochrane Library through June 2015 without year or language restriction, supplemented with hand search, using Preferred Reporting Items for Systematic Reviews and Meta-Analysis and Meta-analysis of Observational Studies in Epidemiology guidelines. We used multivariable adjusted hazard ratios (aHRs) to assess each endpoint. Risk of bias was assessed using the Newcastle-Ottawa scale.

Evidence synthesis: Nineteen studies of low to moderate risk of bias were selected and up to 118 830 patients were pooled. Inclusion criteria and follow-up length varied between studies. Most studies assessed patients treated with external beam radiotherapy, although some included those treated with brachytherapy separately or with the external beam radiation therapy group. The risk of overall (10 studies, aHR 1.63, 95% confidence interval 1.54–1.73, $p < 0.00001$; $I^2 = 0\%$) and prostate cancer-specific (15 studies, aHR 2.08, 95% confidence interval 1.76–2.47, $p < 0.00001$; $I^2 = 48\%$) mortality were higher for patients treated with radiotherapy compared with those treated with surgery. Subgroup analyses by risk group, radiation regimen, time period, and follow-up length did not alter the direction of results.

Conclusions: Radiotherapy for prostate cancer is associated with an increased risk of overall and prostate cancer-specific mortality compared with surgery based on observational data with low to moderate risk of bias. These data, combined with the forthcoming randomized data, may aid clinical decision making.

Patient summary: We reviewed available studies assessing mortality after prostate cancer treatment with surgery or radiotherapy. While the studies used have a potential for bias due to their observational design, we demonstrated consistently higher mortality for patients treated with radiotherapy rather than surgery.

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1. Introduction

Nonconservative treatment options for patients diagnosed with clinically-localized prostate cancer include radical prostatectomy and radiotherapy [1]. Currently, there are no published randomized controlled trials comparing their efficacy. For patients desiring nonconservative treatment, established clinical guidelines recommend either treatment option and patients must ultimately decide for themselves which treatment to undertake [2,3].

Few reviews and meta-analyses have been published on this subject. Recent reviews have focused on patients with high-risk prostate cancer [4,5]. These have reported a benefit of radical prostatectomy over radiotherapy for both overall and prostate cancer specific mortality [4,5]. The limited scope of previous reviews and recent publication of a number of studies assessing prostate cancer-specific and overall survival for patients treated with contemporary forms of radiotherapy [6–8] requires a new, comprehensive meta-analysis.

Our objective was to systematically review and conduct a systematic review and meta-analysis to compare efficacy data on overall and prostate cancer-specific survival among patients treated with radiotherapy or radical prostatectomy for clinically-localized prostate cancer.

2. Evidence acquisition

2.1. Research question

Do patients treated with radical prostatectomy for clinically-localized prostate cancer have improved overall or prostate cancer-specific mortality compared with those treated with radiotherapy?

2.2. Types of studies

We included randomized controlled trials, cohort, and case-control studies. Case series lacking comparator groups were excluded. Other publications including editorials, commentaries, and review articles were excluded. Publications not subject to peer-review (ie, reports of data from vital statistics and dissertations or theses) were also excluded. Where there was more than one publication resulting from the same patient cohort, to prevent the duplication of patients from one cohort, for each of our analyses we selected one study based on a hierarchical assessment of comparability of study groups, time period of study (preference for more recent), and number of patients (Supplementary data).

2.3. Types of participants and exposure

We reviewed studies reporting on men of any age with nonmetastatic prostate cancer treated with any commonly-utilized form of radiotherapy including conformal external beam (EBRT), intensity-modulated (IMRT), brachytherapy, or a combination of radiotherapy modalities with curative treatment intent. We excluded studies assessing adjuvant or salvage therapies as the specific objective. We included studies irrespective of dose and duration of radiotherapy. In

order to be included, studies had to have a comparison group comprising patients treated with radical prostatectomy. Studies assessing nonstandard treatments (such as cryotherapy) were excluded.

2.4. Outcome measures

The primary outcome was overall mortality and the secondary outcome was prostate cancer-specific mortality. Studies reporting surrogate endpoints such as biochemical recurrence only were excluded. Since age, comorbidity, and histologic factors such as grade and stage significantly impact overall and prostate cancer-specific mortality [8,9], we considered studies only reporting multivariable adjusted hazard ratios (aHR). We excluded crude or unadjusted outcome measures since these would provide biased estimates given the known differences in age and comorbidity between patients treated with radiotherapy and surgery.

2.5. Methods of review

We used Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Meta-analysis of Observational studies in Epidemiology guidelines for reporting of this systematic review and meta-analysis [10,11].

2.6. Search strategy

Medline, EMBASE, and EBM Reviews Cochrane Central Register of Controlled Trials databases were searched using the OvidSP search platform for studies indexed from database inception to June 1, 2015 with the assistance of a professional librarian. We used both subject headings and text-word terms for “radical prostatectomy”, “prostate cancer surgery”, “radiotherapy”, “outcome”, “survival/mortality”, and related and exploded terms including medical subject headings terms in combination with keyword searching. A full search strategy is presented in the Supplementary data. No limitations were placed with respect to publication language or publication year. Following the literature search, all duplicates were excluded. References from review articles, commentaries, editorials, included studies, and conference publications of relevant medical societies were reviewed and cross-referenced to ensure completeness. Conference abstracts were excluded.

2.7. Review methods

Two authors performed the study selection independently (C.J.D.W. and R.S.). Disagreements were resolved by consensus with the senior author (R.K.N.). Titles and abstracts were used to screen for initial study inclusion. Full-text review was used where abstracts were insufficient to determine if the study met inclusion or exclusion criteria. The final list of selected studies was agreed upon by urologists (C.J.D.W. and R.K.N.), radiation oncologists (R.C. and C.D.), and an epidemiologist (R.S.). One author (C.J.D.W.) performed all data abstraction including evaluation of study

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