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Review

A systematic review of randomised controlled trials of radiotherapy for localised prostate cancer

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Abstract ***Background:*** Prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males. A systematic review of randomised controlled trials (RCTs) of radiotherapy and other non-pharmacological management options for localised prostate cancer was undertaken.

Methods: A search of thirteen databases was carried out until March 2014. RCTs comparing radiotherapy (brachytherapy (BT) or external beam radiotherapy (EBRT)) to other management options i.e. radical prostatectomy (RP), active surveillance, watchful waiting, high intensity focused ultrasound (HIFU), or cryotherapy; each alone or in combination, e.g. with adjuvant hormone therapy (HT), were included.

Methods followed guidance by the Centre for Reviews and Dissemination and the Cochrane Collaboration. Indirect comparisons were calculated using the Bucher method.

Results: Thirty-six randomised controlled trials (RCTs, 134 references) were included. EBRT, BT and RP were found to be effective in the management of localised prostate cancer. While

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higher doses of EBRT seem to be related to favourable survival-related outcomes they might, depending on technique, involve more adverse events, e.g. gastrointestinal and genitourinary toxicity. Combining EBRT with hormone therapy shows a statistically significant advantage regarding overall survival when compared to EBRT alone (Relative risk 1.21, 95% confidence interval 1.12–1.30). Aside from mixed findings regarding urinary function, BT and radical prostatectomy were comparable in terms of quality of life and biochemical progression-free survival while favouring BT regarding patient satisfaction and sexual function.
There might be advantages of EBRT (with/without HT) compared to cryoablation (with/without HT). No studies on HIFU were identified.
Conclusions: Based on this systematic review, there is no strong evidence to support one therapy over another as EBRT, BT and RP can all be considered as effective monotherapies for localised disease with EBRT also effective for post-operative management. All treatments have unique adverse events profiles. Further large, robust RCTs which report treatment-specific and treatment combination-specific outcomes in defined prostate cancer risk groups following established reporting standards are needed. These will strengthen the evidence base for newer technologies, help reinforce current consensus guidelines and establish greater standardisation across practices.

1. Background

Worldwide, prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males, accounting for 14% (903,500) of the total new cancer cases and 6% (258,400) of the total cancer deaths in males in 2008 [1]. It is currently estimated that 1 in 7 men in the USA will be diagnosed with prostate cancer at some time in their lives (15.3% of men, based on 2008–2010 data), with an estimated prevalence in 2011 of 2,707,821 men living with prostate cancer and an estimated 233,000 new cases for 2014. For those who have the disease, chances of surviving 5 years after diagnosis are good (98.9% based on data from 2004–2010). Nevertheless, it is estimated that 29,480 American men will die from prostate cancer in 2014 [2,3]. Aside from reducing life expectancy, prostate cancer is associated with reduced quality of life in terms of decreased sexual functioning, urinary incontinence and changes in bowel function, all of which may occur prior to treatment and/or worsen after treatment [4].

Prostate cancer also affects society as a whole through premature death and disability as well as resulting human and economic consequences. It has been estimated that approximately $11.9 billion is spent each year in the United States on prostate cancer treatment, with $4.6bn, $6.2bn and $1.1bn spent on initial treatment, continuing care and last year of life, respectively [5,6]. It is clearly important to ensure that, for those in need of treatment, expenditure is targeted so that the right patients are in receipt of the most effective treatment at the correct time.

Current widely accepted management options include active surveillance, watchful waiting, radical prostatectomy (RP), hormone therapy (HT), radiotherapy, (i.e. external beam radiotherapy (EBRT) or brachytherapy (BT)) and chemotherapy. These approaches are applied individually, sequentially or in combination. High intensity focused ultrasound (HIFU) and cryotherapy are also used but to a lesser degree [7].

However, there is a lack of systematic reviews of randomised controlled trials assessing these options for prostate cancer, i.e. RP, radiotherapy (EBRT and BT), HIFU and cryotherapy.

In this systematic review, we aim to assess the efficacy [8] and adverse events associated with radiotherapy (EBRT and/or BT) compared with other non-pharmacological management options in patients with localised prostate cancer.

2. Methods

The systematic review process followed published guidelines [9,10].

2.1. Inclusion criteria

Our review was focused on non-pharmacological interventions. Pharmacological management of patients was only considered if it was an adjunct to main treatment. Published and unpublished randomised controlled trials were included when they reported on adult men (>18 years) with prostate cancer, treated with any form of radiotherapy (EBRT and/or BT), alone or in combination with HT or RP, in comparison to other relevant management options, i.e. RP, active surveillance, watchful waiting, HIFU and cryotherapy. Outcomes considered relevant for our review included mortality outcomes (overall survival, disease-specific survival), progression outcomes (clinical, biochemical and mixed progression-free survival), adverse events (AE; including

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