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Timing of Curative Treatment for Prostate Cancer: A Systematic Review

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Abstract

Context: Delaying definitive therapy unfavourably affects outcomes in many malignancies. Diagnostic, psychological, and logistical reasons but also active surveillance (AS) strategies can lead to treatment delay, an increase in the interval between the diagnosis and treatment of prostate cancer (PCa).

Objective: To review and summarise the current literature on the impact of treatment delay on PCa oncologic outcomes.

Evidence acquisition: A comprehensive search of PubMed and Embase databases until 30 September 2012 was performed. Studies comparing pathologic, biochemical recurrence (BCR), and mortality outcomes between patients receiving direct and delayed curative treatment were included. Studies presenting single-arm results following AS were excluded.

Evidence synthesis: Seventeen studies were included: 13 on radical prostatectomy, 3 on radiation therapy, and 1 combined both. A total of 34 517 PCa patients receiving radical local therapy between 1981 and 2009 were described. Some studies included low-risk PCa only; others included a wider spectrum of disease. Four studies found a significant effect of treatment delay on outcomes in multivariate analysis. Two included low-risk patients only, but it was unknown whether AS was applied or repeat biopsy triggered active therapy during AS. The two other studies found a negative effect on BCR rates of 2.5−9 mo delay in higher risk patients (respectively defined as any with T ≥2b, prostate-specific antigen >10, Gleason score >6, >34−50% positive cores; or D'Amico intermediate risk-group). All studies were retrospective and nonrandomised. Reasons for delay were not always clear, and time-to-event analyses may be subject to bias.

Conclusions: Treatment delay of several months or even years does not appear to affect outcomes of men with low-risk PCa. Limited data suggest treatment delay may have an impact on men with non-low-risk PCa. Most AS protocols suggest a confirmatory biopsy to avoid delaying treatment in those who harbour higher risk disease that was initially misclassified.

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1. Introduction

Delay of definitive therapy has an unfavourable impact on outcomes in different malignancies [1–3]. Because most malignant cells appear to grow exponentially with related systemic spread, we can reasonably assume that treatment delay of some tumours may risk missing the window of curability.

Prostate cancer (PCa) is generally considered a relatively slow-growing malignancy, with screening adding a considerable lead time [4,5]. Delay between diagnosis and active therapy of PCa is often common. Unintended causes for this delay may include the need for pretreatment diagnostics or psychological and logistical reasons. Active surveillance (AS), as opposed to immediate definitive therapy, has garnered considerable support for several reasons in the treatment of low-risk disease. This strategy has introduced a new intended reason for delay in treatment [6,7]. AS is

designed to avoid unnecessary therapy in low-risk PCa, but identification of these tumours can be difficult and may miss the presence of occult higher risk disease.

We review the current medical literature to identify evidence whether treatment delay in PCa results in worse oncologic outcomes. Effects on functional outcome are not addressed.

2. Evidence acquisition

2.1. Study selection

We conducted a systematic review of the electronic databases PubMed and Embase according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement guidelines [8]. Predefined search terms were used to identify articles describing the impact of a delay in treatment or extending the time interval between diagnosis

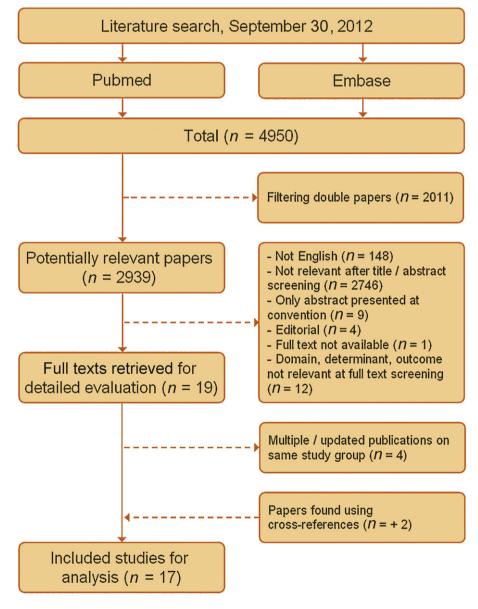


Fig. 1 - Literature search and selection of studies for analysis flowchart.

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