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Review – Prostate Cancer

Low-risk Prostate Cancer: Identification, Management, and Outcomes

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Abstract

Context: The incidence of low-risk prostate cancer (PCa) has increased as a consequence of prostate-specific antigen testing.
Objective: In this collaborative review article, we examine recent literature regarding low-risk PCa and the available prognostic and therapeutic options.
Evidence acquisition: We performed a literature review of the Medline, Embase, and Web of Science databases. The search strategy included the terms: prostate cancer, low risk, active surveillance, focal therapy, radical prostatectomy, watchful waiting, biomarker, magnetic resonance imaging, alone or in combination.
Evidence synthesis: Prospective randomized trials have failed to show an impact of radical treatments on cancer-specific survival in low-risk PCa patients. Several series have reported the risk of adverse pathologic outcomes at radical prostatectomy. However, it is not clear if these patients are at higher risk of death from PCa. Long-term follow-up indicates the feasibility of active surveillance in low-risk PCa patients, although approximately 30% of men starting active surveillance undergo treatment within 5 yr. Considering focal therapies, robust data investigating its impact on long-term survival outcomes are still required and therefore should be considered experimental. Magnetic resonance imaging and tissue biomarkers may help to predict clinically significant PCa in men initially diagnosed with low-risk disease.
Conclusions: The incidence of low-risk PCa has increased in recent years. Only a small proportion of men with low-risk PCa progress to clinical symptoms, metastases, or death and prospective trials have not shown a benefit for immediate radical treatments. Tissue biomarkers, magnetic resonance imaging, and ongoing surveillance may help to identify those men with low-risk PCa who harbor more clinically significant disease.
Patient summary: Low-risk prostate cancer is very common. Active surveillance has excellent long-term results, while randomized trials have failed to show a beneficial impact of immediate radical treatments on survival. Biomarkers and magnetic resonance imaging may help to identify which men may benefit from early treatment.

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1. Introduction

The incidence of prostate cancer (PCa) has increased over the past 2 decades due to the widespread use of prostate specific antigen (PSA) screening [1]. This trend is mostly marked in low-risk localized PCa [2], while a considerable reduction of metastatic PCa at diagnosis has been reported [3–5].

A significant challenge is to differentiate PCa destined to cause clinical symptoms or metastases from more clinically indolent PCa that is highly unlikely to impact survival, even without immediate treatment. To this aim, several risk classifications have been proposed on the basis of clinical and pathological characteristics such as clinical stage, PSA, and biopsy Gleason score. Several local active treatments have been proposed in this setting, such as radical prostatectomy (RP), external beam radiotherapy (EBRT), or active surveillance (AS). Although several different AS protocols have been proposed, it generally consists of monitoring with PSA, prostate exam, with or without magnetic resonance imaging (MRI), and repeat prostate biopsies. It differs from watchful waiting, which is a passive approach where symptomatic progression prompts the subsequent use of palliative treatment.

The aim of this review is to evaluate currently available literature about low-risk PCa and to provide a contemporary overview of diagnostic approaches and available management options.

2. Evidence acquisition

A literature review was performed in June 2016 using the Medline, Embase, and Web of Science databases. The search strategy included the terms "prostate cancer," "low risk," "active surveillance," "focal therapy," "radical prostatectomy," "watchful waiting," "biomarker," "magnetic resonance imaging," alone or in combination. The search was limited to English literature. References cited in selected articles and in review articles retrieved in our search were also used to identify manuscripts that were not included in the initial search. The articles that provided the highest level of evidence were then evaluated. When existing, prospective studies were preferred to retrospective designs. A list of articles judged to be highly relevant by the first and senior authors was circulated among the coauthors and a final consensus was reached on the structure of the review and the articles included. The systematic review was performed in agreement with the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (Fig. 1) [6].

3. Evidence synthesis

Fig. 1 shows a flow diagram of the selection process for this systematic review of the literature. Out a total of 723 articles screened, 189 were initially assessed for eligibility. Of these 121 were subsequently excluded and 31 were selected and included by authors. In total, 99 articles were selected and critically analyzed.

3.1. Definition of low-risk PCa

Low-risk localized disease has generally been defined as clinical stage T1–T2, biopsy Gleason score $\leq$6, and PSA $<$10 ng/ml. Almost all risk classifications utilize these risk factors based on outcome data after whole-gland treatments

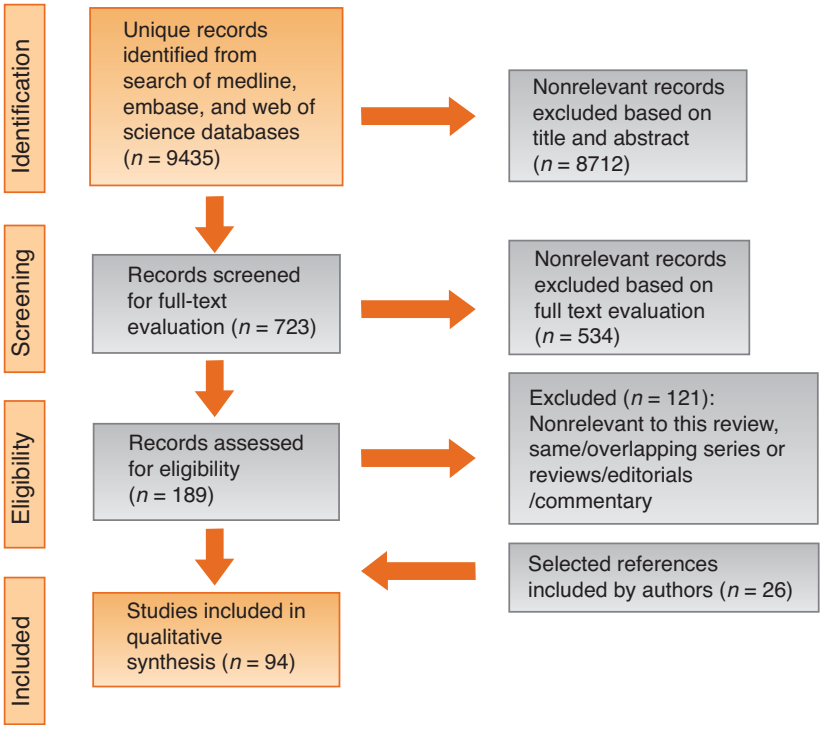

Fig. 1 – Flow diagram of evidence acquisition in a systematic review for patients affected by low risk prostate cancer.

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