

INPLASY

PSA as an ultrasensitive biomarker for patients with recurrent prostate cancer. A systematic review

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von Eyben, FE¹; Kairemo, K²; Kapp, DS³.

Corresponding author:

Finn von Eyben

finn113edler@mail.tele.dk

Author Affiliation:

Center of Tobacco Control Research.

ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 November 2023 and was last updated on 21 November 2023.

INTRODUCTION

Review question / Objective To summarize ultrasensitive PSA assays and clinical studies for outcome of recurrent prostate cancer patients for survival after salvage treatment. Patients: Prostate cancer patients after initial treatment. PSA measured with ultrasensitive PSA assays. Outcome: progression free survival, overall survival.

Rationale The hypothesis for the review is that very early salvage treatment gives better overall survival after salvage treatment than (less) early salvage treatment, or late salvage treatment. Earlier treatment means a smaller tumor burden and less heterogeneity.

Condition being studied Prostate cancer after the initial treatment of localized cancer.

METHODS

Search strategy Search in Pubmed with a defined set search words, further search in relevant publications from their reference lists.

Participant or population Participants in the published publications.

Intervention Repeat measurements of PSA and salvage treatment at specified PSA thresholds for rising PSA values.

Comparator patients after initial treatment for localized cancer who do not develop rising PSA after the PSA nadir after the initial treatment.

Study designs to be included Clinical studies will be analyzed in Forest plots to calculate an overall frequency for an outcome. Stata has a program for summarizing p values into an overall p value.

Eligibility criteria The systematic review has a defined set of inclusion and exclusion criteria. The selection process reduced the initial 300+ hits to selected 115 publications.

Information sources PUBMED and Google Web of Science.

Main outcome(s) PSA measured with ultrasensitive assays can differentiate between patients who have a relapse and patients without a relapse from 3 months after initial radical prostatectomy.

Additional outcome(s) We compare the overall survival for three risk groups for patients with PSA relapse and patients with a slightly later phase of non-metastatic prostate cancer.

Data management Data were evaluated in STATA version 16.0 with updates.

Quality assessment / Risk of bias analysis We summarize survival. So studies with longer follow-up have a higher frequency of deaths of prostate cancer than studies with a short follow-up.

Strategy of data synthesis Conventional Forest plots.

Subgroup analysis Most studies had radical prostatectomy as initial treatment but other patients had radiation as initial treatment. Outcome was related to levels of PSA at start of salvage radiation therapy.

Sensitivity analysis We summarized 66 thousand patients reported over three decades. Much has been changed during the period but the trends for relevance of PSA remained grossly unchanged over 3 decades despite many new treatments in recent years.

Language restriction Mainly English.

Country(ies) involved Denmark, Finland, and USA.

Other relevant information We excluded a publication in Japanese because we do not understand the language and most readers of the review will face the same problem.

The publications did not inform of the salvage treatment but generally patients who relapse after the initial radical prostatectomy are treated with salvage radiation therapy.

The salvage radiation therapy has not changed much during the decades despite many technical improvements.

Treatment is generally given with five treatments per week to a cumulative dose of 60 to 70 Gy.

Keywords biochemical-recurrence-prone prostate cancer, prostate specific antigen (PSA) half-life, PSA nadir, PSA thresholds, survival, ultrasensitive PSA assays.

Dissemination plans The systematic review is being evaluated by the journal *Biomedicine*.

Contributions of each author

Author 1 - Finn von Eyben - Center of Tobacco Control Research.

Email: finn113edler@mail.tele.dk

Author 2 - Kalevi Kairemo - Professor of Nuclear medicine, affiliated with Docrates, Helsinki, Finland, and University of Texas MD Anderson Cancer Center, Houston, Texas, USA.

Email: kalevi.kairemo@gmail.com

Author 3 - Daniel Kapp - Long-term affiliation at Stanford University, California, USA. Professor Kapp has been editor of a journal of gynecologic oncology.

Email: dskap@stanford.edu