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Platinum Priority – Collaborative Review – Prostate Cancer

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# Positive Surgical Margins After Radical Prostatectomy: A Systematic Review and Contemporary Update

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**Abstract**

***Context:*** The clinical significance of positive surgical margins (PSMs) in radical prostatectomy (RP) specimens and the management of affected patients remain unclear.
***Objective:*** To address pitfalls in the pathologic interpretation of margin status; provide an update on the incidence, predictors, and long-term oncologic implications of PSMs in the era of robot-assisted laparoscopic RP (RALRP); and suggest a practical evidence-based approach to patient management.
***Evidence acquisition:*** A systematic review of the literature was performed in April 2013 using Medline/PubMed, Web of Science, and Scopus databases and the Cochrane Database of Systematic Reviews. Studies focusing on PSMs in RP pertinent to the objectives of this review were included. Particular attention was paid to publications within the last 5 yr and those concerning RALRP.
***Evidence synthesis:*** A total of 74 publications were retrieved. Standardized measures to overcome variability in the pathologic interpretation of surgical margins have recently been established by the International Society of Urological Pathology. The average rate of PSMs in contemporary RALRP series is 15% (range: 6.5–32%), which is higher in men with a more advanced pathologic stage and equivalent to the rate reported in prior open and laparoscopic prostatectomy series. The likelihood of PSMs is strongly influenced by the surgeon's experience irrespective of the surgical approach. Technical modifications using the robotic platform and the role of frozen-section analysis to reduce the margin positivity rate continue to evolve. Positive margins are associated with a twofold increased hazard of biochemical relapse, but their association with more robust clinical end points is controversial. Level 1 evidence suggests that adjuvant radiation therapy (RT) may favorably affect prostate-specific antigen recurrence rates, but whether the therapy also affects systemic progression, prostate cancer–specific mortality, and overall survival remains debatable.
***Conclusions:*** Although positive margins in prostate cancer are considered an adverse oncologic outcome, their long-term impact on survival is highly variable and largely influenced by other risk modifiers. Adjuvant RT appears to be effective, but further study is required to determine whether early salvage RT is an equivalent alternative.


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## 1. Introduction

Positive surgical margins (PSMs) after radical prostatectomy (RP) are uniformly considered an adverse outcome associated with failure of the surgery to achieve cure of the prostate cancer (PCa). In 2009, we published a comprehensive review on the issue of positive margins that was based primarily on studies conducted in the late 1990s and early in the first decade of the 2000s [1]. Since then, there has been a dramatic worldwide shift in practice patterns from open to robotic surgery and a substantial increase in RP volume [2]. In addition, data from clinical trials and case series have matured, allowing for better appraisal of the true impact of PSMs on oncologic outcomes and the role of radiation therapy (RT) in this setting. We hence sought to present an update addressing the pitfalls in the pathologic interpretation of margin status and the incidence and long-term oncologic implications of PSMs in the current era of robot-assisted laparoscopic RP (RALRP). A practical evidence-based approach to the management of patients with PSMs is suggested.

## 2. Evidence acquisition

To update our previous review [1], we performed a systematic literature search in April 2013 using the Medline/PubMed, Scopus, and Web of Science databases and the Cochrane Database of Systematic Reviews, including both medical subject headings and free text protocols. The search was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses criteria for systematic reviews (http://www.prisma-statement.org) and was restricted to the term *positive margins* or *surgical margins* and one of the following: *prostate cancer, prostate carcinoma, pathological, radical prostatectomy, robotic-assisted laparoscopic radical prostatectomy, surgical experience, prognosis, oncologic outcomes, survival*, and *radiation therapy*. The following limits were used: humans; gender (male); English language; and publications dating from January 1, 2005 (Fig. 1).

Two authors (O.Y. and K.T.) independently reviewed the abstracts of the retrieved studies and selected the abstracts that were pertinent to the objectives of the present review. The corresponding full-length articles and their linked references were carefully assessed by all authors; particular attention was paid to publications that appeared within the last 5 yr and publications concerning RALRP. Studies published as abstracts or reports from meetings were excluded. When two or more papers reported on updated series of the same cohort, the most recent paper was considered. Only articles reporting complete data with clinical relevance for the present review were included in the final analysis.

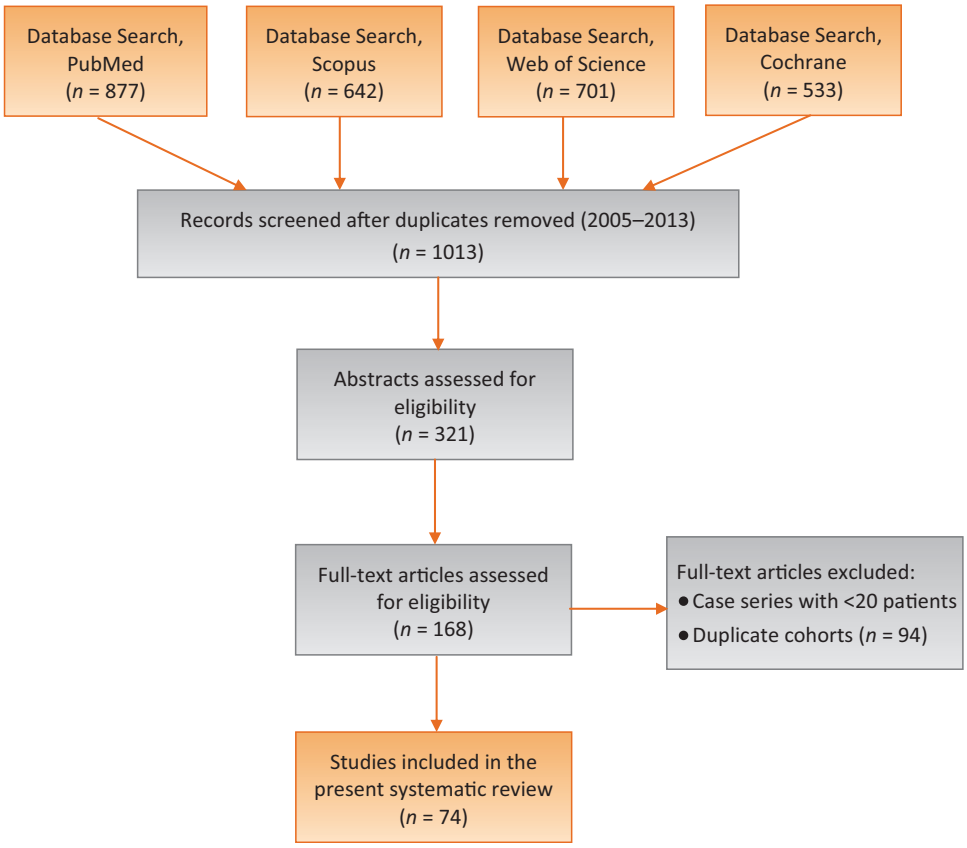


**Fig. 1 – Systematic electronic search method.**