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Systematic Review and Meta-analysis of Studies Reporting Oncologic Outcome After Robot-assisted Radical Prostatectomy

Giacomo Novara [a,], Vincenzo Ficarra [a,b], Simone Mocellin [a], Thomas E. Ahlering [c], Peter R. Carroll [d], Markus Graefen [e], Giorgio Guazzoni [f], Mani Menon [g], Vipul R. Patel [h], Shahrokh F. Shariat [i], Ashutosh K. Tewari [i], Hendrik Van Poppel [j], Filiberto Zattoni [a], Francesco Montorsi [k], Alexandre Mottrie [b], Raymond C. Rosen [l], Timothy G. Wilson [m]*

[a] *University of Padua, Padua, Italy;* [b] *O.L.V. Robotic Surgery Institute, Aalst, Belgium;* [c] *University of California, Irvine, Orange, CA, USA;* [d] *University of California, San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco Veterans Affairs Medical Center, San Francisco, CA, USA;* [e] *Martini-Clinic, Prostate Cancer Centre, University Hamburg-Eppendorf, Hamburg, Germany;* [f] *University Vita-Salute San Raffaele, H. San Raffaele-Turro, Milan, Italy;* [g] *Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA;* [h] *Global Robotics Institute, Florida Hospital Celebration Health, Celebration, FL, USA;* [i] *Weill Medical College of Cornell University, New York, NY, USA;* [j] *University Hospital, Katholieke Universiteit Leuven, Leuven, Belgium;* [k] *University Vita-Salute San Raffaele, H. San Raffaele, Milan, Italy;* [l] *New England Research Institutes, Inc., Watertown, MA, USA;* [m] *City of Hope National Cancer Center, Duarte, CA, USA*

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Abstract

Context: Despite the large diffusion of robot-assisted radical prostatectomy (RARP), literature and data on the oncologic outcome of RARP are limited.
Objective: Evaluate lymph node yield, positive surgical margins (PSMs), use of adjuvant therapy, and biochemical recurrence (BCR)–free survival following RARP and perform a cumulative analysis of all studies comparing the oncologic outcomes of RARP and retropubic radical prostatectomy (RRP) or laparoscopic radical prostatectomy (LRP).
Evidence acquisition: A systematic review of the literature was performed in August 2011, searching Medline, Embase, and Web of Science databases. A free-text protocol using the term *radical prostatectomy* was applied. The following limits were used: humans; gender (male); and publications dating from January 1, 2008. A cumulative analysis was conducted using Review Manager software v.4.2 (Cochrane Collaboration, Oxford, UK) and Stata 11.0 SE software (StataCorp, College Station, TX, USA).
Evidence synthesis: We retrieved 79 papers evaluating oncologic outcomes following RARP. The mean PSM rate was 15% in all comers and 9% in pathologically localized cancers, with some tumor characteristics being the most relevant predictors of PSMs. Several surgeon-related characteristics or procedure-related issues may play a major role in PSM rates. With regard to BCR, the very few papers with a follow-up duration >5 yr demonstrated 7-yr BCR-free survival estimates of approximately 80%. Finally, all the cumulative analyses comparing RARP with RRP and comparing RARP with LRP demonstrated similar overall PSM rates (RARP vs RRP: odds ratio [OR]: 1.21; $p = 0.19$; RARP vs LRP: OR: 1.12; $p = 0.47$), pT2 PSM rates (RARP vs RRP: OR: 1.25; $p = 0.31$; RARP vs LRP: OR: 0.99; $p = 0.97$), and BCR-free survival estimates (RARP vs RRP: hazard ratio [HR]: 0.9; $p = 0.526$; RARP vs LRP: HR: 0.5; $p = 0.141$), regardless of the surgical approach.
Conclusions: PSM rates are similar following RARP, RRP, and LRP. The few data available on BCR from high-volume centers are promising, but definitive comparisons with RRP or LRP are not currently possible. Finally, significant data on cancer-specific mortality are not currently available.

* Corresponding author. Department of Surgical and Oncological Sciences, Urologic Unit, Via Giustiniani 2, 35100 Padua, Italy. Tel. +39 049 8212720; Fax: +39 049 8218757.
E-mail address: giacomonovara@gmail.com, giacomo.novara@unipd.it (G. Novara).

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1. Introduction

Radical prostatectomy (RP) is a standard surgical treatment of clinically localized prostate cancer (PCa) [1]. Patients who undergo RP experience 15-yr cancer-specific mortality (CSM) ranging from 7% to 20%. Conversely, 15-yr biochemical recurrence (BCR)–free survival estimates may be as high as 75% [2,3]. These figures were obtained in series of retropubic RPs (RRPs) performed in US and European referral centers. Robot-assisted RP (RARP) also has become very popular in the United States and Europe; it has been estimated that >75% of RPs are performed using the da Vinci platform (Intuitive Surgical, Inc., Sunnyvale, CA, USA) [4,5].

Literature and data on the oncologic outcome of RARP are limited and sparse. Very few series reported BCR rates at a follow-up duration as long as 5 yr [6,7], which was still insufficient for a comprehensive evaluation of CSM. More data are available on other outcomes that can be considered surrogates for oncologic control (eg, positive surgical margin [PSM] rates). We previously reported that, compared with RRP, RARP was associated with a significantly lower risk of overall PSMs and PSMs in pathologically confined disease, whereas statistically significant differences between RARP and laparoscopic radical prostatectomy (LRP) failed to be identified [8]. However, data on other relevant issues, such as lymph node yield during robotic lymph node dissection and use of adjuvant therapies following RARP, are sparse and controversial [8–12].

Because of the increasing use of RARP as well as the mounting literature in the field of oncologic outcomes of RARP and controversies in the available literature, we elected to update our previous systematic reviews. We aimed at evaluating lymph node yield after RARP, prevalence and risk factors for PSMs after RARP, surgical techniques that are able to improve PSM rates after RARP, use of adjuvant therapy after RARP, and BCR-free survival estimates following RARP. Finally, we aimed at performing a cumulative analysis of all studies comparing the oncologic outcomes of RARP and RRP or LRP.

2. Evidence acquisition

To update our previous systematic reviews [8,9], we performed a literature search in August 2011 using the Medline, Embase, and Web of Science databases. The Medline search included only a free-text protocol using the term *radical prostatectomy* in the title and abstract fields of the records. The following limits were used: humans; gender (male); and publications dating from January 1, 2008. The searches of the Embase and Web of Science databases used the same free-text protocol, keyword, and publication dates.

Two authors (G.N. and V.F.) separately reviewed the records to select RARP series as well as studies that compared RRP with LRP, RRP with RARP, and LRP with RARP, and discrepancies were resolved by open discussion. Other significant studies cited in the reference lists of the selected papers were evaluated, as were studies published after the systematic search. All noncomparative studies reporting the outcome of RARP for >100 cases were collected. The present review included only studies reporting oncologic outcomes (ie, lymph node yield, PSM rates, use of adjuvant therapies, and BCR-free survival rates). Studies published only as abstracts and reports from meetings were not included in the review. All the data retrieved from the selected studies were recorded in an electronic database. Quality control of the electronic data recording was performed on a random sample of papers (approximately 15% of the articles).

All the papers were categorized according to the 2011 level of evidence for therapy studies: systematic review of randomized trials or *n*-of-1 trials (level 1); randomized trials or observational studies with dramatic effect (level 2); nonrandomized controlled cohort/follow-up studies (level 3); case series, case–control studies, or historically controlled studies (level 4); and mechanism-based reasoning (level 5) [13].

2.1. Statistical analysis

Cumulative analysis was conducted using Review Manager v.4.2 software designed for composing Cochrane Reviews (Cochrane Collaboration, Oxford, UK). Statistical heterogeneity was tested using the χ^2 test. A p value <0.10 was used to indicate heterogeneity. Where there was a lack of heterogeneity, fixed-effects models were used for the cumulative analysis. Random effects models were used in case of heterogeneity. For continuous outcomes, the results were expressed as weighted mean differences and standard deviations; for dichotomous variables, results were given as odds ratios (OR) and 95% confidence intervals (CIs). For cumulative analysis of BCR, statistical analyses were performed using Stata 11.0 SE software (StataCorp, College Station, TX, USA). A weighted average of study-specific estimates of the hazard ratio (HR) was calculated using the inverse of variance as the weighting factor. RARP was considered the reference treatment with which either RRP or LRP was compared. The natural logarithm of HR and the corresponding standard error were used as data points for the meta-analysis. In studies performing Cox multivariable survival analysis, HR and CI were usually reported. For studies performing only univariable survival analysis, HR and 95% CI were calculated from survival curves adopting a hierarchical series of steps, as in Parmar et al. [14]. For indirect treatment comparisons, an extended version of the Bucher method [15] was used to obtain HR estimates from studies in which all three surgery types were considered but RARP was not the reference treatment. For all statistical analyses, a two-sided $p < 0.05$ was considered statistically significant.

3. Evidence synthesis

3.1. Quality of the studies and level of evidence

Figure 1 shows the flowchart of this systematic review of the literature. We selected 129 records reporting oncologic outcomes after RARP. Two further studies (one level 2 and one level 3) published during the realization of the systematic review were added [16,17]. Forty-seven abstracts or meeting