

Original article

Surgical margin length and location affect recurrence rates after robotic prostatectomy

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Abstract

Background: Robotic-assisted laparoscopic radical prostatectomy is a current standard treatment for localized prostate cancer, with treatment failure defined by biochemical recurrence (BCR). Open radical prostatectomy series have identified the presence of a positive surgical margin (PSM) as a predictor of long-term recurrence, a measure that is affected by the surgeon's skill. We evaluate the effect of PSM parameters on BCR rates from robotic-assisted laparoscopic radical prostatectomy, across 3 high-volume institutions.

Methods: De-identifiable clinicopathological and histopathological data were prospectively collected for 4,001 patients with at least 3 years of follow-up. Kaplan-Meier plots and 3 statistical models were used to evaluate the effect of margin parameters on BCR, via crude rates, traditional multivariable Cox regression, and a propensity-adjusted Cox regression model.

Results: Overall, 37% of men with a PSM developed BCR compared with 10% of men with negative margins (hazard ratio [HR] = 1.81, 95% CI: 1.47–2.22). Length ≥ 3 mm or a multifocal positive margin was associated with a higher risk of BCR compared with negative margin cases. On multivariable Cox regression analysis of the positive margin cohort, only apical margins significantly predicted BCR relative to basal margins (HR = 2.03, 95% CI: 1.01–4.09), whereas there was no significant difference in BCR rates for posterolateral margins relative to basal margins (HR = 1.62, 95% CI: 0.84–3.11). Propensity-adjusted modeling confirmed a greater effect of apical compared with posterolateral PSM.

Conclusions: A PSM length ≥ 3 mm is predictive of BCR, as is to a lesser extent multiple positive margins. In contrast to open prostatectomy series, posterolateral margins carry a smaller risk of BCR compared with apical margins. © 2015 Elsevier Inc. All rights reserved.

Keywords: Robotic-assisted prostatectomy; Positive surgical margin; Length; Location; Biochemical recurrence

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1. Introduction

Prostate cancer is the most common nondermatological malignancy in Western men and a common cause of cancer-related death [1]. Randomized trials of patients identified from pre-prostate-specific antigen (PSA) screening eras have shown a survival benefit of radical prostatectomy for localized prostate cancer [2]. In the absence of long-term mortality data, biochemical recurrence (BCR), defined as a rise in PSA level, can be used to prognosticate adverse survival outcomes, determine the need for adjuvant salvage therapy, and predict cancer-related death [3].

After prostatectomy, histopathological assessment of the Gleason grade and pathological stage, together with the patient's preoperative PSA level, is used to stratify patients, prognosticate their outcome, and guide further management [4]. A positive surgical margin (PSM), which is defined as the presence of tumor cells at the inked margin is a consistently strong predictor of BCR [5]. A study reported a BCR-free survival of 93.8% and 79.9% in those with negative surgical margins (NSMs) and PSMs, respectively, after covariate adjustment [6]. A PSM, however, may be the result of artifact, intraprostatic incision [7], or extraprostatic disease that has been incompletely resected.

Minimally invasive master-slave “robotic” systems are being increasingly used for radical prostatectomy to address the limitations of a traditional laparoscopic approach, with similar outcomes between operative modalities [8,9]. Tissue handling, retraction, and tension applied at each step are all unique from open radical (ORP) and laparoscopic radical prostatectomy procedures; hence, the effect of margin parameters on outcomes after robotic-assisted radical prostatectomy (RARP) cannot be drawn from such studies. Two recent RARP single-institution series have been published; one establishing the effect of PSMs ≥ 3 mm or multifocal margins compared with those < 3 mm or unifocal margins (hazard ratio [HR] = 2.84, 95% CI: 1.76–4.59) [10,11]. This effect has not been demonstrated in RARP multi-institutional cohorts with long-term follow-up.

The apex and posterolateral regions are the most common locations for PSM in ORP [12]. In a recent review, 11 of 15 studies showed no significant effect of apical PSM on BCR after multivariable analysis [13]. Posterolateral margins are often the result of efforts to preserve the neurovascular bundles, as this region broadly describes where intrafascial or interfascial dissection occurs for nerve sparing. Three recent reports describe a greater effect of a posterolateral margin on BCR rates, whereas only one failed to demonstrate a significant relationship (of any location including posterolateral), likely owing to the small sample size [13,14].

RARP studies have failed to establish any statistically significant conclusions regarding the effect of PSM location on BCR. An institution reported a trend toward a greater effect of apical margins on progression-free survival [15]; initial trends suggest PSM locations in RARP having

different prognostic value when compared with ORP series, where there is more generally accepted importance of posterolateral margins, but still controversy regarding apical margins [11].

We seek to determine the way in which margin parameters after RARP predict BCR across high-volume institutions.

2. Methods

2.1. Patient populations

This is a multi-institutional study involving patients from 3 major RARP treatment centers: University of California Irvine Medical Center, Irvine (USA), Florida Hospital (USA), and Karolinska University Hospital (Sweden). Between January 2002 and October 2013, data were prospectively collected for 7,357 RARP patients. Patients who had received RARP for cT1–3 prostate cancer and met all of the following criteria were included in this study: prostatectomy performed a minimum of 3 years before the end of follow-up; postoperative PSA level (or the presence or absence of BCR) had been recorded; not received adjuvant hormonal or radiotherapy; and the margin status (presence or absence) of the histopathological specimen had been recorded. In total, 3,330 cases were excluded owing to insufficient follow-up with or without adjuvant radiation or hormone therapy, whereas a further 26 cases were excluded exclusively owing to use of adjuvant therapy alone. In total, 4,001 consecutive patients fulfilled the inclusion criteria for this study.

2.2. Surgical technique

Each institution involved in this study have reported their method of RARP, which has been detailed previously [11,16,17]. Subsequent subtle modifications are used by some of the contributing centers but not others (e.g., grades of nerve-sparing dissection, cautery-free technique, local hypothermia, and retrograde dissection) [18–20].

2.3. Histopathological analysis

Comprehensive approaches to histopathological processing and specimen handling have been documented by all 3 centers involved and follows the widely used modified Stanford protocol [21] as previously reported [7]. The following histopathological variables were recorded: prostate volume (grams), pathological stage (TNM), pathological Gleason score, nodal status, the presence or absence of positive margins, the number of PSMs (focality: 0, 1, or ≥ 2), the total length of positive margins (a cumulative measurement across all PSM(s) in millimeters—grouped into NSMs, margin length < 3 mm, or margin length ≥ 3 mm), and the location of any PSM (posterolateral,

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