Impact of positive surgical margins and their locations after radical prostatectomy: comparison of biochemical recurrence according to risk stratification and surgical modality

Abstract

Purpose

We investigated the influence of positive surgical margins (PSMs) and their locations on biochemical recurrence (BCR) according to risk stratification and surgical modality.

Methods

A total of 1,874 post-radical-prostatectomy (RP) patients of pT2–T3a between 2000 and 2010 at three tertiary centers, and who did not receive neoadjuvant/adjuvant therapy, were included in this study. Patients were stratified according to BCR risk: low risk (PSA <10, pT2a-b, and pGS ≤6), intermediate risk (PSA 10–20 and/or pT2c and/or pGS 7), and high risk (PSA >20 or pT3a or pGS 8–10). The median follow-up was 43 months.

Results

PSMs were a significant predictor of BCR in both the intermediate- and high-risk-disease groups (P = .001, HR 2.1, 95% CI 1.3–3.4; P < .001, HR 2.8, 95% CI 2.0–4.1). Positive apical margin was a significant risk factor for BCR in high-risk disease (P = .003, HR 2.0, 95% CI 1.2–3.3), but not in intermediate-risk disease (P = .06, HR 1.7, 95% CI 0.9–3.1). Positive bladder neck margin was a significant risk factor for BCR in both intermediate- and high-risk disease (P < .001, HR 5.4, 95% CI 2.1–13.8; P = .001, HR 4.5, 95% CI 1.8–11.4). In subgroup analyses, robotic RP provided comparable BCR-free survival regardless of risk stratification. Patients with PSMs showed similar BCR-free survival between open and robotic RP (log-rank, P = .897).

Conclusions

Post-RP PSMs were a significantly independent predictor of disease progression in both intermediate- and high-risk disease. Both positive apical and bladder neck margins were significant risk factors of BCR in high-risk disease. Patients with PSMs showed similar BCR-free survival between open and robotic surgery.
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Conclusions Post-RP PSMs were a significantly independent predictor of disease progression in high-risk disease as well as intermediate-risk disease. Both positive apical and bladder neck margins are also significant risk factors of BCR in high-risk disease. Patients with PSMs showed similar BCR-free survival between open and robotic surgery.

Keywords Prostatic neoplasms · Prostatectomy · Neoplasm · Residual · Disease-free survival · Robotics

Introduction

Positive surgical margin (PSM) implies incomplete tumor resection in surgical beds [1]. Its oncological significance to disease progression, however, remains controversial [2]. One recent study reported that PSM is not a significant risk factor for biochemical recurrence (BCR) in low- and high-risk diseases [3].

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Some reports have indicated that PSM rates might be related to surgical modalities and technique [7–9]. Another study recently showed that in high-stage disease, higher PSM rates are associated with robot-assisted laparoscopic radical prostatectomy (RALP) rather than with retropubic radical prostatectomy (RRP), but that in low-stage disease, PSM rates do not differ [10]. However, there has been no study comparing the two modalities for BCR according to risk stratification. Moreover, there is no known comparative RRP/RALP study on how PSMs effect BCR.

In the present study, we investigated the influence of PSMs and their locations on disease progression with pathological stage T2–T3a patients according to risk stratification and surgical modality.

Methods

A total of 3,465 consecutive patients who had undergone RRP or RALP for clinically localized prostate cancer between January 2006 and December 2010 at three tertiary referral centers representing the same institution were enrolled in this study. Upon the approval of our institutional review board, we retrospectively collected clinical and pathological information on those patients. Follow-up data were gathered by means of chart review.

All surgeons, who participated in this study, were experts and experienced enough to open (87–564 cases) or laparoscopic (over 150 cases) prostatectomy, and several reports showed that an experienced open surgeon successfully transferred open surgical skills to a robotic surgery in 8–25 cases [11, 12]. Therefore, with respect to each surgeon, the first 25 patients to undergo RALP were excluded owing to the learning curve. Additionally, a total of 252 patients who had undergone neoadjuvant therapy were excluded from the study. In order to isolate the effect of PSM locations on BCR, 460 patients with seminal vesicle invasion and/or positive lymph nodes, along with 254 patients who had undergone adjuvant therapy, were excluded. Also, 377 patients with <6 months of the follow-up and 24 patients with missing data were excluded. The patients with a detectable range of PSA over 0.2 ng/ml at the first follow-up visit were treated with adjuvant hormone therapy or radiotherapy, so those patients were excluded from the analyses. Thus, our final subjects numbered 1,874 patients with disease of T2 and T3a pathological stages.

The procedure according to which pathological specimens were processed was identical at each of the three hospitals. Prostatectomy specimens were processed according to the whole-mount technique and following the Stanford procedure, and were evaluated by 4 expert uro-pathologists. PSMs, defined as cancer cells reaching the inked surface, were categorized into four groups according to location: apex, bladder neck, postero-lateral, and multifocal. Pathological staging was done using the seventh edition AJCC cancer staging system [13].

Follow-up visits were scheduled at 3-month intervals for 1 year, then semiannually for 1 year, and annually thereafter. Serum PSA level was checked at each follow-up visit. BCR was defined as a PSA >0.2 ng/ml or more on two consecutive measurements. Patients were stratified by BCR risk according to the modified D’Amico criteria as follows: low risk (PSA <10, pT2a–b stage, and GS ≤5), intermediate risk (PSA 10–20 and/or pT2c stage and/or GS 7), and high risk (PSA >20 or pT3a stage or GS 8–10) [14].

Robotic surgery at our institution began in July 2008. In a subgroup analysis comparing robotic with open surgery, patients who had undergone RRP since that time were included. The choice of surgical approach accorded with patient preference after discussion of the risks, benefits, and alternatives with the attending surgeon. RRP was performed using the modified Walsh anatomical modality, and RALP was performed, using the transperitoneal antegrade approach and the da Vinci Robot System. We performed pelvic lymph node dissection (PLND) in most of the high-risk patients in D’Amico criteria, and the necessity of PLND in intermediate-risk patients was determined with the discretion of attending surgeon. The boundary of PLND included obturator, and external and internal iliac lymph nodes in most patients. The nerve-sparing procedure was performed if clinically indicated by patient age, preoperative erectile function, and oncological parameters.

Comparisons between subject groups were conducted using the Student’s t test or Pearson χ² test, and the respective clinicopathological variables were analyzed using Pearson χ² tests. To determine the effect of risk group as well as surgical margin status and its location on BCR risk, Kaplan–Meier curves were generated, and differences were compared by log-rank test and Cox proportional hazard regression analysis. Significant variables on univariate analysis were included in the multivariate model. A two-sided P value <.05 was considered significant. Statistical results were calculated using the SPSS software package (ver. 14.0, SPSS Inc., Chicago, IL, USA).
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