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Original article

The association between nerve sparing and a positive surgical margin during radical prostatectomy

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Abstract

Purpose: A positive surgical margin (SM) during radical prostatectomy (RP) increases risk of biochemical recurrence. We evaluated the effect of nerve-sparing procedures on risk of positive SM for pT2- and pT3-category tumors. We hypothesized that nerve sparing would increase rates of pT2 positive margins.

Methods: We evaluated a historical cohort of 9,915 consecutive RP patients treated at The Ottawa Hospital or Memorial Sloan-Kettering Cancer Center from 2000 to 2010. Patients underwent open, laparoscopic, or robotic RP. The primary outcome was presence of a positive SM stratified by pathologic pT2 and pT3 categories. The association between nerve sparing and positive margin was adjusted for prostate-specific antigen, RP Gleason sum, surgical modality, surgical date, and location in the multivariable model.

Results: Of 6,120 eligible patients, 3,958 (64.7%) had open RP, 1,566 (25.6%) had laparoscopic RP, and 596 (9.7%) had robotic RP. Approximately 8.6% (363/4,199) of patients with pT2-category disease and 25.2% (485/1,921) of patients with pT3-category disease had a positive margin. Patients with pT2-category disease who underwent a bilateral nerve-sparing procedure were more likely to have a positive margin when compared with those who underwent nerve resection on multivariable analysis (relative risk [RR] = 1.52, 95% CI: 0.97–2.39) after adjusting for confounders. Patients with pT3-category disease who underwent a bilateral nerve-sparing procedure had no associated increase in risk of positive margin after adjustment for other variables (RR = 0.96, 95% CI: 0.80–1.16). Prostate incision into tumor (pT2R1) was significantly more likely in patients treated with robotic surgery (RR = 1.76, 95% CI: 1.25–2.48) than in those with open surgery. There was no difference between laparoscopic and open RP (RR = 0.86, 95% CI: 0.65–1.12).

Conclusions: Bilateral nerve sparing is associated with increased risk of positive SMs in patients with pathologic T2-category disease during RP. © 2014 Elsevier Inc. All rights reserved.

Keywords: Prostate; Carcinoma; Prostatectomy; Nerves

1. Introduction

Radical prostatectomy (RP) is a well-established treatment for men with clinically localized prostate cancer. The goals of this procedure are to achieve oncologic control while preserving urinary continence and erectile function, if possible. A nerve-sparing RP preserves the neurovascular bundles adjacent to the posterior-lateral prostate. It is associated with maintenance of erectile function and urinary continence [1–4]. However, a concern with nerve-sparing RP is that the closer dissection plane results in a higher risk of positive surgical margins (SMs). Previous studies

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evaluating the relationship between nerve sparing and positive SMs have produced conflicting results, possibly owing to small sample size, incomplete information about potential confounders, lack of pathologic tumor stage stratification, or being performed in a noncontemporary era [5–11].

Positive SMs can occur in patients who have extraprostatic disease (pT3) and in patients with organ-confined (pT2) disease [12]. Prostate incision into organ-confined tumor can occur when the plane of surgical dissection is carried into the prostate. Pathologically, it is defined as tumor extension to the inked margin in the same plane where benign prostatic acini also extend to the inked margin [13,14]. Prostate incision into tumor (pT2R1) during RP increases the risk of biochemical recurrence and may decrease cancer-specific survival [14,15]. A positive SM has important implications for adjuvant treatment and is possibly an indication of poor surgical quality [16–18].

Our objective was to evaluate the effect of nerve sparing on risk of positive margins in patients with pT2- and pT3-category disease using a large multisurgeon prospective cohort of contemporary RP patients. We hypothesized that the close prostate dissection required for neurovascular bundle preservation would increase the risk of positive SMs.

2. Materials and methods

2.1. Patient selection

After receiving institutional review board approval, we evaluated a historical cohort of 9,915 consecutive RP patients treated at The Ottawa Hospital (n = 866) or Memorial Sloan-Kettering Cancer Center (MSKCC, n = 9,049) between 2000 and 2010 for clinically localized prostate adenocarcinoma. Patients who received preoperative androgen deprivation, who underwent preoperative prostate radiation therapy, who were operated on before 2000, or who had incomplete data were excluded. Data were combined to enhance generalizability through inclusion of a broader range of surgeons and settings.

2.2. Surgical technique

All patients underwent a RP performed by 1 of 19 surgeons at MSKCC or by 1 of 3 surgeons at the Ottawa Hospital. The approach was not standardized and procedures were performed by open, laparoscopic, or robotic technique. Patients underwent nerve resection, unilateral nerve sparing, or bilateral nerve sparing. The decision to spare or resect nerves was at the discretion of the surgeon and patient based on preoperative sexual function and extent of disease. No information was available on intrafascial or interfascial periprostatic dissection. Furthermore, no information was available for the extent of "wide dissection" during non–nerve-sparing procedures.

2.3. Pathologic technique

Dedicated genitourinary pathologists reviewed all pathology specimens at both centers. Intact RP specimens were fixed in formalin, inked to determine SMs in the fresh state, serially sectioned, and entirely submitted for histologic examination. The inked apical margin was assessed via the perpendicular coned technique. The most apical 3-mm portion of the gland is sectioned and further segmented radially in a conelike fashion and embedded. Finally, the remaining bulk of the gland is sectioned from apex to base at approximately 3-mm intervals and entirely submitted. Pathologists assessed prostate specimens for grade, category, SM status, and the presence of extraprostatic extension. A positive SM was consistently defined as tumor extending to the inked surface of the prostatectomy specimen. Prostate incision into tumor (pT2R1) was defined as tumor at the inked margin in the same plane where benign prostatic acini are at the inked margin. The location and extent of prostate incision into tumor was not available.

2.4. Statistical analysis

Descriptive statistics were used to characterize the study subjects. The primary outcome was the presence of a positive SM on the prostatectomy specimen. This was evaluated a priori in the overall cohort and in category-stratified cohorts (pT2 and pT3). The association between nerve sparing and a positive margin was assessed using univariable and multivariable logistic regression analyses. Adjustments for prostate-specific antigen (PSA; continuous), pathologic Gleason sum (categorical <7, 7, and >7), pathologic category (pT2 and pT3; only in the overall model), RP modality (categorical open, pure laparoscopic, and robotic-assisted laparoscopic), year of prostatectomy (continuous), and location (The Ottawa Hospital or MSKCC) were made in the multivariable model. The tests were 2-sided with $P < 0.05$ considered statistically significant. Confidence intervals are 95% when reported. Statistical analyses were conducted using SAS v9.2 (SAS Institute Inc, Cary, NC).

3. Results

Patients who received preoperative androgen deprivation (n = 369), who underwent preoperative prostate radiation therapy (n = 5), who were operated on before 2000 (n = 178), or who had incomplete data on nerve sparing (n = 2,621), pathologic category (n = 298), preoperative PSA (n = 238), or surgical modality (n = 86) were excluded, leaving 6,120 patients included in the analysis. Of the eligible patients, most had clinical T1c-category (3,814/5,872, 65.0%) and Gleason 6 disease on biopsy (3,086/5,877, 52.5%). Detailed patient and disease characteristics are presented in Table 1. Patients underwent open

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