The effect of wide resection during radical prostatectomy on surgical margins

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Abstract

Introduction: The impact of nerve-sparing on positive surgical margins during radical prostatectomy (RP) remains unclear. The objective of this study was to determine the incidence of positive surgical margins with a wide resection compared to a nerve-sparing technique.
Methods: A consecutive, single-surgeon patient cohort treated between August 2010 and November 2014 was reviewed. A standardized surgical approach of lobe-specific nerve-spare or wide resection was performed. Lobe-specific margin status and tumour stage were obtained from pathology reports. Univariable and multivariable associations between nerve management technique and lobe-specific positive surgical margin were determined.
Results: Of 388 prostate lobes, wide resection was performed in 105 (27%) and nerve-sparing in 283 (73%). In 273 lobes without extra-prostatic extension (EPE), 0 of 52 (0%) had a positive margin when wide resection was performed compared to 20 of 221 (9%) if nerve-sparing was performed (p=0.02). In 115 lobes with EPE, 11 of 53 (21%) had a positive margin if wide resection was performed compared to 28 of 62 (45%) if nerve-sparing was performed (p=0.006). In multivariable analysis, the risk of a positive margin was decreased among patients who received wide resection as compared to nerve-spare (RR 0.43, 95% CI 0.26–0.71; p=0.001).
Conclusions: Surgical techniques to reduce positive surgical margins have become increasingly important as more patients with high-risk cancer are selecting surgery. The risk of a positive margin was greatly reduced using a standardized wide resection technique compared to nerve-sparing.

Introduction

Radical prostatectomy (RP) may be performed with nerve-sparing or nerve resection. The purpose of nerve-sparing is to preserve erectile function and urinary continence,[1] while nerve resection is done to maximize oncologic resection and minimize the risk of a positive surgical margin.

A positive margin is recorded if tumour cells are detected at the inked margin of the prostatectomy specimen. The incidence of positive margins is similar in robotic and open procedures and ranges from 6.5–38%.[2] Positive margins are important to avoid because they are associated with cancer recurrence and increased use of adjuvant or salvage treatments.[2,3]

While it seems logical that a wider resection would result in fewer positive margins compared to nerve-sparing, previous studies have failed to consistently identify this association.[4-6] One explanation for this may be use of different surgical approaches for wide periprostatic dissection within and between studies.

Characterizing a surgical approach that minimizes positive margins has become increasingly relevant, as more patients with high-risk disease are selecting surgery and more patients with low-risk disease are being managed with surveillance.[7,8] The purpose of this study was to determine if the incidence of lobe-specific positive surgical margins after prostatectomy was associated with neurovascular bundle dissection technique.

Methods

Institutional ethics review board approval was obtained. A cohort of consecutive patients treated with RP by a single surgeon between August 2010 and November 2014 at one tertiary-care cancer centre (The Ottawa Hospital, Ottawa, ON, Canada) was reviewed. Patient and tumour factors were recorded from the medical record using standardized abstraction.

Surgical technique

Prostatectomy was performed using an open or robotic technique. A standardized surgical approach was used for sparing or resecting the neurovascular bundles. Patients received lobe-specific nerve-sparing or wide resection. The wide resection technique included dissection posterior to Denonvillier's fascia and incision on to the perirectal fat lateral to the neurovascular bundles (Figs. 1 and 2). Otherwise, there was no difference in prostate apex, urethral, or bladder neck dissection between techniques. In most cases, bladder neck-sparing was performed. The decision to perform wide

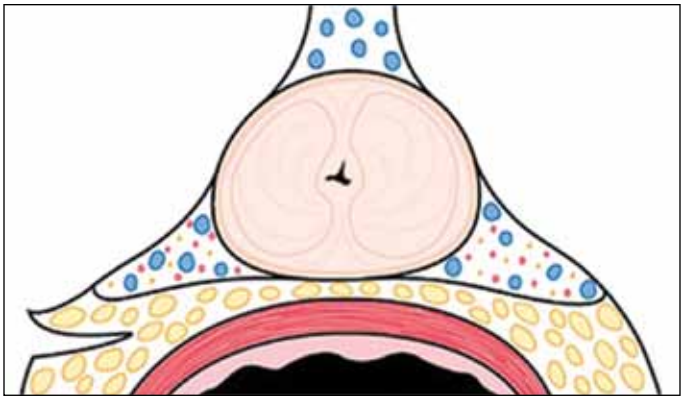

Fig. 1. Illustration of wide resection technique that included dissection posterior to Denonvillier's fascia and incision onto the perirectal fat lateral to the neurovascular bundles.

resection or nerve-sparing was based on preoperative cancer risk, sexual function, and patient preference.

Pathological technique

Prostatectomy specimens were processed and reviewed by a genitourinary pathologist. Specimens were fixed in formalin, inked, and serially sectioned transversely from apex to base. Tumour grade, tumour stage, location of EPE, and location of positive surgical margins were documented in standardized synaptic reports. A positive surgical margin was reported if cancer extended to the inked margin.

Statistical analyses

Patient demographics and disease characteristics were analyzed using descriptive statistics. Univariable and multivariable log binomial regression analyses were used to assess the association between lobe-specific surgical technique (wide resection vs. nerve-sparing) and the incidence of positive surgical margins on the ipsilateral prostate lobe (side-specific). Multivariable associations adjusted for preoperative PSA, biopsy Gleason score, pathological prostate volume, tumour volume, year of surgery, EPE status, and neurovascular bundle management (wide resection or nerve-sparing). Statistical analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, NC).

Results

One hundred and ninety-four (194) patients received prostatectomy during the study period and were included in analyses. The mean patient age was 62.0 years (standard deviation [SD] 6.4) and the mean preoperative prostate-specific antigen (PSA) was 8.8 ng/mL(SD 7.2). Most patients (155, 80%) received a robotic prostatectomy and 39 (20%) received an open prostatectomy. Seventy-four (74, 38%) patients had clinical T1, 96 (49%) patients had clinical T2, and 24 (12%) patients had clinical T3 tumours (Table 1).

Wide resection was performed in 105 (27%) prostate lobes while nerve-sparing was performed in 283 (73%) lobes. Fifty-nine lobes (15%) had positive surgical margins (Table 2). Of the 273 lobes without EPE, 0 of 52 (0%) had positive margins when wide resection was performed and 20 of 221 (9%) had positive margins when nerve-sparing was performed (p=0.02). Of the 115 lobes with EPE, 11 of 53 (21%) had a positive margin when wide resection was performed and 28 of 62 (45%) had a positive margin when nerve-sparing was preformed (p=0.006). No patients experienced a rectal injury.Adjusting for known potential confounders, the risk of a positive margin was 60% less if a wide resection was performed (RR 0.43, 95% CI 0.26–0.71) (Table 3). Later year of surgery (RR 0.77, 95% CI 0.63-0.93), and larger prostate volume (RR 0.98, 95% CI 0.96–1.00) were also associated with a decreased risk of a positive surgical margin. EPE was associated with a higher risk of a positive surgical margin (RR 6.31, 95% CI 3.78–10.52).

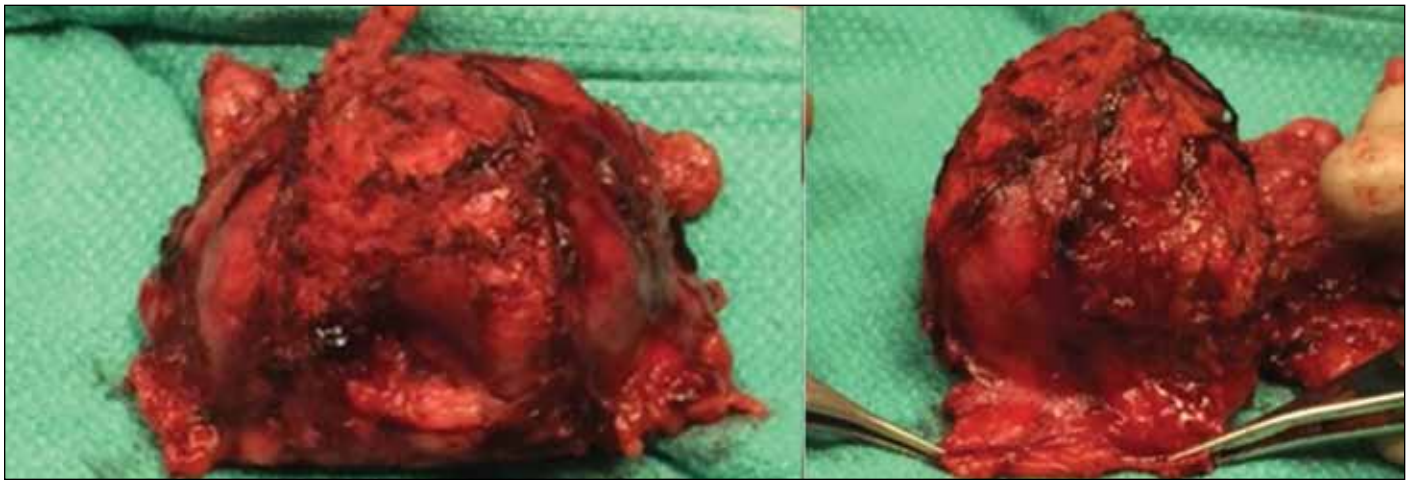

Fig. 2. Coronal (a) and sagittal (b) views of prostatectomy specimen after bilateral wide resection.

Table 1. Patient demographics and disease characteristics

Variable	Value
Total N	194
Age (years), mean ± SD	62.0 ± 6.4
Preoperative PSA (ng/mL), mean ± SD	8.8 ± 7.2
Clinical stage, n (%)	
cT1	74 (38.1)
cT2	96 (49.5)
cT3	24 (12.4)
Pathological stage, n (%)	
pT2	103 (53.1)
pT3	91 (46.9)
Biopsy Gleason score, n (%)	
Gleason 6	45 (23.2)
Gleason 3 + 4	83 (42.8)
Gleason 4 + 3	31 (16.0)
Gleason 8	20 (10.3)
Gleason 9-10	15 (7.7)
Pathological Gleason score, n (%)	
Gleason 6	13 (6.7)
Gleason 3 + 4	104 (53.6)
Gleason 4 + 3	57 (29.4)
Gleason 8	4 (2.1)
Gleason 9-10	16 (8.2)
TRUS prostate volume (mL), mean ± SD	35.1 ± 23.1
Pathological prostate volume (mL), mean ± SD	41.1 ± 21.9
Cancer volume, mean ± SD	5.7 ± 6.2
Year of surgery, n (%)	
2010[a]	6 (3.0)
2011	27 (13.9)
2012	52 (26.8)
2013	59 (30.4)
2014[a]	50 (25.7)
Surgical approach, n (%)	
Open	39 (20.1)
Robotic	155 (79.9)

[a]Incomplete calendar year. SD: standard deviation; TRUS: transrectal ultrasound.

Discussion

Nerve-sparing necessitates close dissection to the prostate and intuitively this should result in an increased risk of a positive surgical margin compared to a wide resection technique. However, previous studies have not consistently demonstrated this association.[4-6] Using a standardized wide resection technique, our patients had a 60% lower risk of a positive margin compared to a nerve-sparing approach. This association was independent of other patient and tumour factors.

Positive surgical margins are important to patients because they are associated with disease recurrence.[2,3,9] A positive margin may also prompt further adjuvant treatments, such as radiotherapy, which exposes patients to the risk of side effects and deterioration in quality of life.[3,10] Methods to predict and avoid positive margins have become increasingly important, as surgeons and patients have opted to observe low-risk tumours and aggressively treat higher risk tumours.[8]

Table 2. Neurovascular bundle management and pathologic results of 388 prostate lobes

Variable	Prostate lobes (N=388)
EPE status, n (%)	
Positive	115 (29.6)
Negative	273 (70.4)
Neuro-vascular bundle status, n (%)	
Wide resection	105 (27.0)
Nerve-spare	283 (72.9)
Surgical margin status, n (%)	
Positive	59 (15.2)
Negative	329 (84.7)

EPE: extra-prostatic extension.

Previous studies have evaluated the association between nerve-sparing and margin status with conflicting results.[4-6,11] One study of over 6000 prostatectomy patients treated at two academic centres found that nerve-sparing increased the risk of a positive margin on multivariable analysis in patients with stage pT2 (RR 1.52, 95% CI 0.97–2.39), but not pT3 disease (RR 0.96, 95% CI 0.80–1.16).[4] Another study reported that nerve-sparing was associated with a lower risk of positive margins after adjusting for age, clinical stage, biopsy grade, year of surgery, and PSA (OR 0.86, 95% CI 0.76–0.97; p=0.012).[6] Possible reasons for these inconsistent findings may be unadjusted confounding, selection bias, or non-uniform surgical technique of wide resection within and between studies. Indeed, non-nerve-sparing does not necessarily equate to a wide, extra-fascial prostate dissection.

The most important finding of this study is that wide resection decreased the absolute risk of a positive margin in patients with EPE by 24% (45% vs. 21%). Given this finding, patients can be presented with reasonable estimates of harm (increased risk of positive surgical margin) and benefits (decreased risk of erectile dysfunction and incontinence) associated with nerve-sparing compared to wide resection.[12-14]

This study has several strengths. The RPs were performed by a single surgeon, ensuring a consistent approach to wide resection and nerve-sparing was used. Furthermore, a consecutive cohort of patients in all prostate cancer risk categories was reviewed, thus limiting the risk of selection bias. Also, we examined surgical technique and positive margins in a lobe-specific fashion, making our results more precise than many previous studies. Finally, our model adjusts for patient and tumour factors, most notably EPE, and found that wide resection decreases margin risk independent of these factors.

The generalizability of this study is unknown, as transfer of the wide dissection technique to other surgeons has not been formally tested. We also found that the rate of positive margins decreased over time, confirming the learning curve previously described for radical prostatectomy.[15] Furthermore, the benefits and risks of wide resection will become clearer as this cohort matures and long-term function and cancer recurrence outcomes become available.

Table 3. Univariable and multivariable associations between patient, tumour, and surgical factors and incidence of side-specific positive surgical margins

	Univariable		Multivariable	
	RR (95% CI)	*p* value	RR (95% CI)	*p* value
Age	1.02 (0.98–1.06)	0.362	—	—
Preoperative PSA	1.02 (0.99–1.05)	0.130	1.01 (0.99–1.02)	0.350
TRUS prostate volume	0.99 (0.97–1.00)	0.071	—	—
Clinical stage				
T1	1.00	—	—	—
T2+T3	0.91 (0.55–1.50)	0.701	—	—
Year of surgery	0.78 (0.65–0.94)	0.011	0.77 (0.63–0.93)	0.007
Pathological prostate volume	0.98 (0.96–1.00)	0.038	0.98 (0.96–1.00)	0.041
Tumour volume	1.02 (1.00 –1.05)	0.114	1.01 (0.98–1.05)	0.506
Biopsy Gleason score				
7 vs 6	0.78 (0.44–1.37)	0.393	0.83 (0.26–2.59)	0.743
>7 vs 6	0.79 (0.34–1.84)	0.581	0.59 (0.15–2.33)	0.448
>7 vs 7	1.01 (0.46–2.20)	0.986	0.71 (0.32–1.58)	0.401
Neurovascular bundle				
Wide resection	0.66 (0.37–1.18)	0.159	0.43 (0.26–0.71)	0.001
Nerve-spare	1.00	—	—	—
EPE				
Positive	4.63 (2.83–7.58)	<0.0001	6.31 (3.78–10.52)	<0.0001
Negative	1.00	—	—	—

CI: confidence interval; EPE: extra-prostatic extension; PSA: prostate-specific antigen; RR: relative risk; TRUS: transrectal ultrasound.

Conclusion

Achieving negative surgical margins for patients with EPE may be increasingly important, as more patients with high-risk cancer choose surgery. Nerve-sparing may still be selected by patients and surgeons to optimize functional outcomes; however, in scenarios where there is a high risk of EPE, the wide resection technique described in this manuscript reduced the risk of a positive surgical margin by 60% compared to nerve-sparing.

Competing interests: Dr. Lavallée is an Advisory Board member for Sanofi and Ferring, and has received grant(s) or honoraria from Sanofi. Dr. Morash is a member of Advisory Boards for Janssen, Sanofi, Abbvie, Astellas, and Ferring. Dr. Cagiannos is an Advisory Board member for Ferring and Abbvie. The remaining authors declare no competing financial or personal interests

This paper has been peer-reviewed.

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