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Original article

Risk factors for biochemical recurrence following radical perineal prostatectomy in a large contemporary series: A detailed assessment of margin extent and location

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Abstract

Objectives: The implications of positive surgical margin (PSM) extent and location during radical perineal prostatectomy (RPP) have not been assessed in a contemporary series. We aimed to examine the incidence, location, and extent of PSM as well as their impact on biochemical recurrence (BCR) following RPP.

Materials and methods: A total of 794 patients underwent RPP by a single surgeon between June 1993 and August 2010. Covariates included age, pathologic T stage, pathologic Gleason sum, preoperative PSA, prostate volume, PSM extent, and location. Life table, Kaplan-Meier, and Cox regression analyses assessed predictors of BCR following RPP.

Results: PSM were recorded in 162 patients (20.4%); of these, 83 (51.2%) were focal (≤1 mm) whereas 79 (48.8%) were broad (>1 mm). Location of PSM was anterior 10.5%, posterior or lateral 14.8%, bladder neck 23.5%, apical 32.1%, and multifocal 19.1%. At a median follow-up of 54 months, the 5-year BCR-free probability was 90.8% in patients with negative margins, 77.5% in patients with focal PSM, and 47.5% in patients with broad PSM. On multivariable analyses adjusted for age, pathologic T stage, pathologic Gleason sum, preoperative PSA, and prostate volume, broad PSM, (HR = 3.49, $P < 0.001$) as well as anterior (HR = 3.77, $P = 0.003$), bladder neck (HR = 2.25, $P = 0.01$) and multifocal (HR = 3.55, $P < 0.001$) PSM were independent predictors of BCR.

Conclusions: In this study, we present oncologic outcomes following RPP in a large contemporary cohort of patients undergoing RPP. In adjusted analyses, broad and anterior PSM carried the highest risk of recurrence after RPP.

Keywords: Prostatic neoplasms; Prostatectomy; Perineal; Margins; Biochemical recurrence

1. Introduction

Radical prostatectomy (RP) represents the standard of care among management options for patients with clinically localized prostate cancer [1]. The ultimate goal of RP is complete removal of all malignant tissue. Modern RP series show a positive surgical margin (PSM) rate of between 11% and 38% [2]. Cancer cells at the inked surgical resection margin may suggest an incomplete local resection, poor cancer control [3–5], and suboptimal patient outcome [6]. Despite the established adverse effect of PSM on the cancer control rate, few investigators have independently assessed the effect of margin extent and location on this outcome [7–12]. A seminal review by Wieder and Soloway demonstrated the influence of surgical approach on location and etiology [13]. Subsequently, Stephenson, et al. showed that the number and extent of PSM significantly influence the risk of biochemical recurrence (BCR) after RP [9]. Con-

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versely, according to their analyses, the empiric prognostic usefulness of subclassifications of PSM was shown to be of little benefit.

Previous data have demonstrated adverse oncologic outcomes associated with PSM in patients undergoing radical perineal prostatectomy (RPP) [14], though the impact of PSM extent and location have not been assessed to date. We hypothesized that our analyses of patients undergoing this underutilized surgical approach would result in different findings than analyses of PSM in open, laparoscopic, or robotic RP subjects. In the current manuscript, we explore the effect of margin extent and location on BCR in a large contemporary cohort of patients undergoing RPP by a single surgeon.

2. Materials and methods

2.1. Patient population

A total of 907 consecutive patients underwent RPP at Munson Medical Center, Traverse City, MI, by a single surgeon between June 1993 and August 2010 and were prospectively entered into an institutional review board (IRB)-approved database. Twenty men who had received prior radiation and 93 men with incomplete pathologic or follow-up data were excluded from the study, leaving 794 available for analyses. Pelvic lymphadenectomy was initially performed on patients with high-risk disease characteristics (Gleason grade 8–10, PSA $>$ 20, cT3 disease) until January 1997 (n = 6), but was not routinely performed thereafter. No patient morphologic or prior surgical characteristics precluded candidacy for RPP, including prior aborted laparoscopic and retropubic prostatectomies, prior renal transplantation, abdominal-perineal resections, morbid obesity, and superior vena cava syndrome. Eighty-six patients had neoadjuvant hormone ablation, 13 for preoperative prostate size reduction, 73 in cases of treatment deferment.

2.2. Surgical technique

RPP was performed as previously described by Harris [15,16]. In summary, the patient's legs are supported in the lithotomy position, with hydraulic leg supports and a 6-in. jell roll placed under the sacrum. An O'Connor-Sullivan drape is used for anorectal access. A Lowsley tractor is placed in the urethra to assist in identification of landmarks and to facilitate manipulation of the prostate. The perineal incision is placed with the apex in the mid-perineum and the ends medial to the ischial tuberosities and anterior to the anus. By elevating the fibrous confluence found immediately posterior to the raphe of the bulbospongiosus muscle with a forceps, the rectourethralis muscle is visualized and divided, revealing Denonvillier's fascia. With elevation of the lateral aspect of the pelvic floor, the space inside the levator ani muscles and lateral to endopelvic fascia is developed. The rectum is swept off the lower aspect of the levator ani.

Denonvillier's fascia is opened transversely between the seminal vesicals and the vas and seminal vesicles are dissected free. The posterior aspect of the prostate–vesicle junction is then developed. When wide excision is intended, the fascia on the lateral aspect of the bladder neck is scored with electrocautery so that all the periprostatic tissues are resected en bloc with the prostate. The neurovascular tissue at the base of the prostate is sealed to complete the wide excision. The lateral aspect of the prostatovesical junction is developed. In nerve-sparing cases, Denonvillier's fascia is incised from the midpoint of the seminal vesicle to the mid apex. With careful sharp dissection, the cavernosal nerve bundles and associated fascia are separated from the prostate from apex to adjacent to the seminal vesicles. Once the neurovascular bundles and associated tissues are separated laterally as far around the prostate as the bladder neck and puboprostatic ligaments, the proximal prostatic pedicle is sealed and divided. The urethra at the apex is dissected out of the prostatic apex up to the veru montanum, where it is divided.

The puboprostatic ligaments are then divided with cauter, and dorsal venous bleeding is controlled with a figure-8 stitch, if necessary. At the bladder neck, the proximal urethra is dissected out of the base of the prostate and divided. If resection of the bladder neck is desired, it is entered in the midline and excised under direct vision of the ureteral orifices. A running anastomosis is completed. If necessary, a 2-layered cystoplasty is performed to reduce a large bladder-neck opening. The bladder-neck urothelium is not everted but rather incorporated into the anastomotic sutures. The levator ani muscles are then reapproximated in the midline with a Penrose drain overlying the rectum. Ambulation and diet are advanced on the day of surgery. The Penrose drain is removed before discharge on the morning of postoperative day 1. The catheter is removed 8 days later and activities are no longer restricted.

2.3. Pathologic assessment and follow-up

RP specimens were surfaced, inked, and pathologic assessment was done according to the Stanford protocol with serial step sections at 3 mm [17]. Resection margins were considered positive if cancer extended to the inked surface [18]. In patients with PSM, specifications regarding the margin extent (focal [$\leq$1 mm] vs. broad [$>$1 mm]) and location (anterior vs. posterolateral vs. bladder neck vs. apical vs. multifocal) were also recorded.

According to institutional protocols, no adjuvant therapy was administered before BCR, which was defined following the guidelines of the American Urologic Association Localized Prostate Cancer Update Panel report $\geq$0.2 ng/ml, with a second confirmatory level of prostate specific antigen of