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Biochemical Recurrence Following Robot-Assisted Radical Prostatectomy: Analysis of 1384 Patients with a Median 5-year Follow-up

Mani Menon [a,d], *Mahendra Bhandari* [a], *Nilesh Gupta* [b], *Zhaoli Lane* [b], *James O. Peabody* [a], *Craig G. Rogers* [a], *Jesse Sammon* [a,*], *Sameer A. Siddiqui* [a], *Mireya Diaz* [a,c]

[a] *Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA*
[b] *Department of Pathology, Henry Ford Hospital, Detroit, MI, USA*
[c] *Department of Biostatistics and Research Epidemiology, Henry Ford Hospital, Detroit, MI, USA*
[d] *Case Western Reserve University, Cleveland, OH; New York University, New York, NY; University of Toledo Schools of Medicine, Toledo, OH, USA*

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Abstract

Background: There is a paucity of data on long-term oncologic outcomes for patients undergoing robot-assisted radical prostatectomy (RARP) for prostate cancer (PCa).
Objective: To evaluate oncologic outcomes in patients undergoing RARP at a high-volume tertiary center, with a focus on 5-yr biochemical recurrence–free survival (BCRFS).
Design, setting, and participants: The study cohort consisted of 1384 consecutive patients with localized PCa who underwent RARP between September 2001 and May 2005 and had a median follow-up of 60.2 mo. No patient had secondary therapy until documented biochemical recurrence (BCR). BCR was defined as a serum prostate-specific antigen $\geq$0.2 ng/ml with a confirmatory value. BCRFS was estimated using the Kaplan-Meier method. Event–time distributions for the time to failure were compared using the log-rank test. Univariable and multivariable Cox proportional hazards regression models were used to determine variables predictive of BCR.
Intervention: All patients underwent RARP.
Measurements: BCRFS rates were measured.
Results and limitations: This cohort of patients had moderately aggressive PCa: 49.0% were D'Amico intermediate or high risk on biopsy; however, 60.9% had Gleason 7–10 disease, and 25.5% had $\geq$T3 disease on final pathology. There were 189 incidences of BCR (31 per 1,000 person years of follow-up) at a median follow-up of 60.2 mo (interquartile range [IQR]: 37.2–69.7). The actuarial BCRFS was 95.1%, 90.6%, 86.6%, and 81.0% at 1, 3, 5, and 7 yr, respectively. In the patients who recurred, median time to BCR was 20.4 mo; 65% of BCR incidences occurred within 3 yr and 86.2% within 5 yr. On multivariable analysis, the strongest predictors of BCR were pathologic Gleason grade 8–10 (hazard ratio [HR]: 5.37; 95% confidence interval [CI], 2.99–9.65; $p < 0.0001$) and pathologic stage T3b/T4 (HR: 2.71; 95% CI, 1.67–4.40; $p < 0.0001$).
Conclusions: In a contemporary cohort of patients with localized PCa, RARP confers effective 5-yr biochemical control.

* Corresponding author. Vattikuti Urology Institute, Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202, USA. Tel. +1 313 916 2062; Fax: +1 313 575 3515.
E-mail address: jsammon1@hfhs.org (J. Sammon).

1. Introduction

Radical prostatectomy (RP) is an effective form of treatment for localized prostate cancer (PCa) [1]. Earlier studies indicate that an estimated 35% of men will experience a biochemical recurrence (BCR) within 10 yr of undergoing RP [2–4]. With the introduction of prostate-specific antigen (PSA) screening, however, there has been a gradual stage and risk migration in PCa, and more men are now diagnosed at an earlier age, with a lower PSA and localized disease [5–7]. Thus, BCR rates from earlier studies may not reflect BCR rates in contemporary patients. Few studies have concentrated on BCR in patients diagnosed after 2000.

In the United States, robot-assisted radical prostatectomy (RARP) has become the surgical treatment of choice for many men with localized PCa. A systematic review of the RARP literature stressed the paucity of BCR data in patients undergoing RARP [8]. Robotic surgery is relatively new, the first robotic urologic program having started at our institution in 2000 [9,10]. The initial patients in this cohort are approaching 10 yr of follow-up. The purpose of this study was to examine oncologic outcomes in patients undergoing RARP between 2001 and 2005.

2. Material and methods

2.1. Patient selection and treatment

From 2000 to 2010, >5000 patients with localized PCa have undergone RARP at our institution using the techniques described by Menon et al [10–12]. Our database comprised 1581 patients who underwent RARP between September 2001 and May 2005 and were eligible for a minimum follow-up of 5 yr. Following exclusion of patients who did not have recorded PSA values postoperatively ($n = 126$), received prior hormone therapy or radiation therapy ($n = 48$), had incomplete biopsy data ($n = 14$), or had adjuvant treatments before documented BCR ($n = 9$), the remaining 1384 patients were the subjects of the present analysis.

All patients had a minimum of six core prostate biopsies, and all biopsies were reviewed by a referee pathologist. The preoperative variables recorded included age, PSA level, biopsy Gleason score, biopsy tumor volume, clinical stage (American Joint Committee on Cancer 2009 guidelines), and body mass index (BMI).

RARP was performed by either MM (1182 patients) or JOP (399 patients). All patients underwent video analysis of the procedure for the first 3 yr of the study, enabling standardization of technique. Nerve sparing was performed in patients who were potent (Sexual Health Inventory for Men >17), the technique evolving during the course of the study [13]. Pelvic lymph node dissection (PLND) was performed only if the probability of lymph node metastasis was >1%, as determined by genetic adaptive neural network analysis [14]. Patients with low- to intermediate-risk disease had PLND limited to the external iliac and obturator zones, whereas extended PLND was performed for patients with palpable T2b–T3 disease, Gleason score of 8–10, or PSA >10 ng/ml.

2.2. Pathologic assessment

The RP specimens were examined according to the Stanford protocol [15]. Pathologic variables evaluated included pathologic stage, Gleason score, tumor volume, prostate weight, lymph node status, perineural invasion, angiolymphatic invasion, and surgical margin status. *Extraprostatic extension* (EPE) was defined as spread of cancer into soft tissue or skeletal muscle; *positive surgical margin* was defined as extension of cancer to the inked surface. Node packets were sent separately. All visible and palpable lymph nodes were dissected and submitted for microscopic examination to evaluate for the presence of metastasis.

2.3. Follow-up

Demographic and follow-up data were collected from a prospective prostatectomy electronic database, institutional electronic medical records, hospital billing records, outpatient medical records, and communication with patients and referring physicians. All patients were queried electronically at 3-mo intervals for the first 12 mo, semiannually during the second year, and annually thereafter. For patients without PSA records within the last 12 mo, follow-up e-mails were sent in April and June 2010. Database management was performed by individuals who were not involved in direct clinical care. The study protocol was approved by the institutional review board of Henry Ford Hospital. Data collection and follow-up correspondence were conducted in accordance with the US Health Insurance Portability and Accountability Act. BCR was defined following the guidelines of the American Urological Association Localized Prostate Cancer Update Panel report [16].

2.4. Statistical analysis

The probability of BCR-free survival (BCRFS) was estimated using the Kaplan-Meier method, and survival curves among groups were compared using the log-rank test. The impact of clinical and pathologic features on BCRFS was analyzed using univariable and multivariable Cox proportional hazard regression models; the proportionality assumption was tested and found to hold (for details, see Appendix). Three models were created in a nonstepwise fashion. The first two models considered preoperative predictors only, including patient age (coded as ≥60 and <60 yr of age), BMI (coded as <25, 25–30, ≥30), perineural invasion (on biopsy), and procedure year; the first incorporated preoperative PSA (coded as <10, 10.1–20, and >20 ng/ml), biopsy Gleason score, and clinical stage; and the second D'Amico risk group. The third model considered predictors of BCR available postoperatively: tumor volume (coded as <15% or ≥15%), pathology Gleason score, pathologic stage (coded as T2, EPE, seminal vesical invasion [SVI]/T4), perineural and angiolymphatic invasion (as determined on final specimen), margin status, and nerve-sparing approach together with age and PSA. All statistical analyses were performed by a qualified biostatistician (MD) using SAS v.9.1 (SAS Institute, Cary, NC, USA). All p values are two-sided and considered statistically significant if <0.05.

3. Results

3.1. Preoperative and pathologic characteristics

Clinical and pathologic variables for the study cohort (1384 patients) are depicted in Table 1. The mean age was 60.0 yr (standard deviation [SD]: ±7.1), and median serum PSA was 5.2 ng/ml (interquartile range [IQR]: 4.2–7.1). Mean BMI was 27.5 (SD: ±3.6), prostate weight (on final specimen) was 48.3 g (SD: ±20.1), and percent tumor volume was 17.5% (SD: ±13.4).

3.2. Follow-up and cancer control

The median follow-up was 5.0 yr (IQR: 3.1–5.8 yr). There were 189 incidences of BCR, 13 patients developed