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Comparative Effectiveness of Robot-assisted Versus Open Radical Prostatectomy Cancer Control

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Abstract

Background: Robot-assisted radical prostatectomy (RARP) remains controversial, and no improvement in cancer control outcomes has been demonstrated over open radical prostatectomy (ORP).
Objective: To examine population-based, comparative effectiveness of RARP versus ORP pertaining surgical margin status and use of additional cancer therapy.
Design, setting, and participants: This was a retrospective observational study of 5556 RARP and 7878 ORP cases from 2004 to 2009 from Surveillance Epidemiology and End Results–Medicare linked data.
Intervention: RARP versus ORP.
Outcome measurements and statistical analysis: Propensity-based analyses were performed to minimize treatment selection biases. Generalized linear regression models were computed for comparison of RP surgical margin status and use of additional cancer therapy (radiation therapy [RT] or androgen deprivation therapy [ADT]) by surgical approach.
Results and limitations: In the propensity-adjusted analysis, RARP was associated with fewer positive surgical margins (13.6% vs 18.3%; odds ratio [OR]: 0.70; 95% confidence interval [CI], 0.66–0.75), largely because of fewer RARP positive margins for intermediate-risk (15.0% vs 21.0%; OR: 0.66; 95% CI, 0.59–0.75) and high-risk (15.1% vs 20.6%; OR: 0.70; 95% CI, 0.63–0.77) disease. In addition, RARP was associated with less use of additional cancer therapy within 6 mo (4.5% vs 6.2%; OR: 0.75; 95% CI, 0.69–0.81), 12 mo (OR: 0.73; 95% CI, 0.62–0.86), and 24 mo (OR: 0.67; 95% CI, 0.57–0.78) of surgery. Limitations include the retrospective nature of the study and the absence of prostate-specific antigen levels to determine biochemical recurrence.
Conclusions: RARP is associated with improved surgical margin status relative to ORP for intermediate- and high-risk disease and less use of postprostatectomy ADT and RT. This has important implications for quality of life, health care delivery, and costs.
Patient summary: Robot-assisted radical prostatectomy (RP) versus open RP is associated with fewer positive margins and better early cancer control because of less use of additional androgen deprivation and radiation therapy within 2 yr of surgery.

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1. Introduction

Prostate cancer (PCa) remains the most commonly diagnosed solid-organ tumor in the United States, with an estimated incidence of 238 590 and PCa-specific mortality of 28 170 in 2013 [1]. In addition, radical prostatectomy (RP) remains the most common treatment for clinically localized PCa, and the robot-assisted approach has been rapidly adopted since it was introduced in 2000 and is currently the most common approach to RP, accounting for 53% of RPs in 2008 [2]. Comparative effectiveness research demonstrates perioperative and functional advantages for robot-assisted RP (RARP) versus open RP (ORP) [2,3], but it remains significantly more costly than open retropubic RP [4], and questions remain about cancer control. Compared with ORP, there are few RARP long-term oncologic outcomes [5]. Although there is a dearth of long-term comparisons of cancer control, positive surgical margins (PSMs) are an important correlate of cancer control and a quality indicator of RP. Open surgeons demonstrate that tactile feedback enables intraoperative decision making that reduces PSMs and improves cancer control [6], but there is an absence of tactile feedback during robotic surgery.

PSM—that is, cancer at the edge of the RP resection specimen—is an independent predictor of biochemical recurrence (BCR) [7,8] and PCa-specific mortality [9,10]. Although tumor characteristics (Gleason score, pathologic stage, prostate-specific antigen [PSA]) may affect the likelihood of PSM, variation in surgeon experience and technique also affect surgical margin status [11]. Although studies from tertiary referral centers have been inconclusive in determining the superiority of one approach over the other, these studies may not be generalizable to community settings, where the majority of RPs are performed. The objective of our study was to perform a population-based comparative effectiveness analysis of PSMs and use of additional cancer therapy following RARP versus ORP.

2. Materials and methods

2.1. Population source

The current study comprised the most recent release of the Surveillance Epidemiology and End Results (SEER)–Medicare linked data. The SEER registries identify 28% of all incident cancer cases in the United States. Medicare insures approximately 97% of all Americans ≥65 yr of age [12].

2.2. Study population

Overall, 22 161 men who had histologically confirmed nonmetastatic PCa (International Classification of Disease [ICD] for Oncology site code 61.9, histologic code 8140) ≥66 yr of age treated with extirpative surgery from January 2004 to December 2010 were identified. We excluded men >80 yr of age ($n = 528$) as well as those with unknown clinical ($n = 287$) and pathologic ($n = 1945$) stage, grade ($n = 571$), PSA at diagnosis ($n = 2078$), positive lymph nodes ($n = 171$), and missing physician identifiers that precluded assessment of surgeon volume ($n = 1844$). PSM is not reported for pT3b (seminal vesicle invasion [SVI]) or pT4 (adjacent organ invasion). Therefore, 1254 pT3b and 220 pT4 RP patients were excluded, resulting in a final study population of 13 402 men.

2.3. Covariates

For each subject, age at diagnosis, race (white vs black vs other), population density (metropolitan vs nonmetropolitan), marital status (married vs unmarried), region (Pacific Coast vs East vs Northern Plains vs Southwest), Gleason score (≤6 vs 7 vs 8–10), PSA (≤10.0 vs 10.1–20.0 vs >20.0 ng/ml), clinical stage (≤T1c vs T2a/T2b vs ≥T2c), pathologic stage (pT2 vs pT3a) were assigned [13]. Census tract socioeconomic status was determined as previously defined [14].

Patients were also classified according to the D'Amico high, intermediate and low risk categories [15]. The Charlson comorbidity index (CCI) was used to categorize comorbid conditions [16]. Moreover, we determined surgeon volume by aggregating the number of procedures [2]. Categorization of surgeon volume was performed using quartiles, which resulted in the following cut-offs adjusted for age: low (3–9), intermediate (10–24), high (25–51), and very high (≥52). Adjustment was made for year of surgery, as outcomes may improve over time [17]. We distinguished RARP (55 866) from ORP (55 840, 55 842, and 55 845) based on the presence of *Current Procedural Terminology*, 4th edition (CPT-4). Of note, as of October 1, 2008, a specific robot-assisted modifier code was introduced: ICD, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code 17.42. From October 1, 2008, and onward, 89% of CPT-4's 55 866 RARP codes had a concomitant ICD-9 17.42 code, thereby confirming the validity of the CPT-4 code used [18,19]. Margin status (negative vs positive) was determined from the site-specific staging codes for prostate [20]. The use of postprostatectomy radiation therapy (RT) or androgen deprivation therapy (ADT) was captured consistent with prior studies [2].

2.4. Statistical analyses

The independent Student t test and χ^2 test were used to compare the statistical significance of differences in means and proportions, respectively. Because of inherent differences between patients undergoing ORP and RARP, adjustment was performed using a 1:1 propensity score–matching ratio [21]. Propensity scores were computed by modeling a logistic regression with the dependent variable as the odds of undergoing RARP and the independent variable as age, race, CCI, marital status, population density, socioeconomic status, surgeon volume, clinical stage, tumor grade, and preoperative PSA. Subsequently, covariate balance between the matched groups was examined. Separate multivariable generalized estimating equation models accounting for surgeon clustering were constructed to compare differences in PSMs at final pathology and the use of additional RT or ADT, respectively. All statistical tests were performed using SPSS v.20 software (IBM Corp., Armonk, NY, USA). All tests were two-sided, with a significance level set at $p < 0.05$.

3. Results

Demographic and tumor characteristics of the study cohort are presented in Table 1, and RARP accounted for 41.2% of RPs during the study period. Men undergoing RARP were more likely to have lower PSA levels at diagnosis ($p < 0.001$) and lower clinical stage disease ($p < 0.001$). In addition, although men undergoing RARP versus ORP were more likely to have Gleason grade 7 disease, they were less likely to have Gleason grade ≤6 and 8–10 disease ($p < 0.001$).

In adjusted analysis (Table 2), there were fewer RARP versus ORP PSMs overall (13.6% vs 18.3%, adjusted odds ratio [OR]: 0.70; 95% confidence interval [CI], 0.66–0.75; $p < 0.001$). In terms of clinical staging, the incidence of

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