



Original Article

Radical prostatectomy then and now: Surgical overtreatment of prostate cancer is declining from 2009 to 2016 at a tertiary referral center

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Abstract

Background: In the era of increasing scrutiny of delivery of quality care, efforts to decrease surgical overtreatment of insignificant prostate cancer (iCaP) continue.

Objective: To quantify the incidence of surgical overtreatment over time among a contemporary series of men diagnosed with CaP.

Methods: We retrospectively reviewed the medical records and pathologic specimens for men with CaP who underwent radical prostatectomy between January 2009 and December 2016 at a tertiary referral center. Overtreatment, defined as presence of iCaP in radical prostatectomy specimens, was the primary endpoint. iCaP was defined as a tumor of Gleason score no more than 6 and a tumor diameter ≤ 10 mm (volume < 0.5 cc). Independent predictors of iCaP were determined using a multivariable model.

Results: A total of 1,283 men were eligible for analysis. Overtreatment was found in 86 (6.7%) patients. The frequency of overtreatment significantly decreased from 15% (24/165) in 2009 to 3% (4/134) of patients in 2016 ($P < 0.001$). In the multivariable analysis, prostate-specific antigen density ≥ 0.15 vs. < 0.15 (odds ratio [OR] 0.30, 95% confidence interval [CI] 0.15–0.64, $P < 0.01$), biopsy Gleason score 3 +4 vs. 3+3 (OR 0.15, 95% CI 0.08–0.29, $P < 0.01$), African American vs. White ethnicity (OR 0.13, 95% CI 0.02–0.96, $P = 0.045$), and year of surgery (OR 0.88, 95% CI 0.77–0.99, $P = 0.03$) remained significant predictors of iCaP at surgery. Over the years of study, the odds of overtreatment decreased by 12% annually (OR 0.88, 95% CI 0.77–0.99, $P = 0.03$). At the same time, the pathological evidence of advanced disease at surgery ($\geq T3a$ with/without lymph node involvement) remained unchanged.

Comment: Surgical overtreatment of CaP has declined to a rate of approximately 3% at this tertiary referral center; further decline is likely. The decline probably has a multifactorial explanation: decreased rate of overdiagnosis, better patient selection for surgery, or change in the referral pattern. © 2018 Elsevier Inc. All rights reserved.

Keywords: Prostate cancer; Overtreatment; Insignificant prostate cancer; Radical prostatectomy; Contemporary

1. Introduction

Overtreatment of prostate cancer (CaP) remains an obstacle in delivering high quality care to these patients. Radical prostatectomy (RP) for nonlethal cancers has been

reported in as many as 40% of cases in some series [1–5]. The possibility for undesirable sequelae of RP is well-known [6,7], reinforcing the consensus that the operation be restricted to cancers of serious potential [8]. An appreciation of the overtreatment issue has resulted in increased use of active surveillance for low-risk lesions [8]. However, any reduction of surgical overtreatment in a contemporary series has yet to be documented.

The advent of widespread prostate-specific antigen (PSA) screening in the 1990s resulted in an increased

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incidence of CaP cases, many of which were of little clinical significance; nevertheless, a concomitant increase in radical prostatectomy, often for insignificant CaP, ensued [9,10]. Thus, overdiagnosis and overtreatment have been linked. The benefits of screening have been called into question [11], resulting in a decline in PSA testing and a reduction in the incidence of CaP cases [12]. Utilization of RP for low risk CaP also appears to have declined [13,14].

Not yet clear is how the above trends may influence patient selection for RP and tissue outcomes in the specimens. The issue has been addressed via statistical modeling of population data [1,2], but actual pathologic data are limited [3–5]. Herein, we used pathological outcomes in a large contemporary series to determine (1) whether the incidence of overtreatment has changed from previous times, and (2) what preoperative variables might explain the change.

2. Patients and Methods

2.1. Patients and outcomes

After Institutional Review Board approval, we retrospectively queried our surgical institutional database to identify men with CaP who underwent RP between January 2009 and December 2016 at our institution. Seven surgeons performed the procedures after shared decision making with patients. We excluded men who received hormonal or radiation treatments prior to surgery. Baseline characteristics and clinical information, including age, ethnicity, body mass index (BMI), PSA, clinical stage, diagnosis to treatment interval, and biopsy Gleason score (GS) were captured. Type of surgery, surgical margin status, number of tumors, size of index tumor, RP GS, and pathological staging were used for analysis. The primary outcome was to evaluate yearly changes in incidence of surgical overtreatment for CaP. Secondary outcomes included assessment of predictors for insignificant CaP (iCaP) at RP. We also evaluated the rate of advanced CaP (\geq T3a with/without lymph node involvement) and concordance between prostate biopsy and RP specimens over time.

2.2. Definition of CaP outcomes

The seventh edition of the American Joint Committee on Cancer tumor–node–metastasis cancer staging system was used for clinical and pathological staging. Clinical staging was assigned by the operating physician and was based on digital rectal exam and cross-sectional imaging. All pathologic specimens were evaluated by one of three experienced genitourinary pathologists. While all RP specimens were read by our genitourinary pathologist, there was no standardized rereview for biopsy samples performed outside of our institution. In order to evaluate the consistency of pathologic evaluation especially reporting extracapsular extension (ECE) over the study period, we chose the first 100 patients

who underwent RP in 2009, 2012, and 2015 and compared with the original reports. We also reviewed the length and GS of ECE. The distribution of ECE is summarized in the Appendix.

Surgical overtreatment is defined here as a RP for iCaP. iCaP is defined as: GS 3+3 = 6 and maximum tumor diameter \leq 10 mm. Tumor volume was not always available in this series, but tumor diameter was always documented. Since tumor diameter and volume are highly correlated, we used diameter \leq 10 mm as a surrogate for tumor volume of $<$ 0.5 cc [15,16].

2.3. Statistical analysis

Descriptive statistics were used to summarize clinical and histopathologic data. Chi-square test or Fisher's exact test was used to compare categorical variables between groups. Analysis of variance tests were used to compare continuous variables with normal distribution (BMI). Univariate and multivariable logistic regression models were used to evaluate predictors iCaP. Variables with $P \leq 0.1$ in univariate analysis were included in multivariable analysis. We also created a prediction model using the beta coefficients to predict surgical overtreatment rates by the year 2020. We evaluated possible interactions and multicollinearity between variables before final model assessment, and performance of the model was assessed using receiver operating curve analysis. Stata 15 software (Stata Corp, College Station, TX) was used. P values $<$ 0.05 were considered statistically significant.

3. Results

3.1. Patient demographics

We identified 1,317 men with CaP who underwent RP. Thirty-four patients received neoadjuvant treatment and were excluded, yielding a cohort of 1,283. Among these 34 patients, 16 men in 2016 and 10 men in 2015 participated in the neoadjuvant clinical trial for high-risk CaP. Details on demographic, clinical, and pathologic data are presented in Tables 1 and 2. Of the 1,283 men included in the cohort, 1,053 (83%) had nonpalpable disease. Robot-assisted radical prostatectomy and open RP were performed in 1,041 (81%) and 242 (19%) patients, respectively. In recent years, more RP surgeries were performed on men \geq 70 years old ($P = 0.03$). There were no differences in the PSA distribution ($P = 0.16$) over time. The percent of GS 3+3 at biopsy and RP specimens decreased from 52% (86 patients) and 32% (53 patients) in 2009 to 13% (17 patients) and 8% (11 patients) in 2016, respectively ($P < 0.001$). At the same time, the percent of biopsy GS ≥ 8 among men who elected RP increased from 9.1% (15 patients) in 2009 to 23.9% (32 patients). Twenty-one patients with GS6 disease (9% of all patients with GS6) had extracapsular extension at surgery. The median size of index tumor was 23 mm (interquartile

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