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Original article

The association of age with perioperative morbidity and mortality among men undergoing radical prostatectomy

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Abstract

Introduction: Older age is considered a relative contraindication to radical prostatectomy (RP). However, data are limited regarding the impact of age on perioperative outcomes following RP. We examined the association of age with perioperative outcomes following RP to inform risk-stratification and management.

Materials and methods: We identified 35,968 men aged 18 to 89 years who underwent RP from 2010 to 2015 in the National Surgical Quality Improvement Program (NSQIP) database. The associations of age with 30-day complications and perioperative morbidity were evaluated using logistic regression, adjusted for patient features. Age was modeled both as a categorical and nonlinear continuous variable.

Results: Median age at surgery was 63 years (IQR: 58–67). Increasing age was associated with greater rates of perioperative morbidity. Compared to men aged <60 years, men aged 70 to 89 years had statistically significantly higher rates of 30-day complications (6.4% vs. 4.4%, $P < 0.0001$), perioperative blood transfusion (6.0% vs. 3.7%, $P < 0.0001$), readmission (4.9% vs. 3.9%, $P < 0001$), and 30-day mortality (0.3% vs. 0.1%, $P < 0.0001$). In multivariable analyses, older age was independently associated with increased risks of perioperative morbidity. Moreover, there was a nonlinear relationship of age with perioperative morbidity, wherein rates of 30-day complications, perioperative blood transfusion, and readmission increased after approximately 70 years of age.

Conclusions: In this national cohort, we observed a nonlinear association of age with perioperative morbidity, with increasing rates of 30-day complications, perioperative blood transfusion, and readmission after approximately 70 years of age. These results have implications for risk-stratification, patient counseling, and treatment selection among older men. © 2017 Elsevier Inc. All rights reserved.

Keywords: Prostate cancer; Complications; Morbidity; Radical prostatectomy; Age; Geriatrics

1. Introduction

Prostate cancer (PCa) is the most prevalent cancer among men in the United States, with an estimated incidence of 180,890 cases in 2016 [1]. Acknowledging the often indolent course of PCa and the effect of competing risks of mortality, contemporary guidelines generally recommend a 10-year life expectancy for the potential benefits of screening and treatment to be realized [2,3]. These considerations have gained increasing public health importance as the population of the United States ages and life expectancy continues to rise [4,5]. Accordingly, a larger proportion of older men may benefit from definitive local therapy including radical prostatectomy (RP).

Data regarding the safety of RP in older patients are sparse and largely limited to single center retrospective series [6–10]. However, these considerations are critical for patients considering definitive local therapy. In particular, it is unclear whether chronological age is independently associated with perioperative risk, or whether there exists an age threshold beyond which perioperative morbidity becomes excessive. We hypothesized that increasing age is associated with increased perioperative morbidity among

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men undergoing RP, and that this relationship is nonlinear. We, therefore, evaluated the association of age with 30-day morbidity and mortality among men undergoing RP using the National Surgical Quality Improvement Program (NSQIP), to better characterize this relationship and improve patient risk-stratification and treatment selection.

2. Materials and methods

2.1. Data source and study population

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) captures perioperative clinical data and 30-day morbidity and mortality for patients undergoing major surgical procedures at participating institutions. Trained clinical reviewers abstract data and the NSQIP employs quality assurance measures to ensure accuracy of data [11].

After obtaining exempt status from our Institutional Review Board, we identified men aged 18 to 89 years who underwent RP in the NSQIP from 2010 to 2015 using Current Procedural Terminology codes 55840, 55842, 55845, and 55866. Men 90 years or older were excluded as they are collapsed into a single age category in the NSQIP.

2.2. Patient characteristics

Perioperative variables recorded included age at surgery, year of surgery, surgical approach (open, minimally invasive), race, American Society of Anesthesiology class, smoking status (smoker within last year, former/never), chronic steroid use, functional status (independent, partially/totally dependent), discharge destination (home, rehab/skilled nursing facility, death), operative time, and presence of the following comorbidities: diabetes, chronic obstructive pulmonary disease, congestive heart failure, hypertension requiring medical treatment, renal failure or dialysis, and bleeding disorder. Age was modeled both as a categorical variable (<60 years, 60–69 years, and 70–89 years) and as a continuous nonlinear variable using restricted cubic splines as described below. Due to the small number of men aged 80 to 89 years ($n = 240$), they were combined into a single category with men aged 70 to 79 years.

2.3. Outcomes

The following outcomes were assessed as part of NSQIP: 30-day complications, perioperative blood transfusion within 72 hours of surgery start, 30-day readmission, 30-day reoperation, and 30-day mortality. Readmission and reoperation data were only available from 2012 to 2015, and these analyses were restricted to those study years. Postoperative complications were further categorized as cardiac, thromboembolic (DVT, PE), infectious (urinary tract infection, sepsis), respiratory, renal, neurologic, and surgical site infection/wound infection.

2.4. Statistical analysis

Baseline characteristics were summarized using medians/interquartile ranges (IQR) and frequency counts/percentages, and compared across age categories using ANOVA and Pearson chi-square test, respectively. Postoperative outcomes were summarized using frequency counts/percentages across age categories using Pearson chi-square test. Multivariable logistic regression was used to evaluate the associations of age group with perioperative endpoints. Effect estimates were summarized using odds ratios (OR) with 95% confidence intervals (95% CI). Models were adjusted for year of surgery, surgical approach, race (white, black, other), American Society of Anesthesiology class (1–2, 3, 4–5), smoking status (smoker within last year, former/never), chronic steroid use, functional status, discharge destination, operative time, and presence of the following comorbidities: diabetes, chronic obstructive pulmonary disease, congestive heart failure, hypertension, renal failure or dialysis, and bleeding disorder. Models were evaluated for multicollinearity using variance inflation factors (VIFs); VIFs were below 2 for each variable in all models, indicating no evidence of multicollinearity. Observations with missing data were dropped, excluding race, which was assigned to an "Unknown" category.

To evaluate for nonlinear associations between age and perioperative endpoints, we constructed separate multivariable logistic regression models for each perioperative endpoint, adjusted for the features above, modeling age as a nonlinear continuous variable using restricted cubic splines with 3 knots [12,13]. Statistical significance of a nonlinear relationship was evaluated by the Wald test. Due to the complexity of interpreting restricted cubic spline models, we estimated rates of each perioperative outcome adjusted for all covariates using marginal effects at the most prevalent value of each covariate (MIRP, year of surgery 2015, white race, American Society of Anesthesiology class 1 to 2, never/former smoker, independent functional status, no steroid use, hypertension requiring medications, and absence of diabetes, chronic obstructive pulmonary disease, congestive heart failure, renal failure/dialysis, or bleeding disorder) and median operative time [14]. We then visualized the nonlinear relationship of age with each perioperative outcome using plots of predicted event rates against age.

Statistical analyses were performed using R version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria). All tests were two-sided, and $P < 0.05$ were considered to be statistically significant.

3. Results

Median age at surgery was 63 years (IQR: 58–67) and age was distributed as follows: <60 years in 12,172 (33.8%) patients, 60 to 69 years in 18,076 (50.3%) patients,

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