10-Year Mortality After Radical Prostatectomy for Localized Prostate Cancer in the Prostate-specific Antigen Screening Era

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OBJECTIVE To provide insight into the impact of radical prostatectomy (RP) on prostate cancer–specific mortality (PCSM) in a primarily prostate-specific antigen screen–detected cohort of men with localized prostate cancer (PCa).

METHODS Between 2000 and 2013, 1864 men consented to participate in a prospective longitudinal outcomes study after RP for localized PCa by a single surgeon. Men lost to follow-up were queried to the National Death Index to acquire mortality data.

RESULTS From our cohort of 1864 men (median age 59 years, median preoperative prostate-specific antigen 5.0, median follow-up 9.1 years), Kaplan-Meier analysis demonstrated 10-year all-cause mortality and PCSM of 4.6% and 1.4%, respectively. Ten-year PCSM for low, intermediate, and high D'Amico risk were 0.9%, 1.0%, and 7.4%, respectively (P <.001). For men with postoperative Gleason score 4-6, 7, and 8-10, 10-year PCSM was 0.8%, 1.0%, and 11.5%, respectively (P <.001). Men with pT2, pT3a, and pT3b disease had 10-year PCSM of 0.7%, 2.6%, and 9.5%, respectively (P <.001). Pathologic stage and grade were the only significant independent predictor of PCSM at 10 years (P = .002 and P = .025, respectively).

CONCLUSION In our series with up to 13 years of follow-up from the National Death Index, 10-year PCSM after RP for clinically localized PCa was very low and strongly predicted by pathologic stage and grade. Death unrelated to PCa was a rare event, suggesting that we are identifying candidates for RP who are likely to live long enough to benefit from surgical intervention. UROLOGY 86: 783–789, 2015. © 2015 Elsevier Inc.

More than 200,000 American men are currently diagnosed annually with prostate cancer (PCa).[1] The overwhelming majority of these newly diagnosed PCa's are clinically localized.[2] Treatment options for clinically localized PCa include radical prostatectomy (RP), radiation therapy, whole gland ablation, focal ablation, active surveillance, and watchful waiting.

The impact of RP on PCa mortality is highly controversial. Between 1989 and 1999, the Scandinavian Prostate Cancer Study Group 4 (SPCG-4) randomized 695 men to RP vs watchful waiting.[3] The RP vs Observation for Localized Prostate Cancer (PIVOT) randomized 731 men to RP vs observation between 1994 and 2002.[4] However, the conclusions from both studies are inconsistent as far as survival advantage of RP.

To our knowledge, there are no other randomized studies comparing RP with watchful waiting to provide insights into the survival advantage of RP in the foreseeable future. Further insights into this controversy will be derived from long-term follow-up of large, single-arm series. Therefore, the objective of the present study is to describe the impact of RP on PCa-specific mortality (PCSM) derived from a primarily screen-detected cohort of men. The unique feature of the present study is that the names of all men failing to respond to our most recent outcome assessment were submitted to the National Death Index (NDI) registry hosted by the United States Center for Disease Control and Prevention (CDC) to minimize underreporting of mortality.[5,6]

METHODS

Between October 2000 and March 2013, 1873 men with localized PCa underwent open radical retropubic prostatectomy by a single surgeon. Of these men, 1864 (99.5%) signed informed

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consent to participate in a prospective longitudinal outcomes study. At the time of signing the consent, men were instructed that they would be requested to complete surveys capturing quality of life, most recent prostate-specific antigen (PSA) level, and any treatments related to their PCa at various future time-points. A full-time data manager was assigned to manage the institutional review board (IRB)-approved database to maximize compliance with follow-up. Mortality from any cause reported before December 31, 2013 was queried from the database.

With IRB approval, the names, social security numbers, and dates of birth of all men lost to follow-up at the most recent outcome assessment were submitted to the NDI registry, which hosts centralized death records from state vital statistics offices in the United States. Any men in our study who were registered as deceased in the NDI between October 1, 2000 and December 31, 2013 were evaluated for timing and cause of death. Men identified by International Classification of Disease (ICD)-10 coded cause of death for malignant neoplasm of the prostate were considered deceased from PCa.

The life expectancy of men in the present study was calculated based on life tables for men in the U.S. population for the year 2006,[7] which represent the midyear of our follow-up. The mean life expectancy according to age at the time of RP for our cohort was determined by multiplying the age-dependent life expectancy by the number of men in the specific age group and dividing this value by the number of men in the study.

The mortality data derived from our prospective outcomes study were combined with the information received from the NDI to generate Kaplan-Meier all-cause survival and PCa-specific survival plots for the study population. Similar Kaplan-Meier plots were generated for subgroups based on age (<65 years vs ≥65 years), D'Amico risk[8] (low, intermediate, or high; Table 1), postoperative tumor grade, and pathologic stage. The 10-year all-cause and PCSM rates were determined within these subgroups using IBM Statistical Package for the Social Sciences (SPSS) version 21.0 (Armonk, NY). Log-rank analysis was used to compare survival times among all subgroups and pairwise between each subgroup. A Cox-proportional hazards model was used to evaluate the association of clinical characteristics and risk of PCSM. Statistical significance was determined based on a 2-tailed P value <.05.

RESULTS

Baseline demographics, preoperative tumor characteristics and pathologic assessment of the surgical specimen are summarized for the 1864 men enrolled in our outcomes study in Table 1. A total of 1789 (96.0%), 1557 (83.5%), and 787 (42.2%) men were eligible for 2-, 5-, and 10-year follow-up, respectively. The median follow-up time was 9.1 years (range 9 months-13.2 years). Biographical information of all 711 (38.1%) men lost to follow-up over the duration of the study was queried to the CDC NDI.

Overall, 73 of 1864 (3.92%) men were reported as deceased from all causes including 19 (1.02%) from PCa. Kaplan-Meier analysis demonstrated cumulative 10-year all-cause mortality and PCSM of 4.6% and 1.4%, respectively (Fig. 1A). Subgroup analysis by D'Amico risk, postoperative Gleason score, and pathologic stage are also shown (Fig. 1B-D; Table 2). Ten-year PCSM for low, intermediate, and high D'Amico risk groups were 0.9%, 1.0%, and 7.4%, respectively (P <.001). For men aged younger than 65 years, 10-year PCSM was 1.3% vs 2.1% for men aged 65 years and older (P = .387), whereas 10-year all-cause mortality was 3.4% for men aged younger than 65 years and 9.9% for men aged 65 years and older (P <.001). For men with postoperative Gleason score 4-6, 7, and 8-10, 10-year PCSM was 0.8%, 1.0%, and 11.5%, respectively (P <.001). Men with organ-confined disease (pT2), extraprostatic extension of tumor without seminal vesicle invasion (pT3a), and extraprostatic extension with seminal vesicle invasion (pT3b)[9] demonstrate 10-year PCSM of 0.7%, 2.6%, and 9.5%, respectively (P <.001). A Cox-proportional hazards model demonstrated that pathologic stage (hazard ratio 2.010; 95% confidence interval, 1.284-3.145), as previously classified, and pathologic grade (hazard ratio 2.488, 95% confidence interval, 1.123-5.514) were the only significant independent predictors of increased PCSM at 10 years (Table 3).

Table 1. Baseline characteristics of radical prostatectomy cohort

Total cohort	1864
Age at RP, median (IQR)	59 (54-64)
Preoperative PSA, median (IQR)	5.0 (4.0-7.1)
Race	n (%)
Caucasian	1677 (90.0)
African American	76 (4.1)
Asian	37 (2.0)
Hispanic	30 (1.6)
Other/not reported	44 (2.4)
Preoperative Gleason score	
≤6	1149 (61.6)
7	598 (32.1)
≥8	117 (6.3)
D'Amico risk stratification[8]	
Low risk (Gleason ≤6; PSA ≤10; cT1-cT2a)	1034 (55.5)
Intermediate risk (Gleason 7; 10 < PSA ≤ 20; cT2b)	658 (35.3)
High risk (Gleason ≥8; PSA >20; cT2c)	172 (9.2)
Postoperative Gleason score	
≤6	909 (48.8)
7	836 (44.8)
≥8	119 (6.4)
Pathologic stage[9]	
Organ confined (pT2)	1415 (75.9)
Extraprostatic extension without seminal vesicle invasion (pT3a)	341 (18.3)
Extraprostatic extension with seminal vesicle invasion (pT3b)	108 (5.8)

IQR, interquartile range; PSA, prostate-specific antigen; RP, radical prostatectomy.

COMMENT

The risk-to-benefit ratio of RP for the management of clinically localized PCa is highly controversial.[10] The reported benefits include reducing the risk of PCa mortality, prevention of local disease progression, prevention of systemic metastasis,[3] and avoidance of androgen deprivation therapy. The reported risks of RP include surgical and perioperative complications,[11,12] urinary