Impact of Patient Age at Treatment on Outcome Following Radical Retropubic Prostatectomy for Prostate Cancer

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Purpose: Historically young patients with prostate cancer have been found to have poorer outcomes. Recent studies suggest favorable pathological findings and improved survival in younger patients undergoing RRP. We assessed age at treatment as a predictor of post-RRP survival.

Materials and Methods: We identified 5,509 patients treated with RRP for prostate cancer at our institution between 1987 and 1995. Age at treatment was classified into categories of younger than 55, 55 to 59, 60 to 64, 65 to 69 and 70 years or older. CSS, sPFS and biochemical PFS were estimated by the Kaplan-Meier method and analyzed using Cox proportional hazard models.

Results: Younger patients had lower preoperative prostate specific antigen, and tumor grade and stage. CSS, sPFS and biochemical PFS were similar across age groups but overall survival decreased with older age at treatment. After multivariate adjustment the risk of cancer death was lower in patients 70 years or older (RR 0.53, 95% CI 0.30 to 0.90), while the risk of progression was lower in all age groups compared to that in men younger than 55 years (RR 0.57 to 0.62). On stratified subset analysis sPFS was progressively worse with younger age in patients with high risk pathological findings. However, the addition of age to multivariate models incorporating preoperative prostate specific antigen, pathological features and adjuvant therapy failed to improve their predictive value for CSS and sPFS.

Conclusions: Despite more favorable clinicopathological features younger patients undergoing RRP for prostate cancer have survival similar to that of older counterparts. Given the greater proportionate impact of prostate cancer on survival, it is particularly important to pursue aggressive treatment in younger patients.

Key Words: prostate, prostatic neoplasms, prostatectomy, age groups, mortality

In previous studies prostate cancer in young patients has been reported to be more aggressive and associated with poor outcomes.[1–3] However, in recent years the widespread use of serum PSA has led to significant stage migration. Furthermore, patients with nonmetastatic prostate cancer are usually offered curative treatment such as RRP, which was not the case in historical series.[2] In fact, an increasing number of younger men are being treated for prostate cancer with RRP, often with favorable pathological findings.[4–7] Some recent studies have also suggested that young patients with prostate cancer have better biochemical outcomes following RP,[6,7] although others demonstrated no difference.[8,9]

However, these findings may have been confounded by the inclusion of patients from the pre-PSA era, small numbers, short followup and the exclusive use of biochemical (PSA) recurrence as the end point. We have previously reported that in patients undergoing RP in the pre-PSA era age at treatment was not a significant predictor of CSS after adjusting for Gleason score.[10] In this study we assessed the impact of patient age on systemic recurrences and death from prostate cancer after RP in a large cohort of patients during the PSA era.

MATERIALS AND METHODS

With approval from the Mayo Clinic Institutional Review Board patients who had undergone RRP for prostate cancer between 1987 and 1995 were identified from the Mayo Clinic Prostatectomy Registry. A total of 5,509 men, who remained after the exclusion of patients who received neoadjuvant therapy prior to surgery or refused research authorization, formed the study cohort. RRP and pelvic lymphadenectomy were performed by a number of different surgeons using standardized techniques. Pathological evaluation was done using a limited sampling technique on frozen tissue sections at surgery with subsequent examination of paraffin embedded sections the following day.[11] Stage and grade were assigned using the 1997 UICC-American Joint Committee on Cancer TNM system and the Gleason system, respectively. DNA ploidy was assessed by flow cytometry.[11] Postoperative adjuvant therapy was defined as that initiated or planned within 90 days following RRP.

Postoperative followup was performed quarterly to semiannually for the first 2 years and annually thereafter by

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TABLE 1. *Clinical and pathological features stratified by age at treatment*

Feature	Total	Younger Than 55	55–59	60–64	65–69	70 or Older	p Value
No. pts	5,509	369	640	1,252	1,721	1,527	
Median mg/ml preop PSA (IQR)	7.8 (4.9–13.9)	6.5 (4.2–11.1)	6.5 (4.3–11.4)	7.5 (4.8–12.8)	8.1 (5.2–14.3)	8.7 (5.3–15.8)	<0.0001
No. biopsy Gleason (%):							0.013
2–4	529 (17.9)	41 (18.1)	66 (18.6)	127 (18.3)	160 (17.6)	135 (17.4)	
5	974 (32.9)	81 (35.7)	125 (35.2)	226 (32.6)	305 (33.5)	237 (30.6)	
6	634 (21.4)	51 (22.5)	78 (22)	146 (21)	200 (22)	159 (20.5)	
7	668 (22.6)	42 (18.5)	73 (20.6)	166 (23.9)	199 (21.9)	188 (24.3)	
8–10	156 (5.3)	12 (5.3)	13 (3.7)	29 (4.2)	46 (5.1)	56 (7.2)	
No. clinical Stage (%):							0.129
T1	1,215 (22.1)	75 (20.3)	156 (24.5)	287 (23)	394 (23)	303 (19.9)	
T2a	2,842 (51.7)	199 (53.9)	335 (52.5)	632 (50.7)	905 (52.8)	771 (50.6)	
T2b	834 (15.2)	53 (14.4)	74 (11.6)	184 (14.8)	229 (13.4)	294 (19.3)	
T3–4	602 (11)	42 (11.4)	73 (11.4)	144 (11.5)	187 (10.9)	156 (10.2)	
No. specimen Gleason (%):							0.0002
2–4	435 (8.4)	39 (10.9)	44 (7.3)	104 (8.8)	128 (7.9)	120 (8.4)	
5	1,788 (34.3)	133 (37)	235 (38.8)	414 (35)	529 (32.5)	477 (33.3)	
6	1,107 (21.3)	78 (21.7)	123 (20.3)	259 (21.9)	366 (22.5)	281 (19.6)	
7	1,526 (29.3)	90 (25.1)	172 (28.4)	332 (28.1)	491 (30.2)	441 (30.8)	
8–10	353 (6.8)	19 (5.3)	32 (5.3)	74 (6.3)	113 (6.9)	115 (8)	
No. pathological stage (%):							<0.0001
T2aN0	1,223 (22.3)	101 (27.4)	158 (24.8)	290 (23.3)	349 (20.3)	325 (21.4)	
T2bN0	1,992 (36.3)	139 (37.8)	253 (39.8)	457 (36.6)	617 (35.9)	526 (34.6)	
T3–4N0	1,815 (33.1)	93 (25.3)	175 (27.5)	398 (31.9)	598 (34.8)	551 (36.2)	
TxN+	461 (8.4)	35 (9.5)	50 (7.9)	102 (8.2)	155 (9)	119 (7.8)	
No. DNA ploidy (%):							<0.0001
Diploid	3,720 (71.6)	275 (77.9)	480 (78.3)	854 (72.4)	1,141 (70.9)	970 (67.5)	
Tetraploid	1,141 (22)	60 (17)	99 (16.2)	264 (22.4)	363 (22.5)	355 (24.7)	
Aneuploid	332 (6.4)	18 (5.1)	34 (5.5)	62 (5.3)	106 (6.6)	112 (7.8)	
No. margin pos (%)	2,135 (38.8)	139 (37.7)	239 (37.3)	464 (37.1)	685 (39.8)	608 (39.8)	0.12
No. adjuvant treatment (%):							
Hormonal	978 (17.8)	64 (17.3)	107 (16.7)	212 (16.9)	305 (17.7)	290 (19)	0.17
Radiation	369 (6.7)	26 (7)	55 (8.6)	91 (7.3)	123 (7.1)	74 (4.8)	0.004
Hormonal + radiation	95 (1.7)	9 (2)	17 (2.6)	24 (2)	23 (1.3)	22 (1.4)	
Median yrs followup (IQR)	10.6 (8.7–12.4)	10.0 (8.7–11.8)	10.5 (8.8–12.3)	10.6 (8.9–12.5)	10.7 (8.7–12.6)	10.8 (8.4–12.5)	0.018

clinical assessment, serum PSA measurement and other investigations as indicated. The Mayo Clinic Prostatectomy Registry monitors outcomes annually, including by correspondence the minority of patients receiving followup elsewhere. Records were 96% up to date. Biochemical progression was defined as PSA greater than 0.4 ng/ml.[12] Systemic progression was defined as demonstrable metastatic disease on radionuclide bone scintigraphy or plain x-ray, or pathological evidence of failure, as on lymph node biopsy. Cause of death was verified from death certificates or physician correspondence.

For statistical analysis age at treatment was categorized into 5 clinically useful groups, including younger than 55, 55 to 59, 60 to 64, 65 to 69 and 70 years or older. Previous studies have used cutoff points of 50, 55 or 59 years to define young patients.[6–9] In this study median patient age was 66 years and patients whose age at RRP was younger than 55 years were considered young to provide a large enough cohort (369 or 6.7%) for valid analysis. bPFS, sPFS, prostate CSS and overall survival were estimated using the Kaplan-Meier method. Associations of age at treatment, and other clinical and pathological features with prostate cancer progression and death were assessed using Cox proportional hazard regression models.

The relative predictive power of these models was evaluated using the c-index. The c-index for a multivariate model is a measure of the accuracy with which predictors included in the model can predict the outcome of interest with a value of 1.0

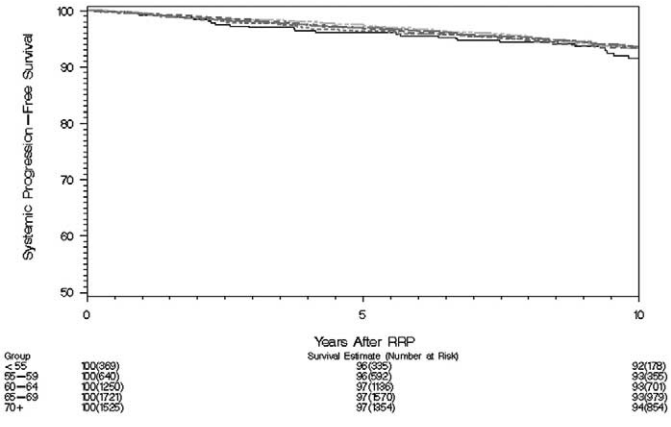

FIG. 1. sPFS after RP for prostate cancer by patient age at treatment.

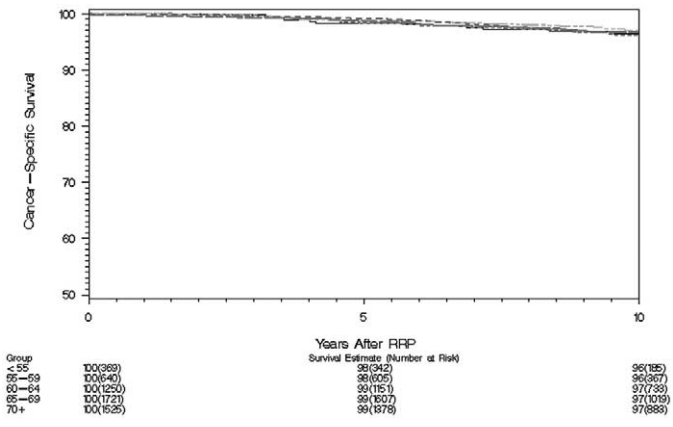

FIG. 2. CSS after RP for prostate cancer by patient age at treatment.