A Contemporary Analysis of Outcomes of Adenocarcinoma of the Prostate With Seminal Vesicle Invasion (pT3b) After Radical Prostatectomy

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Purpose: Despite earlier detection and stage migration, seminal vesicle invasion is still reported in the prostate specific antigen era and remains a poor prognostic indicator. We investigated outcomes in men with pT3b disease in the contemporary era.

Materials and Methods: The institutional radical prostatectomy database (1982 to 2010) of 18,505 men was queried and 989 with pT3b tumors were identified. The cohort was split into pre-prostate specific antigen (1982 to 1992), and early (1993 to 2000) and contemporary (2001 to present) prostate specific antigen eras. Of the 732 men identified in the prostate specific antigen era 140 had lymph node involvement and were excluded from study. The Kaplan-Meier method was used to determine biochemical recurrence-free, metastasis-free and prostate cancer specific survival. Proportional hazard models were used to determine predictors of biochemical recurrence-free, metastasis-free and cancer specific survival.

Results: In the pre-prostate specific antigen, and early and contemporary prostate specific antigen eras, 7.7%, 4.3% and 3.3% of patients, respectively, had pT3bN0 disease ($p > 0.001$). In pT3bN0 cases, the 10-year biochemical recurrence-free survival rate was 25.8%, 28.6% and 19.6% ($p = 0.8$), and the cancer specific survival rate was 79.9%, 79.6% and 83.8% ($p = 0.6$) among the eras, respectively. In pT3bN0 cases in the prostate specific antigen era, prostate specific antigen, clinical stage T2b or greater, pathological Gleason sum 7 and 8–10, and positive surgical margins were significant predictors of biochemical recurrence-free survival on multivariate analysis while clinical stage T2c or greater and Gleason 8–10 were predictors of metastasis-free and cancer specific survival.

Conclusions: Despite a decreased frequency of pT3b disease, and lower rates of positive surgical margins and lymph nodes, patients with seminal vesicle invasion continue to have low biochemical recurrence-free survival. Advanced clinical stage, intermediate or high risk Gleason sum at pathological evaluation and positive surgical margins predict biochemical recurrence. High risk clinical stage and Gleason sum predict metastasis-free and cancer specific survival.

Key Words: prostate, adenocarcinoma, seminal vesicles, prostatectomy, prostate-specific antigen

Abbreviations and Acronyms

ART = adjuvant radiation treatment

BFS = biochemical recurrence-free survival

CSS = prostate cancer specific survival

LN = lymph node

MFS = metastasis-free survival

PSA = prostate specific antigen

RP = radical prostatectomy

SM = surgical margin

SV = seminal vesicle

SVI = seminal vesicle invasion

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TRADITIONALLY, SVI by adenocarcinoma of the prostate at RP is associated with worse pathological features and prognosis.[1,2] In the PSA era, despite earlier detection and stage migration, rates of SVI have decreased

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from greater than 10%, but persist at approximately 6% of all RP specimens.[3] In-depth studies of pathological specimens have distinguished certain types of SVI, with lesser degrees having more a favorable prognosis.[4,5] In the PSA era, SVI is most commonly via extraprostatic extension into the soft tissues adjacent to the prostate and SVs, and subsequently into the wall of the SVs.[4] Nevertheless, SVI is believed to be associated with occult micrometastatic disease, earlier biochemical recurrence and eventual disease progression.[6]

The largest previous analysis of SVI included approximately 300 men and demonstrated a biochemical recurrence rate of greater than 60%.[7] A second analysis of 220 men similarly demonstrated a high rate of recurrence (54%) and no benefit to adjuvant or salvage therapy.[3] Using a larger, comprehensive database from our institution, we investigated outcomes in men with pT3b disease treated predominantly without ART in the contemporary era.

MATERIALS AND METHODS

The institutional review board approved, Johns Hopkins University RP database (1982 to present) was queried for men with pT3b disease. Of approximately 18,505 men who underwent RP 989 had SVI (pT3b disease). All patients at our institution undergo bilateral pelvic LN dissection. All RP specimens were processed. The SVI diagnosis was confirmed under standard protocol with SVI defined as tumor invading the muscular wall of the SV, which can occur by several mechanisms, of which the most common is extraprostatic extension at the base of the prostate, direct tracking along the ejaculatory duct complex, or via isolated, noncontiguous SV deposits.[4,8–10] Of note, the route of invasion was not consistently documented and not considered in analysis. The cohort was grouped into 3 time based cohorts, including the prePSA (1982 to 1992), early PSA (1993 to 2000) and contemporary PSA (2001 to 2010) eras. The split between the early and contemporary PSA eras was based on the penetrance of PSA screening and incorporation of the Partin tables into clinical practice at our institution.[11,12] A total of 257 men underwent RP before 1993 and 732 were identified in the PSA era, including 283 in the early and 447 in the contemporary eras, respectively. Appropriate comparative tests (the t and chi-square tests, and ANOVA) were used to determine differences in preoperative and postoperative characteristics among the eras.

Men with prostate cancer involving pelvic LNs were excluded from further survival analysis. A total of 242 men with LN invasion (N1) were excluded, yielding 155, 217 and 375 evaluable in each era, respectively. The Kaplan-Meier method was used to determine BFS, MFS and CSS among all 3 time cohorts. Men with pT3bN0 disease in the PSA era only were evaluated for predictors of BFS, MFS and CSS using univariate and multivariate proportional hazard models. Variables included preoperative PSA (0 to less than 10, 10 to less than] 20, and 20 or greater), clinical stage (cT2a or less, cT2b, and cT2c or greater), pathological Gleason sum (2–6, 7, and 8–10) and positive SMs. Significant predictors of BFS, MFS and CSS on univariate analysis were included in the multivariate analysis.

RESULTS

A total of 989 men were identified with SVI (pT3b). The SVI rate was 12.7%, 5.7% and 3.9% in the prePSA, and early and contemporary PSA eras, respectively ($p < 0.001$). Table 1 lists clinical and pathological data on all patients among the eras. Based on D'Amico criteria,[13] the rate of high risk prostate cancer decreased significantly as the era progressed (58.5%, 21.9% and 11.8%, respectively, $p < 0.001$). Of note, the rate of positive SMs decreased from 52.7% to 41.4% to 35.1%, and the rate of positive LNs decreased from 39.7% to 23.9% to 16.1% among the eras, respectively ($p < 0.001$).

In men with pT3bN0 disease, the 10-year BFS rate was 25.8%, 28.6% and 19.7% in the prePSA, and the early and contemporary PSA eras, respectively ($p = 0.8$). The MFS rate was 62.9%, 71.9% and 75.7% ($p = 0.3$), and the CSS rate was 79.9%, 79.6% and 83.9%, respectively ($p = 0.6$, fig. 1). Table 2 lists the characteristics of the 592 patients with a median age of 59 ears (range 41 to 73) who had pT3bN0 disease and median PSA 7.7 ng/ml (range 0.1 to 84.1). Notably 202 men (34.2%) had positive SMs. In pT3bN0 cases in the PSA era, preoperative PSA (0 to less than 10, 10 to less than 20, and 20 or greater ng/ml), clinical stage (cT2a or less, cT2b, and cT2c or greater), pathological Gleason sum (2 to 6, 7, and 8 to 10) and positive SMs were significant predictors of BFS, MFS and CSS on univariate analysis, and were included in the final multivariate model. Multivariate analysis revealed that clinical stage cT2c or greater (HR 1.65, 95% CI 1.08–2.51, $p = 0.02$), pathological Gleason 7 (HR 14.4, 95% CI 6.9–29.9, $p < 0.001$), and 8–10 (HR 45.3, 95% CI 21.3–96.4, $p < 0.001$) and positive SMs (1.42, 1.11–1.82, $p = 0.006$) were significant predictors of BFS. Figure 2 shows univariate Kaplan-Meier analysis. Predictors of MFS were clinical stage T2c–T3 (HR 4.3, 95% CI 1.94–9.3, $p < 0.001$) and Gleason 8–10 at RP (HR 7.4, 95% CI 1.8–31.4, $p = 0.01$, fig. 3). Predictors of CSS were clinical stage T2c–T3 (HR 4.1, 95% CI 1.8–9.3, $p < 0.001$) and Gleason 8–10 at RP (HR 3.9, 95% CI 1.35–11.5, $p = 0.01$, fig. 4).

In the contemporary PSA era, 30 men with pT3bN0 (5.1%) received ART, including 19 with positive SMs. A total of 141 men (41.1%) received adjuvant or salvage radiation (73 or 21.5%), hormone therapy (96 or 28.2%) and/or chemotherapy (29 or 8.9%). When the 144 patients who received adjuvant or salvage therapy were excluded, multivariate anal-