The Impact of Obesity on Overall and Cancer Specific Survival in Men With Prostate Cancer

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Abbreviations and Acronyms

ADT = androgen deprivation therapy

BMI = body mass index

BT = brachytherapy

CaPSURE™ = Cancer of the Prostate Strategic Urological Research Endeavor

PSA = prostate specific antigen

RP = radical prostatectomy

XRT = external beam radiation therapy

Submitted for publication October 27, 2008.

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† Financial interest and/or other relationship with TAP Pharmaceuticals, National Cancer Institute, AstraZeneca and Takeda.

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Purpose: We examined the impact of obesity on disease specific and overall survival in patients with prostate cancer.

Materials and Methods: We identified 7,274 men from the Cancer of the Prostate Strategic Urological Research Endeavor database with clinically localized prostate cancer, known body mass index and clinicopathological disease characteristics. Patients were classified by body mass index as normal (less than 25 kg/m^2), overweight (25 to 29.9 kg/m^2), obese (30 to 34.9 kg/m^2) and severely obese (35 kg/m^2 or greater). Associations between body mass index and need for secondary treatment, disease specific survival and overall survival were analyzed using univariate and multivariate models.

Results: Patients were classified by body mass index category as normal (28.8%), overweight (50%), obese (16.4%) and very obese (4.8%). Mean followup was 51.3 ± 38.5 months. During followup there were 1,044 deaths with 220 (21.1%) from prostate cancer. Stratified by body mass index category the groups differed with regard to the need for secondary treatment ($p = 0.05$) and overall mortality ($p < 0.01$) but there were no significant differences with regard to disease specific survival ($p = 0.09$). On multivariate analysis age 65 to 74 years (HR 2.4, $p = 0.002$), age older than 75 years (HR 3.2, $p = 0.0001$), high risk disease (HR 1.6, $p < 0.0001$), conservative treatment (HR 1.2, $p < 0.0001$) and presence of diabetes (HR 1.6, $p < 0.0001$) were associated with decreased overall survival. Only conservative treatment (HR 1.4, $p < 0.0001$), high risk disease (HR 8.4, $p < 0.0001$) and intermediate risk disease (HR 2.5, $p = 0.004$) were associated with decreased disease specific survival.

Conclusions: In a prospective, community based cohort we were unable to establish a relationship between body mass index and prostate cancer disease specific survival or overall survival.

Key Words: prostatic neoplasms, obesity, mortality, body mass index

In the United States prostate cancer is the most common cancer detected and the second leading cause of cancer related death in adult males.[1] In the last 20 years the prevalence of obesity in American men has doubled, increasing to 31% in 2004.[2] A recent study reported that a body mass index greater than 40 kg/m^2 was associated with a greater than 50% increase in cancer mortality across a wide range of malignancies including prostate cancer.[3]

In light of this growing epidemic the urological community has shown significant interest in defining the relationship between obesity and prostate cancer biology. Associations be-

0022-5347/09/1821-0112/0
THE JOURNAL OF UROLOGY®

Vol. 182, 112-117, July 2009
Printed in U.S.A.
DOI:10.1016/j.juro.2009.02.118

tween obesity and higher Gleason scores, advanced stage at diagnosis,[4] adverse pathological features following radical prostatectomy[5] and increased biochemical recurrence rates[6,7] have recently been described.

However, the impact of obesity on prostate cancer specific and overall mortality is less clearly defined. While some series demonstrated no differences in cancer specific survival between obese and normal weight men undergoing radical prostatectomy,[8] recent population based cohort studies reported BMI as an independent risk factor for prostate cancer related death.[9,10] Further confounding these results is the likelihood that obese patients have higher rates of expectant management and nonsurgical treatment methods.[11]

Despite recent attention the exact role of obesity in the development, diagnosis, progression and treatment of prostate cancer is still not well understood. In this study we examined the impact of obesity on rates of secondary treatment, overall survival and disease specific survival in patients with prostate cancer treated with various primary treatment modalities in a large, prospective, community based, observational sample.

MATERIALS AND METHODS

The study population consisted of patients recruited to participate in CaPSURE, a longitudinal, observational, database of men with biopsy proven prostate adenocarcinoma established in 1995. Patients are recruited from 40 primarily community based urology practices (34 community based, 3 Veteran's Administration, 3 academic medical centers) across the United States. All patients with prostate cancer are recruited consecutively by participating urologists who report complete clinical data and followup information on diagnostic testing, treatments, oncological outcomes and health related quality of life. Patients are treated according to physicians' usual practices and followed until death or withdrawal from the study. Informed consent is obtained from each patient under local institutional review board supervision and data accuracy is assured by random sample chart review every 6 months. Mortality information is obtained from the Bureau of Vital Statistics or National Death Index.

As of May 2007, 13,740 men were enrolled in the CaPSURE database. Inclusion criteria for this study were a new prostate cancer diagnosis at CaPSURE enrollment (ie enrolled within 6 months of diagnosis) between 1995 and 2007, clinically localized prostate cancer (T1-T3, NX/N0, M0), and available information regarding clinical risk stratification, BMI and initial/secondary forms of treatment. The records of men undergoing expectant management were excluded from analysis. BMI classes were defined as normal (less than 25 kg/m^2), overweight (25 to 29.9 kg/m^2), obese (30 to 34.9 kg/m^2) or severely obese (35 kg/m^2 or greater). Specific treatment modalities for prostate cancer were defined as RP, XRT, BT, primary ADT or cryotherapy. Patients were categorized as having low, intermediate or high risk disease based on a modification of the D'Amico classification as low risk—stage T1 or 2a, Gleason score less than 7, PSA less than 10 ng/ml; intermediate risk—stage T2b or Gleason score 7 or PSA between 10 and 20 ng/ml; and high risk—any stage greater than T2b, Gleason score greater than 7, PSA greater than 20 ng/ml.[12] Outcomes of interest included overall mortality, prostate cancer specific mortality and receipt of secondary therapy.

Associations among obesity, demographics, treatments and mortality outcomes were analyzed using univariate and multivariate models. Correlation among the variables in the analysis was tested by Spearman's rho. Variables with higher rho were excluded from analysis to avoid collinearity. For categorical and continuous variables the Pearson chi-square and ANOVA tests were used to determine association. Controlling for age, BMI, clinical risk stratification, type of treatment (surgical [RP] vs nonsurgical) and presence of diabetes, Cox proportional hazards models were used to identify independent predictors of secondary treatment, overall mortality and prostate cancer specific mortality. Values were expressed as mean $\pm$ SD with $p \leq 0.05$ considered statistically significant. Associations between BMI and variables of interest were evaluated by Cox proportional hazards models and Kaplan-Meier curves. All analyses were performed using SAS® 9.1 statistical software.

RESULTS

Of the 13,740 patients enrolled in CaPSURE as of May 2007, 7,274 met the study inclusion criteria. The majority of the sample were white (white 89%, black 8%, other race 3%) and 65.8 $\pm$ 8.4 years old (median 66) at diagnosis. Median PSA at diagnosis was 7 ng/ml, and Gleason scores ranged from 2 to 4 (5%), 5 to 6 (58%), 7 (26%), to 8 to 10 (11%). Clinical staging was T1 (45%), T2 (50%) and T3 (5%). Using the Gleason score, PSA and clinical stage to determine clinical risk, 38% of patients were categorized as low risk, 35% as intermediate risk and 27% as high risk by the D'Amico classification. Initial therapy consisted of RP (53%), ADT (14%), BT (11%), cryotherapy (4%), BT plus XRT (3%) and RP plus XRT (1%). With a mean time to secondary treatment of 29.5 $\pm$ 24.7 months (median 21) 1,277 patients (17.6%) had progression to secondary therapy including ADT 79.7%, XRT 15.6%, cryotherapy 2.1%, BT 2% and RP 0.6%. With a mean followup of 51.3 $\pm$ 38.5 months (median 44) there were 1,044 deaths of which 220 (21.1%) were from prostate cancer.

Categorized by BMI patients were classified as normal weight (28.8%), overweight (50%), obese (16.4%) and severely obese (4.8%). Table 1 displays demographic, clinical and pathological characteristics of the sample stratified by BMI category while table 2 describes treatment and outcome characteristics. Groups differed by race/ethnicity ($p < 0.01$), age at diagnosis ($p < 0.01$), PSA at diagnosis ($p < 0.01$), T stage