Current Use of Imaging after Primary Treatment of Prostate Cancer

Ahmed A. Hussein, Sanoj Punnen,* Shoujun Zhao, Janet E. Cowan,†
Michael Leapman, Thanh C. Tran, Samuel L. Washington,
Matthew D. Truesdale, Peter R. Carroll and Matthew R. Cooperberg‡

From the Department of Urology and Helen Diller Family Comprehensive Cancer Center, University of California-San Francisco (AAH, SP, SZ, JEC, ML, TCT, SLW, MDT, PRC, MRC), San Francisco, California, and Department of Urology, Cairo University (AAH), Cairo, Egypt

Abbreviations and Acronyms

ADT = androgen deprivation therapy

BS = radionuclide bone scan

BT = brachytherapy

CAPRA = University of California-San Francisco Cancer of the Prostate Risk Assessment

Cryo = cryosurgery

CT = computerized tomography

EBRT = external beam radiation therapy

MRI = magnetic resonance imaging

PCa = prostate cancer

PSA = prostate specific antigen

RP = radical prostatectomy

Accepted for publication January 22, 2015.

Study received institutional review board approval.

Supported by United States Department of Defense Prostate Cancer Research Program W81XWH-13-2-0074 and a grant from Abbott (CaPSURE).

* Financial interest and/or other relationship with Dendreon.

† Financial interest and/or other relationship with Abbot Laboratories.

‡ Correspondence: Department of Urology, University of California-San Francisco, 1600 Divisadero St., Box 1695, San Francisco, California 94143 (telephone: 415-885-3660; FAX: 415-353-7093; e-mail: mcooperberg@urology.ucsf.edu).

Purpose: Data are limited on imaging after primary treatment of localized prostate cancer.

Materials and Methods: We identified 8,435 men newly diagnosed with nonmetastatic prostate cancer in 1995 to 2012 who were enrolled in CaPSURE™. Patients were followed after primary treatment with radical prostatectomy, cryosurgery, brachytherapy, external beam radiation therapy or androgen deprivation therapy. We assessed the use of bone scan, computerized tomography and magnetic resonance imaging after primary treatment. Factors associated with posttreatment outcomes (number of imaging tests, and time to first imaging and salvage treatment) were evaluated with multivariate Poisson regression and Cox proportional hazards regression.

Results: The incidence of posttreatment bone scan, computerized tomography and magnetic resonance imaging was 20% or less. Last posttreatment log(prostate specific antigen) was associated with multiple posttreatment imaging. Management by radical prostatectomy, cryosurgery, external beam radiation therapy or brachytherapy vs androgen deprivation therapy was associated with a lower likelihood of posttreatment imaging. Of patients who were imaged after treatment 25% with radical prostatectomy and 9% with radiation underwent imaging before prostate specific antigen failure. The 5-year salvage treatment-free survival rate was 81%. Positive findings on posttreatment imaging were associated with a higher risk of salvage treatment.

Conclusions: Patients treated with androgen deprivation therapy for localized disease were most likely to be imaged, primarily by bone scan. Men treated with other therapies were less likely to be imaged and tended to undergo computerized tomography. Imaging may add value to posttreatment prostate specific antigen monitoring to identify disease recurrence and progression. Further studies are needed to establish guidelines for the optimal frequency and imaging type to monitor the treatment response.

Key Words: prostatic neoplasms, diagnostic imaging, prostate-specific antigen, salvage therapy, disease progression

THE role of imaging after PCa diagnosis is primarily to identify metastatic disease and enhance clinical staging with tests such as BS, CT and MRI.[1] Studies show consistent overuse of pretreatment imaging to stage

0022-5347/15/1941-0098/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2015.01.097
Vol. 194, 98-104, July 2015
Printed in U.S.A.

low risk, localized PCa.[2–4] In contrast, data are limited on imaging after primary treatment for PCa.

Posttreatment imaging, which is usually triggered by increasing PSA, is typically used to restage cases. Recurrence definitions after radiotherapy or surgery rely mainly on changes in PSA.[5–7] Studies have shown limited value of CT to detect recurrent disease at low PSA[8] and a high false-negative rate for bone metastasis for BS when postoperative PSA is 6 ng/ml or less and the patient lacks skeletal symptoms.[8,9]

In previous studies overall patterns of imaging in this patient cohort were not systematically assessed. We characterized contemporary trends in the use of BS, CT and MRI after primary PCa treatment. We obtained data from a large, national PCa registry to identify factors associated with posttreatment imaging and in turn clarify whether such imaging affects time to salvage therapy.

METHODS

Data Registry

CaPSURE is a longitudinal registry of patients with biopsy proven PCa recruited from 36 community, 4 veteran and 3 academic urological practices nationwide. Participating urologists recruit patients consecutively at diagnosis and report demographic and clinicopathological characteristics, reflecting real-world practice patterns. Followup data are collected at subsequent office visits and by patient reported questionnaires.[10]

Subjects

A total of 14,715 patients have consented to participate in the CaPSURE study under central institutional review board supervision since 1995. The current study included men newly diagnosed with nonmetastatic PCa who underwent active treatment in 1995 to 2012. Patients on watchful waiting or active surveillance and those with clinical stage N1/M1 or with 1 year or less of posttreatment followup were excluded from analysis. The final cohort underwent RP, Cryo, BT, EBRT or ADT as primary treatment. Men who received neoadjuvant or adjuvant treatment were included in study.

Data Analysis

Demographics (age at diagnosis, race and insurance type), clinical factors at diagnosis (PSA, Gleason grade, cT stage and CAPRA score[11]) and primary treatment modality are shown as the frequency and mean. The CAPRA score ranges from 0 to 10 with validated risk groups defined as low—0 to 2, intermediate—3 to 5 and high—6 to 10.[12] We calculated the imaging rates of BS, CT and MRI within 5 years after primary treatment and before salvage treatment. Biochemical recurrence was defined as 2 consecutive PSA values 0.2 ng/ml or greater after RP, or as a 2 ng/ml increase in PSA after nadir following radiotherapy (the Phoenix definition).[7]

Outcomes

Primary outcomes were the number of posttreatment imaging tests and time to first posttreatment imaging. The initial multivariate Poisson regression model identified factors associated with multiple posttreatment imaging to evaluate the volume of imaging. The second multivariate model assessed time to first posttreatment imaging with Cox proportional hazards regression to determine the risk of any imaging after treatment. Independent variables in the 2 models were primary treatment type, receipt of pretreatment imaging and last posttreatment PSA before the outcome event or last followup. We also evaluated a third outcome, time to salvage treatment, to determine the impact of posttreatment imaging findings on the likelihood of salvage treatment. This Cox model was restricted to men who underwent imaging after treatment. All models were adjusted for age, race, insurance coverage, CAPRA clinical risk, type of clinical site and diagnosis year. Covariates were selected a priori and assessed for interitem correlations with none excluded due to collinearity. We used the Pearson chi-square test, Mantel-Haenszel test for trend and ANOVA for statistical analysis with 2-sided $p < 0.05$ considered significant. All analysis was done with SAS® 9.2.

RESULTS

Of the 14,715 men ever enrolled in CaPSURE 10,977 were diagnosed with localized disease in or after 1995. We selected 8,435 patients treated with RP, Cryo, BT, EBRT or ADT who had any imaging data available and 1 year or greater of followup data as the final study cohort. At diagnosis mean ± SD age was 65 ± 8.6 years, median PSA was 6.3 ng/ml (IQR 4.6–9.7) and 78% of the men were at low or intermediate CAPRA risk (5 or less). Of the patients 48% had private health insurance, 44% had Medicare with or without supplement, 3% had veteran coverage and 5% had other or unreported insurance. The primary treatment type was RP in 4,629 patients (55%, including 104 with adjuvant EBRT), Cryo in 341 (4%), BT in 1,321 (16%), EBRT in 962 (11%) and primary ADT in 1,182 (14%). Median followup was 61 months (IQR 35–97) (supplementary table, http://jurology.com/).

Of the 8,435 patients 1,458 underwent posttreatment imaging with BS, CT and/or MRI. The posttreatment imaging rate by BS, MRI and CT was less than 20%, which decreased with time in patients diagnosed in 1995 to 1999 (20%), 2000 to 2004 (17%) and 2005 to 2012 (13%) ($p < 0.01$). In men with posttreatment imaging BS decreased from 54% to 35% and MRI decreased from 9% to 7% between 1995 and 2012. CT increased from 37% to 58% during the same periods ($p < 0.01$, fig. 1, *A* and *B*).

The rate of posttreatment imaging was the highest in patients who received ADT (37%) and similar in the other treatment groups (range 13% to 15%). BS was the predominant modality after primary