Identification of Recurrence Sites Following Post-Prostatectomy Treatment for Prostate Cancer Using ^{11}C-Choline Positron Emission Tomography and Multiparametric Pelvic Magnetic Resonance Imaging

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Abbreviations and Acronyms

ADT = androgen deprivation therapy

BCR = biochemical recurrence

CT = computerized tomography

MDT = metastasis directed therapy

mpMRI = multiparametric magnetic resonance imaging

PET = positron emission tomography

PSA = prostate specific antigen

RP = radical prostatectomy

RRP = radical retropubic prostatectomy

RT = radiotherapy

Purpose: We describe anatomical sites of recurrence in patients with prostate cancer who had biochemical recurrence following radical prostatectomy and who received radiotherapy and/or androgen deprivation therapy postoperatively. We performed ^{11}C-choline positron emission tomography/computerized tomography and multiparametric magnetic resonance imaging.

Materials and Methods: After radiotherapy and/or androgen deprivation therapy patients who underwent radical prostatectomy were evaluated by ^{11}C-choline positron emission tomography/computerized tomography and multiparametric magnetic resonance imaging to determine recurrence patterns and clinicopathological features. Recurrent sites were described as local only (seminal vesicle bed/prostate fossa, vesicourethral anastomosis and bladder neck) or distant metastatic disease. Features associated with the identification of any distant metastatic disease were evaluated by multivariable logistic regression.

Results: A total of 550 patients were identified. Treatment included androgen deprivation therapy in 108, radiotherapy in 201, and androgen deprivation therapy and radiotherapy in 241. Median prostate specific antigen at evaluation was 3.9, 3.6 and 2.8 ng/ml in patients treated with androgen deprivation therapy, radiotherapy and a combination, respectively. Recurrence developed locally in 77 patients (14%), as distant metastasis only in 411 (75%), and as local and distant metastatic disease in 62 (11%). On multivariable analysis treatment with radiotherapy (OR 7.18, 95% CI 2.92–17.65), and radiotherapy and hormonal therapy (OR 9.23, 95% CI 3.90–21.87, all $p < 0.01$) was associated with increased odds of distant failure at evaluation.

Accepted for publication September 2, 2017.

No direct or indirect commercial incentive associated with publishing this article.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

Supported by the Richard M. Schulze Family Foundation, Jim and Dorothy Nelson, Dorothea Berggren and CTSA (Clinical and Translational Science Awards) Grant UL1 TR000135 from NCATS (National Center for Advancing Translational Sciences), a component of NIH (National Institutes of Health).

The contents are solely the responsibility of the authors and do not necessarily represent the official view of NIH.

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Supplementary references 31 to 36 are available at http://jurology.com/.

0022-5347/18/1993-0726/0
THE JOURNAL OF UROLOGY®

https://doi.org/10.1016/j.juro.2017.09.033
Vol. 199, 726-733, March 2018
Printed in U.S.A.

Conclusions: The combination of ^{11}C-choline positron emission tomography/computerized tomography and multiparametric magnetic resonance imaging successfully identified patterns of recurrence after postoperative radiotherapy and/or androgen deprivation therapy at a median prostate specific antigen of less than 4 ng/ml. Half of this cohort had local only recurrence and/or a low disease burden limited to pelvic lymph nodes. These patients may benefit from additional local therapy. These data and this analysis may facilitate the evaluation of such patients with biochemically recurrent prostate cancer.

Key Words: prostatic neoplasms, neoplasm metastasis, salvage therapy, diagnostic imaging, recurrence

PROSTATE cancer is the most common visceral malignancy in men in the United States and the third most common cause of death. In 2017 it was estimated that 161,360 new cases would be diagnosed and there would be 26,370 deaths from prostate cancer.[1] RP provides excellent long-term oncologic outcomes in clinically localized cases but BCR develops in approximately 40%.[2–5]

Management of biochemically recurrent prostate cancer after RP varies. Currently there is evidence to support the role of RT to the prostatic fossa in the adjuvant and salvage settings[6–8] as well as ADT, particularly in patients at high risk who have locally advanced disease.[9] More recently the outcomes of 2 randomized clinical trials revealed the benefit of combined RT and ADT in the management of post-RP recurrence.[10,11]

Unfortunately recurrences still develop following adjuvant and salvage therapies. Current guidelines recommend treatment with ADT in this setting[12] predicated on the assumption that failures cannot be targeted in a meaningful way. This may in part be due to the limited value of conventional imaging (eg bone scintigraphy and computerized tomography) when the disease burden is lower.[13,14] However, advanced imaging modalities offer improved detection. Local recurrences after RP can be detected by mpMRI.[15] Furthermore, ^{11}C-choline PET/CT has been useful for detecting metastatic recurrences, particularly at PSA greater than 1 ng/ml.[16] Consequently NCCN® (National Comprehensive Cancer Network®) and EAU (European Association of Urology) recognize the usefulness of ^{11}C-choline PET/CT in the evaluation of biochemically recurrent prostate cancer.[17,18] Together mpMRI and ^{11}C-choline PET/CT have improved the localization of disease recurrence at a lower disease burden[19–22] and aided in guiding directed therapies.[23]

Given the existing evidence supporting mpMRI and ^{11}C-choline PET/CT for evaluating patients with biochemically recurrent prostate cancer we evaluated anatomical sites of recurrence and how prior treatment influences recurrence patterns among heavily pretreated patients in whom biochemical failure developed after RP with ADT and/or RT.

MATERIALS AND METHODS

After obtaining institutional review board approval we identified patients who underwent RP and were previously treated with RT and/or ADT, and restaged with ^{11}C-choline PET/CT and mpMRI for biochemical recurrence between 2008 and 2016. Patients were selected based on certain study inclusion criteria, including 1) RP performed as the definitive treatment for clinically localized prostate cancer, 2) subsequent BCR after RP (PSA 0.2 ng/ml),[24] 3) administration of postoperative ADT or RT and 4) lesion visualization on ^{11}C-choline PET/CT and/or mpMRI after BCR.

Clinical variables included age and PSA at surgery, pathological Gleason score, AJCC (American Joint Committee on Cancer) pathological tumor and nodal stage,[25] surgical margin status, PSA at positive ^{11}C-choline PET/CT and mpMRI, the interval from BCR to positive imaging and the sites of recurrence in patients who received ADT, RT and RT plus ADT. RT and ADT were classified as adjuvant or salvage.[26,27]

Our institutional methods of performing ^{11}C-choline PET/CT and mpMRI after RP were previously described.[19] For PET/CT the patients received intravenous injection of ^{11}C-choline (370 to 740 MBq) followed by imaging within 5 minutes of injection. When acquiring mpMRI, 1.5 or 3 Tesla scanners were used to evaluate BCR in the prostate fossa, pelvic lymph nodes and bones using T2-weighted, diffusion-weighted and dynamic contrast enhanced imaging. The number and location of lesions on PET/CT were documented by a radiologist specializing in nuclear medicine.

Local recurrence involved the seminal vesicle bed and/or the prostate fossa, the vesicourethral anastomosis and the bladder neck. Metastatic recurrences included those in pelvic lymph nodes (perirectal, presacral, obturator, common iliac, internal iliac and external iliac), inguinal nodes, perirectal nodes and retroperitoneal nodes, and visceral and osseous disease. Patients were further classified by disease volume using the CHAARTED (Chemo-Hormonal Therapy versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer) trial definition applied to PET/CT with high volume disease classified as visceral metastases, or 4 or more bone lesions with 1 more beyond the vertebral bodies and pelvis as detected by PET/CT.[28]

Patients were stratified by treatment type at BCR, including ADT and/or RT. Variables are summarized as the frequency and percent, or the median and IQR. The association between clinical and pathological features with any metastatic recurrence compared to local only