[^{11}C]Choline Positron Emission Tomography/Computerized Tomography to Restage Prostate Cancer Cases With Biochemical Failure After Radical Prostatectomy and No Disease Evidence on Conventional Imaging

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Abbreviations and Acronyms

ADT = androgen deprivation therapy

CT = computerized tomography

PCa = prostate cancer

PET = positron emission tomography

PSA = prostate specific antigen

PSADT = PSA doubling time

RP = radical prostatectomy

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Study received approval from the Scientific Institute, San Raffaele Hospital ethical committee.

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Purpose: We assessed the value of [^{11}C]choline positron emission tomography/computerized tomography in patients with prostate cancer in whom biochemical failure developed after radical prostatectomy but who showed no disease evidence on conventional imaging.

Materials and Methods: Considered for this study were 2,124 patients treated with radical prostatectomy who underwent [^{11}C]choline positron emission tomography/computerized tomography to restage disease between December 2004 and January 2007. Study inclusion criteria were 1) previous radical prostatectomy and pelvic lymph node dissection, 2) increasing prostate specific antigen beyond 0.2 ng/ml after radical prostatectomy, 3) no lymph node disease at radical prostatectomy, 4) no evidence of metastatic disease on conventional imaging, 5) no androgen deprivation therapy and 6) no adjuvant or salvage radiotherapy. These criteria were satisfied in 109 of the 2,124 patients (5%).

Results: Median prostate specific antigen at imaging was 0.81 ng/ml (range 0.22 to 16.76 ml). Imaging suggested local recurrence in 4 patients (4%) and pelvic lymph node disease in 8 (7%). Scans were positive in 5%, 15% and 28% of patients with prostate specific antigen less than 1, between 1 and 2, and greater than 2 ng/ml, respectively ($p < 0.05$). Prostate specific antigen was the only significant predictor of tomography results ($p < 0.05$).

Conclusions: Positron emission tomography/computerized tomography detected increased [^{11}C]choline uptake, suggesting recurrent disease in 11% of patients with prostate cancer, increasing prostate specific antigen after radical prostatectomy and no evidence of disease on conventional imaging. This modality may be useful to restage disease but it cannot be used to guide therapy.

Key Words: prostate; tomography, emission-computed; choline; prostate-specific antigen; prostatic neoplasms

After RP in patients with PCa biochemical failure, that is persistently increasing plasma PSA beyond 0.2 ng/ml, develops in 15% to 77% in the first 5 years after surgery.[1] In recent years [^{11}C]choline PET/CT has proved useful to restage patients with PCa who have biochemical failure.[2–10] The greatest appeal of this technique is that it allows assessment of disease recur-

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rence at multiple anatomical sites at a single time.[4]

The positive detection rate of [11C]choline PET/CT varies substantially among studies. de Jong et al failed to detect positive scans in patients with PSA less than 5 ng/ml[3] while Krause et al reported a 36% detection rate in patients with PCa who had PSA less than 1 ng/ml.[7] These disparities may be related to methodological differences in sample population recruitment. Previous PET/CT series included patients with biochemical recurrence only as well as those with clinically proven metastatic disease.[3–5,7,11] Also, no distinction was made between patients receiving and not receiving ADT. This may represent a significant limitation due to the potential of ADT to interfere with [11C]choline uptake,[12] and to the inclusion of androgen sensitive and androgen resistant patients in the same cohort. Previous studies also included patients who did and did not previously receive radiotherapy.[4,5,7]

We assessed the ability of [11C]choline PET/CT to detect recurrent disease in patients with PCa and biochemical failure after RP who had no other evidence of disease on conventional imaging.[13]

MATERIALS AND METHODS

Patients

We retrospectively considered 2,124 patients referred to our institution for [11C]choline PET/CT from December 2004 to January 2007 to restage PCa after biochemical failure. Study inclusion criteria were 1) previous RP and pelvic lymph node dissection, 2) biochemical failure, defined as PSA greater than 0.2 ng/ml on at least 2 consecutive measurements 3 months apart, 3) no evidence of lymph node metastasis at RP, 4) no evidence of metastatic disease on clinical examination and several diagnostic conventional imaging techniques, 5) no previous ADT and 6) no previous adjuvant or salvage radiotherapy. At least 1 imaging technique at each analyzed anatomical district had to be negative for metastatic disease. Transrectal ultrasound and transrectal magnetic resonance were used to assess the prostatectomy bed, abdominopelvic CT was used to study lymph nodes, and bone scintigraphy and bone CT were used to assess the skeleton. Imaging was done within 3 months of PET/CT.

This retrospective, single institution study was approved by the Scientific Institute, San Raffaele Hospital ethical committee. An informed consent form for [11C]choline PET/CT and for anonymous publication of disease related information was signed by each patient according to the Declaration of Helsinki.

PET/CT Acquisition

PET/CT was acquired using 3 integrated PET/CT systems, including Discovery™ LS, Discovery ST and Discovery STE. Patients refrained from drinking and fasted at least 6 hours before [11C]choline PET/CT. A CT scout image was acquired to define the body axial extension (from the pelvis to the base of the skull) to be imaged. After low dose CT at 90 mA, 0.8 seconds per rotation and 140 kV 5, 1-minute frames centered on the pelvis were acquired immediately after injecting about a mean ± SD of 438 ± 70 MBq [11C]choline. At the end of dynamic scanning, ie 5 minutes after injection, whole body PET was done.[10]

Image Interpretation

Image readout was done on a Xeleris™ workstation, which enables visualization of PET, CT and fused PET/CT images in the transverse, coronal and sagittal planes. [11C]choline images were read independently by a staff physician (GG) and a senior staff physician (LG) with 3 and 7 years, respectively, of experience with [11C]choline PET/CT. All cases of disagreement (7 of 109 or 6%) were reexamined and a consensus was reached. Each focal tracer accumulation deviating from tracer physiological distribution[14] was considered to suggest disease. [11C]choline PET/CT findings were compared to histological analysis of the surgical lymph node specimen and the vesicourethral anastomosis biopsy, when available.

Group comparisons were done using the t test for continuous variables and the chi-square test for categorical variables. All tests were 2-sided with statistical significance considered at $p < 0.05$.

RESULTS

Of 2,124 patients 109 (5%) met study inclusion criteria. Table 1 lists sample characteristics. Median time from PSA measurement to [11C]choline PET/CT was 18 days. Median PSA was 0.81 ng/ml (mean 1.31 ± 1.91, range 0.22 to 16.76). Median PSADT[15] in 47 cases was 9.96 months (mean 12.42 ± 8.34, range 2.90 to 45.33). PET/CT was positive in 12 of 109 patients (11%) and negative in 97 of 109 (89%). Of the 109 patients with positive scans 8 (7%) had increased [11C]choline uptake in the pelvic lymph nodes. A median of 2 lymph nodes (range 1 to 3) had increased [11C]choline uptake and mean maximal diameter was 8.7 ± 1.3 mm (range 5.4 to 9.7). Four patients (4%) had increased [11C]choline uptake in the prostatectomy bed. No patient had concomitant increased [11C]choline uptake in the prostatectomy bed and the lymph nodes. There was no significant [11C]choline uptake in the retroperito-

Table 1. *Sample clinical characteristics*

Mean ± SD/median age (range)	66.4 ± 6.2/67		(51–83)
Mean ± SD/median ng/ml PSA at PET/CT (range)	1.31 ± 1.91/0.81		(0.22–16.76)
Mean ± SD/median mos to biochemical failure (range)	33	± 22/24	(7–135)
Mean ± SD/median mos to trigger PSA (range)	43	± 28/36	(9–141)
No. pathological T stage (%):			
pT2	76		(70)
pT3a	17		(15)
pT3b	16		(15)
No. Gleason score (%):			
7 or Less	92		(84)
Greater than 7	17		(16)