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^{11}C-choline PET/CT predicts survival in prostate cancer patients with PSA < 1 NG/ml

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Abstract

Purpose The main drawback of ^{11}C-choline PET/CT for restaging prostate cancer (PCa) patients with biochemical failure is the relatively low positive detection rate for prostate specific antigen (PSA) < 1 ng/ml. This study assessed whether ^{11}C-choline PET/CT predicts survival in PCa patients with PSA < 1 ng/ml.

Methods This retrospective study included 210 PCa patients treated with radical prostatectomy who underwent ^{11}C-choline PET/CT from December 1, 2004 to July 31, 2007 due to biochemical failure. PCa-specific survival was estimated using Kaplan–Meier curves. Cox regression analysis was used to evaluate the association between clinicopathologic variables and PCa-specific survival. PCa-specific survival was computed as the interval from radical prostatectomy to PCa-specific death.

Results Median follow-up after radical prostatectomy was 6.9 years (95% confidence interval, CI, 2.0–14.5 years). ^{11}C-choline PET/CT was positive in 20.5% of patients. Median PCa-specific survival was 13.4 years (95% CI, 9.9–16.8 years) in patients with positive ^{11}C-choline PET/CT, and it was not achieved in patients with negative ^{11}C-choline PET/CT (log-rank, chi-square = 15.0, $P < 0.001$). Ten-year survival probabilities for patients with negative ^{11}C-choline PET/CT and for patients with positive ^{11}C-choline PET/CT were 86.0% (95% CI: 80.7%–91.3%) and 63.6% (95% CI: 54.5–72.7%). At multivariate analysis, only ^{11}C-choline PET/CT significantly predicted PCa-specific survival (hazard ratio = 2.54, 95% CI, 1.05–6.13, $P = 0.038$). Patients with pathological ^{11}C-choline uptake in the prostatic bed or in pelvic lymph nodes had longer PCa-specific survival in comparison to patients with pathological tracer uptake in the skeleton (log-rank: chi-square = 27.4, $P < 0.001$).

Conclusion Despite the relatively low positive detection rate for PSA < 1 ng/ml, positive ^{11}C-choline PET/CT predicts PCa-specific survival in this low PSA range. As long as more sensitive radiotracers, such as ^{68}Ga-PSMA-11, do not become more widely available, these results might support a broader use of radiolabeled choline in restaging PCa for PSA < 1 ng/ml.

Keywords Prostate cancer · ^{11}C-choline PET/CT · Survival · Biochemical failure

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Introduction

In the last 20 years, many in-vitro and in-vivo studies have given strong support to the use of positron emission tomography and positron emission tomography/computed tomography (PET/CT) with radiolabeled choline (either ^{11}C-choline or ^{18}F-fluorocholine) in prostate cancer (PCa) patients. Over time, the technique has found robust application in restaging PCa patients with biochemical failure [1–9]. Additionally, promising results have been obtained in the initial staging of high-risk PCa patients [10, 11], to guide radiotherapy [12–15] and possibly in monitoring the response to second-line antiandrogenic therapy [16] or chemotherapy [17, 18].

In the setting of restaging, the major weak point of PET/CT with radiolabeled choline is represented by the relatively low

positive detection rate for low PSA values, when the tumor burden is expected to be low and the therapeutic possibilities are expected to be maximal. Castellucci et al. reported a positive detection rate of 28% for PSA < 1.5 ng/ml [19]. Giovacchini et al. reported 26% for PSA between 0.8 ng/ml and 1.0 ng/ml [5]. Other studies reported similar or more distant values depending on the PSA threshold and on characteristics of the sample [4, 6, 7, 20–23]. For this reason, the European Association of Urology endorses the use of PET/CT with radiolabeled choline in the interval between 1 ng/ml and 2 ng/ml, but not for PSA < 1 ng/ml [24].

During the last few years, emphasis has been given to the potential role that might be played by the radiotracer class of the inhibitors of the prostate specific membrane antigen (PSMA) protein, the most frequently used being ^{68}Ga-PSMA-11 [25–27]. Preliminary comparative data indicate that ^{68}Ga-PSMA-11 could be more sensitive than radiolabeled choline for early detection of PCa recurrence, including in the interval of PSA ≤ 1 ng/ml [25–29].

A few survival studies have already been performed in PCa patients with radiolabeled choline, and they have shown that PET/CT with radiolabeled choline can be used to predict survival in PCa patients [30–32]. However, the two studies performed by Giovacchini et al. [30, 31] were carried out in populations independently from the PSA values of the patients, and therefore mean PSA was higher than 1 ng/ml. Kwee et al. and Caroli et al. performed two studies with PET/CT in metastatic castration-resistant PCa patients [32, 33]. As such, it is still unexplored whether PET/CT with radiolabeled choline provides prognostic information for low PSA. Due to this relevant issue and the ongoing debate on the use of PET/CT with radiolabeled choline for PSA < 1 ng/ml, we designed this retrospective study to assess whether PET/CT with radiolabeled choline predicts PCa-specific survival for PSA < 1 ng/ml.

Patients and methods

Study population This retrospective study included 210 PCa patients who underwent ^{11}C-choline PET/CT for restaging of disease between December 1, 2004 and July 31, 2007. Inclusion criteria were: (1) histologically confirmed prostate adenocarcinoma, (2) primary treatment with radical prostatectomy, (3) biochemical failure, defined as PSA higher than 0.2 ng/ml and rising on at least two consecutive measurements performed 3 months apart, (4) clinical and pathological features of interest for multivariate Cox-regression analysis, (5) availability of follow-up information regarding the survival status, and (6) informed consent agreement.

Follow-up Postoperative clinical surveillance included PSA determinations and rectal examinations every 3 to 12 months.

During follow-up availability of imaging techniques, including ^{11}C-choline PET/CT, computed tomography, ultrasonography, magnetic resonance, and bone scintigraphy was variable among patients.

Median follow-up after radical prostatectomy was 6.9 years (95% confidence interval, CI, 2.0–14.5 years). Median follow-up after ^{11}C-choline PET/CT was 4.0 years (95% CI, 0.2–6.7 years). PCa-specific survival was chosen as primary endpoint. PCa-specific death was defined as death in any patient with metastasis who showed progression without another obvious cause of death [34]. PCa–specific survival was defined as the time between radical prostatectomy and PCa-specific death. At last follow-up, 29/210 patients (13.8%) had died and 24/210 patients (11.4%) had died of PCa. Survival times of patients who were alive at the last follow-up contact were censored.

This single-institution study was approved by the Ethical Committee of the San Raffaele Scientific Institute, Milan, Italy. An informed consent form for the execution of ^{11}C-choline PET/CT scans and for anonymous publication of disease-related information according to the Declaration of Helsinki was signed by each patient.

PET/CT acquisition After a low-dose CT scan, five 1-min frames centered on the pelvis were acquired immediately after the injection of 420 ± 62 MBq of ^{11}C-choline. At the end of dynamic imaging, i.e., about 5 min post-injection, a whole-body PET scan was acquired [5].

Image interpretation PET/CT images were visually interpreted. Images were analyzed by two nuclear medicine physicians with more than 8 years of experience in PET and PET/CT, and discrepancies were solved by consensus. Local recurrence was defined as focal ^{11}C-choline uptake in the post-surgical prostatectomy loge. Lymph node and bone metastases were defined as focal ^{11}C-choline uptake higher than background [5].

Statistical analysis Comparisons of variables between two groups were performed using t-test and chi-square test as needed.

PCa-specific survival was estimated using Kaplan–Meier curves. Differences between survival curves of patients with positive ^{11}C-choline PET/CT and negative ^{11}C-choline PET/CT were evaluated using the log-rank test. Survival rates and their 95% confidence intervals were also derived from Kaplan–Meier curves. The association between ^{11}C-choline PET/CT findings and PCa-specific survival was assessed using Cox proportional hazard regression models. Because of the very low number of fatal events and the moderately large sample size, only factors traditionally associated with PCa-survival [34, 35] were entered, so that convergence could be obtained. To minimize biases on survival times introduced

by therapies started after ^{11}C-choline PET/CT, patients that received any therapy (anti-androgenic therapy, radiotherapy or chemotherapy) after PET/CT were contrasted at multivariate analysis vs patients that did not receive any additional therapy. To verify that our results were independent by the definition of PCa–specific survival, an ancillary Cox-regression analysis was performed in which PCa–specific survival was computed as the interval between the date of ^{11}C-choline PET/CT and the date of PCa-specific death or censoring. The proportional hazards assumption was formally tested using interaction terms between independent variables and time. All these interactions had $P > 0.1$.

To assess the robustness of our results, we also assessed survival as a function of the TNM classification of the American Joint Committee on Cancer (AJCC), assuming ^{11}C-choline PET/CT as gold standard for identification of disease. For the analysis, three groups of patients were defined on the basis of five PET/CT anatomical findings, i.e.: (1) patients with pathological ^{11}C-choline uptake in the skeleton (M1b) and in retroperitoneal lymph nodes (M1a), (2) patients with pathological ^{11}C-choline uptake in pelvic lymph nodes (N1 M0) or in the prostate bed (N0) (grouped together to increase the statistical power), 3) patients with negative ^{11}C-choline PET/CT.

PET/CT results were also related to standard of care imaging studies and biopsies.

Statistical significance was defined as $P < 0.05$. Survival analysis was performed using the SPSS v 18 statistical software package (SPSS Inc., Chicago, IL, USA).

Results

The clinical and pathological characteristics of the sample are reported in Table 1. Median PSA in the whole sample was 0.54 ng/ml. ^{11}C-choline PET/CT was positive in 43/210 patients (20.5%). Patients with positive ^{11}C-choline PET/CT had, in comparison to patients with negative ^{11}C-choline PET/CT, higher PSA, more advanced pathological stage, and received therapy after PET/CT more frequently. On an anatomical basis, pathological ^{11}C-choline uptake was observed in either pelvic (23/210, 11.0%) or in retroperitoneal lymph nodes (6/210, 2.9%), in the skeleton (8/210, 3.8%) and in the post-surgical prostate bed (17/210, 8.1%).

In patients with positive ^{11}C-choline PET/CT, median survival was 13.4 years (95% CI: 9.9–16.8 years). In patients with negative PET/CT, median survival was not achieved owing to the low frequency of fatal events in this group: the difference between the two groups was statistically significant (log-rank, chi-square = 15.0, $P < 0.001$; Fig. 1). Survival probabilities for the whole group, for patients with negative ^{11}C-choline PET/CT and for patients with positive ^{11}C-choline PET/CT

Table 1 Clinical and pathological characteristics of the whole sample and in the subgroups of patients with negative ^{11}C-choline PET/CT and positive ^{11}C-choline PET/CT

	Whole Sample ($n = 210$)	Negative PET/CT ($n = 167$)	Positive PET/CT ($n = 43$)	P
Age (years)				0.403
Mean ± SD (median)	66.5 ± 6.1 (67)	66.3 ± 6.0 (66)	67.3 ± 6.6 (67)	
Range	50–81	50–80	51–81	
PSA (ng/ml)				0.013
Mean ± SD (median)	0.54 ± 0.21 (0.54)	0.52 ± 0.22 (0.52)	0.61 ± 0.20 (0.61)	
Range	0.22–0.99	0.22–0.99	0.25–0.98	
Pathological stage				< 0.001
pT2	107 (51.0%)	96 (57.5%)	11 (25.6%)	
pT3, pT4	80 (38.0%)	59 (35.3%)	21 (48.8%)	
Any T pN1	23 (11.0%)	12 (7.2%)	11 (25.6%)	
Gleason score				0.138
< 7	57 (28.1%)	51 (30.5%)	8 (18.6%)	
7	103 (49.0%)	82 (49.1%)	21 (48.8%)	
> 7	48 (22.9%)	34 (20.4%)	14 (32.6%)	
ADT at PET/CT				0.005
No	149 (71.0%)	126 (75.4%)	23 (53.5%)	
Yes	61 (29.0%)	41 (24.6%)	20 (46.5%)	
Start of any therapy after PET/CT				< 0.001
No	62 (29.5%)	60 (35.9%)	2 (4.7%)	
Yes	148 (70.5%)	107 (64.1%)	41 (95.3%)	

Fig. 1 Kaplan–Meier PCa-specific survival probability curves in patients with negative ^{11}C-choline PET/CT and in patients with positive ^{11}C-choline PET/CT. PCa–specific survival was computed as the interval between the date of prostatectomy and the date of PCa-specific death or censoring
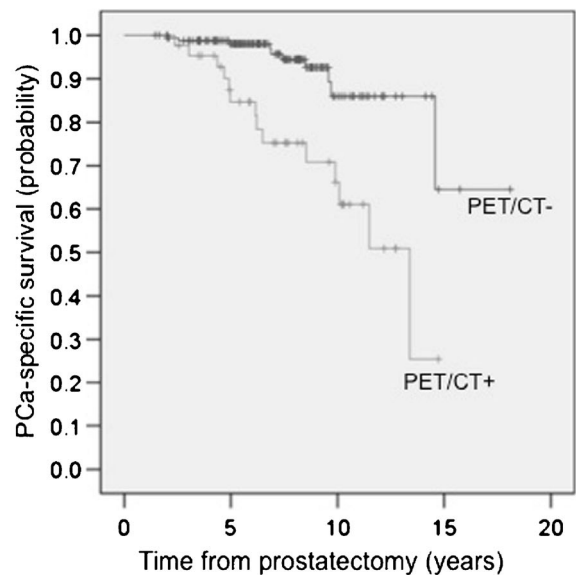
PET/CT-	No. at risk	167	131	24	2	0
	No. PCa-specific deaths	0	3	6	1	0
PET/CT+	No. at risk	43	31	13	0	0
	No. PCa-specific deaths	0	6	5	3	0

PET/CT are reported in Table 2. Survival probabilities were always higher for patients with negative ^{11}C-choline PET/CT than for patients with positive ^{11}C-choline PET/CT. For example, 10-year survival probabilities for patients with negative ^{11}C-choline PET/CT and for patients with positive ^{11}C-choline PET/CT were 86.0% (95% CI: 80.7%–91.3%) and 63.6% (95% CI: 54.5–72.7%).

Results of the Cox regression analysis are shown in Table 3. At univariate analysis, statistical significance was attained by ^{11}C-choline PET/CT ($P < 0.001$), pathological stage ($P = 0.045$), and Gleason score ($P = 0.017$). However, at multivariate analysis statistical significance was maintained only by ^{11}C-choline PET/CT (hazard ratio, HR = 2.54, 95% CI, 1.05–6.13, $P = 0.038$). As expected, patients with higher risk of death were also those that received additional therapy more frequently because of pathological ^{11}C-choline PET/CT. Neglecting this term highly increases the statistical significance of ^{11}C-choline PET/CT (HR = 3.59, 95% CI, 1.50–8.59, $P = 0.004$).

Using the follow-up interval from ^{11}C-choline PET/CT to the date of PCa-specific death or censoring as time variable did

not change the results. Kaplan–Meier analysis showed that median PCa-specific survival was significantly shorter in patients with positive ^{11}C-choline PET/CT (5.9 years) than in patients with negative ^{11}C-choline PET/CT (7.9 years) (log-rank, chi-square = 19.5, $P < 0.001$, Fig. 2). At Cox regression, statistical significance was reached at univariate analysis by ^{11}C-choline PET/CT ($P < 0.001$), pathological stage ($P = 0.018$), and Gleason score ($P = 0.013$). However, at multivariate analysis the statistical significance was maintained only by ^{11}C-choline PET/CT (HR = 2.96, 95% CI, 1.24–7.08, $P = 0.014$).

We also assessed survival according to the TNM classification of the AJCC, as defined by ^{11}C-choline PET/CT. Kaplan–Meier analysis showed that ^{11}C-choline PET/CT could successfully distinguish the three groups of patients defined in their stage according to the ^{11}C-choline uptake, i.e.: (1) patients with pathological ^{11}C-choline uptake in the skeleton (M1b) or in retroperitoneal lymph nodes (M1a), (2) patients with pathological ^{11}C-choline uptake in pelvic lymph nodes (N1 M0) or in the prostate bed (N0), and (3) patients with negative ^{11}C-choline PET/CT (log-rank, chi-square =

Table 2 PCa-specific survival probabilities in the whole group, and in patients with negative and positive ^{11}C-choline PET/CT

	Whole group ($n = 210$)	PET/CT − ($n = 124$)	PET/CT + ($n = 86$)
5-year	95.2%	98.0%	84.7%
	(93.6%–96.8%)	(96.9%–99.1%)	(78.9%–90.5%)
10-year	80.3%	86.0%	63.6%
	(75.8%–84.8%)	(80.7%–91.3%)	(54.5%–72.7%)
15-year	52.3%	64.5%	25.4%
	(38.0%–66.6%)	(45.5%–83.5%)	(6.4%–44.4%)

Table 3 Cox regression analysis of factors predicting PCa-specific survival (calculated from the date of prostatectomy)

	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
[11]C-choline PET/CT	4.43	< 0.001	2.54	0.038
	(1.95–10.07)		(1.05–6.13)	
PSA (ng/mL)	3.27	0.244	1.83	0.594
	(0.44–24.20)		(0.19–17.30)	
Pathological stage		0.045		0.544
pT2pN0	1 (Reference)		1 (Reference)	
pT3pN0 and pT4pN0	3.04	0.034	1.84	0.288
	(1.08–8.49)		(0.59–5.73)	
Any T pN1	4.41	0.020	1.35	0.658
	(1.26–15.44)		(0.35–5.26)	
Gleason score		0.017		0.090
< 7	1 (Reference)		1 (Reference)	
7	1.64	0.406	0.83	0.778
	(0.51–5.30)		(0.23–2.95)	
> 7	4.64	0.013	2.31	0.209
	(1.39–15.52)		(0.62–8.61)	
Start of any therapy after PET/CT	5.35	< 0.001	4.18	0.004
	(2.12–13.5)		(1.58–11.04)	

27.4; $P < 0.001$) (Fig. 3). Median survival was achieved only in M1b/M1a patients (6.2 years, 95% CI, 2.6–9.8 years). In the multivariate analysis, statistical significance was obtained only by ^{11}C-choline PET/CT coded according to the three AJCC-based groups ($P = 0.010$).

At least one standard of care procedure was available in 139/210 patients (66%). Specifically, 5/136 patients (4%) had positive bone scintigraphy, 5/136 patients (4%) had positive abdominal-pelvic contrast-enhanced CT, 22/117 patients (19%) had positive abdominal-pelvic multiparametric magnetic resonance, and 12/127 (9%) patients had positive ultrasonography-guided prostate bed or lymph node biopsy. Since some patients had lesions in different anatomical sites, standard of care procedures were positive in 31/139 patients

Fig. 2 Kaplan–Meier PCa-specific survival probability curves in patients with negative ^{11}C-choline PET/CT and in patients with positive ^{11}C-choline PET/CT. PCa–specific survival was computed as the interval between the date of ^{11}C-choline PET/CT and the date of PCa-specific death or censoring
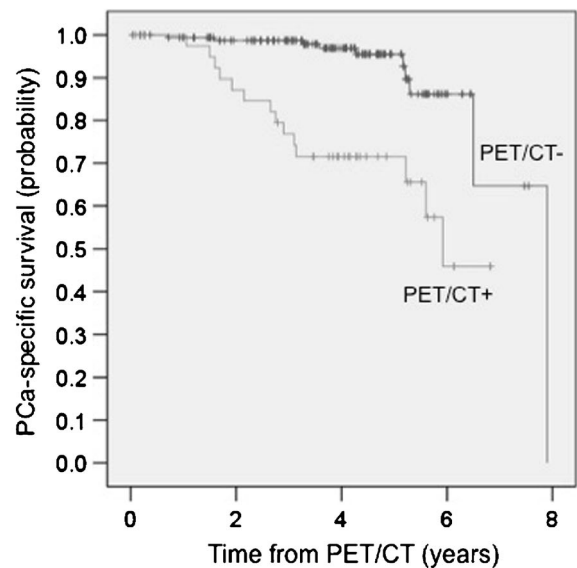
PET/CT-	No. at risk	167	142	86	9	0
	No. PCa-specific deaths	0	2	2	4	2
PET/CT+	No. at risk	43	34	21	4	0
	No. PCa-specific deaths	0	5	6	3	0

Fig. 3 Kaplan–Meier PCa-specific survival probability curves in patients with negative ^{11}C-choline PET/CT (PET/CT-), in patients with positive ^{11}C-choline PET/CT suggestive of local recurrence or pelvic lymph node disease (PET/CT+, N0 and N1 M0, respectively) and in patients with positive ^{11}C-choline PET/CT suggestive of retroperitoneal lymph node disease or bone metastases (PET/CT+, M1a and M1b, respectively)
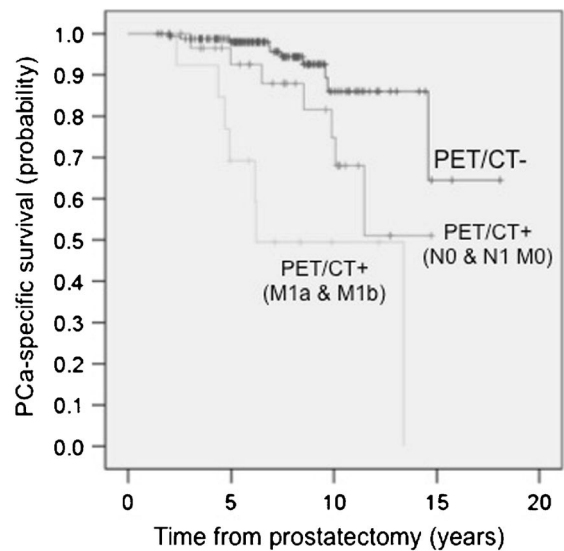
PET/CT-	No. at risk	167	131	24	2	0
	No. PCa-specific deaths	0	3	6	1	0
N1 M0 & N0	No. at risk	30	23	11	0	0
	No. PCa-specific deaths	0	2	3	2	0
M1b & M1a	No. at risk	13	8	2	0	0
	No. PCa-specific deaths	0	4	1	1	0

(22%). Among patients with negative standard of care procedures ($n = 108$), Kaplan–Meier analysis showed that median PCa-specific survival was 4.6 years (95% CI 2.4–20.6) in patients with positive ^{11}C-choline PET/CT ($n = 12$), while median PCa-specific survival was not achieved in patients with negative ^{11}C-choline PET/CT ($n = 96$) (log-rank, chi-square = 6.6, $P = 0.010$).

Since PCa patients treated with anti-androgenic therapy (ADT) were combined to patients not treated with ADT to increase the statistical power, another Cox regression analysis was performed where the variables ^{11}C-choline PET/CT, treatment with ADT at the time of PET/CT, and their interaction were entered. Statistical significance was obtained for the first two variables ($P = 0.003$ and $P = 0.040$), but not for their interaction ($P = 0.203$), indicating that the results were not significantly biased by the mixture of the two clinically different populations. The association between ADT and positive PET/CT (see also Table 1) is a well-replicated finding attributed to the higher number of risk factors or to the more aggressive disease in patients receiving ADT [5, 36, 37].

Discussion

PET/CT with radiolabeled choline has drastically improved imaging of PCa in the last 20 years [37, 38]. This technique has been shown to be useful in different clinical contexts, primarily for restaging patients with biochemical failure [1–9], for initial staging of newly diagnosed high-risk PCa

patients [10, 11], and to guide salvage radiotherapy [12–15]. In patients with biochemical failure after radical prostatectomy, PET/CT with radioactive choline predicts PCa-specific survival, and its prognostic power is greater than any other traditional biochemical or pathological risk factor [30, 31].

In spite of these multiple favorable features, during these years it became evident that PET/CT with radiolabeled choline was affected by an important limit, i.e., the positive detection rate in patients with biochemical failure after radical prostatectomy is relatively low for low PSA values, either PSA < 1 ng/ml or PSA < 1.5 ng/ml, according to the study design. Most studies in these intervals reported positive detection rates ranging between about 20% and an optimistic 45% [1, 4, 6, 19, 21–23, 39, 40]. Studies reported even lower detection rates (11%) in cases of particular inclusion criteria, such as absence of macroscopic disease on conventional imaging [4]. Studies agreed that, also in this low PSA interval, the positive detection rate of PET/CT can be increased by preferably selecting patients with either short PSA doubling time or high PSA velocity [4, 19, 22, 39, 40]; this is, however, impractical for some physicians. This weakness of PET/CT with radiolabeled choline is particularly dismaying considering that it is for low PSA values that the disease burden is expected to be less and the interest of clinicians is highest. Indeed, the European Association of Urology endorses the use of PET/CT with radiolabeled choline for PSA between 1 ng/ml and 2 ng/ml, but not for PSA < 1 ng/ml [41].

The failure of radiolabeled choline to completely satisfy this clinical demand prompted the search for new tracers.

Among these, ^{68}Ga-PSMA-11 (also known as ^{68}Ga-HBED-CC, Glu-urea-Lys(Ahx)-HBED-CC, or ^{68}Ga-PSMA-HBED-CC), often abbreviated as ^{68}Ga-PSMA, represents the most promising tracer for PCa imaging [28, 29]. Comparative studies have consistently reported higher positive detection rate of PET/CT with ^{68}Ga-PSMA compared to PET/CT with radiolabeled choline and differences were noteworthy for PSA < 1 ng/ml [25, 26]. However, there is currently no PET PSMA tracer with FDA/EMA approval, and in many countries the use of ^{68}Ga-PSMA is still restricted by national legislatory rules so that, until formal approval is granted, ^{68}Ga-PSMA can only be used only in experimental clinical trials. Therefore, while on one hand is reasonable to expect that in the very short term radiolabeled choline will still be the main tracer for PCa imaging in many centers, on the other hand PSMA PET agents are expected to replace radiolabeled choline as soon as FDA/EMA approval is obtained.

The results of our current study appear therefore particularly important: even though the positive detection rate of PET/CT with radioactive choline for PSA < 1 ng/ml is low (20.5% in our study), PET/CT findings do have prognostic value also in this narrow PSA interval, and therefore they require proper clinical management. In two retrospective studies with median PSA of 3.4 ng/ml [42] and 2.3 ng/ml [43], PET/CT with radiolabeled choline significantly influenced the clinical management of PCa patients in almost 50% of the cases. Therefore, use of PET/CT with radiolabeled choline for low PSA values requires some trade-off between high rate of false negative scans and good clinical management of positive patients. Moreover, we have shown that the prognostic information of ^{11}C-choline PET/CT is maintained also in patients that have no evidence of disease in standard of care diagnostic procedures. These patients are definitely a subgroup of patients in whom ^{11}C-choline PET/CT plays a critical role for imaging the site of relapse of disease and guiding further therapeutic options [4].

In the two survival studies that our group had previously carried out in two PCa populations not selected on the basis of their PSA value, median PSA was up to 1.82 ng/ml and highest PSA was up to 48.6 ng/ml [30, 31]. In the present study, median and maximum PSA were 0.54 ng/ml and 0.99 ng/ml respectively. Similarly to what we found in the two cited studies, also in the present investigation ^{11}C-choline PET/CT was the only variable that reached statistical significance at multivariate analysis. To the best of our knowledge, the current study represents the first investigation assessing PCa-specific survival with ^{11}C-choline PET/CT in PCa patients treated with radical prostatectomy and experiencing biochemical failure restricted to patients with PSA < 1 ng/ml.

To assess the robustness of our results, we also assessed survival according to the TNM classification of the AJCC, assuming ^{11}C-choline PET/CT as gold standard for identification of disease. Kaplan–Meier analysis showed that ^{11}C-choline PET/CT could successfully distinguish three groups of patients defined in their stage according to the ^{11}C-choline uptake: (1) patients with pathological ^{11}C-choline uptake in the skeleton (M1b) or in retroperitoneal lymph nodes (M1a), (2) patients with pathological ^{11}C-choline uptake in pelvic lymph nodes (N1 M0) or in the prostate bed (N0), and (3) patients with negative ^{11}C-choline PET/CT. The group including patients with skeletal metastases had shorter survival in comparison to patients with PET/CT findings suggestive of pelvic lymph node metastases or local recurrence, consistent with the fact that skeletal metastases represent the primary source of morbidity and mortality in PCa-patients. Overall, these results indirectly support an acceptable clinical accuracy of the technique [37, 44]. Results also were not sensitive to the definition of survival time, because very similar findings were obtained using the interval from prostatectomy and the interval from PET/CT.

Conclusions

In summary, in this group of PCa patients with biochemical failure after radical prostatectomy and PSA < 1 ng/ml, ^{11}C-choline PET/CT has a positive detection rate of 20.5% and predicts PCa-specific survival. Tracers with higher positive detection rate are desirable for the clinical routine. However, until such tracers become more widely available, PET/CT with radiolabeled choline might be more broadly used in this low PSA range for clinical studies.

Compliance with ethical standards

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