

# Effect of positive carbon-11-choline PET/CT results in the therapeutic management of prostate cancer biochemical relapse

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**Objective** Carbon-11-(<sup>11</sup>C)-choline PET/computed tomography (CT) has shown good results in re-staging of prostate cancer (PCa) with raised serum levels of prostate-specific antigen. Our aim was to evaluate the effect of positive <sup>11</sup>C-choline PET/CT results in the therapeutic management of patients with PCa with biochemical relapse (BR) after curative intention treatment.

**Patients and methods** A total of 112 patients with PCa BR and positive <sup>11</sup>C-choline PET/CT were retrospectively evaluated. PET/CT was acquired 20 min after intravenous administration of 555–740 MBq of <sup>11</sup>C-choline. The therapeutic management after <sup>11</sup>C-choline PET/CT was obtained from the clinical records. The minimum follow-up time was 18 months.

**Results** In 80 (71.4%) of 112 patients, <sup>11</sup>C-choline PET/CT showed local recurrence of PCa; in 17 (15.2%) patients, distant recurrence; and in 15 (13.4%) patients, local plus distant recurrence. A second malignancy was detected in five (4.5%) patients. The planned therapeutic management was changed as per positive <sup>11</sup>C-choline PET/CT result in 74 (66.1%) patients and were treated as follows: 31 (27.7%) patients with HT, combined with other treatments in eight (7.1%), 17 (15.2%) with BT, 13 (11.6%) with external beam

radiotherapy, one (0.9%) with RP, and four (3.6%) with chemotherapy. Treatment approach was not modified in 37 (33%) patients. No data was available from one (0.9%) patient.

**Conclusion** Positive <sup>11</sup>C-choline PET/CT result had an important effect in the therapeutic management of patients with PCa and BR, leading to a change in the planned approach in two (66.1%) out of three patients. In addition, in 4.5% of the patients, the <sup>11</sup>C-choline PET/CT allowed the detection of a second malignancy. *Nucl Med Commun* 40:79–85 Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.

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**Keywords:** biochemical relapse, carbon-11-choline, clinical effect, PET/CT, prostate cancer, therapeutic management

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## Introduction

Prostate cancer (PCa) is the commonest neoplasm in men, excluding skin cancer, covering a wide spectrum of biologic behavior, ranging from indolent low-risk disease to highly aggressive castration-resistant PCa. The incidence in necropsies is similar in different countries. It is estimated that 19% of any new male cancer diagnosed in USA will be PCa [1]. The therapeutic options include radical prostatectomy (RP), with pelvic lymph node (LN) dissection if the likelihood of metastases is higher than 2%; external beam radiotherapy (EBRT); hormone therapy (HT); brachytherapy (BT); chemotherapy (ChT); and active surveillance. For a successful treatment, an individualized management of the patients is mandatory depending on the circumstances and risk group [2,3]. In the long term, a good control of the disease is achieved in

most patients, mostly in low-risk patients. However, it has been reported that up to 50% of patients treated with RP or EBRT will develop biochemical relapse (BR) during the follow-up period [4]. The natural evolution of a BR is a clinically detectable recurrence, local or metastatic, in months to years [5].

Serum prostate-specific antigen (PSA) levels and PSA kinetics are useful to detect a BR of PCa. Although PSA rising precedes radiological and clinical changes, it does not localize the site of recurrence. The advances in the available therapeutic options, both localized and systemic, highlight the importance of a precise diagnostic and prognostic tool, as the management of a local or spread disease is different. There is no ideal imaging test for all the circumstances. Transrectal echography is not

routinely recommended, as it does not completely exclude local recurrence and does not check spread disease. Computed tomography (CT) is not recommended for re-staging, as it has a low sensibility for local recurrence, mostly with low serum PSA levels, although it is important for salvage radiotherapy, to define the target volume. MRI gives an excellent imaging quality and good results in loco-regional recurrence, in addition if an endorectal coil is used [6]. However, it does not evaluate distant areas. Bone scintigraphy (BS) detects spread bone disease, although it is useless for soft tissues disease, and it is only recommended with fast PSA kinetics or serum PSA levels higher than 10 ng/ml [2].

In the past decades, molecular imaging with PET/CT has acquired a preponderant role in oncology, as it allows the evaluation of the entire whole body in a single examination, with high contrast of the lesions. Owing to the known limitations of fluorine-18-fluorodeoxyglucose in PCa, some other more specific PET radiotracers have been developed. Choline is a substrate for the synthesis of phosphatidylcholine, which is the major phospholipid in the cell membrane [7]. Choline uptake is mediated by a specific transporter and upregulated along with choline kinase activity in tumour cells. Choline may be labelled both with  $^{18}\text{F}$ -choline or carbon-11-( $^{11}\text{C}$ )-choline-based PET radiotracers have the advantage of an avid uptake by the tumour and involved LNs, with low background uptake. Von Eyben and Kairemo [8] concluded that the choice between the two choline radiotracers and different acquisition protocols had no significant effect on tumour detection. The new 2018 NCCN guidelines on the management of PCa state that  $^{11}\text{C}$ -choline PET/CT or PET/MR may be used to detect recurrence or disease progression after definitive therapy or during systemic therapy [2].

Several reports have evaluated the clinical effect of radiolabelled choline PET/CT results for the management of the BR in PCa [9–12]. In our institution, with an on-site cyclotron, we use  $^{11}\text{C}$ -choline PET/CT as a suitable option for BR assessment to determine which patients may benefit most from the test. In this sense, the aim of the study was to evaluate the therapeutic effect in daily clinical routine of a positive  $^{11}\text{C}$ -choline PET/CT result in patients with BR of PCa after curative intention treatment.

## Patients and methods

### Patients

We carried out a retrospective study including 112 patients with BR of PCa who had a positive  $^{11}\text{C}$ -choline PET/CT result between June 2010 and September 2016. The study was approved by the ethics committee of our institution, and all patients signed a written informed consent. The mean age of the patients was  $69.5 \pm 7$  years, ranging from 56 to 86 years. The mean serum PSA level was  $8.1 \pm 15.9$  ng/ml, ranging from 0.36 to 135 ng/ml.

Initial treatment was RP with or without adjuvant treatment in 43 (38.4%), EBRT with or without adjuvant treatment in 57 (50.9%), BT in 11 (9.8%), and HT in one (0.9%). BR was established by two consecutive increments of PSA over nadir level (unless PSA persistence) in patients initially treated with RP, or a PSA increment of 2 ng/ml over nadir after radiotherapy or HT [2,3]. A total of 15 (13.3%) patients were on HT treatment at the time of PET/CT scan. Clinical records, biochemical parameters, and imaging studies were reviewed during a follow-up period of, at least, 18 months. Table 1 shows the main characteristics of the patients included in the study.

### Carbon-11-choline synthesis

All procedures were performed at the Nuclear Medicine Department of our hospital, using a PET trace 840 cyclotron (General Electric, Uppsala, Sweden) and a Tracerlab FXC Pico module synthesizer (General Electric). The complete synthesis procedure has been reported elsewhere [13]. The radiochemical purity was 99.9% and the enantiomeric purity was 98.5%. The total time for each synthesis was 35 min.

### Carbon-11-choline PET/CT acquisition

All patients refrained from eating for at least 6 h before the PET/CT scan.  $^{11}\text{C}$ -choline PET/CT scans were carried out using a Biograph LSO Pico 3D scan (Siemens

**Table 1 Patient population characteristics (n = 112)**

Parameters	Data
Age (years)	
Mean $\pm$ SD	69.5 $\pm$ 7
Median (range)	70 (56–86)
PSA at carbon-11-choline PET/CT (ng/ml)	
Mean $\pm$ SD	8.1 $\pm$ 15.9
Median (range)	4.47 (0.36–135)
Gleason score (n)	
$\leq 5$	13
6	28
7	56
8	8
9	5
No data available	2
Median (range)	7 (2–9)
Patients on hormonotherapy (n)	15
Initial prostate cancer location (n)	
Left lobe	25
Right lobe	21
Both lobes	61
No data available	5
Perineural invasion (n)	
Yes	42
No	60
No data available	10
PSA at diagnose (ng/ml)	
Mean $\pm$ SD	15.2 $\pm$ 18.6
Median (range)	9.78 (2.34–160)
Nadir PSA (ng/ml)	
Mean $\pm$ SD	0.24 $\pm$ 0.52
Median (range)	0.04 (0–4)
Time diagnose – BR [mean $\pm$ SD (range)] (months)	70.6 $\pm$ 43.7 (12–252)
Patients with second recurrence (n)	20

BR, biochemical relapse; PSA, prostate-specific antigen.

Healthcare Molecular Imaging, Hoffman States, Illinois, USA). A noncontrast enhanced CT scan (50 mAs, 130 KeV, slice thickness 5.0 mm, tube rotation time 0.8 s) was first carried out 20 min after the intravenous injection of 555–740 MBq of  $^{11}\text{C}$ -choline. Immediately after the CT scan, PET acquisition was performed from the skull base to the middle of thighs (six beds/3 min). The information provided by CT was used for attenuation correction of PET images and for anatomical localization. Images were reconstructed in a  $128 \times 128$  matrix, using the ordered subsets expectation maximization iterative method (two iterations, eight subsets).  $^{11}\text{C}$ -choline PET/CT images were represented on axial, sagittal, and coronal slices.

#### Visual analysis of carbon-11-choline PET/CT scans

In this retrospective study,  $^{11}\text{C}$ -choline PET/CT results were obtained from the initial reports performed by two experienced nuclear medicine specialists, based on a visual analysis of the images. For the purpose of this study, no re-evaluation of the images was performed.  $^{11}\text{C}$ -choline PET/CT scans were considered positive when nonphysiological  $^{11}\text{C}$ -choline uptake in a region was greater than the background activity.  $^{11}\text{C}$ -choline PET/CT scans were considered negative when no  $^{11}\text{C}$ -choline uptake was observed outside the physiological radiotracer distribution. The locations of pathological uptake foci were divided as follows: prostate, prostatic bed, LNs, bone, lung, colon, and soft tissue. The results were compared with the final diagnosis, which was based on

clinical and biochemical follow-up, imaging (CT, MRI, ultrasonography, BS and  $^{11}\text{C}$ -choline PET/CT follow-up), or histopathological analysis. The data regarding therapeutic management after  $^{11}\text{C}$ -choline PET/CT scan were compiled from the clinical records during a follow-up time of, at least, 18 months.

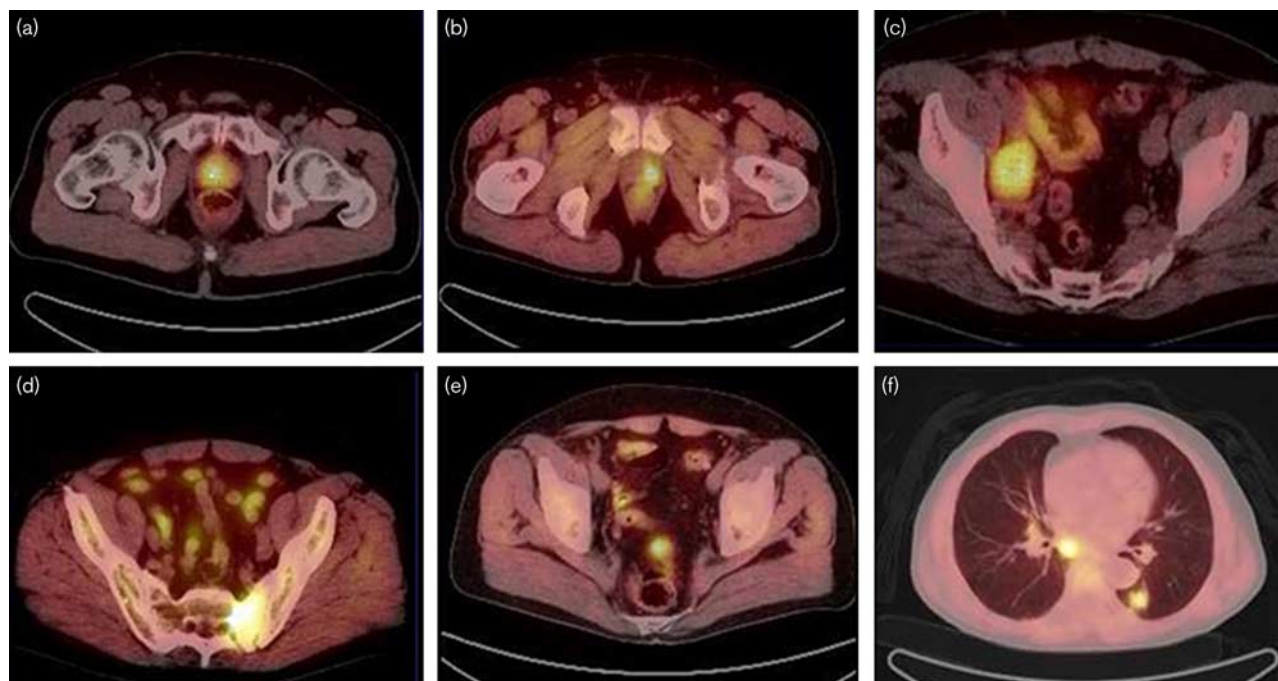
#### Statistical analysis

Continuous variables (age, Gleason index, and trigger PSA) were expressed as mean values, SD, and range. Categorical variables were expressed as percentage or proportion. The Mann–Whitney  $U$ -test was applied to independent variables to evaluate the significance of the results. A statistical significance was established at  $P$  values lower than 0.05. All statistical analyses were performed using AnalystSoft Biostat version 2009 for Windows software (AnalystSoft Inc., Vancouver, British Columbia, Canada).

#### Results

Of 112 patients, 80 (71.4%) had positive  $^{11}\text{C}$ -choline PET/CT uptake in local recurrence of PCa: 50 patients in prostate, 14 patients in prostate bed, 11 patients in regional LNs, and five patients in prostate or prostatic bed plus regional LNs (Fig. 1). Seventeen out of 112 (15.2%) patients had positive  $^{11}\text{C}$ -choline PET/CT uptake in distant recurrence of PCa: eight patients in bone, six patients in distant LNs, two patients in bone plus distant LNs, and one patient in a soft tissue mass. Finally, 15 (13.4%) of 112 patients had positive  $^{11}\text{C}$ -choline PET/CT uptake in local plus distant recurrences:

Fig. 1



Examples of carbon-11-choline PET/CT findings. (a) Prostate. (b) Prostate bed. (c) Pelvic lymph nodes. (d) Bone. (e) Colon cancer. (f) Lung cancer plus mediastinal lymph nodes. CT, computed tomography.

**Table 2** Locations of carbon-11-choline PET/computed tomography foci in the 112 patients

Recurrence	Site of recurrence	Number of patients (%)	Number of patients with treatment change (%)
Local recurrence	Overall	80 (71.4)	49 (61.2)
	Prostate	50	27
	Prostatic bed	14	11
	Regional lymph nodes	11	8
	Prostate or prostatic bed plus regional lymph nodes	5	3
Distant recurrence	Overall	17 (15.2)	11 (64.7)
	Distant lymph nodes	6	3
	Bone	8	6
	Bone plus distant lymph nodes	2	2
	Soft tissue mass	1	0
Local and distant recurrence	Overall	15 (13.4)	12 (80)
	Prostate or prostate bed plus distant lymph nodes	5	4
	Prostate plus regional and distant lymph nodes	1	1
	Regional plus distant lymph nodes	2	2
	Bone plus regional lymph nodes	1	1
	Prostate or prostate bed plus bone	4	2
	Prostate plus bone and distant lymph nodes	2	2

five patients in prostate or prostate bed plus distant LNs, one patient in prostate plus regional and distant LNs, two patients had regional plus distant LNs, one patient in bone plus regional LNs, four patients in prostate or prostate bed plus bone, and two patients in prostate plus bone and distant LNs (Table 2).

Additionally, a second malignancy was detected and treated in five of the 112 (4.5%) patients. In four patients, a synchronous lung cancer was diagnosed, and in one patient, a synchronous colon cancer. They received additional therapy further to the prostate relapse treatment: three patients with lung cancer received ChT, one patient with lung cancer initiated palliative care, and one patient with colon cancer was treated with surgery plus ChT.

The initial treatment of the 112 patients with PCa was RP with or without adjuvant treatment in 43 (38.4%) patients, EBRT with or without adjuvant treatment in 57 (50.9%) patients, BT in 11 (9.8%), and HT in one (0.9%). In the whole population, 74 of 112 patients had their treatment changed as per the positive <sup>11</sup>C-choline PET/CT (66.1%), whereas no change was done in 37 (33%) patients. There were no further data available from one (0.9%) patient.

In 32 (28.6%) of the 43 patients treated with RP, the therapeutic approach after the <sup>11</sup>C-choline PET/CT changed, whereas 10 (8.9%) continued with the same management. There were no data available from one (0.9%) patient. In 34 (30.3%) of the 57 patients treated with EBRT, the positive <sup>11</sup>C-choline PET/CT result led to a therapeutic change, whereas in 23 (20.5%) patients, the treatment was the same. In eight (7.1%) of the 11 patients treated with BT, the therapeutic regime changed after the positive <sup>11</sup>C-choline PET/CT result, whereas three (2.7%) patients stayed with the same approach. Finally, the positive <sup>11</sup>C-choline PET/CT result did not produce any change in the therapy of the patient with HT. Higher percentage of treatment changes were detected after initial treatment with RP (32 of 43 patients, 74.4% of them) or BT (8 of 11 patients, 72.7% of

**Table 3** Relation of initial treatment and management after positive carbon-11-choline PET/computed tomography

Initial treatment	Management after
Radical prostatectomy ± others ( <i>n</i> = 43)	
32	Treatment change
10	Same treatment
1	No data available
External beam radiotherapy ± others ( <i>n</i> = 57)	
34	Treatment change
23	Same treatment
Brachytherapy ( <i>n</i> = 11)	
8	Treatment change
3	Same treatment
Hormonotherapy ( <i>n</i> = 1)	
1	Same treatment

them), whereas less changes were observed with EBRT with or without HT as initial approach (34 of 57 patients, 59.7% of them). There was only one patient treated with HT alone, and therefore, no conclusion is achievable (Table 3).

The 74 patients with therapeutic changes were treated as follows: 31 patients with HT, eight patients with a combination of HT and other treatments (Fig. 2), 17 patients with BT, 13 patients with EBRT, four patients with ChT, and one patient with RP. During the follow-up period, 36 (32.1%) of the 74 patients had disease progression despite the treatment change. On the contrary, 37 of the 74 (33.1%) patients had no evidence of disease progression. There were no further data from one (0.9%) of the 74 patients. Details of planned therapy versus changed therapy are displayed in Table 4.

Of the 37 patients, 20 (33.1%) with no treatment changes after the positive <sup>11</sup>C-choline PET/CT result remained with the same management during the whole surveillance period: four (3.6%) patients started planned EBRT, 10 (8.9%) patients continued AS, three (2.7%) patients continued HT, one (0.9%) patient had planned transurethral resection, one (0.9%) patient had planned BT, and

Fig. 2



75 year old. Prostate cancer, Gleason 3 + 3, treated with radical prostatectomy. At diagnose he had a serum PSA level of 5.4 ng/ml. After 5 years he developed biochemical relapse, with serum PSA level of 6.6 ng/ml. He was planned for active surveillance. Carbon-11-choline PET/CT shows uptake in retroperitoneal lymph nodes. The intended treatment was changed to hormonotherapy and chemotherapy. Progression to metastatic bone disease was detected 2 years later. CT, computed tomography; PSA, prostate-specific antigen.

Table 4 Relation of changes in planned treatment

Planned management	Management changes	N (%)
Total management changes: 74 (66.1%)		
Conversion to focal treatment/new focal treatment: 28 (25%)		
Active surveillance	BT	11 (9.8)
Active surveillance	EBRT	4 (3.6)
HT	BT	6 (5.3)
HT	Surgery	1 (0.9)
EBRT	EBRT + surgery	1 (0.9)
EBRT	Extended EBRT	3 (2.7)
Extended EBRT	EBRT	2 (1.8)
Conversion to systemic treatment: 27 (24.1%)		
Active surveillance	HT	6 (5.3)
Active surveillance	ChT	2 (1.8)
Active surveillance	HT + BT	1 (0.9)
Active surveillance	HT + EBRT	1 (0.9)
Active surveillance	HT + EBRT + BT	1 (0.9)
Surgery	HT	1 (0.9)
EBRT	HT	12 (10.7)
EBRT	HT + EBRT	3 (2.7)
Change in systemic treatment 19 (17%)		
HT	Intensive HT	9 (8)
HT	HT + ChT	5 (4.5)
HT	HT + EBRT	3 (2.7)
HT	HT + BT	2 (1.8)

BT, brachytherapy; ChT, chemotherapy; EBRT, external beam radiotherapy; HT, hormonotherapy.

one (0.9%) patient had palliative care. During the surveillance period, 15 (13.4%) of the 37 patients with no treatment changes had subsequent management changes: seven (6.2%) patients were changed to HT, one (0.9%) patient to BT, one (0.9%) patient to EBRT, four (3.6%) patients to ChT, and two (1.8%) patients to active surveillance from just observation. There was no further information from two of the 37 (1.8%) patients.

There were no follow-up data available from one (0.9%) of the 112 patients.

No significant differences were found in serum PSA levels when BR was diagnosed, PSA levels at diagnose of PCa, PSA nadir, Gleason score, age, and time from diagnose to

Table 5 Statistical differences between patients with and without approach changes

Parameter	Mean value		SD		P value
	With	Without	With	Without	
PSA at PET/CT	6.7	10.8	10.8	2.3	0.47
PSA at diagnose	14.2	17.3	12.2	27.1	0.76
Nadir PSA	0.2	0.4	0.3	0.8	0.57
Gleason	6.7	6.4	1.1	1	0.14
Age	69	70.7	6.7	7.7	0.38
Time Dx – BR	5.7	6.3	3.2	4.5	0.25

BR, biochemical relapse; CT, computed tomography; Dx, diagnose; PSA, prostate-specific antigen.

BR, between patients with treatment change and those with no approach changes (Table 5).

## Discussion

The study showed the high effect of a positive <sup>11</sup>C-choline PET/CT result on the therapeutic approach of patients with BR of PCa after curative intention treatment. The influence was estimated to be as high as two-thirds of the patients included in the study. These results were consistent with the previously reported by others [9–12], especially when the test is considered in terms of relevancy to the patient management.

The serum PSA levels are of utmost importance to decide how the BR has to be treated. However, some degree of uncertainty about the real extent of the recurrence is present, and it may lead to failures or unnecessary treatments. In this context, <sup>11</sup>C-choline PET/CT contributes toward distinguishing between local or distant PCa relapse, with a proved clinical value to re-staging the disease in a wide range of serum PSA levels. In our work, we have local recurrence in 80 (71.4%) of 112 patients, distant recurrence in 17 (15.2%) of 112 patients, or both in 15 (13.4%) of 112 patients. Ceci *et al.* [9] reported an overall detection rate of 62.1% with <sup>11</sup>C-choline PET/CT in patients scheduled for salvage radiotherapy (59 of 95 patients). Local recurrence

was noticed in 40 (67.8%) of 59 patients, distant relapse in 13 (22%) of 59 patients, and local plus distant relapse in six (10.2%) of 59 patients. In patients scheduled for palliative approach, they reported an overall detection rate of 90.1% with  $^{11}\text{C}$ -choline PET/CT (50 out of 55 patients): They observed local recurrence in 24 (48%) of 50 patients, distant relapse in eight (16%) of 50 patients, and local plus distant relapse in 18 (36%) of 50 patients. Colombié *et al.* [11] reported an overall detection rate of 137 (79.7%) of 172 patients with  $^{18}\text{F}$ -fluorocholine PET/CT. In 99 of 137 patients, local recurrence was noticed [41 (29.9%) patients with prostatic bed recurrence and 58 (42.3%) patients with pelvic LN with or without prostatic bed recurrence, overall 72.2%], and in 38 (27.7%) of 137 patients, distant recurrence was reported (bone, lung, extrapelvic LN). However, none of the patients had isolated abdominal LN metastasis. Although the results seem different regarding distant recurrence, there is no distant plus local recurrence group, and this may explain the difference. Gillebert *et al.* [12] reported an overall detection rate of 105 (59%) of 179 patients with  $^{18}\text{F}$ -fluorocholine PET/CT, leading to the detection also of lung cancer in two patients. In 80 of 105 patients, local recurrence was noticed (local recurrence only in 43 patients, regional LN only in 35 patients, and both in two patients); in 13 of 105 patients, a distant recurrence was reported (distant foci only); and in 12 patients, local plus distant recurrence (distant foci plus regional LN in six patients, local plus distant recurrence in two patients, and local plus regional LN plus distant in four patients).

We have been able to estimate the relevance of this information for the therapeutic approach in our population, as it is shown in Tables 2 and 4. Overall, 74 (66.1%) of 112 patients had changed their planned therapeutic approach. Moreover, 15 out of the 37 patients with positive  $^{11}\text{C}$ -choline PET/CT and no treatment changes (13.4%) needed a later therapeutical change, theoretically increasing the effectiveness of the  $^{11}\text{C}$ -choline PET/CT. These results are similar to others. Ceci *et al.* [9] reported a change in 46.7% of their 150 patients with BR of PCa. Considering only positive  $^{11}\text{C}$ -choline PET/CT results (109 patients), the changes raised to 70 out of 109 patients. Of 109 patients, 59 were due for salvage radiotherapy and 45 of them had their initial strategy changed, whereas 50 out of 109 patients were due for palliative treatment and 25 of them had their approach changed. Soyka *et al.* [10] noticed a change in the overall therapeutic plan in 48% (75 out of 156 patients) with BR of PCa, although it raises when you consider only positive  $^{18}\text{F}$ -choline PET/CT results (124 out of 156 patients). Colombié *et al.* [11] reported a change in the therapeutic approach in 43.6% (75 out of 172 patients), with 49.6% (68 out of 137 patients) when you analyze only positive  $^{18}\text{F}$ -fluorocholine PET/CT results. A recent publication from Gillebert *et al.* [12] reported an overall treatment change in 55.9% of patients (100 out of 179 patients). It raised to 74 out of 105 patients when considering only

positive  $^{18}\text{F}$ -fluorocholine PET/CT results. D'Agostino *et al.* [14] reported in their series a significant effect on radiotherapy planning of  $^{11}\text{C}$ -choline PET/CT, determining a change in management in 48.8% of cases, considering all therapeutic indications.

From our results, RP or BT as an initial approach lead to a higher treatment changes (74.4 and 72.7%), compared with EBRT $\pm$ HT (59.7%). These results are consistent with the report of Gillebert *et al.* [12]. They noticed changes in 72% of patients who had RP as an initial treatment, 67% of patients with BT, and 58% with EBRT plus HT, although they also report several treatments and combinations with a variety of results. As an example, seven patients were treated initially with high-intensity focused ultrasound, and six of them (86%) required a different treatment approach than planned.

There were no patients with planned palliative care in our population. Therefore, we have no data regarding whether a positive result with precise lesion location may lead to a different and curative intention approach, as it was observed by Ceci *et al.* [9].

Another issue is to avoid unnecessary HT treatments, to prevent premature castration resistance. Because of our study design, with just  $^{11}\text{C}$ -choline PET/CT positive results, this is not an area where firm conclusions can be obtained. However, in seven (26.9%) of 26 patients, planned HT approach changed to local treatment (six were treated with BT and one with surgery). The details are displayed in Table 4. Colombié *et al.* [11] reported a change from palliative HT to curative approach in 35 (51.5%) of 68 patients. Of the 35 patients, 42.9% had nonplanned EBRT, 31.4% had surgery, 17.1% had cryotherapy, and 8.6% had high-intensity focused ultrasound. The difference in the results may be related to the tendency observed in our results to associate HT to local treatments, as happens in five (19.2%) of 26 patients, treated with EBRT+HT (three patients) or BT $\pm$ HT (two patients).

Over the recent years, PCa has been imaged with  $^{68}\text{Ga}$ -PSMA PET/CT, for both the initial assessment and BR. The interest of this radioligand has been focused on the detection of primary prostate lesions, metastases, and recurrence, showing a high sensitivity even in early BR with low serum PSA levels [15,16]. Nowadays,  $^{68}\text{Ga}$ -PSMA PET/CT has demonstrated substantial higher detection rates than reported from other imaging modalities [17,18]. Regarding the clinical effect of  $^{68}\text{Ga}$ -PSMA PET/CT on patient management, Calais *et al.* [19] analyzed prospectively 161 patients with BR after prostatectomy. In 53% of these patients, there was a modification of the intended management after the result of  $^{68}\text{Ga}$ -PSMA PET/CT. In a meta-analysis, Han *et al.* [20] reviewed 15 studies assessing the effect of  $^{68}\text{Ga}$ -PSMA PET/CT in patients with PCa. They found a pooled proportion of changes in the management in 54% of patients. Interestingly, among several variables attributable to



heterogeneity, PET positivity was the only significant factor. Meta-regression analysis demonstrated that there was a 0.55% increase in the management change for every 1% increase in PET positivity. Recently, Schwarzenboeck *et al.* [21] have reported a clear effect of  $^{68}\text{Ga}$ -PSMA PET/CT in patients with PCa candidate for radiation therapy. In 70% of patients, the result of  $^{68}\text{Ga}$ -PSMA PET/CT modified the planned target volume for irradiation and the use of boosted doses.

Our work has some limitations. The first is the retrospective nature of the study. Before the  $^{11}\text{C}$ -choline PET/CT, the referring physicians were not asked to determine the planned strategy depending on the result of the scan. The information about the influence of positive  $^{11}\text{C}$ -choline PET/CT result was obtained by reviewing the clinical records, but not by a regulated questionnaire where the physicians could have explained his/her intended treatment strategy. Second, the study was carried out in a single center. Nevertheless, although the results represent a real situation in the clinical setting, the findings of the work may not be applicable to a broader population. The third was the lack of long-term follow-up period. In our study, the surveillance period was 18 months. This time seems short to determine the overall patient survival. The fourth was the lack of histopathology diagnosis for all patients. This is a common limitation in this kind of studies owing to ethical or practical issues [22]. Finally, an accurate knowledge of the biodistribution of radiolabelled choline is of great importance for the correct interpretation of PET/CT images and to minimize the potential pitfalls not owing to PCa because of inflammation or benign tumours [23,24].

## Conclusion

Our results confirmed the usefulness of  $^{11}\text{C}$ -choline PET/CT in the management of patients with BR of PCa. The positive result had an important effect in the therapeutic management of patients with PCa and BR, leading to a change in the planned approach in two-thirds of patients with positive PET/CT scan (66.1% of patients). In addition, in 4.5% of the patients, a second malignancy was detected and treated.

## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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