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"Real-world" evaluation of ^{18}F-Choline PET/CT practices in prostate cancer patients and impact on changes in therapeutic strategy

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Abstract

Objectives: The role of ^{18}F-fluorocholine positron emission tomography/computed tomography (^{18}F-Choline PET/CT) in different clinical situations remains controversial and current practices are very heterogeneous. The aim of this study was to evaluate the "real-world" practice of ^{18}F-Choline PET/CT in patients with prostate cancer and its potential impacts on therapeutic strategy.

Methods and materials: This is a retrospective multicenter observational study including 265 consecutive men who underwent ^{18}F-Choline PET/CT for prostate cancer between November 2014 and November 2015. Primary outcome was impact on therapeutic strategy. Secondary outcomes were sensitivity of the ^{18}F-Choline PET/CT and predictive factors associated with positive scans. Statistical analyses comprised Student's *t* test for continuous variables or chi-squared test for qualitative variables.

Results: Median PSA level at the time of PET/CT was 4.19 ng/ml. The decision to perform PET/CT was made after multidisciplinary discussion in 29.8% of cases; most were prescribed by urologists (50.2% of cases). Three main indications were concerned: biochemical recurrence after local treatment (61.1%), initial staging (26.0%), or at the time of progression to castration-resistance (12.9%). Upon biochemical recurrence, ^{18}F-Choline PET/CT allowed identification of ≥1 site(s) with a sensitivity of 80.9%. In multivariate analysis, predictive factors associated with ^{18}F-Choline PET/CT sensitivity were serum PSA level and local treatment type in cases of biochemical recurrence, and PSA doubling time and Gleason score in case of initial staging. ^{18}F-Choline PET/CT results allowed restaging and change in therapeutic strategy in 58.1% of all combined indications.

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Conclusions: Indications of ^{18}F-Choline PET/CT were varied. The detection rate of metastatic lesions was suitable, especially when PSA rate was >1 ng/mL. In most cases, ^{18}F-Choline PET/CT led to a change in therapeutic strategy, particularly in the setting of biochemical recurrence.

Keywords: Biochemical recurrence; Castration-resistance; ^{18}F-Choline PET/CT; Prostate cancer; Staging

1. Introduction

Prostate cancer (CaP) is the second most common cancer in men worldwide, with a wide spectrum of biologic behavior that includes both indolent low-risk disease and highly aggressive castration-resistant prostate cancer (CRCaP) [1].

New treatment options, both localized and systemic, necessitated accurate diagnostic and prognostic tools to refine the individual therapeutic approach at various times throughout CaP management. To effectively manage CaP patients, accurate, reproducible, and validated methods are required to detect and quantify the burden of bone and soft tissue metastases. However, current recommended conventional imaging with bone scintigraphy and computed tomography (CT) scans exhibits significant limitations during detection of nodal disease and bone metastases.

Positron emission tomography (PET) /CT imaging have been demonstrated to have a better sensitivity in detecting metastases compared to conventional imaging, particularly in men suspected of CaP recurrence based on progressive elevation of prostate-specific antigen (PSA) levels after initial localized treatment [2].

Currently, the role of PET in CaP treatment remains uncertain. In clinical practice, there has been a growing interest for ^{18}F-fluorocholine PET/CT (^{18}F-Choline PET/CT) as it can lead to better staging of CaP at different time and therefore may impact patient management by identifying lesion(s) not detectable with conventional imaging procedures and/or by changing the treatment options, from localized to systemic [3].

The present study aimed at addressing the most common indications for ^{18}F-Choline PET/CT in CaP patients in a "real-life" setting, focusing on the potential impact in clinical practice and influence on treatment strategy.

2. Material and methods

2.1. Inclusion criteria and patient data

This is a retrospective multicenter study that included consecutive CaP patients that were referred for a ^{18}F-Choline PET/CT between November 2014 and November 2015. The timing of PET-CT in relation to PSA level, as well as any treatment after scanning, was at the discretion of the treating physician.

Medical records of the patients were reviewed to obtain information regarding characteristics of CaP at diagnosis; prior local and systemic treatments; timing and indication of ^{18}F-Choline PET/CT, and therapeutic strategy before and after ^{18}F-Choline PET/CT. Biochemical recurrence was defined as PSA ≥0.2 ng/ml after prostatectomy and as 2 rises in PSA of ≥2 ng/ml above nadir after radiotherapy. When additional PSA values were available for the calculation of PSA kinetics, PSA doubling time (PSA DT) was calculated as the natural log of 2 divided by the slope of log PSA level, divided by time in months; PSA velocity was calculated as the slope of the linear regression of PSA levels over time in years. Clinicopathologic features were tested for their associations with positive scan results, using Student's *t* test for continuous variables or the chi-squared test for qualitative variables.

All patients were provided with written information regarding the trial. This study received approval from an institutional review board and was conducted according to the principles outlined in the Declaration of Helsinki.

2.2. ^{18}F-Choline PET/CT

In each center, acquisitions were performed on a Siemens mCT Biograph (Siemens, Erlangen, Germany, 2012), from the base of the skull to the knees, at 60 minutes (45–90 minutes) after the ^{18}fluorocholine injection (Iasocholine, then Fluorochol; 3A) with an activity of 4 MBq/kg, associated with concomitant intravenous administration of 20 mg of furosemide. No oral or IV contrast material was used. The scanner was set to 100 mA and 100 kV, modulated by Care Dose 4D and care Kv, to decrease the dose of irradiation; the field of view was 780 mm. CT reconstructions used a smooth medium B30s filter for soft tissue and B70s for bone and lung; sections were 3 mm, with increments of 2 mm. The duration of the ^{18}F-Choline PET/CT acquisition steps was adapted to the patient's weight and varied between 2 and 3 min/step. The ^{18}F-Choline PET/CT data were obtained by iterative reconstruction (2 iterations and 21 subsets) with flight time (TrueX + TOF ultra HD PET), Gaussian filter, and 200 × 200-pixel matrix. The interpretation was performed on a Syngo Via console; interpretation criteria were qualitative and quantitative, using SUV max.

Only PETs that detecting hypermetabolism without suspicious lesions during CT acquisition were considered as inducing a restaging.

3. Results

3.1. Characteristics of the population

A total of 265 consecutive men underwent ^{18}F-Choline PET/CT between November 2014 and November 2015. The median age was 69.3 (50.7–92.5) years. Median PSA value at the time of the PET/CT was 4.19 (0.03–58.0) ng/ml. Prior bone scintigraphy and/or CT scan were performed in most cases (83.4% and 55.8%, respectively) and were negative in 84.1% and 76.8% of patients, respectively.

A total of 162 patients (61.1%) exhibited biochemical recurrence after local treatment, including radical prostatectomy in 52 cases (32.1%), radiotherapy (associated or not with deprivation androgen therapy) in 99 cases (61.1%), and focal therapy in 11 cases (6.8%). In 69 cases (26.0%), ^{18}F-Choline PET/CT was performed for initial staging of high-risk CaP. In 34 cases (12.9%), ^{18}F-Choline PET/CT was performed in patients who progressed to castration-resistance. The decision to perform ^{18}F-Choline PET/CT was made after multidisciplinary discussion in 29.8% of the cases (79/265). The exam was prescribed by urologists in 50.2% (133/265), radiotherapists in 25.7% (68/265), oncologists in 21.1% (56/265), and other physicians in 3.0% (8/265). Clinicopathological characteristics of the study population are presented in Table 1.

3.2. Detection rate and sensitivity of F-Choline PET/CT scan

In cases of biochemical recurrence, ^{18}F-Choline PET/CT allowed to identify 1 or more sites with a sensitivity of 80.9% (131/162), while it was negative in 19.1% of cases. In patients who had previous bone scintigraphy and/or CT scan, a positive lesion on PET was not associated with a detectable lesion on bone scintigraphy in 84.1% of cases and on CT in 76.8% of cases.

In case of positive PET/CT scan, local recurrence was observed in 52 cases (39.7%), among which 42 occurred after radiotherapy or focal therapy and 10 occurred after radical prostatectomy. The occurrence of isolated local PET tracer uptake in the prostate was 38.2% (42/110) in cases of prior local treatment by radiotherapy or focal therapy, vs. 19.2% (10/52) in the prostatic bed in cases of prior local treatment by radical prostatectomy ($P = 0.03$). At the opposite, metastases were observed in 79 cases (60.3%) of positive PET/CT scan, including pelvic nodes only ($n = 24$), extrapelvic nodes ($n = 14$), bone metastases ($n = 35$) and visceral metastases ($n = 6$).

In cases of initial staging of high-risk CaP, ^{18}F-Choline PET/CT detected metastases in 15.9% of cases (11/69), including extrapelvic nodes only in 36.4% (4/11), bone metastases in 54.5% (6/11), and visceral (lung) metastases in 9.1% (1/11).

Finally, in cases of CRCaP, ^{18}F-Choline PET/CT allowed to detect metastases despite normal standard imaging in 26.5% of cases (9/34) and radiological progression of metastatic disease in 14.7% of cases (5/34), including bone metastases ($n = 8$) and visceral metastases ($n = 6$).

3.3. Predictive factors associated with PET/CT positive scans

Predictive factors significantly associated with ^{18}F-Choline PET/CT sensitivity differ according to the indication.

In case of biochemical recurrence, age ($P = 0.008$), serum PSA level ($P < 0.001$), and type of previous local treatment ($P = 0.002$) were found to be associated with PET/CT positivity (Table 2). In multivariate analysis, serum PSA level and type of previous treatment remained independent prognostic factors associated with PET/CT positivity ($P < 0.001$ and $P = 0.03$, respectively). Patients with negative ^{18}F-Choline PET/CT exhibited significantly lower median PSA level (0.75 vs. 2.99 ng/ml, $P < 0.001$). In patients with PSA ≥1 ng/ml at the time of PET/CT, sensitivity was 89.3%, vs. 45.2% in case of PSA < 1 ng/ml ($P < 0.001$). Fig. 1 shows the positivity of the PET / CT according to different PSA thresholds. Prior local treatment by radiotherapy or focal therapy was significantly associated with a higher rate of PET/CT scan positivity, compared to radical prostatectomy ($P = 0.03$).

In case of initial staging, PSA DT doubling time ($P = 0.038$) and Gleason score ($P < 0.001$) were found to be associated with PET/CT positivity, defined by distant metastases detection, (Table 3) and remained independent prognostic factors in multivariate analysis. Patients with positive ^{18}F-Choline PET/CT exhibited significantly shorter PSA DT (5.9 vs. 35 months, $P < 0.038$). In patients with Gleason score >7, distant metastases were detected in 50.0% of cases vs. only 2.2% for Gleason score ≤ 7 ($P < 0.001$).

In the group of patients with CRCaP, 67.6% of them (23/34) were undergoing hormone treatment at the time of ^{18}F-Choline PET/CT. The sensitivity of the exam did not differ significantly according to hormonal therapy exposure (86.9% vs. 81.8%, $P = 0.69$). A Gleason score >7 was associated with PET/CT positivity in univariate analysis ($P = 0.03$) but was not an independent prognostic factor in multivariate analysis (Table 4).

3.4. Impact on therapeutic strategy

Overall, ^{18}F-Choline PET/CT results led to restaging and change in therapeutic strategy in 58.1% of cases (154/265). Focusing on the indication, a change in therapeutic strategy due to ^{18}F-Choline PET/CT restaging was observed in 63.0% (102/162) of biochemical recurrence, 46.4% (32/69) of initial staging, and 58.8% (20/34) of CRCaP. Changes in strategy and treatment planning are detailed in Fig. 2.

Table 1
Patient characteristics

		Overall population ($n = 265$)	Initial staging ($n = 69$)	Biochemical recurrence ($n = 162$)	Castration-resistant prostate cancer ($n = 34$)
Age (y), median [min−max]		69.3 (50.7−92.5)	67.6 (50.7−81.6)	70.1 (53.7−92.5)	74.4 (51.5−87.3)
Initial PSA value at diagnosis (ng/ml), median [min-max]		12.0 (1.9−369.0)	18.0 (3.2−280.0)	9.6 (1.9−369.0)	26.0 (3.8−343.0)
PSA value at the time of F-choline PET/CT (ng/ml), median [min−max]		4.19 (0.03−58.0)	17.0 (0.76−58.0)	2.5 (0.07−44.7)	5.7 (0.03−54.0)
PSA velocity (ng/ml/y), median [min−max]		1.99 (0.05−88.0)	2.31 (0.07−47.0)	1.55 (0.05−35.3)	39.7 (5.7−88.0)
PSA doubling time (mo), median [min−max]		8.5 (0.50−98.0)	24.5 (2.9−98.0)	6.1 (0.99−73.0)	1.8 (0.50−7.0)
Initial T stage, *n* (%)	TX	81 (30.5)	9 (13.0)	56 (34.6)	16 (47.1)
	T1b	2 (0.8)	1 (1.5)	1 (0.6)	0 (0)
	T1c	62 (23.4)	26 (37.7)	31 (19.1)	5 (14.7)
	T2a	25 (9.4)	8 (11.6)	13 (8.0)	4 (11.8)
	T2b	26 (9.8)	5 (7.3)	20 (12.3)	1 (2.9)
	T2c	19 (7.2)	9 (13.0)	7 (4.3)	3 (8.8)
	T3a	44 (16.6)	9 (13.0)	30 (18.5)	5 (14.7)
	T3b	4 (1.5)	2 (2.9)	2 (1.3)	0 (0)
	T4	2 (0.8)	0 (0)	2 (1.3)	0 (0)
Initial N status, *n* (%)	NX	93 (35.1)	15 (21.7)	61 (37.7)	17 (50.0)
	N0	149 (56.2)	43 (62.3)	93 (57.4)	13 (38.2)
	N+	23 (8.7)	11 (16.0)	8 (4.9)	4 (11.8)
Initial M status, *n* (%)	MX	97 (36.6)	15 (21.7)	67 (41.4)	15 (44.1)
	M0	150 (56.6)	44 (63.8)	91 (56.2)	15 (44.1)
	M+	18 (6.8)	10 (14.5)	4 (2.4)	4 (11.8)
Initial Gleason score[a], *n* (%)	Gleason = 6	60 (29.7)	24 (38.1)	33 (28.5)	3 (13.1)
	Gleason = 7	88 (43.6)	21 (33.3)	60 (51.7)	7 (30.4)
	Gleason > 7	54 (26.7)	18 (28.6)	23 (19.8)	13 (56.5)
Prescriber, *n* (%)	Urologist	133 (50.2)	53 (76.9)	73 (45.1)	7 (20.6)
	Radiotherapist	68 (25.7)	7 (10.1)	59 (36.4)	2 (5.9)
	Oncologist	56 (21.1)	7 (10.1)	24 (14.8)	25 (73.5)
	Other	8 (3.0)	2 (2.9)	6 (3.7)	0 (0)
Multidisciplinary decision, *n* (%)	Yes	79 (29.8)	38 (55.1)	33 (20.4)	8 (23.5)
	No	186 (70.2)	31 (44.9)	129 (79.6)	26 (76.5)

[a] Only 202 available.

Table 2
Comparison of patients' characteristics according to the results of F-choline PET/CT in the setting of biochemical recurrence

		Negative PET/CT ($n = 31$)	Positive PET/CT ($n = 131$)	P
Age (y), median (min–max)		65.7 (54.7–85.0)	71.3 (53.7–92.5)	**0.008***
PSA value (ng/ml), median (min–max)		0.75 (0.07–6.80)	2.99 (0.2–44.7)	**<0.001***
PSA velocity (ng/ml/y), median (min–max)		0.96 (0.05–11.5)	1.66 (0.07–35.3)	0.56*
PSA doubling time (mo), median (min–max)		6.89 (1.35–38.4)	6.0 (0.99–73.0)	0.73*
Initial Gleason score[a], n (%)	Gleason = 6	7 (35.0)	26 (27.1)	0.19**
	Gleason = 7	12 (60.0)	48 (50.0)	
	Gleason > 7	1 (5.0)	22 (22.9)	
Initial local treatment, n (%)	Radical prostatectomy	17 (54.8)	35 (26.7)	**0.002****
	Radiotherapy	13 (42.0)	86 (65.7)	
	Focal therapy	1 (3.2)	10 (7.6)	
Prescriber, n (%)	Urologist	16 (51.6)	57 (43.5)	0.41**
	Radiotherapist	13 (42.0)	46 (35.1)	
	Oncologist	1 (3.2)	23 (17.6)	
	Other	1 (3.2)	5 (3.8)	
Multidisciplinary decision, n (%)	Yes	8 (25.8)	25 (19.1)	0.40**
	No	23 (74.2)	106 (80.9)	

Bold values = significant values ($p<0.05$).
*Student t test.
**Chi-square test.
[a] Only 116 available.

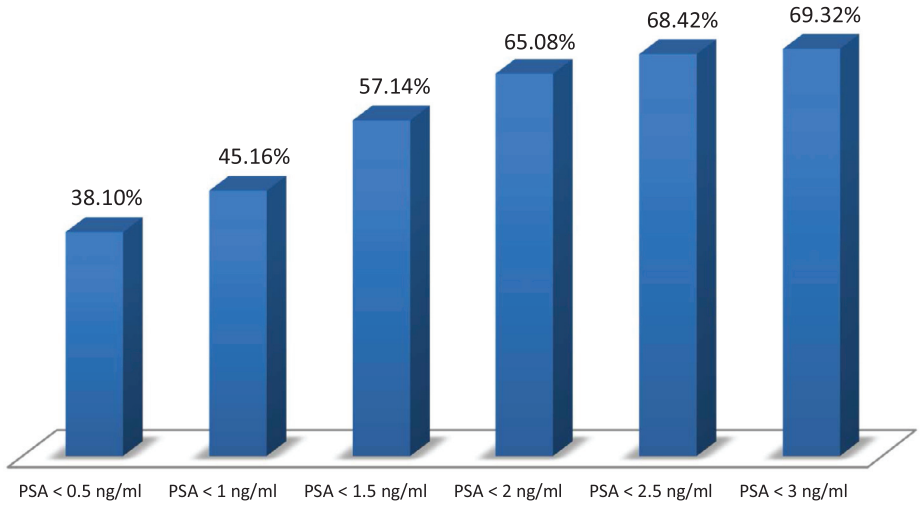

Fig. 1. Positivity of PET/CT in case of biochemical recurrence according to different PSA thresholds.

4. Discussion

Even though published data are promising, the role of PET/CT in treatment planning in CaP management remains under investigation.

In this multicenter series, most ^{18}F-Choline PET/CT were performed in the context of biochemical recurrence. In these circumstances of rising PSA after a primary local treatment, it remains controversial how PET/CT might useful to guide therapeutic strategy. Some reports suggest that local therapeutic approaches may offer durable progression-free survival [4]. The potential interest in PET/CT is related to identifying which patients will benefit from curative local treatment deferring the introduction of long-term hormone therapy and avoiding related side effects. In our series, the impact of ^{18}F-Choline PET/CT results on change in therapeutic strategy was notably high. Indeed, 63% of patients were restaged with PET/CT findings; thus, they could benefit from local salvage therapies (mainly radiotherapy or focal therapy) and/or focal treatment on an oligometastatic disease with ultraselective and highly conformal techniques.

One of the main controversial concerns regarding PET/CT is its predictive value in the early stages of recurrence. In a recent systematic review, Evangelista et al. concluded that PET/CT scan exhibits a high sensitivity for the detection of locoregional and distant recurrence [5]. Further, the overall detection rate of ^{18}F-Choline PET/CT significantly

Table 3
Comparison of patients' characteristics according to the results of F-choline PET/CT for initial staging

		No metastasis on PET/CT ($n = 58$)	Distant metastases on PET/CT ($n = 11$)	P
Age (y), median (min−max)		67.0 (50.7−80.8)	69.9 (54.5−81.6)	0.49*
PSA value (ng/ml), median (min−max)		16.6 (0.76−58.0)	19.0 (1.0−44.7)	0.65*
PSA velocity (ng/ml/y), median (min−max)		2.2 (0.07−47)	6.2 (0.58−21.0)	0.78*
PSA doubling time (mo), median (min−max)		35 (2.9−98.0)	5.9 (4.3−40.2)	**0.038***
Initial Gleason score[a], n (%)	Gleason = 6	23 (43.4)	1 (10.0)	**<0.001****
	Gleason = 7	21 (39.6)	0 (0)	
	Gleason > 7	9 (17.0)	9 (90.0)	
Prescriber, n (%)	Urologist	47 (81.0)	6 (54.5)	0.11**
	Radiotherapist	5 (8.6)	2 (18.2)	
	Oncologist	4 (6.9)	3 (27.3)	
	Other	2 (3.5)	0 (0)	
Multidisciplinary decision, n (%)	Yes	32 (55.2)	6 (54.5)	0.97**
	No	26 (44.8)	5 (45.5)	

Bold values = significant values ($p<0.05$).
*Student t test.
**Fisher exact test.
[a] Only 63 available.

Table 4
Comparison of patients' characteristics according to the results of F-choline PET/CT in case of castration-resistant prostate cancer

		No metastasis on PET/CT ($n = 20$)	Distant metastases on PET/CT ($n = 14$)	P
Age (y), median (min−max)		75.7 (61.6−87.3)	67.1 (51.5−85.3)	0.18*
PSA value (ng/ml), median (min−max)		5.7 (0.10−54.0)	4.4 (0.03−40.0)	0.41*
PSA velocity (ng/ml/y), median (min−max)		69.7 (5.7−88)	9.7 (9.4−12.1)	0.21*
PSA doubling time (mo), median (min−max)		1.1 (0.50−7.0)	2.1 (1.8−2.4)	0.75*
Initial Gleason score[a], n (%)	Gleason = 6	3 (21.4)	0 (0)	**0.03****
	Gleason = 7	6 (42.9)	1 (11.1)	
	Gleason > 7	5 (35.7)	8 (88.9)	
Prescriber, n (%)	Urologist	6 (30.0)	1 (7.1)	0.20**
	Radiotherapist	0 (0)	2 (14.3)	
	Oncologist	14 (60.0)	11 (78.6)	
	Other	0 (0)	0 (0)	
Multidisciplinary decision, n (%)	Yes	4 (20.0)	4 (28.6)	0.69**
	No	16 (80.0)	10 (71.4)	

Bold values = significant values ($p<0.05$).
*Student t test.
**Fisher exact test.
[a] Only 23 available.

increased along with PSA. However, the threshold used to identify specific lesions after PSA increases remains the major concern for clinicians. A strong consensus regarding the optimal values to refer patients is currently lacking, partly because available studies do not share the same initial clinical and pathological patient characteristics. Husarik et al. reported that recurrent disease after biochemical relapse can be reliably localized by ^{11}C-Choline PET/CT in patients with PSA levels of >2 ng/ml [6]. Giovacchini et al. reported that a PSA cut-off value of 1.4 ng/ml can discriminate between a positive and negative ^{11}C-Choline-PET/CT, with a sensitivity rate of 73%. In contrast, they have reported that only 24% of patients with a PSA value <1.4 ng/ml presented a positive PET-CT [7]. These results were consistent with other studies reporting that, with PSA levels <1 ng/ml, the detection rate ranged from 36 to 50% [8,9]. In our study, the sensitivity of ^{18}F-Choline PET/CT in case of biochemical recurrence after local treatment was quite high, since 80.9% of the exams were positive with an optimal PSA cut-off value of 1 ng/ml, above which the sensitivity was 89.3%. However, in patients with a PSA value <1 ng/ml, the sensitivity remains acceptable, since ^{18}F-Choline PET/CT could identify a hypermetabolic focus in almost half the patients (45.2%). This good performance could be explained by the late acquisition at 60 minutes after the ^{18}fluorocholine injection associated with concomitant intravenous administration of 20 mg of furosemide, allowing enhanced detection of local recurrence. In our study, PSA velocity was not associated with PET/CT sensitivity. At the opposite, previous series showing that PSA velocity predicts PET/CT positivity

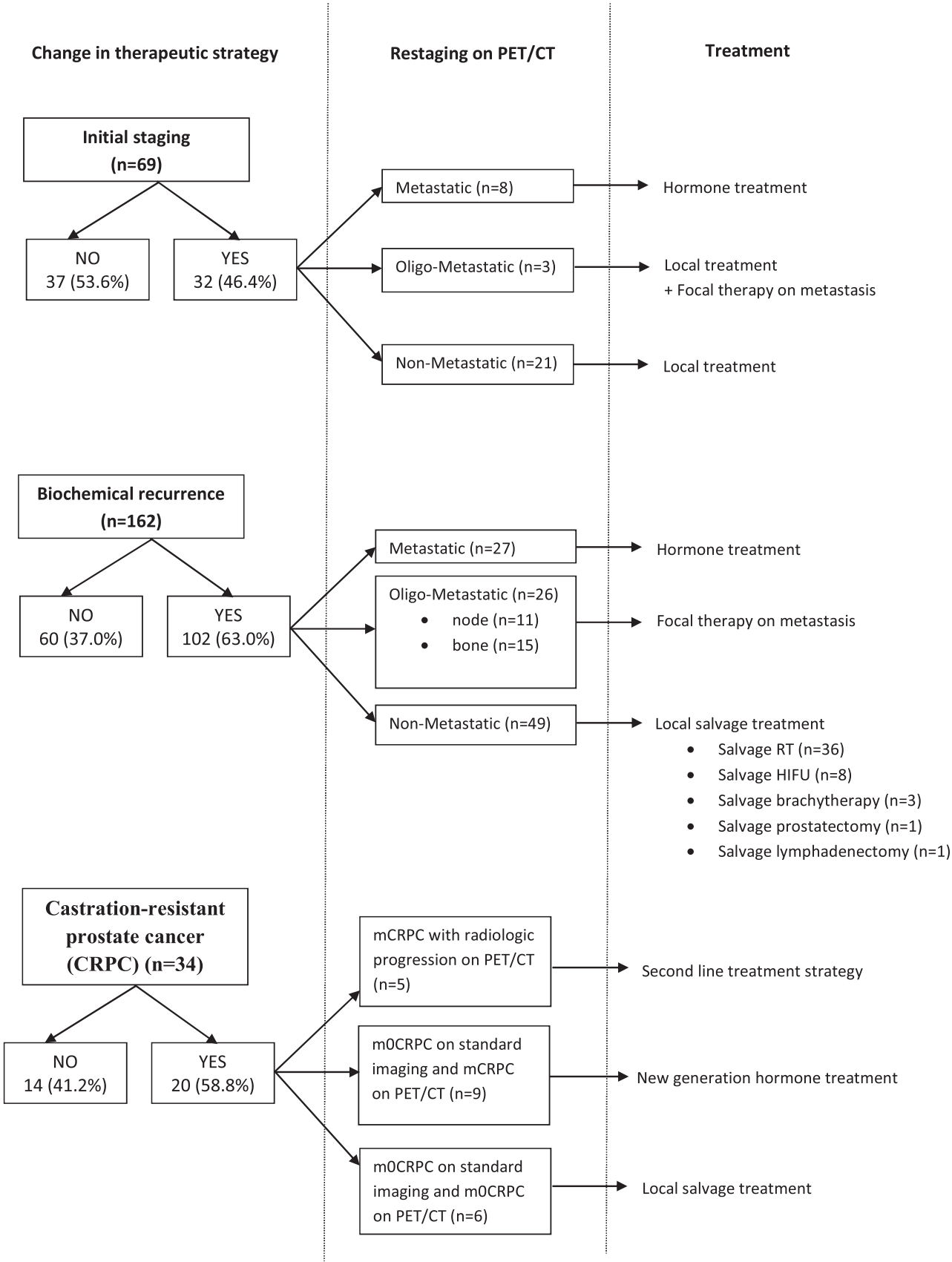

Fig. 2. Restaging of prostate cancer and modification of treatment according to F-Choline PET/CT scan indications and results.

[10,11]. PSA velocity seems to be significantly higher in patients with presumed skeletal metastasis than in patients with presumed local recurrence [10].

Another interesting issue could be the development of new radiopharmaceuticals. PET agents can be divided into those that interrogate tumor metabolism (^{18}F-FDG, ^{11}C-Choline, ^{18}F-Choline, ^{11}C-Acetate, and ^{18}F-FACBC), hormone receptors (^{18}F-FDHT), and other targets such as prostate-specific membrane antigen (PSMA) labeled by Gallium 68 (^{68}Ga-PSMA) and more recently by 18 Fluorine (^{18}F-PSMA) [12]. In a recent meta-analysis, Fanti et al. reported a pooled detection rate of 62%, with similar results in terms of sensitivity to ^{18}F-Choline PET/CT [13]. More recently, data suggest that PSMA based imaging offers higher tumor detection rate compared to choline PET/CT, especially at very low PSA levels during biochemical recurrence [14,15,16]. In addition, PSMA could also be used as theranostic agent, when coupled with a radioligand (Lutetium 177 [^{177}Lu] for example), to delay disease progression in metastatic CRCaP [15]. Although this new diagnostic technique able to detect disease with high sensitivity and specificity might have a clinical impact on patient management, it is still not available in most European centers [17].

Current guidelines do not support the routine use of PET/CT for initial staging. Nevertheless, it seems to have better performances than conventional imaging for nodal staging with a sensitivity of almost 45% [18] and for all patients with suspected metastases [19]. In high-risk CaP patients, this would be useful to detect lymph node metastasis and to eliminate distant metastases before decision of a local treatment. In this population, it has been shown that ^{18}F-Choline PET/CT results could modify the therapeutic approach in nearly 15% to 20% of cases [16]. For preoperative assessment of distant metastases, it should be noted that metastatic bone lesions were found in 10% of cases and that these were not detectable on bone scan in 15% of them. These good diagnostic performances have been confirmed in a prospective study reporting a sensitivity of 91% for the detection of bone metastases in CaP patients [20]. In our series, when performed as part of the initial staging, ^{18}F-Choline PET/CT results change the therapeutic approach in 46% of cases. This is all the more remarkable as many of our patients previously underwent a negative bone scintigraphy and/or CT scan, suggesting that ^{18}F-Choline PET/CT seems to be an optimal imaging modality for patients with suspected metastases and/or with high risk CaP, especially if PSA DT is short and Gleason score >7. Two Italian surveys have shown that in the initial staging of CaP patients referred for curative local treatment, up to 10% of the oncologists would prescribe a pretreatment Choline PET/CT [21,22]. In oligometastatic disease, an important issue is the need to defer hormone therapy. The use of PET/CT will likely increase the proportion of patients who could benefit from a focal therapeutic strategy on metastatic sites, as our series shows in >10% of cases.

Finally, in CRCaP, the relevance of routine PET/CT to improve treatment planning is still debated. Choline PET/CTs are more frequently positive in hormone-resistant patients than in hormone-sensitive patients [7]. In vitro studies have shown that androgen depletion reduces the uptake of Choline in androgen-dependent CaP cells but not in androgen-independent cells [23]. At the era of new generation hormone therapy with several lines of efficient treatments, it will be crucial not to lose the opportunity to switch to another therapeutic strategy. The role of PET/CT may evolve in the coming years to optimize the management of such patients.

The main limitations of our study are its retrospective setting and the lack of data on PPV and specificity. A positive lesion on PET should be interpreted with caution by comparing with other imaging and if possible, by confirming with a biopsy (especially in case of local recurrence). Moreover, we do not have data on the oncological impact of the therapeutic changes described in these 3 subpopulations. Indeed, particularly in the population of patients with biochemical recurrence, the real benefit of local salvage therapies guided by PET results remains controversial, and trials are ongoing to assess this point.

In conclusion, in this multicenter study reflecting current practices in "real-world," the indications of ^{18}F-Choline PET/CT varied widely, including biochemical recurrence, initial staging, or CRCaP. In all these settings, ^{18}F-Choline PET/CT might significantly modify the staging of CaP and therefore lead to a change in patient management and therapeutic approach in more than half of all cases.

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