Which patient with biochemical recurrence after primary treatment for prostate cancer would result in a positive ⁶⁸Ga-PSMA PET/CT?

A clinical tool to guide physicians before suggesting ⁶⁸Ga-PSMA PET/CT

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Introduction and objective

To develop a **clinical nomogram** aimed to predict which **patients with recurrent prostate cancer (PCa) could benefit** from ⁶⁸Gallium-Prostate Specific Membrane Antigen Positron Emission Tomography/Computed Tomography (**⁶⁸Ga-PSMA PET/CT**).

Results

Table1. Overall patient characteristics

Variable	Overall
No. of patients	703
Age (years)	
Median	68
IQR	63-73
Primary treatment, n (%)	
Radical prostatectomy	684 (97.3)
Radiotherapy	19 (2.7)
ISUP grade#, n (%)	
1	67 (9.5)
2	128 (18.2)
3	223 (31.7)
4	155 (22)
5	130 (18.5)
T stage, n (%)	
Missing data	70 (10)
T2-T3a	231 (32.9)
T3b - pT4	402 (57.2)
PLND, n (%)*	
No	148 (21.6)
Yes	536 (78.4)
Nodal status, n (%)*	
Missing data	62 (9.1)
pN0	508 (74.3)
pN1	114 (16.7)
Positive Surgical Margins, n (%)*	
Missing data	101 (14.8)
No	342 (50)
Yes	241 (35.2)
Adjuvant Radiotherapy, n (%)*	
No	502 (73.4)
Yes	182 (26.6)
Salvage Radiotherapy, n (%)*	
No	515 (75.2)
Yes	169 (24.7)
PSA at ⁶⁸ Ga-PSMA PET/CT (ng/ml)	
Median	0.7
IQR	0.4-1.3
PSA ranges at ⁶⁸ Ga-PSMA PET/CT (ng/ml), n (%)	
≤0.2	30 (4.3)
0.21-0.5	213 (30.3)
0.6-1	203 (28.9)
1.1-2	167 (23.8)
>2	90 (12.8)
On-going ADT at ⁶⁸ Ga-PSMA PET/CT, n (%)	
No	587 (83.5)
Yes	116 (16.5)
Time to BCR (months)	
Median	21
IQR	8.8-49
Time to BCR (months)	
>12 months	492 (70)
≤12 months	211 (30)
PSA doubling time (months)	
Median	6
IQR	3.5-9.6
PSA doubling time (months), n (%)	
<3 months	132 (18.8)
3-6 months	215 (30.6)
6-12 months	230 (32.7)
>12 months	126 (17.9)
⁶⁸ Ga-PSMA PET/CT results, n (%)	
Positive	360 (51.2)
Negative	343 (48.8)
Clinical setting, n (%)	
-First PSA recurrence	325 (46.2)
-PSA recurrence after salvage therapy	241 (46.2)
-PSA persistence after surgery	76 (10.8)
-Assessment before systemic treatments	61 (8.7)

Material and methods

703 PCa patients with confirmed **biochemical recurrence (BCR)**

- after **Radical Prostatectomy (n=684)**
- After primary **radiotherapy (n=19)**

Each man underwent **⁶⁸Ga-PSMA PET/CT** to identify the **site of recurrence**.

1) We assessed the **detection rate of ⁶⁸Ga-PSMA PET/CT** in **overall population** and in each **subgroup of patients** (**first PSA relapse, BCR after salvage therapy, PSA persistence after primary therapy and disease progression before starting systemic therapies**).

2) **Multivariate logistic regressions** were used to determine which co-variables independently **predict a positive ⁶⁸Ga-PSMA PET/CT result**.

3) Regression-based coefficients were used to develop **a nomogram predicting positive ⁶⁸Ga-PSMA PET/CT result** and 200 bootstrap resamples were used for internal validation.

Table 2. Patients' characteristics and detection rates according to different clinical setting

Different clinical stages of BCR	N. of patients	Mean PSA (ng/mL)	Detection Rate	Pelvic Relapse*	Distant Relapse*	Oligometastatic (1 to 3 lesions)	Multimetastatic (> 3 lesions)
Group-1 First-time BCR (no salvage therapy)	325	0.9	40.3%	19.4%	20.9%	35.7%	4.6%
Group-2 PSA failure after salvage therapy	241	1.3	54.0%	21.6%	32.4%	42.8%	11.2%
Group-3 Biochemical Persistence post-RP	76	1.1	60.5%	31.6%	28.9%	39.5%	21%
Group-4 *** Restaging before systemic therapy	61	4.7	86.9%	8.2%	78.7%	36%	50.9%
P value	-	<0.001	<0.001	0.3	<0.001	0.2	<0.001
Overall Population	703	1.3	51.2%	20.4%	30.8%	38.5%	12.7%

* Prostate bed and/or pelvic lymph-nodes.

**At least one distant lesion (extra-pelvic lymph nodes and/or bone and/or visceral metastasis).

*** (chemotherapy and/or abiraterone/enzalutamide and/or radioligand-therapy naïve)

Table 3. Uni and multivariate logistic regression to predict positive findings at PSMA PET/CT (n=703)

Variables	UNIVARIATE		MULTIVARIATE	
	OR (95% C.I.)	P value	OR (95% C.I.)	P value
ISUP group				
1	1.0 (Ref)		1.0 (Ref)	
2	1.15 (0.63-2.11)	0.7	1.34 (0.64-2.82)	0.4
3	1.82 (1.04-3.19)	0.04	2.02 (1.02-3.99)	0.04
4	2.15 (1.19-3.87)	0.01	1.76 (0.86-3.59)	0.01
5	2.69 (1.46-4.94)	0.001	2.35 (1.12-4.94)	0.02
PSA at PSMA PET/CT (ng/ml)				
≤0.2	1.0 (Ref)		1.0 (Ref)	
0.21-0.49	1.79 (0.73-4.36)	0.2	1.83 (0.67-4.97)	0.2
0.5-0.99	4.21 (1.73-10.25)	0.002	4.52 (1.66-12.26)	0.003
1-1.99	5.57 (2.26-13.72)	<0.001	6.09 (2.20-16.87)	0.001
≥2	6.25 (2.42-16.19)	<0.001	5.39 (1.78-16.35)	0.003
PSA doubling time (ng/ml/)				
< 3 months	1.0 (Ref)		1.0 (Ref)	
3-5.9 months	0.56 (0.33-0.95)	0.03	0.59 (0.34-1.04)	0.07
6-11.9 months	0.15 (0.09-0.25)	<0.001	0.16 (0.09-0.28)	<0.001
≥12 months	0.03 (0.01-0.05)	<0.001	0.02 (0.11-0.06)	<0.001
Ongoing ADT at BCR				
No	1.0 (Ref)		1.0 (Ref)	
Yes	2.68 (1.74-4.13)	<0.001	1.04 (0.56-1.93)	0.9
Time to BCR (months)				
>12 months	1.0 (Ref)		1.0 (Ref)	
≤12 months	1.39 (1.00-1.92)	0.049	1.03 (0.64-1.68)	0.9
Clinical setting				
-First recurrence after primary treatment	1.0 (Ref)		1.0 (Ref)	
-Recurrence after salvage therapy	1.73 (1.24-2.43)	0.001	1.30 (0.85-1.98)	0.2
-PSA persistence after primary treatment	2.27 (1.36-3.78)	0.002	1.43 (0.70-2.90)	0.3
-Advanced stage PCa	9.81 (4.51-21.31)	0.001	6.05 (2.14-17.11)	0.001
Predictive accuracy	-		82.3%	

Figure 1. Nomogram to predict the likelihood of positive ⁶⁸Ga-PSMA PET/CT result

Figure 2. Calibration plot: after 200 bootstrap resamples, the predictive accuracy of the model was 82%

Figure 3. Decision curve analysis shows a net benefit cut off 10%

Conclusion

Our nomogram could **help physician to select patients with different scenario of recurrence** who may **benefit from ⁶⁸Ga-PSMA PET/CT restaging**.