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^{68}Ga-PSMA-11 PET/MRI in patients with newly diagnosed intermediate or high-risk prostate adenocarcinoma: PET findings correlate with outcomes after definitive treatment

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ABSTRACT

Prostate-specific membrane antigen (PSMA) PET offers superior accuracy to other imaging modalities in initial staging of prostate cancer and is more likely to affect management. We examined the prognostic value of ^{68}Ga-PSMA-11 uptake in primary lesion and presence of metastatic disease on PET in newly diagnosed prostate cancer patients prior to initial therapy. **Methods:** In a prospective study from April 2016 to December 2020, ^{68}Ga-PSMA-11 PET/MRI was done in men with new diagnosis of intermediate or high-grade prostate cancer who were candidates for prostatectomy. Patients were followed up after initial therapy for up to 5 years. We examined the Kendall correlation between PET (intense uptake in primary lesion and presence of metastatic disease) and clinical and pathologic findings (grade group, extraprostatic extension, nodal involvement) relevant for risk stratification, and examined the relationship between PET findings and outcome using Kaplan–Meier analysis. **Results:** Seventy-three men, 64.0±6.3 years of age were imaged. Seventy-two had focal uptake in prostate and in 20 (27%), PSMA-avid metastatic disease was identified. Uptake correlated with grade group and prostate-specific antigen (PSA). Presence of PSMA metastasis correlated with grade group and pathologic nodal stage. PSMA PET had higher per-patients positivity than nodal dissection in patients with only 5-15 nodes removed (8/41 vs. 3/41) but lower positivity if more than 15 nodes were removed (13/21 vs. 10/21). High uptake in primary (SUV_{max}>12.5, P = .008) and presence of PSMA metastasis (P = .013) were associated with biochemical failure, and corresponding hazard ratios for recurrence within 2-years (4.93 and 3.95, respectively) were similar or higher than other clinicopathologic prognostic factors. **Conclusions:** ^{68}Ga-PSMA-11 PET can risk stratify patients with intermediate or high-grade prostate cancer prior to prostatectomy based on degree of uptake in prostate and presence of metastatic disease.

INTRODUCTION

Patients diagnosed with localized prostate adenocarcinoma have generally prolonged natural history, although some patients experience rapid progression after initial curative intent prostatectomy or radiation therapy. Initial risk stratification impacts treatment decisions and subsequent management of prostate cancer patients. Risk stratification is primarily based on clinical tumor stage, histologic grade group, and the prostate-specific antigen (PSA) level *(1)* although incorporating molecular markers is increasingly being considered *(2)*. Imaging is indicated in all men with unfavorable intermediate-, high-, or very high-risk disease *(3,4)*. Presence of nodal or distant metastatic disease on cross-sectional imaging or bone scintigraphy affects management and prognosis. Prostate-specific membrane antigen (PSMA) PET/CT or PET/MRI has significantly better sensitivity and higher diagnostic yield for detection of metastatic disease *(5,6)*. Unfortunately, the outcome data on patients with metastasis that is occult on anatomic imaging and bone scintigraphy is sparse. Extrapolation of data from prostatectomy and pelvic nodal dissection suggests that prognosis of patients with nodal metastasis could be variable *(7)*. After prostatectomy, even in node positive patients, 75% achieve complete biochemical response and are at low risk for recurrence and caner specific mortality *(8)*. There is a need for prognostic models to identify patients at risk for persistent or recurrent disease based on PET from others who do not benefit from overtreatment.

We and others had examined the clinical utility of pre-therapy vertex to mid-thigh ^{68}Ga-PSMA-11 PET as a part of PET/MRI in newly diagnosed prostate cancer patients and correlation with histopathology *(9-11)*. We now examine the association between PET findings and outcomes/biochemical recurrence after initial therapy.

METHODS

Patient Population

The study protocol was approved by the Stanford University Institutional Review Board and all subjects signed a written informed consent form. Patients with newly diagnosed intermediate- or high-risk prostate cancer (PSA ≥10 ng/mL, cT2b or greater, or Gleason score ≥7) who were scheduled for radical prostatectomy were enrolled from April 2016 until December 2020 (NCT02678351). The protocol has been previously described *(11).* Exclusion criteria were androgen deprivation therapy, neoadjuvant chemotherapy, or radiation therapy prior to the planned prostatectomy.

PET/MR Imaging Protocol

^{68}Ga-PSMA-11 was prepared as described previously *(11,12)*. The mean ± SD administered dosage was 160.8±31.1 MBq (range, 91.4–236.4). After uptake time of 50.0±8.9 minutes (range, 40–108) patients were imaged from mid-thighs to vertex using a time-of-flight simultaneous PET/MR scanner (SIGNA, GE Healthcare, Waukesha, WI) in 3D mode for 4 minutes per bed position in 5–9 beds. Delayed pelvic PET/MR including prostate multiparametric MRI (mpMRI) was obtained after voiding, at 70.5±13.4 minutes (range, 43–108) after the initial scan. A two-point Dixon three-dimensional T1-weighted spoiled gradient-echo MR sequence was acquired using the volume coil for MR-attenuation correction.

Image Analysis

PET images acquired prior to October 2017 (33 patients) were independently reviewed in correlation with MRI by two nuclear medicine physicians with 13 and 5 years of experience *(11)*. Subsequent studies were reviewed by one of the original nuclear physicians (AI, greater than 13 years of experience) using MIM version 7 (MIM Software Inc., Cleveland, Ohio). PET findings were communicated with the referring surgeon and the information was used as a part of clinical decision making. Standardized uptake values (SUV) normalized based on body weight were measured for prostate lesions

and physiological activity in liver, spleen, right parotid gland, and mediastinal blood pool separately by a radiologist/nuclear medicine physician (FM, 10 years of experience). For prostate lesions, maximum and peak SUV (SUV_{max} and SUV_{peak}) were recoded for initial images and SUV_{max} was recorded for delayed images. Physiologic activity was recorded using SUV_{mean} per Prostate Cancer Molecular Imaging Standardized Evaluation recommendations *(13)*. Lesion PSMA index was calculated based on SUV_{peak} comparison with blood pool and liver activity *(14)*.

Outcome Analysis

Biochemical persistence and recurrence were assessed via review of all available electronic medical records (including PSA results and clinical notes). Biochemical failure was defined as PSA ≥0.4 ng/mL after prostatectomy or persistent PSA that was followed by adjuvant therapy. Recurrence was defined as a rise in PSA at least 6-weeks after radical prostatectomy with or without adjuvant therapy measuring ≥0.2 ng/mL that was subsequently confirmed by a follow up measurement *(15)* or any rise in PSA that was treated with salvage therapy.

Statistical Analysis

Analysis was performed using MATLAB (R2021B) Statistics and Machine Learning toolbox. A multi-step analysis was performed. PET findings were dichotomized (low versus high uptake in primary lesion, presence of metastatic disease). We next examined the correlation between PET findings and clinical and pathologic parameters in prostate cancer risk stratification. Finally, we examined the relationship between PET findings and outcomes.

There is no a priori threshold for dichotomizing uptake in prostate although uptake higher than twice activity in normal liver parenchyma has been suggested for metastatic lesions *(13, 14)*. To explore a basis for thresholding of the primary prostate lesion (or the dominant lesion if more than one lesion were present) we used histogram and cluster analysis. Shapiro–Wilk test was used to examine normality

of SUV_{max} distribution. We subsequently used cluster analysis of the SUV_{max} based on L1-norm (*k*-medians) with *k* = 2. The resulting categories (low vs. high uptake) were stable for SUV_{max}<12.5 (*n* = 40) or SUV_{max}>20 (*n* = 13), but classification was variable for SUV_{max} between 12.5 and 20 (i.e., *k*-medians results depended on initial state, *n* = 20). We used SUV of 12.5 as the cut-off threshold for future analysis which is close to twice average normal liver activity (11.88 g/mL) in our patients, and more evenly divided the patients into low and high uptake groups compared to a higher cut-off value.

We also explored reliability of physiologic uptake that can define an internal reference per subject *(16)*. Coefficient of variation was used to examine the variability of physiologic uptake. Person correlation coefficient was used to estimate the contribution of factors that systematically affect physiologic uptake in different organs to the overall variability of physiologic uptake.

Metastatic disease on ^{68}Ga-PSMA-11 PET/MRI was categorized as absent versus present (regardless of number of metastases). For clinical parameters, conventional categories were used (PSA level: <10, 10-20, >20, Clinical tumor stage: T1-2a, T2b/c, ≥T3, Grade group: 2, 3, ≥4) *(17)*.

Kendall tau was used to assess correlation between PET findings and clinical and pathologic parameters. A cut off value of $P < 0.05$ was used for significance. Kruskal–Wallis H test was used to examine if similar number of nodes were sampled during pelvic dissection between various groups.

Survival analysis: The relationship between PET findings and outcomes were analyzed using Kaplan Meier survival plots and log-rank test using MatSurv *(18)*.

RESULTS

Patient Characteristics and Pathologic Findings

Seventy-five men were consented for this study (Figure 1). One patient was excluded due to equipment failure. No imaging could be done in one patient and PET/MRI was terminated early (after

acquisition of pelvis and lower abdomen) in another patient due to claustrophobia. The data for prostate lesions and regional lymph nodes includes 73 patients (Table 1,2). The data for distant metastasis and physiologic uptake includes 72 patients.

Sixty-five patients underwent prostatectomy 12.4±15.4 (median, 7, range, 1–95) days after PET. In all cases clinically significant prostate cancer was confirmed. On average 14.83±10.84 lymph nodes (median 13, range: 0–54) from 64 patients were submitted for pathologic examination. The Gleason grade group after prostatectomy correlated with grade group based on initial biopsy (Kendall tau = 0.42, *P* = 0.0002), and was unchanged, revised up, or revised down after prostatectomy in 32, 26, and 5 patients, respectively (Table 3).

In 72 of 73 patients, follow-up data was available (34.4±15.49 months after PET, median, 35.91, range, 4.86–60.7). Persistent disease (based on PSA failure) was documented in 10 patients after prostatectomy and 4 after other treatments. Biochemical recurrence (after initial complete response) was documented in 14 patients after prostatectomy and in 6 patients after prostatectomy and adjuvant therapy.

PET Findings

Except for one patient, focal uptake was identified within the prostate gland. In 7 patients (including a patient with negative PET) MR showed more lesions, and in 26 patients, PET showed more lesions. For the remaining patients, PET-positive lesion was congruent with mpMRI in 36 patients, and incongruent in 1 (Table 4). In 20 patients (27.4%), PET showed focal uptake outside of prostate consistent with metastatic disease in 66 lesions (3.3±4.6 sites per patient, median, 1, range 1–19 , Table 5).

Metastatic Disease on PET versus Pelvic Dissection

Of 16 patients with pathologically proven N1 disease, 9 had PSMA metastasis (56% per patient sensitivity). There were 9 patients that nodal dissection did not reveal metastasis (pN0) but had PSMA metastasis. The extent of a pelvic lymph node dissection confounds the probability of positive lymph nodes. Patients with PSMA metastasis and negative pelvic dissection had on average less than half of the number of lymph nodes sampled compared to patients that both PET and pelvic dissection showed metastatic disease, or only pelvic dissection showed metastatic disease (11.7±5.2 vs. 24.4±13.1 and 27.3±15.7, respectively, $P = 0.012$, Kruskal-Wallis test). The per patient ^{68}Ga-PSMA-11 PET/MRI positivity rate was 2.5 times higher than pelvic nodal dissection when 5–15 nodes were surgically sampled (Table 5).

Degree of ^{68}Ga-PSMA-11 Uptake

For prostate lesions (dominant lesion if multiple lesions are present) the SUV_{max} was 14.53±10.42 (median, 10.64, range, 3.61–50.12 g/mL) and the SUV_{peak} was 9.18±7.21, (median, 6.69, range, 2.13–40.24 g/mL). Figure 2A depicts the histogram of SUV_{max} of the dominant prostate lesion in our dataset. The distribution is asymmetric and non-gaussian ($P < 0.001$, Shapiro-Wilk test). A cut-off value of 12.5 (approximately 55th percentile) was used for subsequent analysis as threshold for "high" uptake. Uptake on initial PET and delayed pelvic PET was highly correlated ($r = 0.968$, Figure 2B) and followed a similar distribution, with the equivalent delayed SUV cut-off of 13.5.

The average uptake in liver, spleen, blood pool, and parotid gland were 5.94±1.53, 9.33±3.11, 1.26±0.24, and 16.08±3.94 g/mL, respectively (corresponding to interpatient coefficients of variation of 0.26, 0.34, 0.19, and 0.25, respectively, Figure 2C). SUV_{max} or SUV_{peak} of the prostate lesion did not correlate with physiologic uptake in the liver, spleen, blood pool, or parotid gland ($r<0.12$ for all tests).

Correlation between physiologic uptake in various organs was weak, with highest between liver and spleen (r = 0.224, P = 0.058, Figure 2D).

Relationship between PET Findings and Clinicopathological Risk Factors

Uptake in primary and presence of PSMA metastasis correlated with several clinical and pathological factors as detailed in Table 6. The notable exception is nonsignificant correlation between clinical or pathologic T-stage (extraprostatic extension) and PET findings (in contrast to *(19)*). High uptake in primary correlated more with pre-prostatectomy PSA level and D'Amico risk category whereas PSMA metastasis correlated more with grade group and nodal involvement.

Relationship between PET Findings and Outcome

High uptake (SUV_{max}>12.5) and presence of PSMA metastasis were associated with biochemical failure or rapid recurrence within 2-years after prostatectomy. In contrast, patients with low uptake in primary who did not have evidence of metastatic disease on PET had low likelihood of experiencing recurrence within the follow up period (Figure 3). The outcomes were worse in patients with high uptake in primary and PSMA metastasis (Figure 4). Results were similar when the analysis included all patients rather than only patients who underwent prostatectomy (P = 0.008 for uptake in primary, P = 0.0135 for PSMA metastasis, and P = 0.001 for the combination of the two). Alternative measures of uptake using body surface area and lean body mass also showed significant differences in survival (P < 0.05) between high and low uptake when a comparable cutoff threshold (about 55 percentile of corresponding population values) was used. Neither SUV_{peak}, nor Lesion-Index *(14)* (defined based on SUV_{peak}) reached statistical significance.

PET findings correlated with the duration of biochemical response after initial therapy (including adjuvant therapy) (Figure 5). The hazard ratio for PET compared to clinicopathologic factors for biochemical recurrence within the first 24 months are depicted in Table 7. High uptake in the primary

cancer and presence of PSMA-avid metastasis were associated with higher hazard ratios for early recurrence compared to clinicopathologic factors, although our sample is too small to allow for statistical comparison and testing independence. Kaplan Meier Survival analysis showed worse outcome for patients with bilateral disease in prostate (based on either PET or MRI) or if PET and MRI results were incongruent that was not statistically significant.

DISCUSSION

In patients with newly diagnosed intermediate- or high-prostate cancer who were candidates for radical prostatectomy, ^{68}Ga-PSMA-11 PET/MRI findings were closely linked with clinical and pathological risk factors. High ^{68}Ga-PSMA-11 uptake in primary lesion and presence of PSMA-avid metastatic disease were negatively associated with response to initial therapy and duration of biochemical response. Our findings add to the evidence of utility of PSMA PET in initial workup of prostate cancer and correlation between PSMA expression and tumor behavior *(20)*.

Dedicated prostate MRI was performed in the same session in conjunction with PET and helped identify prostate lesions (particularly lesions with very low uptake). Uptake and conspicuity increase on delayed PET. Nonetheless most lesions were readily visible on the initial PET including lesions that were identified only on PET or lesions with indeterminate appearance on mpMRI that were not prospectively called. Although survival analysis did not utilize MRI findings, scanner hardware, attenuation correction methodology, and post processing affect image quality and SUV measurements which should be considered before applying our results to data from PET/CT or other PET/MRI systems.

PSMA-PET sensitivity of 56% for nodal involvement here is in line with other studies *(21,22)*. Therefore, absence of PSMA metastasis does not indicate that a pelvic nodal dissection is not required *(23)*. Several patients had nodal involvement on PET that was not confirmed pathologically. PSMA PET has high specificity *(23-26)*, so we suspected under-sampling, corroborated by our analysis. Accurate

surgical staging requires extensive lymphadenectomy which increases surgical morbidity. The positivity rate of PET in our study was 2.5 times higher than limited pelvic dissection (sampling up to 15 lymph nodes), and only slightly lower than extensive pelvic nodal dissection (52% vs 62%). PSMA PET could therefore be supplementary to surgical pathology in staging patients undergoing nodal dissection, particularly if for any reason extensive nodal dissection is not performed. Our survival analysis also suggests that despite limited sensitivity, the prognostic value of PSMA PET (in terms of hazard ratio of biochemical recurrence) can be comparable to pathologic nodal staging given variable prognosis of pN1 disease *(7)*.

PSMA expression and histologic tumor grade are linked *(27)* and PSMA plays a complex role in tumor progression *(28)*, which is consistent with our finding of slower progression in patients with low uptake in primary tumor. Low PSMA expression could reduce the sensitivity of PET for metastatic disease but might have little impact on the overall prognostic value of PSMA PET if cancers with low PSMA expression would have low probabilities for metastatic spread in the first place. ^{68}Ga-PSMA-11 uptake and grade group were correlated in our data (Table 6), which partially explains better prognosis in patients with low uptake in prostate. Nonetheless for every grade group, we noticed that those with SUV_{max}<12.5 tend to have longer recurrence free survivals. Larger studies could shed light into the value of incorporating PSMA uptake in prognostic models of prostate cancer in addition to histologic grade. This question could be particularly relevant in patients who decide not to undergo prostatectomy as in nearly half our patients, the grade group based on initial biopsy changed after prostatectomy.

To simplify our analysis, we categorized uptake to low- versus high. Variations on how this was done (e.g., normalizing based on lean body mass instead of weight) did not affect our results although using SUV_{peak} (which could underestimate uptake in small lesions) did. Uptake categorization and Kaplan-Meier analysis was reproducible on repeat PET/MRI of the pelvis performed after voiding, suggesting that SUV_{max} was a sufficiently robust measure in our study *(29)*. Dichotomizing a continuous

variable is however associated with certain issues such as loss of information *(30)*, and further studies may be needed to confirm the relationship between SUV and duration of biochemical response.

A limitation of our study is that we did not examine how PET findings affected management. Heterogeneity in initial treatment strategies in prostate cancer can confound survival analysis. A few patients elected not to undergo prostatectomy and pursed other treatments after PET. Exclusion of these patients did not change the survival analysis results. As the role of PSMA PET in initial evaluation of patients with prostate cancer evolves our results point to opportunities for optimizing treatment strategies in patients with high uptake in primary lesion or with metastatic disease on PET.

CONCLUSION

PSMA PET in initial evaluation of patients with intermediate and high-risk prostate cancer correlates with the probability of biochemical failure or recurrence at least as well as clinical and pathologic factors. Patients with low uptake in prostate lesions and no evidence of metastatic disease on PET are unlikely to have recurrence within the first 2 years after initial treatment. Patients with high uptake in prostate cancer and metastatic disease are at risk for early recurrence and may require frequent surveillance and aggressive treatments.

DISCLOSURE

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All authors declare that they have no conflict or competing of interest.

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KEY POINTS

Question: Is ^{68}Ga-PSMA-11 PET useful in assessment of risk for failure after prostatectomy or early biochemical recurrence?

Pertinent findings: High ^{68}Ga-PSMA-11 uptake in primary prostate cancer and presence of PSMA-avid metastatic disease on PET are significant adverse prognostic factors after initial therapy.

Implication for patient care: ^{68}Ga-PSMA-11 PET has higher positivity rate than limited pelvic lymphadenectomy for metastatic disease and identifies patients that could benefit from additional treatment or and/or frequent surveillance.

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TABLE 1. Clinical characteristics of patients included in the study (n = 73)

	Mean, SD	Median, range
Age at the time of PET (years)	64.0 ± 6.3	66, 44–75
Weight (kg)	86.0 ± 13.3	85.3, 62.1–138.3
BMI (kg)	27.2 ± 3.4	26.6, 20.9–43.8
PSA (ng/mL)*	12.9 ± 21.1	8.6, 3.0–176

*PSA data not available in one patient.

TABLE 2. Gleason sore and Clinical stage of patients included in the study

		N
Gleason Score (biopsy)[†]		
	3+4	14 (19.2%)
	4+3	20 (27.4%)
	4+4 or 3+5	18 (24.7%)
	4+5	19 (26%)
Clinical T-stage[‡]		
	T1c	33 (45.2%)
	T2a	13 (17.8%)
	T2b	7 (9.6%)
	T2c	6 (8.2%)
	T3a	8 (11%)

[†]Not known in 2 patients. [‡]Not known in 6 individuals.

TABLE 3 Initial biopsy versus prostatectomy

	Grade group based on Initial biopsy		
Final Grade group	*2*	*3*	*4/5*
2	**9**	5	0
3	6	**9**	0
4/5	8	12	**14**

TABLE 4. Laterality of PSMA-avid lesion vs. PIRADS 4 or 5 lesions on prostate mpMRI.

	mpMRI			
PSMA PET	*No lesion*	*R*	*L*	*Bilateral*
No lesion	0	0	1	0
R	1	**13**	1	3
L	1	0	**10**	3
Bilateral	5	10	9	**13**

TABLE 5. Positivity vs. number of lymph nodes removed during pelvic nodal dissection.

	Pelvic dissection			**PSMA PET**		
Number of nodes removed	pN0	pN1	Positivity rate	No metastasis	Metastatic disease	Positivity rate
1 – 2	2	0	0	2	0	0
5 – 15	38	3	7.3%	33	8	19.5%
>15	8	13	61.9%	11	10	52.4%

TABLE 6. Cross-tabulation of the relationship between PET findings and clinical or pathologic risk factors in prostate cancer. Number of patients in each group are specified.

	SUV_{max}			PSMA-avid metastasis		
Prognostic factor	**<12.5**	**>12.5**	*Kendall τ*	**Absent**	**Present**	*Kendall τ*
D'Amico risk category			*0.35 (p = 0.0027)*			*0.15 (p = 0.2)*
Intermediate	21	6		22	5	
High	19	27		31	15	
Grade group			*0.24 (p = 0.034)*			*0.31 (p=0.0058)*
2	17	6		20	3	
3	15	16		24	7	
4/5	8	11		9	10	
PSA			*0.33 (p = 0.0037)*			*0.21 (p = 0.068)*
<10	30	15		36	9	
10-20	8	12		14	6	
>20	1	6		3	5	
Clinical T-stage			*0.23 (p = 0.052)*			*0.08 (p = 0.48)*
T1c	19	14		23	10	
T2a	9	4		13	0	
T2b/c	8	5		8	5	
≥T3	1	8		7	2	
Extraprostatic extension			*0.02 (p = 0.85)*			*0.07 (p = 0.57)*
Negative	16	13		22	7	
Positive	19	17		25	11	
Nodal involvement			*0.18 (p = 0.12)*			*0.34 (p = 0.0036)*
pN0	29	19		39	9	
pN1	6	10		7	9	

TABLE 7. Prognostic factors for biochemical recurrence within 24 months after initial response (unadjusted log-rank hazard ratio, ratio >1 indicates increased probability of recurrence).

Factor	**Hazard ratio (95% CI) (*n* = 72)**	**HR in patients who underwent prostatectomy (n=65)**
SUV_{max}>12.5	4.93 (1.87–13.04)	5.148 (1.94–13.66)
PSMA metastasis	3.95 (1.26–12.42)	4.14 (1.30–13.19)
D'Amico high risk	1.06 (0.39–2.83)	1.11 (0.42–2.96)
Grade group>2	2.74 (1.03–7.34)	3.12 (1.18–8.24)
PSA>10 ng/dL	1.48 (0.56–3.96)	1.72 (0.63–4.69)
≥cT2b	3.53 (1.08–11.56)	4.12 (1.19–14.29)
≥pT3	1.35 (0.52–3.53)	1.35 (0.52–3.53)
pN1	3.57 (1.09–11.72)	3.22 (1.01–10.21)

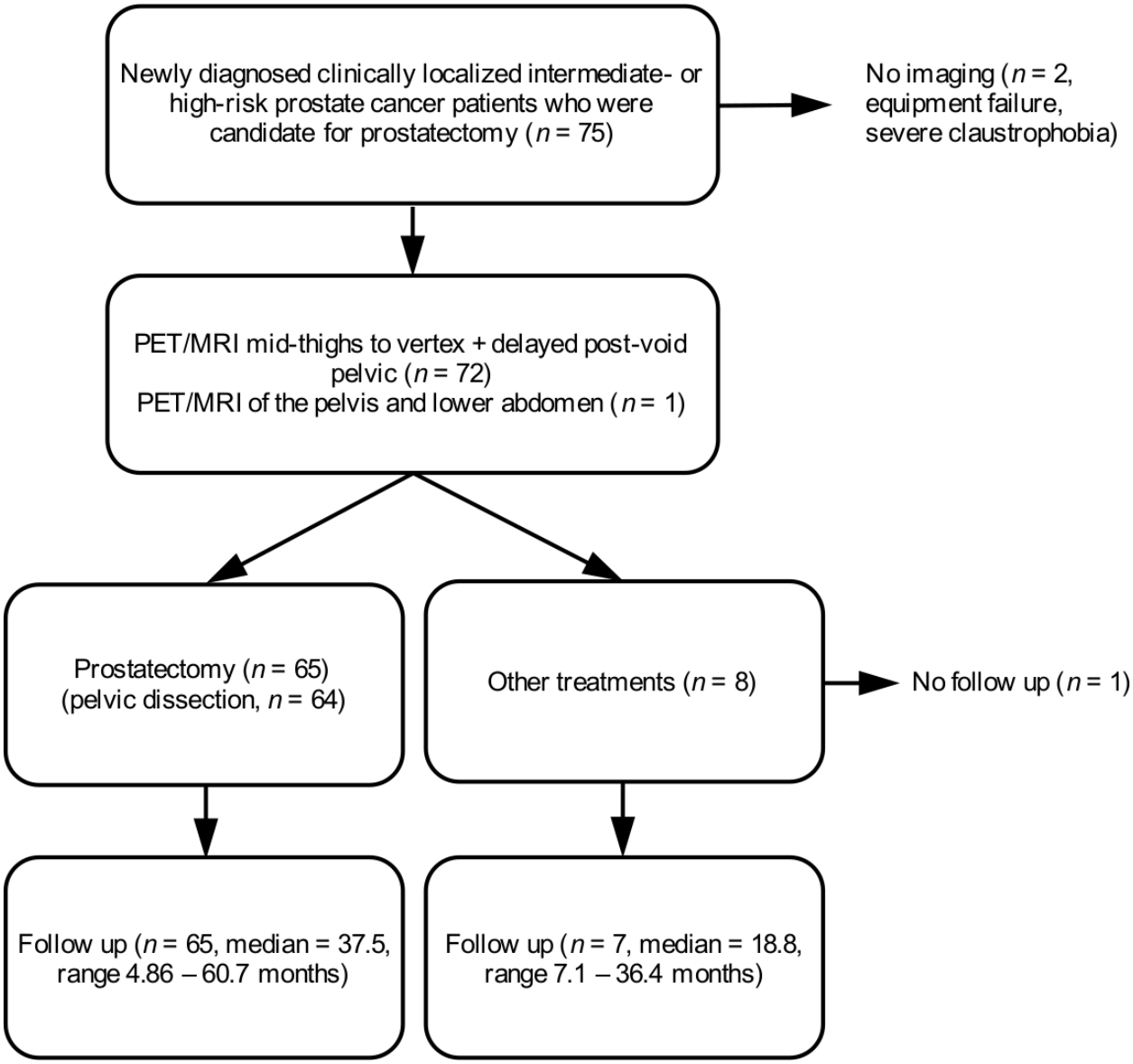


FIGURE 1. Study diagram.

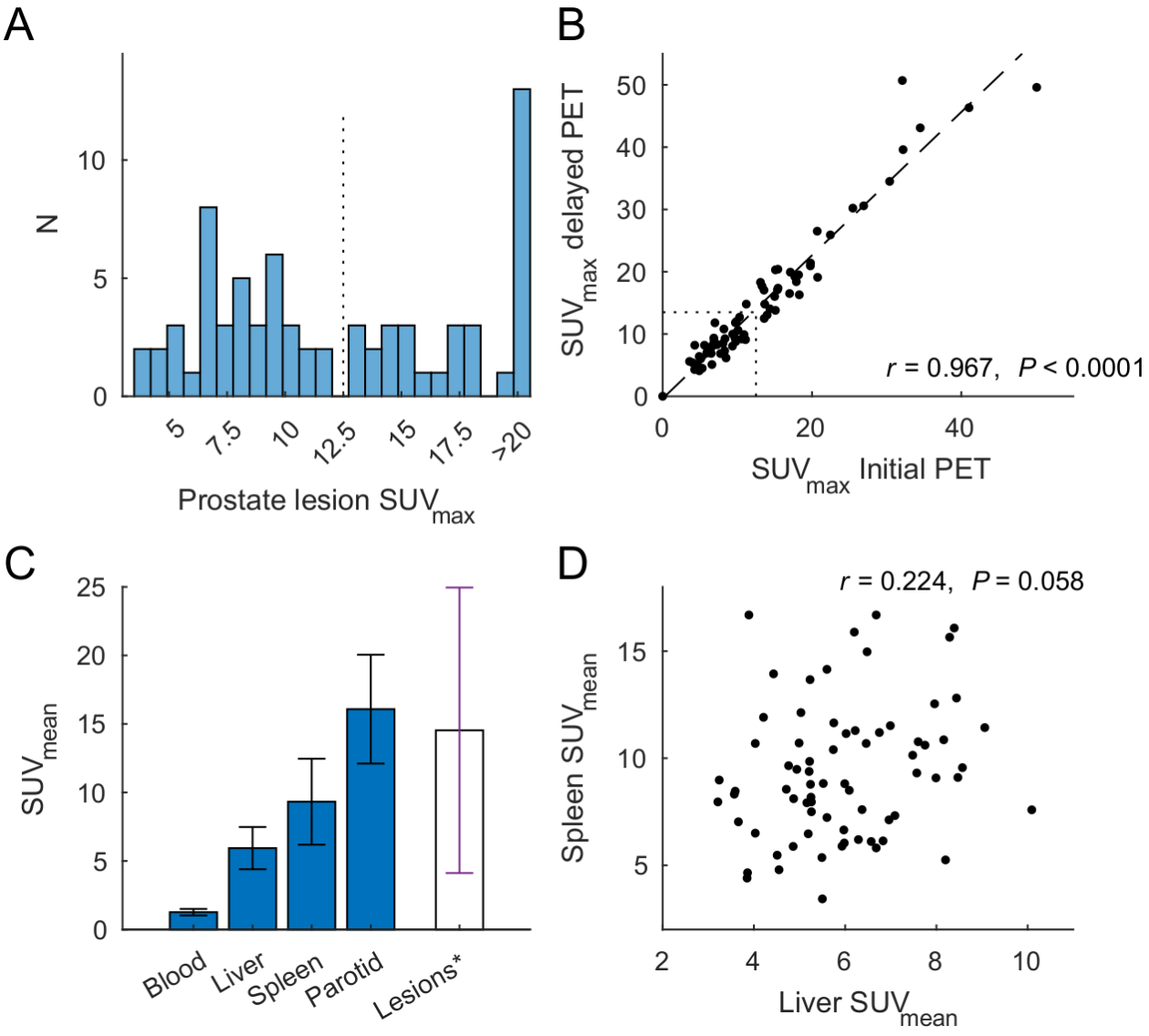


FIGURE 2. Uptake in primary prostate cancer versus physiologic uptake. (A) Histogram of SUV_{max} of the primary lesion on initial PET. (B) Correlation between early and delayed SUV_{max}. (C) Average uptake in blood pool, liver, spleen, and right parotid gland (error bars indicate standard deviation). Lesion uptake (using SUV_{max}) is also plotted for comparison (white bar). (D) Poor within-subject correlation between liver and spleen uptake.

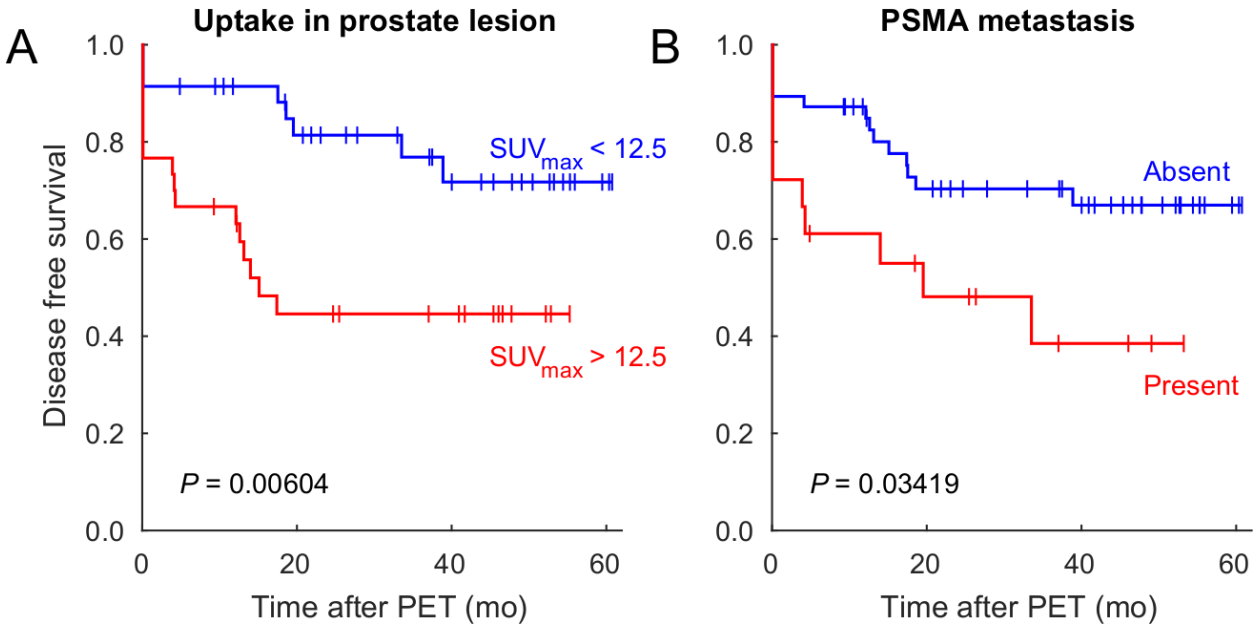


FIGURE 3. Kaplan Meier Analysis for disease free survival after prostatectomy according to the uptake of the primary lesion (A) (SUV_{max} on initial PET), and presence of metastatic disease on PET (B). Censored events are marked with a tick.

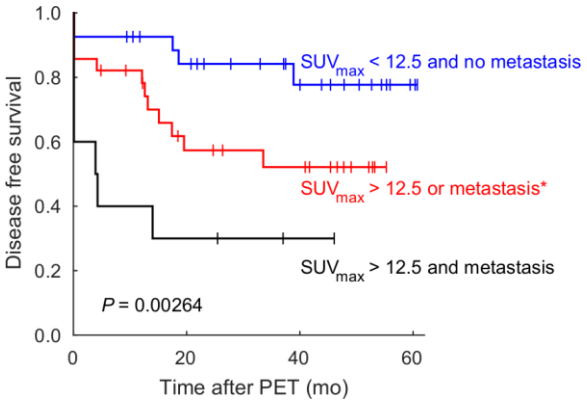


FIGURE 4. Kaplan Meier Analysis for disease free survival after prostatectomy as a function of uptake in primary cancer and presence of metastatic disease. Patient with both high uptake in the primary cancer and metastatic disease on PET had worse survival than patient who had no or only one risk factor.

*Exclusive disjunction.

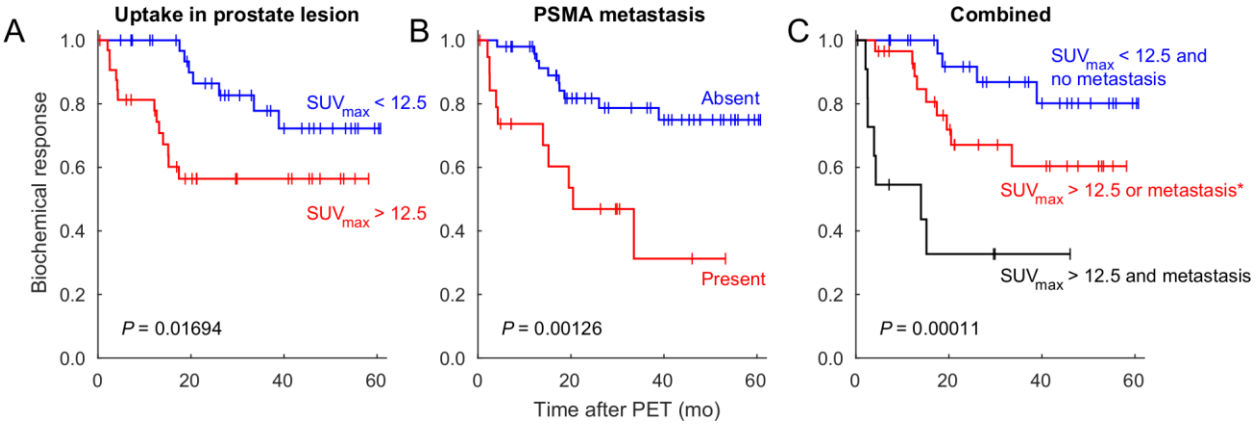
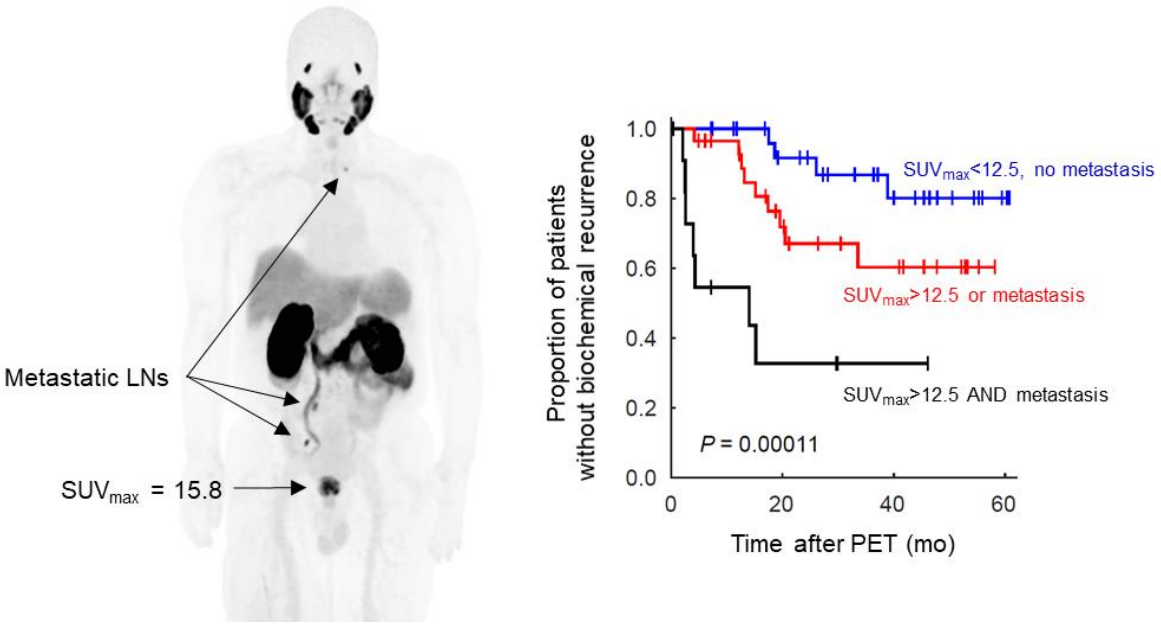


FIGURE 5. Proportion of patients without biochemical progression after initial treatment with or without adjuvant radiation therapy over time according to the uptake of the primary prostate lesion (A), presence of metastatic disease on PET (B), or combination of them (C). *Exclusive disjunction.



Graphical Abstract