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Original Article

European association of urology risk stratification predicts outcome in patients receiving PSMA-PET-planned salvage radiotherapy for biochemical recurrence following radical prostatectomy

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A B S T R A C T

Purpose: The European Association of Urology (EAU) proposed a risk stratification (high vs. low risk) for patients with biochemical recurrence (BR) following radical prostatectomy (RP). Here we investigated whether this stratification accurately predicts outcome, particularly in patients staged with PSMA-PET.
Methods: For this study, we used a retrospective database including 1222 PSMA-PET-staged prostate cancer patients who were treated with salvage radiotherapy (SRT) for BR, at 11 centers in 5 countries. Patients with lymph node metastases (pN1 or cN1) or unclear EAU risk group were excluded. The remaining cohort comprised 526 patients, including 132 low-risk and 394 high-risk patients.
Results: The median follow-up time after SRT was 31.0 months. The 3-year biochemical progression-free survival (BPFS) was 85.7 % in EAU low-risk versus 69.4 % in high-risk patients ($p = 0.002$). The 3-year metastasis-free survival (MFS) was 94.4 % in low-risk versus 87.6 % in high-risk patients ($p = 0.005$). The 3-year overall survival (OS) was 99.0 % in low-risk versus 99.6 % in high-risk patients ($p = 0.925$). In multivariate analysis, EAU risk group remained a statistically significant predictor of BPFS ($p = 0.003$, HR 2.022, 95 % CI 1.262–3.239) and MFS ($p = 0.013$, HR 2.986, 95 % CI 1.262–7.058).
Conclusion: Our data support the EAU risk group definition. EAU risk grouping for BCR reliably predicted outcome in patients staged lymph node-negative after RP and with PSMA-PET before SRT. To our knowledge, this is the first study validating the EAU risk grouping in patients treated with PSMA-PET-planned SRT.

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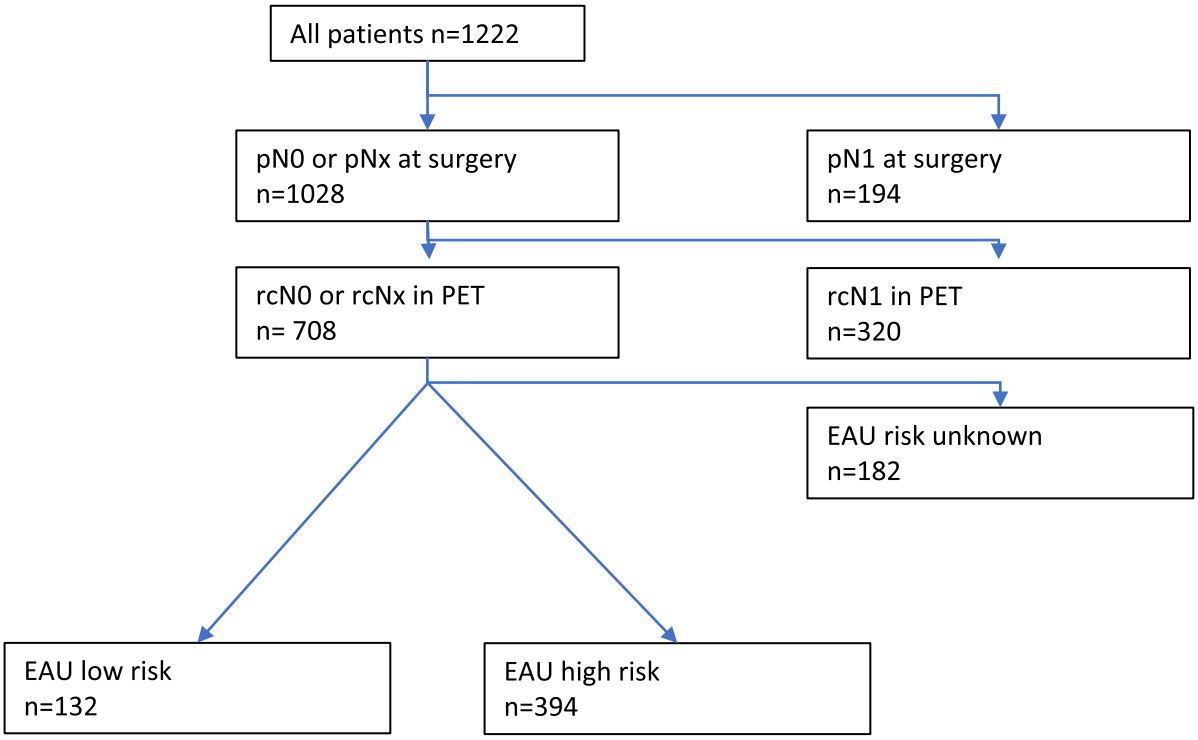


Fig. 1. Flow chart of patient selection.

Introduction

In cases of localized prostate cancer, both radical prostatectomy and external beam radiotherapy provide excellent long-term results; however, approximately 30–50 % of patients with intermediate- and high-risk prostate cancer experience biochemical recurrence (BR) within 10 years following treatment [1]. Salvage radiotherapy (SRT), with or without androgen deprivation (ADT), provides a potential cure for patients with BR after RP [2,3]. While SRT has a well-established effect on biochemical progression-free survival [4], its impacts on overall survival (OS) and cancer-specific survival (CSS) seem to be limited to a subgroup of high-risk patients [4,5]. In particular, patients with a PSA doubling time of <6 months [6] and/or a high ISUP grade group benefit from radiotherapy in terms of OS and CSS [7]. Therefore, the European Association of Urology (EAU) suggests that patients exhibiting BR after RP without pathological lymph node involvement (pN0) should be stratified into risk groups as follows: low-risk BCR defined by a prostate-specific antigen doubling time (PSA-DT) of > 12 months and a ISUP grade group of ≤ 3, or high-risk BCR after RP defined by a PSA-DT of ≤ 12 months or an ISUP grade group of ≥ 4 [7].

The validity of this risk stratification has been demonstrated by studies of retrospective cohorts [8,9]. However, the great majority of patients included in these cohorts were not staged using prostate-specific membrane antigen positron emission tomography (PSMA-PET) before SRT. PSMA-PET is a diagnostic imaging tool with a 75–100 % sensitivity and specificity for prostate cancer [10], which results in adaptation of radiotherapy planning in up to 60 % of cases [11]. High-risk BR patients reportedly harbor a higher rate of PSMA-PET-positive lesions, and a higher probability of positive lymph node detection during PSMA-PET staging before SRT [12]. Thus, it is unclear whether the prognostic value of EAU risk stratification for pN0 patients is also valid among patients without lymph node involvement detected on PSMA-PET.

In this retrospective study, we aimed to evaluate the usefulness of these recommendations, particularly in patients without pathological lymph node involvement at the time of RP, and who were staged as lymph node-negative with PSMA-PET before SRT (rcN0).

Material and methods

Patients

We retrospectively analyzed data obtained from eleven participating centers in Germany (n = 6), Italy (n = 1), Australia (n = 1), Switzerland (n = 2), and Cyprus (n = 1). Information was collected regarding all patients treated with PSMA-PET-based SRT for PSA recurrence or persistence after a radical prostatectomy between August 2013 and June 2020. Patients with distant metastases and patients who received ADT prior to the PSMA-PET scan were excluded from the database, resulting in a total patient number of 1222.

Next, we limited the cohort to patients without pathological lymph node metastases (pN0/x) and without lymph node detection on PSMA-PET images (rcN0), leaving 708 patients. Among these patients, 182 could not be categorized into an EAU risk group. Therefore, the final cohort comprised 526 patients, including 132 EAU low-risk and 394 EAU high-risk patients (Fig. 1). Patient characteristics are described in Table 1.

This study was approved by the local Ethics Committees of the participating centers.

PSMA-PET scans prior to SRT

Prior to SRT, all patients underwent PSMA-PET staging. The majority of PSMA-PET scans were conducted with ^{68}Ga-PSMA-11 (n = 455, 86.7 %) or ^{18}F-PSMA-1007 (n = 55, 10.5 %). Scans were performed according to institutional protocols, and interpreted locally by two experienced readers who followed international recommendations for assessments [13]. The PET protocols have been previously described [14].

Treatment and follow-up

Treatment and follow-up procedures have been described elsewhere

Table 1
Characteristics of patients treated with salvage radiotherapy for prostate cancer, grouped by EAU risk group.

Characteristic	Category	EAU Low-risk n = 132 (25.1 %)	EAU High-risk n = 394 (74.9 %)	P-value
Age, years		69.2 ± 7.1	68.5 ± 7.3	0.323
Initial PSA (ng/ml)	0–10	66 (50.0 %)	164 (41.68 %)	0.200
	10.1–20	26 (19.7 %)	93 (23.6 %)	
	>20	6 (4.5 %)	35 (8.9 %)	
	Unknown	34 (25.8 %)	102 (25.9 %)	
Initial pT stage	2	85 (64.4 %)	175 (44.4 %)	<0.001*
	3a	38 (28.8 %)	141 (35.8 %)	
	3b	4 (3.0 %)	65 (16.5 %)	
	4	1 (0.8 %)	1 (0.3 %)	
	unknown	4 (3.0 %)	12 (3.0 %)	
R stage	R0	81 (61.4 %)	224 (61.9 %)	0.908
	R1/x	51 (38.6 %)	150 (38.1 %)	
R Stage/PSA persistence post-RP	R0& no PSA persistence	61 (46.2 %)	175 (44.4 %)	0.881
	R0& PSA persistence	20 (15.2 %)	63 (16.0 %)	
	R1/x&no PSA persistence	38 (28.8 %)	113 (28.7 %)	
	R1/x&PSA persistence	13 (9.8 %)	32 (8.1 %)	
	unknown	0	11 (2.9 %)	
Time between surgery and BR	≤ 1 year	17 (12.8 %)	156 (39.6 %)	<0.001*
	> 1 year	114 (86.3 %)	221 (56.1 %)	
	unknown	1 (<1%)	17 (4.3 %)	
ISUP Grade Group	1 + 2	93 (70.5 %)	102 (25.9 %)	<0.001*
	3 + 4 + 5	39 (29.5 %)	209 (53.4 %)	
	unknown	0	3 (<1%)	
PSA-doubling	0–6	0	176 (44.7 %)	<0.001*
time (months)	6.1–12	0	134 (34.0 %)	
	>12	132 (100 %)	27 (6.9 %)	
	unknown	0	57 (14.5 %)	
PSA before	≤0.5	88 (66.7 %)	274 (69.5 %)	0.537
SRT (ng/ml)	>0.5	44 (33.3 %)	120 (30.5 %)	
Dose to fossa	≤70	67 (50.3 %)	231 (58.6 %)	0.071
(Gy)	>70	64 (48.2 %)	153 (38.9 %)	
	unknown	2 (1.5)	10 (2.5 %)	
SRT to pelvic lymph nodes	No	131 (99.2 %)	381 (96.7 %)	0.116
	Yes	1 (0.8 %)	13 (3.3 %)	
ADT	yes	29 (22.0 %)	91 (23.1 %)	0.813
	No	103 (78.0 %)	302 (76.6 %)	
	Unknown	0	1 (<1%)	
Duration of ADT	≤12 months	25 (21.6 %)2	47 (11.9 %)25	0.017*
	>12 monthsDuration not available	(0.2 %)2	(6.3 %)19	
		(0.2 %)	(4.8 %)	

in detail [14]. Target volumes and doses were prescribed at the discretion of the treatment center, and according to PSMA-PET findings. Eight of the eleven centers prescribed a boost in cases of local recurrences within the fossa. SRT protocols are listed in Supplemental Table S1.

Routine follow-ups included PSA testing. Patients with biological progression after SRT underwent either PSMA-PET (preferably) or conventional imaging to localize the recurrence. Supplemental Table S2 summarizes the follow-up procedures of the respective centers.

Statistical analysis

Statistical comparisons were performed using the *t*-test for normally distributed continuous data. Pearson's Chi square test was performed to test the independence of categorical variables.

Database retrieval was performed in January 2022. The primary study end-point was BPFS, defined as the time from completing the SRT to BR (defined as the nadir after SRT + 0.2 ng/ml); death from any cause; or the last date recorded alive, whichever came first. Secondary end-points were metastases-free survival (MFS) and overall survival (OS). MFS was defined as the interval between SRT initiation and the date of metastasis or death, whichever occurred first. OS was defined as the time from completing SRT to death from any cause or the last date recorded alive.

BPFS, OS, and MFS were estimated using the Kaplan–Meier method (log-rank test) and the Cox regression model. The cohort of EAU low-risk patients served as the reference group. Univariate analysis was performed, including the following covariates: age, initial PSA, initial pathological T stage (pT stage), resection status (R0-R1/x), International Society of Urological Pathology (ISUP) grade group of the surgery specimen, PSA doubling time, PSA serum values before SRT (PSA before SRT), maximal prescribed dose to parts of the prostatic fossa (i.e. boost to the local recurrence) or the complete prostatic fossa (DPF), and elective radiotherapy to lymph nodes. In multivariate analysis, the ISUP grade group and PSA-doubling time were omitted because they were the factors defining the EAU risk groups. Additionally, the factors included in multivariate analysis were restrained to those that achieved a p-value of < 0.1 in univariate analysis.

Hazard ratios (HRs) were considered significant when the corresponding 95 % confidence interval (95 % CI) excluded 1. All tests were two-sided, with 0.05 serving as the threshold of statistical significance. All calculations were performed using IBM SPSS Statistics Version 28.0 (IBM Corp., Armonk, NY, USA).

Results

The median follow-up time after SRT was 31.0 months (range:4.0–85.5 months). The mean age at diagnosis was 68.6 years (±7.2 years). Among the 526 patients included, 362 (68.8 %) started SRT at PSA levels of ≤ 0.5 ng/ml, and 298 (56.5 %) received a dose of ≤ 70 Gy to the prostatic fossa. Only a small minority of patients received

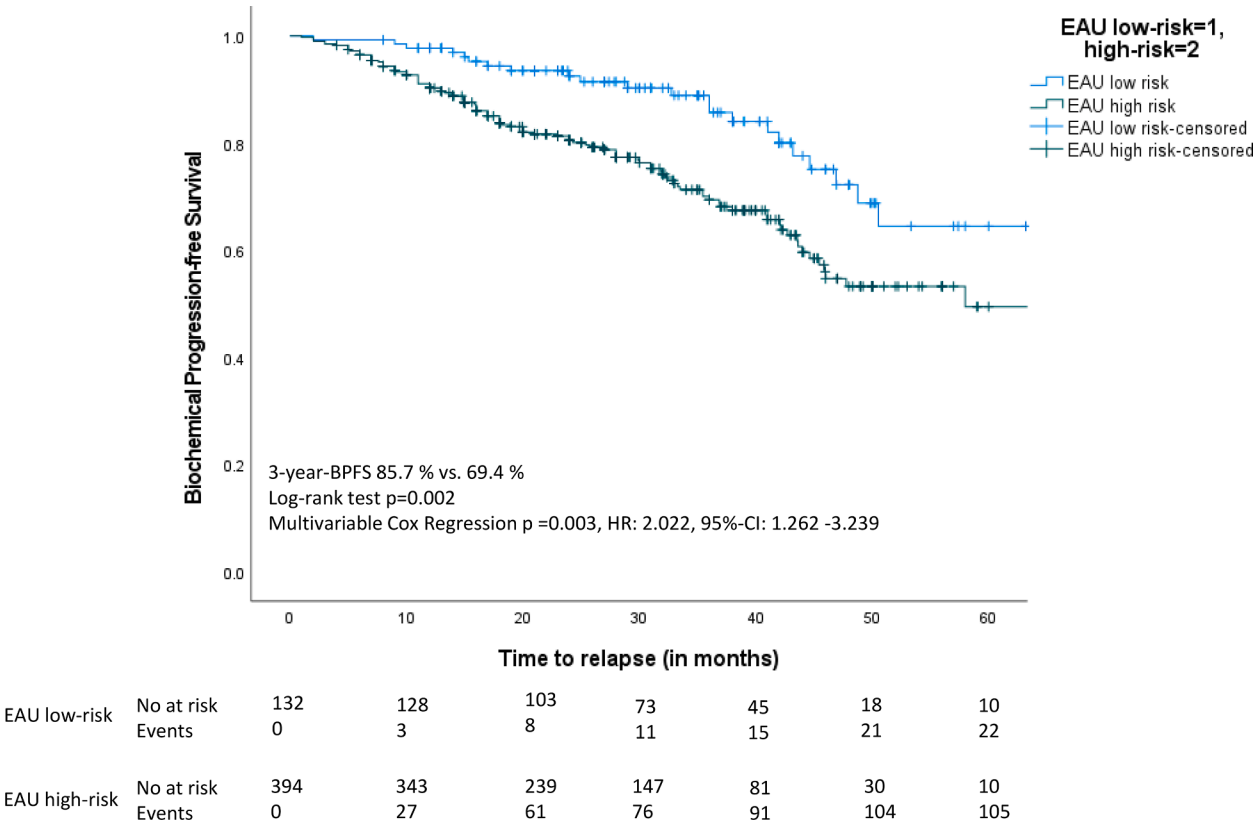
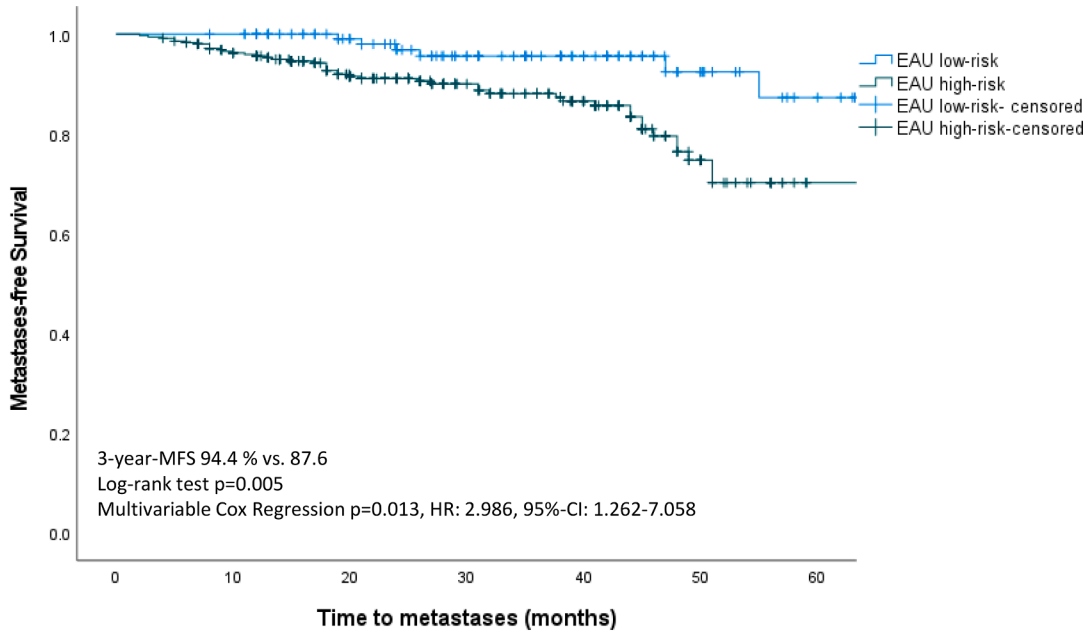


Fig. 2. Biochemical Progression-free Survival in patients with EAU low-risk BR compared to patients with high-risk BR.

Table 2
Univariate and multivariate Cox-regression results for factors that influence BPFS in the complete cohort*Significant difference; PET: positron emission tomography; PSA: prostate-specific antigen; SRT: salvage radiotherapy; pT: Size and extend of primary tumor in surgical specimen, R stage: degrees of microscopic or macroscopic residual tumor after resection, ISUP Grade Group: International Society of Urological Pathology Grade Group.

Factor	Category	Cox-Regression multivariate							
				95 % CI				95 % CI	
		p	HR	Lower	Upper	*p*	HR	Lower	Upper
EAU risk group	Low-risk	0.002*	1.000			0.003*	1.000		
	High-risk		2.048	1.301	3.221		2.022	1.262	3.239
Age (years)	continuous	<0.001*	1.050	1.023	1.078	0.002*	1.045	1.017	1.075
Initial PSA (ng/ml)	≤10	0.895	1.000						
	10.1–20	0.937	1.020	0.628	1.655				
	>20	0.492	1.246	0.665	2.335				
	unknown	0.627	.109	.730	1.686				
pT Stage	2	0.004*	1.000			0.028*	1.000		
	3a/3b/4	0.001	1.809	1.258	2.602	0.023*	1.551	1.063	2.263
	unknown	0.139	2.170	0.779	6.047	0.137	1.338	0.958	7.819
R stage	0	0.032*	1.000			0.008*	1.000		
	1/2/x		0.657	0.448	0.964		0.578	0.386	0.867
ISUP Grade Group	1 + 2	<0.001*	1.000						
	3–5		2.421	1.597	3.669				
PSA-doubling time (months)	≤6	0.288	1.000						
	6–12	0.573	0.875	0.551	1.390				
	>12	0.125	0.711	0.460	1.099				
	unknown	0.559	1.185	0.670	2.098				
PSA before SRT (ng/ml)	≤0.5	0.095	1.000			0.137	1.000		
	>0.5		1.363	0.947	1.962		1.338	0.912	1.965
RT dose (Gy)	≤70	0.052	1.000			0.056	1.000		
	>70		0.692	0.478	1.003		0.695	0.479	1.010
Elective RT to pelvic lymph nodes	No	0.379	1.000						
	Yes		1.565	0.576	4.252				
ADT	Yes	0.918	1.000						
	No	0.682	1.104	0.688	1.770				



EAU low-risk	No at risk	119	118	96	67	47	24	13
	Events	0	0	1	5	5	6	7
EAU high-risk	No at risk	353	314	225	141	101	39	13
	Events	0	13	26	30	35	44	46

Fig. 3. Metastases-free Survival in patients with EAU low-risk BR compared to patients with high-risk BR.

elective lymph node irradiation (n = 14, 2.7 %).

Our cohort included 132 EAU low-risk patients (25.1 %) and 394 EAU high-risk patients (74.9 %). pT3/4 stage was significantly more common among high-risk patients (52.5 % vs. 32.6 %, $p < 0.001$). Additionally, an interval of less than one year between surgery and BR was more common in EAU high-risk patients (39.6 % vs.12.8 %, $p < 0.001$). The rate of patients receiving ADT did not differ between the EAU low-risk and high-risk cohorts. However, the duration of ADT differed between these groups, with EAU high-risk patients being significantly more likely to receive ADT for > 12 months ($p = 0.017$). The groups did not differ in any of the remaining prognostic parameters, other than those defining the risk groups (Table 1).

EAU low-risk patients exhibited a significantly higher 3-year BPFS (85.7 %) than EAU high-risk patients (69.4 %), when compared by univariate Kaplan-Meier analysis ($p = 0.002$, Fig. 2). Univariate analysis also revealed that BPFS was significantly influenced by age; pT stage 2 vs. 3/4; R stage 0 vs. 1/x, and ISUP grade group 1 or 2 vs. 3–5. The influence of RT dose ≤ 70 Gy vs. > 70 Gy was borderline significant (Table 2).

Since prognostic factors were not equally distributed across the two groups, we conducted multivariate Cox-regression analysis to account for potential confounders other than those defining the risk groups. In this multivariate analysis, the difference in BPFS between EAU low-risk and high-risk patients remained statistically significant ($p = 0.003$, HR 2.022, 95 % CI 1.262–3.239). BPFS also remained significantly associated with age, pT stage 2 vs. 3a/b/4, and R stage (Table 2).

Kaplan-Meier analysis revealed that 3-year MFS was significantly higher in EAU low-risk patients compared to EAU high-risk patients (94.4 % vs. 87.6 %, $p = 0.005$, Fig. 3). Other factors that significantly influenced MFS in the univariate analysis included age; pT stage 2 vs. 3/4; ISUP grade group 1 or 2 vs. 3–5; and elective RT to pelvic lymph nodes (Table 3). In multivariate analysis, the EAU risk grouping was the strongest predictor of MFS ($p = 0.013$, HR 2.986, 95 % CI 1.262–7.058). Other factors that remained significant in multivariate analysis included pT stage 2 vs. 3/4, and R stage 0 vs. R1/2/x (Table 3).

OS did not differ between the EAU risk groups ($p = 0.925$). The 3-year OS rate was 99.0 % among low-risk patients, and 99.6 % among high-risk patients (Fig. 4). Cancer-specific survival was not calculated since no deaths caused by prostate cancer were recorded.

Discussion

In this study, we compared the outcomes of low-risk BR patients versus high-risk BR patients, stratified according to the EAU recommendations established in 2019 [7]. These recommendations were derived from a systematic review of data regarding the effects of SRT among patients with biochemical recurrence, in terms of MFS and OS, to establish which patients truly benefit from this treatment. Our present findings support the usefulness of the EAU risk classification in a cohort of lymph node-negative PET-staged patients who received SRT. BPFS and MFS were significantly superior in patients with low-risk BR compared to patients with high-risk BR.

Previous studies have demonstrated higher survival rates in patients with low-risk BR compared to high-risk BR. Tilki et al. evaluated a cohort of 1125 patients with BR, and found significantly higher rates MFS and CSS rates in low-risk patient subgroup. Their cohort included patients who underwent surgery between 1992 and 2006. Therefore, it can be assumed that the great majority of patients did not receive PSMA-PET staging before SRT, and in cases of biochemical recurrence following SRT [4].

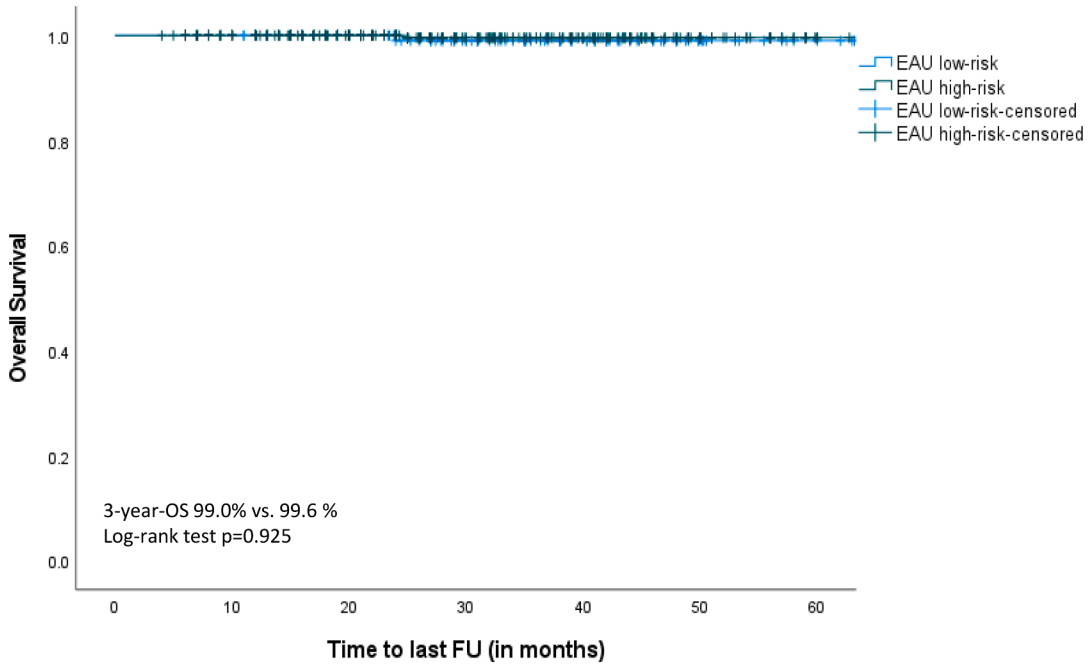
Similar results were obtained in a pooled analysis from ten European high-volume centers, including patients treated with RP between 1989 and 2020. OS and CSS rates were higher among patients with low-risk BR. However, a benefit from early SRT was only found among patients classified as EAU high-risk, not in those classified as low-risk. Notably, PSMA-PET was not conducted in the majority of patients included in that analysis [9].

Information derived from pre-SRT PSMA-PET could substantially

Table 3
Univariate and multivariate Cox-regression results for factors that influence MFS in the complete cohort.

Factor	Category	Cox-regression							
		univariate				multivariate			
				95 % CI				95 % CI	
		p	HR	Lower	Upper	*p*	HR	Lower	Upper
EAU risk group	Low-risk	0.006*	1.000			0.013*	1.000		
	High-risk		3.304	1.407	7.758		2.986	1.262	7.059
Age (years)	continuous	0.187	1.026	0.987	1.067				
Initial PSA (ng/ml)	≤10	0.574	1.000						
	10.1–20	0.818	0.920	0.454	1.864				
	>20	0.460	1.370	0.594	3.157				
	unknown	0.315	0.651	0.282	1.505				
pT Stage	2	0.042*	1.000			0.067	1.000		
	3a/3b/4	0.013*	2.076	1.169	3.685	0.024*	1.957	1.095	3.498
	unknown	0.407	2.354	0.312	17.783	0.328	2.813	0.354	22.350
R stage	0	0.071	1.000			0.047*	1.000		
	1/2/x		0.567	0.306	1.049		0.531	0.284	0.991
ISUP Grade Group	1 + 2	<0.001*	1.000						
	3–5		3.893	1.794	8.845				
PSA-doubling time (months)	≤6	0.095	1.000						
	6–12	0.801	1.092	0.550	2.168				
	>12	0.077	0.497	0.229	1.078				
	unknown	0.308	1.543	0.670	3.551				
PSA before SRT (ng/ml)	≤0.5	0.286	1.000						
	>0.5		1.370	0.769	2.442				
RT dose (Gy)	≤70	0.448	1.000						
	>70		0.801	0.452	1.420				
Elective RT to pelvic lymph nodes	No	0.033	1.000			0.152	1.000		
	Yes		3.606	1.112	11.696		2.394	0.725	7.912
ADT	Yes	0.893	1.000						
	No		0.953	0.463	1.955				

*Significant difference; PET: positron emission tomography; PSA: prostate-specific antigen; SRT: salvage radiotherapy; pT: Size and extend of primary tumor in surgical specimen, R stage: degrees of microscopic or macroscopic residual tumor after resection, ISUP Grade Group: International Society of Urological Pathology Grade Group.



EAU low-risk	No at risk	132	131	111	83	53	23	13
	Events	0	0	0	1	1	1	1
EAU high-risk	No at risk	394	367	284	184	119	55	22
	Events	0	0	0	1	1	1	1

Fig. 4. Overall Survival in patients with EAU low-risk BR compared to patients with high-risk BR.

impact a patient's classification and treatment recommendations [11,15], due to the higher sensitivity for detecting lymph node or distant metastases [16]. This can lead to adaptation of SRT treatment volumes—for example, with the inclusion of pelvic lymph nodes, or application of higher doses to the intraprostatic recurrence and involved lymph nodes. In some cases, SRT is not recommended due to metastatic disease [11]. Notably, it has not been established that PSMA-PET-planned radiotherapy has benefits in terms of OS, CSS, or MFS. However, the question whether PSMA-PET planed SRT actually improves patient outcome is currently under investigation. The randomized PSMA SRT trial (NCT03582774) compares SRT treatment with or without Ga-PSMA-PET in patients with BR after RP. The PSMA-PET procedure is standardized. SRT treatment however is at the discretion of the treating physician [15]. Another study investigates the effect of individualized PSMA-PET planned SRT comparing a standard cohort that dose not receive PET with a cohort that receives SRT with a standardized radiotherapy concept based on a pre-treatment PSMA-PET (NCT04794777) [17].

When comparing EAU risk groups, PSMA-PET staging is particularly important because positive PET results are more common among EAU high-risk patients [12]. Dong et al. performed a pooled analysis of two prospective cohort studies, and found that the PET-positive rate was 82 % among high-risk patients, compared to 49 % in low-risk patients. PSMA-PET revealed lymph node metastases in 50 % of the high-risk cohort vs. 30 % of the low-risk cohort, and distant bone metastases in approximately 20 % of patients in the high-risk cohort compared to roughly 10 % in the low-risk cohort [12]. These results highlight the importance of external validation of the EAU risk groups among patients with PSMA-PET staging, since the high-risk cohort most likely included a relevant percentage of patients with higher stages that were undertreated with SRT only.

In our patient cohort, all patients were staged using PSMA-PET, and patients with lymph node involvement and distant metastases were excluded to ensure that EAU high-risk and low-risk patients did not differ due to disease spread. Furthermore, we restricted the cohort to patients without initial lymph node metastasis, to obtain an even more homogenous patient cohort. The key finding of our study was that even in this selective cohort of patients, the EAU risk groups predicted BPFS and MFS, according to both univariate and multivariate analysis. In contrast to the findings by Tilki et al., we did not demonstrate a difference in cancer-specific survival, as no deaths caused by prostate cancer occurred during our study period [8]. This was probably due to the shorter follow-up time, and the effective salvage methods available for prostate cancer. Our cohort was not suitable for obtaining valuable results concerning OS, since the life expectancy of the included patients was clearly higher than the median follow-up time of 31 months. Only two deaths occurred in our cohort. The MFS rates were comparable between our study and the study of Tilki et al. This might initially seem surprising, considering that in contrast to in their study, all of our patients received salvage treatment and had a disease confined to the prostatic fossa [8]. On the other hand, in cases of biochemical recurrence, the patients in our cohort received staging, most often with PSMA-PET. Therefore, we can assume that we had higher sensitivity for the detection of metastases in our cohort, thereby elevating the rate of metastases in follow-up. In our cohort, approximately 50 % of patients had an initial pT3/4 tumor, and 40 % were staged as R1/x. Both conditions were predictors of worse MFS in multivariate analysis. Furthermore, less than 25 % of patients received ADT, which is a lower rate than one would expect, particularly in the high-risk collective. Moreover, only 14 patients in the whole cohort received elective pelvic lymph node irradiation. The randomised, controlled SPPORT trial found a significant reduction of biochemical progression-free survival in patients receiving SRT including elective nodal irradiation plus ADT compared with those receiving SRT to the prostatic bed (with or without ADT) only [18]. This approach might be useful in order to further improve the outcome of high-risk patients with biochemical recurrence. Other instruments that

might help further stratify patients within the EAU high risk group into patients that benefit from treatment escalation is the are genomic classifiers, such as the Decipher test. The Decipher test is based on 22 RNA biomarkers and has been externally validated in numerous settings in the treatment of prostate cancer. Among others, it has been shown to aid decision-making conserning the addition of ADT in patients with BR after RP. While The EAU risk stratification is an easy to handle clinical tool, genomic classifier test are commercial gene tests and have not approved by the relevant authorities in the majority of countries yet. However, the addition these tests to clinical data should be further investigated.

Certain patients with low-risk biochemical recurrence might not have to be treated at all (i.e. elderly or frail patients). As we do not have a cohort of patients that did not undergo radiotherapy despite of BR, however, our study cannot help to shed light on this question.

One strength of our study is the highly selective cohort of patients. We also must acknowledge certain limitations. First and foremost, the retrospective study design harbors typical weaknesses, such as the unequal distribution of risk factors between the groups, and a potential for selection bias. Moreover, due to the multi-centric design, the standard procedures for PSMA-PET imaging and for SRT, including dose prescription and treatment volume definition, were very heterogenous. Another limitation of this study is the short follow-up time, which prevented analysis of the predictive value of EAU risk grouping on cancer-specific survival and OS, due to the low number of events observed within such a short time span. However, since PSMA-PET staging has only recently become widely available, we were not able to analyze a longer follow-up.

Conclusion

EAU risk grouping for BCR seems to reliably predict BPFS and MFS among patients without lymph node or distant metastases. To our knowledge, this is the first study to validate EAU risk grouping among patients treated with PSMA-PET-planned SRT. Our data support the use of EAU risk stratification in routine clinical practice when treating patients with PSMA-PET-planned SRT. Further prospective studies with longer follow-up are needed to confirm these results.

CRediT authorship contribution statement

Sophia Scharl: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Constantinos Zamboglou:** Writing – review & editing, Data curation. **Iosif Strouthos:** Data curation. **Andrea Farolfi:** Writing – review & editing, Data curation. **Francesca Serani:** Writing – review & editing, Data curation. **Stefan A. Koerber:** Writing – review & editing, Data curation. **Jürgen Debus:** Data curation. **Jan C. Peeken:** Data curation. **Marco M.E. Vogel:** Data curation. **Stephanie G. C. Kroeze:** Data curation. **Matthias Guckenberger:** Writing – review & editing, Data curation. **Manuel Krafcsik:** Writing – review & editing, Data curation, Conceptualization. **George Hruby:** Writing – review & editing, Data curation. **Louise Emmett:** Writing – review & editing, Data curation. **Nina-Sophie Schmidt-Hegemann:** Writing – review & editing, Data curation. **Christian Trapp:** Writing – review & editing, Data curation. **Simon K.B. Spohn:** Data curation. **Christoph Henkenberens:** Data curation. **Benjamin Mayer:** Writing – review & editing, Methodology, Data curation. **Mohamed Shelan:** Writing – review & editing, Data curation. **Daniel M. Aebersold:** Data curation. **Reinhard Thamm:** Methodology, Data curation. **Thomas Wiegel:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2024.110215.

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Further reading

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