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Mortality Risk for Patients with Biopsy Gleason Grade Group 1 Prostate Cancer

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Abstract

Background and objective: We investigated the association of clinical factors at presentation with the presence of unsampled high-risk prostate cancer (PC) and PC-specific mortality (PCSM) and all-cause mortality (ACM) following radical prostatectomy in patients with biopsy Gleason Grade Group (GGG) 1 PC.

Methods: The study population comprised 10 228 patients treated for GGG 1 PC diagnosed via transrectal ultrasound (TRUS)-guided systematic biopsy (SBx; n = 9248) or combined biopsy (CBx; SBx + TRUS/magnetic resonance image [MRI] fusion biopsy; n = 980) from a cohort study at a university hospital in Hamburg, Germany. We used logistic, Fine and Grays, and Cox multivariable regression methods to calculate the adjusted odds ratio (aOR) of adverse pathology and adjusted hazard ratios (aHRs) for early prostate-specific antigen (PSA) failure (≤18 mo), PCSM, and ACM in relation to each clinical factor.

Key findings and limitations: Irrespective of biopsy approach, percent positive biopsies (PPB) >50% and PSA >20 ng/ml were significantly associated with higher risk of adverse pathology (SBx: aOR 1.71 and 3.49; CBx: aOR 1.81 and 2.82, respectively) and early PSA failure (SBx: aHR 1.54 and 4.37; CBx: aHR 2.88 and 7.81, respectively). PPB >50% and PSA >20 ng/ml were also associated with higher risk of PCSM (aHRs 2.56 and 3.71) and ACM (aHRs 1.47 and 2.00) in the SBx group (all $p \leq 0.04$). The study is limited by the single-institution cohort design.

Conclusion and clinical implication: Maintaining the "cancer" classification for patients with GGG 1 and either PPB >50% or PSA>20 ng/ml and considering rebiopsy to identify unsampled high-grade disease may minimize the risk of mortality for this subgroup.

Patient summary: For patients undergoing non-targeted prostate biopsy, approximately 1 in 12 with a biopsy result of grade group 1 prostate cancer may have more aggressive cancer than the result suggests. A very high PSA (prostate-specific antigen) level (>20 ng/ml) or the presence of grade group 1 cancer in more than 50% of the biopsy samples can identify patients at risk.

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1. Introduction

Whether or not biopsy Gleason grade 3 + 3 or Gleason grade group (GGG) 1 [1] findings at prostate biopsy should be called "cancer" remains controversial. This question arose after results from the ProtecT trial were published [2]. Specifically, approximately three-quarters of the patients enrolled in ProtecT had GGG 1 disease and only 3.1% of patients had died from prostate cancer (PC) at median follow-up of 15 yr despite initially being randomized to active monitoring (AM) versus radical treatment with radical prostatectomy (RP) or radiotherapy (RT) and androgen deprivation therapy (ADT). However, given that approximately 61% of the patients in ProtecT who were randomized to AM had eventually undergone radical treatment by 15 yr and had a twofold higher risk of metastatic disease (9.4% with AM vs 4.7% with RT + ADT vs 5.0% with RP), a subgroup of patients in ProtecT might have benefited from earlier radical treatment despite having biopsy GGG 1 PC.

The contemporary combined biopsy (CBx) approach involves transrectal ultrasound (TRUS)-guided systematic biopsy (SBx) plus multiparametric magnetic resonance imaging (mpMRI)/TRUS fusion-guided biopsy. Data are lacking on the ability of clinical parameters at presentation to predict the presence of occult high-risk PC in patients with a GGG 1 diagnosis on CBx. It remains unknown whether this information can identify patients with GGG 1 who are at higher risk of PC-specific mortality (PCSM) and all-cause mortality (ACM).

Given the potential for undergrading due to biopsy sampling error [3] and understaging due to the spatial resolution limits of the imaging modalities currently available [4], we evaluated the impact of clinical parameters [5–8] at presentation on the odds of adverse pathology at RP and of early prostate-specific antigen (PSA) failure for patients diagnosed with clinically localized GGG 1 PC via SBx or contemporary CBx. We also evaluated how prognostic factors at presentation impacted PCSM and ACM risk for patients with longer follow-up in the SBx group.

2. Patients and methods

2.1. Patient population, staging, and treatment

Between February 28, 1992, and September 7, 2023, 10 228 consecutive patients underwent RP for cT1–2N0M0, biopsy GGG 1 adenocarcinoma of the prostate at University Hospital Hamburg-Eppendorf and comprised the primary study cohort. Patients with PSA >20 ng/ml underwent staging via computed tomography or MRI of the pelvis and a bone scan and, more recently, positron emission tomography. Of these patients, 9248 underwent a 12-core TRUS-guided SBx. The median age was 63 yr (interquartile range [IQR] 58–67). A secondary cohort comprised an additional 980 patients (median age 62 yr, IQR 57–67) underwent RP between July 2, 2013, and September 7, 2023 for a diagnosis of biopsy GGG 1 PC; in nearly all of these cases, diagnosis was in accordance with the 2014 International Society of Urological Pathology (ISUP) guidelines on Gleason grading [1] and patients underwent CBx. Use of mpMRI to guide biopsy became standard in 2018 after publication of results from the PRECISION study [3]. Some patients underwent CBx before 2018 and were included in the secondary study cohort. RP specimens were reviewed by a pathologist with expertise in genitourinary pathology. In accordance with federal and institutional guidelines, patients signed an institutional review board–approved, protocol-specific informed consent form permitting prospective collection of deidentified data at baseline and follow-up. These data were entered into a secure, password-protected database for outcome analysis.

2.2. Follow-up

Follow-up started on the day of RP surgery and ended on the date of last follow-up or the date of death, whichever occurred first. The database was last updated on November 30, 2023. During follow-up, patients had a PSA test and rectal examination and were typically seen by a urologist every 3 mo for 1 yr, every 6 mo for an additional 4 yr, and annually thereafter.

2.3. Outcome measures

The outcome measures included adverse pathology at RP, with categories defined as pathological GGG 4 or 5, pT3b or pT4, or positive pelvic lymph nodes (pN1) [9]. Patients with GGG 2 or 3 and tertiary grade 5 were categorized as GGG 4 or 5. ACM was measured from the date of RP to death from any cause, censored at the date of last follow-up for surviving patients; PCSM was defined analogously, but death from causes other than to PC was considered as a competing risk. Documentation of castrate-resistant metastatic PC, with prior imaging identifying metastatic disease, and a rising PSA level with testosterone <20 ng/dl before death were required for assignment of PCSM as the cause of death. Time to PSA failure was defined from the date of RP until post-RP PSA exceeded 0.1 ng/ml. We used 0.1 ng/ml as opposed to the conventional cutoff of 0.2 ng/ml because the American Urological Association guidelines recommend that patients with detectable PSA after RP who are at high risk of clinical progression may be offered salvage RT when their PSA is <0.2 ng/ml [10]. Thus, patients with adverse pathology at RP could have started salvage therapy before their PSA reached 0.2 ng/ml.

2.4. Statistical analysis

The statistical analysis plan is provided in the Supplementary material.

3. Results

3.1. Prognostic factors for adverse pathology

Of the 10 228 patients in the overall cohort, 955/9248 (10.33%) in the SBx group and 77/980 (7.86%) in the CBx group had adverse pathology at RP (Table 1). Patients with significantly higher adjusted odds of adverse pathology irrespective of biopsy approach were more likely to be older (adjusted odds ratio [aOR] 1.05 for SBx, 1.09 for CBx) and to have percent positive biopsies (PPB) >50% (aOR 1.71 for

Table 1 – Adjusted odds ratios for adverse pathology at RP for 10 228 patients diagnosed with Gleason grade group 1 prostate cancer using a TRUS or combined biopsy approach

Clinical Factor	TRUS biopsy (n = 9248)				Combined biopsy (n = 980)			
	Adverse pathology		aOR (95% CI)	p value	Adverse pathology		aOR (95% CI)	p value
	Yes (n = 955)	No (n = 8293)			Yes (n = 77)	No (n = 903)		
Median age at RP, yr (IQR)	65 (60–69)	63 (57–67)	1.05 (1.04–1.07)	<0.001	66 (61–69)	62 (57–66)	1.09 (1.04–1.13)	<0.001
Median year of RP (IQR)	2013 (2010–2016)	2011 (2007–2014)	1.05 (1.03–1.06)	<0.001	2020 (2017–2022)	2019 (2017–2021)	1.01(0.91–1.11)	0.93
PSA category, n (%)								
<4 ng/ml	27 (2.83%)	762 (9.19%)	0.65 (0.43–0.98)	0.04	0	50 (5.54%)	0.20 (0.01–3.29)	0.26
≥4–10 ng/ml	460 (48.17%)	5371 (64.77%)	Reference		38 (49.35%)	545 (60.35%)	Reference	
>10–20 ng/ml	307 (32.15%)	1784 (21.51%)	1.54 (1.31–1.81)	<0.001	27 (35.06%)	262 (29.01%)	1.23 (0.72–2.11)	0.46
>20 ng/ml	161 (16.86%)	376 (4.53%)	3.49 (2.80–4.35)	<0.001	12 (15.58%)	46 (5.09%)	2.82 (1.33–5.99)	0.007
PSA density category, n (%)								
≤0.15 ng/ml cm^3	117 (18.53%)	3310 (39.91%)	Reference		15 (19.48%)	332 (36.77%)	Reference	
>0.15 ng/ml cm^3	778 (81.47%)	4983 (60.09%)	1.97 (1.63–2.39)	<0.001	62 (80.52%)	571 (63.23%)	1.92 (1.03–3.55)	0.04
PPB category, n (%)								
≤50%	772 (80.84%)	7385 (89.05%)	Reference		59 (76.62%)	781 (86.49%)	Reference	
>50%	183 (19.16%)	908 (10.95%)	1.71 (1.42–2.05)	<0.001	18 (23.38%)	122 (13.51%)	1.81 (1.01–3.23)	0.046
cT stage, n (%)								
cT1c	816 (85.45%)	7503 (90.47%)	Reference		65 (84.42%)	836 (92.58%)	Reference	
cT2	139 (14.55%)	790 (9.53%)	1.59 [1.30–1.96] <0.001		12 (15.58%)	67 (7.42%)	2.50 [1.26–4.96] 0.009	

TRUS = transrectal ultrasound; aOR = adjusted odds ratio; CI = confidence interval; RP = radical prostatectomy; IQR = interquartile range; PSA = prostate-specific antigen; PPB = percent positive biopsies.

Table 2 – Proportion of patients with adverse pathology stratified by the number of prognostic factors and biopsy approach

Prognostic factor	Proportion of patients with adverse pathology [a]		p value
	TRUS-guided biopsy (n = 9248) [b]	Combined biopsy (n = 980) [c]	
PSA >20 ng/ml and PPB >50%	48.84% (42/86)	44.44% (4/9)	
PSA >20 ng/ml or PPB >50%	17.86% (260/1456)	12.22% (22/180)	
PSA ≤20 ng/ml and PPB ≤50%	8.47% (653/7706)	6.45% (51/791)	
Total	10.33% (955/9248)	7.86% (77/980)	<0.001

TRUS = transrectal ultrasound guided; PSA = prostate-specific antigen; PPB = percent positive biopsies; GGG = Gleason grade group.
[a] Percentages include patients who had one or more adverse pathologic factors.
[b] 7.48% of 9248 patients had pathological GGG 4 or 5, 5.22% had pT3b or pT4, and 1.77% had pN1.
[c] 5.71% of 980 patients had pathological GGG 4 or 5, 3.14% had pT3b or pT4, and 0.10% had pN1.

SBx, 1.81 for CBx), PSA >20 ng/ml (aOR 3.49 for SBx, 2.82 for CBx), cT2 disease (adjusted odds ratio [aOR] 1.59 for SBx, 2.50 for CBx) ,or PSA density >0.15 ng/ml/cm^3 (aOR 1.97 for SBx, 1.92 for CBx). Patients in the CBx group had a significantly lower risk of adverse pathology at RP (7.86% vs 10.33%; p < 0.001; Table 2).

3.2. aHRs for early PSA failure, PCSM, and ACM

In the SBx group (n = 9248), 591 patients (6.39%) had died at median follow-up of 7.11 yr (IQR 4.01–11.04) and 53 (8.97%) of these deaths were from PC. Among the 9248 patients, 9129 had follow-up of at least 1 mo and 362 PSA failures were observed. Results in Table 3 show that PPB >50% and PSA >20 ng/ml were significantly associated with higher risk of PCSM (aHR 2.56 for PPB >50%, 3.71 for PSA >20 ng/ml) and ACM (aHR 1.47 for PPB >50%, 2.00 for PSA >20 ng/ml; all p ≤0.003).

In the CBx group (n = 980), at median follow-up of 3.03 yr (IQR 1.18–4.97), 19 (2.33%) of 815 patients with follow-up of at least 1 mo had experienced PSA failure. Both PPB >50% and PSA >20 ng/ml were significantly associated with higher risk of early PSA failure irrespective of biopsy approach (SBx: aHR 1.54 for PPB >50% and 4.37 for PSA >20 ng/ml; CBx: aHR 2.88 for PPB >50% and 7.81 for PSA >20 ng/ml), as shown in Table 4 (all $p \leq 0.04$).

3.3. Adjusted PCSM and ACM estimates

In the SBx group (n = 9248), patients with PPB >50% or/and PSA >20 ng/ml had significantly higher adjusted PCSM ($p \leq 0.002$; Fig. 1A) and ACM ($p \leq 0.012$; Fig. 1B) estimates than patients without these clinical factors. The 8-yr adjusted PCSAM point estimates were 6.80% (95% CI 1.10–20.15%), 0.87% (95% CI 0.40–1.68%), and 0.32% (95% CI 0.18–0.53%) for patients with both factors, one factor, and no factors, respectively. The corresponding ACM estimates were 8.49% (95% CI 3.73–18.68%), 6.82% (95% CI 5.31–8.73%), and 4.64% (95% CI 4.09–5.26%).

4. Discussion

We found that patients with GGG 1 PC diagnosed via contemporary CBx and either PPB >50% or PSA >20 ng/ml had significantly higher adjusted odds of adverse pathology at RP and higher risk of early PSA failure. Moreover, in the SBx group, the adjusted risk for both PCSM and ACM was higher for patients with one or both clinical factors. Given

Table 3 – Adjusted hazard ratios for PCSM and ACM for the 9248 patients who underwent TRUS-guided biopsy

Parameter	Patients	PCSM			ACM		
		Events	aHR (95% CI)	p value	Events	aHR (95% CI)	*p* value
Age at RP	9248 [a]	53 [a]	0.99 (0.94–1.03)	0.55	591	1.08 (1.06–1.10)	<0.001
Year of RP	9248 [a]	53 [a]	0.96 (0.91–1.01)	0.08	591	0.98 (0.97–0.999)	0.04
PSA							
<4 ng/ml	789	7	1.58 (0.65–3.83)	0.31	59	1.04 (0.78–1.39)	0.77
≥4–10 ng/ml	5831	26	1.00 (reference)		339	1.00 (reference)	
>10–20 ng/ml	2091	10	1.03 (0.48–2.21)	0.93	138	1.20 (0.97–1.49)	0.09
>20 ng/ml	537	10	3.71 (1.70–8.11)	0.001	55	2.00 (1.48–2.72)	<0.001
PSA density							
≤0.15 ng/ml/cm^3	3487	19	1.00 (reference)		253	1.00 (reference)	
>0.15 ng/ml/cm^3	5761	34	1.13 (0.59–2.19)	0.71	338	0.94 (0.77–1.14)	0.51
PPB							
≤50%	8157	38	1.00 (reference)		501	1.00 (reference)	
>50%	1091	15	2.56 (1.36–4.79)	0.003	90	1.47 (1.17–1.85)	<0.001
cT stage							
cT1c	8319	40	1.00 (reference)		503	1.00 (reference)	
cT2	929	13	1.74 (0.86–3.50)	0.12	88	1.20 (0.95–1.52)	0.13

TRUS = transrectal ultrasound; PCSM = prostate cancer–specific mortality; ACM = all-cause mortality; aHR = adjusted hazard ratio; RP = radical prostatectomy; CI = confidence interval; PSA = prostate-specific antigen; PPB = percent positive biopsies.
[a] The number of patients and number of events represent the total sample size and total event rate given that these two covariates are continuous and include the entire patient population.

Table 4 – Adjusted hazard ratios for early PSA failure for patients who underwent combined or TRUS biopsy with minimum follow-up of 1 mo

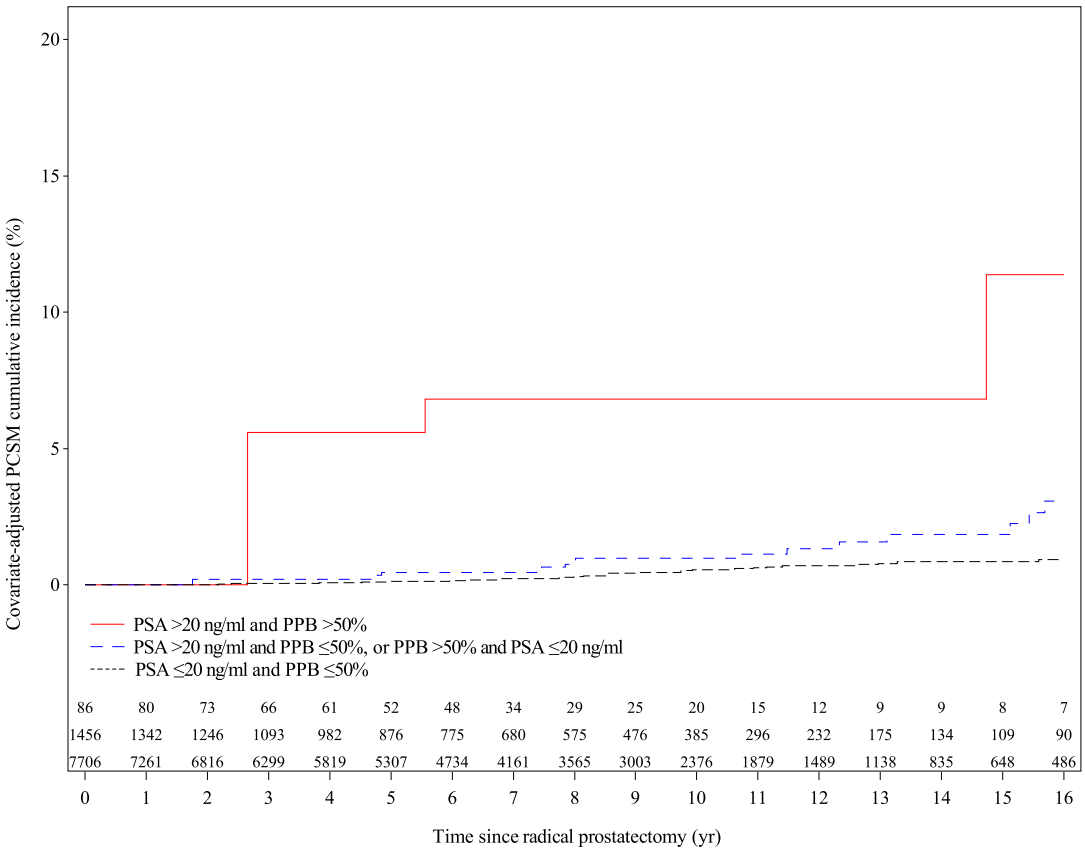
Parameter	TRUS biopsy (*n* = 9129)				Combined biopsy (*n* = 815)			
	Patients	Early PSA failure			Patients	Early PSA failure		
		Events	aHR (95% CI)	*p* value		Events	aHR (95% CI)	*p* value
Age at RP	9129 [a]	362 [a]	1.02 (1.00–1.03)	0.05	815 [a]	19 [a]	0.99 (0.92–1.06)	0.78
Year of RP	9129 [a]	362 [a]	1.01 (0.99–1.03)	0.18	815 [a]	19 [a]	0.81 (0.66–0.99)	0.04
PSA level								
<4 ng/ml	780	9	0.63 (0.32–1.26)	0.19	46	0	0.54 (0.03–11.65)	0.70
≥4–10 ng/ml	5754	145	1.00 (reference)		475	7	1.00 (reference)	
>10–20 ng/ml	2070	139	2.29 (1.78–2.94)	<0.001	246	8	2.37 (0.79–7.06)	0.12
>20 ng/ml	525	69	4.37 (3.20–5.96)	<0.001	48	4	7.81 (2.05–29.74)	0.003
PSA density								
≤0.15 ng/ml/cm^3	3449	61	1.00 (reference)		286	5	1.00 (reference)	
>0.15 ng/ml/cm^3	5680	301	1.77 (1.29–2.43)	<0.001	529	14	0.68 (0.22–2.08)	0.50
PPB								
≤50%	8058	296	1.00 (reference)		704	14	1.00 (reference)	
>50%	1071	66	1.54 (1.18–2.01)	0.002	111	5	2.88 (1.04–7.97)	0.04
cT stage								
cT1c	8209	317	1.00 (reference)		747	17	1.00 (reference)	
cT2	920	45	1.23 (0.90–1.69)	0.20	68	2	1.89 (0.47–7.57)	0.37

TRUS = transrectal ultrasound; aHR = adjusted hazard ratio; RP = radical prostatectomy; CI = confidence interval; PSA = prostate-specific antigen; PPB = percent positive biopsies
[a] The number of patients and number of events represent the total sample size and total event rate given that these two covariates are continuous and include the entire patient population.

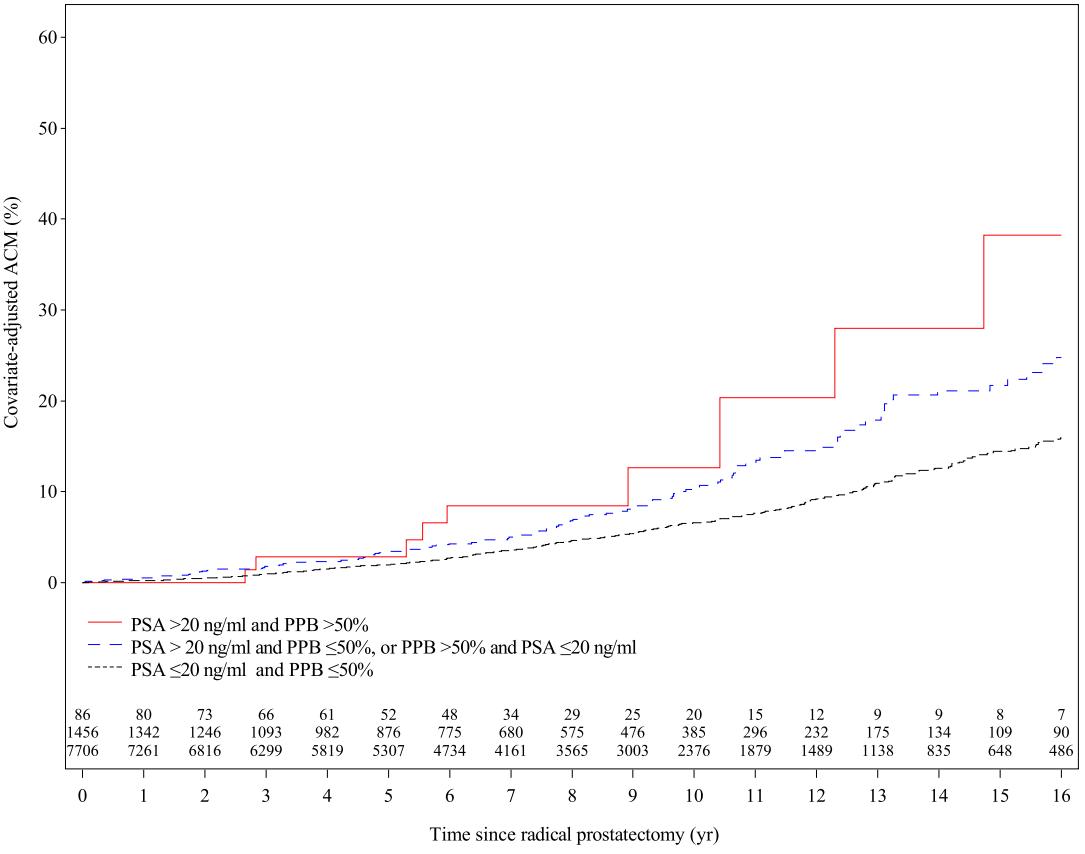
the significant association between PPB >50% and PSA >20 ng/ml and higher adjusted odds for adverse pathology, early PSA failure, and mortality risk, this information could be used to identify patients with GGG 1 who might harbor unsampled higher-grade clinically significant PC. It is possible that if results from the ProtecT trial [2] had been stratified according to the presence of one or more of these clinical factors, higher PCSM rates might have been observed. Specifically, while it has been shown that biopsy GGG1 PC has limited potential for metastasis to the pelvic lymph nodes [11], clinical factors at the time of diagnostic biopsy appear to be able to identify patients who are likely to harbor unsampled higher-grade and higher-stage cancer that confer long-term risk of shorter survival [12]. Therefore, for patients with biopsy GGG 1 PC and either PSA >20 ng/ml or PPB >50%, further evaluation with germline testing and/or molecular classifiers [13] could be considered to better assess the likelihood of unsampled high-grade disease to inform decisions on whether to consider a systematic rebiopsy and to obtain more samples from MRI-visible lesions with a Prostate Imaging-Reporting and Data System score of 3–5.

Fig. 1 – (A) Cumulative incidence estimates of prostate cancer-specific mortality (PCSM) and (B) Kaplan Meier estimates of overall survival or all-cause mortality (ACM) for the 9248 patients diagnosed via transrectal ultrasound-guided prostate biopsy stratified by prostate-specific antigen (PSA; threshold >20 ng/ml) and percent positive biopsy (PPB; threshold >50%). The three rows of numbers below the *x*-axis show the number of patients at risk at that time point for each patient subgroup defined in the legend. The *p* values for pairwise comparisons were as follows. PCSM: both factors versus either factor, $p = 0.035$; both factors versus neither factor, $p < 0.001$; either factor versus neither factor, $p < 0.001$. ACM: both factors versus either factor, $p = 0.283$; both factors versus neither factor, $p = 0.012$; either factor versus neither factor, $p < 0.001$.

A


Covariate-adjusted PCSM cumulative incidence (%)
20
15
10
5
0
PSA >20 ng/ml and PPB >50%
PSA >20 ng/ml and PPB ≤50%, or PPB >50% and PSA ≤20 ng/ml
PSA ≤20 ng/ml and PPB ≤50%
86 80 73 66 61 52 48 34 29 25 20 15 12 9 9 8 7
1456 1342 1246 1093 982 876 775 680 575 476 385 296 232 175 134 109 90
7706 7261 6816 6299 5819 5307 4734 4161 3565 3003 2376 1879 1489 1138 835 648 486
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Time since radical prostatectomy (yr)

B


Covariate-adjusted ACM (%)
60
50
40
30
20
10
0
PSA >20 ng/ml and PPB >50%
PSA > 20 ng/ml and PPB ≤50%, or PPB >50% and PSA ≤20 ng/ml
PSA ≤20 ng/ml and PPB ≤50%
86 80 73 66 61 52 48 34 29 25 20 15 12 9 9 8 7
1456 1342 1246 1093 982 876 775 680 575 476 385 296 232 175 134 109 90
7706 7261 6816 6299 5819 5307 4734 4161 3565 3003 2376 1879 1489 1138 835 648 486
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Time since radical prostatectomy (yr)

A few points warrant further discussion. First, approximately 30%, 18%, and 7% of patients diagnosed via a contemporary TRUS-guided, TRUS/MRI fusion-guided, or CBx approach, respectively, harbor unsampled higher-grade disease [3]. Therefore, many physicians currently use a CBx approach. A study investigating whether additional information can obviate the need for TRUS-guided biopsy in addition to MRI-targeted biopsy is under way [14]. Given the significant association between adverse pathology and either PPB >50% or PSA >20 ng/ml in the CBx group, identification of patients more likely to have adverse pathology at RP may be possible using these parameters. Second, while the actuarial PCSM rates at 8 yr were modest (0.87% for patients with one factor and 6.80% for patients with both factors), these outcomes follow early intervention with RP and might have been higher if the biopsy GGG 1 result had not been called "cancer" and treatment had been delayed. Specifically, categorizing a GGG 1 result as benign could delay the time to a cancer diagnosis and intervention. In addition, only 6.4% of patients had died from any cause at median follow-up of 7.11 yr. Therefore, these 8-yr PCSM estimates apply to patients with short life expectancy. Of note, as shown in Figure 1B, median life expectancy had not been reached by the end of the follow-up period of 16 yr. Therefore, for healthy patients with long life expectancy ($\geq$15 yr), our actuarial PCSM rates may underestimate the true rates.

Finally, to assess long-term mortality risk, we evaluated patients in the SBx group who had longer follow-up given the CBx technique has only been in routine use for 5 yr. Undergrading can occur in approximately 30.2% of patients diagnosed via SBx, compared to 6.7% for diagnosis via CBx [3], so CBx could have identified GGG >1 in some patients in the primary study cohort, who would thus have been excluded. This means that our PCSM and ACM results may have overestimated the actual mortality risks had a CBx approach been used, as reflected in the 2.47% lower incidence of adverse pathology at RP in the CBx group in comparison to the SBx group (Table 2). In addition to possible overestimation of mortality risk because of SBx undergrading, there is also potential for underestimation of the mortality risk for patients with occult high-risk PC whose treatment was delayed and/or whose life expectancy exceeded the 7.11-yr median follow-up in our study; this underestimation increases with increasing life expectancy. In the CBx group, early PSA failure, which is significantly associated with higher risk of both distant metastasis and PCSM following RP [15,16], was nearly three times more frequent for patients with PPB >50% and almost eight times more frequent for patients with PSA >20 ng/ml.

Our study has some limitations. First, data were not available for PSA levels in the year before diagnosis. Therefore, further research is warranted to determine whether a PSA increase >2 ng/ml during the year before diagnosis [17] is associated with significantly higher odds of adverse pathology and risk of PCSM and ACM. Second, this is a single-institution cohort study. Finally, data for the SBx group were collected before the 2014 ISUP guidelines on Gleason grading [1], so PC graded as GGG 1 in some patients might now be graded as GGG 2, with overestimation of the risks of PCSM and ACM for GGG 1 PC. However, it is reassuring that we found that the same clinical factors (PPB >50% and PSA >20 ng/ml) were associated with adverse pathology at RP and early PSA failure in a more contemporary group diagnosed via CBx and whose biopsy GGG 1 results were nearly all assigned after the 2014 ISUP conference [1].

5. Conclusions

Despite the potential study limitations, consideration of how competing risks because of comorbidities can impact longevity is important and allows an informed discussion between the physician and patient on whether observation, active surveillance, or radical treatment is indicated. However, classification of all biopsy GGG 1 cases as benign precludes such a discussion, as this is a heterogeneous group with respect to prognosis. Thus, categorization of GGG 1 PC as benign in patients with PSA >20 ng/ml or PPB >50% could result in higher PCSM risk and shorter survival given the higher adjusted odds of adverse pathology at RP and higher risk of early PSA failure, irrespective of the biopsy approach. Further evaluation with rebiopsy should be considered for these patients to better assess whether they might harbor unsampled high-grade PC.

Author contributions: Anthony V. D'Amico had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Tilki, D'Amico.
Acquisition of data: Tilki, Huland, Graefen.
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Drafting of the manuscript: All authors.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euo.2024.06.009.

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