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European Association of Urology

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

Application of a Prognostic Gleason Grade Grouping System to Assess Distant Prostate Cancer Outcomes

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Article info

Article history:
Accepted November 24, 2016

Associate Editor:
James Catto

Keywords:
Prognostic Gleason score
Prostate cancer
Prostate cancer–specific mortality

Abstract

Background: There is growing enthusiasm for the adoption of a novel grade grouping system to better represent Gleason scores.
Objective: To evaluate the ability of prognostic Gleason grade groups to predict prostate cancer (PCa)–specific mortality (PCSM) and bone metastatic progression.
Design, setting, and participants: We identified patients with PCa enrolled in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry across treatment strategies, including conservative and nondefinitive therapy.
Outcome measurements and statistical analysis: We examined the prognostic ability of Gleason grade groups to predict risk of PCSM and bone metastasis using the Kaplan-Meier method and unadjusted and adjusted Cox proportional hazards models.
Results and limitations: We identified 10 529 men with PCa followed for a median of 81 mo (interquartile range 40–127), including 64% in group I ($< 3 + 4$); 17% in group II (3+4); 9% in group III (4+3); 6% in group IV (4+4); and 4% in group V ($\geq 4 + 5$). Relative to grade group I, the unadjusted risks of PCSM and bone metastasis were significantly associated with prognostic grade groupings for both biopsy and prostatectomy samples (all $p < 0.01$). Pairwise comparisons within Gleason sums collapsed within grade group V were not significant; however, this analysis was limited by a small representation of men with Gleason pattern $\geq 4 + 5$.
Conclusions: The prognostic grade grouping system is associated with risk of PCSM and metastasis across management strategies, including definitive therapy, conservative management, and primary androgen deprivation.
Patient summary: A five-level reporting system for prostate cancer pathology is associated with the risk of late prostate cancer endpoints.
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DOI of original article: http://dx.doi.org/10.1016/j.eururo.2016.11.031.
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http://dx.doi.org/10.1016/j.eururo.2016.11.032
0302-2838/© 2016 Published by Elsevier B.V. on behalf of European Association of Urology.

Please cite this article in press as: Leapman MS, et al. Application of a Prognostic Gleason Grade Grouping System to Assess Distant Prostate Cancer Outcomes. Eur Urol (2016), http://dx.doi.org/10.1016/j.eururo.2016.11.032

1. Introduction

Conceived five decades ago, the Gleason scoring system is a clinical variable strongly associated with prostate cancer (PCa) outcome [1]. With time, incremental modifications to the standards for pathologic reporting have allowed for greater agreement between biopsy and radical prostatectomy (RP) specimens, yet have resulted in the elimination of nearly half of the initially proposed Gleason scores (ie, sums 2–5) [2–4]. A well-recognized communication challenge has emerged whereby the lowest assigned Gleason sum associated with PCa is reported as 6 on a scale from 2 to 10. As a result, a reduction in the practical histologic spectrum may serve to misrepresent the degree of clinical risk and potentially compound the problem of overtreatment for men with low-grade tumors with a perceived higher than actual risk.

A novel grade grouping system offering five tiers consistent with modern reporting conventions has been proposed, and there has been a groundswell of momentum in support of its widespread adoption, including a recent announcement requiring consistent use for publication in major urologic oncology journals, including *European Urology* [5,6]. To date, a number of validation studies examining the ability of this revised Gleason grading reporting system to predict clinical recurrence following definitive therapy have been published, as well as two publications addressing PCa-specific mortality following conservative management and radiotherapy [7–12]. However, it is unknown if a reporting rubric that collapses the highest Gleason sums (group V) will in turn mask differences in clinical outcome within these subcategories, or whether such a system will perform adequately when broadly implemented outside of academic centers and across treatment types. Therefore, we aimed to evaluate the association of prognostic Gleason grade group with risk of PCa-specific mortality (PCSM) and the development of bone metastasis across management strategies among men in a large multicenter registry.

2. Patients and methods

Study participants were enrolled in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry initiated in 1995, which

Table 1 – Baseline clinicodemographic and pathologic characteristics among patients with prostate cancer enrolled in CaPSURE

Value	RP	BT	EB	HT	AS/WW	*p* value
Mean age, yr (SD)	61.6 (7.0)	68.0 (7.2)	70.1 (6.8)	73.0 (8.3)	71.4 (8.5)	<0.01
Median PSA, ng/ml (IQR)	5.8 (4.4–8.6)	6.0 (4.6–8.5)	8.4 (5.5–14.8)	10.6 (6.3–23.2)	6.0 (4.4–8.6)	
Race/ethnicity, *n* (%)						
Native American	17 (<1)	0 (0)	2 (<1)	2 (<1)	0 (0)	<0.01
Asian/Pacific Islander	25 (<1)	4 (<1)	10 (1)	19 (1)	7 (1)	
Latino/Hispanic	50 (1)	37 (3)	14 (1)	19 (1)	10 (1)	
African American	303 (6)	48 (4)	118 (8)	134 (8)	48 (5)	
Caucasian	3711 (73)	907 (66)	1040 (67)	953 (60)	646 (67)	
Mixed	18 (<1)	4 (<1)	2 (<1)	5 (<1)	2 (<1)	
Other	934 (18)	368 (27)	367 (24)	457 (29)	248 (26)	
Clinical T stage, *n* (%)						
T1	2486 (51)	688 (53)	624 (42)	631 (42)	567 (63)	<0.01
T2	2329 (48)	587 (45)	772 (52)	752 (50)	321 (36)	
T3	73 (1)	16 (1)	91 (6)	123 (8)	14 (2)	
Missing	170	77	66	83	59	
Prognostic Gleason group, *n* (%)						
I (2–6)	3471 (69)	999 (73)	791 (51)	700 (44)	815 (85)	<0.01
II (3 + 4)	881 (17)	198 (14)	324 (21)	292 (18)	78 (8)	
III (4 + 3)	391 (8)	94 (7)	203 (13)	225 (14)	42 (4)	
IV (8)	214 (4)	51 (4)	154 (10)	200 (13)	17 (2)	
V (9–10)	101 (2)	26 (2)	81 (5)	172 (11)	9 (1)	
Extended Gleason group, *n* (%)						
2–6	3471 (69)	999 (73)	791 (51)	700 (44)	815 (85)	<0.01
3 + 4	881 (17)	198 (14)	324 (21)	292 (18)	78 (8)	
4 + 3	391 (8)	94 (7)	203 (13)	225 (14)	42 (4)	
4 + 4	181 (4)	36 (3)	132 (9)	152 (10)	14 (1)	
3 + 5	25 (<1)	15 (1)	16 (1)	36 (2)	3 (<1)	
5 + 3	8 (<1)	0 (0)	6 (<1)	12 (1)	0 (0)	
4 + 5	63 (1)	13 (1)	42 (3)	103 (7)	4 (<1)	
5 + 4	20 (<1)	6 (<1)	19 (1)	34 (2)	2 (<1)	
10	7 (<1)	6 (<1)	8 (1)	25 (2)	2 (<1)	
Missing	11	1	12	10	1	
Clinical risk category (CAPRA score), *n* (%)						
0–2 (low)	2257 (59)	722 (64)	321 (31)	306 (27)	471 (72)	<0.01
3–5 (intermediate)	1301 (34)	324 (29)	484 (46)	433 (39)	153 (23)	
6–10 (high)	258 (7)	78 (7)	246 (23)	378 (34)	29 (4)	
Missing	1242	244	502	472	308	

RP = radical prostatectomy; BT = brachytherapy; EB = external beam radiation therapy; HT = hormonal therapy; AS = active surveillance; WW = watchful waiting; CAPRA = Cancer of the Prostate Risk Assessment.

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