Urologic Oncology: Seminars and Original Investigations 37 (2019) 179.e19−179.e28

UROLOGIC ONCOLOGY

Original article

Prognostic value of modified Glasgow Prognostic Score in non−muscle-invasive bladder cancer

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Received 6 August 2018; received in revised form 30 October 2018; accepted 4 November 2018

Abstract

Purpose: To investigate the prognostic value of preoperative modified Glasgow Prognostic Score (mGPS) in patients with non−muscle-invasive bladder cancer (NMIBC) treated with transurethral resection of bladder with or without intravesical therapy.

Material and Methods: We retrospectively reviewed our medical records to identify 1,096 consecutive patients with NMIBC treated with transurethral resection of bladder. The mGPS of each patient was calculated on the basis of preoperative serum C-reactive protein and albumin. Univariable and multivariable Cox regression analyses were performed to investigate the association of mGPS with recurrence-free survival (RFS) and progression-free survival (PFS).

Results: The mGPS of 0, 1, and 2 was observed in 764 (69.7%), 299 (27.3%), and 33 (3.0%) patients, respectively. On univariable analysis, mGPS 2 was associated with worse RFS (Hazard Ratio [HR]: 1.60, 95%; CI: 1.01−2.54). However, on multivariable analyses, which adjusted for the effects of established clinicopathologic features, mGPS 2 did not maintain its independent association with RFS (HR: 1.41, 95% CI: 0.88−2.26). On multivariable analysis, mGPS 1 and 2 were both independently associated with worse PFS compared to mGPS 0 (HR: 2.06, 95% CI: 1.37−3.12 and HR: 3.31, 95% CI: 1.40−7.87, respectively). The inclusion of mGPS improved the discrimination of a standard prognostic model for PFS from 71.6% to 73.8%. In subgroup analyses, mGPS 1 was associated with PFS (HR 2.09, 95% CI: 1.24−3.52) on multivariable analysis in patients with the European Association of Urology high-risk group. Additionally, in patients treated with bacillus Calmette-Guérin, mGPS 2 was associated with disease PFS (HR10.1, 95% CI: 2.61−38.8).

Conclusions: The mGPS independently predicts PFS in patients with NMIBC. Inclusion of mGPS in prognostic models might help identify patients who are more likely to fail standard therapy and experience disease progression and, therefore, may benefit from intensified therapy such as radical cystectomy or inclusion in clinical trials of novel immunotherapeutics. © 2018 Published by Elsevier Inc.

Keywords: Non−muscle-invasive; Bladder cancer; Modified Glasgow prognostic score; Progression; Outcomes

Funding Disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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https://doi.org/10.1016/j.urolonc.2018.11.005
1078-1439/

1. Introduction

The standard treatment of non−muscle-invasive bladder cancer (NMIBC) is transurethral resection of bladder (TURB) followed by intravesical instillation chemotherapy or immunotherapy according to patient's risk of disease recurrence and progression [1]. Despite optimal treatment including adjuvant intravesical instillation therapy, up to 70% of NMIBC patients eventually experience disease recurrence and 10% to 20% experience disease progression to muscle invasive bladder cancer (MIBC) [2].

Current prognostic models rely on clinicopathologic features derived from retrospective analyses [2,3]. External validation studies have found the prognostic accuracy for these models to be limited [4,5]. Therefore, there is need for novel biomarkers to help improve the prediction of response to standard treatment [6,7].

The immune system including the inflammatory response and the tumor's own microenvironment plays an important role in bladder cancer (BC) clinical and biologic behaviors and outcomes [8,9]. In this context, the modified Glasgow Prognostic Score (mGPS), based on serum C-reactive protein (CRP) and albumin levels, has been incorporated in prognostic models for MIBC, showing significant accuracy improvement [10]. There is, however, still no clear data on the role of mGPS in patients with NMIBC.

We hypothesized that preoperative mGPS is associated with worse oncologic outcomes in patients with NMIBC. To test this, we investigated the role of preoperative mGPS in patients treated with TURB with or without adjuvant intravesical therapy for NMIBC.

2. Material and methods

2.1. Patient population and treatment

Following approval by the institutional review board, we retrospectively reviewed 1,117 medical records. Twenty-one patients with pure carcinoma in situ were excluded, as this group is too small for separate analyses. Overall, 1,096 consecutive patients with primary or recurrent NMIBC treated with TURB were included in this study. Immediate single-dose postoperative instillation chemotherapy, adjuvant intravesical chemotherapy, or adjuvant bacillus calmette-guérin (BCG) immunotherapy were administered according to risk categories of disease recurrence and progression as well as according to physicians' discretion based on current guidelines. A second-look TURB was performed based on pathologic and intraoperative findings. All TURB specimens were staged based on the 2009 TNM classification. Tumor grade was based on the 1973 World Health Organization system. All laboratory tests, including serum CRP and albumin, were performed within 30 days before initial TURB. No patients had urinary tract infection or known systematic inflammatory disease in preoperative urinary test and performed imagings such as chest X-ray and abdominal computed tomography. The mGPS was calculated, as previously described [11,12], using serum CRP and albumin of each patient: patients with an elevated CRP level (>0.5 mg/dl) plus hypoalbuminemia were allocated a score of 2, those with only 1 of these factors were allocated a score of 1 and those with normal serum CRP and albumin levels were scored as 0. Patients were assigned into low, intermediate, and high risk group of NMIBC according to European Association of Urology (EAU) guidelines [1].

2.2. Follow-up

Due to the retrospective nature of the study, follow-up was not standardized. However, in general, patients were followed according to guidelines at the time. The postoperative follow-up included physical examination, urinary cytology, and cystoscopy. Imaging of the upper urinary tract was performed based on pathologic features according to guidelines and at physician discretion. Disease recurrence was defined as tumor relapse in the bladder regardless of tumor stage. Disease progression was defined as tumor relapse at stage ≥pT2.

2.3. Statistical analysis

First, the association of mGPS with recurrence-free survival (RFS) and progression-free survival (PFS) rates was estimated using Kaplan−Meier method. The log-rank test was used to determinate the statistical difference between each group. Second, univariable and multivariable Cox regression analyses were performed to assess the association of mGPS with RFS and PFS, after adjusting for the effects of established clinicopathologic features. Third, the discrimination of the obtained models was evaluated using Harrel's C-index. Fourth, exploratory analyses investigated RFS and PFS rates for patients stratified according to the EAU risk stratification and according to the receipt of intravesical BCG therapy. Data were analyzed using STATA 14 (Stata Corp., College Station, TX). A P value of <0.05 was considered significant and all tests were performed 2-sided.

3. Results

3.1. Patient characteristics

The mGPS of 0, 1, and 2 was observed in 764 (69.7%), 299 (27.3%), and 33 (3.0%) patients, respectively. Clinicopathologic features for the overall population and stratified by mGPS are shown in Table 1. Patients with pT1 tumor as well as those in the EAU high risk group were more likely to have a mGPS of 0 ($P = 0.04$ and $P = 0.02$, respectively).

3.2. Association of mGPS with disease recurrence

Within a median follow-up of 64.8 months (IQR: 26.5−110.9), 461 patients (42.1%) experienced disease recurrence. The median time to disease recurrence was 7 months (IQR: 4−16.3).

Table 1
Association of modified Glasgow Prognostic Score with clinicopathologic characteristics in 1,096 patients treated with transurethral resection of the bladder for non−muscle-invasive bladder cancer

Variables	Total	mGPS			*P* value
		0	1	2	
Number of patients, *n* (%)	1,096	764 (70)	299 (27)	33 (3)	
Median age (IQR)	67 (58−74)	67 (58−74)	66 (59−74)	65 (60−73)	0.84
Gender, *n* (%)					0.23
Female	254 (23)	166 (66)	79 (31)	9 (3)	
Male	842 (77)	598 (71)	220 (26)	24 (3)	
Smoking status, *n* (%)					0.18
Never smoked	267 (24)	194 (73)	68 (25)	5 (2)	
Former smoker	322 (30)	234 (73)	78 (24)	10 (3)	
Current smoker	507 (46)	336 (66)	153 (30)	18 (4)	
Prior recurrent rate, *n* (%)					0.58
Primary	916 (84)	634 (69)	252 (28)	30 (3)	
≦1 recurrent/y	88 (8)	67 (76)	20 (23)	1 (1)	
>1 recurrent/y	92 (8)	63 (68)	27 (29)	2 (2)	
Pathological T stage, *n* (%)					0.04
PTa	653 (60)	443 (68)	184 (28)	26 (4)	
pT1	443 (40)	321 (72)	115 (26)	7 (2)	
Pathological tumor grade, *n* (%)					0.12
Grade 1	230 (21)	156 (68)	66 (28)	8 (4)	
Grade 2	383 (35)	258 (67)	108 (28)	17 (5)	
Grade 3	483 (44)	350 (72)	125 (26)	8 (2)	
Concomitant CIS, *n* (%)	47 (4)	34 (4)	11 (4)	2 (6)	0.75
Tumor size, *n* (%)					0.55
<1 cm	352 (32)	253 (72)	92 (26)	7 (2)	
1−3 cm	444 (41)	300 (68)	128 (28)	16 (4)	
>3 cm	300 (27)	211 (70)	79 (27)	10 (3)	
Number of tumors, *n* (%)					0.67
1	704 (64)	492 (70)	193 (27)	19 (3)	
1−7	291 (27)	198 (68)	81 (28)	12 (4)	
≧8	101 (9)	74 (73)	25 (25)	2 (2)	
Intravesical therapy, *n* (%)	472 (43)	329 (43)	129 (43)	14 (42)	0.99
Type of intravesical therapy, *n* (%)					0.09
Early single installation	145 (13)	93 (64)	50 (35)	2 (1)	
Adjuvant chemotherapy	48 (4)	34 (71)	10 (21)	4 (8)	
Adjuvant BCG	279 (26)	202 (72)	69 (25)	8 (3)	
EAU risk groups, *n* (%)					0.02
Low-risk	129 (12)	86 (67)	42 (32)	1 (1)	
Intermediate risk	464 (41)	313 (67)	129 (28)	22 (5)	
High-risk	503 (46)	365 (73)	128 (25)	10 (2)	

BCG = bacillus Calmette-Guérin; CIS = carcinoma in situ; EAU = European Association of Urology; IQR = interquartile range; mGPS = modified Glasgow Prognostic Score.

The 5-year RFS rates for patients with mGPS 0, 1, and 2 were 54.6%, 53.7%, and 43.4%, respectively (Fig. 1A). On univariable analyses, mGPS 2 was associated with worse RFS compared to mGPS 0 (Hazard Ratio [HR]: 1.60, 95% CI: 1.01−2.54, $P = 0.04$). However, after adjusting for effects of established clinicopathologic features (Table 2), mGPS 2 did not retain its independent association with RFS on multivariable analysis (HR: 1.41, 95% CI: 0.88 −2.26, $P = 0.16$).

3.3. Association of mGPS with disease progression

During follow-up, 101 patients (9.2%) experienced disease progression. The median time to disease progression was 25 months (IQR: 8.8-68.3). The 5-year PFS rates for patients with mGPS 0, 1, and 2 were 94.0%, 88.5%, and 87.5%, respectively (Fig. 1B). On univariable analyses, patients with mGPS 1 or 2 had a significantly shorter PFS probability compared to patients with mGPS 0 (HR: 1.91, 95% CI: 1.27−2.87, $P = 0.002$ and HR: 2.54, 95% CI: 1.09 −5.91, $P = 0.03$, respectively). On multivariable analysis, adjusted for effects of standard clinicopathologic features, mGPS 1 and 2 were both independently associated with worse PFS (HR: 2.06, 95% CI: 1.37−3.12, $P = 0.001$ and HR: 3.31, 95% CI: 1.40−7.87, $P = 0.007$, respectively) (Table 2). The addition of mGPS to a base multivariable model for the prediction of PFS improved its discrimination from 71.6% to 73.8%.

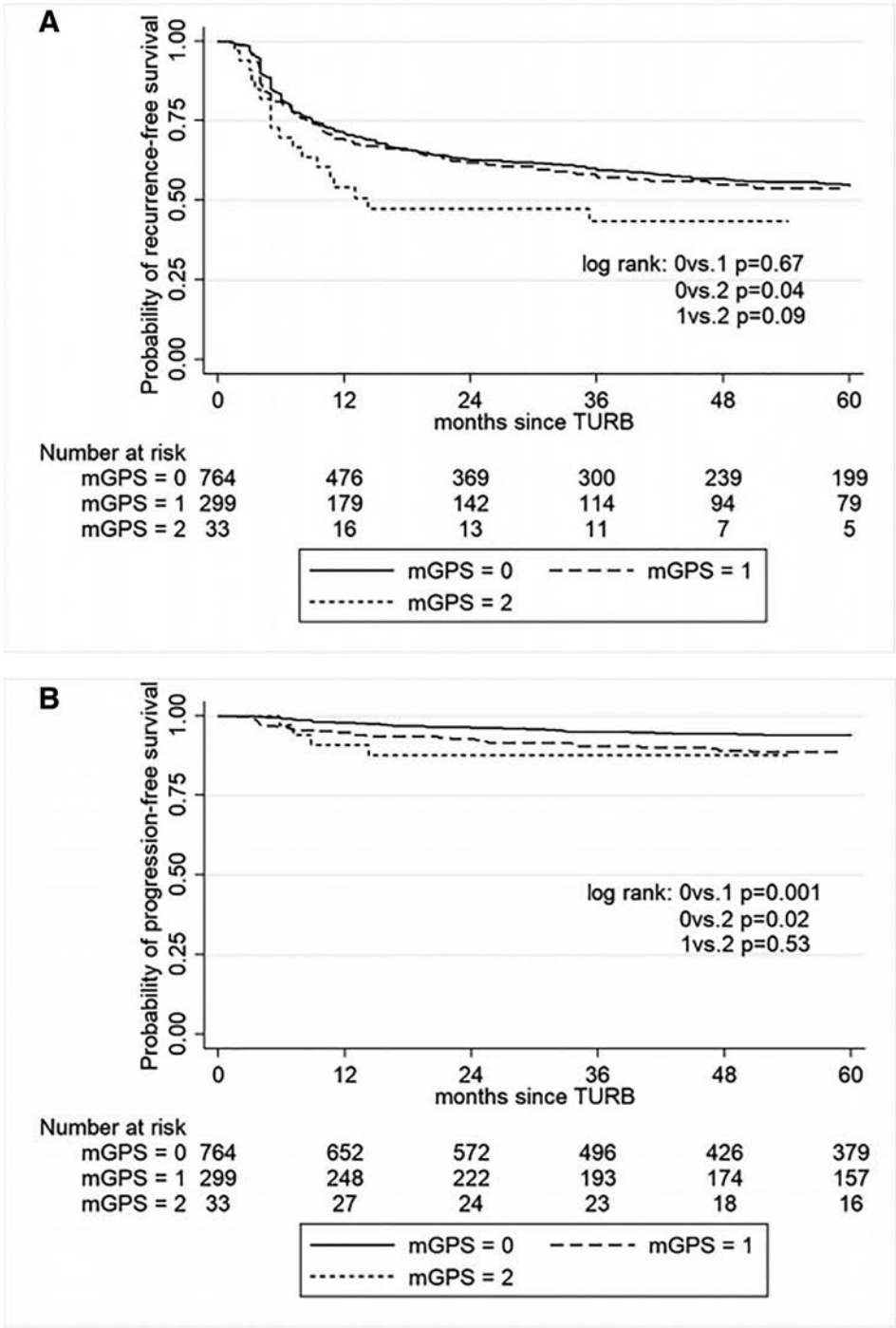

Fig. 1. Recurrence-free survival (A) and progression-free survival (B) estimates in 1,096 patients treated with transurethral resection of the bladder for nonmuscle-invasive bladder cancer, stratified by the modified Glasgow Prognostic Score.

3.4. Subgroup analyses in patients stratified by the EAU risk grouping

A total of 503 patients (45.9%) were stratified into the EAU high risk group. During a median follow-up of 52.4 months (IQR: 20.6−91.8), a total of 188 (37.4%) and 62 (12.3%) patients experienced disease recurrence and progression, respectively. The 5-year RFS of EAU high risk patients with mGPS 0, 1, and 2 were 61.6%, 56.1%, and 46.7%, respectively. However, no significant association could be observed (Fig. 2A). The 5-year PFS rates for mGPS 0, 1, and 2 were 89.6%, 80.9%, and 90.0%, respectively (Fig. 2B). On multivariable Cox regression analysis, after adjustment for effects of standard clinicopathologic features, a mGPS of 1 was associated with shorter PFS compared to a mGPS of 0 (HR: 2.09, 95% CI: 1.24−3.52, $P = 0.006$; Table 3).

Table 2
Univariable and multivariable Cox regression analyses for the prediction of recurrence-free survival and progression-free survival in 1,096 patients treated with transurethral resection of the bladder for non−muscle-invasive bladder cancer

Variable	RFS				PFS			
	Univariable		Multivariable		Univariable		Multivariable	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (continuous)	1.03 (1.02−1.03)	<0.001	1.03 (1.02−1.03)	<0.001	1.04 (1.02−1.06)	<0.001	1.04 (1.02−1.06)	<0.001
Female gender	1.09 (0.88−1.35)	0.43	0.98 (0.79−1.22)	0.89	1.20 (0.77−1.86)	0.42	1.06 (0.68−1.67)	0.79
Prior recurrence rate (ref.: primary)								
≤r recurrence per y	0.66 (0.44−0.98)	0.04	0.83 (0.55−1.25)	0.37	2.09 (1.11−3.95)	0.02	2.18 (1.12-4.23)	0.02
>1 recurrence per y	0.78 (0.55−1.10)	0.16	1.16 (0.81−1.66)	0.43	2.00 (1.13−3.53)	0.02	2.48 (1.34−4.57)	0.004
Pathological T stage								
pT1 vs. pTa	0.84 (0.77−0.93)	0.001	0.65 (0.53−0.81)	<0.001	1.25 (1.03−1.52)	0.02	0.68 (0.47−0.97)	0.04
Pathological tumor grade (ref.: G1)								
G2	2.00 (1.54−2.62)	<0.001	1.57 (1.19−2.07)	0.001	2.56 (1.19−5.52)	0.02	2.34 (1.07−5.12)	0.03
G3	1.25 (0.95−1.64)	0.11	2.47 (1.52−4.01)	<0.001	3.92 (1.87−8.22)	<0.001	7.53 (2.80−20.3)	<0.001
Concomitant CIS	1.01 (0.64−1.60)	0.97	0.88 (0.55−1.41)	0.59	1.37 (0.56−3.38)	0.49	0.88 (0.35−2.20)	0.78
Tumor size, cm (ref.: < 1 cm)								
1−3 cm	0.96 (0.76−1.22)	0.76	1.04 (0.82−1.33)	0.75	1.53 (0.92−2.53)	0.10	1.37 (0.82−2.30)	0.23
>3 cm	2.37 (1.89−2.97)	<0.001	2.28 (1.80−2.90)	<0.001	1.80 (1.08−3.01)	0.03	1.70 (0.99−2.91)	0.054
Number of tumor (ref.: single)								
2−7	1.51 (1.23−1.85)	<0.001	1.47 (1.19−1.81)	<0.001	1.50 (0.96−2.35)	0.08	1.07 (0.67−1.71)	0.77
≥8	1.02 (0.72−1.44)	0.93	1.10 (0.77−1.57)	0.60	2.61 (1.49−4.55)	0.001	1.77 (0.99−3.17)	0.053
Intravesical therapy	0.58 (0.48−0.70)	<0.001	0.61 (0.49−0.76)	<0.001	1.13 (0.76−1.68)	0.55	0.89 (0.57−1.37)	0.59
mGPS (ref.: score 0)								
1	1.03 (0.84−1.27)	0.77	1.06 (0.86−1.30)	0.62	1.91 (1.27−2.87)	0.002	2.06 (1.37−3.12)	0.001
2	1.60 (1.01−2.54)	0.04	1.41 (0.88−2.26)	0.16	2.54 (1.09−5.91)	0.03	3.31 (1.40−7.87)	0.007

CI = confidence interval; CIS = carcinoma in situ; HR = hazard ratio; mGPS = modified Glasgow Prognostic Score; PES = progression-free survival; RFS = recurrence-free survival.

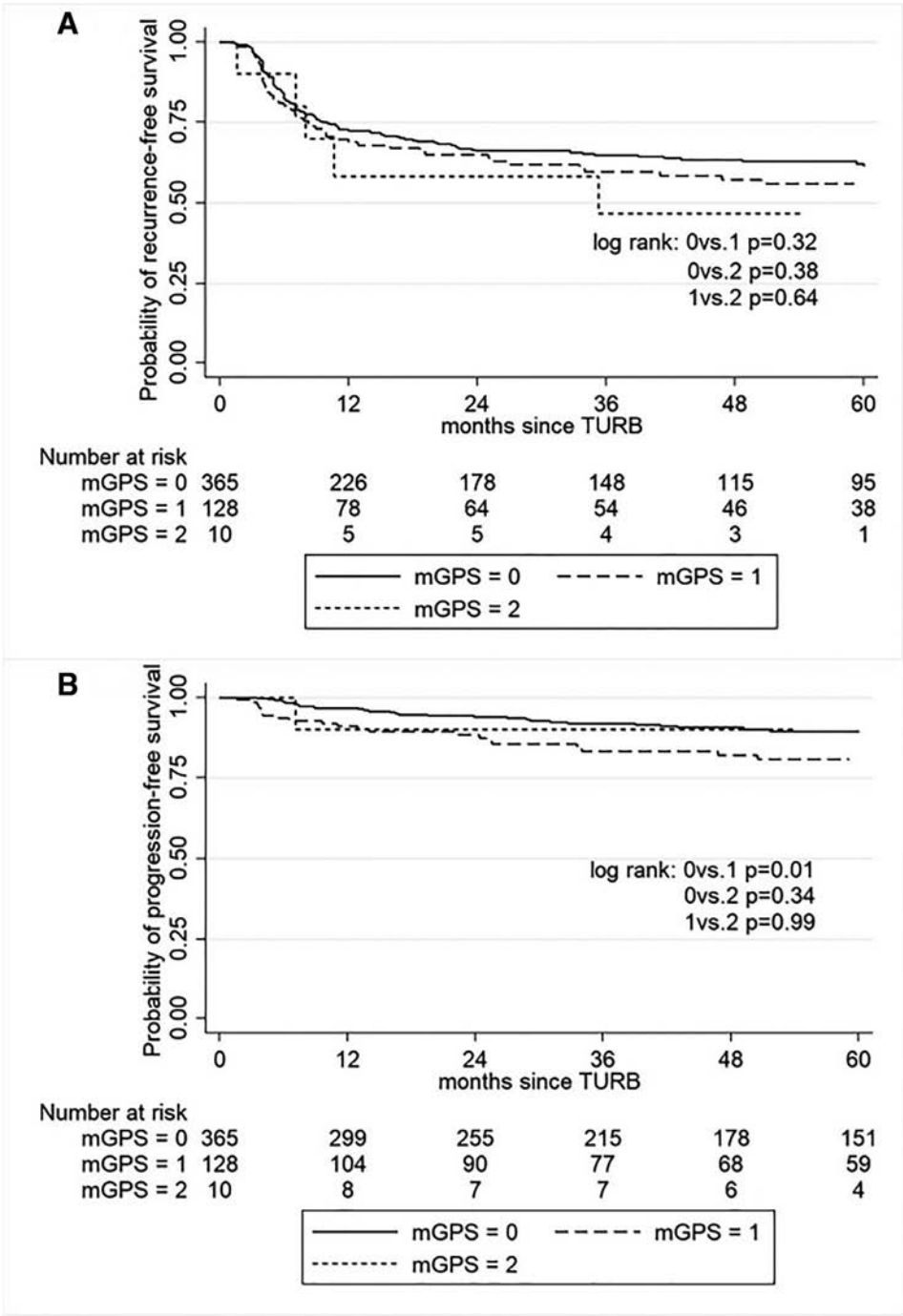

Fig. 2. Recurrence-free survival (A) and progression-free survival (B) estimates in 503 patients with EAU high-risk non−muscle-invasive bladder cancer, stratified by the modified Glasgow Prognostic Score.

3.5. Correlation with response to BCG instillation therapy

On exploratory analyses, we investigated the association of mGPS with response to adjuvant intravesical BCG therapy. A total of 279 patients (25.5%) were treated with adjuvant BCG instillation therapy. The mGPS of 0, 1, and 2 was observed in 202 (72.4%), 69 (24.7%), and 8 (2.9%) BCG patients, respectively. During a median follow-up of 58 months (IQR: 21.9−89.0), 107 (38.4%) and 22 (7.9%) patients experienced disease recurrence and progression, respectively. In this cohort, the 5-year RFS of patients with mGPS 0, 1, and 2 was 57.2%, 59.5%, and 60%, respectively. However, no significant association could be observed (Fig. 3A). The 5-year PFS rates for mGPS 0, 1, and 2 were 95.0%, 90.6%, and 75.0%, respectively. Higher mGPS was associated with shorter PFS (Fig. 3B). On multivariable Cox regression analysis that adjusted for the effects of standard clinicopathologic features, mGPS

Table 3
Multivariable Cox regression analyses for the prediction of progression-free survival in 503 European Association of Urology high risk patients treated with transurethral resection of bladder and 279 patients treated with adjuvant bacillus Calmette-Guérin instillation therapy for non−muscle-invasive bladder cancer

	503 patients with EAU high risk		279 patients treated with BCG	
	PFS		PFS	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age	1.05 (1.02−1.07)	0.001	1.05 (1.004−1.10)	0.03
Gender	1.16 (0.62−2.06)	0.62	0.65 (0.22−1.90)	0.43
pT1 vs. pTa	0.64 (0.46−0.88)	0.006	1.11 (0.71−1.73)	0.64
Concomitant CIS	0.56 (0.22−1.45)	0.23		
Tumor size (ref.: < 1 cm)				
1−3 cm	1.23 (0.62−2.43)	0.55	1.17 (0.30−4.59)	0.82
>3 cm	1.45 (0.73−2.85)	0.29	2.03 (0.54−7.65)	0.30
Number of tumor (ref.: single)				
2−7	1.22 (0.69−2.17)	0.50	1.39 (0.56−3.42)	0.48
≥8	1.89 (0.93−3.84)	0.08	0.83 (0.17−4.07)	0.82
mGPS (ref.: score 0)				
1	2.09 (1.24−3.52)	0.006	1.64 (0.64−4.19)	0.31
2	1.98 (0.46−8.53)	0.36	10.1 (2.61−38.8)	0.001

BCG = bacillus Calmette-Guérin; CI = confidence interval; CIS = carcinoma in situ; EAU = European Association of Urology; HR = hazard ratio; mGPS = modified Glasgow Prognostic Score; PES = progression-free survival.

2 retained its independent association with PFS (HR 10.1, 95% CI: 2.61−38.8, $P = 0.001$) (Table 3).

4. Discussion

In this retrospective study, we investigated the association of mGPS with oncologic outcomes of NMIBC patients treated with TURB with or without adjuvant intravesical instillation therapy. Although some investigators previously described the relationship of conventional GPS with oncologic outcomes in BC patients [10,13], this is the first study, to our knowledge, to investigate prognostic impact of mGPS in NMIBC patients. To address this question, we assessed the prognostic and predictive value of mGPS in a large consecutive cohort of NMIBC patients.

In this cohort of patients with NMIBC, elevated mGPS score was found in 30.3% and 45.9% were stratified into the EAU high risk group. Adjuvant intravesical BCG instillation was administered in 25.5% of patients after TURB. We further found that patients with mGPS of 2 were more likely to experience disease recurrence on univariable analysis and disease progression on multivariable Cox regression analysis. The addition of mGPS to a standard prognostic model for prediction of disease progression improved its discrimination by 2.2%; in other words, 2 out of 100 patients benefited in terms of prediction disease prognosis. Moreover, in patients stratified in the EAU high risk group, mGPS of 1 was significantly associated with worse PFS in multivariable Cox regression analysis. In patients who received BCG instillations, mGPS of 2 was independently associated with shorter PFS than patients with mGPS of 0.

The correlation between inflammation and tumor aggressiveness is generally accepted [14]. Elevated inflammation markers such as CRP and neutrophil-to-lymphocyte ratio have been reported to have a prognostic role in various cancers, especially in patients with advanced tumor stages [15,16]. In NMIBC, Mbeutcha et al. reported an association of high preoperative CRP (>0.5 mg/dl) with worse PFS [9]. Moreover, D'Andrea et al. showed that preoperative neutrophil-to-lymphocyte ratio ≥3 is associated with shorter RFS and PFS in NMIBC patients [8]. Meanwhile, serum albumin reflects nutrition status of the patients, which has also prognostic value in various cancers [17,18]. Niwa et al. demonstrated the relationship between low albumin and worse oncologic outcomes using the albumin-to-globulin ratio in NMIBC patients treated with TURB [19]. Combination of already established biomarkers and those reflecting complementary cancer-related processes may further improve predictive accuracy in this highly variable disease.

The mGPS calculated, using combination of serum CRP and albumin, has been reported to have useful prognostic value in various advanced cancers [11,20,21]. This score reflects both the inflammatory and nutrition status. Combination of these measurements provides a more sensitive biomarker of oncologic outcomes compared to CRP or albumin alone. In this study, we calculated mGPS using CRP >0.5 mg/dl to discriminate patients who are likely to have disease recurrence and progression more clearly than conventional GPS using CRP level of >1 mg/dl in muscle invasive BC patients treated with radical cystectomy [12].

One of the challenging controversies in NMIBC is to identify the patients who are likely to fail therapy and experience disease recurrence and progression to muscle invasive disease. Many tools have been developed to help clinicians and their patients resolve the current inaccuracy in prediction of the course of disease. For example, in NMIBC patients treated with BCG, the Spanish Urological

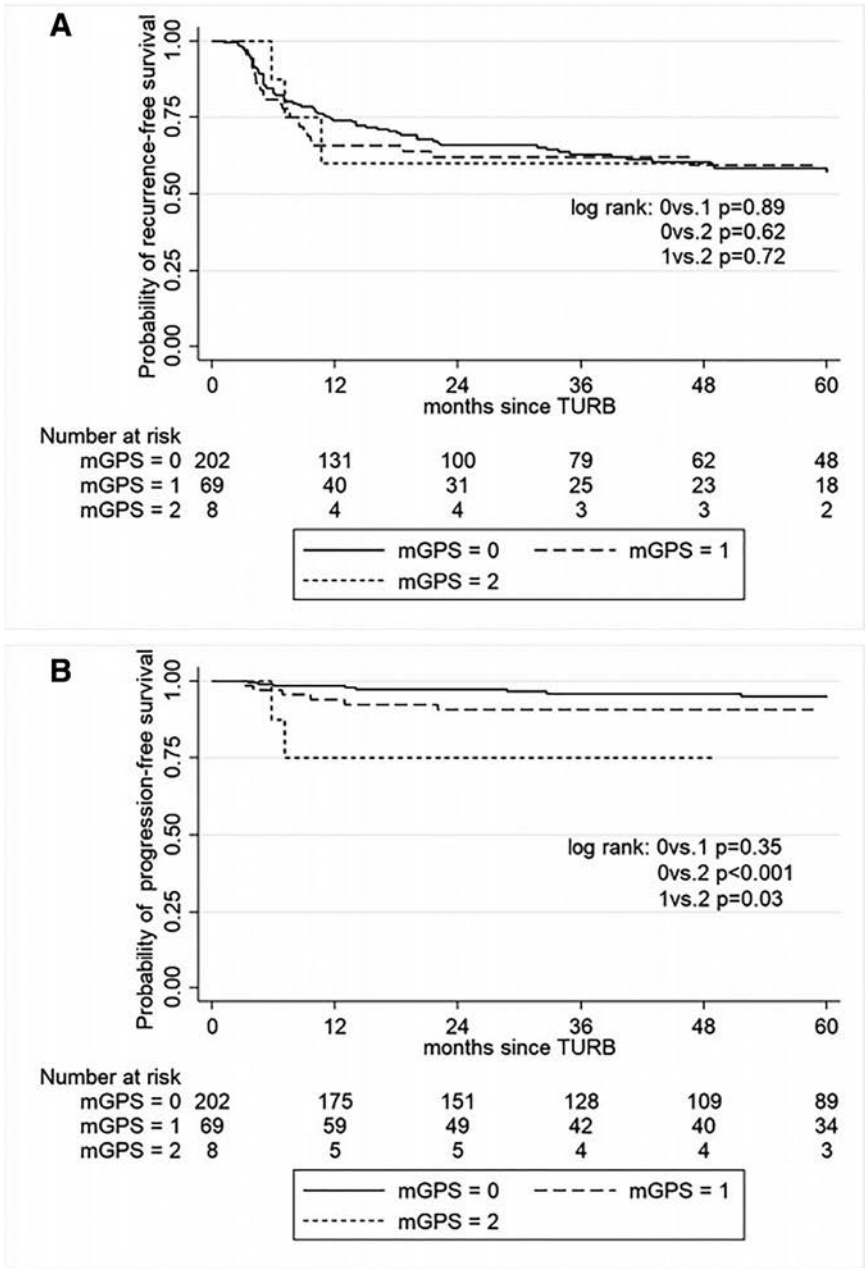

Fig. 3. Recurrence-free survival (A) and progression-free survival (B) estimates in 279 patients treated with transurethral resection of the bladder and adjuvant bacillus Calmette-Guérin immunotherapy for non−muscle-invasive bladder cancer, stratified by the modified Glasgow Prognostic Score.

Club for Oncological Treatment risk table [3] has been established. However, the accuracy of all previous tools for prediction of disease recurrence and progression in NMIBC patients remains suboptimal. Moreover, several investigators demonstrated the variable discrimination of these models when tested in external validation cohorts [5,22]. The accuracy of these tools could potentially be improved by adding biomarkers such as systemic inflammatory biomarker (i.e., mGPS). We found that patients with elevated mGPS are more likely to experience disease progression to muscle invasive disease. Furthermore, in patients with the EAU high risk NMIBC and in patients who received adjuvant BCG treatment, mGPS was associated with shorter PFS. Our results highlight that mGPS might identify the patients who are likely to experience BCG failure and, therefore, benefit from an individualized and closer follow-up, early radical cystectomy or inclusion into clinical trials evaluating novel strategies such as addition checkpoint inhibitors into the treatment of NMIBC. However, the number of patients with mGPS 2 was small, limiting the power of the statistical analyses and weakening unequivocal clinical conclusions.

This study's limitations include its retrospective nature, which may have led to a selection bias. Therefore, our results

should be interpreted within the limits of retrospective design. Moreover, the study is limited by the lack of standardization of the surgical procedures, adjuvant intravesical instillation therapy and follow-up scheduling. All patients treated with BCG received a full course of induction followed by maintenance schedule when tolerated. But, due to differences of BCG maintenance treatment scheduling among centers, we could not account for BCG maintenance treatment completion. TURB specimens were not reviewed by central pathologic assessment and relevant pathologic prognostic factors such as lymphovascular invasion [23] and variant histology [24] were not assessed. Although mGPS has been reported as a prognostic factor especially for patients with advanced cancers, our study included only NMIBC patients treated with TURB. Despite these limitations, we elucidated the relationship between mGPS and disease progression in NMIBC patients treated with TURB. We suggest that this score should be applied to patients with NMIBC or other early-stage cancers. This score can be calculated easily combined with serum CRP and albumin, which is cheap and includes commonly used routine blood examination before surgery. As this is the first retrospective study on mGPS for NMIBC, external validation is needed. Finally, further prospective, well-controlled studies to validate the prognostic value of mGPS in NMIBC patients treated with TURB are needed in the future.

5. Conclusions

The mGPS is significantly associated with PFS in patients with NMIBC treated with TURB with or without intravesical therapy. Preoperative mGPS could help identify the patients who are more likely to experience disease progression to muscle invasive disease and may benefit from intensified therapy such as early radical cystectomy or addition of novel immuno-therapeutics. Additionally, these data could support current tools in predicting disease progression, thereby, improving accuracy of data to guide patient counseling regarding the ideal therapy for each and every one.

Conflict of interest

The authors declare that they have no conflict of interest.

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