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Prognostic Relevance of the Modified Glasgow Prognostic Score in Patients Treated with Enfortumab Vedotin + Pembrolizumab for Metastatic Urothelial Carcinoma: A Multicenter Real-World Analysis of the GUARDIANS Cohort

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Abstract

Background and Objective: Enfortumab vedotin plus pembrolizumab (EV+P) is the first-line standard of care for metastatic urothelial carcinoma (mUC), but outcomes remain heterogeneous despite high response rates. The modified Glasgow Prognostic Score (mGPS), derived from C-reactive protein and albumin, is a prognostic tool across solid tumors but has not been evaluated in patients receiving EV+P. We aimed to determine whether baseline mGPS is independently associated with overall survival (OS) and progression-free survival (PFS) in this population.

Methods: We retrospectively analyzed 310 patients treated with first-line EV+P across 19 German centers in the GUARDIANS registry, stratified by baseline mGPS (0: CRP ≤10 mg/L; 1: CRP >10 mg/L, albumin ≥35 g/L; 2: CRP >10 mg/L, albumin <35 g/L). OS and PFS were estimated by Kaplan–Meier methods and compared by log-rank test. Multivariable Cox regression, adjusted for age, ECOG status, and liver metastases, assessed independent prognostic value and discrimination (Harrell's C-index), which was compared with that of the Bellmunt risk score.

Key Findings and Limitations: mGPS was independently associated with both OS and PFS. mGPS 1 and mGPS 2 (vs. mGPS 0) carried hazard ratios of 2.26 (95% CI 1.19–4.29) and 3.11 (95% CI 1.46–6.63) for OS, and 1.63 (95% CI 1.09–2.45) and 2.36 (95% CI 1.43–3.90) for PFS (all p≤0.018; C-index 0.71 and 0.65, respectively). mGPS discriminated similarly to the established Bellmunt risk score (standalone C-index 0.65 vs. 0.66 for OS and 0.62 vs. 0.60 for PFS). ECOG status was also prognostic; liver metastases were not. Limitations include the retrospective design and immature OS follow-up.

Conclusions and Clinical Implications: mGPS is a simple, independent, readily available prognostic marker for first-line EV+P that may complement established risk factors for stratification and merits prospective validation.

Keywords: enfortumab vedotin; modified Glasgow Prognostic Score; pembrolizumab; prognosis; real-world evidence; urothelial carcinoma

Introduction

Enfortumab vedotin + pembrolizumab (EV+P) has become the standard first-line treatment for locally advanced or metastatic urothelial carcinoma (la/mUC), following the results of the phase III EV-302/KEYNOTE-A39 trial, which demonstrated a substantial improvement in progression-free survival (PFS) and overall survival (OS) compared with platinum-based chemotherapy (median PFS 12.5 vs. 6.3 months; median OS 33.8 vs. 15.9 months at 2.5-year follow-up) [1,2]. Despite these unprecedented response and survival rates, clinical outcomes with EV+P remain heterogeneous. Reliable, low-cost, and readily available markers are needed to complement conventional staging and performance status in risk stratification.

Several clinical prognostic models have been developed for mUC in earlier treatment eras. The Bellmunt risk score, derived in patients receiving second-line chemotherapy after platinum failure, incorporates ECOG performance status, liver metastases, and hemoglobin <10 g/dL as adverse prognostic factors [3], and has subsequently been adapted for the immunotherapy era [4]. In parallel, the inflammation- and nutrition-based Glasgow Prognostic Score (GPS) and its modified version (mGPS) are calculated from only two routine parameters: C-reactive protein (CRP) and serum albumin. It has been validated as a prognostic tool across a broad range of solid tumors, including urological malignancies [5]. For example, mGPS has demonstrated comparable on-treatment prognostic utility in metastatic renal cell carcinoma, where it outperformed prognostic value compared to the well-established IMDC risk score in a Phase 3 clinical trial [6]. In urothelial carcinoma specifically, baseline mGPS has been shown to predict survival in patients treated with immune checkpoint inhibitor (ICI) monotherapy [7] and to provide on-treatment information that complements radiological staging [8]. Comprehensive analysis across tumor types further confirmed the prognostic relevance of GPS/mGPS for ICI efficacy more broadly [9]. It has even been proposed to guide treatment decisions beyond progression on ICI-based therapy [10]. Prognostic models including inflammatory indices have recently been examined in patients receiving EV monotherapy after platinum chemotherapy and ICI [11,12]. However, to our knowledge, the prognostic value of mGPS has not been specifically evaluated in patients treated with the antibody–drug conjugate/checkpoint-inhibitor combination EV+P.

We hypothesized that baseline mGPS would demonstrate prognostic value for OS and PFS in EV+P treated mUC in a large multicenter registry and compared its discrimination with that of the established Bellmunt risk score.

Methods

Study design and patients

This retrospective, multicenter, real-world study included patients with la/mUC who initiated first-line treatment with EV+P, drawn from the GUARDIANS cohort, a German multicenter real-world registry [13]. Eligibility for this sub-analysis, applied to the 468 patients in the parent GUARDIANS registry across 25 German centers, required complete baseline CRP and albumin values, a recorded baseline ECOG performance status, complete vital status, and at least one follow-up or progression assessment; patients not meeting these criteria were excluded (Supplementary Figure S1). Baseline values were harmonized before analysis (albumin in g/L, hemoglobin in g/dL; CRP values reported as "<1 mg/L" were set to 0.9 mg/L), and implausible entries were treated as missing.

Ethical approval

This retrospective study was approved by the Ethics Committee at Heidelberg University, #S-568/2022, with waiver of informed consent.

mGPS definition and comparator

The mGPS was calculated from baseline CRP and albumin, measured 0–20 days prior to the first cycle of EV+P: mGPS 0, CRP ≤10 mg/L; mGPS 1, CRP >10 mg/L and albumin ≥35 g/L; mGPS 2, CRP >10 mg/L and albumin <35 g/L [14].

The original three-factor Bellmunt risk score served as the comparator. To directly benchmark mGPS against this established composite score, baseline hemoglobin values, measured within the same window as CRP and albumin,

were additionally retrieved for the analysis population, enabling calculation of the Bellmunt risk score (ECOG performance status >0, presence of liver metastases, and hemoglobin <10 g/dL, each scored 0 or 1 and summed to define good [0 factors], intermediate [1 factor], or poor [2–3 factors] risk groups) [3]. Because only few patients had all three factors, the number of patients with two and with three factors is reported separately.

Endpoints

OS was defined as the time from EV+P initiation to death from any cause, or last contact for patients alive. PFS was defined as the time from EV+P initiation to radiological or clinical progression, as determined by the treating investigators (not by blinded independent central review or protocol-defined RECIST assessment), or death from any cause, whichever occurred first, or to the date of the most recent staging assessment for patients without a documented progression event. Time-to-event variables were derived directly from documented treatment start, progression/staging, and death dates to ensure internal consistency between OS and PFS.

Statistical analysis

OS and PFS were estimated using the Kaplan–Meier method and compared across mGPS groups using the log-rank test. Cox proportional-hazards regression (Efron approximation for tied event times) was used to estimate univariable and multivariable hazard ratios (HR) with 95% confidence intervals (CI). mGPS was modeled as a categorical variable (mGPS 0 as reference). The multivariable model included mGPS, age (continuous), ECOG performance status (categorical: 0, 1, ≥2; reference 0), and presence of liver metastases (binary). Age, ECOG performance status, and liver metastases were selected a priori as adjustment covariates based on their role in the original and immunotherapy-adapted Bellmunt risk score [3,4]. A multiplicative mGPS×ECOG interaction term was tested in the multivariable model using a likelihood-ratio test, with both variables retained without an interaction term if this test was not statistically significant. Discrimination was assessed with Harrell's C-index (95% confidence intervals from 500 bootstrap resamples); mGPS and the Bellmunt risk score were compared as standalone predictors (univariable Cox models for the mGPS and Bellmunt risk groups) in patients with complete Bellmunt data, with the difference in C-index (mGPS minus Bellmunt) and its 95% confidence interval derived from paired bootstrap resampling. Associations of mGPS with ECOG performance status and sex were assessed with the chi-squared test, with age by the Kruskal–Wallis test, and with ECOG performance status and the Bellmunt risk group additionally by Spearman's rank correlation. All tests were two-sided; $p<0.05$ was considered statistically significant. Statistical analyses were performed using R version 4.5.2 (R Foundation for Statistical Computing).

Results

Patient characteristics

Of the 468 patients in the parent GUARDIANS registry, 310 (66.2%) across 19 centers met inclusion criteria and were included in the primary analysis population (Supplementary Figure S1). Baseline characteristics, overall and stratified by mGPS group, are summarized in Table 1. Median age was 69 years (IQR 59–76) and did not differ significantly across mGPS groups (Kruskal–Wallis p=0.98). 218 patients (70.3%) were male, with a similar sex distribution across mGPS groups (chi-squared p=0.56). ECOG performance status was 0 in 137 (44.2%), 1 in 111 (35.8%), and ≥2 in 62 patients (20.0%), and differed significantly across mGPS groups (p<0.001; Table 1). Liver metastases were present in 68 patients (21.9%). Baseline hemoglobin, enabling calculation of the Bellmunt risk score, was available for 308 patients (99.4%).

mGPS distribution and survival outcomes

Baseline mGPS was 0 in 118 patients (38.1%), 1 in 141 (45.5%), and 2 in 51 (16.5%). Median follow-up, estimated by the reverse Kaplan–Meier method, was 8.7 months (95% CI 7.4–9.9); during this period, 70 OS events (22.6%) and 139 PFS events (44.8%) were observed (Table 1). mGPS was significantly associated with both OS and PFS (log-rank p<0.001 for both; Figure 1). Estimated median OS was not reached in mGPS 0, was 33.7 months in mGPS 1 (95% CI 14.0–not reached), and was 12.5 months in mGPS 2 (95% CI 7.7–not reached). Estimated median PFS was 12.7 months (95% CI 10.5–not reached) in mGPS 0, 7.4 months (95% CI 6.4–10.8) in mGPS 1, and 5.7 months (95% CI 2.6–8.7) in mGPS 2.

Univariable and multivariable Cox regression

In univariable analysis, mortality risk increased stepwise with higher mGPS (mGPS 1 vs. 0: HR 2.61, 95% CI 1.39–4.89; mGPS 2 vs. 0: HR 4.48, 95% CI 2.19–9.18), with a similar pattern for PFS (mGPS 1 vs. 0: HR 1.74, 95% CI 1.17–2.58; mGPS 2 vs. 0: HR 2.80, 95% CI 1.74–4.51). After adjustment for age, ECOG performance status, and presence of liver metastases, mGPS remained independently associated with OS (mGPS 1: HR 2.26, 95% CI 1.19–4.29, p=0.013; mGPS 2: HR 3.11, 95% CI 1.46–6.63, p=0.003) and with PFS (mGPS 1: HR 1.63, 95% CI 1.09–2.45, p=0.018; mGPS 2: HR 2.36, 95% CI 1.43–3.90, p<0.001; Table 2, Figure 2). Model discrimination was moderate (C-index 0.71, 95% CI 0.66–0.78 for OS; 0.65, 95% CI 0.61–0.71 for PFS). ECOG performance status was itself strongly and independently prognostic for OS (ECOG 1 vs. 0: HR 1.93, 95% CI 1.06–3.50; ECOG ≥2 vs. 0: HR 3.06, 95% CI 1.59–5.90) and, to a lesser degree, PFS (ECOG 1 vs. 0: HR 1.31, 95% CI 0.89–1.95; ECOG ≥2 vs. 0: HR 1.89, 95% CI 1.20–2.99; Table 2). Because mGPS and ECOG performance status were correlated (χ^2=30.0, p<0.001; Spearman ρ=0.30), we formally tested for an mGPS×ECOG interaction. This was not significant for OS (likelihood-ratio p=0.634) or PFS (p=0.834), indicating that the two variables can be jointly modeled without an interaction term. Age was not independently associated with either endpoint, and presence of liver metastases showed no significant association with OS or PFS in either univariable or multivariable analysis (Table 2).

Comparison with the Bellmunt risk score

Applying the original three-factor Bellmunt risk score (ECOG performance status >0, liver metastases, and hemoglobin <10 g/dL) to the 308 patients with available hemoglobin values (see Patient characteristics) classified 94 patients (30.5%) as good risk (0 factors), 130 (42.2%) as intermediate risk (1 factor), and 84 (27.3%) as poor risk (2 factors: 71 [23.1%]; 3 factors: 13 [4.2%]; combined as in the original score). As standalone predictors, both mGPS and the Bellmunt risk group were associated with OS and PFS, with hazard ratios of similar magnitude (Table 3).

In these 308 patients, discrimination of mGPS (C-index 0.65, 95% CI 0.59–0.71 for OS; 0.62, 95% CI 0.57–0.67 for PFS) was similar to that of the Bellmunt risk score (C-index 0.66, 95% CI 0.60–0.71 for OS; 0.60, 95% CI 0.55–0.65 for PFS; Table 3). The difference in C-index (mGPS minus Bellmunt) was not significant for either endpoint (OS: −0.007, 95% CI −0.081 to 0.071; PFS: 0.016, 95% CI −0.044 to 0.077). mGPS and the Bellmunt risk group were moderately correlated (Spearman ρ=0.39, p<0.001), indicating partly overlapping prognostic information (cross-tabulation in Supplementary Table S1).

Discussion

In this multicenter real-world cohort of 310 patients treated with first-line EV+P for la/mUC, baseline mGPS was independently associated with both OS and PFS after adjustment for age, ECOG performance status, and presence of liver metastases, with moderate model discrimination. To our knowledge, this is the first description of the prognostic value of mGPS specifically within the EV+P combination setting, extending previous observations of GPS/mGPS as a prognostic tool in mUC treated with ICI monotherapy [7,9], including on-treatment mGPS assessment in mUC [8] and metastatic renal cell carcinoma [6] by the same research group, and EV monotherapy after platinum/ICI failure [11,12].
The attenuation of the mGPS hazard ratios between univariable and multivariable analysis, particularly for mGPS 2 and OS, suggests that part of its prognostic signal is mediated through, or confounded by, ECOG performance status, consistent with the pathophysiological link between systemic inflammation, hypoalbuminemia, and functional decline. Formal likelihood-ratio testing did not, however, support a significant mGPS×ECOG interaction, and a substantial independent effect of mGPS persisted after adjustment. Although mGPS and ECOG performance status were correlated, mGPS is an objective, laboratory-based measure whereas ECOG assessment is inherently observer-dependent. mGPS may therefore provide complementary, more reproducible prognostic information rather than simply recapitulating performance status. In contrast, mGPS was not associated with sex (p=0.563) or age (p=0.976; Table 1), suggesting that, unlike its relationship with performance status, mGPS is not simply a proxy for classical demographic risk factors in this cohort.

A notable finding was the absence of a significant association between liver metastases and OS or PFS in our cohort, in contrast to the original Bellmunt risk score, in which liver metastases is one of three canonical adverse prognostic factors alongside ECOG performance status and hemoglobin <10 g/dL [3]. This is in line with subgroup analyses of the pivotal EV-302 trial, in which the OS/PFS benefit of EV+P over chemotherapy was consistently maintained across baseline subgroups, including patients with liver metastases [1]. Several explanations may be considered. First, EV, as an antibody–drug conjugate targeting Nectin-4, and pembrolizumab, as an ICI, act through mechanisms distinct from cytotoxic chemotherapy, and their combined activity may partially overcome the traditionally poor prognosis conferred by visceral, particularly hepatic, disease. Second, the relatively modest size of the liver-metastasis subgroup in our cohort (n=68, 21.9%) limits statistical power to detect a moderate effect, as reflected in the wide confidence intervals around both the univariable and multivariable estimates (Table 2). Third, part of the prognostic information historically carried by liver metastases may be captured indirectly through mGPS or ECOG in the modern treatment context. This finding should be interpreted with caution and warrants confirmation in larger, ideally pooled, real-world cohorts or within prospective trial datasets.

To directly evaluate the added value of mGPS relative to an established composite risk score, we compared the standalone discrimination of mGPS with that of the original three-factor Bellmunt risk score in the same cohort. Discrimination was similar for both OS and PFS, and the confidence intervals of the difference in C-index included zero. mGPS, which requires only two routine laboratory values, thus performed comparably to a composite score that additionally requires performance status, metastatic site, and hemoglobin. The moderate correlation between the two scores suggests that they capture partly distinct information, but whether combining them improves risk stratification was not assessed here and warrants evaluation in larger cohorts. This comparison was, however, performed within the same real-world dataset used to derive mGPS, and independent external validation of both scores is warranted before either is adopted for clinical decision-making.

Median follow-up in this real-world cohort was short (8.7 months by the reverse Kaplan–Meier method), reflecting the recent introduction of EV+P as first-line standard of care. OS estimates, particularly the non-reached median in the low-risk mGPS 0 subgroup, should therefore be considered statistically immature, and longer follow-up will be required to confirm the stability of these estimates. Nonetheless, the observed number of events (70 OS and 139 PFS events) permitted the multivariable models presented here, although the events-per-variable ratio for OS (approximately 12 per parameter) was at the lower end. This contrasts with the considerably more mature 2.5-year median follow-up reported for the pivotal EV-302/KEYNOTE-A39 trial [2].

This analysis was performed within the German multicenter GUARDIANS cohort, which has previously reported effectiveness and safety outcomes for first-line EV+P in a real-world urothelial carcinoma population [13]. The

present mGPS-focused analysis extends those findings by evaluating a simple, routinely available inflammation-based biomarker within the same multicenter network, and our results can be directly contextualized against the parent GUARDIANS cohort as further real-world data mature.

Strengths of this study include its multicenter design across 19 German centers, a comprehensive, source-data-verified time-to-event dataset, and a systematic evaluation of the relationship between mGPS and classical demographic and clinical prognostic factors. Limitations include the retrospective design, potential residual confounding, a real-world population that included some patients with ECOG ≥2 not represented in the EV-302 trial population, restriction to German centers, immature OS follow-up, and the unavailability of objective response data for this analysis. In total, 158 of 468 patients (33.8%) in the parent registry were not included in this sub-analysis, predominantly reflecting non-systematic baseline CRP/albumin ascertainment across centers rather than missingness among individually screened patients (Supplementary Figure S1), which we consider unlikely to be a material source of bias. The comparison with the Bellmunt risk score, while based on hemoglobin values available for 99.4% of the analysis population, was performed within the same real-world dataset used to derive mGPS rather than in an independent validation cohort, and formal external validation of both scores remains warranted.

Conclusion

In this large multicenter real-world cohort of patients treated with first-line EV+P for la/mUC, the modified Glasgow Prognostic Score was independently associated with both overall and progression-free survival, largely unrelated to age or sex and providing prognostic information complementary to, rather than redundant with, ECOG performance status. Presence of liver metastases, a classical adverse factor in the Bellmunt score, was not independently prognostic in this cohort. As a simple, inexpensive, and routinely available biomarker, mGPS discriminated similarly to the established Bellmunt risk score and may support individualized risk stratification in the EV+P era; it merits prospective validation.

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Data Availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

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Table 1. Baseline characteristics of the analysis population, overall and by mGPS group (n=310)

Characteristic	Overall (n=310)	mGPS 0 (n=118)	mGPS 1 (n=141)	mGPS 2 (n=51)	p
Age, median (IQR), years	69 (59–76)	69 (59–75)	69 (61–75)	67 (59–78)	0.976
Male sex, n (%)	218 (70.3)	79 (66.9)	103 (73.0)	36 (70.6)	0.563
ECOG performance status, n (%)					<0.001
0	137 (44.2)	69 (58.5)	58 (41.1)	10 (19.6)	
1	111 (35.8)	38 (32.2)	52 (36.9)	21 (41.2)	
≥ 2	62 (20.0)	11 (9.3)	31 (22.0)	20 (39.2)	
Primary tumor site, n (%)					0.615
Bladder	209 (67.4)	82 (69.5)	88 (62.4)	39 (76.5)	
Upper tract	81 (26.1)	29 (24.6)	42 (29.8)	10 (19.6)	
Urethra	4 (1.3)	2 (1.7)	2 (1.4)	0 (0.0)	
More than one location	16 (5.2)	5 (4.2)	9 (6.4)	2 (3.9)	
CRP, median (IQR), mg/L*	18 (6–56)	4 (2–7)	36 (20–67)	89 (36–138)	<0.001
Albumin, median (IQR), g/L*	40 (36–43)	42 (40–45)	40 (37–42)	33 (30–34)	<0.001
mGPS, n (%)					
0	118 (38.1)	118 (100)	–	–	
1	141 (45.5)	–	141 (100)	–	
2	51 (16.5)	–	–	51 (100)	
Liver metastases, n (%)	68 (21.9)	16 (13.6)	40 (28.4)	12 (23.5)	0.016
Lung metastases, n (%)	119 (38.4)	39 (33.1)	60 (42.6)	20 (39.2)	0.291
Bone metastases, n (%)	81 (26.1)	23 (19.5)	40 (28.4)	18 (35.3)	0.071
Lymph node involvement, n (%)	228 (73.5)	82 (69.5)	109 (77.3)	37 (72.5)	0.359
Adrenal metastases, n (%)	13 (4.2)	2 (1.7)	11 (7.8)	0 (0.0)	0.013
Peritoneal metastases, n (%)	24 (7.7)	6 (5.1)	11 (7.8)	7 (13.7)	0.155
Brain metastases, n (%)	6 (1.9)	3 (2.5)	3 (2.1)	0 (0.0)	0.532
OS events, n (%)	70 (22.6)	13 (11.0)	39 (27.7)	18 (35.3)	<0.001
PFS events, n (%)	139 (44.8)	38 (32.2)	70 (49.6)	31 (60.8)	<0.001
Median follow-up (reverse KM), months	8.7 (95% CI 7.4–9.9)	–	–	–	–

*p-values from the chi-squared test (categorical variables) or Kruskal–Wallis test (continuous variables) across the three mGPS groups. *CRP and albumin are shown for descriptive completeness only; The ECOG and primary-tumor-site p-values refer to the respective omnibus (3×3 / 4×3) comparisons across mGPS groups.*

Table 2. Univariable and multivariable Cox regression for OS and PFS (n=310)

Variable	OS univar. HR (95% CI)	p	OS multivar. HR (95% CI)	p	PFS univar. HR (95% CI)	p	PFS multivar. HR (95% CI)	p
mGPS 1 vs. 0	2.61 (1.39–4.89)	0.003	2.26 (1.19–4.29)	0.013	1.74 (1.17–2.58)	0.006	1.63 (1.09–2.45)	0.018
mGPS 2 vs. 0	4.48 (2.19–9.18)	<0.001	3.11 (1.46–6.63)	0.003	2.80 (1.74–4.51)	<0.001	2.36 (1.43–3.90)	<0.001
Age (per year)	1.00 (0.98–1.02)	0.807	1.00 (0.98–1.02)	0.808	1.00 (0.98–1.01)	0.508	0.99 (0.98–1.01)	0.356
ECOG 1 vs. 0	2.25 (1.25–4.04)	0.007	1.93 (1.06–3.50)	0.031	1.41 (0.97–2.07)	0.075	1.31 (0.89–1.95)	0.175
ECOG ≥2 vs. 0	4.06 (2.16–7.62)	<0.001	3.06 (1.59–5.90)	<0.001	2.25 (1.44–3.50)	<0.001	1.89 (1.20–2.99)	0.006
Presence of liver metastases	1.50 (0.90–2.48)	0.119	1.15 (0.68–1.94)	0.608	1.29 (0.89–1.88)	0.175	1.11 (0.76–1.62)	0.595

Multivariable model adjusted for mGPS, age, ECOG performance status (categorical), and presence of liver metastases; mGPS 0 and ECOG 0 are the reference categories. Model discrimination: Harrell's C-index 0.71 (95% CI 0.66–0.78) for OS and 0.65 (95% CI 0.61–0.71) for PFS. A formal likelihood-ratio test for an mGPS×ECOG interaction was not significant (OS p=0.634; PFS p=0.834).

Table 3. Association with survival and discrimination of mGPS and the Bellmunt risk score as standalone predictors (n=308)

Predictor (univariable Cox model)	OS HR (95% CI)	p	PFS HR (95% CI)	p
mGPS 1 vs. 0	2.66 (1.42–4.98)	0.002	1.77 (1.19–2.63)	0.005
mGPS 2 vs. 0	4.48 (2.19–9.18)	<0.001	2.80 (1.74–4.51)	<0.001
Bellmunt intermediate vs. good	1.94 (0.96–3.89)	0.064	1.86 (1.18–2.93)	0.008
Bellmunt poor vs. good	4.15 (2.08–8.27)	<0.001	2.59 (1.60–4.20)	<0.001
Model	**C-index OS (95% CI)**		**C-index PFS (95% CI)**	
mGPS	0.65 (0.59–0.71)		0.62 (0.57–0.67)	
Bellmunt risk score	0.66 (0.60–0.71)		0.60 (0.55–0.65)	
Difference (mGPS minus Bellmunt)	−0.007 (−0.081 to 0.071)		0.016 (−0.044 to 0.077)	

Hazard ratios (HR) with 95% confidence intervals (CI) from separate univariable Cox models in the 308 patients with complete Bellmunt risk score data; mGPS 0 and Bellmunt good risk are the reference categories. C-index: Harrell's C-index with 95% CIs from 500 bootstrap resamples; the difference in C-index and its 95% CI were derived from paired bootstrap resampling of the same patients.

Figure 1. Kaplan–Meier estimates by baseline mGPS group in the primary analysis population (N=310; mGPS 0: n=118; mGPS 1: n=141; mGPS 2: n=51). (A) Overall survival. (B) Progression-free survival. Tick marks indicate censored observations. Groups were compared using the log-rank test (p<0.001 for both).

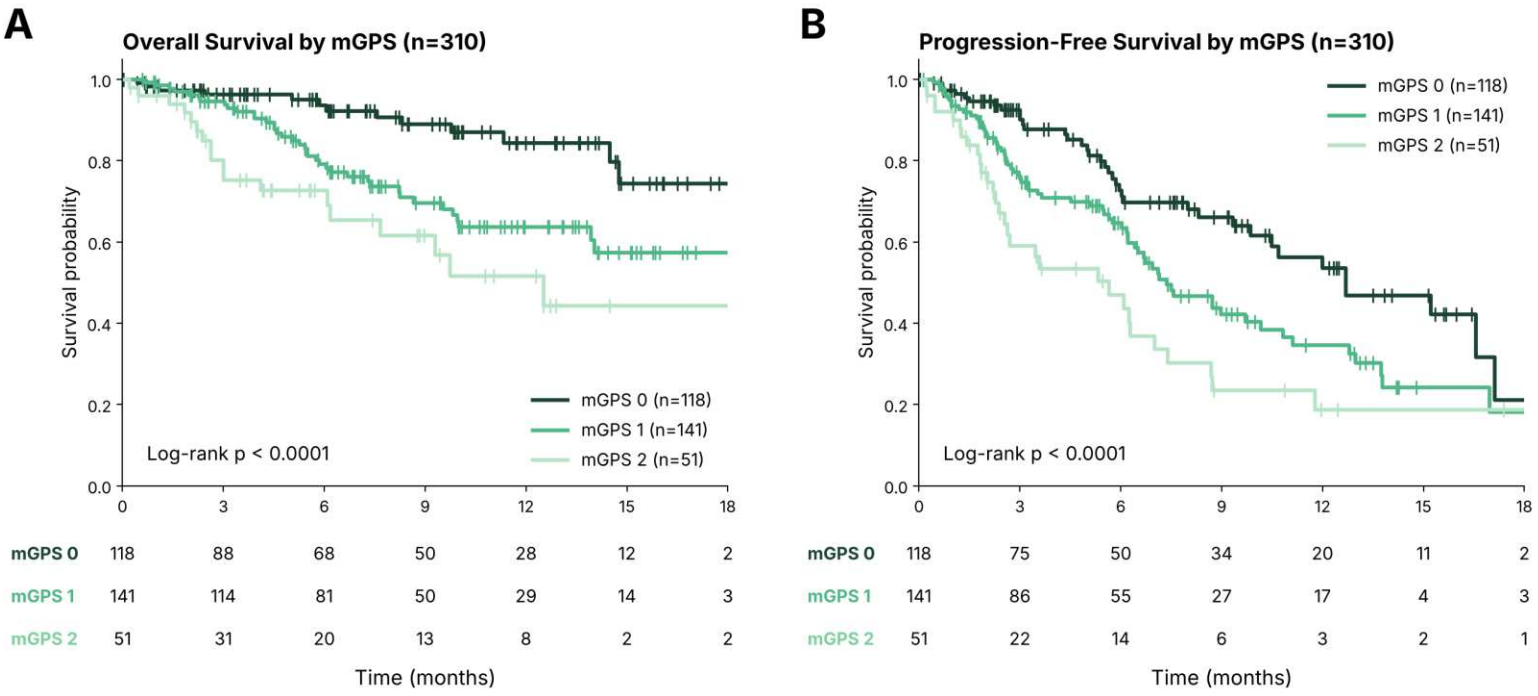
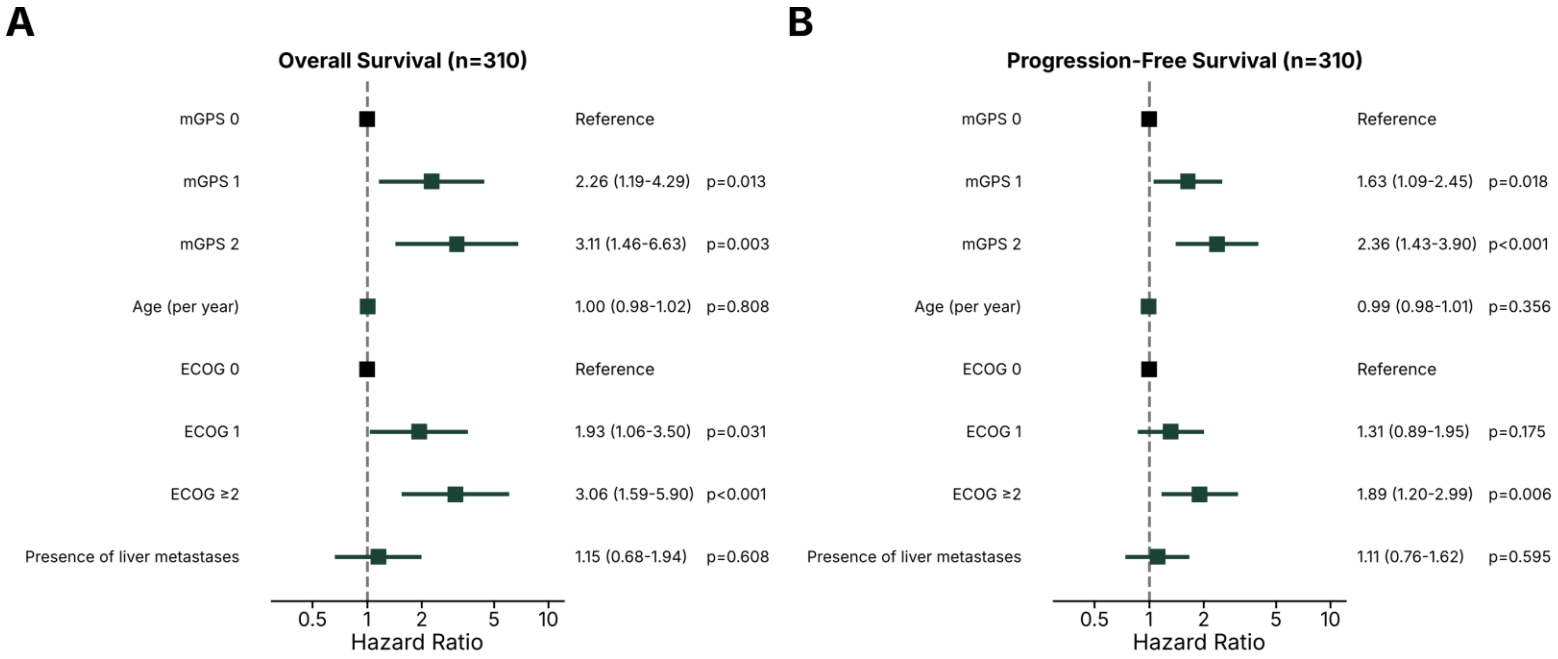


Figure 2. Forest plots of multivariable Cox proportional-hazards regression (N=310). Hazard ratios with 95% confidence intervals are shown for mGPS (reference: mGPS 0), age (per year), ECOG performance status (reference: ECOG 0), and presence of liver metastases, mutually adjusted in a single model. (A) Overall survival. (B) Progression-free survival.



Supplementary Files

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