scientific reports

Check for updates

OPEN

Preoperative ECOG performance status as a predictor of outcomes in upper tract urothelial cancer surgery

Tsung-Mu Yang[1], I-Hsuan Alan Chen[2], Chia-Cheng Yu[2], Chi-Rei Yang[3], Wen-Chi Chen[3,4], Po-Hung Lin[5,6,7], See-Tong Pang[5,6], Steven Kuan-Hua Huang[8,9], Zhi-Hao Chen[8,10], Jen-Shu Tseng[11,12,13], Wun-Rong Lin[11,12], Yao-Chou Tsai[14,15,16], Chih-Chin Yu[15,17], Pi-Che Chen[18], Ian-Seng Cheong[18], Yuan-Hong Jiang[19], Chia-Chang Wu[20,21,22], Hsu-Che Huang[23,24], Ting-En Tai[16], Chung-You Tsai[25,26], Wei-Yu Lin[6,27,28], Yung-Tai Chen[29,30,31], Richard Chen-Yu Wu[32,33], Hsiang-Ying Lee[1,34,35]✉ & Hsin-Chih Yeh[1,34,36]✉

Eastern Cooperative Oncology Group performance status (ECOG-PS) is a widely used functional status measure in oncology, yet its prognostic value in upper tract urothelial carcinoma remains unclear. In this multicenter study of 2473 patients undergoing radical nephroureterectomy, ECOG-PS ≥ 2 was independently associated with worse overall survival (hazard ratio [HR] 2.53, $p < 0.001$), cancer-specific survival (HR 2.02, $p < 0.001$), and disease-free survival (HR 1.50, $p = 0.003$) than those with ECOG-PS 0–1. They also had a higher risk of major perioperative complications (odds ratio 2.46, $p < 0.001$). These findings support ECOG-PS as a valuable preoperative risk stratification tool.

Keywords Eastern cooperative oncology group, Major perioperative complication, Radical nephroureterectomy, Survival outcome, Upper tract urothelial carcinoma

[1]Department of Urology, Kaohsiung Medical University Hospital, No. 100, Tzyou 1st Rd., Sanmin District, Kaohsiung 807377, Taiwan. [2]Division of Urology, Department of Surgery, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan. [3]Department of Urology, China Medical University Hospital, Taichung, Taiwan. [4]Graduate Institute of Integrated Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan. [5]Division of Urology, Department of Surgery, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan. [6]School of Medicine, College of Medicine, Chang Gung University, Taoyuan, Taiwan. [7]Graduate Institute of Clinical Medical Science, College of Medicine, Chang Gung University, Taoyuan, Taiwan. [8]Division of Urology, Department of Surgery, Chi Mei Medical Center, Tainan, Taiwan. [9]Department of Medical Science Industries, College of Health Sciences, Chang Jung Christian University, Tainan, Taiwan. [10]Institute of Biomedical Sciences, National Sun Yat-Sen University, Kaohsiung, Taiwan. [11]Department of Urology, MacKay Memorial Hospital, Taipei, Taiwan. [12]Mackay Medical College, Taipei, Taiwan. [13]Institute of Biomedical Informatics, National Yang Ming Chiao Tung University, Taipei, Taiwan. [14]Department of Surgery, Taipei Tzu Chi Hospital, The Buddhist Tzu Chi Medical Foundation, New Taipei City, Taiwan. [15]School of Medicine, Buddhist Tzu Chi University, Hualien, Taiwan. [16]Department of Urology, Taipei Medical University Hospital, Taipei Medical University, Taipei, Taiwan. [17]Division of Urology, Department of Surgery, Taipei Tzuchi Hospital, The Buddhist Tzu Chi Medical Foundation, New Taipei City, Taiwan. [18]Department of Urology, Ditmanson Medical Foundation, Chiayi Christian Hospital, Chiayi, Taiwan. [19]Department of Urology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation and Tzu Chi University, Hualien, Taiwan. [20]Department of Urology, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan. [21]Department of Urology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan. [22]TMU Research Center of Urology and Kidney (TMU-RCUK), Taipei Medical University, Taipei, Taiwan. [23]Division of Urology, Department of Surgery, Cardinal Tien Hospital, New Taipei City, Taiwan. [24]Department of Life Science, College of Science, National Taiwan Normal University, Taipei, Taiwan. [25]Divisions of Urology, Department of Surgery, Far Eastern Memorial Hospital, New Taipei City, Taiwan. [26]Department of Electrical Engineering, Yuan Ze University, Taoyuan, Taiwan. [27]Division of Urology, Department of Surgery, Chang Gung Memorial Hospital, Chia-Yi, Taiwan. [28]Chang Gung University of Science and Technology, Chia-Yi, Taiwan. [29]Department of Urology, Postal Hospital, Taipei, Taiwan. [30]Department of Urology, Taiwan Adventist Hospital, Taipei, Taiwan. [31]Department of Urology, National Taiwan University Hospital, Taipei, Taiwan.

[32]Department of Urology, E-Da Hospital, Kaohsiung, Taiwan. [33]Department of Information Engineering, I-Shou University, Kaohsiung, Taiwan. [34]Department of Urology, School of Medicine, College of Medicine, Kaohsiung Medical University, Sanmin District, No. 100, Shih-Chuan 1st Rd., Kaohsiung 80708, Taiwan. [35]Graduate Institute of Clinical Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan. [36]Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan. ✉email: ashum1009@hotmail.com; patrick1201.tw@yahoo.com.tw

Upper tract urothelial carcinoma (UTUC) is a rare but aggressive malignancy. While radical nephroureterectomy (RNU) remains the standard of care[1], contemporary 5-yr recurrence-free survival can be as low as 69%[2]. Optimizing perioperative risk stratification remains a critical challenge.

ECOG-PS is a simple and widely used oncology metric[3], and is linked to various cancer types[4–6]. However, its role in UTUC remain uncertain due to conflicting results[7–13]. Most studies suffer from outdated data, small sample sizes, limited control over confounding variables, and heterogeneity in ECOG-PS score cutoff points, which diminishes its prognostic value for clinicians.

Furthermore, some studies have explored the influence of ECOG-PS on perioperative complications after RNU. Raman et al. included ECOG-PS in a preoperative nomogram for surgical risk assessment[14], and one retrospective study identified ECOG-PS ≥ 2 as a predictor of complications[15]. However, due to limited research, the relationship remains uncertain.

Taiwan has a notably high prevalence of UTUC. To better understand the disease, the Taiwan UTUC Collaboration Group, comprising multiple medical centers, established a nearly nationwide database. By utilizing this large-scale multicenter registry, this study aims to evaluate the prognostic significance of preoperative ECOG-PS regarding outcomes and complications in patients undergoing RNU for UTUC.

Methods

Study design and patient population

This retrospective study retrieved data from the UTUC registry database maintained by the Taiwan UTUC Collaboration Group. The database is a multicenter internet-based registry where participating surgeons from sixteen different teaching hospitals registered 6005 cases of UTUC in Taiwan between 1988 and 2023. Each contributing institute followed up on cases and maintained the datasets, with consensus meetings held to systematically address any discrepancies. After excluding patients who did not undergo RNU or had missing data essential for this study, a total of 2473 eligible patients were included in the final analysis. The flowchart of patient selection is presented in the Supplementary Fig. 1. While the reduction in sample size may limit the generalizability of the findings, the exclusion of missing data ensured the validity of the multivariable analysis.

This study was approved by Kaohsiung Medical University Hospital institutional review board (KMUH IRB) (KMUHIRB-E(I)-20,180,214) and was registered at ClinicalTrials.gov (ID: NCT06305130). Our study adhered to the Declaration of Helsinki and institutional regulations. The database is retrospective and contains de-identified information; the KMUH IRB granted an expedited review and waived the need for formal informed consent after verification of the protocol.

Covariates

The selection of covariates was guided by existing literature and clinical expertise. The included covariates were ECOG-PS, age, gender, history of bladder cancer, estimated glomerular filtration rate (eGFR), hypertension, diabetes mellitus, preoperative hydronephrosis, tumor size, tumor location, multifocality, pathological T stage, pathological N stage, histological variant, tumor grade, lymphovascular invasion, surgical margin, tumor necrosis, surgical method (open, hand-assisted laparoscopic, or laparoscopic/robotic surgery), and receipt of systemic chemotherapy (none, adjuvant, or salvage/palliative chemotherapy).

Outcome measurement

Duration of overall survival (OS), cancer-specific survival (CSS), and disease-free survival (DFS) was defined as the time from the pathological diagnosis of UTUC to all-cause death for OS, cancer-specific death for CSS, and either clinical evidence of disease recurrence or cancer-specific death for DFS. After registration in the database, patients' information was regularly updated, with the end date for data inclusion set as June 2024 for this study. However, not all patients had their information updated to this cutoff date. Patients who were still alive were censored at the date of the last data update. The secondary outcome was major complications, defined as any Clavien-Dindo perioperative complication ≥ grade 3 that occurred at any time before hospital discharge.

Statistical analysis

Patients were categorized into low and high ECOG-PS groups (0–1 vs. 2–4) based on two considerations. First, this cutoff is widely used in existing studies to distinguish healthier patients (PS 0–1) from those with poorer functional status (PS 2–4). Second, the small number of patients with PS 3 (n = 23) and PS 4 (n = 7), as shown in Supplementary Fig. 1, along with the requirement for a sufficient number of events per variable in regression analysis, further justified this grouping. Group differences were compared using the chi-square test. Survival curves were generated with the Kaplan–Meier method and compared using the log-rank test. Cox proportional hazards models were applied to explore prognostic factors.

Retrospective studies carry risks of selection bias, recall bias, incomplete data, and uncollected confounders from medical records. To minimize bias from non-randomized assignment, we performed propensity-score matching (PSM) based on the probability of being in a comparison group conditioned on observed covariates. To enhance statistical power while maintaining an adequate control group size, we applied 1:5 optimal matching was performed with a caliper size of 0.2 standard deviation. This approach balances the trade-off between sample

representativeness and bias reduction. All previously mentioned covariates were included in the matching process. Multivariable analyses were also conducted following the matching.

Additionally, we performed a competing-risk model to more accurately estimate the subdistribution hazards in cancer-related outcomes. For CSS, death unrelated to UTUC was considered competing events, while for DFS, all-cause death was treated as a competing event. Logistic regression models were employed to identify determining factors for major perioperative complications. Only covariates demonstrating statistical significance were retained in the multivariable models. This approach was adopted to minimize the risk of overfitting and to ensure model parsimony. A significance level of $p < 0.05$ was applied, and all analyses were performed using Statistical Analysis System version 9.4 (SAS Institute Inc., Cary, NC).

Results

Baseline characteristics

A total of 2,473 patients were included in the analysis (Table 1). The mean and median follow-up times were 44.5 and 36.8 mo, respectively. The mean age at diagnosis was 68.9 yr, and the median age was 69.7 yr. Among them, 2247 had an ECOG-PS score of 0–1, while 226 had an ECOG-PS score of 2–4.

Difference between ECOG-PS groups in primary cohort

Patients with an ECOG-PS score of 2–4 were older and predominantly female. They exhibited lower eGFR and had a higher prevalence of hypertension and diabetes mellitus compared to individuals with an ECOG-PS score of 0–1. Significant differences between the ECOG-PS groups were also observed in preoperative hydronephrosis ($p = 0.037$), pathological T stage ($p = 0.011$), histological variant ($p = 0.002$), lymphovascular invasion ($p < 0.001$), surgical margin ($p < 0.001$), surgical method ($p = 0.002$), and chemotherapy ($p < 0.001$) (Table 1).

Survival analyses of primary cohort

The median OS for the ECOG-PS 0–1 group was 131.6 mo (95% confidence interval [CI] 116.9 to ∞) compared to 43.0 mo (95% CI 31.7–58.3) for the ECOG-PS 2–4 group ($p < 0.001$; Fig. 1a). The 5-yr OS, CSS and DFS rates were 73.9%, 83.6% and 71.6%, respectively, for patients in the ECOG-PS 0–1 group, compared to 41.0%, 64.7% and 55.2% for patients in the ECOG-PS 2–4 group ($p < 0.001$ for all; Fig. 1 and Table 2). The survival curves suggested a clear correlation between higher ECOG-PS scores and poorer survival outcomes. To illustrate the trend of worsening outcomes with increasing ECOG scores, separate survival curves for PS 0–1, 2, 3, and 4 are presented in Supplementary Fig. 2. The results confirm that OS, CSS, and DFS consistently deteriorate as ECOG scores increase ($p < 0.001$ for all).

Multivariable Cox regression models showed that in the primary cohort, an ECOG-PS score of 2–4 is a significant factor for OS, CSS, and DFS (hazard ratio [HR] 2.53, 95% CI 2.01–3.18, $p < 0.001$; HR 2.02, 95% CI 1.49–2.74, $p < 0.001$; HR 1.50, 95% CI 1.13–2.00, $p = 0.006$, respectively; Table 3). The results of univariable and full multivariable analyses are presented in Supplementary Tables 1 and 2.

Survival analyses after propensity-score matching

To minimize the effect of confounders, PSM was performed for the ECOG-PS 0–1 and 2–4 patients. Patients were matched as described in the methodology. All covariates were well balanced between groups after matching (Table 1).

After PSM, Kaplan–Meier analysis still revealed significantly worse OS, CSS, and DFS ($p < 0.001$ for all) for the ECOG-PS 2–4 group (Fig. 2). Multivariable Cox regression models also indicated that ECOG-PS 2–4 was associated with unfavorable OS, CSS, and DFS (HR 2.69, 95% CI 2.14–3.38, $p < 0.001$; HR 2.12, 95% CI 1.53–2.95, $p < 0.001$; HR, 1.53; 95% CI 1.15–2.02, $p = 0.003$, respectively; Table 3). The results of univariable and full multivariable analyses are provided in Supplementary Tables 1 and 2.

Competing-risk models for cancer-related outcomes

To further validate these findings, we applied competing-risk models for CSS and DFS to account for competing events. In the primary cohort, ECOG-PS 2–4 was significantly associated with worse CSS (subdistribution HR [SHR] 1.45, 95% CI 1.13–1.87, $p = 0.004$). For DFS, the association approached but did not reach statistical significance (SHR 1.22, 95% CI 1.00–1.49, $p = 0.05$) (Table 3). In the PSM cohort, the competing-risk model confirmed the significant association between ECOG-PS 2–4 and inferior CSS and DFS (SHR 1.47, 95% CI 1.14–1.89, $p = 0.003$; SHR 1.24, 95% CI 1.02–1.52, $p = 0.036$, respectively; Table 3). The results of univariable and full multivariable competing-risk models are showed in Supplementary Tables 3 and 4.

Other independent factors in survival analysis

As shown in Supplementary Table 2, old age, history of bladder cancer (particularly concurrent bladder cancer), and receipt of systemic chemotherapy were associated with unfavorable OS, CSS, and DFS ($p < 0.05$ for all). Male gender, low eGFR, hypertension, and preoperative hydronephrosis were associated with poorer OS ($p < 0.05$ for all), while laparoscopic/robotic surgery showed a favorable effect on OS ($p = 0.033$).

Tumor-related factors such as larger tumor size, advanced pathological T stage, positive lymph nodes, and lymphovascular invasion were significant predictors of worse OS, CSS, and DFS ($p < 0.05$ for all). Positive surgical margin was linked to unfavorable OS and CSS ($p < 0.05$ for both). Additionally, histological variant was associated with inferior CSS ($p = 0.006$), while high tumor grade was a significant prognostic indicator for worse CSS and DFS ($p = 0.033$ and $p = 0.029$, respectively). Multifocality was associated with inferior DFS ($p = 0.014$).

	Primary cohort (n = 2473)			After PSM (n = 1332)		
Patients	ECOG-PS 0–1 2247 (%)	ECOG-PS 2–4 226 (%)	*p*	ECOG-PS 0–1 1110 (%)	ECOG-PS 2–4 222 (%)	*p*
Clinical characteristics						
Age			< 0.001			0.28
< 70	1204 (53.6)	61 (27.0)		346 (31.2)	61 (27.5)	
> 70	1043 (46.4)	165 (73.0)		764 (68.8)	161 (72.5)	
Gender			0.010			0.45
Male	976 (43.4)	79 (35.0)		410 (36.9)	76 (34.2)	
Female	1271 (56.6)	147 (65.0)		700 (63.1)	146 (65.8)	
History of bladder cancer			0.52			0.94
No	1678 (74.7)	166 (73.5)		823 (74.1)	165 (74.3)	
Previous	180 (8.0)	23 (10.2)		113 (10.2)	21 (9.5)	
Concurrent	389 (17.3)	37 (16.4)		174 (15.7)	36 (16.2)	
eGFR			0.038			0.83
≥ 60	833 (37.1)	68 (30.1)		343 (30.9)	67 (30.2)	
< 60	1414 (62.9)	158 (69.9)		767 (69.1)	155 (69.8)	
Hypertension			< 0.001			0.64
No	955 (42.5)	70 (31.0)		368 (33.2)	70 (31.5)	
Yes	1292 (57.5)	156 (69.0)		742 (66.8)	152 (68.5)	
Diabetes mellitus			0.002			0.50
No	1649 (73.4)	144 (63.7)		746 (67.2)	144 (64.9)	
Yes	598 (26.6)	82 (36.3)		364 (32.8)	78 (35.1)	
Preoperative hydronephrosis			0.037			0.67
No	826 (36.8)	99 (43.8)		463 (41.7)	96 (43.2)	
Yes	1421 (63.2)	127 (56.2)		647 (58.3)	126 (56.8)	
Surgical method			0.002			0.85
Open	572 (25.5)	79 (35.0)		360 (32.4)	76 (34.2)	
HALNU	574 (25.5)	39 (17.3)		208 (18.7)	39 (17.6)	
Laparoscopic/Robotic Surgery	1101 (49.0)	108 (47.8)		542 (48.8)	107 (48.2)	
Systemic chemotherapy			< 0.001			0.80
No	1598 (71.1)	183 (81.0)		906 (81.6)	179 (80.6)	
Adjuvant	489 (21.8)	25 (11.0)		128 (11.5)	25 (11.3)	
Salvage/palliative	160 (7.1)	18 (8.0)		76 (6.8)	18 (8.1)	
Pathological characteristics						
Tumor size			0.50			0.43
< 3 cm	1071 (47.7)	113 (50.0)		592 (53.3)	112 (50.5)	
≥ 3 cm	1176 (52.3)	113 (50.0)		518 (46.7)	110 (49.5)	
Tumor location			0.89			0.98
Pelvis	933 (41.5)	95 (42.0)		464 (41.8)	94 (42.3)	
Ureter	846 (37.7)	87 (38.5)		438 (39.5)	86 (38.7)	
Both	468 (20.8)	44 (19.5)		208 (18.7)	42 (18.9)	
Multifocality			0.64			0.74
No	1418 (63.1)	139 (61.5)		698 (62.9)	137 (61.7)	
Yes	829 (36.9)	87 (38.5)		412 (37.1)	85 (38.3)	
Pathological T stage			0.011			0.68
pTis/ pTa/ pT0	370 (16.5)	33 (14.6)		192 (17.3)	33 (14.9)	
pT1	549 (24.4)	56 (24.8)		293 (26.4)	56 (25.2)	
pT2	445 (19.8)	32 (14.2)		167 (15.0)	32 (14.4)	
pT3	779 (34.7)	84 (37.2)		387 (34.9)	82 (36.9)	
pT4	104 (4.6)	21 (9.3)		71 (6.4)	19 (8.6)	
Pathological N stage			0.19			0.92
pN0	536 (23.9)	45 (19.9)		230 (20.7)	45 (20.3)	
pNx	1593 (70.9)	164 (72.6)		808 (72.8)	161 (72.5)	
pN +	118 (5.3)	17 (7.5)		72 (6.5)	16 (7.2)	
Histological variant			0.002			0.26
No	2005 (89.2)	186 (82.3)		957 (86.2)	185 (83.3)	
Yes	242 (10.8)	40 (17.7)		153 (13.8)	37 (16.7)	

Continued

Patients	Primary cohort (n = 2473)			After PSM (n = 1332)		
	ECOG-PS 0–1 2247 (%)	ECOG-PS 2–4 226 (%)	*p*	ECOG-PS 0–1 1110 (%)	ECOG-PS 2–4 222 (%)	*p*
Grade			0.57			0.60
Low	278 (12.4)	25 (11.1)		139 (12.5)	25 (11.3)	
High	1969 (87.6)	201 (88.9)		971 (87.5)	197 (88.7)	
Lymphovascular invasion			< 0.001			0.10
No	1784 (79.4)	155 (68.6)		834 (75.1)	155 (69.8)	
Yes	463 (20.6)	71 (31.4)		276 (24.9)	67 (30.2)	
Surgical margin			< 0.001			0.39
Free	2136 (95.1)	203 (89.8)		1033 (93.1)	203 (91.4)	
Positive	111 (4.9)	23 (10.2)		77 (6.9)	19 (8.6)	
Tumor necrosis			0.09			0.61
No	1896 (84.4)	181 (80.1)		916 (82.5)	180 (81.1)	
Yes	351 (15.6)	45 (19.9)		194 (17.5)	42 (18.9)	

Table 1. Descriptive characteristics of patients in the primary and propensity score-matched cohorts. *PSM* propensity-score matching, *ECOG-PS* eastern cooperative oncology group performance status, *eGFR* estimated glomerular filtration rate, *HALNU* hand-assisted laparoscopic nephroureterectomy.

Association of ECOG-PS with major perioperative complications

Overall, major perioperative complications occurred in 83 patients (3.7%) in the ECOG-PS 0–1 group and 23 patients (10.2%) in the ECOG-PS 2–4 group (Table 2). Surgical complications, such as bowel perforation and vascular injury, often required urgent intervention or increased recovery time. Major medical complications, including acute kidney injury and arrhythmia, were associated with prolonged hospitalization and higher mortality. Detailed distributions of complications by Clavien-Dindo classification and perioperative complication specifics are provided in Supplementary Table 5.

In the primary cohort, univariable analysis showed a significant association between ECOG-PS 2–4 and major perioperative complications ($p < 0.001$), which remained robust in the multivariable analyses (odds ratio [OR] 2.46, 95% CI 1.50–4.03, $p < 0.001$; Table 4). Similarly, in the PSM cohort, ECOG-PS 2–4 was independently associated with major perioperative complications (OR 2.68, 95% CI 1.51–4.71, $p < 0.001$; Table 4). The results of univariable analysis of both primary and PSM cohorts are presented in Supplementary Table 6.

Discussion

Several studies have explored the relationship between ECOG-PS and survival outcomes in UTUC patients following RNU. Three earlier studies, albeit with small sample sizes and limited control of covariates, addressed this topic. Martinez-Salamanca et al.[7] found an association between ECOG and OS but not CSS, using a cutoff of ECOG 0 versus ≥ 1. In contrast, Morizane et al.[12] and Aziz et al.[11] reported ECOG as a significant factor for CSS, using the same cutoff as our study (ECOG 0–1 vs. 2–4). More recent studies with larger sample sizes and updated data, while not primarily focused on ECOG and had different cutoffs, provide further insights into its prognostic value. These studies generally support the association of ECOG with OS, but findings regarding CSS and DFS remain inconsistent[8–10,13].

The observed 5-yr CSS and DFS in this study were 79% and 70%, respectively, aligning with previous reports on UTUC prognosis[2,7,9,12,13]. Our findings unequivocally demonstrate that a high ECOG-PS score is associated with unfavorable OS, CSS, and DFS in UTUC patients undergoing RNU. Despite PSM, subsequent multivariable adjustment, and competing-risk model, the results remained robust, further supporting the prognostic significance of ECOG-PS.

ECOG-PS is a well-established prognostic factor for OS in patients with various cancers[16–18]. This aligns with findings from most prognostic studies of UTUC[7–11]. Patients with poor overall health conditions typically harbor more comorbidities and healthcare issues. Therefore, it is not surprising to find a strong association between ECOG-PS and OS.

Our study also indicated that high ECOG-PS scores were associated with worse CSS and DFS. However, the association between ECOG-PS and CSS has only been observed in some studies[11–13], and the link between ECOG-PS and DFS was identified in only one study[13]. The inconsistency observed in the literature can be attributed to small sample sizes, variations in ECOG-PS cutoff points, and inadequate control over covariates, which precluded more accurate estimation[7–11]. In contrast, by leveraging the largest cohort with rigorous analysis, our study provides a more precise estimate of the genuine association.

It is important to acknowledge that patients with poor PS often receive less intensive treatment, which may compromise cancer control and patient survival. To address this concern, we included systemic chemotherapy in our multivariable analysis, and our study still highlights ECOG-PS as a robust factor influencing both OS and cancer-related outcomes. This indicates that regardless of whether systemic therapy was administered, individuals with poor PS consistently exhibited inferior outcomes. This evidence supports the notion that the prognostic significance of ECOG-PS is not solely attributed to differences in treatment plans.

We also evaluated the American Society of Anesthesiologists physical status classification (ASA-PS) for additional context. Univariate analyses showed that ASA-PS 3–4 was associated with worse OS ($p < 0.001$), CSS

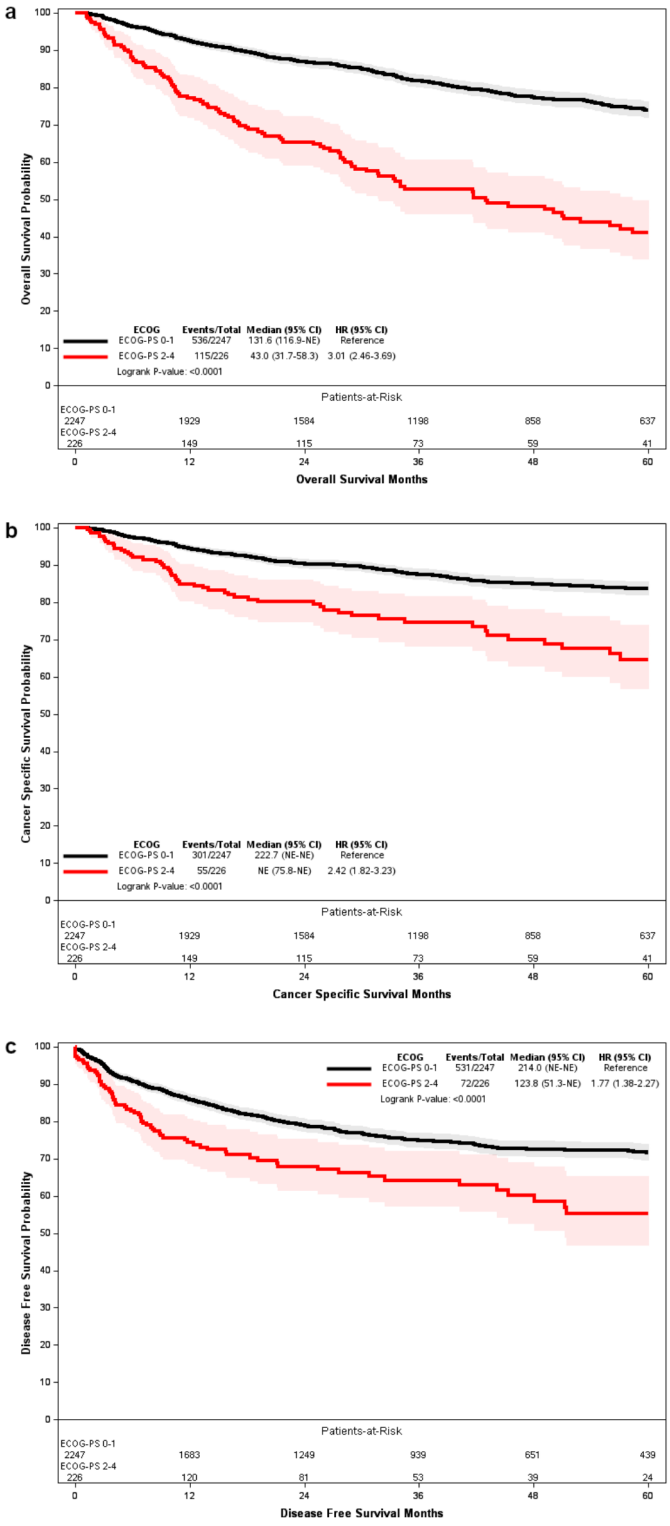

Fig. 1. In Kaplan–Meier analysis, ECOG-PS 2–4 was significantly associated with lower overall, cancer-specific, and disease-free survival in the primary cohort of 2473 patients.

($p = 0.035$), and DFS ($p = 0.017$). However, in multivariable analyses accounting for study covariates, ASA-PS was not significantly associated with any outcomes. In contrast, the significance of ECOG-PS persisted even after adjusting for ASA (Supplementary Table 7). The ASA-PS primarily reflects comorbidity severity rather than overall health[19], and its subjective nature can introduce variability in scoring[20–22], potentially affecting its reliability. Beyond these tools, emerging markers such as the CONUT (Controlling Nutritional Status) score[23]

	OS (5-yr, %)	CSS (5-yr, %)	DFS (5-yr, %)	Major perioperative complications (%)
ECOG-PS				
0–1	73.9	83.6	71.6	10.2
2–4	41.0	64.7	55.2	3.7
*p**	< 0.001	< 0.001	< 0.001	< 0.001

Table 2. Summary of survival and complication outcomes by ECOG-PS Groups. *ECOG-PS* eastern cooperative oncology group performance status, *OS* overall survival, *CSS* cancer-specific survival, *DFS* disease-free survival. **P*-values for survival outcomes were estimated using the log-rank test, while *P*-values for major complications were derived from logistic regression analysis.

	Overall survival		Cancer-specific survival		Disease-free survival	
	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
ECOG-PS						
2–4 versus 0–1	2.53 (2.01–3.18)	< 0.001	2.02 (1.49–2.74)	< 0.001	1.50 (1.13–2.00)	0.006
ECOG-PS (after PSM)						
2–4 versus 0–1	2.69 (2.14–3.38)	< 0.001	2.12 (1.53–2.95)	< 0.001	1.53 (1.15–2.02)	0.003
Competing risk model			**Cancer-specific survival**		**Disease-free survival**	
			SHR (95% CI)	***p***	**SHR (95% CI)**	***p***
ECOG-PS						
2–4 versus 0–1	N/A		1.45 (1.13–1.87)	0.004	1.22 (1.00–1.49)	0.05
ECOG-PS (after PSM)						
2–4 versus 0–1	N/A		1.47 (1.14–1.89)	0.003	1.24 (1.02–1.52)	0.036

Table 3. Multivariable regression analysis of survival outcomes in both primary cohort and propensity score-matched cohort. *HR* hazard ratio, *SHR* subdistribution hazard ratio, *CI* confidence interval, *ECOG-PS* eastern cooperative oncology group performance status, *PSM* propensity-score matching. See Supplementary Table 2 and 4 for the full results of the multivariable analysis.

and sarcopenia[24] have shown promise in predicting surgical outcomes but were not included in this study. Their integration into future research could provide a more comprehensive assessment of patient fitness for surgery.

Several other factors also played pivotal roles in determining survival outcomes. Our results showed that old age and male were associated with worse OS and oncological outcomes, aligning with most of the literature[25,26]. The gender disparity is likely attributable to the higher prevalence of predisposing risk factors, such as smoking among men, which puts the entire urothelium at risk. Concurrent bladder cancer was also associated with worse prognoses, consistent with prior research linking concurrent tumors to higher recurrence, progression, and lower survival rates[27]. Two main hypotheses—field cancerization and intraluminal seeding—have been proposed to explain the multifocality and recurrence patterns of urothelial cancers. Additionally, the literature identifies unique risk factors, such as higher consumption of AA-containing herbs in women and an elevated risk of pan-urothelial carcinoma in this population. However, it remains unclear whether concurrent bladder cancer itself directly affects prognosis or if other genetic, environmental, or unmeasured confounding factors contribute to the observed outcomes. Tumor-related factors including multifocality, tumor size, pathological T stage, pathological N stage, histological variant, grade, lymphovascular invasion, and surgical margin served as significant independent predictors for OS or cancer-related outcomes, as these factors are well-established prognostic indicators for oncological outcomes[25,26,28].

Although 40% of patients in our study had pT3 or pT4 disease, only 21% received systemic chemotherapy, which falls within but toward the lower end of the reported global range (20–50%)[29]. The lower utilization rate may be attributed to patient ineligibility due to medical conditions (e.g., postoperative eGFR < 60%), treatment refusal, or loss to follow-up[30]. Similar challenges have been observed globally[29,31]. Additionally, a persistent negative perception of chemotherapy among the Taiwanese population[30,32], along with variability in treatment attitudes, likely further reduces chemotherapy acceptance.

We observed that up to 4.3% of patients experienced major perioperative complications, a rate consistent with the results of a systematic review, which reported a range from 3.8 to 4.6%[33]. Major surgery can be challenging in patients with high ECOG-PS scores. Previous investigations found poor PS as an independent factor for major perioperative complications in patients undergoing RNU[14,15], while frailty was associated with both major complications and extended hospital stays[34,35]. Our study comprehensively incorporated various clinicopathological parameters, confirming that a high ECOG-PS score is a significant predictor for major perioperative complications in both the primary and PSM cohorts. Given this evident correlation, surgeons should exercise increased caution when performing RNU on such patients.

The limitations of this study include a relatively short follow-up period of less than five years and its observational nature, which inherently carries the risk of residual confounding despite the use of PSM techniques. While

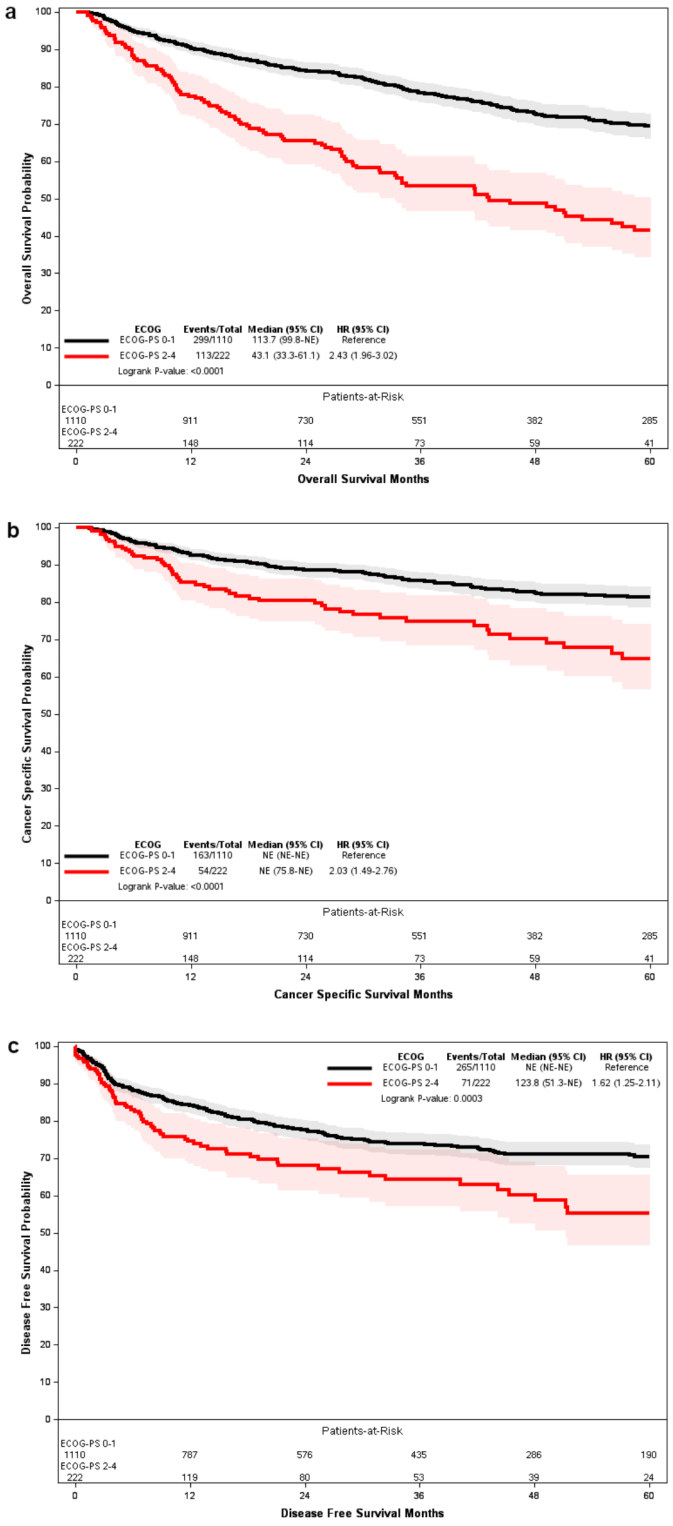

Fig. 2. In Kaplan–Meier analysis, ECOG-PS 2–4 was significantly associated with lower overall, cancer-specific, and disease-free survival in the propensity score-matched cohort of 1332 patients.

we controlled for systemic chemotherapy, specific details such as regimen, dosing, number of chemotherapy cycles, and other adjunctive therapies (e.g., neoadjuvant) were not available in the dataset. Notably, variations in adjuvant and systemic therapies across participating centers could introduce variability in treatment outcomes. Furthermore, although immunotherapy has significantly advanced the treatment of urothelial carcinoma, our database, established before its widespread adoption in Taiwan, lacks data on immunotherapeutic interventions. Additionally, while we included the surgical approach as a covariate, specific operative factors such as surgeon

Variables	All patients		After PSM	
	OR (95% CI)	*p*	OR (95% CI)	*p*
ECOG-PS				
2–4 versus 0–1	2.46 (1.50–4.03)	< 0.001	2.67 (1.51–4.71)	< 0.001
eGFR				
< 60 versus ≥ 60	1.69 (1.06–2.70)	0.029	2.41 (1.18–4.94)	0.016
Hypertension				
Yes versus no	1.57 (1.02–2.44)	0.042		
Preoperative hydronephrosis				
Yes versus no			2.17 (1.19–3.97)	0.012
Surgical margin				
Positive versus free	2.35 (1.23–4.51)	0.010		
Systemic chemotherapy		0.008		
No	Ref	–		
Adjuvant	0.40 (0.20–0.77)	0.007		
Salvage/palliative	0.40 (0.14–1.12)	0.08		

Table 4. Multivariable regression analysis of major perioperative complications in both primary cohort and propensity score-matched cohort. *PSM* propensity-score matching, *OR* odds ratio, *CI* confidence interval, *ECOG-PS* eastern cooperative oncology group performance status, *eGFR* estimated glomerular filtration rate. Major perioperative complications were defined as any Clavien-Dindo complication ≥ grade 3.

experience, surgery duration, and blood loss were unavailable. Incomplete patient data and losses due to the retrospective nature of the study and the prolonged recruitment period further contribute to potential bias. The involvement of multiple institutions over three decades also introduces variability in surgical practices and expertise, which could lead to uncontrolled bias in the results. While ECOG-PS provides a straightforward measure of performance status, incorporating additional frailty indices—such as sarcopenia assessment or the Charlson Comorbidity Index—may enhance prognostic accuracy. Future studies integrating these factors could further refine preoperative risk stratification in UTUC patients.

In conclusion, our study provides robust evidence supporting the prognostic significance of preoperative ECOG-PS in outcomes following RNU. ECOG-PS guides surgical decisions by identifying suitable candidates and stratifying perioperative risks. Patients with better ECOG scores are more likely to tolerate surgery, while those with poorer performance status require careful risk–benefit evaluation. If surgical risks outweigh potential benefits, alternative treatments or supportive care may be more appropriate. Additionally, higher ECOG-PS is associated with increased perioperative complications and slower recovery, highlighting the need for enhanced postoperative care. Despite its limitations, the largest sample size, detailed inclusion of covariates, and comprehensive approach in our study provide important insights into ECOG-PS in risk stratification and patient management.

Data availability

The data are available from the corresponding author on reasonable request.

Received: 1 December 2024; Accepted: 19 March 2025
Published online: 26 March 2025

References

1. Luo, H.-L., Chen, T.-S. & Wu, W.-J. The cancer behavior and current treatment strategy for upper urinary tract cancer. *Urol. Sci.* **33**, 161–169 (2022).
2. Leow, J. J., Orsola, A., Chang, S. L. & Bellmunt, J. A contemporary review of management and prognostic factors of upper tract urothelial carcinoma. *Cancer Treat Rev.* **41**, 310–319 (2015).
3. Sørensen, J. B., Klee, M., Palshof, T. & Hansen, H. H. Performance status assessment in cancer patients. An inter-observer variability study. *Br. J. Cancer* **67**, 773–775 (1993).
4. Mollica, V. et al. The impact of ECOG performance status on efficacy of immunotherapy and immune-based combinations in cancer patients: The MOUSEION-06 study. *Clin. Exp. Med.* **23**, 5039–5049 (2023).
5. Hanaoka, M. et al. The eastern cooperative oncology group performance status as a prognostic factor of stage I-III colorectal cancer surgery for elderly patients: A multi-institutional retrospective analysis. *Surg. Today* **52**, 1081–1089 (2022).
6. Bhargavan, R., Philip, F. A., Km, J. K., Augustine, P. & Thomas, S. Comparison of modified frailty index, clinical frailty scale, ECOG Score, and ASA PS score in predicting postoperative outcomes in cancer surgery: A prospective study. *Indian J. Surg. Oncol.* **15**, 938–945 (2024).
7. Martinez-Salamanca, J. I. et al. Prognostic role of ECOG performance status in patients with urothelial carcinoma of the upper urinary tract: An international study. *BJU Int.* **109**, 1155–1161 (2012).
8. Wu, K.-H. et al. Oncologic impact of delay between diagnosis and radical nephroureterectomy. *Front. Oncol.* **12**, 1025668 (2022).
9. Chromecki, T. F. et al. Chronological age is not an independent predictor of clinical outcomes after radical nephroureterectomy. *World J. Urol.* **29**, 473–480 (2011).
10. Yeh, H.-C. et al. Validation of hyponatremia as a prognostic predictor in multiregional upper tract urothelial carcinoma. *J. Clin. Med.* **9**, 1218 (2020).

11. Aziz, A. et al. Comparative analysis of comorbidity and performance indices for prediction of oncological outcomes in patients with upper tract urothelial carcinoma who were treated with radical nephroureterectomy. *Urol. Oncol.* **32**, 1141–1150 (2014).
12. Morizane, S. et al. Preoperative prognostic factors after radical nephroureterectomy in patients with upper urinary tract urothelial carcinoma. *Int. Urol. Nephrol.* **45**, 99–106 (2013).
13. Capitanio, U. et al. Comparison of oncologic outcomes for open and laparoscopic nephroureterectomy: A multi-institutional analysis of 1249 cases. *Eur. Urol.* **56**, 1–9 (2009).
14. Raman, J. D. et al. Preoperative nomogram to predict the likelihood of complications after radical nephroureterectomy. *BJU Int.* **119**, 268–275 (2017).
15. Kocher, N. J. et al. Incidence and preoperative predictors for major complications following radical nephroureterectomy. *Transl. Androl. Urol.* **9**, 1786–1793 (2020).
16. Vose, J. M. Mantle cell lymphoma: 2017 update on diagnosis, risk-stratification, and clinical management. *Am. J. Hematol.* **92**, 806–813 (2017).
17. Kotecha, R. et al. Meta-analysis of survival and development of a prognostic nomogram for malignant pleural mesothelioma treated with systemic chemotherapy. *Cancers (Basel)* **13**, 2186 (2021).
18. Curry, L. D. et al. Performance status, comorbidities, and cycles of methotrexate exert the greatest influence on outcomes of primary and secondary CNS lymphomas: The Lexington experience. *Ann. Hematol.* **102**, 141–154 (2023).
19. Forsberg, A. Associations between ASA classification, self-estimated physical health, psychological wellbeing and anxiety among Swedish orthopaedic patients. *Int. J. Orthop. Trauma Nurs.* **39**, 100769 (2020).
20. Haynes, S. R. & Lawler, P. G. P. An assessment of the consistency of ASA physical status classification allocation. *Anaesthesia* **50**, 195–199 (1995).
21. Sankar, A., Johnson, S. R., Beattie, W. S., Tait, G. & Wijeysundera, D. N. Reliability of the American society of anesthesiologists physical status scale in clinical practice. *Br. J. Anaesth.* **113**, 424–432 (2014).
22. Curatolo, C. et al. ASA physical status assignment by non-anesthesia providers: Do surgeons consistently downgrade the ASA score preoperatively?. *J. Clin. Anesth.* **38**, 123–128 (2017).
23. Ishihara, H. et al. Preoperative controlling nutritional status (CONUT) score as a novel predictive biomarker of survival in patients with localized urothelial carcinoma of the upper urinary tract treated with radical nephroureterectomy. *Urol. Oncol.* **35**(539), e539-539.e516 (2017).
24. Kocher, N. J. et al. Is sarcopenia and sarcopenic obesity associated with clinical and pathological outcomes in patients undergoing radical nephroureterectomy?. *Urol. Oncol.* **36**(156), e117-156.e122 (2018).
25. Kardoust Parizi, M. et al. Risk stratification of upper tract urothelial carcinoma: A Review of the Current Literature. *Expert Rev. Anticancer Ther.* **19**, 503–513 (2019).
26. Kenigsberg, A. P., Meng, X., Ghandour, R. & Margulis, V. Oncologic outcomes of radical nephroureterectomy (RNU). *Transl. Androl. Urol.* **9**, 1841–1852 (2020).
27. Fang, D. et al. Characteristics and treatment outcomes of pan-urothelial cell carcinoma: A descriptive analysis of 45 patients. *Sci. Rep.* **5**, 18014 (2015).
28. Wang, J. et al. The impact of histological variants in patients with upper tract urothelial carcinoma treated with radical nephroureterectomy. *J. Cancer Res. Clin. Oncol.* **149**, 8279–8288 (2023).
29. Leow, J. J. et al. Neoadjuvant and adjuvant chemotherapy for upper tract urothelial carcinoma: A 2020 systematic review and meta-analysis, and future perspectives on systemic therapy. *Eur. Urol.* **79**, 635–654 (2021).
30. Huang, H.-L., Kung, P.-T., Chiu, C.-F., Wang, Y.-H. & Tsai, W.-C. Factors associated with lung cancer patients refusing treatment and their survival: A national cohort study under a universal health insurance in Taiwan. *PLoS ONE* **9**, e101731 (2014).
31. Huchcroft, S. A. & Snodgrass, T. Cancer patients who refuse treatment. *Cancer Causes Control* **4**, 179–185 (1993).
32. Chen, H., Allan, H. & Lu, Z. J. The social construction of cancer chemotherapy toxicity. *Cancer Nurs.* **36**, E61–E67 (2013).
33. Ni, S. et al. Laparoscopic versus open nephroureterectomy for the treatment of upper urinary tract urothelial carcinoma: A systematic review and cumulative analysis of comparative studies. *Eur. Urol.* **61**, 1142–1153 (2012).
34. Suskind, A. M. et al. Impact of frailty on complications in patients undergoing common urological procedures: A study from the American college of surgeons national surgical quality improvement database. *BJU Int.* **117**, 836–842 (2016).
35. Rosiello, G. et al. Preoperative frailty predicts adverse short-term postoperative outcomes in patients treated with radical nephroureterectomy. *J. Surg. Oncol.* **121**, 688–696 (2020).

Acknowledgements

We thank Yu-Tsai Li for statistical assistance and all members of the Taiwan Upper Tract Urothelial Carcinoma Collaboration Group: Allen W. Chiu, Bing-Juin Chiang, Chao-Hsiang Chang, Chao-Yuan Huang, Cheng-Huang Shen, Cheng-Kuang Yang, Cheng-Ling Lee, Chen-Hsun Ho, Che-Wei Chang, Chia-Chang Wu, Chieh-Chun Liao, Chien-Hui Ou, Chih-Chen Hsu, Chih-Chin Yu, Chih-Hung Lin, Chih-Ming Lu, Chih-Yin Yeh, Ching-Chia Li, Chi-Ping Huang, Chi-Rei Yang, Chi-Wen Lo, Chuan-Shu Chen, Chung-Hsin Chen, Chung-You Tsai, Chung-Yu Lin, Chun-Hou Liao, Chun-Kai Hsu, Fang-Yu Ku, Hann-Chorng Kuo, Han-Yu Weng, Hao-Han Chang, Hong-Chiang Chang, Hsiao-Jen Chung, Hsin-Chih Yeh, Hsu-Che Huang, Ian-Seng Cheong, I-Hsuan Alan Chen, Jen-Kai Fang, Jen-Shu Tseng, Jen-Tai Lin, Jian-Hua Hong, Jih-Sheng Chen, Jungle Chi-Hsiang Wu, Kai-Jie Yu, Keng-Kok Tan, Kuan-Hsun Huang, Kun-Lin Hsieh, Lian-Ching Yu, Lun-Hsiang Yuan, Hao-Lun Luo, Marcelo Chen, Min-Hsin Yang, Pai-Yu Cheng, Po-Hung Lin, Richard Chen-Yu Wu, See-Tong Pang, Shin-Hong Chen, Shin-Mei Wong, Shiu-Dong Chung, Shi-Wei Huang, Shuo-Meng Wang, Shu-Yu Wu, Steven Kuan-Hua Huang, Ta-Yao Tai, Thomas Y. Hsueh, Ting-En Tai, Victor Chia-Hsiang Lin, Wei-Chieh Chen, Wei-Ming Li, Wei-Yu Lin, Wen-Hsin Tseng, Wen-Jeng Wu, Wun-Rong Lin, Yao-Chou Tsai, Yen-Chuan Ou, Yeong-Chin Jou, Yeong-Shiau Pu, Yi-Chia Lin, Yi-Hsuan Wu, Yi-Huei Chang, Yi-sheng Lin, Yi-Sheng Tai, Yu-Khun Lee, Yu-an-Hong Jiang, Yu-Che Hsieh, Yu-Chi Chen, Yu-Ching Wen, Yung-Tai Chen, Zhe-Rui Yang.

Author contributions

Conception and design: H.C.Y.; acquisition of data: all authors; statistical analysis: H.C.Y.; drafting of the manuscript: T.M.Y.; critical revision of the manuscript for important intellectual content: H.C.Y.; obtaining funding: H.C.Y.; supervision: H.C.Y., H.Y.L.; All authors reviewed and approved the final version of the manuscript.

Funding

This study was supported by Kaohsiung Municipal Ta-Tung Hospital (kmtth-111-R011) and the Ministry of Science and Technology (MOST 111-2314-B-037-071-MY3). The study's design, analysis, results, and conclusions were independently developed by the authors and are not influenced by the funding sources.

Declarations

Competing interests
The authors declare no competing interests.

Additional information
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-95128-1.

Correspondence and requests for materials should be addressed to H.-Y.L. or H.-C.Y.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.