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Introduction

The rising global incidence of cancer and the prolonged survival attributable to advances in oncological therapy have led to a marked increase in the frequency of intensive care unit (ICU) admissions among patients with malignancy. It has been reported that cancer patients account for approximately 15% of all ICU admissions [12, 14, 15]. As systemic oncological treatments continue to evolve — including the widespread adoption of immune checkpoint inhibitors and targeted molecular therapies — the clinical profile of cancer patients requiring ICU admission has become increasingly complex, encompassing not only direct tumor-related emergencies but also treatment-associated toxicities and procedure-related complications [16].

Cancer patients constitute a highly heterogeneous group; diverse anatomical tumor localizations, variable disease stages, and a wide spectrum of admission diagnoses make prognostic assessment challenging. A substantial proportion of existing studies have treated cancer patients as a homogeneous population, and multivariable survival analyses stratified by anatomical localization, disease stage, and reason for admission remain limited [7, 16]. Furthermore, short-term ICU mortality — while clinically important — does not fully capture the prognostic burden of critical illness in this population, as functional deterioration and discontinuation of oncological treatment following ICU discharge represent equally important outcomes. Updated, comprehensive data are therefore needed to support clinical decision-making in oncological intensive care.

Despite the growing body of literature on oncological intensive care, several methodological gaps persist. Few studies have formally tested the proportional hazards assumption before survival modeling, assessed multicollinearity among covariates, or validated prognostic model performance using both discrimination and calibration metrics simultaneously. The majority of available data originates from high-volume Western European or North American centers, and single-center data from university hospitals serving mixed oncological populations across diverse admission categories remain limited. Against this background, the present study had two prespecified aims. The primary aim was to determine the independent effects of cancer anatomical localization, cancer clinical status, and reason for ICU admission on 90-day mortality, after adjustment for illness severity and demographic factors, in a single-center cohort of consecutively admitted critically ill cancer patients. The secondary aim was to evaluate the internal discrimination and calibration of a multivariable logistic regression model integrating these cancer-specific descriptors with conventional severity scores.

Material and Methods

Study Design and Patient Selection

This was a single-center, retrospective, observational cohort study of cancer patients admitted to the Internal Medicine and Respiratory ICUs of Trakya University Faculty of Medicine between January 2024 and January 2025. The Non-Interventional Clinical Research Ethics Committee of Trakya University Faculty of Medicine approved the study (onay numarası gelince koyucam). It was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision).

Inclusion criteria were: age ≥18 years, a pathologically confirmed diagnosis of solid or hematological malignancy, and an ICU stay of at least 24 hours during the defined period. Exclusion criteria were: ICU stay shorter than 24 hours, incomplete clinical data, and patients transferred from other institutions whose follow-up data were unavailable. Where a single patient had more than one ICU admission during the study period, the index admission was retained, and subsequent readmissions were excluded. The study was reported in accordance with the STROBE guidelines [11].

Data Collection

The following data were retrospectively extracted from the institutional electronic medical record system using a standardized data collection form: demographic characteristics, Charlson Comorbidity Index (CCI) [3], Clinical Frailty Scale (CFS), Glasgow Coma Scale (GCS), Acute Physiology and Chronic Health Evaluation II (APACHE-II) [8] and Sequential Organ Failure Assessment (SOFA) [17] scores recorded within the first 24 hours of ICU admission, anatomical localization of cancer (seven categories: lung, gastrointestinal tract, renal, head and neck, breast, central nervous system, and a miscellaneous group of solid tumours), clinical status (new diagnosis, remission, progression, relapse, active treatment), reason for ICU admission, ICU length of stay (days), and 90-day mortality (patients alive at day 90 were administratively censored; for those discharged alive before day 90, survival was confirmed through the institutional electronic record and outpatient follow-up, with no patient lost to follow-up before day 90) as the primary outcome. All patients were assigned anonymous identification codes. To preserve statistical stability in the multivariable model, admission categories with fewer than five patients (gastrointestinal emergency, n=4; status epilepticus, n=3; multiple organ failure, n=1) were combined a priori into a single 'Other' category (n=8). All other admission categories were retained at their original granularity.

Statistical Analysis

Continuous variables were expressed as the median with interquartile range (IQR); categorical variables as frequencies and percentages. Normality was assessed with the Shapiro-Wilk test. Mann-Whitney U and chi-square/Fisher's exact tests were used for group comparisons. Survival analysis was performed using the Kaplan-Meier method and Log-Rank test; Bonferroni correction was applied for pairwise comparisons. Independent predictors of 90-day mortality were assessed using binary logistic regression. The multivariable model included 19 dummy/continuous predictors with an events-per-variable ratio of 11.1, exceeding the conventional threshold of 10. Variables with $p<0.10$ in univariable analysis and those with established clinical relevance were included in the multivariable model. Cancer anatomical localization was retained in its original seven categories for all analyses. The chi-square assumptions were satisfied (only one of fourteen expected frequencies fell below 5, within the Cochran ≤20% threshold). The seven categories were used as a single stratification variable in Table 1 and the Kaplan-Meier analyses, and as a six-level dummy set (lung as reference) in the logistic regression. Multicollinearity was assessed using variance inflation factors (VIF). Model discrimination was evaluated using the area under the ROC curve (AUC), with 2000 bootstrap iterations to construct confidence intervals, and calibration using the Hosmer-Lemeshow test. The optimal probability cut-off was identified using the Youden index (J = sensitivity + specificity − 1) and is reported as exploratory, given that it was derived from the same dataset used for model development. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using Python 3.12 (pandas, statsmodels, scipy, lifelines, scikit-learn).

Results

Participants and Baseline Characteristics

Of 315 cancer patients screened, 7 (2.2%) were excluded: 5 with an ICU stay of less than 24 hours, 1 duplicate record identified during data quality review, and 1 readmission of the index patient. The final analytical cohort therefore comprised 308 patients (Figure 1). The median age was 67 years (IQR 61–75), and 189 patients (61.4%) were male. At admission, the median CCI was 8 (IQR 6–10), the median APACHE-II score was 20 (IQR 14–26), and the median SOFA score was 6 (IQR 3–9). The median CFS was 6 (IQR 5–7), and the median admission GCS was 12 (IQR 3–15). The lung was the most common anatomical site of malignancy (33.4%, n=103), followed by the gastrointestinal tract (25.3%, n=78), renal (15.9%, n=49), head and neck (7.5%, n=23), breast (7.5%, n=23), and central nervous system (6.8%, n=21) tumors; a miscellaneous category of solid tumors accounted for the remaining 3.6% (n=11). Acute respiratory failure was the leading reason for ICU admission (41.2%, n=127), followed by shock (31.5%, n=97), postoperative monitoring (19.2%, n=59), cerebrovascular disease (5.5%, n=17), and the 'Other' category (2.6%, n=8). During follow-up, 210 patients died, yielding a 90-day mortality rate of 68.2%; the median ICU length of stay was 6 days (IQR 2–15).

Baseline characteristics stratified by 90-day survival status are summarized in Table 1. Age and sex did not differ between survivors and non-survivors (p=0.614 and p=0.133, respectively). Non-survivors had a higher CCI (p=0.002), a higher CFS (p<0.001), and a lower GCS (p<0.001) than survivors. Cancer anatomical localization across its seven categories was not associated with mortality on chi-square testing (p=0.231), whereas cancer clinical status (p=0.004) and reason for ICU admission (p<0.001) both differed significantly between the two groups; the pairwise pattern underlying these omnibus signals is presented in the unadjusted survival analyses below. Higher APACHE-II and SOFA scores within the first 24 hours of admission were recorded (both p<0.001), as well as a longer ICU length of stay (p<0.001), among non-survivors.

Baseline characteristics stratified by cancer clinical status are summarized in Table 2. Patients in remission were older and had a lower CCI than those with progression or active treatment (both p≤0.001), but APACHE-II and SOFA scores recorded within the first 24 hours of admission did not differ across the five status categories (p=0.612 and p=0.777, respectively).

Unadjusted Survival Analyses

Kaplan-Meier survival analysis by cancer anatomical localization did not demonstrate an overall between-group difference across the seven categories (global Log-Rank χ^2=9.71, df=6, p=0.138). The 90-day restricted mean survival times (RMST) ranged from 31.1 days (95% confidence interval (CI): 23.4–39.3) in patients with gastrointestinal cancer to 54.7 days (95% CI: 39.7–70.2) in patients with central nervous system tumors, with intermediate values for lung (35.8 days, 95% CI: 29.4–43.0), renal (43.7 days, 95% CI: 32.7–55.0), breast (43.2 days, 95% CI: 27.5–58.5), and head and neck (50.0 days, 95% CI: 35.3–64.1) malignancies; the miscellaneous category had an RMST of 40.1 days (95% CI: 16.9–62.7). No pairwise comparison retained statistical evidence after Bonferroni correction for 21 tests (Supplementary Table S1). A pre-specified single comparison contrasting gastrointestinal cancers with all other

localizations combined, motivated by prior literature suggesting an unfavorable prognosis for gastrointestinal malignancies in the ICU setting [7], indicated numerically shorter survival for the gastrointestinal group (Log-Rank χ^2=4.90, p=0.027) (Figure 2).

Survival differed clearly across cancer clinical status categories (Log-Rank χ^2=17.40, df=4, p=0.002). The longest 90-day RMST was observed in the remission group (57.6 days, 95% CI: 48.6–67.4), whereas the shortest was observed in the progression group (30.0 days, 95% CI: 23.0–37.4); intermediate values were recorded for new diagnosis (36.9 days, 95% CI: 29.7–44.9), active treatment (34.4 days, 95% CI: 25.8–43.8), and relapse (41.7 days, 95% CI: 23.6–59.9). Post-hoc pairwise comparisons with Bonferroni correction confirmed shorter survival in the new diagnosis (corrected p=0.009), progression (corrected p<0.001), and active treatment (corrected p=0.009) subgroups compared with patients in remission (Figure 3).

Survival also differed markedly according to reason for ICU admission (Log-Rank χ^2=59.55, df=4, p<0.001). The longest RMST was recorded in patients admitted for postoperative monitoring (75.8 days, 95% CI: 67.4–82.8), whereas the shortest was observed in the 'Other' admission category (22.1 days, 95% CI: 2.4–46.9). Acute respiratory failure (30.2 days, 95% CI: 24.6–36.1), shock (29.2 days, 95% CI: 22.2–36.3), and cerebrovascular disease (39.6 days, 95% CI: 22.6–58.4) all showed substantially shorter restricted mean survival than the postoperative group (Supplementary Table S2). Postoperative monitoring was associated with markedly longer survival than each of the other admission categories (all Bonferroni-corrected p≤0.001) (Figure 4).

Multivariable Analysis — Independent Predictors of 90-Day Mortality

The proportional hazards assumption, assessed using Schoenfeld residuals across 19 model terms, was violated for one covariate (acute respiratory failure dummy, p=0.043). Because the proportional hazards assumption was not uniformly satisfied, and to provide an outcome-aligned estimate for a fixed 90-day time horizon, binary logistic regression was designated as the primary multivariable analysis. The multivariable model included 19 dummy/continuous predictors with an events-per-variable ratio of 11.1, satisfying the conventional threshold of 10 events per variable. No multicollinearity was detected among covariates (maximum variance inflation factor = 2.39). The independent predictors of 90-day mortality identified by the multivariable model are summarized in Table 3. With postoperative monitoring as the reference category, acute respiratory failure emerged as the strongest independent predictor (OR=27.08, 95% CI: 8.93–82.12, p<0.001), followed by cerebrovascular disease (OR=23.93, 95% CI: 4.49–127.57, p<0.001) and shock (OR=8.74, 95% CI: 2.81–27.18, p<0.001). The wide confidence interval for the cerebrovascular disease estimate — reflecting the small subgroup size (n=17) — indicates substantial statistical uncertainty, and this estimate should be interpreted as exploratory.

Among cancer clinical status categories, both a new diagnosis (OR=4.16, 95% CI: 1.38–12.54, p=0.012) and disease progression (OR=2.90, 95% CI: 1.07–7.84, p=0.036) independently predicted higher mortality compared with patients in remission. Each one standard deviation increase in APACHE-II score (OR=3.78, 95% CI: 2.16–6.62, p<0.001) and SOFA score (OR=1.97, 95% CI: 1.17–3.32, p=0.011) was associated with **higher** odds of 90-day mortality. None of the six anatomical localization categories (with lung as the reference) retained independent prognostic value in the

adjusted model; the corresponding adjusted odds ratios were 0.92 (gastrointestinal), 0.70 (renal), 0.46 (head and neck), 0.59 (breast), 0.37 (central nervous system), and 1.89 (miscellaneous), all with p>0.20 and confidence intervals crossing unity. Sex was likewise retained in the model without reaching statistical significance. Age showed a borderline inverse association with 90-day mortality after adjustment (OR=0.69 per 1 standard deviation (SD) increase, 95% CI: 0.46–1.03, p=0.071), despite showing no univariable difference between survivors and non-survivors (median 68 vs 67 years; p=0.614). The CCI did not retain independent prognostic value in the adjusted model (OR=0.94 per 1 SD increase, 95% CI: 0.63–1.41, p=0.781).

Model Performance

The final logistic regression model demonstrated excellent discrimination, with an AUC of 0.897 (95% CI: 0.859–0.931; 2000 bootstrap samples) (Figure 5). Calibration was excellent, as indicated by the Hosmer-Lemeshow goodness-of-fit test (χ^2=4.92, df=8, p=0.766) and by the calibration plot (Figure 6). The Nagelkerke pseudo-R^2 was 0.584, and the Cox-Snell R^2 was 0.417. An optimal probability cut-off identified via the Youden index was 0.784, yielding a sensitivity of 73.3% and a specificity of 88.8%; because this threshold was derived from the same dataset used for model development, it should be regarded as exploratory and requires external validation before clinical application. Model performance parameters are summarized in Table 4.

Discussion

In this single-center retrospective cohort of 308 critically ill cancer patients, three findings emerged as central. First, 90-day mortality was determined far more strongly by the acute clinical context at ICU admission and the underlying oncological trajectory than by tumor anatomical localization, which was neither significant overall nor independently prognostic after adjustment. Second, illness severity scores from the first 24 hours retained substantial independent prognostic weight after adjustment for cancer-specific variables, supporting their use alongside — rather than in place of — oncological descriptors. Third, the apparent inverse association of age with mortality is most consistent with statistical suppression rather than a biological protective effect, as discussed below.

After multivariable adjustment, reason for ICU admission emerged as the strongest predictor of 90-day mortality, with acute respiratory failure, cerebrovascular disease, and shock conveying the highest adjusted odds compared with postoperative monitoring. These findings echo the literature on prognostic factors in oncological intensive care, in which acute respiratory failure and shock are repeatedly identified as the leading drivers of mortality in cancer patients requiring critical care [1, 6, 13, 18]. The clinical implication is that, at the bedside, the syndrome bringing the patient to the ICU carries greater prognostic weight than the underlying tumor site itself.

Cancer clinical status retained independent prognostic value in the adjusted model. Compared with remission, both a new diagnosis (OR=4.2) and disease progression (OR=2.9) carried substantially higher odds of 90-day mortality. That new diagnoses showed an effect size comparable to progression is biologically plausible: such patients often have advanced or undertreated disease and limited time to initiate disease-directed therapy. The independent weight of disease progression aligns with the framework of Vigneron et al. [16], in which disease control status is a primary determinant of post-ICU outcome, and with the scoping review by Codru et al. [4]. Notably, the five status groups did

not differ in admission APACHE-II or SOFA scores (p=0.612 and p=0.777), yet differed markedly in chronic disease burden (remission median CCI 6 vs 9 for progression/relapse/active treatment; p=0.001). This suggests that the prognostic weight of clinical status is mediated through chronic comorbidity and the biological trajectory of the malignancy rather than through acute illness severity at ICU admission.

Anatomical localization did not meet the global significance threshold (p=0.138), and no pairwise comparison survived Bonferroni correction; however, gastrointestinal cancers showed the numerically shortest restricted mean survival and were associated with shorter survival than all other localizations combined in a pre-specified single contrast (p=0.027). This exploratory signal aligns with García de Herreros et al. [7], in which gastrointestinal cancers and liver metastasis were associated with higher in-hospital and 3-month mortality. The unfavorable prognosis of gastrointestinal malignancies in critical care likely reflects a convergence of mechanistic factors: a high prevalence of advanced-stage disease at initial diagnosis, the nutritional depletion and systemic cachexia inherent to these tumors, and the acute surgical emergencies — including obstruction and perforation — that can precipitate ICU admission. Notably, gastrointestinal localization did not emerge as an independent predictor in the logistic regression model, suggesting that its survival signal is largely mediated through the acute syndromes (shock, respiratory failure) and disease-stage variables that already precipitate ICU admission, rather than representing a direct, localization-specific mortality risk. This pattern explains why none of the six anatomical categories retained independent significance in the multivariable model.

Beyond these predictor-specific findings, the overall mortality rate observed in our cohort warrants comparison with the broader literature. Studies of patients with advanced metastatic disease admitted emergently report mortality rates exceeding 70% [4]. The relatively high mortality observed in our cohort is likely attributable to the predominance of acute medical admissions (acute respiratory failure 41.2%, shock 31.5%), the absence of a dedicated oncological ICU, and the high median APACHE-II score of 20, reflecting a physiologically compromised patient population at admission. The Internal Medicine and Respiratory ICU setting, which does not routinely receive elective post-procedural admissions to the same extent as surgical ICUs, may further explain the elevated mortality compared with cohorts reporting a high proportion of postoperative patients. Among cancer patients specifically, ICU mortality rates reaching 59% have been documented in studies evaluating prognostic scoring systems [10]. Taccone et al. [15] documented a hospital mortality rate of 27% in patients with solid tumors admitted to European ICUs — a notably lower figure likely explained by the substantial proportion of postoperative admissions in that cohort. Consistent with this interpretation, in our study, the postoperative monitoring group had a 90-day mortality rate of only 20.3% (12/59), in marked contrast to patients admitted for acute medical indications.

Each one standard deviation increase in APACHE-II score nearly quadrupled the odds of 90-day mortality (OR=3.8), and each SD increase in SOFA score nearly doubled the odds (OR=2.0). These results confirm the prognostic relevance of generic severity scores in oncological intensive care, despite the recognized limitations of APACHE-II in this population [2]. The combined use of cancer-specific descriptors (clinical status, reason for admission) and physiological severity scores delivered substantially better discrimination than would be expected from severity scores in isolation, as reflected in the model's AUC of 0.897 and Nagelkerke R^2 of 0.584. The CCI, despite an apparent

univariable association, did not retain independent prognostic value in the adjusted model, suggesting that its prognostic information is largely captured by the combination of cancer status, reason for ICU admission, and APACHE-II/SOFA scores in this population.

Age showed a borderline inverse association with 90-day mortality after adjustment (OR=0.69 per 1 SD, p=0.071), despite no univariable difference. This is most consistent with statistical suppression rather than a causal protective effect: in critically ill cancer cohorts age is consistently a positive or null predictor [5], and an inverse association emerging only after adjustment is a hallmark of suppression, whereby covariates sharing variance with age (APACHE-II, comorbidity, frailty) absorb its risk and invert the residual coefficient. In our cohort, older patients had higher APACHE-II scores, higher CCI, and more acute respiratory failure admissions, providing the structural setup for this effect. The finding should therefore be read as a statistical artifact, not a biological signal.

The model's discrimination and calibration compare favorably with published prognostic models in oncological intensive care [10, 18] and support integrating cancer trajectory variables with conventional severity scores in bedside prognostic discussions. Nevertheless, the optimal Youden cut-off (0.784; sensitivity 73.3%, specificity 88.8%) was derived from the same dataset used for model development and is therefore likely to be optimistically biased. External validation in independent cohorts — preferably multicenter and prospective — is essential before any threshold-based application in clinical practice, and recent work in this field has emphasized the importance of incorporating performance status and longer-term functional outcomes into such models [9].

Study Limitations

The principal limitations of this study are its single-center, retrospective design and the resulting inability to draw causal inferences. Oncological performance status (ECOG/Karnofsky scale), which has been consistently associated with ICU mortality in prior studies [2, 7], could not be retrospectively extracted from the institutional database and was therefore absent from the multivariable model — a recognized gap that may have led to residual confounding. However, the CFS and GCS were available and confirmed adverse univariable associations with mortality. Limited subgroup sample sizes in certain admission categories (gastrointestinal emergency n=4, status epilepticus n=3, multiple organ failure n=1) and the wide confidence intervals for the cerebrovascular disease predictor (OR=23.9, 95% CI: 4.49–127.57) preclude definitive conclusions for these subgroups. Similarly, the smaller anatomical strata (miscellaneous n=11, central nervous system n=21, head and neck n=23, breast n=23) produced wide confidence intervals in the adjusted localization estimates. However, the absence of any independent localization signal — combined with the non-significant global Log-Rank test — argues that anatomical site is not a major determinant of 90-day mortality in this cohort. The 90-day mortality endpoint, while clinically relevant, does not capture longer-term outcomes such as functional recovery, resumption of oncological treatment, or one-year survival. Future multicenter prospective studies should aim to integrate performance status, standardized nutritional markers (e.g., serum albumin, prognostic nutritional index), and longitudinal functional outcomes to refine prognostic modeling in oncological intensive care. In addition, the proportional hazards assumption tested via Schoenfeld residuals was violated for the acute respiratory failure dummy (p=0.043), which precluded the use of Cox regression as the primary multivariable framework. Binary logistic regression was therefore selected to provide an outcome-aligned estimate at a fixed 90-day

horizon; this trade-off discards the time-to-event structure of the data and should be considered when comparing our adjusted estimates with hazard ratios reported in cohorts where the proportional hazards assumption was satisfied. The development and external validation of a bedside risk-stratification tool incorporating the predictors identified in this model are priorities for future research.

Conclusion

Three findings from this cohort carry direct implications for oncological critical care practice. First, the acute syndrome bringing a cancer patient to the ICU, the patient's underlying disease trajectory, and physiological derangement within the first 24 hours of admission jointly determine 90-day mortality, while tumor anatomical localization does not retain independent prognostic value after adjustment. Second, prognostic discussions and triage decisions in cancer patients should therefore integrate the reason for ICU admission and disease trajectory alongside conventional severity scores, rather than relying on tumor site as a primary prognostic anchor. Third, the predictors identified here offer a coherent framework for a future bedside risk-stratification tool, provided that ECOG/Karnofsky performance status and longer-term functional outcomes are incorporated and that external validation is performed in prospective, multicenter data.