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Early Postoperative Mortality Risk in Cranial Tumor Surgery: Integrating Short-Term Risk With Long-Term Survival to Inform Operative Strategy

hasan ali aydın

drhasanaliaydin@gmail.com

Zonguldak Bülent Ecevit University

emrah keskin

Zonguldak Bülent Ecevit University

murat kalaycı

Zonguldak Bülent Ecevit University

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Abstract

Objective

Early postoperative mortality after cranial tumor surgery is frequently reported but rarely incorporated into operative decision-making as a structured component of risk–benefit assessment. We aimed to quantify preoperative early mortality risk and to examine whether such stratification provides clinically relevant context for surgical decision-making.

Methods

This retrospective cohort included 392 consecutive adults undergoing cranial tumor surgery (189 brain metastases; 203 primary intra-axial tumors). A multivariable logistic regression model was developed to estimate 30- and 90-day postoperative mortality using routinely available preoperative variables (age > 65 years, tumor category, critical location, hemorrhagic presentation, lesion multiplicity, and surgical intent). Model performance was assessed using discrimination, calibration, decision curve analysis, and internal bootstrap validation. Overall survival was analyzed using Kaplan–Meier and Cox proportional hazards models, including landmark analysis among 30-day survivors. A 15% predicted 90-day mortality probability was used to define a clinically interpretable higher-risk category.

Results

Thirty-day mortality occurred in 5.6% and 90-day mortality in 12.5% of patients. The model demonstrated good discrimination (AUC 0.77 for both endpoints; optimism-corrected AUC 0.70 for 30-day and 0.74 for 90-day mortality) and acceptable calibration. Decision curve analysis showed positive net benefit across clinically relevant thresholds. Predicted early mortality risk significantly stratified overall survival: patients with ≥ 15% predicted risk had shorter median survival than lower-risk patients (12 vs. 38 months, $p < 0.001$), and this separation persisted among 30-day survivors (16 vs. 42 months, $p < 0.001$).

Conclusions

Quantified preoperative early mortality risk was associated with both short- and long-term outcomes and may provide structured context for preoperative risk–benefit assessment in cranial tumor surgery. Prospective and external validation are warranted.

Introduction

Cranial tumor surgery remains a central pillar of modern neuro-oncological care, encompassing both metastatic and primary intra-axial neoplasms. In appropriately selected patients, surgical resection provides rapid neurological relief, cytoreduction, tissue diagnosis, and facilitation of multimodal

oncological strategies [1, 2]. Even in an era of increasingly effective systemic therapies and advanced radiotherapeutic techniques, operative intervention continues to shape both immediate and long-term disease trajectories. However, postoperative outcomes remain heterogeneous, and early mortality persists as a clinically consequential and ethically sensitive endpoint.

Early postoperative mortality reflects the convergence of tumor aggressiveness, systemic disease burden, and perioperative physiological vulnerability [3–5]. While systemic and radiotherapeutic options continue to evolve [4, 6], surgical decision-making frequently occurs in complex clinical scenarios characterized by borderline indications and competing treatment pathways [2]. Long-term survival and intracranial disease control remain dominant outcome metrics in the literature [1, 7], yet the short-term perioperative horizon represents a distinct prognostic domain with implications that extend beyond traditional oncological endpoints.

Recent investigations have focused on perioperative adverse events and 30-day outcomes following cranial and skull base surgery [8]. Tumor-specific factors such as hemorrhagic presentation and anatomical complexity have been associated with increased operative risk and postoperative morbidity [9]. Extent of resection remains a key determinant of survival in metastatic disease [7], and several predictive models have been proposed to estimate perioperative events or short-term postoperative survival [9, 10]. Nevertheless, many of these approaches rely on detailed comorbidity indices, registry-derived datasets, or postoperative parameters that may not be readily accessible at the time of initial surgical triage. Moreover, disease-specific series continue to underscore the biological heterogeneity of intracranial tumors and its influence on outcome variability [11, 12].

In daily practice, the early clinical expression of aggressive tumor biology often manifests through observable preoperative features. Hemorrhagic metastases, radiological disease burden, and the integration of stereotactic radiotherapy illustrate how anatomical and biological considerations converge in operative planning [6, 7]. Advanced age and frailty further modulate perioperative vulnerability in elderly patients with brain metastases [13]. Concurrently, modern molecular classification frameworks have refined long-term prognostic stratification across central nervous system tumors [14], although such molecular information is frequently unavailable at the time when operative decisions must be made.

Despite the existence of survival prediction systems and perioperative risk models, an important conceptual gap remains. Most studies address either long-term oncological survival or isolated short-term complications, without examining how quantified early mortality risk may interact with expected long-term survival and operative strategy. Whether formally estimated early postoperative mortality risk can contribute to a structured preoperative risk–benefit assessment—particularly in patients facing aggressive resection versus limited surgical intent—has not been systematically evaluated.

Accordingly, the present study sought to quantify preoperative early mortality risk following cranial tumor surgery and to examine its relationship with overall survival and operative strategy within a consecutive single-center cohort. By integrating short-term risk estimation with survival analyses and operative

intent, we aimed to explore whether early mortality risk may inform a more structured and clinically contextualized approach to surgical triage in contemporary neuro-oncology. This question is clinically relevant when anticipated oncological benefit may be modest and perioperative vulnerability substantial.

Methods

Study Design and Patient Population

This retrospective cohort study included consecutive adult patients who underwent cranial tumor surgery at a single tertiary neurosurgical center. Eligible patients were operated for brain metastases or primary intra-axial tumors. Meningiomas were excluded due to their distinct biological behavior and comparatively lower perioperative mortality risk profile.

The study had two prespecified objectives:
(1) to develop and internally validate a preoperative clinical model estimating 30- and 90-day postoperative mortality, and
(2) to examine whether quantified early mortality risk meaningfully stratifies long-term survival and relates to operative strategy.

The study was conducted in accordance with institutional ethical standards and the principles of the Declaration of Helsinki. Ethical approval was obtained from the Zonguldak Bülent Ecevit University Faculty of Medicine Institutional Ethics Committee (Approval No: 2025/10, May 21, 2025). Given the retrospective design of the study, the requirement for individual informed consent was waived by the ethics committee. This study is a retrospective observational study and does not meet the definition of a clinical trial. Therefore, trial registration is not applicable.

Variables and Outcomes

Only variables available at the time of surgical triage were considered for model development. Preoperative predictors included age (>65 years), tumor category (metastatic vs. primary intra-axial), lesion location (posterior fossa or other critical location vs. non-critical), hemorrhagic presentation, lesion multiplicity, and anticipated surgical intent (gross total resection vs. biopsy/subtotal resection). The primary endpoints were 30-day and 90-day all-cause postoperative mortality. The secondary endpoint was overall survival, defined as the interval from the date of surgery to death or last follow-up. Complete-case analysis was performed, as missing data were minimal and did not exceed 5% for any included variable.

Development of the Early Mortality Model

Separate multivariable logistic regression models were constructed to estimate 30-day and 90-day postoperative mortality. All prespecified preoperative variables were entered simultaneously into the models to preserve clinical interpretability and minimize overfitting through a parsimonious predictor set.

Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Model discrimination was quantified using the area under the receiver operating characteristic curve (AUC).

Calibration was assessed using: (1) Calibration plots across deciles of predicted risk, (2) Calibration intercept and slope and (3) Brier score for overall predictive accuracy.

Internal Validation

Internal validation was performed using bootstrap resampling (≥800 iterations). For each bootstrap sample, model performance was estimated within the resampled dataset and evaluated against the original dataset to quantify optimism.

Optimism-corrected AUC values were calculated by subtracting average optimism from the apparent AUC. Calibration stability across bootstrap iterations was examined to assess potential overfitting.

Clinical Utility and Threshold Exploration

Decision curve analysis (DCA) was performed to evaluate the clinical utility of the model across a range of threshold probabilities. Net benefit was calculated and compared with default “treat-all” and “treat-none” strategies.

A 15% predicted 90-day mortality probability was selected to represent an intermediate-to-high risk zone. This cut-point corresponded to a region of positive net benefit on DCA and was considered clinically interpretable as a level at which perioperative mortality risk may reasonably influence operative decision-making. This threshold was used for stratified survival and interaction analyses.

Survival and Interaction Analyses

Overall survival was analyzed using Kaplan–Meier methods with log-rank testing. Cox proportional hazards models were constructed to evaluate the association between predicted early mortality risk and long-term survival, both as a continuous probability and as a categorized risk level (≥15% vs. <15%).

Landmark analysis restricted to patients surviving beyond 30 days was performed to assess whether early mortality risk continued to stratify survival beyond the immediate postoperative period.

To explore potential effect modification, interaction terms between early mortality risk category and operative strategy (gross total resection vs. limited intent) were evaluated within Cox proportional hazards models.

Statistical Considerations

Continuous variables were summarized as mean ± standard deviation or median (interquartile range), as appropriate. Categorical variables were presented as frequencies and percentages. All analyses were performed using standard statistical software. Statistical significance was defined as a two-sided p-

value <0.05. Effect sizes and confidence intervals were emphasized alongside p-values to support clinically meaningful interpretation.

Results

Cohort Characteristics and Early Outcomes

A total of 392 adult patients were included, comprising 189 (48.2%) brain metastases and 203 (51.8%) primary intra-axial tumors. Meningiomas were excluded by design. Thirty-day mortality occurred in 22 patients (5.6%), and 90-day mortality in 49 patients (12.5%).

Baseline clinical characteristics and unadjusted mortality rates are summarized in Table 1. Higher early mortality was observed among patients aged > 65 years, those with posterior fossa or other critical lesion locations, hemorrhagic presentation, metastatic tumor category, and limited surgical intent. Notably, 90-day mortality exceeded 20% in patients aged > 65 years and in those with critical lesion location or limited surgical intent, reflecting substantial heterogeneity in preoperative risk profiles.

Table 1
Baseline characteristics of the study cohort and early postoperative mortality (N = 392)

Variable	N (%)	30-day mortality (%)	90-day mortality (%)
Age > 65 years	128 (32.7%)	7.8	22.7
Metastatic tumor	189 (48.2%)	7.4	14.8
Posterior fossa / critical location	73 (18.6%)	9.6	21.9
Hemorrhagic presentation	94 (24.0%)	10.6	17.0
Multiple intracranial lesions	59 (15.1%)	6.8	10.2
Biopsy or subtotal resection (limited intent)	165 (42.1%)	10.3	20.0

Multivariable Early Mortality Model

In multivariable logistic regression analysis, limited surgical intent emerged as the strongest independent predictor of both 30-day (OR 5.21, p = 0.002) and 90-day mortality (OR 3.92, p < 0.001). Advanced age (> 65 years) and critical lesion location were independently associated with 90-day mortality, while hemorrhagic presentation and metastatic tumor category demonstrated directional but less consistent associations. Lesion multiplicity did not materially contribute to adjusted model performance. Regression coefficients were used to derive a simplified cumulative risk score to enable individual-level risk estimation.

Model Performance and Validation

The model demonstrated good apparent discrimination for both endpoints (AUC 0.77 for 30-day and 90-day mortality). Internal bootstrap validation revealed modest optimism, with corrected AUC values of 0.70 (30-day) and 0.74 (90-day), indicating stable performance and limited overfitting.

Calibration analyses showed acceptable agreement between predicted and observed mortality across deciles of risk (Fig. 1A–B). Calibration slopes approximated unity in bootstrap samples. Brier scores were low (0.049 for 30-day; 0.095 for 90-day), supporting reasonable probabilistic accuracy.

Decision curve analysis demonstrated positive net benefit across intermediate threshold probabilities for both endpoints (Fig. 2A–B), suggesting that risk estimation provides incremental clinical utility beyond default treatment strategies.

Nomogram and Practical Application

A graphical nomogram derived from the final multivariable model enables individualized estimation of 30- and 90-day mortality risk. Progressive separation of early mortality across low-, intermediate-, and high-risk categories (Fig. 3) illustrates the stepwise gradient of perioperative vulnerability.

Risk Stratification and Survival Interaction

Stratification using the pre-specified ≥ 15% predicted 90-day mortality threshold identified a clinically distinct higher-risk subgroup. Overall survival differed markedly between strata (median OS 9 vs 31 months for high- versus lower-risk patients; log-rank $p = 2.64\times10^{-12}$; Fig. 4). Importantly, this separation persisted beyond the immediate postoperative period. In a 30-day landmark analysis restricted to patients surviving at least 30 days (n = 358), early risk status continued to stratify long-term outcomes (median OS 14 vs 33 months; log-rank $p = 1.15\times10^{-6}$; Fig. 5), indicating that quantified early risk captured vulnerability extending beyond perioperative mortality alone.

Formal Interaction Testing

To formally test whether the association between operative strategy and survival differed by early-risk stratum, an interaction term (risk × surgical intent) was evaluated in an adjusted Cox proportional hazards model. Gross total resection was associated with improved survival (HR 0.47, 95% CI 0.29–0.77; p = 0.0028), whereas the interaction term was not statistically significant ($p_{int} = 0.311$), suggesting no definitive effect modification by risk category at the cohort level.

Exploratory metastasis high-risk analysis

In an exploratory analysis restricted to patients with brain metastases within the high-risk stratum (n = 67), gross total resection was associated with a numerically longer median survival compared with limited surgical intent (12.2 vs. 8 months); however, this difference was not statistically significant (log-rank p = 0.594).

Discussion

Early postoperative mortality following cranial tumor surgery represents a clinically decisive yet insufficiently integrated endpoint in contemporary neuro-oncology. While molecular classification systems and long-term survival models have substantially refined oncological prognostication [15–17], the immediate perioperative horizon—particularly the first 30 to 90 days after surgery—remains less systematically incorporated into operative decision frameworks. The present study sought not only to quantify early mortality risk using preoperatively available variables, but also to examine whether such risk stratification meaningfully contextualizes long-term survival and operative strategy.

Unlike traditional prognostic systems that emphasize tumor biology and extended survival trajectories [18–20], our model targets a distinct temporal domain dominated by the interaction between physiological reserve, surgical burden, and aggressive disease phenotype. Operative decisions frequently precede definitive molecular characterization, particularly in urgent or neurologically unstable patients. Thus, models dependent on postoperative or molecular data may lack real-time applicability. By restricting predictors to universally accessible preoperative variables, the present approach prioritizes translational feasibility at the moment of surgical triage.

Multivariable analysis identified limited surgical intent, advanced age, and critical anatomical location as principal contributors to early mortality risk. Notably, limited surgical intent—defined as biopsy or subtotal resection—emerged as the strongest independent predictor. This observation should not be interpreted as a causal assertion regarding surgical extent. Rather, operative intent likely reflects a composite of anatomical constraint, systemic burden, and biological aggressiveness. In this sense, intent functions as a clinically pragmatic marker of perioperative vulnerability rather than a purely technical variable [21]. To further examine this relationship, a formal interaction term between risk category and surgical intent was evaluated; the absence of a statistically significant interaction suggests that operative strategy does not demonstrate definitive effect modification across risk strata at the cohort level. Subgroup differences observed in metastatic high-risk patients should therefore be interpreted as exploratory and hypothesis-generating.

From a methodological standpoint, the model demonstrated acceptable discrimination (AUC ≈ 0.77) with limited optimism after bootstrap validation. Calibration slopes approximating unity and low Brier scores support reasonable probabilistic accuracy. Decision curve analysis further indicated positive net benefit across clinically relevant thresholds, reinforcing potential clinical utility beyond default strategies. Although the number of early mortality events—particularly for the 30-day endpoint—was modest, the ratio of events to predictors remained within commonly accepted methodological thresholds for logistic regression modeling. Bootstrap resampling was specifically employed to mitigate potential overfitting and to provide optimism-corrected performance estimates, thereby strengthening internal validity.

An important conceptual contribution of this study is the demonstration that early mortality risk stratification extends beyond perioperative death alone. Risk-defined groups exhibited marked separation in overall survival, including in landmark analyses restricted to 30-day survivors. This finding

suggests that early mortality risk captures an integrated signal of biological aggressiveness and systemic vulnerability that continues to influence longer-term outcomes. Tumor biology, although central to survival modeling [15–17], often manifests perioperatively through observable clinical phenotypes such as hemorrhagic presentation, critical location, and advanced age [22, 23]. By operationalizing these features within a simplified scoring structure, the model captures the early clinical footprint of disease severity without reliance on molecular profiling.

Several limitations warrant careful consideration. The retrospective single-center design introduces potential selection bias and limits generalizability. Operative intent was not randomized, and confounding by indication cannot be excluded; surgeons may preferentially select limited resection in patients perceived to be physiologically fragile or anatomically complex. Although multivariable adjustment and interaction testing were performed, residual confounding remains possible. Additionally, external validation in independent cohorts is required before broad clinical implementation. The model was intentionally designed to prioritize preoperative applicability rather than comprehensive oncological prognostication; therefore, it does not substitute for molecularly informed survival frameworks [24, 25].

In conclusion, early postoperative mortality after cranial tumor surgery can be systematically stratified using a minimal set of universally available preoperative variables. By integrating discrimination, calibration, decision-analytic utility, and survival contextualization, the present study reframes early mortality from a retrospective quality metric into a structured component of preoperative risk–benefit assessment. Rather than supplanting established prognostic systems, this approach complements them by informing operative intent and perioperative planning at the time when surgical decisions must be made.

Conclusion

In this single-center cohort, early postoperative mortality after cranial tumor surgery could be systematically stratified using a minimal set of universally available preoperative clinical and radiological variables. Quantified early mortality risk demonstrated stable discrimination, acceptable calibration, and positive decision-analytic utility, and remained associated with long-term survival even beyond the immediate perioperative period.

Although operative intent was not shown to be definitively modified by risk category at the cohort level, formal risk stratification provided a structured framework for contextualizing surgical decision-making. Early mortality risk thus emerges not merely as a retrospective outcome metric, but as a clinically relevant component of preoperative risk–benefit assessment.

Prospective validation and external replication are required before widespread implementation. Nevertheless, integration of quantified early mortality risk into multidisciplinary evaluation may enhance transparency in surgical triage and perioperative planning within contemporary neuro-oncological practice.

Declarations

Author Contributions

HAA conceived and designed the study, contributed to data acquisition, performed the data analysis, and drafted the manuscript.
EK contributed to data collection, interpretation of the results, and critical revision of the manuscript for important intellectual content.
MK contributed to study supervision, interpretation of data, and critical review of the manuscript.

All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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Competing Interests

The authors declare that they have no competing interests.

Ethics Approval and Consent to Participate

The study was conducted in accordance with institutional ethical standards and the principles of the Declaration of Helsinki. Ethical approval was obtained from the Zonguldak Bülent Ecevit University Faculty of Medicine Institutional Ethics Committee (Approval No: 2025/10, May 21, 2025). Given the retrospective design of the study, the requirement for individual informed consent was waived by the ethics committee. This study is a retrospective observational study and does not meet the definition of a clinical trial. Therefore, trial registration is not applicable.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request, in accordance with institutional regulations and data protection policies.

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Figures

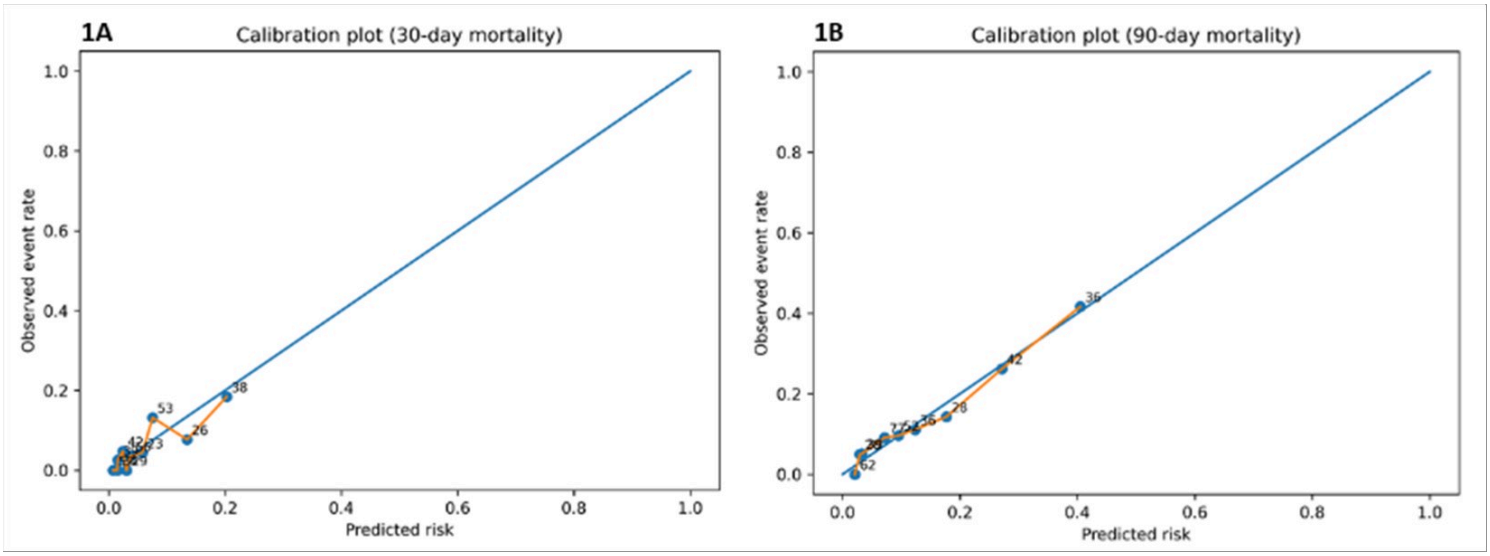


Figure 1

A. Calibration plot for 30-day mortality showing agreement between predicted and observed risk across deciles of predicted probability.

B. Calibration plot for 90-day mortality showing agreement between predicted and observed risk across deciles of predicted probability.

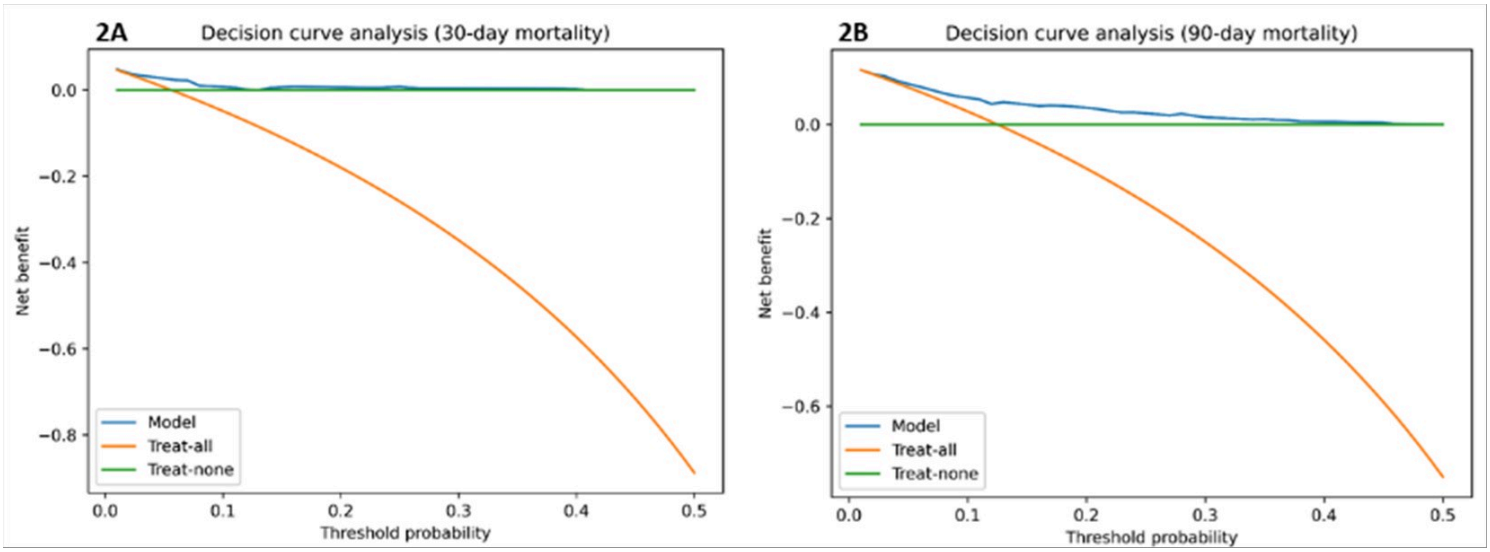


Figure 2

A. Decision curve analysis for 30-day mortality demonstrating net clinical benefit of the prediction model compared with treat-all and treat-none strategies across threshold probabilities.

B. Decision curve analysis for 90-day mortality demonstrating net clinical benefit of the prediction model compared with default treatment strategies across clinically relevant risk thresholds.

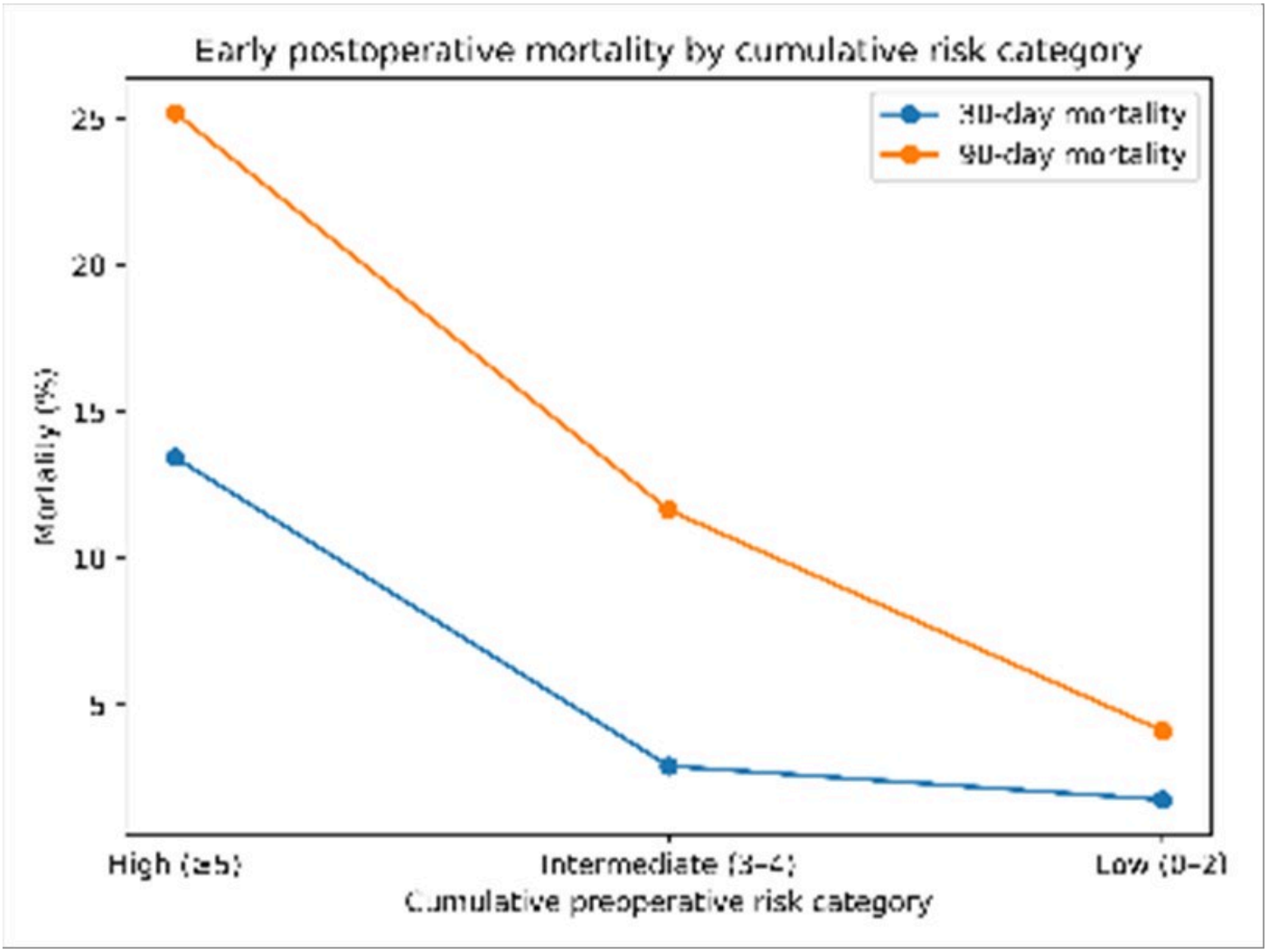


Figure 3

Thirty- and ninety-day postoperative mortality according to cumulative preoperative risk categories (low, intermediate, high), demonstrating a progressive increase in early mortality with increasing risk score.

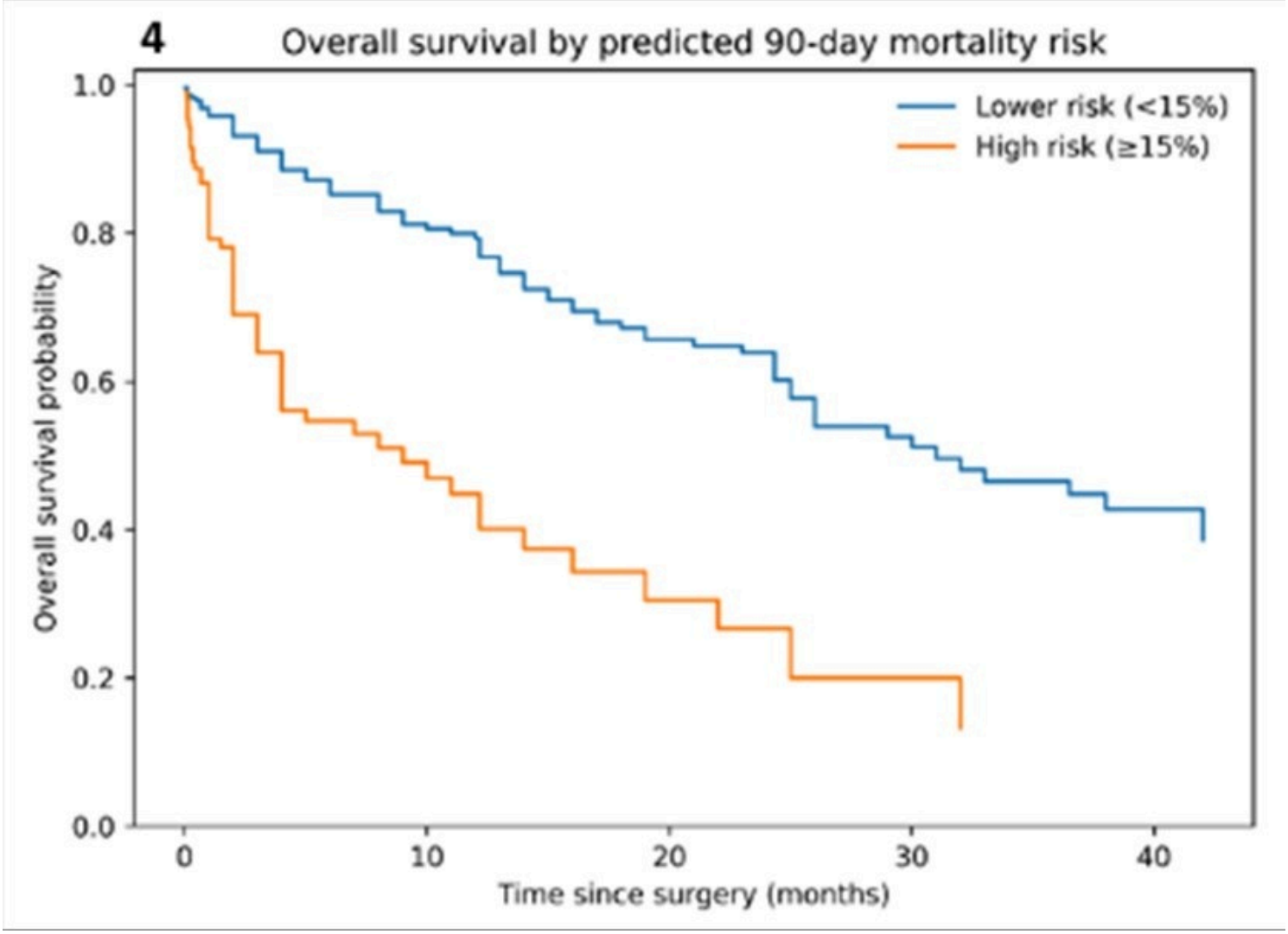


Figure 4

Kaplan–Meier overall survival curves stratified by ≥15% predicted 90-day mortality risk, demonstrating significant separation between higher- and lower-risk groups.

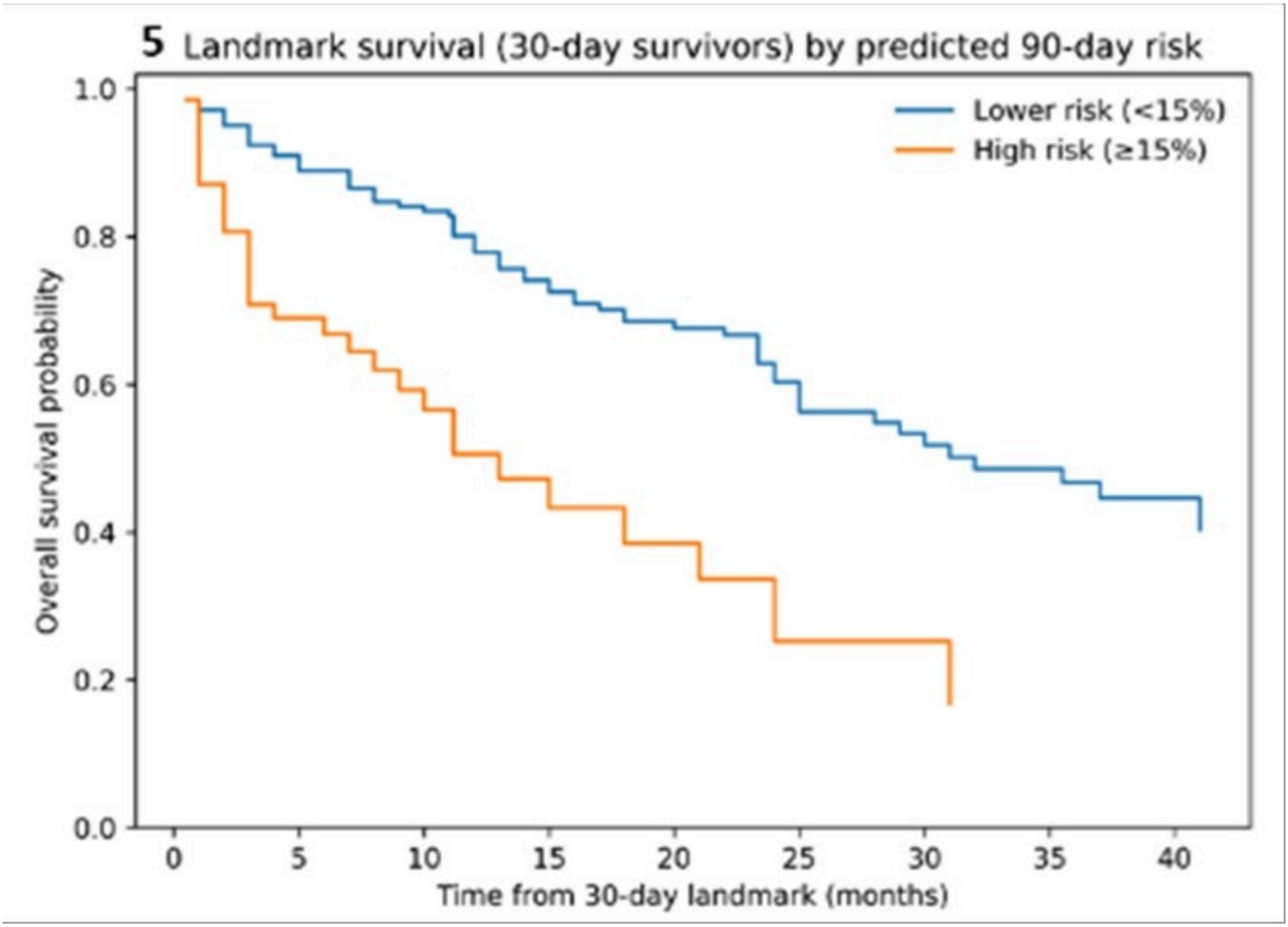


Figure 5

Landmark Kaplan–Meier survival analysis among patients surviving ≥30 days, showing persistent overall survival separation according to early mortality risk category.