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Preoperative Prediction of 30-Day Mortality in Major Abdominal Surgery: Development and Internal Validation of a Firth-Penalized Prognostic Model A Retrospective Cohort Study

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Abstract

Objective

To identify preoperative predictors of 30-day mortality in patients undergoing major abdominal surgery and to develop and internally validate a prognostic prediction model.

Methods

This retrospective cohort study included 1,131 adult patients who underwent major abdominal surgery at the First Hospital of Lanzhou University between January 2020 and December 2024. After excluding two records with implausible INR values (data-entry errors) and 42 with missing INR, 1,087 patients were analyzed. The primary outcome was 30-day postoperative mortality. Because the outcome was rare, Firth penalized logistic regression was used to identify independent preoperative predictors; a full multivariable model was fitted, and a final parsimonious model was used for the nomogram and performance analyses. Model performance was assessed by discrimination (AUC) and calibration, with internal validation by bootstrap resampling. Decision curve analysis (DCA) was performed.

Results

Among 1,087 analyzable patients, 19 (1.7%) died within 30 days. In the full multivariable Firth model (n = 1,051; AUC 0.865), three predictors were independently significant: INR (OR 42.9 per 1 unit, 95% CI 7.9-233.5, P < 0.001), baseline hemoglobin (OR 1.033 per 1 g/L, 95% CI 1.015–1.052, P < 0.001), and emergency surgery (OR 2.72, 95% CI 1.01–7.31, P = 0.047). The final parsimonious model comprising these three predictors showed good discrimination (AUC 0.852; bootstrap-corrected 0.855, 95% CI 0.758–0.945). Mortality rose across INR quartiles (1.0%, 0.4%, 1.1%, and 4.5%), and INR > 1.5 identified a 12.7% mortality risk versus 1.2% at INR ≤ 1.5. Higher baseline hemoglobin was paradoxically associated with increased mortality, with a clear dose-response gradient (3.7% mortality in the highest hemoglobin quartile vs 0.7–1.5% in the lower quartiles).

Conclusion

INR, emergency surgery, and baseline hemoglobin are independent preoperative predictors of 30-day mortality in major abdominal surgery. Elevated INR is a particularly strong early warning signal. The parsimonious nomogram provides a practical tool for risk stratification. The paradoxical hemoglobin-mortality association warrants further investigation.

1. Introduction

Major abdominal surgery encompasses complex procedures involving the liver, biliary system, pancreas, spleen, and gastrointestinal tract. Despite advances in surgical technique, anesthesia, and perioperative care, postoperative mortality remains a substantial clinical concern: more than four million people worldwide are estimated to die within 30 days of surgery each year, making perioperative death a leading contributor to global mortality [1]. Early and accurate identification of patients at elevated risk of death is essential for individualized preoperative planning, resource allocation, and informed consent.

Massive transfusion (MT) and major intraoperative bleeding have long been recognized as key determinants of adverse postoperative outcomes, and several nomograms and predictive models for perioperative transfusion risk have been developed [2, 3]. In an unpublished companion analysis using the same cohort, we identified six preoperative predictors of perioperative massive transfusion and developed a nomogram for transfusion risk stratification. However, transfusion and bleeding represent intermediate events rather than ultimate outcomes; the more clinically meaningful question is which patients will ultimately die. Existing generic risk tools—such as the Surgical Outcome Risk Tool (SORT) and the ACS NSQIP Surgical Risk Calculator—predict 30-day mortality from preoperative variables [4, 5], but SORT relies on procedure-specific coding and ASA grade and has been shown to underpredict risk precisely in the high-risk patients for whom accurate stratification matters most [6]. Few studies have directly modeled 30-day mortality using simple, universally available laboratory indices across a heterogeneous group of major abdominal procedures that includes emergency cases.

A further unresolved issue concerns the role of preoperative hemoglobin. While anemia is conventionally regarded as a risk factor for poor outcomes, recent evidence suggests that elevated hemoglobin and hematocrit may also signal increased risk through hemoconcentration, dehydration, or occult cardiopulmonary and hematologic comorbidity [7–9]. The direction and clinical significance of the hemoglobin-mortality association in major abdominal surgery remain incompletely characterized.

Coagulation status is another candidate predictor. Preoperative INR is a simple, universally available index of hemostasis and hepatic synthetic function, and large registry studies have established that even modest elevations are associated with graded increases in postoperative bleeding and mortality [10, 11]. However, the prognostic value of INR has been examined mainly in specific procedural cohorts, and its contribution within a purely preoperative model for a heterogeneous population of major abdominal surgery—where emergency cases and occult coagulopathy are common—has not been fully characterized.

In this study, we aimed to (1) identify independent preoperative predictors of 30-day mortality, (2) develop and internally validate a Firth-penalized prognostic model with a nomogram, and (3) explicitly examine the dose-response relationships of preoperative INR and hemoglobin with mortality.

2. Methods

2.1 Study design and participants

This was a retrospective cohort study conducted at the First Hospital of Lanzhou University. Adult patients (≥ 18 years) who underwent major abdominal surgery (surgery grade III or IV) between January 2020 and December 2024 were eligible. Patients with incomplete transfusion or mortality records were excluded. The study was approved by the institutional review board, with a waiver of informed consent given the retrospective design.

2.2 Outcome definition

The primary outcome was all-cause 30-day postoperative mortality, defined as death from any cause within 30 days after surgery.

2.3 Candidate predictors

Preoperative (baseline) variables were collected, including demographics (age, sex), comorbidities (hypertension, diabetes mellitus, coronary heart disease), emergency status, and preoperative laboratory indices (hemoglobin, hematocrit, platelet count, INR, prothrombin time, APTT, thrombin time, fibrinogen, ALT, AST, LDH, total and direct bilirubin, total protein, albumin, BUN, and creatinine).

2.4 Statistical analysis

Continuous variables are presented as median with interquartile range (IQR) and compared using the Mann-Whitney U test. Categorical variables are presented as counts with percentages and compared using the Fisher exact test or chi-square test. Data screening identified two implausible INR values (1013 and 15.74, the latter with a concordant prothrombin time outlier of 156.9 s) consistent with data-entry errors; these two records were excluded. INR was additionally missing in 42 patients. Consequently, 1,087 of 1,131 patients had analyzable INR values and constituted the descriptive-analysis cohort; 44 patients (42 with missing INR and 2 with implausible INR) were therefore not available for INR-based analyses. Because 30-day mortality was a rare event (1.7%), univariate and multivariate analyses were performed using Firth penalized logistic regression, which yields finite and less biased estimates in the presence of separation or rare events [5, 16]. Model construction followed a three-step strategy: (1) univariate Firth analysis of all candidate predictors; (2) a full multivariable Firth model including all variables with univariate $P < 0.10$, with AST excluded because of collinearity with ALT (Pearson $r = 0.89$) and APTT excluded because its coefficient could not be stably estimated owing to a single extreme outlier (3835 s, a data-entry error); and (3) a final parsimonious model retaining the independently significant predictors ($P < 0.05$) from the full model, which was used for the nomogram and all performance analyses.

Model performance was assessed by discrimination (AUC) and calibration. Internal validation of the parsimonious model was performed by bootstrap resampling (200 replicates). A nomogram was constructed from the parsimonious model, and DCA was performed to assess net clinical benefit. To explore the hemoglobin-mortality and INR-mortality associations, we examined mortality across quartiles of each variable and stratified by emergency status. Pre-specified sensitivity analyses included (1) refitting the model with hypertension, diabetes mellitus, and coronary heart disease added as

covariates, (2) excluding patients with INR > 2, and (3) refitting the model separately in elective and emergency subgroups. Joint risk stratification by baseline INR strata and hemoglobin quartiles was summarized in a heatmap. For the multivariable models, patients with any missing value among the included predictors were excluded by complete-case analysis (full model n = 1,051; parsimonious model n = 1,087). Analyses were performed using Python 3.13 (pandas, scipy, scikit-learn). A two-sided $P < 0.05$ was considered statistically significant.

3. Results

3.1 Baseline characteristics

A total of 1,087 patients with analyzable INR values were included in the descriptive analysis (median age 59 years; 60.6% male); 44 patients (42 with missing INR and 2 with implausible INR) were excluded from INR-based analyses. Nineteen patients (1.7%) died within 30 days. Patients who died had significantly higher rates of emergency surgery (52.6% vs 20.2%, $P = 0.002$) and massive transfusion (52.6% vs 10.9%, $P < 0.001$), greater intraoperative blood loss (median 1200 vs 300 mL, $P = 0.004$), higher total transfusion volume (10.0 vs 3.5 units, $P < 0.001$), higher baseline hemoglobin (129 vs 102 g/L, $P = 0.039$), higher INR (1.3 vs 1.1, $P < 0.001$), and lower albumin (33.6 vs 38.0 g/L, $P = 0.007$) (Table 1).

Table 1
Baseline characteristics of patients with and without 30-day mortality

Variable	No death (n = 1068)	Death (n = 19)	P value
Age (years)	59.0 (50.0–68.0)	58.0 (55.0–61.5)	0.541
Male sex, n (%)	646 (60.5%)	13 (68.4%)	0.646
Hemoglobin (g/L)	102.0 (87.0–126.0)	129.0 (96.0–141.0)	0.039
Hematocrit (%)	32.1 (27.8–38.2)	39.2 (30.6–42.0)	0.071
Platelet count (×10⁹/L)	185.0 (119.0–260.0)	164.0 (60.0–248.5)	0.232
INR	1.1 (1.0–1.2)	1.3 (1.1–1.8)	< 0.001
Prothrombin time (s)	12.1 (11.4–13.3)	14.0 (12.2–18.6)	< 0.001
APTT (s)	31.5 (29.1–34.0)	35.1 (30.4–38.3)	0.013
Thrombin time (s)	13.9 (12.9–15.1)	16.7 (12.9–18.9)	0.022
Fibrinogen (g/L)	3.2 (2.5–3.9)	2.9 (1.1–3.6)	0.065
ALT (U/L)	20.0 (12.0–38.5)	46.0 (36.5–132.5)	< 0.001
AST (U/L)	25.0 (18.0–43.0)	55.0 (35.5–95.5)	< 0.001
LDH (U/L)	182.0 (151.0–229.0)	181.5 (173.2–304.8)	0.129
Total bilirubin (μmol/L)	15.3 (10.7–26.2)	39.0 (12.2–51.3)	0.031
Direct bilirubin (μmol/L)	3.6 (2.3–6.9)	17.6 (4.3–24.0)	0.011
Total protein (g/L)	63.8 (58.4–71.1)	60.7 (45.7–66.5)	0.075
Albumin (g/L)	38.0 (34.2–42.1)	33.6 (29.0–39.0)	0.007
BUN (mmol/L)	5.3 (4.1–6.8)	5.8 (3.8–7.3)	0.483
Creatinine (μmol/L)	64.4 (54.6–77.0)	71.9 (54.9–90.9)	0.133
Blood loss (mL)	300.0 (150.0–600.0)	1200.0 (200.0–2000.0)	0.004
Transfusion (units)	3.5 (2.5–6.5)	10.0 (3.8–18.2)	< 0.001
Length of stay (days)	13.0 (9.0–18.0)	7.0 (3.2–19.8)	0.038
Emergency surgery, n (%)	216 (20.2%)	10 (52.6%)	0.002
Hypertension, n (%)	200 (18.7%)	4 (21.1%)	0.768
Diabetes mellitus, n (%)	100 (9.4%)	2 (10.5%)	0.697
Coronary heart disease, n (%)	20 (1.9%)	0 (0.0%)	1.000
Massive transfusion, n (%)	116 (10.9%)	10 (52.6%)	< 0.001

3.2 Univariate and multivariate analysis

In univariate Firth analysis, INR (OR 59.2 per 1 unit, P < 0.001), ALT (OR 1.004 per U/L, P < 0.001), AST (OR 1.002 per U/L, P < 0.001), emergency surgery (OR 4.35, P = 0.001), baseline albumin (OR 0.919, P = 0.003), fibrinogen (OR 0.562 per g/L, P = 0.013), PT (OR 1.028 per s, P = 0.033), baseline hemoglobin (OR 1.019, P = 0.023), and thrombin time (OR 1.028, P = 0.038) were significantly associated with 30-day mortality, whereas LDH showed a marginal association (OR 1.001 per U/L, P = 0.053) (Table 2). In the full multivariable Firth model including all ten variables with univariate P < 0.10 (complete-case cohort, n = 1,051; AUC 0.865), three predictors remained independently significant: INR (OR 42.9 per 1 unit, 95% CI 7.9-233.5, P < 0.001), baseline hemoglobin (OR 1.033 per 1 g/L, 95% CI 1.015–1.052, P < 0.001), and emergency surgery (OR 2.72, 95% CI 1.01–7.31, P = 0.047); albumin (OR 0.941, P = 0.112), LDH (OR 0.998, P = 0.236), thrombin time, creatinine, ALT, PT, and fibrinogen were not significant (Table 3, Fig. 1).

Table 2
Univariate analysis of preoperative predictors of 30-day mortality

Variable	OR	95% CI	P value
Age (years)	0.996	0.967–1.026	0.784
Emergency surgery	4.352	1.785–10.613	0.001 *
Hemoglobin (g/L)	1.019	1.003–1.035	0.023 *
Albumin (g/L)	0.919	0.869–0.971	0.003 *
INR	59.219	12.524–280.002	< 0.001 *
Total bilirubin (μmol/L)	1.002	0.999–1.006	0.143
Thrombin time (s)	1.028	1.002–1.056	0.038 *
Creatinine (μmol/L)	1.006	1.000–1.012	0.068
Platelet count (×10⁹/L)	0.997	0.993–1.002	0.202
ALT (U/L)	1.004	1.002–1.005	< 0.001 *
AST (U/L)	1.002	1.001–1.003	< 0.001 *
LDH (U/L)	1.001	1.000–1.002	0.053
Prothrombin time (s)	1.028	1.002–1.055	0.033 *
Fibrinogen (g/L)	0.562	0.356–0.887	0.013 *
APTT (s)	NC*	NC*	NC*

** Statistically significant (P < 0.05). NC: not computable because the coefficient could not be stably estimated owing to a single extreme APTT outlier (3835 s, a data-entry error). Univariate analyses were performed by Firth penalized logistic regression after exclusion of two implausible INR values and 42 records with missing INR.*

Table 3
Multivariate Firth penalized logistic regression for 30-day mortality

Variable	β coefficient	OR	95% CI	P value
(Intercept)	-10.4236	0.000	0.000–0.003	< 0.001*
Emergency surgery	1.0004	2.719	1.011–7.311	0.047*
Hemoglobin (per 1 g/L)	0.0325	1.033	1.015–1.052	< 0.001*
Albumin (per 1 g/L)	-0.0609	0.941	0.873–1.014	0.112
INR (per 1 unit)	3.7597	42.936	7.894–233.529	< 0.001*
Thrombin time (per 1 s)	0.0166	1.017	0.985–1.050	0.312
Creatinine (per 1 μmol/L)	0.0037	1.004	0.994–1.014	0.470
ALT (per 1 U/L)	0.0030	1.003	0.999–1.007	0.104
Prothrombin time (per 1 s)	0.0332	1.034	0.993–1.076	0.106
Fibrinogen (per 1 g/L)	-0.2824	0.754	0.504–1.127	0.169
LDH (per 1 U/L)	-0.0016	0.998	0.996–1.001	0.236

** Statistically significant (P < 0.05). Full multivariable model; Model AUC = 0.865; n = 1051. The final parsimonious three-predictor model (emergency surgery, hemoglobin, INR; n = 1,087) had AUC = 0.852 with bootstrap-corrected AUC = 0.855 (95% CI 0.758–0.945) and was used for the nomogram, ROC, calibration, and DCA.*

The final parsimonious model retained the three independently significant predictors—emergency surgery (OR 3.19, 95% CI 1.25–8.14, P = 0.015), baseline hemoglobin (OR 1.031 per 1 g/L, 95% CI 1.014–1.049, P < 0.001), and INR (OR 124.1 per 1 unit, 95% CI 25.5-603.6, P < 0.001)—and was used for the nomogram and all subsequent performance analyses (n = 1,087). Given the narrow observed INR range (IQR 1.0-1.2), the OR per 0.1-unit INR increment corresponds to approximately 1.62 (exp(0.482)), which is a more clinically interpretable magnitude.

3.3 Model performance and validation

The full multivariable model achieved an AUC of 0.865. The final parsimonious three-predictor model showed good discrimination with an AUC of 0.852 (Fig. 2), essentially preserving the discrimination of the full model while using only routinely available variables. Bootstrap internal validation (200 replicates) yielded a corrected AUC of 0.855 (95% CI 0.758–0.945), indicating negligible overfitting. Calibration was satisfactory (Fig. 3), and DCA demonstrated net clinical benefit (Fig. 4). A nomogram was constructed for clinical use (Fig. 5).

3.4 The INR-mortality relationship

Mortality increased across INR quartiles: 1.0%, 0.4%, 1.1%, and 4.5% in the first through fourth quartiles (0.05–1.04, 1.04–1.10, 1.10–1.21, and 1.21–2.89, respectively) (Fig. 6). At clinically meaningful

thresholds, mortality was 4.3% for INR > 1.2 versus 0.9% for INR ≤ 1.2, and 12.7% for INR > 1.5 versus 1.2% for INR ≤ 1.5—a nearly tenfold gradient.

3.5 The hemoglobin-mortality relationship

We observed a paradoxical positive association between baseline hemoglobin and mortality. This association was consistent across emergency (median 121 g/L in decedents vs 100 g/L in survivors) and elective (133 vs 103 g/L) subgroups, indicating it was not driven by emergency status. Baseline hemoglobin was positively correlated with intraoperative blood loss ($r = 0.231$, $P < 0.001$) but negatively correlated with total transfusion volume ($r = -0.131$, $P < 0.001$). A clear dose-response gradient was evident across hemoglobin quartiles (4.7–87, 87–103, 103–126, and 126–193 g/L): 30-day mortality was 1.5%, 0.7%, 1.2%, and 3.7% in the first through fourth quartiles, respectively (Fig. 7). Patients with hemoglobin > 150 g/L comprised 15.8% of decedents versus 6.2% of survivors.

3.6 Sensitivity analyses and joint risk stratification

All three predictors of the parsimonious model remained independently significant in nearly every sensitivity scenario (**Table S1**). Adding hypertension, diabetes, and coronary heart disease did not alter the model (AUC 0.833; emergency surgery, hemoglobin, and INR all retained significance, whereas none of the comorbidities was significant). Excluding patients with INR > 2 to rule out extreme-value influence left the model essentially unchanged (AUC 0.837; INR $P < 0.001$). In the elective-only subgroup the model performed well (AUC 0.844, n = 861, 9 deaths), while in the emergency subgroup hemoglobin lost significance ($P = 0.063$) although INR remained dominant (AUC 0.794, n = 226, 10 deaths). Baseline INR and hemoglobin jointly stratified risk in an additive fashion (Fig. 8): mortality was 0% across all hemoglobin quartiles among patients with INR ≤ 1.0, but reached 25.0% in patients with INR > 1.5 combined with the highest hemoglobin quartile. Comorbidities (hypertension 18.7% vs 21.1%, diabetes 9.4% vs 10.5%, coronary heart disease 1.9% vs 0%; all $P > 0.69$) were not associated with 30-day mortality in this cohort.

4. Discussion

In this retrospective cohort study of 1,087 patients undergoing major abdominal surgery, we developed and internally validated a preoperative prognostic model for 30-day mortality. In a full multivariable Firth model, three readily available variables—INR, emergency surgery, and baseline hemoglobin—emerged as independently significant. The final parsimonious three-predictor model achieved good discrimination (AUC 0.852) with satisfactory calibration and clear net clinical benefit, and was robust to bootstrap internal validation.

Elevated preoperative INR was the strongest predictor of mortality. Each 0.1-unit increment in INR corresponded to a nearly 1.6-fold increase in the odds of death, and mortality rose from approximately 1% at INR ≤ 1.2 to 12.7% at INR > 1.5. This finding is clinically coherent and aligns with large registry evidence: in an analysis of over 636,000 surgical patients in the ACS NSQIP, Tamim et al. reported a graded association between preoperative INR and 30-day mortality (adjusted OR 2.31 for INR 1.5–1.9

and 2.81 for INR ≥ 2, relative to INR < 1), with an optimal INR threshold of approximately 1.13 for mortality [10]. Our data extend this relationship to a heterogeneous major abdominal surgery cohort in which the outcome was rare, and demonstrate that INR retains independent prognostic value after adjustment for hemoglobin, albumin, and emergency status. Coagulopathy is a well-established marker of hepatic dysfunction, disease severity, and emerging physiological decompensation, and it directly informs bleeding risk and transfusion requirements. Notably, the apparent absence of an INR effect in preliminary screening—owing to numerical instability induced by two implausible data-entry values—underscores the importance of rigorous data quality checks in rare-event modeling. Routine preoperative coagulation screening, often criticized as low-yield in elective surgery populations, may retain substantial prognostic value in unselected major abdominal surgery cohorts that include emergency cases [10, 11].

Emergency surgery was the next strongest predictor of mortality (OR 2.72 in the full model and 3.19 in the parsimonious model), consistent with the established literature showing that urgent and emergent procedures carry substantially higher risk due to uncontrolled pathology, physiological derangement, and limited time for preoperative optimization [12]. In a large cohort of 4,346 patients undergoing emergency abdominal surgery, Tolstrup et al. reported a 30-day mortality of 8%, with age, ASA grade, cirrhosis, chronic nephropathy, and malignancy identified as key risk factors [12]. Baseline albumin was significant in univariate analysis (OR 0.919, P = 0.003) but was attenuated to non-significance in the fully adjusted model (OR 0.941, P = 0.112), consistent with its well-recognized role as a marker of nutritional depletion, hepatic dysfunction, and systemic inflammation, and with meta-analytic evidence that hypoalbuminaemia confers a substantially elevated mortality risk in abdominal and gastrointestinal surgery [13, 14]. The attenuation of the albumin effect in the fully adjusted model likely reflects shared variance with INR and other markers of hepatic synthesis and illness severity.

The most intriguing finding is the paradoxical positive association between baseline hemoglobin and mortality. Conventionally, preoperative anemia is regarded as a risk factor for adverse outcomes [7, 15]. However, our observation of increased mortality at higher hemoglobin levels is consistent with a U-shaped (or J-shaped) relationship between preoperative red cell mass and postoperative risk that has been documented in large surgical cohorts. In a landmark analysis of over 310,000 older veterans undergoing major noncardiac surgery, Wu et al. reported that 30-day mortality increased monotonically with both negative and positive deviations of hematocrit from the normal range, with risk rising once hematocrit exceeded 51% [8]. Similarly, in a cohort of nearly 200,000 patients undergoing major surgery in the ACS NSQIP, Musallam et al. found that a raised preoperative hematocrit was independently associated with increased 30-day mortality (OR 2.23) and venous thromboembolism [9]. Our findings extend this U-shaped relationship to a heterogeneous cohort of major abdominal surgery and demonstrate a clear dose-response gradient, with mortality reaching 3.7% in the highest hemoglobin quartile.

Several mechanisms may underlie the elevated risk associated with high hemoglobin. The most directly supported is blood hyperviscosity: hematocrit is exponentially related to whole-blood viscosity, and elevated red cell mass increases flow resistance, raises cardiac workload, and impairs microcirculatory

perfusion, predisposing to thrombotic and cardiac events [8, 16]. Consistent with a viscosity-mediated mechanism, Wu et al. observed that mortality and cardiac morbidity began to rise once hematocrit exceeded 51%, well below traditional polycythemia thresholds [8]. Second, elevated hemoglobin may reflect hemoconcentration secondary to dehydration or capillary leak, which itself signals greater physiological stress and reduced effective circulating volume. Third, higher hemoglobin may indicate occult cardiopulmonary or hematologic comorbidity—including chronic hypoxemia, obstructive sleep apnea, or polycythemia—that independently increases perioperative risk [17]; uncontrolled polycythemia vera has been associated with fatal perioperative thrombotic complications even during otherwise routine hepatectomy [18]. Fourth, in acute hemorrhage, a relatively preserved hemoglobin may paradoxically delay recognition and treatment of ongoing blood loss, as the initial hemoglobin may remain near-normal because whole blood is lost and compensatory fluid redistribution requires hours to dilute the remaining red cell mass. Importantly, in our data the association was present in both emergency and elective subgroups and was independent of emergency status, suggesting that it is not merely an artifact of acute bleeding presentation. Collectively, these observations indicate that both ends of the hemoglobin spectrum—anemia and erythrocytosis—warrant attention in preoperative risk assessment, and that a U-shaped rather than a monotonic inverse relationship best characterizes the hemoglobin-mortality association.

4.1 Strengths and limitations

This study has several strengths. First, it directly models 30-day mortality—the ultimate clinical endpoint—using purely preoperative information, complementing our unpublished companion analysis on massive transfusion prediction. Second, Firth penalized logistic regression provides valid inference despite the rarity of the outcome, the model construction followed a transparent three-step strategy, and the stability of the three significant predictors across multiple sensitivity scenarios (comorbidity adjustment, exclusion of extreme INR values, and elective/emergency stratification; **Table S1**) supports robustness. Third, we explicitly characterized the dose-response relationships of both INR and hemoglobin with mortality, identifying INR as the dominant preoperative risk signal and replicating the paradoxical hemoglobin-mortality association; the joint INR-hemoglobin stratification grid (Fig. 8) is immediately usable at the bedside, with zero mortality at INR ≤ 1.0 and mortality up to 25.0% for INR > 1.5 combined with the highest hemoglobin quartile. Fourth, all predictors are derived from routine preoperative laboratory tests and basic clinical status, requiring no additional cost or specialized testing.

Several limitations should be acknowledged. First, the retrospective, single-center design may limit generalizability, and the small number of death events (n = 19) precluded robust subgroup modeling. Second, external validation in independent, multicenter cohorts is required. Third, information on specific causes of death, intraoperative complications, and detailed comorbidity severity was not available. Fourth, the wide confidence interval around the INR effect estimate reflects the narrow observed INR range and the rarity of the outcome; the corresponding OR should be interpreted as a strong risk gradient rather than a precise multiplicative effect. Fifth, although bootstrap validation suggested negligible overfitting, the optimism correction should be interpreted cautiously given the small number of events.

5. Conclusion

INR, emergency surgery, and baseline hemoglobin are independent preoperative predictors of 30-day mortality in patients undergoing major abdominal surgery. Elevated INR is a particularly strong and actionable early warning signal. The parsimonious nomogram provides a practical tool for preoperative risk stratification and individualized perioperative planning. The paradoxical positive association between elevated baseline hemoglobin and mortality represents a novel observation that merits further investigation.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board of the First Hospital of Lanzhou University. Given the retrospective nature of the study, the requirement for informed consent was waived by the ethics committee.

Consent for publication

Not applicable. This manuscript contains no individual person's data in any form.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Zhaoyin Su, Shuai Ni, and Daowei Ding contributed equally to this work and participated in study design, data collection, and manuscript drafting. Yunpeng Wang, Jinhao Xu, Yuchen Xie, Rubing Lin, and Ximeng Wang participated in data acquisition, analysis, and critical revision of the manuscript. Yatao Liu and

Nerlich Michael conceived and supervised the study and are the corresponding authors. All authors read and approved the final manuscript.

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Figures

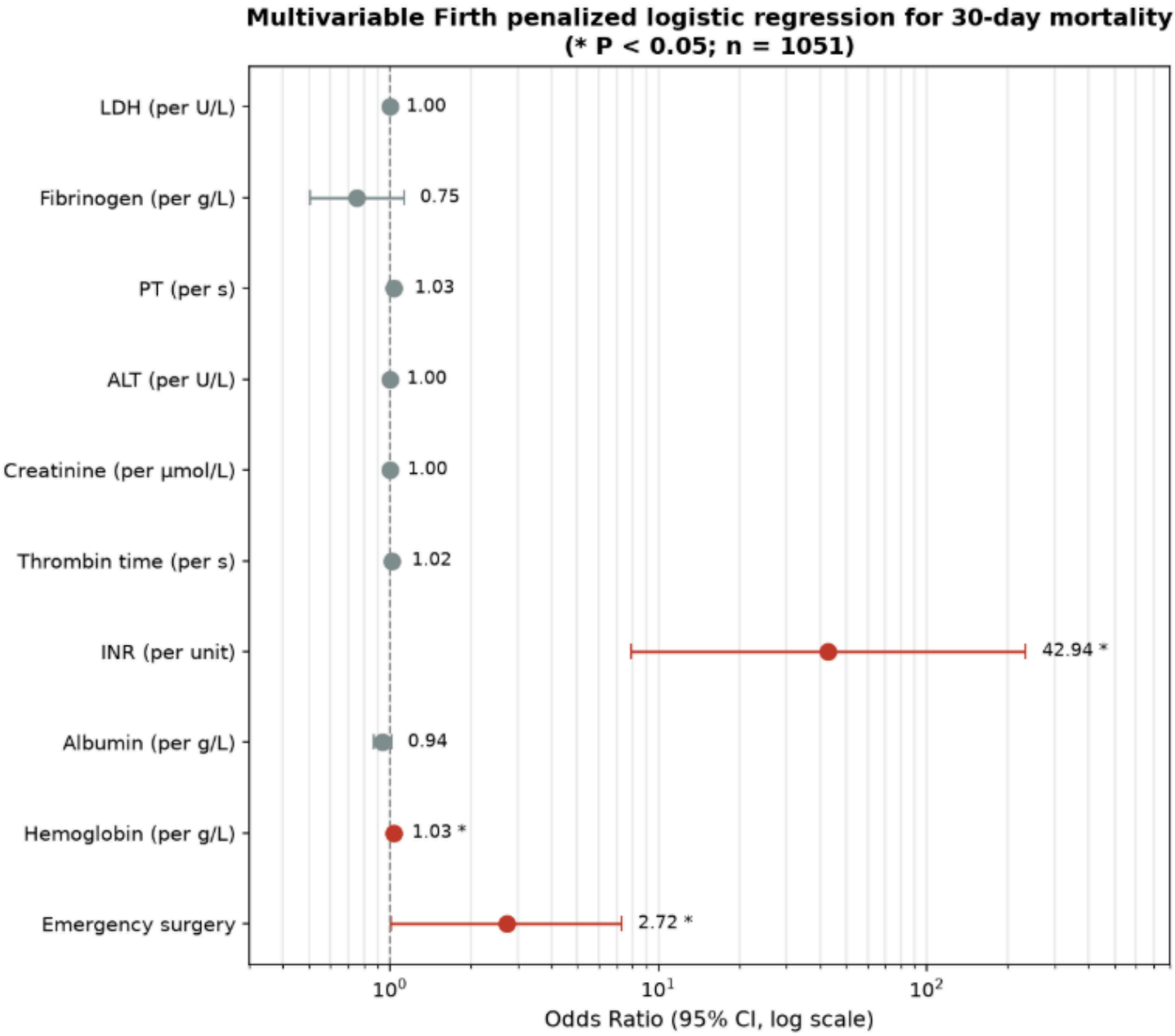

Figure 1

Forest plot of the full multivariable Firth penalized logistic regression model for 30-day mortality (P < 0.05; n = 1051).*

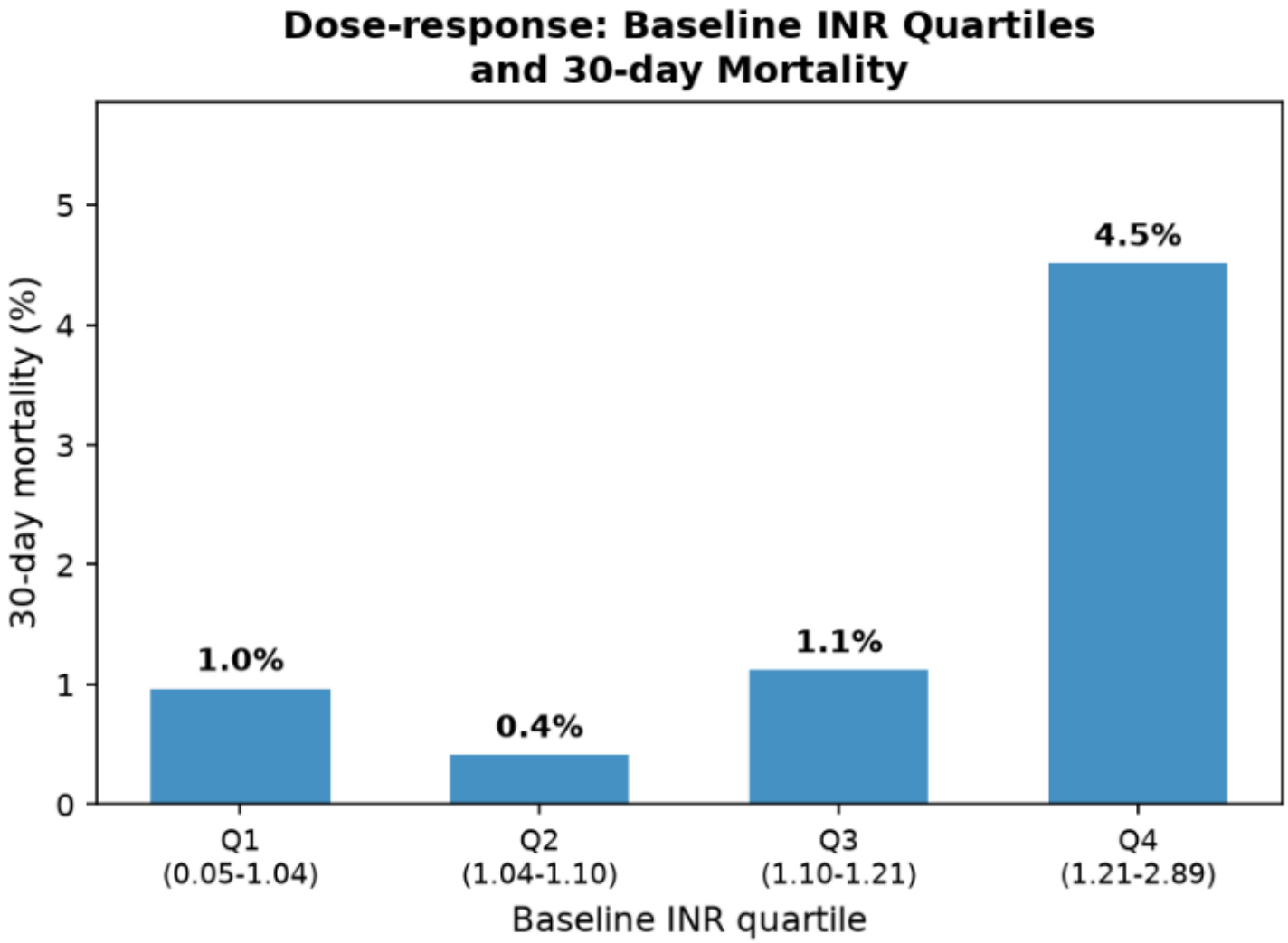

Figure 6

Dose-response relationship between baseline INR quartiles and 30-day mortality.

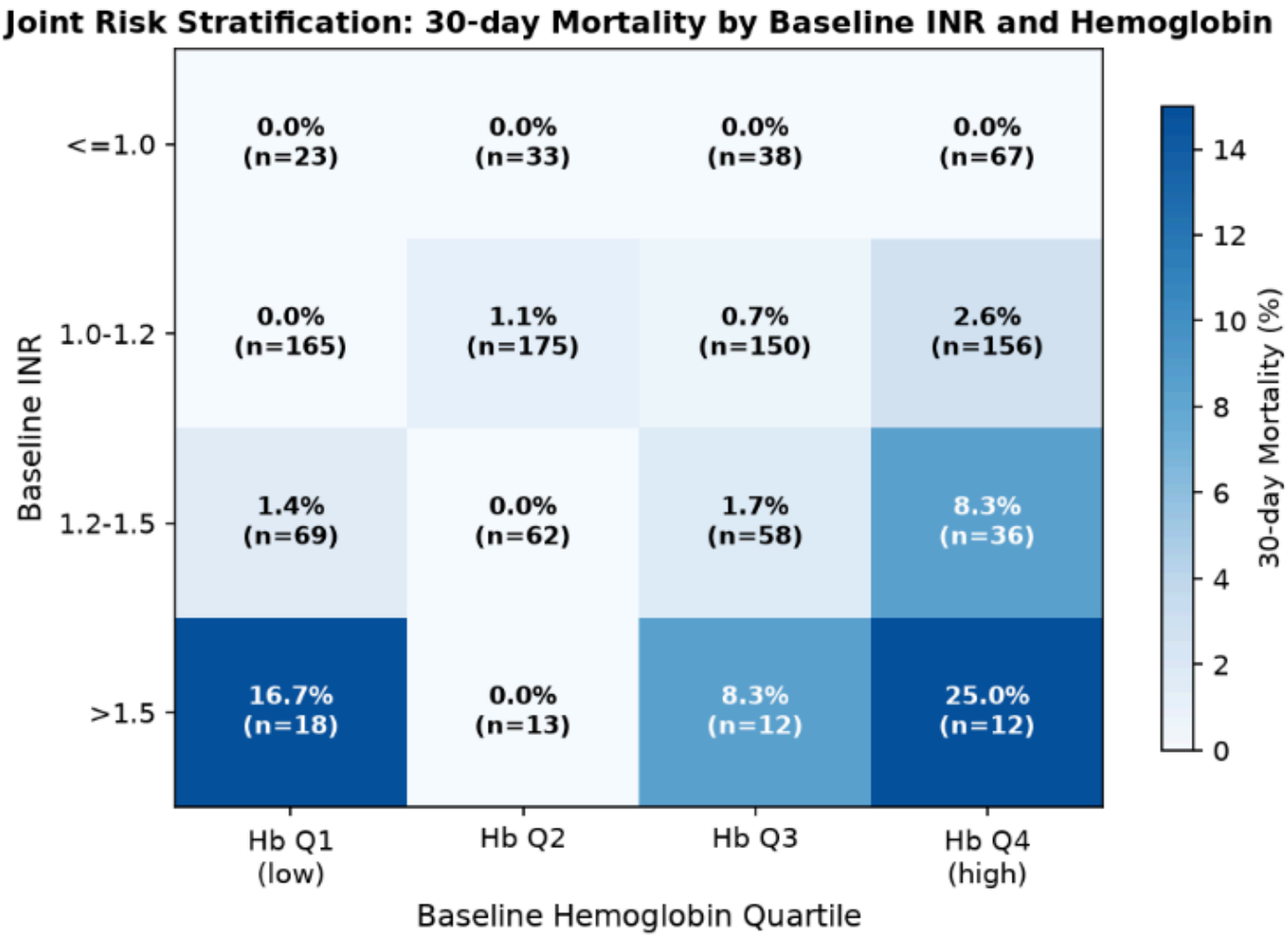

Figure 8

Joint risk stratification heatmap: 30-day mortality by baseline INR strata and hemoglobin quartiles. Cell values show mortality with sample size; cells with fewer than 5 patients are shown as N/A.