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Development of a simple risk score for 30-day mortality in patients with acute hemorrhagic rectal ulcer: a multicenter retrospective study

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Abstract

Purpose

Acute hemorrhagic rectal ulcer (AHRU) occurs mainly in elderlies and may cause massive hematochezia. Factors associated with short-term mortality in AHRU remain unclear. We aimed to identify factors associated with 30-day mortality and develop a risk score in a multi-center, retrospective cohort study.

Methods

We retrospectively analyzed 357 patients with AHRU diagnosed at 11 hospitals during a period 2014–2024. Factors associated with 30-day mortality were assessed using logistic regression analysis. A simple risk score was developed from factors identified in the multivariable analysis and internally validated using 1,000 bootstrap resamples.

Results

Twenty-five patients (7.0%) died within 30 days. Shock index (SI) ≥ 1 (odds ratio [OR], 6.75; 95% confidence interval [CI], 2.67–17.04), invasive malignancy (OR, 6.02; 95% CI, 2.22–16.28), and systemic steroid use (OR, 4.69; 95% CI, 1.66–13.27) were independently associated with 30-day mortality. Similar regression coefficients among the factors suggested a value of point 1 for each factor. Mortality was 2.4%, 11.1%, and 45.5% in patients with scores of 0, 1, and 2–3, respectively. The AUC was 0.80, and the bootstrap-corrected AUC was 0.79 (95% CI, 0.69–0.89).

Conclusion

SI ≥ 1, invasive malignancy, and systemic steroid use were associated with early mortality in patients with AHRU. A simple score based on these three factors may help stratify AHRU patients at a high risk of early mortality.

Introduction

Acute hemorrhagic rectal ulcer (AHRU) is a disease characterized by sudden-onset, painless and massive hematochezia, which typically occurs in elderlies with underlying diseases [1–4]. Although endoscopic hemostasis is usually effective, rebleeding is frequent [5–10]. Mortality is also substantial and is often related to underlying disease rather than uncontrolled bleeding [8, 11].

Several studies have investigated factors associated with mortality in acute lower gastrointestinal bleeding (LGIB) [12–16]. However, the risk factors for AHRU remain unclear. A previous study reported a

30-day mortality rate of 15.0% in patients with AHRU [10]. Because the high mortality in the early phase of AHRU was not attributable to uncontrollable bleeding alone [11], identifying factors associated with short-term mortality and stratifying patients with AHRU at a high mortality is clinically important. Nevertheless, no disease-specific risk score for short-term mortality in AHRU has been established. Accordingly, we aimed to identify factors associated with 30-day mortality and to develop a simple risk score for patients with AHRU.

Methods

Study design and patients

This multicenter retrospective cohort study included consecutive patients diagnosed with AHRU between April 2014 and March 2024 at Iwate Medical University or 10 affiliated hospitals in northern Japan. AHRU was diagnosed on the basis of acute hematochezia and characteristic endoscopic findings of rectal ulcers, according to the clinical definitions of AHRU in previous studies [1, 2, 5, 8, 11]. A total of 357 patients were included in the present analysis.

The study was conducted in accordance with the Declaration of Helsinki. Informed consent for study enrollment was obtained in the form of an opt-out on the website of each participating institution. The study protocol was approved by the Institutional Review Board of Iwate Medical University (MH2025-036) and each participating institution.

Data collection and definitions

Medical records were reviewed for age, sex, body mass index, performance status, place at the onset of AHRU, medications, comorbidities, laboratory findings, and clinical course. Evaluated medications included nonsteroidal anti-inflammatory drugs, antiplatelet agents, anticoagulants, and systemic corticosteroids. Systemic steroid use was defined as ongoing oral or intravenous corticosteroid therapy at AHRU onset. Hypertension, cardiac disease, cerebrovascular disease, chronic pulmonary disease, diabetes mellitus, and invasive malignancy were regarded as comorbidities. Invasive malignancy was defined as an active malignant neoplasm, excluding carcinoma in situ. We also checked white blood cell count, hemoglobin, blood urea nitrogen (BUN), creatinine, albumin, C-reactive protein (CRP), and prothrombin time-international normalized ratio as laboratory variables.

The shock index (SI) was calculated as heart rate divided by systolic blood pressure at the time of the onset of AHRU. SI ≥ 1 was regarded as indicating hemodynamic instability [17, 18]. Overall dose of blood transfusion and the incidence of rebleeding during the clinical course were also evaluated. Rebleeding was defined as recurrent overt rectal bleeding after primary hemostasis.

Outcome

Outcome

The primary outcome was all-cause mortality within 30 days after AHRU onset. Thirty-day survival status was ascertained from the medical records. For patients, who died within 30 days, the presumable cause of death was determined from the clinical documentation.

Statistical analysis

Continuous variables are presented as median with interquartile range (IQR) and categorical variables as number and percentages. Clinical characteristics were compared between patients who survived beyond 30 days and those who died within 30 days using the Mann-Whitney U test for continuous variables and the chi-square test or Fisher exact test for categorical variables, as appropriate. Missing data were handled by complete-case analysis, using available non-missing observations for each analysis.

Univariable logistic regression analysis was performed to evaluate factors associated with 30-day mortality. Given the limited number of outcome events, the number of variables included in the multivariable model was restricted to reduce the risk of overfitting [19]. Variables were selected from those showing strong association in the univariable analysis, with consideration of clinical relevance. Odds ratios (ORs), 95% confidence intervals (CIs), regression coefficients, and *p* values were calculated.

A simple score was developed based on the results of the multivariable analysis. The association between the score and 30-day mortality was evaluated. Mortality was examined across the observed score values, and pairwise comparisons were performed using Fisher exact tests with Bonferroni correction. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC). Internal validation was performed using 1,000 bootstrap resamples, and optimism-corrected performance was estimated. Calibration was assessed using the calibration slope and intercept. Overall prediction error was assessed using the Brier score. A two-sided p value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA) and R version 4.5.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics and 30-day mortality

Among 357 patients with AHRU, 332 survived for more than 30 days, while 25 died within 30 days after the onset of AHRU. 30-day mortality rate was calculated to be 7.0%. Table 1 summarizes the clinical characteristics of the deceased and surviving patients. Systemic steroid use, invasive malignancy, and SI ≥ 1 were more frequent among patients who died within 30 days. These patients also had higher BUN, creatinine, and CRP values and lower albumin value than surviving patients did.

Table 1
Clinical characteristics according to 30-day mortality

Variable	Survived > 30 days (n = 332)	30-day death (n = 25)	*p* value
Age, years, median (IQR)	82 (75–88)	76 (68–82)	0.07
Sex, male/female	148/184	8/17	0.22
BMI, median (IQR)	20.6 (18.1–23.1)	21.6 (18.3–25.0)	0.27
Performance status, median (IQR)	3 (2–4)	3 (3–4)	0.07
In-hospital onset, n (%)	186 (56.2)	16 (64.0)	0.66
NSAID use, n (%)	59 (17.8)	6 (24.0)	0.43
Antiplatelet use, n (%)	86 (25.9)	7 (28.0)	0.82
Anticoagulant use, n (%)	82 (24.7)	6 (24.0)	0.82
Systemic steroid use, n (%)	20 (6.0)	8 (32.0)	< 0.001
Hypertension, n (%)	212 (63.9)	14 (56.0)	0.52
Cardiac disease, n (%)	66 (19.9)	8 (32.0)	0.06
Cerebrovascular disease, n (%)	98 (29.5)	5 (20.0)	0.63
Chronic pulmonary disease, n (%)	26 (7.8)	3 (12.0)	0.44
Diabetes mellitus, n (%)	78 (23.5)	9 (36.0)	0.22
Invasive malignancy, n (%)	32 (9.6)	9 (36.0)	< 0.001
Shock index ≥ 1, n (%)	44 (13.3)	13 (52.0)	< 0.001
Blood transfusion, n (%)	132 (42.6)	16 (69.6)	0.08
Rebleeding, n (%)	71 (21.4)	8 (32.0)	0.22
WBC, /μL, median (IQR)	8000 (6233–14970)	9250 (2910–16780)	0.05
Hemoglobin, g/dL, median (IQR)	10.5 (8.7–12.2)	10.2 (7.8–11.0)	0.12
BUN, mg/dL, median (IQR)	23 (16.6–36.5)	38.7 (24.5–51.1)	< 0.01
Creatinine, mg/dL, median (IQR)	0.87 (0.63–1.35)	1.17 (0.81–3.12)	0.03
Albumin, g/dL, median (IQR)	2.8 (2.4–3.3)	2.3 (1.9-3.0)	< 0.01
CRP, mg/dL, median (IQR)	1.7 (0.57–4.76)	4.3 (1.9–9.7)	< 0.01

Data are median (IQR) or n (%). Percentages are based on available cases. BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; NSAID, nonsteroidal anti-inflammatory drug; PT-INR, prothrombin time-international normalized ratio; WBC, white blood cell count.

Variable	Survived > 30 days (n = 332)	30-day death (n = 25)	*p* value
PT-INR, median (IQR)	1.23 (1.03–1.30)	1.25 (1.07–1.53)	0.13

Data are median (IQR) or n (%). Percentages are based on available cases. BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; NSAID, nonsteroidal anti-inflammatory drug; PT-INR, prothrombin time-international normalized ratio; WBC, white blood cell count.

The causes of death for deceased patients were malignancy in 7 (28.0%), sepsis in 6 (24.0%), pneumonia in 3 (12.0%), hemorrhagic shock in 3 (12.0%), and brain infarction, liver failure, heart failure, urinary tract infection, multiple organ failure, and infective endocarditis in a patient each (4.0%).

Factors associated with 30-day mortality

In univariable logistic regression analysis, BUN, creatinine, albumin, CRP, SI ≥ 1, invasive malignancy, and systemic steroid use were associated significantly with 30-day mortality (Table 2). In the multivariable model, SI ≥ 1 (OR, 6.75; 95% CI, 2.67–17.04; $p < 0.001$), invasive malignancy (OR, 6.02; 95% CI, 2.22–16.28; $p < 0.001$), and systemic steroid use (OR, 4.69; 95% CI, 1.66–13.27; $p = 0.004$) were independent risk factors for 30-day mortality.

Table 2
Logistic regression analysis for 30-day mortality

Variable	Univariable OR (95% CI)	*p* value	Multivariable OR (95% CI)	*p* value
BUN	1.015 (1.004–1.027)	0.006		
Creatinine	1.209 (1.031–1.417)	0.013		
Albumin	0.356 (0.180–0.703)	0.003		
CRP	1.071 (1.010–1.136)	0.018		
Shock index ≥ 1	7.091 (3.042–16.529)	< 0.001	6.748 (2.673–17.035)	< 0.001
Invasive malignancy	5.273 (2.156–12.897)	< 0.001	6.015 (2.222–16.281)	< 0.001
Systemic steroid use	7.341 (2.897–19.062)	< 0.001	4.694 (1.660-13.269)	0.004

BUN, blood urea nitrogen; CI, confidence interval; CRP, C-reactive protein; OR, odds ratio.

Development of the AHRU 30-day mortality risk score

The regression coefficients for SI ≥ 1, invasive malignancy, and systemic steroid use were 1.909, 1.794, and 1.546, respectively. Because the coefficients were similar, a simple unweighted score was constructed by assigning one point to each factor (Table 3), resulting in a total score ranging from 0 to 3. Scores were 0 in 254 patients, 1 in 81, 2 in 21, and 3 in a patient. Because a single patient had a score of 3, patients with scores of 2 and 3 were combined in a group comparing 30-day mortality. Thirty-day mortality was 2.4% (6/254) for patients with score 0, 11.1% (9/81) for patients with score 1, and 45.5% (10/22) for patients with score 2 or 3 (Fig. 1). Mortality differed significantly between patients with score 0 and 1 ($p = 0.008$), between patients with score 1 and 2–3 ($p = 0.002$), and between patients with score 0 and 2–3 ($p < 0.001$).

Table 3
Development of the AHRU 30-day mortality risk score

Predictor	Regression coefficient	Adjusted OR (95% CI)	Assigned points
Shock index ≥ 1	1.909	6.748 (2.673–17.035)	1
Invasive malignancy	1.794	6.015 (2.222–16.281)	1
Systemic steroid use	1.546	4.694 (1.660-13.269)	1
Total score = shock index ≥ 1 (1 point) + invasive malignancy (1 point) + systemic steroid use (1 point).			
Risk groups: low, 0 points; intermediate, 1 point; high, 2–3 points.			

Internal validation

The AUC of the score for the prediction of 30-day mortality was 0.80, and the bootstrap-corrected AUC was 0.79 (95% CI, 0.69–0.89) (Fig. 2). The calibration slope was 1.02 (95% CI, 0.62–1.59), and the calibration intercept was 0.09 (95% CI, -0.85 to 1.61). The Brier score was 0.06 (95% CI, 0.04–0.07).

Discussion

In this multicenter retrospective study, 7.0% of patients with AHRU died within 30 days after onset. SI ≥ 1, invasive malignancy, and systemic steroid use were independently associated with 30-day mortality. A simple score based on three factors stratified patients into groups with 30-day mortality rates of 2.4%, 11.1%, and 45.5%. The score showed a moderate power for the stratification of short-term prognosis.

AHRU often occurs in older patients with poor general condition and serious underlying diseases [1–6, 8, 10, 20]. In fact, Takahashi et al. reported an in-hospital mortality rate of 18% among 72 patients with AHRU. However, Takahashi et al. also reported that none of their 13 deaths was caused by uncontrolled bleeding, whereas malignancy, pneumonia, and sepsis were common causes of death [11]. Therefore, it should be noted that underlying diseases, rather than massive bleeding, are the predominant cause of death in patients with AHRU [21–22].

In our multi-center retrospective cohort, we found a similar trend. Malignancy, sepsis, and pneumonia accounted for 64% of deaths and hemorrhagic shock for 12%. Previous studies of patients with LGIB confirmed advanced age, comorbidities, poor general condition, coagulopathy, and hypovolemia to be closely associated with high mortality [14, 15]. In a recent study of 8,254 patients with acute hematochezia, Tominaga et al. reported that factors related to general condition and underlying diseases were associated with 30-day mortality in patients with acute hematochezia [16]. Our findings confirmed that those two risk factors are significant in patients with AHRU. Also, SI is a simple index for hemodynamic instability, which has been readily applied to patients with acute LGIB [17, 18, 23, 24].

Since SI is an indicator of the blood loss together with the instability to altered hemodynamics [18, 25], the significance of SI in our AHRU seems to be a reasonable observation.

Takahashi et al.[11] reported that malignancy was the most common cause of death in patients with AHRU. In another study by Tominaga et al.[16], malignant tumor with distant metastasis was found to be a predictor of 30-day mortality in patients with acute hematochezia. Advanced or disseminated malignancy contributes to poor general condition, malnutrition, and systemic inflammation, all of which are closely associated with poor prognosis [16, 26].

Systemic steroid use was found to be another risk factor for mortality in patients with AHRU. In general, systemic steroids impair wound healing and increase the risk of infection. In addition, steroid is used in patients with impaired underlying conditions. These may partly explain the contribution of steroid to poor prognosis in AHRU. However, there are controversial reports on the effect of steroids on prognosis in patients with AHRU [9–11].

There have been reported several risk scores, which are presumed to be available for acute gastrointestinal bleeding. However, the populations and the endpoints are different from one score to another. Earlier LGIB scores were scheduled to predict the volume of bleeding [23, 24]. Another score referred to as Oakland score was developed for identifying patients who would be discharged in fair to good conditions [27]. There are other scores, which predict mortality in patients with gastrointestinal bleeding [28–31]. An index recently proposed by Tominaga et al. comprises six factors including laboratory test results [16] and has an excellent prognostic value in patients with LGIB.

We developed a scoring system for patients with AHRU, which specifically predicts 30-day mortality. Because the system comprises three binary factors available at the onset of AHRU, it does not require calculation of laboratory test results. According to the system, the mortality increased from 2.4% at score 0 to 11.1% at score 1 and up to 45.5% at score 2 or 3. The apparent and the bootstrap-corrected AUCs for predicting mortality were 0.80 and 0.79, respectively, suggesting little optimism in discrimination. Consequently, the scoring system provided a simple way to identify patients at a high risk of early mortality. The results seem to suggest a potential of the scoring system as a simple way to stratify patients with AHRU.

This study has several limitations. First, the retrospective nature of the study introduced selection bias, especially regarding the management of the patients, across participating institutions. Second, the sample size was not substantial, particularly in the poor prognosis of only 25 patients. The small number of events seems to have caused model instability and wide confidence intervals, even with the reduction in the risk of overfitting. Third, the score was developed and internally validated in the same cohort. The confidence intervals for the calibration slope and intercept were wide, while calibration showed no clear evidence of major miscalibration. Fourth, detailed information regarding two major risk factors, such as cancer stage, steroid dose and duration was not systematically collected.

Conclusions

Our multi-center, retrospective cohort study revealed SI ≥ 1, invasive malignancy, and systemic steroid use to be independently associated with 30-day mortality in patients with AHRU. A simple scoring system comprising the three factors could stratify patients according to mortality risk with moderate discrimination power. The performance of the scoring system should be validated in other populations.

Declarations

Acknowledgments:

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Author contributions

Makoto Eizuka and Yosuke Toya contributed to the study design, data collection, data analysis, and writing of the manuscript. Hibiki Kamata, Takao Fujiwara, Takahiro Gonai, Takeshi Abe, Kenji Nakagawa, Keika Kato, Shun Yamada, Nozomu Saito, and Mizuki Komai contributed to data collection. Takayuki Matsumoto supervised the study and the writing of the manuscript. All authors read and approved the final manuscript.

Ethics approval:

The study protocol was approved by the Institutional Review Board of Iwate Medical University (MH2025-036) and each participating institution.

Consent to participate:

Informed consent for study enrollment was obtained through an opt-out procedure on the website of each participating institution.

Funding

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Competing interests

The authors declare no conflicts of interest related to this study.

Data availability

The datasets generated and analyzed during the current study are not publicly available because of ethical and privacy restrictions but may be available from the corresponding author on reasonable request and with appropriate institutional approval.

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Figures

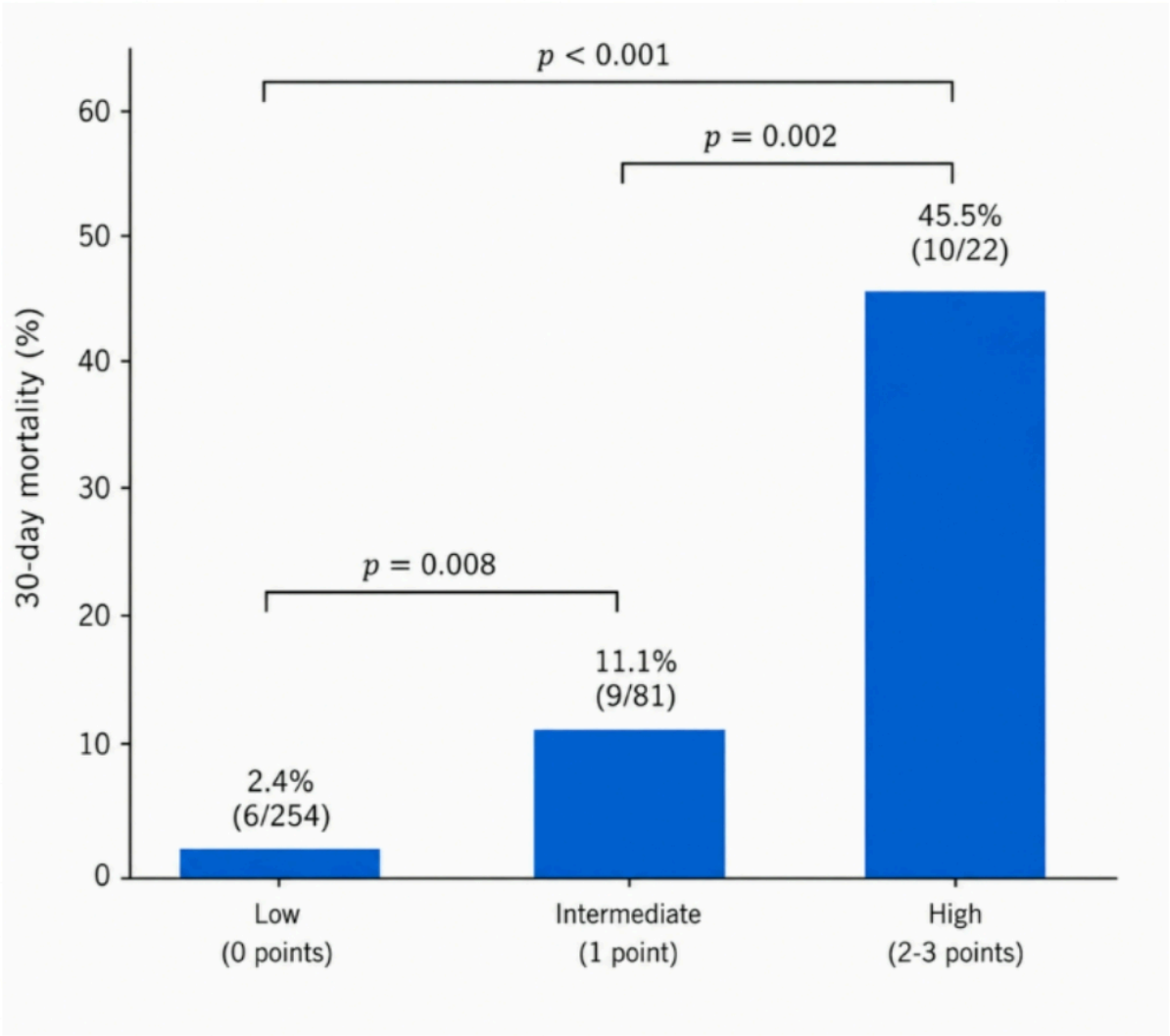


Figure 1

Thirty-day mortality according to the AHRU mortality risk groups. Patients were classified as low risk (0 points), intermediate risk (1 point), or high risk (2-3 points)

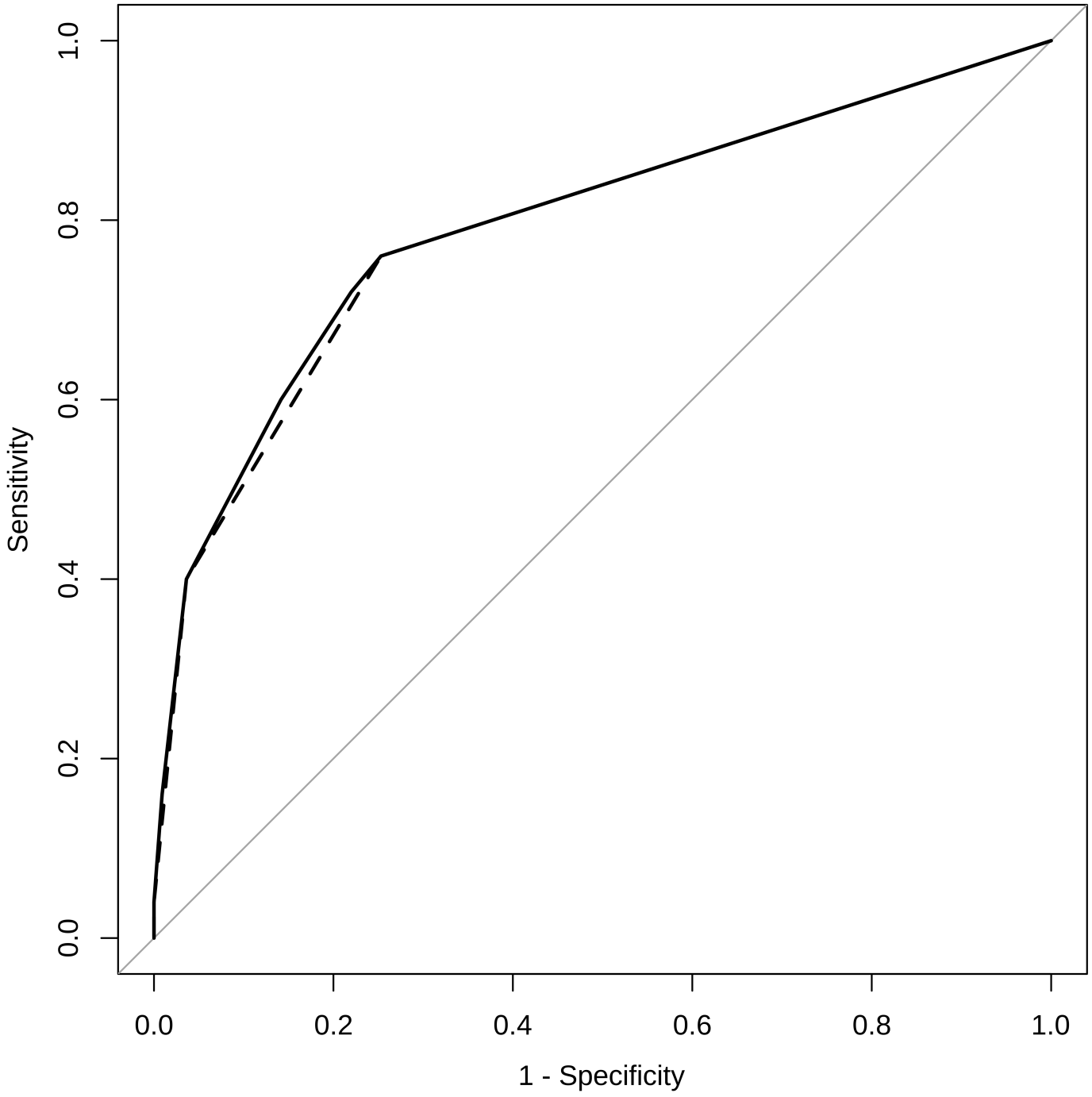


Figure 2

Receiver operating characteristic curves of the AHRU 30-day mortality risk score. The solid line represents the apparent performance, and the dashed line represents the bootstrap-corrected performance