Research Square

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Risk Prediction of Failure of the First Planned Weaning Attempt After Hepatectomy: A Cohort Study Using Firth-Penalized Logistic Regression

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Research Article

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Abstract

Background

To develop and internally validate a parsimonious model for predicting failure of the first planned weaning attempt after hepatectomy.

Methods

We included consecutive patients who underwent a first planned weaning attempt after hepatectomy. The primary outcome was reintubation within 48 h after planned extubation. Candidate predictors were limited to variables available before or at the time of weaning. Firth-penalized logistic regression was used to address the low event rate. All subsets of candidate predictors were compared, and the final model was selected according to optimism-corrected area under the receiver-operating-characteristic curve (AUC) from 500 bootstrap resamples. Discrimination, calibration, and sensitivity analyses were evaluated. Model reporting followed the TRIPOD framework.

Results

Of 416 patients included in the final cohort, 21 (5.0%) experienced weaning failure. The final model was fitted in 414 patients and included the PaO_2/FiO_2 (P/F) ratio at weaning, atelectasis, and hypertension. For each 50-mmHg decrease in the P/F ratio, the odds of weaning failure increased by approximately 1.56-fold. Atelectasis was associated with a higher risk of failure. The apparent AUC was 0.824 (bootstrap 95% CI, 0.74 to 0.93), the optimism-corrected AUC was 0.804, and the optimism-corrected calibration slope was 0.949. Conventional logistic regression and multiple-imputation analyses showed consistent directions of association.

Conclusions

A three-variable model comprising oxygenation status at weaning, atelectasis, and hypertension may provide individualized risk estimates for failure of the first planned weaning attempt after hepatectomy. External validation in independent, multicenter cohorts is required before use in clinical decision support.

Background

Hepatectomy is a major treatment for primary and metastatic liver malignancies[1, 2]. Postoperative pulmonary complications remain an important source of morbidity and mortality after this procedure[3]. Because the liver is adjacent to the diaphragm, surgical traction, diaphragmatic dysfunction, and changes in intra-abdominal pressure can compromise postoperative respiratory mechanics[4]. Patients undergoing

hepatectomy may therefore be vulnerable to pulmonary complications and failure to wean from mechanical ventilation.

Weaning failure is commonly defined as an unsuccessful spontaneous breathing trial or the need to re-establish invasive ventilatory support because of respiratory distress, hemodynamic instability, or inadequate airway protection after planned extubation[5]. This event prolongs intensive care unit (ICU) and hospital stays and is associated with worse outcomes. In high-risk surgical populations, clinical judgment alone may not reliably identify patients at risk of reintubation[6, 7].

Oxygenation is central to weaning assessment. The P/F ratio integrates arterial oxygen tension and inspired oxygen fraction and is widely used to quantify impaired gas exchange[8]. Atelectasis is also common after hepatectomy and may restrict ventilation and increase the work of breathing. In addition, comorbid conditions, including hypertension, cirrhosis, malnutrition, and sarcopenia, may reduce perioperative physiological reserve[9, 10].

Most prediction models for weaning failure have been developed in general ICU or cardiac-surgery populations[11, 12]. A model tailored to the first planned weaning attempt after hepatectomy, using predictors available at the bedside and accounting for a low event rate, remains needed. We therefore developed a multivariable model to predict first planned weaning failure after hepatectomy and internally validated its performance using bootstrap resampling.

Methods

Study design and participants

This retrospective cohort study used convenience sampling to identify patients admitted to the ICU of Peking University People's Hospital after hepatectomy between January 2014 and November 2023. Eligibility criteria were age > 18 years, ICU admission after hepatectomy, and an Acute Physiology and Chronic Health Evaluation II (APACHE II) score > 10. We excluded patients with incomplete records, perioperative cardiorespiratory arrest or other acute catastrophic events, and pre-existing pulmonary disease, including pulmonary infection or chronic obstructive pulmonary disease. The institutional ethics committee approved the study (2021PHB024-001). The patient-selection process is shown in Fig. 1.

Outcome definition

Extubation failure was defined as the need for reintubation for any clinical reason within 48 h after planned extubation. The 48-h window was selected to focus on events related to the first weaning attempt[5].

Candidate predictors and data processing

Electronic medical records were reviewed to obtain demographic characteristics, body mass index, smoking history, comorbidities, previous liver surgery, and preoperative laboratory results. Intraoperative

variables included American Society of Anesthesiologists physical status, open surgery, concomitant procedures, microwave ablation, blood-product transfusion, and operative duration. Postoperative variables available before weaning included APACHE II score at ICU admission, postoperative transfusion, vasoactive-drug use, atelectasis before weaning, and measurements at weaning, including temperature, heart rate, mean arterial pressure, pH, arterial carbon dioxide tension, P/F ratio, lactate, rapid shallow breathing index, and cardiac troponin I.

The P/F ratio was calculated as PaO_2/FiO_2. The ROX index was calculated from SpO_2, back-calculated FiO_2, and respiratory rate at weaning. One P/F value of 3.5 mmHg was considered a data-entry error and excluded. Thirty-nine missing P/F values that had previously been replaced by the cohort mean were not included in the complete-case primary analysis.

Statistical analysis and model development

Analyses were performed using Stata 18.0 (StataCorp LLC). Continuous variables were assessed for normality with the Shapiro-Wilk test and are summarized as mean ± standard deviation or median (interquartile range), as appropriate. Between-group comparisons used t tests or analysis of variance for normally distributed variables and Mann-Whitney U or Kruskal-Wallis tests for non-normally distributed variables.

Univariable Firth-penalized logistic regression was performed for candidate variables available before or at weaning. Firth penalization reduces bias in maximum-likelihood estimates under small-sample and sparse-event conditions. Candidate predictors were restricted to variables that differed between groups and were available before outcome occurrence. ICU length of stay was excluded because it was measured after the weaning outcome. PaO_2 and the P/F ratio were not entered simultaneously because of substantial collinearity. All nonempty subsets of candidate predictors were fitted, and the final model was selected using the highest optimism-corrected AUC from 500 bootstrap resamples. We report apparent AUC, bootstrap confidence intervals, Brier score, calibration intercept, and calibration slope. Sensitivity analyses used conventional logistic regression, multiple imputation, and composite blood-pressure variables. All tests were two-sided, with $P < 0.05$ considered statistically significant.

Results

Patient selection and baseline characteristics

Among 456 consecutive patients who underwent a first planned weaning attempt after hepatectomy, 40 were excluded during data quality control. One patient had an implausible P/F ratio of 3.5 mmHg, and 39 patients had missing P/F values that had previously been replaced by the cohort mean of 389.80 mmHg. To retain an outcome event, one patient with weaning failure and a mean-imputed P/F value was retained. The final cohort included 416 patients, of whom 21 (5.0%) experienced weaning failure within 48 h.

Because hypertension status was missing for two patients, both of whom had successful weaning, the multivariable model was fitted in 414 patients with 21 events.

Compared with patients with successful weaning, those with weaning failure had lower P/F ratios at weaning (median, 227.0 [IQR, 202.5 to 305.0] vs 410.0 [317.5 to 480.0] mmHg; P < 0.001) and lower PaO_2 values (97.6 [84.3 to 122.0] vs 165.3 [127.0 to 192.0] mmHg; P < 0.001). Atelectasis and hypertension were more frequent in the failure group. ICU stay was also longer in this group. The rate of weaning failure was 9.0% (12/133) among patients with hypertension and 3.2% (9/281) among those without hypertension.

Table 1
Selected baseline characteristics of the weaning-failure and weaning-success groups

Characteristic	Weaning failure (n = 21)	Weaning success (n = 395)	P value
Age, years	63.0 (54.0 to 72.0)	61.0 (52.0 to 68.0)	0.419
Male sex	15/21 (71.4%)	264/395 (66.8%)	0.813
Body mass index, kg/m^2	25.4 (22.4 to 28.3)	24.2 (22.1 to 26.5)	0.793
Hypertension	12/21 (57.1%)	121/393 (30.8%)	0.016
Diabetes mellitus	8/21 (38.1%)	77/395 (19.5%)	0.051
P/F ratio at weaning, mmHg	227.0 (202.5 to 305.0)	410.0 (317.5 to 480.0)	< 0.001
PaO_2 at weaning, mmHg	97.6 (84.3 to 122.0)	165.3 (127.0 to 192.0)	< 0.001
Respiratory rate at weaning, breaths/min	20.0 (17.0 to 21.0)	17.0 (15.0 to 20.0)	0.002
Atelectasis	11/21 (52.4%)	82/395 (20.8%)	< 0.001

Data are median (interquartile range) or n/N (%).

Univariable analyses

Univariable Firth-penalized logistic regression was performed for variables that differed between groups and were available before or at weaning, together with exploratory circulatory and oxygenation measures. The P/F ratio showed the highest discrimination among oxygenation measures, with an optimism-corrected AUC of 0.791, followed by PaO_2 (0.779) and the ROX index (0.661). Atelectasis and hypertension were each associated with weaning failure, although their individual discrimination was limited.

Table 2
Univariable Firth logistic regression analyses of candidate predictors

Variable	N	OR (95% CI)	P value	Optimism-corrected AUC
P/F ratio at weaning, per 1 mmHg	416	0.989 (0.985 to 0.994)	< 0.001	0.791
PaO_2 at weaning, per 1 mmHg	416	0.975 (0.963 to 0.987)	< 0.001	0.779
ROX index, per 1 point	414	0.826 (0.716 to 0.953)	0.009	0.661
Atelectasis, yes vs no	416	4.162 (1.737 to 9.975)	0.001	0.659
Hypertension, yes vs no	414	2.951 (1.233 to 7.062)	0.015	0.629
Postoperative hypotension, yes vs no	416	2.935 (1.113 to 7.742)	0.030	0.576

For clinical interpretation, a 50-mmHg decrease in the P/F ratio corresponded to an approximately 1.70-fold increase in the odds of weaning failure in the univariable analysis. The ROX index was calculated using SpO_2, back-calculated FiO_2, and respiratory rate after excluding two implausible values.

Predictor selection

Candidate predictors were restricted to variables with significant between-group differences that were available before or at weaning. ICU length of stay was excluded to prevent outcome leakage. PaO_2 at weaning and the P/F ratio were strongly correlated (Pearson r = 0.950) and were not included in the same model. All 15 nonempty subsets of P/F ratio, PaO_2, atelectasis, and hypertension were fitted with Firth regression and ranked by optimism-corrected AUC. The combination of P/F ratio, atelectasis, and hypertension had the highest optimism-corrected AUC (0.804) and was selected as the final model.

Final multivariable model

Table 3
Final Firth logistic regression model for weaning failure (N = 414; 21 events)

Predictor	β	SE	OR (95% CI)	P value
Intercept	−0.5224	0.8531	Not applicable	0.540
P/F ratio at weaning, per 1 mmHg	−0.0089	0.0024	0.991 (0.986 to 0.996)	< 0.001
Atelectasis, yes vs no	1.0050	0.4681	2.732 (1.092 to 6.838)	0.032
Hypertension, yes vs no	0.6842	0.4641	1.982 (0.798 to 4.923)	0.140

The individual predicted risk was calculated as follows:

$$\text{logit}\,(P) = -0.5224 - 0.0089 \times \text{P/F\:ratio} + 1.0050 \times \text{atelectasis} + 0.6842 \times \text{hypertension}$$

1

Atelectasis and hypertension were coded as 1 for yes and 0 for no. Each 50-mmHg decrease in the P/F ratio was associated with an approximately 1.56-fold increase in the odds of weaning failure. Although hypertension was not statistically significant in the multivariable model, it was retained because of its univariable association and incremental discrimination: the optimism-corrected AUC was 0.804 for the three-variable model and 0.797 for the model containing only P/F ratio and atelectasis.

Model performance

Table 4
Apparent and optimism-corrected performance of the final model

Metric	Apparent	Optimism-corrected
AUC	0.824 (bootstrap 95% CI, 0.74 to 0.93; 2,000 resamples)	0.804
Brier score	0.043	0.045
Calibration slope	1.034	0.949
Calibration intercept	−0.005	−0.152

The optimism-corrected calibration slope of 0.949 suggested limited overfitting, which was consistent with use of Firth penalization at an events-per-variable ratio of 7.0.

Sensitivity analyses

Conventional, non-penalized logistic regression in the same 414 patients yielded similar estimates: P/F ratio, OR 0.991 (95% CI, 0.986 to 0.996); atelectasis, OR 2.764 (95% CI, 1.072 to 7.131); hypertension, OR 2.027 (95% CI, 0.791 to 5.193); and AUC, 0.824.

Multiple imputation in 455 patients with 25 events, using 20 imputed datasets and predictive mean matching after exclusion of the single data-entry error, produced consistent associations: P/F ratio, OR 0.990 (95% CI, 0.985 to 0.995); atelectasis, OR 3.01 (95% CI, 1.27 to 7.15); hypertension, OR 1.74 (95% CI, 0.74 to 4.11); and mean AUC, 0.838 (range, 0.797 to 0.861).

Post hoc composite blood-pressure variables, defined by preoperative hypertension combined with intraoperative or perioperative hypotension, did not improve discrimination. Their optimism-corrected AUCs were 0.793 and 0.797, respectively, compared with 0.804 for hypertension alone. These findings support retention of the simpler comorbidity indicator.

Discussion

In this cohort of patients undergoing a first planned weaning attempt after hepatectomy, we developed and internally validated a three-variable prediction model comprising P/F ratio at weaning, atelectasis, and hypertension. The model demonstrated acceptable discrimination after optimism correction (AUC, 0.804) and favorable calibration (slope, 0.949), providing a quantitative approach to peri-weaning risk stratification.

The P/F ratio was the strongest predictor in the final model. By accounting for inspired oxygen concentration, the P/F ratio characterizes gas-exchange efficiency and oxygenation reserve more directly than PaO_2 alone[8, 13]. In this cohort, each 50-mmHg decrease in P/F ratio was associated with a 1.56-fold increase in the odds of weaning failure. The P/F ratio also discriminated better than PaO_2 and the ROX index. In the early postoperative period after hepatectomy, pain and elevated intra-abdominal pressure may increase respiratory rate and influence the ROX index independently of pulmonary gas exchange, which may partly explain its lower performance[14].

Atelectasis was independently associated with weaning failure[15]. Upper-abdominal incisions and restricted diaphragmatic movement after hepatectomy can promote dependent atelectasis, reduce effective lung volume, impair ventilation-perfusion matching, and increase the work of breathing[16]. Incorporating atelectasis alongside the P/F ratio may therefore capture both functional impairment and structural pulmonary abnormality at the bedside.

Hypertension did not reach conventional statistical significance in the multivariable model; however, it increased model discrimination and remained clinically plausible as a marker of limited cardiovascular reserve, chronic vascular disease, or impaired left-ventricular diastolic function[17]. With only 21 events, variable selection should incorporate predictive contribution, clinical availability, and biological plausibility rather than rely solely on the P value of an individual coefficient[18].

Firth penalization was se lected because the number of weaning-failure events was small[19]. The modest difference between apparent and optimism-corrected performance, together with the consistency of conventional logistic regression and multiple-imputation analyses, supports the stability of the principal associations[6]. Nevertheless, the model should be interpreted as an internally validated exploratory tool rather than a basis for fixed clinical action thresholds.

This study has several limitations. First, its single-center retrospective design may limit generalizability because patient mix, perioperative management, and extubation practices vary across institutions. Second, the limited number of outcome events leaves uncertainty around effect estimates despite penalized regression and bootstrap validation. Third, ascertainment of atelectasis and some perioperative variables relied on existing clinical records and requires standardized definitions in future work. Fourth, model performance was not assessed across the extent of hepatectomy, analgesic strategies, noninvasive respiratory support, or relevant clinical subgroups. Finally, only internal validation was performed. Multicenter prospective external validation and impact studies are needed to determine whether model-guided management improves reintubation rates, ICU stay, and decision making.

Conclusions

The P/F ratio at weaning, atelectasis, and hypertension may jointly estimate the risk of failure of the first planned weaning attempt after hepatectomy. This three-variable Firth logistic regression model showed acceptable internally validated discrimination and calibration and may support peri-weaning risk stratification. Independent external validation and clinically actionable risk thresholds are required before clinical implementation.

Abbreviations

APACHE II
Acute Physiology and Chronic Health Evaluation II
AUC
area under the receiver-operating-characteristic curve
BMI
body mass index
CI
confidence interval
FiO2
fraction of inspired oxygen
ICU
intensive care unit
IQR
interquartile range
OR
odds ratio
PaO2
arterial oxygen tension
P/F ratio
ratio of partial pressure of arterial oxygen to fraction of inspired oxygen
ROX index
ratio of oxygen saturation (SpO2) to respiratory rate
SD
standard deviation
TRIPOD
Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis

Declarations

Ethics approval and consent to participate

The institutional ethics committee approved this study (2021PHB024-001) and waived informed consent because of the retrospective design.

Consent for publication

Written informed consent for publication was waived by the institutional ethics committee because this retrospective observational study used only de-identified routine clinical data without identifiable personal information.

Competing interests

The authors declare no competing interests.

Authors' information

Not applicable.

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Author Contribution

ZJJ conceived and designed the study; ZY and LPY performed the statistical analysis and interpreted the results; WY drafted and revised the manuscript. All authors read and approved the final manuscript.

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Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because they contain protected health information, but a de-identified dataset may be available from the corresponding author on reasonable request and subject to institutional approval.

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Figures

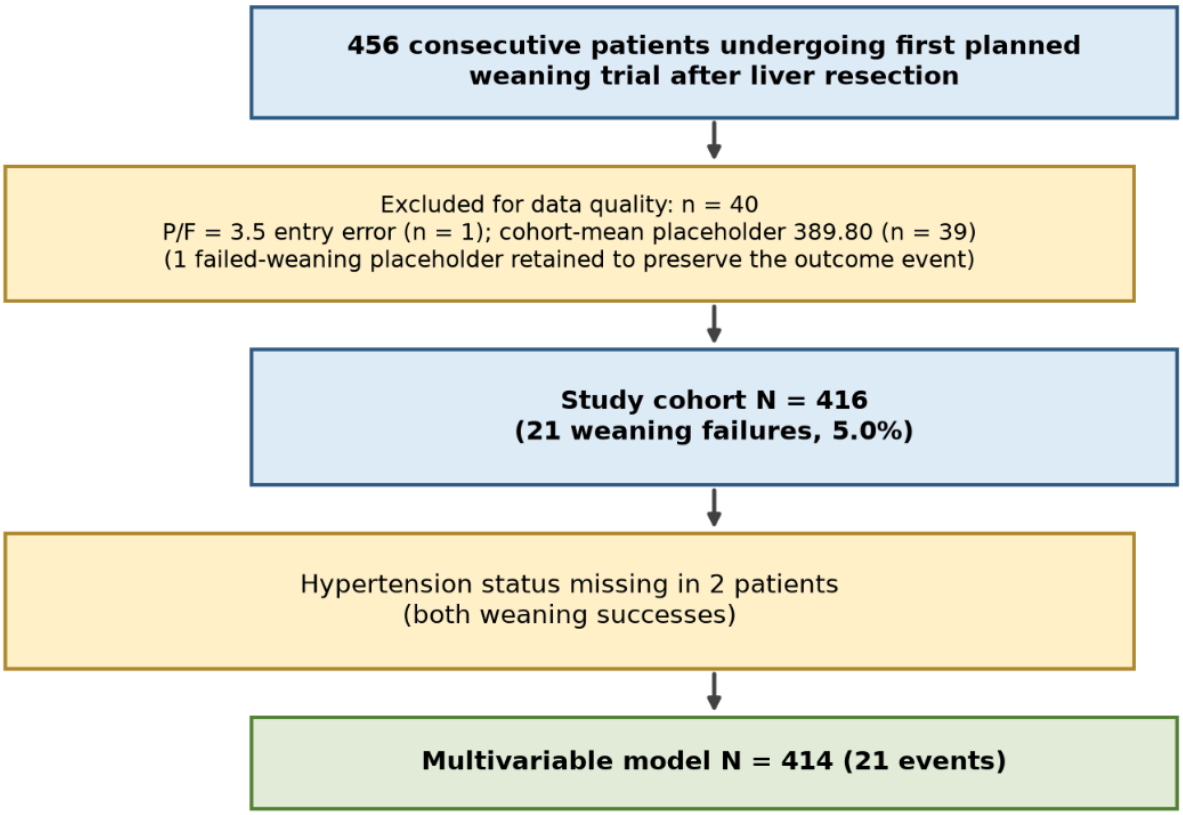

Figure 1

Patient flow diagram.

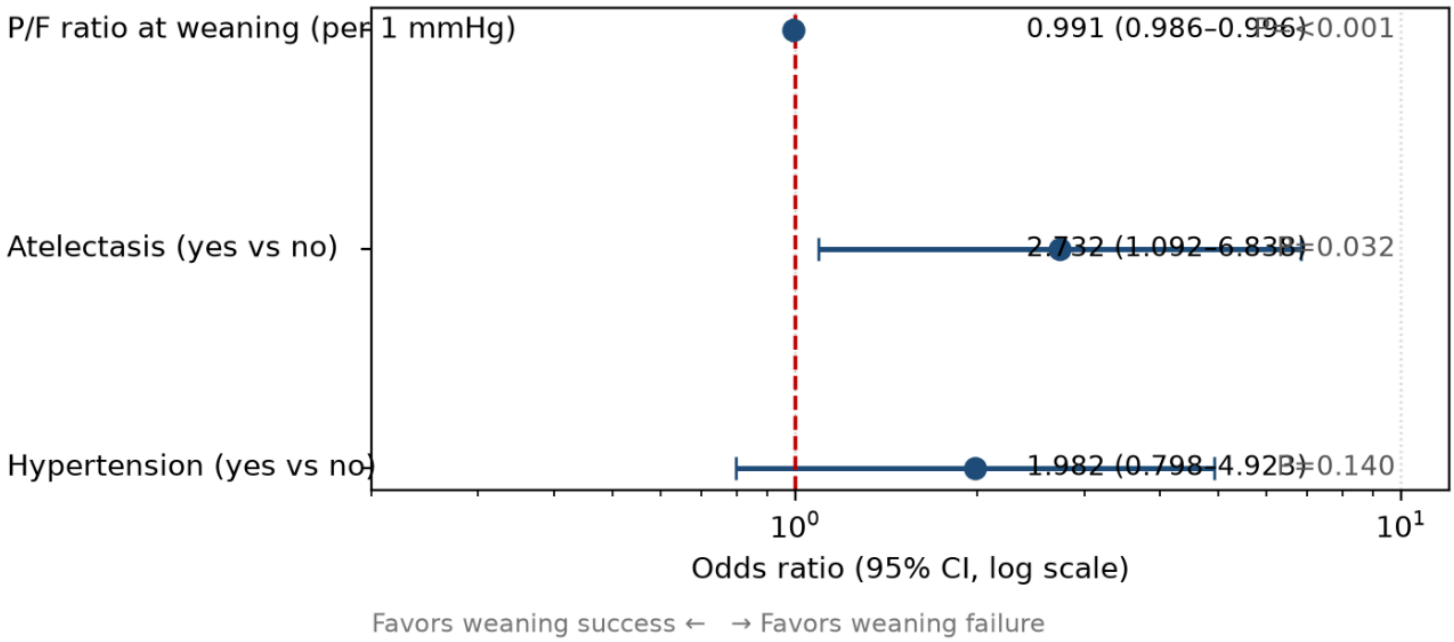

Figure 2

Effect estimates, expressed as odds ratios and 95% confidence intervals on a logarithmic scale, for the final multivariable model.

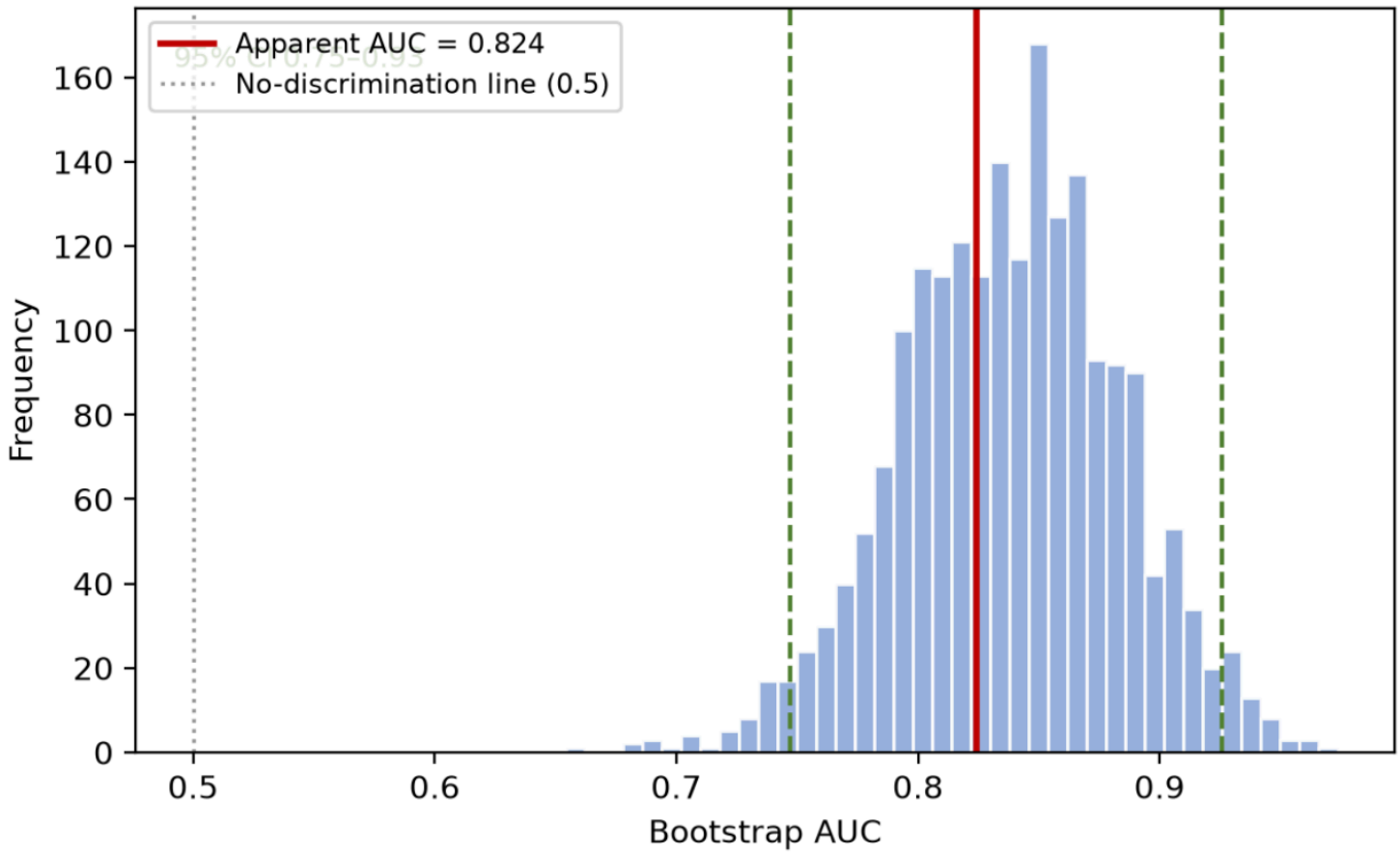

Figure 3

Distribution of apparent AUC values across 2,000 bootstrap resamples of the final model.

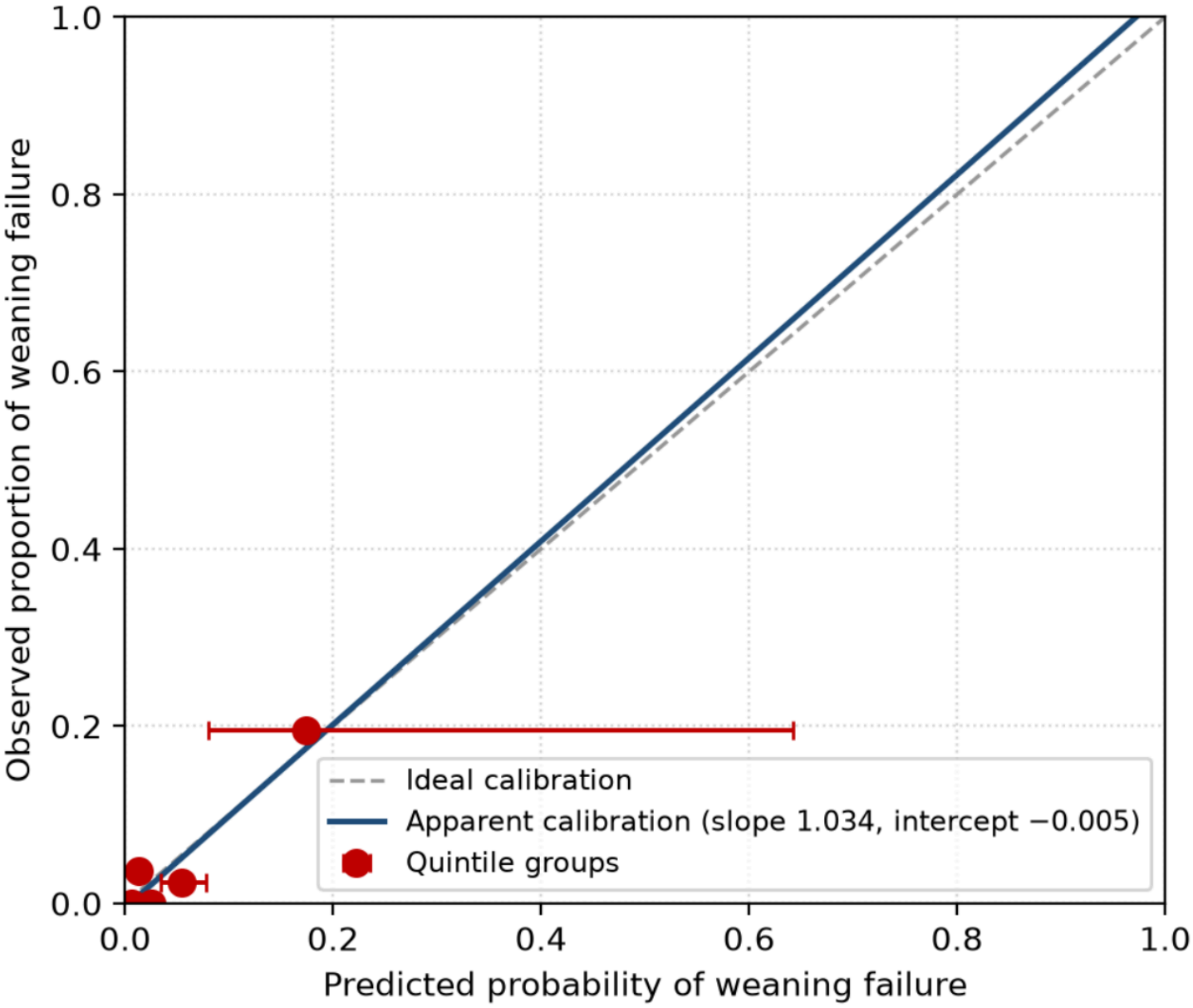

Figure 4

Calibration curve for the final model based on quintile groups (N = 414).