

ORIGINAL ARTICLE

Risk model for predicting failure to rescue after hepatectomy: Cohort study of 1371 consecutive patients

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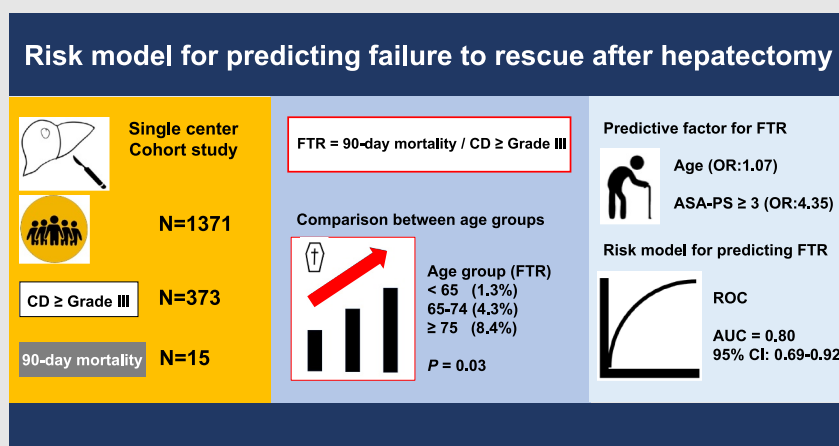
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Graphical Abstract



This study investigated the association between age and failure to rescue (FTR) and develop a risk model for FTR following hepatectomy. Our risk model including age and American Society of Anesthesiologists Physical Status can be clinically relevant and useful for predicting FTR after hepatectomy.

Abstract

Aim: Although hepatectomy is a complex surgical procedure, its incidence among older patients has increased due to global aging. However, few studies have focused on the association between age and failure to rescue (FTR) posthepatectomy. This study aimed to investigate the association between age and FTR and develop a risk model for FTR following hepatectomy.

Methods: We analyzed a total of 1371 consecutive patients who underwent primary hepatectomy between July 2003 and September 2022. The patients were divided into three groups according to their age: young-old (<65 years), pre-old

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; AUC, area under the curve; CDc, Clavien-Dindo classification; CI, confidence interval; C-index, concordance index; FTR, failure to rescue; IQR, interquartile range; OR, odds ratio; ROC, receiver operating characteristic; SSI, surgical site infection.

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(65–74 years), and old group (≥ 75 years). Additionally, the associations among age, FTR, and risk factors for FTR were investigated. Subsequently, a risk model was developed to predict the FTR.

Results: Of the 1371 patients, 373 (27.2%) experienced major complications, and FTR occurred in 15 patients. The older group showed a higher FTR rate (8.4%) than the young-old (1.3%) and pre-old (4.3%) groups ($p = 0.03$). Multivariate analyses indicated that older age (odds ratio [OR] 1.07; 95% confidence interval [CI] 1.00–1.15; $p = 0.045$) and American Society of Anesthesiologists Physical Status score ≥ 3 (OR 4.35; 95% CI 1.24–15.2; $p = 0.02$) were independent predictive factors for FTR. The risk model exhibited an accuracy with an area under the curve of 0.80 (95% CI 0.69–0.92). Calibration plots of the model revealed a concordance index of 0.73.

Conclusions: This study identified an association between age, FTR, and risk factors for FTR posthepatectomy. Together, our risk model is a clinically relevant, internally validated, and useful tool for predicting FTR posthepatectomy.

KEYWORDS

age, failure to rescue, hepatectomy, older adults

INTRODUCTION

The incidence of hepatectomies in older patients has increased due to global aging.¹ As hepatectomy is a complex surgery, its morbidity and mortality rates remain high.² Although we previously reported the feasibility of complex hepatopancreatobiliary surgery in older patients,³ a comprehensive surgical strategy is crucial for older patients undergoing hepatectomy. Currently, attention is focused on managing postoperative complications rather than simply preventing them.

Failure to rescue, defined as the failure to save patients with severe complications, is a quality indicator for managing postoperative complications.^{4,5} It is commonly used to evaluate the effect of hospital volume on patient outcomes.⁶ The significance of FTR following hepatectomy has been previously reported.⁷ Several risk factors for FTR posthepatectomy have been examined, including patient demographics and the effect of hospital volume.^{8–10} However, few studies have focused on the association between age and FTR after hepatectomy. Furthermore, a risk model for predicting FTR after hepatectomy has not yet been established.

This study investigated the association between age and FTR as well as the risk factors for FTR after hepatectomy. Our objective was to develop a risk model for FTR in patients who have undergone hepatectomy.

METHODS

Patients and study design

This retrospective study used a database of 1593 consecutive patients who underwent hepatectomy at our institution between July

2003 and September 2022. Patients who underwent repeat hepatectomy were excluded considering the different surgical risks associated with the severity of adhesions.¹¹ The study was approved by the Ethics Committee of our institution (approval no. 2406–031) and was carried out in accordance with the Declaration of Helsinki. Due to the retrospective nature of this study, informed consent was not required. The study protocol is registered in the UMIN Clinical Trial Registry (UMIN000054484).

Clinical data

The following demographic and clinical data were extracted from our database, including: age; sex; body mass index; ASA-PS¹²; comorbidities such as chronic hepatitis/liver cirrhosis, chronic obstructive pulmonary disease, hypertension, chronic heart failure, cerebrovascular disease, chronic kidney disease, and diabetes; preoperative laboratory tests; liver function according to the Child–Pugh classification; primary liver disease including hepatocellular carcinoma, intrahepatic cholangiocarcinoma, metastatic liver cancer, and others; tumor size; tumor number (solitary or multiple); operative factors; and postoperative outcomes. Patients were divided into three groups according to their ages, including the young-old (<65 years), pre-old (65–74 years), and old group (≥ 75 years).¹³

The operative factors included the surgical approach (open or minimally invasive surgery), type of hepatectomy, operative time, estimated blood loss, blood transfusion, extrahepatic bile duct resection, vascular reconstruction, lymph node dissection, number of liver resection sites (single or multiple), and resection of other organs.

Postoperative outcomes that were evaluated included: a comprehensive complication index¹⁴; complications such as incisional

or organ/space SSI, bile leakage, cholangitis, posthepatectomy liver failure, hemorrhage, sepsis, respiratory complications, cardiac complications, ascites, and others; 30- and 90-day mortality rates; and the length of hospital stay. Postoperative complications were classified and defined according to the CDc $\geq$ II.¹⁵ Complications with CDc $\geq$ III were considered major complications. Bile leakage and posthepatectomy liver failures were evaluated according to the International Study Group of Liver Surgery criteria.^{16,17} Cardiac complications included arrhythmia, heart failure, and ischemic heart disease. Respiratory complications included pneumonia, atelectasis, and pleural effusion.

Objective

The primary objective of this study was to develop a risk model for predicting FTR after hepatectomy. Secondary objectives included determining the incidence of FTR, defined as 90-day mortality in patients with at least one major complication postsurgery, and the risk factors associated with FTR.

Statistical analysis

Initially, patient characteristics and perioperative outcomes stratified by age were assessed in all patients as well as in those with major complications. Following the investigation of FTR, the risk factors for FTR incidence were investigated. Univariate and multivariate analyses were undertaken using a logistic regression model to identify predictive factors for FTR. In multivariate analyses, variables with $p < 0.05$ in univariate analysis were selected. Odds ratios and 95% CI were determined. A risk model was developed to predict FTR using the results of multivariate analyses and clinical knowledge. The performance of the model was evaluated by measuring the AUC using the ROC curve. Subsequently, internal validity was assessed using the bootstrap method to evaluate the discriminative performance of the model.¹⁸ The calibration curve C-index was used to determine the predictive validity of the model.

Values are presented as proportions for categorical data and as medians with IQRs for continuous variables. Statistical analyses were undertaken using the Mann-Whitney *U*-test for continuous variables and Fisher's exact test for categorical variables. All reported p values were two-tailed, with an alpha level of 0.05 considered statistically significant. All statistical analyses were carried out using EZR software (version 1.65; Saitama Medical Center, Jichi Medical University).

RESULTS

Study cohort

Of the 1593 patients, data from 1371 patients were analyzed after excluding 222 who underwent repeat hepatectomy (Figure 1). The

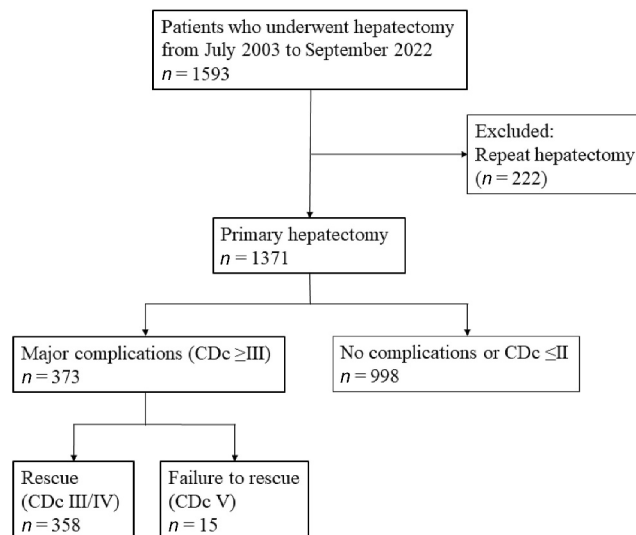


FIGURE 1 Flowchart of the study. CDc, Clavien–Dindo classification.

characteristics of the 1371 patients are summarized in Table 1. There were 920 men (67.1%) and 451 women (32.9%) with a median age of 67.0 (IQR, 59.0–73.0) years. The primary liver diseases included hepatocellular carcinoma ($n = 631$, 46.0%) and metastatic liver cancer ($n = 345$, 25.2%). The median operative time was 298 min (IQR, 229–380 min), and the estimated blood loss was 410 mL (IQR, 190–900 mL). Regarding postoperative outcomes, the incidence of major complications and 90-day mortality rates were 27.2% ($n = 373$) and 1.1% ($n = 15$), respectively. The primary causes of mortality at 90 days included liver failure ($n = 8$), hemorrhage ($n = 2$), and others ($n = 5$; Table S1).

Perioperative outcomes stratified by age are presented in Table 1. No significant differences, with the exceptions of operative time and other organ resection, were observed across operative factors between the young-old (<65 years, $n = 555$), pre-old (65–74 years, $n = 523$), and old group (≥ 75 years, $n = 293$). Regarding postoperative outcomes, the incidence of complications ($p = 0.20$) and major complications ($p = 0.89$) did not differ significantly between the groups; however, the older group exhibited a higher incidence of 90-day mortality (2.4%).

Failure to rescue following hepatectomy

To investigate the incidence of FTR, the characteristics and outcomes of 373 patients with major complications (CDc ≥ 3) were evaluated; these results are presented in Table 2. Common causes of major complications included bile leakage (33.2%), incisional or organ/space SSI (26.0%), and respiratory complications (20.9%). Of the 373 patients, 15 (4.0%) experienced an FTR. The cumulative incidence of FTR is presented in Figure 2a. Of the 15 FTRs, 12 (80%) occurred between postoperative days 30 and 90.

TABLE 1 Patient characteristics categorized by age.

Variable	Total (n = 1371)	Young-old (<65 years) (n = 555)	Pre-old (65–74 years) (n = 523)	Old (≥75 years) (n = 293)	p value
Age, years	67.0 [59.0, 73.0]	57.0 [50.0, 61.0]	70.0 [67.0, 72.0]	78.0 [76.0, 80.0]	<0.001
Sex	Male	920 (67.1)	349 (66.7)	192 (65.5)	0.697
	Female	451 (32.9)	176 (31.7)	101 (34.5)	–
BMI, kg/m ²	22.8 [20.5, 25.1]	22.8 [20.6, 25.0]	22.8 [20.6, 25.3]	22.6 [20.2, 25.0]	0.415
ASA- PS score	1–2	1204 (87.8)	513 (92.4)	235 (80.2)	<0.001
	3–4	167 (12.2)	42 (7.6)	58 (19.8)	–
Comorbidity	CH/LC	524 (38.2)	211 (38.0)	207 (39.6)	0.628
	COPD	46 (3.4)	8 (1.4)	24 (4.6)	0.003
	Hypertension	220 (16.0)	52 (9.4)	96 (18.4)	<0.001
	Chronic heart failure	29 (2.1)	5 (0.9)	13 (2.5)	0.014
	CVD	29 (2.1)	9 (1.6)	8 (1.5)	0.045
	CKD	33 (2.4)	13 (2.3)	14 (2.7)	0.899
	Diabetes	276 (20.1)	84 (15.1)	121 (23.1)	0.001
		4.0 [3.6, 4.3]	4.0 [3.7, 4.3]	4.0 [3.5, 4.1]	<0.001
Albumin, g/dL	0.6 [0.5, 0.9]	0.7 [0.5, 1.0]	0.7 [0.5, 0.9]	0.6 [0.5, 0.8]	0.023
Total bilirubin, mg/dL	102.0 [93.0, 111.0]	102.0 [93.0, 112.0]	102.0 [93.0, 112.0]	102.0 [94.0, 109.0]	0.729
Prothrombin, %	1310 (95.6)	531 (95.7)	504 (96.4)	275 (93.9)	0.244
Child–Pugh grade	A	61 (4.4)	24 (4.3)	19 (3.6)	–
	B				
Tumor factor	HCC	631 (46.0)	243 (43.8)	238 (45.5)	0.580
	ICC	127 (9.3)	41 (7.4)	53 (10.1)	–
	Metastatic liver cancer	345 (25.2)	156 (28.1)	138 (26.4)	–
	Others	268 (19.5)	115 (20.7)	94 (18.0)	–
		3.0 [2.0, 5.0]	3.0 [1.9, 5.5]	2.8 [2.0, 4.7]	0.516
Tumor size, cm	1021 (75.5)	389 (71.2)	395 (76.7)	237 (81.2)	0.004
Tumor number	332 (24.5)	157 (28.8)	120 (23.3)	55 (18.8)	–
Operative factor	Open	1245 (90.8)	509 (91.7)	467 (89.3)	0.330
	MIS	126 (9.2)	46 (8.3)	56 (10.7)	–
					(Continues)

TABLE 1 (Continued)

Variable	Total (n = 1371)	Young-old (<65 years) (n = 555)	Pre-old (65–74 years) (n = 523)	Old (≥75 years) (n = 293)	p value
Type of hepatectomy					
Partial resection or segmentectomy	422 (30.8)	151 (27.2)	175 (33.5)	96 (32.8)	0.610
Sectionectomy	406 (29.6)	176 (31.7)	152 (29.1)	78 (26.6)	–
Bisectionectomy	501 (36.5)	200 (36.0)	185 (35.4)	116 (39.6)	–
Trisectionectomy	42 (3.1)	28 (5.0)	11 (2.1)	3 (1.0)	–
Operative time, min	298 [229, 380]	300 [235, 387]	299 [234, 384]	284 [212, 370]	0.041
Blood loss, mL	410 [190, 900]	460 [200, 1000]	400 [190, 890]	400 [170, 700]	0.060
Blood transfusion	322 (23.5)	116 (20.9)	127 (24.3)	79 (27.0)	0.122
BDR	144 (10.5)	47 (8.5)	65 (12.4)	32 (10.9)	0.102
Vascular reconstruction	109 (8.0)	46 (8.3)	44 (8.4)	19 (6.5)	0.593
LND	324 (23.6)	130 (23.4)	114 (21.8)	80 (27.3)	0.205
Number of resection sites					
Single	1175 (85.7)	461 (83.1)	456 (87.2)	258 (88.1)	0.070
Multiple	196 (14.3)	94 (16.9)	67 (12.8)	35 (11.9)	–
Other organ resections	133 (9.7)	60 (10.8)	56 (10.7)	17 (5.8)	0.032
Outcomes					
Comprehensive complication index	8.6 [0.0, 26.2]	8.6 [0.0, 26.2]	8.6 [0.0, 26.2]	20.9 [0.0, 26.2]	0.129
Any complications	645 (47.0)	251 (45.2)	243 (46.5)	151 (51.5)	0.204
Major complications	373 (27.2)	149 (26.8)	141 (27.0)	83 (28.3)	0.891
30-day mortality	3 (0.2)	0 (0.0)	3 (0.6)	0 (0.0)	0.117
90-day mortality	15 (1.1)	2 (0.4)	6 (1.1)	7 (2.4)	0.025
LOS, days	18.0 [14.0, 26.0]	18.0 [14.0, 26.0]	17.0 [13.0, 25.5]	18.0 [14.0, 26.0]	0.290

Note: Values are reported as median [interquartile range] or number (percentage).

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; BDR, bile duct resection; BMI, body mass index; CH, chronic hepatitis; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; HCC, hepatocellular carcinoma; ICC, intrahepatic cholangiocarcinoma; LC, liver cirrhosis; LND, lymph node dissection; LOS, length of hospital stay; MIS, minimally invasive surgery.

TABLE 2 Characteristics of patients with major complications categorized by age.

Variable		Total (n = 373)	Young-old (<65 years) (n = 149)	Pre-old (65–74 years) (n = 141)	Old (≥75 years) (n = 83)	p value
Age, years		67.0 [60.0, 74.0]	58.0 [52.0, 61.0]	69.0 [67.0, 72.0]	78.0 [76.0, 80.0]	<0.001
Sex	Male	261 (70.0)	110 (73.8)	101 (71.6)	50 (60.2)	0.088
	Female	112 (30.0)	39 (26.2)	40 (28.4)	33 (39.8)	
BMI, kg/m ²		22.5 [20.4, 25.1]	22.3 [20.2, 24.9]	22.6 [20.3, 24.9]	22.8 [21.0, 25.7]	0.706
ASA- PS score	1–2	327 (87.7)	136 (91.3)	125 (88.7)	66 (79.5)	0.035
	3–4	46 (12.3)	13 (8.7)	16 (11.3)	17 (20.5)	–
Comorbidity	CH/LC	129 (34.6)	53 (35.6)	48 (34.0)	28 (33.7)	0.960
	COPD	9 (2.4)	2 (1.3)	4 (2.8)	3 (3.6)	0.420
	Hypertension	49 (13.1)	10 (6.7)	21 (14.9)	18 (21.7)	0.003
	Chronic heart failure	10 (2.7)	3 (2.0)	6 (4.3)	1 (1.2)	0.389
	CVD	7 (1.9)	5 (3.4)	1 (0.7)	1 (1.2)	0.265
	CKD	13 (3.5)	3 (2.0)	4 (2.8)	6 (7.2)	0.142
	Diabetes	64 (17.2)	21 (14.1)	27 (19.1)	16 (19.3)	0.436
Albumin, g/dL		3.8 [3.5, 4.2]	3.9 [3.5, 4.3]	3.8 [3.5, 4.1]	3.8 [3.5, 4.1]	0.202
Total bilirubin, mg/dL		0.7 [0.5, 1.0]	0.7 [0.4, 1.0]	0.7 [0.5, 1.0]	0.7 [0.5, 0.9]	0.522
Prothrombin, %		102.0 [92.0, 112.2]	102.5 [92.0, 112.2]	98.0 [90.0, 113.0]	104.0 [95.0, 111.0]	0.322
Child–Pugh grade	A	345 (92.5)	139 (93.3)	129 (91.5)	77 (92.8)	0.849
	B	28 (7.5)	10 (6.7)	12 (8.5)	6 (7.2)	–
Tumor factor						
Primary disease	HCC	149 (39.9)	51 (34.2)	59 (41.8)	39 (47.0)	0.220
	ICC	52 (13.9)	21 (14.1)	21 (14.9)	10 (12.0)	–
	Metastatic liver cancer	87 (23.3)	43 (28.9)	32 (22.7)	12 (14.5)	–
	Others	85 (22.8)	34 (22.8)	29 (20.6)	22 (26.5)	–
Tumor size, cm		3.1 [2.1, 5.2]	3.2 [2.0, 6.0]	3.0 [2.0, 5.0]	3.0 [2.2, 4.6]	0.749
Tumor number	Single	265 (72.6)	94 (66.2)	102 (72.9)	69 (83.1)	0.029
	Multiple	100 (27.4)	48 (33.8)	38 (27.1)	14 (16.9)	–
Operative factor						
Surgical approach	Open	365 (97.9)	147 (98.7)	136 (96.5)	82 (98.8)	0.420
	MIS	8 (2.1)	2 (1.3)	5 (3.5)	1 (1.2)	–
Type of hepatectomy	Partial resection or segmentectomy	80 (21.4)	29 (19.5)	38 (27.0)	13 (15.7)	0.100
	Sectionectomy	96 (25.7)	46 (30.9)	28 (19.9)	22 (26.5)	–
	Bisectionectomy	175 (46.9)	62 (41.6)	67 (47.5)	46 (55.4)	–
	Trisectionectomy	22 (5.9)	12 (8.1)	8 (5.7)	2 (2.4)	–
Operative time, min		352 [274, 455]	371 [285, 480]	333 [260, 438]	350 [266, 425]	0.022
Blood loss, mL		630 [310, 1340]	615 [335, 1600]	730 [300, 1265]	490 [285, 1000]	0.099
Blood transfusion		124 (33.2)	46 (30.9)	46 (32.6)	32 (38.6)	0.492

(Continues)

TABLE 2 (Continued)

Variable		Total (n = 373)	Young-old (<65 years) (n = 149)	Pre-old (65–74 years) (n = 141)	Old (≥75 years) (n = 83)	p value
BDR		72 (19.3)	24 (16.1)	31 (22.0)	17 (20.5)	0.411
Vascular reconstruction		52 (13.9)	19 (12.8)	26 (18.4)	7 (8.4)	0.105
LND		126 (33.8)	53 (35.6)	42 (29.8)	31 (37.3)	0.432
Number of resection sites	Single	307 (82.3)	116 (77.9)	117 (83.0)	74 (89.2)	0.095
	Multiple	66 (17.7)	33 (22.1)	24 (17.0)	9 (10.8)	–
Other organ resection		50 (13.4)	17 (11.4)	22 (15.6)	11 (13.3)	0.574
Outcomes						
30-day mortality		3 (0.8)	0 (0.0)	3 (2.1)	0 (0.0)	0.064
90-day mortality		15 (4.0)	2 (1.3)	6 (4.3)	7 (8.4)	0.028
Comprehensive complication index		33.5 [26.2, 37.0]	33.5 [26.2, 37.0]	33.5 [26.2, 39.5]	33.5 [26.2, 39.5]	0.415
Major complications	Incisional SSI	16 (4.3)	4 (2.7)	8 (5.7)	4 (4.8)	0.458
	Organ/space SSI	81 (21.7)	34 (22.8)	31 (22.0)	16 (19.3)	0.850
	Bile leakage	124 (33.2)	55 (36.9)	40 (28.4)	29 (34.9)	0.277
	Cholangitis	2 (0.5)	0 (0.0)	2 (1.4)	0 (0.0)	0.191
	Liver failure	14 (3.8)	3 (2.0)	6 (4.3)	5 (6.0)	0.244
	Hemorrhage	15 (4.0)	6 (4.0)	6 (4.3)	3 (3.6)	1.000
	Sepsis	10 (2.7)	3 (2.0)	4 (2.8)	3 (3.6)	0.719
	Respiratory complications	78 (20.9)	26 (17.4)	32 (22.7)	20 (24.1)	0.3986
	Cardiac complications	10 (2.7)	2 (1.3)	8 (5.7)	0 (0.0)	0.023
	Ascites	61 (16.4)	17 (11.4)	30 (21.3)	14 (16.9)	0.075
	Others	75 (20.1)	28 (18.8)	22 (15.6)	25 (30.1)	0.020
LOS, days		29.0 [21.0, 43.0]	30.0 [22.0, 43.0]	29.0 [21.0, 43.0]	28.0 [20.0, 42.5]	0.910

Note: Values are reported as median [interquartile range] or number (percentage).

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; BDR, bile duct resection; BMI, body mass index; CH, chronic hepatitis; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; HCC, hepatocellular carcinoma; ICC, intrahepatic cholangiocarcinoma; LC, liver cirrhosis; LND, lymph node dissection; LOS, length of hospital stay; MIS, minimally invasive surgery; SSI, surgical site of infection.

When stratified by age, no significant differences were observed between the groups in terms of the patient demographic data. The characteristics and results of patients with major complications stratified by age are presented in Table 2. Details of the other causes of major complications are presented in Table S2. Although all the groups had similar comprehensive complication index ($p = 0.42$) and comparable complication severities ($p = 0.83$; Table S3), the older group exhibited a higher FTR rate (8.4%) than those of the young-old (1.3%) and pre-old (4.3%) groups ($p = 0.03$; Figure 2b).

Predictive factors associated with FTR following hepatectomy

Table 3 presents the results of the univariate and multivariate analyses to identify the perioperative factors associated with FTR. In the multivariate analysis, age (OR 1.07; 95% CI 1.00–1.15; $p = 0.045$) and ASA-PS $\geq$ grade 3 (OR, 4.35; 95% CI 1.24–15.2; $p = 0.02$) were independent factors to predict FTR. However, other factors, including tumor and surgical factors, were not significant.

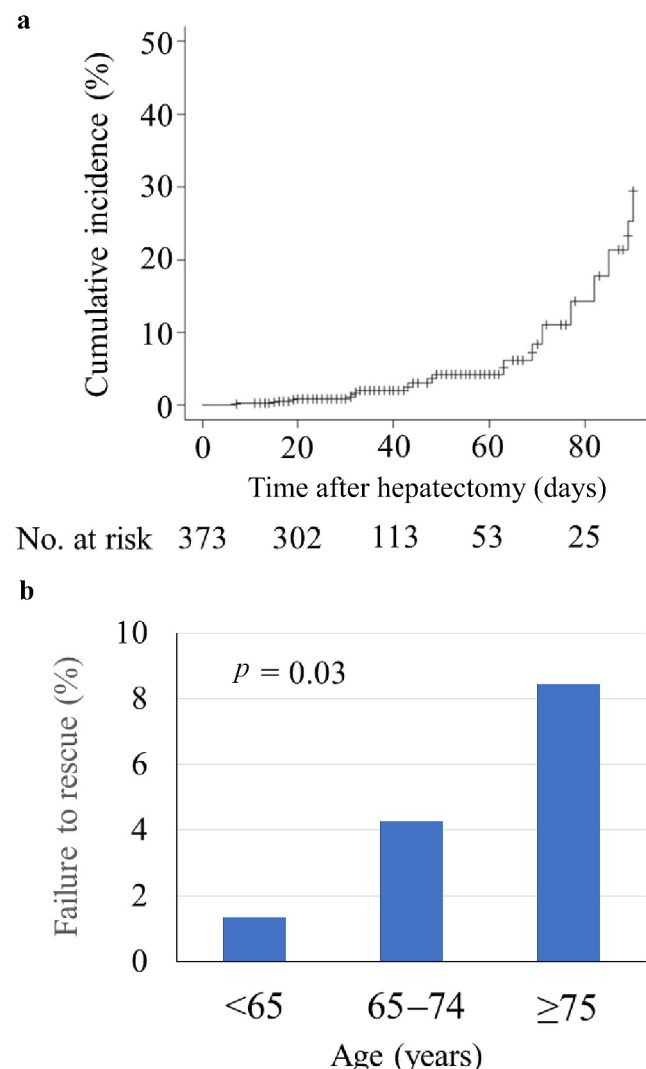


FIGURE 2 (a) Cumulative incidence of failure to rescue (FTR) after hepatectomy. (b) FTR rates stratified by age.

Risk model for predicting FTR following hepatectomy

The predictive probability of the model for FTR was constructed using the results of multivariate analyses as follows (available in Document S1):

$$\begin{aligned} \text{Log } p/(100 - p) = & -9.27191 + 0.06907 \times (\text{Age}) + 1.47004 \\ & \times (\text{ASA-PS} \geq 3) + 1.06836 \times (\text{Albumin} \leq 3) \\ & + 0.01009 \times (\text{Blood transfusion}) + 0.66690 \\ & \times (\text{Operative time} \geq 6 \text{ h}) + 0.96631 \\ & \times (\text{Other organ resection}) + 1.12059 \\ & \times (\text{Vascular reconstruction}) \end{aligned}$$

$$\begin{aligned} \text{EXP} &= \exp[\log p/(100 - p)]p \text{ (predictive probability; \%)} \\ &= [\text{EXP}/(1 + \text{EXP})] \times 100 \end{aligned}$$

The correlation between age and individual risk for FTR, calculated using the risk model, was plotted as a scatter plot (Figure S1). Approximate curves were plotted and stratified using ASA-PS (≤ 2 vs.

≥ 3). The mortality risk was higher in patients with ASA-PS scores ≥ 3 than that of patients with ASA-PS scores ≤ 2 .

Model performance and calibration of the model

Figure 3 indicates the accuracy of the model based on the ROC curve. The AUC was 0.80 (95% CI 0.69–0.92). Calibration plots of the model used to predict the FTR using the bootstrap method are presented in Figure 4. The predicted probability of FTR was highly correlated with the actual probability, particularly in the high-risk group, although it overpredicted the incidence in the lower-risk group. The C-index of the model was 0.73.

DISCUSSION

The present study analyzed the cumulative incidence of FTR and the association between age and FTR in 1371 patients following primary hepatectomy. Most FTRs occurred between postoperative days 30 and 90. Multivariate analyses identified age and the ASA-PS score as independent predictors of FTR. Furthermore, a risk model was developed to predict FTR after hepatectomy, and its performance was confirmed.

In this study, the overall incidence of mortality at 30 and 90 days and the FTR were 0.2%, 1.1%, and 4.0%, respectively. These results are better than those of a nationwide study.^{19,20} Furthermore, our 30- and 90-day mortality rates, stratified by age, were better than the national averages reported in Japan.²¹ These findings may be attributed to our institution being a certified high-volume liver transplant center, performing over 80 hepatectomy procedures annually.^{8,19,22,23} The multidisciplinary approaches to manage specific complications likely contributes to these low incidences of mortality and FTR.

Regarding the effect of age on hepatectomy outcomes, no significant differences were observed in the incidence of major complications between the groups in the overall cohort (Table 1). However, older patients with major complications showed higher FTR rates (Figure 2b). Although older patients were more likely to undergo partial hepatectomy than extended hepatectomy,¹ no significant differences in the surgical factors were detected between the groups in this study. Given that there were no significant differences in demographics among patients with major complications, older patients with major complications may be more susceptible to death. As previously reported,^{9,24} age is an independent risk factor for FTR. Furthermore, the ASA-PS was a predictive factor for FTR. Although the ASA-PS is a subjective tool assessed by anesthesiologists, it is helpful for evaluating the general condition of patients.¹² Therefore, comprehensive perioperative surgical management based on improved recovery after surgery should be provided, particularly for older patients regardless of their ASA-PS score.²⁵ Efforts to prevent major complications are important for high-risk patients.

TABLE 3 Univariate and multivariate analyses of risk factors for predicting failure to rescue.

			Univariate			Multivariate		
Variable		No. of patients	OR	95% CI	p value	OR	95% CI	p value
Age, years		373	1.09	1.02–1.16	0.012	1.07	1.00–1.15	0.045
Sex	Female	112	0.35	0.08–1.56	0.168	–	–	–
BMI, kg/m ²	≥25	100	1.38	0.46–4.15	0.562	–	–	–
ASA-PS score	3–4	46	5.30	1.79–15.70	0.003	4.35	1.24–15.20	0.021
Comorbidity	CH/LC	129	1.69	0.60–4.78	0.320	–	–	–
	COPD	9	3.12	0.37–26.70	0.298	–	–	–
	Hypertension	49	0.46	0.06–3.59	0.460	–	–	–
	CKD	13	2.06	0.25–17.00	0.500	–	–	–
	Diabetes	64	1.81	0.56–5.86	0.325	–	–	–
Preoperative albumin, g/dL	≤3.0	27	5.30	1.56–17.90	0.007	2.91	0.69–12.30	0.146
Preoperative prothrombin, %	≤80	32	2.83	0.76–10.60	0.123	–	–	–
Child–Pugh grade	Grade B	28	3.33	0.88–12.60	0.076	–	–	–
Tumor size, cm	≥3	205	1.59	0.53–4.75	0.406	–	–	–
Tumor number	≥2	100	0.40	0.09–1.79	0.228	–	–	–
Surgical approach	MIS	8	<0.01	0.00–Inf	0.992	–	–	–
Surgical procedure	Bisectionectomy or more	197	2.54	0.80–8.14	0.116	–	–	–
Operative time, h	≥6	160	3.27	1.02–10.50	0.046	1.95	0.51–7.48	0.331
Blood loss, mL	≥1000	106	1.85	0.61–5.65	0.279	–	–	–
Blood transfusion		124	3.17	1.10–9.12	0.032	1.01	0.28–3.65	0.988
BDR		72	1.05	0.29–3.81	0.944	–	–	–
Number of resection sites	≥2	66	0.322	0.04–2.49	0.278	–	–	–
Other organ resection		50	3.48	1.14–10.60	0.029	2.63	0.78–8.91	0.121
Vascular reconstruction		52	3.31	1.08–10.10	0.036	3.07	0.81–11.60	0.100

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; BDR, bile duct resection; BMI, body mass index; CH, chronic hepatitis; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; Inf, infinity; LC, liver cirrhosis; MIS, minimally invasive surgery; OR, odds ratio.

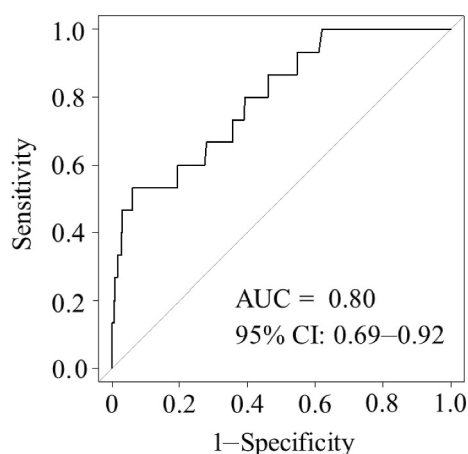


FIGURE 3 Receiver operating characteristic curve and area under the curve (AUC) of the accuracy of the model for failure to rescue following hepatectomy. CI, confidence interval.

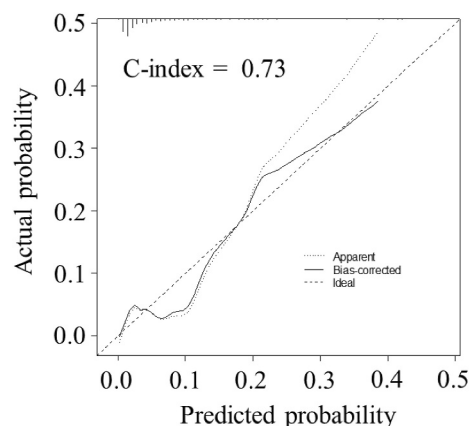


FIGURE 4 Calibration plot of the model for failure to rescue following hepatectomy.

To date, studies investigating FTR after hepatectomy have conventionally focused on the effect of hospital volume on outcomes, indicating a lower risk of mortality in high-volume centers.^{8,19} Furthermore, FTR risk factor analyses have been performed after hepatectomy.^{9,24} However, the predictive value of FTR remains unknown. Therefore, the strength of this study lies in the development of a simple risk model for predicting the FTR after hepatectomy. A risk model was generated using multivariate analyses, including intraoperative factors that were not completely correlated with FTR. Additionally, the model performance and internal validity were assessed. The performance of the model with an AUC of 0.80 was acceptable. Moreover, the calibration plots of the model exhibited good overall agreement with a C-index of 0.73. The risk calculator presented in Document S1 may be useful for predicting FTR after hepatectomy. According to this calculator, the predicted FTR in an 80-year-old patient with ASA-PS grade 3 who required vascular reconstruction was >23%. This information could be communicated to surgeons and patients before surgery, although an estimated high FTR should not be considered a contraindication for hepatectomy.

The present study possesses certain limitations. Although the sample size was relatively large at 1371 patients, including 373 patients with major complications, this was a single-center retrospective study undertaken at a high-volume center, thus potentially contributing to a selection bias for patients undergoing hepatectomy. Due to the retrospective nature of the study, there were minimal missing data on clinical parameters and confounding factors were carefully addressed. As we excluded patients who underwent repeat hepatectomy, the impact of such procedures on FTR was not investigated, necessitating further research in this area. Furthermore, the risk model for FTR demonstrated acceptable discrimination. However, unknown or residual confounding factors may influence FTR. Finally, the risk model was only validated in an internal validation cohort. Therefore, in future studies, this model should be validated using an external cohort.

CONCLUSIONS

The present study demonstrates an association between age and FTR after hepatectomy and suggests that age and the ASA-PS score are significant predictors of FTR after hepatectomy. Our internally validated risk model is clinically relevant for predicting FTR following hepatectomy. Further multicenter studies are required to explore its broader clinical applicability.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

Approval of the research protocol by an Institutional Reviewer Board: N/A.

Informed Consent: N/A.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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