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ORIGINAL ARTICLE

Combination of advanced lung cancer inflammation index and nonalcoholic fatty liver disease fibrosis score as a promising marker for surgical procedure selection for hepatocellular carcinoma

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Abstract

Aim: Methods of predicting severe postoperative complications after anatomical resection for hepatocellular carcinoma are yet to be established. We aimed to clarify the relationship between inflammation-based prognostic scores and liver fibrosis markers and the incidence of postoperative complications after anatomical resection for hepatocellular carcinoma as well as the usefulness of these markers in surgical procedure selection.

Methods: We included 374 patients with hepatocellular carcinoma who had undergone initial hepatectomy between January 2007 and December 2021. The association between inflammation-based prognostic scores or liver fibrosis markers and postoperative complications was evaluated, and severe postoperative complication rates in the high-risk group defined by these markers were compared in terms of surgical procedure.

Results: The advanced lung cancer inflammation index and nonalcoholic fatty liver disease fibrosis score correlated significantly with severe postoperative complications after anatomical resection, with areas under the curve of 0.67 and 0.61, respectively. The combined advanced lung cancer inflammation index and nonalcoholic fatty liver disease fibrosis score resulted in a larger area under the curve (0.69). Furthermore, in the high-risk group determined by the combined score, the anatomical resection group had a significantly higher incidence of severe complications than the partial resection group ($P < 0.01$). There were no significant differences in prognosis among the surgical procedures in the high-risk group.

Conclusion: The combined advanced lung cancer inflammation index and nonalcoholic fatty liver disease fibrosis score serves as a predictive marker for severe postoperative complications after anatomical resection. This combined marker may contribute to appropriate surgical procedure selection.

KEYWORDS
anatomical resection, hepatocellular carcinoma, inflammation, liver fibrosis, postoperative complications

1 | INTRODUCTION

Hepatocellular carcinoma (HCC) is a malignant tumor that develops from hepatocytes and is the most common primary liver cancer.[1] Although there are various treatment options, including radiofrequency ablation, transcatheter arterial chemoembolization, and molecularly targeted therapies, hepatectomy is the most effective.[2–4] Although no conclusions have been reached regarding the optimal surgical procedure for HCC, anatomical resection is presumed to be superior to partial resection.[5] However, previous reports have suggested that anatomical resection carries a greater risk of postoperative complications.[6] Therefore, surgeons are often confused regarding the selection of these procedures.

Many previous reports have demonstrated risk factors for postoperative complications in hepatectomy, such as the serum albumin level, indocyanine green (ICG) retention rate at 15 min, sarcopenia, liver fibrosis, operation time, blood loss, and history of diabetes.[7–10] These factors can be broadly categorized as those related to nutritional status, liver function, and surgery. Among these factors, those related to the nutritional status or liver function can be measured preoperatively and used to predict postoperative complications.

Several methods have been established to assess inflammation status and liver fibrosis before surgery. The usefulness of inflammation-based prognostic scores (IBPSs) has been reported, and there is an association between these scores and postoperative complications.[11–13] On the other hand, convenient scores such as the FIB-4 score,[14] nonalcoholic fatty liver disease fibrosis score (NFS),[15] and aspartate aminotransferase to platelet ratio index (APRI)[16] have also been developed to assess liver fibrosis.

However, the usefulness of these scores for postoperative complication prediction or surgical procedure selection remains controversial.

This study aimed to clarify the relationship between IBPSs and liver fibrosis markers and the incidence of severe postoperative complications after anatomical resection of HCC and assess the usefulness of these markers for surgical procedure selection.

2 | METHODS

2.1 | Study design and patient population

We included 374 patients with HCC who had undergone initial hepatectomy between January 2007 and December 2021 in this study. All surgical procedures were performed at the Division of Gastroenterological, Hepato-Biliary-Pancreatic, Transplantation, and Pediatric Surgery, Department of Surgery, Shinshu University Hospital.

IBPSs and liver fibrosis markers were assessed to determine their relationship with postoperative complications using receiver operating characteristic (ROC) curve analysis. Complication rates were compared between patient groups stratified by cutoff values obtained using ROC curve analysis, and the characteristics of the high-risk group were examined. The above analysis was performed in patients who underwent anatomical resection, and the results were compared with those of patients who underwent partial hepatectomy. In this study, anatomical resection was defined as complete removal of the ≥1 Couinaud segment housing the tumor, encompassing procedures such as segmentectomy, sectionectomy, hemiheptectomy, and bi- and trisectionectomy. Risk factors for severe postoperative complications were also identified. Patients who underwent noncurative resection ($n = 14$) and those who were followed up for <6 mo ($n = 21$) were excluded from the survival analysis.

The study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by the Shinshu University Hospital Ethics Committee (approval number: 5244). Informed consent for enrollment in this study was obtained using an opt-out method on the website, and those who rejected the protocol were excluded.

2.2 | Endpoint assessment and data collection

We evaluated the diagnostic ability of IBPSs and liver fibrosis markers on the incidence of severe postoperative complications in terms of the area under the curve (AUC) calculated by ROC curve analysis and clarified the characteristics of the high-risk group.

The medical records of patients participating in the study were retrospectively reviewed for background data, preoperative laboratory data, operative characteristics, surgical outcomes, and pathological findings. The pathological stage was determined according to the eighth edition of the *TNM Classification of Malignant Tumors* by the Union for International Cancer Control (UICC). Postoperative complications were categorized using Clavien–Dindo classification (CD)[17] and severe postoperative complications were defined as complications of CD IIIa or higher. Posthepatectomy liver failure (PHLF) was defined based on the International Study Group of Liver Surgery (ISGLS) standards of 2011.[18]

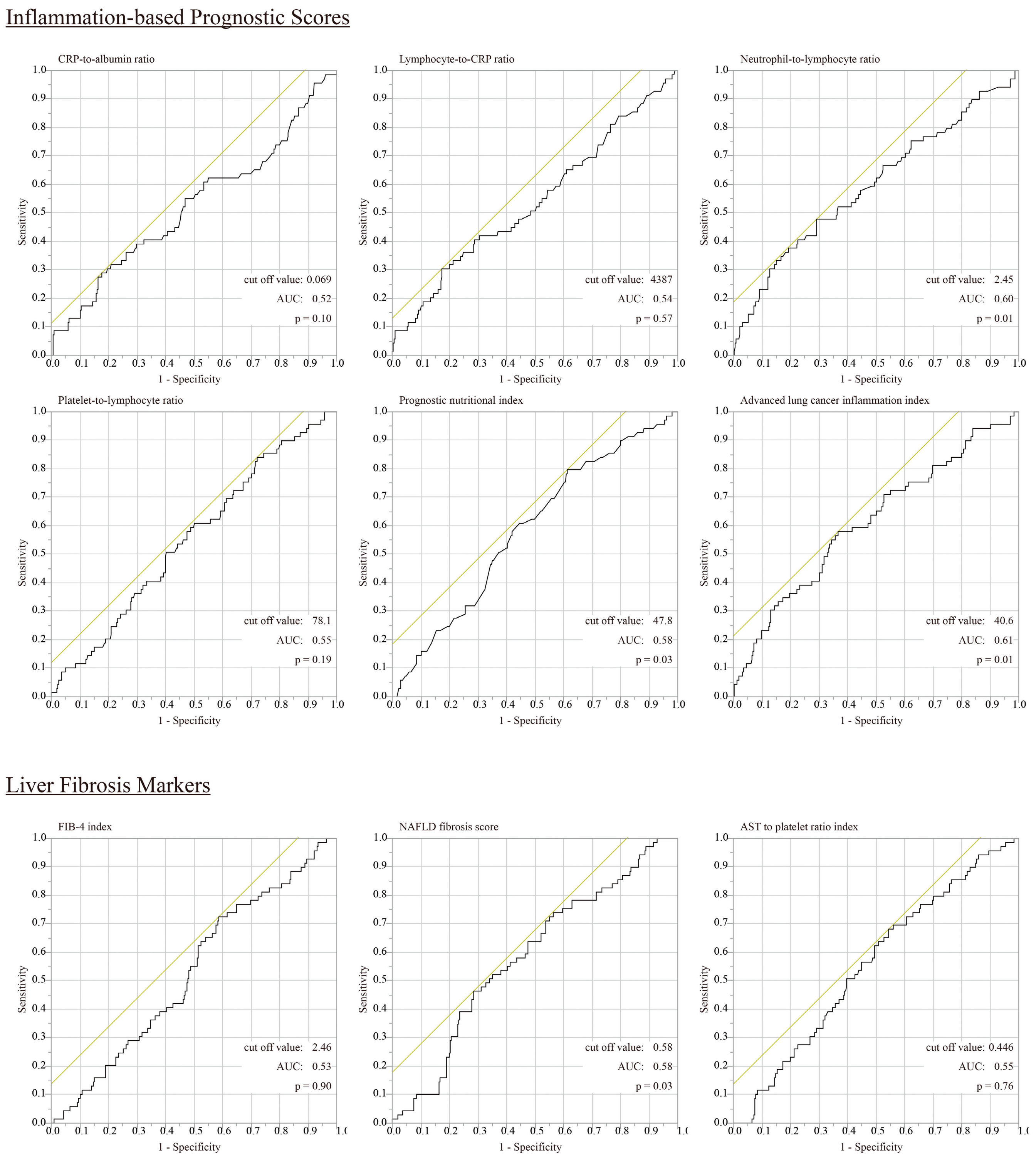


FIGURE 1 Receiver operating characteristic curve analysis of inflammation-based prognostic scores and liver fibrosis markers for severe postoperative complications of hepatectomy for hepatocellular carcinoma. The highest area under the curve values of inflammation-based prognostic scores and liver fibrosis markers were obtained for the advanced lung cancer inflammation index (ALI) (0.61) and nonalcoholic fatty liver disease fibrosis score (NFS) (0.58), and the optimal cutoff values for ALI and NFS were 40.6 and 0.58, respectively. The sensitivity and specificity of ALI at those cutoff values were 66.0% and 63.3%, respectively. The corresponding values for NFS were 46.4% and 71.5%, respectively.

2.3 | Perioperative management and surgical procedure

The future remnant liver volume, ICG retention or clearance rate, and hepatocellular uptake index derived from gadoxetate disodium-enhanced magnetic resonance imaging (MRI) were measured to determine the indications for HCC surgery. The extent of liver resection was determined using Makuuchi's criteria,[19] ICG clearance from the remnant liver,[20] and the remnant hepatocellular uptake index.[21] Laboratory data were checked daily for 3–5 d after surgery, and bilirubin levels in the drainage fluid were measured on postoperative d 1 and 3. Postoperative surveillance was conducted as follows: blood tests, including tumor markers, and ultrasonography, were conducted at intervals of 1–3 mo, and computed tomography or MRI was performed every 6 mo.

2.4 | Statistical analysis

ROC curve analysis was performed; the AUC was calculated. The optimal cutoff value, sensitivity, and specificity of the various scores were obtained using the Youden index. The method of risk assessment for severe postoperative complications was defined by the results of the above-mentioned analyses and validated using bootstrapping with 1000 resamples. Quantitative variables were analyzed using the Wilcoxon rank-sum test and presented as medians with ranges. Categorical variables were analyzed using the χ^2 test or Fisher's exact test. Variables with *P*-values <0.05 were considered statistically significant. Univariate and multivariate analyses were performed to evaluate significant risk factors for the development of severe postoperative complications, and odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. In the multivariate analysis, quantitative variables were stratified into two groups based on the cutoff value obtained from the ROC curve analysis, and a multiple logistic regression model was applied. Survival after surgery was estimated using the Kaplan–Meier method and compared using the log-rank test. We used JMP v. 13.2.1 (SAS Institute, Cary, NC, USA) and R v. 4.3.0 (R Core Team, Vienna, Austria) to perform the above statistical analyses.

3 | RESULTS

3.1 | ROC curve analysis for severe complications

ROC curve analyses were performed for each IBPSs and liver fibrosis marker. The details on each score or marker are presented in Table S1. For IBPSs, the neutrophil-to-lymphocyte ratio, prognostic nutritional index, and advanced lung cancer inflammation index (ALI) were significantly correlated with severe complications (>CD grade IIIa) in terms of the AUC (Figure 1), and ALI showed the highest AUC (0.61). Among the liver fibrosis markers, NFS was the only marker that showed a significant correlation with >CD grade IIIa complications, with an AUC of 0.58 (Figure 1). ALI and NFS, which

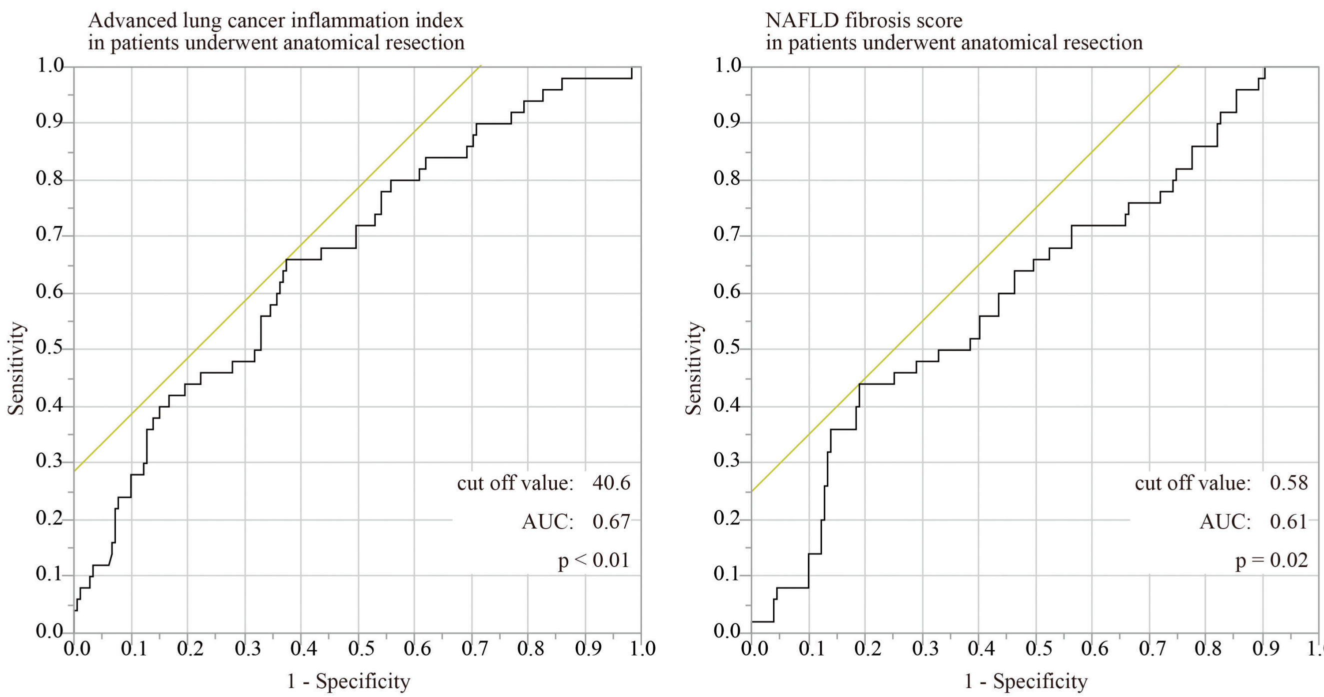


FIGURE 2 Receiver operating characteristic curve analysis of advanced lung cancer inflammation index (ALI) and nonalcoholic fatty liver disease fibrosis score (NFS) for severe postoperative complications in the anatomical resection group. ALI and NFS were significantly correlated with severe postoperative complications, with an AUC of 0.67 and 0.61, respectively.

showed the highest AUC values for IBPSs and liver fibrosis markers, respectively, were further assessed. The optimal cutoff values for ALI and NFS were 40.6 and 0.58, respectively. The sensitivity and specificity of ALI at these cutoff values were 66.0% and 63.3%, respectively. The corresponding values in the NFS group were 46.4% and 71.5%, respectively. When comparing the diagnosability of ALI and NFS with the combinations of these markers, the AUC of the combination calculated using ROC curve analysis was 0.62, which was higher than that of ALI or NFS alone (Figure S1). Moreover, in the anatomical resection groups, ALI, NFS, and their combination

TABLE 1 Patients' background data, operative characteristics, surgical outcomes, and pathological findings.

Variables	High-risk $n = 220$	Low-risk $n = 154$	*P* value
Age*, y	73 (42–85)	68 (16–89)	<0.001**
Sex			0.030**
Male	154 (70.0)	123 (79.9)	
Female	66 (30.0)	31 (20.1)	
Body mass index*, kg/m^2	22.5 (14.0–35.9)	23.0 (13.4–45.2)	0.170
Underlying liver disease			
Hepatitis B virus	92 (41.8)	70 (45.5)	0.485
Hepatitis C virus	94 (42.7)	58 (37.7)	0.326
Alcohol	23 (10.5)	23 (14.9)	0.197
NASH/NAFLD	18 (8.2)	7 (4.6)	0.157
Diabetes mellitus	100 (45.5)	26 (16.9)	<0.001**
Total bilirubin*, mg/dl	0.76 (0.15–1.85)	0.85 (0.36–2.81)	0.031**
Indocyanine green retention rate at 15 min*, %	13.0 (2.6–89.0)	11.9 (2.9–44.0)	0.134
Operative procedure			<0.001**
Hemihepatectomy	34 (15.5)	10 (6.5)	
Sectionectomy	42 (19.1)	29 (18.9)	
Segmentectomy	49 (22.3)	65 (42.2)	
Partial	95 (43.2)	50 (32.5)	
Operation time*, min	357 (106–820)	340 (82–990)	0.114
Blood loss*, ml	325 (0–6600)	300 (0–1850)	0.302
Blood transfusion	37 (16.8)	16 (10.4)	0.075
Mortality	1 (0.5)	0 (0)	1.00
Morbidity			
All grade	138 (62.7)	72 (46.8)	0.002**
Clavien–Dindo classification grade ≥ IIIa	52 (23.6)	17 (11.0)	0.002**
Postoperative hospital stay*, day	14 (7–87)	13 (4–117)	0.009**
UICC staging, 8th edition			0.383
IA	35 (16.0)	34 (22.2)	
IB	72 (32.9)	54 (35.3)	
II	76 (34.7)	47 (30.7)	
IIIA	17 (7.8)	9 (5.9)	
IIIB	16 (7.3)	9 (5.9)	
IVA	1 (0.5)	0 (0)	
IVB	2 (0.9)	0 (0)	

Note: Figures in parentheses are percentage unless otherwise specified.

Abbreviations: NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; UICC, Union for International Cancer Control.

*Median (range). ***P* < 0.05.

were more strongly correlated with >CD grade IIIa complications, with AUC of 0.67, 0.61, and 0.69, respectively (Figures 2 and S1).

3.2 | Assessment of risk factors for severe postoperative complications

Based on the results of the ROC analysis for severe postoperative complications, we defined patients with a low ALI or high NFS as the high-risk group. Table 1 shows the patients' background data, preoperative laboratory data, operative characteristics, surgical outcomes, and pathological findings categorized by the risk calculated using ALI and NFS. Age ($P < 0.01$), sex ($P = 0.03$), history of diabetes mellitus ($P < 0.01$), preoperative serum total bilirubin level ($P = 0.03$), and operative procedure ($P < 0.01$) differed significantly between the high- and low-risk groups.

In the univariate analysis, age > 60 y ($P = 0.04$), diabetes mellitus ($P < 0.01$), ICG retention rate at 15 min ≥ 11.8% ($P < 0.01$), anatomical resection ($P = 0.03$), and high-risk calculated by ALI and NFS ($P < 0.01$) were significantly correlated with the incidence of severe postoperative complications. In multivariate analysis by logistic regression model, the ICG retention rate at 15 min ≥11.8% (OR, 2.19; 95% CI, 1.22–3.94; $P = 0.01$) and high-risk calculated using ALI and NFS (OR, 2.38; 95% CI, 1.27–4.47; $P = 0.01$) were identified as independent risk factors for severe postoperative complications (Table 2).

3.3 | Detailed assessment of postoperative complications

The incidence of severe postoperative complications was compared between the two groups and categorized according to the risks calculated using ALI and NFS. In the entire cohort, the high-risk group had a significantly higher incidence of severe postoperative complications than did the low-risk group (23.6% vs. 11.0%, $P < 0.01$; Figure 3A). Among patients who underwent anatomical resection, severe postoperative complications were significantly more prevalent in the high-risk group than in the low-risk group (30.4% vs. 11.5%, $P < 0.01$; Figure 3A). In contrast, among the patients who underwent partial resection of HCC, there was no significant difference in the incidence of severe complications between the patient groups stratified according to ALI and NFS (14.7% vs. 10.0%, $P = 0.41$; Figure 3A). The results of the analyses and descriptive data on the short-term postoperative outcomes are listed in Table 3. The incidences of PHLF and ascites were significantly higher in the high-risk group than in the low-risk group (PHLF, 21.8% vs. 13.0%, $P = 0.03$; ascites, 8.6% vs. 2.0%, $P < 0.01$). Additionally, the length of postoperative hospital stay was longer in the high-risk group compared with in the low-risk group ($P = 0.01$).

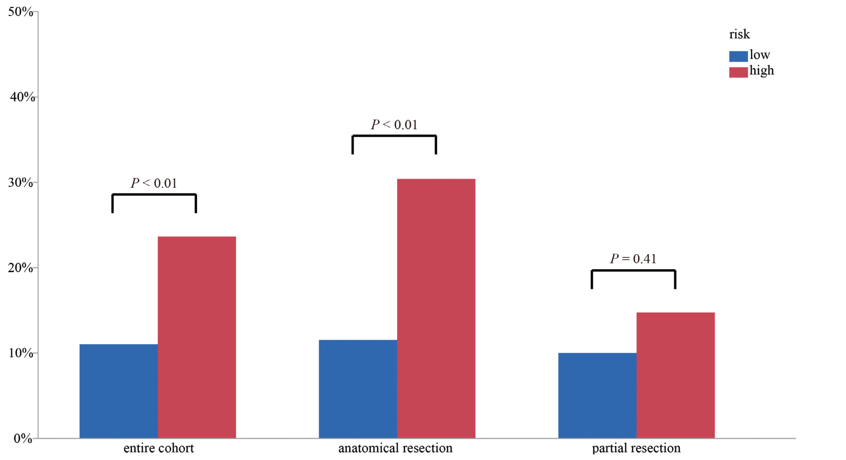
Analyzing the surgical procedures for the high-risk group, the incidence of severe postoperative complications in patients who underwent anatomical resection was significantly higher than that in patients who underwent partial resection (30.4% vs. 14.7%, P

TABLE 2 Uni- and multivariate analyses of risk factors for severe complications.

	Univariate			Multivariate		
Variables	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Age						
<60	Ref					
≥60	2.45	0.94–6.40	0.060			
Diabetes mellitus						
No	Ref			Ref		
Yes	2.08	1.23–3.56	0.007*	1.70	0.96–13.57	0.067
Liver cirrhosis						
No	Ref					
Yes	1.14	0.66–1.98	0.635			
ICG retention rate at 15 min						
<11.8%	Ref			Ref		
≥11.8%	2.39	1.39–4.10	0.001*	2.19	1.22–3.94	0.009*
Anatomic resection						
No	Ref			Ref		
Yes	1.85	1.04–3.29	0.031*	1.60	0.86–2.99	0.141
Risk calculated by advanced lung cancer inflammation index and nonalcoholic fatty liver disease fibrosis score						
Low-risk	Ref			Ref		
High-risk	2.49	1.38–4.51	0.002*	2.38	1.27–4.47	0.006*

Abbreviations: CI, confidence interval; ECOG, Eastern Cooperative Oncology Group.
*$P < 0.05$.

(A)



(B)

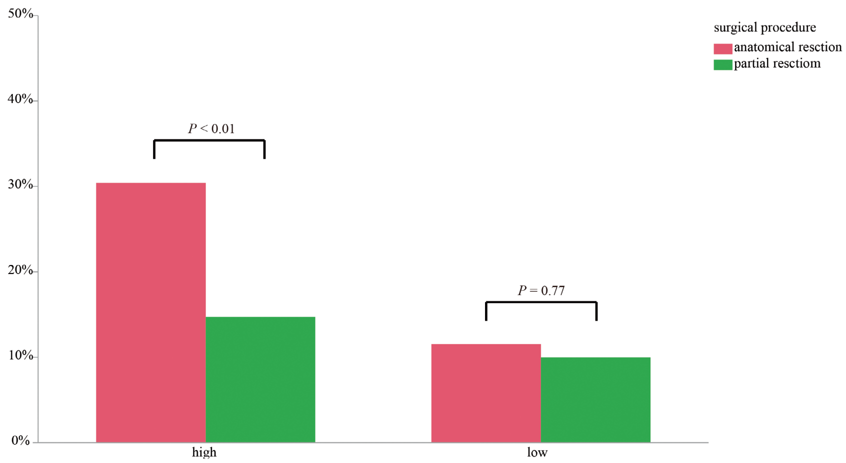


FIGURE 3 Analysis of the incidence rate of severe postoperative complications. The high-risk group had a significantly higher severe postoperative complication rate than the low-risk group in the entire cohort (23.6% vs. 11.0%, $P < 0.01$; A) and in the anatomical resection group (30.4% vs. 11.5%, $P < 0.01$; A). In the partial resection group, there was no significant difference (14.7% vs. 10.0%, $P = 0.41$; A). With regard to surgical procedures for the high-risk group, the severe postoperative complication rates of anatomical resection were significantly higher than those of partial resection (30.4% vs. 14.7%, $P < 0.01$; B). In the low-risk group, there were no significant difference in the rates of severe postoperative complications between anatomical resection and partial resection (11.5% vs. 10.0%, $P = 0.77$; B).

< 0.01; Figure 3B). In contrast, in the low-risk group there was no significant difference in the incidence of severe postoperative complications between anatomical and partial resections (11.5% vs. 10.0%, $P = 0.77$; Figure 3B). Regarding the validation cohort by the bootstrapping method, 95% CI of the incidence of severe postoperative complications in the high-risk group including patients who underwent anatomical and partial resections was 22.4%–38.4% and 7.6%–22.1%, respectively ($P < 0.01$).

3.4 | Characteristics and survival analysis in the high-risk group

The oncological characteristics of the high-risk groups are shown in Table 4. The anatomical group had significantly more advanced disease than the partial resection group in terms of Des-γ-carboxy prothrombin ($P < 0.01$), tumor diameter ($P < 0.01$), and hepatic vein invasion ($P < 0.01$). With regard to background liver fibrosis, the anatomical resection group showed a significantly lower rate of liver cirrhosis than the partial resection group (21.7% vs. 59.5%; $P < 0.01$). Survival analysis revealed that the overall survival (OS) and recurrence-free survival (RFS) rates did not differ significantly between the anatomical and partial resection groups (OS, $P = 0.18$; RFS, $P = 0.21$; Figure 4A,B).

4 | DISCUSSION

In this study, we aimed to clarify the impact of IBPSs and liver fibrosis markers on postoperative complications after anatomical resection for HCC and the potential of these markers in surgical procedure selection. We determined that the combination of ALI and NFS can predict the incidence of severe postoperative complications after anatomical resection, and that this combination marker may play a role in surgical procedure selection.

As mentioned previously, liver function[22,23] and nutritional status[11] are associated with the postoperative complications of hepatectomy. However, few studies have reported an association between inflammatory markers and the risk of postoperative complications of hepatectomy for HCC.[13,24] This is presumed to be because the development of postoperative complications of hepatectomy, especially PHLF, is strongly influenced by liver function. In support of this hypothesis, an association between these markers and postoperative complications has been more frequently reported in cases of liver metastases with no fibrosis in the background liver than in HCC.[25,26] By contrast, liver fibrosis alone is not necessarily a highly accurate marker for predicting severe complications, although some studies have focused on the association between fibrosis and specific complications. In this study, FIB-4 and APRI, which are established predictive markers of liver fibrosis,[14,16] did not correlate with severe complications.

TABLE 3 Short-term postoperative outcomes.

	High-risk	Low-risk	
	n = 220	*n* = 154	*P* value
Mortality	1 (0.5)	0 (0)	1.00
Morbidity			
All grade	138 (62.7)	72 (46.8)	0.002*
Clavien–Dindo classification grade ≥ IIIa	52 (23.6)	17 (11.0)	0.001*
Post-hepatectomy liver failure	48 (21.8)	20 (13.0)	0.027*
Post-hepatectomy bile leakage	20 (9.1)	18 (11.7)	0.416
Ascites	19 (8.6)	3 (2.0)	0.004*
Pleural effusion	26 (11.8)	14 (9.1)	0.397
Incisional surgical site infection	14 (6.4)	14 (9.1)	0.328
Intraperitoneal Infection	12 (5.5)	7 (4.6)	0.021
Postoperative hospital stay, median (range), day	14 (7–87)	13 (4–117)	0.009*

Note: Figures in parentheses are percentage unless otherwise specified.
*$P < 0.05$.

In this context, ALI and NFS correlated significantly with severe complications. First, we discuss the details of ALI and NFS. ALI was investigated by Jafri et al[27] as a prognostic marker for lung cancer and as a score based on inflammation or nutritional status. Previous reports have revealed that ALI has a significant correlation with the long-term outcomes of various types of cancers[27,28]; however, studies examining the relationship between ALI and postoperative complications are limited. The NFS is a score that estimates the extent of lung cancer (LC) in patients with nonalcoholic fatty liver disease; however, its usefulness in viral hepatitis or HCC is controversial, and the NFS is rarely applied to predict surgical outcomes. Moreover, there has been no evidence to date regarding the relationship between these markers and postoperative complications of HCC. Second, we investigated why ALI and NFS could accurately predict the incidence of severe complications. As previously reported, the ALI is evaluated by a combination of albumin and the neutrophil-lymphocyte ratio (NLR), making it a superior marker for nutrition and inflammation status. In general, malnutrition leads to delayed healing of the surgical site and vulnerability to infection due to inhibition of chemical mediators production and migration and adhesion of inflammatory cells or fibroblasts.[29] Additionally, inflammation status, or NLR, has been reported to be associated with interleukin (IL)-6 levels. IL-6 contributes to tissue injury and bacterial invasion via superoxide anion, which could potentially correlate with postoperative complications.[30] The NFS is a noninvasive marker for liver fibrosis along with APRI and FIB-4 score and includes platelet, aspartate aminotransferase (AST), and alanine aminotransferase (ALT), which are closely related to postoperative complications of liver

TABLE 4 Oncological characteristics of high-risk group.

	AR	PR	
Variables	*n* = 115	*n* = 79	*P* value
Alpha fetoprotein*, ng/mL	12.3 (0.7–166 130)	10.4 (1.0–6507)	0.273
Des-γ-carboxy prothrombin*, mAU/mL	218 (9.0–255 600)	40 (8.0–102 283)	<0.001**
Liver cirrhosis	25 (21.7)	47 (59.5)	<0.001**
Tumor diameter*, cm	4.3 (1.3–16.5)	2.7 (1.0–14.0)	<0.001**
Multiple lesion	21 (18.3)	22 (27.9)	0.117
Portal vein invasion	37 (32.2)	17 (21.5)	0.100
Hepatic vein invasion	26 (22.6)	4 (5.1)	<0.001**
UICC stage, 8th edition, *n* (%)			0.176
IA	15 (13.0)	16 (20.3)	
IB	42 (36.5)	28 (35.4)	
II	37 (32.2)	29 (36.7)	
IIIA	11 (9.6)	4 (5.1)	
IIIB	10 (8.7)	2 (2.5)	

Note: Figures in parentheses are percentage unless otherwise specified.
Abbreviations: AR, anatomic resection; PR, partial resection; SEG; segmentectomy, UICC, Union for International Cancer Control.
*Median (range). **$P < 0.05$.

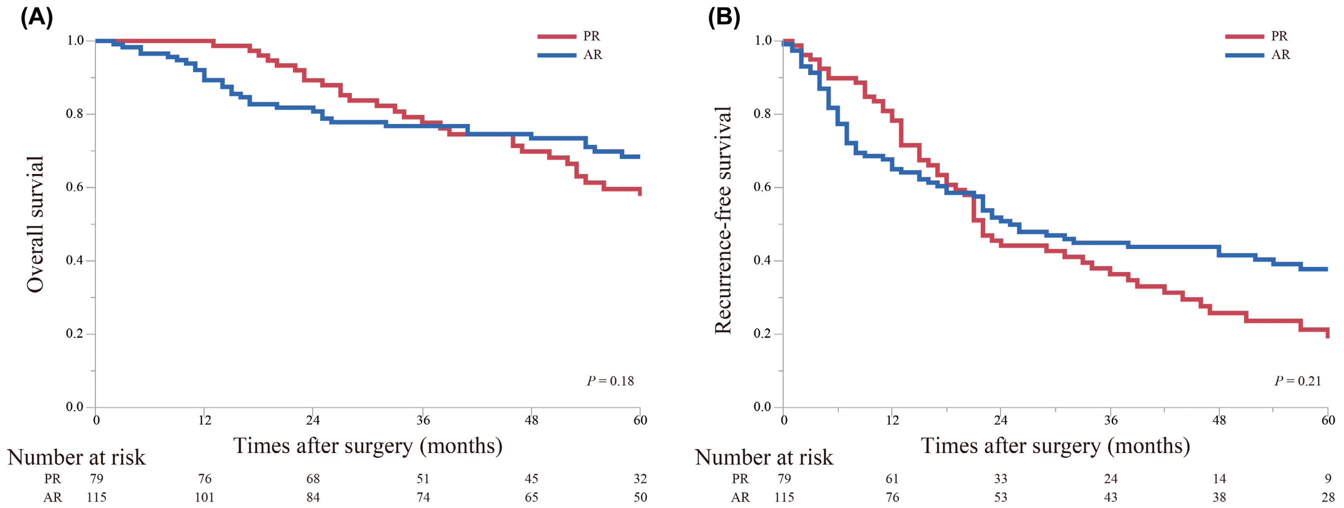


FIGURE 4 Kaplan–Meier curve of overall survival (OS) and recurrence-free survival (RFS) between anatomical resection and partial resection. The OS and the RFS of the anatomical resection group (AR) and the partial resection group (PR) did not show significant difference (OS, $P = 0.18$; RFS, $P = 0.21$; A, B).

resection. In addition, platelets, AST, and ALT play other important roles in predicting postoperative complications: platelets and AST and ALT contribute to liver regeneration by deriving serotonin[31] and liver inflammation, respectively.[32] Importantly, as opposed to APRI or FIB-4, NFS include factors related to impaired glucose tolerance,[33] which are risk factors for postoperative complications of hepatectomy. Moreover albumin, which is an item of both ALI and NFS, is not only a marker for malnutrition, but also of liver function and is closely related to the development of complications, particularly PHLF.[34] Consequently, the risk of severe postoperative complications could be comprehensively assessed.

One of the most impressive findings of the present study was the significantly higher rate of severe postoperative complications of anatomical resection than of partial resection in the high-risk group. These results indicate that adding ALI + NFS to the existing criteria (Makuuchi's criteria,[19] ICG clearance of the remnant liver,[20] and the remnant hepatocellular uptake index[21]) can allow us to select appropriate cases for anatomical resection in terms of preventing severe postoperative complications. The results of the survival analysis were also notable to some extent. Although they did not show precise noninferiority, survival time was comparable between the anatomical and partial resection groups. These findings suggest that using this amalgamation to determine the surgical procedure is acceptable from an oncological perspective.

The present study had some limitations. The main limitation was its single-center, retrospective, nonrandomized design. Another critical problem was that the group that underwent anatomical resection included patients who could not undergo partial resection because of the relationship between the tumor and vessels. Although it was not impossible to exclude these cases retrospectively, we did not add these exclusion criteria because selection bias was expected to occur. Another limitation was the heterogeneity of the patients' backgrounds. In multivariate analysis, anatomical resection was not an independent risk factor for severe complications. We consider this phenomenon to be due to heterogeneity. To overcome these limitations, a prospective randomized study focusing on patients who can undergo partial resection is required.

In conclusion, the combination of ALI and NFS is a predictive marker for the incidence of severe postoperative complications after anatomical resection, and this combination marker could contribute to the selection of surgical procedures.

AUTHOR CONTRIBUTIONS

KH, AS, KK, TN, NK, and YS designed the study and interpreted the data. KH drafted the article. KH, TY, HS, HH, and KY participated in the data analysis. YS supervised the study. All authors critically revised the article, commented on drafts of the article, and approved the final report.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest for this article.

ETHICS STATEMENTS

The protocol for this research project was approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Committee of Shinshu University Hospital, Approval no. 5244. Informed consent for enrollment in this study was obtained using an opt-out method on the website.

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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