

Prognostic utility of the albumin-bilirubin and fibrosis-4 indices for predicting postoperative liver failure following major hepatic resection

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Abstract

Background: Post-hepatectomy liver failure is the principal cause of death after major hepatic resection, and reliable preoperative prediction of the residual functional reserve is essential. This study evaluated the albumin-bilirubin (ALBI) score and the fibrosis-4 (FIB-4) index for predicting post-hepatectomy liver failure. **Methods:** A retrospective cohort of 318 patients undergoing major hepatic resection of three or more segments was analysed. The preoperative ALBI score and FIB-4 index were calculated from routine laboratory data, and patients were stratified by ALBI grade and by a FIB-4 threshold. The primary outcome was post-hepatectomy liver failure defined by the International Study Group of Liver Surgery within 30 days. Independent predictors were identified by multivariable logistic regression, and discriminative ability was compared using the area under the receiver operating characteristic curve. **Results:** Post-hepatectomy liver failure occurred in 19.8% of patients. A higher ALBI grade was independently associated with liver failure (adjusted odds ratio 2.74, 95% confidence interval 1.55-4.85), as was an elevated FIB-4 index (adjusted odds ratio 2.05, 95% confidence interval 1.14-3.69). The ALBI score showed greater discrimination than FIB-4, with an area under the curve of 0.76 versus 0.71. **Conclusion:** The preoperative ALBI score is an independent predictor of post-hepatectomy liver failure and outperformed the FIB-4 index, while the two combined offered modest incremental value, supporting their use in preoperative risk assessment before major hepatic resection.

Keywords: Albumin-bilirubin score, Fibrosis-4 index, Post-hepatectomy liver failure, Hepatic resection, Liver function, Risk prediction

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1. Introduction

The expansion of hepatic surgery to increasingly complex cases has made the preoperative estimation of risk one of the central problems of hepatobiliary practice. As the boundaries of resectability are pushed outward by improved imaging, neoadjuvant therapy, and techniques to augment the future liver remnant, the decisive question at the point of planning is often not whether a tumour can be removed but whether the patient's liver

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can tolerate its removal. Objective, reproducible markers of hepatic reserve that can be obtained from routine investigations are therefore of great practical value, because they inform the choice between resection and alternative treatment, guide the extent of the operation, and identify patients who require measures to enlarge or protect the remnant before surgery.

Hepatic resection is the mainstay of curative treatment for primary and secondary liver malignancy, and advances in surgical technique, anaesthesia, and perioperative care have progressively widened the range of patients who can be offered an operation (Kingham *et al.*, 2015). Yet major hepatic resection, defined conventionally as the removal of three or more contiguous Couinaud segments, remains a formidable undertaking, and its safety is ultimately limited by the capacity of the future liver remnant to sustain metabolic, synthetic, and detoxifying function during the critical early postoperative period (Rahbari *et al.*, 2011).

Post-hepatectomy liver failure is the most feared complication of this surgery and the leading cause of perioperative death after major resection (Balzan *et al.*, 2005). It arises when the residual liver is unable to meet physiological demand, whether because too little parenchyma remains, because the remaining tissue is intrinsically diseased, or because of a combination of the two. Beyond its direct mortality, post-hepatectomy liver failure prolongs intensive-care and hospital stay, precipitates cascading organ dysfunction, and compromises the delivery of adjuvant therapy, so that its avoidance is central to the safe practice of hepatic surgery (Mullen *et al.*, 2007).

The pathophysiology of the complication explains why preoperative assessment matters. In the days after a major resection the remnant must sustain synthetic and detoxifying function while mounting a regenerative response, and both processes place heavy demands on hepatocellular reserve. A liver that is already functionally marginal, or whose architecture is distorted by fibrosis, may be unable to meet these demands, and the resulting failure of synthesis and clearance manifests as the coagulopathy and hyperbilirubinaemia that define the condition. Because this trajectory is largely set at the time of operation, the interval before surgery is when risk can most usefully be estimated and, where possible, reduced.

The prediction of this complication therefore rests on an accurate preoperative assessment of hepatic functional reserve. Traditional tools have important shortcomings. The Child–Pugh classification was devised for patients with cirrhosis and portal hypertension and incorporates subjective variables such as ascites and encephalopathy, which limits its precision in the surgical candidate (Pugh *et al.*, 1973). Dynamic tests such as indocyanine green clearance provide useful information but require specialised equipment and are not universally available, while volumetric assessment of the future liver remnant addresses quantity rather than the quality of the remaining parenchyma (Imamura *et al.*, 2005). There remains a need for objective markers that can be derived from routine blood tests and that capture the functional state of the liver.

The albumin–bilirubin score was developed as an objective, evidence-based measure of liver function that uses only serum albumin and bilirubin, excluding the subjective components of the Child–Pugh system, and it stratifies patients into three grades of progressively worse function (Johnson *et al.*, 2015). The fibrosis-4 index, derived to estimate hepatic fibrosis non-invasively from age, aminotransferase levels, and platelet count, reflects the degree of underlying parenchymal disease, which itself determines the remnant's capacity to regenerate and function (Sterling *et al.*, 2006). The two therefore capture complementary dimensions of hepatic reserve: the ALBI score reflects current synthetic and excretory function, while the FIB-4 index reflects the structural substrate of fibrosis on which that function depends.

Although each index has been studied in the setting of chronic liver disease and hepatocellular carcinoma, the evidence concerning their value for predicting post-hepatectomy liver failure specifically is less developed, and studies that examine both within the same cohort, using a standardised definition of liver failure and rigorous multivariable adjustment, are scarce (Zou *et al.*, 2018). It is therefore unclear whether these indices are independently associated with post-hepatectomy liver failure after major resection, and which of the two, or whether their combination, offers the most useful prediction for the surgeon planning an operation (Fagenson *et al.*, 2020).

This study evaluated whether the preoperative ALBI score and FIB-4 index are independently associated with post-hepatectomy liver failure after major hepatic resection, compared their discriminative ability, and examined whether combining the two improves prediction beyond either alone.

2. Materials and methods

2.1. Study design and setting

This was a retrospective observational cohort study conducted at a tertiary referral centre for hepatobiliary surgery. Consecutive patients who underwent major hepatic resection over a defined study period were identified from a prospectively maintained surgical database. The study was designed and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cohort studies (von Elm et al., 2007). The protocol was approved by the Institutional Review Board, which waived the requirement for individual informed consent given the retrospective use of anonymised data. All procedures conformed to the principles of the Declaration of Helsinki.

2.2. Participants and eligibility criteria

Eligible patients were adults aged 18 years or older who underwent major hepatic resection, defined as the removal of three or more contiguous Couinaud segments, for primary or secondary liver malignancy or for benign disease requiring major resection. Exclusion criteria were emergency surgery, resection of fewer than three segments, a two-stage or staged hepatectomy in which the relevant physiology could not be attributed to a single operation, liver transplantation, concurrent biliary reconstruction for hilar obstruction that independently affects bilirubin, and incomplete laboratory or outcome data. These criteria were applied so that the calculated indices reflected baseline hepatic function and the cohort represented a consistent major-resection population.

2.3. Calculation of the ALBI score and FIB-4 index

Preoperative laboratory values obtained within seven days before surgery were used for all calculations. The albumin–bilirubin score was computed from serum albumin and total bilirubin using the established linear formula, and patients were assigned to ALBI grade 1, 2, or 3 according to the validated grade thresholds, with higher grades indicating poorer liver function. The fibrosis-4 index was calculated from age, aspartate and alanine aminotransferase levels, and platelet count using the established formula, and patients were dichotomised at a threshold derived from the cohort by receiver operating characteristic analysis into low and high FIB-4 groups. Where more than one qualifying laboratory set was available, the value closest to surgery was used, and patients with an acute biliary or infective disturbance of the relevant analytes at the time of sampling had been excluded to prevent transient derangements from distorting the indices. All indices were computed by an investigator blinded to postoperative outcomes, and the parameters are summarised in Table 1.

Table 1: Components and interpretation of the ALBI score and FIB-4 index		
Index	Components	Interpretation
ALBI score	Serum albumin and total bilirubin, combined by the validated linear formula	Grades 1–3; higher grade = worse liver function
FIB-4 index	Age, aspartate and alanine aminotransferase, and platelet count	Higher value = greater hepatic fibrosis
Note: ALBI, albumin–bilirubin; FIB-4, fibrosis-4.		

2.4. Surgical procedure, perioperative care, and outcome

Major hepatic resection was performed by experienced hepatobiliary surgeons using open or minimally invasive techniques according to tumour location, extent of resection, and surgeon preference, with intraoperative ultrasound and parenchymal transection performed by standard methods. The adequacy of the future liver remnant was assessed preoperatively by volumetry, and portal vein embolisation was employed selectively when the remnant was considered insufficient. Perioperative care followed a standardised enhanced-recovery pathway that was uniform across the cohort.

The primary outcome was post-hepatectomy liver failure within 30 days, defined and graded according to the criteria of the International Study Group of Liver Surgery, in which liver failure is identified by an increased

international normalised ratio and concomitant hyperbilirubinaemia on or after the fifth postoperative day, and graded A to C by the intensity of treatment required ([Rahbari et al., 2011](#)). Clinically significant liver failure was defined as grade B or C. Outcomes were adjudicated by two clinicians independent of the operating team and blinded to the index values, with disagreements resolved by consensus.

2.5. Statistical analysis

Recorded covariates comprised age, sex, body mass index, American Society of Anesthesiologists physical status, underlying liver disease, cirrhosis, tumour type, extent of resection, operative approach, intraoperative blood loss, and preoperative portal vein embolisation. Continuous variables are presented as mean with standard deviation or median with interquartile range and were compared using the independent-samples t test or Mann-Whitney U test; categorical variables are expressed as frequencies and percentages and compared using the chi-square or Fisher exact test. The independent association between each index and post-hepatectomy liver failure was assessed by multivariable logistic regression, with results reported as adjusted odds ratios and 95% confidence intervals. The discriminative ability of the ALBI score, the FIB-4 index, and their combination was compared using the area under the receiver operating characteristic curve, and model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test. A two-sided p value below 0.05 was considered statistically significant.

3. Results and discussion

3.1. Patient characteristics

A total of 318 patients met the eligibility criteria and were included in the analysis. The mean age was 61.5 years, and 58.5% were male. Hepatocellular carcinoma accounted for 39.6% of cases, colorectal liver metastases for 41.2%, and other tumours or benign disease for the remainder; underlying chronic liver disease was present in 44.0% of patients and established cirrhosis in 18.6%. A right or extended hemihepatectomy was performed in 57.9% of cases, and preoperative portal vein embolisation had been used in 21.4%. By ALBI grade, 51.3% of patients were grade 1, 40.6% grade 2, and 8.1% grade 3. Baseline characteristics stratified by the occurrence of post-hepatectomy liver failure are presented in Table 2.

Table 2: Baseline characteristics by occurrence of post-hepatectomy liver failure

Characteristic	No PHLF (n = 255)	PHLF (n = 63)	p-value
Age, years, mean (SD)	60.4 (10.9)	65.9 (10.2)	< 0.001
Male sex, n (%)	147 (57.6)	39 (61.9)	0.535
Body mass index, kg/m ² , mean (SD)	25.1 (3.9)	25.8 (4.3)	0.210
ASA III-IV, n (%)	78 (30.6)	31 (49.2)	0.005
Chronic liver disease, n (%)	101 (39.6)	39 (61.9)	0.001
Cirrhosis, n (%)	38 (14.9)	21 (33.3)	< 0.001
Right/extended hepatectomy, n (%)	141 (55.3)	43 (68.3)	0.061
Portal vein embolisation, n (%)	52 (20.4)	16 (25.4)	0.386
Major blood loss, n (%)	61 (23.9)	26 (41.3)	0.006

Note: SD, standard deviation; ASA, American Society of Anesthesiologists; PHLF, post-hepatectomy liver failure.

3.2. Incidence of post-hepatectomy liver failure

Post-hepatectomy liver failure occurred in 63 of 318 patients, an overall incidence of 19.8%; grade A accounted for the majority, and clinically significant grade B or C failure affected 9.7% of the cohort. As shown in Figure

1, the incidence rose steeply across ALBI grades, from 8.9% in grade 1 to 22.6% in grade 2 and 41.7% in grade 3, with a parallel rise in clinically significant failure. A similar gradient was observed by fibrosis status: patients with a high FIB-4 index had more than double the incidence of those with a low index (28.3% versus 13.3%, $p < 0.001$; Table 3).

Table 3: Unadjusted incidence of post-hepatectomy liver failure by FIB-4 category			
FIB-4 category	PHLF, n (%)	No PHLF, n (%)	p-value
High FIB-4 (n = 138)	39 (28.3)	99 (71.7)	< 0.001
Low FIB-4 (n = 180)	24 (13.3)	156 (86.7)	

Note: PHLF, post-hepatectomy liver failure; FIB-4, fibrosis-4.

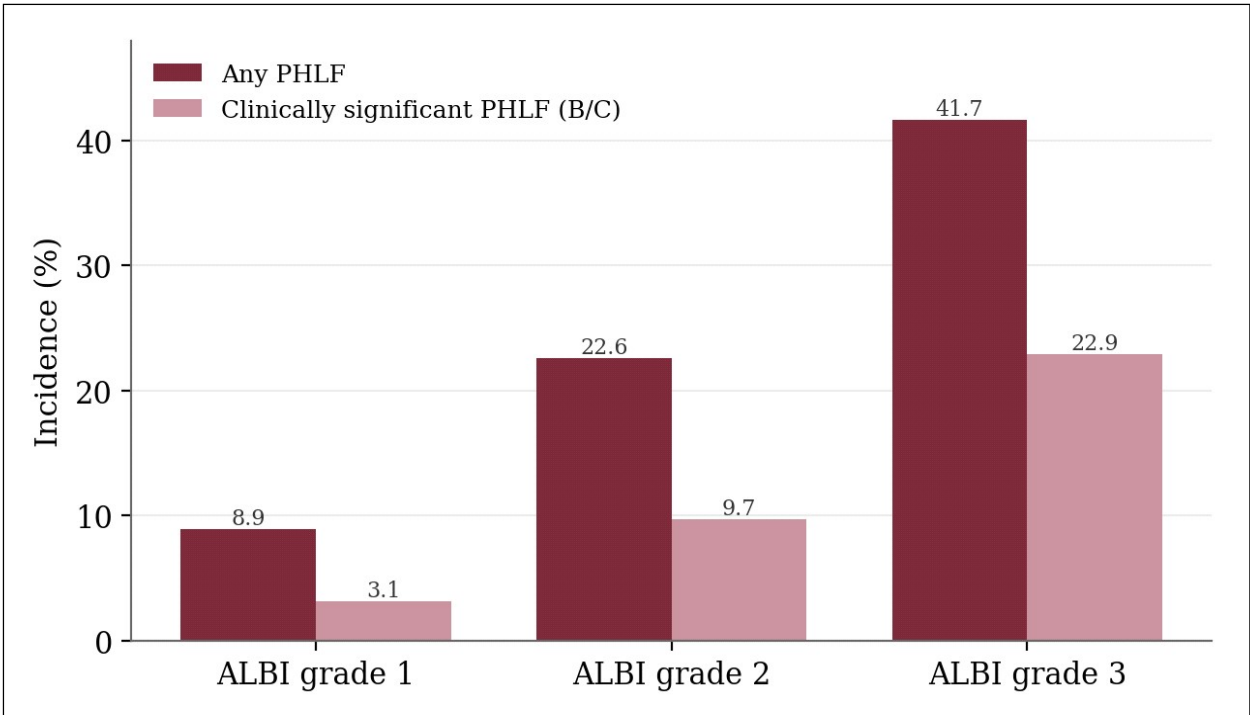


Figure 1: Incidence of post-hepatectomy liver failure across preoperative ALBI grades

3.3. Multivariable analysis

After adjustment for age, American Society of Anesthesiologists physical status, cirrhosis, extent of resection, intraoperative blood loss, and the other index, a higher ALBI grade remained independently associated with post-hepatectomy liver failure, with an adjusted odds ratio of 2.74 per grade increase (95% confidence interval 1.55–4.85, $p < 0.001$). An elevated FIB-4 index was also independently predictive, with an adjusted odds ratio of 2.05 (95% confidence interval 1.14–3.69, $p = 0.017$). Among the clinical covariates, cirrhosis, an extended resection, and major intraoperative blood loss each retained an independent association with liver failure, findings that accord with established surgical experience and lend face validity to the model. Notably, both indices retained significance in the presence of these established risk factors, indicating that they add predictive information rather than merely restating the risk conveyed by cirrhosis and the extent of resection. The adjusted associations are summarised in Table 4.

3.4. Comparative discriminative ability

The two indices differed in discriminative ability. The ALBI score achieved a higher area under the receiver operating characteristic curve than the FIB-4 index (0.76 versus 0.71), and combining the two raised discrimination further to 0.80, indicating that FIB-4 contributed information beyond that captured by ALBI.

Table 4: Multivariable logistic regression for post-hepatectomy liver failure

Variable	Adjusted OR	95% CI	p-value
Higher ALBI grade (per grade)	2.74	1.55–4.85	< 0.001
High FIB-4 index	2.05	1.14–3.69	0.017
Cirrhosis	2.31	1.22–4.38	0.010
Right/extended hepatectomy	1.98	1.06–3.70	0.032
Major blood loss	1.87	1.03–3.40	0.040
ASA III-IV	1.44	0.78–2.66	0.243

The model was well calibrated on the Hosmer–Lemeshow test, with no significant departure between observed and predicted probabilities. These comparisons are summarised in Table 5.

Table 5: Discriminative ability of the indices for post-hepatectomy liver failure

Index	AUC	95% CI	Sensitivity/Specificity
ALBI score	0.76	0.70–0.82	70%/72%
FIB-4 index	0.71	0.64–0.78	64%/67%
ALBI + FIB-4 combined	0.80	0.74–0.85	74%/75%

3.5. Subgroup analysis

The association between a higher ALBI grade and post-hepatectomy liver failure was consistent across clinically relevant subgroups. The effect was preserved in patients with and without cirrhosis, in those undergoing right or extended resection and lesser major resections, and across tumour types, with no statistically significant interaction detected in any comparison. This consistency indicates that the prognostic value of the ALBI score applies broadly across the major-resection population rather than being confined to a particular disease or operative context. The subgroup estimates are presented in Table 6.

Table 6: Association between higher ALBI grade and liver failure across subgroups

Subgroup	Adjusted OR	95% CI	p (interaction)
Cirrhosis present	2.91	1.34–6.32	0.62
Cirrhosis absent	2.58	1.28–5.20	
Right/extended resection	2.83	1.42–5.64	0.77
Lesser major resection	2.61	1.19–5.72	
Hepatocellular carcinoma	2.79	1.31–5.94	0.71
Colorectal metastases	2.64	1.22–5.71	

4. Discussion

Both the ALBI score and the FIB-4 index, obtainable from a routine preoperative blood panel, were independently associated with post-hepatectomy liver failure after major resection, and their combination discriminated

better than either alone. Objective, inexpensive markers can therefore stratify the risk of the most serious complication of hepatic surgery, providing an accessible adjunct to preoperative assessment.

The superiority of the ALBI score is biologically plausible, since its components, albumin and bilirubin, directly index the synthetic and excretory capacity on which the future liver remnant depends. This finding aligns with earlier surgical series in which ALBI predicted post-hepatectomy outcomes, and it extends them by showing that the score retains its value after adjustment for a fibrosis marker ([Andreatos et al., 2017](#)). It is also consistent with reports that ALBI outperforms the Child–Pugh and Model for End-Stage Liver Disease scores in this setting, a difference attributable to its ability to discriminate within the well-compensated range into which most resection candidates fall; in the present cohort, cirrhosis was present in fewer than one in five patients, yet the ALBI grade still stratified risk ([Wang et al., 2018](#)).

The independent contribution of the FIB-4 index reflects a complementary dimension of hepatic reserve. Fibrosis impairs the regenerative response required after major resection, so that a liver with adequate baseline function may nonetheless fail to regenerate once a large volume is removed ([Hobeika et al., 2019](#)). Previous work has linked fibrosis markers to adverse outcomes largely in patients with established chronic liver disease ([Kabir et al., 2021](#)); the present findings suggest the FIB-4 index carries prognostic information across a broader resection population and, importantly, adds to rather than duplicates the ALBI score, since the two together improved discrimination beyond either alone ([Citterio et al., 2016](#)).

The clinical value of these indices lies in their simplicity. Unlike dynamic function tests or volumetric software, both are derived from standard laboratory values and can be generated before surgery at no additional cost, a particular advantage in resource-limited settings ([Toyoda et al., 2016](#)). A patient flagged by a poor ALBI grade or an elevated FIB-4 index might be considered for a more conservative resection, for measures to augment the remnant such as portal vein embolisation, or for closer postoperative surveillance ([van Lienden et al., 2013](#); [Ribero et al., 2007](#)). A pragmatic approach would use the ALBI grade as the principal marker of current function and the FIB-4 index to capture the additional risk conferred by fibrosis, complementing rather than replacing volumetric and dynamic evaluation where these are available.

The overall incidence of post-hepatectomy liver failure and its steep gradient across ALBI grades are in keeping with contemporary series and with the established principle that both the quality of the liver and the volume removed govern the risk of decompensation ([Reissfelder et al., 2011](#); [Farges et al., 1999](#)). This study has limitations. Its retrospective, single-centre design cannot exclude residual confounding, the FIB-4 threshold was derived within the cohort and requires external validation, and the small number of ALBI grade 3 patients limits precision in that subgroup ([Harimoto et al., 2018](#); [Vauthey et al., 2000](#)). Prospective, multicentre validation, and ultimately trials testing whether risk-guided optimisation reduces liver failure, are needed to confirm these findings and to define their role in practice ([Kokudo et al., 2016](#)).

5. Conclusions

The preoperative ALBI score and FIB-4 index are each independently associated with post-hepatectomy liver failure after major hepatic resection, with the ALBI score providing the stronger prediction and the FIB-4 index adding complementary information such that the two combined offer the best discrimination. Because both are derived from routine laboratory data and require no specialised testing, they are practical and attractive markers for incorporation into preoperative risk assessment before major hepatic resection. Prospective, externally validated studies, and ultimately interventional trials of risk-guided optimisation, are required to confirm these findings and to establish whether their use can reduce the incidence of this most serious complication of hepatic surgery.

Ethics approval and consent to participate

The study was approved by the Institutional Review Board, which waived individual informed consent for the retrospective analysis of anonymised data.

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Data availability

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Author contributions

All authors contributed to the conception and design of the study, data acquisition, analysis and interpretation, drafting and critical revision of the manuscript, and approved the final version for submission.

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