The ability of the albumin-bilirubin grade to predict the short-term outcomes and complications following hepatic resection

Original Article

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the 2nd leading cause of cancer-associated mortality globally.

Aim: To evaluate the albumin-bilirubin (ALBI) grade as a prognostic tool in assessing cases undergoing hepatectomy for early postoperative complications in comparison to other scores/grades.

Patients and Methods: This prospective research has been performed on 42 cases with HCC that were subjected to elective hepatic resection at the National Liver Institute at Menoufia University.

Results: The ALBI score had 66.7% sensitivity and 93.9% specificity at a threshold value of greater than 2 with area under the curve (AUC)=0.825 and was highly significant (*P=0.001*). The CHILD score had a 55.6% sensitivity and 75.8% specificity at a threshold value of greater than 5% with AUC=0.640 and was nonsignificant (*P=0.136*). The model for end-stage liver disease score at a threshold value 8.35 had 100% sensitivity and 21.2% specificity, with AUC=0.519, and was nonsignificant (*P=0.868*).

Conclusion: The ALBI score demonstrated greater predictive value for liver cell failure compared with the Child-Pugh score as well as the model for end-stage liver disease score. The ALBI score, as well as bilirubin can be used as independent predictors for liver cell failure and bile leak posthepatic resection in HCC patients.

Key Words: Albumin-bilirubin score, Hepatocellular carcinoma, hepatic resection, model for end-stage liver disease score.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the 2nd leading reason for cancer-associated mortality globally. The morbidity and mortality burden in cases with chronic liver illness is significant, as it occurs in 90% of cases in conjunction with underlying liver illness[1]. Regardless of the development of numerous techniques for HCC treatments in recent decades, liver resection (LR) remains the primary curative therapy that provides the most favorable result[2]. LR is frequently presented with life-threatening complications, including post-hepatectomy liver failure (PHLF)[3].

The incidence of PHLF ranges between 8 and 12%, influenced by various definitions, severity, surgery extent, and intraoperative course. Post-hepatectomy liver failure is identified by the International Study Group of Liver Surgery (ISGLS) as an acquired impairment of liver functions, which is defined as an elevated International Normalized Ratio and hyperbilirubinemia following the fifth day following surgery[4].

Consequently, to decrease the PHLF risk, it is essential to perform a precise preliminary evaluation of cases undergoing LR, which includes the evaluation of portal hypertension & liver function[5].

Multiple markers were previously suggested for this reason, including the liver stiffness evaluation, Child–Pugh, as well as volumetric imaging for future liver residual evaluation. These markers are usually carried out during the preoperative phase[6].

Nevertheless, these assessments are frequently insufficient, time-consuming, or costly in terms of their ability to accurately predict the functional recovery of the liver following surgery. The albumin-bilirubin score, a new noninvasive method for assessing liver function and anticipating survival in HCC cases, has currently demonstrated promising outcomes to predict the long-term prognosis of chronic liver illness and HCC cases, involving post-hepatectomy liver failure prediction. Nevertheless, the albumin-bilirubin grade was not fully endorsed in the evaluation of HCC cases undergoing liver resection, as no definitive outcomes are available for this latter outcome[7].

The main aim of this research was to assess the albumin-bilirubin grade as a prognostic tool in the assessment of cases undergoing hepatectomy for early postoperative complications in comparison to other scores and grades.

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PATIENTS AND METHODS:

This prospective research has been performed on 42 cases with HCC who were subjected to elective hepatic resection at the National Liver Institute at Menoufia University.

The research has been accepted by the local ethics committee of the National Liver Institute at Menoufia University. A written informed consent has been obtained from all cases before the operation.

Inclusion criteria: All cases that underwent resection (anatomical and nonanatomical) for HCC and cases with CP-A liver function.

Operational design

Preoperative evaluation: All cases were subjected to: Full history taking, laboratory studies, and imaging studies, including: computed tomography to confirm the diagnosis of a hepatic lesion, computed tomography volumetric study when needed for assessing residual liver volume specifically when more than two segments is planned for resection, a dynamic abdominal MRI in doubtful cases, and an upper GI endoscopy to detect varices and the need for endoscopic management.

Biopsy is taken when two radiological modalities are not conclusive, and the nature of the lesion needs histopathological examination, most commonly happens in small lesions, where biopsies frequently become mandatory, or in larger hypovascularized lesions. It provides detailed histological information, which is crucial for planning surgery and predicting outcomes.

Albumin-bilirubin (ALBI) grade[8]

The ALBI score has been evaluated utilizing the following formula: [log10 bilirubin (μmol/l) x0.66]+[albumin (g/l) x -0.085]. Cases were then divided into three groups regarding the ALBI score: Grade 1: ALBI less than or equal to -2.60, Grade 2: -2.59 less than or equal to ALBI less than or equal to -1.39 and Grade 3: ALBI greater than -1.39.

Liver resection technique

The right subcostal incision with midline extension (Kehr's or j-shaped incision) was the preferred approach. Mobilization of the liver has been carried out by dividing the falciform, triangular, and coronary ligaments. Further intraoperative US was used for detecting tumor sites, proximity to vessels, excluding tumor multiplicity, and guiding the resection planes. Hilar dissection with inflow control ligation of the hepatic artery branches, portal vein, as well as bile ducts was performed according to the planned type of hepatic resection. In general, anatomical resections were selected according to size and site when the future liver residual was sufficient; or non-anatomical resections were utilized. LRs were categorized as minor (two or fewer segmentations) or major (more than two segmentations) in accordance with Couinaud's classification[9]. Parenchymatous dissection has been performed utilizing either the harmonic scalpel (HARMONIC ACE+ Shears using GEN11 Generator, Ethicon Johonson and Johonson) or clamp crush method, with the objective of ensuring a safety margin of a minimum of 2 cm. Hemostasis was done using spray diathermy and an Argon beam coagulator (VIO 300 D/APC 2, erbe) with ligation of sizable branches of blood vessels and bile ducts with Liga-clips (LT202 Ethicon Johonson and Johonson), ligatures, or sutures. Closure of the wound after inserting drains in the dependent areas and close to cut surfaces.

Postoperative course

Patients were regularly referred to the ICU for at least one day after surgery, monitoring various parameters like pulse, blood pressure, respiratory rate, oxygen saturation, urine output, C.V.P., and drain output. Daily blood complete blood count, serum creatinine, serum albumin, serum bilirubin, and INR were obtained. Portable chest radiography were ordered when necessary. After stabilization, patients were transferred to the general ward, where deep venous thrombosis prophylaxis was performed using elastic stockings. Enteral feeding was mostly initiated on the first postoperative day (POD), and drains were removed based on color and output.

Posthepatectomy liver failure is diagnosed according to ISGLS definition as the impairment of the liver's synthetic (INR), excretory (bilirubin), and detoxifying functions.

Group	Clinical description	Diagnosis	Symptoms
A	Impaired liver function	-Urine Output >0.5 mL/kg/h -BUN <150 mg/dl -Oxygen saturation >90% -INR <1.5	None
B	Deviation from the expected postoperative course, no need for invasive support	-Urine Output ≤0.5 ml/kg/h -BUN <150 mg/dl - Despite the oxygen supply oxygen saturation <90% -INR ≥1.5, <2.0	-Acid -Weight gain -Mild respiratory failure -Confusion -Encephalopathy
C	Multiple organ failure requiring invasive support	-Urine output ≤0.5 ml/kg/h -BUN ≥150 mg/dl - Despite high fractionated oxygen support oxygen saturation ≤85% -INR ≥2.0	- Kidney failure - Hemodynamic instability - Respiratory failure - Massive ascites -Encephalopathy

Also, the posthepatectomy bile leak is diagnosed according to the ISGLS definition, total bilirubin levels in the abdominal drain fluid of three times the serum concentration from the third POD onwards, or the need for interventional or operative treatment of biliary collections, or biliary peritonitis were considered as bile leaks. Leaks were categorized in three grades of severity: grade A required no change in patient management and intraoperatively placed drains were left no longer than POD 7; grade B involved therapeutic interventions different from surgery or retaining intraoperatively placed drains for more than 7 days; grade C leaks were surgically treated by reoperation.

Statistical analysis

The SPPS medcalc ed 26.0 software, IBM, Chicago, IL, Microsoft Excel 2016, and MedCalC program software version 19.1 were utilized to tabulate and statistically analyze the data gathered. For numerical parametric data, descriptive statistics were computed as the mean±SD (standard deviation) and the minimum and maximum of the range. For numerical nonparametric data, the median and 1st and 3rd interquartile ranges were computed. Categorical data were computed as numbers and percentages. The association among the categorical target variable and one or more independent variables was assessed using logistic regression. It is beneficial in conditions where the target variable's outcome might be classified into only two probable categories. The receiver operating characteristic curve is an efficient method to assess the sensitivity and specificity of quantitative diagnostic measures that classify cases into one of two groups.

RESULTS:

Patients' ages varied between 19 and 77 years, with the mean age±SD being 59.0±11.53 years. There was a higher prevalence of men (66.7%) overweighing women (33.3%), with a male-to-female ratio of 2 : 1. The mean BMI±SD was 23.45±3.64 kg/m^2 and ranged from 19 to 32 kg/m^2 (Table 1).

The majority of cases underwent open-approach procedures: 39 (92.9%) cases, minor resections: 35 cases (83.3%) and anatomical resections (4 cases of formal Lt. hepatectomies, 3 formal Rt. Hepatectomies, 14 Lt. lateral, 2 Rt posterior segmentectomies, 3 segmentectomies): 26 (61.9%) cases.

Operative time ranged between 1.5 and 6 h. Blood transfusions were done in 9 (21.4%) cases. The mean blood loss was 240.24±177.5 ml. Bleeding was the commonest complication that occurred intraoperatively, as it occurred in 6 (14.3%) cases. Intraoperative mortality was not reported in any case (Table 2).

Posthepatectomy liver cell failure was diagnosed in 9 (21.4%) cases, seven of them had grade A and two had grade B. All of them recovered with supportive and medical treatment with a mean hospital stay of 21±9 days. In addition, bile leaks were diagnosed in 6 (14.3%) cases. A superficial incisional infection was reported in 6 (14.3%) cases. Respiratory and renal complications were encountered in one case. The mean hospital stay was 10.74±6.74 days and ranged from 3 to 30 days (Table 3).

There was significant relation between Bile leak grade and ALBI score (Table 4).

In univariate analysis, a Major complication, a higher ALBI score, operation length, blood loss, and hospital stay were positively correlated with an increased risk of liver cell failure. In multivariate analysis, using a model adjusted for the previously mentioned parameters, it was found that the ALBI score can be utilized as an independent predictor of liver cell failure (Table 5).

In univariate analysis: higher ALBI score, albumin, bilirubin, MELD score, CHILD score, and hospital stay were positively correlated with an increased bile leak. In multivariate analysis, using a model adjusted for the previously mentioned parameters, it was found that the ALBI score and bilirubin can be used as independent predictors of bile leakage (Table 6).

The ALBI score had 66.7% sensitivity and 93.9% specificity at a threshold value of greater than 2 with the area under the curve (AUC)=0.825 and was highly significant (*P=0.001*). The CHILD score had a 55.6% sensitivity and 75.8% specificity at a threshold value of greater than 5% with AUC=0.640 and was nonsignificant (*P=0.136*). MELD score at a threshold value of 8.35 had 100% sensitivity and 21.2% specificity, with AUC=0.519, and was nonsignificant (*P=0.868*) (Table 7).

Table 1: Baseline characteristics of the examined cases

Parameters	Examined cases (*n*=42) *N* (%)
Sex	
Male	28 (66.7)
Female	14 (33.3)
Age (years)	
Mean±SD	59.0±11.53
Median	61.5
Range	19.0–77.0
BMI (Kg/m^2)	
Mean±SD	23.45±3.64
Median	23.0
Range	19.0–32.0

%, percentage; n, number; SD, standard deviation.

Table 2: Distribution of examined cases regarding operative data

Parameters	Examined cases (n=42) N (%)
Procedure	
Open	39 (92.9)
Laparoscopic	3 (7.1)
Liver resection category	
Minor	35 (83.3)
Major	7 (16.7)
Resection type	
Anatomical	26 (61.9)
Nonanatomical	16 (38.1)
Operation length (hours)	
Mean±SD	3.1±0.97
Median	2.92
Range	1.5–6.0
Blood loss (ml)	
Mean±SD	240.24±177.5
Median	200
Range	0–600
Blood transfusion units	
No	33 (78.6)
1 unit	2 (4.8)
2 units	6 (14.3)
3 units	1 (2.4)
Intraoperative complications	
No	36 (85.7)
Bleeding	6 (14.3)
Intraoperative mortality	
No	42 (100.0)
Yes	0

%, percentage; n, number; SD, standard deviation.

Table 3: Distribution of examined cases regarding postoperative data

Parameters	Examined cases (n=42) N (%)
Post hepatectomy liver failure	
No	33 (78.6)
Yes	9 (21.4)
Bile leak grade	
No	36 (85.7)
Yes	6 (14.3)
Surgical site infection	
No	36 (85.7)
Superficial incisional	6 (14.3)
Respiratory complications	
No	41 (97.6)
Yes	1 (2.4)
Renal complications	
No	41 (97.6)
Yes	1 (2.4)
Hospital-stay (days)	
Mean±SD	10.74±6.74
Median	8.0
Range	3–30

%, percentage; n, number; SD, standard deviation.

Table 4: Relation between Bile leak grade and ALBI score

	Bile leak grade		
ALBI score Mean±SD	No	A	B
	−2.8±0.6	−2.0±0.4	−1.8±0.9
P value		0.006	

SD, standard deviation.

Table 5: Univariate and multivariate regression analysis for factors predicting LCF

	Univariate				Multivariate			
			95% CI				95% CI	
Parameters	*P* value	Odds ratio (OR)	Lower limit	Upper limit	*P* value	Odds ratio (OR)	Lower limit	Upper limit
Age	0.742	1.012	0.943	1.085				
Sex (male)	0.429	1.840	0.407	8.328				
BMI	0.110	0.797	0.604	1.053				
Minor complication	0.59	1.15	0.65	1.88				
Major complication	**<0.001**	2.09	1.48	2.69	0.09	1.04	0.786	1.120
Albumin	0.109	0.344	0.093	1.268				
Bilirubin	0.792	1.060	0.689	1.629				
ALBI score	0.**005**	11.525	2.085	63.700	0.**022**	1.296	1.038	1.619

Lesion size	0.381	1.099	0.889	1.359				
Operation length (h)	0.**006**	4.990	1.581	15.753	0.559	1.702	0.286	10.122
Blood loss	0.**004**	1.007	1.002	1.011	0.923	1.088	0.198	5.988
MELD Score	0.578	0.806	0.376	1.726				
CHILD score	0.378	1.582	0.570	4.392				
Hospital-stay (days)	0.**002**	1.302	1.106	1.533	0.182	1.006	0.997	1.015

B, Regression coefficient; CI, Confidence interval; S.E., Standard error.

Table 6: Univariate and multivariate regression analysis for factors predicting bile leak

	Univariate				Multivariate			
			95% CI				95% CI	
Parameters	*P* value	Odds ratio (OR)	Lower limit	Upper limit	*P* value	Odds ratio (OR)	Lower limit	Upper limit
Age	0.**042**	0.931	0.869	0.998				
Sex (male)	0.110	0.797	0.604	1.053				
BMI	0.267	1.137	0.906	1.427				
Albumin	0.**029**	0.129	0.020	0.813	0.239	0.266	0.029	2.412
Bilirubin	0.**012**	55.942	2.390	1309.242	0.**026**	38.486	1.561	949.037
ALBI score	0.**012**	13.982	1.795	108.946	0.**032**	3.934	1.123	13.783
Lesion size	0.114	1.215	0.954	1.547				
Operation length(h)	0.524	1.313	0.569	3.028				
Blood loss	0.883	1.000	0.996	1.005				
MELD Score	0.**023**	3.082	1.170	8.114	0.588	1.645	0.272	9.949
CHILD score	0.**041**	3.741	1.053	13.291	0.065	3.454	0.925	12.896
Hospital-stay (days)	0.**049**	1.122	1.000	1.259	0.078	1.124	0.987	1.280

Table 7: Validity (area under the curve, sensitivity, specificity) for ALBI score, MELD Score and CHILD score to detect liver cell failure

	Best cut off	Sensitivity	Specificity	PPV	NPV	AUC	*P* value
ALBI score	2.0	66.7%	93.9%	91.6%	73.8%	0.825	**0.001**
Child score	5.0	55.6%	75.8%	69.7%	63%	0.640	0.136
MELD score	8.35	100%	21.2%	56%	100%	0.519	0.868

AUC, area under the curve; NPV, negative predictive value; *P value*, Probability value; PPV, positive predictive value.
*Statistically significant at *P* less than or equal to 0.05.

DISCUSSION

Regarding demographic data of the studied patients, it has been revealed that the mean age of the patients was 59.0±11.53 years, with the majority of males (66.7%) having a mean BMI of 23.45±3.64 kg/m^2.

In accordance with the present research, Sun *et al*.,[10] enrolled 2,301 patients with HCC and revealed that the average age was 50.9±10.8 years, with the majority of males being 86%.

As regard operative data, an open approach was performed in 39 (92.9%) cases, while only 3 cases were performed by laparoscopy. Minor resections were performed in 35 (83.6%) cases, while major resections were done in 7 (16.7%) cases. Anatomical resections have been carried out in 26 (61.9%) cases, while nonanatomical resections were done in 7 (16.7%) cases. Operative time ranged between 1.5 and 6 h. Blood transfusions were done in 9 (21.4%) cases. The mean blood loss was 240.24±177.5 ml. Intraoperative complications were encountered in 33 (27.5%) cases. Bleeding was the commonest complication that occurred intraoperatively, as it occurred in 6 (14.3%)cases and one of them was converted from a laparoscopic to an open procedure. Intraoperative mortality was not reported in any case.

Comparable with the current study, Shehta *et al*.[3] enrolled 268 cases that underwent 1ry liver resection for pathologically confirmed hepatocellular carcinoma; the majority were Child–Pugh grade A (97.4%), cirrhosis was found in (94.8%), a single tumor was found in 90.3% of patients, while the rest had multiple tumors; the mean tumor size was 6 (1.7–20) cm. Open resection has been carried out in most cases (97.8%); minor resection has been carried out in most cases (78.4%). The median operation time was 3 (1.2–7) h, and the mean intraoperative blood loss was 700 (100–6000) cm. Intraoperative blood transfusions were performed in 133 (49.6%) patients.

Posthepatectomy liver cell failure was diagnosed in 9 (21.4%) cases, and seven of them had grade A. In addition, bile leaks were diagnosed in 6 (14.3%) cases. It was managed conservatively in four cases, while the remaining two cases required ERCP. A superficial incisional infection was reported in 6 (14.3%) cases that were managed conservatively with proper antibiotics. Respiratory and renal complications were encountered in one case. The mean hospital stay was 10.74±6.74 days and ranged from three days to 30 days.

Wang *et al*.,[11] revealed that of the 1242 cases, 643 (51.8%) had one or more complications following surgery. Pleural effusion was the most prevalent complication, affecting 197 (15.9%) cases. Ascites happened in 185 (14.9%) cases, and PHLF happened in 166 (13.4%) cases. Grade A posthepatectomy liver failure was observed in 58 (4.7%) cases, grade B in 91 (7.3%), and grade C in 17 (1.4%). The mortality rate following surgery was 1.0% (12 patients).

This study reported that there was a significant relation between Bile leak grade and ALBI score. Our findings were in line with Andreatos *et al*.,[12] who demonstrated that ALBI score was significantly associated with bile leak (grade 1, 7.1%; grade 2, 11.5%; grade 3, 14.0%; *P < 0.001*).

In univariate analysis, a higher ALBI score, operation length, blood loss, and hospital stay were positively correlated with an increased risk of liver cell failure. In multivariate analysis, using a model adjusted for the previously mentioned parameters, it was found that the albumin-bilirubin score can be utilized as an independent predictor of liver cell failure.

In concordance with the current study, Park *et al*.,[12] enrolled 101 patients who had HCC and underwent hepatectomy. PHLF was observed in 32 (31.7%) cases. The multivariable analysis indicated the ALBI score (OR 2.83; 95% CI 1.22–6.55; *P=0.015*) and ALBI grade (OR 2.86; 95% CI 1.08–7.58; *P=0.035*) as independent indicators of PHLF.

In univariate analysis, a higher ALBI score, albumin, bilirubin, MELD score, CHILD score, and hospital stay were positively correlated with an increased bile leak. In multivariate analysis, using a model adjusted for the previously mentioned parameters, it was found that the ALBI score and bilirubin can be used as independent predictors of bile leak.

In concordance with the current study, Andreatos *et al*.,[13] reported that MELD was not correlated with bile leak (MELD <10, 8.4%; MELD ≥10, 11.2%; *P=0.13*), while albumin-bilirubin was (grade 1, 7.1%; grade 2, 11.5%; grade 3, 14.0%; *P<0.001*). Based on multivariable analysis, the development of a BL was related to ALBI grade 2/3 (OR 1.35, 95% CI 1.02–1.80; *P=0.04*). Also, univariate and multivariate analyses demonstrated that higher operation length and blood loss were independent predictors of an increased risk of bile leak.

The ALBI score had 66.7% sensitivity and 93.9% specificity at a threshold value of greater than 2 with AUC=0.825 and was highly significant (*P=0.001*). The CHILD score had a 55.6% sensitivity and 75.8% specificity at a threshold value of greater than 5% with AUC=0.640 and was nonsignificant (*P=0.136*). MELD score at a threshold value of 8.35 had 100% sensitivity and 21.2% specificity, with AUC=0.519, and was nonsignificant (*P=0.868*).

In concordance with the current study, Zou *et al*.,[14] revealed that the area under the curves for the MELD score, Child–Pugh score, ICG R15, and ALBI score to anticipate post-hepatectomy liver failure was 0.665, 0.649, 0.668, and 0.745, respectively. The albumin-bilirubin score demonstrated that PHLF had a superior predictive value compared with the Child–Pugh score, MELD score, and ICG R15.

Moreover, Park *et al*.,[12] showed that the AIBL score's area under the receiver operating characteristic curve was 0.676 (95% CI 0.566–0.785). The best cutoff value of the ALBI score to detect PHLF was –2.62, with a specificity of 56.5% and a sensitivity of 75.0%.

CONCLUSION

The ALBI score demonstrated greater predictive value for liver cell failure compared with the Child–Pugh score and the MELD score. The ALBI score as well as bilirubin can be used as independent predictors for liver cell failure and bile leak post hepatic resection in HCC patients.

CONFLICT OF INTEREST

There are no conflicts of interest.

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