

ORIGINAL ARTICLE

A comparative study on postoperative mortality prediction of SFLI scoring system and Child-Pugh classification in patients with hepatocellular carcinoma

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Summary

Purpose: In our previous study, we have established the clinical significance of the SFLI (scoring formula of liver injury), the purpose of this study was to compare the SFLI system and the Child-Pugh grading system in the prediction of postoperative mortality in patients with hepatocellular carcinoma (HCC).

Methods: 114 patients with HCC who underwent surgical treatment were enrolled. According to the requirement of the indicators for the Child-Pugh classification, various indices (including albumin [ALB], total bilirubin [TBIL], prothrombin time [PT], ascites, and hepatic encephalopathy) were considered in these patients before surgery, and then Child-Pugh grading was performed. Similarly, the serum biochemical markers including ALB, pre-albumin (PA), TBIL, serum creatinine (SCR), international normalized ratio (INR), alanine transaminase (ALT), aspartate transaminase (AST), γ -glutamyl transpeptidase (γ -GT), alkaline phosphatase (ALP), PT, activated partial thromboplastin time (APTT), and thrombin time (TT) were collected before surgery for SFLI analysis. The predicted postoperative mortality rates of these two scoring models and their diagnostic efficacy were analyzed and compared.

Results: According to the Child-Pugh grading system, in level A, B and C were 75, 35, and 4 cases respectively, and the corresponding mortality rates were 1.3% (1/75), 17.1% (6/35) and 75% (3/4). Meanwhile, according to the SFLI classification, the number of patients in the grade I, I+, II, and III were 36, 29, 28, and 21, respectively, and the corresponding mortality rates were 0, 0, 14.3% (4/28), and 28.6% (6/21), respectively. The patient mortality rate increased significantly with increasing grading ($p < 0.01$). These two classification methods were further compared using ROC analysis, in which the area under the curve (AUC) for the Child-Pugh method was 10.2% with a 95% confidence interval (95% CI) 17-18, and the AUC of SFLI was 88.2% with a 95% CI 80-96.

Conclusion: The SFLI scoring system is very useful in the assessment of liver function and postoperative mortality, and its grading standard is much better than the traditional Child-Pugh classification in many aspects.

Key words: Child-Pugh classification, hepatocellular carcinoma, liver reserve function, SFLI scoring system

Introduction

Surgical liver resection is an important method for the treatment of liver diseases, especially for HCC, but liver damage and liver dysfunction of the patients after resection become an important

cause of patient's death [1-3]. Therefore, an accurate preoperative evaluation of liver reserve function is needed for the selection of a reasonable treatment to ensure the safety of liver resection

and to control the bleeding and systemic infection in order to reduce postoperative failure.

There are many methods existing for the evaluation of liver reserve function in clinical practice, among which the traditional Child-Pugh classification method is widely used [4-8]. The Child-Pugh method can accurately assess the conditions of liver damage and liver reserve function in the final stage of cirrhosis, as well as the short-term survival rate of patients with end-stage of HCC.

On the other hand, serum biochemical tests are widely used in the clinic, by which the activities of different enzymes and the contents of dedicated compounds in serum are measured [9]. The serological methods can reflect the synthesis and secretion function of the liver during liver damage and have become the most common and mature methods used to assess liver reserve function [10].

Nonetheless, it is hard to assess the liver reserve function from a single biochemical indicator, since it could be easily affected by other diseases. Therefore, we recently established a Scoring Formula of Liver Injury (SFLI) by combining various biochemical indicators. In the process of constructing the SFLI mathematical scoring formula, we first introduced the "matter element analysis method" into the field of medical liver injury scoring formula for the first time. Matter element analysis method is used in our research to solve the weight problem of each test index in the SFLI scoring formula which was shown to be effective in assessing liver function [11].

In order to confirm that SFLI could accurately and efficiently assess the preoperative liver damage and liver reserve function, and to provide a reference for clinical evaluation and treatment, in this study we compared the SFLI method with the traditional Child-Pugh classification method to predict the postoperative mortality of HCC patients. As a result, we found that the SFLI scoring system is very useful in the assessment of liver reserve function and postoperative mortality, and its grading standard is much better than the traditional Child-Pugh classification in many aspects.

Methods

Case selection criteria and grouping

HCC patients who had undergone liver resection at the First Clinical Medical College of China, Three Gorges University, were enrolled in this study. One hundred and fourteen patients were admitted from December

2011 to December 2013. All patients were subjected to routine diagnostic tests and the sero-clinical indicators were collected for the Child-Pugh classification method (ALB, TBIL, PT, ascites, and hepatic encephalopathy) and the SFLI method (ALB, PA, TBIL, SCR, INR, ALT, AST, γ -GT, ALP, PT, APTT, and TT).

Child-Pugh score

The grade of hepatic encephalopathy, severity of ascites, TBIL, ALB and PT were selected as the evaluation indices, and the liver function was classified as Child-Pugh grade A (5-6 points), grade B (7-9 points), or grade C (≥ 10 points). The detailed Child-Pugh scoring criteria are shown in Table 1.

SFLI score

In our previous study, the matter element analysis method was applied to clinical liver damage assessment for the first time, and we have successfully established a scoring formula named SFLI [11]. The matter element analysis method was mainly used to solve the weight of each measurement indicator in the SFLI scoring formula. The detailed method was as follows:

Table 1. The Child-Pugh scoring criteria

Index	A	B	C
Total bilirubin ($\mu\text{mol/L}$)	<34	34-51	>51
Albumin (g/L)	>35	28-35	<28
Prothrombin time (s)	1-3	4-6	>6
Ascites	none	light	medium
Hepatic encephalopathy (grade)	none	1-2	3-4

(1) Construction of matter element. The range of patient age analyzed was T_m , each indicator was C_n and the measurement data were X_{ji} ($j=1, 2, y, m; i=1, 2, y, n$). The following matter elements were successfully constructed:

	T1	T2	...	T_m	
C1	X11	X21	...	X_{m1}	
Rmn=	C2	X12	X22	...	X_{m2}
	
	Cn	X1n	X2n	...	X_{mn}

Where T represents the patient age range, C represents each measurement indicator, X represents measurement data and Rmn represents the variant symbol.

(2) Determination of the membership degree (U). In order to determinate the weight of each indicator in SFLI, a standard measurement should be obtained. This standard was carried out using the membership degree

(U) as following method:

Indicators with small measurement values gave better results:

$$U_j = \frac{\max X_{ji} - X_{ji}}{\max X_{ji} - \min X_{ji}}$$

Indicators with great measurement values gave better results:

$$U_j = \frac{X_{ji} - \min X_{ji}}{\max X_{ji} - \min X_{ji}}$$

where max X_{ji} and min X_{ji} represent the corresponding maximum and minimum values of X_{ji} in each group classed by age respectively.

(3) Conversion of the membership degree into relevance. As the correlation coefficient (x) is equivalent to the membership function, the correlation coefficient x_{ji} could be determined from the membership coefficient U_{ji}, namely: x_{ji}=U_{ji} (j=1, 2, y, m; i=1, 2, y, n).

(4) Establishment of the fuzzy matter element:

	T1	T2	...	Tm
C1	ξ11	ξ21	...	ξm1
Rξ= C2	ξ12	ξ22	...	ξm2
...
Cn	ξ1n	ξ2n	...	ξmn

Where R is the variant symbol, ξ are the correlation coefficients, C_n are the measurement indicators, n=1,2... and m=1,2...

(5) Solving the weight for each indicator in the SFLI. W_j represents the weight for each indicator:

$$W_j = \frac{\sum_{j=1}^m \xi_{ji}}{\sum_{j=1}^n \sum_{i=1}^m \xi_{ji}}$$

and

$$R_w = \frac{C_1}{W_1} \frac{C_2}{W_2} \dots \frac{C_n}{W_n}$$

The serum markers ALB, PA, TBIL, SCR, INR, ALT, AST, γ-GT, ALP, PT, APTT, and TT were used to construct SFLI using the matter element method [11]. The formula is shown below (Equation 1), in which R represents the final score of SFLI. Accordingly, the liver function was classified into four levels: SFLI level I: 0.770 ≤ R < 1; level I+: 0.712 ≤ R < 0.770; level II: 0.629 ≤ R < 0.712; and level III: 0.401 ≤ R < 0.629.

Equation 1

$$R = \frac{0.0779 * (ALB - 33.51)}{1.91} + \frac{0.0996 * (PA - 105.59)}{26.89} + \frac{0.0979 * (59.05 - TBIL)}{36.56} + \frac{0.072 * (84.55 - SCR)}{20.67} + \frac{0.0844 * (1.25 - INR)}{0.14} + \frac{0.0919 * (63.88 - ALT)}{21.6} + \frac{0.0711 * (89.83 - AST)}{35.23} + \frac{0.0601 * (129.15 - rGT)}{36.99} + \frac{0.0935 * (146.02 - ALP)}{25.92} + \frac{0.0926 * (14.11 - PT)}{4.48} + \frac{0.074 * (36.78 - APTT)}{4.48} + \frac{0.0789 * (17.68 - TT)}{25.92}$$

Statistics

Data were analyzed using SPSS 18.0 software. The measured data were presented as mean ± standard deviation, and the count data were compared using the chi-square test. The diagnostic performance for postoperative mortality of these two assessment models was analyzed using ROC analysis with a significance level α = 0.05.

Results

As shown in Table 2, among the 114 patients enrolled in this study, the number of patients of the Child-Pugh class A, B and C were 75, 35 and 4, respectively, and the corresponding mortality rates were 1.3, 17.1 and 75%. As for the SFLI scoring system, the number of patients in SFLI level I, I⁺, II and III were 36, 29, 28 and 21 respectively,

Table 2. The predicted postoperative mortality in Child-Pugh and SFLI

Scoring system	Patients, n	Postoperative mortality n (%)	p value
Child-Pugh			
A	75	1 (1.3)	< 0.01
B	35	6 (17.1)	
C	4	3 (75.0)	
SFLI			
I	36	0 (0)	< 0.01
I ⁺	29	0 (0)	
II	28	4 (14.3)	
III	21	6 (28.6)	

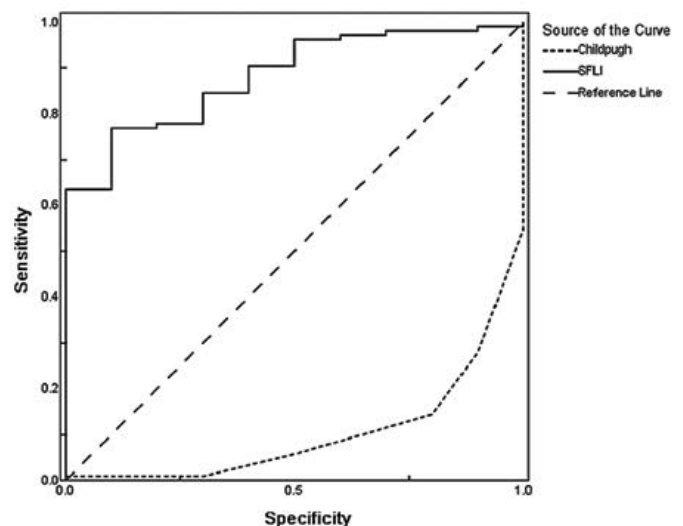


Figure 1. ROC curves of the diagnostic performance for postoperative mortality in Child-Pugh and SFLI. The area under the ROC curve is correlated with the diagnostic accuracy. As a result, the SFLI formula showed better sensitivity and specificity in the prediction compared with Child-Pugh score formula.

with the corresponding postoperative mortality rate being 0, 0, 14.3 and 28.6%. In both scoring systems, the increase in the scores indicated elevated postoperative mortality rate ($p < 0.01$).

As shown in Figure 1, the two evaluation systems were further compared with ROC analysis. The AUC of the Child-Pugh classification system was 10.2%, with a 95% CI of 17-18. And the AUC of the SFLI system was 88.2%, with its 95% CI being 80-96.

Discussion

Liver reserve function quantifies the synthetic function of the liver, and is an important factor affecting the safety of liver surgery. A widely used method to evaluate liver function is the Child-Pugh classification system, in which the liver function is classified into three levels from A to C. The Child-Pugh method is powerful, but has some limitations in the clinic, including lack of continuity, having a clear dome effect, difficulty in making correct classification of ascites and hepatic encephalopathy, and lacking comparability [12]. Instead, we recently developed an objective scoring formula called SFLI to evaluate liver function based on the serum biochemical indicators [11]. In the SFLI method, the liver function falls in one of the following four SFLI levels: I, I⁺, II, and III, with the level III indicating severe liver cirrhosis decompensated stage and ascites.

To evaluate the value of SFLI method in assessing liver reserve function, we compared the SFLI method and the Child-Pugh method in this study. Our data showed that the Child-Pugh method could hardly to accurately predict the surgery

safety since even the lowest risk level A had 1.3% mortality rate. However, SFLI method was better in predicting the surgery safety. One reason was that the SFLI method was able to classify the Child-Pugh level A patients into the SFLI level I⁺ or II, which indicated that the SFLI method is more continuous and therefore more accurate than the Child-Pugh method. The ROC curves further showed that the SFLI method had higher specificity and sensitivity in discriminating postoperative mortality.

Compared to the Child-Pugh method, the SFLI method is more indicative and accurate, having better continuity in the classification, and is more effective in assessing the postoperative prognostic situation. Containing a lot of important serological indicators, the SFLI method could be applied in the evaluation of chronic liver damage, disease-related liver damage, and the liver reserve function in liver cirrhosis and HCC. We hope the SFLI method, complementary to the traditional Child-Pugh classification system, would be a useful tool in clinic trials for evaluating liver function and postoperative mortality.

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Conflict of interests

The authors declare no conflict of interests.

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