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Original Article

MELD score is the better predictor for 30-day mortality in patients with ruptured hepatocellular carcinoma treated by trans-arterial embolization

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Abstract: Background and Aims: Spontaneous hepatocellular carcinoma (HCC) rupture is a catastrophic life-threatening complication that could be rescued by trans-arterial embolization (TAE). However, deteriorated liver function with total bilirubin more than 3 mg/dL was deemed as a relative contraindication. This study was aimed to re-evaluate this relative contraindication. Methods: Patients with ruptured HCC and treated by TAE between February 2005 and December 2016 in Chang Gung Memorial Hospital, Linkou branch were recruited. Pre-TAE characteristics including age, gender, etiology, liver biochemistry, Child-Pugh classification, Model for End-Stage Liver Disease (MELD) score, the presence of shock, tumor staging and post TAE liver function were compared between patients with and without post-TAE 30-day mortality. Results: A total of 186 patients were enrolled. The successful hemostatic rate after embolization was 91.4% and the median overall survival was 224 days. The 30-day cumulative mortality rate is 20.4%. By multivariate logistic regression analysis, male [aOR: 0.25, P=0.034] MELD score [aOR: 13.61, P<0.001], tumor size [aOR: 1.21, P=0.023] are the independent predictors for 30-day mortality. MELD score has better predictability of post-TAE 30-day mortality than total bilirubin level (AUROC: 0.818 vs. 0.668). The cut-off points of MELD score 13 has higher negative predictive value of 95% for post-TAE 30-day mortality. Conclusion: TAE is effective for the initial hemostasis in patients with HCC rupture. MELD score ≥13 rather than only total bilirubin level >3 mg/dL be more predictive of post TAE 30-day mortality.

Keywords: Hemoperitoneum, spontaneous rupture of hepatocellular carcinoma, acute abdominal bleeding, mortality

Introduction

Hepatocellular carcinoma (HCC) is the sixth most common primary liver tumor and the fourth leading cause of cancer-related deaths worldwide [1-3]. Spontaneous HCC rupture with intraperitoneal hemorrhage, incidence ranged from 3-14.5%, is a catastrophic life-threatening complication which ranked the third leading cause of death in HCC patients [4-9]. Despite the decreased incidence of spontaneous HCC rupture due to HCC surveillance program [10] which improve early detection rate, the mortality rate within 30 days of HCC rupture remains high up to 34-71% with median survival duration of 7-21 weeks [11-13].

The primary therapeutic goal in these patients is to achieve stable hemodynamic status rather than anti-cancer treatment. Trans-arterial embolization (TAE) is an efficient and well-tolerated approach to stop tumor bleeding [14-20]. A deteriorated liver function, such as hyperbilirubinemia (total bilirubin level >3.0 mg/dL or >50 μmol/L), was considered as a relative contraindication for TAE in patients with HCC rupture due to high risk of hepatic failure and mortality [15, 18]. However, this cut-off value was derived from two cohorts of less than 50 cases 20 years ago. Since the advance in TAE technique, whether the use of total bilirubin level >3.0 mg/dL alone still being a contraindication or predictive of adverse outcome nowadays is

questionable. Since HCC rupture is a catastrophic event which usually accompanied with shock, hypoperfusion and multi-organ dysfunction, nearly half of the morality cases occur in the first month [17, 21]. In this study, we aims to investigate the predictors of 30-days mortality and compare different prognostic scores in predicting mortality of patients with ruptured HCC receiving TAE.

Material and methods

Patient recruitment

One hundred and eighty-six spontaneous HCC rupture patients receiving trans-arterial embolization between February 2005 and December 2016 in Chang Gung Memorial Hospital, Linkou branch were retrospectively recruited. Spontaneous tumor rupture was diagnosed by the clinical presentation of acute onset abdominal pain, distension or hemodynamic instability accompanied with typical radiological evidence of contrast extravasation from liver tumor by abdominal computed tomography and/or collection of bloody aspiration from abdominal paracentesis [22]. Patients who received TAE at other hospital prior to their arrival to our site or the HCC rupture events occur within 1 week of liver tumor biopsy as procedure complication or lacking the image evidence including CT with or without abdominal paracentesis supporting HCC rupture were all excluded from analysis. The study was approved by the institutional review board of Chang Gung Medical foundation (IRB No, 201701160B0).

The procedure of TAE

The TAE was performed via the right femoral artery access. The 4-Fr RH catheter or RC1 catheter (Terumo Corporation, Ashitaka, Japan) was advanced to common hepatic artery or proper hepatic artery, then 2.7-Fr Progreat microcatheter super selectively cannulated via the guiding catheter into the feeding vessel at least at segmental or subsegment level which supplying possible bleeding tumor (extravasation of contrast medium may not be seen usually). Lipiodol injection to partial stasis in vessel (visualized fluoroscopically), then followed gelfoam slurry injection to complete stasis. Whether lipiodol administration was depended on operator's judgement. Because this procedure was aimed to stop bleeding, "super-selective embolization" was applied to de-vascularize the bleeding vessel or tumors. Embolization was super-selectively done in the vessel as near as possible to bleeding tumor in order to decrease the liver parenchyma damage. TAE technique between patients with PVTT or PVTT was almost same due to emergent status of the patients. Presumably, partial devascularization was done in those patients with PVTT. Actually, there is no standard protocol but super-selective TAE is absolutely necessary. The successful embolization was defined as an angiographically completed procedure without any sign of bleeding and with a clinical stabilization of hemodynamic conditions as well as hemoglobin levels within 48 hours after the initial embolization.

Laboratory methods

Pre-TAE variables including age, gender, etiology, clinical symptoms, vital signs at arrival, presence of shock (systolic blood pressure <90 mmHg), liver biochemistry data, prothrombin time, alpha-fetoprotein, baseline white blood count, the nadir of hemoglobin, creatinine, Albumin-Bilirubin (ALBI) score, Child-Pugh score, Model for End-Stage Liver Disease (MELD) scores, interval from HCC rupture to TAE and post-TAE total bilirubin level were analyzed and compared between patients with and without 30-day mortality post TAE.

Statistical analysis and definitions

Continuous data with normally distribution were expressed as the mean ± standard deviation (SD) and were compared using independent student t test/analysis of variance (ANOVA) while non-normally distribution as median (range) and were compared by Manne-Whitney U test. Whether the variables being normally distribution was tested by Shapiroe-Wilk test which *P* value less than 0.05 regarded as non-normally distributed, vice versa. Categorical variables were compared using the χ^2 test or Fisher's exact test. Logistic regression model was used to identify predictors for 30-day mortality. Receiver operating characteristic (ROC) curve was used to evaluate the predictor of 30-day mortality. The best cut-off value of MELD score, Child-Pugh score, ALBI score and total bilirubin were obtained by Youden Index. All analysis was carried out using the SPSS v. 20 statistical packages (SPSS Inc., Chicago, IL), $P<0.05$ was considered statistically significant.

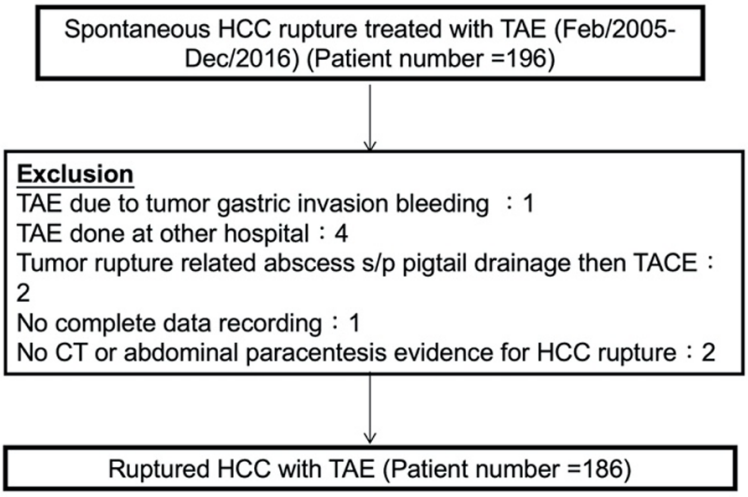

Figure 1. Flowchart of patient recruitment. Abbreviations: HCC-hepatocellular carcinoma; TAE-trans-arterial embolization; TACE-trans-arterial chemoembolization; CT-Computed tomography.

Result

Pre-TAE characteristics of patients with spontaneous ruptured HCC

A total of 186 patients with spontaneous ruptured HCC receiving embolization between February 2005 and December 2016 were recruited, as seen in **Figure 1**. One hundred and fifty-two (81.7%) patients were male with mean age of 62 years. Viral hepatitis (HBV: 44.6%, HCV: 28.5% and HBV/HCV co-infection: 2.7%) accounts for the major etiology and 72.6% patients were diagnosed with liver cirrhosis. 37.6% patients belong to Child-Pugh B and 11.8% patients belong to Child-Pugh C. The median MELD score was 12 (range 6-32). Most patients were advanced stage (77%). 57 (30.6%) patients encountered hemorrhagic shock. Macrovascular invasion and distant metastasis occurred in 58 (31.2%) and was noted in 28 (15.4%) patients respectively, as seen in **Table 1**. In current study, 112 patients died during a median of 224 (0-4225) days follow-up which 84 cases (75%) occurred within 1 year and 38 cases (34%) occurred within the 1st month (**Figure 2**).

Trans-arterial embolization hemostatic effect and long-term outcome

The initial presented symptoms in HCC ruptured patients included abdominal pain (93.5%), shock status (30.6%), dizziness and syncope (7%), and conscious change (2.2%). Success hemostasis by trans-arterial embolization was achieved in 170 (91.4%) patients. Most of the TAE procedure (82.3%) was conducted within three days since the onset of HCC rupture event. During a median of 224 (range 0-4225) days follow-up, one-fifth (N=38, 20.4%) patients died within 30 days post TAE. Tracing the patients who survived more than 30 days, adjuvant anticancer treatments including surgery, trans-arterial chemoembolization, radiotherapy or chemotherapy were provided to prolong the survival.

Among these 38 early mortality patients, 16 (43.2%) patients died of failed hemostasis after TAE, 12 (31.6%) patients died of hepatic failure, 3 (7.9%) died of respiratory failure, 3 (7.9%) died of sepsis, 2 (5.3%) died of gastrointestinal bleeding, 1 (2.63%) died of recurrent HCC rupture after discharge, the rest one patients died of acute renal failure who refused hemodialysis and recurrent HCC rupture at second day post TAE event.

Comparing the 16 patients who failed hemostasis to those stopped bleeding after TAE, these patients have comparable tumor size but higher proportion with multiple tumors (87.5% vs. 60%, P=0.030), initial presentation of shock (87.5% vs. 25.3%, P<0.001), more advanced BCLC staging (BCLC stage C and D: 50% and 43.8% vs. 67.6% and 8.2%, respectively, P<0.001), and higher MELD score as well as Child-Pugh classification (median MELD: 17 vs. 12, and Child-Pugh classification B and C: 37.5% and 56.3% vs. 37.6% and 7.6% both P<0.001) as seen in Supplementary Table 1.

There were only 11 of 186 patients in our study had pre-TAE bilirubin level more than 3 mg/dl. Among these 11 patients, 9 (81.8%) patients had successful hemostasis, numerically lower than that in 161 (92.0%) patients whose pre-TAE serum total bilirubin ≤3 mg/dL though not reaching statistical significance (P=0.410). The cause of death in 6 of the 11 patients whose pre-TAE total bilirubin >3 mg/dL was failed

Table 1. Demographic features of HCC ruptured patients who received TAE and comparison between patients with and without 30-day mortality

Variables	Overall (N=186)	30-Day mortality		*P* value
		No (N=148)	Yes (N=38)	
Age	62.0±13.1	61.74±13.55	62.37±12.17	0.794
Male	152 (81.7%)	126 (85.1%)	26 (68.4%)	0.017
Etiology (HBV/HCV/B+C/Non-B, non-C)	83/53/5/45 (44.6%/28.5%/2.7%/24.2%)	67/42/5/34 (45.3%/28.4%/3.4%/23.0%)	16/11/0/11 (42.1%/28.9%/0%/28.9%)	0.615
Liver cirrhosis	135 (72.6%)	106 (71.6%)	29 (76.3%)	0.563
Child-Pugh classification (A/B/C)	94/70/22 (50.5%/37.6%/11.8%)	88/53/7 (59.5%/35.8%/4.7%)	6/17/15 (15.8%/44.7%/39.5%)	<0.001
MELD score	12 (6-32)	11 (6~24)	18 (10~32)	<0.001
≥13	85 (45.7%)	52 (35.1%)	33 (86.8%)	<0.001
BCLC stage (A/B/C/D)	6/36/123/21 (3.3%/19.7%/66.1%/10.9%)	6/35/100/7 (4.1%/23.6%/67.6%/4.7%)	0/1/23/14 (0%/2.6%/60.5%/36.8%)	<0.001
Tumor number (single/multiple)	70/116 (37.6%/62.4%)	64/84 (43.2%/56.8%)	6/32 (15.8%/84.2%)	0.002
Tumor Max size	8.4 (2~21)	7.75 (2~18)	10.0 (4~21)	0.012
Macrovascular invasion	58 (31.2%)	38 (25.7%)	20 (52.6%)	0.001
Metastasis	28 (15.4%)	19 (12.8%)	9 (23.7%)	0.095
Shock	57 (30.6%)	37 (25.0%)	20 (52.6%)	0.001
Pre-TAE laboratory data				
WBC (mm^3)	11100 (3100-34200)	11100 (3100-32900)	11100 (3700-34200)	0.950
Nadir of Hemoglobin (g/dL)	9.3 (3.4-20.2)	9.35 (5.0-20.2)	9.05 (3.4-14.4)	0.188
Creatinine (mg/dL)	1.15 (0.32-14.63)	1.10 (0.41-14.63)	1.59 (0.32-13.8)	0.021
ALT (U/L)	42 (6-569)	41 (6-569)	44 (15-174)	0.618
Total bilirubin (mg/dL)	1.0 (0.2-19.8)	0.9 (0.2-12.3)	1.55 (0.2-19.8)	0.001
≥3	11 (5.9%)	5 (3.5%)	6 (15.8%)	0.024
Albumin (g/dL)	3.15 (1.46-4.59)	3.26 (1.88-4.59)	2.83 (1.46-4.18)	<0.001
INR	1.2 (0.9-3.2)	1.2 (0.9-3.2)	1.5 (1.0-2.9)	<0.001
AFP (ng/mL)	122 (2-2528998)	91 (2~1172235)	12490 (2~2528998)	0.004
Post-TAE				
Post TAE total bilirubin in 7 days	1.7 (0.3-28.1)	1.6 (0.3-23.6)	6.0 (1.0-28.1)	<0.001
30 days mortality	38 (20.4%)			
Follow up duration (days)	224 (0-4225)			

Abbreviations: BCLC stage: Barcelona Clinic Liver Cancer stage; MELD: Model for End-Stage Liver Disease; Na-MELD score; SIRS: systemic inflammatory response syndrome; WBC: white blood count; Hb: hemoglobin; Cr: creatinine; ALT: alanine aminotransferase; Alb: albumin; ALBI: albumin-bilirubin; INR: international normalized ratio; AFP: α-fetoprotein; TAE: trans-arterial embolization.

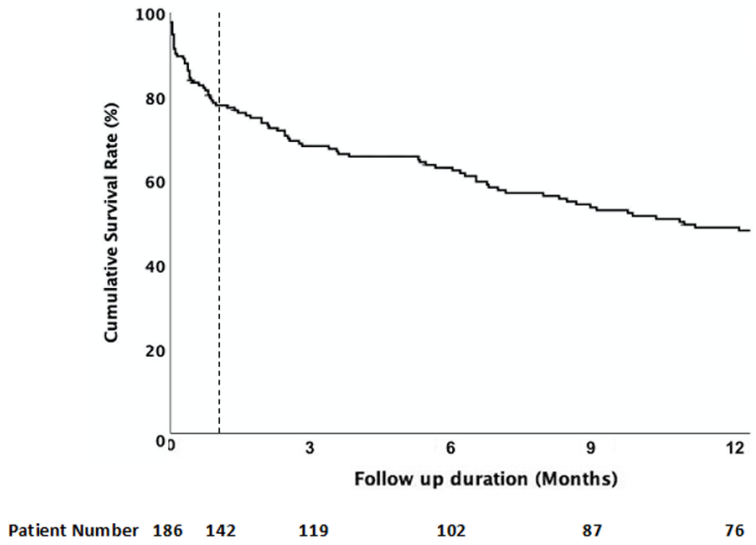

Figure 2. Cumulative survival rate of spontaneous ruptured hepatocellular carcinoma patients.

hemostasis (N=2), liver failure (N=2), renal failure (N=1) and rebreeding after discharge (N=1). The median survival time was shorter in patients whose pre-TAE total bilirubin level >3 mg/dL than those ≤3 mg/dL [25 (2-1019) vs. 236 (0-4225) days, P=0.01]. Two patients with total bilirubin level more than 3 mg/dL survived more than 2 years from HCC rupture event and received subsequent anti-cancer treatment.

Independent factors of post TAE 30-day mortality in HCC ruptured patients

The host characteristics, liver function reserve and HCC staging were compared between ruptured HCC patients received TAE with or without early (<30 days) mortality, as seen in **Table 1**. Pre-TAE variables were comparable between these two groups in terms of age, etiology, cirrhosis, metastasis, the WBC count, the nadir of hemoglobin and ALT level. However, significant higher proportion of patients with advanced Child-Pugh classification, high MELD score, larger tumor size, multiple tumors, high total bilirubin, low albumin, prolonged prothrombin time and advanced HCC stage with vascular invasion were found in the early mortality arm. The presentations with shock at the onset of ruptured HCC were also more frequent in early mortality group (P=0.001).

In multivariate logistic regression analysis, higher MELD score more than 13 [adjusted odds ratio (aOR): 13.61 (95% CI: 3.41~54.28), P<0.001], larger tumor size [aOR: 1.21 (95% CI: 1.03~1.42), P=0.023] were independent predictors for 30-day mortality, as seen in **Table 2**.

The most optimal predicting system for post TAE early mortality in HCC ruptured patients

Three commonly used scoring systems including MELD score, Child-Pugh score and ALBI score were compared for their predictability for post-TAE early mortality (<30 days). The MELD score showed the best Area under the Receiver Operating Characteristic curve (AUROC) as 0.818 (95% CI: 0.750-0.886) followed by Child-Pugh score as 0.799 (95% CI: 0.714~0.884) and ALBI score as 0.757 (95% CI: 0.680~0.834). The AUROC using total bilirubin was only 0.668 (95% CI: 0.558~0.779), significantly lower than that of MELD score (P=0.019) and nearly significantly lower to Child-Pugh score (P=0.055) but similar to ALBI score (P=0.136). There's no statistical difference between AUROC of MELD score and of Child-Pugh score (P=0.372) or ALBI score (P=0.229), as seen in **Figure 3**.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the use of serum total bilirubin >3 mg/dL, MELD score ≥13, Child-Pugh score ≥8 and ALBI score >-1.87 to predict post-TAE 30-day mortality was listed as **Table 3**. Although the use of total bilirubin >3 mg/dL provides highest specificity as 97% yet the sensitivity was lowest among these scores (16%). Taking these information together, MELD score ≥13, Child-Pugh score ≥8 and ALBI score >-1.87 provide good sensitivity and NPV yet MELD score have the highest AUROC than others. The cumulative mortality rate for 30-Day and 1 year in patients with MELD score ≥13 and <13 was 42.9% and 70%, 7.2% and 31.5% respectively (log rank test, P<0.001, as seen in **Figure 4A**). The cumulative mortality rate for 30-Day and 1 year in patients with Child-Pugh score ≥8 and <8 was

Table 2. Logistic regression analysis for independent predictors of 30-day mortality in HCC ruptured patients post TAE

Variables		Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Male (No/%)		0.38 (0.17-0.86)	0.020	0.26 (0.08-0.91)	0.034
Child-Pugh score		1.99 (1.55-2.55)	<0.001		
MELD score	continuous	1.28 (1.17-1.39)	<0.001		
	≥13 points	11.55 (4.25-31.41)	<0.001	13.61 (3.41-54.28)	<0.001
Tumor number (single/multiple)		0.25 (0.10-0.62)	0.003	0.26 (0.07-1.02)	0.053
Tumor Max size		1.15 (1.04-1.26)	0.005	1.21 (1.03-1.42)	0.023
Vascular invasion		3.22 (1.54-6.71)	0.002	2.10 (0.66-6.69)	0.211
Metastasis		2.11 (0.87-5.13)	0.101		
Shock		3.33 (1.59-6.97)	0.001	2.28 (0.74-6.98)	0.150
Pre-TAE					
Creatinine		1.13 (0.94-1.36)	0.184		
Total bilirubin	continuous	1.36 (1.07-1.71)	0.011		
	≥3 mg/dL	5.18 (1.49-18.02)	0.010		
Albumin		0.20 (0.10-0.43)	<0.001	0.39 (0.14-1.07)	0.068
INR		10.42 (3.32-32.75)	<0.001		
AFP		1.00 (1.00-1.00)	0.065		

Abbreviations: BCLC stage: Barcelona Clinic Liver Cancer stage; MELD: Model for End-Stage Liver Disease; SIRS: systemic inflammatory response syndrome; INR: international normalized ratio; AFP: α-fetoprotein; TAE: trans-arterial embolization.

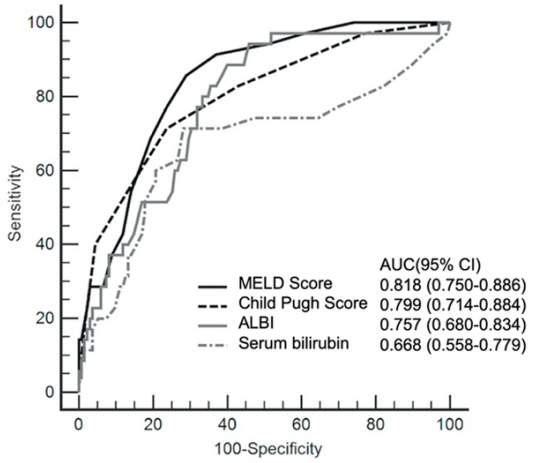

Figure 3. The comparing the Area Under Receiver Operating Characteristic (AUROC) for prediction of post trans-arterial embolization early mortality. Abbreviations: MELD: Model for End-Stage Liver Disease; ALBI: albumin-total bilirubin.

43.9% and 70.2%, 8.8% and 33.6% respectively (log rank test, P<0.001, as seen in **Figure 4B**).

Discussion

This is the largest single-center cohort reporting HCC ruptured patients post TAE outcome. It is important to note that 75% of the overall mortality occurred in the first year while half of these 1-year mortality cases took place in the first month (**Figure 2**). The 30-day mortality rate in current study was 20.4%, not higher than that of 34-71% in previous systemic review and meta-analysis [11-13]. Trans-arterial embolization (TAE) is an effective and well-tolerated treatment for the emergency management of hemoperitoneum especially when hepatic insufficiency or liver cirrhosis [23]. The successful rate of hemostasis was 170 (91.4%) among 186 patients. Since 16 of the 38 (42.1%) early mortality patients died of uncontrolled bleeding, failed to achieve hemostasis by TAE remains the important cause of 30 days mortality.

This study provides the evidence that the use of MELD score ≥13 or Child-Pugh score ≥8 is more suitable and better than using total bilirubin level >3 mg/dL [15, 18] for prediction of post-TAE 30-day mortality in HCC ruptured patients. Although serum total bilirubin level of 3 mg/dL had high specificity as 97% yet not good enough to serve as a prediction tool for its poor sensitivity, and NPV (**Table 3**). Since hepatic failure accounts for one-third of mortality causes in these early mortality patients, the MELD score or Child-Pugh score provides more objective evaluation for liver reserve than using total bilirubin alone. Although many studies

Table 3. Area under the receiver operating characteristic curve (AUROC) for evaluate the predictors of 30-day mortality

	AUROC (95% CI)	Cut-off value	Sensitivity	Specificity	PPV	NPV
Child-Pugh score	0.799 (0.714-0.884)	≥8	71%	76%	44%	91%
MELD score	0.818 (0.750-0.886)	≥13	87%	64%	39%	95%
ALBI score	0.757 (0.680-0.834)	>-1.87	89%	57%	35%	95%
Total bilirubin, mg/dL	0.668 (0.558-0.779)	>1.25	71%	71%	40%	90%
		>3	16%	97%	55%	81%

AUROC: area under ROC curve, NPV: negative predictive value, PPV: positive predictive value.

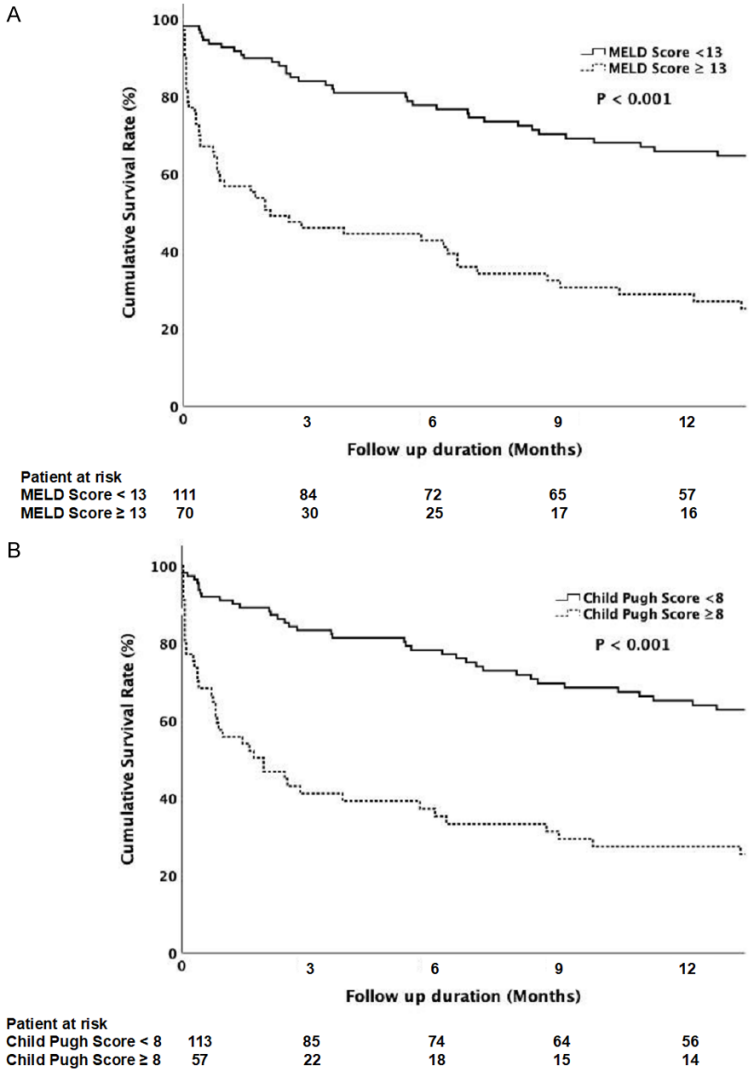

Figure 4. A. Cumulative survival rate of spontaneous ruptured hepatocellular carcinoma patients with MELD score ≥13 and <13. B. Cumulative survival rate of spontaneous ruptured hepatocellular carcinoma patients with Child-Pugh score ≥8 and <8.

adopting pre-therapy MELD score <8-11 for prediction of survival in patients receiving surgical operation or local regional therapy or liver transplantation, limited information that whether a different MELD score cut-off shall be adopted for HCC ruptured patients receiving TAE since these patients' liver function may be acutely deteriorated due to shock or transient hypoperfusion. In this study, the optimal cut-off for short-term prognosis prediction by pre-TAE MELD score ≥13 and Child-Pugh score ≥8 are both higher than that in previous reports which composed mainly HCC patients received surgical resection or local regional therapy or transplantation. Patients whose MELD score or Child-Pugh score above those cut-off value may encounter early mortality (42.8%-43.9%) in spite of the high successful hemostasis rate as 91.4% after TAE.

Emergency embolization for ruptured HCC in patients with hyperbilirubinemia >3.0 mg/dL or >50 μmol/L was discouraged in previous studies [15, 18]. The successful rate by TAE was comparable between patients with pre-TAE total bilirubin >3 and ≤3 mg/dL in current study (81.8 vs. 91.8%, P= 0.410). Instead, patients with higher MELD score and Child-Pugh score are prone to encounter TAE hemostasis failure, which may due to their prolonged INR (median: 1.6 vs. 1.2, P<0.001), as seen in Supplementary Table 1.

Of note, the presence of shock at arrival is not an independent factor for post-TAE 30-Day survival, which conflicts with previous studies [7, 24, 25]. Since the presence of shock has higher probability for short-term mortality in univariate analysis yet not significance after adjustment with other factors, it could be assumed that the presentation with shock has an indirect impact on short-term mortality. These shock patients were prone to have TAE hemostasis failure, which the leading cause of death. The high hemostasis failure rate may be secondary to shock related disseminated intravascular coagulation.

The mechanism of spontaneous rupture is still not clear. A number of hypotheses have been formulated to explain the pathophysiology of spontaneous rupture including large tumor size, subcapsular location, contour protrusion and exophytic tumor growth, tumor necrosis, portal hypertension, increased intratumoral pressure cause from occlusion of hepatic veins by tumor thrombi or invasion and coagulopathy [23]. Our study revealed 50% ruptured HCC is exophytic growth and 78% tumor size was larger than 5 cm. It's worthy of mention that one-fourth of are non-cirrhotic patients, whom may not undergo regular ultrasonography surveillance program. These patients had presented median tumor size as 10 (3.2-18) cm, larger than that in cirrhotic patients (median size: 7.8, (2.0-21) cm, *P* value =0.016).

There are several limitations of the present study: First, all HCC ruptured patients in current study received TAE. We could not provide the predictability of early mortality in those without TAE treatment nor those with other treatment modality. Second, since the study was conducted by retrospective method, it is difficult to assess whether super-selection embolization method provide better survival benefit than traditional one. Third, about one-third (N=81) patients had incomplete post-TAE profile of bilirubin, creatinine, albumin or INR level, we could not provide the information whether changes of these profiles before and after TAE be crucial for outcome prediction.

Conclusions

In conclusion, TAE is an effective approach to rescue HCC ruptured patients. Patients with pre-TAE total bilirubin >3 or ≤3 mg/dL have comparable TAE successful rate. Using MELD score ≥13 is better than total bilirubin level >3 mg/dL in prediction of 30-day mortality after TAE in HCC ruptured patients.

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Disclosure of conflict of interest

None.

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Supplementary Table 1. Comparison of demographic features and pre-TAE variables between patients with successful and failed hemostasis

	Successful hemostasis (N=170)	Failed hemostasis (N=16)	*P* value
Age	61.9±13.4	61.6±12.0	0.924
Male	142 (83.5%)	10 (62.5%)	0.082
Liver cirrhosis	121 (71.2%)	14 (87.5%)	0.242
Etiology (B/C/B+C/Non-B, non-C)	78/48/5/39 (45.9%/28.2%/2.9%/22.9%)	5/5/0/6 (31.2%/31.2%/0%/37.5%)	0.475
Child-Pugh classification (A/B/C)	93/64/13 (54.7%/37.6%/7.6%)	1/6/9 (6.3%/37.5%/56.3%)	<0.001*
BCLC stage (A/B/C/D)	6/35/115/14 (3.5%/20.6%/67.6%/8.2%)	0/1/8/7 (0%/6.2%/50%/43.8%)	<0.003
MELD score	12 (6~32)	17 (11~25)	<0.001*
Tumor number (single/multiple)	68/102 (40%/60%)	2/14 (12.5%/87.5%)	0.030*
Tumor Max size	8.3 (2~21)	10.0 (4~19.8)	0.333
Macrovascular invasion	50 (29.4%)	8 (50%)	0.098
Metastasis	28 (16.5%)	0 (0%)	0.136
Shock	43 (25.3%)	14 (87.5%)	<0.001*
Pre-TAE laboratory data			
WBC (mm^3)	11100 (3100~34200)	11550 (7000~26000)	0.671
Nadir of Hemoglobin (g/dL)	9.45 (5.0~20.2)	8.35 (3.4~14.4)	0.072
Creatinine (mg/dL)	1.14 (0.32~14.63)	1.26 (0.48~13.8)	0.651
ALT (U/L)	41 (6~569)	60 (21~129)	0.853
Total bilirubin (mg/dL)	1.0 (0.2~19.8)	1.4 (0.2~7.7)	0.674
Total bilirubin ≥3 mg/dl	9 (5.3%)	2 (12.5%)	0.525
Albumin (g/dL)	3.20 (1.46~4.59)	2.58 (1.48~4.18)	<0.001*
INR	1.2 (0.9~3.2)	1.6 (1.0~2.6)	<0.001*
AFP (ng/mL)	117 (2~2528998)	13857 (11~830323)	0.066

*Abbreviations: AFP: α-fetoprotein; ALT: alanine aminotransferase; Alb: albumin; ALBI: albumin-bilirubin; BCLC stage: Barcelona Clinic Liver Cancer stage; INR: international normalized ratio; MELD: Model for End-Stage Liver Disease; SIRS: systemic inflammatory response syndrome; TAE: trans-arterial embolization; WBC: white blood count.