Abdominal Radiology (2019) 44:903–911
https://doi.org/10.1007/s00261-019-01895-7

HEPATOBILIARY

Development and validation of an imaging and clinical scoring system to predict early mortality in spontaneous ruptured hepatocellular carcinoma treated with transarterial embolization

Kam-Ho Lee[1] · Man-Lap Donald Tse[1] · Martin Law[1] · Andrew Kai-Chun Cheng[1] · Ho-Yuen Frank Wong[1] · Man-Leung Yu[1] · Yan-Lin Li[1] · Yuen-Chi Ho[1] · Ferdinand Chu[1] · Wendy Wai-Man Lam[1]

Published online: 10 January 2019

Abstract

Purpose To develop and validate a scoring system using a combination of imaging and clinical parameters to predict 30-day mortality in ruptured HCC (rHCC) patients after transarterial embolization (TAE).

Methods 98 consecutive patients with rHCC who underwent abdominal CT and subsequent TAE between January 2007 and December 2016 were retrospectively reviewed. The CT scans were reviewed by two radiologists blinded to the patient outcome. Clinical parameters including serum bilirubin, albumin, INR, creatinine, and hemoglobin were recorded. Independent risk factors for 30-day mortality after TAE were identified using multivariate binary logistic regression, for development of a scoring system. The scoring system was then validated in 20 patients between January 2017 and May 2018.

Results In the development cohort, bilobar tumor distribution (OR = 29.6), clinical parameters of bilirubin > 2.5 mg/dL (OR = 5.9), and albumin < 30 g/L (OR = 4.1) were independent predictors for 30-day mortality. A 6-point score was derived and yielded area-under-the-receiver-operating-characteristic-curve (AUC) of 0.904. A score ≥ 4 resulted in sensitivity of 80.5% and specificity of 91.2% for 30-day mortality. In the validation cohort, AUC for 30-day mortality was 0.939. A score ≥ 4 resulted in sensitivity of 81.2% and specificity of 88.9%. In both development and validation cohorts, the proposed scoring system was better than biochemical components of Child–Pugh score and serum bilirubin to predict 30-day mortality.

Conclusion Imaging and clinical parameters can be combined into a scoring system to accurately predict 30-day mortality after TAE in rHCC patients. The score may help identify and counsel high-risk patients.

Keywords Hepatocellular carcinoma · Spontaneous rupture · Therapeutic embolization · Prognostic factors

Introduction

Hepatocellular carcinoma is a hypervascular tumor that can demonstrate rapid progression and direct invasion of surrounding parenchyma and capsule, leading to spontaneous rupture. Spontaneous rupture of HCC has a reported incidence ranging from less than 3% in Western studies and up to 26% in Asian studies [1–3]. Patients with ruptured HCC (rHCC) usually present with hemodynamic instability secondary to massive hemoperitoneum, and rHCC is more often seen in patients with advanced tumor status where there may be associated coagulopathy and liver failure. The 30-day mortality of spontaneous rupture was reported to be 17–71% in prior studies, with liver failure and re-bleeding or re-rupture being the most common causes of death [1, 3–8]. Transarterial embolization (TAE) has been shown to be effective for hemostasis in unstable patients with rHCC [1, 4, 9, 10]. However, clinical outcomes of rHCC after TAE remain unpredictable and a significant portion of patients succumb early despite successful embolization. A practical clinical tool to predict early mortality after TAE in rHCC is not available in literature.

In this retrospective study, we evaluated the radiological and clinical factors associated with early mortality in patients with spontaneous rupture of HCC following hemostasis by emergency transarterial embolization (TAE). The aim of this study was to develop and validate a simple clinical scoring system to predict early 30-day

✉ Kam-Ho Lee
viclkh88@gmail.com

[1] Department of Radiology, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong, HKSAR, China

mortality in this group of patients, in order to guide radiologists on decision making and patient counseling.

Methods and materials

Study population

This retrospective cohort study was approved by local institutional review board and the requirement to obtained informed consent was waived. All consecutive patients of at least 18 years old with rHCC who underwent TAE between January 2007 and December 2016 were identified from the hospital Radiological Information System and included into the development cohort. Patients with a pre-procedural CT were included. Patients were excluded if pre-procedural CT was not available, diagnosis was uncertain on CT or they were lost to follow-up within 30 days. All cases of HCCs were determined by combination of clinical features including known cirrhosis or chronic hepatitis, or previous HCC; biochemistry including raised serum alpha fetoprotein (AFP); characteristic imaging features including arterial hyperenhancement with contrast washout, capsule or interval growth; and histopathology for cases which underwent resection. Diagnosis of rHCC was based on combination of clinical presentation (including acute abdominal pain, hypotension and/or blood-stained ascites upon paracentesis), and CT findings showing peritumoral hematoma, peritumoral contrast extravasation, disruption of HCC contour, and/or enucleation sign [11, 12]. Patients with rHCC who underwent TAE and had a pre-procedural CT in the period between January 2017 and May 2018 were included into the validation cohort.

Imaging acquisition

Abdominal and pelvis CT images were acquired using commercially available 64-section CT scanner (GE Healthcare, UK). Images were typically acquired with 64×0.625 mm section collimation, a tube rotation time of 800 ms, a tube potential of 100 or 120 kV, automated tube current modulation with tube current between 10 and 300 mA at a noise index of 10 for a slice thickness of 5 mm, and a pitch of 1. For contrast CT studies, iodinated contrast (300 mg I/ml) (GE Healthcare, UK) was administered intravenously at a dose of 2 mL/kg and injection rate at 3 mL/sec. A multiphasic protocol consisting of unenhanced phase, arterial phase (30 s after injection), portovenous phase (75 s after injection), and delayed phase (4 min after injection) was used.

Technique of TAE

All TAEs were performed via a right femoral arterial approach under local anesthesia. The location of ruptured tumor was determined by pre-procedural CT based on the presence of sentinel clot, active contrast extravasation, and/or disruption of HCC contour. Hepatic angiography was performed to determine vascular anatomy. Selective or subsegmental TAE was performed if tumor is solitary and/or a bleeding source was well delineated by CT and/or angiography. In case of multifocal tumors where the exact ruptured tumor could not be localized on angiography, segmental or lobar embolization was performed based on interpretation of CT findings. The choice of embolic agent was decided according to the preference of the operating interventional radiologist. Gelfoam slurry, polyvinyl alcohol particles (PVA) 355–500 μm (Contour, Boston Scientific, MA), or a combination of both was used as embolization agent. If contrast extravasation was noted on angiography, embolization was performed until cessation of contrast extravasation. If no contrast extravasation was noted, embolization was performed until stasis in the target vessel. Technical success was defined as stasis of the feeding artery after embolization.

Data collection

Medical records were reviewed in electronic patient record system with a checklist to evaluate the patients' demographics, laboratory findings, and outcome. Demographic data included age at presentation, sex, and hepatitis status. Laboratory findings included hemoglobin, serum bilirubin, albumin, creatinine levels, and international normalized ratio (INR) on admission prior to TAE, and serum AFP level within 3 months prior to TAE. Sum of biochemical components of Child–Pugh Score (bilirubin, albumin and INR) was calculated [13]. Radiological reports of the TAE were reviewed to determine the choice of embolic agents.

Image evaluation

All computer tomography (CT) images of abdomen and pelvis performed prior to the TAE were reviewed independently on picture archiving and communication system by two radiologists (KHL and DT), with discrepancy resolved by consensus. Both radiologists were blinded to patients' outcomes but were aware of the diagnosis of rHCC. Bilobar distribution, multifocality, number of tumors, maximal dimension of the ruptured tumor, and maximal dimension of the largest tumor were recorded.

Statistical analysis to develop the scoring system and it validation

All categorical variables were presented as frequency and percentage. All continuous variables were presented as median and interquartile range (IQR). The baseline characteristics of the development and validation cohorts were compared using Pearson χ^2 test for categorical variables and Mann–Whitney *U* test for continuous variables.

For both development and validation cohorts, we defined 30-day mortality as the primary end point. Prognostic biochemical and imaging variables were selected on the basis of clinical experience and evidence of literature. Biochemical variables included hemoglobin, serum bilirubin, albumin, INR, and creatinine while imaging variables included multifocality, bilobar distribution, maximal dimension of the ruptured tumor, and maximal dimension of the largest tumor.

Univariate logistic regression analysis was then performed on all candidate variables in order to determine the statistically significant prognostic factors for the 30-day mortality. All statistically significant prognostic factors for 30-day mortality as obtained from the univariate logistic regression were entered into a multiple logistic regression model with backward elimination to identify potential independent predictors for early mortality.

Finally, to develop a practical scoring system, the independent predictors for the 30-day mortality identified by multivariate logistic regression were each assigned points according to the beta regression coefficient values (rounded to the nearest integer) in the logistic regression model [14]. The final risk score was the sum of the points of the variables. Area under the receiver operating characteristic curve (AUC) was calculated to assess the predictive ability of the scoring system. AUC from individual biochemical parameters was also compared to that of the proposed scoring system. We also assessed the calibration of the proposed scoring system for prediction of early mortality using the Hosmer–Lemeshow test. Optimal cut-off values to predict the 30-day mortality were determined by Youden index.

To evaluate the prognostic performance of the scoring system to patients in the validation cohort (rHCC patients during the period between January 2017 and March 2018), AUC with 95% confident interval (CI) and the Hosmer–Lemeshow test results were used. A two-sided *p* value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 24.0 (IBM Corp., Chicago, USA).

Results

Baseline characteristics of development and validation cohort

Between January 2007 and December 2016, a total of 111 patients underwent TAE for rHCC. Of these patients, 13 patients were excluded because pre-procedural CT was unavailable ($n=7$), diagnosis of rHCC was uncertain ($n=4$) or patients were lost to follow-up ($n=2$). 98 patients were therefore included into the development cohort. Between January 2017 and May 2018, 20 patients were included into the validation cohort. Demographics and clinical characteristics of the population were summarized in Table 1. In the development cohort, median age was 65 years (IQR 56–75 years). 90.8% ($n=89$) of patients had background diagnosis of chronic hepatitis or cirrhosis, while 60.2% ($n=59$) of patients were positive for hepatitis B. Serum AFP within 3 months of TAE was available for 84.7% ($n=83$) of patients, with median 208 ng/mL (interquartile range 6–4875 ng/mL). Technical success rate of TAE was 100% for both cohorts. The overall 30-day mortality was 41.8% for the development cohort and 55% for the validation cohort. Most common causes of 30-day mortality in the two cohorts included multiorgan failure ($n=22$), liver failure ($n=16$), and shock ($n=6$). The validation cohort did not differ from the development cohort for clinical, demographic, imaging characteristics or distribution of embolic agents ($p>0.05$).

Prognostic factors and the scoring system

In univariate logistic regression analysis, bilobar distribution ($p<0.001$), multifocality ($p=0.001$), large ruptured tumor size ($p=0.038$), and large maximum tumor size ($p<0.001$) were significant imaging predictors for 30-day mortality, whereas young age ($p=0.021$), low serum albumin ($p=0.036$), and higher serum bilirubin level ($p<0.001$) were significant clinical predictors for 30-day morality. Albumin < 30 g/L and bilirubin > 2.5 mg/dL were significant risk factors of 30-day mortality on univariate logistic regression ($p=0.012$ and $p<0.001$, respectively). In multivariate logistic regression, bilobar distribution, high serum bilirubin level, and low serum albumin level remained independently associated with early mortality (Table 2). The Hosmer–Lemeshow test showed no significant difference between the observed and predicted risks of early morality ($p=0.075$).

Three independent predictors including bilobar distribution, bilirubin, and albumin identified in multivariate logistic regression were included in the final scoring

Table 1 Baseline patient characteristics for the development and validation cohorts

Patient characteristics	Development cohort (98 patients) Number of patients (%)/Median (IQR)	Validation cohort (20 patients) Number of patients (%)/Median (IQR)	*p* value
Age in years	65 (56–75)	60 (54–67)	0.196
Gender			
Male	75 (76.5)	12 (60)	0.126
Female	23 (23.5)	8 (40)	
Race			
Chinese	98 (100)	20 (100)	1
Hepatitis status			
Non-hepatitis B virus	39 (39.8)	10 (50)	0.399
Hepatitis B virus	59 (60.2)	10 (50)	
Imaging parameters	Number of patients (%)/Median (IQR)	Number of patients (%)/Median (IQR)	*p* value
Bilobar distribution	56 (57.1)	13 (65)	0.516
Multifocality	65 (66.3)	12 (60)	0.588
Ruptured tumor size	8.5 (5.4–13.1)	8.4 (6.3–11.8)	0.911
Maximum tumor size	10.1 (7.2–13.7)	10.5 (7.1–12.9)	0.849
Biochemical parameters	Median (IQR)	Median (IQR)	*p* value
Hemoglobin (g/dL)	8.9 (7.2–11.0)	7.9 (7.8–9.5)	0.137
Alpha fetoprotein (ng/mL)	208 (6–4875)	163 (36–721)	0.605
Albumin (g/L)	29 (24–34)	28.5 (25–33)	0.874
Bilirubin (mg/dL)	1.3 (0.7- 2.8)	1.3 (1.0–2.4)	0.54
International normalized ratio	1.3 (1.1–1.4)	1.4 (1.3–1.5)	0.06
Creatinine (mg/dL)	1.1 (0.9–1.7)	1.0 (0.8–1.2)	0.292
Embolic agents	Number of patients (%)	Number of patients (%)	*p* value
Gelfoam slurry	50 (51.0)	12 (60)	0.508
Polyvinyl alcohol particles (PVA)	46 (46.9)	7 (35)	
Gelfoam slurry and PVA	2 (2.1)	1 (5)	

system (Table 3). The beta regression coefficient of each predictor was converted into points rounded to the nearest integer. The total risk score ranged from 0 to 6 points. Median risk score was 3 (IQR 1–4). Optimal cut-off score to predict 30-day mortality was 4 with a Youden index of 0.717. Patients with a score ≥ 4 were considered high risk for 30-day mortality. The cut-off value of ≥ 4 yielded sensitivity of 80.5% (33 out of 41), specificity of 91.2% (52 out of 57), positive predictive value of 86.8% (33 out of 38), and negative predictive value of 86.7% (52 out of 60). The final scoring system model had an AUC of 0.904 (95% CI 0.839, 0.969). The proposed scoring system had a better AUC than sum of biochemical components of Child–Pugh score (0.744; 95% CI 0.645, 0.842) and serum bilirubin alone (0.805; 95% CI 0.717, 0.892) in predicting 30-day mortality (Fig. 1a). According to the proposed scoring system, rHCC patients with risk scores of ≥ 4, 3 , and ≤ 2 could be stratified into high-, intermediate-,and low-risk groups, with predicted probability of 30-day mortality of 86.8, 31.8, and 2.6%, respectively (Table 4) (Figs. 2, 3).

In the validation cohort, the risk score ≥ 4 was predictive of 30-day mortality, with sensitivity of 81.2% and specificity of 88.9%, positive predictive value of 90%, and negative predictive value of 80%. The AUC of the scoring system was 0.939 (95% CI 0.828, 1.00), higher than that of biochemical components of Child–Pugh score (0.621; 95%: 0.372, 0.870) and serum bilirubin alone (0.677; 95% CI 0.435, 0.919) (Fig. 1b). The Hosmer–Lemeshow test showed no significant difference between the observed and predicted risks of outcome ($p = 0.875$). Similar to the development cohort, rHCC patients with risk scores of ≥ 4, 3 , and ≤ 2 could be stratified into high-, intermediate-, and low-risk groups, with predicted probability of 30-day mortality of 90.0, 66.7, and 0%, respectively (Table 4).

Table 2 Results of univariate logistic regression analysis for imaging and clinical variables to predict the 30-day mortality

Variable	Odd ratio (95% CI)	*p*-value
Age	0.96 (0.93–0.99)	0.021
Gender		
Male	2.48 (0.88–6.98)	0.086
Etiologic cause		
Hepatitis B virus	1.06 (0.47–2.40)	0.895
Imaging parameters		
Bilobar distribution	27.44 (7.47–100.84)	< 0.001
Multifocality	5.25 (1.91–14.42)	0.001
Ruptured tumor size (cm)	1.09 (1.01–1.19)	0.038
Maximum tumor size (cm)	1.22 (1.10–1.36)	< 0.001
Biochemical parameters		
Hemoglobin (g/dL)	0.91 (0.78–1.07)	0.26
Albumin (< 30 g/L)	3.96 (1.35–11.61)	0.012
Bilirubin (> 2.5 mg/dL)	9.60 (3.29–27.98)	<0.001
International normalized ratio	3.68 (0.76–17.80)	0.105
Creatinine (mg/dL)	1.00 (0.99–1.00)	0.526
Embolic agents		
Gelfoam slurry	0.87 (0.38–1.95)	0.73

Comparison of 30-day mortality between Gelfoam slurry and PVA

In the development cohort, 50 patients were treated with Gelfoam slurry, 46 with PVA particle, and remaining 2 with combination of both. There was no significant difference in 30-day mortality between the patients treated with Gelfoam slurry and those treated with PVA (40% vs. 43.5%, $p = 0.916$).

Discussion

For patients with rHCC, TAE has become the initial treatment of choice to achieve hemostasis and stabilize the patient, with emergency hepatic resection reserved for only a small group of highly selected patients. Hemostatic success rates range between 53 and 100% [2], though TAE carries a risk of worsening liver function and liver failure, and recurrent bleeding [3, 6, 15, 16]. Our study demonstrated that the proposed scoring system consisting of bilobar tumor distribution, high serum bilirubin, and low serum albumin was associated with risk of early mortality in rHCC patients after TAE. In our development and validation cohorts, a risk score of greater than or equal to 4, out of a total possible 6, was sensitive and specific in predicting 30-day mortality. To the best of our knowledge, this is the first study providing a clinical scoring system for prediction of early mortality of rHCC patients after TAE.

Several prognostic factors were reported to be associated with early mortality in rHCC patients by previous studies. Among these factors, the relationship between hyperbilirubinemia and early mortality was most consistently reported. Ngan et al. reported that emergency TAE was rarely helpful in prolonging survival in patients with bilirubin level > 2.92 mg/dL [17] while Okazaki et al. suggested that embolization for rHCC was contraindicated in patient with total bilirubin level > 3.0 mg/dL [18]. A more recent study by Kung et al. demonstrated that cumulative mortality rate was 71% for patients with a serum total bilirubin level of ≥ 2.7 mg/dL [19]. Our study confirmed that hyperbilirubinemia was a poor prognostic indicator for survival in rHCC patients and showed that the critical level of bilirubin may be lower than previously reported if other risk factors coexist. The cumulative mortality rate was 79% at serum bilirubin level > 2.5 mg/dL in our cohort.

Hypoalbuminemia has been shown to be a strong predictor for early and late mortality in hospitalized patients during acute medical admission and after discharge, respectively [20, 21], likely reflective of the patient's nutritional and generalized disease status. In a study by Li et al. which included 62 patients with rHCC treated with TAE [6], a low albumin level was the only independent risk factor for early mortality. Our results also suggested that moderate hypoalbuminemia (serum albumin level < 30 g/L) was associated with a higher mortality rate at 30 days (54.7%). The prognosis after TAE in patients with mild hypoalbuminemia (serum albumin level, 30–34 g/L) may not be substantially jeopardized.

Bilobar tumor distribution was an independent predictor for early mortality in rHCC patients after TAE, consistent with the results from a previous study by Shin et al. [8]. In our cohort, a substantial portion (52.6%, 10 out of 19) of patients with bilobar distribution of tumor but normal serum bilirubin level died within 30 days after TAE. Among this

Table 3 Results of multivariate logistic regression analysis of statistically significant variables to predict the 30-day mortality

Variable	Beta coefficient	Odd ratio (95% CI)	*p*-value	Score point
Bilobar distribution	3.39	29.63 (6.35–121.69)	< 0.001	3
Bilirubin (> 2.5 mg/dL)	1.78	5.90 (1.56–22.3)	0.009	2
Albumin (< 30 g/L)	1.4	4.06 (1.23–13.39)	0.021	1

The score points were obtained from the rounded integer values of the beta coefficients obtained by the regression

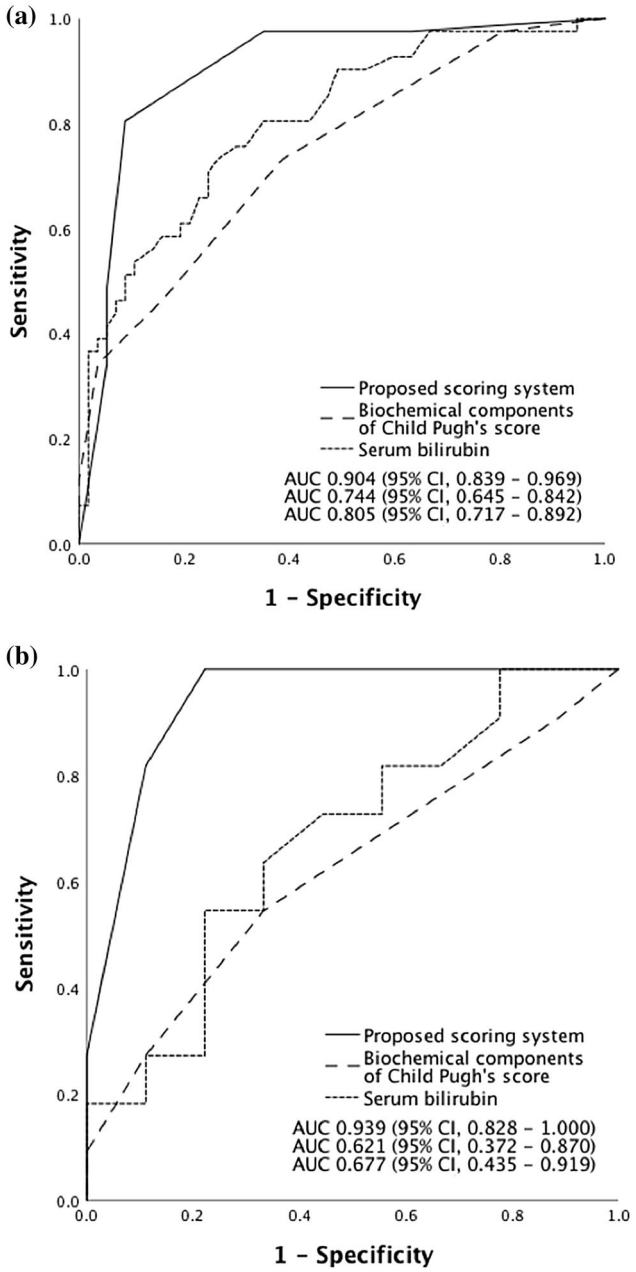

Fig. 1 Graphs showing prediction of 30-day mortality in rHCC patients after TAE in **a** development cohort and **b** validation cohort. Area under the receiver operating characteristic curves (*AUC*) and 95% CIs for 30-day mortality prediction using the proposed scoring system (solid curve), sum of biochemical components of Child–Pugh score (dashed curve), and using serum bilirubin alone (dotted curve)

subgroup of patients, the 30-day mortality rate was 87.5% if there was coexisting moderate hypoalbuminemia (serum albumin level < 30 g/L). We speculate that rHCC patients with bilobar tumor and low serum albumin have impaired liver reserve, leaving them more susceptible to ischemic injury to TAE and post-procedural hepatic decompensation, which are closely linked to early mortality.

Several previous studies have demonstrated that a high Child–Pugh score was associated with poor survival in rHCC patients after TAE [7, 8, 15]. Since hemoperitoneum is present in virtually all patients with rHCC and altered mental status secondary to hypovolemic shock is common, accurate determination of Child–Pugh score in rHCC patients can be challenging. The current proposed scoring system is potentially more accurate than using the sum of biochemical components of Child–Pugh score (bilirubin, albumin and INR) in predicting early mortality, and can be used even when ruptured tumor is the first presentation of HCC.

Leung et al. reported in a retrospective cohort of 112 patients with rHCC that conservative and selective intervention approach resulted in similar in-hospital mortality but a lower intervention rate, when compared to aggressive approach [22]. In their subgroup analysis, the in-hospital mortality rate and survival were better with conservative approach after exclusion of those who were considered 'terminal.' The authors did not define how patients were classified as 'terminal.' Our scoring system, by stratifying patients according to risk of early mortality, can be a useful clinical tool to identify high-risk rHCC patients in which TAE is likely futile and conservative management may be justified, and to aid interventional radiologists in pre-treatment patient counseling.

Absorbable gelatin sponge, PVA, and stainless steel coils are commonly used agents in TAE for rHCC [2, 19]. The present study showed that patients treated with Gelfoam and those treated with PVA had no significant difference in 30-day mortality rate. The choice of embolic agent was not an independent poor prognostic factor in our multivariate analysis. A recent study by Zhou et al. showed that TAE using lipiodol and Gelfoam combined was associated with significantly increased survival compared to TAE using PVA [23], which suggested that addition of the liquid embolic agent lipiodol could penetrate into the terminal hepatic arterioles and portal venules of the tumor, in addition to the proximal embolic effect of Gelfoam.

Our study has limitations. Firstly, the quality of data was limited by its retrospective nature. Given the emergent nature of rHCC, diagnostic work up of the patients was at times incomplete, particularly for patients who present for the first time with rHCC, for whom grading of cirrhosis can be difficult as discussed above. The diagnosis of HCC in our study population was also based on combined clinical, biochemical, and imaging features, without the use of imaging-based scoring systems such as LI-RADS. Secondly, the small sample size of our validation cohort means that while it was able to show early evidence that our scoring system can be used to predict mortality outside of the development cohort, further validation is still required with a larger study population. Thirdly, this single-center cohort study included

Table 4 Summary of the 30-day mortality rates of different risk groups stratified according to proposed risk score in both development and validation cohorts

Risk group	Score	Development cohort		Validation cohort	
		Number of patients	30-day mortality (%)	Number of patients	30-day mortality (%)
Low	≤ 2	38	1 (2.6)	7	0 (0)
Intermediate	3	22	7 (31.8)	3	2 (66.7)
High	≥ 4	38	33 (86.8)	10	9 (90)

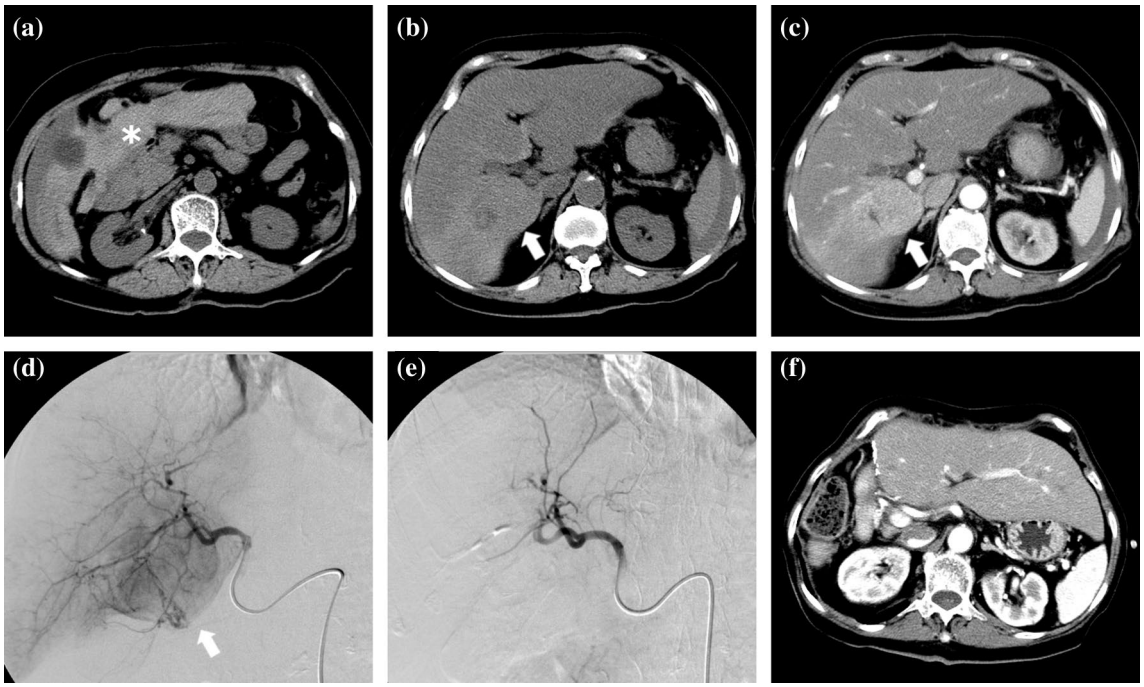

Fig. 2 A 77-year-old patient with rHCC. Pre-contrast axial CT images (**a**, **b**) showed perihepatic hyperdense fluid in keeping with acute hematoma (*). Arterial phase post-contrast axial CT image (**c**) and right hepatic arteriogram (**d**) showed hypervascular HCC in the right lobe (white arrows). Patient had serum bilirubin and albumin within normal limits, thus with overall score of 0. TAE was performed with PVA. Post-embolization right hepatic arteriogram (**e**) showed no further tumor blush. Patient survived and subsequently underwent right hepatectomy with histology confirmed HCC. Follow-up contrast CT at 1 year (**f**) showed hypertrophied left lobe, with no evidence of HCC recurrence

Asian patients with a high proportion of hepatitis B-related HCC; while this is consistent with several other Asian studies [3, 15, 19, 22], further external validation studies are therefore needed to test the general application of our scoring system to other populations.

In conclusion, our study demonstrated that bilobar distribution of tumor, high serum bilirubin (> 2.5 mg/dL), and low serum albumin (< 30 g/L) were independent predictors for early mortality of rHCC patients after TAE. An imaging and clinical scoring system was developed from 98 patients to predict 30-day mortality, with scores of 3, 2, and 1 assigned to each of bilobar distribution, high serum bilirubin, and low serum albumin, respectively, based on the beta coefficients of multivariate logistic regression; the individual scores are then summed to a total risk score from 0 to 6. The scoring system was then validated in a subsequent 20 consecutive patients. The 30-day mortality rate was high up to 90% in rHCC patients with a total risk score ≥ 4 despite treatment by TAE. By stratifying patients into high-, intermediate-, and low-risk groups, the proposed scoring system is a potentially useful clinical tool to aid radiologists and clinicians on decision making and patient counseling in rHCC patients.

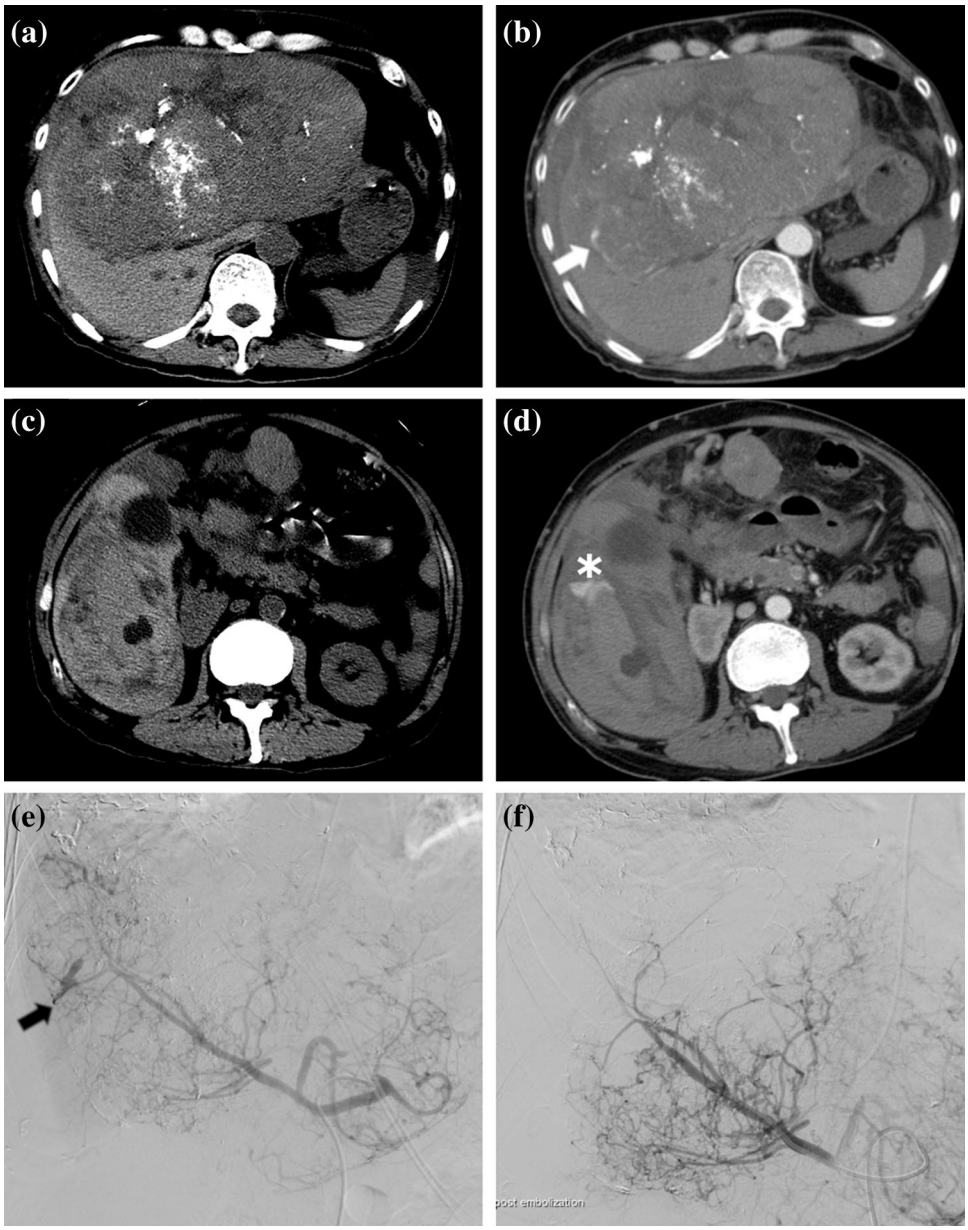

Fig. 3 A 59-year-old patient with rHCC. Pre-contrast (**a**, **c**) and arterial phase post-contrast (**b**, **d**) CT images showed large bilobar tumor with history of previous TACE, showing active extravasation (white arrow) into large perihepatic hematoma (*). Serum bilirubin was normal but albumin was low (28 g/L), giving an overall score of 4 (bilobar distribution: 3 + low serum albumin: 1). Hepatic arteriogram (**e**) showed active extravasation at the same location as demonstrated on CT (black arrow). TAE was performed with PVA at right hepatic artery; post-embolization arteriogram (**f**) showed cessation of bleeding. Nevertheless, patient died 1 day later secondary to shock

References

1. Liu CL, Fan ST, Lo CM, Tso WK, Poon RT, Lam CM, Wong J (2001) Management of spontaneous rupture of hepatocellular carcinoma: single-center experience. J Clin Oncol 19 (17):3725-3732. https://doi.org/10.1200/JCO.2001.19.17.3725
2. Yoshida H, Mamada Y, Taniai N, Uchida E (2016) Spontaneous ruptured hepatocellular carcinoma. Hepatol Res 46 (1):13-21. https://doi.org/10.1111/hepr.12498
3. Moris D, Chakedis J, Sun SH, Spolverato G, Tsilimigras DI, Ntanasis-Stathopoulos I, Spartalis E, Pawlik TM (2018) Management, outcomes, and prognostic factors of ruptured hepatocellular carcinoma: A systematic review. J Surg Oncol 117(3):341-353
4. Chen WK, Chang YT, Chung YT, Yang HR (2005) Outcomes of emergency treatment in ruptured hepatocellular carcinoma in the ED. Am J Emerg Med 23 (6):730-736. https://doi.org/10.1016/j.ajem.2005.02.052
5. Lai EC, Wu KM, Choi TK, Fan ST, Wong J (1989) Spontaneous ruptured hepatocellular carcinoma. An appraisal of surgical treatment. Ann Surg 210 (1):24-28
6. Li WH, Cheuk EC, Kowk PC, Cheung MT (2009) Survival after transarterial embolization for spontaneous ruptured hepatocellular carcinoma. J Hepatobiliary Pancreat Surg 16 (4):508-512. https://doi.org/10.1007/s00534-009-0094-6
7. Monroe EJ, Kogut MJ, Ingraham CR, Kwan SW, Hippe DS, Padia SA (2015) Outcomes of emergent embolisation of ruptured hepatocellular carcinoma in a western population. Clin Radiol 70 (7):730-735. https://doi.org/10.1016/j.crad.2015.03.007
8. Shin BS, Park MH, Jeon GS (2011) Outcome and prognostic factors of spontaneous ruptured hepatocellular carcinoma treated with transarterial embolization. Acta Radiol 52 (3):331-335. https://doi.org/10.1258/ar.2010.100369

9. Miyamoto M, Sudo T, Kuyama T (1991) Spontaneous rupture of hepatocellular carcinoma: a review of 172 Japanese cases. Am J Gastroenterol 86 (1):67-71
10. Xu HS, Yan JB (1994) Conservative management of spontaneous ruptured hepatocellular carcinoma. Am Surg 60 (8):629-633
11. Choi BG, Park SH, Byun JY, Jung SE, Choi KH, Han JY (2001) The findings of ruptured hepatocellular carcinoma on helical CT. Br J Radiol 74 (878):142-146. https://doi.org/10.1259/bjr.74.878.740142
12. Kim HC, Yang DM, Jin W, Park SJ (2008) The various manifestations of ruptured hepatocellular carcinoma: CT imaging findings. Abdom Imaging 33 (6):633-642. https://doi.org/10.1007/s00261-007-9353-7
13. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R (1973) Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 60 (8):646-649
14. Han K, Song K, Choi BW (2016) How to Develop, Validate, and Compare Clinical Prediction Models Involving Radiological Parameters: Study Design and Statistical Methods. Korean J Radiol 17 (3):339-350. https://doi.org/10.3348/kjr.2016.17.3.339
15. Fan WZ, Zhang YQ, Yao W, Wang Y, Tan GS, Huang YH, Yang JY, Li JP (2018) Is Emergency Transcatheter Hepatic Arterial Embolization Suitable for Spontaneously Ruptured Hepatocellular Carcinoma in Child-Pugh C Cirrhosis? J Vasc Interv Radiol 29 (3):404-412 e403. https://doi.org/10.1016/j.jvir.2017.09.022
16. Schwarz L, Bubenheim M, Zemour J, Herrero A, Muscari F, Ayav A, Riboud R, Ducerf C, Regimbeau J, Tranchart H, Lermite E, Petrovai G, Suhol A, Doussot A, Capussotti L, Tuech J, Le Treut Y (2018) Bleeding Recurrence and Mortality Following Interventional Management of Spontaneous HCC Rupture: Results of a Multicenter European Study. World J Surg 42(1):225-232
17. Ngan H, Tso WK, Lai CL, Fan ST (1998) The role of hepatic arterial embolization in the treatment of spontaneous rupture of hepatocellular carcinoma. Clin Radiol 53 (5):338-341
18. Okazaki M, Higashihara H, Koganemaru F, Nakamura T, Kitsuki H, Hoashi T, Makuuchi M (1991) Intraperitoneal hemorrhage from hepatocellular carcinoma: emergency chemoembolization or embolization. Radiology 180 (3):647-651. https://doi.org/10.1148/radiology.180.3.1651524
19. Kung CT, Liu BM, Ng SH, Lee TY, Cheng YF, Chen MC, Ko SF (2008) Transcatheter arterial embolization in the emergency department for hemodynamic instability due to ruptured hepatocellular carcinoma: analysis of 167 cases. AJR Am J Roentgenol 191 (6):W231-239. https://doi.org/10.2214/AJR.07.3983
20. Jellinge ME, Henriksen DP, Hallas P, Brabrand M (2014) Hypoalbuminemia is a strong predictor of 30-day all-cause mortality in acutely admitted medical patients: a prospective, observational, cohort study. PLoS One 9 (8):e105983. https://doi.org/10.1371/journal.pone.0105983
21. Walter LC, Brand RJ, Counsell SR, Palmer RM, Landefeld CS, Fortinsky RH, Covinsky KE (2001) Development and validation of a prognostic index for 1-year mortality in older adults after hospitalization. JAMA 285 (23):2987-2994
22. Leung KL, Lau WY, Lai PB, Yiu RY, Meng WC, Leow CK (1999) Spontaneous rupture of hepatocellular carcinoma: conservative management and selective intervention. Arch Surg 134 (10):1103-1107
23. Zhou C, Zu Q, Wang B, Zhou C, Shi H, Liu S (2018) Efficacy and prognostic factors of transarterial embolization as initial treatment for spontaneously ruptured hepatocellular carcinoma: a single-center retrospective analysis in 57 patients. Jpn J Radiol. https://doi.org/10.1007/s11604-018-0799-z