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## FULL PAPER

# The development of a predictive risk model on post-ablation hemobilia: a multicenter matched case-control study

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**Objective:** This study aimed to develop a predictive risk model for post-ablation hemobilia.

**Methods:** This was a retrospective, multicenter, matched case-control study. The case group comprised patients with hepatocellular carcinoma who developed post-ablation hemobilia ( $n = 21$ ); the control group ( $n = 63$ ) comprised patients with hepatocellular carcinoma but no post-ablation hemobilia; for each case, we included three controls matched for age, sex, platelet count, year of ablation therapy, and center. Univariate and multivariate regression analyses were performed to identify the risk factors for hemobilia. A risk score model was developed based on adjusted odds ratios (ORs).

**Results:** The independent risk factors for occurrence of post-ablation hemobilia were maximum tumor diameter  $>47$  mm [OR = 5.983, 95% CI (1.134–31.551)] and minimum

distance from the applicator to the portal trunk  $\leq 8$  mm [OR = 4.821, 95% CI (1.225–18.975)]. The risk model was developed using the adjusted ORs; thus a score of 6 was assigned to the former and a score of 5 for the latter. The area under the curve of this risk model was 0.76. Significant hemodynamic instability and inaccurate embolization might increase the risk of recurrence of hemobilia.

**Conclusion:** Tumor size  $>47$  mm and distance of the applicator from the portal trunk  $\leq 8$  mm are independent risk factors for hemobilia. A predictive risk model for post-ablation hemobilia was developed using these risk factors.

**Advances in knowledge:** This is the first study that developed a risk score model of post-ablation hemobilia. Risk factors of the recurrence of post-ablation hemobilia were also been identified.

## INTRODUCTION

Percutaneous thermal ablation is widely considered to be an effective and safe minimally invasive therapy for hepatocellular carcinoma (HCC)<sup>1–4</sup> but complications may occasionally occur. One such complication is hemobilia, which is reported in 8.2% of patients undergoing CT-guided ablation.<sup>5</sup> The number of cases of post-ablation hemobilia being reported is increasing due to the rising popularity of ablation therapy.<sup>6</sup>

The mechanism of post-ablation hemobilia is still unclear, but mechanical and thermal injury may both contribute.<sup>7</sup> Trauma during penetration of the liver can easily lead to fistula formation between arteries/veins and bile ducts lying in close proximity (mechanical injury). The heat or cold generated by the applicator during ablation can also damage nearby bile ducts and vessels (thermal injury).

Hemobilia can be massive and can lead to other complications, such as biliary infection and liver failure.<sup>8,9</sup> Conservative medical treatment, transarterial embolization (TAE), endoscopic treatment, and vascular stenting are the usual strategies adopted for management of hemobilia.<sup>5</sup> In some cases, surgery (hepatic artery ligation, hepatectomy, or cholecystectomy) is indicated for treating hemobilia or the related complications<sup>5,10–14</sup>; however, the mortality rate of patients undergoing surgery is as high as 10%.<sup>5</sup>

The ability to accurately predict the risk of post-ablation hemobilia would help reduce its incidence; however, few studies have investigated the risk factors for occurrence of hemobilia. There is also no consensus on the best treatment.<sup>15</sup> The aim of this multicenter, matched case-control study was to develop a risk prediction model for post-ablation hemobilia.

## METHODS AND MATERIALS

### Study design

In this retrospective, multicenter, matched case-control study, the cases were patients with HCC with post-ablation hemobilia at the Cancer Center, Beijing Ditan Hospital, Capital Medical University between January 2008 and December 2018 and at the Center of Interventional Oncology and Liver Diseases, Beijing Youan Hospital, Capital Medical University between January 2012 and October 2018. The inclusion criteria of the cases were:<sup>1</sup> 18–75 years old;<sup>2</sup> diagnosis of HCC;<sup>3</sup> history of ablation therapy for intrahepatic HCC<sup>4</sup>; and diagnosis of post-ablation hemobilia. The diagnosis of HCC was confirmed by either histopathological biopsy or the current practice guideline of the American Association for the Study of Liver Diseases.<sup>16</sup> Hemobilia was suspected according to specific presenting symptoms (*i.e.* melena, hematemesis, abdominal pain, or jaundice) and medical history.<sup>11</sup> Hemobilia was confirmed by high-density material in the biliary system on contrast-enhanced CT or hepatobiliary source of hemorrhage in endoscopy.<sup>7,12</sup> Patients with no gallbladder were excluded.

The controls were selected from the cohort of patients with HCC who underwent ablation treatment without major complications. Major complications was confirmed based on the definition in the standardization of terminology and reporting criteria of image-guided ablation.<sup>17</sup> For each case, three controls were matched by age ( $\pm 5$  years), sex, year of the ablation therapy, and medical center. Additionally, the controls were also matched by platelet count (PLT) ( $\pm 10 \times 10^9 \text{ L}^{-1}$ ), which has been reported to be an independent risk factor of post-ablation hemobilia.<sup>15</sup> As the sample size of the present study was relatively small, matching known independent risk factors would be helpful for generating accurate results. This study was approved by the ethics committees of Beijing Youan Hospital and Beijing Ditan Hospital, Capital Medical University. All patients enrolled in this study provided written informed consents.

The basic clinical characteristics of all patients were reviewed. The minimal distance between the applicator and portal trunk was defined as the minimal distance between the applicator and the first or second branch of the portal vein during ablation therapy. The minimal distance between the applicator and the gallbladder was defined as the minimal distance between applicator and the wall of the gallbladder during ablation therapy. These distances were measured on axial plane images by two authors (JZ and WL) who are specialists with extensive experience on radiological imaging evaluation. Tumors were divided into central tumors (in segments I, IV, V, or VIII) and peripheral tumors (in segments II, III, VI, or VII) based on tumor location.

### Ablation therapy

The ablation therapy was guided by CT. A 22 G puncture needle was used to lead the ablative applicator to insert into the tumor. Then the applicator was advanced into the target. The strategy of radiofrequency ablation (RFA) included power output of 80–120 W for a duration of 6–8 min per session; that of microwave ablation (MWA) included power output of 40–60 W for a duration of 4–6 min per session; and that for cryoablation

included a duration of 12 min per session. A contrast-enhanced CT was performed at the end of the ablation to evaluate technical success and assess for possible complications. In case of residual tumors, supplemental ablation was performed. In case of complications, prompt diagnosis was made and appropriate management was performed. After the ablation, all patients were monitored for 24 h.

### Follow-up

The follow-up time was 6 months. All patients underwent a re-examination at 1 month after the ablation, which included physical examinations, laboratory examinations [blood counts, liver function, and alpha fetoprotein (AFP)], and image examinations [abdominal contrast-enhanced CT or MRI]. The survival status at 6 months after the ablation treatment was reviewed and recorded.

### Statistical analysis

As for the basic characteristic data analysis, frequencies and proportions were used for categorical data, means and standard deviations (SD)/interquartile range (IQR) were used for continuous variables.

The meta-analyses were performed with SPSS v. 17.0 software (SPSS Inc., Chicago, IL). To explore independent risk factors of post-ablation hemobilia, univariate and multivariate analyses were performed by using conditional logistic regression. All continuous variables were transformed into categorical variables. The two-tailed *p* value, odds ratio (OR), and 95% confidence interval (CI) were calculated. All variables with *p* < 0.05 in the univariate analysis were included into the multivariate regression analysis. All variables with *p* < 0.05 in multivariate analysis were included into the risk score model.

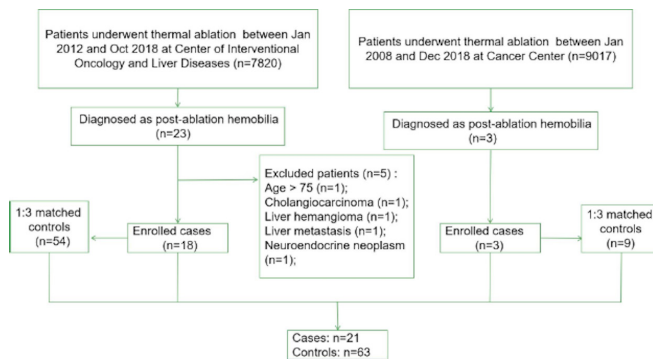
The risk scores were assigned to variables according to adjusted ORs. For each variable, the adjusted OR was rounded to the nearest integral number. The final score equaled the sum of the risk scores of all independent risk factors. The discrimination of the prediction model was assessed by area under curve (AUC) by using receiver operating characteristic (ROC) curve. The risk of post-hemobilia calculated by the risk score model was divided into high risk and low risk based on the cut-off value by using ROC curve.

## RESULTS

### Basic characteristics

From among 16 837 patients who underwent ablations, 26 patients with HCC who developed post-ablation hemobilia were identified. Among these 26 patients, 5 did not meet the study criteria. The remaining 21 patients with HCC and post-ablation hemobilia formed the case group. Another 63 patients matched by year of ablation therapy, center, sex, age, and platelet count (in a ratio of 1:3) formed the control group. [Figure 1](#) shows the details of the selection procedure, and [Table 1](#) summarizes the characteristics of the included patients. Hemobilia was diagnosed by contrast-enhanced CT in 20/21 (95%) patients and by endoscopy in 1/21 (5%) patient. On CT imaging, the presence of high-density material in the biliary system, with an interface

Figure 1. The flowchart of selection procedure.



between blood and bile, was considered diagnostic of hemobilia (Figure 2).

#### Risk score model

Cases and controls were compared to identify the factors associated with post-ablation hemobilia. The variables evaluated in the univariate analysis included presence of ascites, time of puncture, ablation method, number of tumors ablated, maximum diameter of ablated tumors, location of ablated tumors, distance from the applicator to the portal trunk, distance from the applicator to the gallbladder, serum albumin (ALB) level, and prothrombin time (PT).

In univariate analysis, time of puncture, number of tumors ablated, maximum diameter of ablated tumors, minimum

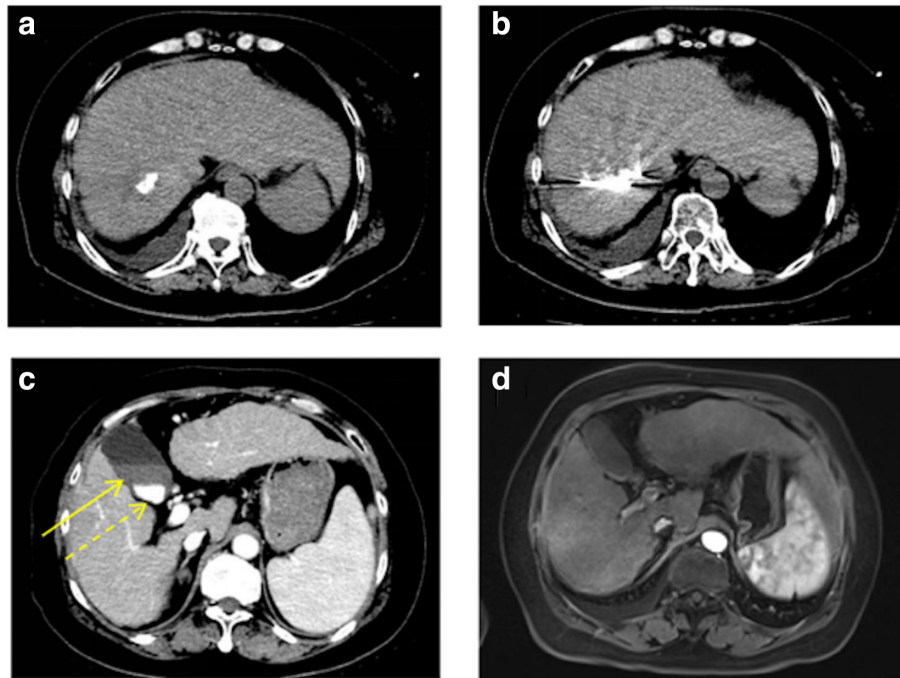
Table 1. Basic characteristics of cases and controls

	Hemobilia group (n = 21)	Control group (n = 63)	p value
Age	54.9 ± 8.02	56.22 ± 7.73	0.505
Sex, n (%)			1.000
Male	16 (76.19%)	48 (76.19%)	
Female	5 (23.81%)	15 (23.81%)	
Virus Hepatitis, n (%)			1.000
Hepatitis B	16 (76.19%)	49 (77.78%)	
Hepatitis C	3 (14.29%)	9 (14.29%)	
None	2 (9.52%)	5 (7.94%)	
Child-Pugh Class, n (%)			1.000
Child-Pugh Class A	18 (85.71%)	55 (87.30%)	
Child-Pugh Class B	3 (14.29%)	8 (12.70%)	
BCLC stage, n (%)			1.000
BCLC 0-A	13 (61.90%)	37 (58.73%)	
BCLC B-C	8 (38.10%)	26 (41.27%)	
Liver cirrhosis, n (%)	18 (85.71%)	54 (85.71%)	1.000
Concurrent ascites, n (%)	1 (4.76%)	9 (14.29%)	0.439
Previous RFA, n (%)	16 (76.19%)	42 (66.67%)	0.587
Previous hepatic surgery, n (%)	1 (4.76%)	8 (12.70%)	0.439
Ablation methods, n (%)			0.403
RFA	11 (52.38%)	38 (60.32%)	
MWA	6 (28.57%)	20 (31.75%)	
Cryoablation	4 (19.05%)	5 (7.94%)	
PLT (×10 <sup>9</sup> L <sup>-1</sup> )	88.38 ± 37.01	89.25 ± 58.8	0.959
TBil (μmol L <sup>-1</sup> )	26.91 ± 15.70	19.39 ± 8.73	0.219

ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BCLC stage, Barcelona clinic liver cancer stage; DBil, Direct bilirubin; HB, Hemoglobin; HCT, Red blood cell specific volume; MWA, Microwave ablation; PLT, Platelet count; RBC, Red blood cell; RFA, Radiofrequency; TBil, total bilirubin; WBC, White blood cell.

(%), the accounting proportion in the related group.

Figure 2. A 58-year-old patient with HCC with post-ablation hemobilia. (a) The pre-operative axial CT image showed an intrahepatic tumor in the right liver lobe, with deposition of lipiodol. (b) Ablation was performed on the target tumor. (c) The intraoperative contrast-enhanced CT image showed that high-density material (the arrow) and contrast agent (the dotted arrow) flowed into the gallbladder. (d) The characteristic CT findings of hemobilia disappeared at 1 month after the ablation. HCC, hepatocellular carcinoma.



distance between the applicator and the portal trunk, ALB, and PT were significantly different between cases and controls ( $p < 0.05$ ; Table 2). On multivariate analysis, maximum diameter of tumor  $>47$  mm [ $p = 0.035$ , OR = 5.983, 95% CI (1.134–31.551)] and minimum distance between the applicator and the portal trunk  $\leq 8$  mm [ $p = 0.024$ , OR = 4.821, 95% CI (1.225–18.975)] were independent risk factors for hemobilia (Table 2).

A risk model was constructed using the adjusted ORs to assign scores for each variable: thus, six points were assigned if the maximum tumor diameter was  $>47$  mm and five points were assigned if the minimum distance between the applicator and the portal trunk was  $\leq 8$  mm (Table 2). The AUC of this risk model was 0.76, indicating that it correctly identified 76% of patients with post-ablation hemobilia. Using the cut-off value calculated by the ROC curve, the patients were separated into high-risk (score  $>2$ ) and low risk (score  $\leq 2$ ) groups. The incidence of post-ablation hemobilia was 52% (16/31) in the high-risk group vs 9% (5/53) in the low-risk group ( $p < 0.05$ ).

#### Management and prognosis

Management of patients with post-ablation hemobilia was with thrombin injection ( $n = 7$ , 33.33%), TAE ( $n = 10$ , 47.62%; Figure 3), antibiotic therapy ( $n = 8$ , 38.10%), and drainage ( $n = 3$ , 14.29%). Thrombin injection was the initial therapy for patients with hemodynamic stability at the onset of hemobilia ( $n = 7$ ). TAE was indicated in several situations. In patients diagnosed with hemobilia by contrast-enhanced CT during CT-guided ablation, TAE was performed immediately if there were signs

of significant hemodynamic instability ( $n = 2$ ) or if there was evidence of significant blood loss in the second contrast-enhanced CT performed at 10 min after thrombin injection ( $n = 6$ ). Significant hemodynamic instability was diagnosed if the patient developed heart rate  $<50$  beats per minute, severe abdominal pain, sudden hematemesis or vomiting, systolic blood pressure  $<80$  mm Hg, or diastolic blood pressure  $<50$  mm Hg.<sup>18</sup> In patients diagnosed with hemobilia after ablation treatment, TAE was performed immediately if there were obvious signs of hemodynamic instability ( $n = 1$ ). Additionally, TAE was performed for patients in whom conservative treatment failed ( $n = 1$ ). During TAE, if the exact bleeding sites were not identified, selective TAE was performed to cover the major arteries in the ablation area. In patients with infection, antibiotic therapy ( $n = 8$ ) and drainage ( $n = 3$ ) were the two main strategies used. Drainage was performed for patients with total bilirubin  $\geq 5$  mg dl<sup>-1</sup> and imaging evidence of duct obstruction.

The prognosis of post-ablation hemobilia was favorable. All the patients with HCC with post-ablation hemobilia were followed up for 6 months and no one died during this period. The symptoms of 17 patients (81%) were resolved within 2 weeks. The characteristic CT findings of hemobilia in all patients disappeared 1 month after the ablation. Additionally, a gallstone was observed in 1 patient at 1 month after the ablation therapy (Figure 4).

Two patients experienced recurrence of hemobilia. Table 3 shows the characteristics of these patients. Hemodynamic instability-related symptoms at the onset of hemobilia and inaccurate

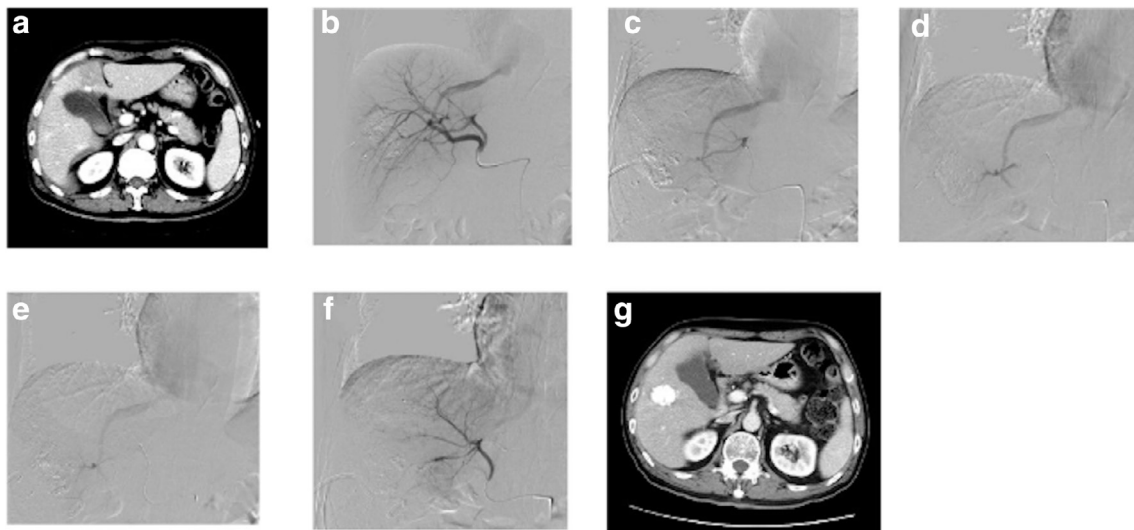
Table 2. The result of univariate analysis

	Hemobilia group (n = 21)	Control group (n = 63)	Univariate analysis			Multivariate analysis				Score
			p	OR	p	$\beta$	p	OR	95% CI	
Ascites										
Yes	1 (5%)	9 (14%)	0.265	0.298	0.035–2.506					
No (Reference)	20 (95%)	54 (86%)								
The times of puncture	5.48 ± 2.46	4.22 ± 2.00								
≤3	3 (14%)	29 (46%)	0.019	6.184	1.341–28.516	1.410	0.206	4.097	0.461–36.383	
>3 (Reference)	18 (86%)	34 (54%)								
Ablation methods										
RFA (Reference)	11 (52%)	38 (60%)								
MWA	6 (29%)	20 (32%)	0.858	1.112	0.346–3.574					
Cryoablation	4 (19%)	5 (8%)	0.187	2.774	0.609–12.647					
The number of ablated tumors	2.38 ± 3.00	1.67 ± 1.00								
≤2 (Reference)	14 (67%)	55 (87%)								
>2	7 (33%)	8 (13%)	0.043	3.678	1.039–13.017	0.868	0.325	2.382	0.423–13.402	
The maximal diameter of tumor (mm)	30.31 ± 19.40	25.96 ± 19.55								
≤47 (Reference)	15 (71%)	57 (90%)								0
>47	6 (29%)	6 (10%)	0.046	3.712	1.023–13.473	1.789	0.035	5.983	1.134–31.551	6
Location of ablated tumors										
Peripheral tumor (Reference)	4 (19%)	19 (30%)								
Central tumor	17 (81%)	44 (70%)	0.359	1.715	0.542–5.427					
The minimal distance between the applicator to the portal trunk (mm)	11.95 ± 11.71	24.76 ± 15.79								
>8 (Reference)	9 (43%)	53 (84%)								0
≤8	12 (57%)	10 (16%)	0.002	4.893	1.805–13.264	1.573	0.024	4.821	1.225–18.975	5
The minimal distance between applicator and gall bladder (mm)	24.67 ± 16.11	33.03 ± 21.11								
>7 (Reference)	19 (90%)	57 (90%)								
≤7	2 (10%)	6 (10%)	1.000	1.000	0.202–4.955					
ALB (g L <sup>-1</sup> )	34.69 ± 4.17	38.70 ± 5.94								
≥35 (Reference)	12 (57%)	52 (83%)								
<35	9 (43%)	11 (17%)	0.025	3.655	1.174–11.377	0.663	0.355	1.941	0.476–7.912	
PT (s)	13.32 ± 1.51	12.52 ± 1.33								
≤13 (Reference)	8 (38%)	45 (71%)								
>13	13 (62%)	18 (29%)	0.007	4.469	1.498–13.335	0.993	0.229	2.700	0.536–13.610	

ALB, Albumin; MWA, Microwave ablation; OR, Odds ratio; PT, Prothrombin time; RFA, Radiofrequency.



Figure 3. A 61 years old patient with HCC with post-ablation hemobilia. (a) The CT image of hemobilia during the ablation therapy. (b) An arterio-portal fistula was observed during diagnostic angiography. (c-e) The embolization of arterio- fistula was performed. (f) The arterio-portal fistula disappeared after embolization. (g) The CT image at 2 months after ablation therapy. HCC, hepatocellular carcinoma.



embolization during TAE were the common factors in these two patients.

#### DISCUSSION

This multicenter, matched case-control study aimed to identify the independent risk factors for hemobilia. Two independent risk factors were identified: maximum tumor diameter >47 mm

and minimum distance between the applicator and the portal trunk of  $\leq 8$  mm. The risk model created using these risk factors had an AUC of 0.76. To our knowledge, this is the first study to report a predictive risk model for post-ablation hemobilia. Additionally, the study suggested that significant hemodynamic instability-related symptoms at the onset of hemobilia and

Figure 4. A 42-year-old patient with HCC with post-ablation hemobilia. (a) The pre-operative axial CT image showed the multiple tumors in the right liver lobe, with deposition of lipiodol. (c) The intraoperative contrast-enhanced CT image showed that high-density material (arrow) filled in the gallbladder. (d) The gallstone (arrow) was observed on the magnetic resonance imaging at 1month after the ablation.

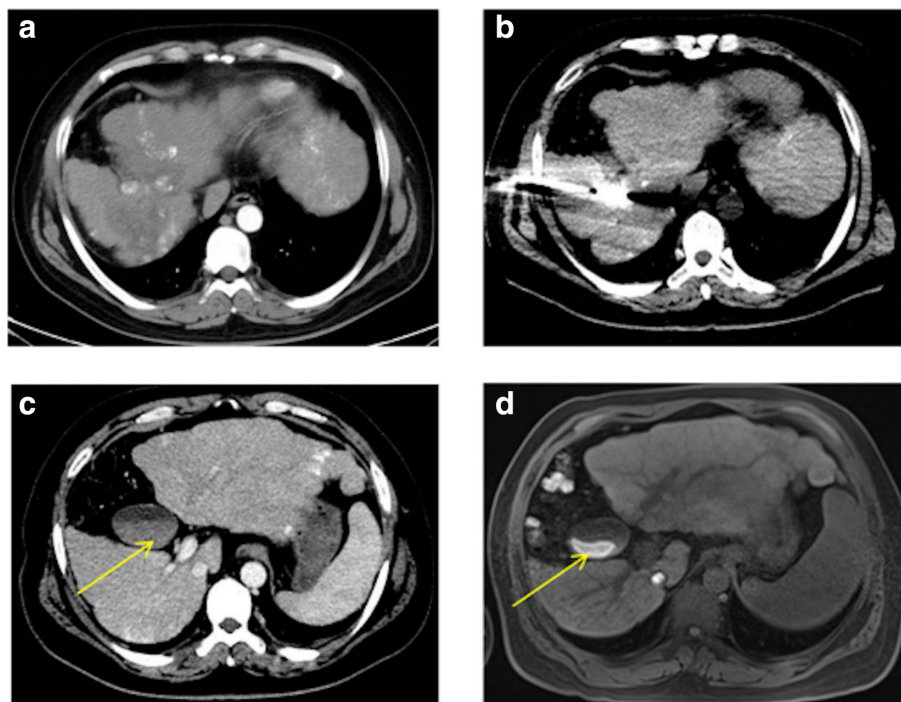


Table 3. The characteristics of patients with or without recurrent hemobilia

		Patients with recurrent hemobilia (n = 2)	Patients without recurrent hemobilia (n = 19)
Child-Pugh Class	A	2 (100%)	17 (89%)
	B	0 (0%)	2 (11%)
BCLC stage	A	1 (50%)	12 (63%)
	B	0 (0%)	5 (26%)
	C	1 (50%)	2 (11%)
Pre-operative PLT ( $\times 10^9 L^{-1}$ )		86	88
Pre-operative PT (s)		12	13
Tumor location	Peripheral tumor	0 (%)	4 (21%)
	Central tumor	2 (100%)	15 (79%)
Number of ablated tumors		3	2.3
The maximal diameter of ablated tumors (mm)		18	31
The minimum distance between the applicator to the portal trunk (mm)		24	10
The minimum distance between applicator and gall bladder (mm)		11	26
The times of puncture		8	5
Ablation methods	RFA	2 (100%)	9 (47%)
	MWA	0 (%)	6 (32%)
	Cryoablation	0 (%)	4 (21%)
The symptoms at the onset of post-ablation hemobilia	During ablation treatment	1. Hematemesis (n = 1) 2. Declined heart rate of 54 beats/min (n = 1)	None
	After ablation treatment	None	1. Abdominal pain (n = 2) 2. Sudden sub xiphoid pain, intense vomiting, profuse sweating, melena and transient unconsciousness (n = 1)
Emergency TAE		2 (100%)	6 (32%)
Embolization of exact bleeding site in the TAE among patients treated by TAE		1/2 (50%)	7/8 (88%)
The time of diagnosis	During ablation	2 (100%)	17 (89%)
	After ablation	0 (%)	2 (11%)

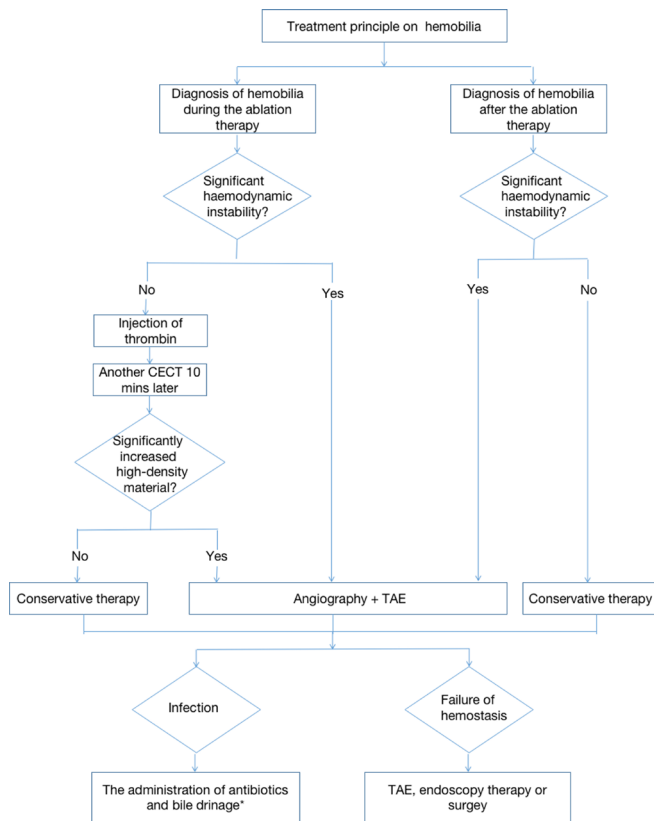
BCLC, Barcelona clinic liver cancer; MWA, microwave ablation; RFA, Radiofrequency ablation; TAE, Trans-arterial embolization.

inaccurate embolization during TAE might increase the risk of recurrence of hemobilia.

Hsieh et al<sup>15</sup> reported that central-type puncture track was an independent risk factor for hemobilia after CT-guided ablation. Although they studied how hemobilia was associated with the relationship between the applicator and the portal vein during ablation treatment, they did not specify a safe distance. In our study, we found that distance  $\leq 8$  mm increased the risk of hemobilia. During pre-operative planning, if it is found that the applicator cannot be placed at a safe distance from the portal trunk, percutaneous ethanol injection (PEI) can be considered. After thermal ablation, adjuvant PEI has been successfully used to eliminate residual tumor tissue lying close to major vessels.<sup>19-21</sup>

Tumor diameter  $>47$  mm was another independent risk factor for hemobilia in the present study; this has not been reported in previous studies. Tumor diameter will obviously influence the distance between the applicator and the portal trunk. Larger tumors are more likely to involve or be close to the portal trunk. Thus, during the ablation of tumors  $> 47$  mm, there is a higher possibility that the applicator will be located  $\leq 8$  mm from the portal trunk. However, in the studies of Hsieh et al<sup>15</sup> and Goto et al<sup>22</sup>, tumor diameter did not significantly affect the risk of post-ablation hemobilia. The smaller mean tumor size in their studies might be the reason why their findings differed from ours. Hsieh et al<sup>15</sup> only included tumors that were considered unsuitable for ultrasound-guided ablation—*i.e.* single tumor  $<5$  cm or 2–3 tumors  $<3$  cm each. In the study of Hsieh et al<sup>15</sup>, tumor sizes in

Figure 5. The treatment algorithm on post-ablation hemobilia. CECT, contrast-enhanced CT; TAE, Trans-arterial embolization. \*In patients with total bilirubin  $\geq 5 \text{ mg dl}^{-1}$  and the evidence of duct obstruction in image examinations, bile drainage is indicated.



the hemobilia group and the control group were  $18.57 \pm 7.66 \text{ mm}$  and  $16.36 \pm 4.93 \text{ mm}$ , respectively. Goto et al<sup>22</sup> only performed ablation on patients with 1–3 tumors  $\leq 3 \text{ cm}$ ; the mean tumor size was  $23 \pm 11 \text{ mm}$  in their study. In our study, the tumor diameters in the hemobilia and the control group were  $30.31 \pm 19.40 \text{ mm}$  and  $25.96 \pm 19.55 \text{ mm}$ , respectively.

We also analyzed the treatment used in our cohort. To our knowledge, there is still no consensus on the treatment for post-ablation hemobilia. Figure 5 shows a treatment algorithm that we propose based on our experience.

The tendency of recurrence is considered as a characteristic of hemobilia.<sup>23</sup> Few studies have explored the exact reasons. Based on our results, significant hemodynamic instability might increase the risk of the recurrence of hemobilia. In general,

there are two types of source of hemobilia, arterial and venous source. Due to the low-pressure gradient between veins and biliary ducts, hemobilia originates from hepatic veins or portal veins would be more likely to be low volume and stop spontaneously (except in cases of portal hypertension).<sup>5,6</sup> The presence of severe hemodynamic instability at the onset of hemobilia indicates high pressure gradient between the injured vessels and bile ducts and high possibility of reopening of the fistula before the wound completely heal, thus, implying a high risk of recurrence. Furthermore, inaccurate TAE, in which the performer failed to identify the exact bleeding source and just performed selective embolization, is not likely to make complete embolization of the injured vessels, thus leading to a high risk of recurrence.

An *in vivo* experiment on dog liver<sup>23</sup> showed that, in the presence of bile, fibrin deposition on vessel wounds and scar formation were significantly reduced. Thus, the healing of fistulas between biliary system and vessels could be slow, with frequent episodes of recurrent hemobilia. In a previous case report,<sup>11</sup> the patient developed upper gastrointestinal hemorrhage and abdominal pain 35 days after ablation treatment. Hemobilia was diagnosed by angiography, and the exact bleeding site was embolized; however, the hemobilia recurred 2 days later. This case is consistent with our theory that significant hemodynamic instability at the onset of hemobilia might increase the risk of recurrence.

The present study has some limitations. First, the small sample size was very small, and different ablation methods were used. Second, the treatment algorithm that we propose is based solely on our experience; there is scope for improvement.

According to our results, the incidence of post-ablation hemobilia is not high. So, from the aspect of causing hemobilia, ablation is a safe therapy. But there is still some room for ablation to reduce the incidence of hemobilia. The results of our study would provide reference on how to make the ablation become safer.

## CONCLUSION

Tumor size  $>47 \text{ mm}$  and distance between the applicator and the portal trunk  $\leq 8 \text{ mm}$  appear to be independent risk factors for occurrence of post-ablation hemobilia. These factors were used to construct a predictive risk model for post-ablation hemobilia.

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