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Impact of metabolic dysfunction-associated fatty liver disease on survival outcomes in patients undergoing radical resection for hepatitis B virus-related hepatocellular carcinoma

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The prevalence of concomitant metabolic dysfunction-associated fatty liver disease (MAFLD) in patients with hepatitis B virus-associated hepatocellular carcinoma (HBV-HCC) is increasing, though the relationship between MAFLD and HBV-HCC remains unclear. The aim of this study is to evaluate the clinical impact of MAFLD on survival outcomes in patients with HBV-HCC after radical resection. Patients with HBV-HCC who underwent radical resection consecutively from January 2015 to December 2020 were included. The retrospective analysis focused on the correlation between histologically confirmed concomitant MAFLD and clinical outcomes. Among the 843 patients with HBV-HCC who underwent radical resection, concomitant MAFLD was observed in 172 (20.4%) patients. In comparison to the non-MAFLD group, the MAFLD group did not have a significant impact on recurrence-free survival (RFS) or overall survival (OS) rates at 1-, 3-, and 5-years (all $P > 0.05$). However, subgroup analysis revealed significantly lower 1-, 3-, and 5-year rates of RFS and OS in the diabetic MAFLD group compared to the non-diabetic MAFLD group (all $P < 0.05$). Moreover, diabetic MAFLD was an independent risk factor associated with poorer OS after radical resection (HR, 1.444; 95% CI 1.082–2.331, $P = 0.032$). Concomitant diabetic MAFLD is associated with a poor prognosis after radical resection in patients with HBV-HCC.

Keywords Metabolic dysfunction-associated fatty liver disease, Hepatocellular carcinoma, Radical resection, Prognosis

Hepatocellular carcinoma (HCC) is the most prevalent primary liver malignancy and ranks as the third leading cause of cancer-related mortality worldwide[1,2]. The infection of Hepatitis B virus (HBV) is a prominent etiological factor for HCC globally, particularly in sub-Saharan Africa and East Asia[3,4]. A survey in China showed that HBV-related HCC (HBV-HCC) accounts for 87.5% of all HCC[5]. Given the scarcity of liver donors and other contributing factors, hepatectomy remains the foremost and most efficacious treatment for early HCC at present[6,7]. It is worth noting that the recurrence rate of HCC after radical resection can be as high as 70% within 5 years, significantly impacting patients' prognosis[8,9]. The prognosis factors for postoperative recurrence of HCC, such as tumor size, number, differentiation, microvascular invasion (MVI), and tumor capsule, have been established as significant factors[10,11].

Nonalcoholic fatty liver disease (NAFLD) has exhibited a progressive increase over the past few decades, reaching a prevalence almost equivalent to that of obesity. It has now emerged as the predominant chronic liver disease worldwide, posing a significant health threat to approximately 25% of the global population[12,13]. The redefinition of NAFLD as metabolic dysfunction-associated fatty liver disease (MAFLD) in 2020 reflects the enhanced understanding of its etiology and pathogenesis[14]. MAFLD terminology has demonstrated superiority in several crucial aspects compared to traditional NAFLD terminology, including its effective identification

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of high-risk liver patients and assessment of extra-hepatic mortality risks such as cardiovascular disease and chronic kidney disease[15–17].

Given the global high prevalence of MAFLD, it is common for HCC patients to exhibit concurrent MAFLD[18]. Furthermore, in the Asia-Pacific region, there is a frequent co-occurrence of HBV-HCC accompanied by MAFLD[19]. However, there is limited knowledge available regarding the association between MAFLD as a comprehensive term for this metabolic disorder and the prognosis of patients with HBV-HCC undergoing hepatectomy. Therefore, this retrospective study aimed to investigate the clinical impact of MAFLD on survival outcomes in patients with HBV-HCC after radical resection.

Methods

Study design and patient selection

The clinical data of patients with HBV-HCC who underwent radical resection at Mengchao Hepatobiliary Hospital of Fujian Medical University from January 2015 to December 2020 were retrospectively collected. This study was approved by the Medical Ethics Committee of Mengchao Hepatobiliary Hospital of Fujian Medical University (No. 2021-035-01). All patients admitted to the hospital have signed a broad consent, which is a specific type of informed consent obtained upon admission. All methods and studies were conducted in accordance with the relevant guidelines and regulations. Our study findings were reported following the Strengthening the Reporting of Observational Studies in Epidemiology Guidelines. The inclusion criteria were patients with HCC confirmed by histological after radical resection and with favorable liver function reserve (Child-Pugh grade A or B). The exclusion criteria were as follows: without HBV infection; hepatocellular-cholangiocarcinoma (HCC - ICC); presence of other malignant tumors; prior invasive treatment [transcatheter hepatic arterial chemoembolization (TACE) or radiofrequency ablation (RFA)]; multiple intrahepatic metastases, invasion of adjacent organs, or distant metastases; incomplete clinical data and perioperative death.

Data collection

The clinical data were retrospectively collected from medical record, including baseline data [(age, sex, body mass index (BMI), alcohol consumption, type 2 diabetes mellitus (T2DM), hypertension, serum biochemistry, HbA1c, high-sensitive C-reactive protein, prothrombin time (PT), white blood cell (WBC), hemoglobin (HB), platelet (PLT), alpha-fetoprotein (AFP), HBsAg, HBV DNA, Child-Pugh grading, BCLC staging, etc.], surgical methods, tumor features (size, number, differentiation, capsule, MVI, microsatellite lesions, etc.), and intraoperative blood transfusion (yes/no).

Definition

The diagnostic criteria in this study for MAFLD require histologically confirmed hepatic steatosis and the presence of at least one of the following: BMI ≥ 23 kg/m^2, T2DM, or metabolic dysregulation (MD)[14]. Cirrhosis was defined by the histopathological presence of pseudolobules. The definition of excessive alcohol consumption was based on alcohol intake of ≥ 30 g/d for men and ≥ 20 g/d for women[20]. Radical resection, also known as R0 resection, was defined as complete tumor removal with no microscopic residual cancer at the resection margin, confirmed by histopathological examination. HCC recurrence was defined as the presence of new lesions in the liver detected by imaging examinations that met the diagnosis criteria of HCC[21].

Follow-up

All patients with HCC were regularly followed up every 3 months for the first 2 years after radical resection, every 6 months from years 2–5, and annually thereafter. Nucleoside antiviral drugs, such as entecavir or tenofovir, were administered in accordance with guidelines. The retreatment strategies for HCC recurrence were discussed by multidisciplinary teams. The primary outcome measures included recurrence-free survival (RFS) and overall survival (OS). RFS was defined as the duration from the date of the radical resection to the date of recurrence or last follow-up. OS was defined as the duration from the date of radical resection to the date of death or final follow-up.

Statistical analysis

SPSS software (version 22.0) and GraphPad Prism 8.0 were used to perform statistical analysis. Continuous variables were presented as medians (interquartile range, IQR) and compared by using either T-test or Mann-Whitney U test. Categorical variables were presented as count (percentages) and compared by using either a $\chi 2$ test or Fisher exact test. RFS and OS were calculated with the Kaplan-Meier method, with group comparisons performed using the log-rank test. Cox regression models were applied to analyze risk factors associated with RFS and OS after radical resection in patients with HBV-HCC. Factors that were significant in the univariate analysis ($P < 0.05$) were included in multivariate analyses of RFS and OS. The hazard ratios (HR) and 95% confidence intervals (CI) were also calculated for each factor. P value < 0.05 indicated statistical significance.

Results

Baseline characteristics of patients with HBV-HCC

A total of 1049 HCC patients who underwent radical resection between 2015 and 2020 were screened for this study. We excluded 206 patients, including 83 patients without HBV infection, 31 patients with HCC-ICC, 12 patients with other malignancies, 29 patients who underwent preoperative TACE, 7 patients who underwent preoperative RFA, 10 perioperative death, and 34 patients with incomplete data. Ultimately, 843 patients with HBV-HCC were categorized into two groups based on the presence or absence of MAFLD: MAFLD group (172,

20.4%) and non-MAFLD group (671, 79.6%). Flow chart for the selection of the study population is shown in Fig. 1.

The 843 patients with HBV-HCC consisted of 688 (81.6%) males and 155 (18.4%) females. The median age was 57.0 (49.0–64.0) years. The proportions of patients with BMI ≥ 23 kg/m^2, T2DM, and MD were 51.5% (434/843), 13.9% (117/843), and 34.1% (287/843), respectively. There were 752 (89.2%) patients with HBV DNA levels ≥ 500 IU/ml, 787 (93.4%) patients with Child-Pugh grade A, and 682 (80.9%) patients with cirrhosis. The median tumor diameter was 4.0 (2.7–6.7) cm. The majority of these tumors were solitary, accounting for 87.3% (736/843) (Table 1). Compared with the non-MAFLD group, the MAFLD group exhibited a higher BMI (24.4 vs. 22.4 kg/m^2, $P < 0.001$) and a greater proportion of patients with combined BMI ≥ 23 kg/m^2, T2DM or MD in the MAFLD group (80.2% vs. 44.1%, 25.0% vs. 11.0%, and 51.2% vs. 29.7%; all $P < 0.001$). Additionally, the ALT levels were also significantly higher in the MAFLD group compared to the non-MAFLD group (35.0 vs. 32.0 IU/L, $P = 0.034$). The two groups did not exhibit any significant differences in terms of other characteristics (all $P > 0.05$) (Table 1).

RFS and OS after radical resection in patients with HBV-HCC

The median RFS of the MAFLD group and non-MAFLD group was 35.0 and 34.0 months, respectively. There were no significant differences in RFS rates at 1-, 3-, and 5-years between the MAFLD group and the non-MAFLD group (82.8%, 46.3%, and 26.8% vs. 80.6%, 47.4%, and 24.1%; $P = 0.361$) (Fig. 2A). The median OS of the MAFLD group and the non-MAFLD group was 56.0 and 54.0 months, respectively. There were also no significant differences in OS rates at 1-, 3-, and 5-years between the two groups (95.4%, 76.3%, and 43.0% vs. 93.9%, 71.5%, and 38.5%; $P = 0.289$) (Fig. 2B).

To further elucidate the impact of different subtypes of MAFLD on survival outcomes in patients with HBV-HCC, they were categorized into two groups based on the presence or absence of T2DM: diabetic MAFLD group (43, 25.0%) and non-diabetic MAFLD group (129, 75.0%).

Subgroup analysis showed that the median RFS of the diabetic MAFLD, non-diabetic MAFLD and non-MAFLD group were 29.0, 36.0, and 34.0 months, respectively. The 1-, 3-, and 5-year RFS rates were significantly lower in the diabetic MAFLD group compared to the non-diabetic MAFLD group (70.6%, 36.6%, and 19.1% vs. 86.9%, 49.5%, and 29.0%, $P = 0.046$). There were no significant differences in RFS rates at 1-, 3-, and 5-years between non-MAFLD group and diabetic MAFLD or non-diabetic MAFLD group (all $P > 0.05$) (Fig. 3A). The median OS of the diabetic MAFLD, non-diabetic MAFLD, and non-MAFLD groups were 45.0, 59.0, and 56.0 months, respectively. The 1-, 3-, and 5-years OS rates were also significantly lower in the diabetic MAFLD group compared to the non-diabetic MAFLD group (93.3%, 65.3%, and 34.7% vs. 95.4%, 80.0%, and 45.8%, $P = 0.039$).

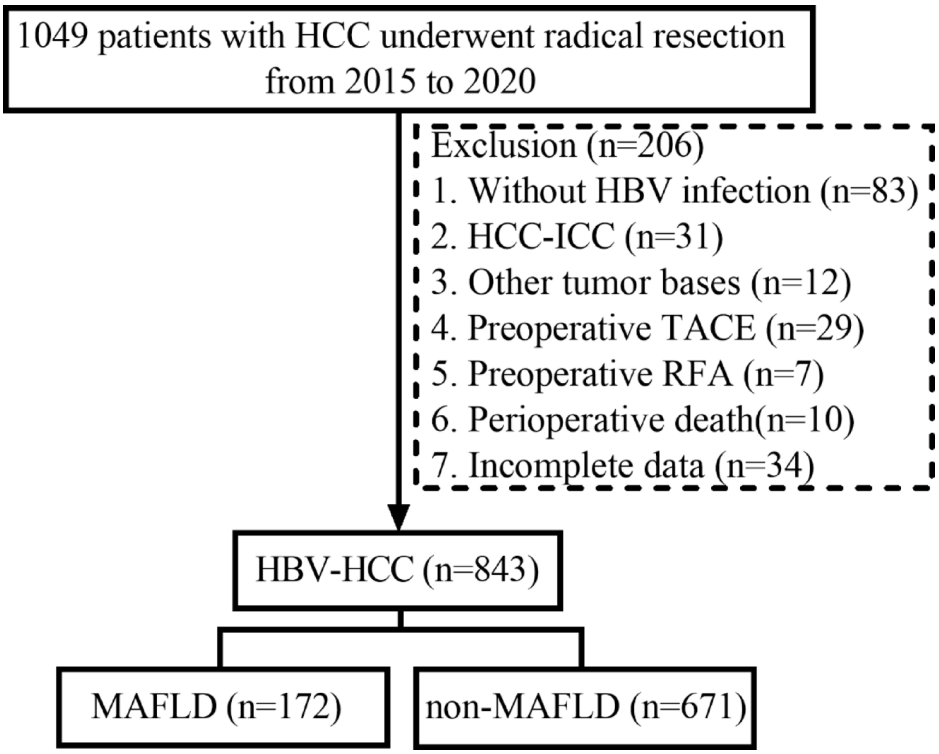

Fig. 1. Flow chart for the selection of the study population. HCC, hepatocellular carcinoma; HBV, hepatitis B virus; HBV-HCC, hepatitis B virus-related hepatocellular carcinoma; MAFLD, metabolic dysfunction-associated fatty liver disease; HCC-ICC, combined hepatocellular- cholangiocarcinoma; TACE, transcatheter hepatic arterial chemoembolization; RFA, radiofrequency ablation.

Variables	Patients ($n=843$)	MAFLD ($n=172$)	non-MAFLD ($n=671$)	P value
Age (years)	57.0 (49.0–64.0)	57.0 (48.0–62.0)	57.0 (49.0–64.0)	0.388
Male	688 (81.6%)	133 (77.3%)	555 (82.7%)	0.104
BMI (kg/m^2)	23.0 (21.1–25.0)	24.4 (22.8–25.8)	22.4 (20.8–24.5)	< 0.001
≥ 23	434 (51.5%)	138 (80.2%)	296 (44.1%)	< 0.001
T2DM	117 (13.9%)	43 (25.0%)	74 (11.0%)	< 0.001
MD	287 (34.0%)	88 (51.2%)	199 (29.7%)	< 0.001
Alcohol consumed	88 (10.4%)	24 (14.0%)	64 (9.5%)	0.091
HBV DNA (≥ 500 IU/mL)	752 (89.2%)	159 (92.4%)	593 (88.4%)	0.125
Cirrhosis	682 (80.9%)	147 (85.5%)	535 (79.7%)	0.110
Child-Pugh grade				0.589
A	787 (93.4%)	159 (92.4%)	628 (93.6%)	
B	56 (6.6%)	13 (7.6%)	43 (6.4%)	
WBC (×10^9/L)	5.5 (4.6–6.6)	5.5 (4.6–6.4)	5.5 (4.5–6.6)	0.690
HB (g/L)	143.0 (139.0-152.0)	143.0 (136.0-154.0)	143.0 (139.0-152.0)	0.839
PLT (×10^9/L)	168.0 (150.0-208.0)	170.5 (149.0-198.8)	167.0 (150.0-209.0)	0.523
PT (s)	13.4 (12.7–13.9)	13.3 (12.7–13.7)	13.4 (12.8–13.9)	0.136
ALB (g/L)	40.0 (38.0–43.0)	40.0 (38.0-43.8)	40.0 (38.0–43.0)	0.633
TBIL (μmol/L)	16.3 (12.0-21.7)	16.6 (11.9–22.8)	16.3 (12.0-21.6)	0.771
ALT (IU/L)	33.0 (23.0–49.0)	35.0 (27.0–51.0)	32.0 (23.0–49.0)	0.034
AFP (μg/L)	47.7 (6.3-697.4)	48.8 (5.8–217.0)	47.7 (6.3-802.2)	0.219
Tumor diameter (cm)	4.0 (2.7–6.7)	4.0 (2.9-6.0)	4.0 (2.5-7.0)	0.753
Number of tumors				0.416
1	736 (87.3%)	147 (85.5%)	589 (87.8%)	
≥ 2	107 (12.7%)	25 (14.5%)	82 (12.2%)	
Tumor differentiation				0.125
Well	12 (1.4%)	4 (2.3%)	8 (1.2%)	
Moderate	390 (46.3%)	67 (39.0%)	323 (48.1%)	
Poor	441 (52.3%)	101 (58.7%)	340 (50.7%)	
Tumor capsule				0.070
Complete	190 (22.5%)	46 (26.7%)	144 (21.5%)	
Incomplete	534 (63.3%)	96 (55.8%)	438 (65.3%)	
No tumor capsule	119 (14.1%)	30 (17.4%)	89 (13.3%)	
Microvascular invasion	460 (54.6%)	91 (52.9%)	369 (55.0%)	0.624
Microsatellite lesions	189 (22.4%)	35 (20.3%)	154 (23.0%)	0.465
BCLC stage				0.945
0	8 (0.9%)	2 (1.2%)	6 (0.9%)	
A	755 (89.6%)	154 (89.5%)	601 (89.6%)	
B	80 (9.5%)	16 (9.3%)	64 (9.5%)	
Surgical method				0.711
Open	437 (51.8%)	87 (50.6%)	350 (52.2%)	
Laparoscopic	406 (48.2%)	85 (49.4%)	321 (47.8%)	

Table 1. Baseline characteristics of patients with HBV-HCC.

There were no significant differences in OS rates at 1-, 3-, and 5-years between non-MAFLD group and diabetic MAFLD group or non-diabetic MAFLD group (all $P > 0.05$) (Fig. 3B).

Prognostic factors for RFS after radical resection in patients with concurrent MAFLD and HBV-HCC

Cox regression analysis revealed that among 172 patients with HBV-HCC in the context of MAFLD, diabetic MAFLD was associated with worse RFS after radical resection (HR, 1.569; 95% CI, 1.035–2.380, $P = 0.034$), but it did not emerge as an independent risk factor ($P = 0.222$). The independent risk factors associated with worse RFS included maximum tumor diameter ≥ 5 cm (HR, 1.654; CI, 1.094–2.498, $P = 0.017$), tumor number ≥ 2 (HR, 1.822; 95% CI, 1.028–3.229, $P = 0.040$), microsatellite lesions (HR, 1.687; 95% CI, 1.003–2.837, $P = 0.049$), and BCLC stage B (HR, 1.862; 95% CI, 1.029–3.368, $P = 0.040$) (Table 2).

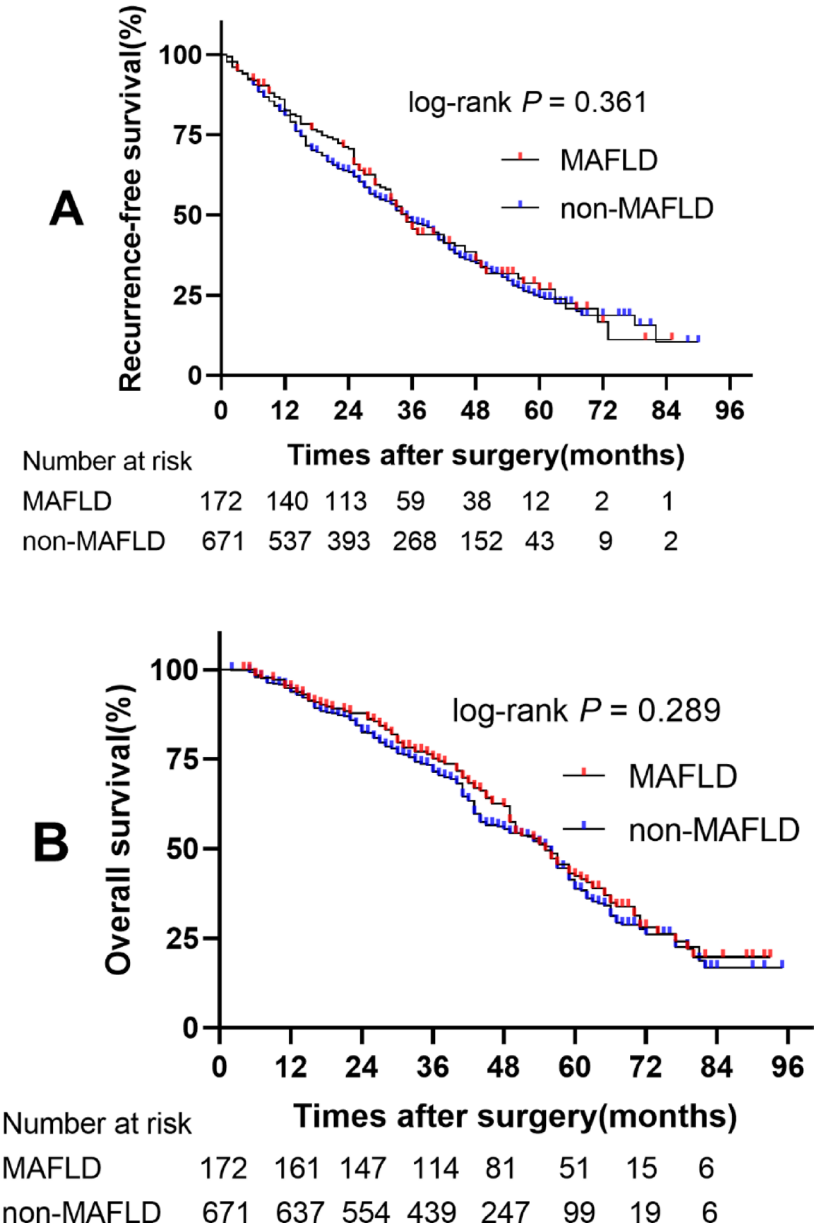

Fig. 2. RFS (**A**) and OS (**B**) in two groups of patients with HBV-HCC. MAFLD, metabolic dysfunction-associated fatty liver disease; HBV-HCC, hepatitis B virus-related hepatocellular carcinoma; RFS, recurrence-free survival; OS, overall survival.

Prognostic factors for OS after radical resection in patients with concurrent MAFLD and HBV-HCC

Cox regression analysis revealed that among 172 patients with HBV-HCC in the context of MAFLD, diabetic MAFLD was associated with worse OS after radical resection (HR, 1.662; 95% CI, 1.094–2.525, $P=0.017$). Furthermore, it was identified as an independent risk factor (HR, 1.444; 95% CI, 1.082–2.331, $P=0.032$). The other independent risk factors associated with worse OS included maximum tumor diameter ≥ 5 cm (HR, 1.399; CI, 1.015–2.139, $P=0.021$), tumor number ≥ 2 (HR, 2.031; 95% CI, 1.161–3.552, $P=0.013$), and poor tumor differentiation (HR, 1.622; 95% CI, 1.011–1.964, $P=0.040$) (Table 3).

Discussion

In this study, we retrospectively evaluated the clinical impact of MAFLD on the long-term prognosis of patients with HBV-HCC after radical resection. We found that concomitant MAFLD in patients with HBV-HCC after radical resection had no impact on either RFS or OS. Notably, within the MAFLD subgroup, diabetic MAFLD was an independent risk factor for poor prognosis in patients with HBV-HCC after radical resection.

HCC patients with concurrent MAFLD are becoming increasingly prevalent due to the rising incidence of MAFLD. The overall prevalence of MAFLD in the population was 38.8%[22], while among overweight/obese

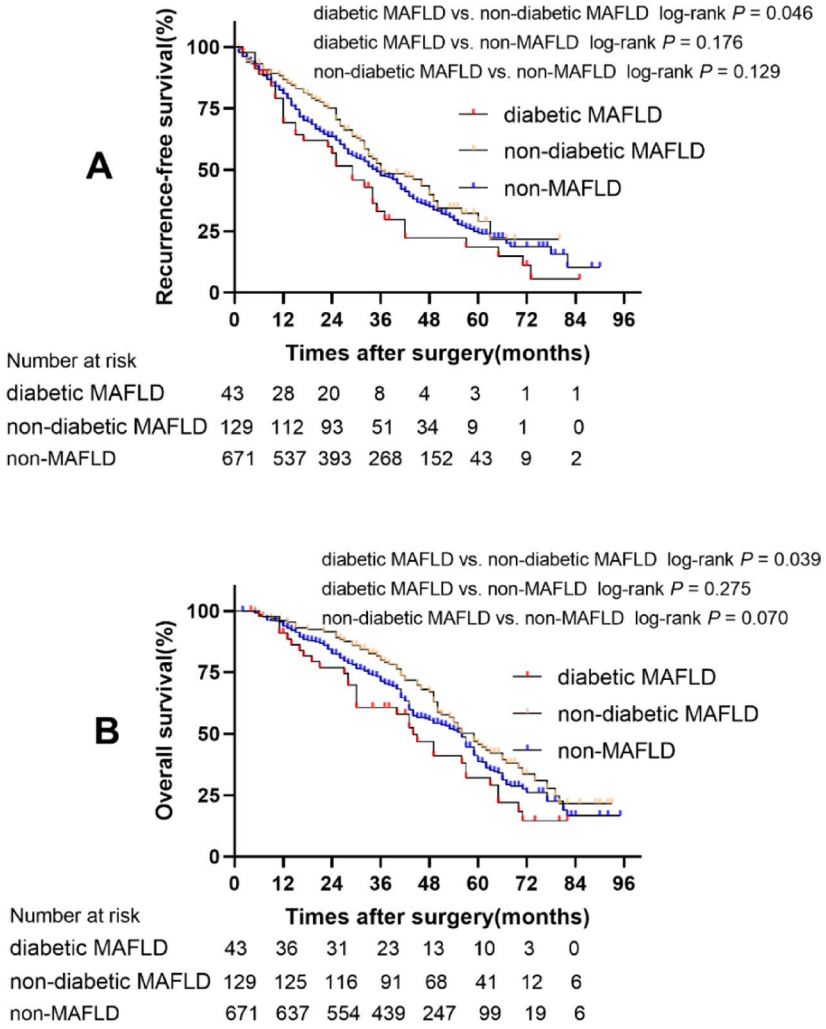

Fig. 3. RFS (**A**) and OS (**B**) in three groups of patients with HBV-HCC. MAFLD, metabolic dysfunction-associated fatty liver disease; HBV-HCC, hepatitis B virus-related hepatocellular carcinoma. RFS, recurrence-free survival; OS, overall survival.

adults, it reached 50.7%[23]. We observed that a substantial proportion of patients with HBV-HCC had MAFLD, accounting for 20.4%. The key disparity in baseline characteristics between the MAFLD group and the non-MAFLD group was the presence of metabolic disorders, with a higher prevalence observed in the MAFLD group. The heterogeneity of MAFLD, which includes various metabolic traits in its diagnostic criteria, accounts for this observed discrepancy. Our study found that the presence of MAFLD does not exert any significant influence on the tumor pathological characteristics of HBV-HCC. This was inconsistent with previous research that patients with concurrent HBV-HCC and MAFLD exhibit superior histological differentiation and lower rates of MVI[19]. Therefore, the confirmation of whether MAFLD influences the tumor pathological features of HBV-HCC requires multi-center and large sample clinical studies, as well as basic research.

The occurrence of postoperative recurrence remains a challenge in achieving satisfactory long-term survival, regardless of the etiology of HCC and the treatment strategy. A multicenter retrospective study of 756 patients who underwent radical hepatectomy abroad demonstrated a recurrence rate of 45.5% at a median follow-up of 36 months[24]. In order to evaluate the impact of MAFLD on the long-term prognosis of patients with HBV-HCC after radical resection, we analyzed the 1-, 3-, and 5-years RFS and OS in both the MAFLD and non-MAFLD groups, revealing no discernible differences. These findings suggest that MAFLD does not impact the RFS and OS rate in patients with HBV-HCC following radical resection. These findings are consistent with previous research[19,25,26]. However, a prior study found that MAFLD was significantly associated with poor prognosis in terms of HCC recurrence and all-cause mortality following surgical resection of HBV-HCC[27]. Nevertheless, this study lacked critical data regarding tumor characteristics (size and number), histopathological parameters (including R0 resection status, MVI, and tumor differentiation grade), serum HBV-DNA levels, and radiological confirmation of HCC recurrence.

However, subgroup analysis showed that the 1-, 3-, and 5-years RFS and OS rates were significantly lower in the diabetic MAFLD group compared to the non-diabetic MAFLD group. Moreover, the presence of diabetic MAFLD was further identified as an independent risk factor for OS. Our findings revealed that among the

Variables	Univariate		Multivariate	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age ≥ 60 (years)	0.759 (0.514–1.120)	0.165		
Male	1.011 (0.646–1.581)	0.963		
Alcohol consumed	1.620 (0.917–2.863)	0.097		
HBV DNA ≥ 500 IU/ml	1.604 (0.652–3.942)	0.303		
AFP ≥ 400 μg/L	10.083 (0.678–1.730)	0.738		
Cirrhosis	0.711 (0.423–1.197)	0.200		
Maximum tumor diameter ≥ 5 cm	1.918 (1.315–2.798)	0.001	1.654 (1.094–2.498)	0.017
Tumor number ≥ 2	2.015 (1.184-3.40)	0.009	1.822 (1.028–3.229)	0.040
Tumor differentiation (poor vs. well or moderate)	1.195 (0.683–2.450)	0.279		
Tumor capsule (no vs. complete or incomplete)	1.115 (0.576–1.752)	0.706		
MVI	1.641 (1.121–2.404)	0.011	1.086 (0.687–1.717)	0.723
Microsatellite lesions	1.953 (1.256–3.038)	0.003	1.687 (1.003–2.837)	0.049
BCLC stage B	1.825 (1.053–3.163)	0.032	1.862 (1.029–3.368)	0.040
Child-Pugh B	1.383 (0.755–2.530)	0.293		
Open surgery	1.690 (1.149–2.486)	0.008	1.406 (0.929–2.128)	0.107
Intraoperative blood transfusion	1.859 (1.126–3.064)	0.015	1.425 (0.846–2.401)	0.183
Diabetic MAFLD	1.569 (1.035–2.380)	0.034	1.334 (0.840–2.119)	0.222

Table 2. Prognostic factors for RFS after radical resection in patients with concurrent MAFLD and HBV-HCC.

Variables	Univariate		Multivariate	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age ≥ 60 (years)	0.944 (0.637–1.398)	0.775		
Male	1.208 (0.825–2.011)	0.468		
Alcohol consumed	1.230 (0.710–2.131)	0.461		
HBV DNA ≥ 500IU/ml	1.877 (0.690–5.108)	0.217		
AFP ≥ 400 μg/L	1.130 (0.704–1.812)	0.613		
Cirrhosis	1.201 (0.670–2.153)	0.538		
Maximum tumor diameter ≥ 5 cm	1.643 (1.110–2.431)	0.013	1.399 (1.015–2.139)	0.021
Tumor number ≥ 2	2.405 (1.417–4.081)	0.001	2.031 (1.161–3.552)	0.013
Tumor differentiation (poor vs. well or moderate)	1.443 (1.017–1.918)	0.007	1.622 (1.011–1.964)	0.040
Tumor capsule (no vs. complete or incomplete)	1.224 (1.037–1.971)	0.037	1.285 (0.917–2.126)	0.136
MVI	1.855 (1.316–2.906)	0.001	1.438 (0.903–2.288)	0.126
Microsatellite lesions	2.105 (1.330–3.332)	0.001	1.541 (0.888–2.674)	0.124
BCLC stage B	1.625 (0.889–2.351)	0.232		
Child-Pugh B	1.597 (0.907–2.814)	0.105		
Open surgery	1.508 (1.019–2.230)	0.040	1.210 (0.779–1.880)	0.397
Intraoperative blood transfusion	1.389 (0.849–2.274)	0.191		
Diabetic MAFLD	1.662 (1.094–2.525)	0.017	1.444 (1.082–2.331)	0.032

Table 3. Prognostic factors for OS after radical resection in patients with concurrent MAFLD and HBV-HCC.

diagnostic criteria for MAFLD, diabetic MAFLD was the only subtype capable of independently identifying a significantly increased mortality rate following radical resection for HBV-HCC. Population-based studies conducted over the past two decades have consistently demonstrated that diabetes was an independent metabolic risk factor for HCC and mortality, both in the general population and in patients with chronic hepatitis B[28,29]. The results of two studies involving patients with biopsy-proven MAFLD-related cirrhosis indicated that diabetes was significantly associated with an increased risk of HCC and mortality[30,31]. Our findings extend previous findings showing that patients with concurrent HBV-HCC and diabetic MAFLD had worse OS after radical resection than patients with non-diabetic MAFLD, which suggests a stronger association of diabetes than other metabolic characteristics with the long-term outcome of HBV-HCC. It is well known that insulin resistance serves as a shared pathophysiological hallmark of both T2DM and MAFLD. During hepatic fat accumulation, intracellular damage and insulin resistance synergistically exacerbate inflammation, fibrosis, and carcinogenesis[32]. Furthermore, elevated insulin levels can activate the insulin-like growth factor 1 signaling pathway, consequently driving tumor cell proliferation and survival[33].

This study has certain limitations. Firstly, due to the inclusion of only patients with HBV-HCC who underwent R0 resection in the study population, it was not feasible to evaluate the impact of MAFLD on the prognosis of non-R0 resection patients with HBV-HCC. The prognosis of non-R0 resection patients, however, was unfavorable, with the characteristics of the tumor itself being the primary determinant influencing their prognosis[34]. Secondly, this study may lead to an underestimation of the MAFLD population due to incomplete clinical data, such as inadequate measurement of waist circumference and HOMA-IR. However, our study included a substantial sample size, thereby enhancing the reliability of the findings. Thirdly, as a retrospective study, the original medical records suffered from inconsistent documentation of detailed surgical classifications (e.g., anatomical resection, non-anatomical resection, or major hepatectomy), precluding a comprehensive analysis of this parameter. Furthermore, our study could not assess the dynamic effects of time-varying variables, including antiviral therapy adherence, BMI, or cardiometabolic risk factors. Future prospective studies systematically collect standardized surgical data and dynamically monitor time-varying variables will be crucial for clarifying the impact of MAFLD on the prognosis of HBV-HCC. Fourthly, the findings of this study, conducted at a single center, necessitate validation through a multi-center study.

In conclusion, concomitant diabetic MAFLD was an independent risk factor for poor prognosis after radical resection in patients with HBV-HCC. Our findings emphasize the necessity of close monitoring and effective treatment for diabetic MAFLD to enhance long-term prognosis for patients with HBV-HCC.

Data availability

Data are available from the first author or corresponding author on reasonable request.

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Author contributions
K.G.X. and K.Y.K. were involved in the conception and design of the study. K.G.X., T.S.L., J.F.K. and Q.B.L. collected and analyzed data. K.G.X. drafted the manuscript. J.F.K. and K.Y.K. revised the manuscript. J.F.K. supervised the study. K.G.X. obtained funding. K.Y.K. was overall guarantor for the study. All authors have revised and approved the final version for publication.

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Declarations

Competing interests
The authors declare no competing interests.

Ethical approval
This study was approved by the Medical Ethics Committee of Mengchao Hepatobiliary Hospital of Fujian Medical University (No. 2021-035-01).

Consent to participate
All patients admitted to the hospital have signed a broad consent, which is a specific type of informed consent obtained upon admission. This enables the utilization of health data in future research without necessitating additional consent during ethical review.

Additional information
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