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Impact of MAFLD on the complications after hepatectomy in patients with HBV-related hepatocellular carcinoma

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Abstract

Metabolic dysfunction-associated fatty liver disease (MAFLD) is a term that was proposed in 2020 by a group of international experts. However, the impact of MAFLD on complications after hepatectomy in patients with hepatocellular carcinoma is not clear. The aim of this study is to explore the influence of MAFLD on the complications after hepatectomy in patients with hepatitis B virus-related hepatocellular carcinoma (HBV-HCC). Patients with HBV-HCC who underwent hepatectomy between January 2019 and December 2021 were consecutively enrolled. The predictors of complications after hepatectomy in HBV-HCC patients were retrospectively analyzed. Among the 514 eligible HBV-HCC patients, 117 (22.8%) were diagnosed with concurrent MAFLD. Post hepatectomy complications occurred in 101 patients (19.6%), including 75 patients (14.6%) with infectious complications and 40 patients (7.8%) with major complications. Univariate analysis showed that MAFLD was not the risk factor for complications after hepatectomy in patients with HBV-HCC ($P > .05$). However, univariate and multivariate analysis revealed that lean-MAFLD was an independent risk factor for post hepatectomy complications in patients with HBV-HCC (odds ratio 2.245; 95% confidence interval 1.243–5.362, $P = .028$). Similar results were found in the analysis of predictors for infectious and major complications after hepatectomy in patients with HBV-HCC. MAFLD commonly coexists with HBV-HCC and is not directly associated with complications after hepatectomy, but lean-MAFLD is an independent risk factor for post hepatectomy complications in patients with HBV-HCC.

Abbreviations: 95% CI = 95% confidence intervals, BMI = body mass index, HBV = hepatitis B virus, HBV-HCC = hepatitis B virus-related hepatocellular carcinoma, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, MAFLD = metabolic dysfunction-associated fatty liver disease, NAFLD = nonalcoholic fatty liver disease, OR = odds ratio, T2DM = type 2 diabetes mellitus.

Keywords: complications, hepatectomy, hepatocellular carcinoma, metabolic dysfunction-associated fatty liver disease

1. Introduction

Primary liver cancer is the 4th most common cause of cancer-related mortality and ranks 6th in terms of incident malignancy worldwide.[1] Hepatocellular carcinoma (HCC) accounts for 75% to 85% of primary liver cancer. The high incidence of HCC in Asia nations compared to other parts of the world is associated with the prevalence of chronic hepatitis B virus (HBV) infection.[2] Although numerous therapeutic options exist, hepatectomy is still the first choice for HCC patients in the current clinical practice.[3,4] The safety of hepatectomy for HCC has improved gradually and the mortality rate has decreased significantly, but postoperative complications are still common,[5,6] which can seriously affect the prognosis of patients.[7–9]

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease closely related to insulin resistance and genetic susceptibility. The global prevalence of NAFLD is approximately 25%.[10] Moreover, incidence of NAFLD- related HCC is also increasing.[11] Considering that HBV is endemic in the Asia-Pacific region, the prevalence of concurrent NAFLD in HBV-related HCC hepatitis B virus-related hepatocellular carcinoma (HBV-HCC) is expected to increase.[12,13] Metabolic dysfunction-associated fatty liver disease (MAFLD), formerly named NAFLD, is a new name proposed in 2020 by a panel of international experts and suggested an accompanying definition.[14] MAFLD more closely highlights the important role of metabolic dysfunction in fatty liver disease than NAFLD.[15] Most importantly, according to this new definition, the exclusion of HBV or hepatitis C virus (HCV) infection or alcohol intake is no longer a prerequisite for diagnosis of MAFLD.

However, coexistence of MAFLD and HCC is common.[16] To date, in the literature, there are no specific data regarding the

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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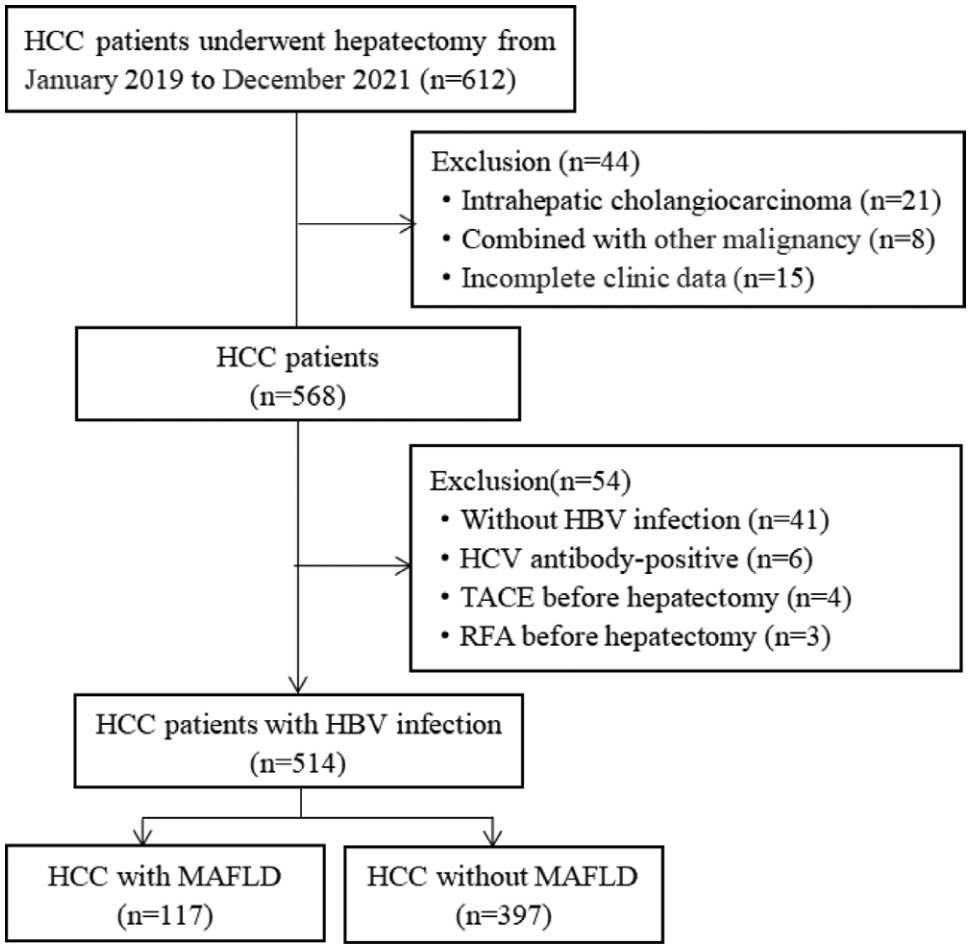

Figure 1. Flow chart for the selection of the study population.

impact of MAFLD on the complications after hepatectomy in HBV-HCC patients. Therefore, in this study, we aimed to evaluate the predictive value of the MAFLD for post hepatectomy complications in patients with HBV-HCC.

2. Methods

2.1. Study population

All patients with HBV-HCC who underwent hepatectomy at Meng Chao Hepatobiliary Hospital of Fujian Medical University from January 2019 to December 2021 were eligible for the study. Patients were selected based on the following inclusion criteria: confirmed HCC by postoperative histopathology; suffered from HBV infection; pathological hepatic steatosis report was available. The exclusion criteria were as follows: intrahepatic cholangiocarcinoma; HCV antibody-positive; combined with other malignancy; preoperative neoadjuvant therapy [including transcatheter hepatic arterial chemoembolization or radiofrequency ablation]; without complete clinical information. This study was approved by the Medical Ethics Committee of Meng Chao Hepatobiliary Hospital of Fujian Medical University (No. 2021-035-01).

2.2. Data collection

All data were obtained retrospectively from medical records, including age, gender, height, body weight, alcohol consumption, hypertension, type 2 diabetes mellitus (T2DM), blood counts, serum biochemistry, coagulation function, alpha-fetoprotein, Hepatitis B surface antigen, HBV DNA, and surgical method and intraoperative blood transfusion. The pathological features of resected tumors (histopathology type, size, numbers, cell differentiation, capsule formation, microvascular invasion, and microsatellite lesions), cirrhosis and hepatic steatosis were recorded. Postoperative complications such as intraabdominal hemorrhage, infection, liver failure, biliary leakage, ascites, and pleural effusion and operative death after hepatectomy were collected. The Child-Pugh score identified patients as grade A (5–6 points), B (7–9 points), or C (10–15points), based on the serum albumin, bilirubin, prothrombin time, and ascites and encephalopathy.

2.3. Definition

The diagnosis of MAFLD was based on the presence of hepatic steatosis (>5%, detected by postoperative liver histopathology) in addition to one of the following 3 criteria: body mass index (BMI) ≥ 23 kg/m^2, T2DM, or metabolic dysregulation.[14] The metabolic dysregulation was defined as the presence of 2 or more of the following abnormalities: high waist circumference, hypertension, abnormal levels of plasma triglycerides or cholesterol, prediabetes or insulin resistance and high level of plasma high-sensitivity C-reactive protein.[14] Lean-MALFD was defined as the patients with MAFLD and BMI < 23kg/m^2. Hepatectomy was defined as complete resection of all microscopic and macroscopic tumors with negative histologic resection margin.[17] Cirrhosis and hepatic steatosis were determined directly by imaging or postoperative hepatic histopathology. Alcohol consumption was defined as male ≥ 30 g/day, female ≥ 20 g/day.[18] HBV infection was defined as the evidence of hepatitis B surface

Table 1

Baseline characteristics of HBV-HCC patients.

Variables	All patients (n = 514)	MAFLD (n = 117)	nonMAFLD (n = 397)	*P* value
Age (yr)	57.0 (48.0–64.0)	56.0 (46.0–62.0)	57.0 (49.0–64.0)	.317
Male	418 (81.3%)	90 (76.9%)	328 (82.6%)	.395
BMI (kg/m^2)	22.9 (21.1–25.0)	24.2 (22.6–25.6)	22.3 (20.7–24.5)	< .001
≥ 23	253 (49.2%)	88 (75.2%)	165 (41.6%)	< .001
T2DM	77 (15.0%)	26 (22.2%)	51 (12.8%)	.013
Metabolic dysregulation	178 (34.6%)	56 (47.9%)	122 (30.7%)	.001
Alcohol consumed	57 (11.1%)	15 (12.8%)	42 (10.6%)	.497
HBV DNA (≥ 500 IU/mL)	403 (78.4%)	87 (74.4%)	316 (79.6%)	.226
Cirrhosis	418 (81.3%)	99 (84.6%)	319 (80.4%)	.298
Child-Pugh grade				.864
A	477 (92.8%)	109 (93.2%)	368 (92.7%)	
B	37 (7.2%)	8 (6.8%)	29 (7.3%)	
Leukocyte count (×10^9/L)	5.5 (4.6–6.6)	5.8 (4.8–6.7)	5.5 (4.5–6.6)	.185
Hemoglobin (g/L)	143.0 (138.0–152.3)	146.0 (137.5–156.0)	143.0 (138.5–152.0)	.366
Platelet count (×10^9/L)	169.0 (147.8–208.3)	173.0 (150.5–218.0)	165.0 (146.0–205.5)	.108
Prothrombin time (s)	13.3 (12.6–13.8)	13.2 (12.4–13.7)	13.3 (12.7–13.9)	.061
Albumin (g/L)	40.0 (38.0–43.0)	41.0 (38.0–44.0)	40.0 (38.0–43.0)	.101
Total bilirubin (μmol/L)	16.3 (12.0–21.7)	16.1 (11.6–22.1)	16.3 (12.0–21.7)	.586
ALT (IU/L)	33.0 (23.0–49.0)	38.0 (27.0–55.0)	31.0 (23.0–48.0)	.009
AFP (μg/L)	48.0 (6.2–620.0)	55.64 (5.6–427.2)	48.0 (6.2–774.1)	.515
Maximum tumor diameter (cm)	4.0 (2.7–6.4)	4.0 (3.0–5.6)	4.0 (2.5–6.8)	.906
Number of tumors				.495
Solitary	452 (87.9%)	105 (89.7%)	347 (87.4%)	
Multiple	62 (12.1%)	12 (10.3%)	50 (12.6%)	
Tumor cell differentiation				.732
Well	8 (1.6%)	1 (0.9%)	7 (1.8%)	
Moderate	228 (44.4%)	54 (46.2%)	174 (43.8%)	
Poor	278 (54.1%)	62 (53.0%)	216 (54.4%)	
Tumor capsule				.445
Complete	111 (21.6%)	21 (17.9%)	90 (22.7%)	
Incomplete	320 (63.2%)	74 (63.2%)	224 (62.0%)	
No tumor capsule	83 (16.1%)	22 (18.8%)	61 (15.4%)	
Microvascular invasion	293 (57.0%)	67 (57.3%)	226 (56.9%)	.948
Microsatellite lesions	107 (20.8%)	20 (17.1%)	87 (21.9%)	.259
BCLC stage				.482
0	4 (0.8%)	0	4 (1.0%)	
A	460 (89.5%)	107 (91.5%)	353 (88.9%)	
B	50 (9.7%)	10 (8.5%)	40 (10.1%)	
Open surgery	246 (47.9%)	51 (43.6%)	195 (49.1%)	.293
Intraoperational blood transfusion	64 (12.5%)	15 (12.8%)	49 (12.3%)	.891

Values are *n* (%) or median (interquartile range).

AFP = alpha-fetoprotein, ALT = alanine aminotransferase, BCLC = Barcelona clinic liver cancer, BMI = body mass index, HBV = hepatitis B virus, HBV-HCC = hepatitis B virus-related hepatocellular carcinoma, MAFLD = metabolic dysfunction-associated fatty liver disease, T2DM = type 2 diabetes mellitus.

Table 2

Complications after hepatectomy in HBV-HCC patients.

Complications	n
Pleural effusion	55 (10.7%)
Ascites	53 (10.3%)
Intraabdominal infection	44 (8.6%)
Pneumonia	33 (6.4%)
Liver failure	8 (1.6%)
Wound infection	7 (1.4%)
Intraabdominal haemorrhage	5 (1.0%)
Bile leakage	3 (0.6%)
Sepsis	2 (0.4%)
Acute renal failure	1 (0.2%)
Cardiovascular event	1 (0.2%)
Death	6 (1.2%)

HBV-HCC = hepatitis B virus-related hepatocellular carcinoma.

antigen-positive and/or HBV DNA-positive. HBV-HCC refers to HCC caused by HBV infection. The severity of complications was graded using Dindo–Clavien classification.[19] Major complications were defined as complications of Clavien classification ≥ III. Among major complications, complications for which surgical or radiologic intervention with antibiotics was needed, such as intraabdominal infection, pneumonia, and wound infection and sepsis were defined as infectious complications.

Table 3

Univariate and multivariate analysis of factors affecting complications after hepatectomy.

	Univariate		Multivariate	
Variables	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
Age ≥ 60 yr	1.678 (1.083–2.599)	.020	1.770 (1.111–2.818)	.016
Female	1.585 (0.943–2.663)	.082		
BMI ≥ 23 kg/m^2	0.984 (0.637–1.521)	.943		
T2DM	1.284 (0.813–2.908)	.134		
Metabolic dysregulation	1.293 (0.826–2.023)	.261		
Hepatic steatosis	0.801 (0.457–1.404)	.438		
Alcohol consumed	1.103 (0.560–2.171)	.777		
HBV DNA > 500 IU/mL	1.145 (0.666–1.968)	.625		
AFP ≥ 400 μg/L	1.056 (0.896–2.807)	.758		
Cirrhosis	1.191 (0.928–2.113)	.373		
Maximum tumor diameter ≥ 5 cm	1.751 (1.130–2.715)	.012	1.378 (0.852–2.229)	.919
Tumor number ≥ 2	1.358 (0.726–2.542)	.338		
Tumor cell differentiation (well or moderate vs poor)	0.804 (0.517–1.248)	.330		
Tumor capsule (complete or incomplete vs no)	1.029 (0.568–1.865)	.926		
Microvascular invasion	1.631 (1.034–2.572)	.036	1.502 (0.916–2.461)	.107
Microsatellite lesions	1.328 (0.795–2.217)	.278		
BCLC stage B	1.172 (0.576–2.378)	.660		
Child-Pugh grade B	2.394 (1.173–4.887)	.016	2.556 (1.195–5.464)	.016
Open surgery	1.879 (1.206–2.928)	.005	1.618 (1.005–2.607)	.048
Intraoperational blood transfusion	1.730 (0.955–3.136)	.071		
Dichotomy of MAFLD (MAFLD vs nonMAFLD)	1.901 (0.876–3.071)	.129		
Trichotomy of MAFLD				
Lean-MAFLD vs nonMAFLD	2.128 (1.104–3.990)	.021	2.245 (1.243–5.362)	.028
nonLean-MAFLD vs nonMAFLD	1.092 (0.818–1.458)	.550		

AFP = alpha-fetoprotein, BCLC = Barcelona Clinic Liver Cancer, BMI = body mass index, CI = confidence interval, HBV DNA = hepatitis B virus DNA, HR = hazard ratio, MAFLD = metabolic associated fatty liver disease, T2DM = type 2 diabetes mellitus.

Postoperative death was defined as death from a postoperative complication within 30 days after hepatectomy.

2.4. Statistical analysis

Statistical analyses were performed using SPSS 23 (SPSS Inc., Chicago, IL). Continuous variables in this study were nonnormal distributed and expressed as medians with interquartile range, while categorical variables were summarized as numbers and relative proportions (%). The differences between 2 groups (MAFLD group vs non MAFLD group, complications group vs no complications group and lean-MAFLD subgroup vs nonlean-MAFLD subgroup) were analyzed using the Mann–Whitney *U* test or Chi-square test. The variables with significant ($P < .05$) in univariate analysis using the above tests were considered as candidates for multivariate analysis using multiple logistic regression. Odds ratio (OR) and the corresponding 95% confidence intervals (95% CI) were provided. *P* values < .05 indicated it was statistically significant.

3. Results

3.1. Baseline characteristics of HBV-HCC patients

Selection of the study population is shown in Figure 1. The baseline characteristics and laboratory data of the study population are shown in Table 1. A total of 514 patients with HBV-HCC were enrolled in this study, including 418 males (81.3%) and 96 females (18.7%). The median patient age was 57 years (48–64years). The number of patients with BMI ≥ 23kg/m^2 was 253 (49.2%), T2DM was 77 (15.0%) and metabolic dysregulation was 178 (34.6%), respectively. The Child-Pugh grades were A and B for 477 (92.8%) and 37 (7.2%) patients, respectively. The median maximum tumor diameter was 4.0 cm (2.7–6.4 cm). Most of them were solitary tumors (452, 87.9%) (Table 1).

Patients were categorized into 2 groups based on the presence of MAFLD: MAFLD group (117, 22.8%) and non MAFLD group (397, 77.2%). Compared with the non MAFLD group, patients in the MAFLD group had a significantly higher BMI ($P < .001$) and had higher alanine aminotransferase ($P = .009$). The proportions of BMI ≥ 23kg/m^2 (75.2%), T2DM (22.2%) and metabolic dysregulation (47.9%) in the MAFLD group were higher than those of the non MALFD group (41.6%, 12.8% and 30.7%, respectively, $P < .05$). There were no significant differences in regard to other baseline characteristics between the 2 groups ($P > .05$) (Table 1).

3.2. Complications after hepatectomy in HBV-HCC patients

The overall morbidity rate of complications after hepatectomy was 19.6% (101/514). Post hepatectomy complications included pleural effusion (55, 10.7%), ascites (53, 10.3%), intraabdominal infection (44, 8.6%), pneumonia (33, 6.4%), liver failure (8, 1.6%), wound infection (7, 1.4%), intraabdominal hemorrhage (5, 1.0%), bile leakage (3, 0.6%), sepsis (2, 0.4%), and acute renal failure (1, 0.2%) and cardiovascular event (1, 0.2%). Major complications occurred in 40 (7.80%) patients. Infectious complications were found in 75 (14.6%) patients. Six patients (1.2%) died from postoperative complications. The causes of postoperative death included liver failure (n = 2), intraabdominal hemorrhage (n = 1), bile leakage (n = 1), sepsis (n = 1), and cardiovascular event (n = 1) (Table 2).

3.3. Predictors of complications after hepatectomy in HBV-HCC patients

Univariate analysis demonstrated that age, maximum tumor diameter, microvascular invasion, Child-Pugh grade, surgical method and lean-MAFLD were significant factors influencing post hepatectomy complications, and while MAFLD was not directly associated with complications. Multivariate analysis showed that lean-MAFLD was an independent risk factor for post hepatectomy complications (OR 2.245; 95% CI

Table 4

Univariate and multivariate analysis of factors affecting infectious and major mplications after hepatectomy.

	Infectious complications		Major complications	
Variables	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
Univariate analysis				
Age ≥ 60 yr	2.014 (1.228–3.303)	.006	1.469 (1.108–2.89)	.016
Female	1.105 (0.597–2.044)	.750	1.504 (0.708–3.193)	.288
BMI ≥ 23 kg/m^2	0.962 (0.589–1.570)	.876	0.846 (0.442–1.619)	.614
T2DM	2.198 (1.236–5.134)	.041	1.192 (0.753–3.287)	.084
Metabolic dysregulation	1.478 (0.898–2.434)	.124	0.893 (0.449–1.778)	.748
Hepatic steatosis	1.037 (0.595–1.805)	.899	0.811 (0.375–1.750)	.593
Alcohol consumed	1.468 (0.723–2.983)	.288	1.162 (0.883–2.578)	.819
HBV DNA > 500 IU/mL	1.842 (1.063–3.919)	.058	1.325 (0.570–3.082)	.078
AFP ≥ 400 μg/L	0.976 (0.570–1.671)	.929	1.149 (0.576–2.291)	.694
Cirrhosis	1.112 (0.584–2.117)	.747	1.328 (0.541–3.259)	.536
Maximum tumor diameter ≥ 5 cm	2.343 (1.425–3.852)	.001	1.626 (1.025–3.726)	.028
Tumor number ≥ 2	1.582 (1.048–2.937)	.036	1.306 (0.804–2.108)	.131
Tumor cell differentiation (well or moderate vs poor)	0.857 (0.523–1.406)	.542	0.961 (0.502–1.838)	.904
Tumor capsule (complete or incomplete vs no)	1.013 (0.520–1.975)	.970	1.099 (0.446–2.707)	.837
Microvascular invasion	1.613 (0.963–2.702)	.069	2.787 (1.298–5983)	.009
Microsatellite lesions	1.242 (0.696–2.215)	.463	1.494 (0.720–3.097)	.281
BCLC stage B	1.324 (0.615–2.851)	.474	1.147 (0.709–1.997)	.304
Child-Pugh grade B	2.730 (1.286–5.794)	.009	1.973 (1.128–5.382)	.018
Open surgery	1.915 (1.388–2.861)	.001	2.144 (1.092–4.208)	.027
Intraoperational blood transfusion	1.595 (0.820–3.103)	.169	2.593 (1.201–5.598)	.015
Dichotomy of MAFLD (MAFLD vs nonMAFLD)	1.429 (0.896–3.443)	.183	1.188 (0.612–2.305)	.128
Trichotomous of MAFLD				
Lean-MAFLD vs nonMAFLD	2.102 (1.413–3.204)	.037	2.478 (1.291–4.449)	.011
nonLean-MAFLD vs nonMAFLD	1.088 (0783–1.513)	.616	1.025 (0.646–1.625)	.917
Multivariate analysis				
Age ≥ 60 yr	2.108 (1.283–3.442)	.004	2.157 (1.185–3.250)	.002
T2DM	1.314 (0.691–2.922)	.327	NA	
Maximum tumor diameter ≥ 5 cm	1.786 (1.109-3.642)	.021	1.764 (1.082–3.180)	.032
Tumor number ≥ 2	1.321 (0.646–2.704)	.346	NA	
Microvascular invasion	NA		1.534 (0.891–2.546)	0.124
Child-Pugh grade B	2.610 (1.159–3.876)	.018	2.027 (1.179–5.057)	.003
Open surgery	1.981 (1.150–3.211)	.015	1.662 (0.801–3.450)	.173
Intraoperational blood transfusion	NA		1.713 (0.729–4.180)	.217
Trichotomous of MAFLD				
Lean-MAFLD vs nonMAFLD	2.325 (1.313–4.152)	.036	2.841 (1.122–5.742)	.014
nonLean-MAFLD vs nonMAFLD	1.381 (0.693–2.128)	.412	1.126 (0.796–3.124)	.764

AFP = alpha-fetoprotein, BCLC = Barcelona Clinic Liver Cancer, BMI = body mass index, CI = confidence interval, HBV DNA = hepatitis B virus DNA, HR = hazard ratio, NA = not adopted, MAFLD = metabolic associated fatty liver disease, T2DM = type 2 diabetes mellitus.

1.243–5.362, P = .028). Furthermore, age ≥ 60yr, Child-Pugh grade B and open surgery were the other independent risk factors for complications after hepatectomy (Table 3).

3.4. Predictors of infectious and major complications after hepatectomy in HBV-HCC patients

Univariate analysis revealed that the presence of lean-MAFLD, but not MAFLD, was significantly associated with infectious and major complications after hepatectomy in HBV-HCC patients (all P < .05). Multivariate analysis also showed that lean-MAFLD was an independent risk factor for infectious (OR 2.325, 95% CI 1.313–4.152, P = .036) and major complications (OR 2.841, 95% CI 1.122–5.742, P = .014). Furthermore, age ≥ 60yr, maximum tumor diameter ≥ 5 cm and Child-Pugh grade B were the other independent risk factors for infectious and major complications after hepatectomy (Table 4).

3.5. Comparison of baseline characteristics between lean-MAFLD and nonlean-MAFLD patients

The baseline characteristics of the patients with HCC in the lean-MAFLD (BMI < 23kg/m^2) and nonlean-MAFLD (BMI ≥ 23kg/m^2) subgroups are summarized in Table 5. Compared with the nonlean-MAFLD patients, lean-MAFLD patients were older (P = .024) and had higher serum alpha-fetoprotein (P = .014), and the proportions of T2DM and metabolic dysregulation were higher (52.6% vs 16.3%, P = .04; 78.9% vs 41.8%, P = .003; respectively). The other clinical and pathological characteristics, such as age, maximum tumor diameter and microvascular invasion, were comparable between the 2 subgroups (all P > .05).

4. Discussion

In this study, we retrospectively assessed the impact of MAFLD for the complications after hepatectomy in patients with HBV-HCC. The main findings were that MAFLD was not directly associated with complications after hepatectomy in HBV-HCC patients, but lean-MAFLD was an independent risk factor for post hepatectomy complications. Similar results were found in the analysis of predictors for major and infectious complications in patients after hepatectomy.

Our findings were consistent with the results in other studies showing patients with HBV infection or HBV-HCC complicated with MAFLD were very common.[20–23] In our study, 22.8% (117/514) patients with HBV-HCC fulfilled the diagnosis criteria of MAFLD. The major differences of baseline characteristics between the MAFLD group and the non MAFLD group in this HBV-HCC cohort were the metabolic

Table 5

Comparison of characteristics between lean-MAFLD and nonlean-MAFLD patients.

Variables	lean-MAFLD (n = 19)	nonlean-MAFLD (n = 98)	*P* value
Age (yr)	61.0 (47.0–67.0)	56.0 (45.0–65.3)	.024
Male	14 (73.6%)	76 (77.6%)	.714
T2DM	10 (52.6%)	16 (16.3%)	.004
Metabolic dysregulation	15 (78.9%)	41 (41.8%)	.003
Alcohol consumed	3 (15.8%)	12 (12.2%)	.672
HBV DNA (≥ 500 IU/mL)	13 (68.4%)	74 (75.5%)	.517
Cirrhosis	17 (89.5%)	82 (83.7%)	.521
Child-Pugh grade			.766
A	18 (94.7%)	91 (92.9%)	
B	1 (5.3%)	7 (7.1%)	
Leukocyte count ($\times 10^9$/L)	5.9 (5.4–6.7)	5.7 (4.6–6.7)	.361
Hemoglobin (g/L)	147.0 (139.0–156.0)	145.5 (136.0–156.3)	.589
Platelet count ($\times 10^9$/L)	171.0 (151.0–227.0)	173.0 (149.8–218.0)	.909
Prothrombin time (s)	12.2 (12.6–13.6)	13.3 (12.6–13.7)	.082
Albumin (g/L)	40.0 (38.0–43.0)	41.0 (38.0–44.0)	.612
Total bilirubin (μmol/L)	17.5 (11.7–21.0)	16.0 (11.4–22.6)	.770
ALT (IU/L)	43.0 (29.0–69.0)	38.0 (27.0–53.5)	.508
AFP (μg/L)	73.0 (5.8–1075.1)	39.6 (5.4–324.1)	.014
Maximum tumor diameter (cm)	4.0 (3.0–5.0)	4.0 (3.0–5.8)	.988
Number of tumors			.090
Solitary	15 (78.9%)	90 (91.8%)	
Multiple	4 (21%)	8 (8.2%)	
Tumor cell differentiation			.255
Well	0 (0.0%)	1 (1.0%)	
Moderate	12 (63.2%)	42 (42.9%)	
Poor	7 (36.8%)	55 (56.1%)	
Tumor capsule			.954
Complete	4 (21.1%)	18 (18.4%)	
Incomplete	11 (57.9%)	60 (61.2%)	
No tumor capsule	4 (21.1%)	20 (20.4%)	
Microvascular invasion	13 (68.4%)	54 (55.1%)	.283
Microsatellite lesions	3 (15.8%)	17 (17.3%)	.869
BCLC stage			.912
A	18 (94.7%)	89 (90.8%)	
B	1 (5.3%)	9 (9.2%)	
Open surgery	8 (42.1%)	43 (43.9%)	.887
Intraoperational blood transfusion	4 (21.1%)	11 (11.2%)	.241

Values are *n* (%) or median (interquartile range).

AFP = alpha-fetoprotein, ALT = alanine aminotransferase, BCLC = Barcelona clinic liver cancer, BMI = body mass index, HBV = hepatitis B virus, MAFLD = metabolic dysfunction-associated fatty liver disease, T2DM = type 2 diabetes mellitus.

profiles including BMI, T2DM and metabolic dysregulation, but not the other clinical and pathological features, and indicating that MAFLD commonly coexists with HBV-HCC but does not influence the characteristics of HBV-HCC. Our results were also consistent with observations from other research that NAFLD and obesity did not impact postoperative complications in HCC patients following curative hepatectomy.[24–27]

We found, in this research, that MAFLD was not directly related with post hepatectomy complications in HBV-HCC patients. However, we further divided the patients with HBV-HCC into lean-MAFLD and nonlean-MAFLD subgroups. Notably, the incidence of post hepatectomy complications of lean-MAFLD patients were significantly higher than those of nonlean-MAFLD patients. Furthermore, according to multivariate analysis results, lean-MAFLD was an independent risk factor for post hepatectomy complications of HBV-HCC patients. Similar results were found in the analysis of predictors for infectious and major complications after hepatectomy. These results may suggest that lean-MAFLD is a predictor for complications after hepatectomy in HBV-HCC patients. While the pathophysiology of lean-MAFLD is still not fully understood, many metabolic factors are involved in the diagnosis. Despite showing a "healthy" body weight, lean-MAFLD individuals exhibited the same pattern of insulin resistance and free fatty acid distribution as obese patients.[28] Lean-MAFLD patients account for 20.7% of the MAFLD population, were older and had higher all-cause mortality rate.[29] A study has shown that lean-MAFLD was related with an increased risk of liver-related events.[30] Another study also found that lean-MAFLD was a risk factor for tumor recurrence among patients with HBV-HCC after curative resection.[23] In our study, we also found that the lean-MAFLD subgroup was older and had higher metabolic dysregulation than the nonlean-MAFLD subgroup, which may explain the higher risk of post hepatectomy complications in the lean-MAFLD subgroup.

Furthermore, we also found that the other predictive factors for the post hepatectomy complications of HBV-HCC patients in this cohort were age, Child-Pugh grade, maximum tumor diameter and open surgery, which were also consistent with previous studies.[31–35]

Our study had some inherent limitations. First, this study was a retrospective single medical center analysis. Second, we only enrolled patients with HBV-HCC. Whether MAFLD has a similar influence on the post hepatectomy complications of HCC caused by different etiologies (such as HCV infection) remains to be investigated. Third, some data cannot be obtained from electronic medical records, such as waist circumference and glycosylated hemoglobin, resulting in the exclusion of some individuals from the evaluation.

In conclusion, our preliminary results indicated that MAFLD is commonly concurrent with HBV-HCC and is not directly related to complications after hepatectomy in HBV-HCC

patients, but lean-MAFLD is an independent risk factor for post hepatectomy complications. Prospective clinical studies involving larger clinical samples and multi-center are warranted to evaluate the generalizability of our results and to deepen our understanding of MAFLD.

Author contributions

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