

Association of steatotic liver disease with long-term oncological outcomes after hepatic resection for hepatocellular carcinoma

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Abstract: Hepatic steatosis manifests in obesity and systemic metabolic disorders. The nomenclature has recently shifted from nonalcoholic fatty liver disease/nonalcoholic steatohepatitis to steatotic liver disease (SLD), which includes metabolic dysfunction-associated steatotic liver disease, metabolic dysfunction-associated steatotic liver disease with increased alcohol intake, and alcohol-related liver disease. This study retrospectively evaluated the association between SLD and long-term oncological outcomes in 85 patients undergoing hepatic resection for hepatocellular carcinoma (HCC) between 2018 and 2022. SLD was histologically defined as steatosis involving $\geq 5\%$ of non-tumorous hepatocytes. Of these patients, 47 did not have SLD (non-SLD group) and 38 had SLD. We compared recurrence-free survival (RFS) and overall survival (OS) between these groups. Patients with SLD exhibited a higher body mass index and more advanced fibrosis than those without SLD, whereas lifestyle-related diseases were comparably prevalent. Median RFS was not reached in the non-SLD group and was 21 months in the SLD group (log-rank $p = 0.054$). In exploratory multivariable analysis, SLD was associated with a higher cause-specific hazard of recurrence after adjustment for age, Barcelona Clinic Liver Cancer stage, viral hepatitis status, and diabetes mellitus (adjusted hazard ratio, 1.939; 95% confidence interval, 1.003–3.748). No significant association between SLD and OS was noted (hazard ratio, 0.962; 95% confidence interval, 0.399–2.315). These findings suggest a possible association between SLD and HCC recurrence after hepatic resection, whereas its association with OS remains uncertain.

Keywords: metabolic dysfunction, MASLD, SLD, overall survival, recurrence-free survival

1. Introduction

The global prevalence of steatotic liver disease (SLD) is estimated to be 25–40% and it continues to rise, driven by the increasing incidence of obesity and diabetes mellitus (DM) (1). A subset of patients with SLD develops steatohepatitis with progressive fibrosis, eventually leading to cirrhosis and hepatocellular carcinoma (HCC) (1).

Traditionally, the term nonalcoholic fatty liver disease (NAFLD) was widely used to describe fatty liver, encompassing a clinical spectrum from simple steatosis to nonalcoholic steatohepatitis (NASH) (2). In 2023, an international consensus proposed a new nomenclature collectively terming these conditions SLD, which includes metabolic dysfunction-associated steatotic liver disease (MASLD), alcohol-related liver

disease (ALD), and MASLD with increased alcohol intake (MetALD) (3). This updated classification enables a more comprehensive assessment of the respective contributions of metabolic dysfunction and alcohol consumption to hepatic steatosis.

In tandem with this classification shift, the epidemiology of HCC has evolved. Although the development of antiviral therapies has effectively controlled chronic viral hepatitis—leading to a decline in virus-related HCC—the proportion of cases associated with metabolic dysfunction and alcohol consumption continues to increase (4–6). Therefore, establishing new clinical evidence that reflects the evolving etiology of HCC is important.

Previous studies investigating the prognosis of patients with NASH-related HCC (NASH-HCC) have yielded conflicting results. Some studies demonstrate

better outcomes for patients with NASH-HCC than for those without, whereas others report the opposite (7-9). These discrepancies may be attributable to ambiguous definitions of the non-NASH cohort and varying proportions of viral- and alcohol-related liver diseases among the populations studied. Most of those non-NASH cases were associated with viral hepatitis, so the observed differences may have been confounded by the underlying liver disease rather than metabolic factors themselves. Moreover, these studies relied on the Brunt classification (10), a histological assessment that fundamentally differs from the recently proposed MASLD definition based on metabolic dysfunction. Consequently, previous findings regarding NASH-HCC cannot be directly extrapolated to SLD-related HCC.

Therefore, the current study aimed to evaluate the association between histologically defined SLD in the non-tumorous liver and recurrence-free survival (RFS) and overall survival (OS) in patients undergoing hepatic resection for HCC.

2. Patients and Methods

2.1. Study design and patients

This study was approved by the Medicine Research Ethics Committee and the Institutional Review Board of Kyorin University (project number R06-180, approval number 2510). All clinical investigations were conducted in accordance with the Declaration of Helsinki (as revised in 2013). The requirement for written informed consent was waived by the institutional ethics committee because of the retrospective nature of the study, and an opt-out approach was used to provide patients with the opportunity to decline participation.

Between April 2018 and December 2022, 86 patients with HCC underwent initial hepatic resection at this hospital. Following established diagnostic criteria, we histologically defined SLD as steatosis involving $\geq 5\%$ of non-tumorous hepatocytes (3). We excluded repeat hepatectomies for recurrent HCC. Of the total patients, 47 did not have SLD and 38 exhibited SLD in the background liver; one patient was excluded due to insufficient non-tumorous liver tissue for reliable histological assessment. Based on diagnostic criteria incorporating cardiometabolic risk factors and alcohol consumption history, the 38 patients with SLD were subclassified into MASLD ($n = 17$) and MetALD/ALD ($n = 21$) cohorts (3). No patients presented with specific-etiologic or cryptogenic SLD (Figure 1).

2.2. Definition and classification of SLD

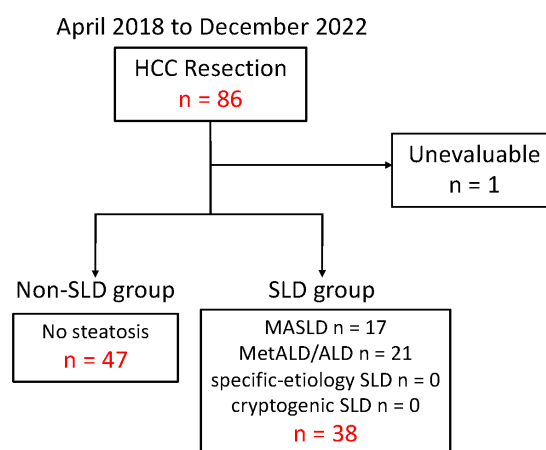
MASLD was diagnosed according to international consensus criteria. Patients with $\geq 5\%$ hepatic steatosis were classified as having MASLD if they exhibited at least one of the following cardiometabolic risk factors:

overweight/obesity (body mass index [BMI] ≥ 23 kg/m² for Asians), impaired glucose metabolism (hemoglobin A1c [HbA1c] $\geq 5.7\%$, type 2 DM, or antidiabetic treatment), elevated blood pressure ($\geq 130/85$ mmHg or antihypertensive treatment), hypertriglyceridemia (≥ 150 mg/dL or lipid-lowering treatment), or reduced high-density lipoprotein (HDL) cholesterol (< 40 mg/dL in men or < 50 mg/dL in women). We incorporated medication use into the corresponding cardiometabolic criteria. We excluded waist circumference and the homeostasis model assessment of insulin resistance (HOMA-IR) from the assessment because these data were unavailable for most patients. Consequently, MASLD was diagnosed based solely on the available cardiometabolic criteria (3).

Alcohol consumption was calculated using patient-reported drinking habits and quantities documented in medical records. To meet the MASLD criteria, alcohol consumption could not exceed 140 g/week for women and 210 g/week for men (3). Because alcohol consumption was retrospectively assessed from medical records, precise differentiation between MetALD and ALD was not possible in all patients. Therefore, these categories were combined as MetALD/ALD. This distinction was not central to the current study, which primarily focused on the association between histologically defined SLD and oncological outcomes.

According to guidelines, hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are not diagnostic components of MASLD; rather, they are considered separate or coexisting liver disease etiologies (3).

2.3. Histopathological assessment



Patients were observed until September 2025

Figure 1. Patient classification according to the presence of SLD. Abbreviations: ALD, alcohol-related liver disease; HCC, hepatocellular carcinoma; MASLD, metabolic dysfunction-associated steatotic liver disease; MetALD, MASLD with increased alcohol intake; SLD, steatotic liver disease.

We identified histopathological findings from the original pathology reports. A gastrointestinal pathologist (A.H.), blinded to clinical outcomes, independently reassessed hepatic steatosis in the non-tumorous liver in all of the patients. The pathologist estimated the percentage of steatotic hepatocytes and classified patients according to the General Rules for the Clinical and Pathological Study of Primary Liver Cancer: st0, < 5%; st1, 5%–33%; st2, 34%–66%; and st3, ≥ 67% (11).

We retrospectively obtained all other pathological variables—including inflammatory activity, fibrosis stage, vascular invasion, and resection margin status (R0)—from the original reports, which had been routinely reviewed and approved by at least two board-certified pathologists, including a liver pathology specialist. Inflammatory activity in the non-tumorous liver was semiquantitatively graded as absent, mild, or moderate-to-severe, based on histological scoring systems proposed by the Nonalcoholic Steatohepatitis Clinical Research Network (12) and the METAVIR system (13). For statistical analysis, we dichotomized inflammatory activity as absent or present (mild or moderate-to-severe). All non-R0 resections were classified as R1 (microscopic margin positivity); no patients had macroscopic residual disease (R2).

2.4. Clinical and surgical variables

Baseline clinical characteristics included age, sex, BMI, a history of DM, hypertension, dyslipidemia, alcohol consumption, HbA1c, triglycerides (TG), and HDL cholesterol.

Baseline hepatic function parameters included a history of HBV or HCV infection, serum alpha-fetoprotein (AFP) levels, and protein induced by vitamin K absence or antagonist-II (PIVKA-II) levels. Liver function was evaluated using the fibrosis-4 index, albumin-bilirubin (ALBI) score, indocyanine green retention rate at 15 minutes (ICG-R15), and Child–Pugh classification.

Assessed surgical and pathological characteristics included major hepatectomy (defined as the resection of three or more Couinaud segments) (14), tumor number, tumor size, microvascular invasion, fibrosis stage (≥ F3), and Barcelona Clinic Liver Cancer (BCLC) stage ≥ B.

2.5. Follow-up and outcome definitions

The primary outcomes were RFS and OS. We also recorded postoperative recurrence and subsequent therapies. All patients were observed until September 2025.

After hepatic resection, patients were regularly followed with clinical assessments, laboratory tests, tumor markers (AFP and PIVKA-II), and contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) on an outpatient basis.

Depending on the patient's clinical condition, imaging was generally performed every 3–4 months during the early postoperative period and every 3–6 months thereafter. Recurrence was diagnosed based on characteristic HCC findings on contrast-enhanced CT, MRI, or other imaging modalities.

RFS was defined as the time from hepatic resection to the first documented recurrence. Patients who died without recurrence were censored at the date of death. Patients who remained recurrence-free were censored at the data cutoff date (September 30, 2025), whereas those lost to follow-up before the data cutoff were censored at the date of their last adequate assessment of recurrence. OS was defined as the time from hepatic resection to death from any cause or the last known date alive. Surviving patients were censored at the last known date alive.

2.6. Statistical analysis

Statistical analyses were performed using the software IBM SPSS Statistics (version 25.0; IBM Corp., Armonk, NY, USA). Continuous variables are expressed as medians with interquartile ranges and were compared using the Mann–Whitney *U* test. Categorical variables were compared using the chi-squared test or Fisher's exact test, as appropriate. Missing data were not imputed, and statistical analyses were performed using available cases for each variable. We estimated the median duration of follow-up using the reverse Kaplan–Meier method. Survival curves for RFS and OS were estimated using the Kaplan–Meier method and compared using the log-rank test. Survival estimates at each time point are reported with 95% confidence intervals (CIs), with the numbers at risk presented below the curves. A two-tailed *p* value < 0.05 was considered statistically significant. An exploratory subgroup analysis excluding patients with viral hepatitis was performed using the same endpoint definitions and censoring rules as in the primary analysis.

The association of SLD with recurrence was evaluated using cause-specific Cox proportional hazards regression, with recurrence as the event and deaths without recurrence treated as censored observations. A multivariable cause-specific Cox proportional hazards model incorporating SLD, age, BCLC stage, viral hepatitis status, and DM was constructed. SLD, DM, viral hepatitis status, and BCLC stage were coded as binary variables (SLD: non-SLD = 0, SLD = 1; DM: absent = 0, present = 1; viral hepatitis: absent = 0, HBV/HCV = 1; BCLC stage: 0/A = 0, B/C = 1), whereas age was modeled as a continuous variable per 1-year increase. Covariates were selected based on clinical relevance rather than univariable statistical significance. Hepatic functional reserve, histological fibrosis, and resection margin status were considered as potential covariates but were not included in the final model because of the limited number of recurrence events

and the risk of overfitting. The proportional hazards assumption for SLD was assessed using an interaction term between SLD and the natural logarithm of time. The linearity assumption for age was assessed by adding a quadratic term for mean-centered age to the Cox model.

3. Results and Discussion

Baseline clinical characteristics are summarized in Table 1. The median ages were 73 and 75 years in the non-SLD and SLD groups, respectively. The proportion of male patients was similar in the groups (81% vs. 84%). BMI was significantly higher in the SLD group than in the non-SLD group (24.7 vs. 22.2 kg/m², $p = 0.01$). The prevalence of lifestyle-related diseases did not differ significantly between the groups. Approximately 30% of patients in both groups were positive for HBV or HCV, and all had received antiviral therapy. The median FIB-4 index, ICG-R15, Child–Pugh classification, ALBI score,

AFP, and PIVKA-II levels did not differ significantly between the groups.

Surgical and pathological characteristics are summarized in Table 2. Tumor size tended to be larger in the non-SLD group than in the SLD group, but this difference was not significant (56 mm vs. 40 mm, $p = 0.10$). Advanced fibrosis ($\geq F3$) was observed significantly more frequently in the SLD group than in the non-SLD group (58% vs. 30%, $p = 0.01$). An exploratory analysis revealed a weak positive correlation between the FIB-4 index and histological fibrosis ($r = 0.279$, $p = 0.010$) (Supplementary Methods/Results, <https://www.globalhealthmedicine.com/site/supplementaldata.html?ID=130>). The degree of hepatic steatosis was assessed in the 85 evaluable patients, and 47 were classified as st0 (< 5% steatosis) and 38 as st1 (5%–33% steatosis). No patients were classified as st2 (34%–66%) or st3 ($\geq 67\%$).

The median duration of follow-up, estimated using

Table 1. Baseline clinical characteristics of patients with HCC who underwent liver resection

Variable	Non-SLD ($n = 47$)	SLD ($n = 38$)	p value
Age, years (median [range])	73 (30–88)	75 (52–86)	0.86
Sex, males (%)	38 (81%)	32 (84%)	0.69
Body mass index, kg/m ² (median [IQR])	22.2 (19.8–24.9)	24.7 (21.9–26.7)	0.01
Diabetes mellitus (%)	21 (45%)	22 (58%)	0.23
Hemoglobin A1c, % (median [IQR])	5.9 (5.8–6.9)	6.5 (5.9–7.1)	0.07
Hypertension (%)	27 (57%)	22 (58%)	0.96
Dyslipidemia (%)	22 (47%)	23 (61%)	0.21
Triglycerides, mg/dL (median [IQR])	99 (71–132)	106 (79–143)	0.41
HDL-cholesterol, mg/dL (median [IQR])	46 (39–58)	46 (36–55)	0.49
Alcohol consumption history (%)	29 (62%)	21 (55%)	0.55
HBV infection (%)	8 (17%)	9 (24%)	0.44
HCV infection (%)	6 (13%)	2 (5%)	0.24
Antiviral therapy among HBV/HCV patients, n (%)	14 (100%)	11 (100%)	–
FIB-4 index (median [IQR])	2.64 (1.93–3.11)	3.38 (2.12–4.01)	0.12
ICG-R15 (%) (median [IQR])	11.6 (7.4–13.1)	13.5 (8.4–16.1)	0.23
ALBI score (median [IQR])	–2.53 (–2.80––2.29)	–2.73 (–2.90––2.50)	0.18
Child–Pugh $\geq B$ (%)	3 (6%)	1 (3%)	0.42
AFP level, ng/mL (median [IQR])	4.5 (2.6–31.0)	9.3 (4.9–35.5)	0.07
PIVKA-II level, ng/mL (median [IQR])	189 (27–1803)	321 (70–751)	0.43

Note: Data are presented as n (%) or the median (IQR). Available sample sizes for variables with missing data were as follows: Triglycerides, $n = 46/37$; HDL cholesterol, $n = 39/34$ (non-SLD/SLD, respectively). Abbreviations: AFP, alpha-fetoprotein; FIB-4, fibrosis-4 index; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDL, high-density lipoprotein; ICG-R15, indocyanine green retention rate at 15 minutes; IQR, interquartile range; PIVKA-II, protein induced by vitamin K absence or antagonist-II, SLD, steatotic liver disease.

Table 2. Surgical and pathological characteristics of patients with HCC who underwent liver resection

Variable	Non-SLD ($n = 47$)	SLD ($n = 38$)	p value
Major hepatectomy (%)	11 (23%)	8 (21%)	0.80
Tumor number ≥ 2	6 (13%)	8 (21%)	0.31
R0 resection (%)	41 (87%)	36 (95%)	0.23
Tumor size, mm (median [range])	56 (10–170)	40 (10–150)	0.10
Microvascular invasion (%)	27 (57%)	18 (47%)	0.36
Micro portal vein invasion	23 (49%)	15 (39%)	0.38
Micro hepatic arterial invasion	2 (4%)	1 (3%)	0.69
Micro hepatic vein invasion	9 (19%)	3 (8%)	0.14
Inflammation (%)	19 (40%)	19 (50%)	0.38
Fibrosis stage $\geq F3$ (%)	14 (30%)	22 (58%)	0.01
BCLC stage $\geq B$ (%)	12 (26%)	6 (16%)	0.27

Abbreviations: BCLC, Barcelona Clinic Liver Cancer; HCC, hepatocellular carcinoma; SLD, steatotic liver disease.

the reverse Kaplan–Meier method, was 57 months in the non-SLD group and 64 months in the SLD group.

We observed a total of 44 RFS events (recurrences) and 20 OS events (deaths), including six deaths before recurrence. The non-SLD group experienced 19 RFS events and 10 deaths, including four deaths before recurrence. The SLD group experienced 25 RFS events and 10 deaths, including two deaths before recurrence.

Median RFS was not reached in the non-SLD group and was 21 months (95% CI: 11.3–30.7 months) in the SLD group (log-rank $p = 0.054$). In univariable cause-specific Cox proportional hazards analysis, the HR for recurrence associated with SLD was 1.776 (95% CI: 0.977–3.236; $p = 0.060$). In multivariable cause-specific Cox analysis adjusted for age, BCLC stage, viral hepatitis status, and DM, the HR for recurrence associated with SLD was 1.939 (95% CI: 1.003–3.748; $p = 0.049$) (Table 3). The multivariable model included 85 patients and 44 recurrence events, with no missing data for the included covariates. There was no evidence of violation of the proportional hazards assumption for SLD ($p = 0.910$). In addition, the quadratic term for mean-centered age was not significant ($p = 0.423$), providing no evidence of a nonlinear association between age and the hazard of recurrence. Median OS was not reached in either group, with no significant differences between the

groups (log-rank $p = 0.930$). In univariable analysis, SLD was not significantly associated with OS (HR = 0.962; 95% CI: 0.399–2.315; $p = 0.930$) (Figure 2). The 3-year RFS estimates were 55.0% (95% CI: 38.2–69.0%) in the non-SLD group and 31.4% (95% CI: 16.3–47.7%) in the SLD group, while the corresponding 3-year OS estimates were 86.2% (95% CI: 72.0–93.5%) and 88.5% (95% CI: 72.2–95.4%), respectively.

In the exploratory subgroup analysis excluding patients with viral hepatitis, median RFS was 22 months (95% CI: 0.4–43.6 months) in the non-SLD group and 27 months (95% CI: 14.7–39.3 months) in the SLD group, with no significant differences between the cohorts (log-rank $p = 0.399$). In univariable analysis, SLD was not significantly associated with RFS (HR = 1.328; 95% CI: 0.681–2.588; $p = 0.404$). Median OS was 79 months (95% CI: 52.6–105.4 months) in the non-SLD group and 68 months (95% CI: 54.1–82.0 months) in the SLD group, with no significant differences between the cohorts (log-rank $p = 0.936$). Similarly, SLD was not significantly associated with OS in univariable analysis (HR = 0.959; 95% CI: 0.346–2.661; $p = 0.936$) (Supplementary Figure S1, <https://www.globalhealthmedicine.com/site/supplementaldata.html?ID=130>).

Recurrence and subsequent therapies are summarized in Table 4. Following recurrence, locoregional therapy

Table 3. Cox proportional hazards analyses for recurrence-free survival

Variable	Univariable HR (95% CI)	p value	Multivariable HR (95% CI)	p value
SLD (vs. non-SLD)	1.776 (0.977–3.236)	0.060	1.939 (1.003–3.748)	0.049
Age, years	0.971 (0.938–1.006)	0.105	0.971 (0.940–1.003)	0.072
BCLC stage ($\geq B$ vs. 0/A)	2.585 (1.326–5.037)	0.005	2.631 (1.318–5.253)	0.006
DM (yes vs. no)	0.685 (0.378–1.241)	0.212	0.599 (0.315–1.137)	0.117
Viral hepatitis status (yes vs. no)	0.461 (0.221–0.962)	0.039	0.518 (0.242–1.110)	0.091

Abbreviations: BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval; DM, diabetes mellitus; HR, hazard ratio; RFS, recurrence-free survival; SLD, steatotic liver disease.

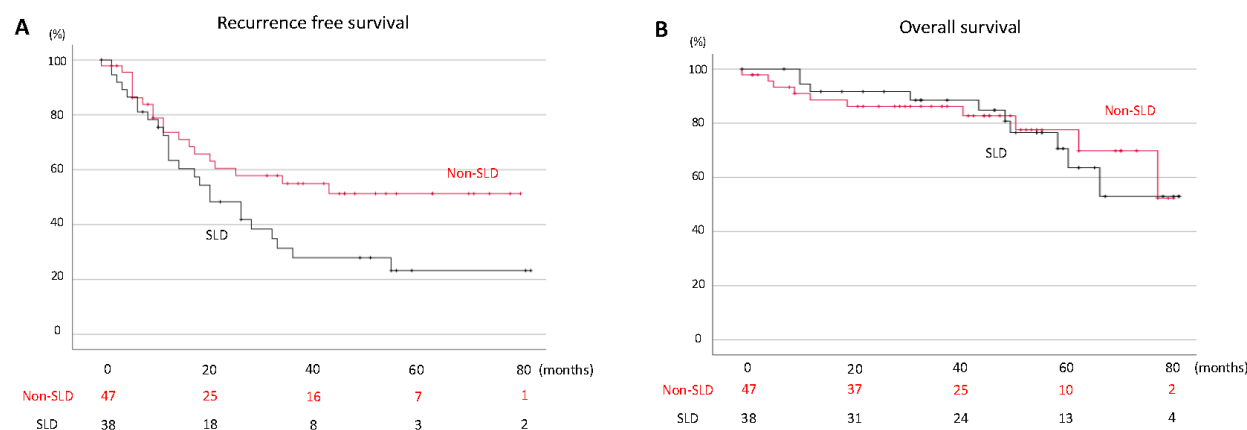


Figure 2. Kaplan–Meier curves for RFS and OS in patients with and without SLD. (A) RFS curves for patients with and without SLD (log-rank $p = 0.054$); **(B)** OS curves for the same patient groups (log-rank $p = 0.930$). Censored data are indicated by tick marks on the Kaplan–Meier plots. Abbreviations: OS, overall survival; RFS, recurrence-free survival; SLD, steatotic liver disease.

Table 4. Patterns of first recurrence among patients with recurrent HCC

Variable	Non-SLD (<i>n</i> = 47)	SLD (<i>n</i> = 38)	<i>p</i> value
Recurrence	19	25	
Site of first recurrence	<i>n</i> = 19	<i>n</i> = 25	
Intrahepatic recurrence	15 (79%)	22 (88%)	0.42
Extrahepatic recurrence	4 (21%)	3 (12%)	
Subsequent therapy	<i>n</i> = 19	<i>n</i> = 25	
Surgery/RFA/TACE	10 (53%)	21 (84%)	0.024
Chemotherapy/BSC	9 (47%)	4 (16%)	

Abbreviations: BSC, best supportive care; HCC, hepatocellular carcinoma; RFA, radiofrequency ablation; SLD, steatotic liver disease; TACE, transcatheter arterial chemoembolization.

(surgery/radiofrequency ablation/transcatheter arterial chemoembolization) was administered more frequently in the SLD group (84% vs. 53%), whereas chemotherapy or best supportive care was more common in the non-SLD group (16% vs. 47%, $p = 0.024$).

The findings of this exploratory study suggested a possible association between SLD and recurrence after hepatic resection for HCC, but it was not significantly associated with OS. These findings should be interpreted cautiously given the limited sample size and number of events.

The prognostic impact of SLD in patients with HCC remains controversial (15,16). Most previous studies have focused on NAFLD/NASH, where the conventional diagnostic framework required excluding other liver disease etiologies, including viral hepatitis and significant alcohol consumption. This restriction likely limited the evaluation of SLD in patients with multiple coexisting etiologies. In contrast, the recently introduced SLD/MASLD classification provides a positive diagnostic framework based on hepatic steatosis and cardiometabolic risk factors, allowing for the coexistence of other liver disease etiologies. In our cohort, approximately 30% of patients had HBV or HCV infections; however, all had received antiviral therapy.

Large cohort studies indicate that SLD increases the risk of HCC development (17,18). Chronic inflammation and lipotoxicity in SLD may induce persistent hepatocellular injury and impaired liver regeneration through mechanisms including endoplasmic reticulum stress and mitochondrial dysfunction, thereby contributing to the progression of hepatic fibrosis (19). Such a persistent carcinogenic background may contribute to recurrence after hepatic resection. Indeed, advanced fibrosis occurred significantly more frequently in the SLD group in our cohort. No significant association between SLD and OS was noted. One possible explanation is that our cohort was restricted to patients with sufficient hepatic functional reserve to undergo resection, with no significant differences in Child–Pugh classification, ALBI score, or ICG-R15 between the groups. Differences in post-recurrence treatment patterns, including the more frequent administration of locoregional therapies in the SLD group, may also have contributed; however, these explanations remain

hypothetical. The adjusted association between SLD and recurrence was imprecisely estimated, and there was no significant association with it in the exploratory virus-excluded subgroup. Therefore, these findings warrant cautious interpretation.

Previous studies have suggested that the prognostic impact of metabolic liver disease in HCC is complex. Coexisting obesity and DM correlate with poorer RFS and OS after hepatic resection for HCC (20). Conversely, SLD is not an independent predictor of HCC recurrence after radiofrequency ablation (21), nor is MAFLD independently associated with oncological outcomes after hepatic resection (22). These findings suggest the oncological impact of SLD depends not only on hepatic steatosis itself but also on accompanying metabolic abnormalities and the underlying liver condition.

These findings highlight the potential relevance of SLD in postoperative surveillance, although their clinical implications require further validation. No significant association between SLD and OS was noted, but our findings suggest that the presence of SLD alone may not necessarily preclude hepatic resection in appropriately selected patients with preserved hepatic functional reserve. Moreover, SLD is associated with an increased risk of cardiovascular disease and metabolic dysfunction (23). Therefore, long-term postoperative management should include not only surveillance for HCC recurrence but also management of metabolic risk factors, including obesity and DM, and cardiovascular risk.

This study has several limitations. First, the retrospective, single-center design, relatively small sample size, and limited number of RFS and OS events may have introduced selection bias and reduced statistical power. The limited number of recurrence events also restricted the number of covariates that could be included in the multivariable model to avoid overfitting. Therefore, residual confounding due to hepatic functional reserve, histological fibrosis, resection margin status, or other unmeasured factors cannot be excluded. Moreover, the retrospective assessment of alcohol consumption and metabolic factors may have limited the accuracy of etiological SLD subclassification, and particularly the distinction between MetALD and ALD. Second, restricting the study population to patients with sufficient hepatic functional reserve to undergo resection limits

the generalizability of our findings to those with more advanced liver dysfunction. Third, all patients with SLD presented with mild steatosis (st1); none exhibited moderate or severe steatosis. Additionally, analyzing hepatic inflammatory activity solely as a binary variable (absent or present) precluded a detailed assessment of severity. Consequently, we were unable to evaluate associations between steatosis or inflammation severity and postoperative outcomes. Fourth, conventional measures of hepatic functional reserve—including ICG-R15, Child–Pugh classification, and ALBI score—may not fully capture the heterogeneous parenchymal injury or impaired regenerative capacity associated with SLD.

In conclusion, this exploratory study suggests a possible association between SLD and HCC recurrence after hepatic resection, whereas its association with OS remains uncertain. Further studies with larger cohorts need to be conducted to validate these findings and clarify the prognostic significance of SLD in patients with HCC.

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