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RESEARCH

Myosteatosis and the survival of patients with hepatocellular carcinoma: a meta-analysis

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Abstract

Myosteatosis, characterized by fat infiltration into skeletal muscle, is increasingly recognized as a prognostic factor in hepatocellular carcinoma (HCC), although the results were not consistent. This meta-analysis aimed to summarize impact on overall survival (OS) and progression-free survival (PFS) in patients with HCC.A systematic search of PubMed, Embase, and Web of Science was conducted to identify observational studies reporting survival outcomes in HCC patients with and without myosteatosis. Pooled hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using a random-effects model. A total of 24 retrospective cohort studies involving 7436 HCC patients were included. Myosteatosis was significantly associated with poorer OS (HR: 1.60, 95% CI: 1.40–1.83, $p < 0.001$, $I^2 = 65\%$) and PFS (HR: 1.53, 95% CI: 1.33–1.76, $p < 0.001$, $I^2 = 36\%$). Subgroup analysis revealed a stronger association in Asian studies (HR: 1.74 for OS; 1.57 for PFS) compared to European studies (HR: 1.08 for OS; 1.05 for PFS). The prognostic impact remained significant regardless of anticancer treatment type, myosteatosis assessment method, sex-specific or universal cutoff values, and follow-up duration (p for subgroup differences all > 0.05). The results remained significant in studies adjusting for sarcopenia (HR: 1.89 for OS; 1.50 for PFS). Meta-regression analyses did not suggest any of the following variables may affect the results, including sample size, mean ages of the patients, proportions of men, follow-up durations, and study quality scores (p all > 0.05). Myosteatosis is independently associated with worse survival in HCC patients, particularly in Asian populations. These findings highlight the significance of assessing muscle quality as a prognostic factor in HCC.

Keywords Hepatocellular carcinoma · Myosteatosis · Survival · Progression · Meta-analysis

Abbreviations

HCC	Hepatocellular carcinoma
OS	Overall survival
PFS	Progression-free survival
HR	Hazard ratio
CI	Confidence interval
CT	Computed tomography
MRI	Magnetic resonance imaging
IMAC	Intramuscular adipose content
SMD	Skeletal muscle density
TACE	Transarterial chemoembolization
TAE	Transarterial embolization
TKI	Tyrosine kinase inhibitor
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
NOS	Newcastle–Ottawa Scale
PROSPERO	International Prospective Register of Systematic Reviews
BMI	Body mass index
MASLD	Metabolic dysfunction-associated steatotic liver disease
RFA	Radiofrequency ablation
CAR-T	Chimeric antigen receptor T-cell therapy

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Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and a leading cause of cancer-related mortality worldwide [1, 2]. The global incidence of HCC continues to rise, particularly in regions with high

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hepatitis B and C virus prevalence, alcohol-related liver disease, and metabolic dysfunction-associated steatotic liver disease (MASLD) [3]. Despite advances in surveillance and therapeutic strategies, the prognosis of HCC remains poor, with a five-year survival rate below 20% in most populations [4]. Treatment options for HCC are diverse and depend on tumor stage, liver function, and patient performance status [5]. Curative approaches, such as surgical resection and liver transplantation, are feasible in early-stage disease [6], while locoregional therapies, including transarterial chemoembolization (TACE) and radiofrequency ablation (RFA), are commonly used for intermediate-stage tumors [7]. Systemic treatments, such as tyrosine kinase inhibitors (TKIs), immune checkpoint inhibitors, and combination regimens, have expanded options for patients with advanced disease [8]. However, treatment response varies, underscoring the need for reliable prognostic markers to refine risk stratification and optimize patient management [9].

In this context, the identification of novel predictors of survival is crucial for improving clinical outcomes in HCC. Myosteatosis, defined as pathological fat infiltration within skeletal muscle, has emerged as a potential prognostic factor in cancer patients [10, 11]. Unlike sarcopenia, which refers to a loss of muscle mass and strength, myosteatosis reflects alterations in muscle composition and quality [12]. It is commonly assessed using computed tomography (CT) or magnetic resonance imaging (MRI) at the level of the third lumbar vertebra, with specific parameters such as skeletal muscle density (SMD) and intramuscular adipose content (IMAC) used to quantify fat infiltration [13, 14]. The presence of myosteatosis is often associated with systemic inflammation, insulin resistance, and metabolic dysfunction, which may contribute to cancer progression and poor survival outcomes [15–17].

In patients with HCC, myosteatosis may promote an unfavorable prognosis through several mechanisms, such as chronic inflammation, hyperinsulinemia, increased circulating free fatty acids, and oxidative stress, which can create a tumor-promoting microenvironment [18]. Despite emerging evidence linking myosteatosis to poor outcomes in HCC, findings across studies remain inconsistent. Some reports suggest a strong association between myosteatosis and reduced overall survival (OS) and progression-free survival (PFS) in patients with HCC [19–36], while others have found no significant impact [37–42]. Differences in study populations, imaging modalities, cutoff values, and adjustment for confounders such as sarcopenia may account for these discrepancies. Given these uncertainties, in this study, we performed a meta-analysis aiming to systematically evaluate the association between myosteatosis and survival outcomes in patients with HCC.

Methods

The study adhered to PRISMA 2020 [43, 44] and the Cochrane Handbook for Systematic Reviews and Meta-analyses [45] guidelines for conducting this meta-analysis, including for the study protocol design, data extraction, statistical analysis, and results presentation. The protocol of the meta-analysis has been registered at PROSPERO with the identifier CRD42025637129.

Literature search

To identify studies pertinent to this meta-analysis, we searched PubMed, Embase, and Web of Science databases using an extensive array of search terms, which included: (1)"myosteatosis"OR"muscle density"OR"muscle attenuation"OR"intramuscular adipose tissue content"OR"intramuscular adipose tissue infiltration"OR"intramuscular adipose tissue deposition"OR"intramuscular fat content"OR"intramuscular fat infiltration"OR"intramuscular fat deposition"; and (2)"hepatocellular cancer"OR"hepatocellular tumor"OR"hepatocellular carcinoma"OR"hepatocellular neoplasm"OR"liver cancer"OR"liver tumor"OR"liver carcinoma"OR"liver neoplasm"OR"HCC"OR"hepatic cancer"OR"hepatic tumor"OR"hepatic carcinoma."The search was restricted to studies conducted on human subjects and included only full-length articles published in English in peer-reviewed journals. Additionally, the references of relevant original and review articles were manually screened to identify any additional eligible studies. The literature search covered the period from the inception of the databases to January 18, 2025. The detailed search strategy for each database is shown in **Supplemental File 1**.

Inclusion and exclusion criteria

The inclusion criteria for potential studies were defined according to the PICOS framework:

P (patients): Adult patients (aged 18 years or older) with confirmed diagnosis of HCC, regardless of the cancer etiology, stage, or main anticancer treatments.

I (exposure): Patients with myosteatosis. The methods, parameters, and cutoffs for the diagnosis of myosteatosis were consistent with those used in the original studies.

C (comparison): Patients without myosteatosis.

O (outcome): Survival outcomes, including OS and PFS, compared between patients with and without myosteatosis. In general, OS is defined as the time from treatment

initiation to death from any cause, while PFS is defined as the time from treatment initiation to disease progression or death, whichever occurs first.

S (study design): Observational studies with longitudinal follow-up, such as cohort studies, nested case–control studies, or post hoc analyses of clinical trials; no minimum follow-up duration or specific covariate adjustment in multivariate analyses was required for inclusion, in order to comprehensively capture all relevant observational evidence.

Studies were excluded if they were reviews, editorials, meta-analyses, preclinical research, or involved patients without HCC, lacked myosteatosis as exposure, or did not report the survival outcomes of interest. In cases where multiple publications appeared to involve overlapping cohorts (e.g., from the same institution with similar enrollment periods), we included only the study with the largest sample size or most comprehensive data to avoid double counting of patients.

Study quality assessment and data extraction

The literature search, study selection, quality assessment, and data extraction were independently performed by two authors. Key data—including hazard ratios (HRs), confidence intervals (CIs), and study characteristics—were cross-checked for consistency. Discrepancies were resolved through discussion and, when needed, consultation with the corresponding author. Study quality was assessed using the Newcastle–Ottawa Scale (NOS) [46], which evaluates selection, control of confounding factors, and outcome measurement and analysis, with scores ranging from 1 to 9, where a score of 9 indicates the highest quality. Studies with the NOS scores of 7 or above were generally considered as high-quality studies [46]. For this meta-analysis, we considered the exposed cohort representative if patients were consecutively or randomly selected. Adjustment for other confounding factors was credited if variables beyond age and sex were included in the multivariate models. A follow-up duration of at least 36 months was considered sufficient for the outcome to occur, and adequacy of follow-up was defined as having less than 10% loss to follow-up. Data extracted for analysis included study characteristics (author, year, country, and design), participant details (number of patients, mean age, sex, and main anticancer treatments), images (CT or MRI), parameters (IMAC or SMD), or cutoffs (sex-specified or not) for evaluating myosteatosis, number of patients with myosteatosis, mean follow-up durations, and variables adjusted when the association between myosteatosis and the survival outcomes of patients with HCC was analyzed.

Statistical analyses

The associations between myosteatosis and OS/PFS of patients with HCC were summarized as HRs and corresponding 95% CIs, compared between patients with and without myosteatosis. The HRs and their standard errors were derived from 95% CIs or p values and subsequently log-transformed to stabilize variance and achieve a normalized distribution [45]. To assess heterogeneity, we used the Cochrane Q test and I^2 statistics [47], with $I^2 < 25\%$, 25 ~ 75%, and > 75% indicating low, moderate, and high heterogeneity. A random-effects model was applied to integrate the results, accounting for study variability [45]. Via excluding individual studies sequentially, a sensitivity analysis was performed to evaluate the robustness of the findings. In addition, subgroup analyses were performed to evaluate study characteristics on the outcomes, such as study country (Asian versus non-Asian), main anticancer treatments, parameters (IMAC or SMD) or cutoffs (sex-specified or not) for evaluating myosteatosis, mean follow-up durations, or whether sarcopenia was adjusted when the association between myosteatosis and the survival outcomes of patients with HCC was analyzed. For continuous variables such as follow-up duration, the median value across included studies was used to define subgroups (e.g., short vs. long follow-up), a common practice in meta-analyses when no standardized thresholds exist. Regarding diagnostic criteria for myosteatosis, studies were classified as using'sex-specific'cutoffs if different thresholds were applied for men and women, and'universal'if a single cutoff was applied to all participants, in accordance with the methods described in the original studies. In addition, univariate meta-regression analyses were performed to evaluate the influence of study characteristics in continuous variables on the outcome, such as sample sizes of the studies, mean ages of the patients, proportions of men, follow-up durations, and study quality scores in NOS [45]. Publication bias was assessed by visually inspecting funnel plot symmetry, where substantial asymmetry may suggest small-study effects or selective publication. Egger's regression test was also performed to statistically detect funnel plot asymmetry, with p values < 0.05 indicating potential bias [48]. Analyses were performed using RevMan (version 5.1; Cochrane Collaboration, Oxford, UK) and Stata software (version 12.0; Stata Corporation, College Station, TX, USA).

Results

Study identification

The study selection process is summarized in Fig. 1. A total of 236 potentially relevant records were initially identified

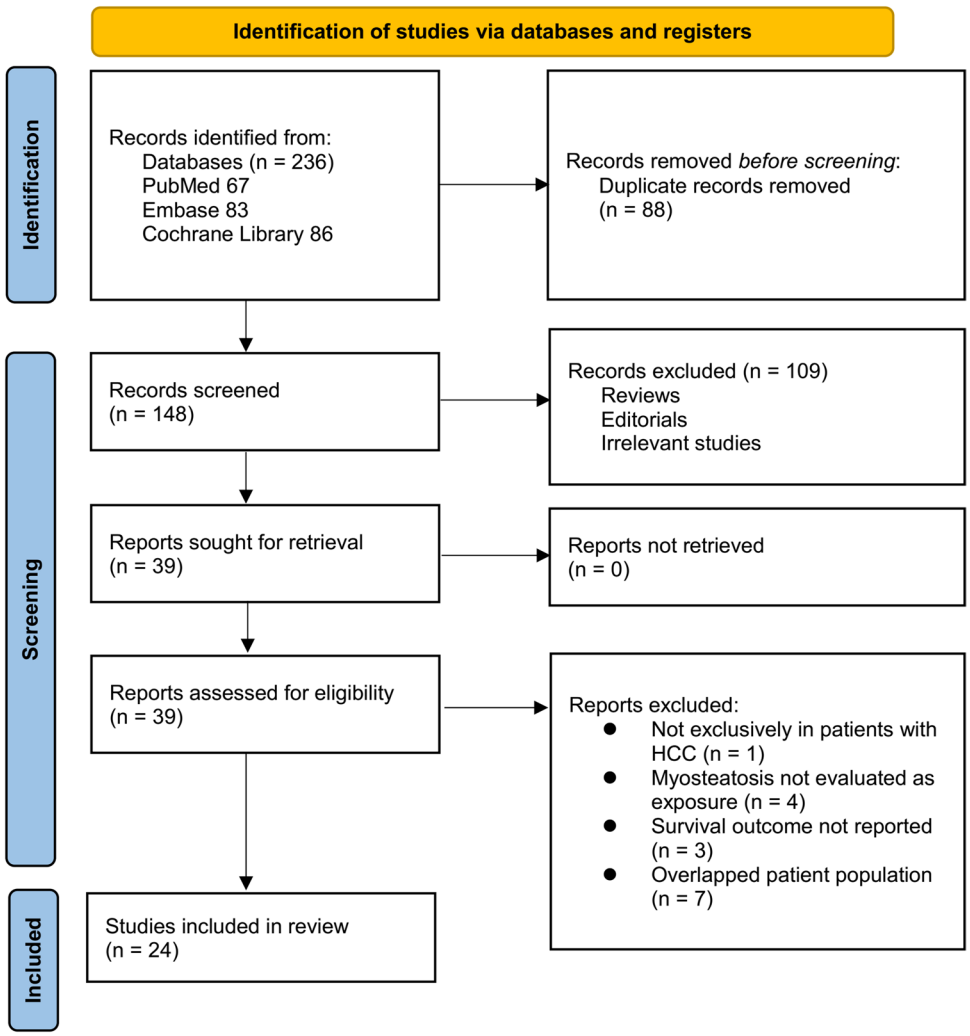

Fig. 1 Flowchart of database search and study inclusion

from the three databases searched and screening of citations of related articles, with 88 duplicates removed. Screening of titles and abstracts resulted in the exclusion of 109 articles that did not meet the objectives of the meta-analysis. The full texts of the remaining 39 articles were independently reviewed by two authors, leading to the exclusion of 15 studies for various reasons detailed in Fig. 1. Ultimately, 24 studies were included in the quantitative analysis [19–42].

Overview of the study characteristics

Table 1 shows the summarized characteristics of the available studies included in the meta-analysis. Overall, 24 retrospective cohorts, published between 2015 and 2025, and performed in Japan, Indonesia, Korea, German, China, Italy, and Thailand, were involved in the meta-analysis [19–42]. A total of 7436 patients with HCC were included in these studies. The mean ages of the patients varied from 50.0 to 74.0 years, and the proportion of men varied from 65.9 to 100.0%. The main anticancer treatments were surgical resection in seven studies [20, 21, 23, 27, 28, 35, 39], liver transplant in two studies [30, 32], TACE or transarterial embolization (TAE) in four studies [22, 25, 38, 42], immunotherapy in four studies [24, 26, 31, 33], and TKIs in five studies [29, 34, 36, 40, 41]. The main anticancer treatments were not specified in one study [19], and a comprehensive treatment involving TACE, RFA, surgical resection, chemoradiotherapy, and supportive treatment was used in another study [37]. All the included studies evaluated myosteatosis using CT imaging at the level of the third lumbar vertebra except one study [41], in which the MRI imaging at the same level was used. Myosteatosis was evaluated using IMAC in six studies [20, 21, 27, 28, 35, 38] and using SMD in the other 18 studies [19, 22–26, 29–34, 36, 37, 39–42]. A sex-specified cutoff for the diagnosis of myosteatosis was used in 11 studies [19–22, 25, 27, 32, 33, 35, 38, 42], and a universal cutoff was used in the other 13 studies [23, 24, 26, 28–31, 34, 36, 37, 39–41]. Accordingly, 3260 patients (43.8%) had myosteatosis. The median follow-up durations were 10 to 71 months. The outcome of OS was reported in 21 studies

Table 1 Characteristics of the included studies

Study	Country	Design	No. of patients included	Mean age (years)	Men (%)	Main anticancer treatment	Methods for myosteatosis evaluation	Parameter for myosteatosis evaluation	Cutoff values of myosteatosis parameters	No. of patients with myosteatosis	Median follow-up duration (months)	Outcomes reported	Variables adjusted
Kaibori [20]	Japan	RC	141	NR	75.9	Surgical resection	CT, L3	IMAC	Previously defined cutoffs: −0.44 for men and −0.31 for women	71	48	OS and PFS	Age, sex, BMI, sarcopenia, ICGR15, albumin, total bilirubin, prothrombin time, AST, platelet count, AFP, PIVKA-II, operative blood loss, tumor stage, and tumor size
Fujiwara [19]	Japan	RC	1257	68.8	65.9	Not specified	CT, L3	SMD	Maximally selected rank statistics determined cutoffs: men: ≤44.4 HU; women: ≤39.3 HU	1069	30	OS	Age, sex, viral status, BCLC stage, treatment methods for BCLC stage 0/A, prothrombin time, presence of previous treatment, and presence of CKD
Mardian [22]	Indonesia	RC	100	55	74	TACE or supportive treatment	CT, L3	SMD	Previously defined: men: ≤44.4 HU; women: ≤39.3 HU	65	13	OS	Age, sex, BMI, sarcopenia, visceral adiposity, viral status, Child–Pugh Class, cancer stage, and AFP

Table 1 (continued)

Study	Country	Design	No. of patients included	Mean age (years)	Men (%)	Main anticancer treatment	Methods for myosteatosis evaluation	Parameter for myosteatosis evaluation	Cutoff values of myosteatosis parameters	No. of patients with myosteatosis	Median follow-up duration (months)	Outcomes reported	Variables adjusted
Hamaguchi [21]	Japan	RC	606	68	79.9	Surgical resection	CT, L3	IMAC	Previously defined cutoffs: −0.36 for men and −0.23 for women	258	43	OS and PFS	Age, sex, BMI, etiology, previous treatment, comorbidities, Child–Pugh Class, tumor size, stage, number, surgical characteristics, and sarcopenia
Sano [37]	Japan	RC	187	69.9	72.7	TACE, RFA, surgical resection, chemoradiotherapy, and supportive treatment	CT, L3	SMD	Previously defined cutoffs: <41 HU in patients with a BMI <25 kg/m^2 and <33 HU in those with BMI ≥25 kg/m^2	110	30	OS	Age, sex, Child–Pugh Class, etiology, and cancer stage
Jang [23]	Korea	RC	160	55.2	75	Surgical resection	CT, L3	SMD	ROC curve analysis determined cutoffs: men: ≤46.1 HU; women: ≤48.4 HU	NR	71	OS and PFS	Age, sex, obesity, etiology, PLT, albumin, MELD-Na score, AFP, cancer stage, and sarcopenia

Table 1 (continued)

Study	Country	Design	No. of patients included	Mean age (years)	Men (%)	Main anticancer treatment	Methods for myosteatosis evaluation	Parameter for myosteatosis evaluation	Cutoff values of myosteatosis parameters	No. of patients with myosteatosis	Median follow-up duration (months)	Outcomes reported	Variables adjusted
Meister [39]	Germany	RC	100	67	72	Surgical resection	CT, L3	SMD	Previously defined cutoffs: < 41 HU in patients with a BMI < 25 kg/m^2 and < 33 HU in those with BMI ≥ 25 kg/m^2	60	30	OS and PFS	Age, sex, BMI, ASA Class, cirrhosis, tumor size, surgery characteristics, and sarcopenia
Yi [24]	China	RC	52	50	84.6	Immunotherapy	CT, L3	SMD	The lowest tertile	36	10	OS and PFS	Age, sex, and hemoglobin
Masetti [38]	Italy	RC	151	73.2	76.8	TAE	CT, L3	IMAC	Previously defined cutoffs: −0.44 for men and −0.31 for women	115	26	OS	None
Yamamoto [40]	Japan	RC	65	74	76.9	Lenvatinib	CT, L3	SMD	Median: 32.2 HU	32	13	OS and PFS	Age, sex, etiology, BMI, Child–Pugh Class, BCLC stage, metastatic status, and sarcopenia
Shi [27]	China	RC	245	56	80.8	Surgical resection	CT, L3	IMAC	ROC curve analysis determined cutoffs specified by sex	170	28	PFS	Age, sex, BMI, AFP, albumin, cirrhosis, surgery characteristics, tumor size, and sarcopenia

Table 1 (continued)

Study	Country	Design	No. of patients included	Mean age (years)	Men (%)	Main anticancer treatment	Methods for myosteatosis evaluation	Parameter for myosteatosis evaluation	Cutoff values of myosteatosis parameters	No. of patients with myosteatosis	Median follow-up duration (months)	Outcomes reported	Variables adjusted
Yoshikawa [41]	Japan	RC	65	74	76.9	Lenvatinib	MRI, L3	SMD	Median: 32.2 HU	32	30	PFS	Age, sex, tumor number, size, ICGR15, tumor stage, differentiation, AFP, PIVKA-II, and sarcopenia
Chen [26]	Taiwan (China)	RC	111	59	87.4	Immunotherapy	CT, L3	SMD	Previously defined cutoffs: <41 HU in patients with a BMI <25 kg/m^2 and <33 HU in those with BMI ≥ 25 kg/m^2	16	31	OS and PFS	Age, sex, HBsAg, anti-HCV, AFP, Child–Pugh Class, BCLC stage, lines of therapy, and sarcopenia
Bannangkoon [25]	Thailand	RC	611	61.4	72.8	TACE	CT, L3	SMD	Previously defined: men: ≤ 44.4 HU; women: ≤ 39.3 HU	237	42	OS	Age, sex, chronic lung disease, and CKD

Table 1 (continued)

Study	Country	Design	No. of patients included	Mean age (years)	Men (%)	Main anticancer treatment	Methods for myosteatosis evaluation	Parameter for myosteatosis evaluation	Cutoff values of myosteatosis parameters	No. of patients with myosteatosis	Median follow-up duration (months)	Outcomes reported	Variables adjusted
Ishida [28]	Japan	RC	188	68.9	84.6	Surgical resection	CT, L3	IMAC	ROC curve analysis determined cutoff: −0.46	NR	60	OS and PFS	Age, sex, sarcopenia, PLT, albumin, total bilirubin, prothrombin time, AST, ALT, AFP, PIVKA-II, operative blood loss, and surgery characteristics
Kang [29]	Korea	RC	245	67	86.1	Sorafenib	CT, L3	SMD	Previously defined cutoffs: < 41 HU in patients with a BMI < 25 kg/m^2 and < 33 HU in those with BMI ≥ 25 kg/m^2	22	15	OS and PFS	Age, sex, obesity, DM, hypertension, tumor number, size, metastatic status, Child–Pugh Class, AFP, cancer stage, and sarcopenia
Liu [31]	China	RC	116	54	77.6	Immunotherapy	CT, L3	SMD	Previously defined cutoffs: < 41 HU in patients with a BMI < 25 kg/m^2 and < 33 HU in those with BMI ≥ 25 kg/m^2	59	20	PFS	Age, sex, ECOG PS, Child–Pugh Class, BCLC stage, metastatic status, AFP, and sarcopenia

Table 1 (continued)

Study	Country	Design	No. of patients included	Mean age (years)	Men (%)	Main anticancer treatment	Methods for myosteatosis evaluation	Parameter for myosteatosis evaluation	Cutoff values of myosteatosis parameters	No. of patients with myosteatosis	Median follow-up duration (months)	Outcomes reported	Variables adjusted
Li [31]	China	RC	224	55	85.3	LT	CT, L3	SMD	P Previously defined cutoffs: < 41 HU in patients with a BMI < 25 kg/m^2 and < 33 HU in those with BMI ≥ 25 kg/m^2	82	18	OS	Age, sex, BMI, MELD score, diabetes status, etiology
Surov [34]	Germany	RC	784	66.4	82.3	TACE	CT, L3	SMD	Previously defined: men: ≤ 28 HU; women: ≤ 23.8 HU	160	60	OS	Age, sex, total bilirubin, BCLC stage, and tumor burden scores
Lu [32]	China	RC	673	53.4	100	LT	CT, L3	SMD	Maximally selected rank statistics determined cutoffs: men: ≤ 37.5 HU	187	31	OS and PFS	Age, BMI, cirrhosis, hepatitis B, Child–Pugh Class, tumor size, number, differentiation, AFP, and sarcopenia
Ouyang [33]	China	RC	305	55.6	87.9	Immunotherapy	CT, L3	SMD	ROC curve analysis determined cutoffs: men: ≤ 31.2 HU; women: ≤ 27 HU	37	17	OS	Age, sex, etiology, cirrhosis, ECOG PS, BCLC stage, tumor number, size, albumin, total bilirubin level, ALT, AST, AFP, and sarcopenia

Table 1 (continued)

Study	Country	Design	No. of patients included	Mean age (years)	Men (%)	Main anticancer treatment	Methods for myosteatosis evaluation	Parameter for myosteatosis evaluation	Cutoff values of myosteatosis parameters	No. of patients with myosteatosis	Median follow-up duration (months)	Outcomes reported	Variables adjusted
Surov [42]	10 European countries	RC	363	66.1	87.1	SIRT/ sorafenib	CT, L3	SMD	Previously defined cutoffs: <41 HU in patients with a BMI <25 kg/ m^2 and <33 HU in those with BMI ≥25 kg/m^2	148	30	OS	Age, sex, ECOG PS, albumin, PLT, BCLC stage, and extrahepatic metastases
Luo [36]	Taiwan (China)	RC	81	68.4	82.7	Lenvatinib	CT, L3	SMD	Previously defined cutoffs: <41 HU in patients with a BMI <25 kg/ m^2 and <33 HU in those with BMI ≥25 kg/m^2	36	20	OS and PFS	Age, sex, underweight, HbsAg, HCV status, AFP, other therapy, tumor size, BCLC stage, ALBI grade, and sarcopenia
Lee [35]	Japan	RC	606	68	79.9	Surgical resection	CT, L3	IMAC	Previously defined cutoffs: −0.36 for men and −0.23 for women	258	36	OS and PFS	Age, sex, underweight, HbsAg, HCV status, AFP, SCr, ALT, AST, PT, PLT, ALBI grade, tumor features, and sarcopenia

AFP, alpha-fetoprotein; ALBI, albumin-bilirubin; ALT, alanine aminotransferase; ASA, American Society of Anesthesiologists; AST, aspartate aminotransferase; BCLC, Barcelona Clinic Liver Cancer; BMI, body mass index; CKD, chronic kidney disease; CT, computed tomography; DM, diabetes mellitus; ECOG PS, Eastern Cooperative Oncology Group performance status; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HU, Hounsfield unit; ICGR15, indocyanine green retention rate at 15 min; IMAC, intramuscular adipose content; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; NR, not reported; MRI, magnetic resonance imaging; OS, overall survival; PFS, progression-free survival; PIVKA-II, protein induced by vitamin K absence-II; PLT, platelet count; PT, prothrombin time; RC, retrospective cohort; RFA, radiofrequency ablation; ROC, receiver operating characteristic; SCr, serum creatinine; SIRT, selective internal radiation therapy; SMD, skeletal muscle density; TACE, transarterial chemoembolization; TAE, transarterial embolization

[19–26, 28–30, 32–40, 42], and the outcome of PFS was reported in 15 studies [20, 21, 23, 24, 26–29, 31, 32, 35, 36, 39–41]. Since one of the included studies reported the outcome in men and women separately [35], these datasets were independently included in the meta-analysis, making 22 and 16 datasets available for the outcome of OS and PFS. The multivariate analyses were performed in all studies except one study, in which the univariate analysis was performed [38]. In total, 16 of the 24 included studies [20–23, 26–29, 31–33, 35, 36, 39–41] adjusted for sarcopenia in their multivariate analyses. In addition to sarcopenia, commonly adjusted variables included age, sex, BMI, liver function markers (e.g., Child–Pugh Class, albumin, bilirubin), tumor-related characteristics (e.g., size, stage, AFP), and treatment modality. The specific covariates adjusted for in each study are detailed in Table 1. The included studies achieved NOS scores ranging from six to nine, reflecting a generally moderate to high quality of methodology and reporting (Table 2).

Association between myosteatosis and OS in patients with HCC

Overall, 21 studies [19–26, 28–30, 32–40, 42] with 22 datasets evaluated the association between myosteatosis and OS in patients with HCC. A moderate heterogeneity was observed among these studies (p for Cochrane Q test <0.001; $I^2=65\%$). The pooled results showed that overall, myosteatosis was associated with poorer OS in patients with HCC (HR: 1.60, 95% CI: 1.40 to 1.83, $p<0.001$; Fig. 2A). Sensitivity analyses by excluding one study at a time showed similar results (HR: 1.55 to 1.65, p all <0.05). Specifically, excluding the only study with univariate meta-analysis showed consistent results (HR: 1.63, 95% CI: 1.42 to 1.87, $p<0.001$; $I^2=65\%$). In addition, the sensitivity analysis limited to studies with NOS score of 7 or higher also showed consistent results (HR: 1.63, 95% CI: 1.43 to 1.85, $p<0.001$; $I^2=55\%$). Moreover, the subgroup analysis showed that the association between myosteatosis and poor OS of HCC was significant in Asian studies but not in European studies (HR: 1.74 versus 1.08; p for subgroup difference <0.001; Table 3). Further subgroup analysis suggested that the association between myosteatosis and poor OS of HCC may not be significantly affected by main anticancer treatments, parameters for evaluating myosteatosis, whether the cutoffs for the diagnosis of myosteatosis were sex-specific or universal, or the median follow-up durations of the studies (p for subgroup difference all >0.05; Table 3). In addition, a stronger association between myosteatosis and poor OS was observed in studies with adjustment of myosteatosis (HR: 1.89, 95% CI: 1.53 to 2.33, $p<0.001$; Table 3). Finally, meta-regression analyses did not suggest any of the following variables may significantly affect the results, including sample size, mean ages of the patients, proportions of men, follow-up durations, and study quality scores (p all >0.05; Table 4).

Association between myosteatosis and PFS in patients with HCC

The pooled results of 16 datasets from 15 studies [20, 21, 23, 24, 26–29, 31, 32, 35, 36, 39–41], all with multivariate analyses, showed that myosteatosis also was associated with poorer PFS in patients with HCC (HR: 1.53, 95% CI: 1.33 to 1.76, $p<0.001$; Fig. 2B) with moderate heterogeneity (p for Cochrane Q test $=0.07$; $I^2=36\%$). Further sensitivity analysis by excluding one study at a time did not significantly change the results (HR: 1.45 to 1.58, p all <0.05). Specifically, the sensitivity analysis including only studies with NOS score of 7 or higher also showed consistent results (HR: 1.54, 95% CI: 1.34 to 1.76, $p<0.001$; $I^2=36\%$). Subsequent subgroup analyses indicated that the association between myosteatosis and poor PFS in HCC patients was significant in Asian studies but not in European studies (HR: 1.57 vs. 1.05). However, the difference between subgroups was not statistically significant ($p=0.08$; Table 3). Similar to the findings for OS, further subgroup analyses indicated that the association between myosteatosis and poor PFS was not significantly affected by the primary anticancer treatments, the parameters used to evaluate myosteatosis, whether the diagnostic cutoffs were sex-specific or universal, or the median follow-up durations of the studies (p for subgroup difference all >0.05; Table 3). Moreover, the association between myosteatosis and poor PFS remains significant in subgroup of studies with adjustment of myosteatosis (HR: 1.50, 95% CI: 1.31 to 1.72, $p<0.001$; Table 3). Lastly, meta-regression analyses did not suggest any of the following variables could significantly modify the results, such as sample size, mean ages of the patients, proportions of men, follow-up durations, and study quality scores (p all >0.05; Table 4).

Publication bias

The funnel plots for the meta-analyses assessing the association between myosteatosis and OS/PFS of patients with HCC are shown in Fig. 3A and B. Visual inspection of the plots reveals symmetry, indicating a low risk of publication bias. These findings are further supported by Egger's regression analyses (for OS: $p=0.42$; for PFS: $p=0.35$).

Discussion

This meta-analysis provides comprehensive evidence that myosteatosis is significantly associated with worse survival outcomes in patients with HCC. By pooling data from 24 retrospective cohort studies with 7436 patients, we found

Table 2 Study quality evaluation via the Newcastle–Ottawa Scale

Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at baseline	Control for age and sex	Control for other confounding factors	Assessment of outcome	Enough long follow-up duration	Adequacy of follow-up of cohorts	Total
Kaibori [20]	0	1	1	1	1	1	1	1	1	8
Fujiwara [19]	1	1	1	1	1	1	1	0	1	8
Mardian [22]	0	1	1	1	1	1	1	0	1	7
Hamaguchi [21]	1	1	1	1	1	1	1	1	1	9
Sano [37]	0	1	1	1	1	1	1	0	1	7
Jang [23]	0	1	1	1	1	1	1	1	1	8
Meister [39]	0	1	1	1	1	1	1	0	1	7
Yi [24]	0	1	1	1	1	0	1	0	1	6
Masetti [38]	1	1	1	0	0	1	1	0	1	6
Yamamoto [40]	0	1	1	1	1	1	1	0	1	7
Shi [27]	1	1	1	1	1	1	1	0	1	8
Yoshikawa [41]	0	1	1	1	1	1	1	0	1	7
Chen [26]	0	1	1	1	1	1	1	0	1	7
Bannangkoon [25]	0	1	1	1	1	1	1	1	1	8
Ishida [28]	1	1	1	1	1	1	1	1	1	9
Kang [29]	0	1	1	1	1	1	1	0	1	7
Liu [31]	0	1	1	1	1	1	1	0	1	7
Li [31]	0	1	1	1	1	1	1	0	1	7
Surov [34]	0	1	1	1	1	1	1	1	1	8
Lu [32]	0	1	1	1	1	1	1	1	1	8
Ouyang [33]	0	1	1	1	1	1	1	0	1	7
Surov [42]	1	1	1	1	1	1	1	1	1	8
Luo [36]	0	1	1	1	1	1	1	0	1	7
Lee [35]	1	1	1	1	1	1	1	1	1	9

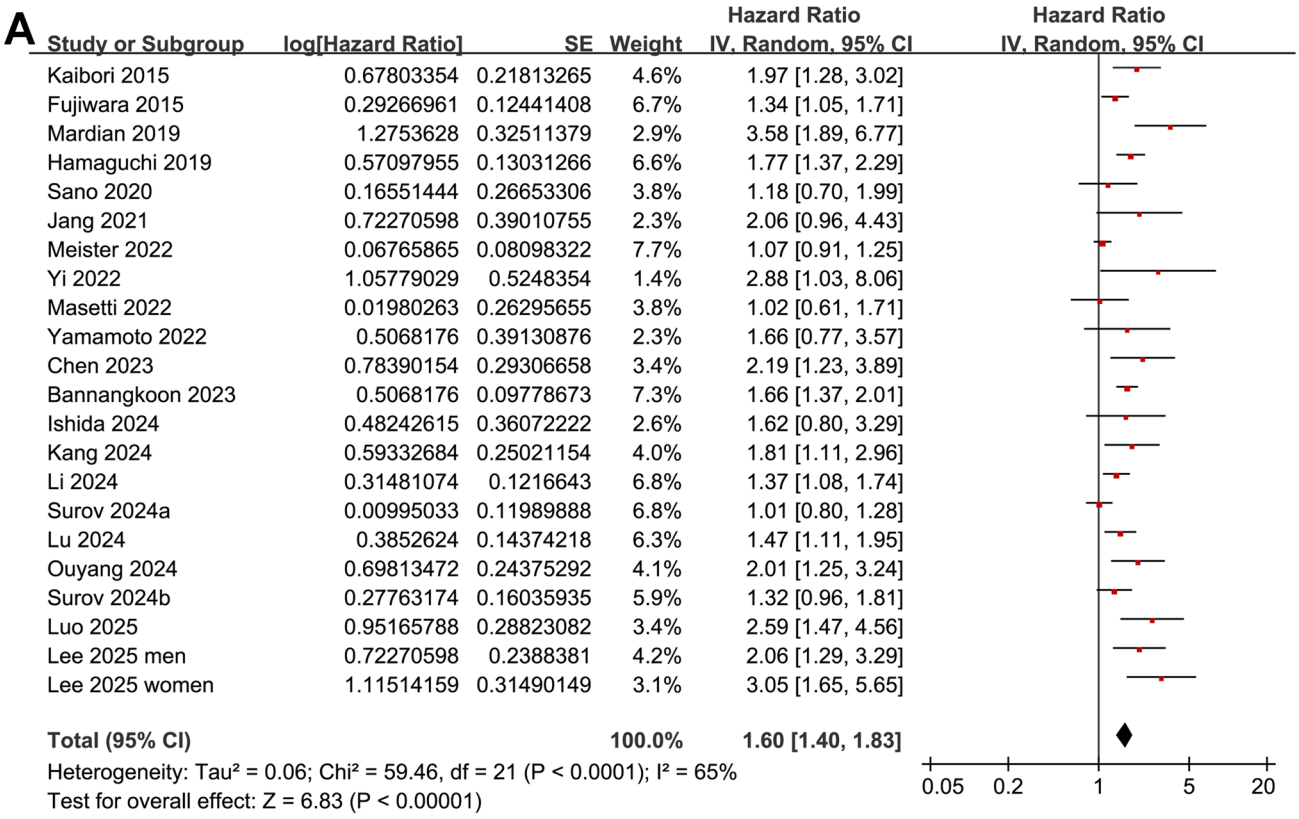

Fig. 2 Forest plots for the meta-analyses of the association between myosteatosis and survival outcomes of patients with HCC; **A**, forest plots for the meta-analysis of OS; and **B**, forest plots for the meta-analysis of PFS

that myosteatosis was independently linked to poorer OS and PFS. Subgroup analyses demonstrated that the association remained robust across different study populations and methodologies, with a stronger effect observed in Asian studies compared to European studies. The results also remained significant regardless of anticancer treatment type, myosteatosis assessment methods, sex-specific or universal cutoffs, and follow-up duration. Notably, studies adjusting

Table 3 Results of subgroup analyses

	OS					PFS				
Subgroup	No. of studies	HR (95% CI)	I^2	p for subgroup effects	p for subgroup difference	No. of studies	HR (95% CI)	I^2	p for subgroup effects	p for subgroup difference
Location of study										
Asia	18	1.74 [1.55, 1.95]	30%	< 0.001		15	1.57 [1.36, 1.81]	34%	< 0.001	
Europe	4	1.08 [0.96, 1.22]	0%	0.18	< 0.001	1	1.05 [0.68, 1.62]	–	0.82	0.08
Anticancer treatments										
Surgical resection	7	1.78 [1.30, 2.43]	77%	< 0.001		8	1.53 [1.22, 1.92]	54%	< 0.001	
Liver transplant	2	1.41 [1.18, 1.69]	0%	< 0.001		1	1.39 [1.08, 1.79]	12%	0.01	
TACE or TAE	4	1.49 [0.97, 2.28]	85%	0.07		0	–	–	–	
Immunotherapy	3	2.16 [1.53, 3.05]	0%	< 0.001		3	2.12 [1.44, 3.11]	0%	< 0.001	
TKIs	4	1.69 [1.25, 2.29]	33%	< 0.001	0.25	4	1.45 [1.13, 1.86]	0%	0.003	0.32
Parameter for myosteatosis										
IMAC	6	1.80 [1.42, 2.29]	38%	< 0.001		6	1.72 [1.29, 2.30]	62%	< 0.001	
SMD	16	1.53 [1.32, 1.78]	66%	< 0.001	0.26	10	1.45 [1.23, 1.70]	14%	< 0.001	0.30
Cutoffs for myosteatosis										
Sex-specific	11	1.66 [1.37, 2.00]	70%	< 0.001		6	1.64 [1.28, 2.10]	62%	< 0.001	
Not sex-specific	11	1.52 [1.25, 1.85]	53%	< 0.001	0.54	10	1.47 [1.23, 1.76]	14%	< 0.001	0.50
Mean follow-up duration										
< 30 months	8	1.84 [1.39, 2.43]	55%	< 0.001		6	1.85 [1.40, 2.45]	22%	< 0.001	
≥ 30 months	14	1.52 [1.30, 1.77]	68%	< 0.001	0.23	10	1.41 [1.22, 1.64]	30%	< 0.001	0.09
Adjusted for sarcopenia										
Yes	14	1.89 [1.53, 2.33]	69%	< 0.001		15	1.50 [1.31, 1.72]	31%	< 0.001	
No	8	1.32 [1.13, 1.54]	49%	< 0.001	0.007	1	6.15 [1.25, 30.26]	–	0.03	0.08

CI, confidence interval; HR, hazard ratio; I^2, heterogeneity index; IMAC, intramuscular adipose content; OS, overall survival; PFS, progression-free survival; SMD, skeletal muscle density; TACE, transarterial chemoembolization; TAE, transarterial embolization; TKIs, tyrosine kinase inhibitors

Table 4 Results of univariate meta-regression analysis

Variables	HR for OS			HR for PFS		
	Coefficient	95% CI	P values	Coefficient	95% CI	P values
Sample size	− 0.00031	− 0.00076 to 0.00014	0.17	− 0.00031	− 0.00096 to 0.00035	0.33
Mean age (years)	− 0.017	− 0.039 to 0.006	0.14	− 0.018	− 0.039 to 0.004	0.10
Men (%)	− 0.0040	− 0.0128 to 0.048	0.35	− 0.00016	− 0.00777 to 0.00745	0.97
Follow-up duration (months)	− 0.0048	− 0.0150 to 0.0054	0.34	− 0.0036	− 0.0147 to 0.0076	0.51
NOS	0.063	− 0.119 to 0.246	0.47	− 0.048	− 0.237 to 0.140	0.59

HR, hazard ratio; OS, overall survival; PFS, progression-free survival; CI, confidence interval; NOS, Newcastle–Ottawa Scale;

for sarcopenia demonstrated an even stronger association between myosteatosis and poor survival, suggesting that muscle quality deterioration may play an important role in the prognosis of HCC beyond muscle mass loss alone. Further meta-regression analyses did not suggest that the results were significantly modified by sample sizes of the included studies, mean ages of the patients, proportions of men, follow-up durations, and study quality scores. These findings support the emerging recognition of myosteatosis as an adverse prognostic factor in HCC and highlight the need for further research to refine its clinical relevance.

To the best of our knowledge, two previous meta-analyses have evaluated the association between myosteatosis and prognosis of patients with HCC. An early meta-analysis included two studies published before 2024 showed that myosteatosis was not associated poor OS in patients with HCC who were treated with TACE [49]. A subsequent meta-analysis included six studies published before 2023 suggested that myosteatosis may be associated with an increased risk of mortality in patients with HCC [50]. Compared to these meta-analyses, our study has several methodological strengths. First, our study is the most updated, incorporating multiple newly published studies that were not included in these previous reviews, thereby increasing statistical power and generalizability. With a larger sample size and broader geographic representation, our meta-analysis provides a more comprehensive assessment of the prognostic role of myosteatosis in HCC. Moreover, our study included a wider range of treatment modalities, reflecting real-world clinical diversity, and performed multiple subgroup analyses to confirm the robustness of the findings. These methodological strengths enhance the reliability of our conclusions and contribute to a deeper understanding of the prognostic significance of myosteatosis in HCC.

The underlying mechanisms linking myosteatosis to poor OS in HCC are multifactorial and involve both pathophysiological and clinical pathways. From a biological perspective, myosteatosis is associated with chronic systemic inflammation, oxidative stress, and mitochondrial dysfunction, all of which contribute to muscle deterioration and impaired metabolic homeostasis [51, 52]. Fat infiltration within skeletal muscle has been shown to disrupt muscle fiber integrity, impair glucose utilization, and promote insulin resistance, creating a tumor-promoting microenvironment [11, 53]. Additionally, myosteatosis may lead to immune system dysregulation, reducing the host's ability to mount an effective antitumor response [54]. Clinically, myosteatosis is often linked to poor nutritional status, sarcopenia, and reduced functional reserve, which may compromise a patient's ability to tolerate aggressive cancer therapies [55]. Furthermore, myosteatosis may influence the efficacy [56] and toxicity of anticancer treatments [25]. Patients with myosteatosis may experience altered drug metabolism and increased toxicity due to impaired liver and muscle function [51], leading to suboptimal treatment responses and higher rates of treatment-related complications. These factors collectively contribute to worse survival outcomes in HCC patients with myosteatosis [18]. In addition, metabolic syndrome and MASLD—conditions increasingly recognized as key drivers of hepatocarcinogenesis—are frequently associated with chronic inflammation, hyperinsulinemia, and ectopic fat deposition, including within skeletal muscle [57]. This fat infiltration contributes to insulin resistance, mitochondrial dysfunction, and immune dysregulation, all of which can impair the host's antitumor response and promote cancer progression [10]. These mechanisms may be more pronounced in certain populations, particularly in regions with a higher prevalence of MASLD or obesity-related HCC, thereby contributing to geographic variation in the prognostic impact of myosteatosis [58].

Results of the subgroup analysis showed that the association between myosteatosis and poor survival outcomes of patients with HCC was significant in studies from Asian countries ($n = 18$), but not in those from European countries ($n = 4$). This geographic variation may be attributed to differences in HCC etiology, such as a higher prevalence of hepatitis B virus infection in Asia compared to hepatitis C virus or metabolic dysfunction-associated steatotic liver disease (MASLD) in Europe [59, 60]. Additionally, genetic background, body composition profiles, lifestyle factors, and access to or choice of anticancer treatments (e.g., use of curative vs. palliative therapies) may contribute to

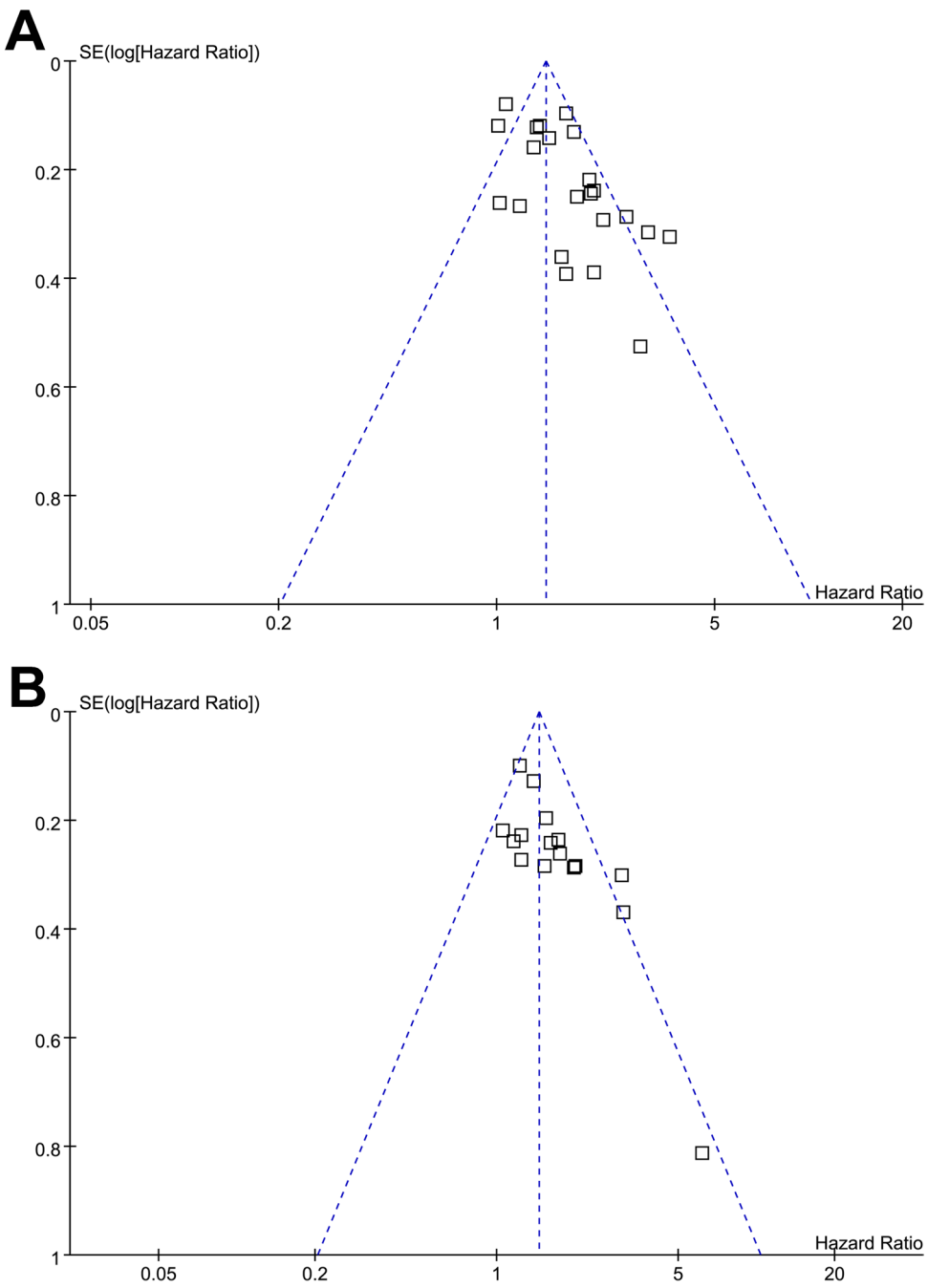

Fig. 3 Funnel plots for evaluating the publication bias underlying the meta-analyses; **A**, funnel plots for the meta-analysis of the association between myosteatosis and OS of patients with HCC; and **B**, funnel plots for the meta-analysis of the association between myosteatosis and PFS of patients with HCC

differential prognostic implications of myosteatosis [61]. Nonetheless, the limited number of European studies may have reduced statistical power and contributed to the observed lack of significance. Further multicenter studies with balanced geographic representation are needed to validate these findings.

Despite its strengths, this study has several limitations. First, all included studies were retrospective, introducing the potential for selection bias and recall bias [62]. Second, the retrospective design of all included studies may introduce inherent biases, including selection bias and residual confounding. Important variables such as detailed HCC etiology (e.g., HBV vs. HCV vs. MASLD), tumor stage at diagnosis, and comorbidity profiles were not uniformly reported or adjusted for across studies, which may have influenced the pooled estimates. Specifically, while tumor stage at diagnosis is a key prognostic factor and influences treatment decisions in HCC, stratified data by tumor stage were rarely reported across the included studies. As a result, we were unable to perform subgroup analyses based on this variable, and the lack of stage-specific adjustment may introduce residual confounding. Moreover, the majority

of included studies were conducted in Asian populations, potentially limiting the generalizability of our findings to other regions with different patient demographics and clinical practices. Furthermore, optimal methods and cutoff values for defining myosteatosis remain uncertain. While most studies used CT-based SMD or IMAC at the third lumbar vertebra, heterogeneity in measurement techniques and thresholds may affect comparability across studies. Third, given the study-level nature of this meta-analysis, we were unable to conduct an individual patient data analysis, which could provide more precise risk stratification and adjustment for confounding variables. Additionally, while HCC has diverse etiologies, including hepatitis B, hepatitis C, alcohol-related liver disease, and MASLD, we were unable to determine whether the impact of myosteatosis on survival varies by HCC etiology due to limited data. Furthermore, the presence of moderate heterogeneity suggests underlying differences in study populations, assessment methods, and treatment strategies that could not be fully accounted for in this analysis. Moreover, as with all observational studies, causality cannot be established, and prospective studies are needed to validate our findings. Finally, while no significant publication bias was detected, the possibility of small-study effects or unpublished negative studies cannot be fully excluded. Therefore, the pooled estimates should still be interpreted with some caution.

The clinical implications of this study are important but should be interpreted with caution. While myosteatosis is a promising prognostic marker in HCC, it is premature to consider it a direct therapeutic target. Instead, these findings underscore the importance of assessing muscle quality in routine clinical practice and incorporating myosteatosis evaluation into risk stratification models for HCC. Future research should focus on refining the criteria for diagnosing myosteatosis, exploring its predictive value for treatment response, and investigating potential interventions to mitigate its impact on survival. Large-scale prospective studies with standardized imaging protocols and predefined cutoff values are needed to further elucidate the clinical utility of myosteatosis in HCC management. Additionally, integrating myosteatosis assessment with other prognostic factors, such as liver function parameters, immune status, and genetic biomarkers, may improve patient stratification and guide personalized treatment approaches. Emerging evidence also suggests that myosteatosis may reflect disease severity in MASLD and may be influenced by BMI and body fat percentage [63]. Given the growing burden of MASLD-associated HCC, future studies should explore the prognostic relevance of myosteatosis in this subgroup, while controlling for metabolic parameters, adiposity, and hepatic fibrosis severity. Such investigations may help clarify the interplay between metabolic dysregulation, muscle quality, and cancer outcomes. On the other hand, to enhance clinical applicability, future efforts should focus on standardizing the assessment of myosteatosis in routine oncology and hepatology practice. This includes developing consensus guidelines on imaging protocols (e.g., CT acquisition parameters at the L3 vertebral level), establishing universally accepted cutoff values (potentially stratified by sex, BMI, or ethnicity), and validating reproducibility across software platforms and institutions. Integrating myosteatosis measurement into radiology reports or risk stratification tools could help guide treatment planning and follow-up strategies for patients with HCC.

Conclusions

In conclusion, this meta-analysis provides up-to-date evidence that myosteatosis may be an independent predictor of poor survival in patients with HCC. The findings remain robust across different treatment modalities and assessment methods, and after adjustment of sarcopenia, with a particularly pronounced effect observed in Asian populations. While the mechanisms underlying this association are complex and multifactorial, myosteatosis likely contributes to poor outcomes through both metabolic and clinical pathways. Despite some limitations, this study represents the most comprehensive analysis to date, reinforcing the need for further research into the prognostic and clinical significance of myosteatosis in HCC. Future studies should focus on optimizing diagnostic criteria, validating findings in prospective cohorts, and investigating strategies to mitigate the adverse effects of myosteatosis on cancer outcomes.

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Author contributions Yongjuan Wu, Guangyuan Cheng, and Qingsong Yang designed the study. Yongjuan Wu and Guangyuan Cheng performed database search, study identification, study quality evaluation, and data extraction. Yongjuan Wu, Guangyuan Cheng, and Jun Han performed statistical analyses. Yongjuan Wu and Qingsong Yang interpreted the results. Yongjuan Wu and Guangyuan Cheng wrote the manuscript. All authors revised the manuscript and approved the submission.

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Data availability The authors confirm that the data supporting the findings of this study are available within the article. Further inquiries can be directed to the corresponding author.

Declarations

Conflict of interest The authors declare no competing interests.

Ethics approval Institutional Review Board approval was not required because this is a meta-analysis.

Consent to participate Not applicable.

Consent to publish Not applicable.

References

1. Vogel A, Meyer T, Sapisochin G, Salem R, Saborowski A. Hepatocellular carcinoma. Lancet. 2022;400(10360):1345–62. https://doi.org/10.1016/s0140-6736(22)01200-4.
2. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. CA Cancer J Clin. 2025;75(1):10–45. https://doi.org/10.3322/caac.21871.
3. Singh SP, Madke T, Chand P. Global epidemiology of hepatocellular carcinoma. J Clin Exp Hepatol. 2025;15(2): 102446. https://doi.org/10.1016/j.jceh.2024.102446.
4. Singal AG, Zhang E, Narasimman M, Rich NE, Waljee AK, Hoshida Y, et al. HCC surveillance improves early detection, curative treatment receipt, and survival in patients with cirrhosis: a meta-analysis. J Hepatol. 2022;77(1):128–39. https://doi.org/10.1016/j.jhep.2022.01.023.
5. Tümen D, Heumann P, Gülow K, Demirci CN, Cosma LS, Müller M, et al. Pathogenesis and current treatment strategies of hepatocellular carcinoma. Biomedicines. 2022. https://doi.org/10.3390/biomedicines10123202.
6. Tabori NE, Sivananthan G. Treatment options for early-stage hepatocellular carcinoma. Semin Intervent Radiol. 2020;37(5):448–55. https://doi.org/10.1055/s-0040-1720950.
7. Inchingolo R, Posa A, Mariappan M, Spiliopoulos S. Locoregional treatments for hepatocellular carcinoma: current evidence and future directions. World J Gastroenterol. 2019;25(32):4614–28. https://doi.org/10.3748/wjg.v25.i32.4614.
8. Doycheva I, Thuluvath PJ. Systemic therapy for advanced hepatocellular carcinoma: an update of a rapidly evolving field. J Clin Exp Hepatol. 2019;9(5):588–96. https://doi.org/10.1016/j.jceh.2019.07.012.
9. Kramer RJ, Moris D. Advances in detecting, prognosticating, and treating hepatocellular carcinoma: advances and outcomes. Cancers Basel. 2024. https://doi.org/10.3390/cancers16122165.
10. Wang L, Valencak TG, Shan T. Fat infiltration in skeletal muscle: Influential triggers and regulatory mechanism. iScience. 2024;27(3):109221. https://doi.org/10.1016/j.isci.2024.109221.
11. Aleixo GFP, Shachar SS, Nyrop KA, Muss HB, Malpica L, Williams GR. Myosteatosis and prognosis in cancer: systematic review and meta-analysis. Crit Rev Oncol Hematol. 2020;145:102839. https://doi.org/10.1016/j.critrevonc.2019.102839.
12. Koo BK. Assessment of muscle quantity, quality and function. J Obes Metab Syndr. 2022;31(1):9–16. https://doi.org/10.7570/jomes22025.
13. Garcia-Diez AI, Porta-Vilaro M, Isern-Kebschull J, Naude N, Guggenberger R, Brugnara L, et al. Myosteatosis: diagnostic significance and assessment by imaging approaches. Quant Imaging Med Surg. 2024;14(11):7937–57. https://doi.org/10.21037/qims-24-365.
14. Amini B, Boyle SP, Boutin RD, Lenchik L. Approaches to assessment of muscle mass and myosteatosis on computed tomography: a systematic review. J Gerontol A Biol Sci Med Sci. 2019;74(10):1671–8. https://doi.org/10.1093/gerona/glz034.
15. Bathe OF. Tumor metabolism as a factor affecting diversity in cancer cachexia. Am J Physiol Cell Physiol. 2025;328(3):C908–20. https://doi.org/10.1152/ajpcell.00677.2024.
16. Scopel Poltronieri T, de Paula NS, Chaves GV. Skeletal muscle radiodensity and cancer outcomes: a scoping review of the literature. Nutr Clin Pract. 2022;37(5):1117–41. https://doi.org/10.1002/ncp.10794.
17. Cardaci TD, VanderVeen BN, Huss AR, Bullard BM, Velázquez KT, Frizzell N, et al. Decreased skeletal muscle intramyocellular lipid droplet-mitochondrial contact contributes to myosteatosis in cancer cachexia. Am J Physiol Cell Physiol. 2024;327(3):C684–97. https://doi.org/10.1152/ajpcell.00345.2024.
18. Jadzic J, Djonic D. Hepatocellular carcinoma and musculoskeletal system: a narrative literature review. World J Gastroenterol. 2024;30(15):2109–17. https://doi.org/10.3748/wjg.v30.i15.2109.
19. Fujiwara N, Nakagawa H, Kudo Y, Tateishi R, Taguri M, Watadani T, et al. Sarcopenia, intramuscular fat deposition, and visceral adiposity independently predict the outcomes of hepatocellular carcinoma. J Hepatol. 2015;63(1):131–40. https://doi.org/10.1016/j.jhep.2015.02.031.
20. Kaibori M, Ishizaki M, Iida H, Matsui K, Sakaguchi T, Inoue K, et al. Effect of Intramuscular adipose tissue content on prognosis in patients undergoing hepatocellular carcinoma resection. J Gastrointest Surg. 2015;19(7):1315–23. https://doi.org/10.1007/s11605-015-2838-8.
21. Hamaguchi Y, Kaido T, Okumura S, Kobayashi A, Shirai H, Yao S, et al. Preoperative visceral adiposity and muscularity predict poor outcomes after hepatectomy for hepatocellular carcinoma. Liver Cancer. 2019;8(2):92–109. https://doi.org/10.1159/000488779.
22. Mardian Y, Yano Y, Ratnasari N, Choridah L, Wasityastuti W, Setyawan NH, et al. Sarcopenia and intramuscular fat deposition are associated with poor survival in Indonesian patients with hepatocellular carcinoma: a retrospective study. BMC Gastroenterol. 2019;19(1):229. https://doi.org/10.1186/s12876-019-1152-4.
23. Jang HY, Choi GH, Hwang SH, Jang ES, Kim J-W, Ahn JM, et al. Sarcopenia and visceral adiposity predict poor overall survival in hepatocellular carcinoma patients after curative hepatic resection. Transl Cancer Res. 2021;10(2):854–66.
24. Yi X, Fu Y, Long Q, Zhao Y, Li S, Zhou C, et al. Myosteatosis can predict unfavorable outcomes in advanced hepatocellular carcinoma patients treated with hepatic artery infusion chemotherapy and anti-PD-1 immunotherapy. Front Oncol. 2022;12: 892192. https://doi.org/10.3389/fonc.2022.892192.
25. Bannangkoon K, Hongsakul K, Tubtawee T, Ina N, Chichareon P. Association of myosteatosis with treatment response and survival in patients with hepatocellular carcinoma undergoing chemoembolization: a retrospective cohort study. Sci Rep. 2023;13(1):3978. https://doi.org/10.1038/s41598-023-31184-9.
26. Chen B-B, Liang P-C, Shih TT-F, Liu T-H, Shen Y-C, Lu L-C, et al. Sarcopenia and myosteatosis are associated with survival in patients receiving immunotherapy for advanced hepatocellular

carcinoma. Eur Radiol. 2023;33(1):512–22. https://doi.org/10.1007/s00330-022-08980-4.
27. Shi S, Zhao Y-X, Fan J-L, Chang L-Y, Yu D-X. Development and external validation of a nomogram including body composition parameters for predicting early recurrence of hepatocellular carcinoma after hepatectomy. Acad Radiol. 2023;30(12):2940–53. https://doi.org/10.1016/j.acra.2023.05.022.
28. Ishida T, Miki A, Sakuma Y, Watanabe J, Endo K, Sasanuma H, et al. Preoperative bone loss predicts decreased survival associated with microvascular invasion after resection of hepatocellular carcinoma. Cancers. 2024. https://doi.org/10.3390/cancers16112087.
29. Kang MK, Song JE, Jang SY, Kim BS, Chung WJ, Lee C, et al. The clinical significance of myosteatosis in survival outcomes in patients with hepatocellular carcinoma treated with sorafenib. Cancers. 2024;16(2):454.
30. Li Z, Zhao Y, Xie Y, Zhang L, Sun Y, Yang K, et al. Impact of CT-relevant skeletal muscle parameters on post-liver transplantation survival in patients with hepatocellular carcinoma. Hep Intl. 2024;18(5):1516–27. https://doi.org/10.1007/s12072-024-10708-z.
31. Liu M, Jin Q, Wang H, Li Y. Progressive sarcopenia and myosteatosis predict prognosis of advanced HCC patients treated with immune checkpoint inhibitors. Front Immunol. 2024. https://doi.org/10.3389/fimmu.2024.1396927.
32. Lu D, Hu Z, Chen H, Khan AA, Xu Q, Lin Z, et al. Myosteatosis and muscle loss impact liver transplant outcomes in male patients with hepatocellular carcinoma. J Cachexia Sarcopenia Muscle. 2024;15(5):2071–83. https://doi.org/10.1002/jcsm.13554.
33. Ouyang J, Yang Y, Xu Y, Wang Z, Zhou Y, Zhao H, et al. How different body compositions affect the prognosis of HCC undergoing immunotherapy: the paradoxical phenomenon of BMI. Radiol Med (Torino). 2024. https://doi.org/10.1007/s11547-024-01933-5.
34. Surov A, Wienke A, Borggrefe J, Hinnerichs M, Seidensticker R, Öcal O, et al. Skeletal muscle quality predicts overall survival in advanced liver hepatocellular carcinoma treated with SIRT and sorafenib: a subanalysis of the SORAMIC trial. United Eur Gastroenterol J. 2024;12(8):1016–27. https://doi.org/10.1002/ueg2.12627.
35. Lee PC, Cheng TY, Ho CT, Huang KW, Chau GY, Huang YH, et al. Gender different impacts of muscle mass and adipose tissue on patients with hepatocellular carcinoma undergoing surgical resection. Liver Int. 2025;45(2): e16237. https://doi.org/10.1111/liv.16237.
36. Luo P-J, Chuang K-I, Ni C-F, Yeh H-Y, Wu M-S, Hsieh Y-Y, et al. Sarcopenia and myosteatosis are associated with low survival in patients receiving lenvatinib for unresectable hepatocellular carcinoma. J Formos Med Assoc. 2025. https://doi.org/10.1016/j.jfma.2025.01.001.
37. Sano A, Tsuge S, Kakazu E, Iwata T, Ninomiya M, Tsuruoka M, et al. Plasma free amino acids are associated with sarcopenia in the course of hepatocellular carcinoma recurrence. Nutrition. 2020;84: 111007. https://doi.org/10.1016/j.nut.2020.111007.
38. Masetti C, Pugliese N, Lofino L, Colapietro F, Ceriani R, Lleo A, et al. Myosteatosis is not associated with complications or survival in HCC patients undergoing trans arterial embolization. J Clin Med. 2022;12(1):262.
39. Meister FA, Lurje G, Verhoeven S, Wiltberger G, Heij L, Liu WJ, et al. The role of sarcopenia and myosteatosis in short- and long-term outcomes following curative-intent surgery for hepatocellular carcinoma in a European cohort. Cancers Basel. 2022. https://doi.org/10.3390/cancers14030720.
40. Yamamoto T, Imai N, Kuzuya T, Yokoyama S, Yamamoto K, Ito T, et al. Changes in body composition predict the time to treatment failure of lenvatinib in patients with advanced hepatocellular carcinoma: a pilot retrospective study. Nutr Cancer. 2022;74(9):3118–27. https://doi.org/10.1080/01635581.2022.2049322.
41. Yoshikawa K, Shimada M, Morine Y, Ikemoto T, Saito Y, Yamada S, et al. Clinical impact of myosteatosis measured by magnetic resonance imaging on long-term outcomes of hepatocellular carcinoma after radical hepatectomy. BMC Surg. 2023;23(1):281. https://doi.org/10.1186/s12893-023-02188-z.
42. Surov A, Wienke A, Borggrefe J, Auer TA, Gebauer B, Mähringer-Kunz A, et al. Albumin-muscle density score predicts overall survival in patients with hepatocellular cancer undergoing treatment with transarterial chemoembolization. J Cancer Res Clin Oncol. 2024;150(12):515. https://doi.org/10.1007/s00432-024-06043-3.
43. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372: n71. https://doi.org/10.1136/bmj.n71.
44. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372: n160. https://doi.org/10.1136/bmj.n160.
45. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane handbook for systematic reviews of interventions version 6.2. The Cochrane Collaboration. 2021;www.training.cochrane.org/handbook.
46. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2010;http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
47. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58. https://doi.org/10.1002/sim.1186.
48. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629–34.
49. Long J, Zhang X, Mi W, Shi J, Ren H, Wang Q. The predictive value of sarcopenia and myosteatosis in trans-arterial (chemo)-embolization treated HCC patients. Aging (Albany NY). 2024;16(1):389–401. https://doi.org/10.18632/aging.205375.
50. Kamiliou A, Lekakis V, Xynos G, Cholongitas E. Prevalence of and impact on the outcome of myosteatosis in patients with hepatocellular carcinoma: a systematic review and meta-analysis. Cancers Basel. 2024. https://doi.org/10.3390/cancers16050952.
51. Henin G, Loumaye A, Leclercq IA, Lanthier N. Myosteatosis: Diagnosis, pathophysiology and consequences in metabolic dysfunction-associated steatotic liver disease. JHEP Rep. 2024;6(2): 100963. https://doi.org/10.1016/j.jhepr.2023.100963.
52. Dondero K, Friedman B, Rekant J, Landers-Ramos R, Addison O. The effects of myosteatosis on skeletal muscle function in older adults. Physiol Rep. 2024;12(9): e16042. https://doi.org/10.14814/phy2.16042.
53. Zhu Y, Hu Y, Pan Y, Li M, Niu Y, Zhang T, et al. Fatty infiltration in the musculoskeletal system: pathological mechanisms and clinical implications. Front Endocrinol (Lausanne). 2024;15:1406046. https://doi.org/10.3389/fendo.2024.1406046.
54. Setiawan T, Sari IN, Wijaya YT, Julianto NM, Muhammad JA, Lee H, et al. Cancer cachexia: molecular mechanisms and treatment strategies. J Hematol Oncol. 2023;16(1):54. https://doi.org/10.1186/s13045-023-01454-0.
55. West MA, van Dijk DPJ, Gleadowe F, Reeves T, Primrose JN, Abu Hilal M, et al. Myosteatosis is associated with poor physical fitness in patients undergoing hepatopancreatobiliary surgery. J Cachexia Sarcopenia Muscle. 2019;10(4):860–71. https://doi.org/10.1002/jcsm.12433.
56. Hong S, Kim KW, Park HJ, Ko Y, Yoo C, Park SY, et al. Impact of baseline muscle mass and myosteatosis on the development of

early toxicity during first-line chemotherapy in patients with initially metastatic pancreatic cancer. Front Oncol. 2022;12: 878472. https://doi.org/10.3389/fonc.2022.878472.
57. Li Y, Li L, Zhang Y, Lu J, Tang X, Bi C, et al. Clinical and pathological characteristics of metabolic dysfunction-associated steatotic liver disease and the key role of epigenetic regulation: implications for molecular mechanism and treatment. Ther Adv Endocrinol Metab. 2025;16:20420188251321600. https://doi.org/10.1177/20420188251321602.
58. Kim HS, Kim HK, Jung CH. Association of myosteatosis with nonalcoholic fatty liver disease, severity, and liver fibrosis using visual muscular quality map in computed tomography. Diabetes Metab J. 2023;47(2):304–5. https://doi.org/10.4093/dmj.2023.0058.
59. Ashtari S, Pourhoseingholi MA, Sharifian A, Zali MR. Hepatocellular carcinoma in Asia: prevention strategy and planning. World J Hepatol. 2015;7(12):1708–17. https://doi.org/10.4254/wjh.v7.i12.1708.
60. Kim DY. Changing etiology and epidemiology of hepatocellular carcinoma: Asia and worldwide. J Liver Cancer. 2024;24(1):62–70. https://doi.org/10.17998/jlc.2024.03.13.
61. Revoredo S, Del Fabbro E. Hepatocellular carcinoma and sarcopenia: a narrative review. Ann Palliative Med. 2023;12(6):1295–309.
62. Powell JT, Sweeting MJ. Retrospective studies. Eur J Vasc Endovasc Surg. 2015;50(5):675. https://doi.org/10.1016/j.ejvs.2015.07.005.
63. Hsieh YC, Joo SK, Koo BK, Lin HC, Lee DH, Chang MS, et al. Myosteatosis but not sarcopenia predisposes NAFLD subjects to early steatohepatitis and fibrosis progression. Clin Gastroenterol Hepatol. 2023;21(2):388–97. https://doi.org/10.1016/j.cgh.2022.01.020.