Prevalence of sarcopenia among patients with hepatocellular carcinoma: A systematic review and meta-analysis

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Abstract. Sarcopenia is a common condition in patients with hepatocellular carcinoma (HCC). Sarcopenia affects the prognosis of patients with HCC and reduces their quality of life. However, to date, there has been no systematic review and meta-analysis to assess the prevalence of sarcopenia in patients with HCC, to the best of our knowledge. PubMed, Embase, Web of Science and the Cochrane Library were comprehensively screened for relevant literature published from March 2001 to June 2022. A random effect analysis was conducted to pool the incidence rates for each study. Subgroup and meta-regression analyses were used to investigate the latent sources of heterogeneities. The Newcastle-Ottawa Scale was used to estimate the quality of the included studies. The I^2 statistic was used to evaluate heterogeneity between studies. In total, 48 studies encompassing 8,959 patients were included in the meta-analysis. The results of the present meta-analysis showed that nearly half (42%) of the patients with HCC had sarcopenia (95% CI, 0.36-0.48). The morbidity of sarcopenia in studies with a high proportion of males (45%) was higher compared with the morbidity observed in studies with a lower proportion of males (37%). In addition, the incidence rate in younger patients (46%) was found to be higher compared with the incidence rate in older patients (39%). In conclusion, the findings in the present systematic review revealed that a large number of patients with HCC suffer from sarcopenia, indicating the necessity of developing screening and intervention measures to improve the outcome in these patients.

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Introduction

Hepatocellular carcinoma (HCC) is a malignancy with a high global morbidity (1), and is one of the primary malignancies that account for cancer-associated mortality (2). According to the latest estimations of the World Health Organization, >1 million patients will succumb to HCC by 2030 (3). Although numerous therapeutic options, including liver transplantation, surgical operation and ablation therapy, are available, HCC is associated with poor outcomes (4). Several factors are significantly related to the outcome of HCC, including sex, race, the degree of liver damage and comorbidity (5).

Early detection and systematic treatment can improve the survival rate of patients with cancer. Nutritional supplements and physical improvements, including timely supplementation of protein and vitamins, and low intensity aerobic exercise, also play a critical role in enhancing the clinical efficacy of the treatments for HCC. Recently, physical parameters, such as muscle strength and fat content, have been used as evaluation factors to predict patient prognosis (6).

Sarcopenia is usually interpreted as a progressive attenuation of muscle volume and a gradual decline in muscle performance, which can cause adverse clinical events (7). Sarcopenia is caused by ageing as well as diverse chronic illnesses, such as diabetes, heart failure and cancer. It has been confirmed that sarcopenia is prevalent in various tumors, including gastric cancer, lung cancer and colorectal cancer, and has an adverse impact on patient prognosis (8). To the best of our knowledge, certain reviews have shown that sarcopenia is closely related to lower survival rates and higher rates of postoperative syndrome in patients with HCC (9,10). Therefore, unravelling the accurate incidence rate of sarcopenia in HCC is important for early screening, formulating adequate intervention measures and improving patient prognosis.

To date, no meta-analysis has assessed the incidence of sarcopenia among patients with HCC, to the best of our knowledge. The evidence obtained from the present meta-analysis will provide accurate and effective epidemiological information to help prevent and treat sarcopenia. Therefore, the

purpose of the present study was to systematically dissect the published literature on the morbidity of sarcopenia among patients with HCC.

Materials and methods

Search strategy and study retrieval. An extensive and systematic literature review was conducted according to the PRISMA guidelines (11). Relevant literature published from March 2001 to June 2022 in the English language was systematically searched in PubMed (https://www.nih.gov/), Embase (https://www.embase.com/), Web of Science (https://www.webofscience.com) and the Cochrane Library (http://www.cochranelibrary.com). The detailed retrieval strategy is presented in Appendix S1. Two authors independently retrieved the titles and abstracts to select potentially suitable articles. Subsequently, the content of these articles was assessed to determine which studies to include and exclude. Reasons for inclusion and exclusion were recorded. All discrepancies were resolved by discussion. All potential studies were entered into EndNote X9 (Clarivate Plc) and duplicate studies were removed. The Prospero registration no. of the present systematic review is CRD42022328912 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022328912).

Inclusion and exclusion criteria. The inclusion criteria were as follows: i) Subject population: Patients with HCC; ii) disease of concern: Sarcopenia (at present, there is no unanimous standard for sarcopenia; therefore, the original definition in each study was retained); iii) the incidence or number of sarcopenia cases was reported; and iv) research type: Prospective or retrospective cohort study. The exclusion criteria were as follows: i) Lack of accurate diagnostic standards for sarcopenia; ii) books, case reports, editorials, letters to the editor and reviews; and iii) non-English writing.

Data extraction and quality assessment. Two investigators separately extracted comprehensive data from the eligible studies. The data filtered from every study contained the following information: i) First author name; ii) study type; iii) publication date; iv) sample size; v) number of individuals with sarcopenia; vi) country where the study was performed; vii) proportion of male patients; ix) average age and x) diagnostic criteria for sarcopenia. Quality assessment was performed separately by two investigators utilizing the Newcastle-Ottawa Scale (NOS) (12). Any disagreements were resolved by a third senior author.

Data synthesis and analysis. In the present study, all statistical analyses were performed using STATA software version 12.0 (StataCorp LP). The incidence rates from the included studies were pooled using a randomized effect meta-analysis (13). Heterogeneity was evaluated using the I^2 test. Values of 75, 50 and 25% from the I^2 test indicated high, medium and low heterogeneity, respectively (14). To clarify the possible sources of heterogeneity, subgroup and meta-regression analyses were performed on region, average age, proportion of male patients, diagnostic criteria, sample size and year of publication. Publication bias was tested using the Egger's test. The asymmetry of the funnel plot was corrected using the trim-and-fill method (15). $P<0.05$ was considered to indicate a statistically significant difference.

Results

Literature search results. In total, 2,923 relevant studies were retrieved, including 832 from PubMed, 819 from Embase, 583 from Cochrane and 689 from Web of Science. After removing duplicates and reading the titles and abstracts, a total of 2,776 studies were excluded. After screening the full texts, 48 studies that met the inclusion criteria were included. A flowchart of the document retrieval process is presented in Fig. 1.

Basic characteristics of included studies and quality assessment. The important features of the studies included in the present meta-analysis are presented in Table I. A total of 8,959 participants were enrolled in the eligible studies (16-63). A large number of the studies included in the current review were performed in Asia, especially in Japan, and 15 documented studies were performed outside Asia, such as Africa (n=4), North America (n=4) and Europe (n=7). The studies included in the present meta-analysis were published between 2013 and 2022. The sample size of patient cohorts in the analyzed studies ranged from 40 to 1,257 patients. Of these, two were observational studies, three were prospective studies and the rest were retrospective studies.

In 43 articles, to define sarcopenia, the skeletal muscle near the third lumbar vertebra was detected by computed tomography (CT), while three of the 43 studies also used grip strength measured using a hand grip dynamometer. In four studies, CT was used to detect the psoas muscle near the third lumbar spine. In addition, one study used magnetic resonance imaging to detect the fat-free muscle area (FFMA) near the superior mesenteric artery.

NOS was used to assess risk bias (Table SI). Based on the scores, all included studies were regarded as high-quality studies (score ≥7).

Morbidity of sarcopenia among patients with HCC according to meta-analysis and subgroup analysis. The pooled incidence rate of sarcopenia among patients with HCC was 42% (95% CI, 0.36-0.48). Remarkable heterogeneity was observed among the 48 studies (I^2=97.9%, $P<0.001$) (Fig. 2).

The prevalence of sarcopenia was 44% in Africa, 40% in North America, 56% in Europe and 39% in Asia, although the I^2 statistic showed significant heterogeneity among the studies included in each subgroup, except for Africa (Table II; Fig. S1A).

Considering the proportion of male patients included in the present study, 75% was used as the analysis cut-off. The prevalence of sarcopenia in the subgroup with a high proportion of male patients was higher compared with the prevalence in the subgroup with a low proportion of males (45 vs. 37%, respectively; Table II; Fig. S1B).

In the subgroup analysis, the incidence rate of sarcopenia based on average age was found to be higher in young patients (<60 years old; 46%) compared with the incidence in elderly patients (≥60 years old; 39%; Table II; Fig. S1C).

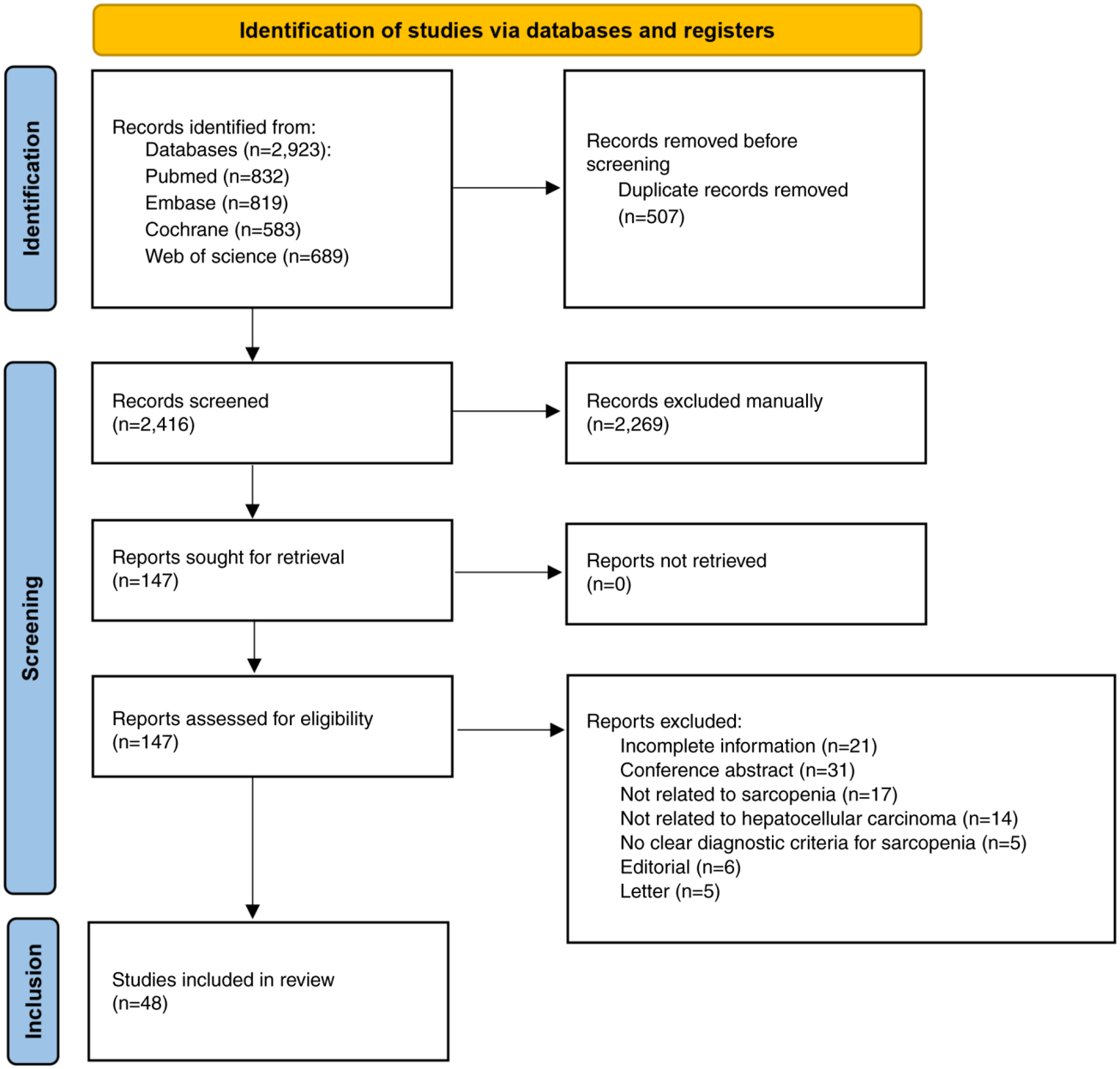

Figure 1. Flow chart of review search on prevalence of sarcopenia among patients with hepatocellular carcinoma.

Furthermore, in the subgroup analysis with different diagnostic criteria, the male skeletal muscle index (SMI) of 42 cm^2/m^2 and female SMI of 38 cm^2/m^2 was used as the cut-off. The morbidity of sarcopenia was higher in the studies with SMI > cut-off (50%), followed by SMI selectively > cut-off (44%), equal to the cut-off (41%) and < cut-off (23%) (Fig. S1D). In addition, the studies using SMI combined with body mass index as the diagnostic standard had a higher incidence rate of sarcopenia (43%) compared with the studies using SMI combined with hand grip strength (24%). Interestingly, when using other diagnostic methods, such as the psoas muscle index (PMI) or FFMA, the incidence rate of sarcopenia was the highest (54%) among all diagnostic criteria used. All aforementioned subgroup analyses are depicted in Fig. S1.

Meta-regression analysis: Year of publication and total sample size. The year of publication of the data collected for the current review did not affect the incidence rate of sarcopenia in the meta-regression analysis (regression coefficient, 0.004; 95% CI, 0.171-0.262; P=0.68; Table III). However, the total sample size could explain ~40% of the heterogeneity among these studies in the meta-regression analysis (regression coefficient, -0.0003; 95% CI, 0.0006 to -0.0001; P<0.001; Table III).

Publication bias. In the current meta-analysis, potential publication bias was found according to the asymmetry of the funnel plot (Fig. S2) and Egger's test (P<0.001; 95% CI, 6.93-12.09). Subsequently, the trim-and-fill method was used to correct the asymmetry of the funnel plots. The processed data showed that the results were not reversed after the addition of six studies (P<0.0001; 95% CI, 0.32-0.43), which further indicated that despite publication bias, the original results were relatively stable (Fig. 3).

Table I. Characteristics of studies included in the present systematic review and meta-analysis.

First author, year	Country	Study design	Sample size	Mean age, years	Male sex, %	Number of patients with sarcopenia	Methods used for detecting sarcopenia	Definition of sarcopenia, cm^2/m^2	(Refs.)
Alsebaey *et al*, 2021	Egypt	Retrospective	262	59.6	69.5	113	CT: L3-SMI	L3-SMI ≤50 for men and ≤39 for women	(16)
Akce *et al*, 2020	USA	Retrospective	57	66.0	77.2	28	CT: L3-SMI	L3-SMI <43 for men and ≤39 for women	(17)
Begini *et al*, 2017	Italy	Retrospective	92	71.6	70.6	37	CT: L3-SMI	L3-SMI ≤53 for men, ≤41 for women with BMI ≥25 and <43 for men and women with BMI< 25	(18)
Dong *et al*, 2022	China	Retrospective	40	59.0	92.5	23	CT: L3-SMI	L3-SMI <42 for men and <38 for women	(19)
Guichet *et al*, 2021	USA	Retrospective	82	65.0	79.0	25	MRI: FFMA at the level of the SMA	FFMA ≤32 cm^2 for men and ≤29 cm^2 for women	(20)
Ha *et al*, 2018	South Korea	Retrospective	178	59.7	79.0	62	CT: L3-SMI	L3-SMI <46 for men and <43 for women	(21)
Hirota *et al*, 2020	Japan	Observational	138	77.0	65.2	42	CT: L3-SMI; Hand dynamometer: Dominant hand	L3-SMI <42 for men and <38 for women; grip strength <26 kg for men and <18 kg for women	(22)
Imai *et al*, 2017	Japan	Retrospective	351	70.4	68.9	33	CT: L3-SMI	L3-SMI <36 for men and <29 for women	(23)
Kim *et al*, 2018	South Korea	Retrospective	92	54.0	100.0	72	CT: L3-PMI	PMI <16 mm/m	(24)
Kobayashi *et al*, 2019	Japan	Retrospective	465	67.6	78.9	62	CT: L3-SMI	L3-SMI <40 for men and <31 for women	(25)
Kobayashi *et al*, 2018	Japan	Retrospective	102	69.0	68.6	31	CT: L3-SMI	L3-SMI <42 for men or <38 for women	(26)
Kotoh *et al*, 2020	Japan	Retrospective	53	72.0	77.3	15	CT: L3-SMI; Grip strength dynamometer: Dominant hand	L3-SMI <42 for men or <38 for women; handgrip strength <26 kg in men or <18 kg in women	(27)
Kroh *et al*, 2019	Germany	Retrospective	70	67.7	70.0	33	CT: L3-SMI	L3-SMI <43 in men with BMI <25 or <53 in men; and SMI <41 irrespective of BMI in women	(28)

Table I. Continued.

First author, year	Country	Study design	Sample size	Mean age, years	Male sex, %	Number of patients with sarcopenia	Methods used for detecting sarcopenia	Definition of sarcopenia, cm^2/m^2	(Refs.)
Lanza *et al*, 2020	Italy	Retrospective	142	73.0	77.4	121	CT: L3-SMI	L3-SMI <55 for men and <39 for women	(29)
Lee *et al*, 2019	South Korea	Retrospective	156	59.0	82.1	99	CT: L3-SMI	L3-SMI <49 for men and <41 for women	(30)
Levolger *et al*, 2015	Netherlands	Retrospective	90	62.0	70.0	52	CT: L3-SMI	L3-SMI <52 for men and <40 for women	(31)
Liao *et al*, 2021	China	Retrospective	727	53.4	83.7	123	CT: L3-SMI	L3-SMI <41 for men and <31 for women	(32)
Meister *et al*, 2022	Netherlands	Retrospective	100	67.0	72.0	54	CT: L3-SMI	L3-SMI <50 for men and <39 for women	(33)
Meza-Junco *et al*, 2013	USA	Retrospective	116	58.0	84.0	35	CT: L3-SMI	L3-SMI <43 in men with BMI <25 or <53 in men with BMI >25; and SMI <41 irrespective of BMI in women	(34)
Salman *et al*, 2021	Egypt	Prospective	97	53.4	74.2	42	CT: L3-SMI	L3-SMI<43 in men with BMI <25 or <53 in men with BMI >25; and SMI <41 irrespective of BMI in women	(35)
Salman *et al*, 2020	Egypt	Prospective	52	53.9	73.0	27	CT: L3-SMI	L3-SMI <43 in men with BMI <25 or <53 in men with BMI >25; and SMI <41 irrespective of BMI in women	(36)
Shiba *et al*, 2018	Japan	Retrospective	68	74.0	60.3	22	CT: L3-SMI	L3-SMI <44 for men and <41 for women	(37)
Takagi *et al*, 2016	Japan	Retrospective	254	65.7	81.4	118	CT: L3-SMI	L3-SMI <46 for men and <38 for women	(38)
Antonelli *et al*, 2018	Italy	Retrospective	96	69.0	78.0	47	CT: L3-SMI	L3-SMI ≤41 in women, ≤53 for men with BMI ≥25 and <43 for men and women with BMI <25	(39)
Harimoto *et al*, 2013	Japan	Retrospective	186	66.0	77.0	75	CT: L3-SMI	L3-SMI <44 for men and <41 for women	(40)

Table I. Continued.

First author, year	Country	Study design	Sample size	Mean age, years	Male sex, %	Number of patients with sarcopenia	Methods used for detecting sarcopenia	Definition of sarcopenia, cm^2/m^2	(Refs.)
Nishikawa *et al*, 2017	Japan	Retrospective	232	72.0	78.0	151	CT: L3-SMI	L3-SMI <36 for men and <30 for women	(41)
Chen *et al*, 2022	China	Retrospective	111	59.0	87.4	57	CT: L3-SMI	L3-SMI <41 for men and <35 for women	(42)
Naganuma *et al*, 2017	Japan	Retrospective	69	72.0	74.0	35	CT: L3-SMI	L3-SMI <42 for men and women	(43)
Mardian *et al*, 2019	Japan	Retrospective	100	55.0	74.0	31	CT: L3-SMI	L3-SMI <36 for men and <30 for women	(44)
Badran *et al*, 2020	Egypt	Retrospective	262	59.6	69.5	113	CT: L3-SMI	L3-SMI <50 for men and <39 for women	(45)
Hou *et al*, 2022	China	Retrospective	153	-	83.6	77	CT: L3-PMI	L3-PMI <5 for men and <4 for women	(46)
Imai *et al*, 2020	Japan	Retrospective	61	67.3	86.8	25	CT: L3-SMI	L3-SMI <42 for men and <38 for women	(47)
Endo *et al*, 2020	Japan	Retrospective	63	71.0	84.1	11	CT: L3-SMI	L3-SMI <42 for men and <38 for women	(48)
Choi *et al*, 2020	South Korea	Retrospective	238	59.0	81.1	135	CT: L3-PMI	PMI <5 for men and <1 for women	(49)
Harimoto *et al*, 2016	Japan	Retrospective	139	-	70.5	57	CT: L3-SMI	L3-SMI <44 for men and <41 for women	(50)
Kamachi *et al*, 2016	Japan	Retrospective	92	71.9	70.6	61	CT: L3-SMI	L3-SMI <52 for men and <39 for women	(51)
Zhang *et al*, 2022	China	Retrospective	228	58.9	76.7	89	CT: L3-SMI	L3-SMI <46 for men and <34 for women	(52)
Yabusaki *et al*, 2016	Japan	Retrospective	195	66.0	80.0	89	CT: L3-SMI	L3-SMI <44 for men and <41for women	(53)
Fujiwara *et al*, 2015	Japan	Retrospective	1257	68.8	65.9	139	CT: L3-SMI	L3-SMI <39 for men and <30 for women	(54)
Acosta *et al*, 2019	USA	Retrospective	119	59.0	78.2	61	CT: L3-SMI	L3-SMI <52 for men and <39 for women	(55)
Yang *et al*, 2022	China	Prospective	155	60.0	87.1	22	CT: L3-SMI; hand dynamometer: Dominant hand	L3-SMI <51 for men and <37 for women; grip strength <28 kg for men or <18 kg for women	(56)

Table I. Continued.

First author, year	Country	Study design	Sample size	Mean age, years	Male sex, %	Number of patients with sarcopenia	Methods used for detecting sarcopenia	Definition of sarcopenia, cm^2/m^2	(Refs.)
Hamaguchi *et al*, 2019	Japan	Retrospective	606	68.0	80.0	84	CT: L3-SMI	L3-SMI <40 for men and <31 for women	(57)
Uojima *et al*, 2020	Japan	Retrospective	100	71.5	75.0	59	CT: L3-SMI	L3-SMI <42 for men and <38 for women	(58)
Takada *et al*, 2018	Japan	Retrospective	214	71.0	77.0	123	CT: L3-SMI	L3-SMI <42 for men and <38 for women	(59)
Tan *et al*, 2022	China	Retrospective	70	41.6	100.0	38	CT: L3-PMI	L3-PMI <6 for men	(60)
Kim *et al*, 2021	South Korea	Retrospective	102	61.3	85.3	23	CT: L3-SMI	L3-SMI <42 for men and <38 for women	(61)
Iritani *et al*, 2015	Japan	Retrospective	217	72.0	67.2	24	CT: L3-SMI	L3-SMI <36 for men and <29 for women	(62)
Voron *et al*, 2015	France	Observational	109	61.6	84.4	59	CT: L3-SMI	L3-SMI <52 for both men and women	(63)

L3, the third lumbar vertebra; SMI, skeletal muscle index; FFMA, fat-free muscle area; PMI, psoas muscle index; BMI, body mass index; SMA, superior mesenteric artery; -, not known.

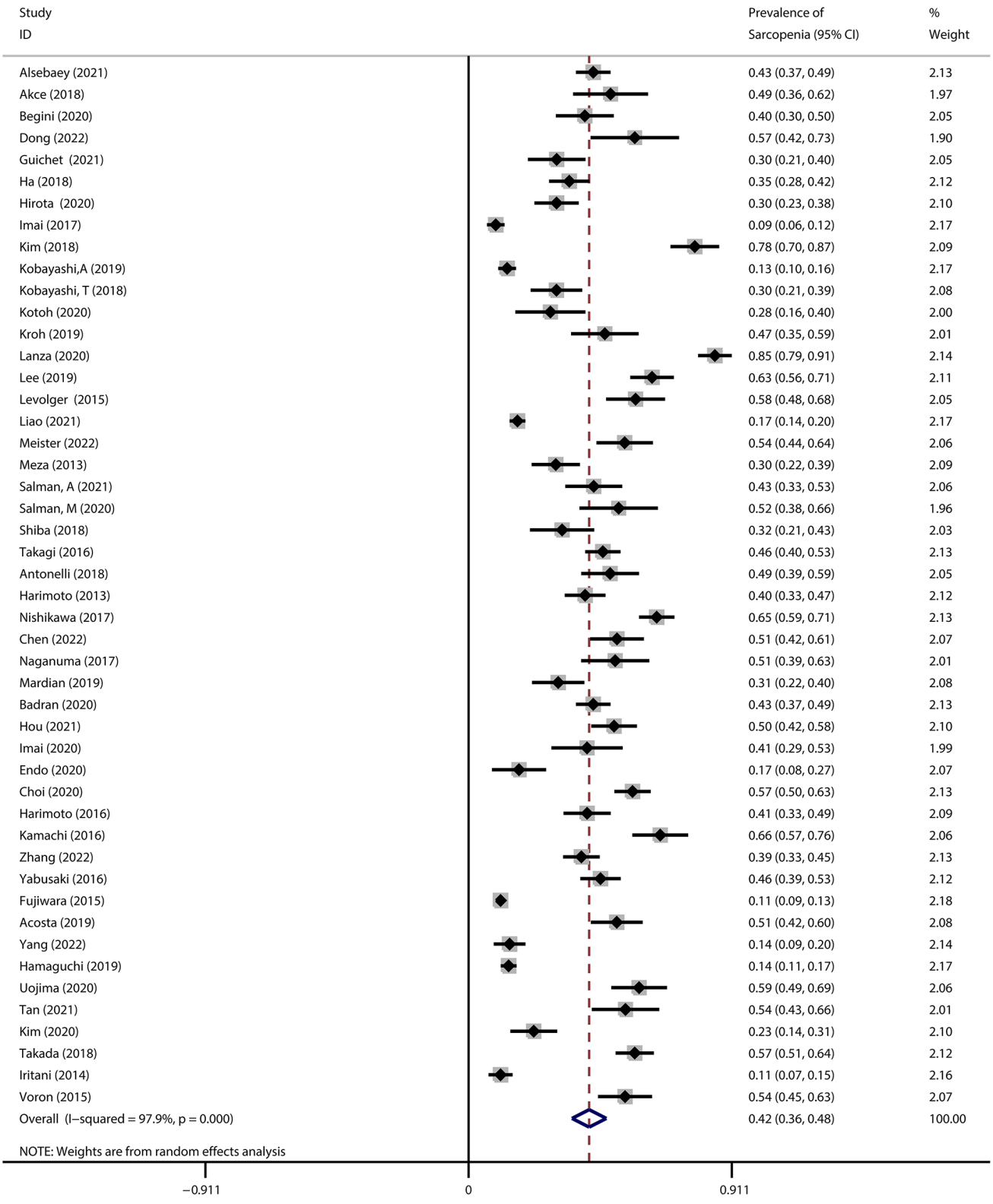

Figure 2. Prevalence of sarcopenia among patients with hepatocellular carcinoma: A random-effect meta-analysis.

Discussion

To the best of our knowledge, the present study performed the first systematic review and meta-analysis on the morbidity assessment of sarcopenia among patients with HCC. The current meta-analysis included 48 studies that evaluated the morbidity of sarcopenia among patients with HCC and were performed across nine countries. The outcomes of the present comprehensive analysis demonstrated that current evidence on the morbidity of sarcopenia among patients with HCC varied considerably depending on the region, average age, proportion of male patients and diagnostic criteria used.

Overall, the present meta-analysis confirmed that a high proportion of patients with HCC suffered from sarcopenia

Table II. Subgroup analysis of all studies based on region, average age, proportion of male patients and diagnostic criteria.

A, Region

Subgroups	Studies, n	Prevalence, %	95% CI	Heterogeneity among studies I^2	Heterogeneity among studies P-value
Africa	4	44	0.40-0.48	0.0	0.687
North America	4	40	0.28-0.52	81.9	0.001
Europe	7	56	0.42-0.70	93.8	<0.001
Asia	33	39	0.32-0.45	97.9	<0.001

B, Average age

Subgroups	Studies, n	Prevalence, %	95% CI	Heterogeneity among studies I^2	Heterogeneity among studies P-value
<60	16	46	0.37-0.56	96.6	<0.001
≥60	30	39	0.31-0.47	98.2	<0.001

C, Proportion of male patients

Subgroups	Studies, n	Prevalence, %	95% CI	Heterogeneity among studies I^2	Heterogeneity among studies P-value
<75%	18	37	0.29-0.45	97.1	<0.001
≥75%	30	45	0.36-0.53	98.0	<0.001

D, Diagnostic criteria

Subgroups	Studies, n	Prevalence, %	95% CI	Heterogeneity among studies I^2	Heterogeneity among studies P-value
SMI >42 cm^2/m^2 for men and SMI >38 cm^2/m^2 for women	16	50	0.42-0.57	93.6	<0.001
SMI=42 cm^2/m^2 for men and SMI=38 cm^2/m^2 for women	7	41	0.27-0.54	93.4	<0.001
SMI <42 cm^2/m^2 for men and SMI <38 cm^2/m^2 for women	8	23	0.15-0.31	98.0	<0.001
SMI >42 cm^2/m^2 for men or SMI >38 cm^2/m^2 for women	3	44	0.38-0.51	52.6	0.121
SMI combined with BMI	6	43	0.36-0.50	60.1	0.028
SMI combined with grip strength	3	24	0.12-0.36	84.7	0.001
Other methods	5	54	0.40-0.68	92.6	<0.001

SMI, skeletal muscle index; BMI, body mass index.

(42%). The morbidity of sarcopenia in Europe (56%) was higher compared with that in other continents, especially Asia (39%). In addition, the incidence rate of sarcopenia in studies with a high proportion of male patients (45%) was higher than that in studies with a low proportion of male patients (37%). It was also revealed that the studies with PMI or FFMA as the diagnostic standard had the highest incidence of sarcopenia (54%) among all diagnostic criteria used. When SMI was greater than the cut-off value of the diagnostic criteria for both male and female patients, the incidence rate was also high (50%). Surprisingly, the morbidity rate of sarcopenia in the young age group (46%) was higher than that in the old age group (39%). All the epidemiological data were significantly higher than those of healthy individuals, indicating that sarcopenia is an urgent problem

Table III. Meta-regression analysis based on year of publication and total sample size.

Variable	Regression coefficient	P-value	95% CI	Adjusted R^2-value, %
Year of publication	0.0040	0.680	-0.1710-0.2620	24.2
Total sample size	-0.0003	<0.001	-0.0006-(-0.0001)	40.8

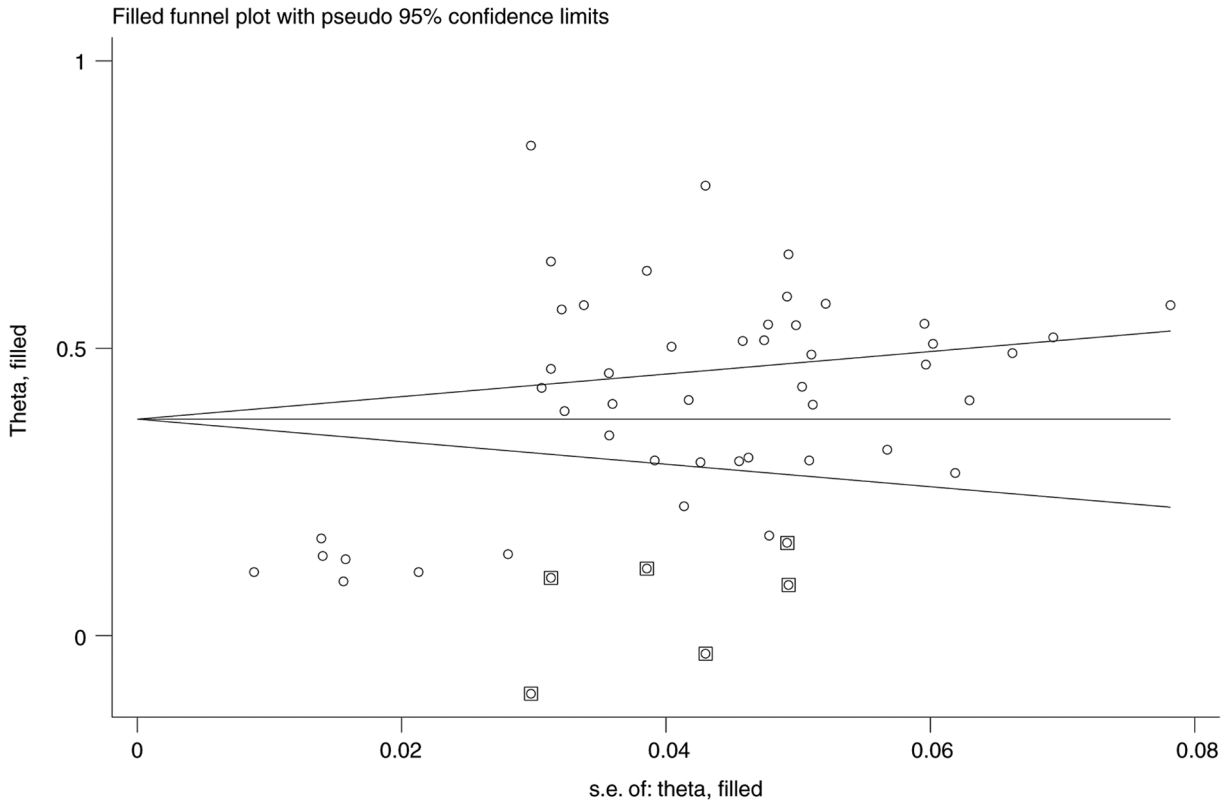

Figure 3. Publication bias: Funnel plot adjusted by the trim-and-fill method.

occurring in patients with HCC, and further research into its prevention and treatment is required to improve patient prognosis (64).

The present systematic review and meta-analysis had several limitations that need to be addressed. Firstly, most of the included studies were conducted in Asia, especially Japan; therefore, the incidence rate of sarcopenia in patients with HCC reported in the present study did not fully represent the global trend. Secondly, only studies published in English were included; therefore, the results of studies published in other languages were omitted.

In the present study, nearly half of the patients with HCC exhibited sarcopenia. Numerous studies have also reported that sarcopenia significantly negatively affects the survival outcomes of patients with HCC. Several important factors contribute to the high morbidity associated with sarcopenia in patients with HCC. First, cancer leads to changes in the patients' lifestyle, such as decreased physical activity and reduced food intake, which can lead to the loss of muscle volume and insufficient protein intake, thus aggravating the degree of sarcopenia (65,66). Second, in HCC proinflammatory cytokines(including IL-6 and TNF-a) are released, thereby interfering with related molecular pathways (such as the PI3K/Akt and Akt-mTOR pathways), which consequently causes muscle recession (67). Third, HCC disrupts the normal metabolic mechanisms in the human body, such as reducing the content of testosterone, thereby slowing down muscle growth (68). In addition, HCC can affect cellular processes, leading to cell autophagy, oxidative stress and mitochondrial dysfunction, which ultimately leads to muscle cell atrophy (69). In summary, multiple factors may jointly contribute to the high incidence rate of sarcopenia in patients with HCC.

The current analysis showed that studies with a high proportion of male patients had a higher morbidity of sarcopenia compared with studies with a lower proportion of males patients, which was consistent with the prevalence of sarcopenia reported in the general population (70). The possible reasons for the difference in the incidence rate of sarcopenia between sexes include different hormone profiles and distinct muscle sensitivities when hormone levels decrease (71). Therefore, biological and genetic differences may be the most important factors affecting the changes observed. It may be hypothesized that sarcopenia can have a higher incidence rate in the older age group compared with younger individuals;

however, the opposite conclusion was reached by the present study. A potential reason for this may be the higher malignancy of HCC in the younger population (72).

The current meta-analysis showed considerable heterogeneity; therefore, a cautious interpretation of the pooled data is necessary. This heterogeneity may be owing to the features of the patients and methodological differences in the included studies. Therefore, a subgroup analysis was performed by region, male proportion, average age and diagnostic criteria, to resolve the potential sources of heterogeneity. Subsequently, by conducting a meta-regression analysis, it was found that the total sample size could explain nearly half of the heterogeneity.

The present systematic review confirmed that the morbidity of sarcopenia is high in patients with HCC, indicating the benefits of early screening and prevention of sarcopenia in this population. However, in the near future, more in-depth research is needed on the causes of sarcopenia in patients with HCC. Additionally, efforts should be made to study the precautions and treatment of sarcopenia in patients with HCC.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

JW was responsible for study design. LH was in charge of analyzing the data. JL and HL wrote the manuscript and conducted the acquisition and interpretation of data. JL and LH confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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