Ji et al. World Journal of Surgical Oncology (2024) 22:229
https://doi.org/10.1186/s12957-024-03516-0

World Journal of Surgical Oncology

REVIEW Open Access

Impact of imaging-diagnosed sarcopenia on outcomes in patients with biliary tract cancer after surgical resection: a systematic review and meta-analysis

Jun Ji[1], Shizheng Mi[1], Ziqi Hou[1], Zhihong Zhang[1], Guoteng Qiu[1], Zhaoxing Jin[1] and Jiwei Huang[1*]

Abstract

Background and aims Sarcopenia has been associated with poor prognosis in patients with malignant tumors. However, its impact on the outcomes of patients with biliary tract cancer (BTC) undergoing surgical resection remains unclear and warrants further review. This study aims to summarize the available evidence on this issue.

Methods A systematic search was conducted in PubMed, Embase, Web of Science, and the Cochrane Library for eligible studies up to March 10, 2024. We extracted data on overall survival (OS), recurrence free survival (RFS), and postoperative major complications from the included studies as the outcomes of interest. Following data synthesis and analysis, we assessed the heterogeneity and performed subgroup analyses. Additionally, the potential for publication bias was evaluated.

Results A total of 26 studies involving 4292 BTC patients were ultimately retrieved. The findings indicated that sarcopenia was significantly associated with reduced OS in BTC patients after surgery (adjusted HR: 2.03, 95% CI: 1.65–2.48, $P<0.001$, $I^2=57.4\%$). Moreover, sarcopenia may also be linked to poorer RFS (adjusted HR: 2.15, 95% CI: 1.79–2.59, $P<0.001$, $I^2=0\%$) and increased postoperative major complications (OR: 1.22, 95% CI 1.02–1.47, $P=0.033$, $I^2=29.2\%$) as well. Notably, no significant publication bias was detected through funnel plots and Egger's tests.

Conclusion Sarcopenia is associated with poorer OS in BTC patients following surgery. Additionally, it may serve as a prognostic indicator for poorer RFS and increased postoperative major complications. Further studies are warrant to standardize existing definitions and validate these findings.

Keywords Biliary tract cancer, Sarcopenia, Survival, Postoperative complication, Meta-analysis

*Correspondence:
Jiwei Huang
huangjiwei@wchscu.cn
[1]Division of Liver Surgery, Department of General Surgery, West China Hospital, Sichuan University, Chengdu 610041, China

Introduction

Biliary tract cancer (BTC) refers to a range of invasive adenocarcinomas originating from the biliary tract. Based on its anatomical origin within the biliary system, it includes intrahepatic cholangiocarcinoma (iCC), perihilar cholangiocarcinoma (pCC), distal cholangiocarcinoma (dCC), and gallbladder carcinoma (GBC) [1, 2]. While BTC accounts for less than 1% of all human cancers, it poses a significant burden on local healthcare systems in regions where liver fluke infections are prevalent, as well as in areas where routine cholecystectomy is not readily available [2]. The majority of BTC patients are already in the advanced stage at the initial diagnosis, with a 5-year survival rate of only 7–20% [3]. Curative resection is the primary treatment for resectable BTC, but it is fraught with challenges including high surgical complexity, severe postoperative complications, and short-term recurrence. Therefore, preoperative evaluation and selection of BTC patients who could benefit from surgery are essential. Recently, body composition parameters such as skeletal muscle mass (SMM) and visceral adipose tissue (VAT) have gained prominence in preoperative evaluation [4]. Growing evidence suggests that these parameters may be more strongly associated with cancer prognosis than body mass index (BMI) [5, 6].

Sarcopenia, first described by Rosenberg in 1989, refers to the age-dependent decline in SMM [7, 8]. In 2016, it was officially designated as a distinct disease (M62.84) by the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) [9]. Sarcopenia is now considered a "muscle failure", characterized by a decline in quality, quantity, and function [4]. The SMM can be assessed using various techniques such as computed tomography (CT), magnetic resonance imaging (MRI), bioelectrical analysis (BIA) and dual-energy X-ray absorptiometry (DXA) [10]. Among these, CT is considered the most effective and convenient method for preoperative measurement. The measurement of SMM at the level of the L3 vertebra via CT has been standardized by both the European Working Group on Sarcopenia in Older People (EWGSOP) and the Asian Working Group for Sarcopenia (AWGS) [4, 11]. Imaging-diagnosed sarcopenia has been identified as a potential risk factor for the survival of patients undergoing surgical resection for gastrointestinal and hepatopancreatobiliary malignancies [12]. A few meta-analyses have indicated that sarcopenia serves as a prognostic factor for both complications and survival rates among BTC patients [13–15]. However, these analyses are limited by the inclusion of a small number of studies and the inclusion of conference abstracts, which may have incomplete data, thereby affecting the interpretability of the conclusions. Furthermore, with the emergence of new clinical studies over the past two years providing additional evidence, it is essential to reassess the relationship between sarcopenia and the prognosis of BTC patients undergoing surgical resection [16–19].

Therefore, it is necessary to summarize and update existing evidence to field this gap. In this study, we conducted a systematic review and meta-analysis to evaluate the impact of imaging-diagnosed sarcopenia on the outcomes of BTC patients following surgical resection.

Methods

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) 2020 guideline (Table S1) [20]. Additionally, the review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO NO. CRD42024522755).

Search strategy

From inception to March 10, 2024, we systematically searched PubMed, Embase, Web of Science, and the Cochrane Library using a combination of subject headings and free textwords. Relevant studies were retrieved using the following keywords: "cholangiocarcinoma", "bile duct cancer", "biliary tract cancer", "gallbladder cancer", "sarcopenia", "skeletal muscle", "psoas muscle", "muscular atrophy", and "body composition". The detailed search strategy is available in Table S2. The search was independently conducted by two researchers (Ji and Mi).

Inclusion and exclusion criteria

The inclusion criteria were defined as follows: (1) Patients: individuals diagnosed with BTC who underwent surgical resection; (2) Exposure and Comparison: preoperative sarcopenia and non-sarcopenia diagnosed by CT or MRI; (3) Outcomes: overall survival (OS), recurrence-free survival (RFS), progression-free survival (PFS), and postoperative major complications classified according to the Clavien-Dindo classification system [21]; (4) Study Types: randomized controlled trials (RCTs) or cohort studies.

The exclusion criteria were outlined as follows: (1) animal studies, case reports, reviews, conference abstracts, ongoing studies, single-arm studies, and letters; (2) lack of available outcome data; (3) duplicated cohorts; (4) sarcopenia diagnosed by techniques other than CT or MRI, such as BIA and DXA; (5) sarcopenia diagnosed after surgical resection.

Selection of studies and data extraction

The retrieved studies were independently screened by two researchers (Ji and Mi). The process involved an initial screening of titles and abstracts to remove duplicates, followed by a full-text review to determine inclusion based on the predefined criteria. In instances where

multiple versions of the same study were identified, only the most recent version was included. Any disparities between the two researchers were resolved by a third experienced researcher (Huang). The included studies meeting the criteria were then separately extracted by the aforementioned researchers using a pre-designed data extraction sheet. The extracted key details mainly included study characteristics (first author, issuing time, study design, study period, region of study and sample size), patient characteristics (population, age, gender and tumor type), exposure characteristics (imaging techniques, measurement approach and gender-specific cut-off values), and clinical outcomes (OS, RFS, DFS and postoperative major complications). The primary endpoint was OS, with secondary endpoints including postoperative major complications and recurrence related outcomes such as RFS.

Quality assessment

Two researchers (Hou and Zhang) independently evaluated the risk of bias in the included studies, with all researchers discussing the outcomes. The Newcastle-Ottawa Scale (NOS) was utilized for cohort studies [22], with a score of ≥7 indicating a low risk of bias. The NOS assesses three main aspects: (1) selection of patients; (2) comparability between groups; (3) outcome and follow-up. Any discrepancies were resolved through discussion and consensus. The Grades of Recommendation, Assessment, Development and Evaluation Working Group (GRADE) framework was employed to assess the level of evidence [23].

Statistical analysis

For survival-related outcomes, we extracted and pooled both crude and adjusted hazard ratios (HR) with 95% confidence intervals (CIs) separately. For binary outcomes such as postoperative major complications, we used odds ratios (OR) with 95% CIs. Statistical heterogeneity was assessed using Cochrane's Q test and the I^2 statistics, with $I^2 \geq 50\%$ indicating significant heterogeneity. The random-effect model was employed when significant heterogeneity was present [24], otherwise, a fixed-effect model was used. Subgroup analyses were performed based on study region, tumor type, and measurement of sarcopenia to explore potential sources of heterogeneity. Sensitivity analysis was conducted by systematically removing each included study one at a time to assess the robustness of the results. Publication bias and asymmetry were qualitatively assessed using the funnel plot when more than 10 articles were included, and Egger's test was conducted for quantitative assessment [25]. In this study, P-value < 0.05 was deemed statistically significant. Statistical analysis was all performed using Stata/MP version 17.0 (Stata Corporation, College Station, TX, USA).

Results

Search results and study quality

The primary search across four databases yielded 518 records, with 221 identified as duplicates. After excluding 237 records based on title and abstract screening, 60 records underwent full-text screening. Ultimately, 26 studies were included in the meta-analysis [16–19, 26–47]. The detailed screening process is illustrated in Fig. 1.

These studies included in the analysis were published between 2015 and 2024. Among them, only one was a prospective cohort study [36], while the others were retrospective studies. Most studies were conducted in East-Asia, with 19 studies in total [16, 18, 19, 27–29, 31, 33–36, 38–44, 46], including 12 from Japan [16, 18, 28, 29, 31, 34, 39–43, 46]. Studies from non East-Asia regions were distributed as follows: Germany [17, 32, 37, 47], France [45], the Netherlands [26], and the United States [30]. Overall, these studies included 4292 individuals, with sample sizes ranging from 41 to 460. The average or median age of the patients ranged from 58 to 74 years. The studies focused on different tumor types, with 10 studies focusing on iCC [17, 19, 27, 29, 32, 34, 36, 38, 45, 46], 6 studies on pCC [16, 26, 41, 42, 44, 47], 2 studies on dCC [31, 39], 2 studies on GBC [35, 40], and the remaining studies including multiple types. Among the included studies, 18 specified that they only included patients who underwent curative intent resection [16, 19, 26–28, 30, 31, 33, 35–40, 43–46], while the others did not explicitly mention. Among the 26 studies included in our analysis, 14 studies reported the use of postoperative adjuvant chemotherapy in patients with BTC [16–18, 27–31, 33–35, 45–47]. Commonly used chemotherapeutic agents included Gemcitabine, S-1, and others. However, detailed information on the specific regimens, duration, and tolerability of adjuvant chemotherapy was often lacking in the studies. Measurements of sarcopenia were all taken at the level of the third lumbar vertebra (L3), including skeletal muscle index (SMI), psoas muscle index (PMI), total psoas area (TPA), and psoas muscle thickness to height (PMTH). Different cut-off values were used, stratified by gender and BMI. Only one study reported both SMI and PMI [37]. Considering the results of the study above, the hazard ratio (HR) with 95% CIs of PMI was included in the meta-analysis. Based on the prevalence data available, the pooled prevalence of sarcopenia in BTC patients is 53.7% (95% CI 48.4%-59.1%). Detailed study characteristics are shown in Table 1.

The vast majority of included studies were evaluated as low-risk bias, with a median score of 7.5 stars (Table 2). According to the GRADE framework, the specific details of evidence level evaluation are shown in Table S3, with levels ranging from very low to moderate.

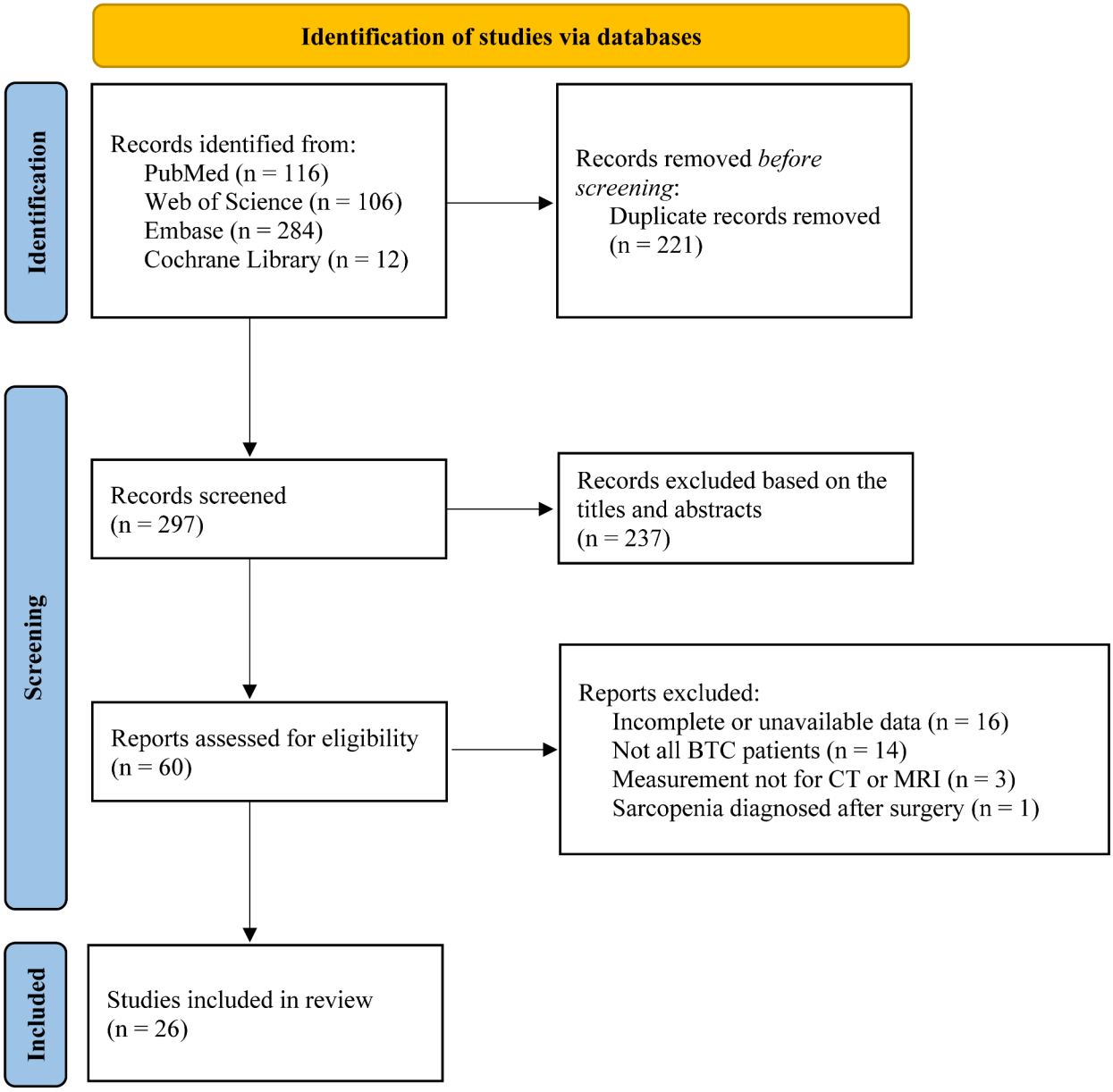

Fig. 1 The search strategy flowchart of the process for the identification of eligible studies

Overall survival

Not all included studies reported HRs and its 95% CIs for OS. A total of 18 studies (n=2754) reported crude results [16, 17, 19, 26–30, 33–38, 41, 45–47], and similarly, 18 studies (n=2847) reported adjusted results [16–19, 26–30, 32–37, 39, 40, 42], which were analyzed separately. The pooled crude results indicated that patients with imaging-diagnosed sarcopenia had poorer OS after surgical resection (HR: 2.02, 95% CI: 1.81–2.24, P<0.001; Fig. 2A). Moreover, the meta-analysis of adjusted results showed consistent findings (adjusted HR: 2.03, 95% CI: 1.65–2.48, P<0.001; Fig. 2B). Regarding statistical heterogeneity, the pooled result of the univariate analyses showed low heterogeneity (I^2=47.4%), while the pooled adjusted result showed moderate heterogeneity (I^2=57.4%).

Subgroup analyses were conducted to explore potential sources of heterogeneity based on study region, tumor type, and measurement of sarcopenia. The subgroup analyses results regarding OS are shown in Table 3. In non East-Asian regions [17, 26, 30, 37, 45, 47], sarcopenia was significantly associated with impaired OS after surgery (HR: 1.69, 95% CI: 1.42–2.02, P<0.001), with low heterogeneity (I^2=0%). In East-Asian regions such as Japan [16, 28, 29, 34, 41, 46], China [19, 27, 36, 38] and Korea [33, 35], sarcopenia was also associated with

Table 1 Baseline characteristics of included studies

Study (time)	Region	Study period	Sample size (with sarcopenia, %)	Age (years)	Male (%)	Tumor type	Imaging	Measurement	Cut-off value
Coelen et al. (2015) [26]	Netherlands	1998–2013	100 (42, 42.0%)	sarcopenia 61 ± 11, non-sarcopenia 62 ± 9 [b]	64 (64.0%)	pCC	CT	L3-SMI	Male: 46.8 cm^2/m^2, Female: 39.1 cm^2/m^2
Zhou et al. (2015) [27]	China	2000–2014	67 (33, 49.3%)	61 (47–81) [a]	22 (32.8%)	iCC	CT	L3-SMI	Male: 43.75 cm^2/m^2, Female: 41.10 cm^2/m^2
Okumura et al. (2016) [28]	Japan	2004–2013	207 (71, 34.3%)	sarcopenia 69.8 ± 8.1, non-sarcopenia 65.4 ± 10.1 [b]	111 (53.6%)	BTC	CT	L3-PMI	Male: 6.15 cm^2/m^2, Female: 3.98 cm^2/m^2
Okumura et al. (2017) [29]	Japan	2004–2015	109 (69, 63.3%)	68 (61–73) [a]	67 (61.5%)	iCC	CT	L3-SMI	Male: 52.5 cm^2/m^2, Female: 41.2 cm^2/m^2
Umetsu et al. (2018) [31]	Japan	2008–2015	65 (48, 73.8%)	72 (31–81) [a]	47 (72.3%)	dCC	CT	L3-PMI	Male: 5.93 cm^2/m^2, Female: 3.54 cm^2/m^2
Chakedis et al. (2018) [30]	United States	2007–2016	78 (30, 38.5%)	sarcopenia 67 ± 10, non-sarcopenia 68 ± 19 [b]	34 (43.6%)	BTC	CT	L3-PMI	Male: non-obese 6.25 cm^2/m^2, obese 7.32 cm^2/m^2, Female: non-obese 4.21 cm^2/m^2, obese 5.16 cm^2/m^2
Hahn et al. (2019) [32]	Germany	1997–2018	143 (76, 53.1%)	64.2 (56–72) [a]	79 (55.2%)	iCC	CT/MRI	L3-PMI	Male: 5.7 cm^2/m^2, Female: 5.1 cm^2/m^2
Yoon et al. (2019) [33]	Korea	2009–2015	371 (185, 49.9%)	66.2 ± 9.6 [b]	224 (60.4%)	BTC	CT	L3-SMI	Male: 50.0 cm^2/m^2, Female: 43.1 cm^2/m^2
Yugawa et al. (2019) [34]	Japan	2000–2017	61 (30, 49.2%)	sarcopenia 69 (53–87), non-sarcopenia 60 (39–82) [a]	44 (72.1%)	iCC	CT	L3-TPA	Male: 34.6 cm^2, Female: 18.1 cm^2
Lee et al. (2020) [35]	Korea	2001–2013	158 (88, 55.7%)	64 (55–70) [a]	58 (65.9%)	GBC	CT	L3-SMI	Male: 52.4 cm^2/m^2, Female: 38.5 cm^2/m^2
Deng et al. (2021) [36]	China	2012–2019	121 (53, 43.8%)	65 (40–87) [a]	52 (43.0%)	iCC	CT	L3-PMI	Male: 8.60 cm^2/m^2, Female: 6.04 cm^2/m^2
Joerdens et al. (2021) [37]	Germany	2011–2021	77 (NR)	68.5 (41–89) [a]	37 (48.7%)	BTC	CT	L3-SMI /L3-PMI	Male: L3-SMI 48.48 cm^2/m^2, L3-PMI: 3.29 cm^2/m^2, Female: L3-SMI 36.69 cm^2/m^2, L3-PMI: 1.94 cm^2/m^2
Tamura et al. (2021) [39]	Japan	2002–2017	111 (89, 80.2%)	72 (39–85) [a]	86 (77.5%)	dCC	CT	L3-SMI	Male: 55.0 cm^2/m^2, Female: 36.0 cm^2/m^2

Table 1 (continued)

Study (time)	Region	Study period	Sample size (with sarcopenia, %)	Age (years)	Male (%)	Tumor type	Imaging	Measurement	Cut-off value
Li et al. (2021) [38]	China	2009–2017	460 (281, 61.1%)	58 (49–64) [a]	223 (48.5%)	iCC	CT	L3-SMI	Male: 42.6 cm^2/m^2, Female: 37.8 cm^2/m^2
Ashida et al. (2022) [40]	Japan	2002–2014	88 (22, 25%)	72 (NA) [a]	53 (60.2%)	GBC	CT	L3-PMI	Male: 7.3 cm^2/m^2, Female: 5.0 cm^2/m^2
Yasuta et al. (2022) [41]	Japan	2006–2017	56 (38, 67.9%)	70 (39–81) [a]	38 (67.9%)	pCC	CT	L3-SMI	Male: non-obese 43.0 cm^2/m^2, obese 53.0 cm^2/m^2, Female: 41 cm^2/m^2
Asai et al. (2023) [42]	Japan	2008–2018	456 (152, 33.3%)	sarcopenia 72 (65–77), non-sarcopenia 68 (61–73) [a]	308 (67.5%)	pCC	CT	L3-PMI	Male: 6.42 cm^2/m^2, Female: 4.73 cm^2/m^2
Ikuta et al. (2023) * [43]	Japan	2010–2022	211 (114, 54.0%)	72 (39–88) [a]	116 (55.0%)	BTC	CT	L3-PMTH	17.5 mm/m
Jung et al. (2023) [44]	Korea	2005–2022	317 (150, 47.3%)	65.6 ± 9.0 [b]	202 (63.7%)	pCC	CT	L3-PMI	Male: 6.74 cm^2/m^2, Female: 3.39 cm^2/m^2
Lacaze et al. (2023) [45]	France	2004–2016	91 (55, 60.4%)	NA	NA	iCC	CT	L3-SMI	Male: 52.4 cm^2/m^2, Female: 38.5 cm^2/m^2
Hayashi et al. (2023) [16]	Japan	2013–2019	89 (63, 70.8%)	NA	55 (61.8%)	pCC	CT	L3-PMI	Male: 6.36 cm^2/m^2, Female: 3.92 cm^2/m^2
Taniai et al. (2023) [46]	Japan	2007–2019	41 (28, 68.3%)	63 (55–68) [a]	21 (51.2%)	iCC	CT	L3-TPA	Male: 31.47 cm^2, Female: 14.94 cm^2
Wang et al. (2023) [17]	Germany	2009–2022	162 (103, 63.6%)	66 (58–74) [a]	76 (46.9%)	iCC	CT	L3-SMI	Male: non-obese 43.0 cm^2/m^2, obese 53.0 cm^2/m^2, Female: 41 cm^2/m^2
Utsumi et al. (2024) [18]	Japan	2010–2022	147 (64, 43.5%)	74 (38–92) [a]	91 (61.9%)	BTC	CT	L3-PMI	Male: 5.10 cm^2/m^2, Female: 3.69 cm^2/m^2
Wang et al. (2024) [47]	Germany	2010–2022	204 (114, 55.9%)	68 (58–74) [a]	139 (66.5%)	pCC	CT	L3-SMI	Male: non-obese 43.0 cm^2/m^2, obese 53.0 cm^2/m^2, Female: 41 cm^2/m^2
Zhao et al. (2024) [19]	China	2015–2021	302 (192, 63.6%)	63 (57–69) [a]	151 (50%)	iCC	CT	L3-SMI	Male: 53.5 cm^2/m^2, Female: 39.9 cm^2/m^2

BTC biliary tract cancer, CT computed tomography, MRI magnetic resonance imaging, L3 third lumbar vertebra, SMI skeletal muscle index, PMI psoas muscle index, TPA total psoas area, PMTH psoas muscle thickness to height, iCC intrahepatic cholangiocarcinoma, pCC perihilar cholangiocarcinoma, dCC distal cholangiocarcinoma, GBC gallbladder cancer, NA not available

*Inverse probability weighting-adjusted, [a] Data presented as median, [b] Data presented as mean

Table 2 Quality assessment of included studies

NOS	Respective	Selection	Ascertainment of exposure	Demonstration	Comparability	Outcome	Follow-up	Adequacy of follow-up	Overall
Coelen et al. (2015) [26]	★	★	★	★	★	★	★		7
Zhou et al. (2015) [27]	★	★	★	★	★	★	★	★	8
Okumura et al. (2016) [28]	★	★	★	★	★	★	★	★	8
Okumura et al. (2017) [29]	★	★	★	★	★	★	★		7
Umetsu et al. (2018) [31]	★	★	★	★	★	★	★		7
Chakedis et al. (2018) [30]	★	★	★	★	★★	★	★		8
Hahn et al. (2019) [32]	★	★	★	★		★	★		6
Yoon et al. (2019) [33]	★	★	★	★	★	★	★		7
Yugawa et al. (2019) [34]	★	★	★	★	★	★	★		7
Lee et al. (2020) [35]	★	★	★	★	★	★	★	★	8
Deng et al. (2021) [36]	★	★	★	★		★	★	★	7
Joerdens et al. (2021) [37]	★	★	★	★	★	★	★		7
Tamura et al. (2021) [39]	★	★	★	★		★	★		6
Li et al. (2021) [38]	★	★	★	★	★★	★	★		8
Ashida et al. (2022) [40]	★	★	★	★	★	★	★	★	8
Yasuta et al. (2022) [41]	★	★	★	★	★	★	★	★	8

Table 2 (continued)

NOS	Respective	Selection	Ascertainment of exposure	Demonstration	Comparability	Outcome	Follow-up	Adequacy of follow-up	Overall
Asai et al. (2023) [42]	★	★	★	★	★	★	★	★	8
Ikuta et al. (2023) [43]	★	★	★	★	★★	★	★	★	9
Jung et al. (2023) [44]	★	★	★	★	★	★	★		7
Lacaze et al. (2023) [45]	★	★	★	★	★	★	★		7
Hayashi et al. (2023) [16]	★	★	★	★	★	★	★		7
Taniai et al. (2023) [46]	★	★	★	★	★	★	★		7
Wang et al. (2023) [17]	★	★	★	★	★	★	★	★	8
Utsumi et al. (2024) [18]	★	★	★	★	★	★	★	★	8
Wang et al. (2024) [47]	★	★	★	★	★	★	★	★	8
Zhao et al. (2024) [19]	★	★	★	★	★	★	★	★	8

impaired OS after surgery (HR: 2.31, 95% CI: 1.87–2.86, $P<0.001$). In the adjusted HR results, consistent findings were observed. These results suggest that patients with sarcopenia may have a poorer OS following surgical resection, regardless of whether they are in non East-Asian or East-Asian regions.

In the subgroup by tumor type, we concentrated on studies that included only one type of tumor, as some studies included multiple tumor types without providing detailed original data. In the analysis of crude results of OS, 9 studies focused on iCC [17, 19, 27, 29, 34, 36, 38, 45, 46], 4 studies focused on pCC [16, 26, 41, 47], and 1 study included only GBC patients [35]. The results indicate that patients with pCC and iCC who have sarcopenia have poorer OS. In the analysis of adjusted results of OS, 7 studies focused on iCC [17, 19, 27, 29, 32, 34, 36], 3 studies on pCC [16, 26, 42], 2 studies on GBC [35, 40], and only 1 study included dCC patients [39]. After adjusting for perioperative factors, tumor-related factors, and other confounders, low SMM in pCC, iCC, and GBC patients remained negatively associated with OS.

In the subgroup based on measurement, we found that BTC patients diagnosed with sarcopenia using different parameters (SMI [17, 19, 26, 27, 29, 33, 35, 38, 41, 45, 47], PMI [16, 28, 30, 36, 37], TPA [34, 46]) had lower OS after surgical resection compared to those without sarcopenia, with low statistical heterogeneity. In the pooled adjusted results [16–19, 26–30, 32, 33, 35–37, 39, 40, 42], we obtained consistent findings.

Recurrence

Similarly, not all eligible studies reported HRs and its 95% CIs for recurrence-related outcomes. A total of 11 studies ($n=1940$) reported crude results for RFS [16, 17, 19, 27–29, 34–36, 38, 47], while 8 studies reported adjusted results ($n=1081$) [18, 27–29, 34–36, 43]. Additionally, 2 studies reported unadjusted results for DFS [45, 46]. In the pooled result of 11 studies above, sarcopenic patients showed poorer RFS (HR: 1.81, 95% CI: 1.42–2.31, $P<0.001$; Fig. 3A), while the multivariate analysis of 8 studies yielded similar pooled result (adjusted HR: 2.15, 95% CI: 1.79–2.59, $P<0.001$; Fig. 3B). Moderate

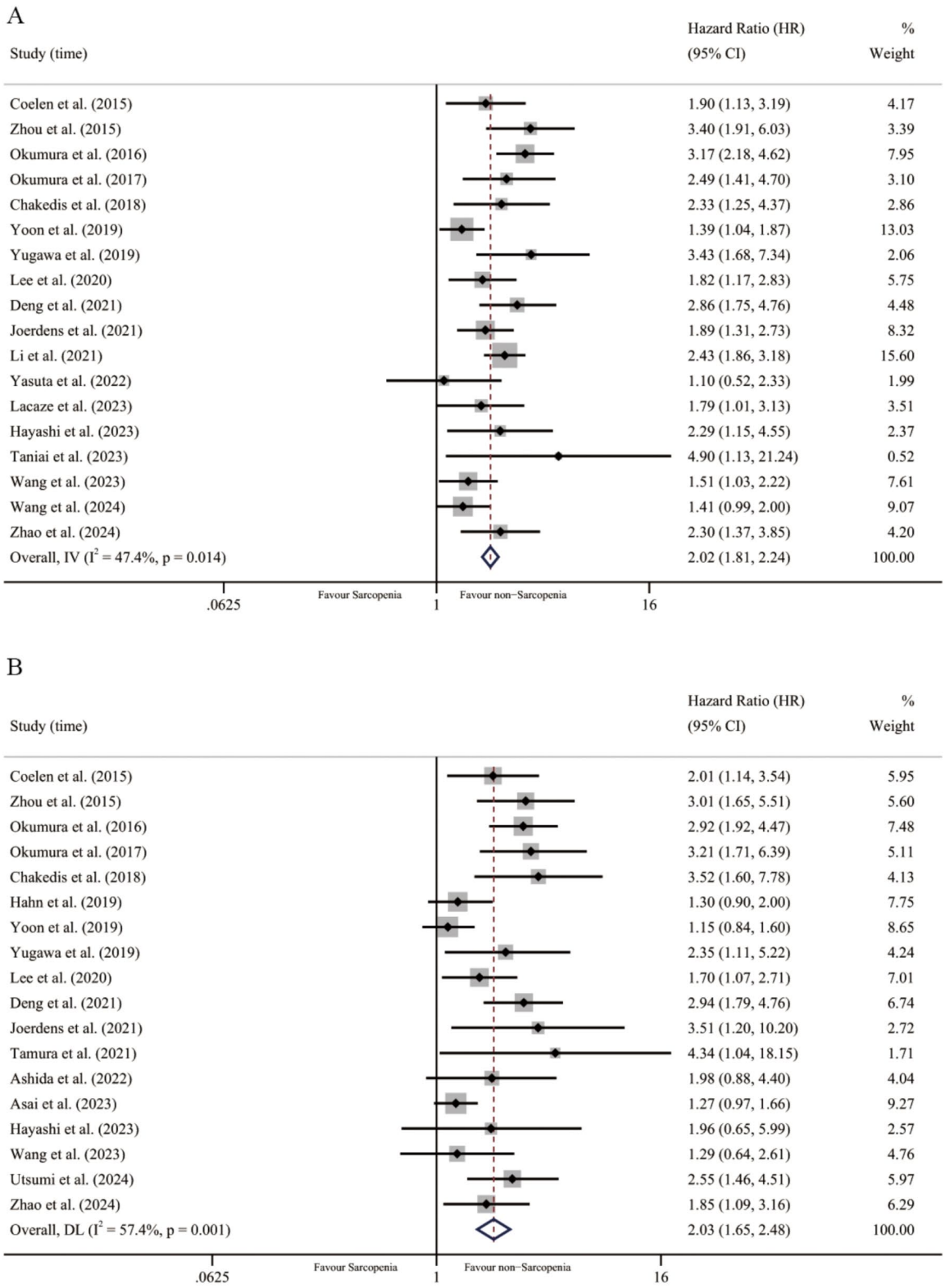

Fig. 2 Forest plots of the association between sarcopenia and OS for BTC patients after surgical resection. (**A**) crude results and (**B**) adjusted results

Table 3 Subgroup analyses results of included studies

Subgroup		Crude results of OS			Adjusted results of OS		
		HRs	*P* value	I^2	HRs	*P* value	I^2
Study region	non East-Asian regions	1.69 (1.42–2.02)	< 0.001	0%	1.88 (1.26–2.82)	0.002	47.9%
	East-Asian regions	2.31 (1.87–2.86)	< 0.001	53.3%	2.09 (1.64–2.67)	< 0.001	62.6%
Tumor type	iCC	2.33 (1.99–2.73)	< 0.001	21.8%	2.10 (1.54–2.87)	< 0.001	51.4%
	pCC	1.57 (1.22–2.02)	< 0.001	0%	1.47 (1.08–1.99)	0.015	17.5%
	dCC	NA	NA	NA	NA	NA	NA
	GBC	NA	NA	NA	1.77 (1.18–2.64)	0.006	0%
Measurement	SMI	1.83 (1.62–2.08)	< 0.001	46.7%	1.89 (1.40–2.55)	< 0.001	54.4%
	PMI	2.48 (2.01–3.05)	< 0.001	3.5%	2.16 (1.57–2.96)	< 0.001	66.2%
	TPA	3.69 (1.91–7.12)	< 0.001	0%	NA	NA	NA

OS overall survival, HRs Hazard ratios, iCC intrahepatic cholangiocarcinoma, pCC perihilar cholangiocarcinoma, dCC distal cholangiocarcinoma, GBC gallbladder cancer, NA not available, SMI skeletal muscle index, PMI psoas muscle index, TPA total psoas area, NA not available

heterogeneity was observed in the crude results, whereas low heterogeneity was noted in the adjusted results (crude RFS: I^2=67.0%; adjusted RFS: I^2=0%). Due to limited data available, we were unable to perform a meta-analysis for PFS.

In the subgroup analysis by study region, 9 studies were conducted in East-Asia [16, 19, 27–29, 34–36, 38], while 2 studies were conducted in non East-Asian regions [17, 47]. The results showed that patients with preoperative sarcopenia in East-Asia were significantly associated with poorer RFS (HR: 2.03, 95% CI: 1.63–2.52, P<0.001, I^2=47.4%). In non East-Asia, the result did not show a statistically significant difference (P=0.656). Subsequently, we conducted other subgroup analyses of the crude results of RFS (Figure S1). In the subgroup by tumor type, we found that sarcopenic patients with iCC were associated with shorter RFS after surgery [17, 19, 27, 29, 34, 36, 38], but the result showed significant heterogeneity (HR: 1.95, 95% CI: 1.39–2.74, P<0.001, I^2=72.2%). In patients with pCC [16, 47], we did not observe a statistically significant difference in RFS (P=0.053). In the subgroup by measurement, we found that sarcopenia diagnosed by both SMI [17, 19, 27, 29, 35, 38, 47] and PMI [16, 28, 36] was associated with shorter RFS (SMI: HR: 1.58, 95% CI: 1.17–2.12, P=0.003, I^2=68.6%; PMI: HR: 2.23, 95% CI: 1.65–3.02, P<0.001, I^2=22.8%). In addition, in the adjusted results, we found that 8 studies all came from East-Asia, so subgroup analysis by study region was not applicable [18, 27–29, 34–36, 43]. Three studies [29, 34, 36] reported adjusted RFS for iCC patients, showing a significant association between sarcopenia and shorter RFS (adjusted HR: 2.21, 95% CI: 1.58–3.08, P<0.001, I^2=0%). In the subgroup analysis based on measurement parameters, we obtained results consistent with crude results (SMI: adjusted HR: 1.95, 95% CI: 1.39–2.75, P<0.001, I^2=0%; PMI: adjusted HR: 2.14, 95% CI: 1.63–2.80, P<0.001, I^2=0%) [18, 27–29, 35, 36].

Postoperative complications

The meta-analysis, which investigated the correlation between preoperative imaging-diagnosed sarcopenia and postoperative major complications, comprised a total of 12 studies, involving 2237 patients [17, 18, 26–31, 33, 35, 42, 44]. Postoperative major complications were defined as Clavien-Dindo classification ≥ III. Using a fixed-effect model, we found that preoperative sarcopenia was positively associated with a higher incidence of major complications (OR: 1.22, 95% CI 1.02–1.47, P=0.033, I^2=29.2%). Subsequently, we conducted further subgroup analyses (Figure S2). Interestingly, in subgroup analyses based on study region and tumor type, we did not find any subgroup that showed statistically significant differences. In the subgroup analysis based on measurement, we found that sarcopenia assessed by SMI [17, 26, 27, 29, 33, 35] was associated with an increased incidence of postoperative major complications, and the heterogeneity test reveal quite low statistical heterogeneity (OR: 1.45, 95% CI 1.06–1.98, P=0.02, I^2=0%). Although sarcopenia assessed by PMI showed a positive trend with postoperative major complications [18, 28, 30, 31, 42, 44], it did not reach statistical significance (OR: 1.08, 95% CI 0.72–1.61, P=0.373, I^2=58.3%).

Sensitivity analysis and publication bias

We conducted sensitivity analyses for OS, RFS, and postoperative major complications (Figure S3). The results of the sensitivity analyses indicate that our findings of OS and RFS are robust, with no individual study significantly influencing the results. However, the sensitivity analysis of the postoperative major complications showed that during the process of deleting the studies one by one, there was a situation of unstable results. Furthermore, the funnel plots for all outcomes did not exhibit obvious asymmetry (Figure S4). Quantitative assessment of publication bias using Egger's test also did not reveal significant statistical differences (OS: P=0.222, RFS: P=0.913, postoperative major complications: P=0.952), further confirming the robustness of the findings.

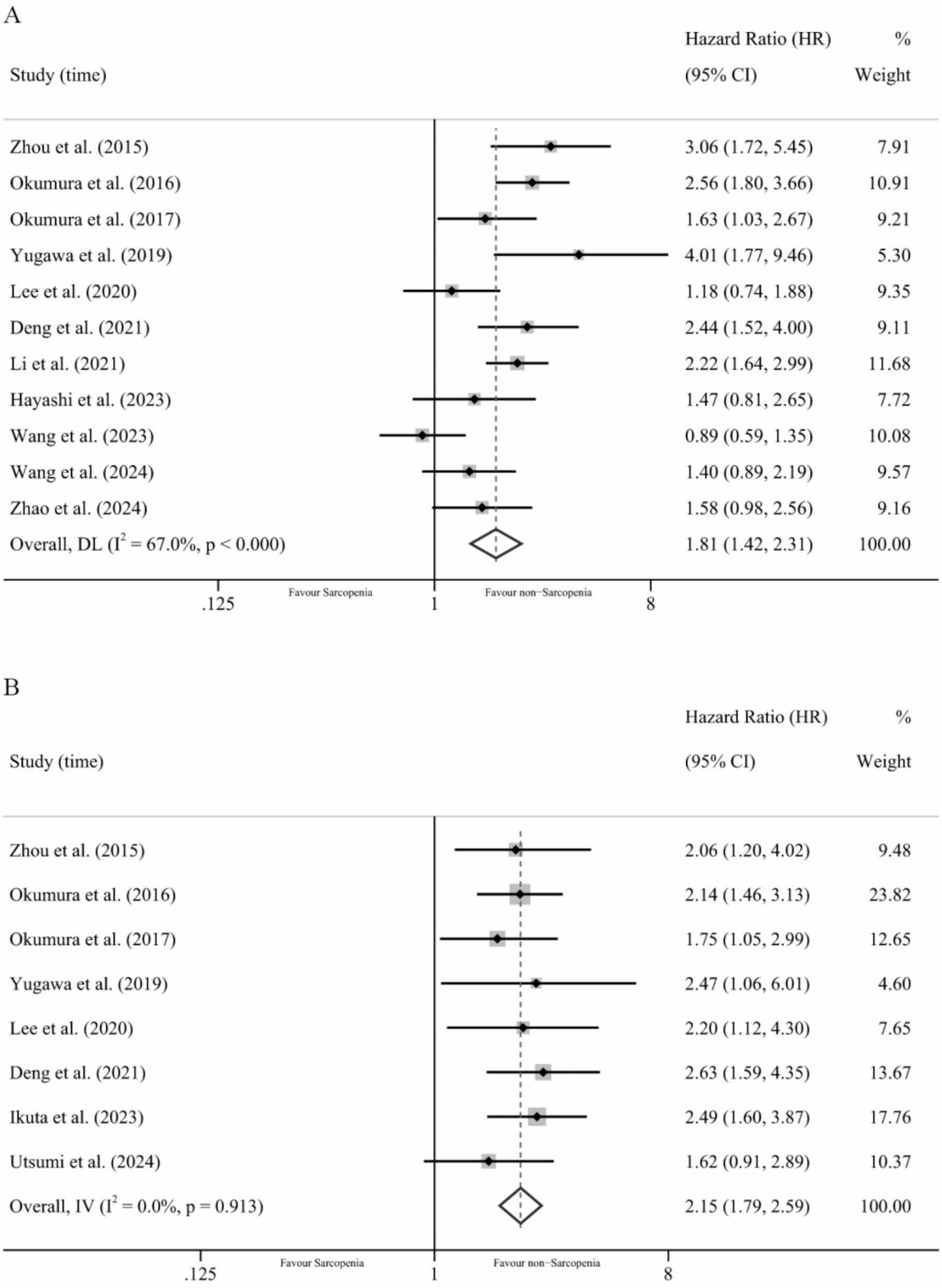

Fig. 3 Forest plots of the association between sarcopenia and RFS for BTC patients after surgical resection. (**A**) crude results and (**B**) adjusted results

Discussion

This study included a total of 26 cohort studies involving 4292 BTC patients from various regions. We synthesized available prevalence data and found that approximately half of BTC patients may have sarcopenia before undergoing surgical resection. The primary results indicate that preoperative imaging-diagnosed sarcopenia is linked to poorer OS in BTC patients. Furthermore, sarcopenia may be associated with a higher risk of recurrence after surgery and an increased risk of postoperative major complications. These findings highlight sarcopenia as an excellent prognostic factor. Unlike previous meta-analyses that included a small number of studies and non full-text studies, our study only included studies that diagnosed sarcopenia via CT or MRI to align with clinical practice, enhancing the generalizability and applicability of the results. Additionally, as a result of our study's more extensive literature search and rigorous inclusion process, a greater number of BTC patients were included, facilitating more reliable and detailed subgroup analyses.

Given the clinical heterogeneity among the eligible studies, we conducted subgroup analyses of survival related outcomes based on available parameters. In the subgroup analysis based on study region, a significant association was observed between preoperative sarcopenia and poorer OS in BTC patients, regardless of whether they were from East-Asia or non East-Asia. However, the statistical heterogeneity observed during the analysis raised our concern. The subgroup of non East-Asian yielded the significant result with low statistical heterogeneity (unadjusted $I^2=0\%$; adjusted $I^2=47.9\%$), while the East-Asia subgroup exhibited moderate statistical heterogeneity (unadjusted $I^2=53.3\%$; adjusted $I^2=62.6\%$). We speculate that the lack of uniform criteria may be a contributing factor. Some studies used receiver operating characteristic (ROC) curve to set cut-off values [28, 36], while others adopted definitions from previous studies, such as the definition by Hamaguchi [16], or even the cut-off value from European populations [35, 48]. This discrepancy likely contributed to the clinical heterogeneity observed. Therefore, it remains necessary to establish unified standards for the East-Asian population through large-scale population data. The differences in sample sizes between studies and varying follow-up characteristics are also potential sources of heterogeneity [49, 50]. Additionally, both the primary analysis and subgroup analysis showed the adjusted results appeared to have greater heterogeneity than the crude results. This may be due to the differences in confounding factors across varying multivariate models in the original studies. However, the consistent pooled HR values of the two types of results indicate the robustness of our conclusions.

The tumor type influences various oncological characteristics and treatment strategies, leading to diverse outcomes among BTC patients. In the subgroup analysis by tumor type, stratification effectively reduced statistical heterogeneity. Inspiringly, we found consistent results across different types of BTC subgroups, indicating a significant association between preoperative diagnosis of sarcopenia and OS. This underscores the importance of identifying and managing sarcopenia in all BTC patients, providing appropriate interventions, and ensuring meticulous postoperative follow-up. Additionally, we found that the impact of sarcopenia on OS appeared more pronounced in iCC patients compared to pCC, likely due to the higher likelihood of achieving R0 resection and lower recurrence rates in iCC cases. Conversely, tumor types with poorer prognoses like pCC and dCC may be more influenced by tumor-specific factors and surgical outcomes. Due to the high recurrence rate after resection, some patients would receive postoperative adjuvant therapy. In most studies, the proportion of patients receiving adjuvant chemotherapy was similar across groups. However, there may be a lower proportion of patients with low muscle mass receiving adjuvant chemotherapy [33, 35], possibly related to differences in drug tolerance. In the subgroup analysis based on measurement, we found sarcopenia assessed by SMI and PMI at the L3 level showed strong prognostic value. Particularly, PMI appeared to be closely linked to survival prognosis. The simplicity of measuring PMI allows radiologists to include it directly in abdominal CT reports, which could serve as a crucial reference for surgeons during preoperative evaluations in the future. Therefore, it is essential to discuss and explore the efficacy of different measurement parameters and their corresponding cut-off values to standardize future research and clinical practice.

Our study findings align with previous research, demonstrating an association between sarcopenia and postoperative major complications [44, 51]. Patients with malignant tumors and sarcopenia often exhibit poor nutritional status and reduced healing capacity, along with elevated levels of pro-inflammatory cytokines in circulation, such as IL-6 [52]. In the case of BTC patients, this may predispose them to severe postoperative biliary tract infections [53]. In the subgroup analysis based on measurement, we found that SMI was predictive of postoperative major complications, whereas PMI was not. This difference could be attributed to the measurement principles, as SMI focuses on total skeletal muscle content while PMI only considers the psoas muscle. A prospective cross-sectional study also suggested that PMI may not fully replace SMI in assessing cancer-related sarcopenia [54]. Hence, further research is warranted to investigate the predictive capacity of sarcopenia for postoperative complications, especially when using SMI as a measurement indicator.

Sarcopenia impacts the survival of BTC patients through various mechanisms. Firstly, skeletal muscle, as the body's reservoir, plays a crucial role in storing proteins and nutrients, which can be mobilized during periods of inadequate intake, such as the perioperative period or during chronic diseases, thereby enhancing patient tolerance to treatments [55, 56]. Conversely, sarcopenic patients may have lower treatment tolerance, leading to reduced survival [57]. For instance, Jung et al. [44] observed that BTC patients with preoperative sarcopenia had a significantly higher frequency and duration of ICU admission (77.3% vs. 47.9%, 2.45 vs. 0.89 days). Additionally, sarcopenia is associated with an imbalance between protein synthesis and degradation, which can increase cellular apoptosis and reduce the regenerative capacity of normal cells [58]. Notably, immunity and inflammation are currently considered key mechanisms through which sarcopenia affects survival. Sarcopenia is linked to systemic inflammation, which occurs at both preclinical and clinical stages [52, 59]. This inflammatory state contributes to elevated levels of IL-6 and activates the tumor necrosis factor (TNF) cascade, promoting tumor invasion and migration [60]. Inflammatory factors such as TNF-α and IL-6 play crucial roles in promoting muscle atrophy. The former directly breaks down and metabolizes skeletal muscle, while the latter, in synergy with other inflammatory mediators, inhibits protein synthesis in muscle cells [61].

Previous studies have highlighted the potential benefits of preoperative exercise and nutritional supplementation in reducing the incidence of sarcopenia in cancer patients and improving postoperative outcomes [62, 63]. Recently, researchers have developed preoperative nutritional protocols, such as the PROtocol for NuTritional risk in Oncology (PRONTO), aimed at identifying patients with low SMM and improving their prognosis [64]. Overall, preoperative improvement of underlying sarcopenia in patients is an important management measure in multidisciplinary cancer treatment.

To the best knowledge, our study represents the most extensive review to date of the impact of sarcopenia on the outcomes of BTC patients following surgery. We conducted detailed subgroup analyses and discussed the reasons for heterogeneity to ensure the robustness of our results. However, our study also has several limitations. Firstly, since all included studies were non-RCTs, the ability to draw causal inferences is limited. Secondly, there are potential sources of heterogeneity that are challenging to avoid, such as age, varying cut-off values, surgical type, adjuvant therapy, treatment for recurrence, and follow-up duration. Our study was limited by the lack of data on the use of preoperative PET/CT in the included studies, potentially introducing bias into the findings [65]. Last but not least, due to data availability constraints, we were unable to analyze and evaluate patients' muscle quality and specific function, which may have impacted the comprehensiveness of sarcopenia diagnosis.

Conclusion

In summary, our study revealed a significant correlation between sarcopenia and diminished OS following surgical resection of BTC. Additionally, sarcopenia may be linked to worse RFS and an increased incidence of postoperative major complications. We recommend that BTC patients undergo preoperative sarcopenia assessment, with regular monitoring and appropriate interventions. Additionally, we look forward to more large-scale prospective studies to standardize existing definitions and validate these findings.

Abbreviations

AWGS	Asian Working Group for Sarcopenia
BIA	Bioelectrical analysis
BMI	Body mass index
BTC	Biliary tract cancer
CIs	Confidence intervals
CT	Computed tomography
dCC	Distal cholangiocarcinoma
DXA	Dual-energy X-ray absorptiometry
EWGSOP	European Working Group on Sarcopenia in Older People
GBC	Gallbladder carcinoma
GRADE	Grades of Recommendation, Assessment, Development and Evaluation Working Group
HR	Hazard ratio
iCC	Intrahepatic cholangiocarcinoma
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
ICU	Intensive care unit
IL-6	Interleukin-6
L3	The third lumbar vertebra
MRI	Magnetic resonance imaging
NOS	Newcastle-Ottawa Scale
OR	Odds ratio
OS	Overall survival
pCC	Perihilar cholangiocarcinoma
PFS	Progression-free survival
PMI	Psoas muscle index
PMTH	Psoas muscle thickness to height
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analysis
PRONTO	PROtocol for NuTritional risk in Oncology
PROSPERO	International Prospective Register of Systematic Reviews
RCTs	Randomized controlled trials
RFS	Recurrence-free survival
ROC	Receiver operating characteristic
SMI	Skeletal muscle index
SMM	Skeletal muscle mass
TNF	Tumor necrosis factor
TPA	Total psoas area
VAT	Visceral adipose tissue

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-024-03516-0.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Acknowledgements
Not applicable.

Author contributions
All authors contributed to the study conception and design. Data collection, screening and extraction were performed by Ji and Mi. Quality assessment was performed by Ji, Hou and Zhang. Statistical analysis was performed by Ji, Jin and Qiu. Interpretation of data was performed by Ji, Mi and Huang. Drafted and revised the manuscript were performed by Ji and Huang. All authors read and approved the final manuscript.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval
Not applicable.

Consent to participate
Not applicable.

Consent to publish
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 4 May 2024 / Accepted: 27 August 2024
Published online: 02 September 2024

References

1. Valle JW, Kelley RK, Nervi B, et al. Biliary tract cancer. Lancet. 2021;397(10272):428–44.
2. Vogel A, Bridgewater J, Edeline J, et al. Biliary tract cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. Annals Oncology: Official J Eur Soc Med Oncol. 2023;34(2):127–40.
3. Banales JM, Marin JJG, Lamarca A, et al. Cholangiocarcinoma 2020: the next horizon in mechanisms and management. Nat Rev Gastroenterol Hepatol. 2020;17(9):557–88.
4. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31.
5. Xia L, Zhao R, Wan Q, et al. Sarcopenia and adverse health-related outcomes: an umbrella review of meta-analyses of observational studies. Cancer Med. 2020;9(21):7964–78.
6. Surov A, Wienke A. Prevalence of sarcopenia in patients with solid tumors: a meta-analysis based on 81,814 patients. JPEN J Parenter Enter Nutr. 2022;46(8):1761–8.
7. Rosenberg IHJTAJoCN. Summary comments: epidemiological and methodological problem in determining nutritional status of older persons. 1989;50:1231–3.
8. Rosenberg IH. Sarcopenia: origins and clinical relevance. J Nutr. 1997;127(5 Suppl):S990–1.
9. Anker SD, Morley JE, von Haehling S. Welcome to the ICd-10 code for sarcopenia. J Cachexia Sarcopenia Muscle. 2016;7(5):512–4.
10. Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr. 2017;36(1):49–64.
11. Chen L-K, Liu L-K, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. J Am Med Dir Assoc. 2014;15(2):95–101.
12. Levolger S, van Vugt JL, de Bruin RW, JN IJ. Systematic review of sarcopenia in patients operated on for gastrointestinal and hepatopancreatobiliary malignancies. Br J Surg. 2015;102(12):1448–58.
13. Watanabe J, Matsui R, Sasanuma H, et al. Body composition assessment and sarcopenia in patients with biliary tract cancer: a systematic review and meta-analysis. Clin Nutr. 2022;41(2):321–8.
14. Surov A, Pech M, Omari J, et al. Low skeletal muscle mass in cholangiocarcinoma treated by surgical resection. A meta-analysis. HPB: Official J Int Hepato Pancreato Biliary Association. 2022;24(7):997–1006.
15. Shin SP, Koh DH. Clinical impact of sarcopenia on cholangiocarcinoma. Life (Basel Switzerland). 2022;12(6).
16. Hayashi K, Abe Y, Kitago M, et al. Prognostic impact of preoperative skeletal muscle change from diagnosis to surgery in patients with perihilar cholangiocarcinoma. Ann Gastroenterol Surg. 2023;7(3):523–32.
17. Wang G, Otto CC, Heij LR, et al. Impact of altered body composition on clinical and oncological outcomes in intrahepatic cholangiocarcinoma. J Clin Med. 2023;12:24.
18. Utsumi M, Inagaki M, Kitada K et al. Prognostic significance of Sarcopenia and systemic inflammatory markers in biliary tract cancer: a retrospective cohort study. J Gastrointest Cancer. 2024.
19. Zhao Z, Bo Z, Ye N, et al. Impact of Sarcopenia on postoperative outcomes after hepatectomy in older patients with intrahepatic cholangiocarcinoma: a multicentre cohort study. Liver Int. 2024;44(1):155–68.
20. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
21. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg. 2009;250(2):187–96.
22. Wells GA, Wells G, Shea B et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2014.
23. Atkins D, Eccles M, Flottorp S, et al. Systems for grading the quality of evidence and the strength of recommendations I: critical appraisal of existing approaches the GRADE working group. BMC Health Serv Res. 2004;4(1):38.
24. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60.
25. 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.
26. Coelen RJ, Wiggers JK, Nio CY, et al. Preoperative computed tomography assessment of skeletal muscle mass is valuable in predicting outcomes following hepatectomy for perihilar cholangiocarcinoma. HPB: Official J Int Hepato Pancreato Biliary Association. 2015;17(6):520–8.
27. Zhou G, Bao H, Zeng Q, et al. Sarcopenia as a prognostic factor in hepatolithiasis-associated intrahepatic cholangiocarcinoma patients following hepatectomy: a retrospective study. Int J Clin Exp Med. 2015;8(10):18245–54.
28. Okumura S, Kaido T, Hamaguchi Y, et al. Impact of the preoperative quantity and quality of skeletal muscle on outcomes after resection of extrahepatic biliary malignancies. Surgery. 2016;159(3):821–33.
29. Okumura S, Kaido T, Hamaguchi Y, et al. Impact of skeletal muscle mass, muscle quality, and visceral adiposity on outcomes following resection of intrahepatic cholangiocarcinoma. Ann Surg Oncol. 2017;24(4):1037–45.
30. Chakedis J, Spolverato G, Beal EW, et al. Pre-operative sarcopenia identifies patients at risk for poor survival after resection of biliary tract cancers. J Gastrointest Surgery: Official J Soc Surg Aliment Tract. 2018;22(10):1697–708.
31. Umetsu S, Wakiya T, Ishido K, et al. Effect of sarcopenia on the outcomes after pancreaticoduodenectomy for distal cholangiocarcinoma. ANZ J Surg. 2018;88(9):E654–8.
32. Hahn F, Muller L, Stohr F, et al. The role of sarcopenia in patients with intrahepatic cholangiocarcinoma: prognostic marker or hyped parameter? Liver Int. 2019;39(7):1307–14.
33. Yoon SB, Choi MH, Song M, et al. Impact of preoperative body compositions on survival following resection of biliary tract cancer. J Cachexia Sarcopenia Muscle. 2019;10(4):794–802.
34. Yugawa K, Itoh S, Kurihara T, et al. Skeletal muscle mass predicts the prognosis of patients with intrahepatic cholangiocarcinoma. Am J Surg. 2019;218(5):952–8.
35. Lee EC, Park SJ, Lee SD, et al. Effects of sarcopenia on prognosis after resection of gallbladder cancer. J Gastrointest Surgery: Official J Soc Surg Aliment Tract. 2020;24(5):1082–91.
36. Deng L, Wang Y, Zhao J et al. The prognostic value of sarcopenia combined with hepatolithiasis in intrahepatic cholangiocarcinoma patients after surgery: a prospective cohort study. Eur J Surg Oncology: J Eur Soc Surg Oncol Br Association Surg Oncol. 2021;47(3 Pt B):603–12.

37. Jordens MS, Heinrichs L, Loosen SH, et al. Sarcopenia predicts cancer mortality in male but not in female patients undergoing surgery for cholangiocellular carcinoma. Cancers (Basel). 2021;13:21.
38. Li H, Dai J, Lan T, et al. Combination of albumin-globulin score and skeletal muscle index predicts long-term outcomes of intrahepatic cholangiocarcinoma patients after curative resection. Clin Nutr. 2021;40(6):3891–900.
39. Tamura S, Ashida R, Sugiura T, et al. The prognostic impact of skeletal muscle status and bone mineral density for resected distal cholangiocarcinoma. Clin Nutr. 2021;40(5):3552–8.
40. Ashida R, Yamamoto Y, Aramaki T, et al. Preoperative skeletal muscle fat infiltration is a strong predictor of poorer survival in gallbladder cancer underwent surgery. Clin Nutr ESPEN. 2022;52:60–7.
41. Yasuta S, Sugimoto M, Kudo M, et al. Early postoperative decrease of skeletal muscle mass predicts recurrence and poor survival after surgical resection for perihilar cholangiocarcinoma. BMC Cancer. 2022;22(1):1358.
42. Asai Y, Yamaguchi J, Mizuno T, et al. Impact of preoperative muscle mass and quality on surgical outcomes in patients undergoing major hepatectomy for perihilar cholangiocarcinoma. J Hepato-Biliary-Pancreat Sci. 2023;30(2):202–11.
43. Ikuta S, Aihara T, Nakajima T, et al. Preoperative psoas muscle thickness to height ratio predicts poor survival after resection of biliary tract cancer. Vivo. 2023;37(2):879–86.
44. Jung HE, Han DH, Koo BN, Kim J. Effect of Sarcopenia on postoperative ICU admission and length of stay after hepatic resection for Klatskin tumor. Front Oncol. 2023;13:1136376.
45. Lacaze L, Bergeat D, Rousseau C, et al. High visceral fat is associated with a worse survival after liver resection for intrahepatic cholangiocarcinoma. Nutr Cancer. 2023;75(1):339–48.
46. Taniai T, Haruki K, Yanagaki M, et al. Osteosarcopenia predicts poor prognosis for patients with intrahepatic cholangiocarcinoma after hepatic resection. Surg Today. 2023;53(1):82–9.
47. Wang G, Mantas A, Heij LR et al. Body composition is associated with postoperative complications in perihilar cholangiocarcinoma. Cancer Med. 2024;13(1).
48. Prado CM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol. 2008;9(7):629–35.
49. Li SJ, Jiang H, Yang H, et al. The dilemma of heterogeneity tests in meta-analysis: a challenge from a simulation study. PLoS ONE. 2015;10(5):e0127538.
50. Vale CL, Tierney JF, Stewart LA. Effects of adjusting for censoring on meta-analyses of time-to-event outcomes. Int J Epidemiol. 2002;31(1):107–11.
51. Beaudart C, Rizzoli R, Bruyere O, et al. Sarcopenia: burden and challenges for public health. Arch Public Health. 2014;72(1):45.
52. Jimenez-Gutierrez GE, Martinez-Gomez LE, Martinez-Armenta C, et al. Molecular mechanisms of inflammation in sarcopenia: diagnosis and therapeutic update. Cells. 2022;11:15.
53. Scheede-Bergdahl C, Watt HL, Trutschnigg B, et al. Is IL-6 the best pro-inflammatory biomarker of clinical outcomes of cancer cachexia? Clin Nutr. 2012;31(1):85–8.
54. Pigneur F, Di Palma M, Raynard B, et al. Psoas muscle index is not representative of skeletal muscle index for evaluating cancer sarcopenia. J Cachexia Sarcopenia Muscle. 2023;14(4):1613–20.
55. Burns HJ. Nutritional support in the perioperative period. Br Med Bull. 1988;44(2):357–73.
56. Sartori R, Romanello V, Sandri M. Mechanisms of muscle atrophy and hypertrophy: implications in health and disease. Nat Commun. 2021;12(1):330.
57. Uojima H, Chuma M, Tanaka Y, et al. Skeletal muscle mass influences tolerability and prognosis in hepatocellular carcinoma patients treated with lenvatinib. Liver Cancer. 2020;9(2):193–206.
58. Argiles JM, Busquets S, Stemmler B, Lopez-Soriano FJ. Cachexia and sarcopenia: mechanisms and potential targets for intervention. Curr Opin Pharmacol. 2015;22:100–6.
59. Feliciano EMC, Kroenke CH, Meyerhardt JA, et al. Association of systemic inflammation and sarcopenia with survival in nonmetastatic colorectal cancer: results from the C SCANS study. JAMA Oncol. 2017;3(12):e172319.
60. Liu D, Wang X, Chen Z. Tumor necrosis factor-alpha, a regulator and therapeutic agent on breast cancer. Curr Pharm Biotechnol. 2016;17(6):486–94.
61. Picca A, Coelho-Junior HJ, Calvani R, et al. Biomarkers shared by frailty and sarcopenia in older adults: a systematic review and meta-analysis. Ageing Res Rev. 2022;73:101530.
62. Kobayashi D, Ishigure K, Mochizuki Y, et al. Multi-institutional prospective feasibility study to explore tolerability and efficacy of oral nutritional supplements for patients with gastric cancer undergoing gastrectomy (CCOG1301). Gastric Cancer. 2017;20(4):718–27.
63. Nakajima H, Yokoyama Y, Inoue T, et al. Clinical benefit of preoperative exercise and nutritional therapy for patients undergoing hepato-pancreato-biliary surgeries for malignancy. Ann Surg Oncol. 2019;26(1):264–72.
64. Muscaritoli M, Bar-Sela G, Battisti NML et al. Oncology-led early identification of nutritional risk: a pragmatic, evidence-based protocol (PRONTO). Cancers (Basel). 2023;15(2).
65. Yoo J, Lee JM, Yoon JH, et al. Additional value of integrated (18)F-FDG PET/MRI for evaluating biliary tract cancer: comparison with contrast-enhanced CT. Korean J Radiol. 2021;22(5):714–24.

Publisher's note