Clinical Nutrition 41 (2022) 321–328

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Meta-analyses

Body composition assessment and sarcopenia in patients with biliary tract cancer: A systematic review and meta-analysis

Jun Watanabe [a, b, *], Ryota Matsui [c], Hideki Sasanuma [a], Yoichi Ishizaki [c], Tetsu Fukunaga [d], Kazuhiko Kotani [b], Naohiro Sata [a]

[a] Department of Surgery, Division of Gastroenterological, General and Transplant Surgery, Jichi Medical University, Shimotsuke, Tochigi, Japan
[b] Division of Community and Family Medicine, Jichi Medical University, Shimotsuke, Tochigi, Japan
[c] Department of Surgery, Juntendo University Urayasu Hospital, Urayasu, Chiba, Japan
[d] Department of Gastroenterology and Minimally Invasive Surgery, Juntendo University Hospital, Tokyo, Japan

ARTICLE INFO

Article history:
Received 3 August 2021
Accepted 4 December 2021

Keywords:
Biliary tract cancer
Body composition
Meta-analysis
Mortality
Sarcopenia
Systematic review

SUMMARY

Background: Sarcopenia, as assessed by body composition, can affect morbidity and survival in several gastrointestinal cancer. However, the impact of sarcopenia, referring to both quantity and quality of skeletal muscle, in biliary tract cancer (BTC) is debatable. We aimed to investigate the impact of sarcopenia on morbidity and mortality in patients with BTC.
Methods: Electronic databases and trial registries were searched through July 2021 to perform random-effects meta-analyses. Study selection, data abstraction and quality assessment were independently performed using the Grading of Recommendations, Assessment, Development, and Evaluation approach.
Results: Twenty-nine studies (4443 patients) were included; 28 used computed tomography and one used dual-energy X-ray absorptiometry to assess body composition. Eighteen studies reported the impact of pre-operative sarcopenia on postoperative outcomes; namely, sarcopenia increased post-operative complications (risk ratio = 1.23, 95% confidence interval [CI] = 1.07 to 1.41; I^2 = 2%), and decreased recurrence-free survival (hazard ratio [HR] = 2.20, 95% CI = 1.75 to 2.75; I^2 = 0%) in multivariable analyses. Low muscle quantity (HR = 2.26, 95% CI = 1.75 to 2.92; I^2 = 66%) and quality (HR = 1.75, 95% CI = 1.33 to 2.29; I^2 = 50%) decreased overall survival in multivariable analyses. The certainty of the evidence was low because of heterogeneity and imprecision.
Conclusions: In sarcopenia, low muscle quantity and quality by body composition conferred an independent risk of morbidity and mortality in patients with BTC. Further studies are needed to confirm these findings and mitigate risk.

1. Introduction

Biliary tract cancer (BTC) refers to any malignant tumor that mainly occurs in the biliary tract, including intrahepatic (ICC) and extrahepatic cholangiocarcinoma (ECC), perihilar cholangiocarcinoma (PHC), gallbladder carcinoma (GC), and ampullary carcinoma [1–3]. BTC is common in eastern Asia and it is an aggressive malignancy with poor prognosis—less than half of patients present with unresectable disease, and the 5-year overall survival (OS) rate is only 5%–15% [4]. The main treatment modality of BTC is surgical resection, and the elderly population undergoing this procedure is steadily increasing [1–3].

Among such elderly populations, prognosis has improved in recent years. For this reason, the relationship between carious gastrointestinal cancers and sarcopenia, which refers to an age-related decrease in skeletal muscle mass, has been attracting

Abbreviations: BTC, biliary tract cancer; CI, confidence interval; CT, computed tomography; ECC, extrahepatic cholangiocarcinoma; GC, gallbladder cancer; HR, hazard ratio; ICC, intrahepatic cholangiocarcinoma; OS, overall survival; PHC, perihilar cholangiocarcinoma; RR, risk ratio; RFS, recurrence-free survival.

* Corresponding author. Department of Surgery, Division of Gastroenterological, General and Transplant Surgery, Jichi Medical University, Shimotsuke, Tochigi, 329-0498, Japan. Fax: +81 285 44 3234.
E-mail addresses: m06105jw@jichi.ac.jp (J. Watanabe), supreme0818@gmail.com (R. Matsui), h-ssnm@jichi.ac.jp (H. Sasanuma), ishizaki@juntendo.ac.jp (Y. Ishizaki), t2fukunaga@juntendo.ac.jp (T. Fukunaga), kazukotani@jichi.ac.jp (K. Kotani), sata2018@jichi.ac.jp (N. Sata).

https://doi.org/10.1016/j.clnu.2021.12.005

attention recently. To assess sarcopenia, body composition is the main focus [5]. In fact, sarcopenia may be a poor prognostic factor in patients after surgery for various malignancies, such as esophageal, gastric, colon, pancreatic, and hepatic cancer [6–9]. A previous systematic review of gastrointestinal and hepatopancreatic cancer revealed that sarcopenia predicts poor morbidity and mortality [6,9]. However, no systematic review of sarcopenia has been carried out in patients with BTC. Unlike other cancers, BTC can be difficult to treat because it is aggressive and has complex anatomical relationships [1–3]. Therefore, researchers must investigate whether sarcopenia impacts on prognosis in BTC.

The definition and concept of sarcopenia has changed over the years. According to the European Working Group on Sarcopenia in Older People 2 (EWGOSP2), diagnosis should consider both quantity and quality of skeletal muscle [5]. Even when patients have sufficient muscle quantity, they may show a reduction of muscle function and strength due to poor muscle quality [5]. When assessing body composition for sarcopenia, dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance (BIA) mainly assess muscle quantity, while computed tomography (CT) assesses both quantity and quality [5]. It follows that previous systematic reviews of gastrointestinal and hepatopancreatic malignancies mainly assessed muscle quantity [6–9]. Thus, researchers must investigate the impact of preoperative sarcopenia, especially as assessed by CT, on malignancy outcomes [6–9].

Clarifying the relationship of sarcopenia, as assessed by body composition especially using CT, with outcomes seems to be useful for the treatment of patients with BTC. Therefore, the present study aimed to compare the morbidity and mortality between patients with sarcopenia and BTC, as assessed by body composition, and patients without sarcopenia. The present study, via a systematic review and meta-analysis based on the available reports observed the impact of sarcopenia, as assessed by body composition on morbidity and mortality in patients with BTC.

2. Materials and methods

The Preferred reporting items for systematic review and meta-analysis 2020 (PRISMA-2020) were followed [10]. The protocol was published in protocols.io (dx.doi.org/10.17504/protocols.io.bwgqpbvw).

2.1. Inclusion criteria of the articles for the review

Studies that assessed body composition in patients with BTC were included. No restrictions based on language, country, observation period, or publication year, were applied. All papers, including published and unpublished articles, conference abstracts and letters, were included in accordance with the recommendations in the Cochrane handbook [11]. Review articles and case reports were excluded. Prospective or retrospective cohort studies, and case–control studies were included. Studies were included if they involved patients with BTC aged over 18 years, and they were excluded if they had mixed populations, in which the outcomes of patients with either benign disease or cancer at another site could not be separated from those of patients with BTC. Exposure was defined as diagnosis of sarcopenia by body composition, assessed by any method based on either the volume or characteristics of muscle and/or adipose compartments within the body. The outcomes were OS, recurrence-free survival (RFS), and postoperative complications categorized according to the Clavien-Dindo classification $\geq$ III [12]. The studies in the qualitative synthesis included patients preoperatively, prechemotherapy, and prepercutaneous transhepatic biliary drainage as assessed by body composition (DXA, BIA and CT), while the studies in the quantitative synthesis (meta-analyses) included only preoperative patients with BTC as assessed by CT.

2.2. Search method

The following databases were searched: MEDLINE (PubMed), the Cochrane Central Register of Controlled Trials (Cochrane Library), and EMBASE (Dialog) (Appendix 1). The following databases for ongoing or unpublished trials were also searched: the World Health Organization International Clinical Trials Platform Search Portal (ICTRP); and ClinicalTrials.gov (Appendix 1). The reference lists of studies, including international guidelines [13–17] as well as the reference lists of eligible studies and articles citing eligible studies, were searched.

2.3. Data collection and analysis

Two independent reviewers (JW and RM) screened the titles and abstracts and then assessed the eligibility based on the full texts. Two independent reviewers (JW and RM) then performed data extraction and evaluated the risk of bias independently using the Newcastle–Ottawa Quality Rating Scale (NOS) [18]. Two reviewers (JW and RM) evaluated the certainty of evidence based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [19]. Disagreements between the two reviewers were resolved by discussion; when this failed, a third reviewer acted as an arbiter (KK). We contacted original authors when relevant data were missing. Summary of findings table was made for the following outcomes, based on the Cochrane handbook [11]: OS, RSF, and major postoperative complications.

2.4. Statistics

The hazard ratios and 95% confidence intervals (CIs) for OS and RFS were pooled in preoperative patients with BTC. The relative risk ratios (RRs) and 95% CIs for major postoperative complications were pooled. Intention-to-treat analysis was performed on dichotomous data as much as possible. Statistical heterogeneity was evaluated by visual inspection of forest plots and by calculating the I^2 statistic (I^2 values of 0%–40%: may not be important; 30%–60%: may represent moderate heterogeneity; 50%–90%: may represent substantial heterogeneity; 75%–100%: considerable heterogeneity) [11]. When there was substantial heterogeneity ($I^2 > 50\%$), we assessed the reason for the heterogeneity. The clinical trial registry systems (ClinicalTrials.gov and ICTRP) were searched to assess reporting bias. Potential publication bias was assessed by visual inspection of the funnel plot [11]. Meta-analysis with a random-effects model was performed using Review Manager software (RevMan 5.4.2). To elucidate the influence of effect modifiers on results, subgroup analyses of the following factors were performed when sufficient data were available: cancer type (BTC, ICC, ECC, or GC) and method of assessing body composition (CT, DXA, or BIA). Sensitivity analyses were planned to assess whether the results of the review withstood the decisions made during the review process. In one of these analyses, studies that used imputed statistics were excluded; the other only included participants who completed the study with complete data.

3. Results

Figure 1 shows the study flowchart. A total of 1264 records were searched on July 9, 2021. After screening, 29 studies (4443 patients) were included in qualitative synthesis [20–48]. Eighteen studies (2923 patients) were ultimately included in the quantitative synthesis (meta-analysis) [20–24,29–31,35,37,38,41–46,48]. Although we followed the Cochrane handbook's recommendation of

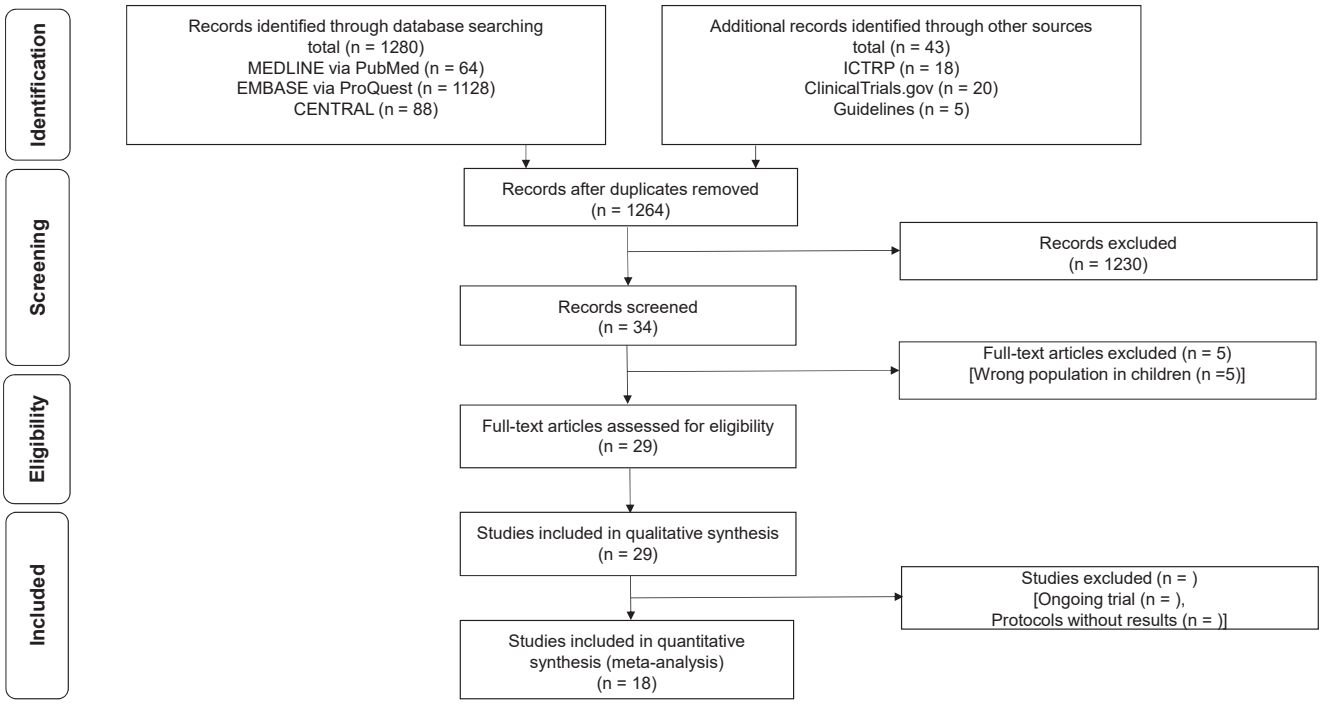

Fig. 1. Flow of the study selection process.

including unpublished data and ongoing studies in the systematic review, no such elements were identified in our search.

Table 1 summarizes the characteristics of the eligible studies. All 29 studies were retrospective cohort studies; 19 were published as articles, while 10 were published as conference abstracts. Of the 29 studies, nine focused on BTC, five on PHC, eight on ICC, four on ECC, and three on GC. Twenty-eight studies assessed body composition for sarcopenia using CT, while one used DTX. Of the 28 studies that used CT to assess skeletal muscle quantity, seven only reported measurements of body composition, while 20 reported their normalization to height and one reported neither. Of the nine studies that used CT to assess skeletal muscle quality, seven only reported measurements of the mean CT value, while two reported their normalization to subcutaneous fat. With regards to timing, 24 studies assessed body composition before surgery, four before chemotherapy, and one before percutaneous transhepatic biliary drainage. Study quality was assessed using NOS; the median was 8 and the range between 2 and 9.

3.1. Body composition assessment in BTC

Table 2 summarizes the findings using the GRADE approach.

3.2. Postoperative complications

Ten studies reported postoperative complications [21–24,29,31,35,42,44]. Sarcopenia assessed by CT increased the postoperative complications (RR = 1.23, 95% CI = 1.07 to 1.41; I^2 = 2%) (Fig. 2).

3.3. RFS

Seven studies reported RFS [23,24,29,35,43,48]. On univariable analysis, sarcopenia assessed as low muscle quantity by CT was a significant risk factor for RFS (HR = 1.89, 95% CI = 1.12 to 3.17; I^2 = 91%) (Fig. 3A). On multivariable analysis, sarcopenia was an independent prognostic factor for RFS (HR = 2.20, 95% CI = 1.75 to 2.75; I^2 = 0%) (Fig. 3B).

3.4. OS

Sixteen studies reported OS [20,23,24,29–31,35,37,38,41–46,48]. On univariable analysis, sarcopenia assessed by CT and defined as low muscle quantity (HR = 2.01, 95% CI = 1.47 to 2.73; I^2 = 85%) (Fig. 4A) was a significant risk factor for OS, as was sarcopenia assessed by CT and defined as low muscle quality (HR = 1.91, 95% CI = 1.61 to 2.27; I^2 = 0%) (Fig. 5A). On multivariable analysis, sarcopenia assessed as low muscle quantity (HR = 2.26, 95% CI = 1.75 to 2.92; I^2 = 66%) (Fig. 4B) and quality (HR = 1.75, 95% CI = 1.33 to 2.29; I^2 = 50%) (Fig. 5B) by CT were independent prognostic factors for OS.

3.5. Additional analysis

Subgroup analyses of cancer type were performed (Appendix Figs. 1–7), in which RFS (P < 0.00001) (Appendix Fig. 2) and OS of muscle quantity (P = 0.04) (Appendix Fig. 4) differed significantly by univariable analysis, but not by multivariable analysis for PFS (Appendix Fig. 3) and OS (Appendix Fig. 5). Subgroup analyses of body composition assessment methods could not be performed because the studies included in the quantitative synthesis (meta-analysis) all used CT. Sensitivity analysis only involving participants who completed the study with complete data were consistent with the original results (Appendix Figs. 8–12). The prespecified sensitivity analyses excluding studies that used imputed statistics could not be performed because no studies used imputed statistics. Funnel plots were visualized as symmetrical, indicating minimal publication bias for reporting of postoperative complications, RFS, and OS (Appendix Figs. 13–16).

4. Discussion

The present systematic review and meta-analysis revealed that sarcopenia, as assessed by body composition, could confer a significantly high rate of postoperative complications and an independently high risk of RFS and OS in patients with BTC. This is new information about the impact of sarcopenia on morbidity and

Table 1
The characteristics of the eligible studies.

Authors [ref no.]	Year	Country	Study type	Study design	Cancer type	Subject no.	Sarcopenia no.	Age	Methods	Muscle quantity	Muscle quality	NOS
Mir [20]	2012	France	P	R	BTC	28	10	63	NR	NR	–	6
Coelen [21]	2015	Netherland	A	R	PHC	97	41	NR	CT	SMA	–	4
Otsuji [22]	2015	Japan	P	R	PHC	256	85	67	CT	TPA	–	6
Zhou [23]	2015	China	P	R	ICC	67	33	61	CT	SMI	–	9
Okumura [24]	2016	Japan	P	R	ECC	207	71	68	CT	PMI	IMAC	9
Van Vugt [25]	2016	Netherland	A	R	PHC	241	112	66	CT	SMI	MA	5
Ashida [26]	2017	Japan	A	R	GC	88	22	NR	CT	PMI	IMAC	4
Cho [27]	2017	Korea	P	R	BTC	524	212	61	CT	SMI	–	8
Nakamura [28]	2017	Japan	A	R	ICC	50	20	NR	CT	TPA	–	4
Okumura [29]	2017	Japan	A	R	ICC	109	69	68	CT	SMI	MA	9
Van Rijssen [30]	2017	Netherland	P	R	BTC	166	130	65	CT	SMI	MA	9
Chakedis [31]	2018	USA	P	R	BTC	117	30	NR	CT	PMI	MA	9
Gao [32]	2018	China	A	R	GC	88	NR	NR	CT	SMA	–	3
Gaspersz [33]	2018	Netherland	A	R	BTC	96	27	NR	CT	SMI	–	2
Limpawattana [34]	2018	Thailand	P	R	BTC	75	46	57	DXA	–	–	8
Umetsu [35]	2018	Japan	P	R	ECC	65	48	72	CT	PMI	–	8
Yamao [36]	2018	Japan	A	R	ICC	66	10	NR	CT	SMA	–	4
Hahn [37]	2019	Germany	P	R	ICC	293	164	66	CT	PMI	–	9
Kitano [38]	2019	Japan	P	R	ECC	110	31	70	CT	SMI	–	9
Lacaze [39]	2019	France	A	R	ICC	102	NR	NR	CT	SMI	MA	5
Meguro [40]	2019	Japan	A	R	BTC	46	NR	76	CT	PMI	–	4
Van Vugt [41]	2019	Netherland	P	R	PHC	233	103	66	CT	SMA	MA	8
Yoon [42]	2019	Korea	P	R	BTC	371	185	66	CT	SMI	MA	9
Yugawa [43]	2019	Japan	P	R	ICC	61	30	65	CT	PMA	–	8
Lee EC [44]	2020	Korea	P	R	GC	158	88	64	CT	SMI	–	9
Lee BM [45]	2020	Korea	P	R	BTC	353	159	67	CT	SMI	–	9
Tamura [46]	2020	Japan	P	R	ECC	111	89	72	CT	SMI	–	9
Zhang [47]	2020	China	P	R	PHC	144	NR	66	CT	SMI	–	8
Deng [48]	2021	China	P	R	ICC	121	66	65	CT	PMI	–	9

A, conference abstract; BTC, biliary tract cancer; CT, computed tomography; ECC, extrahepatic cholangiocarcinoma; GC, gallbladder cancer; ICC, intrahepatic cholangiocarcinoma; IMAC, intramuscular adipose tissue content; MA, muscle attenuation; NOS, the Newcastle–Ottawa Quality Rating Scale; NR, not reported; P, published articles; PHC, perihilar cholangiocarcinoma; PMA, psoas muscle area; PMI, psoas muscle index; R, retrospective cohort study; SMA, skeletal muscle area; SMI, skeletal muscle index.

Table 2
Summary of findings.

The impact of sarcopenia assessed by body composition in patients with biliary tract cancer				
Patient or Population: Adults, Setting: Preoperative, Exposure: Sarcopenia, Comparison: Non-sarcopenia				
Outcomes	Relative Effect (95% CI)	Patient Number (Studies)	Certainty of the Evidence (GRADE)	Comments
Postoperative complications	RR 1.23 (1.07–1.41)	1574 (10 non-RCT)	Low[a]	Sarcopenia may increase postoperative complications.
Recurrent free survival (multivariable)	HR 2.20 (1.75–2.75)	630 (6 non-RCT)	Low[b]	Sarcopenia may reduce recurrent free survival.
Overall survival (multivariable) assessed with muscle quantity	HR 2.26 (1.75–2.92)	1887 (13 non-RCT)	Low[b,c]	Sarcopenia of muscle quantity may reduce overall survival.
Overall survival (multivariable) assessed with muscle quality	HR 1.75 (1.33–2.29)	1444 (7 non-RCT)	Moderate[b]	Sarcopenia of muscle quality probably reduce overall survival.

CI, confidence interval; HR, hazard ratio; RCT, randomized control trials; RR, risk ratio. GRADE Working Group grades of evidence; High certainty: We are very confident that the true effect lies close to that of the estimated effect. Moderate certainty: We are moderately confident in the estimated effect. The true effect is likely to be close to the estimated effect, but there is a possibility that it is substantially different. Low certainty: Our confidence in the estimated effect is limited: The true effect may be substantially different from the estimated effect. Very low certainty: We have very little confidence in the estimated effect. The true effect is likely to be substantially different from the estimated effect.

[a] Downgraded because of non-RCT.
[b] Downgraded because of imprecision due to the small sample size.
[c] Downgraded because of inconsistency due to substantial heterogeneity.

mortality in BTC based on a systematic review of studies that considered both skeletal muscle quantity and quality (a recent concept of sarcopenia) as assessed by CT mainly. The present study findings would imply that sarcopenia should be assessed before surgical treatment of patients with BTC.

In previous systematic reviews of gastrointestinal and hepatopancreatic malignancies [5–8], sarcopenia, as assessed by body composition, increased postoperative complications and mortality, with HRs of 1.70 (esophageal cancer), 2.12 (gastric cancer), 1.78 (pancreatic cancer), 3.19 (hepatic cancer), and 1.85 (colorectal cancer) for mortality or survival [5–8]. In the present review, sarcopenia conferred increased postoperative complications, as well as decreased RFS (HR = 2.20) and OS (HR = 1.75) in patients with BTC. These findings are consistent with previous reviews reporting poor outcomes in patients with sarcopenia [5–8]. Thus, this study was valuable in that it expanded knowledge of sarcopenia in gastroenterological malignancies to include BTC.

In the present review, most studies used CT among the several methods (CT, DXA, or BIA) to assess body composition. Although previous reviews have also used often used CT [5–8], the impact of

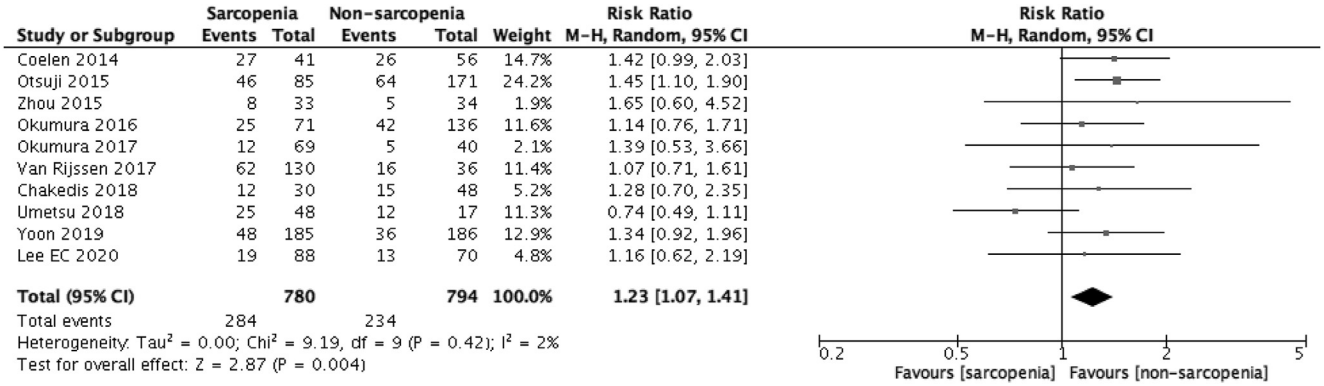

Fig. 2. Forest plot of postoperative complications.

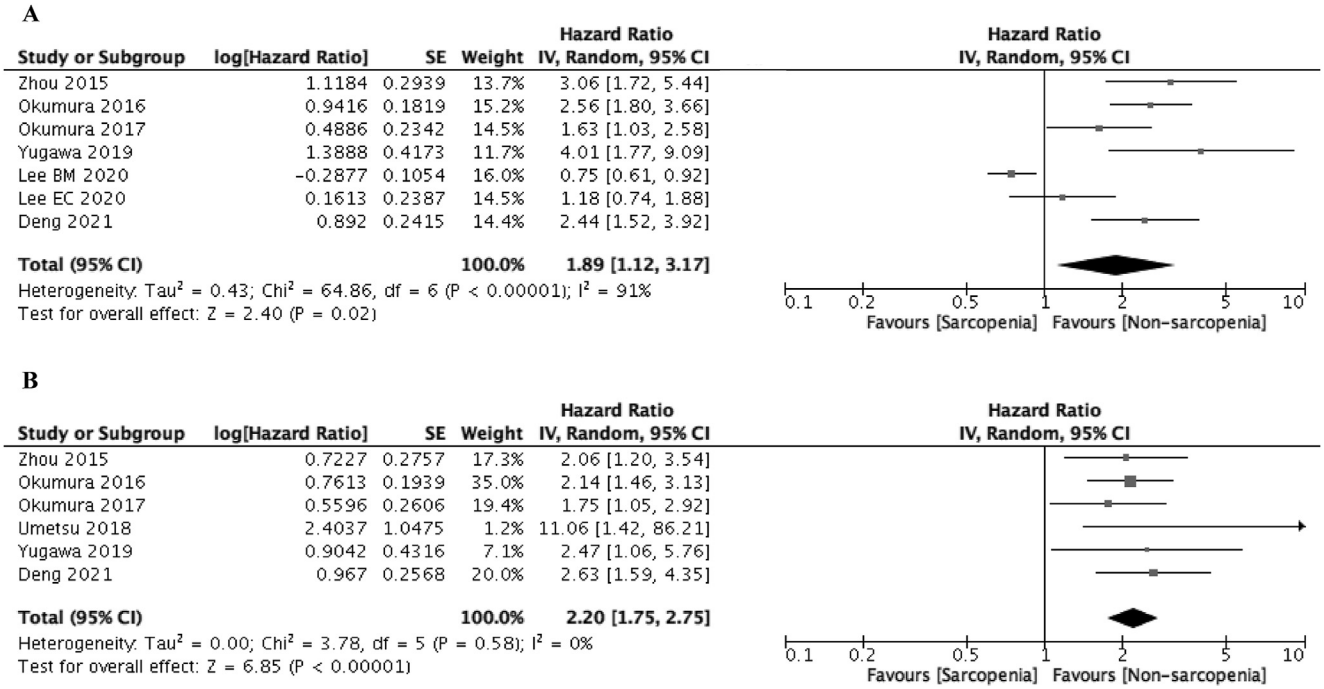

Fig. 3. Forest plot of recurrence-free survival on A) univariable and B) multivariable analysis.

assessment of body composition using CT on postoperative outcomes has not been comparted to the other assessment methods. Even though CT was recently recognized as the gold standard method to assess body composition, which refers to both the quantity and quality of skeletal muscle, the choice of methods for the body composition assessment in clinical practice is under consideration. While the present review observed the impact of body composition, assessed using CT (manifesting partly the muscle quality), on postoperative outcomes, it could not compare CT with DXA or BIA in terms of the measured impact of body composition on outcomes. Moreover, the impact was not markedly higher than in previous reviews [5–8], indicating that muscle quality and quantity cannot be completely separated, but that they are highly correlated [24]. Moreover, the methodology for assessing muscle quality has not yet been standardized. Seven of the nine studies in the present review [25,29–31,39,41,42] used mean CT values as the quality measure; however, this value is greatly influenced by CT equipment and scanning conditions [49]. Another two studies [24,26] used intramuscular adipose tissue content, standardized to subcutaneous fat, which is unaffected by the scanning device [50]. The best methodologies for assessing body composition in patients undergoing BTC surgery should be further determined in an evidence-based way.

The mechanisms responsible for the relationship between sarcopenia and increased risk of morbidity/mortality are still unclear. Potential factors include age-related changes [51] and cancer cachexia [52]. Skeletal muscle quantity and quality can be compromised by a variety of factors, including age-related changes in the body composition and hormonal environment, positive energy balance, inflammatory pathways, and insulin resistance [51]. In addition, cancer cachexia causes an involuntary loss of muscle mass and increased adipocyte lipolysis, stimulating systemic inflammation and cytokine networks [52]. Inflammation and insulin resistance promote cancer progression because tumor cells activate various growth and survival signaling pathways [53,54].

Intervention to maintain muscle quantity and quality may improve survival, but no studies have evaluated long-term survival [55]. Approaches to enhance skeletal muscle quantity and quality include exercise [56] and oral nutritional support [57]. Preoperative

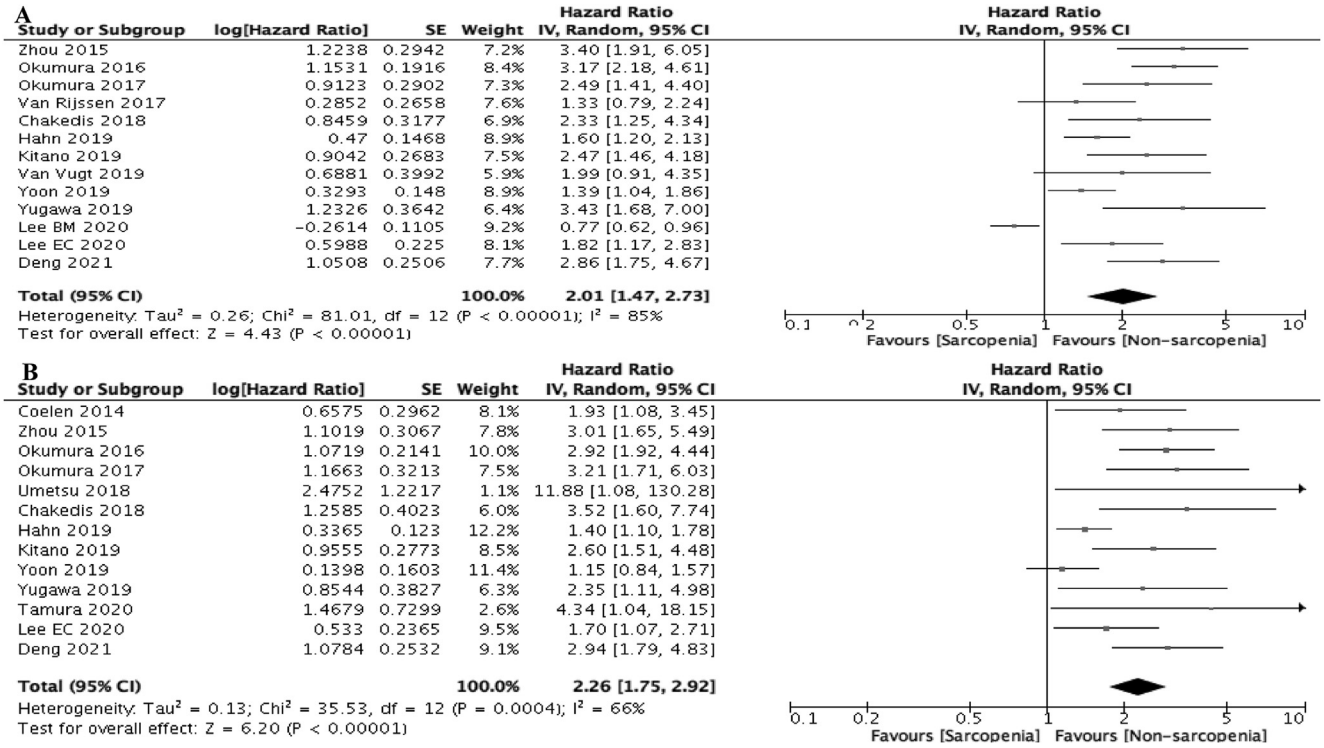

Fig. 4. Forest plot of overall survival assessed as low muscle quantity on A) univariable and B) multivariable analysis.

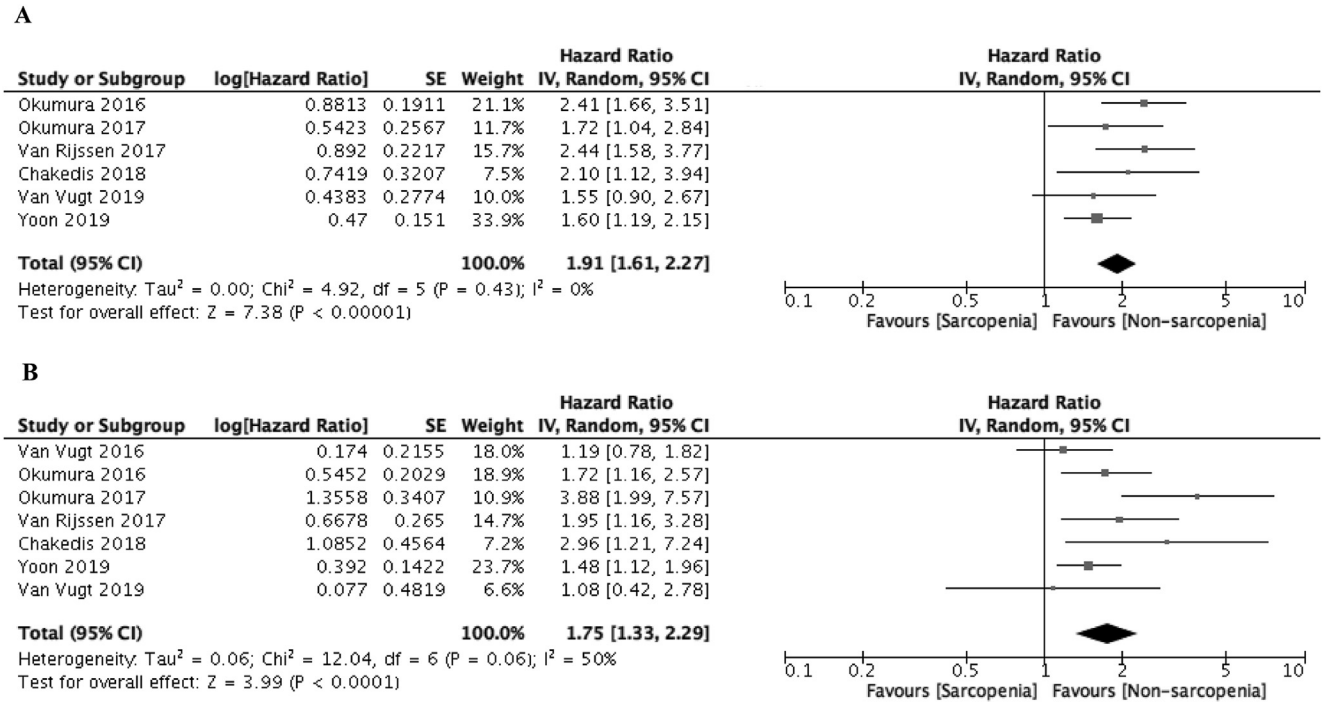

Fig. 5. Forest plot of overall survival assessed as low muscle quality on A) univariable and B) multivariable analysis.

rehabilitation and nutritional support may reduce morbidity and improve survival [58,59]. In the elderly population, exercise, especially strength training, is reported to improve the muscle quality compared to the muscle quantity [60,61]. Further studies are needed to elucidate the effects of methods that improve skeletal muscle quantity and quality in cancer patients.

The present study had several limitations. First, the overall strength of the conclusion was limited because the studies had high heterogeneity in their methods and techniques of body composition assessment, and because the small sample size led to imprecision. Further large studies using standardized measures of body composition are needed. Second, variability in cancer type was an

important confounder. However, in the multivariable subgroup analyses, RFS and OS did not differ significantly among cancer types. Third, many other studies have assessed body composition in mixed cohorts that included patients with liver or/and pancreatic cancer; these studies were therefore not suitable for inclusion in this review. However, we adopted a rigorous method of searching based on the PRISMA statement [10]. Forth, sarcopenia based on physical performance was not assessed, since the body composition assessment used in the present review could not directly evaluate physical performance.

5. Conclusion

The present systematic review and meta-analysis revealed that sarcopenia, as assessed by body composition, was associated with a significantly high rate of postoperative complications and an independently high risk of RFS and OS in patients undergoing BTC surgery. These findings suggested that the medical team in-charge of treatment should be aware of the presence of sarcopenia and adjust the care given accordingly, because it is related to postoperative complications and prognosis. Further studies are needed to confirm these findings and mitigate the negative effects.

Funding

This work was supported by JSPS KAKENHI Grant Number JP21K21121.

Author contributions

Conceptualization, J.W. and K.K.; methodology, J.W. and K.K.; software, J.W.; validation, J.W., R.M., and K.K.; formal analysis, J.W. and K.K.; investigation, J.W., R.M., and K.K.; resources, N/A; data curation, J.W., R.M., and K.K.; writing of original draft preparation, J.W.; writing, review and editing, J.W., R.M., H.S., Y.I., T.F., K.K., and N.S.; visualization, J.W.; supervision, H.S., Y.I., T.F., K.K., and N.S.; project administration, J.W. and K.K.; funding acquisition, N/A. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2021.12.005.

References

[1] Gamboa AC, Maithel SK. The landmark series: gallbladder cancer. Ann Surg Oncol 2020;27:2846–58.
[2] Cloyd JM, Ejaz A, Pawlik TM. The landmark series: intrahepatic cholangiocarcinoma. Ann Surg Oncol 2020;27:2859–65.
[3] Soares KC, Jarnagin WR. The landmark series: hilar cholangiocarcinoma. Ann Surg Oncol 2021. https://doi.org/10.1245/s10434-021-09871-6 [Epub ahead of print].
[4] Bridgewater J, Lopes A, Wasan H, Malka D, Jensen L, Okusaka T, et al. Prognostic factors for progression-free and overall survival in advanced biliary tract cancer. Ann Oncol 2016;27:134–40.
[5] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16–31.
[6] Levolger S, van Vugt JL, de Bruin RW, IJzermans JN. Systematic review of sarcopenia in patients operated on for gastrointestinal and hepatopancreatobiliary malignancies. Br J Surg 2015;102:1448–58.
[7] Boshier PR, Heneghan R, Markar SR, Baracos VE, Low DE. Assessment of body composition and sarcopenia in patients with esophageal cancer: a systematic review and meta-analysis. Dis Esophagus 2018;31.
[8] Kamarajah SK, Bundred J, Tan BHL. Body composition assessment and sarcopenia in patients with gastric cancer: a systematic review and meta-analysis. Gastric Cancer 2019;22:10–22.
[9] Bundred J, Kamarajah SK, Roberts KJ. Body composition assessment and sarcopenia in patients with pancreatic cancer: a systematic review and meta-analysis. HPB 2019;21:1603–12.
[10] 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.
[11] Higgins JPT, Thomas J. Cochrane handbook for systematic reviews of interventions version 6.2, 2021. 2021. Cochrane, https://training.cochrane.org/handbook/current. [Accessed 3 July 2021].
[12] Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187–96.
[13] Version 3.2021 NCCN clinical practice guidelines in oncology: hepatobiliary cancers. 2021. Available online: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. [Accessed 3 July 2021].
[14] Valle JW, Borbath I, Khan SA, Huguet F, Gruenberger T, Arnold D, ESMO Guidelines Committee. Biliary cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2016;27:v28–37.
[15] Khan SA, Davidson BR, Goldin RD, Heaton N, Karani J, Pereira SP, et al. Guidelines for the diagnosis and treatment of cholangiocarcinoma: an update. Gut 2012;61:1657–69.
[16] Bridgewater J, Galle PR, Khan SA, Llovet JM, Park JW, Patel T, et al. Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma. J Hepatol 2014;60:1268–89.
[17] Shroff RT, Kennedy EB, Bachini M, Bekaii-Saab T, Crane C, Edeline J, et al. Adjuvant therapy for resected biliary tract cancer: ASCO clinical practice guideline. J Clin Oncol 2019;37:1015–27.
[18] Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The newcastle-ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Univ Liverpool, Liverpool, UK; 2011. Available online: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. [Accessed 3 July 2021].
[19] Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64:383–94.
[20] Mir O, Coriat R, Dhooge M, Perkins G, Boudou-Rouquette P, Brezault C, et al. Feasibility of gemcitabine and oxaliplatin in patients with advanced biliary tract carcinoma and a performance status of 2. Anti Cancer Drugs 2012;23:739–44.
[21] Coelen RJS, Wiggers JK, Nio CY, Van Dieren S, Besselink MGH, Busch ORC, et al. Impact of sarcopenia on outcomes following resection of perihilar cholangiocarcinoma. Unit Eur Gastroenterol J 2014;2:A197.
[22] Otsuji H, Yokoyama Y, Ebata T, Igami T, Sugawara G, Mizuno T, et al. Preoperative sarcopenia negatively impacts postoperative outcomes following major hepatectomy with extrahepatic bile duct resection. World J Surg 2015;39:1494–500.
[23] Zhou G, Bao H, Zeng Q, Hu W, Zhang Q. Sarcopenia as a prognostic factor in hepatolithiasis-associated intrahepatic cholangiocarcinoma patients following hepatectomy: a retrospective study. Int J Clin Exp Med 2015;8:18245–54.
[24] Okumura S, Kaido T, Hamaguchi Y, Fujimoto Y, Kobayashi A, Iida T, et al. Impact of the preoperative quantity and quality of skeletal muscle on outcomes after resection of extrahepatic biliary malignancies. Surgery 2016;159:821–33.
[25] van Vugt JLA, Gaspersz MP, Vugts J, Willemssen FEJA, Groot Koerkamp B, IJzermans JNM. Skeletal muscle density, but not skeletal muscle mass, is associated with impaired survival in patients with suspected perihilar cholangiocarcinoma and may identify patients at risk for early death. J Cachexia Sarcopenia Muscle 2016;7:635.
[26] Ashida R, Sugiura T, Okamura Y, Ito T, Yamamoto Y, Uesaka K. Prognostic impact of quality and quantity of skeletal muscle for advanced gallbladder cancer. J Hepatobiliary Pancreat Sci 2017;24:A40.
[27] Cho KM, Park H, Oh DY, Kim TY, Lee KH, Han SW, et al. Skeletal muscle depletion predicts survival of patients with advanced biliary tract cancer undergoing palliative chemotherapy. Oncotarget 2017;8:79441–52.
[28] Nakamura I, Hatano E, Hai S, Okada T, Asano Y, Uyama N, et al. The impact of sarcopenia on outcomes following resection of intrahepatic cholangiocarcinoma. J Hepatobiliary Pancreat Sci 2017;24:A299.
[29] Okumura S, Kaido T, Hamaguchi Y, Kobayashi A, Shirai H, Fujimoto Y, et al. Impact of skeletal muscle mass, muscle quality, and visceral adiposity on outcomes following resection of intrahepatic cholangiocarcinoma. Ann Surg Oncol 2017;24:1037–45.
[30] Van Rijssen LB, van Huijgevoort NC, Coelen RJ, Tol JA, Haverkort EB, Nio CY, et al. Skeletal muscle quality is associated with worse survival after pancreatoduodenectomy for periampullary, nonpancreatic cancer. Ann Surg Oncol 2017;24:272–80.

[31] Chakedis J, Spolverato G, Beal EW, Woelfel I, Bagante F, Merath K, et al. Preoperative sarcopenia identifies patients at risk for poor survival after resection of biliary tract cancers. J Gastrointest Surg 2018;22:1697–708.
[32] Gao S, Wang D. Sarcopenia as an independent prognostic factor in patients following surgery for gallbladder cancer. Int J Clin Exp Med 2018;11:877–83.
[33] Gaspersz M, Belkouz A, Dierks J, Groot JW, Rentinck M, Nio C, et al. The association between sarcopenic overweight and chemotherapy toxicity in bile duct and gallbladder cancer patients treated with gemcitabine and cisplatin. HPB 2018;20:S315.
[34] Limpawattana P, Theerakulpisut D, Wirasorn K, Sookprasert A, Khuntikeo N, Chindaprasirt J. The impact of skeletal muscle mass on survival outcome in biliary tract cancer patients. PLoS One 2018;13:e0204985.
[35] Umetsu S, Wakiya T, Ishido K, Kudo D, Kimura N, Miura T, et al. Effect of sarcopenia on the outcomes after pancreaticoduodenectomy for distal cholangiocarcinoma. ANZ J Surg 2018;88:E654–8.
[36] Yamao T, Yamashita Y, Umezaki N, Tsukamoto M, Arima K, Miyata T, et al. Sarcopenia and caveolin-1 expression in cancer-associated fibroblasts in intrahepatic cholangiocarcinoma. Cancer Sci 2018;109.
[37] Hahn F, Müller L, Stöhr F, Mähringer-Kunz A, Schotten S, Düber C, et al. The role of sarcopenia in patients with intrahepatic cholangiocarcinoma: prognostic marker or hyped parameter? Liver Int 2019;39:1307–14.
[38] Kitano Y, Yamashita YI, Saito Y, Nakagawa S, Okabe H, Imai K, et al. Sarcopenia affects systemic and local immune system and impacts postoperative outcome in patients with extrahepatic cholangiocarcinoma. World J Surg 2019;43:2271–80.
[39] Lacaze L, Bergeat D, Rousseau C, Sulpice L, Val-Laillet D, Boudjema K, et al. Visceral fat assessed by third lumbar vertebra (L3)-targeted CT affects survival and recurrence after curative liver resection for intra hepatic cholangiocarcinoma (ICC). Clin Nutr 2019;38:S101.
[40] Meguro K, Hosono K, Watanabe S, Nakajima A. Effects of sarcopenia and background factors on elderly biliary cancer patients receiving chemotherapy. Unit Eur Gastroenterol J 2019;7:497.
[41] van Vugt JLA, Gaspersz MP, Vugts J, Buettner S, Levolger S, de Bruin RWF, et al. Low skeletal muscle density is associated with early death in patients with perihilar cholangiocarcinoma regardless of subsequent treatment. Dig Surg 2019;36:144–52.
[42] Yoon SB, Choi MH, Song M, Lee JH, Lee IS, Lee MA, et al. Impact of preoperative body compositions on survival following resection of biliary tract cancer. J Cachexia Sarcopenia Muscle 2019;10:794–802.
[43] Yugawa K, Itoh S, Kurihara T, Yoshiya S, Mano Y, Takeishi K, et al. Skeletal muscle mass predicts the prognosis of patients with intrahepatic cholangiocarcinoma. Am J Surg 2019;218:952–8.
[44] Lee EC, Park SJ, Lee SD, Han SS, Kim SH. Effects of sarcopenia on prognosis after resection of gallbladder cancer. J Gastrointest Surg 2020;24:1082–91.
[45] Lee BM, Cho Y, Kim JW, Jeung HC, Lee IJ. Prognostic significance of sarcopenia in advanced biliary tract cancer patients. Front Oncol 2020;10:1581.
[46] Tamura S, Ashida R, Sugiura T, Okamura Y, Ito T, Yamamoto Y, et al. The prognostic impact of skeletal muscle status and bone mineral density for resected distal cholangiocarcinoma. Clin Nutr 2020;40:3552–8.
[47] Zhang JX, Ding Y, Yan HT, Zhou CG, Liu J, Liu S, et al. Skeletal-muscle index predicts survival after percutaneous transhepatic biliary drainage for obstructive jaundice due to perihilar cholangiocarcinoma. Surg Endosc 2020;22.
[48] Deng L, Wang Y, Zhao J, Tong Y, Zhang S, Jin C, et al. The prognostic value of sarcopenia combined with hepatolithiasis in intrahepatic cholangiocarcinoma patients after surgery: a prospective cohort study. Eur J Surg Oncol 2021;47:603–12.
[49] Kitajima Y, Eguchi Y, Ishibashi E, Nakashita S, Aoki S, Toda S, et al. Age-related fat deposition in multifidus muscle could be a marker for nonalcoholic fatty liver disease. J Gastroenterol 2010;45:218–24.
[50] Marcus RL, Addison O, Kidde JP, Dibble LE, Lastayo PC. Skeletal muscle fat infiltration: impact of age, inactivity, and exercise. J Nutr Health Aging 2010;14:362–6.
[51] Koliaki C, Liatis S, Dalamaga M, Kokkinos A. Sarcopenic obesity: epidemiologic evidence, pathophysiology, and therapeutic perspectives. Curr Obes Rep 2019;8:458–71.
[52] Rydén M, Arner P. Fat loss in cachexia—is there a role for adipocyte lipolysis? Clin Nutr 2007;26:1–6.
[53] Srikanthan P, Hevener AL, Karlamangla AS. Sarcopenia exacerbates obesity-associated insulin resistance and dysglycemia: findings from the national health and nutrition examination survey III. PLoS One 2010;5:e10805.
[54] Chang ML, Yang Z, Yang SS. Roles of adipokines in digestive diseases: markers of inflammation, metabolic alteration and disease progression. Int J Mol Sci 2020;21:8308.
[55] Cruz-Jentoft AJ, Sayer AA. Sarcopenia. Lancet 2019;393:2636–46.
[56] Zhang Y, Zou L, Chen ST, Bae JH, Kim DY, Liu X, et al. Effects and moderators of exercise on sarcopenic components in sarcopenic elderly: a systematic review and meta-analysis. Front Med 2021;8:649748.
[57] Wright J, Baldwin C. Oral nutritional support with or without exercise in the management of malnutrition in nutritionally vulnerable older people: a systematic review and meta-analysis. Clin Nutr 2018;37:1879–91.
[58] Tsukagoshi M, Harimoto N, Araki K, Kubo N, Watanabe A, Igarashi T, et al. Impact of preoperative nutritional support and rehabilitation therapy in patients undergoing pancreaticoduodenectomy. Int J Clin Oncol 2021;26:1698–706.
[59] Tomassini S, Abbasciano R, Murphy GJ. Interventions to prevent and treat sarcopenia in a surgical population: a systematic review and meta-analysis. BJS Open 2021;5:zraa069.
[60] Escriche-Escuder A, Fuentes-Abolafio IJ, Roldán-Jiménez C, Cuesta-Vargas AI. Effects of exercise on muscle mass, strength, and physical performance in older adults with sarcopenia: a systematic review and meta-analysis according to the EWGSOP criteria. Exp Gerontol 2021;151:111420.
[61] Strasser EM, Hofmann M, Franzke B, Schober-Halper B, Oesen S, Jandrasits W, et al. Strength training increases skeletal muscle quality but not muscle mass in old institutionalized adults: a randomized, multi-arm parallel and controlled intervention study. Eur J Phys Rehabil Med 2018;54:921–33.