Computed Tomography-Assessed Sarcopenia Indexes Predict Major Complications following Surgery for Hepatopancreatobiliary Malignancy: A Meta-Analysis

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Keywords

Sarcopenia · Computed tomography · Major complications · Surgery · Hepatopancreatobiliary

Abstract

Background: Computed tomography (CT)-assessed sarcopenia indexes have been reported to predict postoperative morbidity and mortality; however conclusions drawn from different indexes and studies remain controversial. **Aim:** The purpose of this meta-analysis was to evaluate various CT-assessed sarcopenia indexes as predictors of risk for major complications in patients undergoing hepatopancreatobiliary surgery for malignancy. **Methods:** Medline/PubMed, Web of Science, and Embase databases were systematically searched to identify relevant studies published before June 2018. PRISMA guidelines for systematic reviews were followed. The pooled risk ratio (RR) for major postoperative complications (Clavien-Dindo $\geq$ III) was estimated in patients with sarcopenia versus patients without sarcopenia. Data extracted were meta-analyzed using Review Manager (version 5.3). **Results:** Twenty-eight studies comprising 6,656 patients were included in this study. CT-assessed sarcopenia indexes, such as skeletal muscle index (SMI, RR 1.36; 95% CI

1.14–1.63; $p = 0.0008$; $I^2 = 24\%$), psoas muscle index (PMI, RR 1.35; 95% CI 1.15–1.58; $p = 0.0002$; $I^2 = 0\%$), muscle attenuation (MA, RR 1.40; 95% CI 1.14–1.73; $p = 0.002$; $I^2 = 4\%$), and intramuscular adipose tissue content (IMAC, RR 1.63; 95% CI 1.28–2.09; $p < 0.0001$; $I^2 = 0\%$) were all predictors of postoperative major complications, although moderate heterogeneity existed and cutoffs for these indexes to define sarcopenia varied. **Conclusions:** All commonly used CT-assessed sarcopenia indexes, such as SMI, PMI, MA, and IMAC can predict the risk of major postoperative complications; however, a consensus on the cutoffs for these indexes to define sarcopenia is still lacking.

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Introduction

With the developments in surgical technique and concept of perioperative management, the morbidity and mortality after surgery have greatly improved [1–3]; however, postoperative complications have still been a major concern for clinicians, and preoperative risk assessment has remained of paramount significance in improving the outcomes of patients. As an index of function capacity,

the predictive value of sarcopenia in the occurrence of postoperative complications has been reported in a variety of studies [4–7].

The term “sarcopenia” was initially proposed by Rosenberg [8], and it described the loss of skeletal muscle mass in aged people. In 2010, the European Working Group [9] on Sarcopenia in Older People recommended that Sarcopenia be defined as a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death in 2010. According to different etiologies, sarcopenia can be classified into the following 2 categories: primary sarcopenia caused by aging, and secondary sarcopenia, a pathological process, which is disease, activity or nutrition related.

Sarcopenia can be estimated and diagnosed by many validated techniques [10], which include dual X-ray absorptiometry, bio-electric impedance analysis, and computed tomography (CT) scanning. Considering the accessibility and simplicity, CT scanning is the most commonly used technique in clinical practice. A variety of studies have reported that CT-assessed sarcopenia indexes [11–14] can predict the risk of postoperative complications, especially major complications; however, conclusions drawn from different indexes and studies have remained controversial to some extent.

This meta-analysis aims to explore whether these commonly reported CT-assessed sarcopenia indexes can predict the risk of incidence of major postoperative complications following surgery for hepatopancreatobiliary malignancy.

Methods

Literature Search

A comprehensive literature search was performed according to PRISMA guidelines using Medline/PubMed, Web of Science, and Embase databases to identify studies on CT-assessed sarcopenia indexes in patients undergoing hepatopancreatobiliary surgery for malignancy before June 2018. The search query included (“sarcopenia” OR “muscle mass” OR “muscle depletion” OR “body composition”) AND (“cancer” OR “neoplasm”) AND (“liver resection” OR “hepatectomy” OR “pancreatectomy” OR “pancreaticoduodenectomy” OR “bile duct”). In case of omission, the Google Scholar was also searched and the references lists of all primary studies were reviewed for relevant studies.

Study Selection

Two reviewers independently evaluated every retrieved study. The inclusion criteria were as follows: (1) patients undergoing surgery for hepatopancreatobiliary malignancy, (2) major postoperative complications were reported and graded according to the Cla-

vien-Dindo classification, and (3) patients were grouped according to the CT-assessed sarcopenia indexes. Exclusion criteria were as follows: (1) studies did not comprise outcome of interest, (2) full-text article was not available, (3) conference abstracts, (4) postoperative complications were not graded according to Clavien-Dindo classification, and (5) patients were grouped according to CT-assessed indexes that were not related to sarcopenia. Furthermore, if 2 studies were performed at the same medical center, and the population sample was repeatedly reported, then, the study with a larger sample size was included.

Data Extraction

Two reviewers independently identified and extracted data from the original studies independently. When there was a discord between the 2 reviewers, a discussion was performed within the study team until an agreement was reached. The extracted data included the general characteristics of the study, the definition and cutoffs of CT-assessed sarcopenia indexes, the prevalence of sarcopenia, and the incidence of major postoperative complications (Clavien-Dindo [15] $\geq$ III).

Quality Assessment

The Newcastle-Ottawa assessment scale [16] was used to assess the quality of the included studies. In each study, the following 3 items were used to assess the quality of methodology: Selection, Comparability, and Outcome.

Statistical Analysis

Review Manager (Revman, version 5.3; The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) was used to perform this meta-analysis. The value of I^2 was used to assess the heterogeneity among studies. I^2 values of 25, 50, and 75% were considered to correspond to low, moderate, and high levels of heterogeneity respectively. When the value of I^2 exceeded 50%, the DerSimonian and Laird random effects model [17] was used to pool estimates; otherwise, the Mantel Haenszel fixed effects model [18] was applied. The outcomes were described as risk ratio (RR) and their associated 95% CI and $p < 0.05$ was considered statistically significant.

Results

Study Selection

A total of 836 references were identified from database searching, of which 58 articles were identified as relevant. From these 58 records, 30 were excluded (not graded by Clavien-Dindo classification, 3; no outcome of interest, 13; repeated report, 2; other treatments, 3; not grouped by sarcopenia indexes, 3; grouped according to indexes not related with sarcopenia, 4; postoperative muscle change, 2). Ultimately, 28 studies comprising 6,656 patients were included in this meta-analysis [11–14, 19–42] (as shown in Fig. 1).

Study Characteristics

The general characteristics of the included studies are presented in Table 1. Fifteen studies [11, 13, 20–23, 25, 27,

Fig. 1. Study selection process.

31, 33, 34, 36, 39, 40, 42] were performed in Japan, with 4 in Netherlands [19, 28, 37, 41], 4 in America [12, 14, 29, 30], 1 in France [24], 1 in Canada [38], 1 in Austria [35], 1 in Korea [32], and 1 in China [26]. Among the included studies, 13 studies were directed at liver [11, 13, 19–29] malignancy, 2 bile duct [30, 31], 6 pancreas [12, 14, 32–35], 2 periampullary [36, 37], 4 periampullary and pancreas [38–41], and 1 hepatopancreatobiliary [42]. The sample size ranged from 67 to 763. All of the studies were cohort studies and 26 studies were retrospective in nature [11–14, 19–40] and 2 studies were prospective [41, 42]. The quality score ranged from 5 to 7.

Calculation Formula of CT-Assessed Sarcopenia Indexes

Based on the 28 included studies, 8 types of CT-assessed sarcopenia indexes were reported, which included skeletal muscle index/total abdominal muscle area (SMI/TAMA), SMA/BSA index (SBI), psoas muscle index/total psoas muscle area (PMI/TPA), muscle attenuation/radiation attenuation (MA/RA), intramuscular adipose tissue content (IMAC), Hounsfield units average classification (HUAC), lean psoas muscle area (LPMA), and Total psoas muscle volume (TPV). The formula for calculating each index is showed in Table 2.

Definition of Sarcopenia

Based on the included 28 studies, sarcopenia was defined by using various indexes and cutoffs. The reported prevalence of sarcopenia ranged from 13.3 to 78%. All of the image analysis was based on CT, and the third lumbar vertebra was the most commonly used level. SMI/TAMA was the most commonly used index, and it was used in 16 studies [11, 13, 19, 21, 23–28, 32, 34, 36–39], with SBI in 2 studies [40, 42], PMI/TPA in 7 studies [12, 20, 22, 29–31, 33], MA/RA in 5 studies [13, 24, 37, 38, 41], IMAC in 4 studies [20, 27, 31, 33], HUAC in 1 study [35], LPMA in 1 study [14], and TPV in 1 study [12] (Table 3).

Cutoff for the Sarcopenia Index

Predefined or study-specific cutoffs were used to define sarcopenia. Predefined cutoffs were adopted in 8 studies [11, 20, 24–28, 39], and optimum stratification, receiver operator characteristic curve and study-specific percentiles were used in the other studies [12–14, 21–23, 29–38, 40–42]. Sex-specific cutoffs were employed in almost all of the included studies, and on comparison with males, females showed a relatively lower muscle mass and MA (Table 3).

Table 1. General characteristics of the studies included in this review

Reference	Country	Study period	Study design	No. of patients	Disease type	Quality assessment (NOS)
Coelen et al. [19], 2015	Netherlands	1998–2013	Retrospective	100	Liver	7
Hamaguchi et al. [20], 2016	Japan	2005–2014	Retrospective	492	Liver	7
Higashi et al. [21], 2016	Japan	2007–2013	Retrospective	144	Liver	6
Kobayashi et al. [11], 2017	Japan	2005–2015	Retrospective	465	Liver	6
Okumura et al. [13], 2017	Japan	2004–2015	Retrospective	109	Liver	7
Coelen et al. [22], 2015	Japan	2008–2014	Retrospective	256	Liver	5
Takagi et al. [23], 2016	Japan	2007–2013	Retrospective	254	Liver	6
Voron et al. [24], 2015	France	2006–2012	Retrospective	109	Liver	5
Yabusaki et al. [25], 2016	Japan	2003–2014	Retrospective	195	Liver	6
Zhou et al. [26], 2015	China	2000–2014	Retrospective	67	Liver	6
Kobayashi et al. [27], 2018	Japan	2005–2014	Retrospective	124	CRLM	6
Lodewick et al. [28], 2014	Netherlands	2005–2012	Retrospective	171	CRLM	5
Peng et al. [29], 2011	USA	2000–2009	Retrospective	259	CRLM	6
Chakedis et al. [30], 2018	USA	2007–2016	Retrospective	78	Bile duct	6
Okumura et al. [31], 2016	Japan	2004–2013	Retrospective	207	Bile duct	6
Amini et al. [12], 2015	USA	1996–2014	Retrospective	763	Pancreas	6
Choi et al. [32], 2018	Korea	2008–2015	Retrospective	180	Pancreas	6
Okumura et al. [33], 2015	Japan	2004–2013	Retrospective	230	Pancreas	6
Okumura et al. [34], 2017	Japan	2004–2015	Retrospective	301	Pancreas	7
Onesti et al. [14], 2016	USA	2005–2012	Retrospective	260	Pancreas	7
Wagner et al. [35], 2018	Austria	2006–2015	Retrospective	424	Pancreas	5
Sui et al. [36], 2018	Japan	2005–2014	Retrospective	354	Periampullary	6
Van Rijssen et al. [37], 2017	Netherlands	2000–2012	Retrospective	166	Periampullary	7
Stretch et al. [38], 2018	Canada	2003–2011	Retrospective	123	Periampullary/pancreas	6
Nishida et al. [39], 2016	Japan	2010–2014	Retrospective	266	Periampullary/pancreas	5
Takagi et al. [40], 2017	Japan	2007–2013	Retrospective	219	Periampullary/pancreas	6
van Dijk et al. [41], 2017	Netherlands	2008–2013	Prospective	186	Periampullary/pancreas	5
Takagi et al. [42], 2017	Japan	2013–2014	Prospective	154	HPB	5

CRLM, colorectal liver metastasis; HB, hepatobiliary surgery; HPB, hepatopancreatobiliary surgery.

Main Effects: Major Postoperative Complications SMI, TAMA, and SBI

As both the SBI and SMI indexes both reflected the total skeletal muscle mass, one adjusted for height and the other for body surface area, and the data were pooled to-

gether. As shown in Figure 2a, based on 18 studies [11, 13, 19, 21, 23–28, 32, 34, 36–39, 40, 42] comprising 3,501 patients and 782 major complications, low preoperative SMI was associated with an increased risk of major complications (RR 1.36; 95% CI 1.14–1.63; $p = 0.0008$; $I^2 = 24\%$).

Table 2. Formulae for calculating CT-assessed sarcopenia indexes

SMI/TAMA	All skeletal muscle mass/height ²
PMI/TPA	Total psoas muscle area/height ²
TPV	Total psoas muscle volume/height ²
SBI	All skeletal muscle mass/body surface area
MA/RA	Mean CT value of the cross-sectional area of the skeletal muscle HU
LPMA	LPMA = total psoas area × lean PMD; lean PMD = (mean psoas density + 85)/170; PMD = (left mean + right mean)/2
IMAC	CT attenuation of the multifidus muscles (+ erector spinae; HU)/CT attenuation of subcutaneous adipose tissue (HU)
HUAC	HUAC = (RHUC + LHUC)/2; RHUC = (right HU × right psoas area)/(total psoas area); LHUC = left HU × left psoas area)/(total psoas area)

PMI and TPA

As shown in Figure 2b, based on 7 studies [12, 20, 22, 29–31, 33] comprising 2,285 patients and 479 major complications, low preoperative PMI was associated with an increased risk of major complications (RR 1.35; 95% CI 1.15–1.58; $p = 0.0002$; $I^2 = 0\%$).

MA and RA

As shown in Figure 2c, based on 5 studies [13, 24, 37, 38, 41] comprising 885 patients and 221 major complications, preoperative incidence of sarcopenia, which was defined by MA/radiation attenuation on CT was associated with an increased risk of major complications (RR 1.40; 95% CI 1.14–1.73; $p = 0.002$; $I^2 = 4\%$).

Intramuscular Adipose Tissue Content

As shown in Figure 2d, based on 4 studies [20, 27, 31, 33] comprising 1,053 patients and 206 major complications, preoperative incidence of sarcopenia, which was defined by IMAC in CT was associated with an increased risk of major complications (RR 1.63; 95% CI 1.28–2.09; $p < 0.0001$; $I^2 = 0\%$).

HUAC, TPV, and LPMA

Due to the scarcity of original studies reporting the HUAC [35], TPV [12], and LPMA [14] indexes, the data were not pooled. In the 3 included studies, both lower HUAC (HR 1.55, 95% CI 0.98–2.45, $p = 0.014$) and TPV (OR 1.69, 95% CI 1.16–2.46, $p = 0.006$) were both associated with an increased risk of major postoperative complications. Also, patients with lower LPMA also showed a higher incidence of major complications when compared to those with higher LPMA ($p < 0.05$).

Discussion

With the developments in surgical technique and concept of perioperative management, the postoperative incidences of morbidity and mortality have greatly decreased; however, the condition is still not satisfactory, and the incidence of major complications after hepatopancreatobiliary surgery is still high [48–50]. The prevention and treatment of major complications have remained of paramount significance in improving the outcomes of patients, and the preoperative risk evaluation and clinical intervention are effective measures to prevent the occurrence of major complications. The role of sarcopenia as an effective predictor of postoperative complications has been reported in many clinical studies [51–53]. In patients with end-stage liver disease and awaiting transplantation, a model including sarcopenia could even surpass the MELD score in predicting waiting list mortality [54]. A variety of studies [19, 30, 32] have also explored the role of sarcopenia in the occurrence of complications in patients undergoing hepatopancreatobiliary surgery. In these studies, sarcopenia was defined by various indexes; however, the conclusions drawn from different studies and various indexes have remained controversial. This meta-analysis aimed to evaluate whether these different CT-assessed sarcopenia indexes could predict the postoperative risk of major complications in patients undergoing hepatopancreatobiliary surgery for malignancy. It was noted that the outcome validated the role of CT-assessed sarcopenia indexes, such as SMI, PMI, MA, and IMAC as effective predictors, although the cutoffs for these indexes to define sarcopenia still varied.

Sarcopenia is a broad concept that comprises the following 3 aspects: contents of muscle mass, muscle

Table 3. Definition of sarcopenia

Reference	Modality and level	Index	Sex-specific cutoff values	Prevalence of sarcopenia, <i>n</i> (%)	Way to identify cutoff values
Coelen et al. [19], 2015	CT/L3	SMI	Males: 46.8 cm ² /m ² ; females: 39.1 cm ² /m ²	42 (42)	Optimal stratification
Hamaguchi et al. [20], 2016	CT/umbilical	PMI, IMAC	PMI: males: 6.089 cm ² /m ² ; females: 4.020 cm ² /m ² IMAC: males: 0.324; females: -0.138	141 (28.7) 219 (44.5)	Adopt the standards of Hamaguchi 2015 [43]
Higashi et al. [21], 2016	CT/L3	SMI	SMI: males: 43.2 cm ² /m ² ; females: 35.3 cm ² /m ²	72 (50)	Median
Kobayashi et al. [11], 2017	CT/L3	SMI	SMI: males: 40.31 cm ² /m ² ; females: 30.88 cm ² /m ²	62 (13.3)	The data of 657 healthy LDLT donors [44]
Okumura et al. [13], 2017	CT/L3	SMI, MA	SMI: males: 52.5 cm ² /m ² ; females: 41.2 cm ² /m ² MA: males: 38.3; females: 31.0	69 (63.3) 53 (48.6)	Receiver operator characteristic curve
Coelen et al. [22], 2015	CT/L3	TPA	Males: 536 mm ² /m ² ; females: 378 mm ² /m ²	85 (33.2)	Lowest tertile
Takagi et al. [23], 2016	CT/L3	SMI	Males: 46.4 cm ² /m ² ; females: 37.6 cm ² /m ²	118 (46.5)	Optimum stratification
Voron et al. [24], 2015	CT/L3	SMI	Males: 52.4 cm ² /m ² ; females: 38.9 cm ² /m ²	59 (54.1)	Adopt the standards of Fearon 2011 [45]
Yabusaki et al. [25], 2016	CT/L3	SMI	Males: 43.75 cm ² /m ² ; females: 41.10 cm ² /m ²	89 (45.6)	Adopt the standards of Vledder 2012 [46]
Zhou et al. [26], 2015	CT/L3	SMI	Males: 43.75 cm ² /m ² ; females: 41.10 cm ² /m ²	33 (49.3)	Adopt the standards of Vledder 2012 [46]
Kobayashi et al. [27], 2018	CT/L3	SMI, IMAC	SMI: males: 40.31 cm ² /m ² ; females: 30.88 cm ² /m ² IMAC: males: -0.358; females: -0.229	24 (19.4) 74 (59.7)	The data of 657 healthy LDLT donors [44]
Lodewick et al. [28], 2014	CT/L3	SMI	Females: 41 cm ² /m ² Males: 43 cm ² /m ² (BMI <25); 53 cm ² /m ² (BMI >25)	80 (46.8)	Adopt the standards of Martin 2013 [47]
Peng et al. [29], 2011	CT/L3	TPA	TPA: 500 mm ² /m ²	41 (15.8)	Optimum stratification
Chakedis et al. [30], 2018	CT/L3	PMI	Males: 7.32 cm ² /m ² ; females: 5.16 cm ² /m ² (BMI >30) Males: 6.25 cm ² /m ² ; females: 4.21 cm ² /m ² (BMI <30)	30 (38.5)	Optimum stratification
Okumura et al. [31], 2016	CT/L3	PMI, IMAC	PMI: males: 6.15 cm ² /m ² ; females: 3.98 cm ² /m ² IMAC: males: -0.341; females: -0.096	71 (34.3) 91 (44.0)	Receiver operator characteristic curve
Amini et al. [12], 2015	CT/L3	TPA, TPV	TPA: males: 564.2 mm ² /m ² ; females: 414.5 mm ² /m ² TPV: males: 17.2 cm ³ /m ² ; females: 12.0 cm ³ /m ²	192 (25.2) 152 (19.9)	Optimum stratification
Choi et al. [32], 2018	CT/L3	SMI	Males: 45.3 cm ² /m ² ; females: 39.3 cm ² /m ²	60 (33.3)	Lowest tertile
Okumura et al. [33], 2015	CT/L3	PMI, IMAC	PMI: males: 5.896 cm ² /m ² ; females: 4.067 cm ² /m ² IMAC: males: -0.343; females: -0.256	64 (27.8) 142 (61.7)	Receiver operator characteristic curve
Okumura et al. [34], 2017	CT/L3	SMI, MA	SMI: males: 47.1 cm ² /m ² ; females: 36.6 cm ² /m ² MA: males: 35.1; females: 30.7	120 (39.9) 144 (47.8)	Receiver operator characteristic curve
Onesti et al. [14], 2016	CT/L4	LPMA	LPMA: 601–1,412 cm ²	86 (33.1)	Lowest tertile
Wagner et al. [35], 2018	CT/L3	HUAC	Males: 16.29; females: 15.69	145 (34.2)	Lowest quartile
Sui et al. [36], 2018	CT/L3	SMI	Males: 40.5 cm ² /m ² ; females: 33.5 cm ² /m ²	87 (24.6)	Lowest quartile
Van Rijssen et al. [37], 2017	CT/L3	SMI, MAI	SMI: males: 53.5 cm ² /m ² ; females: 46.4 cm ² /m ² MAI: males: 36.3; females: 36.0	130 (78) 81 (48.8)	Optimum stratification
Stretch et al. [38], 2018	CT/L3	SMI, MA	Males: 47.7 cm ² /m ² ; females: 36.5 cm ² /m ² MA: 30	50 (40.7) 31 (25.2)	Lowest 40th percentile Lowest quartile
Nishida et al. [39], 2016	CT/L3	SMI	Females: 41 cm ² /m ² Males: 43 cm ² /m ² (BMI <25); 53 cm ² /m ² (BMI >25)	132 (49.6)	Adopt the standards of Martin 2013 [47]
Takagi et al. [40], 2017	CT/L3	SBI	Males: 68.5 cm ² /m ² ; females: 52.5 cm ² /m ²	55 (25.1)	Lowest quartile
van Dijk et al. [41], 2017	CT/L3	RA	MAI: males: 33.9; females: 30.9	62 (33.3)	Lowest tertile
Takagi et al. [42], 2017	CT/L3	SBI	Males: 71.6 cm ² /m ² ; females: 55.3 cm ² /m ²	38 (24.7)	Lowest quartile

Fig. 2. a Forest plot comparing major complications in patients with low SMI versus patients with normal SMI. **b** Forest plot comparing major complications in patients with low PMI versus patients with normal PMI. **c** Forest plot comparing major complications in patients with low MA versus patients with normal MA. **d** Forest plot comparing major complications in patients with high IMAC versus patients with normal IMAC.

(For figure 1d see next page.)

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strength, and physical performance. It can be divided into 3 stages according to the severity of the condition. The “pre-sarcopenia” stage is characterized by the loss of muscle mass without any impact on muscle strength or physical performance. The “sarcopenia” stage is characterized by low muscle mass, plus low muscle strength or low physical performance. “Severe sarcopenia” is the stage identified when all 3 criteria of the definition are met [9]. The complexity of contents directly leads to the diversification of the methods to define sarcopenia. Dual X-ray absorptiometry, bio-electric impedance analysis, and CT can all be employed to measure muscle mass [9]. Even when only CT was employed, various indexes were used to define sarcopenia in different studies. According to these studies, CT-assessed sarcopenia indexes could be classified into 2 groups – SMI and PMI. While both SMI and PMI presented only the muscle quantity [19–20], MA, IMAC, HUAC, and LPMA were related to muscle quality [13, 14, 27, 35].

Among the muscle quantity indexes, SMI [19] calculated all the skeletal muscle mass, which included bilateral rectus abdominis, external oblique, internal oblique, transverse abdominal, psoas, and paraspinal muscles. However, PMI [20] calculated only the muscle mass of psoas. Apparently, measuring the psoas muscle area alone is much easier and less time-consuming; however, it is still unknown whether the psoas muscle alone adequately represents the muscle condition of the whole body. Rutten et al. [55] found a weak correlation between PMI and SMI in the assessment of sarcopenia in ovarian cancer, pointing out that psoas muscle was prone to be focally affected by degenerative diseases of the lumbar spine and this affection might be confused the muscle atrophy caused by cancer. Baracos [56] also indicated that psoas muscle alone does not reveal the muscle condition of the whole body. The characteristic of PMI as a reflection of the skeletal muscle condition of the whole body may need

further discussion. Indeed PMI was reported to be an effective predictor of major postoperative complications in many clinical studies [57–59] and our meta-analysis has also validated this role.

Among the muscle quality indexes, MA [13] represents the mean CT value of all the skeletal muscles in a targeted cross-sectional section and IMAC [20] is calculated by dividing the CT value of the multifidus muscles by the CT value of subcutaneous fat. Both HUAC [35] and LPMA [14] reveal both the muscle mass and the CT value of the bilateral psoas muscles, although the formulae for calculating these indexes vary. In previous studies [60, 61], sarcopenia was mainly defined by the skeletal muscle mass, and it was considered that muscle strength and physical performance were directly related to the muscle mass. However, it has now been noted that patients with adequate muscle mass might have a decreased level of muscle function and physical performance [37]. Therefore, numerous clinical researches have started to employ muscle quality to define sarcopenia. As CT-assessed muscle quality indexes, MA and IMAC have been confirmed to be valid predictors of major complications and survival in many studies [62, 63], and these conclusions were consistent with the outcomes of this meta-analysis. Owing to the scarcity of original publication, the overall effect of HUAC and LPMA could not be pooled; however, the predictive value of these 2 indexes has also been confirmed in other studies [64, 65].

In many studies, it has been verified that CT-assessed sarcopenia indexes are associated with postoperative short- and long-term outcomes; however, a consensus on cutoffs for these indexes is still lacking. Among the studies included in this analysis, some studies defined the cutoff by directly adopting predefined cutoffs and some performed optimum stratification or receiver operating characteristic curve. This lack of consensus has directly hampered sarcopenia evaluation in clinical practice and

academic communication, and more researches need to be performed to reach an agreement.

One point that deserves attention is that most of the I^2 values in this study were rather low, suggesting negligible heterogeneity, which further enhances the credibility of the outcome. In fact, the study designs of most of the included studies were similar owing to the nature of the prognosis analysis of sarcopenia, especially with respect to participants' selection and image analysis in the original studies. In the IMAC part (Fig. 2d), all of the included studies were retrospective cohort studies, all of the participants were Japanese and 3 studies used identical image-processing software. This uniformity in study designs might explain the rather small heterogeneity.

In summary, this meta-analysis showed that both CT-assessed muscle quantity sarcopenia indexes, SMI and PMI, and muscle quality indexes, MA and IMAC, were

effective predictors of major postoperative complications in patients following hepatopancreatobiliary surgery, and that more studies are needed to confirm the effectiveness of HUAC and LPMA. Thus, sarcopenia should be included in the preoperative risk evaluation, and to achieve this goal, a consensus on the cutoffs for sarcopenia indexes should soon be established.

Disclosure Statement

The authors declare no conflicts of interest.

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