Radiological Assessment of Sarcopenia and Its Clinical Impact in Patients with Hepatobiliary, Pancreatic, and Gastrointestinal Diseases: A Comprehensive Review

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Abstract

Sarcopenia is 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. The diagnosis of sarcopenia is based on documentation of two of the three criteria: low muscle mass, low muscle strength, and low physical performance. Imaging-based assessment of muscle mass is preferred in both clinical and research settings. Anthropometry for the evaluation of muscle mass is prone to errors and is not recommended in the clinical setting.

There is a lack of literature on the radiological assessment of sarcopenia and its association with prognosis in hepatobiliary, pancreatic, and gastrointestinal diseases. Thus, we aim to provide a review of studies that utilized radiological methods to assess sarcopenia and evaluate its impact on outcomes in patients with these diseases.

Keywords

- sarcopenia
- CT
- MRI

Introduction

Sarcopenia is 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.[1] Sarcopenia can be classified as primary and secondary according to the age at onset and associated inciting factors. Aging has been classically associated with primary sarcopenia, whereas secondary sarcopenia can result in any age group and is related to the underlying disease process.[2] Due to its increased relevance in determining outcomes in the geriatric population, cancer patients, and patients with chronic illness, sarcopenia is recognized as a disease entity in the International Classification of Diseases Tenth Revision (ICD-10).[3] The sarcopenia disease burden is expected to increase to around 200 million by the end of 2050 due to its higher prevalence in the long-term care and community-dwelling population.[4]

Sarcopenia progresses through three main stages: presarcopenia, sarcopenia, and severe. Prolonged muscle disuse results in fatty infiltration within the myofibrils with a reduction in muscle attenuation and conversion of type II myofibrils to type I. This leads to impaired muscle contractility and reduction in muscle power.[5] The current recommendation for diagnosis of sarcopenia is based on documentation of two of the three criteria: low muscle mass, low muscle strength, and low physical performance. Clinical examinations for detecting sarcopenia are effective when there is a reduction in muscle power, which may manifest as difficulty or inability to maintain posture, balance, or perform repeated maneuvers.[6] As a result, clinical examinations alone will not suffice for the early detection of

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Table 1 Sarcopenia measurement at CT

Parameters	Comments
Muscle area	Cross-sectional area within region of interest with attenuation −29 and +150 HU
Intermuscular adipose tissue area	Cross-sectional area within region of interest with attenuation −190 and −30 HU
Muscle density	Mean attenuation of tissue contained within the region of interest, after applying attenuation thresholds of −29 and +150 HU
Muscle fat density	Mean attenuation of tissue contained within the region of interest, after applying attenuation thresholds of −190 and −30 HU
Skeletal muscle index	Cross-sectional area of skeletal muscle at L3/height^2. The most widely used thresholds to diagnose CT sarcopenia are SMI <52.4 cm^2/m^2 in men and SMI <38.5 cm^2/m^2 in women
Psoas muscle index	Cross-sectional area of psoas muscles at L4 level/height^2

Abbreviations: CT, computed tomography; SMI, skeletal muscle index.

sarcopenia, and radiological investigations have become increasingly important. Dual-energy X-ray absorptiometry (DEXA), computed tomography (CT), and magnetic resonance imaging (MRI) are most widely used for the assessment of sarcopenia. Various parameters and criteria have been used to diagnose sarcopenia.[7]

Although, readily available, ultrasound is not reproducible and no widely accepted consensus is available for cut-off values of sarcopenia.

DEXA is readily available, cost-effective, and reproducible. It is a widely accepted modality for sarcopenia assessment. The lean mass derived from DEXA scan can be used to calculate the appendicular skeletal mass index (ASMI), which is a measure of sarcopenia on DEXA.

CT is considered the gold standard for body composition analysis and is used as a screening tool for assessment of sarcopenia (►**Table 1**). Skeletal muscle index (SMI) is the most commonly used parameter for sarcopenia. It is calculated at the level of L3 or L4 on a CT scan by segmentation (►**Fig. 1**).[1] Peripheral quantitative CT (pQCT) is a novel imaging modality primarily used to investigate bone mineral content. pQCT produces a cross-sectional image that enables quantification of three-dimensional tissue structure and skeletal muscle evaluation. It has extremely low radiation exposure and short scan time with relatively lower cost; however, it lacks standardization. The limitations of CT are exposure to ionizing radiation and inability to distinguish between intra-myocellular fat and intermuscular fat.

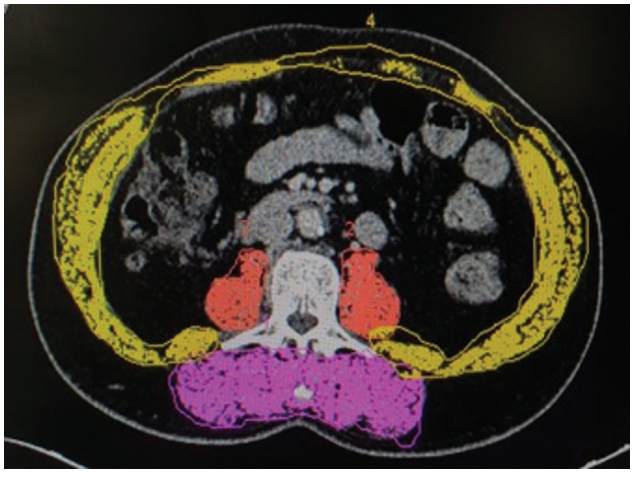

Fig. 1 Computed tomography (CT) image of a 50-year-old male who had vague abdominal pain. Image depicts utilization of segmentation technique in CT for calculating skeletal mass index at L3 level. In this case, the skeletal mass index was 60 cm^2/m^2 (>52.4 cm^2/m^2 cut-off), suggesting that there is no sarcopenia.

MRI can assess muscle composition by using several semiquantitative or quantitative sequences without the need of ionizing radiation. Muscle quality abnormalities, such as muscle disruption, edema, myosteatosis, and myofibrosis can also be evaluated on MRI (►**Fig. 2**). T2 mapping, magnetic resonance spectroscopy, Dixon sequence, diffusion tensor imaging, and strain rate tensor imaging can be used for assessment of sarcopenia.[4] Though MRI can differentiate between intra-myocellular fat and intermuscular fat (which was a drawback of CT), it is costly and time-consuming and there are no specific cut-offs for diagnosis of sarcopenia.

Sarcopenia is frequently detected in patients with hepatobiliary, gastrointestinal, and pancreatic disorders and has been associated with decreased overall survival (OS), a higher mortality rate, hospitalization, and postoperative complications. Because these patients frequently undergo imaging for diagnosis or follow-up, radiological tests can effectively assess sarcopenia in this group of patients.

This review aims to review studies that utilized radiological methods for assessing sarcopenia and evaluate its impact on outcomes in patients with hepatobiliary, pancreatic, and gastrointestinal diseases.

We systematically reviewed the PUBMED database with the search terms “sarcopenia” AND “imaging.” Studies were eligible for inclusion if they evaluated the impact of sarcopenia diagnosed by imaging in hepatobiliary, pancreatic, and gastrointestinal systems. Exclusion criteria included case series (<10 patients), case reports, letters to editors, reviews, meta-analysis, pediatric studies (age < 12 years), studies that evaluated sarcopenia clinically without utilizing radiological tests, and those with insufficient data. We collected data from the selected studies regarding patient demographics, type of study, the origin of the study population, the

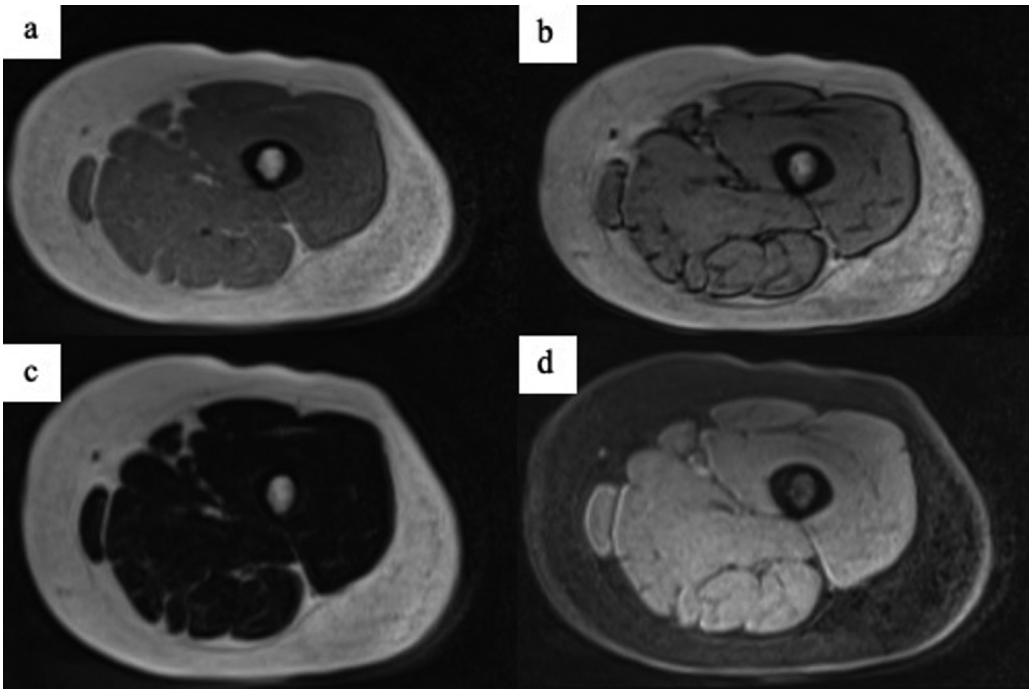

Fig. 2 Dixon MRI sequence of the right thigh in a 64-year-old woman. Axial T1W in-phase (**a**), out of-phase (**b**), 100% fat images (**c**), and 100% water images (**d**) are shown. The images depict reduction in the muscle bulk with fatty infiltration of the muscles (as seen by chemical shift artefact on out-of-phase image). These findings are suggestive of myosteatosis and sarcopenia. MRI, magnetic resonance imaging.

radiological method used for sarcopenia detection, measurement techniques, muscle site, area, and cut-off values. In addition, predictive outcomes and complications related to the prevalence and degree of sarcopenia in these diseases were recorded.

Radiological Assessment of Sarcopenia

Our literature search yielded 305 studies. After filtering out duplicates and screening titles and abstracts, 136 studies met the inclusion criteria.[8–143] ►**Table 2** enumerates all these studies.

These studies were published from 2012 to 2022. The total number of subjects/patients evaluated in these studies was 33,960. Abdominal CT was the most common imaging modality in these studies. The most common measurement parameter used for the measurement of sarcopenia in CT and MRI was SMI in 80 (58.8%) studies. The other commonly used parameters included psoas muscle area, transverse psoas muscle thickness (TPMT), and total abdominal muscle areas, which were used in 10, 4, and 3 studies, respectively. In MRI, sarcopenia was estimated using fat-free muscle areas, while in DEXA, ASMI was utilized. In addition to muscle area quantification, some of the studies used mean muscle attenuation values ($n = 14$) or intramuscular adipose content ($n = 6$) for qualitative assessment of myosteatosis. Most of these studies utilized L3 levels for the measurement of sarcopenia.

These studies' cut-off criteria for diagnosing sarcopenia showed marked heterogeneity with 24 different gender-specific cut-off values for SMI. The most common cut-off value for SMI was less than 52.4 cm^2/m^2 in males and less than 38.5 cm^2/m^2 in females. Few studies also employed cut-off values based on body mass index. Some studies relied on a change in SMI measurement on serial imaging. For assessment of myosteatosis, average muscle attenuation cut-off values varied from 31.4 to 41 HU.

Sarcopenia and Chronic Liver Disease

Eleven studies analyzed the impact of sarcopenia on clinical outcomes in patients with chronic liver disease (CLD; ►**Table 3**).[17,63,66,67,71,88,90,93,100,125,128]

There were 2,789 patients (aged 54 to 68.4 years). Most studies were retrospective. Two studies also recruited a control group.[67,90] Abdominal CT was the commonest modality used (nine studies). The commonest parameters were SMI and TPMT. In addition, one of these studies evaluated the relationship between sarcopenia and response after transjugular intrahepatic portosystemic shunts,[90] while two other studies compared sarcopenia with biochemical markers of cirrhosis.[71,125] Overall, these studies showed that sarcopenia has a negative impact on survival and is associated with the development of acute decompensation.

Sarcopenia and Hepatocellular Carcinoma

Cancer is associated with reduced fat and muscle stores with resultant wasting and cachexia in later stages. The prevalence of sarcopenia in patients with CLD and hepatocellular carcinoma (HCC) is higher (►**Table 4**).

Sarcopenia in this group of patients is associated with negative impact on outcomes. There were 34 studies (7,836 patients, age 53.9 to 73 years) reporting radiological assessment of sarcopenia and its prognostic impact in CLD patients with HCC.[10,15,16,18]

Table 2 Diagnostic modalities, measurement methods, and cut-off values for diagnosing sarcopenia

Author	Year	*N*	Disease	Modality	Parameter	Cut-off values (SMI and PMI in cm^2/m^2, TPMT in mm/m, PMA, SMA, and FFMA in cm^2, TPA in mm^2/m^2, muscle attenuation [MA] in HU), TPV in cm^3/m, ASMI in kg/m^2)
Peng et al[8]	2012	557	PDAC	CT	TPA	M < 611, F < 454
Tandon et al[9]	2012	142	LT	CT/MRI	SMI	M < 52.4, F < 38.5
Dodson et al[10]	2013	216	HCC	CT	TPA	M < 477, F < 338
Krell et al[11]	2013	207	LT	CT	TPA	M < 1449.2, F < 954.3
Montano-Loza et al[12]	2014	248	CLD	CT	SMI	M ≤ 53, F ≤ 41 (BMI ≥ 25) and ≤ 43 (for both M and F with BMI < 25)
Broughman et al[13]	2015	87	CRC	CT	SMI	M ≤ 53, F ≤ 41 (BMI ≥ 25) and ≤43 (for both M and F with BMI < 25)
Choi et al[14]	2015	484	PDAC	CT	SMI	M ≤ 42.2, F ≤ 33.9
Fujiwara et al[15]	2015	1,257	HCC	CT	SMI MA	M < 36.2, F < 29.6 M < 44.4, F < 39.3
Hamaguchi et al[16]	2015	477	HCC	CT	PMI	M < 6.089, F < 4.020
Hiraoka et al[17]	2015	988	CLD	CT	PMI	M < 4.24, F < 2.5
Iritani et al[18]	2015	217	HCC	CT	SMI	M < 36.0, F < 29.0
Jeon et al[19]	2015	145	LT	CT	PMI	M < 7.7 (20–50 y) and <6.6 (>50 y) F < 4.6 (20–50 y) and <4.4 (>50 y)
Jones et al[20]	2015	100	CRC	CT	PMA	M < 54.5, F < 38.5
Levolger et al[21]	2015	90	HCC	CT	SMI	M < 52.0, F < 39.5
Nault et al[22]	2015	52	HCC	CT	SMI	M < 55, F < 39
Okumura et al[23]	2015	230	PDAC	CT	PMI	M < 5.896, F < 4.067
Valero et al[24]	2015	96	HCC	CT	TPV	M < 34.9, F < 23.3
Voron et al[25]	2015	109	HCC	CT	SMI	M < 52.4, F < 38.9
van Vugt et al[26]	2015	206	CRC	CT	SMI	M ≤ 52.4, F ≤ 38.5
Zhang et al[27]	2017	114	IBD	CT	SMI	M ≤ 55, F ≤ 39
Kobayashi et al[28]	2016	241	HCC	CT	PMI	M < 6.089, F < 4.020
Holt et al[29]	2016	32	IBD	CT	SMA	M <161.9, F < 104.8
Fujikawa et al[30]	2016	69	IBD	CT	TPA	M < 56.7 and F < 35.5
Hamaguchi et al[31]	2016	492	HCC	CT	PMI	M < 6.089, F < 4.020
Nishida et al[32]	2016	266	PDAC	CT	SMI	M ≤ 53, F ≤ 41 (BMI ≥ 25) and ≤43 (for both M and F with BMI < 25)
Reisinger et al[33]	2016	87	CRC	CT	SMI	M < 50.5, F < 39.7
Sandini et al[34]	2016	124	PDAC	CT	TAMA	M ≤ 53, F ≤ 41 (BMI ≥ 25) and ≤43 (for both M and F with BMI < 25)
Zhang et al[35]	2017	204	IBD	CT	SMI	M ≤ 55, F ≤ 39
Yabusaki et al[36]	2016	195	HCC	CT	SMI	M ≤ 43.75 F ≤ 41.1
Black et al[37]	2017	447	GIC	CT	SMI	M < 43, F < 41
Bamba et al[38]	2017	72	IBD	CT	SMI	M ≤ 42, F ≤ 38

Table 2 (*Continued*)

Author	Year	*N*	Disease	Modality	Parameter	Cut-off values (SMI and PMI in cm^2/m^2, TPMT in mm/m, PMA, SMA, and FFMA in cm^2, TPA in mm^2/m^2, muscle attenuation [MA] in HU), TPV in cm^3/m, ASMI in kg/m^2)
Begini et al[39]	2017	92	HCC	CT	SMI	M $\leq$ 53, F $\leq$ 41 (BMI $\geq$ 25) and $\leq$43 (for both M and F with BMI $<$ 25)
Boer et al[40]	2016	91	CRC	CT	TPA/TAMA/MEAN HU	Cut-off not mentioned
Hamaguchi et al[41]	2017	250	LT	CT	SMI	M $<$ 40.31, F $<$ 30.88
Hanaoka et al[42]	2017	133	CRC	CT	MPM, TPA	345.8
Imai et al[43]	2017	351	HCC	CT	SMI	M $\leq$ 36, F $\leq$ 29
Cravo et al[44]	2017	71	IBD	CT	SMI	M $\leq$ 53, F $\leq$ 41 (BMI $\geq$ 25) and $\leq$43 (for both M and F with BMI $<$ 25)
Nishikawa et al[45]	2017	232	HCC	CT	SMI	M $\leq$ 36.2, F $\leq$ 29.6
Dedhia et al[46]	2018	29	IBD	MRI	PSM	3.55
Pedersen et al[47]	2017	178	IBD	CT	TPI	M $<$ 611, F $<$ 454
van Roekel et al[48]	2017	104	CRC	CT	SMI	47.8
Shintakuya et al[49]	2017	132	CP	CT	SMI	M $<$ 39.4, F $<$ 30.1
Takagi et al[50]	2017	219	PDAC	CT	SMI	M: 68.5, F $<$ 52.5
van Vugt et al[51]	2017	452	GI CANCER	CT	SMI	M $\leq$ 52.4, F $\leq$ 38.5
Wada et al[52]	2017	32	LT	CT	TPA TPV	M $<$ 796, F $<$ 506.8 M $<$ 146.9, F $<$ 86.2
Yamashima et al[53]	2017	40	HCC	CT	TPMT/HEIGHT	18.27 $\pm$ 3.09
Yoon et al[54]	2017	203	AP	CT	SMI	M $\leq$ 52.4, F $\leq$ 38.5
Ozola-Zālīte et al[55]	2019	265	CP	CT	TPA	M: 3.3, F: 2.5
Antonelli et al[56]	2018	96	HCC	CT	SMI	M $\leq$ 53, F $\leq$ 41 (BMI $\geq$ 25) and $\leq$43 (for both M and F, BMI $<$ 25)
Chae et al[57]	2018	36	LT	CT	PMI	308.8
van der Kroft et al[58]	2018	80	CRC	CT	SMI MA	M $\leq$ 53, F $\leq$ 41 (BMI $\geq$ 25) and $\leq$43 (for both M and F, BMI $<$ 25) 34.1
Deng et al[59]	2018	101	CRC	CT	ΔSMI	3.28
Huguet et al[60]	2018	173	CLD	CT	TPTI	15.22
Kobayashi et al[61]	2018	102	HCC	CT	SMI	M $\leq$ 42, F $\leq$ 38
Levolger et al[62]	2018	122	LARC	CT	ΔSMI	M: 1.95, F: 4.53
Praktiknjo et al[63]	2018	116	CLD	MRI	MA FFMA[a]	M $<$ 3,523 mm^2, F $<$ 3,153 mm^2 M $<$ 3,197 mm^2, F $<$ 2,895 mm^2
Shirai et al[64]	2018	402	HCC	CT	PMI	M $<$ 6.36, F $<$ 3.92
Sugimoto et al[65]	2018	323	PDAC	CT	SMI	M $\leq$ 49.9, F $\leq$ 39.4
Tachi et al[66]	2018	362	CLD	CT	SMI MEAN HU	M $<$ 42, F $<$ 38 $<$41 (BMI $<$ 25), $<$33 (BMI $\geq$ 25)

(*Continued*)

Table 2 (*Continued*)

Author	Year	*N*	Disease	Modality	Parameter	Cut-off values (SMI and PMI in cm^2/m^2, TPMT in mm/m, PMA, SMA, and FFMA in cm^2, TPA in mm^2/m^2, muscle attenuation [MA] in HU), TPV in cm^3/m, ASMI in kg/m^2)
Tachi et al[67]	2018	288	CLD	CT	SMA	<31
Takada et al[68]	2018	214	HCC	CT	SMI	M ≤ 42, F ≤ 38
Thiberge et al[69]	2018	162	IBD	CT	SMI	M ≤ 55.4, F ≤ 38.9
van Vugt et al[70]	2018	224	LT	CT	SMI	M < 50.4, F < 41.8
Velasquez et al[71]	2018	211	CLD	CT	SMI	M ≤ 53, F ≤ 41 (BMI ≥ 25) and ≤43 (for both M and F, BMI < 25)
van Vugt et al[72]	2018	816	CRC	CT	SMI MEAN HU	M ≤ 53, F ≤ 41 (BMI ≥ 25) and ≤43 (for both M and F, BMI < 25) < 41 (BMI < 25), <33 (BMI ≥ 25)
Xiao et al[73]	2018	3,051	CRC	CT	SMI	M ≤ 52.3, F ≤ 38.6
Acosta et al[74]	2019	168	LT	CT	SMI	M ≤ 52.4, F ≤ 38.5
Bieliuniene et al[75]	2019	100	CP/PDAC	CT/MRI	SMI	M < 45.4, F < 34.4
Choi et al[76]	2018	188	LARC	CT	SMI	M ≤ 52.4, F ≤ 38.5
Dohzono et al[77]	2019	78	GIC	CT	PMA	M < 482.8, F < 326.3
Esser et al[78]	2019	172	LT	CT	TPA PD PMI SMI	M < 1,561, F < 1,464 <38.5 M < 6.36, F < 3.92 M < 50 and F < 39
Galata et al[79]	2020	230	IBD	CT/MRI	SMI	M ≤ 41.5, F ≤ 31.8
Hamaguchi et al[80]	2019	606	HCC	CT	SMI/IMAC	M < 40.31, F < 30.88
Herod et al[81]	2019	169	CRC	CT	MEAN PSOAS DENSITY	<43.5
Jang et al[82]	2019	284	CP	CT	SMI	M < 52.4, F < 38.5
Jochum et al[83]	2019	47	LARC	CT	SMI	M ≤ 52.4, F ≤ 38.5
Kamo et al[84]	2019	277	LT	CT	SMI/IMAC	M ≤ 40.3, F ≤ 30.8
Kitano et al[85]	2019	110	IHS	CT	SMI	F ≤ 41, M ≤ 53 (BMI ≥ 25) and M/F ≤ 43 (BMI < 25)
Kobayashi et al[86]	2019	465	HCC	CT	SMM	M < 40.31, F < 30.88
Kuo et al[87]	2019	126	LT	CT	SMI	M < 48
Lindqvist et al[88]	2019	53	LT	DEXA/CT	ASMI[b] FFMI[b], SMI	M < 7.59 F < 5.47 M < 43 F < 41
Mardian et al[89]	2019	100	HCC	CT	SMI/MEAN HU	M ≤ 36.2, F ≤ 29.6
Praktiknjo et al[90]	2019	168	CLD	CT	TPMT	M: 17.8, F: 14
Agalar et al[91]	2020	65	CRC	CT	SMI	M ≤ 52.4, F ≤ 38.5
Badran et al[92]	2020	262	HCC	CT	SMI	M ≤ 50, F ≤ 39
Beer et al[93]	2020	265	CLD	MRI	TPMT	M < 12, F < 8
Cabo et al[94]	2020	97	LT	CT	PMA	M < 784.0, F < 642.1
Celentano et al[95]	2021	31	IBD	MRI	TPA/ SMA	M: 11.93, F: 9.77 M: 73.49, F: 65.85
Dhaliwal et al[96]	2020	57	LT	CT/MRI	PMA	M < 1,561, F < 1,464

Table 2 (*Continued*)

Author	Year	*N*	Disease	Modality	Parameter	Cut-off values (SMI and PMI in cm^2/m^2, TPMT in mm/m, PMA, SMA, and FFMA in cm^2, TPA in mm^2/m^2, muscle attenuation [MA] in HU), TPV in cm^3/m, ASMI in kg/m^2)
Pinto Dos Santos et al[97]	2020	368	LT	CT	PMI	6.3
Han et al[98]	2020	1,384	LARC	CT	SMI	M $\leq$ 52.4, F $\leq$ 38.5
Grillot et al[99]	2020	88	IBD	CT	SMI	M $\leq$ 52.4, F $\leq$ 38.5
Romagna et al[100]	2020	83	CLD	CT	SMI	M $\leq$ 50, F $\leq$ 39
Salman et al[101]	2020	52	CLD	CT	SMI	F $\leq$ 41, M $\leq$ 53 (BMI $\geq$ 25) and M/F $\leq$ 43 (BMI $<$ 25)
Schaffler-Schaden et al[102]	2020	85	CRC	CT	SMI	M $<$ 43, F $<$ 41
Shakhbazov et al[103]	2020	34	CP	CT	TPA	M $<$ 492, F $<$ 362
Shirdel et al[104]	2020	974	CRC	CT	SMI/SMR	39.4, 41.0
Takada et al[105]	2020	153	HCC	CT	PMI	M $<$ 6.36, F $<$ 3.92
Tankel et al[106]	2020	185	CRC	CT	TIP	F $\leq$ 41, M $\leq$ 53 (BMI $\geq$ 25) and M/F $\leq$ 43 (BMI $<$ 25)
Trikudananthan et al[107]	2020	138	CP	CT	SMI	M $\leq$ 52.4, F $\leq$ 38.5
Xie et al[108]	2020	298	CRC	CT	SMI	M $\leq$ 49.5, F $\leq$ 29.9
Yeh et al[109]	2020	136	HCC	CT	PMI	M $<$ 4.24, F $<$ 2.50
Zager et al[110]	2021	121	IBD	CT/MRI	PMA	95.12 $\pm$ 263.2
Akce et al[111]	2021	57	HCC	CT/MRI	SMI	M $<$ 43, F $<$ 41
Akturk et al[112]	2021	107	AP	CT	TIP	NA
Alsebaey et al[113]	2021	262	HCC	CT/MRI	SMI	M $<$ 50, F $<$ 39
Argillander et al[114]	2021	233	CRC	CT	ΔSMI	$>$1 SD
Bamba et al[115]	2021	187	IBD	CT	SMI	M $<$ 42, F $<$ 38
Box et al[116]	2021	220	PDAC	CT	SMI	M $\leq$ 53, F $\leq$ 41 (BMI $\geq$ 25) and $\leq$43 (for both M and F BMI $<$ 25)
Cárcamo et al[117]	2021	359	CRC	CT	SMI MEAN HU	M $\leq$ 53, F $\leq$ 41 (BMI $\geq$ 25) and $\leq$43 (for both M and F, BMI $<$ 25) $<$41 (BMI $<$ 25), $<$33 (BMI $\geq$ 25)
Boparai et al[118]	2021	44	IBD	CT	SMI	M $\leq$ 36.5, F $\leq$ 30.2
Guichet et al[119]	2021	82	HCC	MRI	FFMA[a]	M $\leq$ 31.97, F $\leq$ 28.95
Irwin et al[120]	2021	106	LT	CT	SMI	M $<$ 50, F $<$ 39
Jang et al[121]	2021	160	HCC	CT	PMA	M $<$ 3.33 F $<$ 2.38
Lee et al[122]	2021	2,333	CRC	CT	SMI	M $<$ 52.4, F $<$ 38.5
Lim et al[123]	2021	266	HCC	CT	SMI	M $<$ 49.6, F $<$ 43.1
Maddalena et al[124]	2021	56	CRC	CT	SMI	M $\leq$ 53, F $\leq$ 41 (BMI $\geq$ 25) and $\leq$43 (for both M and F BMI $<$ 25)
Mihai et al[125]	2021	52	CLD	CT	SMI	M $\leq$ 52.4, F $\leq$ 38.5
Salinas-Miranda et al[126]	2021	105	PDAC	CT	ΔSMI	2.8
Murachi et al[127]	2021	34	CRC	CT	SMI	M $\leq$ 6.36, F $\leq$ 3.24
Paternostro et al[128]	2021	203	CLD	CT	TPMT	M $<$ 12: F $<$ 8
Qayyum et al[129]	2021	36	HCC	CT	T12 SMI	M $<$ 11.4, F $<$ 8.2

(*Continued*)

Table 2 (*Continued*)

Author	Year	*N*	Disease	Modality	Parameter	Cut-off values (SMI and PMI in cm^2/m^2, TPMT in mm/m, PMA, SMA, and FFMA in cm^2, TPA in mm^2/m^2, muscle attenuation [MA] in HU), TPV in cm^3/m, ASMI in kg/m^2)
Jördens et al[130]	2021	75	IHCC	CT	SMI, PMI	54.26, 1.685
Seror et al[131]	2021	110	HCC	CT	SMI	M < 52, F < 38
Williet et al[132]	2021	79	PDAC	CT	PMI	M < 5.73, F < 4.37
Wu et al[133]	2021	137	HCC	CT	TPA	M < 39.1
Wu et al[134]	2021	271	LT	CT	PMI	2.63
Yasueda et al[135]	2022	56	IBD	CT	SMI	M < 6.36, F < 3.92
Yıldırım et al[136]	2021	219	PDAC	CT	SMI	M < 52, F < 38
Zheng et al[137]	2021	75	HCC	CT	ΔPMA	NA
Wackenthaler et al[138]	2022	37	LT	CT	PMA	M < 52.4, F < 38.5
Chong et al[139]	2022	1,011	LT	CT	ΔSMI	29.4
da Silva Dias et al[140]	2022	178	CRC	CT	SMI	M ≤ 49.82, F ≤ 35.85
Özkul et al[141]	2022	115	PDAC	CT	SMI	M ≤ 56.44, F ≤ 43.36
Rom et al[142]	2022	117	PDAC	CT	SMI	M < 52, F < 38
Sato et al[143]	2022	92	CRC	CT	SMI	M < 42.6, F < 36.8

Abbreviations: AP, acute pancreatitis; ASMI, appendicular skeletal muscle index; CLD, chronic liver disease; CP, chronic pancreatitis; CRC, colorectal carcinoma; CT, computed tomography; DEXA, dual energy X-ray absorptiometry; FFMA, fat free muscle area; FFMI, fat free muscle index; GIC, gastrointestinal cancer; SMI, skeletal muscle index; HCC, hepatocellular carcinoma; IBD, inflammatory bowel disease; IMAC, intramuscular adipose content; LARC, locally advanced rectal carcinoma; LSN, liver surface nodularity; LT, liver transplant; MA, muscle area; MPM, morphological changes in psoas muscle; MRI, magnetic resonance imaging; PDAC, pancreatic ductal adenocarcinoma; PMA, psoas muscle area; PMI, psoas muscle index; PSMA, paraspinous muscle area; PTI, transverse psoas muscle thickness index; TAMA, total abdominal muscle area; TPA, total psoas area; TPMT, transverse psoas muscle thickness; TPV, total psoas volume.
Note: All these parameters are used in CT except in [a]MRI and [b]DEXA.

21,24,25,28,31,36,39,43,45,53,56,61,64,68,74,80,86,89,92,101,105,109,111,119,-121,123,129,131,133,137 There were 32 retrospective and 2 prospective studies. The studies included both newly diagnosed and advanced HCCs. Twelve studies included patients with HCC who underwent hepatectomy or transplant. In six studies, patients were on systemic chemotherapy or immunotherapy[53,56,68,111,129,133] and in another seven studies, patients underwent locoregional therapies.[10,21,61,109,119,123,137] The most common modality was CT ($n = 33$), and the commonest parameter was SMI. Most studies reported poor outcomes including OS and HCC recurrence in patients with sarcopenia.

Sarcopenia and Liver Transplant

In this subgroup, there were 20 retrospective studies (4,168 patients) that assessed outcomes of sarcopenia in patients who underwent liver transplantation or had been waitlisted for the transplant procedure (►**Table 5**).[9,11,12,19,41,52 57,60,70,78,84,87,94,96,97,113,120,133,138,139]

Two studies included patients who underwent emergent liver transplant following acute liver failure.[87,139] SMI was the most common parameter. Sarcopenia was associated with increased mortality, graft failure, reduced OS, and increased postoperative complications and infections in these studies, except for the study by Dhaliwal et al,[96] in which there was no difference in clinical outcomes between sarcopenic and nonsarcopenic patients. A study by van Vugt et al showed that sarcopenia is associated with increased health care costs and longer hospital stay following transplantation.[70]

Sarcopenia and Inflammatory Bowel Disease

Studies predominantly assessed the relationship of sarcopenia with adverse outcomes and postoperative complications in patients with inflammatory bowel disease. There were 16 studies (1,589 patients, age 17.9 to 43.8 years).[27,29,30,35,38,44,46,47,69,79,95,99,110,115,118,135] Ten studies specifically were related to Crohn's disease (►**Table 6**). One study assessed the feasibility of MRI for the detection of skeletal muscle mass.[95] In contrast, the rest of the studies evaluated the association of sarcopenia with adverse outcomes such as the need for surgery, increased hospitalization, abscesses, and fistula formation. CT was the commonest imaging modality used, and SMI was the parameter employed for the assessment of sarcopenia and muscle mass.

Sarcopenia and Biliary, Pancreatic, Gastrointestinal, and Colorectal Malignancy

Association between cancer and muscle function has been increasingly evaluated over the last decade. There is an association between sarcopenia with mortality, OS,

Table 3 Studies reporting association of sarcopenia with outcomes in patients with chronic liver disease

Author	Year	Country of origin	Study type	Study population	*N*	Age (y)	Modality: parameter	Outcomes
Beer et al[93]	2020	Austria	Retrospective	CLD	265	5	MRI: TPMT	Sarcopenia was an independent risk factor for mortality in patients with CLD ($p = 0.005$).
Praktiknjo et al[90]	2019	Germany	Prospective	CLD patients undergoing TIPS	168	56[a]	CT: TPMT/ height	Patients with sarcopenia showed significantly higher rates of mortality, ascites, overt hepatic encephalopathy, and acute on chronic liver failure than the nonsarcopenic group ($p < 0.001$).
Praktiknjo et al[63]	2018	Germany	Retrospective	CLD patients	116	58[a]	MRI: FFMA	Sarcopenic patients showed no clinical improvement after TIPS and had higher mortality.
Lindqvist et al[88]	2019	Sweden	Retrospective	CLD with liver transplant	53	57[a]	DEXA/CT: ASMI/SMI	ASMI measured with DEXA is a useful alternative method to SMI measured with CT when a CT scan is not clinically indicated or available.
Hiraoka et al[17]	2015	Japan	Retrospective	Chronic hepatitis	988	68.4	CT: psoas index	Frequency of presarcopenia was higher in chronic hepatitis regardless of age ($p < 0.01$)
Tachi et al[66]	2018	Japan	Retrospective	CLD	362	68.4	CT: SMI	Lower BMI ($p < 0.001$), myosteatosis ($p < 0.001$), lower ALT ($p = 0.010$), and female gender ($p = 0.034$) were significantly associated with skeletal volume loss.
Tachi et al[67]	2018	Japan	Prospective	CLD	288	67.5	CT: SMA	Cirrhosis ($p < 0.001$) and lower SMA ($p = 0.017$) were significantly associated with HCC development in patients with CLD.
Paternostro et al[128]	2021	Austria	Prospective	CLD with HVPG measurements	203	55	CT: TPMT	Sarcopenia was an independent risk factor for mortality ($p = 0.007$), irrespective of severity of portal hypertension.
Romagna et al[100]	2020	Brazil	Retrospective	CLD	83	56	CT: SMI	Sarcopenia has a high prevalence among patients with CLD. However, it is not significantly associated with predictors of severity of cirrhosis.
Moctezuma-Velázquez et al[71]	2018	Canada	Retrospective	CLD	211	55	CT: SMI	Low testosterone levels are associated with sarcopenia in male cirrhotic patients ($p = 0.002$), and the frequency of hypotestosteronemia ($p = 0.006$) was also higher. There were no significant differences in female patients.
Mihai et al[125]	2021	Romania	Retrospective	HCV CLD treated with antivirals	52	59	CT: SMI	Low creatinine serum level correlates with sarcopenia ($p = 0.031$)

Abbreviations: ACLF, acute on chronic liver failure; ALT, alanine aminotransferase; ASMI, appendicular skeletal mass index; CLD, chronic liver disease; FFMA, free fat muscle area; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HVPG, hepatic venous pressure gradient; MELD (model for end-stage liver disease); SMA, skeletal mass attenuation; SMI, skeletal mass index; TIPS, transjugular Intrahepatic portosystemic shunt; TPMT, transverse psoas muscle thickness.
[a]Median, rest mean.

Table 4 Studies reporting association of sarcopenia with outcomes in patients with hepatocellular carcinoma

Author	Year	Country of origin	Study type	Study population	Number	Age (y)	Modality: parameter	Outcomes
Fujiwara et al[15]	2015	Japan	Retrospective	HCC	1,257	68.8	CT: SMI, MA	Sarcopenia ($p = 0.001$) and visceral adiposity ($p = 0.005$) independently predicted mortality in patients with HCC.
Jang et al[121]	2021	Republic of Korea	Retrospective	HCC + hepatectomy	160	55	CT: PMI, PMA, visceral adipose tissue	PMI showed a positive correlation with PMA ($\rho = 0.493$, $p < 0.001$) in HCC patients. In curatively resected HCC patients, sarcopenia and high visceral adiposity predict poor OS but not RFS, while PMA did not predict OS.
Akce et al[111]	2021	Atlanta, Georgia	Retrospective	HCC + immunotherapy.	57	NA	CT: SMI	After controlling for baseline Child–Pugh score and NLR, sex-specific sarcopenia does not predict OS.
Seror et al[131]	2021	France	Retrospective	HCC	110	67.7	CT: SMI	The combination of liver surface nodularity and sarcopenia help predict severe postoperative complications ($p < 0.001$).
Badran et al[92]	2020	Egypt	Prospective	HCC	262	59.6	CT: SMI	Sarcopenia was associated with lack of response to therapy, liver decompensation, and higher mortality in HCC.
Mardian et al[89]	2019	Indonesia	Prospective	HCC	100	55.03	CT: SMI, MA	Patients with sarcopenia had shorter median survival than the reference groups (both $p < 0.0001$).
Voron et al[25]	2015	France	Retrospective	HCC + hepatectomy	109	61.6	CT: skeletal muscle mass	Sarcopenia was found to be an independent predictor of poor OS (HR = 3.19; $p = 0.013$) and DFS (HR = 2.60; $p = 0.001$) in patients with HCC.
Salman et al[101]	2020	Egypt	Prospective	HCC	52	53.9	CT: SMI	Sarcopenia was an independent prognostic factor for 1-year deaths.
Acosta et al[74]	2019		Retrospective		168	59		

Table 4 (*Continued*)

Author	Year	Country of origin	Study type	Study population	Number	Age (y)	Modality: parameter	Outcomes
		Lexington, Kentucky		HCC + transplant for HCC			CT: skeletal muscle mass	Alpha-fetoprotein level >100 mg/dL ($p = 0.034$) and male gender ($p = 0.002$) were independently associated with the presence of sarcopenia in patients who underwent liver transplant for HCC.
Guichet et al[119]	2021	New York, United States	Retrospective	HCC + 90Y radioembolization.	82	65	MRI: FFMA	Patients with sarcopenia were found to have increased mortality at 180 days (31.8 vs. 8.9%) and 1 year (68.2 vs. 21.2%).
Imai et al[43]	2017	Japan	Retrospective	HCC	351	70.4	CT: skeletal muscle volume	Sarcopenic patients died significantly earlier than nonsarcopenic patients ($p = 0.007$).
Begini et al[39]	2017	Rome, Italy	Retrospective	HCC	92	71.9	CT: SMI	Mean OS was reduced in sarcopenic HCC patients ($p = 0.001$).
Takada et al[68]	2018	Japan	Retrospective	HCC + chemotherapy − sorafenib	214	71	CT: SMI	OS in patients with presarcopenia tended to be worse than in patients without presarcopenia (median 252 vs. 284 days; $p = 0.16$).
Nishikawa et al[45]	2017	Japan	Retrospective	Unresectable HCC	232	72	CT: SMI	The objective response rate and disease control rate to sorafenib in the sarcopenia group were significantly lower compared with those in the nonsarcopenia group ($p = 0.0146$ and $p = 0.0151$, respectively).
Takada et al[105]	2020	Japan	Retrospective	HCC	153	73	CT: SMI	The median event-free survival in HCC was significantly worse in presarcopenia ($p = 0.016$)
Qayyum et al[129]	2021	United States	Retrospective	HCC + immunotherapy	36	70	CT: SMI	Sarcopenia was associated with reduced survival and HCC necrosis in patients treated with systemic

(*Continued*)

Table 4 (*Continued*)

Author	Year	Country of origin	Study type	Study population	Number	Age (y)	Modality: parameter	Outcomes
								targeted therapy ($p = 0.037$ for women, $p = 0.015$ for men).
Levolger et al[21]	2015	Netherlands	Retrospective	HCC + thermal ablation	90	62	CT: SMI	Sarcopenia was associated with poor survival in patients with potentially curable HCC, mainly due to an increase in treatment-related mortality ($p = 0.002$).
Antonelli et al[56]	2018	Rome, Italy	Retrospective	HCC + chemotherapy − sorafenib	96	69	CT: SMI	The sarcopenic group showed shorter OS ($p = 0.01$) and shorter time on treatment with sorafenib ($p = 0.004$).
Wu et al[133]	2021	Taiwan	Retrospective	HCC + chemotherapy − sorafenib	137	70	CT: muscle area at L3.	Patients with sarcopenia exhibited poorer OS than patients without sarcopenia ($p < 0.001$).
Hamaguchi et al[80]	2019	Japan	Retrospective	HCC + hepatectomy	606	68	CT: SMI	OS and RFS were significantly lower ($p < 0.001$ and $p = 0.016$) among patients with sarcopenia undergoing resection for HCC.
Shirai et al[64]	2018	Japan	Retrospective	HCC + hepatectomy	402	67	CT: PMI	Preoperative low muscle mass in males and low muscle quality in males and females were significantly associated with pulmonary dysfunction in patients undergoing hepatectomy for HCC.
Zheng et al[137]	2021	China	Retrospective	HCC + TACE	75	54.5	CT: BMD, cross-sectional area of paraspinal muscles	Cross-sectional area of paraspinal muscles, Child–Pugh class, and portal vein thrombosis were associated with prognosis of HCC.
Kobayashi et al[86]	2019	Japan	Retrospective	HCC + hepatectomy	465	65	CT: skeletal muscle mass	Patients with sarcopenic obesity displayed worse median OS ($p = 0.002$) and worse median RFS ($p = 0.003$). Preoperative sarcopenic

Table 4 (*Continued*)

Author	Year	Country of origin	Study type	Study population	Number	Age (y)	Modality: parameter	Outcomes
								obesity was an independent risk factor for death ($p = 0.005$) and HCC recurrence ($p = 0.006$) after hepatectomy.
Yeh W et al[109]	2020	Taiwan.	Retrospective	HCC + thermal ablation	136	65.4	CT: PMI	Presarcopenia was found to be an independent prognostic factor of OS ($p = 0.026$), but not of recurrence of HCC after radiofrequency ablation.
Lim J et al[123]	2021	Korea	Retrospective	HCC + TACE	266	69.9	CT: SMI	Patients with sarcopenia had a shorter life expectancy than those without sarcopenia ($p = 0.007$) after TACE.
Kobayashi et al[61]	2018	Japan	Retrospective	HCC + TACE	102	69	CT: SMI	Sarcopenia was found to be an independent prognostic factor in patients who underwent TACE for HCC ($p = 0.037$).
Kobayashi et al[28]	2015	Japan	Retrospective	HCC + hepatectomy	241	65	CT: IMAC, PMI	Postoperative depletion of skeletal muscle quality at 6 months was associated with HCC recurrence ($p = 0.024$).
Hamaguchi et al[16]	2016	Japan	Retrospective	HCC + hepatectomy	492	68[a]	CT: IMAC	Preoperative high IMAC was an independent risk factor for increased major postoperative complications ($p = 0.049$) and infectious complications ($p = 0.021$).
Yabusaki et al[36]	2016	Japan	Retrospective	HCC + hepatectomy	195	66	CT: SMI	Sarcopenia was associated with higher cumulative recurrence rate ($p = 0.13$).
Iritani et al[18]	2015	Japan	Retrospective	HCC	217	72	CT: SMI	Sarcopenic patients showed a significantly lower OS than those without sarcopenia ($p = 0.004$). Sarcopenic patients who were overweight (BMI > 22) died earlier ($p = 0.012$).
Dodson et al[10]	2013	United States	Retrospective	HCC + TACE	216	60		

(*Continued*)

Table 4 (*Continued*)

Author	Year	Country of origin	Study type	Study population	Number	Age (y)	Modality: parameter	Outcomes
							CT: total psoas area	Sarcopenia was independently associated with increased risk of death ($p = 0.04$) after TACE.
Valero et al[24]	2015	United States	Retrospective	HCC + hepatectomy	96	61.9	CT: total psoas area	The presence of sarcopenia was an independent predictive factor of postoperative complications ($p = 0.01$).
Hamaguchi et al[16]	2015	Japan	Retrospective	HCC + hepatectomy	477	68[a]	CT: intramuscular adipose tissue content	The OS and RFS were significantly lower in patients with sarcopenia than in nonsarcopenic patients ($p < 0.0001$, $p = 0.0012$, respectively). Sarcopenia was significantly associated with death ($p < 0.0001$) and HCC recurrence ($p = 0.0007$) after hepatectomy.
Yamashima et al[53]	2017	Japan	Retrospective	HCC + chemotherapy − sorafenib	40	71.5	CT: PMI	Patients with mild muscle atrophy exhibited a significantly longer OS compared with patients with severe muscle atrophy ($p = 0.045$).

Abbreviations: BMD, bone mineral density; EFS, event-free survival; FFMA, free fat muscle area; HCC, hepatocellular carcinoma; MA, mean muscle attenuation; MA, mean muscle attenuation; NLR, neutrophil-to-lymphocyte ratio; OS, overall survival; PFS progression-free survival; PMA, psoas muscle attenuation; PMI, psoas muscle index; SMA, skeletal mass attenuation; SMI, skeletal muscle index; TACE, trans arterial chemoembolization; Y90, yttrium 90.
[a]Median, rest mean.

Table 5 Studies reporting association of sarcopenia with outcomes in liver transplant patients

Author	Year	Country of origin	Study design	Study population	*N*	Age (y)	Modality: parameter	Outcomes
Irwin et al[120]	2021	South Africa	Retrospective	LT recipients	106	50[a]	CT: SMI	One year after transplant, myosteatosis was associated with higher mortality ($p = 0.049$), greater risk of allograft failure ($p = 0.021$), and longer hospital and ICU stays compared with those without myosteatosis.
Kuo et al[87]	2019	United States	Retrospective	Urgent LT	126	53[a]	CT: SMI	Sarcopenia was strongly associated with posttransplant mortality in men.
Alsebaey et al[113]	2021	Egypt	Retrospective	LT recipients	262	59.6	CT: SMI	MELD sarcopenia was found to be better prognostic model than the MELD scores alone in HCC patients awaiting liver transplantation.
Wu et al[134]	2021	Taiwan	Retrospective	LT recipients	271	51.93	CT: PMI	Female recipients with major postoperative complications had significantly lower mean PMI values ($p = 0.028$).
Krell et al[11]	2013	United States	Retrospective	LT recipients	207	51.7	CT: total psoas area	A lower TPA was associated with increased risk of posttransplant infectious complications and mortality ($p = 0.003$).
Dhaliwal et al[96]	2020	United States	Retrospective	Re-OLT	57	50	CT: PMI	Patients without sarcopenia had a trend toward longer median time between the first and second transplant.
Pinto Dos Santos et al[97]	2020	Germany	Retrospective	OLT recipients	368	57.5[a]	CT: PMI	Sarcopenia was found to be an independent predictor of early post-LT survival in male patients and not in females.
Tandon et al[9]	2012	Canada	Retrospective	Listed for LT	142	53[a]	CT: SMI	Male sex, Child–Pugh class C cirrhosis were independent predictors of sarcopenia. Sarcopenia was associated with increased waiting-list mortality.
Jeon et al[19]	2015	Korea	Retrospective	Follow-up LT recipients	145	50.2	CT: PMI	Newly developed sarcopenia was associated with increased mortality.
Cabo et al[94]	2020	Spain	Retrospective	LT recipients	97	55.8	CT: PMI	Sarcopenia was associated with a higher incidence of postoperative complications ($p = 0.08$).

(*Continued*)

Table 5 (*Continued*)

Author	Year	Country of origin	Study design	Study population	*N*	Age (y)	Modality: parameter	Outcomes
Chong et al[139]	2022	United States	Retrospective	Urgent LT	1011		CT: SMI	Progressive perioperative sarcopenic deterioration was associated with inferior patient and graft survival in high-acuity LT.
Esser et al[78]	2019	Austria	Retrospective	Listed for LT	172	54.6	CT: total psoas area, psoas muscle density	Sarcopenia was associated with inferior patient and graft survival ($p < 0.05$).
Chae et al[57]	2018	Korea	Retrospective	LT recipients	473	52	CT: PMI	PMI change $\leq -11.7\%$ between the day before surgery and postoperative day 7 was an independent predictor of patient mortality after LDLT.
van Vugt et al[70]	2018	Netherlands	Retrospective	Listed for LT	224	56	CT: SMI	It was found that an incremental increase in SMI was significantly associated with a decrease in total hospital costs ($p = 0.045$).
Kamo et al[84]	2019	Japan	Retrospective	LT recipients	277	54	CT: SMI	Patients with sarcopenic obesity showed worse OS after LT compared with nonsarcopenic/nonobese patients ($p = 0.002$).
Montano-Loza et al[12]	2014	Canada	Retrospective	LT recipients	248	55	CT: SMI	Sarcopenic patients had longer hospital stays ($p = 0.005$) and a higher risk of perioperative bacterial infections ($p = 0.04$) after LT.
Hamaguchi et al[41]	2017	Japan	Retrospective	LT recipients	250	54[a]	CT: SMI	Low SMI was associated with increased risk of death after LDLT ($p = 0.002$).
Huguet et al[60]	2018	France	Retrospective	Listed for LT	173	54.7	CT: psoas thickness	Low psoas thickness was associated with increased mortality ($p = 0.034$).
Wada et al[52]	2017	Japan	Retrospective	LT recipients	32	54	CT: total psoas volume, total psoas area	Preoperative volume of the skeletal muscle is a better predictor of postoperative risks in LDLT than preoperative area of the skeletal muscle.

Abbreviations: LT, liver transplantation; MELD, modified end stage liver disease score; OLT, orthotopic liver transplant; OS, overall survival; PMI, psoas muscle index; POC, postoperative complications; Re-OLT, liver re-transplantation; SMI, skeletal muscle index.

[a]Median, rest mean

Table 6 Studies reporting association of sarcopenia with outcomes in patients with inflammatory bowel disease

Author	Year	Country	Study type	Study population	Age (Y)	Modality: parameter	Outcomes
Boparai et al[118]	2021	India	Retrospective	CD	34	CT: SMI	Sarcopenia and increased visceral fat associated with increased rate of surgery ($p = 0.01$) and ($p = 0.002$), respectively.
Grillot et al[99]	2020	France	Retrospective	CD	NA	CT: SMI	Sarcopenic CD patients had significantly more abscesses (51 vs. 16.7%, $p = 0.001$), hospitalizations (61.2 vs. 36.1%, $p = 0.022$), and digestive surgery (63.3 vs. 27.8%, $p = 0.001$) than nonsarcopenic patients during the follow-up.
Zhang et al[27]	2017	China	Prospective	CD	32	CT: SMI	Major POC in patients with sarcopenia (15.7 vs. 2.3%, $p = 0.027$) compared with nonsarcopenic patients.
Zager et al[110]	2021	Israel	Retrospective	CD	35.9	CT/MRI: PMI	Patients with major POC had lower mean psoas muscle index ($p = 0.03$).
Bamba et al[38]	2017	Japan	Retrospective	IBD	NA	CT: SMI	Presence of sarcopenia ($p = 0.015$) was a significant factor predicting intestinal resection. Cumulative operation-free survival rate was significantly lower for sarcopenic patients ($p = 0.003$).
Yasueda et al[135]	2022	Japan	Retrospective	CD	NA	CT: SMI	Operation time was significantly longer, hemorrhage occurred more often in the sarcopenia group. CD activity index at 6 months post-op had significantly decreased in the nonsarcopenia group ($p = 0.01$) but not in the sarcopenia group ($p = 0.20$).
Celentano et al[95]	2021	United Kingdom	Retrospective	CD	NA	MRI: TPA/SMA	Incidence of 30-day POC was higher in patients with sarcopenia.
Zhang et al[35]	2017	China	Prospective	IBD	NA	CT: SMA/VFA/SFA	Sarcopenia ($p = 0.007$) was a negative predictor of high Mayo score in UC patients. Sarcopenic patients with UC had high probability of need for colectomy.
Cravo et al[44]	2017	Portugal	Retrospective	CD	43	CT: SMI	Sarcopenia associated with increased risk of severe phenotypes (stricturing/penetrating disease and recurrent surgeries) in patients with CD.
Bamba et al[115]	2021	Japan	Prospective	IBD	NA	CT: SMI	Sarcopenia was a significant factor for predicting intestinal resection ($p = 0.015$). The cumulative operation-free survival rate was significantly lower for sarcopenic patients than in all IBD patients ($p = 0.003$).
Galata et al[79]	2020	Germany	Retrospective	CD	37.2	CT/MRI: SMI	SMI was an independent risk factor for major postoperative complications ($p = 0.002$; odds ratio= 0.914).
Holt et al[29]	2016	Australia	Retrospective	CD	43.8	CT: SMA	Sarcopenia found to be more prevalent in ambulatory CD patients and is predictive of lower bone mineral density.
Dedhia et al[46]	2018	United States	Retrospective	UC	17.9	MRI: PSMA	Reduced PSMA was associated with increased complication rates ($p = 0.04$).
Fujikawa et al[30]	2016	Japan	Retrospective	UC	39.8	CT: TPA	Sarcopenia was an independent risk factor for surgical-site infections ($p = 0.03$).
Pedersen et al[47]	2017	United States	Retrospective	IBD	42.7	CT: TPI	Sarcopenia affects surgical outcomes among patients younger than 40 years
Thiberge et al[69]	2018	France	Retrospective	CD	41	CT: SMI	SMI was reduced in patients with adverse outcome, compared with patients without surgery or death ($p = 0.07$)

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; PMI, psoas muscle index; POC, postoperative complications; PSMA, paraspinal muscle area; SFA, subcutaneous fat area; SMA, skeletal muscle area; SMI, skeletal muscle index; TPA, total psoas area; TPI, total psoas index; UC, ulcerative colitis; VFA, visceral fat area.

recurrence-free survival, and postoperative complications. In this review, we found 13 studies[8,14,23,32,34,65,85,126,130,132,136,141,142] that reported on pancreatic and biliary malignancies and 31 studies[13,20,26,33,37,40,42,48,51,58,59,62,72,73,76,77,81,83,91,98,102,104,106,108,114,117,122,124,127,140,143] that reported on gastrointestinal and colorectal malignancies (►**Tables 7** and **8**).

Six studies compared outcomes of sarcopenia in these malignancies following chemotherapy.[76,91,124,126,127,144] Most studies also report the effect of sarcopenia on postoperative complications and OS in these patients who had undergone surgical resection of malignancy. One study had reported the influence of sarcopenia and muscle mass on the development of pancreatic fistula formation in patients following pancreatoduodenectomy.[32] A study by van Vugt et al showed that sarcopenia is associated with increased health care costs in patients with malignancy of the alimentary tract.[51]

Sarcopenia and Pancreatitis

Ten studies evaluated the radiological detection of sarcopenia in patients with pancreatitis (chronic pancreatitis in eight and acute pancreatitis in two).[49,50,54,55,75,82,103,107,112,116] Of these studies, two studies evaluated outcomes in chronic pancreatitis patients undergoing total pancreatectomy with auto islet transplantation[103,107] (►**Table 9**).

Expert Opinion and Future Directions

Sarcopenia is gaining importance as a prognostic marker of several diseases. In the context of hepatobiliary, pancreatic, and gastrointestinal disorders, more than 100 studies have reported the negative impact of sarcopenia assessed at radiological investigations on clinical outcomes. Radiological assessment is preferred to evaluate skeletal muscle mass, a key component of sarcopenia. Anthropometry-based evaluation of muscle mass is unreliable. CT is the most common radiological modality utilized for assessing sarcopenia as it is widely available. Most patients with hepatobiliary, pancreatic, and gastrointestinal diseases undergo CT as a part of their evaluation. Various parameters are used to evaluate sarcopenia at CT. Several cut-off values have been proposed. Due to this variability, as well as the need for manual measurements, the utilization of imaging for the clinical assessment of sarcopenia is hampered. Therefore, till recently, radiological assessment of sarcopenia has been used in the research setting only. Standardizing radiological methods and the cut-off for assessing sarcopenia is necessary. Automating measurements will significantly help allow the seamless incorporation of imaging in the clinical assessment of sarcopenia. Artificial intelligence can be utilized to achieve this. Finally, in the future, indices that account for both obesity and sarcopenia may be developed, and these may fully explore the impact of body composition on the outcomes.

Table 7 Studies reporting association of sarcopenia with outcomes in biliary and pancreatic malignancy

Author	Year	Country	Study type	Study population	*N*	Age mean	Modality: parameter	Outcomes
Jördens et al[130]	2021	Germany	Retrospective	Cholangiocarcinoma	75	70	CT: SMI/PMI	Sarcopenia is associated with significantly reduced median OS.
Sandini et al[34]	2016	Italy	Retrospective	PDAC post-pancreatoduodenectomy	124	72	CT: TAMA	Sarcopenic obesity is a strong predictor of major complications after pancreatoduodenectomy for cancer.
Sugimoto et al[65]	2018	United States	Retrospective	PDAC post-pancreatoduodenectomy	323	65	CT: SMI	Smaller sex-standardized SMI associated with shorter OS ($p = 0.011$) and shorter RFS ($p = 0.007$)
Özkul et al[141]	2022	Turkey	Retrospective	PDAC	115	64.9	CT: SMI	SMI was found as poor prognostic factors for OS ($p = 0.009$).
Choi et al[14]	2015	Korea	Retrospective	PDAC + chemotherapy	484	60	CT: SMI	Sarcopenia during chemotherapy ($p < 0.001$) was poor prognostic factor for OS
Okumura et al[23]	2015	Japan	Retrospective	PDAC post-pancreatoduodenectomy	230	67	CT: PMI	Low muscle mass and low muscle quality were independent prognostic factors of poor OS ($p < 0.001$; $p < .001$)

Author Contribution

S. F.: data curation, writing—original draft preparation; S. S.: data curation, writing—original draft preparation;

Table 7 (*Continued*)

Author	Year	Country	Study type	Study population	*N*	Age mean	Modality: parameter	Outcomes
								and RFS ($p = 0.007$; $p = 0.004$), respectively.
Rom et al[142]	2022	Israel	Retrospective	PDAC post-pancreatoduodenectomy	111	67	CT: SMI/IMAC/VSR	Low SMI correlated with poor OS ($p = 0.007$), DSS ($p = 0.006$), and RFS ($p = 0.01$)
Nishida et al[32]	2016	Japan	Retrospective	PDAC post-pancreatoduodenectomy	266	69	CT: skeletal muscle mass	Sarcopenia ($p = 0.007$) was an independent risk factor for the development of clinically relevant POPF.
Salinas-Miranda et al[126]	2021	Canada	Retrospective	PDAC + chemotherapy	105	61.7	CT: ΔSMI	ΔSMI was prognostic for OS with a HR of 1.2 (95% CI: 1.08–1.33, $p = 0.001$).
Peng et al[8]	2012	United States	Retrospective	PDAC post-pancreatoduodenectomy	557	65.7	CT: TPA	Sarcopenia associated with an increased risk of death at 3 years (HR = 1.63; $p < 0.001$).
Williet et al[132]	2021	France	Retrospective	PDAC	79	NA	CT: PMI	Sarcopenia associated with decreased OS.
Yıldırım et al[136]	2021	Spain	Retrospective	PDAC	219	66.6	CT: SMI	Survival of the patients with normal nutritional status was significantly longer than that of those who were malnourished ($p < 0.001$).
Kitano et al[85]	2019	Japan	Prospective	Cholangiocarcinoma	110	71[a]	CT: SMI	Presence of sarcopenia was an independent predictor of poor OS ($p = 0.0008$).

Abbreviations: DSS, disease-specific survival; HR, hazard ratio; IMAC, intramuscular adipose tissue content; OS, overall survival; PDAC, pancreatic ductal adenocarcinoma; PMI, psoas muscle index; POC, postoperative complications; POPF, postoperative pancreatic fistula; RFS, recurrence-free survival; SMI, skeletal muscle index; TAMA, total abdominal muscle area; TPA, total psoas area; VSR, visceral-to-subcutaneous adipose tissue area ratio; ΔSMI, change of skeletal muscle index.
[a]Median, rest mean

Table 8 Studies reporting association of sarcopenia with outcomes in gastrointestinal/colorectal malignancies

Author	Year	Country	Study type	Study population	*N*	Age (years)[a]	Modality: parameter	Outcomes
Dohzono et al[77]	2019	Japan	Retrospective	GIC	78	68.3	CT: PMA	Lower paravertebral muscle density was an independent poor prognostic factor (HR: 2.23 [95% CI: 1.24–3.99], $p = 0.007$).
Deng et al[59]	2018	Taiwan	Retrospective	CRC	101	63.7	CT: SMI and MA	Progressive sarcopenia after diagnosis of colorectal cancer has a significant negative prognostic association with OS and PFS ($p < 0.05$).
Murachi et al[127]	2021	Japan	Retrospective	CRC + chemotherapy	34	65	CT: SMI	Sarcopenia was significantly associated with poorer OS (median 3.2 vs. 5.3 months, $p = 0.031$).
Maddelena et al[124]	2021	Italy	Retrospective	CRC + chemotherapy	56	67	CT: SMI	Baseline sarcopenia did not affect survival and was not related to worse treatment toxicity[b].
Hanaoka et al[42]	2017	Japan	Retrospective	CRC + surgery	133	68.3	CT: morphologic change of the psoas muscle (MPM) at L3 vertebrae	Severe sarcopenia was identified as an independent factor associated with infectious complications (OR: 4.26, 95% CI: 1.38–13.10).
Broughman et al[13]	2015	United States	Retrospective	CRC + surgery	87	77	CT: SMI	Sarcopenia was found to be highly prevalent among older patients with early-stage CRC.
Lee et al[122]	2021	Korea	Retrospective	CRC	2333	60.4	CT: SMI	Both OS and RFS were lower in patients with persistent sarcopenia 2 to 3 years postoperatively than in those who recovered (OS: 96.2% vs. 90.2%, $p = 0.001$; RFS: 91.1% vs. 83.9%, $p = 0.002$).
Xie et al[108]	2020	China	Retrospective	CRC	298	67	CT: SMI	Sarcopenia was an independent risk factor for POCs ($p = 0.008$) and independent predictor for poor PFS ($p < 0.001$) and OS ($p < 0.001$).
Agalar et al[91]	2020	Turkey	Prospective	CRC + chemotherapy	65	54.4	CT: SMI	Low SMI is associated with adverse postoperative outcomes in elderly patients undergoing CRC surgery.
Argillander et al[114]	2021	Netherlands	Retrospective	CRC + surgery	233	76	CT: ΔSMI	Muscle wasting was associated with reduced OS (HR: 2.8, $p = 0.002$).
van Roekel et al[48]	2017	Netherlands	Retrospective	CRC	104	64.3	CT: SMI	No significant association of sarcopenia with long-term health-related quality of life in stage I–III CRC survivors[b].

Table 8 (*Continued*)

Author	Year	Country	Study type	Study population	*N*	Age (years)[a]	Modality: parameter	Outcomes
Reisinger et al[33]	2016	Netherlands	Prospective	CRC	87	65.6	CT: SMI	Low muscle mass in patients undergoing surgery for CRC was associated with an increased postoperative inflammatory response ($p = 0.007$).
van Vugt et al[72]	2018	Netherlands	Prospective	CRC + surgery	816	70	CT: SMI/mean HU	Low skeletal muscle mass ($p = 0.018$) and density ($p = 0.045$) were independently associated with severe POC.
Xiao et al[73]	2018	Canada	Cross-sectional study	CRC	3051	56	CT: SMI	Pre-existing co-morbidities were more prevalent in sarcopenic patients with CRC.
Jochum et al[83]	2019	United States	Retrospective	LARC	47	59.3	CT: SMI	POCs were significantly higher in sarcopenic patients ($p = 0.03$).
Cárcamo et al[117]	2021	Chile	Retrospective	CRC	359	64	CT: SMI/mean HU	Sarcopenia does not independently influence survival in nonmetastatic CRC[b].
da Silva Dias et al[140]	2022	Portugal	Retrospective	CRC + chemotherapy	178	62	CT: SMI	Sarcopenia was associated with higher incidence of drug-limiting toxicities ($p = 0.030$).
Sato et al[143]	2022	Japan	Retrospective	CRC + stent + surgery	92	70.5	CT: SMI	Sarcopenia was an independent predictor of POC ($p = 0.001$) and infectious complications ($p < 0.001$).
Choi et al[76]	2018	South Korea	Retrospective	LARC	188	61	CT: SMI	Sarcopenia was negatively associated with OS in locally advanced CRC patients who underwent neoadjuvant chemoradiation therapy and curative resection ($p = 0.013$).
Herrod et al[81]	2019	United Kingdom	Retrospective	CRC + surgery	169	68	CT: mean psoas density at the level of the L3 vertebra	Sarcopenia was associated with an increased risk of POCs ($p = 0.007$) and an increased risk of anastomotic leak ($p = 0.026$).
Shirdel et al[104]	2020	Sweden	Retrospective	CRC	974	67.1	CT: SMI/SMR	Sarcopenia and myosteatosis were associated with decreased cancer-specific survival.
Tankel et al[106]	2020	Israel	Retrospective	CRC + surgery (LAP)	185	68	CT: TPI and HUAC	Sarcopenia was significantly associated with preoperative comorbidities, peri-operative mortality, and a greater incidence of respiratory, cardiac, and serious POC and those aged >75 were at particular risk of morbidity ($p = 0.002$)

(*Continued*)

Table 8 (*Continued*)

Author	Year	Country	Study type	Study population	*N*	Age (years)[a]	Modality: parameter	Outcomes
								following elective laparoscopic CRC surgery.
Han et al[98]	2020	Korea	Retrospective	LARC	1384	59	CT: SMI	5-year OS rate was significantly lower in sarcopenic patients ($p = 0.003$) and patients with sarcopenic obesity ($p = 0.02$).
Schaffler-Schaden et al[102]	2020	Austria	Retrospective	CRC	85	77	CT: SMI	SMI is a significant prognostic factor for early cancer recurrence in nonobese CRC patients ($p = 0.04$).
van der Kroft et al[58]	2018	Germany	Prospective	CRC	80	69	CT: SMI/MA	Muscle attenuation and sarcopenia were not significantly associated with postoperative complications[b].
Levolger et al[62]	2018	Netherlands	Retrospective	LARC	122	61	CT: ΔSMI	Loss of skeletal muscle mass during chemoradiotherapy was independently associated with lower DFS ($p = 0.025$) and distant metastasis-free survival ($p = 0.013$).
Black et al[37]	2017	United Kingdom	Prospective	CRC and EGC	447	75	CT: SMI	Among the CRC patients, survival was shorter for those with sarcopenia ($p = 0.017$) or low levels of subcutaneous fat ($p = 0.005$).
Boer et al[40]	2016	Netherlands	Retrospective	CRC + surgery	91	71.2	CT: TPA/TAMA/mean HU	Sarcopenia was an independent risk factor for POCs ($p \leq 0.002$) and an independent predictor of worse OS (HR: 8.54; 95% CI: 1.07–68.32).
Jones et al[20]	2015	United Kingdom	Prospective	CRC	100	70	CT: PMA	Sarcopenia was associated with a significantly increased risk of developing major complications ($p = 0.01$).
van Vugt et al[26]	2015	Netherlands	Retrospective	CRC	206	62.1	CT: SMI	Sarcopenic patients underwent significantly more reoperations than the nonsarcopenic patients (25.6 vs. 12.1%; $p = 0.012$). SMI independently associated with the risk of severe POC ($p = 0.018$).
van Vugt et al[51]	2017	Netherlands	Prospective	GIC	452	65	CT: SMI	Low skeletal muscle mass was independently associated with increased hospital costs ($p = 0.015$).

Abbreviations: CI, confidence interval; CRC, colorectal carcinoma; DFS, disease-free survival; EGC, esophagogastric cancer; GIC, gastrointestinal cancer; HR, hazard ratio; HUAC, Hounsfield unit average calculation; LARC, locally advanced rectal carcinoma; MA, muscle attenuation; OR, odds ratio; OS, overall survival; PMA, psoas muscle area; POC, postoperative complications; SMI, skeletal muscle index; SMR, skeletal muscle radiodensity; STS, short-term survival; TAMA, total abdominal muscle area; TPA, total psoas area; TPI, total psoas index.

[a]Mean age.

[b]Studies which showed no significant correlation between sarcopenia and clinical outcome.

Table 9 Studies reporting association of sarcopenia with outcomes in pancreatitis

Author	Year	Country	Study design	Study population	*N*	Age (years)	Modality: parameter	Outcomes
Trikudananthan et al[107]	2020	United States	Prospective	CP undergoing TPAIT	138	40	CT: SMI	Sarcopenia ($p = 0.023$) was an independent predictor of low islet yield.
Ozola-Zālīte et al[55]	2019	Latvia, Lithuania, and Denmark	Retrospective	CP	265	54.3	CT: TPA	Sarcopenia was found to be present in 1 of 5 patients with CP (prevalence 20.4%)
Bieliuniene et al[75]	2019	Lithuania, Kazakhstan, Denmark	Prospective cohort	CP	100	58.3	CT/MRI: SMI	34% patients had sarcopenia. The presence of osteopenia/osteoporosis predicted the presence of sarcopenia ($p = 0.02$).
Shakhbazov et al[103]	2020	United States	Retrospective	CP undergoing TPAIT	34	43.1	CT: TPA	Patients with sarcopenia experienced more complications (83.3%) compared with patients without sarcopenia (50%). However, differences were not significant ($p = 0.31$).[a]
Box et al[116]	2021	United States	Retrospective	CP	220	64.1[b]	CT: SMI/SFI	SFI $\geq$2.9 was significantly associated with POPFs (OR: 8.2).
Shintakuya et al[49]	2017	Japan	Prospective	CP	132	70[b]	CT: SMI	Sarcopenia was independently associated with pancreatic exocrine insufficiency ($p < 0.001$).
Jang et al[82]	2019	South Korea	Prospective	CP	284	62.6	CT: SMI	Sarcopenic obesity was the only independent predictor for POPF (OR: 2.65).
Akturk et al[112]	2021	Turkey	Retrospective	AP	107	NA	CT: TPI	Lower volume and density of psoas muscle was associated with worse CTSI and larger pancreatic necrosis in patients with AP.
Yoon et al[54]	2017	South Korea	Retrospective	AP	203	53.3	CT: SMI/SAT/VAT/VMR	VMR demonstrated the highest area under the ROC curve (0.757, 95% confidence interval: 0.689–0.825) in predicting moderately severe or severe AP.
Takagi et al[50]	2017	Japan	Retrospective	CP	219	65.9	CT: SMI	Sarcopenia was significantly associated with a higher incidence of in-hospital mortality ($p = 0.004$) and infectious complications ($p < 0.001$).

Abbreviations: AP, acute pancreatitis; CI, confidence interval; CP, chronic pancreatitis; CTSI, computed tomography severity index; POC, postoperative complications; POPF, postoperative pancreatic fistula; ROC curve, receiver operating characteristic curve; SAT, subcutaneous adipose tissue; SFI, subcutaneous fat area indexed for height; SMI, skeletal muscle index; TPA, total psoas area; TPAIT, total pancreatectomy with auto islet transplantation; TPI, total psoas index; VAT, visceral adipose tissue; VMR, visceral muscle to fat ratio.

[a]Sarcopenia is not associated with outcome in this study.

[b]Median, rest mean.

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