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REVIEW

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Low skeletal muscle mass and postoperative morbidity in surgical oncology: a systematic review and meta-analysis

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Abstract

Background Sarcopenia might function as an indicator for frailty, and as such as a risk factor for the development of postoperative complications. The aim of this study was to meta-analyse the relation between preoperative sarcopenia and the development of severe postoperative complications in patients undergoing oncological surgery.

Methods PubMed and Embase databases were systematically searched from inception until May 2018. Included were studies reporting on the incidence of severe postoperative complications and radiologically determined preoperative sarcopenia. Studies reporting the skeletal muscle as a continuous variable only were excluded. Data were extracted independently by two reviewers. Random effect meta-analyses were applied to estimate the pooled odds ratio (OR) with 95% confidence intervals (95% CI) for severe postoperative complications, defined as Clavien-Dindo grade ≥3, including 30-day mortality. Heterogeneity was evaluated with I^2 testing. Analyses were performed overall and stratified by measurement method, tumour location and publication date.

Results A total of 1924 citations were identified, and 53 studies (14 295 patients) were included in the meta-analysis. When measuring the total skeletal muscle area, 43% of the patients were sarcopenic, versus 33% when measuring the psoas area. Severe postoperative complications were present in 20%, and 30-day mortality was 3%. Preoperative sarcopenia was associated with an increased risk of severe postoperative complications (OR_{pooled}: 1.44, 95% CI: 1.24–16.8, $P<0.001$, I^2=55%) and 30-day mortality (OR_{pooled}: 2.15, 95% CI: 1.46–3.17, $P<0.001$, I^2=14%). A low psoas mass was a stronger predictor for severe postoperative complications compared with a low total skeletal muscle mass (OR_{pooled}: 2.06, 95% CI: 1.37–3.09, OR_{pooled}: 1.32, 95% CI: 1.14–1.53, respectively) and 30-day mortality [OR_{pooled}: 6.17 (95% CI: 2.71–14.08, OR_{pooled}: 1.80 (95% CI: 1.24–2.62), respectively]. The effect was independent of tumour location and publication date.

Conclusions The presence of low psoas mass prior to surgery, as an indicator for sarcopenia, is a common phenomenon and is a strong predictor for the development of postoperative complications. The presence of low total skeletal muscle mass, which is even more frequent, is a less informative predictor for postoperative complications and 30-day mortality. The low heterogeneity indicates that the finding is consistent over studies. Nevertheless, the value of sarcopenia relative to other assessments such as frailty screening is not clear. Research is needed in order to determine the place of sarcopenia in future preoperative risk stratification.

Keywords Sarcopenia; Postoperative complications; Radiology; Surgery

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Introduction

Surgery is part of the multimodality treatment of most solid tumours. Though very effective, surgical treatment may lead to postoperative complications.[1,2] Especially in frail patients, these complications can lead to permanent functional loss and negatively influence survival and long-term quality of life.[3,4] The benefits of surgery should therefore be carefully weighed against these negative sequelae.[5,6] For this purpose, there has been increasing attention for methods to identify frail patients in recent years.[4] In some cases, the presence of factors associated with frailty may lead to the decision not to perform a certain surgical procedure. In other cases, interventions may be undertaken to improve a patient's performance preoperatively in order to undergo surgery under the most optimal circumstances.

The presence of preoperative sarcopenia can be a possible method for detecting frail patients. Sarcopenia describes the loss of skeletal muscle mass associated with increased age, so called primary sarcopenia, or secondary to systemic conditions such as cancer or an inflammatory state.[7,8]. The advantage of the use of sarcopenia over other screening methods for frailty, such as extensive questionnaires and assessments, is its objective, quantitative and relatively quick nature. Furthermore, the presence of sarcopenia can be determined on images routinely obtained in the oncological workup, and does therefore not require additional testing of the patient. Sarcopenia can be diagnosed with the use of clinical tests and/or measurement of the skeletal muscle mass.[8] A common method for the detection of sarcopenia is the CT-based estimation of the lean skeletal muscle mass.[9,10]

Both a negative and a positive effect of the presence of sarcopenia on the development of severe complications have been reported. [11–18] Therefore, we performed a systematic review and meta-analysis of all the studies that recorded incidences of severe postoperative complications in patients with or without sarcopenia, undergoing oncological surgery for any type of solid tumour.

Methods

Search strategy

The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines were followed in this systematic review and meta-analysis.[19,20]

We searched the PubMed and Embase databases for studies reporting on sarcopenia and postoperative complications published form the inception of each database to May 1, 2018. The search terms were 'sarcopenia', 'postoperative complications', 'neoplasms', and 'surgery', with synonyms for each (see Supplementary File S1 for search strategy). No filters or restrictions were applied.

Selection criteria

The following studies were included: Studies should report on the development of severe postoperative complications in the first 30 days after surgery in adult patients. Patients had to undergo surgical resection of any type of malignancy. Only studies were included that applied a CT-based assessment of skeletal muscle mass with use of the skeletal muscle area (SMI) and psoas area (TPI) on the level of the third lumbar vertebra. Furthermore, only studies were included when the presence or absence of sarcopenia was based on a clearly defined cut-off. Studies were excluded when skeletal muscle mass was reported as a continuous variable. Studies describing only a specific type of postoperative complication or studies that did not distinguish severe complications from less severe or overall complications were excluded. Non-English studies were excluded. When different publications described the same set of patients, the most recent study was included in the here presented meta-analysis.

Endpoints

The primary endpoint was the presence of severe postoperative complications within the first 30 days after surgery. Severe complications were classified with use of the Clavien-Dindo scale; complications with score of $\geq$3 were considered severe postoperative complications.[21] The 30-day mortality was considered separately. Data about the 30-day mortality was obtained in two different ways: firstly, as the 30-day mortality apart from the severe complications in studies that reported them separately and secondly, as a grade V complication on the Clavien-Dindo scale, being a subgroup of the total number of postoperative complications. Therefore, in the latter studies, the data about patients with grade V complications were used in both the analysis regarding the severe postoperative complications and in the analysis regarding the 30-day mortality.

Data extraction and quality assessment

The first author, year of publication, total study population, median age, gender, location of the malignancy, number of patients with and without sarcopenia and the number of patients with postoperative complications was extracted from each study.

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We assessed the methodological quality of the included studies using the Newcastle-Ottawa scale for cohort studies.[22] This scale assesses the patient selection, comparability and outcomes. The outcomes of the assessments were converted in order to classify each study as having a good, fair or poor methodological quality. Two reviewers (L. W. and A. H.) independently performed the process of study selection, data extraction and quality assessment. Disagreements were resolved by consensus.

Statistical analysis

For each study. we calculated odds ratios (ORs) and 95% confidence intervals (95% CI) for postoperative complications in patients with and without preoperative sarcopenia. A random-effect model was used for all analyses as we expected considerable variation in types of cancer and cut-off values for the definition of sarcopenia. Heterogeneity was assessed with use of the I^2 statistics and was interpreted as follows: 0–40% low heterogeneity, 30–60% moderate heterogeneity, 50–90% substantial heterogeneity and 75–100% considerable heterogeneity.[23] To explore sources of heterogeneity, we performed subgroup analysis with studies stratified by: measurement method of sarcopenia (total skeletal muscle mass versus psoas mass), tumour location and publication date. The stratification was performed for both severe postoperative complications and 30-day mortality separately. We only included strata considering two or more studies. The null hypothesis, that the relationship between sarcopenia and postoperative complications or 30-day mortality is equal across the defined strata, was tested with a X^2 test. All analyses were performed with use of Review Manager (RevMan) 5.3. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Results

Included studies

A total of 1924 articles was identified by our search. A total of 140 studies met the eligibility criteria and of those studies 53 were included in the meta-analysis (*Figure* 1). Cross reference search did not provide additional studies.

Quality of the included studies

A summary of the methodological quality of the included studies is presented in *Table* 1. A total of 20 studies (38%) did have a good methodological quality. In the remaining 33 studies (62%), the methodological quality was poor, due to a low score on the comparability domain.

Study characteristics

The included studies concerned 14 295 patients. The most reported tumour location was hepatiopancreaticobiliary (22/53 studies), followed by upper gastro intestinal (GI) (12/53 studies), and lower GI (12/53 studies). The estimated pooled median age of the included studies was 61 years. A total of 25 (47%) studies reported a median age $\geq$65 years. The majority of the patients, 78%, in the included studies was male. Half (26/53) of the included studies were published before 2017 and 27 studies in 2017 and 2018. Characteristics of the included studies are displayed in *Table* 2.

Sarcopenia

In 40/53 studies (75%), the total skeletal muscle mass was used to determine sarcopenia. The psoas mass was used in 13/53 (25%) of the studies. The cut-off values used to determine low total skeletal muscle mass and low psoas mass, respectively, are listed in *Table* S1, ranging from 40.5 to 71.6 in male patients and 33.5 to 55.3 in female patients for low total skeletal mass and ranging 4.3–7.8 in males and 3.8–6.4 in females for low psoas mass. A total of 5938 patients (42%) were sarcopenic. In studies using the total skeletal muscle mass, a total of 4849 patients (43%) were considered sarcopenic, versus 1089 patients (33%) in studies measuring the psoas area.

Severe postoperative complications

A total of 2920 patients (20%) with severe postoperative complications were recorded. A total of 1398 patients with sarcopenia (24%) and 1522 patients without sarcopenia (18%) developed a severe postoperative complication (see *Figure* 2). OR_{pooled}: 1.44 (95% CI 1.24–16.8, $P<0.001$).

The I^2 was 55%, representing moderate heterogeneity. The outcomes of the analysis did not change when only studies with good methodological quality were included in the analysis (*Figure* S1). Subgroup analysis on the effect of the use of total skeletal muscle mass or psoas mass showed a significant difference between the subgroups (P 0.04). The pooled OR for the effect of the presence of sarcopenia on the development of severe postoperative complications was 1.32 (95% CI 1.14–1.53) in studies using total skeletal muscle mass and 2.06 (95% CI 1.37–3.09) in studies using the psoas mass (*Figure* 3a). Subgroup analysis based on tumour location or date of publication showed no differences between the subgroups. (*Figures* S2 and S3).

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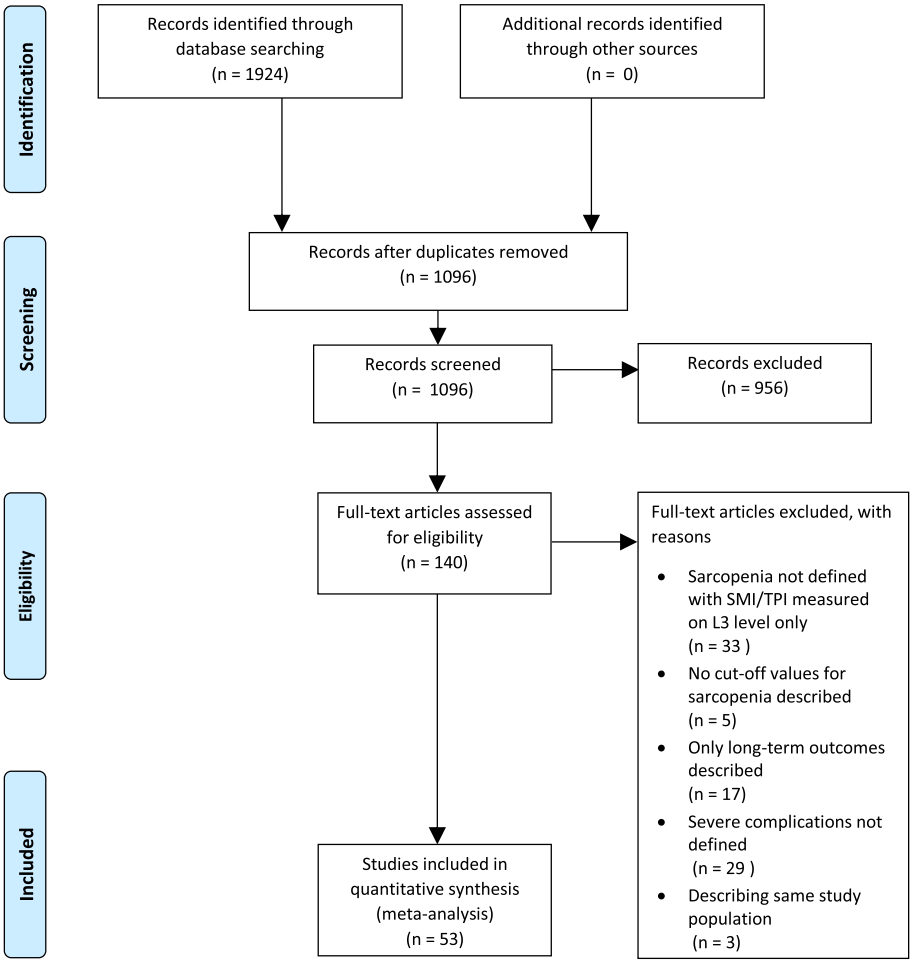

Figure 1 Flowchart of included studies

Thirty-day mortality

A number of 25 studies with a total of 6411 patients reported on 30-day mortality. Sarcopenia was present in 46% of the patients, and the pooled 30-day mortality was 3%. In patients with sarcopenia, 30-day mortality was 4% and in patients without sarcopenia 2% [OR_{pooled}: 2.15 (95% CI 1.46–3.17, $P<0.001$)] (*Figure* 4). The I^2 was 14%, indicating little heterogeneity.

Subgroup analysis for the effect of the use of the total skeletal muscle mass or the psoas mass for the detection of sarcopenia showed a significant difference between the subgroups. The pooled OR for the effect of sarcopenia on the 30-day mortality in studies using the total skeletal muscle mass was 1.80 (95% CI 1.24–2.62) versus 6.17 (95% CI 2.71–14.08) in studies using the psoas mass, $P<0.001$ (*Figure* 3b).

The subgroup analyses on the effect of tumour location and date of publication showed no significant differences between the subgroups. Subgroup analyses are presented in *Figure*s S2 and S3.

Discussion

In this meta-analysis 14 295 surgical oncological patients were included from 53 studies, where 20/53 were good quality studies. Results did not change when only good quality studies were included. Most studies (22/53) concerned patients diagnosed with a hepaticopancreaticobiliary malignancy. The prevalence of radiologically determined sarcopenia is relatively high, with a prevalence of 43% when sarcopenia was based on total skeletal mass and 33% for sarcopenia based on psoas mass. Preoperative sarcopenia was associated with an increased risk of severe postoperative complications (OR_{pooled}: 1.44, 95% CI: 1.24–16.8, $P<0.001$, I^2=55%) and 30-day mortality (OR_{pooled}: 2.15, 95% CI: 1.46–3.17, $P<0.001$, I^2=14%). A low psoas mass was a stronger predictor for severe postoperative complications (OR_{pooled}: 2.06, 95% CI: 1.37–3.09, OR_{pooled}: 1.32, 95% CI: 1.14–1.53, respectively) and 30-day mortality compared with a low total skeletal muscle mass [OR_{pooled}: 6.17 (95% CI: 2.71–14.08), OR_{pooled}: 1.80 (95% CI: 1.24-2.62), respectively].

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Table 1 Methodological quality of the included studies with regard to our study question

Study	Selection	Comparability[a]	Outcome	Overall quality
Amini, 2015[24]	+	+	+	+
Banaste, 2017[16]	+	-	+	-
Chemama, 2016[25]	+	+	+	+
Choi, 2018[26]	+	+	+	+
Coelen, 2015[27]	+	+	+	+
Elliot, 2017[28]	+	-	+	-
Grotenhuis, 2016[29]	+	-	+	-
Harada, 2015[30]	+	-	+	-
Harimoto, 2013[31]	+	+	+	+
Higashi, 2015[32]	+	+	+	+
Jarvinen, 2018[33]	+	-	+	-
Jones, 2015[34]	+	-	+	-
Kudou, 2017[35]	+	+	+	+
Kuwada, 2018[36]	+	+	+	+
Levolger, 2015[37]	+	-	+	-
Lodewick, 2015[38]	+	-	+	-
Malietzis, 2016[39]	+	-	+	-
Mason, 2017[40]	+	-	+	-
Mayr, 2018[41]	+	+	+	+
Nakamura, 2018[42]	+	-	+	-
Nakashima, 2018[43]	+	-	+	-
Nakanishi, 2018[44]	+	+	+	+
Nimomiya, 2017[45]	+	-	+	-
Nishida, 2016[46]	+	-	+	-
Nishigori, 2016[47]	+	-	+	-
Okumura, 2016 [48]	+	-	+	-
Okumura, 2015a[49]	+	-	+	-
Okumura, 2015b[50]	+	-	+	-
Otsuji, 2015[51]	+	+	+	+
Ouchi, 2016[52]	+	-	+	-
Pędziwiatr, 2016[18]	+	+	+	+
Peng, 2011[53]	+	+	+	+
Peyton, 2016[54]	+	-	+	-

(*Continues*)

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Table 1 (continued)

Study	Selection	Comparability[a]	Outcome	Overall quality
Rutten, 2017[55]	+	-	+	-
Saeki, 2018[56]	?	-	+	-
Sakurai, 2017[15]	+	-	+	-
Da Silva, 2018[57]	+	+	+	+
Smith, 2014[58]	+	+	+	+
Sui, 2017[59]	+	-	+	-
Takagi, 2016 [60]	+	-	+	-
Takagi, 2017a[61]	+	-	+	-
Takagi, 2017b[62]	+	-	+	-
Takeda, 2018[63]	+	-	+	-
Tegels, 2015[64]	+	-	+	-
Umetsu, 2018[65]	+	-	+	-
Valero, 2015[66]	+	+	+	+
Van der Kroft, 2018[67]	+	+	+	+
Van Vught, 2015[68]	+	+	+	+
Van Vught, 2017[69]	+	-	+	-
Van Vught, 2018[70]	+	+	+	+
Voron, 2015[71]	+	-	+	-
Wagner, 2018[72]	+	-	+	-
Zhuang, 2016[73]	+	+	+	+

[a]Studies were considered of good quality on the comparability domain if either selected cohorts or a multivariate analysis on the effect of sarcopenia on the development of postoperative complications were present.

The effect on the risk of severe complications was independent of tumour location and publication date.

Our analysis showed that the presence of low psoas mass prior to surgery is a stronger predictor for the development of postoperative complications when compared with the presence of low total skeletal muscle mass. This finding has not been reported earlier. This makes the measurement of the psoas mass a more adequate risk factor than the measurement of the total skeletal muscle mass in the selection of patients with an increased risk of developing postoperative complications. A possible explanation for the greater effect of a low total psoas mass compared with a low total skeletal muscle mass might be that the quantification of the psoas muscles reflects the physical condition of a patient better than the total skeletal muscle area. The relation between a low psoas mass and a decreased physical performance has been discussed in literature.[74,75] The psoas muscles are only active during standing, bending, and lifting, representing an active lifestyle.[76] A decreased psoas mass could therefore indicate that the patient is less active, has a decreased physical condition, and might subsequently be more frail and vulnerable for the development of postoperative complications. Furthermore, when a postoperative complication does occur, the impact of the complication could possibly be less well compensated, which can lead to a higher mortality risk in the postoperative period. Another aspect is that low psoas mass is also related to longer term postoperative mortality among different groups of patients.[24,77,78] Thus suggesting that low psoas mass might not only reflect a decreased physical condition on the short term but also represent physical changes with effects lasting over time.

The use of radiologically determined sarcopenia in preoperative risk stratification has some restrictions. Radiologically assessed sarcopenia is present in a large number of patients. When measured with total skeletal muscle mass, sarcopenia is present in almost half of the study population, and when

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Table 2 Characteristics of included studies

Study	Population (N)	Age[a]	Males		Location of malignancy[b]	SMI/TPI	Sarcopenia	
			N	%			N	%
Amini, 2015[24]	763	67 (58–74)	418	55	HPB	TPI	192	25.1
Banaste, 2017[16]	214	59 (24–78)	105	49	Lower GI	SMI	90	42.1
Chemama, 2016[25]	97	53 (46–62)	37	38	Lower GI	SMI	39	40.0
Choi, 2018[26]	180	64 ± 9	98	54	HPB	SMI	60	33.3
Coelen, 2015[27]	100	62 ±9	64	64	HPB	SMI	42	42.0
Elliot, 2017[28]	192	62 ± 9	156	81	Upper GI	SMI	49	25.5
Grotenhuis, 2016[29]	120	62 (19–78)	88	73	Upper GI	SMI	54	45.0
Harada, 2015[30]	256	NR[c]	234[d]	92	Upper GI	TPI	84	32.8
Harimoto, 2013[31]	186	67 ± 11	NR	NR	HPB	SMI	75	40.3
Higashi, 2015[32]	144	65 ± 10	108	75	HPB	SMI	72	50.0
Jarvinen, 2018[33]	115	63 ±9	86	75	Upper GI	SMI	92	80.0
Jones, 2015[34]	100	69 ±10	60	60	Lower GI	TPI	15	15.0
Kudou, 2017[35]	148	NR	NR	NR	Upper GI	SMI	42	28.4
Kuwada, 2018[36]	491	~71[e]	348	71	Upper GI	SMI	123	25.1
Levolger, 2015[37]	90	62 (22–86)	63	70	HPB	SMI	52	57.8
Lodewick, 2015[38]	171	64 (24–86)	104	61	HPB	SMI	80	46.8
Malietzis, 2016[39]	805	69 (961–77)	472	59	Lower GI	SMI	485	60.2
Mason, 2017[40]	698	62 ±7	698	100	Urogenital	SMI	388	55.6
Mayr, 2018[41]	327	70 (63–75)	262	80	Urogenital	SMI	108	33.0
Nakamura, 2018[42]	328	71 (38–87)	195	59	Other	TPI	183	55.8
Nakashima, 2018[43]	341	NR	289	85	Upper GI	SMI	171	50.1
Nakanishi, 2018[44]	494	66 ± 12	298	60	Lower GI	SMI	298	60.3
Nimomiya, 2017[45]	265	65 ± 10	164	62	HPB	SMI	170	64.2
Nishida, 2016[46]	266	69 (27-87)	181	68	HPB	SMI	132	49.6
Nishigori, 2016[47]	199	~65[e]	164	82	Upper GI	SMI	149	74.8
Okumura, 2016 [48]	207	~67[e]	111	54	HPB	TPI	71	32.4
Okumura, 2015a[49]	230	67 (32–87)	124	54	HPB	TPI	64	32.1
Okumura, 2015b[50]	109	68 (63–74)	67	62	HPB	SMI	69	63.3
Otsuji, 2015[51]	256	67 (34–85)	162	63	HPB	TPI	85	33.2
Ouchi, 2016[52]	60	69 (43–88)	35	58	Lower GI	TPI	20	33.3
Pędziwiatr, 2016[18]	124	66 (range NR)	73	59	Lower GI	SMI	34	27.4
Peng, 2011[53]	259	58 ± 12	155	60	HPB	TPI	41	15.8
Peyton, 2016[54]	128	63 (31–85)	85	66	Urogenital	TPI	32	25.0
Rutten, 2017[55]	216	63 (16–85)	0	0	Urogenital	SMI	70	32.4
Saeki, 2018[56]	157	65 (range NR)	122	78	Upper GI	SMI	85	54.1
Sakurai, 2017[15]	569	67 ± 11	396	70	Upper GI	SMI	142	24.9
Da Silva, 2018[57]	250	NR	0	0	Urogenital	SMI	56	22.4
Smith, 2014[58]	200	66 ± 12	141	71	Urogenital	TPI	77	38.5
Sui, 2017[59]	354	70 ± 11	203	57	HPB	SMI	87	24.6
Takagi, 2016 [60]	254	66 ± 11	207	82	HPB	SMI	118	46.5
Takagi, 2017a[61]	154	65 ± 13	90	58	HPB	SMI	38	24.7
Takagi, 2017b[62]	219	66 ±12	143	65	HPB	SMI	55	25.1
Takeda, 2018[63]	144	~61[e]	102	71	Lower GI	SMI	37	25.7
Tegels, 2015[64]	152	70 (37–88)	87	57	Upper GI	SMI	86	56.6
Umetsu, 2018[65]	65	72 (31–81)	47	72	HPB	TPI	48	73.8
Valero, 2015[66]	96	62 ± 12	59	61	HPB	TPI	47	49.0
Van der Kroft, 2018[67]	63	NR	39	64	Lower GI	SMI	33	52.4
Van Vught, 2015[68]	206	~61[e]	100	49	Lower GI	SMI	90	43.7
Van Vught, 2017[69]	452	65 (58–71)	278	62	Lower GI	SMI	206	45.6
Van Vught, 2018[70]	816	~70[e]	440	54	Lower GI	SMI	412	50.5
Voron, 2015[71]	109	62 ±13	92	84	HPB	SMI	59	54.1
Wagner, 2018[72]	424	63 (19–87)	203	48	HPB	TPI	145	34.2
Zhuang, 2016[73]	937	64 ± 15	730	78	Upper GI	SMI	389	41.5

[a]Mean ± SD, median (range), a: interquartile range.
[b]HPB: liver, pancreas, bile ducts; Upper GI: esophagus, stomach; Lower GI: colon, rectum, peritoneal carcinomatosis; urogenital: kidney, prostate, bladder, ovary, endometrium; Other.
[c]NR: not reported.
[d]Estimated, based on both included and excluded patients.
[e]Estimated, calculation based on mean/median age in different groups.

measured with psoas mass in one-third of the patients. The lower prevalence of the low psoas mass emphasizes its better suitability over the total skeletal muscle mass to select those patients that are at an increased risk for the development of postoperative complications. The widespread presence of sarcopenia reduces its discriminative value between those at an increased risk and those not at an increased risk for the development of postoperative complications. In addition,

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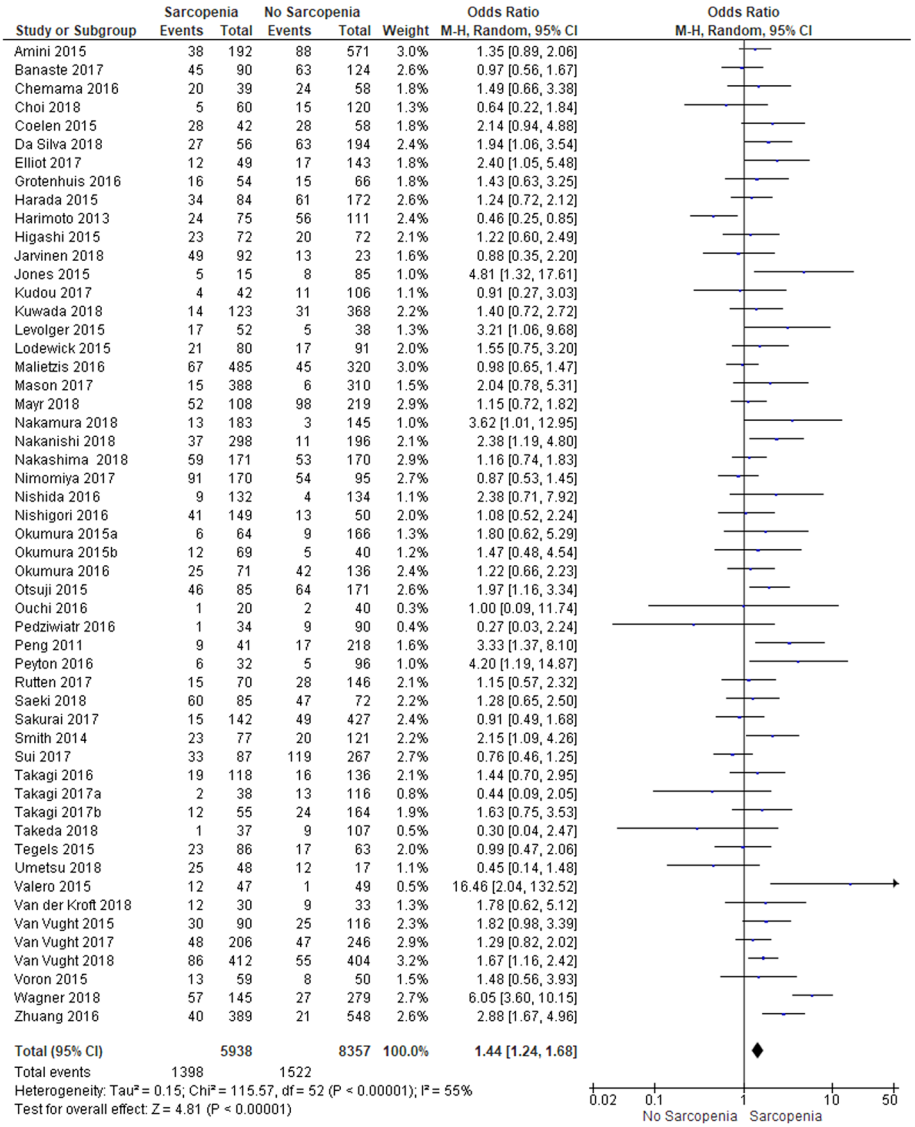

Figure 2 Sarcopenia and the development of severe postoperative complications

in this work, the reported value of a low psoas mass as predictor for the development of postoperative complications is outperformed by tests incorporating strength and coordination, i.e. the Timed Up and Go (TUG) (OR: 3.43, 95% CI 1.14–10.35 versus OR_{pooled}: 2.06, 95% CI: 1.37–3.09, respectively).[79] A less clear picture is present when the predictive value of a low psoas mass is compared with the presence of frailty. Different frailty assessments yield different ORs for the prediction of postoperative complications, with ORs ranging 1.80–6.40.[3,4] The OR for low psoas mass is in the lower range of this spectrum. This indicates that the value of the assessment of the psoas mass as a replacement for frailty screening is limited. Nevertheless, sarcopenia is a cause of physical frailty, and assessment of sarcopenia might help to select those patients that are physical frail.[80] Therefore, despite the limited value of radiologically assessed sarcopenia as a stand-alone risk factor, screening on sarcopenia with use of the psoas mass might be an addition to existing multi-domain assessments.

An important strength of this meta-analysis is the quality of the studies used in this analysis. Next to the 17 studies marked as having a good methodological quality, a total of 25 other studies did perform a multivariate analysis for other outcomes. With the presence of a multivariate analysis in itself as an indicator of quality, almost 80% of the studies included in this meta-analysis can be considered as having a good methodological quality. Another strong point is the fairly high homogeneity in this meta-analysis, thus showing that the results are consistent across studies and can be used in the general population of patients with abdominal malignancies. Furthermore, this research showed that there is no selection bias for patients undergoing surgical treatment for

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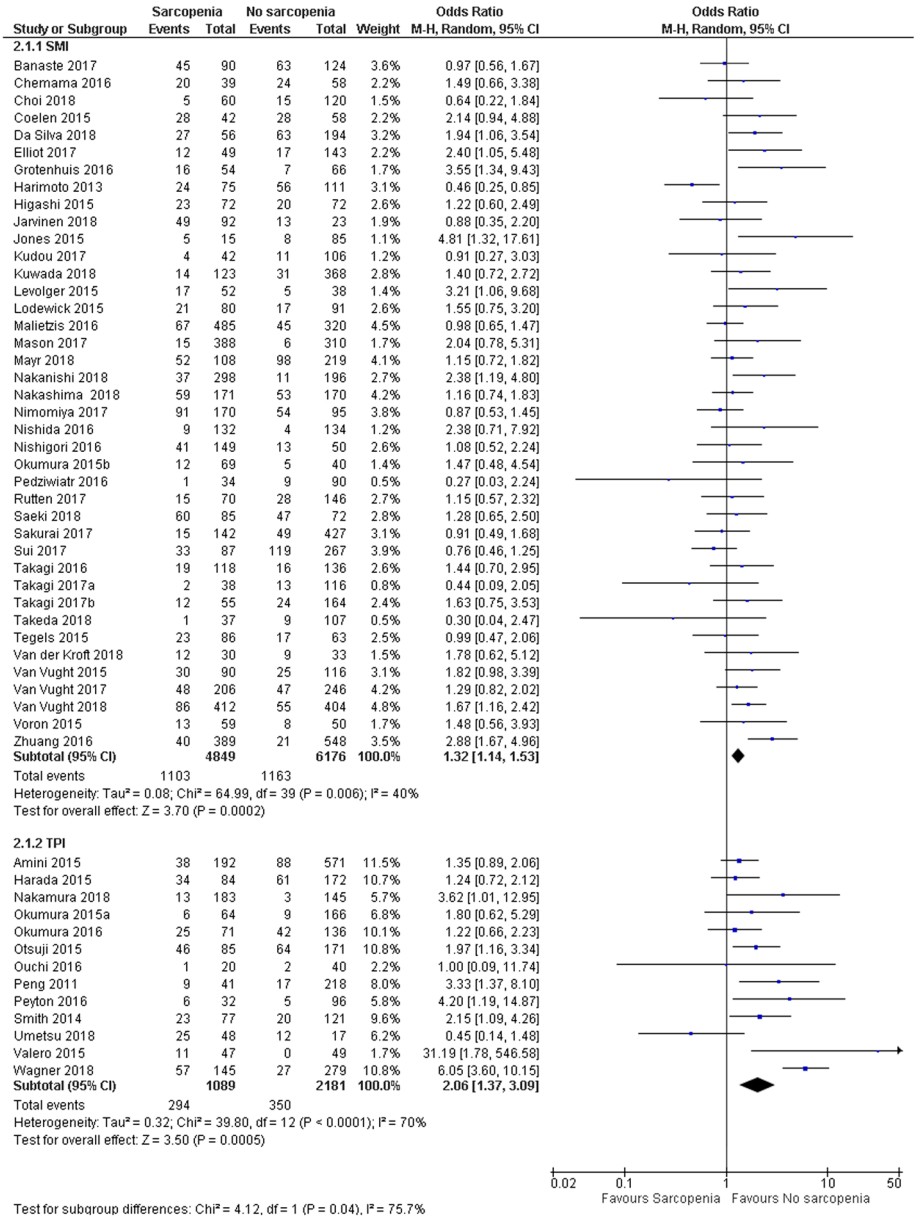

Figure 3 Predictive value of total skeletal muscle mass and total psoas mass (a) Severe postoperative complications

a malignancy based on 'eyeballing' for the presence of sarcopenia. The number of patients with sarcopenia undergoing oncologic surgery remains relatively stable over the years. If the selection bias was present, a decrease in the number of patients with sarcopenia who underwent major oncological surgery should be expected. This study also has some limitations. First, all included studies were retrospective cohort studies, with known disadvantages regarding risk of bias and potential missing data. Secondly, the used cut-off values for total skeletal muscle mass and psoas mass in the studies included in this analysis varied greatly. In the studies included in this meta-analysis, a total of 37 different cut-off values, divided in 24 different values for studies using the total skeletal muscle mass and 13 different values for studies using the psoas mass, were used, limiting the degree of comparability between the outcomes of the different studies. Furthermore, the number of studies reporting on the psoas mass is relatively small. However, with over 3000 patients included in these studies, the number of included patients is deemed large enough to reliably determine the differences between the psoas mass and the total skeletal muscle mass as a risk factor for postoperative morbidity. Another limitation is the exclusion of studies investigating the influence of the total skeletal muscle mass as a continuous variable

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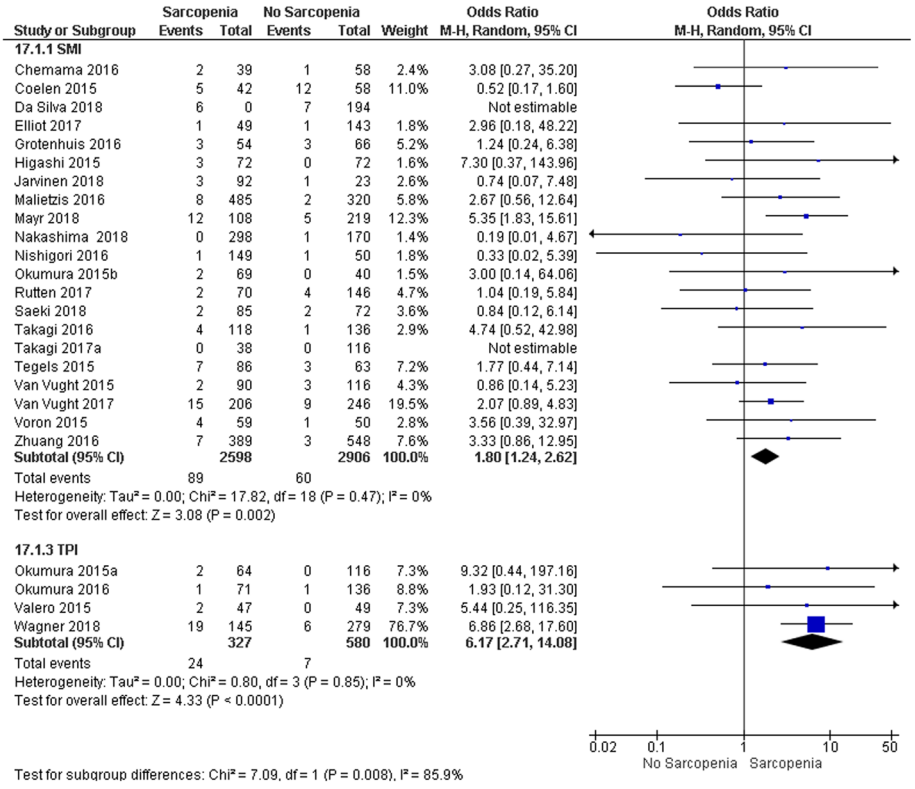

Figure 3 (b) 30-day mortality

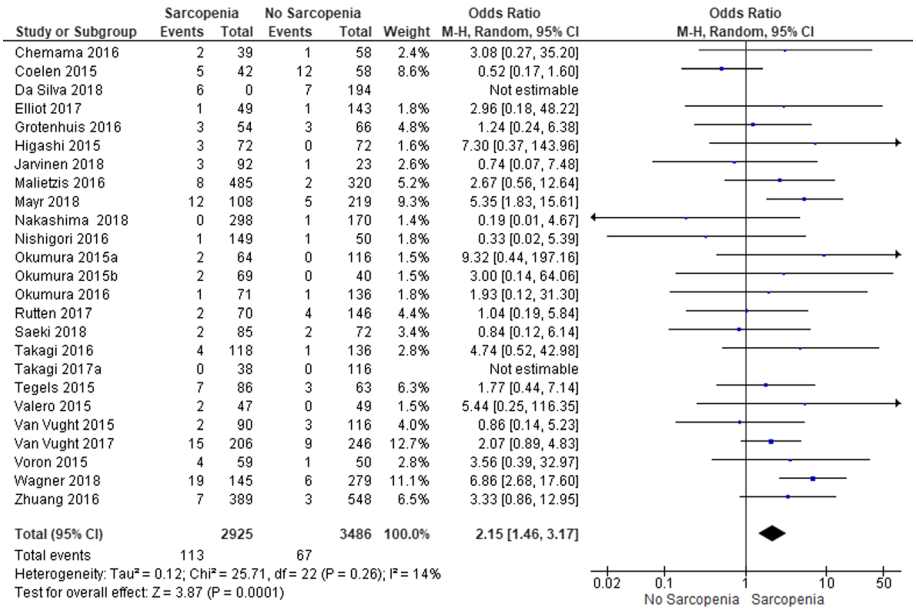

Figure 4 Sarcopenia and 30 day mortality

(*N*=5), without cut-off values to determine sarcopenia, on the development of sarcopenia. The exclusion of these studies does lead to missing of data, but evaluation of these studies showed the same trend in the relationship between skeletal muscle mass and sarcopenia as was described in this meta-analysis.

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Based on the results of this meta-analysis, several subjects for future research arise. An important subject is combining the radiologically assessed psoas mass with tools assessing muscle strength and functioning, and possible also including factors as coordination and cognition. Assessment of the psoas mass adds quantification of the lean skeletal muscle mass to the existing information. This might lead to a better assessment of the patient physical condition and might subsequently further improve preoperative risk stratification. Furthermore, the position of sarcopenia relative to frailty in the preoperative risk stratification should be evaluated. As mentioned, sarcopenia can contribute to frailty, but it does not equal frailly.[80] Therefore, it is not clear whether patients who are deemed frail are the same patients who are considered sarcopenic. Research is needed to explore the agreements and differences between those patient groups in order to determine the place of sarcopenia in future preoperative risk stratification. Another topic is the standardization of cut-off values for both total psoas mass and total skeletal muscle mass. As mentioned above, use of standardized cut-off values improves the comparability between studies. Furthermore, with standardization, it becomes more clear, which patients are considered sarcopenic and have increased risk of developing postoperative complications, improving the utility of radiologically assessed in clinical practice. An entirely other subject of future research is the preoperative 'treatment' of sarcopenia. Literature showed that resistance training can be effective to improve muscle strength, skeletal muscle mass and physical function.[81] However, the effects of resistance training on postoperative outcomes is unclear. Furthermore, the benefits of resistance training are not limited to sarcopenic patients alone but to all elderly, regardless of whether or not they have sarcopenia,[82] which advocates for the encouragement of physical activity in all elderly, not limited to those suffering from sarcopenia.

In summary, radiologically assessed preoperative sarcopenia is associated with the development of postoperative complications. The presence of low psoas mass surpasses the presence of low skeletal muscle mass as a risk factor for the development of severe postoperative complications, and even more so as a risk factor for 30-day mortality, in patients undergoing surgery for a solid malignancy. The addition of assessment of the total psoas mass to existing screening tools focussing on muscle strength and coordination could lead to further improvement of preoperative risk stratification in surgical oncology.

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Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Data S1. Supporting Information
Figure S1. Comparison of studies with a good versus a poor methodological quality
Figure S1a. Severe postoperative complications
Figure S1b. 30-day mortality
Figure S2. Stratification by tumour location
Figure S2a. Severe postoperative complications: grouped tumour location
Figure S2b. Severe postoperative complications: specific tumour location
Figure S2c. 30-day mortality: grouped tumour location
Figure S2d. 30-day mortality: specific tumour location
Figure S3a. Severe postoperative complications
Figure S3b. 30-day mortality

Conflict of interest

None declared.

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