

Review



## The Predictive Value of Low Muscle Mass as Measured on CT Scans for Postoperative Complications and Mortality in Gastric Cancer Patients: A Systematic Review and Meta-Analysis

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Supplementary Materials:

#1	#2	#3	#4
Stomach	Cancer*	"Muscle mass"	"Computed Tomography"
Gastric	Neoplas*	"Skeletal muscle"	СТ
Cardia	Malignan*	"Psoas muscle"	CAT
	Tumor*	Myopenia	Scan*
	Tumour*	Sarcopen*	
	Oncolog*	"Total muscle area"	
	Carcinoma*	"Body composition"	
	"Squamous cell	"Total Psoas Area"	
	carcinoma*"		
	Adenocarcinoma*	"Muscle wasting"	
		"Muscle attenuation"	
		"Muscular atrophy"	
MeSH-terms:	MeSH-terms:	MeSH-terms:	MeSH-terms:
- Stomach	- Neoplasms	- Sarcopenia	-"Tomography, X-Ray
-"Stomach neoplasms"	- Carcinoma	-"Muscular atrophy"	Computed"
- Cardia	-"Neoplasms squamous	-"Psoas muscle"	- Radiography
-"Gastrointestinal	cell"	-"Muscle, skeletal"	
neoplasms"	-Adenocarcinoma	-"Body composition"	
Emtree-terms:	Emtree-terms:	Emtree-terms:	Emtree-terms:
- Stomach (exp)	- 'Malignant neoplasm'	- 'Muscular atrophy'	- 'Computer assisted
	(exp)	- 'Skeletal muscle' (exp)	tomography'
	(exp)	( 1 /	0 1 5
		- 'Body composition'	- 'Digital imaging' (exp)

## Table S1. Overview of search strategy.

	Low Risk of Bias	Moderate Risk of Bias	High Risk of Bias
	Adequate reporting of patient	Moderate reporting of patient	Inferior reporting of patient
	cohort. In- and exclusion criteria	cohort and in- and exclusion	cohort and in- and exclusion
Study	mentioned clearly. Baseline	criteria. Moderate description of	criteria. Inferior description of
participation	study sample is well described	baseline study sample for	baseline study sample for
	for important patient	important patient	important patient
	characteristics.	characteristics.	characteristics.
	Adequate reporting of response	Moderate reporting of response	Inferior reporting of response
	rate, reasons for loss to follow	rate, reasons for loss to follow	rate, reasons for loss to follow
Study attrition	up, and attempts to collect data	up, and attempts to collect data	up, and attempts to collect data
	from patients who dropped out	from patients who dropped out	from patients who dropped out
	of study.	of study.	of study.
	Adequate reporting of the	Moderate reporting of the	Inferior reporting of the method
	method of muscle mass	method of muscle mass	of muscle mass assessment
Prognostic	assessment. Blinded and	assessment. Blinded and	Not-blinded or inexperienced
factor	experienced investigator. Cutoff	experienced investigator. A	investigator A data-dependent
measurement	value for low muscle mass was	data-dependent cutoff value	cutoff value was used for the
	based on large patient cohorts	was used for the definition of	definition of low muscle mass
	and not data-dependent.	low muscle mass.	definition of fow induce muss.
	Adequate reporting of	Moderate reporting of definition	Inferior reporting of definition
Outcome	definition of outcomes, duration	of outcomes, duration of follow-	of outcomes, duration of follow-
measurement	of follow-up, and method of	up, and method of outcome	up, and method of outcome
	outcome measurement.	measurement.	measurement.
	Adequate accounting for	Moderate accounting for	Inferior accounting for possible
	possible confounders: BMI,	possible confounders: BMI,	confounders: BMI, gender,
	gender, smoking/alcohol, TNM	gender, smoking/alcohol, TNM	smoking/alcohol, TNM stage,
Cr. 1	stage, performance score,	stage, performance score,	performance score, histological
Study	histological type, therapy	histological type, therapy	type, therapy (surgery,
confounding	(surgery, chemotherapy),	(surgery, chemotherapy),	chemotherapy), comorbidity,
	comorbidity, tumor location,	comorbidity, tumor location,	tumor location, regression
	regression grade in case of	regression grade in case of	grade in case of chemotherapy,
	chemotherapy, nutritional	chemotherapy, nutritional	nutritional status.
	status.	status.	
Ctatistical		Meta-analysis with	Meta-analysis with
Statistical	Meta-analysis with univariable	activation and the second	activation and the second
roporting	analysis only.	significant in the univariable	significant in the univariable
reporting		analysis $(n < 0.05)$	analysis (n < 0.1)

Table S2. Applied definitions of the 3-point scale per domain of QUIPS.

				nent		
	anticip	tion atrition	ostic fact	or neasure	renent confound	ne ical Anali
	Study	Study	Progre	OUTCOL	Study	Statist
Tegels 2015	Low	Low	Low	Low	High	High
Huang 2016	Low	Low	Low	Low	Moderate	Moderate
Nishigori 2016	Low	Low	Moderate	Low	Low	Low
Wang 2016	Low	Low	Low	Low	Moderate	Moderate
Zhuang 2016	Moderate	Low	Moderate	Low	Low	Low
Kudou 2017	Low	Low	Low	Moderate	High	High
Sakurai 2017	Low	Low	Moderate	Moderate	Moderate	Moderate
Mirkin 2017	Moderate	Low	Moderate	Moderate	High	High
Zheng 2017	Low	Low	Moderate	Low	Moderate	Moderate
Kuwada 2018	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Lu 2018	Low	Low	Moderate	Moderate	Moderate	Moderate
Nishigori 2018	Low	Low	Low	Moderate	Low	Low
O'Brien 2018	High	Low	Low	Moderate	Moderate	Moderate
Zhang 2018	Low	Low	Moderate	Low	Moderate	Moderate
Siezerga 2019	Low	Low	Low	Moderate	Low	Low

Figure S1. Overview of the risk of bias score of the included studies following QUIPS.



Figure S2. Funnel plot of included studies reporting on postoperative complications.



Figure S3. Funnel plot of included studies reporting on severe postoperative complications.



Figure S4. Funnel plot of included studies reporting on overall mortality.



Figure S5. Funnel plot of included studies reporting on disease-specific mortality.

			Low muscle mass	Normal muscle mass		Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
2.1.1 Univariable ana	lyses						
Huang 2016	0.761	0.219	179	294	20.3%	2.14 [1.39, 3.29]	
Kuwada 2018	0.399	0.237	123	368	18.8%	1.49 [0.94, 2.37]	
Nishigori 2016	0.383	0.423	97	60	9.0%	1.47 [0.64, 3.36]	
Sierzega 2019	0.936	0.376	60	78	10.7%	2.55 [1.22, 5.33]	
Subtotal (95% CI)			459	800	58.8%	1.86 [1.41, 2.44]	◆
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> = 2.30,	df = 3 (l	P = 0.51); I² = 0%				
Test for overall effect:	Z = 4.43 (P < 0.00	001)					
2.1.2 Multivariable an	alyses						
O'Brien 2018	1.255	0.419	20	36	9.1%	3.51 [1.54, 7.97]	
Wang 2016	1.613	0.414	32	223	9.3%	5.02 [2.23, 11.30]	
Zhang 2018	1.224	0.491	24	132	7.1%	3.40 [1.30, 8.90]	
Zhuang 2016	1.102	0.282	389	548	15.6%	3.01 [1.73, 5.23]	<b>_</b>
Subtotal (95% CI)			465	939	41.2%	3.51 [2.43, 5.08]	•
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> = 1.05,	df = 3 (l	° = 0.79); I² = 0%				
Test for overall effect:	Z = 6.68 (P < 0.00	001)					
Total (95% CI)			924	1739	100.0%	2.43 [1.83, 3.24]	•
Heterogeneity Tau <sup>2</sup> =	0.06: Chi <sup>2</sup> = 10.77	df = 7	(P = 0.15); P = 35%				
Test for overall effect:	7 = 6 09 (P < 0 00	001	0 - 0.10/1 - 00/0				D.01 0.1 1 10 100
Test for subgroup diff	erences: Chi <sup>2</sup> = 7	41 df=	1 (P = 0 006) F = 86.5	96			Favours low muscle mass Favours normal muscle mass

**Figure S6.** Sensitivity analysis: forest plots of univariable and multivariable odds ratios for postoperative complications for gastric cancer patients with low muscle mass versus normal muscle mass.

			Low muscle mass	Normal muscle mass		Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
2.2.1 Univariable ana	lyses						
Huang 2016	0.264	0.432	176	294	16.9%	1.30 [0.56, 3.04]	<b>+</b>
Kuwada 2018	0.329	0.339	123	368	20.7%	1.39 [0.72, 2.70]	
Nishigori 2016	-0.799	0.773	97	60	8.2%	0.45 [0.10, 2.05]	
Subtotal (95% CI)			396	722	45.7%	1.21 [0.74, 1.98]	*
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> = 1.83,	df = 2 (l	P = 0.40); I <sup>2</sup> = 0%				
Test for overall effect:	Z = 0.74 (P = 0.46)						
2.2.2 Multivariable ar	alyses						
O'Brien 2018	1.255	0.419	20	36	17.4%	3.51 [1.54, 7.97]	<b>_</b>
Sierzega 2019	1.29	0.529	60	78	13.6%	3.63 [1.29, 10.25]	
Zhuang 2016	1.102	0.282	389	548	23.3%	3.01 [1.73, 5.23]	_ <b>_</b>
Subtotal (95% CI)			469	662	54.3%	3.23 [2.12, 4.91]	•
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> = 0.15,	df = 2 (l	P = 0.93); I <sup>2</sup> = 0%				
Test for overall effect:	Z = 5.48 (P < 0.000	001)					
Total (95% CI)			865	1384	100.0%	2.01 [1.22, 3.31]	◆
Heterogeneity: Tau <sup>2</sup> =	0.20; Chi <sup>2</sup> = 10.87	, df = 5	(P = 0.05); I <sup>2</sup> = 54%				
Test for overall effect:	Z = 2.73 (P = 0.008	3)					0.01 0.1 1 10 100
Test for subgroup diff	erences: Chi² = 8.8	39. df =	1 (P = 0.003), I <sup>2</sup> = 88.	7%			Favours low muscle mass Favours normal muscle mass

**Figure S7.** Sensitivity analysis: forest plots of univariable and multivariable odds ratios for severe postoperative complications for gastric cancer patients with low muscle mass versus normal muscle mass.

			low muscle mass	Normal muscle mass		Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.1.2 Multivariable a	nalysis						
Kuwada 2018	0.378	0.186	123	368	16.3%	1.46 [1.01, 2.10]	
Nishigori 2018	0.693	0.245	76	101	11.7%	2.00 [1.24, 3.23]	_ <b></b>
O'Brien 2018	2.39	0.627	20	36	2.5%	10.91 [3.19, 37.30]	
Sakurai 2017	0.47	0.165	142	427	18.4%	1.60 [1.16, 2.21]	
Sierzega 2019	0.663	0.299	60	78	8.8%	1.94 [1.08, 3.49]	<b>_</b>
Zheng 2017	0.678	0.175	103	590	17.4%	1.97 [1.40, 2.78]	
Zhuang 2016	0.501	0.11	389	548	24.9%	1.65 [1.33, 2.05]	+
Subtotal (95% CI)			913	2148	<b>100.0</b> %	1.80 [1.47, 2.21]	•
Heterogeneity: Tau <sup>2</sup> :	= 0.03; Chi <sup>2</sup> = 10.92, (	df = 6 (P	= 0.09); I <sup>2</sup> = 45%				
Test for overall effect	t: Z = 5.73 (P < 0.0000	)1)					
Total (95% CI)			913	2148	100.0%	1.80 [1.47, 2.21]	◆
Heterogeneity: Tau <sup>2</sup> :	= 0.03; Chi <sup>2</sup> = 10.92, (	df = 6 (P	= 0.09); l <sup>2</sup> = 45%				
Test for overall effect	t: Z = 5.73 (P < 0.0000	11)					0.02 0.1 1 10 50
Test for subgroup di	fferences: Not applica	able					Favours low muscle mass Favours normal muscle mass

**Figure S8.** Sensitivity analysis: forest plots of univariable and multivariable odds ratios for overall survival for gastric cancer patients with low muscle mass versus normal muscle mass.