BMC Cancer

SYSTEMATIC REVIEW Open Access

Incidence and risk factors of sarcopenia in gastric cancer patients: a meta-analysis and systematic review

Mingyue Fu[1], Xuehong Wang[2*], Jing Zhou[1] and Jianfeng Wang[1]

Abstract

Background This meta-analysis was to assess the incidence and risk factors of sarcopenia in gastric cancer (GC) patients and to provide clinical implications for the prevention and improvement of sarcopenia in GC patients.

Methods PubMed, Embase, Cochrane, Web of Science, CNKI, Wanfang, and VIP databases (language was limited to Chinese and English) were searched for observational studies. The random-effects model was used to analyze the incidence of GC combined with sarcopenia and the odd ratio (OR) and 95% confidence interval (CI) of risk factors.

Results 1244 studies were retrieved and 20 eligible studies were included. The meta-analysis revealed that the incidence of sarcopenia in GC patients was 26.6% (95% CI: 21%~32%). Age (OR = 1.128, 95% CI: 1.056 ~ 1.204, $P < 0.001$), male (OR = 1.054, 95% CI: 0.620 ~ 1.791, $P < 0.005$), body mass index (OR = 1.117, 95% CI: 0.881 ~ 1.414, $P < 0.001$), nutritional risk screening 2002 (OR = 3.953, 95% CI: 2.038 ~ 7.668, $P < 0.05$), and tumor diameter > 3 cm (OR = 1.515, 95% CI: 1.021 ~ 2.248, $P < 0.05$) may be risk factors for sarcopenia in GC patients. In contrast, tumor stage (OR = 1.907, 95% CI: 0.967 ~ 3.763, $P > 0.05$), gastrectomy approach (OR = 1.837, 95% CI: 1.237 ~ 2.727, $P > 0.05$), differentiation type (OR = 0.586, 95%CI: 0.325 ~ 1.059, $P > 0.05$), and severe adverse reactions (NLR, HB, ALB) after chemotherapy (OR = 0.926, 95%CI: 0.793 ~ 1.082, $P > 0.05$) had no significant correlation with sarcopenia in GC patients.

Conclusions This meta-analysis shows an increased prevalence of sarcopenia in GC patients. This analysis, which focused on Asian populations, suggested that high nutritional risk was a risk factor for sarcopenia in GC patients. Age over 65 years and tumor diameter over 3 cm may be risk factors for sarcopenia. Men may be prone to sarcopenia. Targeting these risk factors may be beneficial in the prevention of sarcopenia in GC patients.

Keywords Gastric cancer, Sarcopenia, Incidence, Risk factors

*Correspondence:
Xuehong Wang
lindawang0710@hotmail.com
[1]Qinghai University Affiliated Hospital (School of Clinical Medicine), Qinghai University, Qinghai Xining 810016, China
[2]Department of Gastroenterology, Qinghai University Affiliated Hospital, No.29 Tongren Road, Chengxi District, Qinghai Xining, Qinghai Province 810000, China

Introduction

Sarcopenia is an age-related progressive and systemic skeletal muscle disease that manifests as accelerated loss of muscle mass and function and is associated with adverse outcomes, such as falls, functional decline, frailty, and death [1]. Various diseases including cancer, organ failure, chronic infections, and aging can result in sarcopenia and severely destroy the integrity and function of skeletal muscle [2]. The incidence of secondary sarcopenia, especially gastrointestinal tumors with sarcopenia, is much higher than that of primary sarcopenia. Gastric cancer (GC) is one of the most common gastrointestinal tumors worldwide, and it ranks fifth in terms of global incidence and fourth in terms of global mortality, posing a serious threat to people's health [3]. GC is a multifactorial process resulting from genetic, environmental, and biological factors. Muscle mass is extremely important in the treatment of GC. One study has illustrated that the main cause of death in GC patients is postoperative sarcopenia rather than the cancer itself [4].

According to the different diagnostic criteria for sarcopenia published by the European Working Group on Sarcopenia in Old People (EWGSOP) in 2010 and 2019, the incidence of sarcopenia in GC patients was 17% and 19%, respectively [5]. One study has reported that the current prevalence of sarcopenia in GC patients is 30.5% [6]. With the increasing incidence of GC, sarcopenia in GC patients is getting much more attention [7]. However, the pathogenesis of sarcopenia in GC is complicated, and the incidence is different across tumor stages and sizes, possibly due to differences in case selection, evaluation criteria, and baseline characteristics of patients. Sarcopenia has gained attention as an adverse factor in cancer. Many studies have investigated the significant impact of sarcopenia on the prognosis of GC patients, but there is a paucity of evidence to predict sarcopenia in GC patients, which has become an important issue. This paper reviews the incidence and risk factors of sarcopenia in GC patients. Observational studies related to sarcopenia in GC patients were retrieved. In the meta-analysis, the combined odds ratio (OR) and its 95% confidence interval (CI) were calculated to assess the relationship between GC and various outcome indicators.

Methods

This systematic review and meta-analysis followed the PRISMA statement and was registered with the International Prospective Register of Systematic Reviews (No. CRD42023446996) (https://www.crd.york.ac.uk/PROSPERO). When heterogeneity was present, a random-effects model was used. Egger's test was used to detect publication bias.

Literature search

Case-control studies and cohort studies published in Chinese or English were searched for in PubMed, Embase, Cochrane, Web of Science, CNKI, Wanfang, and VIP databases until September 1, 2023 using the following MeSH terms: gastric cancer, sarcopenia, and risk factors. The detailed PubMed search strategy is provided as supplementary material. The retrieved literature was imported to EndNoteX9. Literature retrieval was undertaken independently by Fu Mingyue and Zhou Jing, and any discrepancies were addressed through discussion with Wang Xuehong. Additionally, references in relevant literature were browsed to obtain eligible studies.

Selection criteria

The included studies analyzed the risk factors and clinical effects of sarcopenia on the prognosis of GC patients. According to the PICOS principle, the inclusion criteria were formulated [8–9]. The patients in the study were GC patients with or without sarcopenia. The exposure factors were population characteristics such as sex, age, comorbidities, and other factors. The outcome measure was the association of these risk factors with sarcopenia in GC patients with 95% CI. The types of studies were retrospective studies and randomized clinical trials (RCTs). Meanwhile, the following studies were excluded: (1) the full text could not be obtained (not public or the article was charged) or the original research data could not be extracted; (2) case report abstracts, conference papers, and other non-original articles, reviews, and meta-analyses; (3) repeated published literature and (4) animal experiments.

Data extraction

The titles and abstracts of the retrieved studies were independently reviewed by 2 investigators, and studies that met the inclusion criteria were selected for full-text assessment. All data and information were recorded on a pre-designed table. Extracted information encompassed first author, date and country of publication, study design, number of participants, median age, median body mass index (BMI) (kg/m^2), clinical stage of GC, diagnostic indicators of sarcopenia, and outcome indicators.

Risk of bias evaluation

Eligible studies were appraised using the Newcastle-Ottawa Scale (NOS) [10] in 3 dimensions: selection, comparability, and exposure (case-control studies). The quality score ranged from 0 to 9, with ≥6 scores representing high quality. Any disagreements were addressed by discussion with Wang Xuehong.

Data synthesis and statistical analyses

Meta-analyses were implemented to compute the OR and 95% CI to assess the correlation of GC combined with sarcopenia with age, sex, BMI, nutritional risk, and tumor size. Heterogeneity was analyzed using the Q test and I^2 test. The fixed-effects model (Mantel-Haenszel, $P > 0.05$ or $I^2 < 50\%$) assumed that different results across studies were by chance. The random-effects model (M-H heterogeneity, $P < 0.05$ or $I^2 > 50\%$) argued that results varied across studies. When heterogeneity was presented, the random-effects model was considered more appropriate than the fixed-effects model, leading to wider CI and more conservative effect estimates. Publication bias was appraised via visual inspection of funnel plots. Begg's and Egger's tests were adopted to determine publication bias. Sensitivity analyses, meta-regression, and subgroup analyses were implemented to further ascertain heterogeneity. STATA 15.0 software was applied for statistical analyses.

Results

Literature search results and general characteristics

1,244 retrieved reports were imported into EndNoteX9. 526 duplicates were deleted, and 698 reports were excluded due to guidelines, case reports, reviews, ineligible control groups, incomplete presentation, and irrelevant endpoints. 20 articles were finally included. All articles included were observational studies, with 9 retrospective and 11 prospective articles (Fig. 1). These articles were conducted in China, Japan, Korea, India, Ireland, and Turkey. The median age, BMI range, definition of sarcopenia, and GC stage were extracted from the sarcopenia and non-sarcopenia groups. Diagnostic criteria (skeletal muscle index (SMI)/hand grip strength/6-m gait speed), measurement methods for muscle mass (CT/MRI/DXA/BIA), and cut-off points for diagnosis were extracted. Sarcopenia was defined as $< 34.9\ cm^2/m^2$ for women and $< 40.8\ cm^2/m^2$ for men in China, $< 38\ cm^2/m^2$ for women and $< 42\ cm^2/m^2$ for men in Japan, and $< 38.5\ cm^2/m^2$ for women and $< 52.4\ cm^2/m^2$ for men in South Korea. The definition criteria were different across countries, and GC from the early to advanced stages were studied. Age and body weight were mostly consecutive data, which are detailed in Table 1.

Quality evaluation results

In the NOS assessment, each of the 8 items was rated as "yes," "no," "unclear," or "not applicable". Whether the study should be included or excluded should be determined through group discussion. The quality scores for retrospective and prospective studies were all ≥6, with 1 article scored 6 points, 11 articles scored 7 points, 5 articles scored 8 points, and 3 articles scored 9 points. The scores are listed in Table 1. Of the recruited papers [11–30], there were 4,782 cases, of which 1,098 cases were GC combined with sarcopenia, with an incidence of 26.6% (95% CI: 0.215 ~ 0.318) (Fig. 2).

Outcome indicators

Age

Twelve papers investigated the correlation between GC combined with sarcopenia and age, with substantial heterogeneity ($I^2 = 72.9\%$, $P < 0.001$). A random-effects model was used for meta-analysis. The results denoted that GC patients > 65 years old had increased risk of sarcopenia (OR = 1.128, 95% CI: 1.056 ~ 1.204, $P < 0.001$). The multivariate analysis (OR = 1.453, 95% CI: 0.887 ~ 2.381) and univariate analyses (OR = 1.116, 95% CI: 1.035 ~ 1.202) yielded similar results. Subgroup analysis indicated a risk in patients over 65 (OR = 1.133, 95% CI: 1.060 ~ 1.212, $P < 0.001$) or 75 years old(OR = 1.958, 95% CI: 1.278 ~ 3.001, $P < 0.01$) (Fig. 3).

Gender

Five papers examined the association between GC combined with sarcopenia and gender, with significant heterogeneity ($I^2 = 68.9\%$, $P < 0.01$). A random-effects model was utilized for meta-analysis. The results pointed out that the risk of sarcopenia was increased in male GC patients (OR = 1.054, 95% CI: 0.620 ~ 1.791, $P < 0.01$). The multivariate (OR = 1.150, 95% CI: 0.150 ~ 8.827) and univariate (OR = 1.105, 95% CI: 0.625 ~ 1.952) analyses yielded consistent results (Fig. 4).

BMI

Six papers investigated the correlation between GC combined with sarcopenia and BMI, with notable heterogeneity ($I^2 = 71.6\%$, $P < 0.01$). The results of meta-analysis using a random-effects model demonstrated that the risk of sarcopenia was greatly increased in GC patients with low BMI (OR = 1.117, 95% CI: 0.881 ~ 1.414, $P < 0.01$). The univariate analysis suggested increase in the risk of sarcopenia in GC patients with low BMI (OR = 1.139, 95% CI: 0.897 ~ 1.447). However, only 1 paper conducted multivariate analysis (OR = 0.403, 95% CI: 0.078 ~ 2.082, $P < 0.01$), suggesting that BMI is a continuous variable, and the risk of sarcopenia increases as BMI decreases (Fig. 5).

Tumor diameter

Four papers examined the association between GC combined with sarcopenia and tumor diameter, with marked heterogeneity ($I^2 = 68.9\%$, $P < 0.01$). A random-effects model was used for meta-analysis. The results signified that the risk of sarcopenia was increased in GC patients with > 3 cm tumor diameter (OR = 1.515, 95% CI: 1.021 ~ 2.248, $P < 0.01$). The multivariate (OR = 2.090, 95% CI: 1.230 ~ 3.551) and univariate (OR = 1.344, 95%

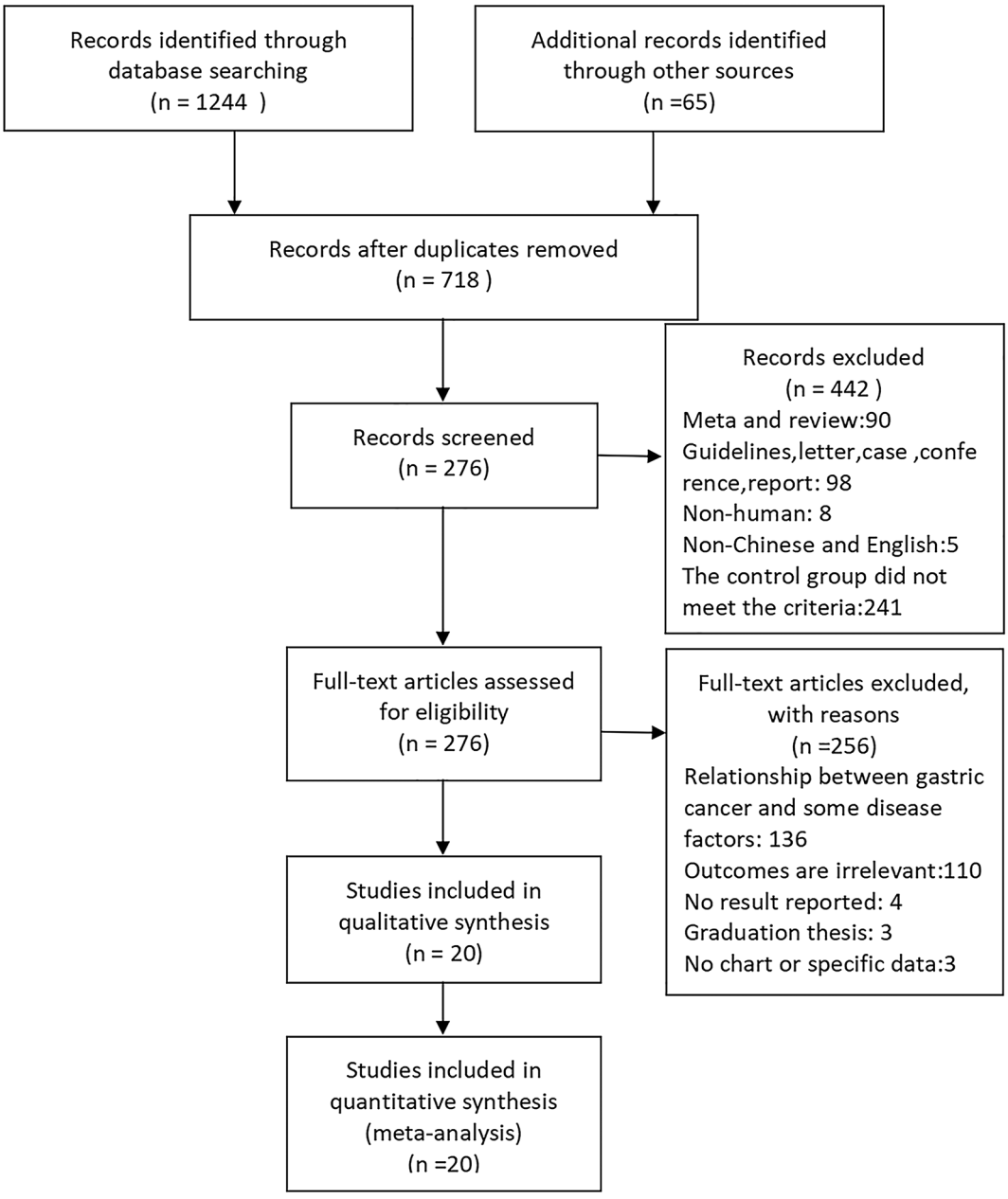

Fig. 1 Flow chart of literature inclusion

CI: 0.920 ~ 1.962) analyses implied that GC patients with larger tumors had increased risk of sarcopenia, suggesting that larger tumor is a risk factor for sarcopenia (Fig. 6).

Risk of malnutrition

Nutritional risk screening NRS2002 was used as the scoring standard [31]. Four papers investigated the association between GC combined with sarcopenia and NRS, and the heterogeneity among papers was notable ($I^2 = 76.2\%$, $P < 0.01$). Using the random-effect model, meta-analysis displayed that the overall risk of sarcopenia was visibly enhanced in GC patients with NRS > 3 score (OR = 3.953, 95% CI: 2.038 ~ 7.668, $P < 0.001$), indicating that NRS2002 score > 3 was a risk factor for GC with sarcopenia. The multivariate (OR = 3.441, 95% CI: 1.623 ~ 7.295) and univariate analyses (OR = 4.199, 95% CI: 1.673 ~ 10.540) found that the risk of sarcopenia was greatly elevated in those with higher NRS scores (Fig. 7).

Other outcome indicators

The correlation analysis of GC combined with sarcopenia and tumor stage displayed that the higher tumor stage was correlated with a risk of sarcopenia in GC

Table 1 Characteristics of the included articles

Authors	Published years	Study design	Country of publication	Sample size	Age Median(SD)		BMI(kg/m2)		Staging of gastric cancer	Diagnosis of sarcopenia	NOS
					Sarcopenia	Nonsarcopenia	Sarcopenia	Nonsarcopenia			
Yongjing He	2023	Retrospective cohort	China	125	67(60.3,70.0)	63(53.0,69. 0)	20. 17.90 ± 2.37	120.64 ± 3.13	Stage IV gastric cancer	ASMI: female < 5.7 kg/m^2,male < 7.0 kg/m^2	7
Hiroyuki Hisada	2022	Retrospective cohort	Japan	767	77(66–95)	73(66–95)	22.4 (12.9–31.1)	23.4 (11.3–37.9)	Early gastric cancer	SMI: female<38.0 cm^2/m^2,male<42.0 cm^2/m^2	7
Xiangwei Sun	2021	Prospective cohort	China	267	72.31(7.89)	63.08 (9.99)	18.5 ≤ BMI < 23	18.5 ≤ BMI < 23	Gastric cancer	SMI: female < 34.9 cm^2/m^2,male < 40.8 cm^2/m^2 GS: female < 18 kg, male < 26 kg	9
Ramanan Sinduja	2021	Prospective cohort	India	100	/	/	17.8 ± 2.54	22.54 ± 3.12	Gastric cancer	SMI: female < 34.9 cm^2/m^2,male < 40.8 cm^2/m^2	9
Oguz Erkul, MD	2021	Prospective study	Turkey	146	72.0 ± 8.7	61.6 ± 11.3	23.3 (19.8–25.7)	25.9 (23.2–30.0)	Gastric cancer	SMI: female<41 cm^2/m^2, male<43 cm^2/m^2(BMI < 25)/53 cm^2/m^2(BMI>25); GS: female < 16 kg, male < 27 kg	7
Hye Jin Kim, MD	2021	Retrospective study	Korea	576	58.0 (44.5–72.0)	62.0 (55.0–70.0)	21.25 ± 3.04	24.02 ± 3.08	I-III gastric cancer	SMI: female < 38.5 cm^2/m^2,male < 52.4 cm^2/m^2	7
Hong-Bo Zou	2021	Prospective cohort	China	135	74.00 (13.00)	63.00 (18.00)	20.63 (2.41)	23.30 (2.62)	Gastric cancer	SMI: female < 34.9 cm^2/m^2,male < 40.8 cm^2/m^2	7
Feng-Min Zhang	2021	Prospective cohort	China	507	74 (69-77.5)	63 (56–69)	22.1 (3.0)	23.0 (2.8)	Stage I gastric cancer.	SMI: female < 34.9 cm^2/m^2,male < 40.8 cm^2/m^2;HS: female < 18 kg, male < 26 kg	7
KEITA KOUZU	2020	Retrospectively study	Japan	67	72.1 ± 7.8	70.0 ± 8.6	21.3 ± 2.9	22.6 ± 3.2	II-III gastric cancer	PMI: female ≤ 0.704 cm^2/m^2, male ≤ 0.766 cm^2/m^2	8
TA TSURO TAMURA	2019	Retrospective study	Japan	153	74 (38–83)	68 (32–83)	17.9(13.4–23)	22.6 (15.7–33.4)	Gastric cancer	MMI: female<13.33 kg/m^2,male<15.44 kg/m^2	8
KAZUYOSHI YAMAMOTO	2019	Retrospective Studies	Japan	90	78 (67–83)	75 (66–91)	18.9 (15.6–26.9)	22.7 (16.8–32.2)	Early gastric cancer	SMI: female 6.42(kg/m^2),male 8.87(kg/m^2), HS: female < 20 kg, male < 30 kg	7
Bo Shi	2019	Retrospective analysis	China	279	61.15 ± 12.56(TPA)59. 95 ± 12.37(SMA)	54.61 ± 12.12(TPA) 53.16 ± 11.84(SMA)	20.41 ± 2.85(TPA)19 .77 ± 2.42(SMA)	21.64 ± 2.91(TPA) 22.62 ± 2.70(SMA)	Gastric cancer	SMA: female<30.5 cm^2/m^2,male 40.6 cm^2/m^2);TPA female<343.0 mm^2/m^2, male<430.0 mm^2/m^2	9
Tianhao	2018	Prospective cohort	China	93	59.54 ± 9.69)	59.54 ± 9.69)	20.49 ± 2.66	23.97 ± 3.05	Gastric cancer	SMI: female ≤ 5.7 kg/m^2,male ≤ 7 kg/m^2	8
Stephen O'Brien	2018	Retrospective analysis	Ireland	56	67.4 ± 12.7	70.3 ± 10.2	23 ± 2.9	27.2 ± 4.4	Gastric cancer	SMI: female<38.5 cm^2/m^2,male<52.4 cm^2/m^2	7
Liangling Ma	2018	Prospective cohort	China	184	75(6)	71(6.75)	20.84(2.43)	22.98(2.90)	Advanced gastric cancer	SMI: female<38.5 cm^2/m^2,male<52.4 cm^2/m^2	6

Table 1 (continued)

Authors	Published years	Study design	Country of publication	Sample size	Age Median(SD)		BMI(kg/m2)		Staging of gastric cancer	Diagnosis of sarcopenia	NOS
					Sarcopenia	Nonsarcopenia	Sarcopenia	Nonsarcopenia			
Yasunari Fukuda	2016	Retrospective cohort	Japan	99	78 (67–85)	75 (66–91)	19.2 (15.6–26.9)	22.8(16.8–32.2)	Gastric cancer	SMI: female<6.42 kg/m^2,male<8.87 kg/m^2	8
Su-Lin Wang, MD1	2016	Prospective cohort	China	255	74.66 (6.80)	63.77 (10.66)	20.08 (2.65)	22.65 (2.78)	Gastric cancer	SMI: female ≤ 29.0 cm^2/m^2,male ≤ 36.0 cm^2/m^2, HS: female < 18 kg, male < 26 kg	8
Dong-Dong Huang, MD	2016	Prospective study	China	470	74(10)	63(4)	20.58 (2.50)	23.53 (2.77)	Early and advanced gastric cancer	SMI: female<34.9 cm^2/m^2,male<40.8 cm^2/m^2; HGS: female < 18 kg, male < 26 kg	7
DongDong Huang	2016	Prospective cohort	China	173	76 (7)	76 (7)	20.62 (2.51)	23.13 (2.98)	Gastric cancer	SMI: female < 34.9 cm^2/m^2,male< 40.8 cm^2/m^2	7
Chong-Jun Zhou	2016	Prospective study	China	240	76 (6.5)	71 (7)	20.70 (2.40)	23.12 (2.92)	Gastric cancer	SMI: female < 34.9 cm^2/m^2,male< 40.8 cm^2/m^2	7

Note: Appendicular skeletal muscle mass (ASMI); Skeletal muscle index (SMI); Hand grip strength (HGS, GS, HS); Muscle mass index (MMI); Psoas muscle index (PMI); Total psoas muscle index (TPA)

patients (OR = 1.907, 95% CI: 0.967 ~ 3.763, $P = 0.953$). In the correlation analysis of gastrectomy approaches, both multivariate (OR = 1.837, 95% CI: 1.237 ~ 2.727) and univariate (OR = 1.702, 95% CI: 1.125 ~ 2.574) analyses manifested that the risk of sarcopenia was higher in patients undergoing total gastrectomy than partial gastrectomy. The correlation analysis indicated that GC differentiation level (OR = 0.586, 95% CI: 0.325 ~ 1.059) and severe adverse reactions (NLR, HB, ALB) after chemotherapy (OR = 0.926, 95% CI: 0.793 ~ 1.082, $P = 0.054$) were not significantly associated with sarcopenia in GC patients. However, the above indexes with $P > 0.05$ (not statistically significant) should be further verified.

Sensitivity analysis, publication bias and meta-analysis

Given the high heterogeneity in the above analyses, the source of heterogeneity could not be found through sensitivity analysis. The pooled risk estimates were calculated again for each study, and the results were stable. The subgroup analysis based on regional distribution did not find the source of heterogeneity. The Egger's test confirmed that meta-analysis results were reliable for the 20 included papers, without noticeable publication bias ($P < 0.05$) (Fig. 8).Meta-regression was performed on age, sex, NRS, BMI, tumor size, tumor stage, gastrectomy method, tumor differentiation, and inflammatory indicators (NLR, HB, ALB) of adverse reactions after chemotherapy to determine the source of heterogeneity. The results implied that advanced age, high NRS score, males, and low BMI ($P < 0.005$) were positively correlated with the risk of sarcopenia in GC patients and were significant risk factors.

Discussion

Despite marked heterogeneity in the prevalence across studies, the overall prevalence of sarcopenia in GC patients was 26.6%. Our analyses concluded that the likelihood of sarcopenia in GC patients increased with age over 65 years, but not 70 years. The prevalence of sarcopenia varies from studies and depends on the definition [32]. Sarcopenia is now officially recognized as a muscle disease in the International Classification of Diseases (ICD-10: M62 [84]) [33]. Multiple mechanisms may be involved in the onset and progression of sarcopenia. Muscle wasting in sarcopenic patients is thought to interact with systemic inflammation, immune dysfunction, and nutritional deficiencies. Muscle loss changes over time and the actual measurable variables are muscle mass, strength, and physical performance, so diagnostic criteria are lacking. The most used definitions are EWGSOP2010 [34], revised EWGSOP2 (2019) [35], and the Asian Working Group on Sarcopenia (AWGS) [36]. According to the AWGS 2010 version, sarcopenia is defined as low muscle mass, which does not reflect

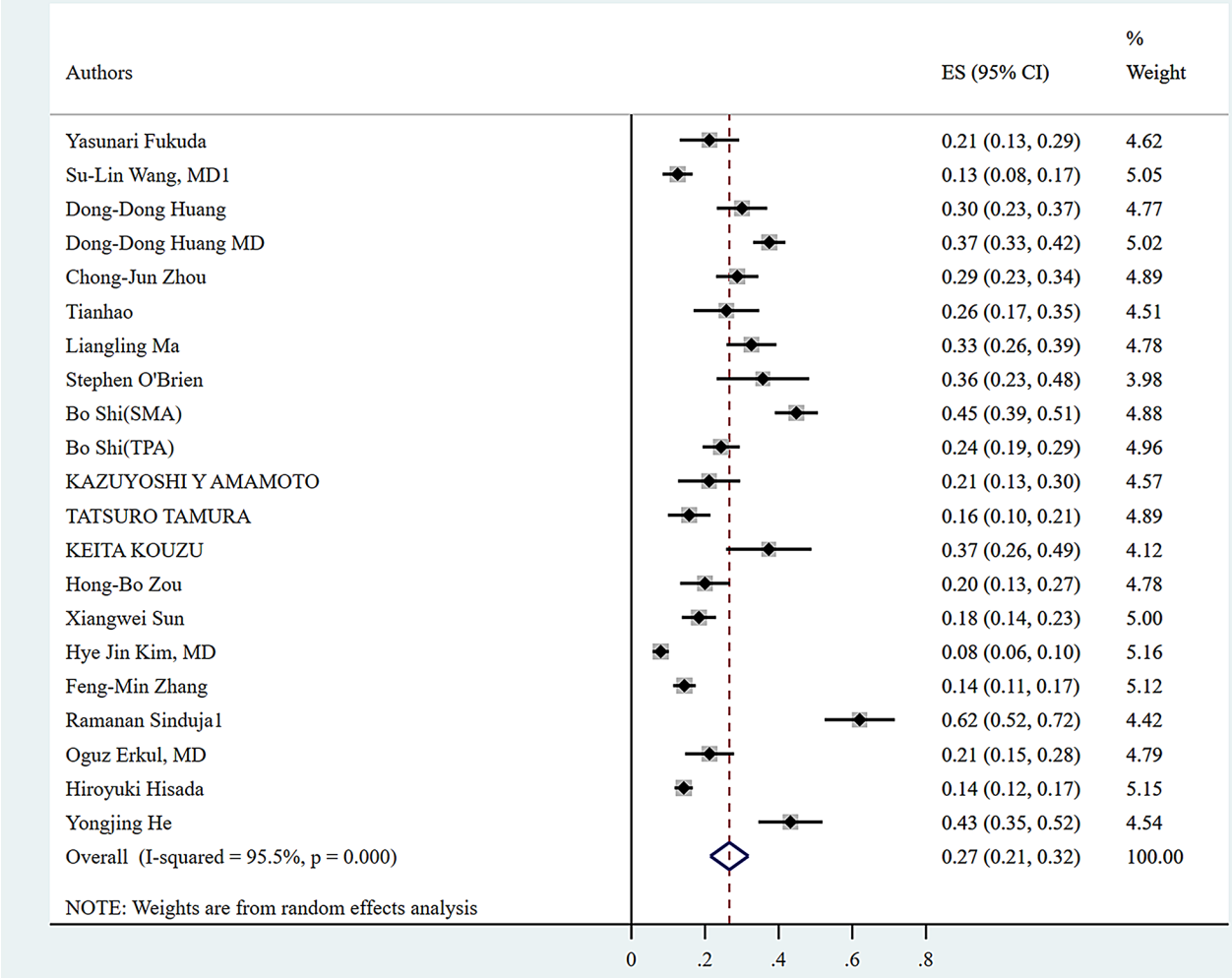

Fig. 2 Forest plot of the incidence of sarcopenia in GC patients

muscle function. The 2019 version is now commonly used and has different thresholds for Asians. A meta-analysis found that the prevalence of sarcopenia was 10% in individuals over 60 years and increased to 20% when diagnosed using bioelectrical impedance analysis (BIA) [37]. Another study reported the prevalence of sarcopenia in GC patients was between 12.5% and 69.8% [38]. However, another meta-analysis of 58,404 community residents aged ≥ 60 years estimated that the overall prevalence of sarcopenia was 10%. Compared to dual-energy X-ray absorptiometry (DXA), the overall prevalence of sarcopenia was slightly increased when muscle mass was measured using BIA, whereas the estimated prevalence differed, and the heterogeneity was not clear [39]. This heterogeneity may be related to the underlying mechanisms of GC-associated sarcopenia, including abnormal nutrition metabolism, muscle atrophy caused by decreased exercise, mitochondrial dysfunction, oxidative damage, cytokine levels, chemotherapy-induced sarcopenia (possibly due to mitochondrial damage), age-related hormonal changes (previous investigations found that the median age was 70 years), cell apoptosis, and ferroptosis. Due to individual differences, the source of heterogeneity could not be clarified through literature. Although the primary literature used relatively consistent definitions of sarcopenia, such as BIA, DXA, and a combination of

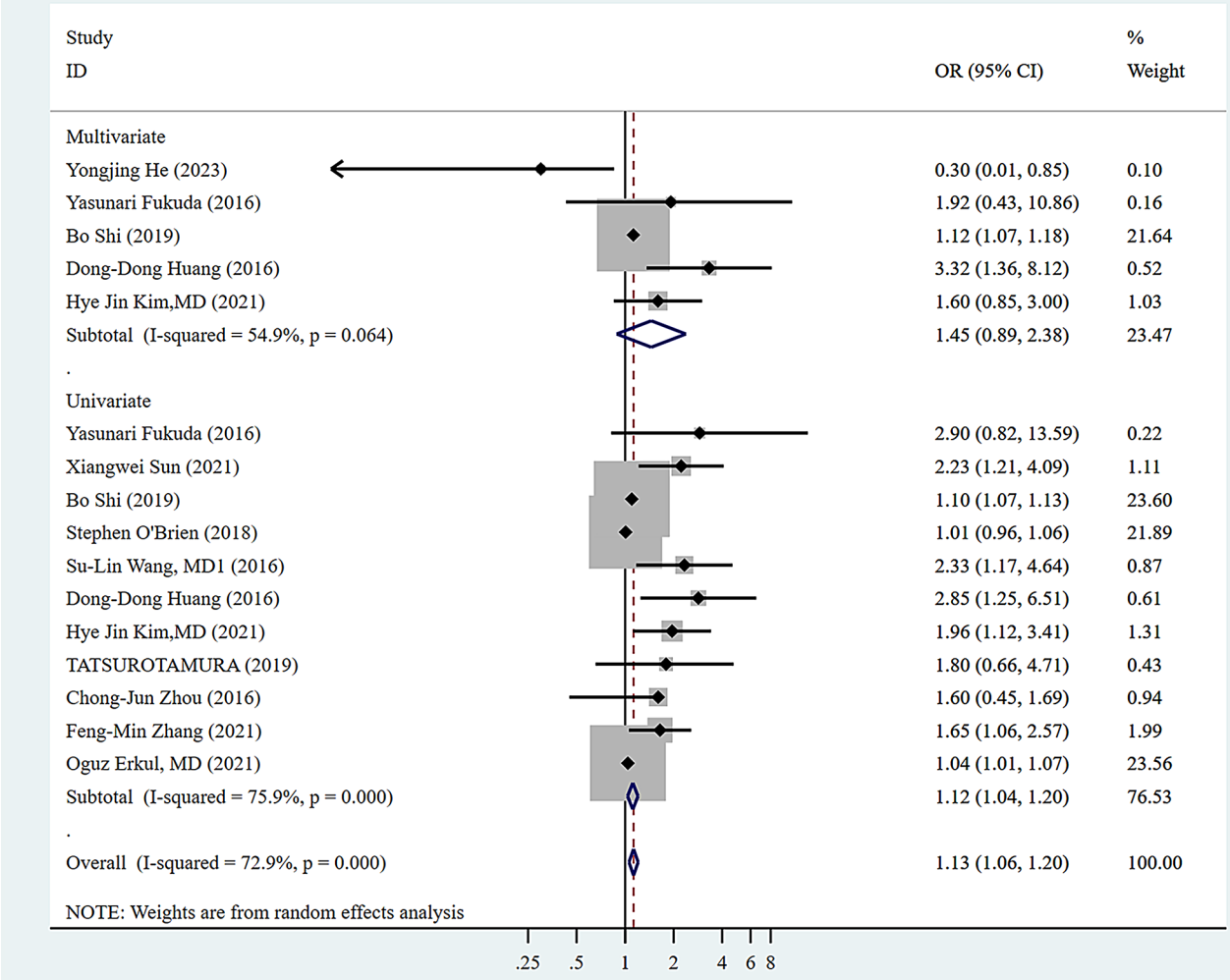

Fig. 3 Forest plot of subgroup analysis by age

muscle mass, muscle strength, and gait speed, there are still differences in the prevalence across studies, possibly resulting from different methodologies, thresholds, and diagnostic altitudes, leading to clinical heterogeneity. In addition to the above potential mechanisms, regional differences between Asian and European populations are also a source of heterogeneity. Literature has found that genetics, lifestyles, geographical differences, and body compositions in white American cohorts are also different from those in Asian populations [40].

Males were also a risk factor for sarcopenia in GC patients. A cross-sectional study in East China based on AWGS criteria found that the prevalence of sarcopenia was 19.2% in men and 8.6% in women [41]. The AWGS criteria are more suitable for Asian populations. The prevalence increases with age, and males are more likely to develop sarcopenia. Potential mechanisms of sex differences in the prevalence of sarcopenia include the following aspects. Muscle mass decreases progressively with age in males, which is not significant or only marginally significant in women [42]. Muscle mass and function are remarkably reduced in early menopause due to a significant decrease in estrogen [43], and not so much in the post-menopause stage. Additionally, testosterone and insulin-like growth factor-1 (IGF-1) levels decline noticeably with age in males, leading to a rapid loss of muscle

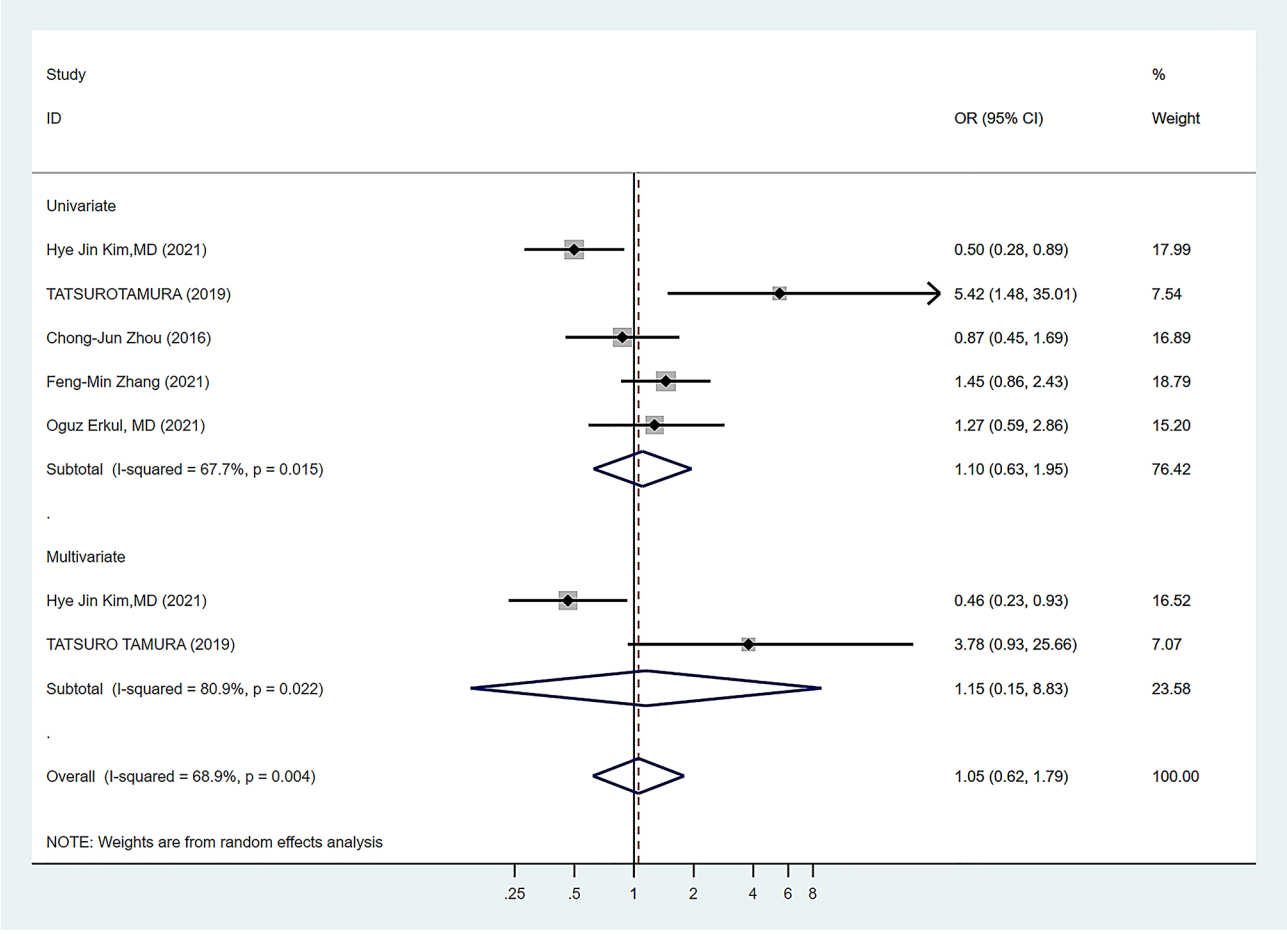

Fig. 4 Forest plot of subgroup analysis by male

mass and strength, which greatly increases the risk of sarcopenia in older men. IGF-1 is a common index that regulates muscle growth and repair, and IGF-1 levels do not change with age in older females [44]. Of course, some studies have shown that the etiology of sarcopenia in GC patients is multifactorial, including tumors, aging itself, socio-demographic factors, lifestyles, and health conditions, rather than sex [45]. It is worthwhile to explore whether sex is associated with sarcopenia in GC.

The included literature used CT to quantify the total cross-sectional skeletal muscle area at the third lumbar vertebrae (L3 SMA), which was further quantified by body surface area, and body weight was monitored to obtain SMI. The range of critical values for L3 SMA in GC patients combined with sarcopenia was different across the primary literature, and the standardized ranges of BMI and SMI were also different across countries. This paper identified low BMI as a potential risk factor for sarcopenia in GC. The reference range of BMI for sarcopenia in GC in the original Turkish literature was 19.8–25.7, with < 23 falling into the low BMI. According to the univariate analysis, the risk of sarcopenia in GC was raised in those with low BMI. Some papers have suggested that overweight or obesity, as measured by BMI, is negatively associated with the risk of sarcopenia. This negative association is possibly related to muscle mass, and higher BMI is associated with an enhanced risk of sarcopenia after adjusting for muscle mass [46]. BMI is expected to

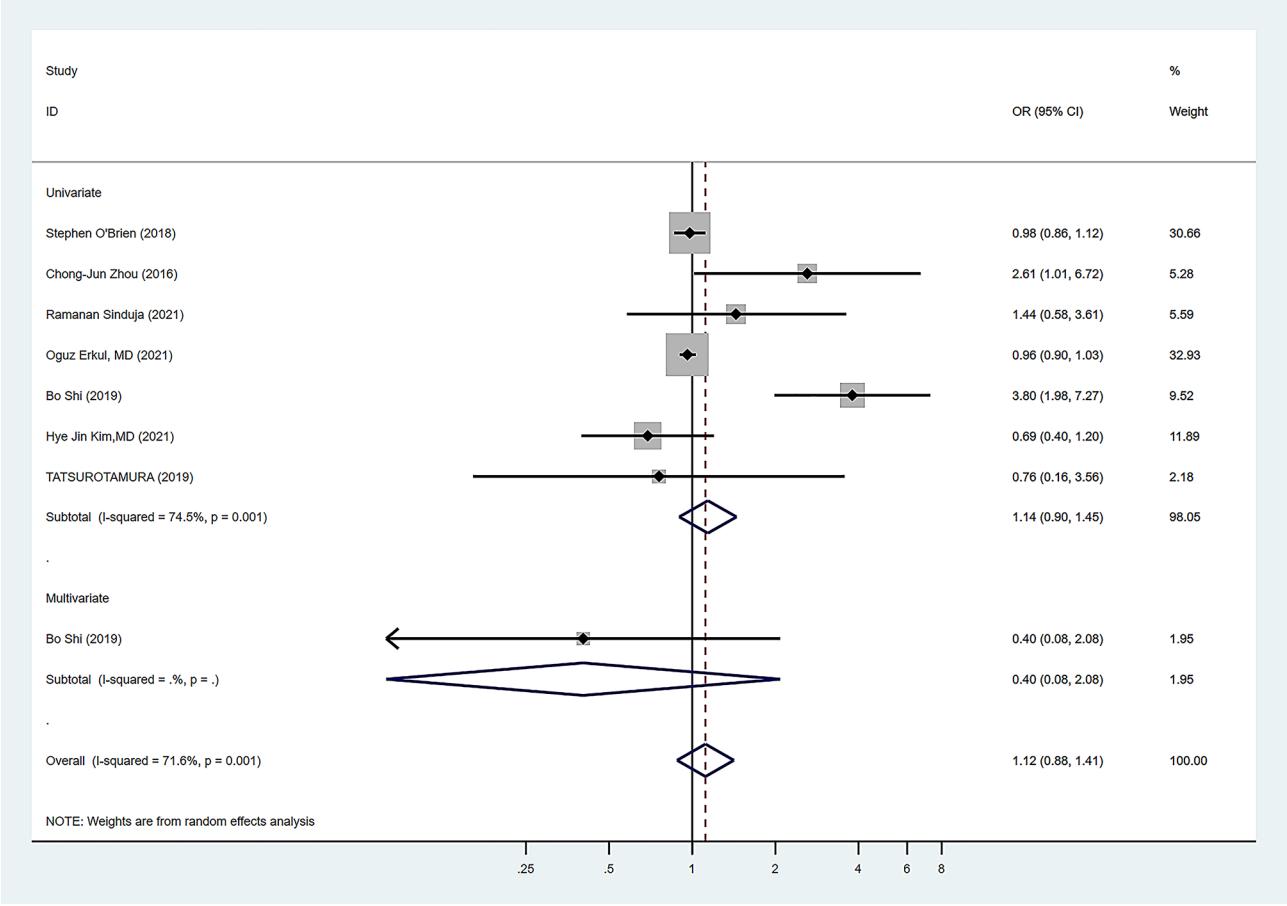

Fig. 5 Forest plot of subgroup analysis by BMI

be a risk factor for sarcopenia in GC. The evidence from these studies is low-quality, with only a few prospective cohort studies. Therefore, the effect of BMI on sarcopenia in GC should be viewed with caution in practical settings because of the possible reverse causality and confounding factors.

The NRS2002 score is computed based on disease severity (0 ~ 3 points), nutritional status (0 ~ 3 points), and age (≥ 70 years + 1 point). A score of ≥ 3 is considered at nutritional risk and < 3 is considered not at nutritional risk. Our analysis concluded that those with high NRS2002 scores had a strikingly increased risk of sarcopenia in GC. Currently, the NRS2002 is a simple and reliable tool for nutritional risk assessment and predicts postoperative outcomes in patients undergoing major surgery. Preoperative nutritional risk assessment has been widely practiced in the clinic, and malnutrition has been recognized as a public health problem. Many GC patients have poor nutritional status due to cancer pain, dietary restrictions, malabsorption, and chronic blood loss. Nutritional risk is strongly associated with increased mortality and postoperative complications in GC [47]. One meta-analysis elicited that the malnutrition risk in cancer patients ranged from 12.8 to 80.8% and that cancer patients at risk of malnutrition had poor overall survival. Hence, the NRS2002 could be a favorable tool for risk stratification of cancer patients [48]. The physical activity and nutritional status of GC patients seem to be associated with the risk of sarcopenia.

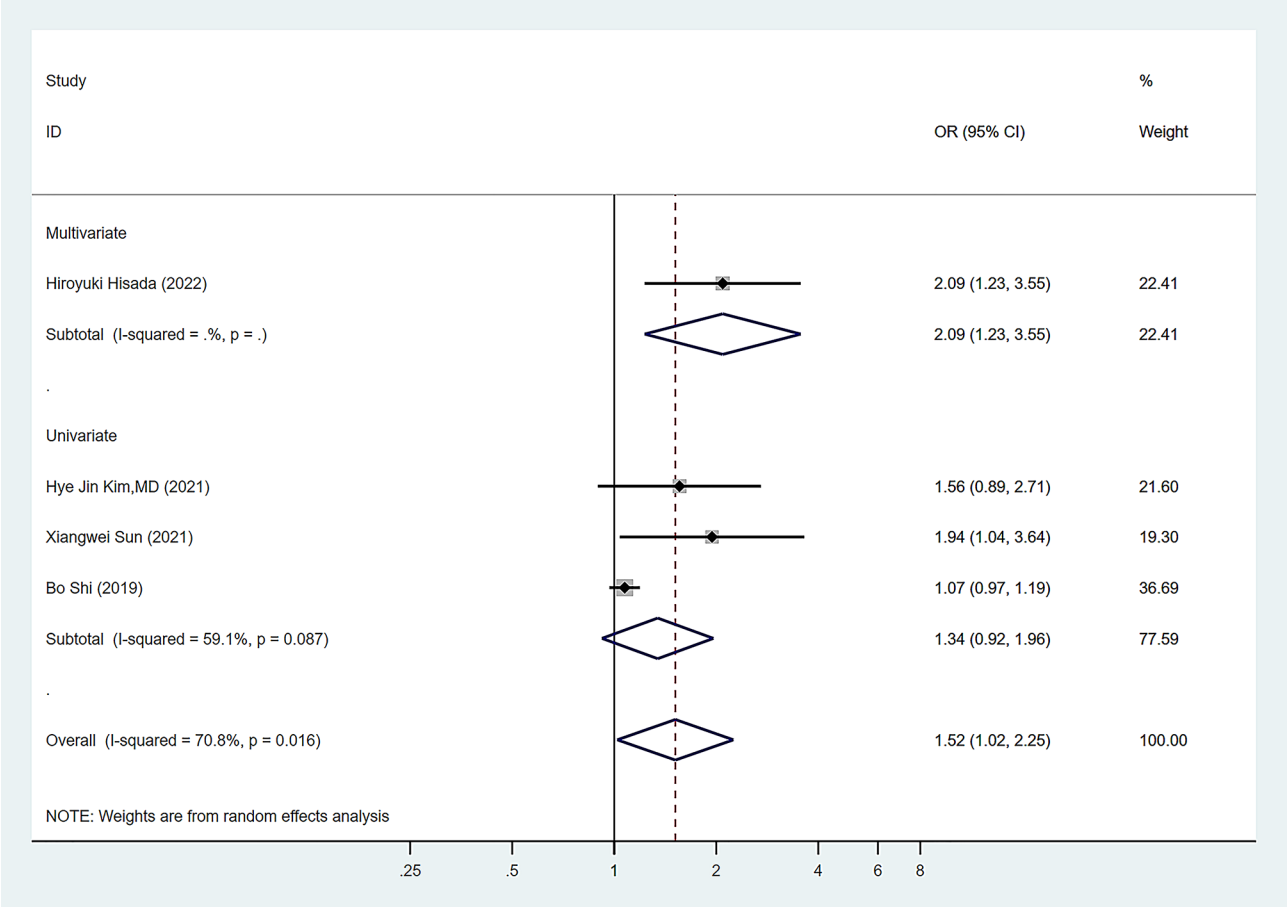

Fig. 6 Forest plot of subgroup analysis by tumor diameter

Furthermore, our findings unraveled that the larger tumor size was associated with a higher risk of sarcopenia in GC patients. A foreign study discovered that tumor size could be used as a five-year prognostic factor for patients with advanced GC [49]. Based on the SEER database, a study demonstrated that the prediction value of tumor size (the "T" stage of the tumor-node-metastasis staging system for many solid tumors) in the clinical prognosis of GC patients was uncertain and contradictory. It finally concluded that tumor size could not be used as a prognostic predictor for GC [50]. Establishing criteria for tumor size is a rather critical issue when classifying GC based on tumor size. While tumor stage, tumor differentiation, inflammatory indicators (NLR, HB, ALB) of adverse reactions after chemotherapy, and total gastrectomy approach had an OR value > 1, but $P > 0.05$, without statistical significance. Whether they can be used as risk factors should be further examined. Tumor stage and size are interrelated, and the optimal threshold for tumor size is different across infiltration depths [51]. Many studies have found that the risk of sarcopenia is inversely related to serum albumin concentration, with higher concentrations associated with a lower risk [52]. In recent years, the relationship between nutritional status and inflammatory indicators on the clinical prognosis of patients with diverse tumors, including GC, has also received increasing attention. Many hematological indexes such as C-reactive protein-albumin ratio,

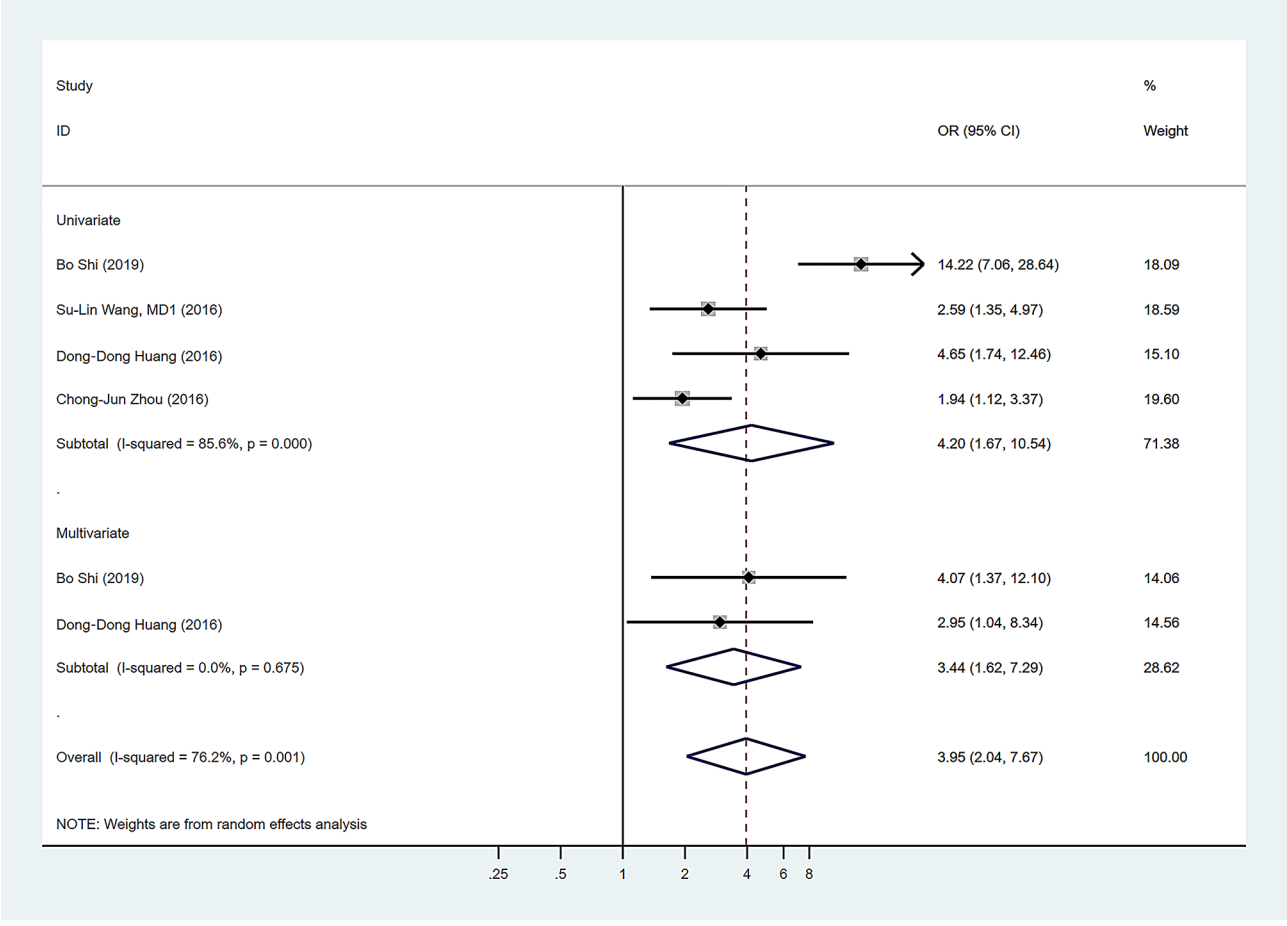

Fig. 7 Forest plot of subgroup analysis by NRS

neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and prognostic nutritional index have been reported as prognostic factors for sarcopenia in GC patients [53]. These studies suggested that all these inflammatory indexes could be predictors for sarcopenia. However, these indexes have different limitations and do not fully reflect the incidence and prognosis of GC patients. For example, a few papers investigated the gastrectomy approach so it may require further validation. Increasing literature proves that cancer patients have an elevated risk of sarcopenia, but it is unclear whether GC or other tumors develop independently. Abundant data are needed to further determine whether the pathogenesis and the five-year survival rate of GC are related to sarcopenia. The prevention and treatment of early sarcopenia are not only valuable for improving the quality of life of patients but also for improving their survival rate and reducing the risk of cancer.

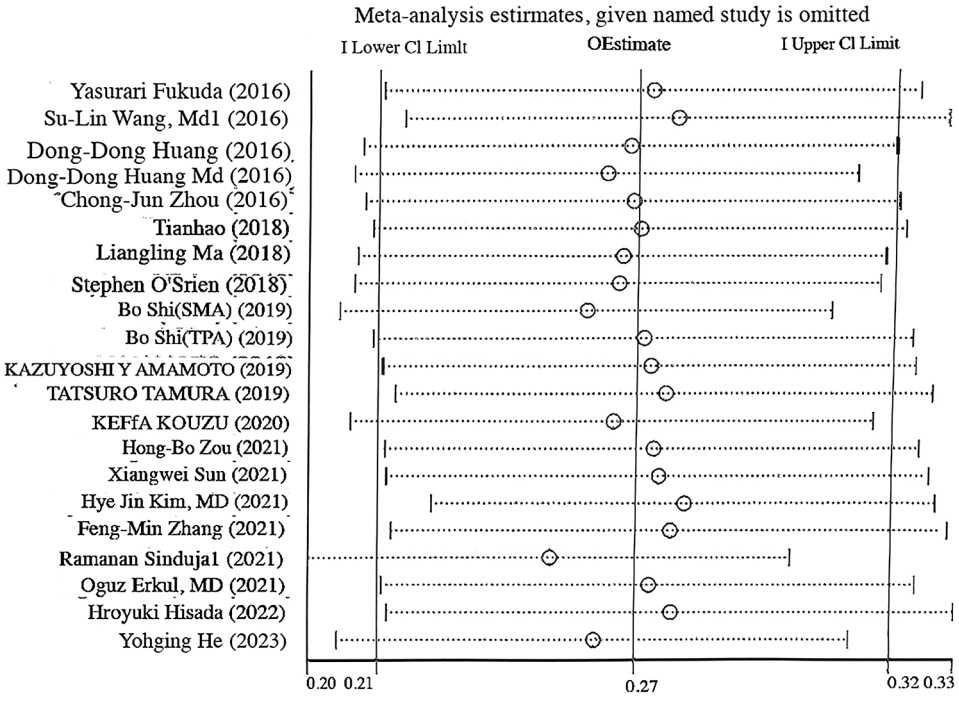

Fig. 8 Forest plot of sensitivity analysis

Conclusion

In this meta-analysis, the incidence of sarcopenia in GC patients was 26.6% in the Asian population. A high nutritional risk index was a risk factor for sarcopenia, while over 65 years old and tumor diameter > 3 cm may be risk factors. Whether males and other factors including tumor stage, resection methods, and adverse reactions after chemotherapy are associated with sarcopenia needs further investigation. Because the mechanism of GC-related sarcopenia is not clear, and few articles focus on the mechanism and differences among various factors, this article only analyzes the incidence of sarcopenia in GC patients. The mechanism between various risk factors and sarcopenia needs to be further studied. The incidence of sarcopenia in GC patients is higher than that in the general population, which can affect the survival and condition of patients. More research is needed to develop more appropriate treatment methods for GC patients with sarcopenia. In the future, more genome-wide association analysis, epigenetics, transcriptomics, proteomics, metabolomics, and microbiome studies of sarcopenia will be conducted. These studies could deepen the understanding of the etiologic basis of GC combined with sarcopenia from genetic and molecular perspectives. In addition, potential interactions between genetics and environmental factors are worth exploring.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-13766-0.

Supplementary Material 1: Table S1. Search strategy

Supplementary Material 2

Acknowledgements
Not applicable.

Author contributions
All authors contributed to the study conception and design. Mingyue Fu: Writing - original draft preparation， Writing - review and editing conceptualization, methodology. Formal analysis and investigation, Visualization; Xuehong Wang: Funding acquisition, Project administration; Jiangfeng Wang: Supervision; JingZhou: Data Curation, Resources; Mingyue Fu, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding
This work was supported by Key Clinical Specialty Construction Project of Qinghai Province (2022－118) and Clinical Medical Research Center for Digestive Diseases of Qinghai Province (2019-SF-L3).

Data availability
The datasets used and/or analyse d during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 16 May 2024 / Accepted: 18 February 2025
Published online: 16 April 2025

References

1. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing.* 2010;39(4):412–23.
2. Sartori R, Romanello V, Sandri M. Mechanisms of muscle atrophy and hypertrophy: implications in health and disease. Nat Commun. 2021;12(1):330.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–49.
4. Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, Compher C, Correia I, Higashiguchi T, Holst M, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr. 2017;36(1):49–64.
5. Zhuang CL, Shen X, Zou HB, Dong QT, Cai HY, Chen XL, Yu Z, Wang SL. EWGSOP2 versus EWGSOP1 for sarcopenia to predict prognosis in patients with gastric cancer after radical gastrectomy: analysis from a large-scale prospective study. Clin Nutr. 2020;39(7):2301–10.
6. Haiducu C, Buzea A, Mirea LE, Dan GA. The prevalence and the impact of sarcopenia in digestive cancers. A systematic review. Rom J Intern Med. 2021;59(4):328–44.
7. Zhang FM, Wu HF, Shi HP, Yu Z, Zhuang CL. Sarcopenia and malignancies: epidemiology, clinical classification and implications. Ageing Res Rev. 2023;91:102057.
8. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009;62(10):1006–12.
9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev. 2021;10(1):89.
10. Wells GA, Wells G, Shea B, Shea B, O'Connell D, Peterson J, Welch, Losos M, Tugwell P, Ga SW et al. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses. In: *2014;* 2014.
11. Zhou CJ, Zhang FM, Zhang FY, Yu Z, Chen XL, Shen X, Zhuang CL, Chen XX. Sarcopenia: a new predictor of postoperative complications for elderly gastric cancer patients who underwent radical gastrectomy. J Surg Res. 2017;211:137–46.
12. Huang DD, Zhou CJ, Wang SL, Mao ST, Zhou XY, Lou N, Zhang Z, Yu Z, Shen X, Zhuang CL. Impact of different sarcopenia stages on the postoperative outcomes after radical gastrectomy for gastric cancer. Surgery. 2017;161(3):680–93.
13. Huang DD, Chen XX, Chen XY, Wang SL, Shen X, Chen XL, Yu Z, Zhuang CL. Sarcopenia predicts 1-year mortality in elderly patients undergoing curative gastrectomy for gastric cancer: a prospective study. J Cancer Res Clin Oncol. 2016;142(11):2347–56.
14. Wang SL, Zhuang CL, Huang DD, Pang WY, Lou N, Chen FF, Zhou CJ, Shen X, Yu Z. Sarcopenia adversely impacts postoperative clinical outcomes following gastrectomy in patients with gastric cancer: A prospective study. Ann Surg Oncol. 2016;23(2):556–64.
15. Fukuda Y, Yamamoto K, Hirao M, Nishikawa K, Nagatsuma Y, Nakayama T, Tanikawa S, Maeda S, Uemura M, Miyake M, et al. Sarcopenia is associated with severe postoperative complications in elderly gastric cancer patients undergoing gastrectomy. Gastric Cancer. 2016;19(3):986–93.
16. Ma L, Zhang F, Wang S, Yu Z. Effect of sarcopenia on postoperative complications in elderly patients with advanced gastric Cancer after radical gastrectomy. J Math Med. 2018;31(2):170–3.
17. O'Brien S, Twomey M, Moloney F, Kavanagh RG, Carey BW, Power D, Maher MM. O'Connor OJ, Ó'Súilleabháin C: sarcopenia and Post-Operative morbidity and mortality in patients with gastric Cancer. J Gastric Cancer. 2018;18(3):242–52.
18. Tian H, Zhou D, Ye C, Tian F, Zhang Y, Gao X, Li G, Wang X. Effect of preoperative sarcopenia on clinical outcomes in patients with gastric cancer: a prospective cohort study. Parenter Enter Nutr. 2018;25(03):166–70.
19. Shi B, Liu S, Chen J, Liu J, Luo Y, Long L, Lan Q, Zhang Y. Sarcopenia is associated with perioperative outcomes in gastric Cancer patients undergoing gastrectomy. Ann Nutr Metab. 2019;75(4):213–22.
20. Yamamoto K, Hirao M, Nishikawa K, Omori T, Yanagimoto Y, Shinno N, Sugimura K, Miyata H, Wada H, Takahashi H, et al. Sarcopenia is associated with impaired overall survival after gastrectomy for elderly gastric Cancer. Anticancer Res. 2019;39(8):4297–303.
21. Tamura T, Sakurai K, Nambara M, Miki Y, Toyokawa T, Kubo N, Tanaka H, Muguruma K, Yashiro M, Ohira M. Adverse effects of preoperative sarcopenia on postoperative complications of patients with gastric Cancer. Anticancer Res. 2019;39(2):987–92.
22. Kouzu K, Tsujimoto H, Sugasawa H, Ishibashi Y, Itazaki Y, Tsuchiya S, Kishi Y, Ueno H. Impact of postoperative reduced skeletal muscle on prognosis after recurrence in gastric cancer. Mol Clin Oncol. 2021;14(1):3.
23. Zhang FM, Zhang XZ, Zhu GL, Lv LQ, Yan XL, Wu WX, Wang SL, Chen XL, Zhuang CL, Yu Z. Impact of sarcopenia on clinical outcomes of patients with stage I gastric cancer after radical gastrectomy: A prospective cohort study. Eur J Surg Oncol. 2022;48(3):541–7.
24. Zou HB, Yan XL, Dong WX, Yu DY, Zhang FM, Zhou LP, Shen ZL, Cai GJ, Zhuang CL, Yu Z. Sarcopenia is a predictive factor of poor quality of life and prognosis in patients after radical gastrectomy. Eur J Surg Oncol. 2021;47(8):1976–84.
25. Kim HJ, Lee ES, Kim BJ, Kim WS, Park JY, Kim JG, Park JM, Kim JW, Chi KC, Kang H. Risk factors and clinical outcomes of postgastrectomy sarcopenia newly developed after curative resection for gastric cancer. Med (Baltim). 2022;101(6):e28699.
26. Erkul O, Cekic AB, Cansu A, Yildirim R, Guner A. Effects of sarcopenia on postoperative outcomes in patients who underwent gastrectomy for gastric Cancer. J Surg Res. 2022;274:196–206.
27. Sinduja R, Anandhi A, Sureshkumar S, Barathi D, Mahalakshmy T, Kate V. Role of sarcopenia in predicting the postoperative morbidity and perioperative mortality in patients undergoing elective surgery for gastric Cancer. J Gastrointest Cancer. 2022;53(4):939–47.
28. Sun X, Xu J, Chen X, Zhang W, Chen W, Zhu C, Sun J, Yang X, Wang X, Hu Y, et al. Sarcopenia in patients with normal body mass index is an independent predictor for postoperative complication and Long-Term survival in gastric Cancer. Clin Transl Sci. 2021;14(3):837–46.
29. Hisada H, Tsuji Y, Obata M, Cho R, Nagao S, Miura Y, Mizutani H, Ohki D, Yakabi S, Takahashi Y, et al. The impact of sarcopenia on short- and long-term outcomes of endoscopic submucosal dissection for early gastric cancer. J Gastroenterol. 2022;57(12):952–61.
30. He Y, Wei H, Liu W, Pan L, Wang Y, Li S. Risk factors of sarcopenia in patients with gastric cancer. Electron Jourmal Metabolism Nutr Cancer. 2023;10(1):95–100.
31. Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr. 2003;22(4):415–21.
32. Yuan S, Larsson SC. Epidemiology of sarcopenia: prevalence, risk factors, and consequences. Metabolism. 2023;144:155533.
33. Falcon LJ, Harris-Love MO. Sarcopenia and the new ICD-10-CM code: screening, staging, and diagnosis considerations. Fed Pract. 2017;34(7):24–32.
34. Cruz-Jentoft AJ, Baeyens J-P, Bauer JM, Boirie Y, Cederholm T, Landi F, Cruz-Gómez A. European working group on sarcopenia in older people. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. In: *2010*; 2010.
35. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31.
36. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, Chou MY, Chen LY, Hsu PS, Krairit O, et al. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. J Am Med Dir Assoc. 2014;15(2):95–101.
37. Shafiee G, Keshtkar A, Soltani A, Ahadi Z, Larijani B, Heshmat R. Prevalence of sarcopenia in the world: a systematic review and meta- analysis of general population studies. J Diabetes Metab Disord. 2017;16:21.
38. Palmela C, Velho S, Agostinho L, Branco F, Santos M, Santos MP, Oliveira MH, Strecht J, Maio R, Cravo M, et al. Body composition as a prognostic factor of neoadjuvant chemotherapy toxicity and outcome in patients with locally advanced gastric Cancer. J Gastric Cancer. 2017;17(1):74–87.
39. Shafiee G, Keshtkar A, Soltani A. Prevalence of sarcopenia in the world: a systematic review and meta- analysis of general population studies. J Diabetes Metab Disord. 2017);16:21.
40. Zhou Y, Wu K, Shen H, et al. Geographical differences in osteoporosis, obesity, and sarcopenia related traits in white American cohorts. Sci Rep. 2019).;9:12311.

41. Du Y, Wang X, Xie H, Zheng S, Wu X, Zhu X, Zhang X, Xue S, Li H, Hong W, et al. Sex differences in the prevalence and adverse outcomes of sarcopenia and sarcopenic obesity in community dwelling elderly in East China using the AWGS criteria. BMC Endocr Disord. 2019;19(1):109.
42. Shimokata H, Ando F, Yuki A, Otsuka R. Age-related changes in skeletal muscle mass among community-dwelling Japanese: a 12-year longitudinal study. Geriatr Gerontol Int. 2014;14(Suppl 1):85–92.
43. Tiidus PM. Benefits of Estrogen replacement for skeletal muscle mass and function in post-menopausal females: evidence from human and animal studies. Eurasian J Med. 2011;43(2):109–14.
44. Yamada M, Nishiguchi S, Fukutani N, Tanigawa T, Yukutake T, Kayama H, Aoyama T, Arai H. Prevalence of sarcopenia in community-dwelling Japanese older adults. J Am Med Dir Assoc. 2013;14(12):911–5.
45. Gao Q, Hu K, Yan C, Zhao B, Mei F, Chen F, Zhao L, Shang Y, Ma Y, Ma B. Associated factors of sarcopenia in Community-Dwelling older adults: A systematic review and Meta-Analysis. Nutrients 2021, 13(12).
46. Liu C, Wong PY, Chung YL, Chow SK, Cheung WH, Law SW, Chan JCN, Wong RMY. Deciphering the obesity paradox in the elderly: A systematic review and meta-analysis of sarcopenic obesity. Obes Rev. 2023;24(2):e13534.
47. Ma BW, Chen XY, Fan SD, Zhang FM, Huang DD, Li B, Shen X, Zhuang CL, Yu Z. Impact of sarcopenia on clinical outcomes after radical gastrectomy for patients without nutritional risk. Nutrition. 2019;61:61–6.
48. Zang Y, Xu W, Qiu Y, Gong D, Fan Y. Association between risk of malnutrition defined by the nutritional risk screening 2002 and postoperative complications and overall survival in patients with cancer: A Meta-Analysis. Nutr Cancer. 2023;75(8):1600–9.
49. Im WJ, Kim MG, Ha TK, Kwon SJ. Tumor size as a prognostic factor in gastric cancer patient. J Gastric Cancer. 2012;12(3):164–72.
50. Xiao J, Shen K, Fan H, Wang G, Liu K, Wang Y, Ma X, Ni P, Xu Z, Yang L. Prognostic value of tumor size in gastric cancer: A retrospective cohort study based on SEER database. Int J Surg Pathol. 2023;31(7):1273–82.
51. Liang Y, Liu L, Xie X, Xia L, Meng J, Xu R, He D. Tumor size improves the accuracy of the prognostic prediction of lymph Node-Negative gastric Cancer. J Surg Res. 2019;240:89–96.
52. Almouaalamy N, Adem SH, Alsubhi AA, Alansari AB, Yahya MA, Alsadan SA. Sarcopenia and associated risk factors in oncology outpatients in specialized cancer centers in Saudi Arabia: a cross-sectional study. Ann Med Surg (Lond). 2023;85(6):2592–7.
53. Ding P, Lv J, Sun C, Chen S, Yang P, Tian Y, Zhou Q, Guo H, Liu Y, Zhao Q. Combined systemic inflammatory immunity index and prognostic nutritional index scores as a screening marker for sarcopenia in patients with locally advanced gastric cancer. Front Nutr. 2022;9:981533.

Publisher's note