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Review

Epidemiology of sarcopenia: Prevalence, risk factors, and consequences

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ABSTRACT

Sarcopenia is a geriatric condition featured by a progressive loss of muscle mass and function and associated with various adverse health outcomes. In this review, we aimed to summarize the epidemiological features of sarcopenia as well as consequences and risk factors of the disease. We performed a systematic review of meta-analysis on sarcopenia to collect data. The prevalence of sarcopenia varied between studies and depending on definition used. Sarcopenia was estimated to influence 10 %–16 % of the elderly worldwide. The prevalence of sarcopenia was higher among patients compared to general populations. The prevalence of sarcopenia ranged from 18 % in diabetic patients to 66 % in patients with unresectable esophageal cancer. Sarcopenia is associated with a high risk of a wide range of adverse health outcomes, including poor overall and disease-progression free survival rate, postoperative complications, and longer hospitalization in patients with different medical situations as well as falls and fracture, metabolic disorders, cognitive impairment, and mortality in general populations. Physical inactivity, malnutrition, smoking, extreme sleep duration, and diabetes were associated with an increased risk of sarcopenia. However, these associations were mainly based on non-cohort observational studies and need confirmation. High-quality cohort, omics, and Mendelian randomization studies are needed to deeply understand the etiological basis of sarcopenia.

1. Introduction

Sarcopenia is a geriatric condition featured by a progressive loss of muscle mass and function and has been associated with several adverse health outcomes, including fracture, functional decline, and mortality [1]. Except commonly affecting the elderly, it can also onset in mid-life [1] and become prevalent among certain populations, such as patients with cancer [2], kidney dysfunction [3], liver disease [4], and metabolic disorders [5]. Sarcopenia is also an important prognostic indicator for survival and clinical complications in these patients [2–5]. Even though sarcopenia has received attention of intense research, it is poorly concluded about its epidemiological features, risk factors, and complications. This review aims to summarize the epidemiological features of sarcopenia as well as consequences and risk factors of the disease.

2. Materials and methods

To summarize available data in a comprehensive way, we performed a systematic review of meta-analysis on sarcopenia (Fig. 1). We searched "sarcopenia" and "meta" in the PubMed database and obtained 726 studies after removing publications before 2010 when most definitions of sarcopenia were published [1]. Two authors independently reviewed the 726 studies and classified included studies into two categories that are studies on risk factors and on consequences. We excluded studies on sarcopenia components instead of sarcopenia as a binary phenotype, studies on obesity sarcopenia, and studies without performed meta-analysis. We extracted information on title, PubMed ID, publication year, first author, population (general population or patients), number of studies included in meta-analysis, total sample size, prevalence of sarcopenia, the associations, and heterogeneity.

3. Results

We included 130 studies in the systematic review of risk factors and consequences of sarcopenia, among which 25 and 109 studies were on risk factor and consequences, respectively. Although this review did not aim to estimate prevalence of sarcopenia in a comprehensive way, we extracted corresponding data to complement the current evidence of prevalence of sarcopenia shown in previous studies, especially among patients with different medical conditions.

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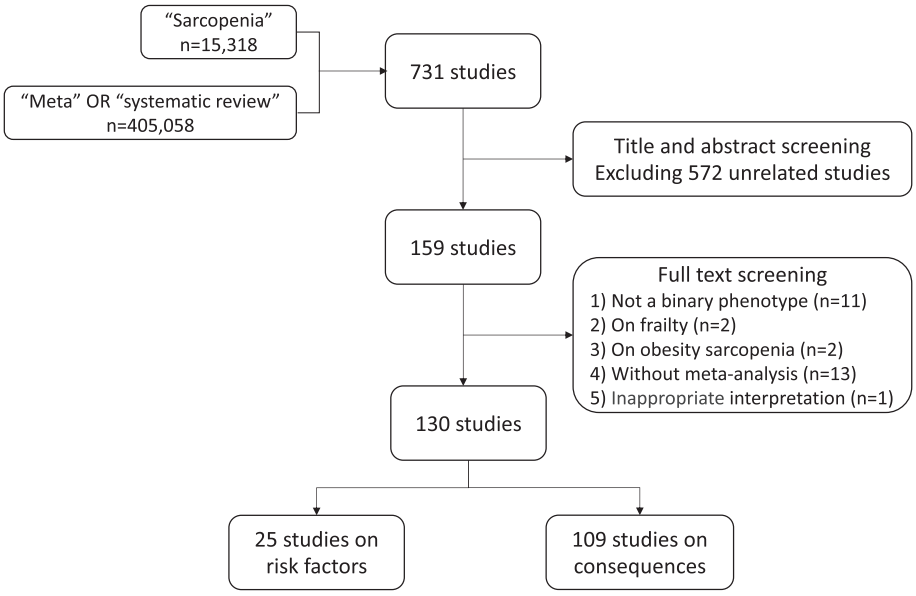

Fig. 1. Flow chart of the systematic review.

3.1. Definitions and prevalence of sarcopenia

Before 2010 when the definition of sarcopenia was proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) [6], low muscle mass was used to define the disease [7], which is partial and could not reflect muscle function. Nowadays, the most commonly used definition of sarcopenia is that recommended by EWGSOP, which was updated as EWGSOP2 in 2019 [8]. This definition was supported by the Asian Working Group on Sarcopenia albeit with different cutoffs for Asians [9] and this is the only definition endorsed by a range of international scientific societies [1]. There are also other definitions for sarcopenia, including the International Working Group on Sarcopenia (IWGS) [10] and the Foundation for the National Institute of Health (FNIH) [11]. These definitions have been summarized in Table 1. Sarcopenia has now been formally recognized as a muscle disease in the International Classification of Disease (ICD-10: M62 [84]) [12].

Even though recent studies used comparatively consistent definitions for sarcopenia, different cut-offs and applied measurements (i.e., bioelectrical impedance (BIA) or dual-energy x-ray absorptiometry (DXA)) make it still difficult to estimate disease prevalence in a homogeneous manner, which is reflected by a wide range of prevalence of sarcopenia in the majority of meta-analyses (Supplementary Table 1). Despite this, there are several meta-analyses with comprehensively collected data on the prevalence of sarcopenia by commonly used definitions, which is informative to understand the epidemiological features of sarcopenia.

The prevalence of sarcopenia varies largely between studies and depends on definition used to define the disease (Table 2) [13,14]. In the systematic review by Nascimento PR et al. [13], the global prevalence of sarcopenia ranged from 5 % (95 % confidence interval [CI] 1 %–10 %) for EWGSOP2 to 17 % (95 % CI 11 %–23 %) for IWGS among the elderly. However, the highest prevalence of sarcopenia was observed for EWGSOP (22 %, 95 % CI 20 %–25 %) and the lowest was for FNIH (11 %, 95 % CI 9 %–14 %) in the study by Petermann-Rocha F et al. [14]. The pooled prevalence of all definitions was around 10 % (95 % CI 7 %–12 %) in Nascimento PR et al. study [13] and 16 % (95 % CI 15 %–17 %) in Petermann-Rocha F et al. study [14]. Even though two studies were based on generally healthy populations, like community-dwelling elderlies, the estimated prevalence of sarcopenia differed, and the reasons for this heterogeneity remain unclear. In another meta-analysis of 58,404 community-dwelling participants aged 60 years and older, the overall global prevalence of sarcopenia was estimated to be 10 % and found to be slightly higher when using BIA compared to DXA to measure muscle quantity [15].

The prevalence of sarcopenia was much higher in different patient groups compared to the general population (Table 3). In the included studies reporting pooled prevalence, the prevalence of sarcopenia ranged from 18 % in patients with diabetes [5] to 66 % in patients with unresectable esophageal cancer [16]. A high prevalence of sarcopenia was also observed in patients with kidney and liver disease [4,17], who need surgery [18], and with different site-specific cancers [2,19–23].

3.2. Consequences of sarcopenia

In studies involving patients with different medical conditions, mortality, survival, and postoperative complications were the primarily studied and observed outcomes (Supplementary Table 1). Overall, baseline sarcopenia or preoperative sarcopenia was associated with an increased risk of short- and long-term mortality, poor overall and progression-free survival rate, overall and severe complications, postoperative infection, and prolonged hospitalization in most included studies (Supplementary Table 1). However, the risks varied between different patient groups concerning mortality and survival rate (Fig. 2) and other consequences. The all-cause mortality of sarcopenia was the highest among patients with emergency laparotomy (odds ratio [OR] = 3.50, 95 % CI 2.54–4.81) [24] and the lowest among patients with radical cystectomy (hazard ratio [HR] = 1.41, 95 % CI 1.22–1.62) [25] (Fig. 2). Likewise, the risk of poor overall survival was observed to be highest among patients with lung cancer (OR = 3.07, 95 % CI 2.45–3.85) and to be lowest among patients with esophageal cancer (HR = 1.12, 95 % CI 1.04–1.20) (Fig. 2). Of note, even though the comparison of the magnitude of the associations might reflect seriousness of sarcopenia in the risk of death and poor survival among different patient groups, it should be interpreted with caution for following reasons. First, there were moderate to high heterogeneity between studies in these combined associations. Second, certain associations with large CI due to small sample sizes were imprecise. Third, some studies were mainly based on a retrospective design where measurement error of sarcopenia might bias the results. Last but not least, the associations might be largely influenced by used definitions of sarcopenia and possibly by different measurements of muscle mass, which confined the comparability of these associations. Sarcopenia was additionally associated with an increased risk of disease progression in patients with liver diseases [26,27], an increased risk of osteoporosis in individuals with chronic obstructive

Table 1
Commonly used definitions of sarcopenia and cut-offs of indicators after 2010.

Classification	Definition	Muscle mass	Muscle strength	
		ASM (kg) or ASM/height^2 (kg/m^2)	Grip strength (kg)	Gait speed (m/s)
EWGSOP	* Low muscle mass * Low grip strength or slow gait speed	Based on BIA: Men < 8.31–10.75 kg/m^2 Women < 6.42–6.75 kg/m^2 Based on DXA: Men < 7.23–7.26 kg/m^2 Women < 5.45–5.67 kg/m^2	Men < 30 Women < 20	Men and women < 0.8
EWGSOP2	* Low muscle mass * Low grip strength	Based on DXA: Men < 7.0 kg/m^2 Women < 5.5 kg/m^2	Men < 27 Women < 16	Men and women < 0.8
AWGS	* Low muscle mass * Low grip strength or slow gait speed	Based on BIA: Men < 7.0 kg/m^2 Women < 5.7 kg/m^2 Based on DXA: Men < 7.0 kg/m^2 Women < 5.4 kg/m^2	Men < 26 Women < 18	Men and women < 0.8
IWGS	* Low muscle mass * Slow gait speed	Based on BIA: Men < 7.23 kg/m^2 Women < 5.67 kg/m^2 Based on DXA: Men < 7.23 kg/m^2 Women < 5.67 kg/m^2	–	Men and women < 1.0
FNIH	* Low muscle mass * Low grip strength	Men < 19.75 kg Women < 15.02 kg	Men < 26 Women < 16	Men and women < 0.8

AWGS, Asian Working Group for Sarcopenia; BIA, bioelectrical impedance; DXA, dual-energy x-ray absorptiometry; EWGSOP, European Working Group on Sarcopenia in Older People; EWGSOP2, European Working Group on Sarcopenia in Older People 2; FNIH, Foundation for the National Institute of Health; IWGS, International Working Group on Sarcopenia.

pulmonary disease [28], and an increased risk of major adverse cardiovascular outcomes and heart failure-related hospitalization in patients with coronary artery disease [29].

The focus of consequences of sarcopenia differed between studies in patients and general populations. With exception for an increased risk of mortality, sarcopenia was further associated with a high risk of cognitive impairment, osteoporosis, falls, fracture, functional decline, hospitalization, metabolic syndrome, diabetes, nonalcoholic liver disease, liver fibrosis, hypertension, depression, and dysphagia among general populations (Table 4). Even though most these associations were based on meta-analyses of cohort studies, the causality remained uncertain due to residual confounding and measurement errors. In addition, the associations may differ using different definitions of sarcopenia, which may also partly explain the high heterogeneity in certain studies. However, falls appeared to be robustly associated with sarcopenia regardless of definition used for sarcopenia [30].

3.3. Risk factors for sarcopenia

There are comparatively fewer studies exploring the risk factors for sarcopenia (Supplementary Table 2). Overall, evidence of these studies was low with a few prospective cohort studies. Thus, the associations reported in previous meta-analysis of risk factors for sarcopenia (Table 5) should be interpreted with caution due to the possibility of reverse causality and confounding affecting the results.

Overweight or obesity measured by body mass index was inversely associated with the risk of sarcopenia [31–33]. However, this inverse association might be biased by muscle mass, which is positively correlated with body mass index [31]. After adjustment for muscle quantity, higher body mass index was associated with an increased risk of sarcopenia [31]. This association was partly in line with a positive association between visceral fat area (a more precise indicator of fat accumulation) and the risk of sarcopenia [5], which indicates that purely excessive fat is not a protective factor for sarcopenia. Instead, sarcopenic obesity affecting 11 % of global older adults has been associated with various adverse outcomes [34].

Among lifestyle factors, physical activity and nutritional status determined by dietary intake or nutrient supplementation appear to be associated with the risk of sarcopenia [5,32,35,36]. In addition, a mixed promotion of physical activity and nutritional supplementation may also be an effective intervention in sarcopenic patients [37,38]. To detail corresponding prevention and therapeutic strategies, studies on comparative effects of individual and combinations of different types of physical activities and dietary patterns are warranted. Alcohol consumption was not associated with the risk of sarcopenia [32,39,40]. Smoking was associated with an increased risk of sarcopenia in a meta-analysis of 29 studies with moderate heterogeneity [32]. Shorter and longer sleep durations were positively associated with the risk of sarcopenia [32,41]. Whether other sleep-related traits, like poor sleep quality and insomnia, are associated with sarcopenia deserves exploration.

Diabetes and its complications, and osteoporosis were associated with a high risk of sarcopenia [32,42,43] and these diseases may also be the consequences of sarcopenia as shown above. The bidirectional associations imply mutual influences between muscle and bone systems and between muscle and endocrine systems. Other comorbidities, like heart diseases [32], cognitive impairment [32], respiratory diseases [32], depression [32,44], anorexia [32], and Parkinson's disease [45] were also positively associated with the risk of sarcopenia. However, whether certain associations, like that for heart diseases and cognitive impairment, are causal or linked by confounders, such as ageing, needs to be investigated. Regarding the link between sarcopenia and metabolic

Table 2
Prevalence of sarcopenia by commonly used definitions after 2010 in two recent systematic reviews.

Definition	Data from Carvalho do Nascimento PR [13]			Data from Petermann-Rocha F [14]		
	No. of studies	N	Prevalence (%)	No. of studies	N	Prevalence (%)
EWGSOP	31	36,811	11 (7–14)	48	200,590	22 (20–25)
EWGSOP2	4	6624	5 (1–10)	3	5720	10 (2–17)
AWGS	13	17,070	8 (3–15)	46	27,940	15 (13–17)
IWGS	5	6993	17 (11–23)	12	11,890	14 (9–18)
FNIH	5	13,338	15 (5–28)	20	27,864	11 (9–14)
All above	58	80,836	10 (7–12)	129	274,004	16 (15–17)

AWGS, Asian Working Group for Sarcopenia; EWGSOP, European Working Group on Sarcopenia in Older People; EWGSOP2, European Working Group on Sarcopenia in Older People 2; FNIH, Foundation for the National Institute of Health; IWGS, International Working Group on Sarcopenia.

Table 3
Prevalence of sarcopenia in patients with different medical situations.

PMID	First author	Population	Studies	N	Prevalence
34399402	Meyer HJ	Patients in critically ill	9	1563	26.3–71.1 %
30389220	Hajibandeh S	Patients with abdominal surgery	20	5324	12.0–56.6 %
28386715	Jones K	Patients with abdominal surgery	24	5267	15–65 %
34078275	Zhang XM	Patients with an intensive care	14	3249	41 %
32131764	Zhang XM	Patients with breast cancer	6	5497	15.9–66.9 %
34337889	Takenaka Y	Patients with cancer receiving immune checkpoint inhibitors	26	2501	21.9–75.0 %
34785325	Tantai X	Patients with cirrhosis	22	6965	37.50 %
34406490	Xie H	Patients with colorectal cancer	19	15,889	12.0–68.2 %
33481108	Trejo-Avila M	Patients with colorectal cancer	44	18,891	37 %
34904651	Feng L	Patients with diabetes	45	12,237	18 %
36235729	Wathanavasin W	Patients with dialysis	41	7576	25.60 %
34989172	Shu X	Patients with dialysis	30	6162	4–68 %
35284466	Xu XT	Patients with diffuse large B-cell lymphoma	12	2324	23.9–55.6 %
30955115	Hua H	Patients with digestive carcinoma surgery	11	2419	11.6–33.0 %
35347823	Ng ZQ	Patients with emergency laparotomy	12	2461	29.50 %
35379520	Park B	Patients with emergency laparotomy	12	6737	34.50 %
35288290	Dakis K	Patients with endovascular aortic aneurysm repair	11	2385	40.30 %
35077542	Chen F	Patients with esophageal cancer	26	4515	14.4–80 %
32193528	Papaconstantinou D	Patients with esophageal cancer	11	1979	14.4–83 %
34249675	Jin SB	Patients with esophageal cancer	11	1485	15.8–60.7 %
29846548	Boshier PR	Patients with esophageal cancer	18	3193	16–75 %
32040700	Wang PY	Patients with esophagectomy	14	2387	36.1–55.3 %
34496449	Li YX	Patients with female cancer	23	3495	46.90 %
29987739	Yang Z	Patients with gastric cancer	13	4262	6.8–57.7 %
34601314	Chen F	Patients with gastric cancer resection	20	7615	6.8–44.8 %
31796090	Su H	Patients with gastrointestinal cancer	70	21,875	2.1–83.3 %
33739153	Wang H	Patients with gastrointestinal oncological surgery	43	16,716	32.3 %
32822372	Pipek LZ	Patients with gastrointestinal surgery	11	4265	6.8–35.9 %
35194194	Sutton EH	Patients with gynecological cancer	27	4286	11–59.2 %
32117787	Hua X	Patients with head and neck cancer	11	2483	6.6–64.6 %
32994071	Findlay M	Patients with head and neck cancer and radiotherapy	7	1059	6.6–64.6 %
32090284	Jia S	Patients with hematopoietic stem cell transplantation	7	1752	35.5–49.0 %.
35876662	Edwards A	Patients with papillomavirus-positive oropharyngeal cancer	9	744	42.90 %
36403578	Zhang JZ	Patients with kidney transplantation	23	2535	26 %
29065187	Kim G	Patients with liver cirrhosis	20	4037	25–70 %
33671958	Wu WT	Patients with lumbar degenerative spine disease	14	1953	24.80 %
31128115	Yang M	Patients with lung cancer (NSCLC)	13	1810	43 %
31128115	Yang M	Patients with lung cancer (SCLC)	13	1810	52 %
32768316	Surov A	Patients with malignant hematological diseases	7	1578	24.6–66.1 %
35578299	Jiang T	Patients with mechanical ventilation	17	3582	43.00 %
35817000	Surov A	Patients with melanoma receiving immunotherapy	6	719	40.20 %
30348603	Deng HY	Patients with non-small cell lung cancer	6	1213	14.0–55.8 %
30266663	Mintziras I	Patients with pancreatic cancer	11	2297	45.40 %
34714876	Takenaka Y	Patients with patients with head and neck cancer	18	3233	13.9–74.7 %
35749415	Zhu Y	Patients with rectal cancer	7	2377	25.6–68.2
32213202	Hu X	Patients with renal cell carcinoma	5	771	25–68 %
36316941	Yuxuan L	Patients with renal cell carcinoma	18	3591	43 %
35794004	Jogiat UM	Patients with resectable esophageal cancer	21	3966	48.10 %
26882087	Shachar SS	Patients with solid tumors	38	7843	11–74 %
31280971	Xia W	Patients with trauma	10	2867	25.0–71.1 %
34479652	Ai Y	Patients with type 2 diabetes	28	16,800	6.3–47.1 %
36151845	Jogiat UM	Patients with unresectable esophageal cancer	5	783	66 %
32268990	Guo Z	Patients with urologic cancer	17	3948	25–68.9 %
30871883	Hu X	Patients with urothelial carcinoma	12	2075	20–75 %

NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

PMID	First author	Population	Studies	N	Indicator	Association
35347823	Ng ZQ	Emergency laparotomy	12	2461	30−day mortality OR	3.50 (2.54−4.81)
35347823	Ng ZQ	Emergency laparotomy	12	2461	1−year mortality OR	3.49 (2.16−5.65)
29987364	Sun G	Nonmetastatic colorectal cancer	12	5337	Mortality OR	3.45 (1.69−7.02)
30955115	Hua H	Digestive carcinoma surgery	11	2419	30−day mortality RR	3.36 (1.60−7.60)
31519557	Buentzel J	Lung cancer	15	2521	Mortality HR	3.13 (2.06−4.76)
31280971	Xia W	Trauma	10	2867	1−year mortality RR	3.11 (1.94−4.96)
33841929	Kawaguchi Y	Lung cancer	10	2643	Poor overall survival OR	3.07 (2.45−3.85)
35379520	Park B	Emergency laparotomy	12	6737	1−year mortality OR	2.80 (1.50−5.60)
34399402	Meyer HJ	Critically ill	9	1563	Mortality HR	2.78 (2.05−3.75)
34714876	Takenaka Y	Head and neck cancer	18	3233	Poor overall survival HR	2.50 (1.95−3.21)
35752855	Yang TR	Emergency laparotomy	11	3795	30−day mortality OR	2.42 (1.93−3.05)
33739153	Wang H	Gastrointestinal oncological surgery	43	16716	30−day mortality rate OR	2.38 (1.56−3.63)
35749415	Zhu Y	Rectal cancer	7	2377	Poor overall survival HR	2.37 (1.13−4.98)
34785325	Tantai X	Cirrhosis	22	6965	Mortality HR	2.30 (2.01−2.63)
34078275	Zhang XM	An intensive care	14	3249	Mortality OR	2.28 (1.83−2.83)
32090284	Jia S	Hematopoietic stem cell transplantation	7	1752	Poor overall survival OR	2.27 (1.33−3.85)
31128115	Yang M	Lung cancer	13	1810	Poor overall survival HR	2.23 (1.68−2.94)
30389220	Hajibandeh S	Abdominal surgery	20	5324	30−day mortality RR	2.15 (1.51−3.05)
34521369	Xue Q	Coronary artery disease	10	3707	Mortality HR	2.15 (0.89−5.22)
32117787	Hua X	Head and neck cancer	11	2483	Poor overall survival HR	2.15 (1.66−2.79)
35685536	Liu W	Sepsis	10	2396	Mortality risk RR	2.14 (1.60−2.87)
35578299	Jiang T	Mechanical ventilation	17	3582	Mortality OR	2.13 (1.70−2.67)
35542968	Yang L	Biliary tract cancer	18	3261	Poor overall survival HR	2.12 (1.46−3.10)
32994071	Findlay M	Head and neck cancer and radiotherapy	7	1059	Poor overall survival HR	2.07 (1.47−2.92)
28386715	Jones K	Abdominal surgery	24	5267	30−day mortality RR	2.06 (1.02−4.17)
32268990	Guo Z	Urologic cancer	17	3948	Poor overall survival HR	2.06 (1.44−2.95)
32220072	Wong A	Head and neck cancer	10	2181	Poor overall survival HR	1.98 (1.64−2.39)
30389220	Hajibandeh S	Abdominal surgery	20	5324	1−year mortality RR	1.97 (1.53−2.53)
32768316	Surov A	Malignant hematological diseases	7	1578	Poor overall survival HR	1.94 (1.30−2.90)
35284466	Xu XT	Diffuse large B−cell lymphoma	12	2324	Poor overall survival HR	1.90 (1.52...2.37)
35430544	Ribeiro HS	Chronic kidney disease	8	2117	Mortality HR	1.87 (1.35−2.59)
30871883	Hu X	Urothelial carcinoma	12	2075	Poor overall survival HR	1.87 (1.43−2.45)
33481108	Trejo−Avila M	Colorectal cancer	44	18891	Poor overall survival HR	1.83 (1.57−2.14)
36235729	Wathanavasin W	Dialysis	41	7576	Mortality risk OR	1.83 (1.40−2.39)
36316941	Yuxuan L	Renal cell carcinoma	18	3591	Poor overall survival HR	1.83 (1.41−2.37)
34989172	Shu X	Dialysis	30	6162	Mortality risk HR	1.82 (1.38−2.39)
32221737	McSharry V	Epithelial ovarian cancer	6	1226	5−year survival OR	1.80 (1.00−3.20)
34496449	Li YX	Female cancer	23	3495	Poor overall survival HR	1.78 (1.38−2.30)
32213202	Hu X	Renal cell carcinoma	5	771	Poor overall survival HR	1.76 (1.35−2.31)
33997307	Li HL	Cancer	81	12731	Mortality HR	1.74 (1.46−2.07)
34513704	Li S	Cancers receiving immune checkpoint inhibitors	19	1763	Poor overall survival HR	1.73 (1.36−2.19)
31567976	Li J	Urologic tumors	16	2264	Poor overall survival HR	1.73 (1.48−2.01)
29065187	Kim G	Liver cirrhosis	20	4037	Mortality HR	1.72 (1.27−2.32)
32131764	Zhang XM	Breast cancer	6	5497	Mortality HR	1.71 (1.25−2.33)
34601314	Chen F	Gastric cancer resection	20	7615	Poor overall survival rate HR	1.71 (1.53−1.91)
34166897	Deng HY	Solid cancers receiving immune checkpoint inhibitors	9	740	Poor 1−year overal survival RR	1.71 (1.39−2.10)
32221737	McSharry V	Epithelial ovarian cancer	6	1226	3−year survival OR	1.70 (0.80−3.50)
29846548	Boshier PR	Esophageal cancer	18	3193	Poor overall survival HR	1.70 (1.33−2.17)
29987739	Yang Z	Gastric cancer	13	4262	Poor overall survival HR	1.70 (1.45−1.99)
36415154	Fang P	Esophageal cancer	41	5965	Poor overall survival HR	1.68 (1.54−1.83)
35817000	Surov A	Melanoma receiving immunotherapy	6	719	Poor overall survival HR	1.67 (1.11−2.52)
35922276	O'Connell RM	Hepatic resection for colorectal liver metastases	13	2936	Poor overall survival HR	1.65 (1.10−2.48)
30348603	Deng HY	Non−small cell lung cancer	6	1213	Poor overall survival RR	1.63 (1.13−2.33)
28386715	Jones K	Abdominal surgery	24	5267	Poor 1−year survival RR	1.61 (1.36−1.91)
33182031	Wang J	Non−small cell lung cancer	9	576	Poor 1−year survival RR	1.61 (1.24−2.10)
31796090	Su H	Gastrointestinal cancer	70	21875	All−cause mortality HR	1.60 (1.37−1.87)
31280971	Xia W	Trauma	10	2867	30 days mortality RR	1.60 (1.21−2.13)
30496385	Deng HY	Esophageal cancer	11	1520	Poor overall survival HR	1.58 (1.35−1.85)
33209496	Xu L	Hepatocellular carcinoma	6	1420	Poor overall survival HR	1.57 (1.34−1.84)
35794004	Jogiat UM	Resectable esophageal cancer	21	3966	Poor overall survival HR	1.56 (1.25−1.95)
34337889	Takenaka Y	Cancer receiving immune checkpoint inhibitors	26	2501	Poor overall survival HR	1.55 (1.32−1.82)
36151845	Jogiat UM	Unresectable oesophageal cancer	5	783	Poor overall survival HR	1.51 (1.21−1.89)
30266663	Mintziras I	Pancreatic cancer	11	2297	Poor overall survival HR	1.48 (1.26−1.74)
26882087	Shachar SS	Solid tumours	38	7843	Poor overall survival HR	1.44 (1.32−1.56)
33763255	Ibilibor C	Radical cystectomy	5	1447	All−cause mortality HR	1.41 (1.22−1.62)
34406490	Xie H	Colorectal cancer	19	15889	Poor overall survival HR	1.40 (1.25−1.58)
35194194	Sutton EH	Gynaecology cancer	27	4286	Poor overall survival HR	1.40 (1.20−1.64)
32747410	Allanson ER	Gynecological cancer	13	2446	Poor overall survival HR	1.33 (1.08−1.64)
35288290	Dakis K	Endovascular aortic aneurysm repair	11	2385	Poor 5−year survival OR	1.30 (1.03−1.72)
34249675	Jin SB	Esophageal cancer	11	1485	Poor overall survival HR	1.29 (1.08−1.54)
35077542	Chen F	Esophageal cancer	26	4515	Poor overall survival HR	1.12 (1.04−1.20)

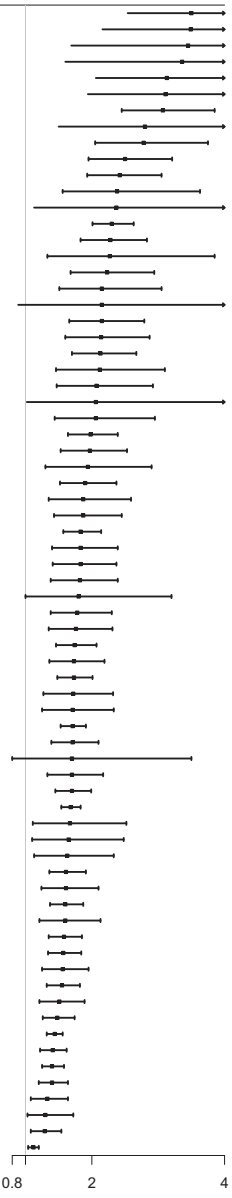

Fig. 2. Mortality and survival associated with sarcopenia in patients with different medical conditions. HR, hazard ratio; OR, odds ratio; RR, relative risk.

diseases, like diabetes and cardiovascular disease, some hypotheses concerning chronic inflammation [46], excessive oxidative stress [47], insulin resistance [48], endothelial dysfunction [47], and liver dysfunction [49], have been proposed to explain these associations. However, given that sarcopenia and metabolic diseases often coexist among populations and possibly have mutual influences, it is difficult to determine which is the cause of the link. Even though some studies found that a prior diagnosis of sarcopenia was associated with an increased risk of cardiovascular disease [50,51], whether the observed association was the consequences of shared risk factors, or reflect a causal association needs further research.

There were differences in inflammation [52], clinical biomarkers [53], blood 25-hydroxyvitamin D [54], adiponectin [55], and pulse wave velocity [56] between sarcopenic patients and non-sarcopenic individuals. These associations need to be confirmed in prospective cohort studies or other studies that can minimize reverse causation and strengthen causality. In addition, gut microbiota may play a role in the development of sarcopenia [57]. Thus, whether probiotics, prebiotics, and bacterial products have preventive and therapeutic potentials deserves exploration.

4. Limitations

Several limitations of this study need discussion. First, this is a review of published meta-analyses. Thus, some novel risk factors and rare consequences of sarcopenia may have been missed due to a few original studies on these topics. Second, even though this review identified many factors and morbidities associated with sarcopenia, the listed associations need to be carefully considered, particularly associations with high heterogeneity between studies or from low-quality studies. Third, this review was mainly based on evidence from observational studies, which cannot provide information on causality of the observed associations.

5. Future directions

5.1. Omics for sarcopenia

There are genome-wide association analyses on components of

Table 4
Consequences of sarcopenia in general populations.

PMID	First author	Consequences of sarcopenia	No. of studies	N	Heterogeneity
28778327	Liu P	All-cause mortality HR = 1.60 (1.24–2.06)	6	7367	Low
30420343	Zhang X	All-cause mortality HR = 1.86 (1.42–2.45)	6	1494	Low
28647519	Kelley GA	All-cause mortality OR = 3.64 (2.94–4.51)	12	14,169	Low
34315158	Xu J	Mortality HR = 2.00 (1.71–2.34)	56	42,108	Moderate
36362701	Su YC	Mortality HR = 9.57 (3.17–28.94)	38	27,226	High
28095426	Beaudart C	Mortality OR = 3.60 (2.96–4.37)	17	>22,000	Moderate
26844538	Chang SF	Mortality HR = 1.87 (1.61–2.18)	10	3797	Low
35670963	Chen X	Cognitive impairment OR = 1.75 (1.57–1.95)	26	18,788	High
27816484	Chang KV	Cognitive impairment OR = 2.25 (1.21–4.17)	7	5994	High
31917049	Peng TC	Cognitive impairment OR = 2.25 (1.70–2.97)	15	10,410	Low
31233073	Cabett Cipolli G	Cognitive impairment OR = 2.50 (1.26–4.92)	6	7045	High
33909650	Teng Z	Osteopenia OR = 2.08 (1.66–2.60)	25	47,744	High
36401390	Yu X	Osteoporosis OR = 3.06 (2.30–4.08)	56	796,914	High
30665817	Zhang X	Falls OR = 1.52 (1.32–1.77)	10	10,073	Moderate
30993881	Yeung SSY	Falls OR = 1.89 (1.33–2.68)	33	52,838	Moderate
32115209	Chen H	Fracture HR = 1.50 (1.08–2.08)	5	27,990	High
29500527	Zhang Y	Fracture RR = 1.34 (1.13–1.58)	9	31,513	Low
34674498	Nielsen BR	Fracture RR = 1.37 (1.18–1.59)	4	7257	High
36362701	Su YC	Fractures HR = 9.66 (5.07–18.38)	38	27,226	High
30993881	Yeung SSY	Fractures OR = 1.71 (1.44–2.03)	33	52,838	Low
33491032	Huang P	Hip fractures HR = 1.42 (1.18–1.71)	5	23,359	Moderate
28647519	Kelley GA	Functional decline OR = 2.58 (1.33–4.99)	12	14,169	High
28095426	Beaudart C	Functional decline OR = 3.03 (1.80–5.12)	17	>22,000	High
36362701	Su YC	Hospitalization HR = 11.80 (4.86–28.65)	38	27,226	High
30134867	Zhang X	Hospitalization HR = 1.57 (1.26–1.94)	5	2832	Low
29549649	Zhao Y	Hospitalization RR = 1.40 (1.04–1.89)	8	4174	Moderate
29547573	Zhang H	Metabolic syndrome OR = 2.01 (1.63–2.47)	12	35,581	High
34652699	Veronese N	Diabetes OR = 2.07 (1.40–3.62)	17	54,676	Low
30048963	Pan X	NAFLD OR = 1.29 (1.12–1.49)	6	19,024	High
29451179	Wijarnpreecha K	NAFLD OR = 1.54 (1.05–2.26)	5	27,804	High
30048963	Pan X	Fibrosis OR = 1.57 (1.29–1.90)	6	19,024	Low
32762638	Bai T	Hypertension OR = 1.29 (1.00–1.67)	12	21,301	Moderate
28633395	Chang KV	Depression OR = 1.82 (1.16–2.86)	10	33,030	High
30272106	Zhao WT	Dysphagia OR = 4.06 (2.27–7.29)	5	913	Low

HR, hazard ratio; NAFLD, nonalcoholic fatty liver disease; OR, odds ratio; RR, relative risk. Heterogeneity was assessed by reported I^2 statistic (low 0–24.9 %; moderate 25–74.9 %; high 75–100 %).

sarcopenia, such as muscle mass (fat-free mass) [58] and grip strength [59]. However, the genetic architecture underlying sarcopenia considering both muscle mass and strength remains unclear [60]. A large-scale international genetic consortium collecting unified data on sarcopenia is warranted. Similarly, more studies are needed on epigenetics, transcriptomics, proteomics, metabolomics, and microbiome on sarcopenia. Such studies could deepen the understanding of the etiological basis of sarcopenia from genetic and molecular perspectives as well as facilitate prevention strategy formulation and drug development for the disease. In addition, potential gene-environmental interactions in sarcopenia are of interest to explore.

5.2. *High-quality cohort studies and Mendelian randomization analysis*

High-quality prospective cohort studies are lacking in this field, especially concerning the exploration of the risk factors for sarcopenia. Except for focusing on clinical patients who are vulnerable to sarcopenia, cohort studies with accurate measurements of muscle quantity and function in generally healthy population are needed to provide evidence to formulate primary prevention strategies. In addition, Mendelian randomization analysis is a widely used epidemiological tool that can strengthen causal inference by using genetic variants as unbiased instrumental variables for the potential risk factor [61]. The causality of observed associations for sarcopenia should be examined using Mendelian randomization analysis.

6. Conclusion

This review summarized evidence on epidemiological features of sarcopenia (Fig. 3). Even though the prevalence of sarcopenia varies according to definition used, it is a prevalent disease among the elderly and patients with varying medical conditions. Sarcopenia is associated with a high risk of a wide range of adverse health outcomes, including poor survival rate, postoperative complications, and longer hospitalization in patients as well as falls and facture, metabolic disorders, cognitive impairment, and mortality in general populations. Physical inactivity, malnutrition, smoking, extreme sleep duration, and diabetes and several other comorbidities were associated with an increased risk of sarcopenia. However, these associations were mainly based on non-cohort observational studies and require confirmation. High-quality cohort, omics, and Mendelian randomization studies are needed to understand the etiological basis of sarcopenia with the aims of preventing and better managing the disease.

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CRediT authorship contribution statement

Shuai Yuan: Conceptualization, Methodology, Data curation, Investigation, Writing – original draft, Visualization. **Susanna C. Larsson:** Conceptualization, Methodology, Investigation, Resources, Writing – review & editing, Supervision.

Declaration of competing interest

The authors have no conflict of interest to declare.

Table 5
Risk factors for sarcopenia.

PMID	First author	Risk factor	No. of studies	N	Heterogeneity
36443946	Liu C	Obesity OR = 0.66 (0.48–0.91) Obesity OR = 3.08 (1.65–5.74) after adjusting for muscle mass	34	–	High
27170042	Steffl M	Alcohol consumption OR = 0.77 (0.67–0.88)	13	13,155	Moderate
36014771	Hong SH	Alcohol consumption OR = 1.00 (0.83–1.20)	19	422,870	Moderate
28553092	Steffl M	Physical inactive OR = 2.22 (1.82–2.70)	25	40,007	Moderate
30409494	Shen Y	Malnutrition OR = 1.74 (1.36–2.24)	16	3585	Moderate
35096921	Zhang Y	Omega-3 PUFAs highest vs. lowest OR = 0.41 (0.26–0.65) Omega-6 PUFAs highest vs. lowest OR = 0.64 (0.33–1.24)	6	6648	Moderate
31832982	Pourmotabbed A	<6 v.s. 6–8 h OR = 1.71 (1.11–2.64) >8 v.s. 6–8 h OR = 1.52 (1.23–1.88)	4	17,551	Moderate
34959843	Gao Q	Age in years OR = 1.12 (1.10–1.13) Female OR = 1.10 (0.80–1.51) Underweight OR = 3.78 (2.55–5.60) Overweight/obesity OR = 0.27 (0.17–0.44) Smoking OR = 1.20 (1.10–1.21) Alcohol consumption OR = 0.92 (0.84–1.01) Physical inactivity OR = 1.73 (1.48–2.01) Malnutrition OR = 2.99 (2.40–3.72) Long sleep duration OR = 2.30 (1.37–3.86) Short sleep duration OR = 3.32 (1.86–5.93) Diabetes OR = 1.40 (1.18–1.66) Cognitive impairment OR = 1.62 (1.05–2.51) Heart diseases OR = 1.14 (1.00–1.30) Respiratory diseases OR = 1.22 (1.09–1.36) Osteopenia OR = 2.73 (1.63–4.57) Osteoarthritis OR = 1.33 (1.23–1.44) Disability for activities of daily living OR = 1.49 (1.15–1.92) Depression OR = 1.46 (1.17–1.83) Falls OR = 1.28 (1.14–1.44) Anorexia OR = 1.50 (1.14–1.96) Anemia OR = 1.39 (1.06–1.82)	68	98,502	Moderate to high
34652699	Veronese N	Diabetes OR = 1.64 (1.20–2.22)	17	54,676	Moderate
32772138	Anagnostis P	Type 2 diabetes OR = 1.55 (1.25–1.91)	15	6526	Moderate
35002965	Qiao YS	Diabetes OR = 2.09 (1.62–2.70) Diabetic complications OR = 2.09 (1.62–2.70)	7	6783	Moderate Low
34095184	Chung SM	Diabetes OR = 1.64 (1.20–2.22)	6	7022	Moderate
36053982	Wannarong T	Diabetic peripheral neuropathy OR = 1.62 (1.30–2.02)	5	4287	Low
34997702	Li Z	Depression OR = 1.57 (1.32–1.86)	15	16,869	High
36401390	Yu X	Osteoporosis OR = 2.63 (1.98–3.49)	17	–	High
36413812	Ponsoni A	Parkinson's disease OR = 3.98 (2.22–7.10)	9	1015	Moderate
34479652	Ai Y[a]	Age OR = 4.73 (4.30–5.19) Higher HbA1c OR = 1.16 (1.05–2.47) Osteoporosis OR = 1.16 (1.05–2.47)	28	16,800	High
34904651	Feng L[a]	Age OR = 1.10 (1.07–1.14) Glycated hemoglobin OR = 1.16 (1.09–1.24) Visceral fat area OR = 1.03 (1.02–1.05) Duration of diabetes OR = 1.06 (1.00–1.11) High-sensitivity C-reactive protein OR = 1.33 (1.12–1.58) Exercise OR = 0.37 (0.18–0.76) Metformin use OR = 0.39 (0.19–0.79)	45	12,237	Low to moderate
36403578	Zhang JZ[a]	Age OR = 1.08 (1.05–1.10) Female OR = 0.31 (0.16–0.61) Lower body mass index OR = 0.57 (0.39–0.84)	23	2535	Low to moderate

OR, odds ratio; PUFAs, polyunsaturated fatty acids.

[a] These studies were not based on general populations (Ai Y study in patients with type 2 diabetes; Feng L study in patients with diabetes; and Zhang JZ study in patients with kidney transplantation).

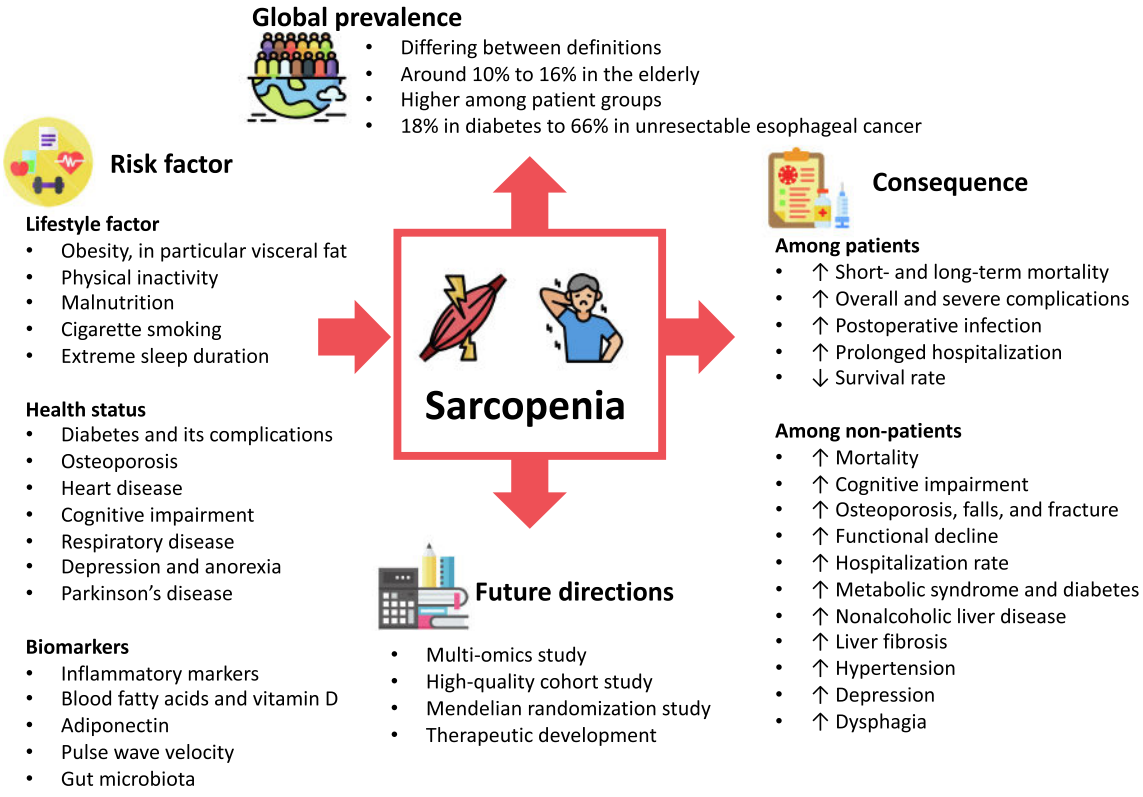

Fig. 3. Summary of risk factors and consequences of sarcopenia.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.metabol.2023.155533.

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