REVIEW



# Association between body composition indices and vascular health: a systematic review and meta-analysis

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### Abstract

**Objective** This systematic review explores the intricate relationship between body composition, with a specific focus on skeletal muscle mass, and vascular health indices, including measures of arterial stiffness—pulse wave velocity (PWV) and cardio-ankle vascular index (CAVI)—as well as arterial structure, specifically carotid artery intima-media thickness (cIMT). **Methods** An extensive literature search, encompassing PubMed, Scopus, EMBASE, Web of Science, and Google Scholar, was conducted until January 2024. Inclusion criteria involved original observational studies, with cross-sectional or longitudinal designs, reporting body composition parameters and vascular health measures. The Newcastle–Ottawa Scale (NOS) assessed study quality. Statistical analyses utilized Stata 17.0, employing random-effects meta-analysis, sensitivity analysis, and evaluation of publication bias.

**Results** Fifteen observational studies (n = 21,215) met the inclusion criteria. Pooled analyses revealed a positive association between fat-free mass (FFM) and carotid intima-media thickness (IMT) (effect size [ES]: 1.79, 95% CI 1.68–1.91), highlighting a relationship with arterial structure. Similarly, body fat percentage (BFP) was positively associated with PWV (ES: 1.45, 95% CI 1.15–1.82), and FFM showed a positive association with CAVI (ES: 1.46, 95% CI 0.78–2.71), both measures of arterial stiffness. Subgroup analyses revealed a non-significant association between appendicular skeletal muscle (ASM) and IMT (ES: 1.01, 95% CI 0.76–1.35).

**Conclusion** This meta-analysis highlights the complex relationship between body composition and vascular health. Subgroup analyses suggest the need for further research into specific body composition indices and their clinical implications. *Level of evidence*: III evidence obtained from well-designed cohort and cross-sectional studies.

Keywords Body composition  $\cdot$  Arterial health  $\cdot$  Meta-analysis  $\cdot$  Vascular health  $\cdot$  Cardiovascular risk

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### Introduction

Loss of skeletal muscle mass, a crucial factor in diagnosing sarcopenia, increases with age and in the presence of diverse chronic health conditions such as inflammation, malignancy, malnutrition, endocrine disorders, chronic kidney disease (CKD), and chronic heart failure (CHF) [1]. Chronic heart failure resulting from various cardiovascular diseases (CVDs) is a common factor that contributes to sarcopenia [1]. Reduced muscle mass has been linked to significant age-related outcomes including falls, fractures, osteoporosis, diminished quality of life, and a decline in independence [2]. As muscle is the largest glucose-utilizing tissue in the body [3], a loss of muscle tissue may also predispose to altered glucose metabolism due to a decline in insulin sensitivity [2]. The factors mentioned above are thoroughly characterized as causal influences on the progression of CVD, specifically atherosclerotic vascular diseases.

Vascular damage, including arteriosclerosis and atherosclerosis, is the prevailing underlying pathogenesis of CVD, particularly in the elderly population [1]. The stiffening of arteries advances with aging, hypertension, atherosclerosis, and vascular remodeling, characterized by smooth muscle cell proliferation and deposition of the extracellular matrix [4]. Consequently, advancement of arterial stiffening leads to elevated central blood pressure, vascular endothelial dysfunction, and capillary artery injury, ultimately resulting in organ damage [4]. Apart from noting that the risk factors for arterial stiffness can predict sarcopenia, several mechanisms may directly connect the loss of muscle tissue with heightened arterial stiffness. These mechanisms include inflammatory cytokines and changes in glucose handling, while low physical activity is recognized as a risk factor contributing to both arterial stiffness and muscle mass loss [2].

Scuteri et al. reported that pulse wave velocity (PWV) is a suitable marker for assessing arterial stiffness and early vascular aging [5, 6]. The cardio-ankle vascular index (CAVI) is a novel measurement tool designed to evaluate arterial stiffness. It reflects the stiffness of the aorta, femoral artery, and tibial artery, incorporating the measurement of brachial–ankle pulse wave velocity (baPWV) and blood pressure [7]. Furthermore, ultrasound measurements of carotid artery intima–media thickness (cIMT) are widely employed as surrogate markers for tracking the development of atherosclerosis and assessing the risk of CVD [8].

Rodriguez et al. investigated pulse wave velocity (PWV) as an indicator of arterial stiffness and revealed a significant association between lower muscle mass and increased arterial stiffness [2]. Several studies have suggested an association between the changes in body composition indices and arterial stiffness. Nevertheless, available data on this matter are not yet conclusive [9–12].

In this systematic review, we explore the intricate link between body composition, specifically skeletal muscle mass, and arterial health. Our primary objective is to provide a comprehensive synthesis of existing evidence, focusing on established markers like PWV, CAVI, and cIMT. By clarifying the association between body composition changes and vascular outcomes, our review aims to inform clinicians and researchers, offering insights for future interventions to address cardiovascular risks associated with these alterations.

### **Material and methods**

#### Literature search and inclusion criteria

We conducted a comprehensive literature review by searching databases including PubMed, Scopus, EMBASE, Web of Science, and Google Scholar until January 2024. The search terms for body composition parameters included body composition, lean mass, skeletal muscle mass, fat-free mass, fat-free mass index, skeletal muscle mass index, fat mass, fat mass index, sarcopenia, endocrine disorders. Those terms were combined with search terms for vascular health including vascular health, vascular function, cardiovascular diseases, arterial stiffness, carotid intima–media thickness, intima–media thickness, pulse wave velocity, PWV, cardioankle vascular index, CAVI, carotid artery intima–media thickness, cIMT, IMT, atherosclerosis. The literature search was limited to human studies published in English.

Studies were considered potentially eligible if they satisfied the following criteria: (i) were original observational studies; (ii) possessed a cross-sectional or longitudinal design; (iii) reported a measure of body composition parameter, reported a measure of arterial stiffness and performed a statistical assessment of the relationship between these measures in order to determine the association between these measures; (iv) provided data on odds ratios (ORs) along with their corresponding 95% confidence intervals (CIs).

Explicit exclusion criteria included non-observational studies, animal or cell-based studies, reviews, other metaanalyses, and individual case reports. We limited our analysis to observational studies because we aimed to establish the natural incidence of both body composition changes and increased arterial stiffness. Interventional studies could alter both arterial stiffness and muscle tissue measures, potentially influencing their association.

All the articles incorporated in the study were published in English. The selection process for these studies is illustrated in Fig. 1. This systematic review adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [13].

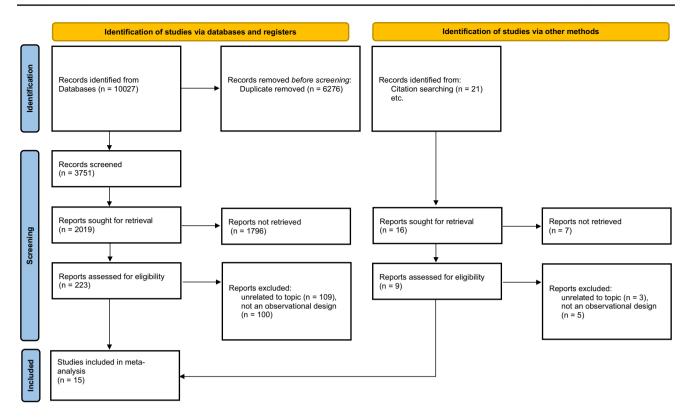


Fig. 1 PRISMA flow diagram for selection process of the studies

Pre-registration code of the systematic review and metaanalysis protocols in PROSPERO is 517,205.

#### **Study selection**

After eliminating duplicates, two authors (MN and BA) independently reviewed the titles and abstracts obtained from the initial search. The screening phase involved reviewing titles and abstracts to identify potentially relevant articles based on the inclusion criteria. Both authors (MN and BA) thoroughly examined the full-text articles to confirm their alignment with the criteria for inclusion and exclusion. In instances of disagreements, a third author (ARA) reevaluated the issues.

#### Data extraction and quality assessment

Data extraction was independently performed by two reviewers (MN and MM) and any discrepancies were resolved through consensus. We extracted information about the first author, year of publication, country, study design, population, age, number of participants, sex, assessment of body composition, assessment of vascular health, and findings of the study. The meta-analysis included effect estimates that were either fully adjusted and reported in the studies, or unadjusted estimates when fully adjusted estimates were not provided. It should be noted that 'full adjustment' refers to effect estimates that account for potential confounding variables, such as age, sex, BMI, physical activity, smoking status, and comorbidities (e.g., hypertension, diabetes), which could influence the relationship between body composition parameters and arterial stiffness.

The Newcastle–Ottawa Scale (NOS), a tool specifically designed for evaluating nonrandomized studies in systematic reviews and meta-analyses, was used [14]. The NOS consists of eight items categorized into three sections: selection, comparability, and exposure. Each item in the NOS provides response choices. The star system is used to semiquantitatively assess the quality of the studies, assigning a maximum of 1 star per item to the highest quality studies. However, when evaluating comparability, an exception is made, allowing for the assignment of 2 stars. Thus, the NOS operates on a scale from 0 to 9 stars [15]. The details regarding the extraction of data and the assessment of quality can be found in Table 1.

#### **Statistical analysis**

All statistical analyses were conducted using Stata, version 17.0 (Stata Corp, College Station, TX, USA). The effect sizes were aggregated using the random-effects method (DerSimonian–Laird) for the meta-analysis. The  $I^2$  index and

First author, year (reference no.)	Country	Design	Population	N (F/M)	Age (year)	Assessment of body composition	Assessment of vascu- lar health (parameter, vascular site)	Finding	SON
Tolosa-Álvarez, 2023 (17)	Spain	Cross-sectional	Patients with high- risk obesity	59 (32/27)	> 18	Assessment of body composition variables such as fat mass, fat-free mass, and body water using BIA	PWV (using four cuffs placed on the extremities)	There was a positive correla- tion between fat mass content and PWV. Independent associations with pathological PWV were found for both BMI and fat mass content, suggest- ing their roles as significant factors influencing arterial stiffness	4
Takase, 2023 (18)	Japan	Cross-sectional	General population	12,985 (9112/3873) ≥20	≥ 20	Assessment of BF%, FMI, FFMI using BIA	cIMT was measured using ultrasound imaging equipment	FMI was not associ- ated with cIMT in most FFMI sub- groups. But, FFMI was positively asso- ciated with cIMT independently of FMI	×
Shin, 2021 (19)	South Korea	South Korea Cross-sectional	Patients with type 2 diabetes	1185 (491/694)	> 30	Assessment of ASM using DXA	cIMT was measured using high-res- olution B-mode ultrasonography	Low ASM may be independent risk factors for high cIMT in patients with type 2 diabetes	9
Rong, 2020 (20)	China	Cross-sectional	Elderly people who received general medical examina- tions in Tianjin First Center Hospital	450 (184/266)	> 65	Assessment of ASM using BIA	baPWV was measured using automatic athero- sclerosis tester	ASMI was negatively associated with baPWV in com- munity-dwelling elderly in China	Q

Table 1 (continued)									
First author, year (reference no.)	Country	Design	Population	N (F/M)	Age (year)	Assessment of body composition	Assessment of vascular health (parameter, vascular site)	Finding	SON
Harada, 2020 (1)	Japan	Retrospective cross-sectional analysis	Patients with CVD	310 (131/179)	72±12	Assessment of ASM using BIA	AVI, API, FMD was assessed using an instrument that analyzes pulse wave, instrument that assesses arterial stiffness, high-resolution ultrasound device equipped with a 10-MHz linear array transducer, respectively	Advanced vascular damage, such as increased arte- rial stiffness and peripheral resist- ance, might play an important role in the reduction in skeletal muscle mass, possibly through damage to skeletal muscle tissue in CVD patients	Ś
Zhang, 2019 (21)	China	Cross-sectional	Older individuals	1002 (582/420)	≥65	Assessment of ASM using BIA	baPWV was meas- ured using the Vas- cular Profiler-1000 device	Increased baPWV is associated with lower relative skel- etal muscle mass (ASM/Ht <sup>2</sup> )	9
Iorio, 2019 (22)	Italy	Cross-sectional	Free-living elderly subjects	52 (38/14)	> 65	Assessment of body composition variables such as fat mass, fat-free mass, and body water using BIA	CAVI was measured using a Vasera VS-1000	Low muscle mass and high fat mass were both associated with an increase in the cardiovascular risk profile, estimated by means of CAVI, in a healthy free- living population	4
Heo, 2018 (23)	South Korea	South Korea Cross-sectional	General population	1869 (1274/595)	30-64	Assessment of ASM using BIA	IMT was assessed using B-mode ultra- sonography	Low ASM is associ- ated with carotid arterial wall thick- ening in men with lower BMIs	9
Vianna, 2018 (24)	Brazil	Cross-sectional	Healthy young adults 1574 (770/804)	1574 (770/804)	Adult age	Fat mass and abdomi- PWV using ultra- nal adipose tissue sound using plethysmog- raphy	PWV using ultra- sound	Visceral fat thickness and fat mass were the strongest body fat measures related to PWV	۲

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NOS	plex 5 ss seem lly tional predic-	ss is 4 ith low nunity- er when nulti-	unk 5 rreases fat ociated ated ning	was 4 men body ared ally bdomi- ät was ent PWV	ipos- 4 ziated this
Finding	The more complex BIA measures seem of no clinically relevant additional value in the predic- tion of CVD	Arterial stiffness is associated with low SMI in community- dwelling older adults, even when adjusting by multi- ple factors	Increases in trunk mass and decreases in peripheral fat mass are associated with accelerated arterial stiffening	Mean baPWV was higher in women with normal body weight compared to not viscerally obese, and abdomi- nal visceral fat was an independent factor for baPWV	Abdominal adipos- ity was associated with cIMT in this
Assessment of vascu- lar health (parameter, vascular site)	PWV	CAVI was deter- mined using VaSera1500	Measurements include arterial diameter, disten- sion, pulse wave transit time, and intima-media thickness in specific arteries, using ultra- sound imaging	baPWV was measured using a volume plethysmo- graphic instrument	cIMT using B-mode ultrasound
Assessment of body composition	Assessment of body composition vari- ables using BIA	Absolute skeletal muscle mass, body fat percentage, absolute fat mass, and segmental muscle mass, using BIA	Total and regional body fat and lean masses were meas- ured with a whole- body DXA	Body fat mass and lean mass using DXA. The abdomi- nal and mid-thigh adipose tissue areas and the mid-thigh muscle area were quantified by CT	Fat distribution using CT
Age (year)	18-70	≥65	$36.5 \pm 0.6$	22-67	24–59
N (F/M)	691 (448/243)	175 (91/84)	277 (145/132)	150 females	100 females
Population	A multi-ethnic sample of non- institutionalized individuals living in the capital Para- maribo	Community-dwelling older adults	Healthy adults	Healthy females	Healthy females
Design	Cross-sectional	Cross-sectional	Cohort	Cross-sectional	Cross-sectional
Country	Suriname	Japan	Netherland	Korea	USA
First author, year (reference no.)	Diemer, 2017 (25)	Sampaio, 2014 (7)	Schouten, 2011 (26)	Lee, 2007 (27)	Lo, 2006 (28)

(continued)	
Table 1	

Ferreira, 2004 (29) Netherlands Cross-sectional Apparently healthy 336 (175/161) adults		VASCULAL SUC)	
	36 Regional body fat and body lean mass were measured with a whole-body DXA	tt Measurement of mass various parameters with at specific vascular DXA sites, encompassing local and regional aspects of arte- rial stiffness and elasticity	Trunk fat is adversely 5 associated with large artery stiff- ness, whereas some degree of protec- tion is conferred by peripheral fat and lean mas

rial velocity pulse index; API: arterial pressure volume index; CAVI: cardio-ankle vascular index

Cochrane's Q test were used to evaluate the heterogeneity between studies. The I<sup>2</sup> interpretation is as follows: low if  $I^2 < 30\%$ , moderate if  $I^2 = 30-75\%$ , and high if  $I^2 > 75\%$ . To further explore the effects of the studies and the influence of different variables on the study outcomes, a sensitivity analysis was conducted. Publication bias was assessed using Begg's rank correlation and visual inspection of funnel plots.

### Results

### Literature search

By conducting an initial search using keywords relevant to our topic, we identified a total of 10,027 full-text articles. After removing duplicate studies and applying the inclusion and exclusion criteria in two distinct stages (title and abstract review), we ultimately incorporated 15 eligible observational studies in our review. Figure 1 provides an overview of the primary research outcomes and the process employed for selecting pertinent studies.

This meta-analysis included 15 articles and 21,215 participants in total [1, 7, 16–28] (Table 1).

### Characteristics of study design and patient sampling

Table 1 summarizes the diverse characteristics of included studies. Fourteen studies were cross -sectional and one study was cohort [25]. Eleven studies [7, 17, 20–28] included a sample of healthy (older or younger) men and women. Four studies sampled participants with high-risk obesity [16], type 2 diabetes [18], elderly people who received general medical examinations in Tianjin first center Hospital [19], and patients with CVD [1]. All participants included in this meta-analysis were aged  $\geq$  18 years old. The sample size of included studies ranged from 52 to 12,985 participants. Studies were conducted in South Korea [18, 22], USA [27], Spain [16], Japan [1, 7, 17], Italy [21], China [19, 20], Brazil [23], Suriname [24], Netherland [25, 28], and Korea [26]. Thirteen studies involved both sexes, but two researches conducted in females or males [26, 27] only.

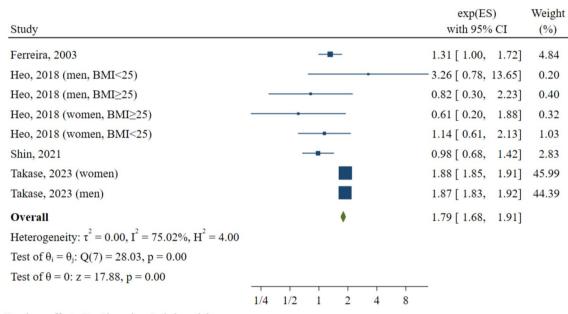
# Assessment of vascular health and body composition

The majority of studies assessed PWV, a measure of arterial stiffness; other studies assessed CAVI, another indicator of arterial stiffness, and cIMT, a measure of arterial structure. These studies also included measurements of various parameters at specific vascular sites, encompassing both local and regional aspects of arterial health and elasticity (Table 1).

Most studies reported a measure of muscle mass (Table 1). Three studies used radiological imaging to determine lean tissue including dual-energy X-ray absorptiometry (DXA), one study used computed tomography (CT) [11, 14, 15, 18, 25], in another one body fat mass and lean mass was assessed using DXA, while the abdominal and mid-thigh adipose tissue areas and the mid-thigh muscle area were quantified by CT. Other studies utilized bioelectrical impedance analysis (BIA).

### Pooled analysis of the association between fat-free mass (FFM) and intima-media thickness (IMT)

The meta-analysis included a total of four studies (with eight effect sizes) investigating the association between FFM and cIMT, a measure of arterial structure. The overall effect size (ES) for this association was estimated to be 1.79 (95% CI 1.68–1.91; Fig. 2), indicating a positive and statistically significant relationship between FFM and IMT (Table 2). The analysis revealed a high level of heterogeneity among the studies ( $I^2$ =75.02%,  $P_{heterogeneity}$  < 0.001) (Table 2).



Random-effects DerSimonian-Laird model

Fig. 2 Forest plot of the association between fat-free mass and carotid intima-media thickness

Table 2 Overall and subgroup estimates of meta-analysis on the association between body composition indices and arterial stiffness

Body composition and vascular association	Overall/subgroups	No. of effect size	References	ES (95%CI)	<i>I</i> <sup>2</sup> (%)	P heterogeneity	P heterogeneity between sub- groups
FFM and IMT	Overall	8	(18, 19, 23, 29)	1.79 (1.68–1.91)	75.02	< 0.001	_
	ASM and IMT	5	(19, 23)	1.01 (0.76–1.35)	0.00	0.45	_
FFM and PWV	Overall	6	(20, 21, 25, 26)	1.08 (0.45-2.56)	86.94	< 0.001	_
	ASMI and PWV	3	(20, 21)	0.00 (0.00-3032.71)	92.97	< 0.001	< 0.001
FFM and CAVI	Overall	3	(1, 7, 22)	1.46 (0.78–2.71)	89.05	< 0.001	_
BFP and PWV	Overall	5	(17, 24–26)	1.45 (1.15–1.82)	74.86	< 0.01	_
Peripheral fat and PWV	Overall	3	(26, 27, 29)	0.86 (0.65-1.16)	76.03	0.02	_
Trunk fat and PWV	Overall	3	(26, 27, 29)	1.11 (0.90–1.37)	86.72	< 0.01	-

ES: effect size; FM: fat mass; BFP: body fat percentage; FFM: fat-free mass; IMT: intima-media thickness; PWV: pulse wave velocity; CAVI: cardio-ankle vascular index; ASM: appendicular skeletal muscle mass; FFMI: fat-free mass index; ASMI: appendicular skeletal muscle index

### Subgroup analysis: appendicular skeletal muscle (ASM) and IMT

A subgroup analysis was conducted to specifically examine the association between ASM and cIMT, a measure of arterial structure, encompassing a total of two studies (with five effect sizes) (Table 2). The subgroup's overall ES was estimated to be 1.01 (95% CI 0.76–1.35), suggesting a moderate and non-statistically significant positive association between ASM and cIMT. The corresponding heterogeneity statistics as follows:  $I^2 = 0.00\%$  and  $P_{heterogeneity} = 0.45$ , indicating a high degree of consistency in the findings across the included studies.

# Pooled analysis of the association between fat-free mass (FFM) and pulse wave velocity (PWV)

The meta-analysis incorporated a total of four studies (with six effect sizes) exploring the association between FFM and PWV, a measure of arterial stiffness. The overall ES for this association was estimated to be 1.08 (95% CI 0.45–2.56; Fig. 3), suggesting a positive but non-significant association between FFM and PWV. The wide confidence interval (0.45–2.56) indicates substantial uncertainty regarding the true magnitude of the association. The meta-analysis revealed a high level of heterogeneity among the studies ( $I^2 = 86.94\%$ ,  $P_{heterogeneity} < 0.001$ ), indicating substantial variability in effect sizes (Table 2).

### Subgroup analysis: appendicular skeletal muscle index (ASMI) and PWV

(2025) 30:3

A subgroup analysis was conducted to explore the association between ASMI and PWV, a measure of arterial stiffness, comprising a subset of two studies (with three effect sizes). The overall ES for this subgroup was estimated to be 0.00 (95% CI 0.00–3032.71), suggesting a null association between ASMI and PWV. There was a high level of heterogeneity among the studies in this ASMI and PWV subgroup ( $I^2$ =92.97%,  $P_{heterogeneity}$  < 0.001) (Table 2).

# Pooled analysis of the association between body fat percentage (BFP) and PWV

The meta-analysis incorporated a total of four studies (with five effect sizes) investigating the association between BFP and PWV. The overall ES for this association was estimated to be 1.45 (95% CI 1.15–1.82; Fig. 4), indicating a positive and statistically significant association between BFP and PWV, with corresponding heterogeneity statistics as follows:  $l^2 = 74.86\%$  and  $P_{heterogeneity} < 0.01$  (Table 2).

# Pooled analysis of the association between fat-free mass (FFM) and cardio-ankle vascular index (CAVI)

The meta-analysis included a total of three studies investigating the association between FFM and CAVI, a measure of arterial stiffness. The overall ES for this association was estimated to be 1.46 (95% CI 0.78–2.71; Fig. 5), suggesting a positive association between FFM and CAVI, with corresponding heterogeneity statistics as follows:  $I^2 = 89.05\%$ and  $P_{\text{heterogeneity}} < 0.001$  (Table 2).

Study			exp(ES with 95%		Weight (%)
Diemer, 2017 (men)			2.44 [ 1.06,	5.63]	22.39
Diemer, 2017 (women)			1.79 [ 1.00,	3.17]	25.18
Rong, 2020 (men)			0.00 [ 0.00,	0.00]	0.46
Rong, 2020 (women)			0.00 [ 0.00, 7	77.62]	0.06
Zhang, 2019			0.98 [ 0.97,	1.00]	28.34
Schouten, 2015			0.66 [ 0.32,	1.38]	23.57
Overall		٠	1.08 [ 0.45,	2.56]	
Heterogeneity: $\tau^2 = 0.69$ , $I^2 = 86.94\%$ , $H^2 = 7.6$	6				
Test of $\theta_i = \theta_j$ : Q(5) = 38.28, p = 0.00					
Test of $\theta = 0$ : $z = 0.17$ , $p = 0.86$					
	1/198070406286+28 1/2.30584300922e+18 1/268435456.0007341	31,99999999	9998356		

Random-effects DerSimonian-Laird model

Fig. 3 Forest plot of the association between fat-free mass and pulse wave velocity

Study							exp(ES) with 95% CI	Weigh (%)	
vianna, 2018							1.35 [ 1.28, 1.4	3] 38.36	5
Diemer, 2017				•			6.72 [ 1.52, 29.7	4] 2.19	)
Diemer, 2017		-					- 11.10 [ 2.66, 46.3	1] 2.36	5
Schouten, 2015							1.12 [ 0.84, 1.4	8] 24.52	2
Tolosa-Álvarez, 2023	-	·					1.49 [ 1.27, 1.7	5] 32.58	3
Overall							1.45 [ 1.15, 1.8	2]	
Heterogeneity: $\tau^2 = 0.03$ , $I^2 = 74.86\%$ , $H^2 = 3.98$									
Test of $\theta_i = \theta_j$ : Q(4) = 15.91, p = 0.00									
Test of $\theta = 0$ : $z = 3.21$ , $p = 0.00$									
	1	2	4	8	16	32	-		

Random-effects DerSimonian-Laird model

Fig. 4 Forest plot of the association between body fat and carotid pulse wave velocity

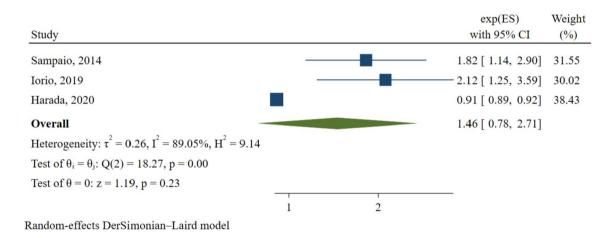


Fig. 5 Forest plot of the association between fat-free mass and cardio-ankle vascular index

### Sensitivity analysis

To evaluate whether any study had a dominant impact on the meta-analysis, we performed a sensitivity analysis by systematically excluding one study at a time and re-evaluating the effect size. Notably, upon the exclusion of the study by Takasa et al. [17], which had the highest weight in the analysis, the recalculated ES was 1.27 (95% CI 0.91–1.77) with a P-value of 0.15, indicating a nonsignificant association between FFM and IMT. In addition, upon the exclusion of the study by Schouten et al. [25], with the cohort design, the recalculated ES was 1.01 (95% CI 1.007–1.023) with a highly significant association between trunk fat mass and PWV (P < 0.001). In this analysis, no other study significantly influenced the outcomes or heterogeneity.

### Deringer

### **Publication bias**

Visual inspection of the funnel plot indicated no publication bias in the studies that investigated the association between FFM and IMT (Begg's test P=0.90), FM and IMT (Begg's test P=0.76), FFM and PWV (Begg's test P=0.70), BFP and PWV (Begg's test P=0.46), FFM and CAVI (Begg's test P=0.29), peripheral fat and PWV (Begg's test P=1.00), as well as trunk fat and PWV (Begg's test P=1.00).

### Discussion

This meta-analysis reveals a complex interplay between body composition and vascular health, emphasizing a negative association between fat-free mass and arterial health. Subgroup analyses for ASM, FFMI, and cIMT suggest the need for further investigation. Heterogeneity underscores factors contributing to variability. The findings highlight the multifaceted nature of body composition indices in vascular health, calling for deeper research into mechanisms and clinical implications.

The relationship between muscle mass and vascular health is complex and not fully understood. While some studies suggest that vascular dysfunction may contribute to muscle atrophy, our findings support a positive association between increased FFM and increased arterial stiffness and thickness, including cIMT and CAVI. This suggests that increased muscle mass may not necessarily protect against vascular dysfunction, and further research is needed to explore the mechanisms underlying these associations. The observed links between FFM and arterial stiffening emphasize the need to consider both the benefits and potential risks of increased muscle mass in the context of vascular health.

Several studies have examined the association between arterial stiffness and skeletal muscle mass [9, 12, 28–32]. However, the findings of these studies are inconclusive, revealing discrepancies in their results. In contrast to studies that found no association [9] or a negative association [28]. some have reported a positive association between the fatfree mass index and arterial stiffness [33-35]. This suggests that individuals with a higher fat-free mass index more frequently exhibit increased arterial stiffness. Liu et al. discovered that sarcopenia, defined as low muscle mass combined with low muscle strength or low physical performance, was not associated with mean cIMT in Taiwanese patients of either sex [36]. In another study [22], diminished skeletal muscle mass was independently linked to the highest quartile of IMT and the presence of carotid artery plaques among a group of middle-aged Korean men with lower BMIs. However, this association was not observed in individuals with higher BMIs. In women, there was no noteworthy correlation between low skeletal muscle mass and the highest quartile of IMT or the presence of carotid artery plaque, irrespective of BMI. There was no association between ASM and a high cIMT in another study [18]. The absence of an association might be explained by the observation that individuals in the lowest ASM tertile were less prone to central obesity, insulin resistance, and dyslipidemia compared to those in the highest tertile [18]. In a study involving 421 obese middle-aged European men and women, FFM was identified as a contributor to elevated cIMT, independent of FM and other atherosclerotic risk factors [33]. The China Kadoorie Biobank study revealed that FFM exhibited a stronger association with cIMT compared to FM [34]. One potential mechanism could be that the elevated metabolic demands of FFM necessitate an increase in the blood flow [37]. Another study demonstrated that stroke volume and cardiac output exhibited a stronger association with FFM than adipose mass, diabetes, and age [35]. It was reported that an increase in FFM through exercise training was associated with a concurrent increase in left ventricle mass and wall thickness [38]. Evidence suggests that the cardiovascular system, including arterial wall thickness, undergoes structural adaptations to accommodate increased blood flow associated with higher muscle mass. Mechanisms such as elevated blood pressure and left ventricular hypertrophy may contribute to this adaptation, as suggested in several studies [33, 34, 37, 38]. These findings highlight the potential link between a higher fat-free mass index (FFMI) and elevated cIMT, which may reflect a physiological response rather than a pathological process.

However, a recent study [39] in 2561 asymptomatic Korean individuals found that low skeletal muscle mass was independently associated with increased arterial stiffness, as measured by the CAVI. Specifically, both sarcopenia classes I and II showed significant associations with higher CAVI, even after adjusting for age, gender, BMI, and common comorbidities. It should be noted that further longitudinal studies should be performed to elucidate the causal relationship between sarcopenia and CAVI. A review of 17 studies [40] found that most studies show an inverse association between arterial stiffness and muscle mass or strength, particularly in individuals with cardiovascular disease (CVD) risk factors. A recent meta-analysis of 38 studies [41] found a pooled prevalence of sarcopenia of 35% in CVD patients, compared to 13% in the general population. The prevalence was highest in those with acute decompensated heart failure (61%), chronic heart failure (32%), and cardiac arrhythmia (30%). This suggests that CVDs significantly increase the risk of sarcopenia, emphasizing the need for early detection and interventions like exercise. A systematic review on the 33 studies [42] found significant associations between vascular dysfunction and muscle health, with negative correlations between vascular dysfunction and muscle strength (10 studies), mass (9 studies), and function (5 studies). Nine studies also showed positive correlations between muscle mass and microvascular health.

The impact of fat mass on arterial stiffness was thoroughly examined. Regardless of age, an increase in visceral adiposity corresponded to heightened arterial wall stiffness, whereas weight loss was linked to a reduction in arterial stiffness [43, 44]. The Baltimore Longitudinal Study of Aging revealed that leptin could mediate the association between abdominal adiposity and arterial stiffness, while adiponectin and resistin were independent correlates of baPWV [45].

The relationship between CVD development and body fat is recognized to be influenced not only by fat content but also by its distribution in the body, a connection observed even in individuals maintaining a healthy weight [46]. In this context, previous findings have indicated that truncal adiposity and waist circumference (representing abdominal visceral fat) exhibit an inverse association with the distensibility and compliance of both carotid and femoral arteries [47]. Hence, it appears that both visceral and truncal adiposity are associated with increased arterial stiffness. Concerning limb composition, fat stored within the muscle may have more adverse effects than fat accumulated in the depots [48].

Body composition is influenced by various factors including corticosteroids, growth, sex hormones, genetic factors, and intrauterine growth [28]. Moreover, behavioral characteristics, such as smoking, alcohol consumption, and physical activity, may influence both body composition and properties of large arteries [49]. Associations between measures of central and peripheral adiposity and the stiffness of the carotid and brachial arteries might have been influenced by confounding and/or mediation from other cardiovascular risk factors, as additional adjustments for these variables led to a decrease in the observed associations. The total/ HDL cholesterol ratio and cardiopulmonary fitness emerged as the primary confounders or intermediates in these relationships, implying that these variables may constitute a pathway through which body composition influences arterial properties.

### **Strength and limits**

This meta-analysis, one of the first to investigate the association between body composition indices and vascular health, conducts a comprehensive synthesis of 15 observational studies involving 21,215 participants, and provides valuable insights into the relationship between body composition measures and vascular health markers. The inclusion of diverse study populations enhances the generalizability of findings. Rigorous meta-analytical methods and focused subgroup analyses contribute to the reliability of our conclusions. However, observed heterogeneity in some analyses remain limitations. The inclusion of both cross-sectional and longitudinal studies introduces methodological diversity, and the restriction to English-language studies may lead to language bias. Another limitation of this study is the low retrieval rate, with only 10% of the initially identified reports included in the final analysis. This may have led to a potential underrepresentation of available data and could affect the generalizability of our findings. The impact of this low inclusion rate on the comprehensiveness of the results should be considered when interpreting the conclusions of this study. While the findings highlight positive associations between fat-free mass and arterial health, mechanistic insights and causal relationships remain incomplete. Future research addressing these limitations is crucial for a more nuanced understanding of the interplay between body composition and cardiovascular health.

### What is already known on this subject?

Several studies have suggested an association between the changes in body composition indices and arterial stiffness. Nevertheless, available data on this matter are not yet conclusive.

### What does this study add?

This study reveals a negative link between fat-free mass and arterial health indices, emphasizing the intricate relationship between body composition and vascular health. Subgroup analyses highlight the need for focused investigations into specific body composition indices, underlining their complex implications. This synthesis underscores the multifaceted nature of body composition in affecting arterial health. Further research into mechanisms and clinical implications is crucial for a deeper understanding of the interplay between body composition and cardiovascular health, providing valuable insights for future interventions.

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Author contributions B.A., and M.V. conceived and designed the study. B.A., M.N., S.MM and R.Y. conducted the systematic search, screened articles, and read the full texts for eligibility. B.A., A.RA., S.MM, and R.Y. extracted data from the original studies and evaluated the studies for risk of bias. B.A., A.RA., A.V, and Z.S contributed to the interpretation of the results and wrote the first draft of the manuscript. M.V. critically revised the manuscript. All authors have read and approved the final manuscript.

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#### Declarations

Ethics approval and consent to participate Not applicable.

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