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REVIEW

Role of Arterial Stiffness and Carotid Intima-Media Thickness on Subclinical Atherosclerosis and Cardiovascular Risk Assessment

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ABSTRACT

Subclinical atherosclerosis precedes overt cardiovascular disease and can be detected through surrogate markers such as arterial stiffness (AS) and carotid intima-media thickness (CIMT). This review examines the diagnostic and prognostic roles of AS and CIMT, highlighting their potential to improve cardiovascular risk stratification. Although traditional risk prediction models remain the cornerstone of primary prevention, they often fail to identify individuals at risk who lack conventional risk factors. Emerging evidence suggests that integrating CIMT and AS into risk assessment may improve the reclassification of individuals with intermediate risk. However, their routine use remains controversial due to methodological heterogeneity, variability in predictive value, and the prioritization of alternative imaging biomarkers such as carotid plaque or coronary artery calcium (CAC). This article critically assesses the strengths and limitations of AS and CIMT, discussing their potential utility as biomarkers, explores their application into clinical practice, and comprehensively summarizes the latest research.

Keywords: Arterial stiffness; Carotid intima-media thickness; Subclinical atherosclerosis; Cardiovascular disease; Cardiovascular risk assessment

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Key Summary Points

Traditional cardiovascular risk prediction models often fail to identify individuals at risk for atherosclerotic cardiovascular disease (ASCVD) who lack conventional risk factors, highlighting an unmet need for improved biomarkers.

Arterial stiffness (AS) and carotid intima-media thickness (CIMT) are non-invasive surrogate markers of subclinical atherosclerosis, but their clinical utility in risk stratification remains controversial.

This review explored whether integrating AS and CIMT into cardiovascular risk assessment could enhance the detection of subclinical atherosclerosis and improve risk classification beyond traditional models.

AS and CIMT are independently associated with increased risk of cardiovascular events. AS, in particular, has been linked to reclassification of up to 15% of intermediate-risk individuals, while CIMT offers modest predictive improvement, particularly for cerebrovascular events.

Despite their prognostic value, routine clinical use of AS and CIMT is limited by methodological inconsistencies and lack of standardization. Nonetheless, they may be particularly useful in refining risk in intermediate-risk patients, younger adults, and those with non-traditional risk profiles.

INTRODUCTION

Atherosclerosis is the primary underlying cause of cardiovascular diseases, which remain the leading cause of mortality worldwide. In 2021, atherosclerotic cardiovascular diseases (ASCVDs) accounted for approximately 20 million deaths globally, representing 37% of all noncommunicable disease-related deaths in individuals under 70 years of age [1]. As a progressive condition, atherosclerosis often begins early in life and remains asymptomatic for extended periods before the development of atherosclerotic plaques [2, 3]. Prior to the onset of symptomatic disease, structural and functional changes occur in the arterial walls, which can be detected using non-invasive imaging techniques. Meta-analyses have demonstrated that carotid intima-media thickness (CIMT) and arterial stiffness (AS) serve as surrogate markers of subclinical atherosclerosis, with well-documented utility in middle-aged and older adults [4–11].

The Cardiovascular Risk in Young Finns Study provided compelling evidence supporting this approach. This longitudinal study revealed that individuals with carotid plaques or elevated CIMT had approximately twice the risk of developing ASCVD over a 16-year follow-up period compared to those without these characteristics, detecting an ASCVD incidence of 2.5% in young adulthood [12]. In addition to CIMT, AS is another key parameter of vascular aging that also emerges in the initial stages of vascular disease [10]. Soderstrom et al. identified a positive association between aortic pulse wave velocity (a-PWV) and CIMT in younger, middle-aged healthy individuals. This finding suggests that individuals with elevated a-PWV, even in the absence of carotid plaques, are also at increased risk for developing ASCVD [9].

In this review, we explore the assessment of subclinical atherosclerosis using AS and CIMT measurements, and how these markers may improve the performance of ASCVD risk prediction models. We examine traditional risk assessment tools alongside recent updates from clinical guidelines, trials, and registries. We also address current methodologies for measuring AS and CIMT, as well as their potential clinical value as biomarkers of ASCVD, a topic that continues to generate substantial debate.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

SHORTCOMINGS OF TRADITIONAL ASCVD RISK PREDICTION MODELS AND THE NEED FOR ALTERNATIVE BIOMARKERS

Assessing ASCVD risk is fundamental to primary prevention, helping in decision-making on the necessity and intensity of interventions such as aspirin, antihypertensive therapy, and lipid management [13]. Traditional risk factors include family history, hypertension, dyslipidemia, smoking, and diabetes [13, 14]. However, many individuals with ASCVD do not exhibit these conventional risk factors, highlighting the need for accurate predictive models. Additionally, the risk varies across populations based on age, gender, and ethnicity [15, 16].

Risk assessment tools estimate an individual's probability of developing ASCVD within a given timeframe, helping identify those at high risk who would benefit most from preventive measures. Traditional cardiovascular risk models, such as the Framingham Risk Score [17] and the Systemic Coronary Risk Estimation [18], estimate a 10-year risk based on conventional factors. Although various risk scores estimate the likelihood of a first cardiovascular event in adults, they should be applied based on the population they were developed for: US-based models (e.g., Pooled Cohort Equations, FRS) [17, 19] are recommended for American patients, while European models (e.g., SCORE, PROCAM) [18, 20] are more suitable for European populations. Because their applicability in low- and middle-income countries remains limited, in 2019, the WHO CVD Risk Chart Working Group updated its risk prediction charts, adapting them to 21 global regions using age-specific incidences and regional risk factor data from 79 countries [21].

Despite their usefulness in predicting cardiovascular events, these models have several limitations. First, they exclude non-traditional risk factors such as chronic inflammation, socioeconomic status, and family history of premature ASCVD, which can influence cardiovascular risk. Second, they typically estimate only 10-year risk, failing to capture long-term risk or the progression of subclinical atherosclerosis. Third, as previously mentioned, their generalizability to diverse ethnic and geographic populations remains uncertain, limiting their applicability in global clinical practice. Finally, they lack direct assessment of atherosclerosis, leading to potential misclassification of individuals at intermediate risk and either overestimation or underestimation of their actual cardiovascular risk.

Several ASCVD clinical practice guidelines provide structured approaches to stratify patients and guide interventions. While methodologies differ, they share the common goal of identifying individuals at elevated risk and optimizing their management.

The American College of Cardiology (ACC) and the American Heart Association (AHA) advocate for a risk-based approach centered on the Pooled Cohort Equations (PCE), which estimate the 10-year ASCVD risk in adults aged 40–75. This model, complemented by the ASCVD Risk Estimator, recommends traditional risk factor screening every 4–6 years from age 20. For younger individuals outside the PCE model, lifetime or 30-year risk estimation provides an alternative perspective. In cases of borderline (5% to < 7.5%) or intermediate-risk (≥ 7.5% to < 20%), coronary artery calcium (CAC) scoring serves as an additional tool to refine risk assessment and guide decisions regarding statin therapy [13].

Similarly, the European Society of Cardiology (ESC) employs the SCORE system, categorizing individuals into low, moderate, high, or very high-risk groups based on the probability of both fatal and non-fatal cardiovascular events [22]. Unlike the ACC/AHA approach, systematic risk assessment is generally reserved for those with major risk factors, excluding younger, asymptomatic individuals, specifically men under 40 and women under 50 without risk factors. Patients with established ASCVD, diabetes, moderate-to-severe renal disease, or genetic lipid disorders are immediately classified as high or very high-risk, warranting a stepwise intensification of treatment with lipid-lowering and blood pressure management strategies.

In the United Kingdom, the National Institute for Health and Care Excellence (NICE) follows

a similar risk-based approach but utilizes the QRISK tool to determine treatment eligibility. Here, the emphasis is placed on lifestyle interventions as the first-line strategy, with pharmacological therapy reserved for individuals at moderate-to-high risk. Specifically, statin therapy is recommended for those with an estimated 10-year ASCVD risk ≥ 10%, as well as for patients with familial hypercholesterolemia, aligning with the overarching principles of risk-based prevention [23].

Overall, no single risk calculator is suitable for all patients. The integration of diverse scoring systems, alongside additional refinements such as imaging, may allow for a personalized approach that balances therapeutic benefits with potential harms, ensuring optimal cardiovascular risk management.

INTEGRATING AS AND CIMT INTO ASCVD RISK ASSESSMENT

The Added Value of AS in Clinical Practice

Pathophysiology and Clinical Implications of AS

AS is a key indicator of vascular aging and an independent risk factor for ASCVD. It results from structural and functional changes in the arterial wall, including intimal thickening, endothelial dysfunction, calcium deposition, and collagen accumulation. These alterations contribute to increased PWV, premature wave reflection, left ventricular hypertrophy, coronary artery and cerebrovascular atherosclerosis [10, 24–26]. Evidence suggests that AS precedes hypertension and target organ damage, making it a valuable marker for early cardiovascular risk assessment [27].

One of the first studies to demonstrate the robust link between AS and atherosclerosis across different vascular territories was The Rotterdam Study, emphasizing its systemic implications [28]. Furthermore, AS has been shown to be closely related to CIMT and carotid plaques, particularly in younger middle-aged individuals and women. The arterial wall changes that lead to increased CIMT are similar to those causing AS, supporting their relationship. Notably, individuals with high AS but no carotid plaques may still be at elevated CVD risk despite the absence of atherosclerosis [9]. Since AS may manifest before overt structural changes, its measurement could enhance early detection and preventive strategies for cardiovascular disease.

Methods for Assessing AS: Strengths and Limitations

Several techniques are used to assess AS, categorized into PWV, pulse wave analysis (PWA), and local arterial stiffness measurements. PWV, the gold standard, measures the speed of pressure wave propagation through arteries, with carotid-femoral PWV (cf-PWV) being the most validated due to its strong association with ASCVD risk [10] (Fig. 1). cf-PWV is included in European guidelines and is considered more reliable than peripheral artery assessments [22]. A variant of this method is ultrafast PWV (uf-PWV), which

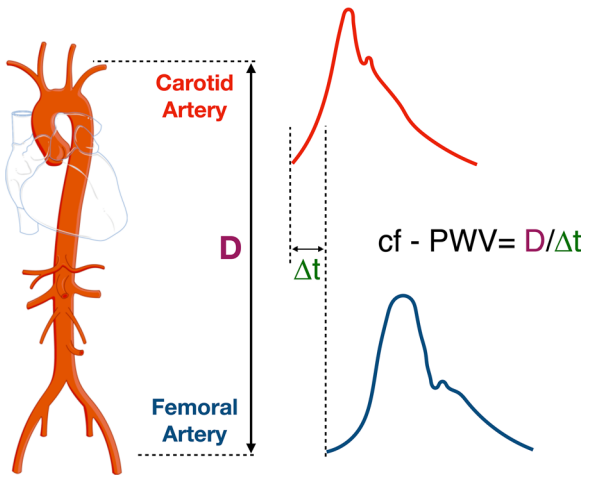

Fig. 1 Cf-PWV assessment. PWV is determined by measuring the time taken for the pulse wave to travel between the carotid and femoral arteries. Pressure-sensitive transducers placed over these sites record pulse waveforms, and Δt is calculated using the foot-to-foot method, which identifies the delay between the onset (foot) of the carotid and femoral pulse waves. The travel distance (D) between the recording sites is measured along the body surface. *Cf-PWV* carotid femoral-pulse wave velocity, *Δt* transit time, *D* distance

improves temporal resolution and reproducibility but requires further validation [29]. The normal and reference values for PWV have been defined by "The Reference Values for Arterial Stiffness Collaboration" [30].

Beyond PWV, other hemodynamic markers provide complementary information. The augmentation index (AIx) reflects arterial wave reflection and systemic stiffness, while arterial compliance and the β-stiffness index quantify vascular elasticity and rigidity, independent of blood pressure [31]. Techniques such as vascular ultrasound and MRI assess wall thickness, distensibility, and the elastic modulus, refining arterial characterization. Speckle tracking ultrasound, an emerging technique, uses 2D echocardiography synchronized with ECG to track carotid artery wall motion, providing angle-independent strain and strain rate assessments [32, 33] (Fig. 2). Another technique to consider is the cardio-ankle vascular index (CAVI). It measures AS via blood pressure cuffs on the arms and ankles and reflects stiffness across the aorta and lower-limb arteries. Unlike PWV, CAVI is less affected by blood pressure at the time of measurement, and it is operator-independent. Despite its advantages, its predictive value for ASCVD and mortality remains under investigation due to limited studies [24, 34].

Each method offers distinct advantages and limitations, with the choice of technique depending on clinical context, feasibility, and required precision. Integrating multiple assessment tools may enhance cardiovascular risk stratification and guide targeted prevention strategies.

Role of AS as Biomarker of ASCVD

AS is a well-established predictor of ASCVD risk, including coronary heart disease (CHD), and stroke. Several studies have reinforced the utility of AS as a predictor or ASCVD events. A meta-analysis by Zhong et al., including 19 studies with 19,908 participants, reported that a 1-SD increase in cf-PWV corresponded to a 25% higher risk of ASCVD events, while a 1-m/s increase led to a 12%, respectively. For ASCVD

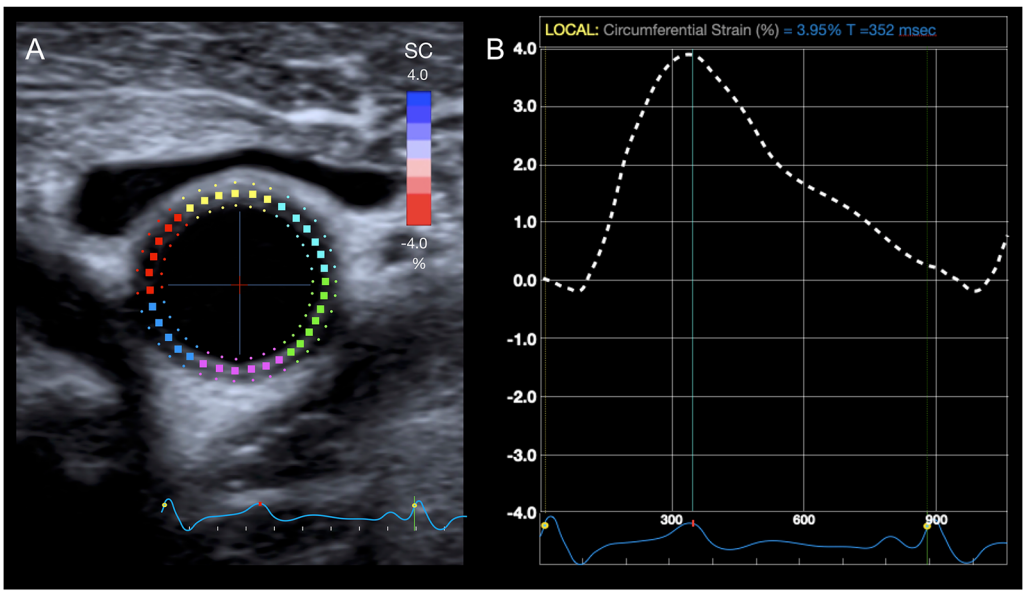

Fig. 2 Speckle tracking strain imaging of the CCA. **A** Short-axis ultrasonography of the CCA, where the region of interest is outlined by a color-coded circumferential strain map. Each of the six segments included in the strain analysis is represented with a different color. **B** The strain curve illustrates the temporal variation of the carotid artery deformation throughout the cardiac cycle. The peak carotid arterial strain occurs at 352 ms, with a maximum circumferential strain of 3.95%. *CCA* common carotid artery

mortality, a 1-SD increase in cf-PWV resulted in a 23% increased risk and a 1-m/s increase was associated with a 9% increased risk [10]. Further supporting this, another meta-analysis in high-ASCVD-risk populations in Asia found that a 1-SD increase in the CAVI was associated with a 20% higher ASCVD risk [24]. Additionally, the Framingham Offspring Cohort demonstrated that individuals with both high central pulse pressure and high cf-PWV had a 52% increased risk of ASCVD [1]. More evidence from The Framingham Heart Study (FHS) demonstrated that higher PWV was associated with a 48% increased risk of incident ASCVD events and significantly improved risk prediction when added PWV to standard risk factors [35].

The ARIC and the MESA studies likewise provided evidence of the link between AS and stroke, demonstrating that increased AS parameters and carotid distensibility were independently associated with higher stroke incidence [36, 37]. The Rotterdam Study concluded that individuals in the highest tertile of PWV had an adjusted hazard ratio (HR) of 2.34 for stroke. Furthermore, a 1-SD increase in PWV was linked to an HR of 1.28 [28]. Research about carotid distensibility also found that patients in the quartile with the lowest distension had a 2.1 times higher prevalence of a previous stroke compared with the patients in the quartile with the highest distension [38]. In agreement with these findings, Van Sloten et al. observed that a 1-SD increase in carotid distensibility predicted stroke with an HR 1.18 [39]. Similarly, carotid-cerebral PWV has been associated with atherosclerotic burden and stenosis severity, particularly in patients with acute ischemic stroke [40] and cf-PWV was also associated with increased risk of dementia (HR 1.60) over 15 years in the Cardiovascular Health Study (CHS) Cognition Study [41].

With respect to CHD, a 9.4-year follow-up Danish study found that each 1-SD increase in cf-PWV was associated with a 16–20% higher risk of developing coronary artery disease (CAD) [42]. In patients with existing CAD, elevated AS has been linked to increased mortality and cardiovascular events [26]. Additionally, a study of 372 patients undergoing percutaneous coronary intervention (PCI) identified high brachial-ankle PWV (ba-PWV) as a strong predictor of cardiac death after PCI [43]. Table 1 (Ref. [28, 36–39, 44]) summarizes the findings of major studies on the association between AS and the risk of ASCVD events.

AS also has a special consideration in cardiovascular outcomes in various populations. In patients with chronic kidney disease (CKD), it acts as an independent predictor of cardiovascular mortality [45] and in individuals with diabetes and metabolic syndrome, it is associated with worsened cardiovascular outcomes [46]. It has also been observed that stiffness parameters were higher in patients with head and neck tumors who had received radiotherapy as part of their treatment [47]. Additionally, in COVID-19 patients, increased arterial stiffness was linked to a 27% higher in-hospital mortality risk in a Spanish cohort [48].

Regarding the assessment of vascular stiffness in ASCVD risk models, patients at intermediate risk in the FHS could be reclassified into a higher or lower ASCVD risk category based on AS measurements [28, 35]. Up to 15% of these patients could be reclassified into a higher (14.3%) or lower (1.4%) risk category when arterial stiffness was assessed [35]. According to the evidence, carotid ultrasound and PWV are recognized in the 2024 European Society of Hypertension (ESH) guidelines for their role in risk stratification and treatment decisions [49]. While studies suggest that AS predicts future ASCVD risk and improves risk classification, its widespread clinical adoption remains limited. Measurement complexities and substantial publication bias have contributed to this limitation. Consequently, the 2021 ESC guidelines, despite acknowledging its prognostic value, do not recommend its routine use [22]. Similarly, the 2019 AHA guidelines also do not support the use of arterial stiffness measurement for ASCVD risk assessment in asymptomatic adults [13].

Table 1 Summary of the studies reporting the association of AS and CIMT with future stroke and/or CHD

Study	Country and year of publication	Population (mean age)	Follow-up (years)	Outcome (*n*)	Measurement and adjusted HR (95% CI)
ARIC [58]	Sweden 2005	5163 (60)	7.0	CHD (113)	CIMT 1.27 (0.61–2.65) Plaque 1.99 (1.13–3.49)
ARIC [36]	USA 2012	10,407 (55)	13.8	Stroke (383)	AD 1.19 (1.02–1.39) SI 1.14 (1.04–1.25)
BLSA [59]	China 2018	1376 (69)	5.2	Stroke (136) or CHD (70)	CIMT 0.8 (0.33–1.69) Plaque 2.0 (1.24–3.25)
CAPS [60]	Germany 2006	5056 (50)	4.2	Stroke (107)	CIMT 1.11 (0.97–1.28)
CCCC [61]	Taiwan 2008	2190 (56)	10.5	Stroke (94) CHD (68)	CIMT 1.47 (1.28–1.69) CIMT 1.38 (1.12–1.70)
CHS [62]	USA 2000	4476 (72)	6.2	Stroke (284)	CIMT 1.36 (1.25–2.28)
EAS [63]	UK 2007	1007 (69)	12.0	Stroke or CHD (137)	CIMT 1.59 (1.07–2.37)
FATE [64]	Canada 2011	1574 (49)	7.2	Stroke or CHD (111)	CIMT 1.86 (1.53–1.28)
FHS [65]	USA 2011	2965 (58)	7.2	Stroke or CHD (296)	CIMT 1.13 (1.02–1.24)
Hoorn [39]	The Netherlands 2014	579 (67)	7.6	Stroke or CHD (130)	AD 1.22 (0.95–1.56) AC 1.19 (1.00–1.41)
IMPROVE [66]	Europe 2017	3703 (64)	3.0	Stroke (73) CHD (125)	CIMT 2.76 (1.66–4.60) CIMT 1.58 (1.06–2.37)

Table 1 continued

Study	Country and year of publication	Population (mean age)	Follow-up (years)	Outcome (*n*)	Measurement and adjusted HR (95% CI)
MDCS [58]	Sweeden 2005	5163 (57)	7.0	CHD (113)	CIMT 1.36 (1.21–1.54) Plaque 2.40 (1.58–3.64)
MESA [37]	USA 2021	5918 (62)	7.7	Stroke (105)	AD 0.05 (0.00–0.75)
MESA [44]	USA 2015	389 (59)	9.5	CHD (33)	LD 3.30 (0.96–11.14)
MESA [67]	USA 2008	6698 (45–84)	3.9	Stroke (59) CHD (159)	CIMT 1.40 (1.20–1.80) CIMT 1.20 (1.00–1.40)
Three City Study [68]	France 2011	5895 (65–85)	5.4	CHD (223)	CIMT 0.80 (0.50–1.10)
PROG-IMT [69]	USA 2012	36,984 (NR)	7.0	Stroke (1339)	CIMT 1.21 (1.09–1.35)
Rotterdam [28]	The Netherlands 2006	2835 (71)	10.0	Stroke (63) CHD (101)	Third tertile: PWV 2.34 (1.13–4.82) AD 2.44 (1.33–4.45)
Rotterdam [70]	The Netherlands 2012	3580 (64)	12.2	Stroke (207)	CIMT 1.33 (1.18–1.50)
SMART [38]	The Netherlands 2004	3950 (63)	NR	Stroke (260)	Third tertile: AD 2.10 (1.10–4.10)
Suita [71]	Japan 2018	4724 (60)	12.7	Stroke (221) CHD (375)	CIMT 1.12 (0.99–1.26) CIMT 1.20 (1.10–1.30)
Tromsø [72]	Norway 2011	6584 (60)	10.8	Stroke (397)	CIMT 1.08 (0.95–1.22) Plaque 1.23 (1.09–1.38)
Xie [73]	China 2011	1734 (43–79)	5.0	Stroke (63) or CHD (81)	CIMT 1.59 (1.04–2.45)

AC Arterial Compliance, *AD* Arterial Distensibility, *AS* Arterial Stiffness, *CHD* Coronary Heart Disease, *CIMT* Carotid Intima-Media Thickness, *LD* Longitudinal Displacement, *NR* Not Reported, *PWV* Pulse Wave Velocity, *SI* Stiffness Index

The Added Value of CIMT in Clinical Practice

Pathophysiology and Clinical Implications of CIMT

CIMT refers to the thickness of the inner two layers of the carotid artery wall: the intima and media. CIMT increases over time due to aging and atherosclerosis and the progressive accumulation of lipids and inflammatory cells, combined with smooth muscle proliferation, results in arterial wall thickening and AS. Over time, atherosclerosis can progress to plaque formation and arterial stenosis, impairing blood flow and increasing the risk of stroke, myocardial infarction, or other acute vascular events [2, 6, 50–52].

Carotid atherosclerosis has traditionally been assessed based on the degree of stenosis (Fig. 3). However, CIMT and AS have been proposed as valuable surrogate markers for early atherosclerosis, complementing traditional assessments. In a recent systematic review, Song et al. reported that in 2020, approximately 28% of individuals aged 30–79 years in the general population had an abnormal CIMT, implying this effect applies to just over 1 billion people [3]. A meta-analysis of 21,494 participants from 20 studies within the Proof-ATHERO (Prospective Studies of Atherosclerosis) consortium, indicated that individuals in the top quartile compared with those in the bottom quartile of baseline CIMT had a 30% higher risk of developing carotid plaque [7]. However, longitudinal studies yield mixed results regarding whether higher baseline CIMT predicts future plaque development [37, 53, 54].

Methods for Assessing CIMT: Strengths and Limitations

CIMT is primarily measured using B-mode ultrasound. The Mannheim Carotid Intima-Media Thickness and Plaque Consensus provides standardized guidelines for CIMT measurement [55]. In longitudinal B-mode ultrasound imaging, CIMT appears as a double-line pattern between the intimal-luminal and medial-adventitial interfaces of the carotid artery wall. Measurement is typically performed in a plaque-free

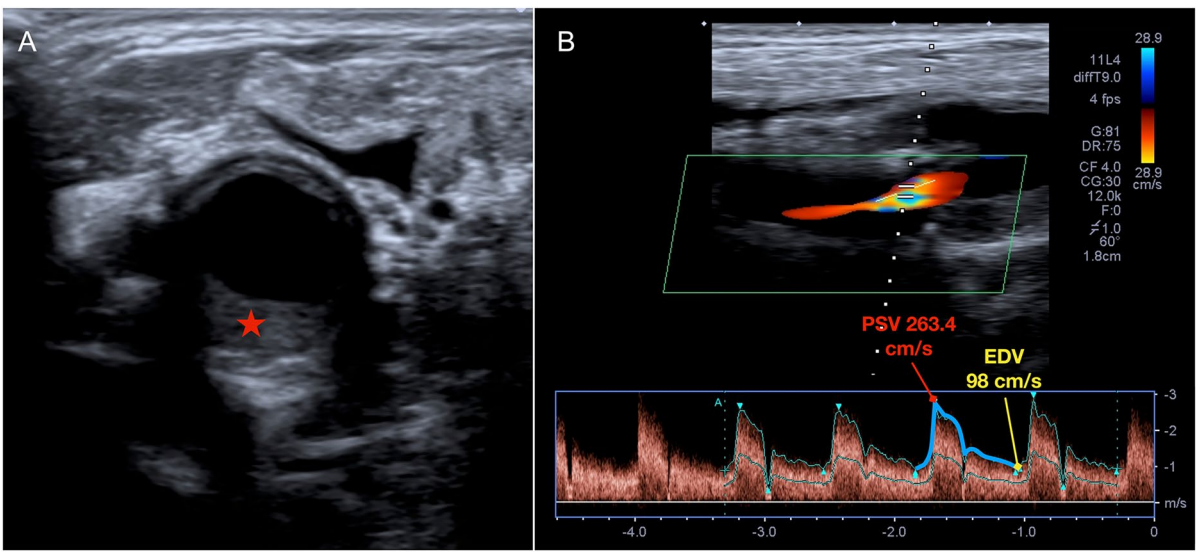

Fig. 3 Ultrasound imaging of the carotid bifurcation. **A** Cross-sectional ultrasound view of the CCA reveals an echolucent plaque (*red asterisk*) causing luminal narrowing. **B** Longitudinal view showing the plaque extending into the origin of the ICA. Doppler velocity analysis indicates a 70% stenosis, based on a PSV of 263 cm/s, exceeding the 230 cm/s threshold for severe stenosis. *CCA* common carotid artery, *ICA* internal carotid artery, *PSV* peak systolic velocity, *EDV* end diastolic velocity

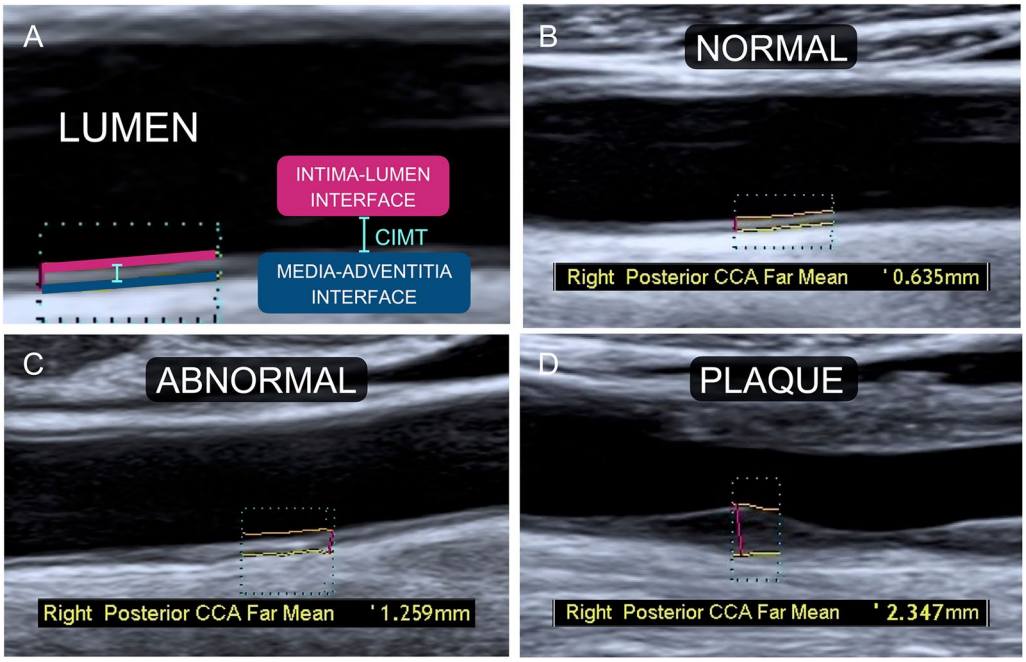

Fig. 4 Measurement of CCA-CIMT. Schematic representation illustrating CIMT as the distance between the intima-lumen and media-adventitia interfaces (**A**). Longitudinal B-mode ultrasound images of the CCA show a normal CIMT of 0.635 mm (**B**), increased wall thickness with a CIMT of 1.259 mm (**C**), and focal, non-calcified arterial wall thickening reaching 2.347 mm, which is considered a plaque (**D**). *CIMT* carotid intima-media thickness, *CCA* common carotid artery

region of the common carotid artery (CCA), most commonly in the distal segment (Fig. 4).

Standardized measurement protocols are essential to ensure reproducibility. Semiautomated and fully automated reading software have been developed to enhance measurement precision, reducing the subjectivity associated with manual readings [55]. Despite these advancements, several challenges persist in CIMT measurement. A major limitation is the absence of universally accepted reference values, as CIMT varies significantly among different populations and ethnic groups. The European Society of Cardiology (ESC) defines abnormal CIMT as values exceeding 0.9 mm [56], whereas the American Society of Echocardiography (ASE) recommends using the 75th percentile of a reference population as a threshold [57]. Mean CIMT values in healthy adults generally range between 0.65 and 0.90 mm and increase at an average rate is approximately 0.01–0.04 mm per year [11, 25].

An important distinction to consider is between CIMT and carotid plaque. Touboul et al. defined carotid plaque as focal thickening that protrudes into the lumen by at least 0.5 mm or 50% of the surrounding CIMT, or as a CIMT value exceeding 1.5 mm [55]. Misclassifying early-stage plaques as increased CIMT remains a potential source of measurement error [7]. It is also important to note that since the annual change in CIMT is small, the resolution of ultrasound devices may limit the accurate assessment of CIMT progression over short periods [25].

Role of CIMT as Biomarker of ASCVD

The role of CIMT as a biomarker of atherosclerosis and its utility in ASCVD risk prediction remain subjects of ongoing debate, despite several studies demonstrating that increased CIMT is associated with higher risks of stroke and myocardial infarction. Table 1 (Ref. [58–73]) summarizes the results of several major studies

related to the association between CIMT and risk of ASCVD events.

A meta-analysis by van den Oord et al. reported that 1-SD deviation increase in CIMT was associated with a 31% increase in stroke risk and a 26% increase in myocardial infarction risk [6]. Similarly, Kumar et al. reported a strong association between increased CIMT with risk of ischemic stroke as compared to control subjects. Additionally, silent brain ischemic events in stroke-free individuals were also associated with increased CIMT [75].

Regarding CHD, Stein et al. reported that a CIMT value above the 75th percentile for the patient's age, sex, and race/ethnicity is indicative of increased cardiovascular risk and thus may indicate a more aggressive risk-reducing therapy [57]. However, it lacks prospective follow-up data supporting interventions in medical therapy based on CIMT values. In addition, Abeysuriya et al. emphasize that CIMT is a strong predictor of CHD and an independent phenotype of early atherosclerosis. In their study, the CHD group showed a significantly higher CIMT compared to the non-CHD group [15]. Other multicenter studies have shown the association between CIMT and increased CHD risk, emphasizing its value in prediction [58, 59, 61, 63–68, 71]. However, some of these studies caution against using CIMT alone, as its predictive ability is limited without other risk factors, with the Framingham Offspring Study and ARIC study suggesting that combining CIMT with additional factors improves CHD risk prediction [78, 79].

When incorporated into cardiovascular risk models, CIMT provides only modest improvements in predictive accuracy [6, 76]. The Rotterdam Study found a net reclassification improvement of 0.8% overall and 3.6% in intermediate-risk individuals [70]. Despite these associations, the clinical utility of CIMT in routine risk stratification remains uncertain. The 2021 ESC guidelines and the AHA/ACC guidelines do not recommend CIMT for systematic risk assessment due to a lack of methodological standardization and its limited incremental predictive value [13, 22]. Conversely, the 2022 Japan Atherosclerosis Society (JAS) guideline [80], along with other authors, recommends considering CIMT for assessing subclinical atherosclerosis and preventing ASCVD, despite the modest improvement in risk prediction models. This recommendation is particularly relevant for intermediate-risk populations due to the clinical significance of even a slight increase in CIMT [6, 81, 82].

It is also important to note that carotid plaque assessment has been shown to be more effective than CIMT in predicting cardiovascular outcomes, with up to 35% greater accuracy in CVD risk prediction compared to CIMT [4, 79]. Moreover, studies suggest that CAC is a stronger predictor of CHD than CIMT [53, 83], although CIMT remains significantly associated with stroke risk [67].

Other factors, such as ethnic variations and genetic predispositions, may also influence CIMT's predictive value. Studies indicate that CIMT progression rates and baseline values vary significantly between populations, with African American individuals displaying higher CIMT than European or Hispanic populations [16]. This suggests that CIMT's role in risk prediction may require individualized approaches rather than universal thresholds.

CONCLUSIONS

Early identification of individuals at risk for ASCVD is crucial in preventive medicine. AS and CIMT have been established as independent predictors of cardiovascular events and can therefore be considered valuable biomarkers for detecting subclinical atherosclerosis. While AS has a strong association with hypertension and CHD, CIMT has proven to be a better predictor of cerebrovascular events.

Regarding their role in ASCVD risk assessment, incorporating AS into traditional models can lead to the reclassification of up to 15% of individuals into higher or lower risk categories. However, CIMT provides only a modest improvement to risk prediction models, with limited incremental value over traditional scores. Although major clinical practice guidelines recommend CAC as the preferred imaging biomarker, AS and CIMT offer a non-radiation

alternative. This makes them particularly valuable in specific scenarios, such as intermediate-risk individuals where traditional risk scores yield ambiguous results, patients with a strong family history of ASCVD but no conventional risk factors, and young adults with early signs of metabolic syndrome, where vascular changes may be present but not yet clinically apparent.

The integration of AS and CIMT into clinical decision-making remains uncertain, largely due to methodological inconsistencies, including variability in measurement techniques, the lack of universally accepted reference values, and differences in study populations. To address these challenges, future research should prioritize the development of standardized measurement protocols and validate these biomarkers in large-scale randomized controlled trials. Additionally, comparative effectiveness studies directly assessing AS, CIMT, and CAC would be valuable, as well as the integration of these biomarkers into risk prediction algorithms powered by AI-driven models. Such approaches could enhance risk stratification by incorporating AS and CIMT alongside other clinical and imaging data, ultimately improving personalized risk assessment.

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Declarations

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REFERENCES

1. Martin SS, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, et al. 2024 Heart disease and stroke statistics: a report of US and global data from the American Heart Association. Circulation. 2024;149(8):e347–913.

2. Flore R, Ponziani FR, Tinelli G, Arena V, Fonnesu C, Nesci A, et al. New modalities of ultrasound-based intima-media thickness, arterial stiffness and non-coronary vascular calcifications detection to assess cardiovascular risk. Eur Rev Med Pharmacol Sci. 2015;19(8):1430–41.

3. Song P, Fang Z, Wang H, Cai Y, Rahimi K, Zhu Y, et al. Global and regional prevalence, burden, and risk factors for carotid atherosclerosis: a systematic review, meta-analysis, and modelling study. Lancet Glob Health. 2020;8:e721-729.

4. Inaba Y, Chen JA, Bergmann SR. Carotid plaque, compared with carotid intima-media thickness, more accurately predicts coronary artery disease events: a meta-analysis. Atherosclerosis. 2012;220(1):128–33.

5. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. Circulation. 2007;115:459–67.

6. Van den Oord SCH, Sijbrands EJG, ten Kate GL, van Klaveren D, van Domburg R, van der Steen FW, et al. Carotid intima-media thickness for cardiovascular risk assessment: systematic review and meta-analysis. Atherosclerosis. 2013;228(1):1–11.

7. Tschiderer L, Seekircher L, Izzo R, Mancusi C, Manzi MV, Baldassarre D, et al. Association of intima-media thickness measured at the common carotid artery with incident carotid plaque: individual participant data meta-analysis of 20 prospective studies. J Am Heart Assoc. 2023;12(12): e027657.

8. Takase M, Nakaya N, Nakamura T, Kogure M, Hatanaka R, Nakaya K, et al. Carotid intima media thickness and risk factors for atherosclerosis: Tohoku Medical Megabank Community-Based Cohort Study. J Atheroscler Thromb. 2023;30(10):1471–82.

9. Söderström M, Grönlund C, Liv P, Nyman E, Näslund U, Wester P. Aortic arterial stiffness associates with carotid intima-media thickness and carotid plaques in younger middle-aged healthy people. Blood Press. 2024;33(1):2405161.

10. Zhong Q, Hu MJ, Cui YJ, Liang L, Zhou MM, Yang YW, et al. Carotid-femoral pulse wave velocity in the prediction of cardiovascular events and mortality: an updated systematic review and meta-analysis. Angiology. 2018;69(7):617–29.

11. Willeit P, Tschiderer L, Allara E, Reuber K, Seekircher L, Gao L, PROG-IMT and the Proof-ATHERO Study Groups, et al. Carotid intima-media thickness progression as surrogate marker for cardiovascular risk: meta-analysis of 119 clinical trials involving 100,667 patients. Circulation. 2020;142(7):621–42.

12. Raitakari OT, Magnussen CG, Juonala M, Kartiosuo N, Pahkala K, Rovio S, et al. Subclinical atherosclerosis in young adults predicting cardiovascular disease: the Cardiovascular Risk In Young Finns Study. Atherosclerosis. 2024;393: 117515.

13. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. J Am Coll Cardiol. 2019;74(10):1376–414.

14. Wallace ML, Ricco JA, Barrett B. Screening strategies for cardiovascular disease in asymptomatic adults. Prim Care. 2014;41(2):371–97.

15. Abeysuriya V, Perera BPR, Wickremasinghe AR. Regional and demographic variations of carotid artery intima and media thickness (CIMT): a systematic review and meta-analysis. PLoS ONE. 2022;17(7): e0268716.

16. Nonterah EA, Crowther NJ, Klipstein-Grobusch K, Oduro AR, Kavousi M, Agongo G, et al. Racial and ethnic differences in the association between classical cardiovascular risk factors and common carotid intima-media thickness: an individual participant data meta-analysis. J Am Heart Assoc. 2022;11(15): e023704.

17. D´Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743–53.

18. Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J. 2003;24(11):987–1003.

19. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63(25):2935–59.

20. Assmann G, Schulte H, von Eckardstein A. Hypertriglyceridemia and elevated lipoprotein(a) are risk factors for major coronary events in middle-aged men. Am J Cardiol. 1996;77(14):1179–84.

21. WHO CVD Risk Chart Working Group. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. Lancet Glob Health. 2019;7(10):e1332–45.

22. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021;42(34):3227–337.

23. National Institute for Health and Care Excellence (NICE). Cardiovascular disease: risk assessment and reduction, including lipid modification. 2023. Available at: https://www.nice.org.uk/guidance/ng238 (Accessed: 2025 Mar 22)

24. Matsushita K, Ding N, Kim ED, Budoff M, Chirinos JA, Fernhall B, et al. Cardio-ankle vascular index and cardiovascular disease: Systematic review and meta-analysis of prospective and cross-sectional studies. J Clin Hypertens (Greenwich). 2019;21(1):16–24.

25. Kim GH, Youn HJ. Is carotid artery ultrasound still useful method for evaluation of atherosclerosis? Korean Circ J. 2017;47(1):1–8.

26. Lee GP, Kim HL. Incremental value of the measures of arterial stiffness in cardiovascular risk assessment. Rev Cardiovasc Med. 2022;23(1):6.

27. Kaess BM, Rong J, Larson MG, Hamburg NM, Vita JA, Levy D, et al. Aortic stiffness, blood pressure progression, and incident hypertension. JAMA. 2012;308(9):875–81.

28. Mattace-Raso FUS, van der Cammen TJM, Hofman A, van Popele NM, Bos ML, Schalekamp MADH, et al. Arterial stiffness and risk of coronary heart disease and stroke. The Rotterdam study. Circulation. 2006;113(5):657–63.

29. Zhu ZQ, Chen LS, Wang H, Liu FM, Luan Y, Wu LL, et al. Carotid stiffness and atherosclerotic risk: non-invasive quantification with ultrafast ultrasound pulse wave velocity. Eur Radiol. 2019;29(3):1507–17.

30. Reference Values for Arterial Stiffness' Collaboration. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: "establishing normal and reference values." Eur Heart J. 2010;31(19):2338–50.

31. Kim HL. The value of serial measurement of arterial stiffness in cardiovascular disease. Rev Cardiovasc Med. 2024;25(1):7.

32. Bjällmark A, Lind B, Peolsson M, Shahgaldi K, Brodin LA, Nowak J. Ultrasonographic strain imaging is superior to conventional non-invasive measures of vascular stiffness in the detection of age-dependent differences in the mechanical properties of the common carotid artery. Eur J Echocardiogr. 2010;11(7):630–6.

33. Teixeira R, Vieira MJ, Gonçalves A, Cardim N, Gonçalves L. Ultrasonographic vascular mechanics to assess arterial stiffness: a review. Eur Heart J Cardiovasc Imaging. 2016;17(3):233–46.

34. Saiki A, Ohira M, Yamaguchi T, Nagayama D, Shimizu N, Shirai K, et al. New horizons of arterial stiffness developed using Cardio-Ankle Vascular Index (CAVI). J Atheroscler Thromb. 2020;27:732–48.

35. Mitchell GF, Hwang SJ, Vasan RS, Larson M. Arterial stiffness and cardiovascular events the Framingham Heart Study. Circulation. 2010;121(4):505–11.

36. Yang EY, Chambless L, Sharrett AR, Virani SS, Liu X, Tang Z, et al. Carotid arterial wall characteristics are associated with incident ischemic stroke but not coronary heart disease in the Atherosclerosis Risk in Communities (ARIC) Study. Stroke. 2012;43(1):103–8.

37. Baradaran H, Delic A, Wong KH, Sheibani N, Alexander M, McNally JS, et al. Using ultrasound and inflammation to improve prediction of ischemic stroke: a secondary analysis of the multi-ethnic study of atherosclerosis. Cerebrovasc Dis Extra. 2021;11(1):37–43.

38. Dijk JM, van der Graaf Y, Grobbee DE, Bots ML. Carotid stiffness indicates risk of ischemic stroke and TIA in patients with internal carotid artery stenosis the SMART study. Stroke. 2004;35:2258–62.

39. Van Sloten TT, Schram MT, van den Hurk K, Dekker JM, Nijpels G, Henry RMA, et al. Local stiffness of the carotid and femoral artery is associated with incident cardiovascular events and all-cause mortality. J Am Coll Cardiol. 2014;63(17):1739–47.

40. Fu X, Liu Q, Zeng X, Huang S, Huang R. Association between cerebral arterial stiffness and large artery atherosclerosis in acute ischemic stroke. J Stroke Cerebrovasc Dis. 2018;27(11):2999–3000.

41. Cui C, Sekikawa A, Kuller LH, Lopez OL, Newman AB, Kuipers AL, et al. Aortic stiffness is associated with increased risk of incident dementia in older adults. J Alzheimers Dis. 2018;66:297–306.

42. Willum-Hansen T, Staessen JA, Torp-Pedersen C, Rasmussen S, Thijs L, Ibsen H, et al. Prognostic value of aortic pulse wave velocity as index of arterial stiffness in the general population. Circulation. 2006;113:664–70.

43. Ki YJ, Choi DH, Lee YM, Lim L, Song H, Koh YY. Predictive value of brachial-ankle pulse wave velocity for long-term clinical outcomes after percutaneous coronary intervention in a Korean cohort. Int J Cardiol. 2014;175:554–9.

44. Gepner AD, Young R, Delaney JA, Tattersall MC, Blaha MJ, Post WS, et al. Comparison of coronary artery calcium presence, carotid plaque presence, and carotid intimamedia thickness for

cardiovascular disease prediction in the multiethnic study of atherosclerosis. Circ Cardiovasc Imaging. 2015;8: e002262.

45. Ticulescu CR, Vriz O, Sparacino L, Popescu BA, Ginghina C, Nicolosi GL, et al. Incremental value of arterial stiffness over traditional risk factors in predicting subclinical cardiovascular remodeling in patients with moderate chronic renal failure. Angiology. 2011;62(8):662–8.

46. Liang X, Li D, Wang Z, Cheng Y, Mou K, Ye C, et al. Aortic stiffness measured by carotid femoral-pulse wave velocity at different stages of normal glucose, prediabetes, and diabetes mellitus: a systematic review and meta-analysis. Rev Cardiovasc Med. 2024;25(9):339.

47. Fernandez-Alvarez V, Nieto CS, Alvarez FL. Arterial stiffness as an ultrasound biomarker of radiation-induced carotid artery disease. Vasa. 2021;50(5):348–55.

48. Rodilla E, Lopez-Carmona MD, Cortes X, Cobos-Palacios L, Canales S, Saez MC, et al. Impact of arterial stiffness on all-cause mortality in patients hospitalized with COVID-19 in Spain. Hypertension. 2021;77:856–67.

49. Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, Muiesan ML, et al. 2024 European Society of Hypertension clinical practice guidelines for the management of arterial hypertension. Eur J Intern Med. 2024;126:1–15.

50. Catalano M, Lamberti-Castronuovo A, Catalano A, Filocamo D, Zimbalatti C. Two-dimensional speckle-tracking strain imaging in the assessment of mechanical properties of carotid arteries: feasibility and comparison with conventional markers of subclinical atherosclerosis. Eur J Echocardiogr. 2011;12(7):528–35.

51. Mancini GB, Dahlöf B, Diez J. Surrogate markers for cardiovascular disease-structural markers. Circulation. 2004;109(Suppl.IV):22–30.

52. Vlachopoulos C, Xaplanteris P, Aboyans V, Brodmann M, Cifkova R, Cosentino F, et al. The role of vascular biomarkers for primary and secondary prevention. A position paper from the European Society of Cardiology Working Group on peripheral circulation endorsed by the Association for Research into Arterial Structure and Physiology (ARTERY) Society. Atherosclerosis. 2015;241(2):507–32.

53. Blaha MJ, Yeboah J, Al Rifai M, Liu K, Kronmal R, Greenland P. Providing evidence for subclinical CVD in risk assessment. Glob Heart. 2016;11(3):275–85.

54. Garg PK, Bhatia HS, Allen TS, Grainger T, Pouncey AL, Dichek D, et al. Assessment of subclinical atherosclerosis in asymptomatic people in vivo: measurements suitable for biomarker and mendelian randomization studies. Arterioscler Thromb Vasc Biol. 2024;44(1):24–47.

55. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarenco P, Bornstein N, et al. Mannheim carotid intima-media thickness and plaque consensus (2004–2006–2011): an update on behalf of the Advisory Board of the 3rd and 4th Watching the Risk Symposium 13th and 15th European Stroke Conferences, Mannheim, Germany, 2004, and Brussels, Belgium, 2006. Cerebrovasc Dis. 2012;34(4):290–6.

56. Mancia MG, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2013;2013(34):2159–219.

57. Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. J Am Soc Echocardiogr. 2008;21:93–111.

58. Rosvall M, Janzon L, Berglund G, Engstrom G, Hedblad B. Incident coronary events and case fatality in relation to common carotid intima-media thickness. J Intern Med. 2005;257:430–7.

59. Zhang Y, Fang X, Hua Y, Tang Z, Guan S, Wu X, et al. Carotid artery plaques, carotid intima-media thickness, and risk of cardiovascular events and all-cause death in older adults: a 5-year prospective, community-based study. Angiology. 2018;69(2):120–9.

60. Lorenz MW, von Kegler S, Steinmetz H, Markus HS, Sitzer M. Carotid intima-media thickening indicates a higher vascular risk across a wide age range: prospective data from the Carotid Atherosclerosis Progression Study (CAPS). Stroke. 2006;37(1):87–92.

61. Chien KL, Su TC, Jeng JS, Hsu HC, Chang WT, Chen MF, et al. Carotid artery intima-media thickness, carotid plaque and coronary heart disease and stroke in Chinese. PLoS ONE. 2008;3: e3435.

62. O´Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolson SK. Carotid artery intima and media thickness as a risk factor of myocardial

infarction and stroke in older adults. N Engl J Med. 1999;340(1):14–22.

63. Price JF, Tzoulaki I, Lee AJ, Fowkes GR. Ankle brachial index and intima media thickness predict cardiovascular events similarly and increased prediction when combined. J Clin Epidemiol. 2007;60(10):1067–75.

64. Anderson TJ, Charbonneau F, Title LM, Buithieu J, Rose MS, Conradson H, et al. Microvascular function predicts cardiovascular events in primary prevention: long-term results from the Firefighters and Their Endothelium (FATE) study. Circulation. 2011;123(2):163–9.

65. Polak JF, Pencina MJ, Pencina KM, O´Donnell CJ, Wolf PA, D´Agostino RB. Carotid-wall intima-media thickness and cardiovascular events. N Engl J Med. 2011;365(3):213–21.

66. Amato M, Veglia F, de Faire U, Giral P, Rauramaa R, Smit AJ, et al. Carotid plaque thickness and common carotid IMT show additive value in cardiovascular risk prediction and reclassification. Atherosclerosis. 2017;263:412–9.

67. Folsom AR, Kronmal RA, Detrano RC, O´Leary DH, Bild DE, Bluemke DA, et al. Coronary Artery Calcification Compared with Carotid Intima-Media Thickness in Prediction of Cardiovascular Disease Incidence: The Multi-Ethnic Study of Atherosclerosis (MESA). Arch Intern Med. 2008;168(12):1333–9.

68. Plichart M, Celermajer DS, Zuerik M, Helmer C, Jouven X, Ritchie K, et al. Carotid intima-media thickness in plaque-free site, carotid plaques and coronary heart disease risk prediction in older adults. The three-city study. Atherosclerosis. 2011;219(2):917–24.

69. Lorenz MW, Polak JF, Kavousi M, Mathiesen EB, Völzke H, Tuomainen TP, Sander D, et al. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. Lancet. 2012;379(9831):2053–62.

70. Elias-Smale SE, Kavousi M, Verwoert GC, Koller MT, Steyerberg EW, Mattace-Raso FUS, et al. Common carotid intima-media thickness in cardiovascular risk stratification of older people: the Rotterdam study. Eur J Prev Cardiol. 2012;19(4):698–705.

71. Kokubo Y, Watanabe M, Higashiyama A, Nakao YM, Nakamura F, Miyamoto Y. Impact of intima-media thickness progression in the common carotid arteries on the risk of incident cardiovascular disease in the Suita Study. J Am Heart Assoc. 2018;7: e007720.

72. Mathiesen EB, Johnsen SH, Wilsgaard T, Bonaa KH, Lochen ML, Njolstad I. Carotid plaque area and intima-media thickness in prediction of first-ever ischemic stroke: a 10-year follow-up of 6584 men and women: the Tromsø Study. Stroke. 2011;42(4):972–8.

73. Xie W, Liang L, Zhao L, Shi P, Yang Y, Xie G, et al. Combination of carotid intima-media thickness and plaque for better predicting risk of ischaemic cardiovascular events. Heart. 2011;97(16):1326–31.

74. Kumar P, Sharma R, Misra S, Kumar A, Nath M, Nair P, et al. CIMT as a risk factor for stroke subtype: a systematic review. Eur J Clin Invest. 2020;50(11): e13348.

75. Finn C, Giambrone AE, Gialdini G, Delgado D, Baradaran H, Kamel H, et al. The association between carotid artery atherosclerosis and silent brain infarction: a systematic review and meta-analysis. J Stroke Cerebrovasc Dis. 2017;26(7):1594–601.

76. Ruijter HM, Peters SAE, Anderson TJ, Britton AR, Dekker JM, Eijkemans MJ, et al. Common carotid intima-media thickness measurements in cardiovascular risk prediction a meta-analysis. JAMA. 2012;308(8):796–803.

77. Bots ML, Groenewegen KA, Anderson TJ, Britton AR, Dekker JM, Engström G, et al. Common carotid intima-media thickness measurements do not improve cardiovascular risk prediction in individuals with elevated blood pressure: the USE-IMT collaboration. Hypertension. 2014;63(6):1173–81.

78. Enserro DM, Vasan RS, Xanthakis V. Twenty-year trends in the American Heart Association cardiovascular health score and impact on subclinical and clinical cardiovascular disease: the Framingham offspring study. J Am Heart Assoc. 2018;7(11): e008741.

79. Nambi V, Chambless L, Folsom AF, et al. Carotid intima-media thickness and presence or absence of plaque improves prediction of coronary heart disease risk: the ARIC (Atherosclerosis Risk in Communities). Study J Am Coll Cardiol. 2010;55:1600–7.

80. Okamura T, Tsukamoto K, Arai H, Fujioka Y, Ishigaki Y, Koba S, et al. Japan Atherosclerosis Society (JAS) guidelines for prevention of atherosclerotic cardiovascular diseases 2022. J Atheroscler Thromb. 2024;31:641–853.

81. Naqvi TZ, Lee MS. Carotid intima-media thickness and plaque in cardiovascular risk assessment. JACC Cardiovasc Imaging. 2014;7(10):1025–38.

82. Ruijter HM, Peters SAE, Groenewegen KA, Anderson TJ, Britton AR, Dekker JM. Common carotid intima-media thickness does not add to Framingham risk score in individuals with diabetes mellitus: the USE-IMT initiative. Diabetologia. 2013;56(17):1494–502.

83. Bell KJL, White S, Hassan O, Zhu L, Scott AM, Clark J, et al. Evaluation of the incremental value of a coronary artery calcium score beyond traditional cardiovascular risk assessment: a systematic review and meta-analysis. JAMA Intern Med. 2022;182(6):634–42.