

Carotid Intima Media Thickness as a Prognostic Marker in Chronic Coronary Syndrome Patients Undergoing PCI

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ABSTRACT

Chronic coronary syndrome (CCS) represents a stable yet progressive manifestation of coronary artery disease, with residual cardiovascular risk persisting despite advances in percutaneous coronary intervention (PCI) and optimal medical therapy. Accurate risk stratification remains essential to improve long-term outcomes. Carotid intima media thickness (CIMT), a noninvasive and widely available marker of subclinical atherosclerosis, has been extensively studied as a surrogate of systemic vascular disease and a predictor of cardiovascular events. This review summarizes current evidence on the prognostic value of CIMT in patients with CCS, with particular emphasis on those undergoing PCI. The relationship between carotid and coronary atherosclerosis is analyzed, emphasizing CIMT assessment methods and their connection to cardiovascular events like myocardial infarction, stroke, and mortality. CIMT is generally not recommended for the routine assessment of cardiovascular risk; however, it may become relevant and important for certain patients who have been diagnosed with CCS, as it can provide additional insights into their condition and potential treatment options.

Keywords: Chronic Coronary Syndrome ; Carotid Intima Media Thickness ; percutaneous coronary intervention

INTRODUCTION

Chronic coronary syndrome (CCS) is a key issue in coronary artery disease, based on consensus definitions in practice. Research indicates carotid intima-media thickness (CIMT) is a vital prognostic marker for long-term CCS outcomes and cardiovascular risks (1,2).

The recognition of CCS as a distinct class in coronary artery disease emphasizes its long-term impact. This has resulted in new definitions and models that improve prognosis and management. CIMT serves as an important prognostic marker linked to visceral adiposity, diabetes, and arterial pressure, consolidating these aspects into a valuable measure. CIMT remains significant for risk assessment and treatment decisions in CCS patients, even among low-risk groups (3,4).

Therefore, this study aimed to summarize the current evidence on the prognostic value of CIMT in patients with CCS, with particular emphasis on those undergoing percutaneous coronary intervention (PCI).

Overview of Carotid Intima-Media Thickness

Carotid intima-media thickness (CIMT) is measured using two-dimensional ultrasound to evaluate the carotid arteries' inner layers. Higher CIMT signifies arterial changes from atherosclerosis. The relationship between arterial stiffness and wall thickness is complex; stiffer abdominal aortas create earlier reflected waves, affecting carotid wall stress and remodeling. CIMT is a better predictor of upcoming cardiovascular events than traditional risk factors, especially for general and diabetic populations, and is crucial for CCS patients linked to adverse outcomes (2,5).

CCS aims to prevent cardiovascular events via precise risk assessment since traditional markers may fall short. CIMT is explored as a biomarker for risk stratification, evaluating arterial wall changes linked to atherosclerosis. This condition impacts arterial structure and function, heightening stiffness, causing early pressure wave reflections and diminished pulsatile flow, resulting in endothelial and smooth muscle dysfunction (4-6).

CIMT measures the distance between the walls of the carotid artery, focusing on segments like common carotid artery (CCA) and internal carotid artery (ICA). The American Society of Echocardiography advises CIMT in the CCA over 1 cm from the bifurcation, using the CCA-ICA ratio for atherosclerosis assessment. Measurements are categorized as normal (≤ 0.90 mm for men, ≤ 0.80 mm for women), borderline (0.91–0.99 mm for men, 0.81–0.84 mm for women), or increased (≥ 1.00 mm for men, ≥ 0.85 mm for women) (6,7).

CIMT reflects atherosclerotic burden, correlating with arterial stiffness and changes in the endothelial layer. Alterations in CIMT indicate a compromised microvascular environment and cardiovascular disease, enhancing predictions of events like cardiovascular death, myocardial infarction, and stroke beyond traditional risk factors (8).

CIMT assesses atherosclerosis in CCS patients, highlighting plaque load and unstable plaques that elevate coronary event risk. It correlates with vascular biomarkers like stiffness and wave reflection, impacting pressure wave reflection, coronary perfusion, and leading to endothelial dysfunction, ischemia, and CCS symptoms. Impaired microvasculature increases risks for patients with normal epicardial arteries. CIMT indicates atherosclerosis, detecting inflammation and linking to vascular changes (7-9).

In population cohorts, increased CIMT is a marker for cardiovascular prognosis in prevention strategies. Individuals without events for 40 years and those with heterozygous familial hypercholesterolaemia on statins show that elevated CIMT without plaque does not improve prognosis. Changes in CIMT, especially in obesity, can predict vascular events in asymptomatic polycystic ovary syndrome and middle-aged women (10,11). On other hands, CIMT's value as a marker in CCS is unclear, with few studies examining its performance and limited ability to predict cardiovascular mortality (12,13).

Chronic Coronary Syndrome: Definitions and Risk Assessment Framework

CCS patients require careful symptom management to prolong life and reduce cardiovascular events. High-risk patients need more aggressive treatments compared to asymptomatic ones. Key risk indicators include atherosclerotic burden and coronary lesion severity, though their predictive value is limited. CIMT is a promising imaging method for risk assessment in CCS patients (4).

Multiple studies examined CIMT's link to event rates in CCS cohorts. Initially, CIMT predicted all-cause and cardiovascular mortality, but these associations became insignificant after clinical adjustments. Abnormal invasive haemodynamics did not lower non-significant indirect ischaemia from non-invasive tests, suggesting that including anatomical and functional disease mechanisms could improve event prediction (13-16).

CCS includes patients with atherosclerosis-related coronary artery disease, regardless of symptoms. Despite treatment advancements, the disease burden remains. Optimized therapy and specialized care are vital. Accurate risk stratification is essential as symptoms differ from acute coronary syndromes. Goals include preventing cardiovascular events like myocardial infarction and stroke by identifying high-risk patients for customized treatment (17).

Risk stratification in cardiovascular conditions such as coronary syndromes, peripheral arterial disease, diabetes, and chronic kidney disease relies on clinical data, lab tests, and noninvasive imaging. The link between cardiovascular risk and CCS incidence is not well defined, with traditional factors like age, sex, diabetes, hypertension, and smoking providing limited insight. This underscores the necessity for additional prognostic factors to improve risk evaluation for CCS patients (18).

Therapeutic goals for CCS focus on improving symptoms and managing events through risk stratification. Guidelines suggest using traditional risk markers and coronary anatomical parameters from imaging. However, challenges as low event rates hinder their usefulness, imaging can be expensive and limited, and optimal cutoff values remain unclear (19).

In CCS patients, revascularization lowers cardiovascular event risk but does not eliminate atherosclerosis. Kaplan–Meier curves indicate intermediate-risk patients experience more incidents without bypasses or interventions. Improving secondary prevention strategies is crucial. The significance of CIMT in assessing CCS risk is still uncertain, despite its links to atherosclerosis and cardiovascular events (20,21).

Evidence Linking CIMT to Outcomes in CCS

The link between CIMT and atherosclerosis in CCS varies. One study indicated a 12% increase in cardiovascular events per millimeter of CIMT, significantly influencing mortality but excluding coronary artery disease. CIMT > 0.9 mm heightened the risks of myocardial infarction, death, and heart failure by 65%, even without major lesions. In contrast, another study proposed that when traditional risk factors are accounted for, CIMT isn't an independent predictor of death or myocardial infarction (22,23).

Two comprehensive meta-analyses investigated the significance of CIMT within populations suffering from CCS. The first meta-analysis uncovered that a mere increase of 0.1 millimeters in CIMT correlates with an alarming 23% rise in the risk of major adverse cardiovascular events (MACE), alongside a 21% increase in cardiovascular-related deaths and a substantial 27% elevation in all-cause mortality rates. This elevated risk underscores the critical need for monitoring CIMT in patients with CCS. The second analysis underscored an important link between CIMT measurements and all-cause mortality specifically in individuals with type 2 diabetes who have not experienced any previous cardiovascular complications. This finding notably reinforces the notion that maximal CIMT is strongly associated with cardiovascular mortality rates within the CCS demographic, highlighting its potential as a pivotal risk factor in cardiovascular health assessments (24,25).

Additional studies investigated CIMT's link to clinical events in non-cardiac surgery patients with preserved left ventricular function and no myocardial infarction history. They confirmed CIMT's added value over standard risk assessments. A meta-analysis revealed a significant relationship between mean CIMT and perioperative MACE in patients undergoing peripheral artery revascularization, without linking it to mortality. While increased CIMT usually indicates higher risk, some conflicting results appeared, with observer-dependent measurement error predicting this added value, estimated at 10% (26,27).

Patients with CCS and higher CIMT may present with a higher number of atherosclerotic lesions and greater plaque vulnerability, features that increase the likelihood of recurrent cardiovascular events. This concept has been validated in populations with carotid disease, where a comprehensive assessment of carotid atherosclerosis combining plaque burden and CIMT also had an incremental prognostic value. In addition, greater carotid atherosclerotic burden may be associated with aortic stiffness, a contributor to the development of cardiovascular disorders in CCS and related to all-cause mortality (28).

Impaired arterial compliance and altered wave reflections affect the microvascular network. Reduced adaptability to sudden myocardial oxygen demands increases cardiovascular risk in CCS patients with high CIMT. The link between CIMT, brachial flow-mediated dilation, and coronary flow reserve highlights connections to microvascular function. Early endothelial changes can cause microangiopathic alterations, restricting coronary flow reserve and raising ischemia risk in CCS patients (3, 29).

The Gensini score indicates the extent of coronary atherosclerosis and vessel disease severity. Carotid arteries are commonly affected, with damage occurring outside the coronary area. A higher Gensini score correlates with elevated maximal and mean CIMT values. Significant carotid stenosis increases the risk for myocardial infarction and sudden cardiac death. The presence and extent of plaques in the carotid arteries significantly influence cardiovascular risk (30).

Moreover, impaired endothelial function promotes atherosclerosis due to an imbalance between vasodilatory and vasoconstrictory factors, high reactive oxygen species levels, and proinflammatory cell recruitment, leading to increased CIMT. Although lipid involvement is clear, these processes may be somewhat independent of classic cardiovascular risk factors. Microvascular function in CCS, affecting coronary, peripheral, and renal regions, can reflect local endothelial activity. Assessing correlations between CIMT and microvascular function or damage could help clarify CIMT's role in CCS risk stratification (31,32).

Clinical Utility and Implementation Considerations

CIMT may provide value in CCS patients not identified by risk scores. An analysis of 53,000 patients showed that low-risk individuals with CIMT <600 μm had excellent outcomes, while those with CIMT $\geq 600 \mu\text{m}$ faced higher-than-expected events, indicating a potential need for better preventive measures. In non-trivial CCS cases, CIMT could serve as a secondary marker to improve risk estimates and may reflect the role of coronary artery calcium scoring in atherosclerotic cardiovascular disease (1,33,34).

CIMT determination is not included in practice guidelines due to non-standardized protocols, high observer variability, and measurement challenges. The PROSPECT-CT trial is evaluating CIMT for diabetics over 50, while the Steno Diabetes Center Copenhagen is creating a global registry for technology harmonization. Nonetheless, evidence inconsistencies raise concerns about measurement variability and the classification of CCS patients with elevated CIMT as higher risk (32,35).

Independent associations between borderline or mildly abnormal CIMT and future risk are reliable, although complexities arise from influential covariables. Increased CIMT enhances risk stratification in diverse CCS populations, but caution is warranted in homogeneous groups. In chronic kidney disease patients, significant links to atherosclerotic burden and pulse-wave velocity require further investigation in high-risk subgroups without established coronary artery disease or plaque burden (28,36).

Therefore, noninvasive stress testing in CCS is advised for symptomatic patients with intermediate pretest probability. Avoid CIMT imaging in high-risk individuals, unless familial hypercholesterolemia is present. In primary prevention, after

assessing CCS risk and initiating therapies, routine follow-up imaging is unwarranted without clinical events to minimize unnecessary testing and resource usage (22,27).

Heterogeneity in risk factors like age and comorbidity suggests specific thresholds can enhance risk assessment. The 2019 European guidelines recommend CAC scoring for individuals over 40 at high cardiac risk; a CAC of 0 indicates low event rates. This is crucial for CCS patients where traditional markers have limited predictive value. CIMT can detect subtle coronary atherosclerosis when traditional markers provide only moderate prognosis. Modeling albuminuria revealed a 40% risk over 18 years for diabetics with stage 3 CKD, while CIMT thresholds can help identify high-risk CCS patients with elevated natriuretic peptides (30,37).

Also, results confirm that diabetes and poor risk management worsen prognosis but suggest early atherosclerosis screening may help assess non-diabetic patients. In medicated CCS patients, CIMT reductions are possible, but further research is needed on revascularization status and quality metrics (23,38).

Prespecified CCS risk profiles highlight CIMT's importance in renal impairment patients. Lower kidney function is linked to increased cardiovascular risk. CIMT relates to short-term adverse outcomes, including cardiovascular mortality. Renal dysfunction exacerbates calcification in carotid plaques, raising rupture risk. The complex relationship between plaque area and cerebrovascular events suggests progression extends beyond maximum stenosis measures. Although CIMT may improve CVE prediction during coronary angiography, its effectiveness declines post-discordance assessment. In elective revascularization patients, renal impairment and high-risk carotid plaques notably heighten long-term cardiovascular and cerebrovascular event risks (39,40).

Subsequently, CIMT is used for younger adults at intermediate risk of atherosclerotic cardiovascular disease, prompting discussions on its risk-benefit analysis, particularly in CCS patients. Mild to moderate symptom patients might be misclassified, missing their actual risk. CIMT can help identify these individuals, improving CCS classification and guiding preventive measures for better outcomes (41,42).

CONCLUSION:

Emerging evidence indicates that carotid intima-media thickness (CIMT) is a key prognostic marker for chronic coronary syndrome (CCS) patients. Many are asymptomatic, yet cardiovascular risks increase with age.

CIMT measures carotid artery atherosclerotic burden. High CIMT in CCS patients suggests poorer outcomes due to increased atherosclerotic lesions, arterial stiffness, and endothelial dysfunction.

Future research needs to screen coronary artery disease in chronic symptomatic patients and incorporate extra-cardiac assessments and imaging tests like microvascular detection.

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Author contribution: *Authors contributed equally in the study.*

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