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Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Review

Carotid intima-media thickness for cardiovascular risk assessment: Systematic review and meta-analysis

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ARTICLE INFO

Article history:

Received 11 October 2012

Received in revised form

16 January 2013

Accepted 16 January 2013

Available online xxx

Keywords:

Carotid ultrasound

Intima-media thickness

Atherosclerosis

Risk prediction

ABSTRACT

Objective: B-mode ultrasound measurement of the carotid intima-media thickness (CIMT) is a widely used marker for atherosclerosis and is associated with future cardiovascular events. This article provides a review and meta-analysis of the published evidence on the association of CIMT with future cardiovascular events and its additional value to traditional cardiovascular risk prediction models.

Methods: A systematic review and meta-analysis of the evidence on the association of CIMT with future cardiovascular events and the additional value of CIMT to traditional cardiovascular risk prediction models was conducted. The association of CIMT with future cardiovascular events and the additional value of CIMT were calculated using random effects analysis.

Results: The literature search yielded 1196 articles of which 15 articles provided sufficient data for the meta-analysis. A 1 SD increase in CIMT was predictive for myocardial infarction (HR 1.26, 95% CI 1.20–1.31) and for stroke (HR 1.31, 95% CI 1.26–1.36). A 0.1 mm increase in CIMT was predictive for myocardial infarction (HR 1.15, 95% CI 1.12–1.18) and for stroke (HR 1.17, 95% CI 1.15–1.21). The overall performance of risk prediction models did not significantly increase after addition of CIMT data. The areas under the curve increased from 0.726 to 0.729 ($p = 0.8$).

Conclusions: CIMT as measured by B-mode ultrasound is associated with future cardiovascular events. However, the addition of CIMT to traditional cardiovascular risk prediction models does not lead to a statistically significant increase in performance of those models.

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Contents

1. Introduction	00
2. Historical perspective on carotid intima-media thickness measurement	00
3. How to measure CIMT?	00
4. Carotid intima-media thickness and cardiovascular risk prediction; a meta-analysis	00
4.1. Methods	00
4.1.1. Search strategy and data extraction	00
4.1.2. Statistical analysis	00
5. Results	00
6. Discussion	00
6.1. Limitations	00

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¹ Relationships with industry: No relationship with industry to declare.

7. Conclusion	00
Acknowledgment	00
References	00

1. Introduction

Data from the European Society of Cardiology demonstrates that cardiovascular disease accounts for 38–42% of the mortality in Europe [1]. Atherosclerosis is the underlying cause of the majority of clinical cardiovascular events. This generalized inflammatory disease is characterized by an accumulation of lipids, inflammatory cells, and development of scar tissue covered by a fibrous cap build within the walls of large and medium-sized arteries [2].

Individuals with subclinical atherosclerosis should preferably be identified at an early stage, so that primary preventive measures can be initiated [3]. The development of atherosclerosis usually takes decades, and one of the first detectable stages of atherosclerosis is thickening of the arterial wall. Carotid ultrasound is a widely used imaging modality for the detection of subclinical atherosclerosis [4]. B-mode ultrasound measurement of carotid intima-media thickness (CIMT) is frequently used for non-invasive evaluation of subjects at risk of atherosclerosis. Still, the exact risk of cardiovascular events associated with an increased CIMT in general populations is not entirely clear. More importantly, the additional value of CIMT measurement on top of currently used risk prediction models is not entirely clear as well.

Therefore the goals of this review and meta-analysis were 1. to provide a short historical perspective on CIMT measurement using ultrasound, 2. to discuss current CIMT acquisition and measurement methods, 3. to assess the association of CIMT with future cardiovascular events using up-to-date data from cohort studies, 4. to determine the additional value of CIMT measurement in

cardiovascular-risk prediction and 5. to provide recommendations for future studies on the role of CIMT for cardiovascular risk assessment.

2. Historical perspective on carotid intima-media thickness measurement

In 1986, Pignoli et al. reported the first in vitro results of a study investigating the arterial wall thickness with real-time B-mode ultrasound [5]. In that initial study, the distance between two parallel echogenic lines correlated well with the intima-media thickness (IMT) measured on pathologic examination. The authors concluded that B-mode ultrasound represented a useful tool for the measurement of IMT of human arteries in vivo. Subsequently, Persson et al. demonstrated in an in vivo study that IMT measurement with B-mode ultrasound was highly reproducible [6]. Partly because of the easily accessible anatomical position of the carotid arteries, the carotid CIMT has become a frequently used measurement in clinical practice and scientific studies.

CIMT is a well-studied phenotype of atherosclerosis. Using B-mode ultrasound the CIMT can be assessed quickly, non-invasively at a relatively low cost [7,8]. The measurement of CIMT is widely used as a non-invasive indicator of (subclinical) atherosclerosis and is both used in prospective follow-up studies to investigate the relationship of CIMT with future cardiovascular events and in clinical intervention trials to monitor changes of any given treatment [8,9]. Based on the assumption that change in CIMT is directly correlated with change in cardiovascular risk, CIMT is a frequently used surrogate endpoint in clinical trials [10–13].

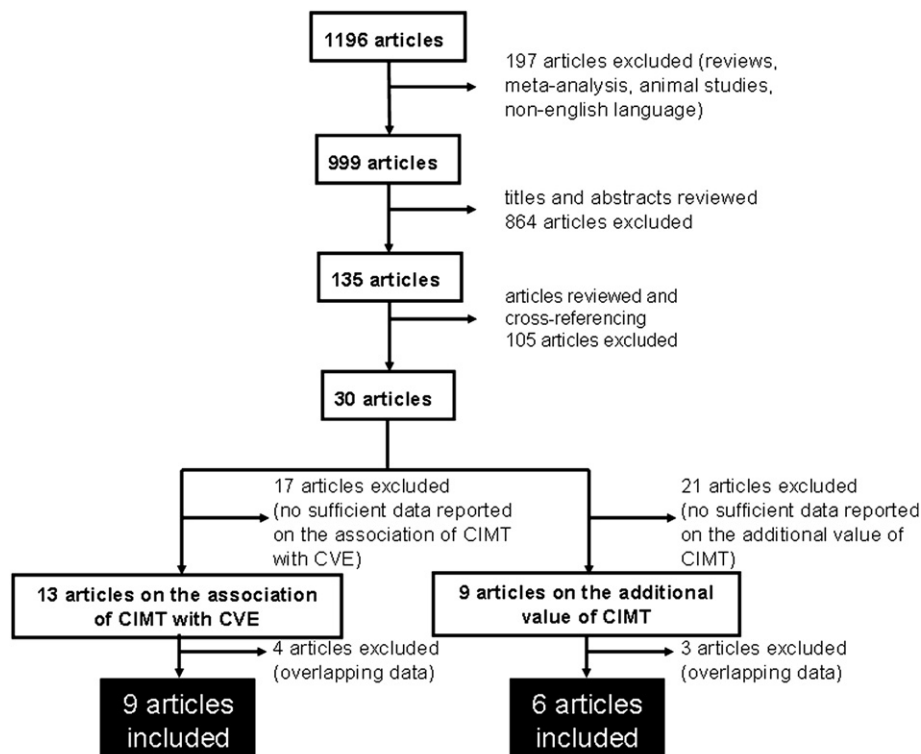


Fig. 1. Flowchart of the literature search strategy.

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