



Reflections in Internal Medicine

Can and should carotid ultrasound be used in cardiovascular risk assessment? The internist's perspective

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ABSTRACT

Cardiovascular risk management is a major and challenging task for internists. Risk scores using algorithms based on traditional risk factors are helpful in identifying patients in whom intensive prevention strategies are warranted. However there remains a need for more accurate screening tools to allow clinicians to individualize the primary prevention programs to their patients.

Approximately 40–80% of apparently healthy, asymptomatic subjects exhibit increased thickness of the lamina intima-media of the carotid artery or have atherosclerotic carotid plaques. These abnormalities can be measured safely and at low cost by ultrasound. Subclinical carotid lesions are strongly associated with generalized atherosclerotic burden and the risk of future cardiovascular events. Although many cardiovascular risk management guidelines recommend the use of these parameters incorporation in clinical practice is still not commonplace.

Based on the current literature it can be stated that in high risk patients there is no additional value of carotid ultrasound because even in the absence of carotid lesions these patients should receive an intensive risk reduction regime. In the large low-intermediate risk group however carotid ultrasound findings carry subtle but possibly clinically relevant information about cardiovascular risk profile. The effect of treatment decisions based on carotid ultrasound parameters has not been studied. Sequential measurements to monitor progression and evaluate treatment response on an individual basis are not sufficiently reproducible.

We therefore recommend the use of carotid ultrasound in low to intermediate risk patients but emphasize the importance of interpreting the results in conjunction with all cardiovascular risk factors and avoid follow-up measurements.

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1. Introduction

Ultrasonography can be used to measure the different vascular layers of the carotid artery and detect the presence of atherosclerotic plaques. The thickness of the lamina intima and media (carotid intima-media thickness or cIMT) has been extensively used in clinical trials as a surrogate marker of cardiovascular disease. This parameter as well as plaque detection could potentially also be useful as a screening tool for subclinical atherosclerosis on an individual patient basis. The current review aims to evaluate the evidence for the clinical use of carotid ultrasound. The following case example illustrates the point.

1.1. Case example

During your outpatient clinic you are visited by a 55 year old male. He has been under your care for cardiovascular risk management for the last 3 years. You are treating him for hypertension, with a thiazide diuretic and an ACE inhibitor; his blood pressure is relatively well regulated with values around 140/85 mm Hg. His BMI is 32 kg/m² with predominantly visceral adiposity. Fasting blood glucose levels are slightly elevated but HbA1c is normal and stable. His LDL-C is 3.2 mmol/L with an HDL-C of 0.9 mmol/L, fasting triglycerides are 2.2 mmol/L. He has no specific complaints, leads a sedentary lifestyle which makes it difficult for you to determine whether he has angina on exertion. You have advised him to stop smoking and two months ago he quit after 35 pack-years.

Your Framingham risk calculator tells you that he is currently at intermediate risk for suffering a heart attack in the next 10 years (15.3%). This does not warrant more aggressive management of his cardiovascular risk factors. However your clinical intuition gives you an uneasy feeling about your patient partly because had he not quit smoking

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his risk score would be significantly higher (28.4%) and the impending diabetes is not taken into account in the prediction model. All your efforts during his visits are aimed at determining whether the obviously present risk factors have led to the development of atherosclerosis. If so, you feel it is justifiable to aim for secondary prevention targets for blood pressure and lipids and are considering adding a statin and aspirin to his treatment regimen.

Could ultrasound examination of the carotid arteries of your patient help you decide? Although many guidelines on cardiovascular disease prevention recommend using cIMT and carotid plaque detection in risk assessment strategies its implementation in clinical practice is still not commonplace. This may partly be explained by conflicting data on the additional value of cIMT above risk assessment tools such as the Framingham [1] PROCAM [2] and SCORE [3] algorithms among others.

The current review will summarize the pathophysiological and epidemiological basis for the use of IMT measurement and carotid plaque detection as possible predictors of future cardiovascular events. Technical and methodological considerations important for the interpretation of results will be addressed first. Three main issues considering clinical applicability in individual patients will be discussed:

- Is the presence of subclinical carotid atherosclerosis representative of generalized and particularly coronary atherosclerosis?
- Does the presence of subclinical carotid atherosclerosis increase the risk of suffering a cardiovascular event?
- Can progression of subclinical carotid atherosclerosis be used to monitor the efficacy of cardiovascular risk management in individual patients?

The review will conclude with recommendations on implementation of carotid ultrasound in a clinical setting.

1.2. Technical and methodological considerations

B-mode ultrasound imaging is able to visualize the intima-media complex of large arteries. The thickness of these vascular structures can be measured offline. Several autopsy studies have validated these measurements and found them to be highly accurate when compared

with histological findings in the same arterial segment [4,5]. Early atherosclerotic changes in these arteries (smooth muscle cell proliferation, fatty streaks and non-stenotic plaques) can be detected by thickening of these vascular structures (Fig. 1). Carotid ultrasound is able to visualize morphological changes in the arterial wall, before the advanced stages of atherosclerosis are reached. It is therefore possible to identify vascular damage in patients before they develop clinical signs and symptoms.

In a substantial percentage of asymptomatic adults this form of subclinical atherosclerosis is present. Salonen et al. observed lesions in 80% of male subjects in the general population by the age of 60 years [6]. Carotid ultrasound is a non-invasive, safe and inexpensive imaging modality. However, there is as of yet no standardized international imaging protocol dictating how to perform IMT measurements and plaque detection. In general, all current ultrasound devices provide sufficient resolution to assure accurate measurement, Fig. 2 shows a representative example.

Ultrasound investigations are prone to operator variability, but several studies show excellent inter- and intra-observer reproducibility in the case of IMT measurement [7–9]. The most frequently used location for the measurement is the most cranial 1 cm of the common carotid artery, but the carotid bifurcation and the internal carotid artery are other possible sites for measurement. Further differences in protocols arise because most authors calculate the mean IMT over 1 cm whereas others use the maximum value. As atherosclerosis is an asymmetrical process the angle at which the artery is approached by the operator can vastly influence the end results. Some authors try to limit the variance this causes by measuring IMT at several angles and using the mean value. Unilateral versus the average of bilateral measurements is another factor limiting uniformity. Due to these and other factors it remains unclear how to define normal IMT values. In healthy young adults IMT will be approximately 0.5 mm slowly increasing with age. It is unclear where the threshold for higher cardiovascular risk lies and if this threshold is comparable in different populations (diabetics vs. non-diabetics; men vs. women; CKD vs. non-CKD; ethnic differences etc.). cIMT values exceeding 0.9 mm are thought to imply increased cardiovascular risk. Atherosclerotic plaque is defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding cIMT value or demonstrates a thickness > 1.5 mm.

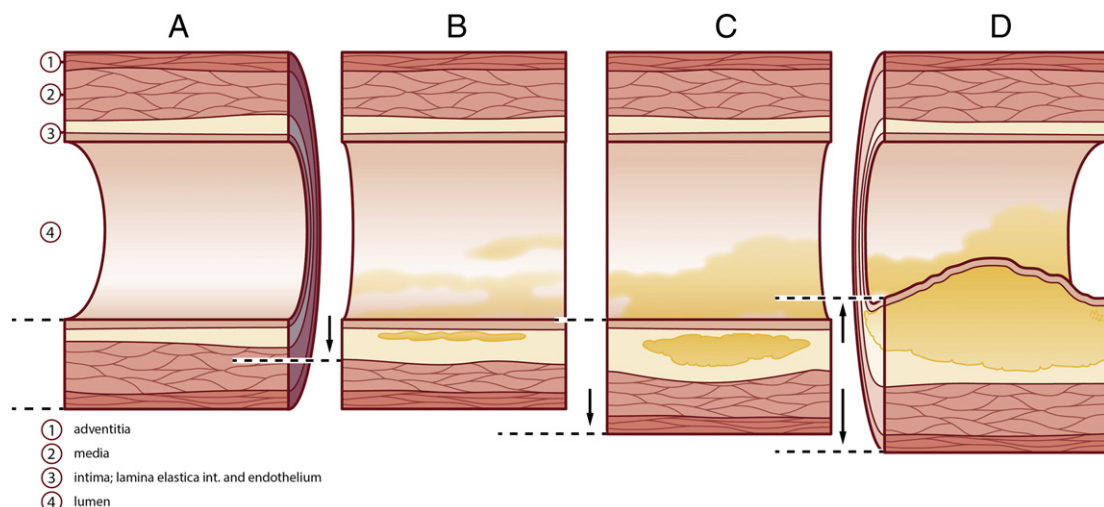


Fig. 1. Schematic representation of the progression of arterial atherosclerosis over a period of decades. A) Normal arterial architecture as seen in healthy young subjects. B) Formation of fatty streaks in the arterial wall can be seen in post-mortem microscopy as early as in adolescence and represents a physiological vascular response to injury. Although these arterial changes can be a precursor of manifest atherosclerosis, the absence of or adequate management of vascular risk factors can keep progression in check. Current imaging techniques are unable to objectify or quantify these subtle changes. C) With advancing age and under the influence of vascular risk factors the fatty streaks can progress to overt intimal thickening. In this stage of the atherosclerotic process the artery responds by an outward remodeling. The artery hereby preserves its lumen diameter and flow. Imaging studies with angiography and Doppler duplex will therefore not detect this early stage of atherosclerosis. Ultrasound measurement of intima media thickness however is sensitive enough to identify these lesions. D) Finally the atherosclerotic plaque starts encroaching into the lumen causing flow changes and stenosis which lead to tissue dysfunctions downstream. In this stage all imaging modalities are useful in diagnosing and evaluating the lesions, however a window for early intervention has passed.

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