Validation of a New Algorithm for Detection of Coronary Artery Disease Using Carotid and Femoral Vascular Ultrasound

Thesis Submitted for partial fulfillment of Master Degree in Cardiovascular Medicine

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Abstract

Background: Atherosclerosis is a systemic disease and patients presenting with atherosclerotic coronary artery disease (CAD) usually have associated vascular disease and the reverse is true. Clinical application of this association in detecting CAD is lacking.

Objective: (a) To investigate the relationship between the carotid and femoral atherosclerosis as assessed by ultrasonography, and the severity of coronary atherosclerosis, provided by coronary angiography. (b) To assess the validity and applicability of the new algorithm for detection of significant CAD.

Methods: Peripheral arterial duplex evaluation was performed for 97 consecutive patients (65 men and 32 women; mean age 59±4.5 years) undergoing coronary angiography for a variety of indications. Common carotid and common femoral intima media thickness (IMT), carotid total plaques dimension product (PDP) and CARFEM index were determined in all patients.

Results: As the number of affected coronary arteries increased, there was a proportional increase in the mean of CCA IMT, total PDP and CARFEM Index (P= .025, < 0.001 and 0.017 respectively). Sensitivity, specificity, positive and negative predictive values of the proposed algorithm were 90.3% 72%, 90.3% and 72% respectively.

The sensitivity and specificity were 93% and 91% respectively in non-diabetics compared to 86.2% and 57% in diabetics; 95% and 90% in women compared to 88% and 60% in men.

Conclusion: Carotid and femoral duplex ultrasonography provides a simple and easy non-invasive tool for detection of significant CAD.

Key Words: Carotid duplex ■ femoral duplex ■ Coronary artery disease ■ strategy

Abbreviations

AoIMT	**Aortic Intima-Media Thickness:**
CA	**Carotid Angiography**
CAD	**Coronary Artery Disease**
CARFEM	**Carotid Femoral Index**
CCA	**Common Carotid Artery**
CEMRA	**Contrast-enhanced MRA**
CFA	**Common Femoral Artery**
CIMT	**Carotid Intima Media Thickness**
CRP	**C-reactive protein**
CT	**Computed Tomography**
DM	**Diabetes Mellitus**
DSA	**Digital Subtraction Angiography**
DUS	**Duplex Ultrasound**
ECG	**Electrocardiogram**
ECST	**European Carotid Surgey Trialists**
EDV	**End Diastolic Velocity**
FBS	**Fasting Blood Sugar**
HDL	**High Density Lipoprotein**
HRT	**Hormone Replacement Therapy**
HTN	**Hypertension**
ICA	**Internal Carotid Artery**
IMT	**Intima Media Thickness**
LAD	**Left Anterior Descending**
LCX	**Left Circumflex**
LDL	**Low Density Lipoprotein**
Lp- PLA2	**Lipoprotein-associated phospholipase A2**

LVSD	**Left Ventricular Systolic Dysfunction**
Lyso PC	**Lysophosphatidylcholine**
LMS-CAD	**Left main stenosis-coronary artery disase**
MET-Sx	**Metabolic Syndrome**
MI	**Myocardial Infarction**
MIP	**Maximum Intensity Projection**
MOSTA	**Multiple overlapping thin-slab acquisition**
MRA	**Magnetic Resonant Angiography**
NASCET	**North American Symptomatic Carotid Endarterectomy Trial**
NPV	**Negative Predictive Value**
PDP	**Plaque Dimension Product**
PPV	**Positive Predictive Value**
PS	**Plaque Score**
PSV	**Peak Systolic Velocity**
PWT	**Posterior Wall Thickness**
QALE	**Quality- adjusted life expectancy**
QALY	**Quality- adjusted life year**
RCA	**Right Coronary artery**
SPECT	**Single Photo Emission Computed Tomography**
SFA	**Superficial Femoral Artery**
TIA	**Transient Ischemic Attack**
TOF	**Time-of-flight (type of MRI technique)**
VA	**Vertebral artery**
VLDL	**Very Low Density Lipoprotien**

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Introduction *and Aim of the Work*

Atherosclerosis is a systemic disease initially characterized by impairment of functional properties of the vascular wall.[1,2,3]Although certain areas of the vasculature are particularly prone to atherosclerotic disease, it is relatively unusual for individuals to have disease localized solely to one area.[4]

Based on this concept, many studies related carotid artery disease and coronary heart disease, and there have been six main areas of research regarding this relation. Firstly, the prevalence and degree of increased Carotid Intima Media Thickness (IMT) has been related to risk factors for cardiovascular disease[5,6] and the prevalence of symptomatic coronary heart disease[7,8] in cross -sectional studies, and to the risk of development of coronary heart disease in cohort studies of asymptomatic normal subjects.[9,10] These studies have demonstrated a strong association between diseases at the two sites. Secondly, the prevalence of carotid plaque and peripheral vascular disease has been assessed in cross-sectional studies of patients known to have coronary heart disease already.[11,12] Nearly 50% of patients have either clinical or imaging evidence of vascular disease in one or more other territory. Thirdly, the value of noninvasive measurements of carotid and peripheral vascular disease in the prediction of severe coronary artery disease has been proved in cohort studies of patients with suspected ischemic heart disease.[7,13] Fourthly, the value of non-invasive measurements of carotid and peripheral vascular disease in the prediction of future coronary vascular events has been assessed in cohort studies of patients known to have coronary artery disease.[14] Fifthly, non-invasive measurements of carotid and peripheral vascular disease were found valuable in excluding severe coronary artery disease in certain subsets of the population with possibility of CAD e.g. prior to valve surgery in patients with no previous ischemic symptoms,[15]to differentiate between ischemic and non ischemic types of cardiomyopathy [16] and to exclude significant CAD in women presenting with atypical chest pain.[17]

Most of the above studies focused on the use of a single ultrasonographic parameter like the Intima Media Thickness of the carotid arteries or occurrence of

plaques.[18] However, few studies attempted to define multiple quantitative variables, which would help to predict the presence and extent of CAD.

One of these studies is Abdelwahab A. et al who studied the relation between the different duplex parameters and the extent of coronary atherosclerosis. By means of ultrasonography, the carotid and femoral arteries were examined and correlated the results to the degree of coronary atherosclerosis found in each patient as assessed by an invasive coronary angiographic evaluation in order to define the most helpful ultrasonographic parameters in identifying CAD. Common carotid and common femoral Intima Media Thickness (IMT), carotid plaque count, length, score, plaque dimensions product (PDP), femoral plaque count and Carotid-Femoral index (CARFEM) were determined in patients undergoing coronary angiography for a variety of indications. The study could construct a new step-wise algorithm for detection of significant coronary artery disease by this simple non-invasive tool.[19]

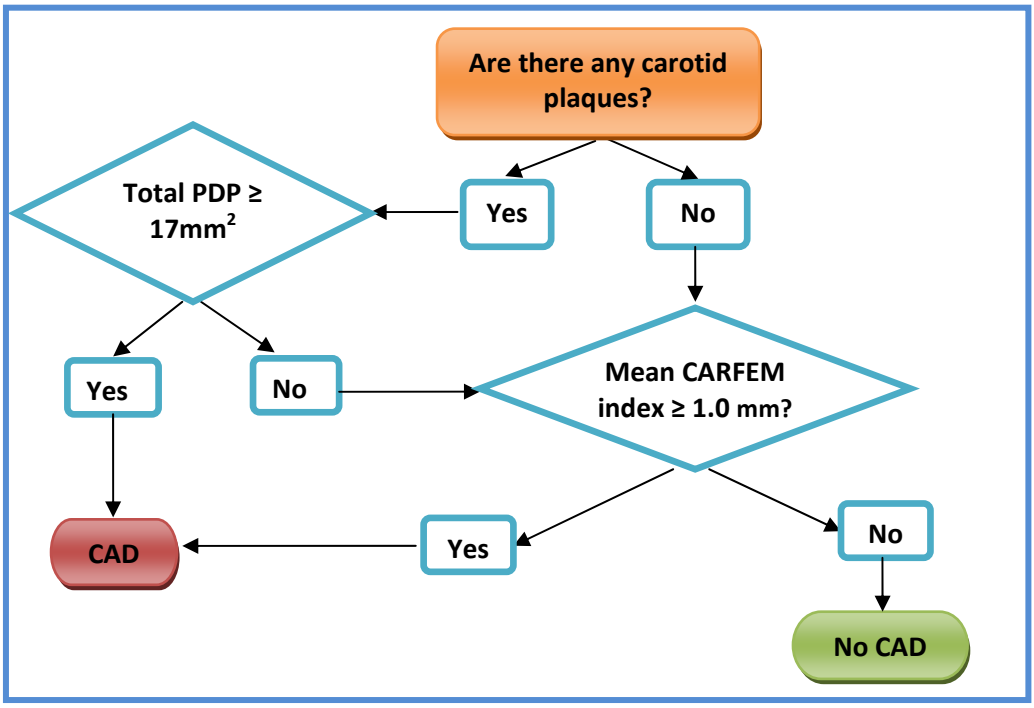

Figure 1: Proposed algorithm for detection of significant CAD using Carotid and Femoral Ultrasound. By Abdelwahab et al [19]

The aim of the work is:

1-To study the relationship between the carotid and femoral atherosclerosis as assessed by ultrasonography, and the severity of coronary atherosclerosis, provided by coronary angiography.

2- To assess the validity and applicability of this new algorithm, for detection or exclusion of significant coronary artery disease by using carotid and femoral vascular ultrasounds.

Pathogenesis of atherosclerosis

ARTERIAL ANATOMY, PHYSIOLOGY, AND PATHOLOGY:

Cross-section histological examination of arteries reveals 3 concentric regions: the intima, media, and adventitia (Fig.2). The boundaries of the intima from the luminal to abluminal sides include the endothelium, a surface monocellular layer with extraordinary biochemical properties, a basement membrane, and the final layer before the media, the internal elastic lamina. The intima is normally extremely thin with endothelial cells in alignment with the direction of flow, except in areas of flow disturbance, such as bifurcations or branches.

Normal endothelium is an organ system intimately involved in local vascular regulation. Nitric oxide is produced by endothelial cells and is antithrombogenic, antiproliferative, and vasodilating. Normal endothelial cells also have synthetic capability for endothelin, which is a powerful vasoconstrictor and is promitogenic, and for the vasodilator prostacyclin. Numerous surface receptors are present, including low density lipoprotein receptors.

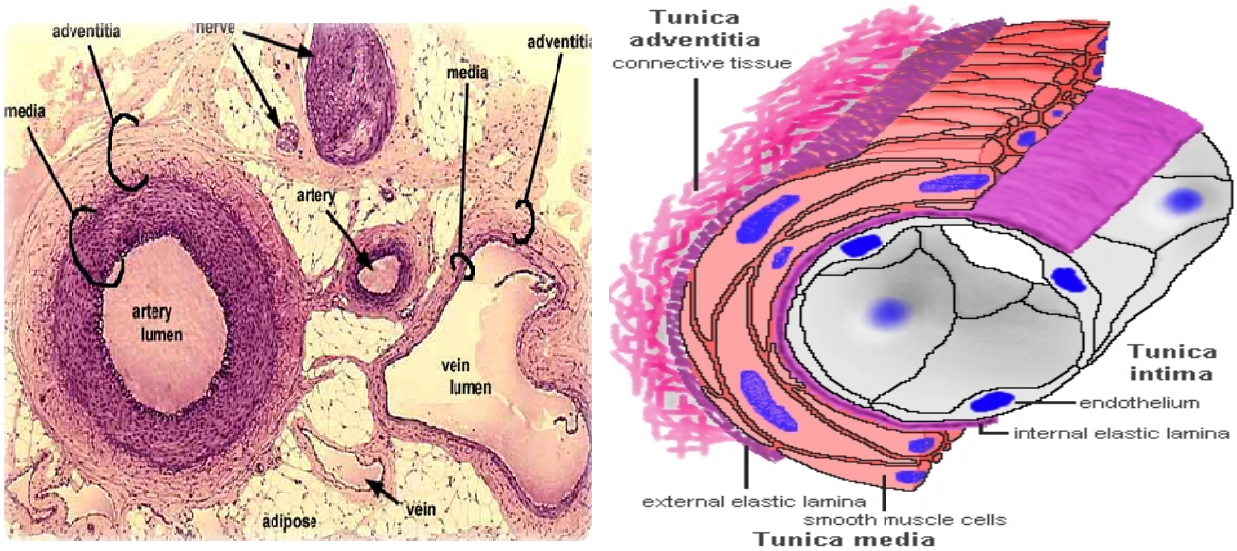

Figure 2. (A) Histological cross section of blood vessels; artery and vein. (B), Note the three components of arterial wall; Intima, media and adventitia.[20]