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ΙΑΤΡΙΚΗ ΣΧΟΛΗ
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"ΣΥΣΧΕΤΙΣΗ ΤΟΥ INTIMA-MEDIA THICKNESS ΣΤΗ ΜΗΡΙΑΙΑ ΑΡΤΗΡΙΑ ΚΑΙ ΤΗΣ ΚΑΡΔΙΑΓΓΕΙΑΚΗΣ ΝΟΣΟΥ"

υπό

ΞΕΝΟΦΩΝΤΑ ΜΙΛΤΙΑΔΗ ΣΑΚΕΛΛΑΡΙΟΥ

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Υπεβλήθη για την εκπλήρωση μέρους των

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1. Introduction

The Framingham Heart Study has contributed importantly to the understanding of the causes of coronary heart disease, stroke and other cardiovascular diseases. The major risk factors studied at Framingham include cigarette smoking, hypertension, high serum cholesterol and various cholesterol fractions, low levels of high-density lipoprotein (HDL) cholesterol and diabetes mellitus. Advancing age is also included as a risk factor in the Framingham charts because of increased absolute risk with aging. It is widely acceptable that the extent of atherosclerosis is being increased with multiple risk factors. It has, also, emphasized the importance of multiple risk factors profile in the prediction and prevention of cardiovascular diseases. The Framingham scores offer both general and specific applications as they suggest priorities for instituting primary prevention strategies and point to factors deserving increased emphasis and those needing less attention. These scores admonish healthcare professionals to look at the whole patient and to recognize the cumulative nature of risk factors. A multifactorial approach to risk reduction offers the best opportunity for both saving patients at high risk and preventing development of high-risk status in the first place. (1, 2) Risk factors of coronary artery disease are associated with disease of extra coronary arteries. Intima media thickness (IMT) of extra coronary arteries such as carotid and femoral arteries is considered a significant marker of atherosclerotic coronary and peripheral vascular diseases. B-mode ultrasound is increasingly being used to measure non-invasively the IMT of carotid and femoral arteries.

Methods

Two online bibliographic databases were used to produce the final list of references for this review: PubMed (US National Library of Medicine®) and Ovid (Ovid Technologies, Inc). The literature search was based on several keywords combinations. Initially we searched the literature applying the keywords: intima media thickness. The above keywords were used in combination with terms as major adverse cardiac events , cardiac events , myocardial infarction and cardiac death. In the search string, other terms were also included, such as femoral artery and lower limb. The purpose of the latter was to narrow the search results to only

those related to femoral artery. Once the automatic literature search was completed, a manual selection ensured that only related articles were includedin the final list of references, as presented in this review.

2. B-mode ultrasound in the assessment of intima media thickness

Atherosclerosis most often develops gradually and slowly, starting from childhood and proceeding into adulthood with varying velocity and susceptibility to complications. The first structural change that can be detected in atherosclerosis is an increase in intima media thickness. IMT is an important atherosclerotic risk marker. However, this increase is not synonymous with subclinical atherosclerosis, but is related to it. Indeed, increase in IMT is also the result of non-atherosclerotic processes such as smooth muscle cell hyperplasia and fibrocellular hypertrophy leading to medial hypertrophy and compensatory arterial remodeling. Therefore, this process may be an adaptive response to changes in flow, wall tension, or lumen diameter. The uniform thickening progresses in straight arterial segments as the patient ages and all known vascular risk factors accelerate this process. Therefore IMT is an important atherosclerotic risk marker but cannot be accepted as a risk factor and should not be subjected to treatment.

Screening for multisite artery diseases is important in asymptomatic adults at moderate cardiovascular risk, as well as in hypertensive patients. The clinician searches for evidence of asymptomatic organ damage, which can further determine cardiovascular risk and lead to re classification of intermediate risk patients into low or high risk categories.

Examination of arterial wall gives every clinician an opportunity to evaluate subclinical alterations in wall structure that precede and predict future cardiovascular clinical events. B-mode ultrasonography is a non-invasive, safe, easily performed, reproducible, sensitive, relatively inexpensive and widely available method for detection of early stages of atherosclerosis and is accepted as one of the best methods for evaluation of arterial wall structure.

One of the main problems in interpreting IMT results from clinical trials is the differences in measurement methodology. To avoid this problem standards for IMT measurement have been developed. The preferred type of equipment is a high-resolution B-mode system (B-mode imaging is preferred over M-mode imaging), equipped with a linear array

transducer > 7 MHz with minimal compression (<10:1) and footprint of at least 3 cm. In addition, focus depth (30-40 mm), frame rate (>15-25 Hz) and gain settings should be adjusted optimally to facilitate edge detection. In addition, intima media thickness should be measured along a segment of the artery free of atherosclerotic plaque with clearly defined lumen-intima and media-adventitia interfaces within a 10-mm-in-length straight arterial segment. Arterial wall segments should be assessed longitudinally and perpendicular to the ultrasound beam usng a horizontal position of the artery in the image sector in order to optimize the visualization of lumen-intima interface. (3)

Intima media thickness is defined by the two parallel echogenic lines (double line pattern), which correspond to the lumen-intima and the media-adventitia interfaces. Ultrasonically, these interfaces are well defined only in the far arterial wall. Even when the near wall IMT is well visualized, its measurement is gain-dependent and unreliable. With the advancement in technology and computer software, accurate measurement and the interpretation of carotid and femoral IMT can be made with greater reliability and reproducibility. Computer software can now automatically define the IMT within 0.01 mm. In order to reduce variation or error in IMT measurements, leading to non-identical results of repeated measurements from the same subject, automated edge detection as opposed to the manual tracing of the echo interfaces not only simplified the reading of ultrasound images but also produced results with low variability. Researchers also demonstrated a reduction in the inter-observer error by using ultrasound images from both arterial sides rather than from one. Finally, the use of external reference points to measure intima media thickness reduced the intra-ob server error by approximately 38%. (4) Figure 1 (4)

High resolution B-mode ultrasound examination of the intima media thickness is a well accepted, highly reproducibly method for the evaluation of atherosclerosis. However, it is essential to determine reference values for IMT in order to interpret exactly these measurements. In all age groups men showed significantly higher IMT of all examined vessels in comparison to women. The mean IMT ranged from 0.50 to 1.04 mm in men in the age groups < or = 35 years and > or = 65 years, respectively. For women, corresponding IMT values ranged from 0.40 to 0.53 mm. Age was found to be a significant determinant of IMT of all examined vessels. IMT was positively related to age in both men and women, with the estimated yearly increase in IMT being 0.016 mm in men and 0.008 mm in women. B-mode ultrasound is also useful

in order to determine plaque occurrence in the wall of the femoral artery. Plaque frequency is also associated with age in both men and women, as more than 50% of men aged > or = 55 years and women > or = 65 years had plaques.(5, 6)As concerns the reproducibility of ultrasound measurements of arterial wall thickness, studies have shown that the reproducibility of intima media thickness measurements in segments prone to atherosclerosis, such as common carotid artery, the bulbous, internal carotid artery and common femoral artery is reliable, even in patients with increased artery wall thickness. For the common femoral artery of normal control subjects the within- and between-observer mean differences were 0.005 mm (-0.119 to 0.129) and 0.015 mm (-0.081 to 0.111), respectively. To obtain good reproducibility it is recommended to use the same ultrasonographer to scan patients in follow-up studies. (7)However, atherosclerotic disease is caused by a combination of systemic and local factors affecting local flow conditions. Especially at the iliac-femoral artery region there is a large degree of bilateral asymmetry. In details, the IMT distribution at the right common femoral artery is more skewed (P90 right: 1.11 mm, left 1.01 mm; P < 0.001), which is mirrored by a significantly higher plaque prevalence. Since atherosclerotic lesions are more prevalent at the right than at the left femoral artery, the choice of body site is very important when assessing vascular health. (8)

Since intima media thickness may be regarded as the closest investigation to an arterial biopsy, the morphological and dimensional information obtained from ultrasound scans may be used in addition to classical risk factors for risk assessment. B-mode scanning could become an important non-invasive, accurate and reproducible method to assess cardiovascular risk in the future, taking however into account the standards of measurement, as they are described above.

3. Intima media thickness in asymptomatic clinically healthy individuals and its relationship with cardiovascular risk factors

Studies have examined intima media thickness in children, adolescents and adults with no known cardiovascular disease. Sex differences occur only at an adult age for intima media thickness. Femoral IMT was not affected by age or by sex up to 18 years of age, whereas after it increased sharply in men and remained higher than in women. Femoral artery geometry seems to be related to blood pressure and body growth. Values were correlated with systolic blood pressure only in men,

and with fat-free mass in children and young adults. Smoking, body mass index and fat mass were associated with intima media thickness only in adults.(9) Although many studies have shown a significant correlation between IMT measured by high resolution ultrasound and the presence of coronary artery disease or cardiovascular risk factors, reference values for the value of intima media thickness in healthy individuals had not yet been established. Depairon el al found that the mean femoral IMT was 543 +/- 63 microns in women and 562 +/- 74 microns in men with no family or personal history of cardiovascular disease or cardiovascular risk factors. Between the ages of 20 and 60, the femoral IMT increased by 1.2 microns per year in women and 3.1 microns in men. (10)

Intima media thickness and impaired endothelial function has significant correlation with cardiovascular risk factors. Studies have shown that cardiovascular risk factors are associated with impaired endothelial function and increased IMT, and that the presence of increased carotid and femoral IMT is significantly correlated with endothelial dysfunction. More detailed, studies revealed a lower flow mediated vasodilatation in patients with increased carotid and femoral IMT in comparison with patients without peripheral atherosclerosis. (11)

Intima media thickness was tested for correlation with blood pressure, cardiac structures and several clinical and biological parameters. The IMT was thicker in hypertensive than in normotensive individuals (0.67 +/- 0.13 and 0.62 +/- 0.16 vs 0.54 +/- 0.09 and 0.52 +/- 0.11 mm, respectively, $P<0.0001$). In normotensive subjects these was significant correlation between IMT and age, body mass index and 24-h systolic blood pressure, whereas in hypertensive patients the femoral IMT was correlated only with 24-h diastolic blood pressure and age. As regards echocardiographic findings, femoral IMT was associated with left posterior wall and interventricular septum in hypertensive patients. Figure 2, Figure 3 (12)

Besides elevated blood pressure, type 2 diabetes mellitus is an important risk factor for the development of atherosclerosis. Early subclinical manifestation of atherosclerosis can be recognized by measuring the thickness of the intima and media. For this reason researchers examined vessel changes and the extent of possible risk factors in patients with newly diagnosed type 2 diabetes and control persons without diabetes mellitus. They found that there was an increase in subclinical atherosclerosis in type 2 diabetics already during the first year after diagnosis, primarily on the common carotid artery

and secondary on the femoral artery. (13) It is well established that impaired glucose regulation is associated with detrimental cardiovascular outcomes such as cardiovascular disease risk factors or intima media thickness. For this reason researchers examined whether these associations are mediated by body mass index, waist circumference or fasting serum insulin. They found that there was a graded relationship between impaired glucose regulation categories and both major cardiovascular risk factors and femoral IMT. However, these relationships were only partly mediated by body mass index, waist and insulin. These results suggest that increased cardiovascular risk factors association with impaired glucose regulation in also mediated by factors other than the considered markers of adiposity and insulin resistance. (14)An other study examined the association between intact insulin, insulin propeptides and femoral artery intima media thickness. It was found that only smoking, systolic blood pressure and ApoB but not insulin or insulin propeptides were assocated with femoral atherosclerosis. (15)In most studies the well established correlation between intima media thickness and the risk of cardiovascular and cerebrovascular events and death is usually measured in patients with multiple vascular risk factors, which makes it difficult to establish whether each cardiovascular risk factor has, per se, an effect in IMT. For this reason researchers examined five “pure” groups of patients, each presenting only one of the following risk factors: hypertension, obesity, overweight, smoking and hyperclolesterolaemia. They found that overweight was the least important risk factor with regard to intima media thickness, followed by smoking, hypercholesterolaemia, hypertension and finally obesity, which emerged as the greatest risk factor. They also managed to build a scale of severity of the vascular risk factors considered and compute a composite general score, which provides an univocal risk estimation at single-patient level. This risk score can be very useful for preventive treatment and estimation of frequency of instrumental examinations. (16)

As a conclusion, these studies demonstrate that structural wall changes detected in each arterial segment were influenced by major cardiovascular risk factors, although with different intensities for each one. Amongst the several factors which have an impact on target organs, age, male gender, high blood pressure and diabetes mellitus type 2 appear to be the main predictors of increased thickening of the arterial wall.

4. Intima media thickness and cardiovascular disease

The variation in severity of cardiovascular disease is reflected in the intima media thickness of peripheral arteries. To prove this state, researchers measured IMT in both carotid and femoral artery in patients with familial hypercholesterolemia and they found that all IMT in both artery groups were severely thickened with respect to normal controls. In particular, the mean IMT of the common femoral artery is thicker in familiar hypercholesterolemic individuals with cardiovascular disease compared with those without. Furthermore, the highest IMTs and the largest absolute differences were observed in the common femoral artery (1.23 +/- 0.46 mm vs 1.10 +/- 0.51 mm; P = 0.006). However, some patients had abnormal IMT of the femoral artery, whereas in others the carotid artery is more affected. For this reason, combined assessment of the carotid and femoral arterial walls may provide a more accurate estimation of total atherosclerotic lesions. (17) Although the common carotid IMT is considered as a marker of cardiovascular disease, the value of the common femoral IMT is not well defined. For this reason, researchers try to evaluate the value of common femoral IMT alone or in combination with the common carotid artery IMT as a marker of cardiovascular disease. They calculated Framingham Heart Study (FHS) risk score for each patient participated in the study and correlated it with the carotid IMT, femoral IMT, and the combined IMT measured at both arterial sites. Common carotid and common femoral IMT showed similar correlation with the FHS risk score. In addition, the combination of IMT from both arterial sites was found to have similar correlation with the FHS risk score to carotid IMT alone (carotid IMT: $r = 0.28$, $p = 0.035$, and $r = 0.35$, $p = 0.007$, respectively, femoral IMT: $r = 0.38$, $p = 0.003$, and $r = 0.43$, $p = 0.001$, respectively, carotid-femoral IMT: $r = 0.37$, $p = 0.005$, and $r = 0.46$, $p = 0.0001$, respectively). (18) A more recent study compared the intima media thickness of the internal carotid artery with the IMT of the common and external carotid, vertebral and femoral arteries and the abdominal aorta to assess the possibility of using these arteries as markers of atherosclerotic disease. Considering IMT equal or greater than 0.8 mm, there was positive and significant correlation between the values obtained for the examined arteries. As a result, routine examinations of either one of these arteries can ad important findings regarding early diagnosis for higher risk patients concerning atherosclerotic disease. (19)

Different ultrasonic arterial wall measurements have been used as predictors of future myocardial infarction or stroke. The Cyprus Study tried to determine the relationship of the number of carotid and femoral bifurcations with plaque and total plaque thickness (sum of the maximum plaque measurements taken from the four bifurcations of scanned carotid and femoral arteries) with the prevalence of clinical cardiovascular disease. Since total plaque thickness was associated with 6.87-fold (2.42 to 19.43) increased odds of cardiovascular disease prevalence, more prospective studies have to be conducted in order to document associations with incident cardiovascular disease events. (20)
In addition to this, Griffin et al tried to determine the relationship of total plaque area (the sum of the atherosclerotic plaque measurements from both carotid and both common femoral arteries) with prevalence of cardiovascular disease and compare it with intima media thickness. After scanning both carotid and both femoral bifurcations with ultrasound and adjusting for conventional risk factors, they found that total plaque area seems to be more significantly associated with the prevalence of cardiovascular disease than IMT. (21)
Intima media thickness (IMT) is a marker of cardiovascular disease. Studies demonstrate that the variation in severity of cardiovascular disease seen in patients with major cardiovascular risk factors is reflected in intima media thickness. However, the combined IMT measurement of different kind of arteries, such as carotid and femoral artery, may have a better correlation with cardiovascular risk score than those of each artery alone. In addition, there are also some different ultrasound arterial wall measurements (number of carotid and femoral bifurcations with plaque, total plaque thickness and total plaque area) that can be used as predictors of future myocardial infarction or stroke. These findings need further investigation in prospective studies in order to use them as routine examinations for early diagnosis of higher risk patients.

5. Intima media thickness and coronary artery disease

We already know that the combined thickness of the intima and media of the carotid artery, as measured noninvasively by ultrasound, is associated with the prevalence of cardiovascular disease and an icreased risk of myocardial infarction and stroke in older adults without a history of cardiovascular disease. (22)

In order to examine the association of occult atherosclerosis of peripheral arteries with the presence and severity of obstructive coronary artery disease, patients without a history or presence of cerebrovascular or peripheral artery disease who underwent routine coronary angiography, examined by duplex ultrasound. Occult atherosclerosis is indicated by the estimation of intima media thickness of the peripheral arteries and the severity of coronary artery disease by the number of the diseased vessels. Intima media thickness was found to have a significant correlation with the presence of obstructive CAD. IMT of carotid and femoral artery were independent predictive factors of obstructive coronary artery disease, with specificity of 74% and 60% and sensitivity of 76% and 70%, respectively. So the assessment of occult atherosclerosis by ultrasound in both the carotid and the femoral arteries is significantly associated with the presence and the severity of CAD. Another study enrolled patients who had undergone coronary angiography due to symptoms of CAD and proved significantly higher values of femoral IMT in patients with CAD than in those without CAD. In the same study was found that there is a strong positive correlation between femoral IM and the severity of CAD. There was also a positive correlation between femoral IMT and levels of triglycerides, body mass index, male gender and smoking. In addition there was a negative correlation between femoral IMT and the level of high-density lipoprotein-cholesterol. As a consequence, femoral IMT may be a novel cardiovascular risk marker. Lisowska et al enrolled patients who had undergone coronary angiography due to symptoms of CAD and tried to find the relationship between intima media thickness, renal function and extent of coronary artery disease. They found that GFR values in CAD patients significantly negatively correlated with intima media complex and lower values of GFR in patients with three-vessel disease than in those patients with one- or two-vessel disease. This correlation between the value of GFR and intima media thickness confirmed the usefulness of this noninvasive method for the estimation of preclinical stages of atherosclerosis in patients with impaired renal function. (23, 24, 25) Figure 5 (23), Figure 6, 7 (24), Figure 8 (25) Finally, researchers tried to assess the relation between individual IMT from peripheral arteries, scores incorporating IMT from the carotid and femoral arteries and the extent and severity of coronary artery disease. For this reason they measured intima media thickness from both carotid and femoral arteries and they develop an IMT score including the number of sites with abnormal IMT (range 0-8). A high risk IMT score can predict an extended

coronary artery disease and the performance of revascularization procedures and all cardiovascular events during a follow-up 0f 14.5 +/- 2.4 months. As a conclusion IMT incorporating data from common and internal carotid artery, carotid bifurcation and femoral artery are well correlated with the extent of coronary atherosclerosis, much better than individual IMT. (26)

We have already mentioned that ultrasound assessments of intima media thickness and plaques in peripheral arteries are widely used as markers of coronary atherosclerosis. Researchers studied patients with stable angina pectoris, assessed intima media thickness, lumen diameter and plaques in the carotid and femoral arteries and related it to the risk of cardiovascular death or non-fatal myocardial infarction, or revascularization during follow-up (median 3 years). Carotid and femoral vascular changes were differently related to cardiovascular events. As concerns femoral artery, both intima media thickness and plaques were related to revascularization. Femoral IMT was aldo related to cardiovascular death or myocardial infarction. However, evaluations of plaques provided better prediction than assessment of intima media thickness in patients with stable angina. Since intima media thickness assessed in peripheral arteries correlated with presence and progression of atherosclerosis in coronary arteries, IMT measurements may help to select high risk patients and evaluate the efficacy of the therapy used. For this reason patients treated with PCI due to acute myocardial infarction underwent ultrasound examination of the IMT complex, including common carotid artery, carotid bulb and common femoral artery. During the follow-up an increase of IMT complex value compared to initial IMT values of all examined peripheral arteries was observed. Even higher were IMT values in non-compliant to standard pharmacological treatment patients. In addition, patients with higher IMT values were reported to have cardiac events more frequently during the follow-up. This study suggest that ultrasound IMT complex assessment of peripheral arteries in everyday clinical practice allows monitoring efficacy of pharmacological therapy in coronary artery disease patients after myocardial infarction, as well as treatment intensification if necessary. (27, 28)

Atherosclerosis is a generalized, progressive disease that may simultaneously affect several arterial trees of the body. Among other efforts in the direction of management of atherosclerosis, early detection of subclinical (asymptomatic) CAD and subsequent prevention of possible future ischemic events is one of our most important tasks.

IMT changes of both the carotid and femoral arteries appeared to be independent predictors of both the existence and the severity of obstructive CAD. However, an isolated CCA IMT measurement may be an inadequate parameter of systemic atherosclerosis, because its sensitivity and specificity are too low to identify patients with significant coronary artery disease. It has been demonstrated that a complex evaluation of different arteries IMT increases the predictive value of these measurements. Finally, ultrasonographic measurement of IMT may be quite useful in atherosclerosis progress monitoring in patients after myocardial infarction, assessing the risk of revascularization procedures and the efficacy of pharmacological therapy.

6. Intima media thickness and peripheral vascular disease

Risk Intervention Study tried to investigate the occurrence of ultrasound assessed morphological changes in the right common femoral artery and relate these findings to the ankle-arm index and to symptoms of lower-extremity arterial disease in hypertensive subjects at high cardiovascular risk. There were more and larger plaques, as well as thicker mean and maximum intima media complexes, in the high risk group than in the low risk group. Plaque occurrence and mean intina media thickness in the right common femoral artery were significantly associated with ankle-arm index both in the right and left leg. In the high risk group, 11% suffered from symptoms of right lower-extremity artery disease, 20% had an ankle-arm index < or = 0.9, 62% had moderate or large plaques (compared with 28% in the low risk group), and 77% had an enlarged intima media complex. Taking these findings account, this study suggested that ultrasound measurements of the intima media thickness of the common femoral artery is a valuable method to evaluate morphological changes related to atherosclerotic disease in the lower extremity. In another study researchers tried to investigate whether peripheral vascular disease of the lower extremity per se affects the arterial viscoelastic properties and intima media thickness of the carotid and femoral arteries. Patients with peripheral vascular disease had significantly impaired femoral elastic properties and stiffness index as well as significantly elevated intima media thickness. Since peripheral vascular disease affects the femoral wall mechanics and morphology similarly to other cardiovascular risk factors and events, the parameters mentioned above may provide further information for cardiovascular risk assessment in addition to the classical risk factors and the

Framingham equation. Indeed, some guidelines have suggested that additional factors such as peripheral arteries scan may influence the clinician's decision to intervene with therapy. (29, 30) Figure 9 (29)

7. Femoral intima media thickness in asymptomatic younger population

Although the clinical manifestations of cardiovascular diseases occur during and after middle age, autopsy studies in youth have shown that cardiovascular risk factors are related to the early stages of coronary atherosclerosis. IMT of carotid and femoral arteries is considered surrogate indicator of atherosclerotic coronary and peripheral vascular diseases in middle aged and older adults. In addition, the use of the Framingham Risk Score in predicting coronary artery disease has been demonstrated in middle-aged and older population. However, the association between FRS and femoral artery IMT has not been studied in asymptomatic younger population. As part of the Bogalusa Heart Study, a study of early natural history of atherosclerosis, many studies examined the relationship between FRS and femoral artery IMT in asymptomatic younger adults.

Femoral artery IMT was measured by B-mode ultrasound in 1080 black and white subjects (aged 24-43 years; 71% white, 43% male) enrolled in the Bogalusa Heart Study. Individuals in the top versus bottom fifth percentiles distribution of femoral intima media thickness were compared for traditional cardiovascular risk factors profile. Femoral IMT showed gender difference (men more than women), but no racial difference. In a multivariate model, systolic blood pressure, age, male gender, cigarette smoking, and total cholesterol/high-density lipoprotein cholesterol ratios related independently, in that order, to intima media thickness. Mean IMT increased with an increasing number of risk factors defined as values above the age-, race-, and gender-specific 75^{th} percentile of systolic blood pressure, waist circumference, total cholesterol/high-density lipoprotein cholesterol ratio, and insulin along with smoking status, with respective mean IMT values of 0.66, 0.69, 0.73, and 0.79 mm for 0, 1 to 2, 3, and 4 to 5 risk factors. The odds ratio for patients with > / = 3 risk factors versus no risk factors having IMT in the top fifth percentile was 4.7.

These studies demonstrated the deleterious impact of higher FRS, indicative of multiple risk factors, on the IMT of femoral artery. This observed association is indicative of the impact of multiple

cardiovascular risk factors on the early stages of atherosclerosis in extra coronary arteries and, by inference, in coronary arteries. The noninvasive ultrasound evaluation of femoral IMT in these studies expands earlier autopsy findings, showing a strong association between multiple cardiovascular risk factors and early phases of atherosclerosis in young adults. The results of these studies demonstrated the utility and validity of the Framingham Risk Score to imply in younger asymptomatic subjects. Even after stratification by race, FRS was independently associated with femoral IMT. This result reinforced the importance of multiple risk factors profiling in early life regardless of race. FRS was related significantly with femoral IMT in a sample younger than the original Framingham population aged 30-70 years. These results demonstrated the utility of FRS even in investigating early peripheral vascular diseases in younger individuals. The findings of these studies that the femoral IMT increased considerably with increased FRS in asymptomatic young adults, supporting the concept of the importance of multivariate risk profile and the attendant accelerated atherosclerosis systemically. The observed adverse effect of multiple risk factors on the femoral IMT parallel the earlier autopsy results showing marked increases in the extent of coronary atherosclerosis in young subjects with increasing number of risk factors. However, having measurements of only one femoral arterial site is a limitation of these studies. Further studies of femoral IMT in different arterial segments, especially on the femoral bifurcation, are needed to compare the results as with different carotid segments. (31, 32, 33, 34)

We have already mentioned that coronary artery disease is insidiously manifested in younger patients. However, Heartscore is not well validated for individuals less than 40 years of age. In the latest guidelines a relative risk chart is provided with the proposal to be used for young adults aged less than 60 years instead of projecting risk at the age of 60 years. Stamatelopoulos et al enrolled young Greeks of age less than 40 years and middle-aged adults aged 40-60 years without clinically overt cardiovascular disease of diabetes and measured flow-mediated dilatation of brachial artery, carotid and femoral intima media thickness, carotid-radial and carotid-femoral pulse wave velocity. They used the European Society of Cardiology online heartscore calculator for mortality risk and Systematic Coronary Risk Evaluation risk charts for relative risk. Heartscore used for mortality risk was significantly correlated with all measured vascular markers in young individuals. As a consequence Heartscore was a strong identifier of the most of the measured markers

of early atherosclerosis and can be used as a prognostic tool in terms of primary prevention for participants younger than 40 years old. (35)
As a conclusion, a higher FRS, indicative of multiple cardiovascular risk factors, has a significant impact on the femoral artery IMT. Studies demonstrated a strong association between multiple cardiovascular risk factors and early phases of atherosclerosis in young adults. These results proved the utility and validity of the FRS to imply also in younger population, reinforcing the importance of multiple risk factors profiling in early life.

8. Effect of drug treatment on the intima media thickness and atherosclerotic process

Peripheral vascular disease is a common condition often associated with cardiovascular risk factors and events. These risk factors and events are significantly correlated to an increased carotid and femoral intima media thickness. In addition, treatment of these risk factors is associated with a decrease or diminished progression of the IMT, paralleled by a reduction in cardiovascular events and an improvement in the symptoms associated with peripheral vascular disease. As a consequence, additional predictors of cardiovascular risk like the IMT, may now influence the decision to intervene with medication. This evidence is particularly strong for lipid lowering therapy. (4)
Since an increased intima media thickness is an early indicator of the atherosclerotic process, researchers investigated the early effect of atorvastatin on the common carotid artery and the common femoral artery, by measuring IMT in these peripheral arteries of hyperlipidaemic patients referred with peripheral vascular disease. Patients, median age 69 years had a common femoral artery IMT mean (SD) of 0.83 (0.13) mm pre-treatment, 0.80 (0.09) mm after 4 weeks, and 0.69 (0.14) mm after 8 weeks treatment with 20mg/day atorvastatin. This cholesterol-lowering induced decrease in common femoral artery intima media thickness achieved significantly after 8 weeks of treatment and may be attributable to an anti-inflammatory effect. In future IMT measurements may be a useful tool to rapidly assess the effect of drug treatment on the atherosclerotic process. Other studies also used ultrasound as a noninvasive surrogate marker of cardiovascular disease and tried to prove that by reducing risk factors, progression of atherosclerosis was inhibited. Researchers treated patients with familiar hypercholesterolemia with simvastatin, 80 mg/d, for 2 years. They found

a decrease in intima media thickness of 0.081 mm (CI -0.109 to -0.053), with its largest reduction in the femoral artery (-0.283). As a consequence, high-dose simvastatin therapy reduces arterial wall IMT, with its largest effect on the femoral artery. In addition, patients with familiar hypercholesterolemia who were treated with both statin and antihypertensive medication experienced a significantly greater benefit in terms of IMT reduction. The Atorvastatin versus Simvastatin Atherosclerosis Progression study examined the long-term effects of statins on femoral IMT and plaque scoring in patients with familiar hypercholesterolemia. This study indicates increased efficacy of atorvastatin 80 mg in retarding progression of atherosclerosis in the femoral artery compared with simvastatin 40 mg. Interestingly, in the carotid arteries these statins influenced intima media thickness to a greater extent whereas in the femoral artery the effects were more pronounced on plaque frequency. These findings underscore the generalized effects of lipid lowering on atherosclerosis. (36, 37, 38)

9. Conclusion

Intima media thickness is a significant marker of atherosclerotic disease. However, no consensus guidelines are available on which site and how IMT sampling should be performed. It is the “phenotype” of the early phases of atherosclerotic disease and is related to the main traditional risk factors. Although threshold IMT values for the prediction of cardiovascular events have not been identified, high IMT values are associated with an increased occurrence of cardiovascular events. Indeed, an IMT > or = 0.9 mm was demonstrated to be associated with an increased cardiovascular risk. In comparison to carotid IMT, femoral IMT is more strictly correlated with the severity of coronary artery disease and the need for revascularization in effort angina. The simultaneous measurement of carotid and femoral IMT may improve risk stratification in patients with coronary heart disease. The challenge for the future is to establish an IMT cut-off value for a better definition of the individual cardiovascular risk.

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21. Griffin M, Nicolaides A, Tyllis T, Georgiou N, Martin RM, Bond D, Panayiotou A, Tziakouri Ch, Dore CJ, Fessas CH. Plaque area at carotid and common femoral bifurcations and prevalence of clinical cardiovascular disease. IntAngiol. 2010 Jun;29(3):216-25
22. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med. 1999 Jan 7;340(1):14-22
23. Kafetzakis A, Kochiadakis G, Laliotis A, Peteinarakis I, Touloupakis E, Igoumenidis N, Katsamouris A. Association of subclinical wall changes of carotid, femoral, and popliteal arteries with obstructive coronary artery disease in patients undergoing coronary angiography. Chest. 2005 Oct;128(4):2538-43
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26. Lekakis JP, Papamichael C, Papaioannou TG, Stamatelopoulos KS, Cimponeriu A, Protogerou AD, Kanakakis J, Stamatelopoulos SF. Intima-media thickness score from carotid and femoral arteries predicts the extent of coronary artery disease: intima-media thickness and CAD. Int J Cardiovasc Imaging. 2005 Oct;21(5):495-501

27. Lisowska A, Knapp M, Bolińska S, Lisowski P, Krajewska A, Sobkowicz B, Musiał WJ. The importance of intima-media thickness (IMT) measurements in monitoring of atherosclerosis progress after myocardial infarction. Adv Med Sci. 2012 Jun 1;57(1):112-7
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30. Cheng KS, Tiwari A, Baker CR, Morris R, Hamilton G, Seifalian AM. Impaired carotid and femoral viscoelastic properties and elevated intima-media thickness in peripheral vascular disease. Atherosclerosis. 2002 Sep;164(1):113-20
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32. Paul TK, Srinivasan SR, Chen W, Li S, Bond MG, Tang R, Berenson GS. Impact of multiple cardiovascular risk factors on femoral artery intima-media thickness in asymptomatic young adults (the Bogalusa Heart Study). Am J Cardiol. 2005 Feb 15;95(4):469-73
33. Paul TK, Chen W, Srinivasan SR, He J, Berenson GS. Contrast of the impact of multiple cardiovascular risk factors on the femoral and carotid intima-media thickness in asymptomatic young adults: the Bogalusa Heart Study. Atherosclerosis. 2011 Jun;216(2):359-64
34. Timir K. Paul, Wei Chen, Sathanur R. Srinivasan, Janet Rice, AhmetToprak, Jiang He, and Gerald S. Berenson. Framingham risk score is associated with femoral artery intimamedia thickness in asymptomatic young adults (The Bogalusa Heart Study). Atherosclerosis. 2010 December ; 213(2): 627–631
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37. De Sauvage Nolting PR, de Groot E, Zwinderman AH, Buirma RJ, Trip MD, Kastelein JJ. Regression of carotid and femoral artery intima-media thickness in familial hypercholesterolemia: treatment with simvastatin. Arch Intern Med. 2003 Aug 11-25;163(15):1837-41
38. van Wissen S, Smilde TJ, de Groot E, Hutten BA, Kastelein JJ, Stalenhoef AF. The significance of femoral intima-media thickness and plaque scoring in the Atorvastatin versus Simvastatin on Atherosclerosis Progression (ASAP) study. Eur J CardiovascPrevRehabil. 2003 Dec;10(6):451-5

Figures

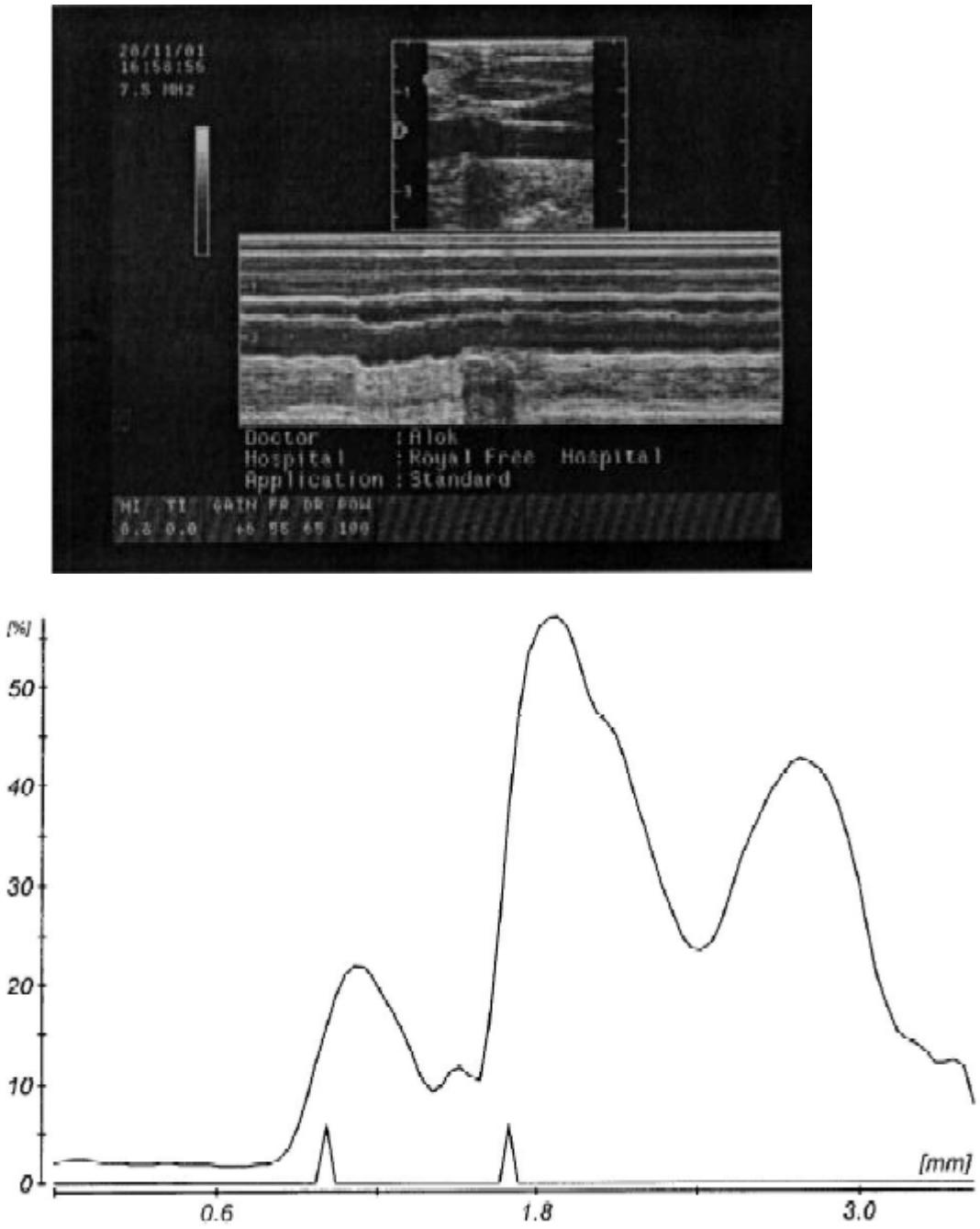

Figure 1 (up) B-mode and M-mode image of the common carotid artery (CCA) in a 72-year-old woman. (bottom) The distance density curve has been generated automatically from the radio frequency (RF) signal and the distance between markers (lumen–intima and media–adventitia interfaces) represent the IMT (in this case 0.70 mm).

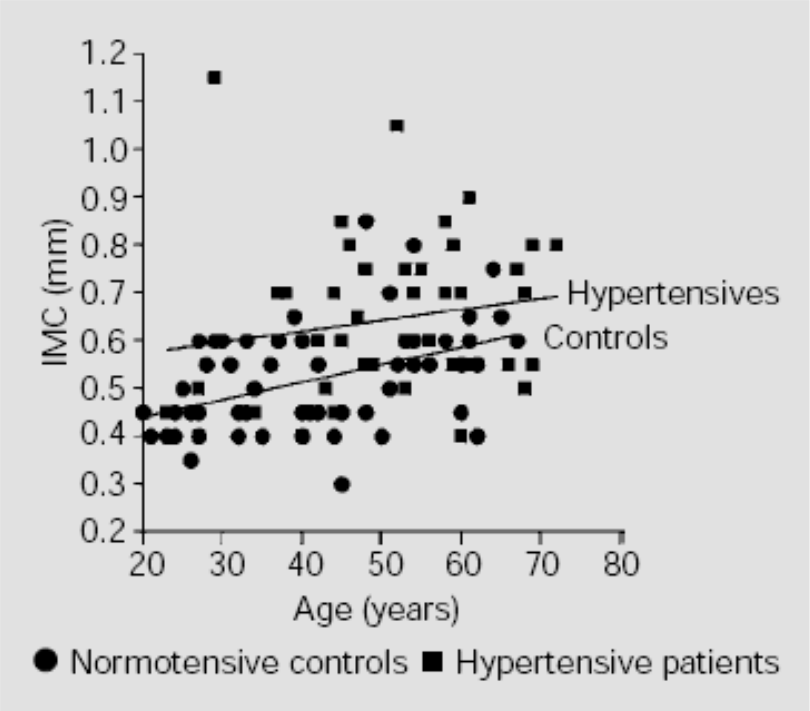

Figure 2 Correlation between common femural intima-media complex (IMC) and age for normotensive controls (N = 63) and hypertensive patients (N = 52). The equation for IMC-normotensives was: y = 0.367 + (0.0036 x age) and for IMC hypertensives: y = 0.529 + (0.0023 x age). The intercepts, but not the slopes,were different.

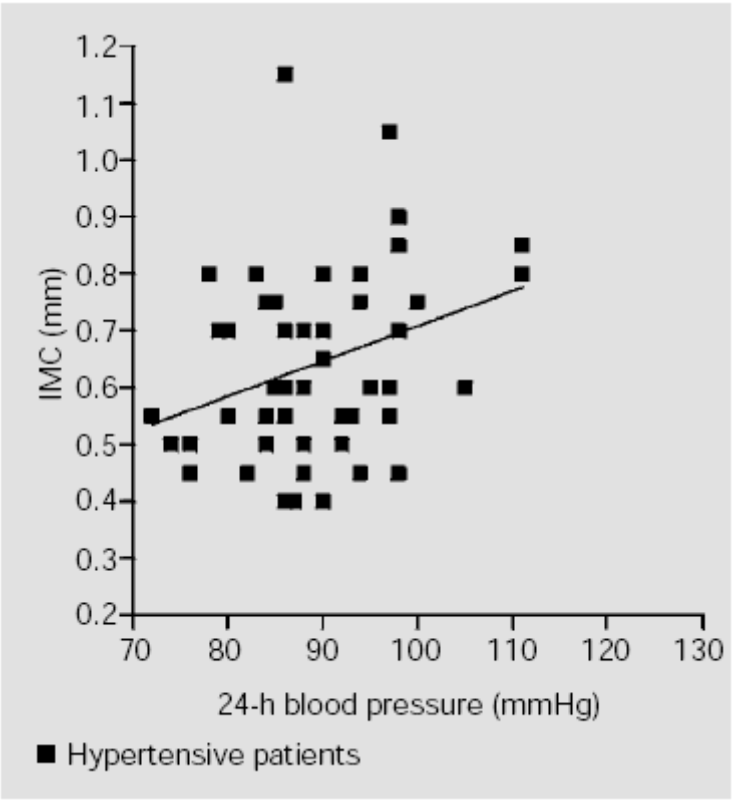

Figure 3 Correlation between common femural intima-media complex (IMC) and 24-h DBP. Hypertensive patients (N = 52). The equation for IMC-hypertensives was: y = 0.09 + (0.0062 x 24-h DBP).

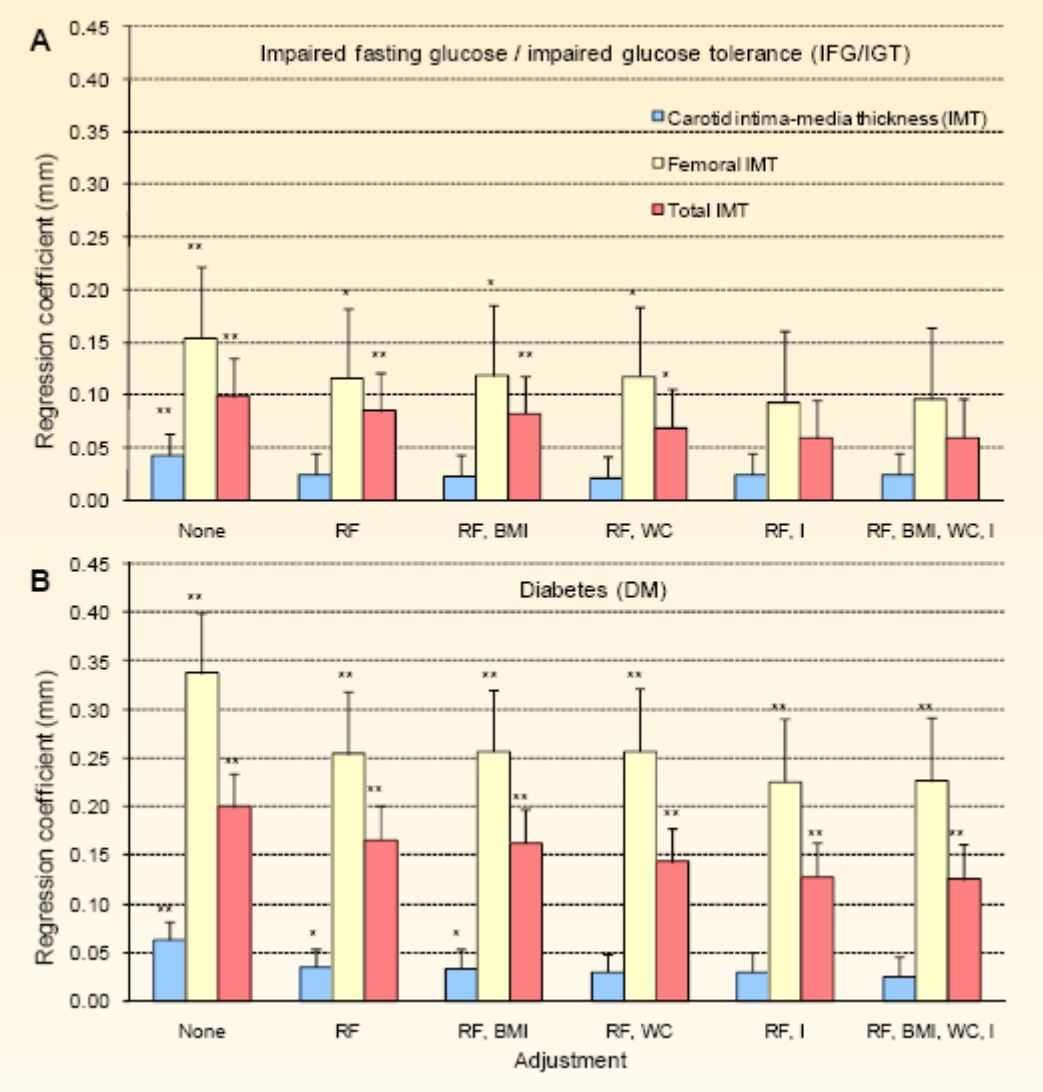

Figure 4 Associations between intima-media thickness (IMT) and categories of impaired glucose metabolism upon incremental adjustment for covariates (regression coefficients with their standard errors). Panel A: impairedfasting glucose / impaired glucose tolerance (IFG/IGT); Panel B: diabetes (DM).

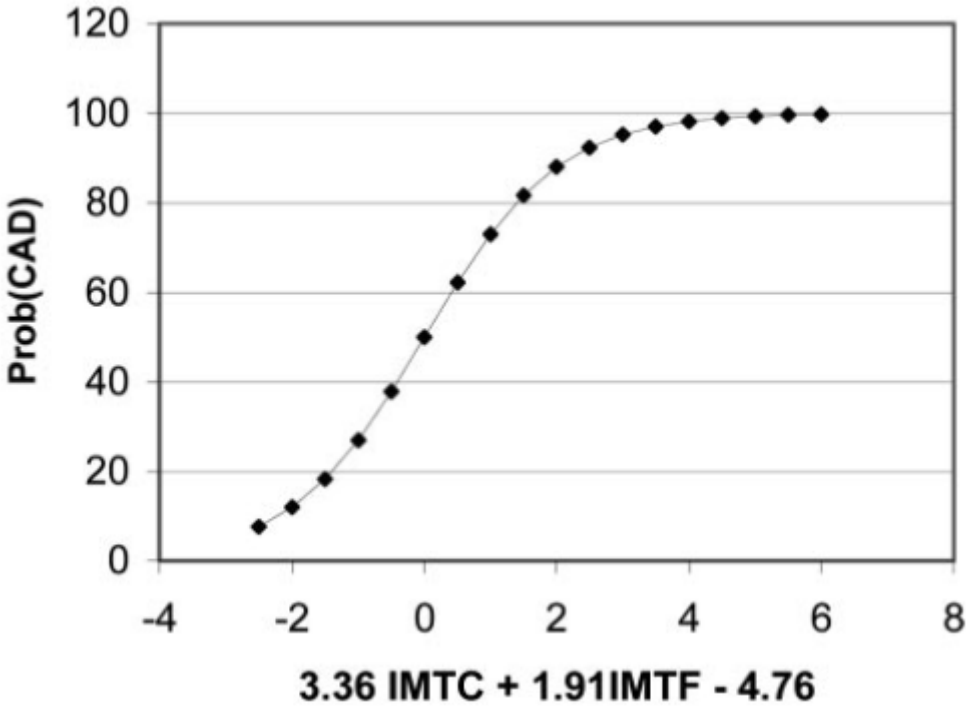

Figure 5 Estimated probability (prob) of CAD as a function of IMTC and IMTF.

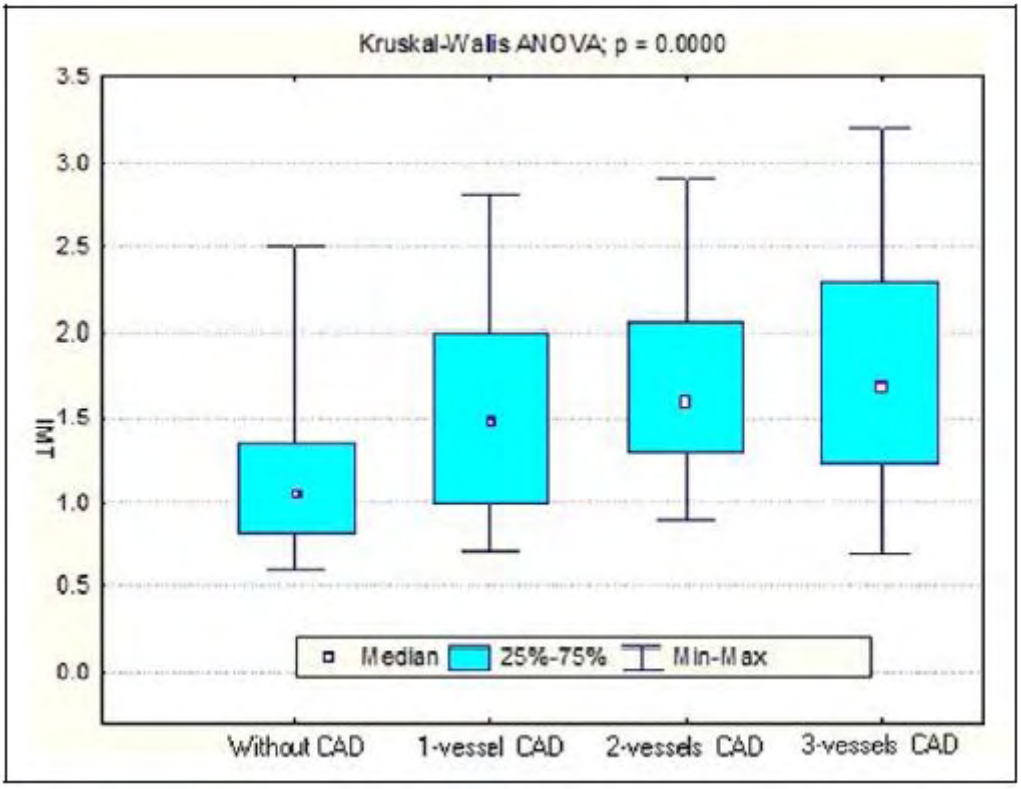

Figure 6 Nonparametric analysis of variance femoral intima media thickness (IMT) and coronary artery disease (CAD).

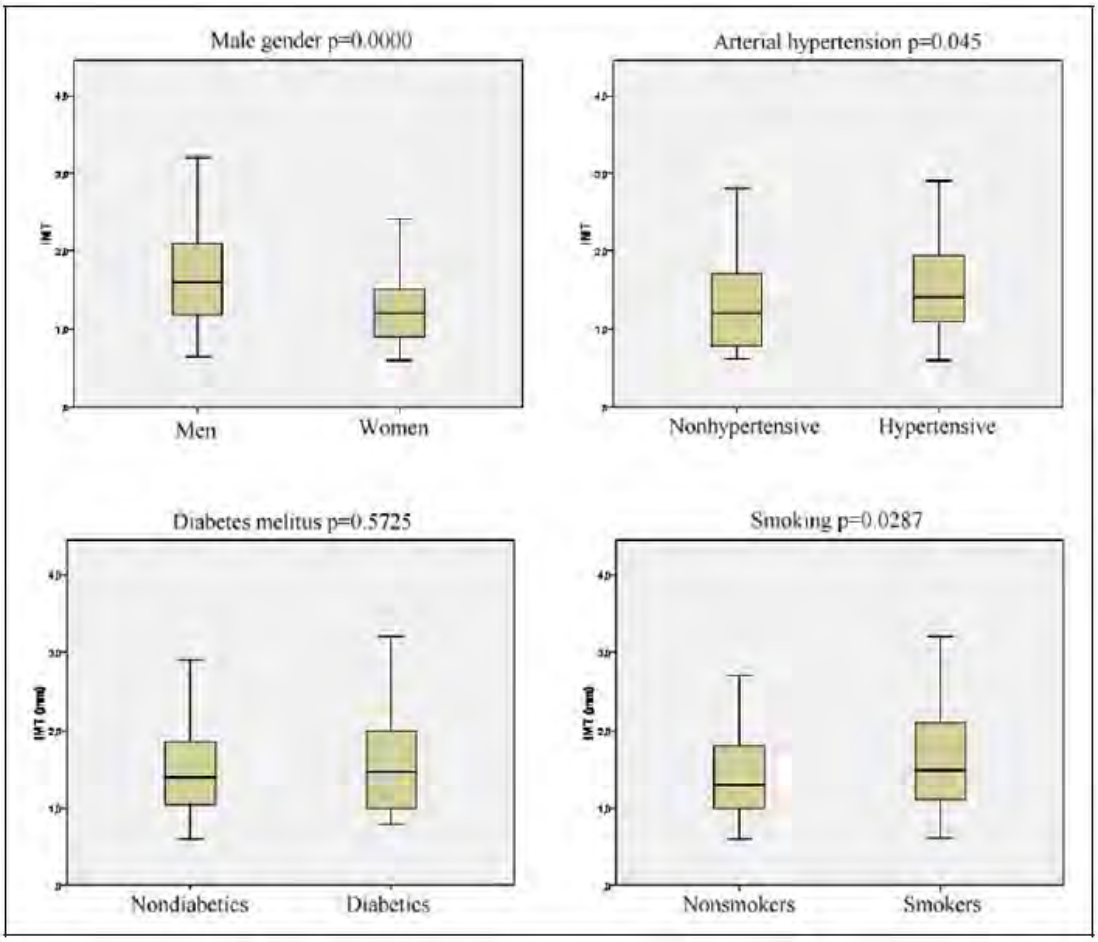

Figure 7 Correlation of femoral intima–media thickness (IMT) and qualitative risk factors.

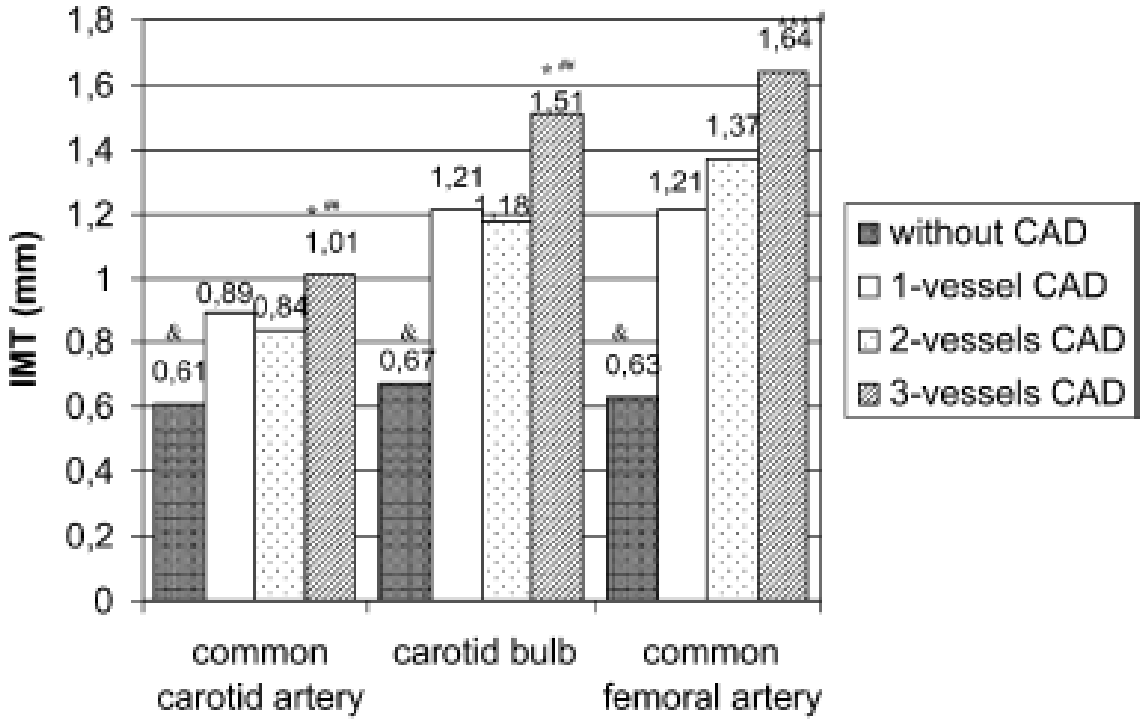

Figure 8 Correlation between CCA, carotid bulb and CFA IMT values and coronary artery lesions in study groups patients and controls.

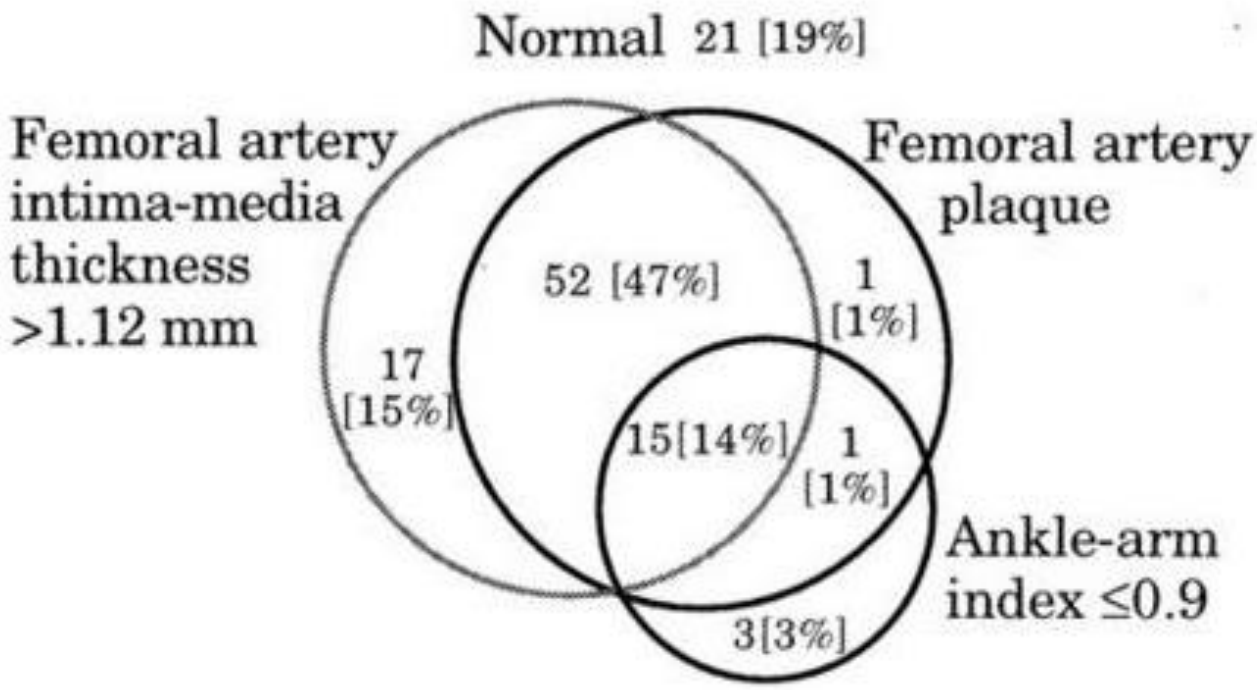

Figure 9 Diagram illustrating the overlap between different methods to diagnose peripheral artery disease in the right leg in hypertensive patients at high cardiovascular risk. The femoral arterial atherosclerotic plaques were of moderate or large size.

ΕΥΡΗΜΑΤΑ ΜΕΛΕΤΩΝ

4. Cheng KS, Mikhailidis DP, Hamilton G, Seifalian AM. A review of the carotid and femoral intima-media thickness as an indicator of the presence of peripheral vascular disease and cardiovascular risk factors. Cardiovasc Res. 2002 Jun;54(3):528-38

Cardiovascular risk factors and events are significantly related to an increased carotid and femoral IMT, scanning with B-mode ultrasound. More importantly, treatment of these risk factors is associated with a decrease or a diminished progression of the IMT, paralleled by a reduction in cardiovascular events and an improvement in the symptoms associated with peripheral vascular disease.

5. Temelkova-Kurktschiev T, Fischer S, Koehler C, Mennicken G, Henkel E, Hanefeld M. Intima-media thickness in healthy probands without risk factors for arteriosclerosis. Dtsch Med Wochenschr. 2001 Feb 23;126(8):193-7

In the group aged 40-54 years the men showed significantly higher IMT of all examined vessels in comparison to the women. In the group aged 55-70 years somewhat higher IMT of the common carotid artery and significantly higher IMT of the arteries of the lower extremity were observed in men. In multivariate analysis age was found to be a significant determinant of IMT of all examined vessels.

6. Junyent M(1), Gilabert R, Núñez I, Corbella E, Cofána M, Zambón D, Ros E. Femoral ultrasound in the assessment of preclinical atherosclerosis.Distribution of intima-media thickness and frequency of atheroma plaques in a Spanish community cohort]. Med Clin(Barc). 2008 Nov 1;131(15):566-71

Reference values for femoral IMT, expressed as 25th, 50th, and 75th percentiles by sex and 5 age groups, were obtained. The 50th percentiles of mean IMT ranged from 0.50 to 1.04 mm in men in the age groups < or = 35 years and > or = 65 years, respectively. For women, corresponding IMT values ranged from 0.40 to 0.53 mm. IMT was positively related to age in both men ($r = 0.44$; $p < 0.001$) and women ($r = 0.23$; $p = 0.019$). From the regression equations of IMT versus age, the estimated yearly increase in IMT was 0.016 mm in men and 0.008 mm in women. More than 50% of men aged > or = 55 years and women aged > or = 65 years had plaques

7. Smilde TJ, Wollersheim H, Van Langen H, Stalenhoef AF Reproducibility of ultrasonographic measurements of different carotid and femoral artery segments in healthy subjects and in patients with increased intima-media thickness.ClinSci (Lond). 1997 Oct;93(4):317-24

For the common femoral artery of normal control subjects the within- and between-observer mean differences were 0.005 mm (-0.119 to 0.129) and 0.015 mm (-0.081 to 0.111), respectively. The reproducibility of intima-media thickness measurements in the common carotid artery is reliable, even in patients with increased artery wall thickness. Also in other segments prone to atherosclerosis, such as the bulbous, internal carotid artery and common femoral artery, a good reproducibility was found. To obtain good reproducibility it is highly recommended to use the same ultrasonographer to scan patients in follow-up studies.

8. Bossuyt J, Van Bortel LM, De Backer TL, Van De Velde S, Azermai M, Segers P, De Buyzere M, Van Daele C, Rietzschel E; Asklepios Investigators. Asymmetry in prevalence of femoral but not carotid atherosclerosis. J Hypertens 2014 Jul;32(7):1429-34

The IMT distribution at the right common femoral artery is more skewed (P90 right: 1.11 mm, left 1.01 mm; P < 0.001), which is mirrored by a significantly higher plaque prevalence (right: 21.9 vs. left: 15.7%; P < 0.001).

9. Sass C, Herbeth B, Chapet O, Siest G, Visvikis S, Zannad F. Intima-media thickness and diameter of carotid and femoral arteries in children, adolescents and adults from the Stanislas cohort: effect of age, sex, anthropometry and blood pressure. J Hypertens. 1998 Nov;16(11):1593-602

Sex differences occur only at an adult age for intima-media thickness. In young subjects femoral artery geometry seems to be related to blood pressure and body growth.

10. Depairon M, Tutta P, van Melle G, Hayoz D, Kappenberger L, Darioli R. Reference values of intima-medial thickness of carotid and femoral arteries in subjects aged 20 to 60 years and without cardiovascular risk factors. Arch Mal Coeur Vaiss. 2000 Jun;93(6):721-6

The mean femoral IMT was 543 +/- 63 microns in women and 562 +/- 74 microns in men (NS). Between the ages of 20 and 60, the femoral IMT increased by 1.2 microns per year (NS) in women and 3.1 microns (p < 0.002) in men. Multiple regression analysis including gender and individual values of age, body mass index and lipid profile confirmed that only age was significantly correlated to the increase in thickness.

11. Corrado E, Muratori I, Tantillo R, Contorno F, Coppola G, Strano A, Novo S. Relationship between endothelial dysfunction, intima media thickness and cardiovascular risk factors in asymptomatic subjects. IntAngiol. 2005 Mar;24(1):52-8

Patients with cardiovascular RF showed an impaired FMD (p < 0.05). Femoral IMT is correlated with age (p < 0.005) and male gender (p < 0.02). Lower FMD in patients with increased carotid and femoral IMT in comparison with patients without peripheral atherosclerosis (p = 0.01).

12. Plavnik FL, Ajzen S, Kohlmann O Jr, Tavares A, Zanella MT, Ribeiro AB, Ramos OL. Intima-media thickness evaluation by B-mode ultrasound. Correlation with blood pressure levels and cardiac structures. Braz J Med Biol Res. 2000 Jan;33(1):55-64

The IMC was thicker in hypertensive than in normotensive subjects (0.67 +/- 0.13 and 0.62 +/- 0.16 vs 0.54 +/- 0.09 and 0.52 +/- 0.11 mm, respectively, P<0.0001). In normotensive patients, the simple linear regression showed significant correlations between IMC and age, body mass index and 24-h systolic blood pressure for both the carotid and femoral arteries. In hypertensives the carotid IMC was correlated with age and 24-h systolic blood pressure while femoral IMC was correlated only with 24-h diastolic blood pressure.

13. Frost D, Fröhlich B, Beischer W. Subclinical arteriosclerosis in patients with newly diagnosed type 2 diabetes mellitus. Demonstration by high-resolution ultrasound measurements of intima-media thickness of the common carotid and femoral arteries. Dtsch Med Wochenschr. 2000 May 26;125(21):648-54

Mean IMT of the CCA was 0.76 +/- 0.20 mm in the patients and 0.64 +/- 0.16 mm in the controls ($p < 0.01$). The IMT of the FA, however, was not significantly different in the two groups (patients: 0.80 + 0.30 mm, controls: 0.75 +/- 0.31 mm)

14. Faeh D, William J, Yerly P, Paccaud F, Bovet P. Diabetes and pre-diabetes are associated with cardiovascular risk factors and carotid/femoral intima-media thickness independently of markers of insulin resistance and adiposity. CardiovascDiabetol. 2007 Oct 24;6:32

Age-adjusted levels of the major CVD risk factors worsened gradually across IGR categories (NFG < IFG/NGT < IFG/IGT < DM), particularly HDL-cholesterol and blood pressure (p for trend < 0.001). With regards to IMT, the association was null with IFG/NGT, weak with IFG/IGT and stronger with DM (all more markedly at femoral than carotid levels).

15. Bokemark L, Wikstrand J, Fagerberg B; Atherosclerosis and Insulin Resistance Study. Intact insulin, insulin propeptides, and intima-media thickness in the femoral artery in 58-year-old clinical healthy men--the Atherosclerosis and Insulin Resistance Study. Angiology. 2001 Apr;52(4):237-45

Smoking, systolic blood pressure, and ApoB but not insulin or insulin propeptides were independently associated with femoral atherosclerosis.

16. Berni A, Giuliani A, Tartaglia F, Tromba L, Sgueglia M, Blasi S, Russo G. Effect of vascular risk factors on increase in carotid and femoral intima-media thickness. Identification of a risk scale. Atherosclerosis. 2011 May;216(1):109-14

Overweight was shown to be the least important risk factor with regard to intima-media thickening, followed by smoking, hypercholesterolaemia, hypertension and finally obesity, which emerged as the greatest risk factor

17. Wittekoek ME, de Groot E, Prins MH, Trip MD, Büller HR, Kastelein JJ. Differences in intima-media thickness in the carotid and femoral arteries in familial hypercholesterolemic heterozygotes with and without clinical manifestations of cardiovascular disease. Atherosclerosis. 1999 Oct;146(2):271-9

All IMTs in familial hypercholesterolemic heterozygotes were severely thickened with respect to normal controls. Furthermore, the highest IMTs and the largest absolute differences were observed in the common femoral artery (1.23 +/- 0.46 mm vs 1.10 +/- 0.51 mm; $P = 0.006$). Some FH patients have abnormal IMT of the femoral artery, whereas in others the carotid artery is more affected.

18. Giannoukas AD, Antoniou GA, Saleptsis V, Baros C, Griffin M, Nicolaides AN. Common femoral artery intima-media thickness as marker for cardiovascular disease in asymptomatic adults. Vasa. 2009 May;38(2):147-54

The carotid and femoral IMT separately and in combination were found to be correlated with the FHS risk score, calculated based on either the total cholesterol or low density lipoprotein plasma levels (carotid IMT: $r = 0.28$, $p = 0.035$, and $r = 0.35$, $p = 0.007$, respectively, femoral IMT: $r = 0.38$, $p = 0.003$, and $r = 0.43$, $p = 0.001$, respectively, carotid-femoral IMT: $r = 0.37$, $p = 0.005$, and $r = 0.46$, $p = 0.0001$, respectively).

19. Neiva Neto EC, Piatto MJ, Paschôa AF, Godoy Ide B, Schlaad SW, Van Bellen B. Intima-media thickness: correlation between carotids, vertebral artery, aorta and femoral arteries. IntAngiol. 2015 Jun;34(3):269-75

Considering IMT equal or greater than 0,8mm, there was positive and significant correlation between the values obtained for the examined arteries (internal, external and common carotid, femoral arteries and the abdominal aorta).

20. Griffin M, Nicolaides A, Tyllis T, Georgiou N, Martin RM, Bond D, Panayiotou A, Tziakouri C, Doré CJ, Fessas C. Carotid and femoral arterial wall changes and the prevalence of clinical cardiovascular disease. Vasc Med. 2009 Aug;14(3):227-32

Maximum thickness of IMT in the carotid bifurcation (IMTmax) and number of carotid and femoral bifurcations with plaque and total plaque thickness (TPT) (sum of the maximum plaque measurements taken from the four bifurcations scanned)were associated with 2.9-fold (1.22 to 7.07) and 6.87-fold (2.42 to 19.43) increased odds of CVD prevalence, respectively.

21. Griffin M, Nicolaides A, Tyllis T, Georgiou N, Martin RM, Bond D, Panayiotou A, Tziakouri Ch, Dore CJ, Fessas CH. Plaque area at carotid and common femoral bifurcations and prevalence of clinical cardiovascular disease. IntAngiol. 2010 Jun;29(3):216-25

Total plaque area appears to be more strongly associated with the prevalence of cardiovascular disease than IMT. This finding warrants further prospective studies.

22. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med. 1999 Jan 7;340(1):14-22

The relative risk of myocardial infarction or stroke increased with intima-media thickness ($P<0.001$).The relative risk of myocardial infarction or stroke (adjusted for age and sex) for the quintile with the highest thickness as compared with the lowest quintile was 3.87 (95 percent confidence interval, 2.72 to 5.51).

23. Kafetzakis A, Kochiadakis G, Laliotis A, Peteinarakis I, Touloupakis E, Igoumenidis N, Katsamouris A. Association of subclinical wall changes of carotid, femoral, and popliteal arteries with obstructive coronary artery disease in patients undergoing coronary angiography. Chest. 2005 Oct;128(4):2538-43

IMTC, IMTF, IMTP, and UB showed significant correlation with the presence of obstructive CAD, but only IMTC and IMTF were independent predictive factors, with specificity of 74% and 60% and sensitivity of 76% and 70%, respectively.

24. Kirhmajer MV, Banfic L, Vojkovic M, Strozzi M, Bulum J, Miovski Z. Correlation of femoral intima-media thickness and the severity of coronary artery disease. Angiology. 2011 Feb;62(2):134-9

Significantly higher values of femoral IMT in patients with CAD than in those without CAD ($P = .0000$). A strong positive correlation between femoral IMT and the severity of CAD expressed by the Gensini Score ($P = .0000$).

25. Lisowska A, Musiał WJ, Lisowski P, Knapp M, Małyszko J, Dobrzycki S. Intima-media thickness is a useful marker of the extent of coronary artery disease in patients with impaired renal function. Atherosclerosis. 2009 Feb;202(2):470-5

Higher values of IMT in the peripheral arteries were observed in patients with CAD than in those without (CCA-0.91 vs 0.61 mm, carotid bulb-1.31 vs 0.67, CFA-1.38 vs 0.63 respectively, p<0.0001). Lower values of GFR in patients with three-vessel disease were observed than in those patients with one- or two-vessel disease (p<0.05).

26. Lekakis JP, Papamichael C, Papaioannou TG, Stamatelopoulos KS, Cimponeriu A, Protogerou AD, Kanakakis J, Stamatelopoulos SF. Intima-media thickness score from carotid and femoral arteries predicts the extent of coronary artery disease: intima-media thickness and CAD. Int J Cardiovasc Imaging. 2005 Oct;21(5):495-501

A high risk IMT score predicted an extended coronary artery disease although a low or medium risk IMT score cannot exclude the possibility of multivessel disease. Also, a high risk group could predict the performance of revascularization procedures and all cardiovascular events during a follow-up of 14.5 +/- 2.4 months.

27. Lisowska A, Knapp M, Bolińska S, Lisowski P, Krajewska A, Sobkowicz B, Musiał WJ. The importance of intima-media thickness (IMT) measurements in monitoring of atherosclerosis progress after myocardial infarction. Adv Med Sci. 2012 Jun 1;57(1):112-7

Non-compliant patients had statistically significant higher IMT values after follow-up when compared to compliant subjects (1.62 vs 1.20, p=0.017). Patients with higher IMT values were reported to have cardiac events more frequently during the follow-up (p<0.05).

28. Held C, Hjemdahl P, Eriksson SV, Björkander I, Forslund L, Rehnqvist N. Prognostic implications of intima-media thickness and plaques in the carotid and femoral arteries in patients with stable angina pectoris. Eur Heart J. 2001 Jan;22(1):62-72

Femoral intima-media thickness was related to cardiovascular death or myocardial infarction, as well as to revascularization, whereas femoral plaques were only related to the latter.

29. Suurküla M, Fagerberg B, Wendelhag I, Agewall S, Wikstrand J. Atherosclerotic disease in the femoral artery in hypertensive patients at high cardiovascular risk. The value of ultrasonographic assessment of intima-media thickness and plaque occurrence. Risk Intervention Study (RIS) Group. ArteriosclerThromb Vasc Biol. 1996 Aug;16(8):971-7

Plaque occurrence and mean intima-media thickness in the right common femoral artery were significantly associated with ankle-arm index both in the right and left leg.

30. Cheng KS, Tiwari A, Baker CR, Morris R, Hamilton G, Seifalian AM. Impaired carotid and femoral viscoelastic properties and elevated intima-media thickness in peripheral vascular disease. Atherosclerosis. 2002 Sep;164(1):113-20

Subjects with PVD have significantly altered femoral elastic properties including Petersen's elastic modulus (5.94 (4.98) vs 3.64 (3.27) mmHg x 10(3), P=0.025) and stiffness index (58.42 (47.76) vs 36.96 (33.43), P=0.033). The femoral (1.05 (0.39) vs 0.69 (0.31) mm, P<0.001) IMTs are also significantly elevated in PVD patients.

31. Paul TK, Srinivasan SR, Wei C, Li S, Bhuiyan AR, Bond MG, Tang R, Berenson GS. Cardiovascular risk profile of asymptomatic healthy young adults with increased femoral artery intima-media thickness: The Bogalusa Heart Study. Am J Med Sci. 2005 Sep;330(3):105-10

The top and bottom fifth percentiles of IMT differed with respect to age (P<0.001), systolic blood pressure (P<0.05), diastolic blood pressure (P<0.05), total cholesterol (P<0.01), low-density lipoprotein (LDL) cholesterol (P<0.001), non-high-density lipoprotein (HDL) cholesterol (P<0.01) and smoking status (P<0.01)

32. Paul TK, Srinivasan SR, Chen W, Li S, Bond MG, Tang R, Berenson GS. Impact of multiple cardiovascular risk factors on femoral artery intima-media thickness in asymptomatic young adults (the Bogalusa Heart Study). Am J Cardiol. 2005 Feb 15;95(4):469-73

Systolic blood pressure, age, male gender, cigarette smoking, and total cholesterol/high-density lipoprotein cholesterol ratios related independently, in that order, to IMT.), with respective mean IMT values of 0.66, 0.69, 0.73, and 0.79 mm for 0, 1 to 2, 3, and 4 to 5 risk factors.

33. Paul TK, Chen W, Srinivasan SR, He J, Berenson GS. Contrast of the impact of multiple cardiovascular risk factors on the femoral and carotid intima-media thickness in asymptomatic young adults: the Bogalusa Heart Study. Atherosclerosis. 2011 Jun;216(2):359-64

Systolic blood pressure followed by age were the major determinant risk factors for the IMT of all arterial segments except carotid bulb for which age was the major predictor.

34. Timir K. Paul, Wei Chen, Sathanur R. Srinivasan, Janet Rice, AhmetToprak, Jiang He, and Gerald S. Berenson. Framingham risk score is associated with femoral artery intimamedia thickness in asymptomatic young adults (The Bogalusa Heart Study). Atherosclerosis. 2010 December ; 213(2): 627–631

A significant positive linear relationship between tertiles of FRS and IMT of femoral artery was noted in whites and blacks alike (p for trend < 0.0001).

35. Stamatelopoulos KS, Papamichael CM, Zacharoulis A, Papaioannou T, Kollias GE, Kyrkou K, Chrysochoou EE, Voidonikola P, Alevizaki M, Lekakis JP. Heart score calculated in individuals younger than 40 years is related to vascular markers of early atherosclerosis. Eur J CardiovascPrevRehabil. 2008 Dec;15(6):619-24

In Heartscore calculator mortality risk (MR) 60 in the younger significantly correlated with all measured vascular markers whereas Systematic Coronary Risk Evaluation risk charts for relative risk (RR) significantly correlated with carotid IMT.

36. Youssef F, Seifalian AM, Jagroop IA, Myint F, Baker D, Mikhailidis DP, Hamilton G. The early effect of lipid-lowering treatment on carotid and femoral intima media thickness (IMT). Eur J Vasc Endovasc Surg. 2002 Apr;23(4):358-64

Patients (14 men; 11 women), median age 69 years (range: 48-81) had a CFA-IMT mean (SD) of 0.83 (0.13) mm pre-treatment, 0.80 (0.09) mm after 4 weeks, and 0.69 (0.14) mm after 8 weeks (p=0.0003).

37. De Sauvage Nolting PR, de Groot E, Zwinderman AH, Buirma RJ, Trip MD, Kastelein JJ. Regression of carotid and femoral artery intima-media thickness in familial hypercholesterolemia: treatment with simvastatin. Arch Intern Med. 2003 Aug 11-25;163(15):1837-41

Mean +/- SD combined baseline IMT was 1.07 +/- 0.23 mm. After treatment with simvastatin for 2 years, this IMT decreased by a mean of 0.081 mm (95% confidence interval, -0.109 to -0.053; P<.001), with its largest reduction in the femoral artery (-0.283 mm; P<.001).

38. van Wissen S, Smilde TJ, de Groot E, Hutten BA, Kastelein JJ, Stalenhoef AF. The significance of femoral intima-media thickness and plaque scoring in the Atorvastatin versus Simvastatin on Atherosclerosis Progression (ASAP) study. Eur J CardiovascPrevRehabil. 2003 Dec;10(6):451-5

IMT was measured at baseline and at 2 years. At baseline, femoral IMT was 1.69 mm in the atorvastatin group and 1.61 mm in the simvastatin group; at 2 years, IMT increased by 0.06 mm (P=0.24) and 0.15 mm (P=0.012), respectively. No significant differences were obvious between these two treatment arms (P=0.26). Femoral plaques were present in 64.7% in the atorvastatin group and 56.1% in the simvastatin group at baseline; after 2 years, these proportions rose to 66.0% (P=0.47) and 67.3% (P=0.02), respectively (P=0.87 between treatment arms).