Rapid ultrasound score as an indicator of atherosclerosis' clinical manifestations in a population of hypertensives: the interrelationship between flow-mediated dilatation of brachial artery, carotid intima thickness, renal resistive index and retina resistive index of central artery

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Abstract

Objective: Flow-mediated dilatation (FMD) of brachial artery, renal resistive index (RRI), retina resistive index of central artery (RRICA) and carotid intima-media thickness (IMT) have been used for ultrasound assessment of cardiovascular risk as good surrogate markers of pre-clinical atherosclerosis. We investigated the interrelationship of these four parameters and examined whether an integrated score is a good indicator of atherosclerotic disease in hypertensives.

Methods: One-hundred fifty-two consecutive subjects were enrolled in this study between April 2004 and April 2005. Each patient underwent cerebral computed tomography, coronarography, carotid, renal, central retinal and femoral arteries Doppler ultrasonographic evaluation. Statistical analysis was performed using ANOVA, Fisher test, Pearson correlation and stepwise regression analyses.

Results: FMD, RRICA, IMT and RRI were significantly correlated with each other. In multiple regression analysis age, pulse pressure, hypertension duration were independently related with the four parameters. Eighty-one findings of total atherosclerotic disease (ADAD were recorded overall (15 cerebrovascular disease, 20 coronary heart disease or myocardial infarction, 22 carotid plaques and 24 low limb plaques). Using an integrated score we were able to divide the population into three scoring bands. In the lowest band we classified 87 patients with 16% of total AD; in the intermediate 40 patients with 30% of total AD, in the highest 25 patients with 54% of total AD. Differences between groups were significant ($p<0.05$).

Conclusion: A potential benefit of these integrated, low-cost and easy-to-detect parameters, is the stratification of patients with atherosclerotic risk. This method may prove useful in discovering those with atherosclerosis in a pre-clinical stage for whom therapy initiated before complications could reduce the risk for a cerebro-cardio-vascular event. *(Anadolu Kardiyol Derg 2014; 14: 9-15)*

Key words: echocardiography, peripheral vascular disease, score for atherosclerosis, regression analysis, sensitivity, specificity

Introduction

Hypertension has been identified as the leading risk factor for mortality, and is ranked third as a cause of disability-adjusted life-years (1). More than a quarter of the world's adult population (totaling nearly one billion) had hypertension in 2000, and this proportion will increase to 29% (1.56 billion) by 2025 (2-4). Therefore, it should be addressed as an important public-health challenge worldwide. Prevention, detection, treatment, and control of this condition should receive high priority. The magnitude of the burden of hypertension needs not only an increase in awareness, treatment, and control of this condition, but also concerted efforts that target primary prevention (4).

Atherosclerosis is an essential link between hypertension as a risk factor and the clinical disease, such as a cerebro-vascular accident, myocardial infarction or arteriopathy of the lower limb. It develops over many years and it is clinically expressed as a

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cerebro-cardio-vascular complication. Progress in noninvasive ultrasound techniques of investigating arteries makes it possible to detect atherosclerosis early, before it becomes symptomatic.

A number of methods have been applied for the noninvasive ultrasound assessment of cardiovascular risk. These include flow-mediated dilatation (FMD) of the brachial artery, renal resistive index (RRI), retina resistive index of central artery (RRICA) and carotid intima-media thickness (IMT). IMT detects morphological changes of carotid artery, consisting of both an intimal atherosclerotic process and medial hypertrophy; in fact, examination of the carotid arteries with measurement of IMT can predict both stroke and myocardial infarction (5-14).

Impairment of vascular endothelial function is the initial step in the development of atherosclerosis. Endothelial dysfunction is an important determinant of altered vascular reactivity and plays a major role in the genesis of micro- and macro-vascular complications. Impairment of endothelial dependent vasodilatation, is due mostly to reduced endothelial-produced nitric oxide (NO) (15). It is altered in all conditions of increased cardio-vascular risk, such as hypertension, smoke, hypercholesterolemia. Several studies demonstrated that the reduction of NO-mediated vasodilatation is predictive of coronary and cerebro-vascular events (16, 17).

FMD, induced by reactive hyperemia, is known to be an endothelium dependent process. It can be detected using high resolution in the superficial arteries such as brachial artery and it was demonstrated to be an early marker of cardiovascular atherosclerotic damage (18-20).

Hypertension comes right after diabetes as the cause of end stage renal disease. Hypertension is directly linked to the development of end stage renal disease, and it can also accelerate the decline in renal function in patients with other diseases involving the kidneys. The increasing incidence of end stage renal disease in patients with essential hypertension may be related to underdiagnosis of renal damage in patients with hypertension. RRI is demonstrated to be a specific prognostic index of renal disease progression (21-23). Hypertension induced damage to small cerebral vessels and it is traditionally estimated by fundoscopic exam. However opposite to the 1930s, when the Keith Wagener and Baker classification of hypertensive eye ground changes in four grades was formulated, today Grades 1 and 2 arteriolar changes are often noted, but there is no evidence that these have an important prognostic value. Therefore, it is doubtful whether grades 1and 2 retinal changes can be used as evidence of target organ damage to stratify global cardiovascular risk (24). More selective methods for investigating ocular damage in hypertension are being developed, but remain research applications. CT and MRI have proven to be effective in identifying ischemic injury within minutes of arterial occlusion. Despite the clinical relevance of these observations, the limited availability, the time-consuming nature and the cost of MRI does not yet allow a widespread use for screening purposes. Recently, central artery of retina resistive index (RRICA) was introduced for qualitative assessment of cerebral small-vessel disease. Patients with vascular risk factors such as hypertension, often show an important reduction of systolic and diastolic central artery velocity of the retina. This flow parameter is useful for quantitative assessment of cerebral small vessel serious diseases (25).

These four methods have been used in a clinical setting because they are good surrogate markers of clinical atherosclerosis. The impact of risk factors on atherosclerosis, such as hypertension, hyperlipidemia, diabetes mellitus, can be evaluated by these four ultrasound parameters and therefore they can improve with appropriate therapy (26, 27). In addition, ultrasound is largely used, easily available and not expensive, which makes it a perfect method for screening purposes.

Several studies have demonstrated a significant correlation between RRI and carotid IMT (28) and between RRI and RRICA (29), a negative correlation between FMD and IMT (30) and between FMD and coronary heart disease (31). In addition, no data has yet been published on the interrelation of these four measurements together. Atherosclerosis is a multi-organ disease, and in this perspective a multi-district exam, based on the combination of these four parameters, may be useful to study the whole atherosclerotic process.

Therefore, the aim of this study is to investigate whether the connection of these four ultrasound parameters is an effective tool for the stratification of atherosclerosis in a population of hypertensive. Our ultimate goal is to produce a final score (which is a result of FMD, RRI, RRICA, IMT single measurements) and to evaluate how this score could be an indicator for hypertensive patients.

Methods

Study population

One hundred fifty-two consecutive subjects were enrolled in this study between April 2004 and April 2005. They were recruited from outpatients and inpatients (from coronary intensive care unit or Emergency room). The characteristics of the study subjects are shown in Table 1. Thirty healthy volunteers were examined for reference values.

Inclusion criteria: All patients were affected by hypertension between the first and the second stage. Hypertension was diagnosed following guidelines (24). Each patient had in his medical record all the following tests before being recruited. These tests included cerebral computed tomography (CT), coronarography, carotid and femoral Echo-Doppler evaluation. Exams were made 2 years before the start of the study. If a single test was not included in the medical record, this was performed in our unit at the time of the admission.

Exclusion criteria: Patients with renal failure, congestive heart failure, atrial fibrillation, severe valvular heart disease and subclavia artery occlusion, bilateral carotid surgery, bilateral or unilateral occlusion of carotid artery were excluded from the study.

Each patient signed an informed consent form for the study.

Study protocol

A history and risk factors were assessed at the first examination. Smokers included current or former smokers. Physical examination and laboratory tests were performed in all subjects. Subjects were fasting for at least 8 to 12 h before the study, and they were studied in a quiet, temperature controlled room. All medications were withheld for at least four half-lives when possible. In addition, subjects were not exercising and not ingesting substances that might affect FMD such as caffeine, high-fat foods and vitamin C or use tobacco for at least 4 to 6 h before the study. The parameters machine was operating nonstop during each study. In addition, the sonographer was not aware of patient history in order to have a blind data collection. Toshiba Power Vision 6000 (Toshiba, Japan), equipped with a variable-frequency phased-array transducer and tissue Doppler imaging (TDI) was used for all ultrasound examinations.

Assessment of atherosclerotic disease

Clinical atherosclerotic disease:

a) Myocardial infarction and stable or unstable angina, coronary revascularization procedures or coronary stenosis >60% at coronarography (32).
b) Cerebro-vascular stroke. Ischemic stroke was diagnosed by CT evidence of stroke without intracranial hemorrhage;
c) Carotid and or femoral plaques stenosing vessel lumen >50%, carotid and femoral surgery or transluminal angioplasty.

Blood pressure measurement

Blood pressure (BP) was measured by mercury sphygmomanometer with an appropriate size rubber cuff. Readings were based on Korotkoff first and fifth phase sounds. Three consecutive BP readings were obtained with the subject in supine position after a rest for at least 15 minutes. The average of the last 2 readings was used for the analyses, recorded to the nearest 2 mm on the scale. Measurements were performed early in the morning and carried out by a trained investigator.

Laboratory tests

We determined lipid profile, and fasting plasma glucose, by standard laboratory methods.

Renal Color-Doppler ultrasonography

Based on the mean and distribution of RRI in normal volunteers, the normal upper limit was found to be 0.60±0.03. RRI examinations were performed with 3.5 mHz transducer, with subject in supine position; the transducer was placed on the lumbar portion, the kidney was displayed by tomographic echography Blood flow was visualized with color-Doppler sonography superimposed on tomographic image. Thereafter, Doppler signal was obtained from the arcuate arteries at the corticomedullary junction. RRI was calculated by the following equation: peak systolic wave - peak diastolic wave/peak systolic wave. RRI was determined at least three times for one kidney and then averaged. The mean RRI of the right and left kidneys was used for the subsequent analyses (33). The total examination time was 1 minutes for each kidney. All measurements were made by one sonographer at the time of examination.

Table 1. Reference ranges and scores of ultrasound parameters considered

Test	Range	Score	Test	Range	Score
1. FMD (%)	≥4	0	3. IMT (mm)	≤0.7	0
	≥2 <4	1		>0.7 ≤0.9	1
	<2	2		>0.9	2
2. RRI	≤0.60	0	4. RRICA	≤0.75	0
	>0.60 ≤0.75	1		>0.75 ≤0.80	1
	>0.75	2		>0.80	2
			5. RIBA (15 seconds)	≤0.80	0
				≥0.80 ≤0.90	1
				>0.90	2

The table shows the reference ranges of FMD, RRI, RRICA, IMT to consider in order to provide a score for each single parameter. Total scoring is calculated from the sum of these four single measurements. In addition, a fifth parameter, the resistive index of brachial artery at 15 seconds from ischemia. (RIBA) was also measured in order to provide further data on endothelial function.
RRICA - retina resistive index of central artery; FMD - flow-mediated dilatation the brachial artery; IMT - carotid intima-media thickness; RIBA - resistive index of brachial artery; RRI - renal resistive index

Common carotid artery scan

Examination of the carotid was performed with a transducer frequency of 7.5 MHz. An electrocardiography (ECG) monitor integrated with the monitor machine was also applied. All measurements were made by one sonographer at the time of examination. Measurements involved a primary transverse and longitudinal scanning of common carotid artery, bifurcation and internal carotid. The IMT was measured on the far wall of the middle segment of the common carotid artery as the distance between the lumen-intima interface and the media-adventitia interface at 10 mm proximal to the bifurcation. All measurements were made at R-wave peak at a site free of plaque. Near and far wall of carotid were scanner longitudinally and transversally to assess the presence of plaques. The presence of plaques was defined as localized echo structures encroaching into vessel lumen for which the distance between the media adventitia interface and internal side of the lesion was=1.3 mm, or as the presence of calcification (34).

Color Doppler ultrasonography of central artery of retina

Orbital Doppler sonographic examinations were performed with 7.5 -MHz linear probe. Sterile coupling gel was applied to closed eyelids, and all of the settings of the machine were adjusted to low flow determination (low pulse repetition frequency, high Doppler gain). The color Doppler images of the vessels were obtained in axial or oblique plans. Central retinal arteries were found within the distal 5 mm part of the optic nerves (the ophthalmic artery is the first intracranial branch of the internal carotid artery. It enters the orbit through the optic canal as the main artery. Most of its branches, including the central retinal artery arise within the posterior third of the orbit). The central retinal artery enters the optic nerve distal to the optic canal and ends in the retina In pulsed Doppler mode resistive index was calculated (resistive index: peak systolic- end diastolic peak/ peak systolic). Based on the mean and distribution of RRICA in normal volunteers, the normal upper limit was found to be 0.70±0.03 (25). The total examination time was 1 minutes.

Measurement of FMD and flow of brachial artery

The right brachial artery was scanned over a longitudinal section, 3-5 cm above the right elbow.

Depth and gain settings were optimized to identify the lumen-to-vessel wall interface. An ECG monitor integrated with the machine was also applied. When an adequate image was obtained, the surface of the skin was marked, and the arm was kept in the same position throughout the study. A pneumatic tourniquet placed around the forearm distal to the target artery was inflated to a pressure of 250 mm Hg, and inflation was held for 5 min. Increased flow was then induced by sudden cuff deflation. A second scan was performed continuously for 60 s before and 120s after cuff deflation. The ultrasound images were recorded on S-VHS videotape. The diameter of the brachial artery was measured from the anterior to the posterior interface between the media and adventitia ("m line")at a fixed distance. The mean diameter was calculated from four cardiac cycles synchronized with the R-wave peaks on the ECG. All measurements were made at end diastole to avoid possible errors resulting from variable arterial compliance. Maximal vasodilatation was observed 45 -60 s after cuff release. The change in diameter caused by FMD was expressed as the percent change relative to that in the initial resting scan. A midartery pulsed Doppler signal was obtained upon immediate cuff release and no later than 15 s after cuff deflation to assess hyperemic velocity (35). In addition, we evaluated also the percentage of telediastolic velocity peak in comparison with systolic velocity peak (resistive index of brachial artery=RIBA) before compression and at 15 s from decompression.

Composition of the score

The score is composed by the combination of RRI, RRICA, IMT, FMD single evaluations. Each of these parameters was divided into tertiles according ranges reported in Table 2. A score from 0 to 2 was based on the Table.

The sum was calculated, and the population grouped into three bands respectively with a total score of 0-4, >4-6, >6-8.

In addition, a fifth parameter, the resistive index of brachial artery (RIBA=systolic velocity peak diastolic velocity peak/systolic velocity peak) was also measured to provide further data on endothelial function.

Statistical analysis

Statistical analysis was carried out by GB-STAT version 6.50 (Dynamic Microsystems, Inc., Silver Spring, MD, USA). Comparison among groups was performed using the ANOVA test. Comparisons of categorical data were made using Fisher's exact test. Pearson's correlation coefficients were used to investigate the linear connection between variables. Stepwise forward regression analysis was performed to assess which factors independently influence FMD, RRI, ACR, IMT and was used to determine which variable was selected first. Significance was defined as $p<0.05$. The results are expressed as means±SD.

For RRI, IMT, RRICA, RIBA and FMD inter and intra-reader variability was good (K>0.80).

Results

Relationship between estimated indexes and clinical variables

All parameters were significantly correlated with each other; Table 3 shows the Pearson's correlation matrix between FMD, IMT, RRI and RRICA. Dividing the population sample into three groups according the score, the baseline characteristics of the groups significantly differ only for duration of hypertension and pulse pressure ($p<0.05$).

Stepwise forward regression analysis was performed with RRI, FMD, IMT, RRICA as dependent variables. Age, pulse pressure, and duration of hypertension were all independently and significantly ($p<0.05$) related with RRI, FMD, IMT, RRICA; in addition to the mentioned variables total cholesterol was significantly related with IMT and fasting plasma glucose with RRICA.

Table 4 shows sensibility, specificity, negative predictive value (NPV) and positive predictive value (PPV) for a score >6 substituting the flow mediated post ischemic dilatation (FMD) with the resistive index of brachial artery (RIBA). It was observed an advance in terms of sensitivity (from 0.48 to 0.51), specificity (from 0.95 to 0.98) and positive predictive value (from 0.80 to 0.92) if we consider RIBA rather than FMD in the assessment of endothelial function.

Atherosclerotic disease in relation to score classification

As shown in Figure 1, in the lowest rank (0-4 points) we classified 87 patients; in the intermediate rank we classified 40 patients; in the highest rank we classified 25 patients. We recorded 81 findings of total atherosclerotic disease (AD) among the entire sample (15 stroke, 20 coronary heart disease or myocardial infarction, 22 carotid plaque and 24 low limb plaque) in 42 patients. 16% of the total atherosclerotic disease were found in the lowest band (13 a.d in 7 patients), 30% of total AD in the intermediate band (25 AD in 15 patients) and 54% of total AD in highest one (43 AD in 20 patients). Differences among groups were statistically significant ($p<0.05$).

Discussion

Analyzing the baseline characteristics of the population sample, we found a significant difference regarding duration of hypertension among the three groups ($p<0.05$). The patients in the group A (score 0-4) have a duration of hypertension of 6±7 years, in the group B (score >4-6) have a duration of hypertension of 8±5 years and in the group C (score >6-8) have a duration of hypertension of 9±7 years. The higher prevalence of AD within higher scoring group compared with the others, as duration of hypertension, could be considered a risk factor itself. Except for pulse pressure, we found no significant differences regarding the other baseline variables recorded; however, a negative trend could still be observed in the higher scoring group, especially considering metabolic parameters, systolic and diastolic pressure. A correlation could be seen among the four ultrasound parameters examined. In fact, high RI in renal and ophthalmic districts correlates with an increase in IMT and with the post-ischemic diastolic flow decreased in the brachial artery. This finding is consistent with the assumption that atherosclerosis is generally a multi-district disease. Consequently, brachial FMD, carotid IMT, RRI and RRICA evaluate different aspects of atherosclerosis as well as different arterial sites. An array of tests should provide better discrimination than a single test. The score described in this report, represents an effort to quantify the evidence for early atherosclerotic disease. This score therefore provides a continuum from no evidence for disease to strong evidence for atherosclerotic disease.

The scoring system was designed so that for each single parameter a score from 0 to 2 was provided. This allowed us to divide the studied population into three bands with severe, moderate and low atherosclerotic manifestations. In particular, in the highest band (>6-8 pts) a significant prevalence of cardiovascular events (57%) was observed, such as strokes, myocardial infarction or plaques >50% as demonstrated by CT, coronarography or echocardiograms provided by the patients or performed at time of admission. This band comprising 16% of the whole population sample had 54% of all atherosclerotic diseases. Moreover, this rank includes 73% of the cerebral vascular disease and 60% of coronary heart disease of the entire population studied (Fig. 1).

However, an important potential benefit of this screening procedure is the identification of individuals with low-intermediate scores (0-6 pts) in which we can detect an atherosclerosis in a pre-clinical stage as demonstrated by CT or coronarography investigations. Our score is based on the combination of four parameters. As explained in the methods, the fourth parameter can be either the post ischemic flow mediated dilatation of the brachial artery (FMD) or the resistive index (RIBA) of the same artery. In particular, we observed that these two parameters do not equally correspond. In fact, in our population sample, when substituting RIBA with the post ischemic dilatation of the brachial artery (FMD) an increase in sensitivity was observed (from 0.48 to 0.51) and positive predictive value (from 0.80 to 0.92). This can be explained considering that NO is the major vasodilator, which acts most consistently in the peripheral resistive arteries (small muscle arteries) (36). The impairment of NO-mediated post-ischemic dilatation in small muscle arteries not necessarily corresponds to a reduced brachial artery dilatation in terms of diameter. In fact, if vascular reactivity is altered, it causes high resistances in peripheral small muscle arteries after ischemia, and consequently brachial artery diameter might even increase for more mechanical dilatation. Therefore, RIBA is a more punctual index of peripheral flow changes. Furthermore, it should also be considered that RIBA is a ratio and so less subject to intra- inter-operator variability. Accordingly, the resistive index

Table 2. Clinical characteristics of study patients in relation with total score

Variables	Score 0-4 (A)	Score >4-6 (B)	Score >6-8 (C)	*P*
Number of patients	87	40	25	n.s.
Age, years	60±13	63±8	65±9	n.s.
Male, %	59	61	62	n.s.
Body mass index, kg/m^2	29±4	28±5	27±2	n.s.
Smokers, %	31	29	30	n.s.
Systolic BP, mm Hg	148±9	150±11	152±14	n.s.
Diastolic BP, mm Hg	92±8	91±7	94±8	n.s.
Pulse pressure, mm Hg	55±7	59±8*	57±9	p<0.05
Heart rate, beats/min	72±11	69±10	73±13	n.s.
Duration of hypertension, years	6±7	8±5	9±7†	p<0.05
Fasting plasma glucose, mg/dL	107±28	115±25	119±27	n.s.
Total cholesterol, mg/dL	197±36	201±30	210±33	n.s.
Triglycerides, mg/dL	131±55	141±47	140±51	n.s.
HDL-cholesterol, mg/dL	51±10	49±8	47±9	n.s.

Data are presented as mean±SD and percentage
ANOVA and Fisher test
*A vs. B; †A vs. C.
HDL - high-density lipoprotein; n.s.- non-significant result.

Table 3. Pearson correlation matrix between FMD, IMT, RRI and RRICA

	IMT	RRI	RRICA	FMD	RIBA
AGE	r 0.55	r 0.51	r 0.52	r -0.58	r 0.54
IMT		r 0.48	r 0.45	r -0.40	r 0.49
RRI			r 0.53	r -0.52	r 0.50
RRICA				r -0.46	r 0.48
FMD					r -0.37

RRICA - retina resistive index of central artery; FMD - flow-mediated dilatation the brachial artery; IMT - carotid intima-media thickness; RIBA - resistive index of brachial artery; RRI - renal resistive index

Table 4. Sensitivity (Sens.), specificity (Spec.), negative predictive value (NPV) and positive predictive value (PPV) of tests with score >6 using post ischemic dilatation of the brachial artery (FMD) and resistive index of brachial artery (RIBA)

	Sens.	Spec.	NPV	PPV
Score >6 (with FMD)	0.48	0.95	0.83	0.80
Score >6 (with RIBA)	0.51	0.98	0.83	0.92

of brachial artery (RIBA) should be preferred to post ischemic flow-mediated dilatation of the brachial artery (FMD) in our score.

Study limitations

Several limitations of this study deserve comment.

First, it was not possible to withhold vasoactive medications to all the patients. This could have coherently affected our measurements. However, it should be considered that in these patients vasoactive drugs would normalize the hemodynamic indexes such as RRICA, FMD, RIBA and RRI rather than shifting to pathologic values. Therefore, we hypothesized that if we could have suspended the vasoactive treatments in all the subjects our method would even increase its positive predictive value.

Second, we inquired only about traditional cardiac risk factors and did not examine "novel" risk factors, which might plays a major role in endothelial function and atherosclerosis. For example, hyperhomocysteinemia or elevated C-reactive protein levels have shown to inhibit peripheral arterial vasoreactivity (37, 38) but were not tested in this patient population.

Third, it is possible that age or gender are related to the observed relationship between scoring and AD. It is known that AD increases with the normal aging process. However, in subgroup analysis, age did not appear to be a significant confounding parameter. Therefore, older age does not fully explain the increase in AD in those patients placed in the higher scoring band.

Fourth, we have not screened the population for waist-hip ratio, which, in association with other baseline parameters that we recorded, is an indicator of metabolic syndrome. Waist-hip ratio was demonstrated to be an indicator endothelial function (39), and it could also influence the other scoring parameters.

Fifth, three of the four parameters identified are not used in common practice and, except one (IMT), there are no generally accepted standardized measures, however, our reference parameters are obtained from a population of healthy volunteers and are in agreement with the values reported in other studies in the literature (18-30).

Sixth, our report is the foundation for a follow-up perspective study, which is actually on-going, aimed at evaluating the predictivity of our scoring system, especially to those patients with low-intermediate scoring.

Conclusion

Hypertension and other traditional risk factors have limited predictive value, recent technologic progress now allows the diagnosis of early disease, a two stages preventive strategy can be proposed: screening for traditional risk factors, followed by investigation of pre-clinical atherosclerosis. The traditional primary preventive screening for risk factors discovers many individuals who have no vascular precursors of atherosclerosis and excludes many individuals destined to develop progressive atherosclerosis (40). In this context, our method could be a good start for the very first selection of those patients with cardiovascular risk factors to be sent to more complex tests such as CT or coronarography. It provides an opportunity to evaluate large patient populations in a noninvasive method and may turn useful in avoiding unnecessary exams. Therefore, the use of integrated, low-cost and easy to detect ultrasound parameters could improve the specificity and sensitivity of discovering those individuals for whom preventing the progression of vascular disease is possible. The scoring system adopted can be a good surrogate marker of multi-organ damage. It should be also underlined how the method is highly reproducible, relatively inexpensive and largely available.

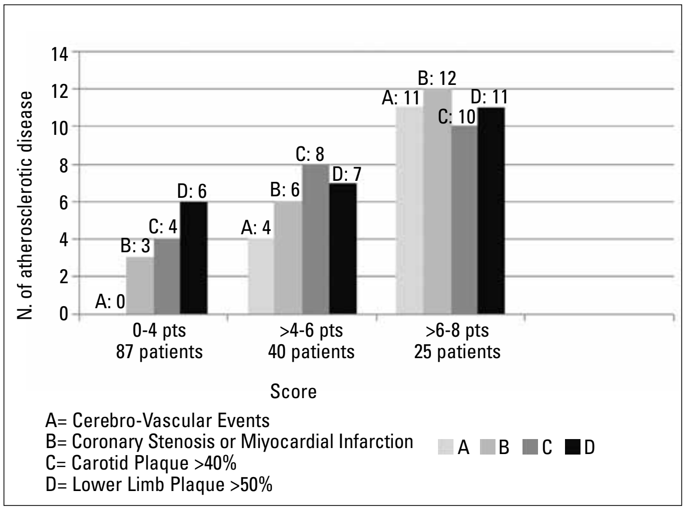

Figure 1. Atherosclerotic disease in relation to final score classification. Distribution of the population within the three scoring bands (0-4 pts, 4-6 pts, 6,8 pts). For each band is reported the number of the diverse atherosclerotic disease (AD) assessed. 81 AD were recorder among the whole sample

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