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Peripheral Vascular Endothelial Function Testing as a Noninvasive Indicator of Coronary Artery Disease

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OBJECTIVES We studied whether assessment of endothelium-dependent vasomotion (EDV) with brachial artery ultrasound (BAUS) imaging predicts the presence or absence of coronary artery disease (CAD) as defined by exercise myocardial perfusion imaging (ExMPI).

BACKGROUND Abnormalities in EDV can be detected in arteries before the development of overt atherosclerosis, and its presence may predict poor long-term prognosis. Brachial artery ultrasound during reactive hyperemia is a noninvasive method of assessing peripheral EDV.

METHODS Clinically-indicated ExMPI along with BAUS were performed in 94 subjects (43 women, 51 men). Coronary artery disease was defined by myocardial ischemia or infarction on single photon emission computed tomography images. Flow-mediated dilation (FMD) after upper arm occlusion was defined as the percent change in arterial diameter during reactive hyperemia relative to the baseline.

RESULTS Subjects with CAD by ExMPI (n = 23) had a lower FMD (6.3 ± 0.7%) than those without CAD by ExMPI (n = 71) (10.5 ± 0.6%; p = 0.0004). Flow-mediated dilation was highly predictive for CAD with an odds ratio of 1.32 for each percent decrease in FMD (p = 0.001). Based on a receiver-operator analysis, an FMD of 10% was used as a cut-point for further analysis. Twenty-one of 23 subjects who were positive for ExMPI had an FMD <10% (sensitivity 91%), whereas only two of 40 subjects with an FMD ≥10% were ExMPI-positive (negative predictive value: 95%). There was a correlation between the number of cardiac risk factors and FMD. Individuals with an FMD <10% exercised for a shorter duration than those with an FMD ≥10% (456 ± 24 vs. 544 ± 31 s, respectively; p = 0.02).

CONCLUSIONS Assessment of EDV with BAUS has a high sensitivity and an excellent negative predictive value for CAD and, thus, has the potential for use as a screening tool to exclude CAD in low-risk subjects. Further standardization of BAUS is required, however, before specific cut-points for excluding CAD can be established. (J Am Coll Cardiol 2001;38:1843–9)

Impaired endothelium-dependent vasomotion (EDV) is a diffuse disease process resulting in abnormal regulation of blood vessel tone and the loss of several atheroprotective effects of the normal endothelium (1). Abnormal EDV can be detected in the coronary circulation before the development of angiographically significant atherosclerotic plaque (2), and this has been shown to be associated with an increased risk of future cardiac events (3,4). Although assessment of coronary artery endothelial function has the advantage of examining the vascular bed with the greatest clinical relevance, it requires a specialized invasive procedure that is costly and not without risk.

In addition to the coronary circulation, endothelial dysfunction occurs concurrently in peripheral arteries, and the assessment of peripheral EDV provides an opportunity to evaluate larger patient populations in a noninvasive fashion (5). Brachial artery ultrasound (BAUS) imaging during reactive hyperemia is a widely used tool for quantifying EDV (6), and impaired peripheral endothelial function may also be a marker of increased future cardiovascular risk (7). Brachial artery ultrasound can detect abnormalities in EDV in subjects at risk for atherosclerosis (8), and medical interventions and lifestyle changes that reduce coronary artery disease (CAD) risk are associated with improved peripheral endothelial function (9–12).

Previous studies have shown a modest correlation between abnormalities in peripheral artery EDV detected by BAUS and coronary artery EDV defined by coronary angiography with vasoactive medications (13,14). A majority of patients presenting for cardiovascular evaluation, however, do not undergo invasive vascular testing. Therefore, we evaluated whether flow-mediated dilation (FMD) of the brachial artery predicts the presence or absence of CAD defined by exercise myocardial perfusion imaging (ExMPI) in low- to intermediate-risk subjects.

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Abbreviations and Acronyms

CAD = coronary artery disease
BAUS = brachial artery ultrasound
EDV = endothelium-dependent vasomotion
ExMPI = exercise myocardial perfusion imaging
FMD = flow-mediated dilation
LVEF = left ventricular ejection fraction
NMD = nitroglycerin-mediated vasodilation
ROC = receiver operator characteristic
SPECT = single photon emission computed tomography

METHODS

Patient population. Consecutive subjects over 18 years of age without prior history of CAD who presented for clinically indicated ExMPI at the New England Medical Center (Boston, Massachusetts) were recruited and enrolled in this study. All subjects gave their written informed consent to participate, and the protocol was approved by the institutional Human Investigation Review Committee. Subjects were instructed to fast overnight, to refrain from smoking, ingesting alcohol or caffeine on the day of testing and to hold any vasoactive medications for 12 h before the imaging studies. Exclusion criteria included an inability to exercise, recent myocardial infarction or unstable angina (within three months), congestive heart failure or significant valvular heart disease.

The presence or absence of the following cardiovascular risk factors was assessed in each subject: male gender, hypertension (systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg or being on an antihypertensive medication), hyperlipidemia (total serum cholesterol >220 mg/dl or taking lipid-lowering medication), diabetes mellitus (treated with an oral hypoglycemic agent or insulin or having fasting glucose levels >140 mg/dl), family history of CAD (having first or second degree relatives with premature cardiovascular disease), postmenopause and smoking (having smoked at least five cigarettes per day within the last month).

Stress testing protocol. Subjects performed a symptom-limited treadmill test utilizing a Bruce exercise protocol under standard supervision and continuous electrocardiographic monitoring. Subjects received intravenous technetium-99m sestamibi for stress perfusion imaging 1 to 2 min before the completion of exercise. Exercise stress images were acquired approximately 30 min after the completion of exercise. Gated single photon emission computed tomography (SPECT) imaging was also performed at this time for analysis of left ventricular function (expressed as left ventricular ejection fraction [LVEF]). Resting perfusion images were obtained before the exercise portion of the test. The SPECT images were analyzed by readers blinded to the study protocol and BAUS results, and were considered positive if perfusion abnormalities were detected (myocardial ischemia or infarction) and negative if no perfusion abnormalities were found.

Endothelial function testing. At least 2 h after completion of the ExMPI, BAUS testing was performed after a protocol (11) similar to that described by Celermajer et al. (15). Longitudinal brachial artery images were obtained with a high-resolution (10 MHz) linear-array vascular transducer (General Electric, Vingmed, System Five, Horten, Norway). Subjects were studied under quiet conditions while they were in the supine position in a temperature-controlled room. After a 10-min equilibrium period, baseline two-dimensional images of the right brachial artery were obtained approximately 2 cm above the antecubital fossa. A blood pressure cuff (Hokanson, Bellevue, Washington) placed proximal to the imaging transducer on the upper arm was inflated to suprasystolic pressure for exactly 5 min. The vessel was imaged continuously for 1 min after release of occlusion, and reactive hyperemia was confirmed by pulse-wave Doppler interrogation. Baseline resting brachial artery dimensions were again obtained 10 min later. Subjects were given sublingual nitroglycerin (400-μg tablet), and the brachial artery was imaged for 5 min.

Endothelium-*dependent* vasomotion was determined by the maximal brachial artery diameter after exactly 60 s of reactive hyperemia compared with the baseline vessel diameter and was expressed as percent FMD. Endothelium-*independent* vasodilation was defined as the maximum brachial artery diameter 5 min after administration of nitroglycerin compared with the baseline vessel diameter and was expressed as percent nitroglycerin-mediated dilation (NMD). Brachial artery measurements were performed with ultrasonic calipers by independent observers blinded to the ExMPI results. Maximal end-diastolic brachial arterial diameter was calculated within a 5-cm segment of the vessel as the mean of five evenly spaced measurements of the distance from the near to the far arterial wall along a line perpendicular to the long axis of the artery. Mean intraobserver and interobserver variability of brachial reactivity measurements in our laboratory on normal volunteers were 1.9% and 2.8%, respectively.

Statistical analysis. A sample size of approximately 90 patients was chosen to provide 80% power (at $\alpha = 0.05$) to determine an absolute difference of 2% in FMD (16). Data were entered into Excel and analyzed with SPSS (Version 10.0, SPSS, Inc., Chicago, Illinois). Data are expressed as mean ± SEM. Univariate analysis (t test) and Spearman rank correlation were performed to demonstrate potential associations with FMD. Multivariate stepwise logistic regression analysis (forward selection with likelihood ratio criterion for selection variables; 0.05 to enter, 0.10 to remove) was used to estimate the relationship between FMD and CAD and to evaluate for potential confounders, including age, gender, presence of hypertension, hypercholesterolemia, diabetes mellitus, tobacco use and family history of premature CAD. A receiver operator characteristics (ROC) curve was generated to determine the predictive power of FMD for CAD. Multiple linear regression

Table 1. Subject Population and Characteristics

	Study Population (n = 94)	Men (n = 51)	Women (n = 43)
Age, yrs	56 ± 2	56 ± 2	56 ± 2
Body mass index, kg/m^2	29 ± 1	28 ± 1	29 ± 1
Diabetes mellitus, n (%)	9 (10)	6 (12)	3 (7)
Hypertension, n (%)	45 (48)	22 (43)	23 (53)
Smoking			
Active, n (%)	11 (12)	8 (16)	3 (7)
Former, n (%)	18 (19)	9 (18)	9 (21)
Postmenopausal women, n (%)			33 (77)
Family history of CAD, n (%)	46 (49)	23 (45)	23 (53)
Hypercholesterolemia, n (%)	43 (46)	25 (49)	18 (42)
Total cholesterol, mg/dl	207 ± 5	203 ± 8	211 ± 7
LDL, mg/dl	122 ± 6	125 ± 7	117 ± 9
HDL, mg/dl	51 ± 2	47 ± 2	56 ± 3
LVEF (%)	63 ± 1	58 ± 1	69 ± 1
Aspirin, n (%)	23 (24)	16 (31)	7 (16)
Beta-blocker, n (%)	20 (21)	12 (24)	8 (19)
Calcium-blocker, n (%)	14 (15)	6 (12)	8 (19)
ACE inhibitor, n (%)	22 (23)	14 (27)	8 (19)
Nitrates, n (%)	8 (9)	6 (12)	2 (5)
Statin, n (%)	27 (29)	16 (31)	11 (26)

ACE = angiotensin-converting enzyme; CAD = coronary artery disease; HDL = high-density lipoprotein cholesterol; LDL = low-density lipoprotein cholesterol; LVEF = left ventricular ejection fraction; Statin = 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor.

analysis was performed to estimate the relationships between FMD and exercise time and to evaluate and adjust for possible confounding of age and cardiac risk factors. In all analyses, a p value <0.05 was considered statistically significant.

RESULTS

Subject population. Ninety-four subjects (43 women, 51 men) with an average age of 56 ± 1 year were enrolled and completed both exercise stress imaging and peripheral endothelial function testing. Characteristics of the study population are listed in Table 1. There were no significant differences in baseline characteristics between men and women. Of the entire population, 45 subjects had a history of hypertension; 9 had diabetes mellitus, and 45 had hypercholesterolemia. Most women (77%) were postmenopausal, and 21% were taking hormone replacement therapy. Subjects had an average total cholesterol of 207 ± 5 mg/dl, low-density lipoprotein cholesterol level of 122 ± 6 mg/dl and high-density lipoprotein cholesterol level of 51 ± 2 mg/dl. The mean LVEF was 63 ± 1%. The number of patients taking the medications most commonly used by study subjects is listed in Table 1.

Relationship between FMD and CAD. Flow-mediated dilation was significantly lower (6.3 ± 0.7%) in the 23 subjects with a positive ExMPI for CAD compared with the 71 subjects with no evidence of CAD by SPECT imaging (10.5 ± 0.6%; p = 0.0004) (Fig. 1, Table 2). Endothelium-*independent* vasomotion was not statistically different between the positive and negative ExMPI groups (NMD: 16.8 ± 1.8% vs. 18.6 ± 0.9%, respectively). There were no significant differences in baseline brachial artery dimensions between the two groups (Table 2). Sensitivity and specificity, along with positive and negative predictive values, of BAUS for detection of CAD were analyzed at various FMD cut-points (Table 3). For an FMD cut-point of 6%, the sensitivity was limited while the specificity was relatively high (43% vs. 80%, respectively) with a negative predictive value of 81%. For an FMD cut-point of 14%, the sensitivity improved significantly while the specificity decreased (100% vs. 34%, respectively), and the negative predictive value improved to 100%. An ROC curve examining the ability of FMD to predict CAD yielded an area under the curve of 0.75 (p = 0.001) (Fig. 2). Based on these analyses, an FMD of 10% was chosen as a cut-point for further analysis as this maximized the negative predictive value and had the least impact on sensitivity.

Forty subjects had an FMD ≥10%, while 54 had an FMD <10%. Twenty-one of 23 subjects with a positive ExMPI had an FMD <10% (sensitivity 91%). Furthermore, only two of 40 subjects with an FMD ≥10% had a positive ExMPI, resulting in a negative predictive value of 95%. Thus, 39% of subjects with an FMD <10% had a positive ExMPI, whereas only 5% of subjects with an FMD ≥10% had CAD by nuclear imaging (Fig. 3).

Relationship between FMD and cardiac risk factors. The average number of cardiac risk factors among all subjects was 3.0 ± 0.1. The number of cardiac risk factors correlated with FMD (Spearman correlation coefficient −0.250; p < 0.02). The 63 subjects with three or fewer cardiac risk factors had a higher FMD (10.2 ± 0.6%) than the 31 subjects with more than three risk factors (8.1 ± 0.9%; p = 0.04). Subjects without CAD who had an FMD <10% (n = 33) had a greater number of risk factors

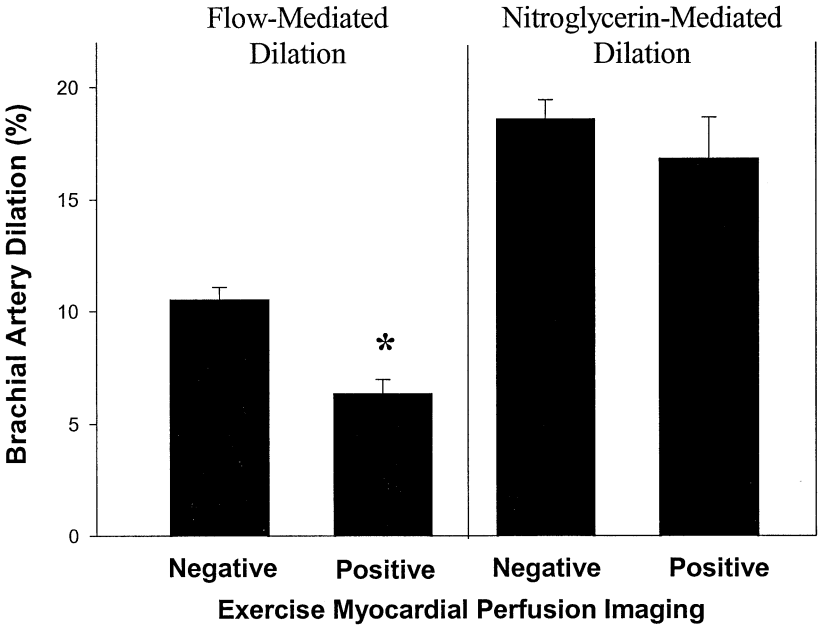

Figure 1. Endothelium-dependent and independent vasomotion. Flow-mediated dilation of the brachial artery during reactive hyperemia (endothelium-dependent vasomotion) in subjects with negative exercise myocardial perfusion imaging (ExMPI) is significantly higher than it is in subjects with positive ExMPI. Nitroglycerin-mediated dilation of the brachial artery (endothelium-independent vasomotion) is essentially unchanged between groups. Values are expressed as mean ± standard error. *p = 0.0004.

compared with subjects without CAD who had an FMD ≥10% (n = 38), though this did not achieve statistical significance (3.1 ± 0.2 vs. 2.6 ± 0.2, respectively; p = 0.1).

Flow-mediated dilation was independently highly predictive for CAD with an odds ratio of 1.32 (95% confidence intervals: 1.11 to 1.56) for each percent decrease in FMD (p = 0.001). Furthermore, male gender, hypercholesterolemia and diabetes mellitus were independent predictors of CAD (p = 0.01, 0.004 and 0.02, respectively). Multivariate stepwise logistic regression analysis showed that the odds ratio for FMD to predict CAD, adjusted for these variables, was 1.29. Age, hypertension, smoking and family history of CAD were not predictors of CAD in this analysis. Univariate analysis revealed that gender, hypertension, hypercholesterolemia and menopausal state were not predictors of FMD, while age and diabetes mellitus were predictors (p = 0.02 and p = 0.045, respectively).

Table 2. Brachial Artery Ultrasound Measurements

	ExMPI Positive	ExMPI Negative	p Value
n	23	71	
Baseline diameter (mm)	4.0 ± 0.2	3.8 ± 0.1	0.2
FMD diameter (mm)	4.3 ± 0.2	4.2 ± 0.1	0.7
%FMD	6.3 ± 0.7	10.5 ± 0.6	0.0004
Rebaseline diameter (mm)	4.0 ± 0.2	3.8 ± 0.1	0.3
NMD diameter (mm)	4.7 ± 0.1	4.6 ± 0.1	0.5
%NMD	16.8 ± 1.8	18.6 ± 0.9	0.4

Mean ± standard error.
ExMPI = exercise myocardial perfusion imaging; FMD = flow-mediated dilation; NMD = nitroglycerin-mediated dilation.

Relationship between FMD and exercise parameters. There was a significant relationship between FMD and duration of exercise (Spearman correlation coefficient: 0.280; p = 0.01). Length of treadmill exercise time during ExMPI differed between those with an FMD ≥10% and those with an FMD <10% (Table 4). Among all subjects, individuals with FMD <10% had an average exercise time of 456 ± 24 compared with 544 ± 31 s in subjects with FMD ≥10% (p = 0.02). This relationship was also statistically significant for the subset of individuals with negative ExMPI (444 ± 29 vs. 547 ± 32 s, p = 0.02). Subjects with a positive ExMPI exercised for a similar duration as those with an FMD <10% in the negative ExMPI group (483 ± 37 vs. 444 ± 29 s; p = NS). While age itself predicts exercise time, multiple linear regression analysis revealed that age was not a significant confounding variable for the relationship between FMD and exercise time. There were no significant differences in electrocardiographic criteria for ischemia at peak exercise stress level between the groups.

DISCUSSION

Evaluation of EDV by high-resolution BAUS has evolved into a widely used noninvasive method of determining peripheral endothelial function in healthy individuals and in patients with a variety of cardiovascular diseases. Previous reports have noted a correlation between abnormalities in FMD of the brachial artery and the presence of CAD by coronary angiography (13,14). In this study, we compared BAUS directly to exercise testing with SPECT imaging. Exercise myocardial perfusion imaging is a highly validated

Table 3. Flow-Mediated Dilation in Subjects Undergoing Exercise Myocardial Perfusion Imaging

	ExMPI(+)	ExMPI(−)	Sens	Spec	NPV	PPV
FMD < 6%	10	14				
FMD ≥ 6%	13	57	43	80	81	42
FMD < 8%	17	23				
FMD ≥ 8%	6	48	74	68	89	43
FMD < 10%	21	33				
FMD ≥ 10%	2	38	91	54	95	39
FMD < 12%	21	47				
FMD ≥ 12%	2	24	91	34	92	31
FMD < 14%	23	58				
FMD ≥ 14%	0	13	100	18	100	28

ExMPI = exercise myocardial perfusion imaging; FMD = flow-mediated dilation; NPV = negative predictive value; PPV = positive predictive value; Sens = sensitivity; Spec = specificity.

method for detecting CAD, quantifying myocardial ischemia and viability, determining prognosis and evaluating the adequacy of revascularization (17–19). In addition to assessing the presence and extent of CAD, this testing modality provides physiologic data regarding myocardial perfusion and exercise capacity. Among patients with suspected but not known CAD, the percentage of individuals presenting for nuclear stress testing who have a normal scan may be as high as 75% (20). This is confirmed in this study where only 25% of subjects studied had a positive ExMPI for CAD. Therefore, much interest lies in developing less expensive noninvasive modalities for excluding CAD and assessing the severity of cardiovascular risk.

Defining CAD risk by peripheral endothelial function testing. The data presented above indicate that assessment of peripheral endothelial function with BAUS may be helpful in defining CAD risk in a low- to intermediate-risk population. In this study, FMD was significantly lower in individuals with CAD defined by nuclear imaging compared with those with normal ExMPI. Furthermore, FMD was an independent predictor of CAD. In the subjects without CAD by ExMPI, however, approximately one-half of the subjects had an FMD <10%, suggesting a relatively limited specificity of this technique for detecting CAD. It is important to note that abnormalities in EDV develop in patients with cardiac risk factors before the development of overt atherosclerosis (21). This study is consistent with these observations. Subjects with normal nuclear scans but with an FMD <10% had more cardiac risk factors than those with an FMD ≥10%. In addition, the actual number of cardiac risk factors had a modest correlation with endothelial function. Subjects with few cardiac risk factors had a larger FMD compared with those with numerous cardiac

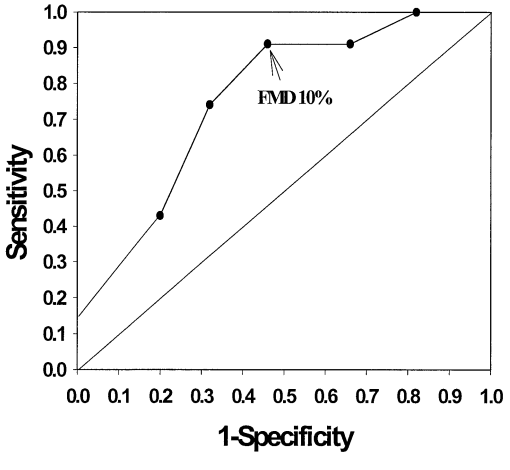

Figure 2. A receiver operator characteristics curve is shown examining the ability of flow-mediated dilation (FMD) to predict coronary artery disease defined by exercise myocardial perfusion imaging. An FMD of 10% **(arrow)** was chosen as a cut-point for further analysis based on the high sensitivity and negative predictive value. The area under the curve was 0.75 (p = 0.001).

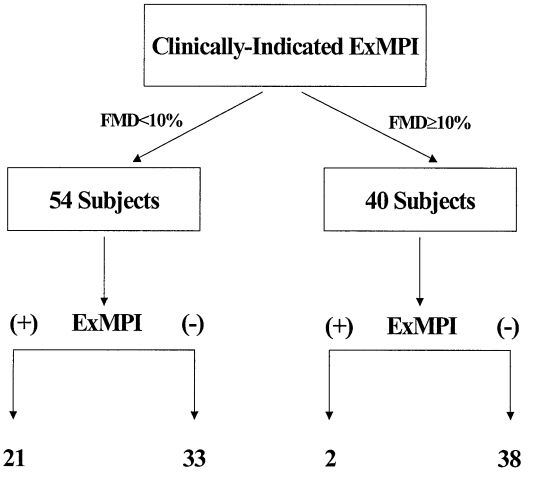

Figure 3. Flow diagram detailing the 94 subjects undergoing exercise myocardial perfusion imaging. Subjects were divided based on a flow-mediated dilation (FMD) cut-point of 10%. Of the 54 subjects with an FMD <10%, 21 had positive exercise myocardial perfusion imaging (ExMPI), while 33 had no evidence of coronary artery disease (CAD). The sensitivity of an FMD <10% for CAD was 91%. Two of the 40 subjects with an FMD ≥10% had CAD by ExMPI resulting in a negative predictive value of 95%.

Table 4. Exercise Treadmill Time and Flow-Mediated Dilation

	FMD <10%	FMD ≥10%	p Value
Exercise time (s), all subjects	456 ± 24	544 ± 31	0.02
Exercise time (s), negative ExMPI subjects	444 ± 29	547 ± 32	0.02

Mean ± standard error.
ExMPI = exercise myocardial perfusion imaging; FMD = flow-mediated dilation.

risks. Thus, in a subset of patients without CAD by ExMPI, FMD is impaired in association with cardiac risk factors, thereby decreasing the specificity of this technique for predicting the presence of CAD.

In contrast, normal FMD reflects a low cardiac risk factor burden and is likely to be associated with a low risk of developing CAD. We, therefore, examined the ability of preserved FMD to predict the absence of CAD. We chose an FMD value of 10% as a cut-point for analysis to optimize the negative predictive value of BAUS to predict the absence of CAD, while preserving the sensitivity of the test. With this analysis, BAUS was found to be an effective test for excluding CAD with a negative predictive value of 95%. The relatively poor positive predictive value of BAUS likely results from impaired endothelial function due to the presence of cardiac risk factors. This decrease in peripheral FMD may precede the development of atherosclerotic stenoses that would be detected by ExMPI. Thus, abnormal FMD detected by BAUS does not necessarily indicate that CAD has developed, whereas normal EDV indicates a low likelihood of advanced disease. Brachial artery ultrasound may, therefore, be useful as a screening tool before ExMPI, especially in subjects with low CAD probability. Such an approach might ultimately reduce the number of normal SPECT scans performed. To validate this further and to explore the potential clinical utility of BAUS-based screening, future prospective studies comparing BAUS to ExMPI using a predefined cut-point (10% in our series of subjects) are warranted.

Exercise capacity and endothelial function. Exercise capacity in patients with known or suspected CAD is helpful for prognosis (22). While it is known that regular exercise can prevent the age-associated decline in EDV and can attenuate reductions in arterial compliance (23,24), no prior study has determined whether endothelial function is associated with exercise capacity. The present data indicate that changes in brachial artery diameter may potentially be related to exercise performance. Among all subjects, those with decreased FMD exhibited significantly shorter exercise duration than those with a larger FMD. In the subset of individuals with normal nuclear scans, exercise time was also shorter in subjects with an FMD <10% when compared with those with an FMD ≥10%. In addition, subjects with an FMD <10% exercised for approximately the same duration regardless of whether the ExMPI was positive or negative. We believe this is the first study showing a possible correlation between EDV and exercise capacity, an important physiologic marker and predictor of cardiovascular events. Further studies focusing on endothelial function and exercise ability are needed.

Study limitations. Several limitations of this study deserve comment. First, we compared BAUS to ExMPI, not to coronary angiography or intravascular ultrasound. While these invasive techniques are considered the gold standard for detection of CAD, ExMPI has evolved into a reliable and frequently used technique for detecting CAD. Exercise myocardial perfusion imaging allows for an assessment of the physiologic relevance of coronary artery stenosis and for the evaluation of a broader subject population than would be encountered in an angiographic study, especially in lower risk individuals of interest for this study. The sensitivity of ExMPI, however, is approximately 90%, and, though some patients with obstructive CAD may have been missed in this study, this is likely a small number and is unlikely to have significantly altered the findings. Second, assessment of cardiac risk factors is inherently imperfect because some individuals were undergoing treatment with medications while others were not. We inquired only about traditional cardiac risk factors and did not examine "novel" risk factors, which might play a role in endothelial function and atherosclerosis. For example, hyperhomocysteinemia or elevated C-reactive protein levels have been shown to inhibit peripheral arterial vasoreactivity (25,26) but were not tested in this patient population. It is also possible that differences in the distribution of risk factors (or gender) between the positive and negative ExMPI groups could also have contributed to the differences observed in FMD. However, the trend toward more risk factors in the positive ExMPI group was not statistically significant, and, though there were fewer women in the positive ExMPI group, there was not a significant difference in FMD between men and women. Third, it is possible that age is related to the observed relationship between the decline in exercise performance and abnormalities in endothelial function. It is known that FMD decreases with the normal aging process. However, in subgroup analysis, age did not appear to be a significant confounding variable for duration of exercise time. Thus, older age does not fully explain the decrease in exercise time in those with abnormal endothelial function. In addition, it is likely that exercise itself can acutely affect endothelial function. In order to ensure that exercise itself did not change vasomotor tone, FMD was evaluated at least 2 h after the cessation of treadmill exercise. Finally, while our results indicate an FMD cut-point of 10%, this may not be applicable to other laboratories performing BAUS because of the lack of standardization of this methodology (27). At

this point, there is no uniformly accepted technique for performing BAUS, and there is a wide variability in normal ranges between laboratories. This is based on certain technical aspects of the procedure, such as cuff position and duration of vessel occlusion, which can alter the degree of FMD. We chose to perform upper arm occlusion because of the larger percent FMD that can be achieved and, thus, the larger differences between groups being studied.

Conclusions. These results support the notion that evaluation of peripheral vascular endothelial function can accurately exclude CAD in subjects undergoing noninvasive assessment for atherosclerosis. Determination of peripheral endothelial function can confirm a low probability of CAD in low-risk individuals and, thus, may obviate the need for more elaborate testing. For those in whom abnormal EDV is detected, further evaluation with techniques such as ExMPI appears warranted. Peripheral vascular function testing may also provide information regarding exercise capacity and the impact of cardiac risk factors on arterial function. If further prospective studies with larger populations confirm these findings, BAUS may become useful as a screening tool for excluding CAD in lower risk subjects undergoing evaluation for suspected CAD.

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