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Efficiency of coronary artery disease screening guidelines in asymptomatic and atypical chest pain type 2 diabetic patients

THESE

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RESUME

Objectifs. Evaluer la prévalence de maladie coronarienne chez les patients diabétiques de type 2 asymptomatiques ou avec angor atypique selon les recommandations américaines de l'American Diabetes Association et de l'American College of Cardiology.

Méthodes. Cent cinquante-quatre patients diabétiques de type 2 asymptomatiques ou avec angor atypique et présentant au minimum 2 facteurs de risque cardio-vasculaires additionnels ont été dépistés par échocardiographie de stress (71%, n=109), scintigraphie myocardique de perfusion (26%, n=40) ou l'association des 2 examens (3%, n=5).

Résultats. L'échocardiographie de stress s'est révélée positive chez 16 patients (14%) et 14 ont eu une coronarographie révélant des sténoses significatives chez 12 (86%). La scintigraphie myocardique de perfusion était positive chez 16 patients (36%). Huit patients ont eu une coronarographie et 4 (50%) présentaient des sténoses significatives.

Au total, 31 patients (20%) ont montré des signes d'ischémie lors de l'examen non-invasif et 15 (10%) ont présenté des sténoses significatives à la coronarographie. Les facteurs prédictifs indépendants de la maladie coronarienne étaient le tabagisme (OR 6.5, p=0.05), la microalbuminurie (OR 3.9, p=0.03), ainsi que les souffles fémoraux (OR 17.1, p=0.008).

Conclusions. En suivant les recommandations américaines, un patient sur cinq présentait une ischémie lors des examens non-invasifs, tandis que 1 sur 10 avait des sténoses significatives à la coronarographie. L'analyse multivariée suggère que des marqueurs des complications micro- et macro-vasculaires en combinaison avec des facteurs de risque cardio-vasculaire classiques pourraient améliorer le pouvoir diagnostic de ces recommandations.

SUMMARY

Aims. We evaluated the prevalence of coronary artery disease in asymptomatic and atypical chest pain type 2 diabetic patients according to the American Diabetes Association and American College of Cardiology guidelines.

Methods. Asymptomatic or atypical chest pain type 2 diabetic patients (n=154), with at least two additional cardiovascular risk factors, were screened for coronary artery disease using stress echocardiography (71%, n=109), myocardial perfusion imaging (26%, n=40) or both (3%, n=5).

Results. Stress echocardiography was positive in 16 patients (14%) and 14 had a coronary angiography, revealing significant stenoses in 12 (86%). Myocardial perfusion imaging was positive in 16 patients (36%). Eight patients underwent angiography and 4 (50%) presented significant stenoses.

Overall, 31 patients (20%) demonstrated signs of ischemia on non-invasive tests and 15 (10%) presented significant stenoses on coronary angiography. Independent predictors of coronary artery disease were smoking (OR 6.5, p=0.05), microalbuminuria (OR 3.9, p=0.03) and femoral murmur (OR 17.1, p=0.008).

Conclusions. Following the guidelines, one in five diabetic patient presented ischemia on non-invasive tests, while one in ten presented significant coronary stenoses. Multivariate analysis suggests that adding markers of micro- and macro-vascular complications to classical cardiovascular risk factors may enhance the diagnostic efficiency of the guidelines.

TITLE

EFFICIENCY OF CORONARY ARTERY DISEASE SCREENING GUIDELINES IN ASYMPTOMATIC AND ATYPICAL CHEST PAIN TYPE 2 DIABETIC PATIENTS

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KEYWORDS

Diabetes mellitus, coronary artery disease, silent myocardial ischemia, stress echocardiography, myocardial perfusion imaging.

ABBREVIATIONS

ADA-ACC	American Diabetes Association and American College of Cardiology
ALFEDIAM	French Diabetes Association
CA	Coronary Angiography
CAD	Coronary Artery Disease
MPI	Myocardial Perfusion Imaging
NNS	Number Needed to Screen
SE	Stress Echocardiography
SPECT	Single Photon Emission Computed Tomography

INTRODUCTION

Cardiovascular diseases are a major burden in the diabetic population as shown by large prospective epidemiological studies [1]. Coronary artery disease (CAD) remains the single most important cause of death associated with diabetes mellitus, with the mortality due to CAD being three times higher in diabetic patients than in non-diabetic patients [2]. Moreover, the risk of myocardial infarction in diabetic patients is similar to that of non-diabetic patients with a previous myocardial infarction [3]. These findings suggest that all type 2 diabetic patients should be considered from a secondary prevention perspective [3, 4]. Consequently, diabetic patients are now classified in the same high-risk category as that previously reserved for patients with known CAD [5, 6]. In addition, CAD is often silent in diabetic patients [7], thus contributing to the disease being undetected until acute complications, such as non-fatal myocardial infarction or sudden death, occur. The systematic screening for diabetic retinopathy and nephropathy has been shown to be efficient in reducing these microvascular complications. Paradoxically, to date, there has been no studies on the efficiency of systematic screening for coronary disease in diabetic patients for the reduction of cardiovascular mortality and morbidity [8]. Early and systematic screening for CAD may decrease the morbidity and mortality seen in this very high-risk population. Several expert groups have published recommendations over the last years for the screening of coronary artery disease in the diabetic population. The first guidelines were published by the French Diabetes Association (ALFEDIAM) in 1995 and recommend screening asymptomatic type 2 diabetic patients with at least one additional cardiovascular risk factor [9]. The American Diabetes Association and the American College of Cardiology (ADA-ACC) published a set of guidelines in 1998 and recommend screening asymptomatic type 2 diabetic patients with at least two additional cardiovascular risk factors [10]. In 2000, the Swiss guidelines [11] were published and these are based on the American guidelines. Despite these recommendations, few studies have been conducted to investigate their diagnostic efficiency, as defined by the proportion of the patients

found to present CAD. This prospective study addresses this issue by using the ADA-ACC guidelines to assess the prevalence of abnormal non-invasive tests and significant CAD in asymptomatic type 2 diabetic patients and in those with atypical chest pain.

PATIENTS AND METHODS

Patients. Between February 1998 and July 2002, 154 consecutive Caucasian type 2 diabetic patients without history of CAD and with either no chest pain (n=113, 73%) or atypical chest pain (n=41, 27%) were prospectively screened for CAD using stress echocardiography or myocardial perfusion imaging. Chest pain was defined according to the Rose questionnaire. Patients with typical angina pectoris, a history of CAD or ECG modifications were excluded from the study. Moreover, all the patients needed to have at least two additional cardiovascular risk factors to be included in the study, as stated in the ADA-ACC guidelines [10]. These patients were recruited and followed-up in an ambulatory setting at the diabetology clinic of the Lausanne University Hospital, Switzerland. The study complies with the Swiss CAD screening guidelines in diabetic patients and all patients gave their informed consent to participate in the screening tests.

Screening algorithm. Enrolled patients were screened for the presence of coronary artery disease according to the ADA-ACC guidelines [10]. Of the 154 patients qualifying for screening, all echogenic patients (n=109, 71%) underwent stress echocardiography (SE), while non-echogenic patients (n=40, 26%) were referred for myocardial perfusion imaging (MPI) and 5 (3%) had both tests. Patients demonstrating a moderate or large area of myocardial ischemia ($\geq$ 2 segments) on SE or MPI were referred for coronary angiography (CA). When ischemia was limited to a small area (< 2 segments), no angiogram was performed in accordance with the ADA-ACC guidelines [10].

Stress echocardiography (SE). Two-dimensional transthoracic echocardiographic images were obtained from the standard parasternal and apical windows before, during, and after stress. All images were recorded in a digital quad-screen format for simultaneous visualisation of wall motion. Dobutamine (3 min stages of 10, 20, 30 and 40 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was the preferred stress agent (n=87, 76%). Dobutamine stress was considered maximal if 85% of the maximal predicted heart

rate for age was reached. If this endpoint was not reached, atropine was added in 4 fractionated doses of 0.25 mg each minute, up to a maximal cumulative dose of 1 mg. Dipyridamole was used as an alternate pharmacological stress agent in patients with contraindications to dobutamine (e.g. severe hypertension or supraventricular tachycardia). Dipyridamole was injected intravenously at a dose of 0.56 mg · kg^{-1} over 4 minutes followed by 4 minutes of observation and then, if negative, followed by 0.28 mg · kg^{-1} over 2 minutes. At the end of the perfusion, atropine was added up to 1 mg. Standard 12-lead ECG and blood pressure were continuously monitored throughout the test. All images were interpreted by two experienced observers and discrepancies were resolved by consensus. The left ventricular wall was divided into 16 segments according to the recommendations of the American Society of Echocardiography [12]. The test was considered positive for the presence of ischemia if new onset or worsening wall motion abnormalities appeared during stress compared to rest. The test was suggestive of previous myocardial infarction if wall motion abnormalities were present both at rest and during stress.

Single photon emission computed tomography myocardial perfusion imaging (SPECT-MPI). We used a conventional 1-day protocol with either dual-isotope Tl-201 at rest (111MBq) and Tc-99m-MIBI (Sestamibi) during stress (925MBq) in lean subjects or with single-isotope Tc-99m-MIBI (370MBq for stress, 925MBq for rest) in more corpulent subjects (BMI $\geq$ 30 kg·m^{-2}). SPECT studies were performed on a dual-headed gamma camera (*Siemens E.-Cam*, Siemens, Erlangen, Germany) using low-energy, high-resolution parallel-hole collimators. Resting studies began 10-15 minutes after the rest Tl-201 or Tc-99m-MIBI injection, and stress imaging started 30-45 minutes after the stress Tc-99m-MIBI injection. Exercise testing was performed with a modified-Bruce protocol on a bicycle-ergometer (n=20, 44%) using 2-minute step increments (25 or 30W) in order to reach 85% of the maximal predicted heart rate for age. In patients unable to perform a complete exercise test (n=25, 56%), pharmacological stress testing was performed using a 4-minute dipyridamole infusion (0.56 mg · kg^{-1}), eventually completed by some low dose exercise (isometric

handgrip or 25-60 W bicycle stress) to alleviate side effects of dipyridamole. The radionuclide tracer was injected at peak exercise that was maintained at least 1, preferably 2 minutes. For pharmacological stress, the tracer injection was performed 3 minutes after the end of dipyridamole infusion. At least one hour separated both stress and rest studies. Standard 12-lead ECG and blood pressure measurements were recorded every 2 minutes during stress and recovery. Two experienced readers evaluated rest and stress images as well as ECG-gated cine images. Discrepancies were resolved by consensus. Regional radiotracer distributions were analysed visually on short-, horizontal- and vertical-long axis views as well as semi-quantitatively on polar maps using the Emory Cardiac Toolbox software [13]. Stress-induced ischemia was defined as moderate or greater-than-moderate improvement of regional perfusion on rest images as compared to stress images. A myocardial scar was considered when the perfusion abnormalities remained unchanged between stress and rest.

Coronary angiography (CA). Coronary angiography was performed transcutaneously through one of the femoral arteries. Significant coronary stenoses were defined as a narrowing in the cross-sectional area of more than 70% of any of the 3 major coronary arteries and of ≥ 50% on the left main coronary artery. CAD was diagnosed if one or more coronary stenoses were found at CA. The angiograms were reviewed by 2 experienced observers and discrepancies were resolved by consensus. No serious complications during and after coronary angiography were reported.

Clinical data. Type 2 diabetes was defined according to the World Health Organization criterias [14]. Hypertension was diagnosed if the patient was receiving antihypertensive drugs or if blood pressure at rest was higher than 135/85 mmHg on two occasions. Dyslipidemia was recognized if the patient was taking lipid-lowering drugs, if triglycerides were above 2.2 mmol/l or if at least two of the following criteria were present : total cholesterol > 5.0 mmol/l, LDL > 3.0 mmol/l, HDL < 0.9 mmol/l, total cholesterol / HDL ratio > 5.0. Microalbuminuria was diagnosed when the ratio

albumin to creatinine in a morning urinary spot was ≥ 2.5 mg/mmol for men and ≥ 3.5 mg/mmol for women. Macroalbuminuria was diagnosed if urinary albumin excretion was above 300 mg per day. Abdominal obesity was present if the waist to hip ratio was above 0.85 for women and 0.90 for men.

Statistical analyses. Continuous variables, normally distributed, were expressed in means with standard deviation and the Student's t test was used for comparisons. Non-normally distributed continuous variables were expressed as median, with 10^{th} - 90^{th} percentiles and the Mann-Whitney U test was used for comparisons. Categorical variables were expressed in frequency and differences were based on the chi-square test. For statistical purposes, the presence of coronary artery disease was defined as a positive SE or SPECT-MPI in the absence of coronary angiography or as the presence of at least one significant coronary stenosis on CA. Forward stepwise logistic regression analysis was performed to determine independent predictors of CAD. The 10-years absolute cardiovascular risk was calculated using the Framingham equation [15]. All statistical analyses were performed using JMP 5.0 (SAS Institute, Cary, USA) and a p value ≤ 0.05 was considered statistically significant.

RESULTS

One hundred fifty-four type 2 diabetic patients without history of CAD and with either no chest pain (n=113, 73%) or atypical chest pain (n=41, 27%) were screened according to the guidelines of the ADA-ACC. The patients' clinical characteristics are shown in Table 1. Patients were mostly males (67%) with a mean age of 60 years and a median diabetes duration of 7 years. Among the cardiovascular risk factors, hypertension, dyslipidemia and abdominal obesity were highly prevalent (79%, 84% and 97%), micro/macro-albuminuria was present in 36% and 37% were currently smokers. The median Framingham 10-years absolute cardiovascular risk was 23%.

Stress echocardiography. Stress echocardiography was performed in 114 patients and was positive in 16 (14%): 7 (44%) patients presented only ischemia, 6 (37%) had ischemia and evidence of a previous silent myocardial infarction and another 3 (19%) demonstrated evidence of silent myocardial infarction without ischemia (Figure 1). Coronary angiography was performed in 14 of the 16 patients with a positive SE. The 2 remaining patients had minor echocardiographic abnormalities (no angiography performed according to the guidelines). Significant stenoses were observed in 12 of these 14 patients (86%): 5 patients had 3-vessel disease, 3 had 2-vessel disease and 4 had single-vessel disease (Figure 1). The positive predictive value of SE to detect significant coronary stenoses was estimated to be 86% (CI: 0.60 - 0.96).

SPECT-MPI. Myocardial perfusion imaging was performed in 45 patients and was abnormal in 16 (36%): in 13 (81%) patients only ischemia was observed, 2 (13%) had ischemia and evidence of previous silent myocardial infarction and 1 (6%) demonstrated evidence of previous silent myocardial infarction without ischemia (Figure 1). Coronary angiography was performed in 8 of these patients and revealed significant stenoses in 4 (50%) (Figure 1). The angiogram showed 2-vessel disease in 3 patients and single-vessel disease in 1. We did not observe any 3-vessel disease.

The 8 remaining patients did not undergo CA (refusal n=2, minimal perfusion defects confined to one segment n=6). The positive predictive value of SPECT–MPI to detect angiographically significant coronary stenoses was calculated to be 50% (CI: 0.22 - 0.78).

Overall results of non-invasive tests. Non-invasive tests were positive in 31 patients (20%), with 15 (10%) presenting significant stenoses at coronary angiography. Five patients had both tests and the results were concordant: 4 had both screening tests negative, while one patient had both exams positive. Table 2 shows univariate predictors for the presence of CAD. Patients presenting atypical chest pain did not have a higher risk of presenting a positive screening test. Markers of vascular complications were found to be the main factors associated with the presence of CAD: carotid and femoral murmurs for macrovascular disease, and micro/macro-albuminuria, diabetic retinopathy and erectile dysfunction for microvascular disease. It is worth noting that hypertension and dyslipidemia did not predict CAD in our population. Independent predictors of CAD in forward stepwise logistic regression were femoral murmur, microalbuminuria and smoking (Table 3).

CAD prediction score. The results of the multivariate analysis were used to create a composite score for predicting the presence of CAD. One point was assigned for each of the three former independent predictors found (smoking, micro-/macro-albuminuria and femoral murmur). One point was assigned to each because of the arbitrary need to have a simple equation. In a receiver operating characteristic analysis this score was able to satisfactorily predict the presence of CAD in this population with an area under the curve of 0.74 (CI: 0.67 – 0.81, $p < 0.001$).

Treatment of patients with established CAD. The subsequent management of the 15 patients presenting with significant stenoses at coronary angiography is shown in Table 4. Fifty-four percent of these patients (n=8) underwent invasive revascularization procedures, which included coronary artery bypass grafting and coronary angioplasty.

DISCUSSION

This study evaluates, for the first time, the efficiency of the ADA-ACC guidelines for the screening of CAD in asymptomatic or atypical chest pain type 2 diabetic patients. Systematic screening for CAD with SE or SPECT-MPI found that 20% of the patients had a positive screening test. Subsequently, coronary angiography identified significant stenoses in 10% of the patients leading to slightly more than half of them (54%) undergoing subsequent revascularization procedures.

The results of this study are consistent with previous data from the literature using different CAD screening guidelines. Janand-Delenne et al. [16] conducted a similar study following the ALFEDIAM guidelines [9] using stress ECG and SPECT-MPI in asymptomatic type 1 and 2 diabetic patients. They found a 15% prevalence of abnormal screening tests across both patient groups. However when only the type 2 diabetic patients were considered, the prevalence rose to 18.4%. Furthermore, the prevalence of coronary stenoses ≥ 50% was 9.6%, despite the fact that coronary angiography was refused by 6 of 32 patients. In an other study with a similar design, Torremocha et al. reported abnormal non-invasive studies (stress ECG and SPECT-MPI) in 11.1% of the patients, with significant stenoses in 9.7% [17]. In type 2 diabetic patients, De Lorenzo et al., using SPECT-MPI as a screening test, observed a 26% prevalence of abnormal perfusion scans, with abnormal scans being predictive of future cardiac events [18]. Despite some variability in the prevalence of CAD in the previous and other studies [19-24], likely to be due to differences in patient selection criteria, ethnic groups, screening algorithms and screening tests, our findings are in agreement. However, when Paillole et al. performed systematic coronary angiographies in all of their 59 diabetic patients without known CAD, but with typical and atypical chest pain or ST modifications, they found a 34% prevalence of significant stenoses at coronary angiography [25]. Despite the fact that their population was at higher risk due to the presence of typical angina or ST segment abnormalities in some patients, this would indicate that the 10% prevalence of significant

stenoses found in our study could only constitute a lower limit. Indeed, because the sensitivity of stress echocardiography and SPECT-MPI is around 80% to 84% [26], 16 to 20% of the patients theoretically have a false negative non-invasive test, leading to an underestimation of the prevalence of significant stenoses. In our study, 54% of the patients with significant stenoses and 5% of the screened population were revascularized. In the previously mentioned studies by Janand-Delenne et al. and Torremocha et al. [16, 17], respectively 37% and 43% of the patients presenting with significant stenoses underwent revascularization procedures.

In our study, both stress echocardiography and myocardial perfusion imaging were used as screening methods for the detection of ischemia. According to the literature, both methods have comparable sensitivity and specificity [26]. Interestingly, the prevalence of positive screening tests was 2.5-fold higher in the SPECT-MPI group as compared to the SE group (36% vs. 14%, $p = 0.002$). This significant difference questions the relative value of each technique for the detection of CAD in diabetic patients. Despite the lack of studies comparing these two tests in this population, some elements suggest that these two methods do not necessarily provide the same information. The first evidence is related to the different detection techniques these two tests use to diagnose ischemia. SPECT-MPI evaluates the differential increase in regional myocardial perfusion to a physical or pharmacological stress, which depends on both coronary epicardial and microcirculatory blood flow. In contrast, stress echocardiography analyses changes in systolic function (wall motion and contractility) during stress. The flow redistribution seen as regional differences in perfusion on SPECT-MPI, leading to oxygen supply and demand imbalance, happens earlier in the ischemic cascade than systolic dysfunction observed with stress echocardiography [26, 27]. The second important difference between these two tests is inherent to their relative threshold for the detection of ischemia. Stress echocardiography has a relatively high threshold, as it requires at least 20% of the myocardial thickness and 5% of ventricular mass to be ischemic before anomalies in systolic function can be detected [28]. Therefore a small area of ischemia caused by

distal vessel disease, such as seen in diabetes, may not be visualized on SE [29]. In contrast, SPECT-MPI is a very sensitive technique that can visualize, if microvascular disease is present, an inhomogeneity or maldistribution of myocardial blood flow not inducing yet any alteration of contractility. Such perfusion abnormalities are frequently observed in high-risk patients and are related to a diminished coronary flow reserve. Indeed, decrease in intracoronary fractional flow reserve has been shown to be associated with reversible defects on SPECT-MPI [30-32]. This also explains the lower positive predictive value found in our study of SPECT-MPI to detect angiographically significant coronary stenoses compared to SE (SPECT-MPI 50% CI:22-78 vs. SE 86% CI:60-96, p = NS). At first, abnormal SPECT-MPI were not associated with significant coronary stenoses and were considered as false positive. However, in term of microcirculatory status, several studies suggest that some of these may actually be true positive. Kaul et al. [33] reported that 35% of abnormal scans were related to the presence of non-occlusive (<50%) coronary stenoses, thus suggesting a possible underestimation of the coronary obstruction. Moreover, Verna et al. [34] demonstrated occult atherosclerotic plaques and an abnormal vasodilatory capacity, in respectively, 95% and 80% of the patients with angiographically "normal" coronary arteries and reversible defects on SPECT-MPI using intravascular ultrasonography and doppler. This suggests that non-significant epicardial stenoses and microvascular dysfunction are often combined and may have an additive effect leading to a further reduction on coronary flow reserve.

Markers of macro- and micro-vascular complications, such as femoral murmur and microalbuminuria were found to be the main predictors of coronary artery disease in our study. Classic cardiovascular risk factors, such as hypertension and dyslipidemia, were not predictive of CAD. This was found in other studies and could be related to their high prevalence in the studied population, which has been shown to reduce discriminative power [16, 17]. In the DIAD study [35], performed in asymptomatic type 2 diabetic patients, the cardiovascular risk factors were not

discriminative either. In addition, the Framingham 10-years absolute cardiovascular risk did not predict the presence of CAD in this population, a finding also observed in the study by Torremocha et al. [17]. These observations suggest that all cardiovascular risk factors do not have the same strength to predict CAD and therefore their respective importance in the guidelines should be reassessed. Markers of micro- and macro-vascular damage, such as microalbuminuria and the presence of atherosclerosis in the peripheral vasculature, in combination with some cardiovascular risk factors, such as smoking, could be helpful to select a subgroup of patients with a higher CAD probability. Thus a group in whom screening strategies could prove to be more efficient and cost-effective.

Following current guidelines, the number of patients needed to be screened (NNS) to find one patient with a positive non-invasive test was 5, the NNS to detect one patient with significant coronary stenoses was 10 and the NNS for one patient to benefit from revascularization was 20. The cost of these non-invasive screening tests is important, yet, since a significant proportion of patients did benefit from revascularization, a significant decrease in mortality and morbidity is expected. This is presently studied by the BARI 2D trial [36] which is an ongoing multicenter study evaluating the effect of early revascularization procedures in reducing mortality and morbidity in type 2 diabetic patients with mild and stable cardiac symptoms.

Finally, as R.W. Nesto suggested [8], the justification for screening depends of whether detection of CAD leads to treatment strategies that ultimately reduce cardiovascular morbidity and mortality.

Limitations of the study. Studies with a larger number of patients are necessary to corroborate our results. Furthermore, we possibly underestimated the true prevalence of coronary artery disease in our population, because angiography was not performed in all patients with ischemia on non-

invasive tests (ischemia limited to 1 segment and in those who refused). Detection of occult atherosclerotic plaques by intravascular ultrasound and measurement of the fractional flow reserve would have been useful to observe whether abnormal non-invasive tests in patients without significant stenoses were true or false positive. All diabetic patients were recruited from a tertiary diabetic referral centre supposedly having more complicated patients therefore our results might not be extended to the diabetic population in general. Finally, our results cannot be extended further to type 1 diabetes because of the different physiopathology and cardiovascular risk factors found in this population. It would have been interesting to follow-up the studied population for the occurrence of cardiovascular events in order to determine the prognostic impact of this screening strategy.

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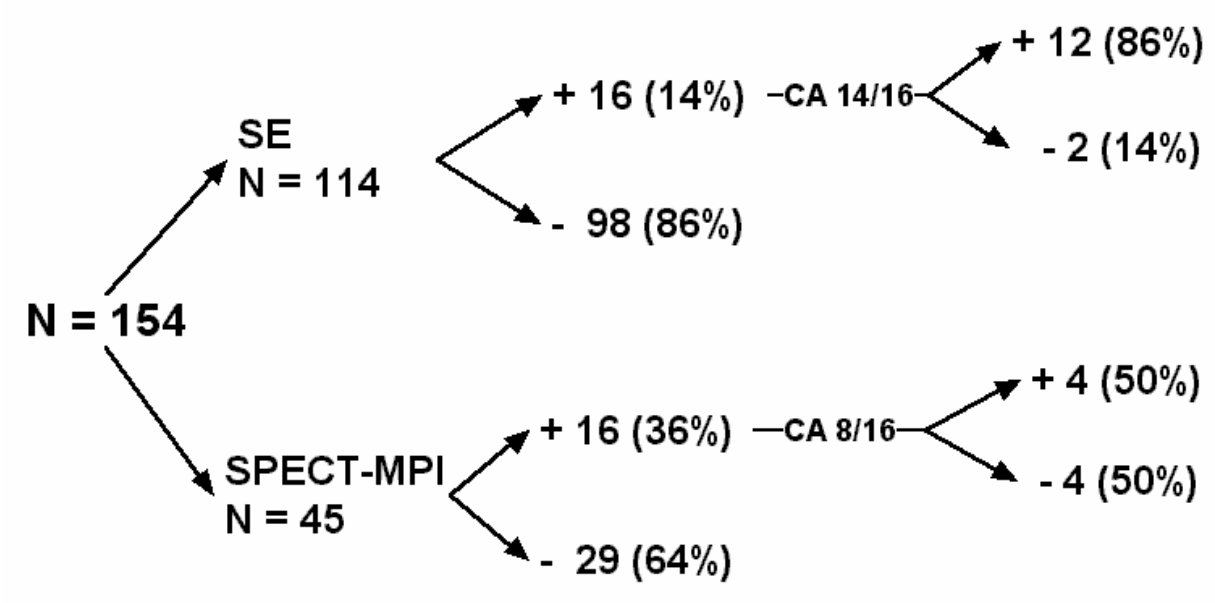
Figure 1. Overview of the screening results



Legends

SE : Stress Echocardiography, SPECT-MPI : Single Photon Emission Computed Tomography, CA : Coronary Angiography

Table 1. Clinical characteristics of diabetic subjects (n = 154)

Male gender	67 %
Age (years)	60 ± 9
Asymptomatic	73 %
Atypical chest pain	27 %
Exertional dyspnea	27 %
Claudication	13 %
Diabetes duration (years)	7 (2-22)
Smoking / stopped / never smoked	37% / 28% / 35 %
Hypertension	79 %
Dyslipidemia	84 %
Micro/macro-albuminuria	36 %
Familial history of CAD	32 %
Abdominal obesity	97 %
Framingham's 10-years absolute CV risk	23 % (11-37)

Table 2. Univariate predictors of CAD (n = 154)

	CAD +	CAD -	OR	P
Male gender	83 %	64 %	2.4	0.07
Age (years)	60 ± 8	60 ± 9	-	NS
Diabetes duration (years)	8 (2-22)	7 (2-22)	-	NS
Atypical chest pain	25 %	27 %	0.9	NS
Exertional dyspnea	46 %	23 %	2.3	0.02
Cardiovascular risk factors				
Hypertension	79 %	79 %	1.0	NS
Dyslipidemia	88 %	83 %	1.4	NS
Smoking	88 %	62 %	3.6	0.01
Familial history of CAD	47 %	30 %	1.9	0.13
Micro/macro-albuminuria	55 %	32 %	2.2	0.05
Abdominal obesity	100 %	96 %	-	NS
Physical inactivity	56 %	58 %	0.9	NS
Framingham 10yrs absolute CV risk	26 % (12-37)	22 % (11-35)	-	NS
Number of CV risk factors	5 (3-6)	4 (2-6)	-	0.009
Clinical examination				
Carotid murmur	14 %	5 %	2.2	0.15
Claudication	24 %	11 %	2.0	0.12
Peripheral pulses absent	48 %	27 %	2.1	0.05
Femoral murmur	27 %	5 %	3.8	0.001
Diabetic proliferative retinopathy	29 %	7 %	3.5	0.002
Erectile dysfunction	58 %	24 %	3.2	0.004
Systolic blood pressure (mmHg)	146 ± 20	143 ± 17	-	NS

Diastolic blood pressure (mmHg)	87 ± 13	87 ± 10	-	NS
Body mass index (kg/m2)	29.2 ± 4.7	30.1 ± 5.6	-	NS
Waist-hip ratio	1.02 ± 0.05	0.98 ± 0.07	-	0.06
Laboratory values				
HbA1c (%)	8.2 (6.8-11.4)	8.4 (6.4-12.9)	-	NS
Total cholesterol (mmol/l)	5.6 ± 1.4	5.7 ± 1.2	-	NS
HDL cholesterol (mmol/l)	1.2 ± 0.3	1.2 ± 0.4	-	NS
LDL cholesterol (mmol/l)	3.3 ± 1.1	3.5 ± 1.0	-	NS
Triglycerides (mmol/l)	2.0 (0.9-3.3)	2.0 (1.2-4.0)	-	NS
Creatinine clearance (ml/min)	87 (65-113)	87 (56-131)	-	NS

Table 3. Stepwise model of independent predictors of CAD

	OR	P
Micro/macro-albuminuria	3.9	0.03
Smoking	6.5	0.05
Femoral murmur	17.1	0.008
Gender	-	0.70
Age	-	0.56

Table 4. Management of the patients with established CAD (n=15)

Medical treatment only	7 (47%)
Coronary artery bypass grafting	4 (27%)
Percutaneous transluminal coronary angioplasty	4 (27%)

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