Coronary Artery Disease in Asymptomatic Type-2 Diabetic Women. A Comparative Study between Exercise Test, Cardiopulmonary Exercise Test, and Dipyridamole Myocardial Perfusion Scintigraphy in the Identification of Ischemia

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Summary

Background: **Cardiovascular disease is the leading cause of morbidity and mortality among diabetic individuals. Myocardial ischemia is frequently asymptomatic, thus leading to a late diagnosis and worse prognosis. Diabetic women are known to have a cardiovascular death risk higher than that in men.**

Objectives: **To assess the prevalence of coronary artery disease (CAD) in asymptomatic diabetic women. To compare the results of exercise test (ET), cardiopulmonary exercise test (CPET), and dipyridamole myocardial perfusion scintigraphy (MPS) with the findings of coronary angiography, (ANGI) in order of identify the most accurate method in the detection of significant CAD.**

Methods: **A total of 104 diabetic women were assessed with ET, CPET and MPS in the period within two months from the ANGI. MIBI-^{99m}Tc scintigraphy was performed using the gated-SPECT technique. Pearson's chi-square, Student's t tests were used for the statistical analysis and also the logistic regression analysis.**

Results: **The prevalence of CAD in the group studied was 32.7%. For the ET, an effective test (p=0.045), the chronotropic incompetence (p=0.031), and the exercise time performed (p=0.022) showed a significant association with DAC. For CPET, peak VO2 and HR achieved were associated with CAD (p=0.004 and p=0.025, respectively). Most of the MPS variables showed a significant association with CAD (p=0.001, for all).**

Conclusions: **The results obtained may suggest a high prevalence of CAD in diabetic women. Thus, this population should be investigated from the cardiovascular point of view even without cardiac symptom. Of the noninvasive diagnostic methods used, dipyridamole MPS was the one that showed the highest discrimination power in relation to diabetic women with CAD. (Arq Bras Cardiol 2007;88(5):263-269)**

Key words: **Diabetes Mellitus, Type 2; coronary arteriosclerosis; women; exercise test; respiratory function tests; radionuclide imaging.**

Introduction

The prevalence of diabetes mellitus (DM) has been growing fast and continuously in the past decades, thus acquiring epidemic proportions[1]. Paradoxically to the reduction in coronary artery disease (CAD) mortality, diabetic individuals have presented a significant increase in mortality[1]. Cardiovascular disease is the leading cause of morbidity and mortality, affecting approximately half of the diabetic patients[1]. In this group of patients, myocardial ischemia is frequently silent, thus leading to a late diagnosis and worse prognosis[1].

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Since the 1990's, studies[2-4] have demonstrated differences in the investigation of CAD according to the patient's gender, and these differences have been attributed to the lower incidence and atypical symptoms among females. However, diabetic women are known to have a cardiovascular death risk 7.5 times higher than non-diabetic women[18]. Since the presence of cardiovascular events (CE) may be modified by an appropriate screening and adequate intervention and treatment, early diagnosis may be of great benefit.

The objective of the present study is to assess the prevalence of CAD among type-2 diabetic women without cardiovascular symptoms and also to identify the most effective diagnostic method to detect significant CAD in the group mentioned, by comparing the findings of exercise test (ET), cardiopulmonary exercise test (CPET), and dipyridamole (DIPY) myocardial perfusion scintigraphy (MPS) with those of coronary angiography (ANGI).

Methods

Initially, 120 type-2 diabetic women aged between 40 and 80 years and diagnosed with DM for at least five years were included. Women with functional limitation or symptoms suggestive of ischemia were excluded. The patients were recruited (after study approval by the institution's ethics and research committee) via telephone call or mail and were included in the study after a baseline interview, clinical evaluation, and signature of the informed consent form. After the interview, 16 patients were excluded (because of symptoms suggestive of ischemia or difficulty to attend follow-up appointments to undergo tests). A total of 104 patients remained in the study and had their glycosylated hemoglobin (Hb_1Ac), ET, CPET, MPS, and ANGI performed with a maximum 2-month interval and with no revascularization procedures between the tests. According to previous recommendation, medications that could interfere with the analysis of the diagnostic tests were discontinued. The tests were analyzed by two specialists in each area, and they had no information on the results of the other tests.

Glycosylated hemoglobin determination - This determination was performed in our institution, using the automated immunoturbidimetric method (Roche™). Values ranging from 4.8 to 6.0 units were considered normal.

Coronary angiography - The coronary arteries were analyzed as regards the degree of stenosis using both visual and quantitative analysis and the percentage of stenosis was calculated automatically by a standard formula. Obstructions ≥ 50% were considered as significant CAD. Detection of collateral circulation (CC) was only considered relevant as a justification for the discrepancies between ANGI and the other methods, as well as to verify associations with ST-segment alterations during DIPY.

Exercise test - The protocol used was the already standardized modified Bruce protocol[5]. The variables determined in the ET and later compared with ANGIO were: exercise time (Δt), blood pressure (BP) behavior, ST-segment analysis, presence of typical exercise-induced chest pain (CP), and presence of chronotropic incompetence (CI) or of complex exercise-induced arrhythmias.

The ET was interpreted, according to the presence of electrocardiographic and clinical alterations, as suggestive of ischemia in the presence of ST-segment depression (ST-depression) ≥ 1.5 mm in relation to baseline or CP suggestive of exercise-induced ischemia. Also, it was interpreted as abnormal (anl) if complex exercise-induce arrhythmias, abnormal behavior of BP (drop or systolic BP plateau) and of heart rate (inappropriate elevation of heart rate in response to exercise in the absence of medications) were found. The presence of ventricular extrasystoles, whether paired or in salvos, or of nonsustained exercise-induced ventricular tachycardia was considered a complex arrhythmia. The presence of exercise-induced decrease in systolic BP ≥10 mmHg or maintenance of BP with increasing effort was considered BP decrease and plateau behavior, respectively. The inappropriate elevation of heart rate (HR) was considered abnormal and called CI, and was assessed by the formula previously described by Azarbal[6].

Cardiopulmonary exercise test - The following variables were analyzed and compared to the results of ANGI: maximum oxygen consumption (VO_2max) or oxygen consumption at exercise peak (VO_2peak), anaerobic threshold (AT), oxygen pulse (VO_2peak pulse) and drop in O_2 pulse (DPO_2) at exercise peak. The other variables determined by CPET, such as HR behavior, exercise time, and ST-segment analysis followed the same criteria described for the ET.

Dipyridamole myocardial perfusion scintigraphy - MPS with DIPY and in baseline conditions was performed with MIBI-^{99m}Tc according to the two-day standard protocol. Images were acquired using the gated-SPECT technique[7]. Dipyridamole was injected at a dose of 0.56 mg/kg/min in four minutes (min). A total of 20 miliCuries (mCi) or 740 megaBecquerel (MBq) of MIBI-^{99m}Tc were administered in the second minute after DIPY infusion, which was considered the time point of maximal hyperemia. The images were acquired 60 min after the radiopharmaceutical was injected. ECGs were performed before, during, and for six minutes after the end of DIPY infusion. DIPY-MPS was considered suggestive of ischemia if ST-depression or intensification of ST-depression ≥ 1.0 mm; ST-elevation ≥ 1.0 mm; or clinical manifestations suggestive of ischemia were found[8]. The adverse effects that occurred during the administration of dipyridamole were readily reverted with the use of endovenous aminophylline. The baseline phase was performed between 24 – 72 hours after the DIPY phase.

The images were processed by the QGS software program[7,9]. Gated-SPECT provided a reproduction of cardiac wall contractility, end-systolic and diastolic volume indexes (ESV and EDV, respectively), and left ventricular ejection fraction (LVEF) index. Qualitative assessment of the radiopharmaceutical concentration in 17 myocardial segments was used to analyze the perfusion images. According to the homogeneity, or lack of homogeneity, of uptake in the myocardial segments, MPS were considered as: normal, if the indicator concentration was homogeneous in both phases; suggestive of ischemia, if there was a reversible low indicator uptake in one or more myocardial segments after stress; suggestive of fibrosis if there was a fixed low uptake in one or more segments in both phases; and suggestive of ischemia and fibrosis if there was fixed and reversible low uptake in one or more segments in both phases.

The analysis of left ventricular (LV) systolic function was based on information from the gated-SPECT. The variables obtained were: wall contractility (normal or abnormal); systolic wall thickening (normal or abnormal), and dilation in the stress and baseline phases. The presence of LV dilation was analyzed by taking into consideration the ESV and EDV recommended in the literature. In the QGS software program analysis, ESV equal to 84+/- 26 ml and EDV equal to 33+/- 17 ml were considered normal[9]. Also, the presence of cavity dilation in the stress phase was analyzed in comparison with basal one (transient LV dilation), using visual analysis and the TID (transient ischemic dilation) index, with values higher than 1.22 representing significant dilation[10,11]. Other variables obtained were the presence of abnormal pulmonary radionuclide uptake[12]; LVEF in the post-DIPY and baseline phases, with values ≥ 50% being considered normal for the QGS software program; and the presence of a > 5% decrease in LVEF values in the exercise phase in relation to baseline.

Statistical analysis - The Pearson's chi square test was used to compare the patient groups in relation to categorical variables, and the Student's t test was used in relation to numeric variables for non-related samples. Discriminant analysis was used to differentiate women with significant CAD. Logistic regression analysis was also performed. P values <0.05 were considered significant. Interobserver agreement for each method was assessed using the kappa statistics (categorical variables), and intraclass correlation coefficient (numeric variables).

Results:

After the statistical analysis, a 32.7% prevalence of significant CAD was observed among diabetic women with no cardiovascular symptoms. Of the 104 patients studied, 34 had a ≥ 50% stenosis.

Coronary angiography - Of the 34 patients with significant stenosis as analyzed by quantitative ANGI, 22 had 1-vessel disease; seven had two-vessel disease; and five had three-vessel disease. The anterior descending artery was affected in 13 patients; the right coronary in 18 patients; the circumflex in 8; the diagonal artery in 3; the marginal branch in one patient; and the ventricular posterior branch in two patients. No patient presented lesions in the left main coronary artery.

Clinical variables - No clinical characteristic enabled discrimination of patients with CAD using the univariate analysis, as shown in Table 1. Using the multivariate logistic regression analysis (Table 2), the variables predictive of CAD were smoking (0.002), and abnormal Hb_1Ac values (0.041).

Noninvasive diagnostic methods - Interobserver agreement for the presence of ischemia on ET was high ($\kappa = 0.787$). For CPET, interobserver agreement was also high in relation to VO_2max ($\rho = 0.974$), ventilatory AT ($\rho=0.900$) and O_2 pulse ($\rho = 0.867$) determinations. The agreement for determination of DPO_2 was low ($\kappa= 0.426$). Interobserver agreement for MPS in relation to the presence of perfusion alterations was high ($\kappa= 0.810$) and the agreement between qualitative and quantitative analysis of ANGIO in relation to the presence of CAD was also high ($\kappa= 0.833$).

Variables of the exercise test - Values of sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio (LR-), and accuracy (A) found for the ET were 44.1%; 61.4%; 35.7%; 69.3%; 73%; 71.3% and 55.7%, respectively. The ET variables that were associated with CAD were: effective test (p=0.045), CI (p=0.031), exercise time (p=0.022) and maximum HR achieved (p=0.027), as shown in Table 3.

Cardiopulmonary exercise test variables - The variables that were associated with CAD were VO_2 peak (p= 0.004) and maximum heart rate achieved (p=0.025), as shown in Table 4. Values of SE, SP, PPV, NPV, LR+, LR-, and A found for CPET in relation to the diagnosis of CAD were 44.1%, 72.8%, 44.1%, 72.8%, 61.4%, 59.2% and 63.4%, respectively.

Scintigraphy variables - Most of the DIPY-MPS variables showed an association with the presence of CAD (Table 5). The presence of ischemia and fibrosis showed a significant association (p=0.001 for both). No significant association was observed between the presence of CC and ST-depression during DIPY infusion ($p = 0.467$). Of the nine patients who presented ST-depression during DIPY infusion, four (44.4%) had significant CC. Also, no association was observed between the presence of ST-depression and CAD ($p = 0.053$). The values of SE, SP, PPV, NPV, LR+, LR- , and A found for DIPY-MPS in the diagnosis of CAD were 94%; 97%; 94%; 97%; 98%; 95.8% and 96.1%, respectively. During DIPY infusion, no severe side effects such as death or MI were observed in the population studied. We observed that: 21 patients (20.1%) had CP; 9 (8.6%) had ST-depression; 14 (13.4%) had headache; 18 (17.3%) had dizziness; 4 (3.8%) had nausea; 2 (1.9%) had complex ventricular arrhythmias; 6 (5.7%) had facial rash; 2 (1.9%) had hypotension and 4 (3.8%) had shortness of breath.

Discussion

The high prevalence of CAD found in the group studied (32.7%) may be explained by the particular characteristic of our Institution. Given that it is one of the cardiology referral centers in the State of Sao Paulo, it serves a large number of patients with multiple risk factors for CAD, thus characterizing a population with a high pretest probability (Table 1).

According to the consensus published in 1988 by the American Diabetes Association[1], the estimated prevalence of CAD for patients with DM is of 55%.

No studies demonstrating the prevalence of CAD, specifically among women with type-2 DM with no cardiovascular symptoms, are available in the literature.

No clinical and epidemiological characteristic showed a significant association with CAD in the group studied using univariate analysis. Using logistic regression analysis, however, abnormal Hb_1Ac values and smoking were factors discriminating patients with CAD in this population (Table 2).

The first challenge in the diagnosis of CAD in diabetic women is to determine the best method for an initial screening.

Traditional resting ECG adds little information in the identification of patients with CAD, since it only rules out or suggests the presence of acute CE or previous myocardial infarction (MI)[13]. Baseline ECG in women frequently shows ventricular repolarization abnormalities (VRA), thus making it hardly relevant in the diagnosis of CAD[13]. In premenopause, ECG specificity is known to be even lower because estrogen-related VRA are more frequent, and estrogen is considered responsible for vasoconstriction of the coronary network, thus resulting in the abnormalities mentioned[13]. VRA are restricted to the ST-segment and the T wave, and are similar to those observed during the use of digitalis, which has molecules structurally similar to those of estrogen[13]. Of the 104 patients evaluated, 39 (37.5%) presented VRA on baseline ECG.

ET is largely used as the method of choice in the initial investigation of CAD; according to the literature, it has sensitivity (SE) and specificity (SP) values lower in females than in males (approximately 61% and 69%, respectively)[5,8]. As previously mentioned, we found lower values in the present study.

Diabetic women also frequently have peripheral vascular insufficiency[1]. In the group studied, 43 patients (42%) had an ineffective ET, which may be one of the reasons for the low SE found. Another limitation was the large number of tests considered "falsely" suggestive of ischemia because of the VRA. Henzlova et al[13] compared three groups of women who had undergone MPS after exercise. Although the MPS had been normal, the patients that were on hormone replacement therapy had 39% of ET compatible with ischemia, in comparison with 22% in the premenopausal group, and 17% in the postmenopausal group, both not receiving estrogens. Of the 39 patients (37.5%) who had a baseline ECG with VRA in the group studied, 10 (33.3%) had ET suggestive of ischemia in the absence of significant CAD, which probably made SP low.

Exercise time (Δt) may indirectly reflect the patients' functional capacity[5,8]. In the group studied, despite the lower limb limitation and low Δt, a significant association was observed between Δt and the presence of CAD (p=0.022). The heart rate achieved was also associated with CAD. In the

Table 1 – Clinical and epidemiological characteristics of the groups with and without CAD on ANGI. HBP: high blood pressure; Hb1Ac: glycosylated hemoglobin; anl: abnormal; SD: standard deviation

	without DAC (70)	WITH DAC (34)	p
Mean age (SD)	59.18 (9.97)	59.79(8.79)	0.542
Mean Hb1Ac (SD)	6.76(2.19)	7.17(1.92)	0.345
HBP	70 (67.3%)	34 (32.7%)	---
Smoking	17(24%)	13(38%)	0.141
Dyslipidemia	61(87%)	31(91%)	0.546
Obesity	59(84%)	26(76%)	0.333
Sedentary lifestyle	64(91%)	32(94%)	0.721
Family history	45(64%)	21(62%)	0.802
Anl Hb1Ac	37(53%)	21(62%)	0.391
Menopause	56(80%)	24(70%)	0.130

Table 2: Logistic regression analysis of the clinical and epidemiologic characteristics. Anl Hb1Ac: abnormal glycosylated hemoglobin; OR: odds ratio

	Coefficient	Standard error	p	O.R.
Anl Hb1Ac	1.236	0.604	0.041	3.443
Smoking	3.118	1.018	0.002	22.610
Family history	0.896	0.634	0.158	2.449
Obesity	-0.869	0.592	0.142	0.419

Table 3- Exercise test variables in the groups of patients with and without CAD. Anl BP: abnormal blood pressure behavior at exercise; CI: chronotropic incompetence; HR max: maximum heart rate achieved with exercise; SD: standard deviation

	Without CAD (70)	WITH CAD (34)	p
Ischemia	27(38%)	15(44%)	0.589
Chest pain	16(23%)	14(41%)	0.053
Efficient	46(66%)	14(41%)	0.045
Anl BP	35(50%)	15(44%)	0.573
Complex arrhythmia	20(28%)	12(35%)	0.486
CI	37(53%)	26(76%)	0.031
Exercise time (SD)	7.53(2.56)	6.27(2.70)	0.022
HR max- mean (SD)	142.07(20.38)	132.45(20.43)	0.027

group of patients with CAD, HR was, on average, equal to 132.45 bpm, and in the patients without CAD, it was equal to 142.07 bpm, with p=0.027 (Table 3).

HR is known to increase linearly during dynamic exercise according to the increase in the workload and O_2 consumption. A higher HR elevation is usually observed among females in relation to males[5], and it is known that an inadequate increase in HR may be an important sign of CAD. Azarbal et al[6] verified that CI is an important predictor of mortality and should be incorporated in risk stratification algorithms of ET. However, the authors described that MPS was a better predictor of mortality and of CE in relation to the presence of CI. In the present study, a significant association was observed between CI and CAD (p=0.031). Of the 34 patients with significant CAD, 26 (73.5%) showed criteria of CI.

As previously mentioned, CPET may provide valuable information on functional capacity. In this study, we attempted to assess the value of CPET in the diagnosis of CAD in asymptomatic diabetic women. Because of the lower cost in relation to MPS and of the possibility of association of ECG and clinical variables obtained with exercise with functional parameters, CPET is perhaps a noninvasive diagnostic method with a higher cost-effectiveness ratio than ET and DIPY-MPS.

Few studies on the usefulness of CPET in the investigation of CAD have been published[14,15]. Klainman et al[14] demonstrated

Table 4- CPET variables in the groups of patients with and without CAD. DPO2: drop in oxygen saturation during exercise; ECG: electrocardiogram; VO2 peak: maximum oxygen consumption at exercise peak; AT: anaerobic threshold; HR: heart rate

	WITHOUT CAD (70)	WITH CAD (34)	p
DPO_2	26(37%)	8(23%)	0.360
Ischemia on ECG	19(27%)	15(44%)	0.292
VO_2peak- mean (SD)	16.41(4.57)	13.59(3.55)	0.004
$O_{2\ SATURATION}$ - mean (SD)	8.24 (2.35)	8.00(2.06)	0.626
AT- mean (SD)	11.75(3.61)	11.71(3.58)	0.953
Exercise time -mean (SD)	9.02(2.36)	8.54(2.94)	0.417
HR max - mean (SD)	142.21(20.75)	130.85(20.19)	0.025

Table 5: Scintigraphy variables in the groups of patients with and without CAD. LV: left ventricle; ECG ischemia: ECG during DIPY suggestive of ischemia; SD: standard deviation; TID: transitory ischemic dilation; LVEF: left ventricular ejection fraction; ESV: end-systolic volume; EDV: end-diastolic volume

	Without CAD	WITH CA D	p
Ischemia	2	28	0.001
Fibrosis	3	13	0.001
Abnormal perfusion	4	32	0.001
LV dilation	15	15	0.017
TID	4	11	0.001
Pulmonary uptake	0	4	0.003
Drop in LVEF	29	16	0.651
Abnormal thickening	10	26	0.001
Abnormal contractility	18	25	0.001
ECG ischemia	3	6	0.053
Chest pain during infusion	12	9	0.166
LVEF post- DIPY –mean (SD)	0.59(0.13)	0.47(0.15)	0.001
Baseline LVEF – mean (SD)	0.60 (0.12)	0.50(0.14)	0.001
ESV – mean (SD)	38.51(29.15)	61.44(48.16)	0.001
EDV – mean (SD)	83.34(34.72)	107.59(49.08)	0.001

that ventilatory variables are decreased with exercise when healthy patients are compared to those with CAD. In the present study, peak VO_2 and HR achieved with exercise were observed to be associated with the presence of CAD (p=0.004 and p=0.025, respectively). The SE value found for CPET in the diagnosis of CAD was also low: equal to 44.1%. The SP value, in turn, was higher than that of ET (72.8%). Of the 34 patients with CAD on ANGI, only 15 had a CPET suggestive of ischemia. On the other hand, of the 70 patients without significant CAD, 51 had a CPET not suggestive of ischemia at exercise.

The identification of severity and extent of perfusion defects enables the degree of functional consequences of a coronary stenosis to be established. Since not always does an anatomical coronary artery lesion produce ischemic alterations, there are situations in which a joint anatomical and functional investigation would be the most appropriate management.

In addition to the importance in risk stratification and clinical management, MPS is considered an important noninvasive method that adds diagnostic accuracy to ET for both genders[16,17]. Its high SP is particularly useful to identify women with ET considered "false negative"[8]. The mean SE and SP values for planar thallium-201-MPS are 84% and 87%, respectively, and for SPECT-MPS, the mean SE increases to 88%, without decreasing SP (87%). With the advances in methodology, there were increases in SE and SP values. Smanio et al found SE and SP values of 95% and 94.1%, respectively, using the gated-SPECT technique[18].

To date, a small number of studies on MPS in women is found in the literature. Taillefer et al[19] compared thallium-201 to MIBI-^{99m}Tc in 115 women and found no significant difference in SE between the two radiopharmaceuticals[19]. However, there was a great increase in SP with the gated-SPECT technique (92% vs. 67%, respectively).

Previous studies[20,21] found similar values for DIPY and adenosine testing in relation to the images obtained after

exercise. Verani et al[20] confirmed the superiority of DIPY-MPS in relation to submaximal ET in the diagnosis of CAD. Because of the low functional capacity found in the group studied (43% of ineffective ET), an important investigation was made using a method that did not require strenuous effort and had a high diagnostic power, such as the DIPY-MPS.

Few studies[20,25] verified the value of MPS in asymptomatic diabetic patients. For this purpose, the multicenter DIAD study (Detection of Ischemia in Asymptomatic Diabetics) enrolled patients from 14 American and Canadian centers[26], and found 22% of ischemia in asymptomatic type-2 diabetic subjects. Rajagopalan et al[25] found 826 patients (58%) with ischemia among 1427 asymptomatic diabetics. Prior et al[24] and Lerner et al[27] identified perfusion defects in 37% of the 133 asymptomatic diabetic individuals (of both genders) who underwent MPS. Of these, 30% were reversible, thus suggesting ischemia.

In this study, SE and SP values of MPS in the diagnosis of CAD were high (94% and 97%, respectively), and similar to those described in the literature[16]. Most of the MPS variables were associated with CAD (Table 5). Of the 34 patients with significant lesion on ANGI, only two (1.9%) were not identified by MPS; both showed preserved perfusion and contractility. The lesions were probably not functionally significant. Of the 70 patients without CAD on ANGI, 68 had normal MPS.

Functional information is also useful in the diagnosis and prognosis of CAD[16, 28]. In this study, we verified that baseline and post-DIPY LVEF values showed association with CAD (p=0.001 for both). However, the LVEF decrease after DIPY in relation to baseline did not show a significant association with CAD (p=0.651).

Yamagishi et al's study[28] demonstrated that the decrease in LVEF values after stress promotes an increase in SE for the detection of multivessel disease. We can try to explain this discrepancy of the literature by the presence of alterations in microcirculation that are common in diabetics and which can cause subendocardial ischemia and drop in LVEF during pharmacological testing in the absence of an anatomically severe obstructive lesion.

Systolic thickening and contractility alterations also showed a significant association with CAD (p = 0.001). The presence of LV dilation and pulmonary MIBI uptake in the stress phase were also verified to be associated with CAD (p = 0.017 and p = 0.003, respectively). In patients with resting or stress-induced LV dysfunction there can be a radiopharmaceutical extravasation into the pulmonary interstitial space due to the increase in end-diastolic pressure[12]. Additionally, with the prolonged circulatory time, increased radioactivity is observed in the lung fields. Although this phenomenon is more frequent in thallium-201 MPS, it can also be observed with Mibi-^{99m}Tc.

Another variable analyzed was transient left ventricular dilation (TID) after dipyridamole infusion. The presence of TID after the stress phase is usually related to LV failure and has a strong association with CAD with stress-induced ischemic dysfunction, which has an unquestionable predictive value in the determination of survival[11]. Hansen et al[12] studied 1129 patients and verified a significant association between the presence of TID after DIPY infusion and CAD[12], and attributed this ventricular cavity dilation to a diffuse subendocardial hypoperfusion. In the group studied, a significant association was observed between the presence of TID and CAD (p = 0.001).

When clinical and electrocardiographic variables during DIPY infusion were analyzed, CP and ECG alterations were observed not to have a significant association with CAD (p = 0.166 and 0.053, respectively). ST-depression during DIPY infusion may be secondary to the "flow steal" phenomenon[20]. However, no association between ST-depression and significant CC on ANGI was observed in this group either (p = 0.467).

The method proved safe and the side effects presented were similar to those described in the literature[21].

Study limitations and clinical implications

The qualitative analysis of the perfusion images was a study limitation. The interpretation using quantitative analysis by scores described in the literature is neither routinely used in our service nor in most of the clinical nuclear medicine services. Therefore, it would not make sense to investigate CAD with a methodology that is not actually used in daily clinical practice.

Finally, we understand that this study is of great value in the clinical management of diabetic women. Knowing that the cardiovascular risk is high in patients with DM, and that women have clinical manifestations which are difficult to characterize, preventive cardiovascular assessment is warranted in the group studied. The presence of VRA on baseline ECG leads to lower accuracy of exercise tests in the identification of CAD. In addition to the frequently observed low functional capacity in diabetic women, the value of methods that depend on the performance of strenuous exercise is limited. On the other hand, it is not cost-effective to perform an anatomical investigation in all diabetic women.

As a consequence of the arguments shown, we can presume that performing a safe technique that has a high diagnostic and prognostic power, such as MPS associated with pharmacological testing with dipyridamole, may be the method of choice in the initial assessment of diabetic women, even in the absence of cardiovascular symptoms.

As a primary conclusion, the results obtained showed that the prevalence of CAD in diabetic women with no cardiovascular symptoms is high (32.7%), and this population should be investigated from the cardiovascular point of view. Also, we conclude that the noninvasive diagnostic method that showed the highest power to discriminate women with CAD was DIPY-MPS; thus, this should be the gold standard method for this group of patients.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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