Silent myocardial ischaemia and risk factors in a diabetic Afro-Caribbean population

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Abstract

Aims. – In Guadeloupe, an island in the French West Indies, diabetes has a prevalence recently reported to be 10%. Myocardial ischaemia is more frequently silent in diabetics, and needs to be screened for and monitored, once identified. This study aimed to evaluate the prevalence of silent myocardial ischaemia (SMI) in a diabetic population and to analyze its associated cardiovascular risk (CVR) factors.

Methods. – This was a cross-sectional study of 147 patients with associated CVR factors, defined according to the 2004 SFC/ALFEDIAM guidelines. Exercise stress tests, myocardial performance imaging and stress echocardiography were performed. Ancova and logistic regression were used in the statistical analyses.

Results. – The patients’ mean age was 62 years, and 53% were male. Mean duration of diabetes was 14 years. Overall, 23.1% had SMI, and these patients more frequently had a personal history of cardiovascular disease vs those without SMI. On multivariate logistic-regression analyses, the adjusted odds ratios of SMI were significantly increased in patients with a personal history of cardiovascular disease (4.36, 95% CI: 1.36–13.96; \( P = 0.01 \)) and left ventricular hypertrophy (LVH) (2.46, 95% CI: 1.03–5.86; \( P = 0.04 \)).

Conclusion. – The prevalence of SMI in our Afro-Caribbean diabetic population was 23.1%. Searching for a personal history of cardiovascular disease and LVH may help to identify patients who need to be screened for SMI.

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Keywords: Silent myocardial ischaemia; Diabetes; History of cardiovascular disease; Left ventricular hypertrophy

Résumé

Ischémie myocardique silencieuse et facteurs de risque chez des patients diabétiques d’origine afro-caribéenne.

Introduction. – La prévalence du diabète de type 2 en Guadeloupe est de 10 %. Chez les diabétiques, l’ischémie myocardique est plus souvent silencieuse et doit être investiguée quand elle est mise en évidence.

Objectif. – L’objectif de l’étude était d’évaluer la prévalence de l’ischémie myocardique silencieuse dans une population caribéenne de diabétiques et d’analyser les facteurs de risque cardiovasculaire associés à celle-ci.

Méthodes. – Il s’agissait d’une étude transversale menée chez 147 patients avec facteurs de risque associés définis selon les recommandations conjointes SFC/ALFEDIAM de 2004. Une épreuve d’effort et une scintigraphie myocardique ont été réalisées. Sur le plan statistique une analyse Ancova et une régression logistique ont été utilisées.

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Résultats. – La moyenne d’âge était de 62 ans, 53 % étaient des hommes. L’ancienneté du diabète était de 14 ans. Parmi les patients, 23,1 % avaient une ischémie myocardique silencieuse. Les patients avec ischémie myocardique silencieuse avaient plus fréquemment des antécédents cardiovasculaires. L’odd ratio de l’ischémie myocardique silencieuse était significativement augmenté en cas d’antécédent cardiovasculaire 4,36 (1,36–13,96), \( P = 0,01 \) et en présence d’hypertrophie ventriculaire gauche 2,46 (1,03–5,86), \( P = 0,04 \) dans l’analyse de régression logistique multivariée.

Conclusion. – La prévalence de l’ischémie myocardique silencieuse dans la population diabétique étudiée était de 23,1 %. Les antécédents cardiovasculaires et la présence d’une hypertrophie ventriculaire gauche étaient associés à la présence d’une ischémie myocardique silencieuse. La recherche de ces facteurs pourrait aider à mieux cibler les patients diabétiques qui devraient bénéficier d’un dépistage systématique de l’ischémie myocardique silencieuse en Guadeloupe.

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Mots clés : Ischémie myocardique silencieuse ; Diabète ; Antécédents cardiovasculaires ; Hypertrophie ventriculaire gauche ; Antilles françaises ; Afro-Caribéens

1. Introduction

In Guadeloupe, an island in the French West Indies, the prevalence of type 2 diabetes is as high as 10.1% in the general population vs only 4.39% in mainland France [1]. Diabetes is an independent cardiovascular risk factor and a major public health problem that is growing worldwide. Cardiovascular events are two to threefold more frequent [2] and more severe [3,4] in diabetic patients than in non-diabetic subjects. Indeed, 65–80% of deaths in diabetic patients are of cardiovascular origin [5].

The condition of silent myocardial ischaemia (SMI) was identified 40 years ago [6]. The disease is the result of a transient decrease in myocardial perfusion with no thoracic pain, and is two to seven times more frequently seen in diabetic patients [7]. Also, SMI is associated with more frequent cardiovascular events, with a hazard ratio of 2.79 [8]. In 2004, the French Society of Cardiology (SFC) and French Language Association for the Study of Diabetes and Metabolic Diseases (ALFEDIAM) published guidelines for the detection of SMI in diabetes to improve the detection of patients at high cardiovascular risk [9].

The present study aimed to evaluate the prevalence of SMI in an Afro-Caribbean diabetic population screened according to the 2004 SFC/ALFEDIAM guidelines, and to analyze the association of cardiovascular risk factors with SMI.

2. Patients and methods

2.1. Study population

The present cross-sectional study was conducted between March 2003 and June 2006 at the cardiovascular unit of the University Hospital of Guadeloupe. The type 1 or 2 diabetic patients were asymptomatic, and fulfilled the following criteria, as assessed by the 2004 SFC/ALFEDIAM guidelines. Included were type 2 diabetic patients aged more than 60 years or with diabetes of more than 10 years’ duration, with at least two of the following risk factors: dyslipidaemia, with total cholesterol more than 6.45 mmol/L and/or low-density lipoprotein (LDL) cholesterol more than 4.128 mmol/L, high-density lipoprotein (HDL) cholesterol less than 0.903 mmol/L, triglyceride (TG) more than 2.28 mmol/L and/or treatment with a lipid-lowering drug given for dyslipidaemia; blood pressure (BP) more than 140/90 mmHg or treatment with antihypertensive medications; current smoker or stopped smoking for less than three years; and major cardiovascular event before age 60 years in a first-degree family relative. Also included were type 1 diabetic patients aged more than 45 years, treated for more than 15 years and with at least two other risk factors. Patients with type 1 or 2 diabetes with peripheral artery disease or carotid atheroma, or proteinuria due to renal insufficiency were included. In addition, patients with either type 1 or type 2 diabetes with microalbuminuria and at least two other risk factors, and those beginning physical activity after the age of 45 years were also included. Finally, also included were diabetic patients undergoing dialysis or with a renal transplant, who had been assessed by a stress test at a recent cardiovascular assessment. Patients with angina were excluded from the study.

2.2. Data collection

2.2.1. Medical history

Data on age, gender, weight, height, and duration of diabetes and family history of cardiovascular disease were recorded for all participating patients. Any previous medical history of cardiovascular disease, such as ischaemic heart disease, stroke, heart failure and/or peripheral artery disease, was also recorded. In addition, body mass index (BMI) and body surface area (according to the DuBois and DuBois formula) were calculated. Obesity was defined as BMI more than or equal to 30 kg/m².

2.2.2. Blood pressure measurement

BP was measured after a cardiac ultrasound examination in the sitting position, using an automated recorder (Welch Allyn) with a suitably sized cuff. The average of three systolic BP (SBP) and diastolic BP (DBP) measurements was calculated. Pulse pressure (PP) was calculated as SBP–DBP.

2.2.3. Biological parameters

Serum creatinine was recorded and creatinine clearance (Cl creat) calculated using the Cockcroft–Gault (CG) and Modification of Diet in Renal Disease (MDRD) formulas. Renal failure was defined as a Cl creat less than 60 mL/min according to the CG formula. Proteinuria was defined as urinary albuminuria more than 200 mg/L in the first morning urinary excretion, and microalbuminuria was defined as albuminuria between 20 and 200 mg/L in the first morning urinary excretion. Nephropathy
was defined as renal failure and/or proteinuria. The lipid-profile parameters measured were total cholesterol, HDL cholesterol, LDL cholesterol (calculated by the Friedewald formula when TG less than 4.56 mmol/L), TG and glycated haemoglobin (HbA1c). Dyslipidaemia was defined according to the SFC/ALFEDIAM 2004 guidelines [9].

2.2.4. Echocardiography

This was performed by an experienced cardiologist using the Philips HDI 5000 sonography system, equipped with a P4-2 phased-array probe. Interventricular wall thickness (IVST) and left ventricular posterior wall thickness (PWT) were measured at end-diastole. Left ventricular internal diameter was also measured at both end-diastole (LVID d) and end-systole (LVID s). End-diastolic measurement criteria included the Penn convention [10]. Left ventricular mass (LVM) was calculated by the formula LVM = (1.04 × [(IVST + LVID d + PWT) 3 – (LVID d) 3]) –13.6. Left ventricular hypertrophy (LVH) was defined according to the SFC/ALFEDIAM guidelines [13,14]. Three test outcomes were possible:

- myocardial perfusion imaging was normal;
- perfusion defects were less than 10% of the left ventricle (LV), and follow-up was suggested;
- perfusion defects were more than 10% of the LV and coronaryography was suggested.

Dobutamine stress echocardiography was performed when myocardial perfusion imaging was unavailable. Dobutamine was given at 10–40 mcg/kg/min with atropine (0.25 mg/min), but was started at the 20-mcg/kg/min step if 85% of the theoretical maximum frequency had not been achieved [15]. There were two possible test outcomes: normal; or positive, with the appearance of hypokinesia in two contiguous segments—in which case, coronaryography was proposed.

SMI was defined as either a positive maximum exercise test, abnormal myocardial perfusion imaging with perfusion defects more than 10% of the LV, or a positive stress echocardiography.

2.2.5. Atheroma

This was assessed by Doppler echography, with atheroma classified as either carotid or lower-limb atheroma with or without stenosis.

2.2.6. Assessment of silent myocardial ischaemia

Three different tests were performed to assess SMI: exercise tests; myocardial perfusion imaging; and stress echocardiography. Anti-ischaemic agents were stopped 48 h before the tests were carried out.

An exercise test was performed according to the guidelines unless contraindicated [12], using a treadmill, following the Bruce protocol, or a bicycle with a 30-W increase in power output every three min. Three test outcomes were possible. First, the test could be completed at maximum intensity (85% of the theoretical maximum frequency, test duration of more than 440 s), but with positive signs of myocardial ischaemia—namely, ST depression of more than 1 mm at 80 ms after J (ST depression horizontal or descending) or more than 1.5 mm at 80 ms after J (ascending ST depression)—in three contiguous leads. The test was also considered positive in cases of severe haemodynamic and rhythm disorders (rhythm disorder, conduction disorder, low output, thoracic pain, or massive and abrupt ST depression) thus, indicating the need for coronaryography. Second, the stress test could be negative, indicating that no further tests are necessary and, third, the stress test could be submaximum or non-discriminatory (small or doubtful chance of positivity), thus suggesting the need for myocardial perfusion imaging or stress echocardiography.

Myocardial perfusion imaging was indicated when either exercise was not possible, the patient had a left bundle branch block or a pacemaker, or a previous exercise test had been either submaximum or non-discriminatory. Thallium-201 and technetium-99 m sestamibi were used in combination with either the exercise test (treadmill or bicycle) or the pharmacological agent dipyridamole, prescribed according to the French guidelines [13,14]. Three test outcomes were possible:

- myocardial perfusion imaging was normal;
- perfusion defects were less than 10% of the left ventricle (LV), and follow-up was suggested;
- perfusion defects were more than 10% of the LV and coronaryography was suggested.

2.2.7. Coronarography

This was proposed when SMI was positively present, according to the SFC guidelines [9]. Coronary stenosis was defined as a narrowing of at least 50%.

2.3. Statistical analysis

Data are expressed as means ± standard deviation (SD) for continuous variables and as numbers (percentages) for categorical variables. TG levels were log10-transformed before the analyses. For comparisons, patients were categorized into two groups according to the presence or absence of an SMI. The chi2 test and analysis of covariance (Ancova) were used to compare percentages and values between patients, with adjustments for age and gender.

Multivariate logistic regressions were performed with a backwards-stepwise procedure, and with all significant covariates at the level of $P < 0.10$ in the univariate analysis. SPSS version 18.0 (SPSS Inc., Chicago, IL, USA) and SYSTAT for Windows version 12 (SYSTAT Software Inc, San Jose, CA, USA) software were used for the data analyses. All $P$ values were two-sided, and were considered significant when less than 0.05.

3. Results

A total of 161 asymptomatic patients were admitted to the hospital cardiovascular unit to be investigated for SMI. Reasons for suspecting SMI were according to the SFC/ALFEDIAM guidelines (Fig. 1). Of the 161 patients, 14 had a stress test that was either submaximum or non-discriminatory. The remaining 147 patients were successfully analyzed. Exercise tests were the only investigation performed in 59 patients, while 83 patients underwent myocardial perfusion imaging, and five had stress echocardiography.
Table 1
Clinical characteristics of the Afro-Caribbean type 2 diabetic patients included in the study.

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Silent myocardial ischaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>No (n = 113)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>147</td>
<td>62.0 (8.8)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>147</td>
<td>58 (51.3%)</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>145</td>
<td>13.9 (8.2)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>147</td>
<td>104 (92%)</td>
</tr>
<tr>
<td>Personal history of CVD</td>
<td>147</td>
<td>8 (7.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>147</td>
<td>99 (87.6%)</td>
</tr>
<tr>
<td>Smoker</td>
<td>147</td>
<td>15 (13.3%)</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>145</td>
<td>86 (77.5%)</td>
</tr>
<tr>
<td>Nephropathy*</td>
<td>143</td>
<td>60 (53.6%)</td>
</tr>
<tr>
<td>BMI</td>
<td>139</td>
<td>27.7 (4.2)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>147</td>
<td>138.8 (20.6)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>147</td>
<td>80.1 (9.8)</td>
</tr>
<tr>
<td>LVH</td>
<td>138</td>
<td>25 (23.4%)</td>
</tr>
<tr>
<td>Carotid atheroma</td>
<td>96</td>
<td>45 (58.4%)</td>
</tr>
<tr>
<td>Lower-limb atheroma</td>
<td>96</td>
<td>52 (67.5%)</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>145</td>
<td>713.2 (226)</td>
</tr>
<tr>
<td>Cl creat by CG (mL/min)</td>
<td>140</td>
<td>76.0 (36.4)</td>
</tr>
<tr>
<td>Cl creat by MDRD (mL/min)</td>
<td>145</td>
<td>81.7 (38.5)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>145</td>
<td>4.9 (1.3)</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>134</td>
<td>1.4 (0.5)</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>134</td>
<td>3.0 (1.1)</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>145</td>
<td>1.3 (0.8)</td>
</tr>
<tr>
<td>Albuminuria (g/L)</td>
<td>126</td>
<td>0.8 (4.0)</td>
</tr>
</tbody>
</table>

Data are presented as means (SD) or n (percent), and adjusted for age and gender; CVD : cardiovascular disease; BMI : body mass index; SBP : systolic blood pressure; DBP : diastolic blood pressure; LVH : left ventricular hypertrophy; Cl creat : creatinine clearance; CG : Cockcroft–Gault formula; MDRD : modification of diet in renal disease; HDL/LDL : high-density/low-density lipoprotein.

* Excluding microalbuminuria.

The characteristics of the study population are presented in Table 1. Overall, 53% of the patients were male, 93% had type 2 diabetes and 7% had type 1 diabetes. The mean age (SD) of the study population was 61.9 (8.6) years and the mean duration of diabetes was 14.2 (8.3) years. Overall, 87.8% of the population was hypertensive, 78.6% had dyslipidaemia, 15.6% were smokers and 27% had LVH. Seventeen patients (11.6%) had a personal history of cardiovascular disease: eight had suffered a stroke; six had lower-limb atheromatous arteritis; and three had ischaemic heart disease. A total of 143 patients had data available for the evaluation of nephropathy: 78 (54.5%) patients had nephropathy; 21 (15%) patients were undergoing dialysis; 27 (19%) patients had renal insufficiency; and 30 (21%) patients had proteinuria without renal insufficiency.

SMI was diagnosed in 34 patients (23.1%). These patients more frequently had a personal history of cardiovascular disease than those without SMI (P = 0.004). LVH was found in 42% of patients with SMI vs 23% without SMI (P = 0.06). A non-significant difference in Cl creat, calculated by the MDRD formula, was found between the two groups, with a lower value for patients with SMI (P = 0.06; Table 1).

The three parameters that were significant in the univariate analysis (history of cardiovascular disease, LVH and Cl creat by MDRD) were included in the multivariate logistic-regression analysis. The adjusted odds ratios (ORs) (95% CI) at step 1 are presented in Table 2. At step 2, the factors associated with SMI were a personal history of cardiovascular disease (OR: 4.36 [1.36–13.96]; P = 0.01) and LVH (OR: 2.46 [1.03–5.86]; P = 0.04; Table 2).

Of the 34 patients with SMI, 10 had an indication for coronary angiography, which was not performed, 13 had a normal
in patients with SMI, whereas Gomez et al. [29] found age and PP to be associated factors and, in the DIAD study, the Valsalva manoeuvre, BP, male gender and duration of diabetes were significantly different [21]. Gender, age, total cholesterol, proteinuria and an abnormal electrocardiography (ECG) trace at rest were the associated risk factors identified in the multivariate analysis of the Milan Study on Atherosclerosis and Diabetes (MiSAD) [16]. Furthermore, in their review, Cosson et al. [30] reported that carotid or lower-limb arterial disease, proteinuria, male gender, age more than 60 years and the presence of two or more cardiovascular risk factors (smoking, microalbuminuria, dyslipidaemia, hypertension, family history of premature cardiac disease and cardiac autonomic neuropathy) were the best predictors of SMI.

Treatment with statins [31], angiotensin-converting enzyme (ACE) inhibitors [32], antiplatelet agents [33] and beta-blockers [34], and control of BP [35] all have proven efficacy in diabetic patients. In addition, intensified multifactorial interventions proved to be effective in the Steno-2 study [36]. However, other studies and editorials have questioned the benefit of screening for SMI [21,37] as well as the benefits of revascularization in asymptomatic diabetic patients [37,38]. Nevertheless, screening for SMI is important to more intensively treat patients with SMI. Indeed, therapeutic management should be even more aggressive, as SMI cases should be considered secondary-prevention patients. Thus, patient management would be aimed at target values for BP, LDL cholesterol and HbA1c.

The limitations of our present study include the small number of patients, its cross-sectional design, and the recruitment of the study population from hospital medical consultations, which may not be representative of the overall population in Guadeloupe. Another issue is that myocardial perfusion imaging was not carried out in all patients, which might have led to underestimation of the prevalence of SMI. Finally, several patients indicated for coronaryography failed to undergo the procedure. Again, this may have led to underestimates the rate of coronary stenosis among patients with SMI. However, despite of these limitations, to our knowledge, this is first study of SMI to be carried out in Afro-Caribbean diabetic patients according to the SFC/ALFEDIAM 2004 guidelines.

4. Discussion

In the present study, an Afro-Caribbean diabetic population was screened for SMI according to the French 2004 SFC/ALFEDIAM guidelines [9], resulting in an SMI prevalence of 23%. Clinical factors associated with SMI were a personal history of cardiovascular disease and LVH.

The reported prevalence of SMI ranges from 6.4% in diabetics without risk factors [16] to 59% [17]. In the present study population, the prevalence of SMI was lower than those previously reported for diabetic patients with additional risk factors [8,17,18]. Furthermore, 25% of our studied population were screened for SMI because of dialysis or atheroma diagnosed by Doppler ultrasonography. As these two factors are strongly statistically linked to coronary artery disease and SMI, such patients may be at higher risk than the patients included in previous studies [19,20].

Our rate of significant coronary artery stenosis (21% of patients with SMI) was relatively low compared with the data from Koistinen et al. and Valensi et al. [7,18], but was similar to the revascularization rate reported by Miller et al. [17]. However, the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study reported a low rate of coronary revascularization (9% of the screened population), and a few patients with SMI were recommended for coronary angiography in Wackers et al. [21].

Considering that our study population was at very high risk, the low rate of SMI might be explained by the lower rate of coronary events, but greater frequency of cerebrovascular events, found in Afro-Caribbean and West-African populations vs Caucasian populations [22–27]. Indeed, the United Kingdom Prospective Diabetes Study (UKPDS) showed that the hazard-ratio associated with Afro-Caribbean ethnicity for myocardial infarction vs Caucasians was 0.3 (0.2–0.6) [28].

Finding the variables associated with SMI would help to better identify patients that should be evaluated for SMI. Indeed, an interesting finding in our present study was the variables associated with the presence of SMI in our sample population: a personal history of cardiovascular disease (stroke and peripheral artery disease) and LVH. Valensi et al. [8] found age, male gender, low HDL cholesterol and high TG to be more frequent coronary angiogram, 10 had coronary lesions and seven had significant coronary lesions, justifying coronary revascularization (5% of the screened population, 21% of patients with SMI).

Table 2
Multivariate logistic regression for silent myocardial ischaemia.

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Step 1 (n = 138)</th>
<th>Step 2 (n = 138)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted OR (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td>Personal history of CVD</td>
<td>4.12 (1.21–14.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>LVH</td>
<td>2.39 (0.94–6.06)</td>
<td>0.06</td>
</tr>
<tr>
<td>Cl creat (by MDRD)</td>
<td>1.00 (0.99–1.01)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

OR : odds ratio; CVD : cardiovascular disease; LVH : left ventricular hypertrophy; Cl creat : creatinine clearance; MDRD : Modification of Diet in Renal Disease formula.
Furthermore, a history of cardiovascular disease and presence of LVH were associated with SMI. Searching for these risk factors in patients selected according to the French guidelines might prove helpful for identifying those patients requiring screening for SMI. Longitudinal studies including more patients should also be of future interest.

**Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article.

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