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Original article

A randomized study comparing isotope and echocardiography stress testing in the screening of silent myocardial ischaemia in type 2 diabetic patients☆

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Abstract

Aims. – This study aimed to compare the positive predictive value (PPV) of stress myocardial scintigraphy (SPECT) and of dobutamine echocardiography (DE) in the diagnosis of significant coronary artery stenosis (CAD) in asymptomatic type 2 diabetic patients, and to assess long-term clinical outcomes according to silent myocardial ischaemia (SMI) screening.

Methods. – A total of 204 asymptomatic type 2 diabetic patients at high cardiovascular (CV) risk were prospectively randomized to undergo either SPECT ($n = 104$) or DE ($n = 100$). Coronary angiography was proposed in cases of SMI, with revascularization of suitable lesions. Intensive treatment of CV risk factors was prescribed for all patients. Death and myocardial infarction (MI) were recorded during the 3-year follow-up.

Results. – Clinical characteristics were similar in the two testing groups. The prevalence of SMI and significant CAD were 13% and 4%, respectively, in the SPECT group *vs* 11% and 5%, respectively, in the DE group (not significant [NS]). The PPV for the detection of significant CAD was 29% for SPECT and 45% for DE (NS). Seven patients (3%) underwent initial revascularization. The 3-year rate of CV death and MI was 2.5%, and similar in both groups.

Conclusion. – Rates of SMI and significant CAD in asymptomatic high-risk type 2 diabetic patients receiving intensive care of risk factors are low, and SPECT and DE are similar in the detection of SMI and CAD. Coronary revascularization and intensive CV risk-factor therapy are associated with a low rate of adverse CV events at 3 years, whichever stress test was used.

Keywords: Type 2 diabetes; Silent myocardial ischaemia; Screening; Stress myocardial scintigraphy; Dobutamine echocardiography; Cardiovascular death; Prospective study; Positive predictive value

Résumé

Étude randomisée comparant échocardiographie et scintigraphie de stress dans le dépistage de l'ischémie myocardique silencieuse chez les diabétiques de type 2.

Objectif. – Comparer la valeur prédictive positive de la scintigraphie myocardique de stress (SPECT) et l'échocardiographie sous dobutamine (ED) dans le diagnostic de sténoses coronaires significatives (CAD) chez les diabétiques de type 2 (DT2) asymptomatiques ; comparer le pronostic clinique à long terme selon la méthode de dépistage.

Méthodes. – Deux cent quatre patients asymptomatiques, DT2 à haut risque cardiovasculaire, ont été randomisés entre SPECT ($n = 104$) et ED ($n = 100$). Une coronarographie a été réalisée en cas d'ischémie myocardique silencieuse (IMS), avec revascularisation si les lésions étaient accessibles. Les facteurs de risque étaient traités de manière intensive. Le suivi clinique a porté sur le taux de décès de cause cardiaque et d'infarctus à trois ans.

☆ Trial registration: ClinicalTrials.gov number, NCT00202670.

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Résultats. – Les caractéristiques cliniques étaient comparables dans les deux groupes. La prévalence de l'IMS et de la CAD était respectivement de 13 et 4 % dans le groupe SPECT, et de 11 et 5 % dans le groupe ED (NS). Les valeurs prédictives positives pour la détection de CAD significative étaient de 29 % pour la SPECT et 45 % pour l'ED (NS). Une revascularisation initiale a été réalisée chez sept patients (3 %). Le taux de décès-infarctus à trois ans était de 2,5 %, identique dans les deux groupes.

Conclusions. – Les fréquences d'IMS et de CAD significatives chez les DT2, asymptomatiques, avec traitement intensif des facteurs de risque sont faibles. SPECT et ED sont comparables en termes de détection d'IMS et de CAD. La revascularisation coronaire et le traitement intensif des facteurs de risque sont associés à un faible taux d'événement cardiaque à trois ans, quel que soit le test utilisé.

Mots clés : Diabète de type 2 ; Ischémie myocardique silencieuse ; Dépistage ; Étude prospective ; Décès cardiovasculaires ; Scintigraphie myocardique de stress ; L'échocardiographie du stress ; Valeur prédictive

1. Introduction

The prevalence of type 2 diabetes is dramatically increasing worldwide [1]. Cardiovascular events, often with atypical features, represent the primary cause of death in this patient population. Also, the prevalence of silent myocardial ischaemia (SMI) is greater in diabetic patients and is associated with a poor prognosis [2].

To prevent adverse cardiac events, the current guidelines recommend detection of asymptomatic coronary artery disease (CAD) in type 2 diabetics who are at high cardiovascular risk [3,4]. Electrocardiography (ECG) stress testing is recommended, but is frequently inconclusive in type 2 diabetic patients. However, the contributions of stress thallium-201 single photon emission tomography (SPECT) and dobutamine echocardiography (DE) have yet to be established.

Despite a number of trials involving type 2 diabetic patients, the usefulness of SMI screening remains controversial, especially in the context of intensive risk-factor therapy [5,6]. In addition, several studies could find no prognostic benefit of systematic revascularization in cases of stable CAD [7–9]. However, most of these studies excluded high-risk patients, such as those with left main stenosis, three-vessel disease or severe left ventricular dysfunction [6,7–9].

The aims of the present study were to compare DE and SPECT in the detection of CAD in type 2 diabetic patients at high cardiovascular risk, and to evaluate the long-term prognosis according to the stress test used.

2. Methods

2.1. Patients

A total of 204 patients with type 2 diabetes were prospectively recruited between November 2003 and September 2008 from the diabetes department of Pitié-Salpêtrière Hospital in Paris, France. The inclusion and exclusion criteria used are listed in Table 1.

Diabetes was diagnosed according to the report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [10]. Patients with latent autoimmune diabetes in adults and secondary diabetes were excluded. Associated cardiovascular risk factors were defined as: age > 55 years for men and > 60 years for women; current smoking; family history of premature CAD (< 55 years for men, < 65 years for women); obesity; high blood pressure; and dyslipidaemia (Table 1). In addition, all patients underwent evaluation for diabetes complications, including fundoscopy, microalbuminuria and proteinuria assays of 24-h urine samples, and ultrasound visualization/examination of peripheral arteries. Severe microangiopathy was defined as the presence of panphotocoagulation retinopathy and/or macroproteinuria (> 300 mg/day). Peripheral (or carotid) arterial disease was defined as ≥ 50% stenosis in one or more vessel on Doppler imaging. All patients gave their informed consent to participate, and the study was approved by the local institutional ethics committee.

2.2. Study design

Altogether, 204 patients were randomized to undergo either stress thallium-201 single photon emission tomography (SPECT) or dobutamine echocardiography (DE) for the diagnosis of SMI. Treatment with nitrates, beta-blockers and

Table 1
Inclusion and exclusion criteria.

Inclusion criteria
Patients with type 2 diabetes, > 55 years (men) or > 60 years (women) of age, with no clinical symptoms of coronary artery disease **AND**
Peripheral or carotid occlusive arterial disease **OR**
Macroalbuminuria (> 300 mg/day) **OR**
Abnormal ECG (specific repolarization changes, Q waves in contiguous derivations or bundle branch block) **OR**
Heart failure (LVEF < 40%) **OR**
At least two of the following risk factors
High blood pressure, defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on more than two occasions, or the use of antihypertensive therapy
Dyslipidaemia, defined as plasma LDL cholesterol > 1.3 g/L, HDL cholesterol < 0.35 g/L, triglycerides > 1.5 g/L, or the use of lipid-lowering therapy
Obesity (BMI > 30 kg/m^2)
Family history of premature coronary artery disease
Current smoking (> 10 cigarettes/day)
Retinopathy (panphotocoagulation)
Exclusion criteria
Symptoms of coronary artery disease
History of coronary artery disease (previous myocardial revascularization, coronary angioplasty or surgery)
Acute coronary syndrome (history or current)
Latent autoimmune diabetes in adults
Secondary diabetes