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Impacts of cardiac rehabilitation on ventricular repolarization indexes and ventricular arrhythmias in patients affected by coronary artery disease and type 2 diabetes

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A B S T R A C T

Background: The benefits of cardiac rehabilitation in diabetic patients are well recognized. We aimed to assess its impact on ventricular repolarization indexes and the occurrence of ventricular arrhythmias in patients with coronary artery disease (CAD) and diabetes type 2.
Methods: From January 2012 to August 2013, 122 consecutive patients [diabetics ($n = 59$) and non diabetics ($n = 63$)] were prospectively enrolled in an out-patient rehabilitation program. Clinical examination, 12-lead ECG, 24-Holter ECGs and maximal exercise testing were performed at the beginning and end of the rehabilitation program in all patients.
Results: Diabetic patients showed significant decreases of repolarization indexes: QTc (−6.4%; $p = 0.006$), QTc disp (−22.6%; $p = 0.050$) and JTc (−9.4%; $p = 0.003$). At the end of the rehabilitation program diabetic patients showed a higher decrease in ventricular arrhythmias according to Lown classes' grading in comparison to non diabetics (-1.05 ± 0.84 vs -0.74 ± 0.91; $p = 0.048$). Insulin therapy was associated with a lower decrease in Lown classes compared to oral anti-diabetics (-0.95 ± 0.80 vs -1.61 ± 0.84; $p < 0.001$).
Conclusion: Cardiac rehabilitation provided an improvement in the majority of ventricular repolarization indexes in patients with diabetes type 2 and CAD, decreasing the frequency of ventricular arrhythmias, particularly in those not treated by insulin.

Introduction

The benefit of regular exercise for patients with cardiovascular disease, as well as for healthy individuals is well recognized. Cardiac rehabilitation has been shown to be beneficial as well as safe for patients with a history of myocardial infarction,[1–3] percutaneous coronary interventions (PCI) or/and coronary artery bypass graft (CABG). Indeed, current European and American guidelines both assign a class I to cardiac rehabilitation in such a population.[4,5] Furthermore, it was established that various cardiac rehabilitation programs, including in-hospital or out-patient modalities, not only increase exercise capacity and improve quality of life in patients affected by coronary artery disease (CAD), but also decrease cardiac mortality, particularly that due to ventricular arrhythmias.[1–3,6]

On the other hand, diabetes mellitus is a chronic and very common condition, especially in patients with CAD. Moreover, diabetic patients have increased cardiovascular mortality, in which malignant ventricular arrhythmias seem to be implicated.[7–9]

Despite the development of invasive and non-invasive cardiac investigations, the 12-lead surface electrocardiogram (ECG) remains an essential tool for the clinician, not only for its prognostic value, but also for the information about ventricular repolarization it provides.[10] In fact, repolarization indexes are recognized as

Conflicts of interest: none.

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markers of myocardial electrical instability, and thus may predict sudden cardiac death.[10–12]

Through the literature, the effects of cardiac rehabilitation in diabetic patients, regarding ventricular repolarization and arrhythmias remain unclear. The aim of the current study was to assess the impact of an out-patient cardiac rehabilitation program in patients affected by type II diabetes and CAD, on ventricular repolarization indexes and ventricular arrhythmias.

Methods

Study population

We performed a prospective comparative study pre- and post-cardiac rehabilitation between diabetic and non diabetic human subjects. From January 2012 to August 2013, consecutive patients affected by CAD, addressed by their referring physicians for cardiac rehabilitation were screened. The criteria for including patients in a rehabilitation program were as follows: 1) absence of active ischemia as assessed by a clinical examination and exercise testing; 2) absence of any acute myocardial infarction in the 40 days before enrollment; 3) absence of congestive heart failure in the last 7 days; and 4) a stable medical therapy for 2 weeks before starting the rehabilitation. The exclusion criteria from the current study included: 1) class IA or III antiarrhythmic medications; 2) inability to complete the rehabilitation program; 3) absence of sinus rhythm at entry or during the rehabilitation program; 4) complete right or left bundle branch block; 5) patients with pacemaker or pre-excitation; 6) presence of electrolyte abnormalities and 7) diabetes mellitus type 1.

All non-diabetic patients were screened for diabetes before enrollment using fasting serum glucose and glycosylated hemoglobin. Clinical examination, 12-lead ECG, 24-Holter ECGs and a maximal exercise testing, using a ramp treadmill protocol with maximal metabolic equivalents (METs) measurement were performed at the beginning and end of the rehabilitation program in all patients.

The study was in compliance with the declaration of Helsinki and all study subjects signed an informed consent form before enrollment.

Protocol of cardiac rehabilitation

All patients completed a 20 exercise sessions out-patient cardiac rehabilitation program during 5 weeks (4 sessions per week). Each session consisted of approximately 15 min of stretching and calisthenics for warm-up, followed by 30 min of continuous upright aerobic and dynamic exercises (combination of walking and bicycling), 10 min light isometric exercises (hand weights), and 15 min of cool-down stretching and calisthenics. Total duration of each session was approximately 1 h and 10 min. Exercise intensity was prescribed individually so that patients' heart rates were approximately 80% of the maximum heart rate. Heart rate, blood pressure, and exercise intensity were monitored and supervised by a senior cardiologist during the exercise session. In addition to the rehabilitation sessions, approximately 1–3 times per week of exercise outside the formal program was encouraged and all patients received psychological and dietary counseling.

Electrocardiographic measurements

A12-lead ECG was performed in all patients, after 30 min of rest, at a paper speed of 25 mm/s and voltage of 10 mm/mV. For the analysis of the ECG, a manual measurement of the values using a digital caliper with measuring range of 0–20 mm, 0.01 mm resolution, and 0–100 ± 0.02 mm accuracy was performed by one blinded experienced cardiologist. The value obtained was converted to milliseconds (ms). Extrasystolic and post-extrasystolic cycles were excluded from the measurement. We considered the T-wave peak as the steepest point, and the T-wave end as the point of return to the baseline. The T-wave end was obtained by the intersection point of the tangent line of the terminal portion of the T-wave with the isoelectric line. When the U-wave was present, the T-wave end was considered as the nadir between the T-wave and the U-wave. The derivations in which it was not possible to define the T-wave end due to low voltage were discarded. Measurement of the QT interval (the interval from the start of the QRS complex to the end of the T-wave) was performed in all 12 leads, and the longest and the shortest intervals measured were selected. The QT interval was corrected according to Bazett's formula which consists in QT by the square root of the RR interval ($QTc = QT/\sqrt{RR}$), thus providing the QT interval value adjusted for heart rate.

QTc interval dispersion (QTc disp) was obtained by the difference between the maximum (QTc max) and the minimum (QTc min) of QTc intervals in the 12-lead electrocardiogram. The JT interval was measured from the end of the QRS complex, which was defined as the point at which the QRS complex returned to the TP isoelectric baseline (J point), to the end of the T wave. JT interval was corrected (JTc) according to Bazett's formula ($JTc = JT/\sqrt{RR}$) and JT interval dispersion (JTc disp) was also obtained by the difference between the maximum and the minimum of JTc intervals. ΔQTc and ΔQTc disp were defined as the difference between QTc and QTc disp before and after rehabilitation, respectively. ΔJTc and ΔJTc disp were defined as the difference between JTc and QTc disp before and after rehabilitation, respectively.

Holter electrocardiography

A 24-h ambulatory holter ECG monitoring (12-channel, digital-DMS® Cardioscan-12, recorder 300-7) was performed before out-patient cardiac rehabilitation and 2 days after the last training session and analyzed by a blinded experienced rythmologist. The grading system of Lown[12] was used to evaluate the ventricular premature beats: class 0 = no ventricular premature beats; class 1 = lower than 30 ventricular premature beats/hr; class 2 = more than1 ventricular premature beats/min or 30 ventricular premature beats/hr; class 3 = multiform ventricular premature beats or ventricular couplets were present; class 4 = ventricular tachycardia of 3 or more beats was present and class 5 = early-cycle ventricular premature beats (R on T phenomenon).

Class 0 to grade 2 were considered as low classes, while those equal or greater than class 3 were considered as high classes. ΔLown grading was defined as the difference between classes before and after cardiac rehabilitation.

Statistical analysis

The sample size was calculated considering the changes in QTc disp (ΔQTc disp). We hypothetized that cardiac rehabilitation will be more beneficial in presence of type 2 diabetes than in non diabetic patients, with a ΔQTc disp absolute difference of 15 ms, with the assumption that standard deviations of ΔQTc disp within groups will be 25 ms and that covariate has an R-squared of 0.2. Choosing a power of 80% and a 2-sided α level of 0.05, at least 88 patients (44 in each group) would be required to reach statistical evidence. Considering a rate of drop out around 20%, at least 105 patients need to be enrolled.

Continuous variables were presented as mean ± standard deviations, and were compared using Student unpaired t test. Categorical variables were presented as counts and percentages and