Incidence and Prevalence of Unrecognized Myocardial Infarction in People With Diabetes

A substudy of the Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes (RECORD) study

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OBJECTIVE—To examine the prevalence and incidence of unrecognized myocardial infarction in a contemporary population with type 2 diabetes.

RESEARCH DESIGN AND METHODS—We performed a retrospective analysis of the electrocardiograms (ECGs) recorded at baseline and after 2 years for the first 1,004 type 2 diabetic individuals to be randomized in the Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes (RECORD) study.

RESULTS—ECGs suitable for analysis were obtained from 669 participants. The prevalence of unrecognized Q-wave myocardial infarction at baseline was 1.9% (n = 13). The incidence of unrecognized Q-wave myocardial infarction at the end of 2 years of follow-up was 1.5/1,000-person-years (n = 2). One-third (13 of 39) of prevalent and one-quarter (2 of 8) of incident myocardial infarctions were unrecognized.

CONCLUSIONS—Although the prevalence and incidence of myocardial infarction was low, unrecognized Q-wave myocardial infarctions made up a substantial proportion of all events.

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Although usually accompanied by typical symptoms, some myocardial infarctions (MIs) are not clinically recognized. Unrecognized MIs are thought to be important because there is some evidence that they carry a similar prognosis to recognized MIs (1–3). People with diabetes are considered to be more at risk for unrecognized MIs than those without diabetes, but few data have directly addressed this issue. Consequently, we examined the prevalence and incidence of clinically unrecognized MI in a contemporary population with type 2 diabetes enrolled in the Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes (RECORD) study.

RESEARCH DESIGN AND METHODS

The design of the RECORD study has been described in detail previously (4). In brief, the RECORD study enrolled 4,458 people with type 2 diabetes that was inadequately controlled with metformin or sulfonylurea monotherapy. History of MI was obtained from the trial case-report forms completed by the study investigators.

This report describes a retrospective analysis of the electrocardiograms (ECGs) recorded at baseline and after 2 years in the study for the first 1,004 people to be randomized. The ECG recordings were coded independently by two cardiologists using a list derived from the Minnesota Code Classification System for Electrocardiographic Findings. When the two cardiologists did not agree, the ECG was reviewed by a third cardiologist. A fourth cardiologist reviewed all ECGs that were identified with potential features of MI and made the final decision whether the ECG demonstrated an MI.

A prevalent unrecognized Q-wave MI was defined as a Q wave (Minnesota codes 1-1 through 1-2 only) in the absence of a previous clinical history of MI at baseline (1,5–9). An incident unrecognized Q-wave MI was defined as a Q wave (Minnesota codes 1-1 through 1-2 only) in the absence of an event as adjudicated by the end point committee using European Society of Cardiology definitions during the course of the study (5,6,8,9). The incident population only included people without Q waves on their baseline ECG.

Data have been summarized for the combined treatment groups using simple descriptive statistics. Incidence rates per 1,000 person-years of follow-up have been calculated as the number of people with an event during the first 2 years of follow-up/total person-years.

RESULTS

The analysis excluded 335 of the 1,004 randomized people: 25 had no baseline ECG, 99 had no ECG at 2 years, 82 withdrew from study, 16 died during follow-up (7 were adjudicated as cardiovascular deaths), ECGs for four

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individuals were not available for unknown reasons, and 109 ECGs were not suitable for 12-lead analysis. ECGs were available and suitable for analysis at baseline and at 2 years for 669 people, and Q waves were present in 21 on their baseline ECG. Therefore, 648 people (with no Q waves at baseline) were evaluable for the incidence rate calculation of MIs. Table 1 describes the baseline characteristics of the 669 people included in this analysis.

A history of MI was ascertained in 26 participants (3.9% [95% CI 2.6–5.7]). Of these, eight had a Q wave present on their baseline ECG, and 18 had no Q wave. Q waves were present on the baseline ECG (i.e., an unrecognized Q-wave MI) in 13 people (1.9% [1.1–3.3]) with no history of MI. The overall prevalence of MI, identified by history or ECG criteria (recognized Q-wave/non–Q-wave MI + unrecognized Q-wave MI), was 5.8% (4.3–7.9; n = 39). Unrecognized Q-wave MIs constituted 33% of all of these MIs.

Among the 648 people with no Q waves at baseline, there were six adjudicated MIs, one of which resulted in a Q wave, and Q waves developed in an additional two people that were not associated with an adjudicated MI (i.e., two people had an unrecognized Q-wave MI). The incidence of unrecognized Q-wave MI was 1.5 (95% CI 0.0–3.6)/1,000 person-years, and unrecognized Q-wave MIs accounted for two of eight (25%) of all incident MIs documented using both approaches. The incidence of any detected MI during the 2-year period was 8 of 648 or 6.2 (1.9–10.4)/1,000 person-years.

Table 1—*Baseline characteristics*

Variable	*n* (%)	Mean (SD)
Total population	669	—
Male	346 (51.7)	—
Age (years)	—	58.8 (8.2)
White	666 (99.6)	—
Duration of diabetes (years)	—	7.2 (5.2)
Physiologic measurements	—	—
BMI (kg/m^2)	—	31.2 (4.6)
Systolic blood pressure (mmHg)	—	139.7 (15.4)
Diastolic blood pressure (mmHg)	—	83.1 (8.9)
Heart rate (bpm)	—	73.8 (8.4)
Medical history	—	—
Angina-stable	66 (9.9)	—
Clinical history of MI	26 (3.9)	—
Hypertension	541 (80.9)	—
Hyperlipidemia	106 (15.8)	—
Percutaneous coronary intervention	11 (1.6)	—
Coronary artery bypass grafting	13 (1.9)	—
Transient ischemic attack	13 (1.9)	—
Stroke	13 (1.9)	—
Peripheral arterial disease	21 (3.1)	—
Diabetic retinopathy	80 (12)	—
Heart failure	5 (0.7)	—
Current smoker	103 (15.4)	—
Previous smoker	146 (21.8)	—
Neuropathy	38 (5.7)	—
Laboratory measurements	—	—
HbA_{1c} (%)	—	7.9 (0.7)
Fasting plasma glucose (mmol/L)	—	9.8 (2.2)
Total cholesterol (mmol/L)	—	5.4 (1.0)
Microalbuminuria	96 (14.3)	—
Macroalbuminuria	8 (1.2)	—
Drug therapy		—
Metformin monotherapy	344 (51.4)	—
Sulfonylurea monotherapy	325 (48.6)	—
Statin	110 (16.4)	—
β-Blocker	161 (24.2)	—
Angiotensin-converting enzyme inhibitor	257 (38.4)	—
Antiplatelet	144 (21.5)	—

CONCLUSIONS—In absolute numbers, the prevalence and incidence of unrecognized Q-wave MIs were low in this substudy of RECORD, but because the prevalence and incidence of recognized MI was also low, a notable proportion of all detected MIs were unrecognized Q-wave MIs: 33% of prevalent MIs and 25% of incident MIs were unrecognized Q-wave MIs.

An Australian prospective observational cohort study (n = 1,269) is the only other study to examine the prevalence of unrecognized Q-wave MI in a cohort with type 2 diabetes. The prevalence of unrecognized Q-wave MI was 3.9%, making up 44% of all Q-wave MIs (7).

Three previous studies have examined the incidence of unrecognized MI in people with diabetes (5,10,11). All reported a higher incidence of unrecognized MI than in this RECORD cohort. The greater absolute prevalence and incidence of unrecognized MI in other studies most likely reflects the higher rates of cardiovascular disease at baseline. We acknowledge that ours is a relatively young clinical trial cohort, with small numbers of participants and events. Our findings may be subject to some uncertainty and may not be applicable to older, unselected populations with diabetes.

Most previous studies of "unrecognized MI" have used the presence of Q waves to indicate an event (12). We believe that many unrecognized MIs will be missed by the requirement of a Q wave. In our own population, only 8 of 26 patients with a baseline history of MI had Q waves, and only 1 of 6 adjudicated incident MIs resulted in a Q wave on the ECG. Any study using ECG criteria, and particularly Q waves only, is therefore likely to considerably underestimate the true burden of disease. Because of uncertainty about the validity of a diagnosis of MI solely based on ECG findings, clinical definitions in line with European Society of Cardiology guidelines were used to adjudicate events in RECORD (4). Thus, although including unrecognized Q-wave MIs would have increased the number of events, we judged that they would not add to the rigor of the study.

We found in this analysis of people with diabetes in the RECORD study that unrecognized Q-wave MIs made up a substantial proportion of all detected MIs. In view of the small numbers in

our analysis, further studies (or meta-analyses of studies) are needed to confirm (or refute) our findings and recommend how best to establish the true burden of MI in people with diabetes.

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