Heart Rate Recovery After Exercise Is a Predictor of Silent Myocardial Ischemia in Patients With Type 2 Diabetes

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OBJECTIVE—Slow heart rate recovery (HRR) predicts all-cause mortality. This study investigated the relationship between silent myocardial ischemia (SMI) and HRR in type 2 diabetes.

RESEARCH DESIGN AND METHODS—The study enrolled 87 consecutive patients with type 2 diabetes and no chest symptoms. They underwent treadmill exercise testing and single-photon emission computed tomography imaging with thallium scintigraphy. Patients with abnormal myocardial perfusion images also underwent coronary angiography.

RESULTS—SMI was diagnosed in 41 patients (47%). The SMI group showed slower HRR than the non-SMI group (18 ± 6 vs. 30 ± 12 bpm; P < 0.0001). HRR was significantly associated with SMI (odds ratio 0.83 [95% CI 0.75–0.92]; P = 0.0006), even after adjustment for maximal exercise workload, resting heart rate, maximum heart rate, rate pressure product, HbA1c, use of sulfonamides, and a history of cardiovascular disease.

CONCLUSIONS—HRR can predict SMI in patients with type 2 diabetes.
Comparison of the SMI and non–SMI groups

There were no differences of clinical characteristics between the two groups (Table 1). The 1- and 3-min heart rates were similar in both groups, but the SMI group showed slower HRR (18 ± 6 vs. 30 ± 12 bpm; P < 0.0001) along with a higher resting heart rate (P = 0.01), lower maximum heart rate (P < 0.001), lower rate pressure product (P = 0.0032), and lower max METs. The number of patients who achieved the target heart rate was not significantly different between the two groups (P = 0.13).

Multivariate logistic regression analysis was performed to assess parameters significantly associated with myocardial ischemia, using the following variables: HRR, use of sulfonamides, and history of cardiovascular disease. As a result, HRR was significantly associated with SMI (odds ratio 0.83 [95% CI 0.75–0.92], P = 0.0006) and was also significantly associated with significant angiographic stenosis, even after adjustment for the above covariates (0.84 [0.75–0.94]; P = 0.0017).

CONCLUSIONS—Many physicians screen asymptomatic persons by stress testing, but it has a low specificity (8). Furthermore, it has been reported that a decrease of the chronotropic reserve predicts CAD (9).

Our findings indicated that slow HRR after exercise strongly predicts SMI in patients with type 2 diabetes. Slow HRR similarly predicts myocardial ischemia at the microvascular and macrovascular levels.

Possible mechanisms of SMI include autonomic denervation of the myocardium (10–12), a higher pain threshold during exercise testing (13), higher endorphin levels (14), and increased production of anti-inflammatory cytokines that may block pain transmission and increase the neural activation threshold (15).

The prevalence of SMI may exceed 20% among asymptomatic patients with type 2 diabetes (3). In this study, the prevalence was a high 47%, probably because our cohort included patients with electrocardiogram abnormalities, at least two risk factors for CAD in addition to diabetes, or a history of CAD (13).

Table 1—Comparison of the SMI and non–SMI patients

| Variable                          | SMI patients (n = 41) | Non–SMI patients (n = 46) | OR (95% CI) | P value* |
|-----------------------------------|-----------------------|---------------------------|-------------|----------|
|                                   |                       |                           | Univariate  | Multivariate |
| Female sex                        | 8 (20)                | 13 (28)                   | —           | —        |
| Age (years)                       | 66 ± 11               | 62 ± 10                   | —           | —        |
| BMI (kg/m²)                       | 24.0 ± 3.3            | 24.1 ± 3.1                | —           | —        |
| Duration of diabetes (years)      | 11.0 ± 6.3            | 10.3 ± 9.1                | —           | —        |
| Current smoker                    | 13 (32)               | 22 (48)                   | —           | —        |
| Family history of diabetes        | 20 (49)               | 33 (72)                   | —           | —        |
| Hypertension                      | 30 (73)               | 36 (78)                   | —           | —        |
| Hyperlipidemia                    | 29 (71)               | 27 (59)                   | —           | —        |
| Cardiovascular disease            | 6 (15)                | 5 (11)                    | 1.01 (0.15–6.87) | 0.6 0.99 |
| Diabetic treatment                |                       |                           | —           | —        |
| Diet only                         | 8 (20)                | 11 (24)                   | —           | —        |
| Oral hypoglycemic agent           | 23 (56)               | 25 (54)                   | —           | —        |
| Use of sulfonamides               | 16 (39)               | 17 (37)                   | 1.02 (0.31–3.4) | 0.84 0.97 |
| Insulin                           | 10 (24)               | 10 (22)                   | —           | —        |
| ACE inhibitors or ARB             | 28 (68)               | 24 (52)                   | —           | —        |
| Statins                           | 24 (59)               | 21 (46)                   | —           | —        |
| Calcium channel blockers          | 11 (27)               | 9 (20)                    | —           | —        |
| Serum cholesterol (mmol/L)        | 4.97 ± 1.01           | 4.97 ± 0.88               | —           | 0.96     |
| Total                             | 2.77 ± 0.88           | 2.82 ± 0.72               | —           | 0.72     |
| Serum triglycerides (mmol/L)      | 3.65 ± 2.09           | 4.34 ± 2.95               | —           | 0.2      |
| HbA1c (%)                         | 7.6 ± 1.8             | 6.9 ± 1.3                 | 0.7 (0.47–1.04) | 0.05 0.08 |
| Heart rate (bpm)                  |                       |                           | —           | —        |
| Resting                           | 87 ± 11               | 81 ± 12                   | 1.01 (0.95–1.08) | 0.01 0.67 |
| Maximum                           | 133 ± 14              | 143 ± 13                  | 0.98 (0.91–1.05) | <0.001 0.54 |
| 1-min                              | 115 ± 14              | 113 ± 15                  | —           | 0.45     |
| 3-min                              | 95 ± 12               | 90 ± 11                   | —           | 0.05     |
| Recovery                          | 18 ± 6                | 30 ± 12                   | 0.83 (0.75–0.92) | <0.0001 0.0006 |
| Maximum METs                      | 7.2 ± 2.1             | 9.0 ± 1.7                 | 0.79 (0.56–1.12) | <0.0001 0.19 |
| Rate pressure product             | 25,316 ± 4,739        | 28,368 ± 4,641            | 1.0 (0.99–1.01) | 0.0032 0.41 |
| Achievement of THR                | 25 (61)               | 33 (76)                   | —           | 0.13     |

Data are mean ± SD or number (%). ARB, angiotensin-receptor blocker; OR, odds ratio; THR, target heart rate. *The t test or χ² test was used to assess differences between the SMI group and non–SMI group. Multivariate logistic regression analysis was performed to identify the parameters significantly associated with myocardial ischemia using heart rate recovery, max METs, resting heart rate, maximum heart rate, rate pressure product, HbA1c, use of sulfonamides, and history of cardiovascular disease.
This study had the limitations of being performed at a single institution and in a small patient population. Accordingly, the relation between HRR and SMI should be assessed by a larger study with pathophysiologic data in the future.

Although it is possible that our results were influenced by the difference of exercise parameters between the two groups, we conclude that HRR is useful for easy detection of SMI in high-risk type 2 diabetic patients to allow primary prevention and that HRR is significantly associated with SMI even after adjustment for the influence of exercise parameters.

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HRR predicts SMI in type 2 diabetes