EXPERIMENTAL & CLINICAL Cardiology

EXPERIMENTAL & CLINICAL CARDIOLOGY

Title: "Relationship Between Heart Rate Recovery After Exercise and Maximal Oxygen Uptake in Sedentary Patients with Type 2 Diabetes"

Authors: Angelo Cataldo, Dario Cerasola, Daniele Zangla, Giuseppe Russo, Rosalia Lo Presti and Marcello Traina

Relationship between heart rate recovery after exercise and maximal oxygen uptake in sedentary patients with type 2 diabetes

Original article

Angelo Cataldo[1], Dario Cerasola[1], Daniele Zangla[1], Giuseppe Russo[1], Rosalia Lo Presti[1], Marcello Traina[1]

[1] Sport and Exercise Sciences DISMOT Research Unit, University of Palermo, Italy

ABSTRACT

AIMS: Heart rate recovery after exercise (HRR) is an estimate of autonomic modulation of the heart, and has been shown to be inversely associated with type 2 diabetes. Type 2 diabetes is associated with decreased maximal oxygen consumption (VO$_2$max). Aim of our study was to assess the relationship between HRR and VO$_2$max in sedentary patients with type 2 diabetes.

METHODS: Maximal exercise testing to determine VO$_2$max (ml · Kg^{-1} · min^{-1}) was performed in 16 sedentary patients with type 2 diabetes (DP) and in 16 age-matched sedentary healthy controls (HS). HRR (bpm) 2 min after cessation of the exercise was recorded. Simple linear regression was used to assess the relations between HRR and VO$_2$max.

RESULTS: VO$_2$max and HRR were significantly lower in DP compared to HS (P = 0.002 and P = 0.008 respectively). A correlation between HRR and VO$_2$max has been found, stronger in DP (r = 0.672, P = 0.004) than HS (r = 0.620, P = 0.01).

CONCLUSIONS: Our study suggests that regular physical activity aimed to improve the levels of VO$_2$max in subjects with diabetes may improve the HRR and reduce the risk of cardiovascular events.

Key words: Autonomic nervous system; Diabetes, HRR; Physical activity; VO$_2$max

INTRODUCTION

Heart rate recovery (HRR) is the rate at which heart rate decreases, usually within minutes, after moderate to heavy exercise, and is regulated by autonomic nervous system [1]. HRR immediately after exercise is a marker of parasympathetic function that has been shown to be inversely associated with insulin resistance, metabolic syndrome, and type 2 diabetes [2]. Attenuated HRR following maximal exercise testing is an important predictor of mortality in healthy adults [3], in patients with cardiovascular disease [4] and with diabetes [5].

The recent "Look AHEAD" study [6] suggested that lifestyle intervention aimed to improve cardiovascular fitness, defined as the estimated metabolic equivalent level based on the treadmill work load, has a beneficial effect upon autonomic nervous system function as reflected in the improvement of heart rate recovery after exercise in adults with type 2 diabetes. However, that study did not analyze changes in maximal oxygen consumption (VO_2max), which is considered the best measure of overall cardiorespiratory fitness and an important predictor of cardiovascular and all-cause mortality [7], and its relationship with HRR.

Previous studies have shown that HRR is related to VO_2max in athletes [8,9], but to our knowledge there are no studies that have investigated this relationship in sedentary type 2 diabetic patients.

Aim of our study was to assess the relationship between HRR measured 2 min after peak of exercise, as index of autonomic nervous function, and VO_2max, as index of cardiovascular fitness, in sedentary patients with type 2 diabetes.

METHODS

We recruited sixteen (eight male and eight female) patients with type 2 diabetes (DP) and sixteen (nine male and seven female) healthy subjects (HS). They were aged 40 to 70, and were classified sedentary according the criteria of the International Physical Activity Questionnaire (IPAQ) [10]. All DP were being treated with diet and antiglycemic agents. Significant cardiovascular disease was excluded in all subjects by an instrumental examination. Each subject gave written informed consent to participate, following an explanation of the nature and purpose of the study. The procedures were conducted in compliance with the Declaration of Helsinki and were approved by the IRB Committee at our Institution. All the physiological evaluations were performed at the Laboratory of Sport and Exercise Sciences "DISMOT" Research Unit of the University of Palermo, Italy.

All tests were performed between 8 and 10 a.m., after a 12-h overnight fast. Stature and body mass were measured before starting the tests using a stadiometer and an electronic weighing scales respectively (SECA,

Germany). All subjects performed a graded exercise test to exhaustion on treadmill, according standard and modified Bruce protocols. The test was stopped when one or more of the following criteria were met: attainment of a VO_2max plateau < 2.2 ml $\cdot$ Kg^{-1} $\cdot$ min^{-1}; respiratory exchange ratio (RER) > 1.10; maximal heart rate (HRmax) close to theoretical value of 220-age; the subject was unable to maintain the required work rate.

A disposable facemask with a 50-80ml dead space (Cosmed V2, Cosmed Srl, Italy) was used to collect expired air throughout the test. Oxygen uptake (VO_2) was recorded with a breath-by-breath measurement system (Cosmed Quark CPET, Cosmed Srl, Italy) and maximal oxygen uptake (VO_2max) was defined as the highest consecutive 30-s average value achieved during the test. The flow meter and gas analyzers were calibrated before each test, according to the manufacturer's instructions.

During the tests the heart rate of each participant was recorded using a short-range radio telemetry system (Polar Electro Oy, Finland). Heart rate recovery (HRR) was defined as the difference between heart rate at peak exercise and heart rate 2 minutes after cessation of the exercise (Figure 1).
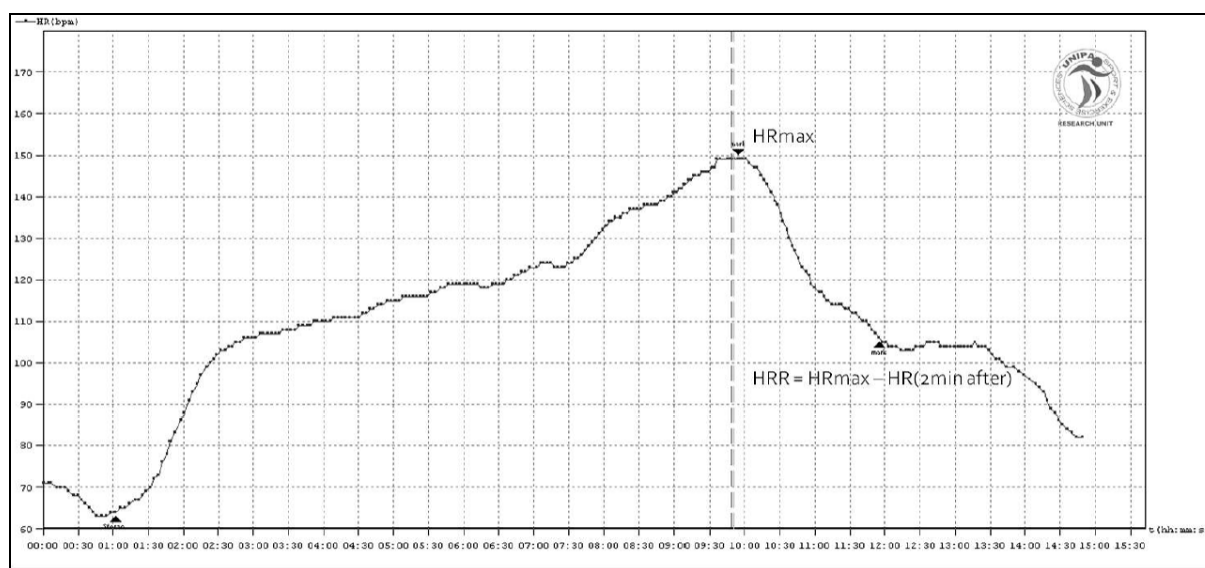

Figure 1. Representative data showing heart rate (HR) during exercise test. HRmax and HRR are indicated.

The cool-down period after cessation of exercise consisted of walking on treadmill at 2.0 Km/h of speed and 0% of grade. An abnormal heart rate recovery was defined as a value of ≤ 22 beats per minute (bpm) at 2min after exercise [11]. All responses were monitored and grafically displayed throughout rest, exercise, and cool-down.

Data are presented as means $\pm$ standard deviation (SD). Differences between groups were assessed with two-tailed Student's *t*-test for unpaired data. A simple linear regression model was used to assess the relations

between HRR and VO$_2$max. Pearson product moment correlation coefficient (r) was used to determine the association between the considered parameters. The P value less than 0.05 was considered statistically significant.

RESULTS

The characteristics of subjects are shown in Table 1. The two groups were similar in age and body weight. BMI was higher in DP (29.9 ± 3.2 vs. 26.9 ± 4.2, P = 0.03). At rest, HR and VO$_2$ were similar in both groups.

Table 1: Characteristics of patients with type 2 diabetes (DP) and healthy subjects (HS) (means ± SD).

	DP (n = 16)	HS (n = 16)	P-value
Age (y)	57 ± 7.5	53 ± 6.9	0.100
Body height (cm)	165 ± 7.7	166 ± 9.8	0.826
Body weight (Kg)	81 ± 9.4	74 ± 15.5	0.136
BMI (Kg · m^{-2})	29.9 ± 3.2	26.9 ± 4.2	0.033 *
HRrest (bpm)	74 ± 12.1	74 ± 12.8	0.899
HRmax (bpm)	130 ± 16.1	143 ± 13.5	0.024 *
VO$_2$rest (ml · Kg^{-1} · min^{-1})	3.78 ± 1.2	3.63 ± 0.9	0.703
VO$_2$max (ml · Kg^{-1} · min^{-1})	20.6 ± 4.3	28.2 ± 8.1	0.002 **
HRR (bpm)	28 ± 8.4	37 ± 8.9	0.008 **

*Difference between DP and HS: * Significant (P < 0.05), ** Very significant (P < 0.01).*
BMI, body mass index; HR, heart rate; VO$_2$, oxygen uptake; HRR, heart rate recovery.

Termination of exercise was due to volitional fatigue for all subjects and no subject demonstrated abnormal physiological response to exercise. HRmax was significantly lower in DP than in HS (130 ± 16.1 vs. 143 ± 13.5 bpm; P = 0.024). VO$_2$max was significantly lower in DP compared to HS (20.6 ± 4.3 vs. 28.2 ± 8.1 ml · Kg^{-1} · min^{-1}, P = 0.002).

HRR was significantly lower in DP (28 ± 8.4 vs. 37 ± 8.9 bpm, P = 0.008). An abnormal value (HRR < 22 bpm) was found only in 4 DP (25%).

When linear regression analysis was performed, a significant positive correlation between HRR and VO$_2$max has been found in both DP (Figure 2) and HS (Figure 3) (r = 0.672, P = 0.004 and r = 0.620, P = 0.01 respectively).
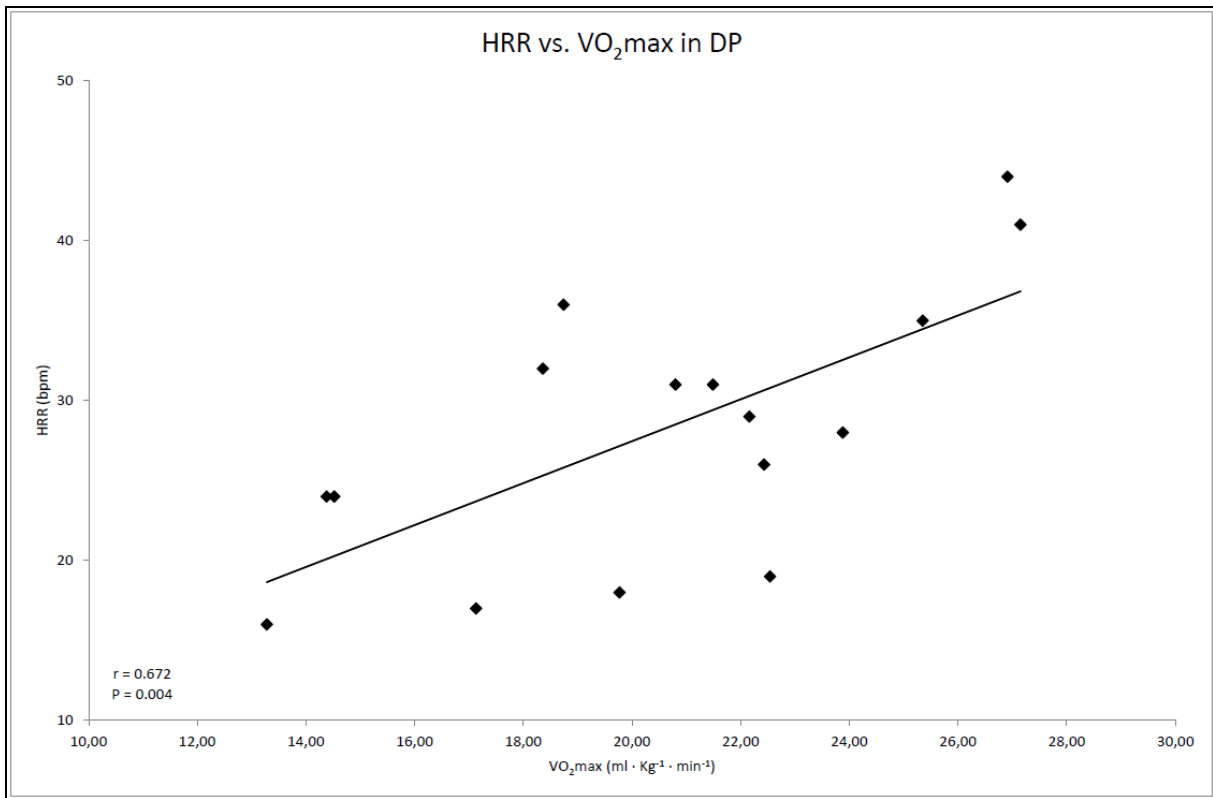
Figure 2. Correlation between heart rate recovery (HRR) and maximal oxygen uptake (VO2max) in patients with diabetes (DP).
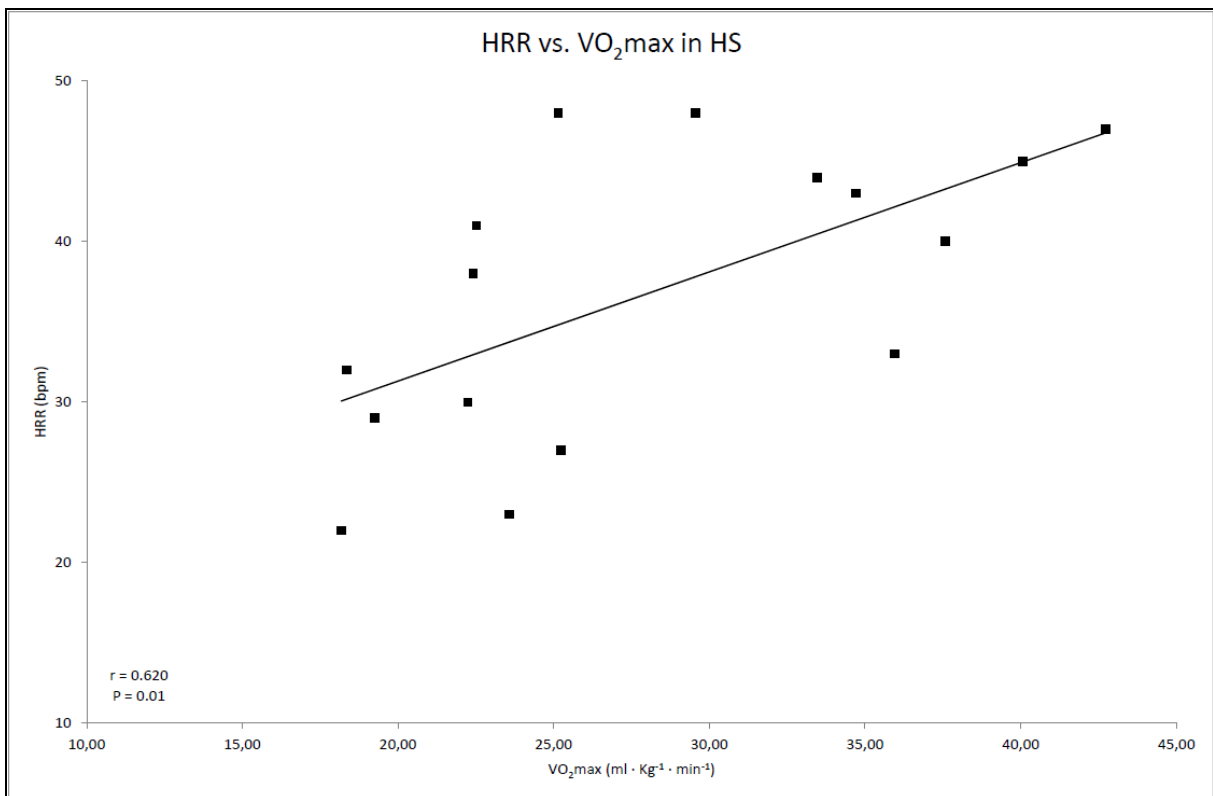

Figure 3. Correlation between heart rate recovery (HRR) and maximal oxygen uptake (VO2max) in healthy subjects (HS).

DISCUSSION

The heart rate recovery immediately after exercise is considered to be a function of the autonomic nervous system, and a consequence of parasympathetic reactivation and sympathetic withdrawal [11]. Several studies have identified the reduced HRR as a predictor of cardiovascular and all-cause mortality in patients referred for exercise testing [3,12], in patients with cardiovascular disease [4,13,14], and in patients with diabetes [5]. It has been shown that HRR is reduced in individuals with diabetes and with impaired fasting glucose levels [15], and that the development of abnormal HRR is indicative of autonomic dysfunction even in pre-diabetic subjects [2]. The recent "Look AHEAD" study [6] suggested that lifestyle intervention aimed to improve cardiovascular fitness has a beneficial effect upon autonomic nervous system function as reflected in the improvement of heart rate recovery after exercise in adults with type 2 diabetes.

In our study we evaluated the VO$_2$max, which is considered the best measure of overall cardiorespiratory fitness and an important predictor of cardiovascular and all-cause mortality [7], and its relationship with HRR after exercise in sedentary patients with type 2 diabetes.

In our study the mean value of VO$_2$max was significantly lower in DP compared to HS (20.6 ± 4.3 vs. 28.2 ± 8.1 ml · Kg^{-1} · min^{-1}, $P = 0.002$); this finding is consistent with the observation that sedentary patients with diabetes have decreased physical fitness, as measured by VO$_2$max, compared to similarly sedentary healthy subjects [16]. HRR after exercise was significantly lower in DP compared to HS (28 ± 8.4 vs. 37 ± 8.9 bpm, $P = 0.008$) and a significant correlation with VO$_2$max is showed in both DP and HS ($r = 0.672$, $P = 0.004$ vs. $r = 0.620$, $P = 0.01$). This correlation was stronger in DP, despite of their lower levels of VO$_2$max, compared to HS , so that we can assume that the exercise-induced muscle and cardiovascular adaptations resulting in an increase in VO$_2$max (e.g., increased muscle capillarizzation, increased blood flow and cardiac output, alterations in the symphato-vagal balance and changes in substrate utilizzation) improve the efficiency of the metabolic processes and contribute to increase HRR after exercise, especially in subjects with low levels of physical fitness.

Therefore, the reduction of HRR may reflect not only the imbalance of the autonomic system, but also the decreased physical fitness demonstrated in our study by the reduced values of VO$_2$max.

Regular physical activity that allows to increase the levels of VO$_2$max may improve HRR and reduce the risk of cardiovascular events in patients with diabetes.

CONCLUSIONS

Heart rate recovery after exercise may be considered an index of physical fitness, and exercise testing with measurements of HRR is an useful tool for the assessment of the combination of cardiovascular fitness and autonomic function.

In sedentary patients with type 2 diabetes regular exercise aimed to increase VO$_2$max has also a beneficial effect on the function of the autonomic nervous system which is reflected in the improved HRR.

REFERENCES

1. Shetler K, Marcus R, Froelicher VF, Vora S, Kalisetti D, Prakash M, Myers J, Do D. Heart rate recovery: validation and methodological issues. J Am Coll Cardiol 2001;38:1980-1987.

2. Sacre JW, Jellis CL, Coombes JS, Marwick TH. Diagnostic accuracy of heart-rate recovery after exercise in the assessment of diabetic cardiac autonomic neuropathy. Diabet Med 2012;29(9):e312-20.

3. Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart rate recovery immediately after exercise as a predictor of mortality. N Eng J Med 1999;341:1351-57.

4. Lahiri MK, Kannankeril PJ, Goldberger JJ. Assessment of autonomic function in cardiovascular disease. J Am Coll Cardiol 2008;51(18):1725-1733.

5. Cheng YJ, Lauer MS, Earnest CP, Church TS, Kampert JB, Gibbons LW, Blair SN. Heart recovery following maximal exercise testing as a predictor of cardiovascular disease and all-cause mortality in men with diabetes. Diabetes Care 2003;26:2052-2057

6. Ribisl PM, Gaussoin SA, Lang W, Bahnson J, Connelly SA, Horton ES, Jakicic JM, Killean T, Kitzman DW, Knowler WC, Stewart KJ, Look AHEAD Research Group. Lifestyle intervention improves heart rate recovery from exercise in adults with type 2 diabetes: results from the Look AHEAD study. J Obes 2012:309196.

7. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002;346(11):793–801.

8. Dimkpa U. Post-exercise heart rate recovery: an index of cardiovascular fitness. JEPonline 2009;12(1):19-22.

9. Cataldo A, Cerasola D, Zangla D, Russo G, Sahin FN, Traina M. Assessment of autonomic function as marker of training status: the role of heart rate recovery after exercise. EJSS Journal 2014;2(1):ahead-of-print.

10. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003;35(8):1381-1395.

11. Shetler K, Marcus R, Froelicher VF, Vora S, Kalisetti D, Prakash M, Do D, Myers J. Heart rate recovery: validation and methodologic issues. J Am Coll Cardiol 2001;38:1980-1987.

12. Nishime EO, Cole CR, Blackstone EH, Pashkow FJ, Lauer MS. Heart rate recovery and treadmill exercise score as predictors of mortality in patients referred for exercise ECG. The J Am Med Assoc 2000;284:1392-1398.

13. Pitsavos CH, Chrysohoou C, Panagiotakos DB, Kokkinos P, Skoumas J, Papaioannou I, et al. Exercise capacity and heart rate as predictor of coronary heart disease events in patients with heterozygous familial hypercholesterolemia. Atherosclerosis 2004;173(2):347-352.

14. Watanabe J, Thamilarasan M, Blackstone EH, Thomas JD, Lauer MS. Heart rate recovery immediately after treadmill exercise and left ventricular systolic dysfunction as predictors of mortality; the case of stress echocardiography. Circulation 2001;104:1911-1916.

15. Panzer C, Lauer MS, Bricke A, Blackstone E, Hoohwerf B. Association of fasting plasma glucose with heart rate recovery in healthy adults: a population-based study. Diabetes 2002;51:803-807.

16. Reusch JEB, Bridenstine M, Regensteiner JG. Type 2 diabetes mellitus and exercise impairment. Rev Endocr Metab Disord 2013;14(1):77-86.