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# ASSESSMENT OF CARDIAC AUTONOMIC FUNCTION BY POST EXERCISE HEART RATE RECOVERY IN DIABETICS

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## Abstract

***Background and Aims:*** *Autonomic dysfunction in type 2 diabetes mellitus (DM) patients may translate into an increased cardiovascular morbidity and mortality. Autonomic system regulates 'heart rate recovery' (HRR), an important predictor of cardiovascular mortality, which can be assessed using the exercise electrocardiogram (ECG). Hence, utilizing HRR, this study assessed the autonomic function of the cardiovascular system after one minute of exercise stress test in both, patients with and without type 2 DM.* ***Materials and Methods:*** *A prospective case control study involving 50 patients with type 2 DM and 50 without type 2 DM, matched for age and sex, was carried out. Each subject underwent an exercise stress test by treadmill using the Bruce protocol. Cardiovascular parameters like heart rate was recorded using a 12 lead ECG along with blood pressure.* ***Results:*** *Patients with T2DM had lesser HRR after exercise ($p < 0.001$). Exercise capacity was significantly reduced among patients with T2DM when compared to controls ($p = 0.01$). A multiple linear regression analysis ($R^2=0.26$) revealed that duration of diabetes ($\beta=-0.02$, $p=0.048$) and resting systolic blood pressure (SBP) ($\beta=-010$, $p=0.048$) are independent predictors of HRR.* ***Conclusion:*** *The study revealed HRR to be significantly reduced among patients with type 2 DM. HRR may hint at the presence of cardiac autonomic dysfunction and predict the cardiovascular mortality.*

**key words**: *Cardiac autonomic dysfunction; Diabetes mellitus; Exercise capacity; Heart rate; Systolic blood pressure*

## Background and aims

The heart rate is regulated by the various autonomic nerve fibers that innervate the heart. There is a sympathetic withdrawal and a parasympathetic reactivation during the first few minutes after maximum exercise due to which the heart rate decreases - heart rate recovery (HRR), which is a protective mechanism and prevents sudden cardiac deaths [1,2].

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Autonomic dysfunction impairs exercise tolerance, HRR and causes orthostatic changes which are associated with sudden cardiac deaths [3]. HRR also independently predicts the acute cerebrovascular accidents and the all-cause mortality [4,5]. Various studies have also revealed a low HRR after exercise as a strong predictor of mortality in patients, independent of ischemia [6-8].

Type 2 diabetes mellitus (T2DM) also predisposes patients towards development of cardiovascular autonomic neuropathy (CAN), a chronic microvascular complication [9]. Autonomic dysfunction is one of the principal mechanisms responsible for increased morbidity and mortality in cardiovascular disease (CAD) patients with T2DM than CAD patients without T2DM [10-12].

The assessment of autonomic dysfunction requires the patients to undergo a battery of non-standardized maneuvers to measure changes in heart rate, blood pressure and the skin galvanic response. The exercise electrocardiogram (ECG) is available in various institutes which can serve as an easily accessible, inexpensive and a non-invasive test for assessing cardiovascular autonomic neuropathy.

The study evaluated the cardiac autonomic function by measuring the HRR after one minute of exercise stress test in patients with T2DM and compare it subjects without T2DM.

Material and methods

Subsequent to approval by the local institutional ethics committee, 50 patients with T2DM matched for age and sex with 50 patients without T2DM (Controls), were recruited in the present case-control study. Before enrollment, a written informed consent was obtained from the patients. The patients with age >60 years, a history of cardiovascular disease and those receiving beta-blockers were excluded from the study. Patients having dementia and any other condition that could have caused an inability to perform the exercise like diabetic neuropathy, ulcers were also excluded.

The treadmill exercise stress testing via Bruce protocol [13] by treadmill was carried out in all study subjects. The subjects were evaluated until they achieved their maximal exercise capacity. The subject's cardiovascular parameters were recorded and monitored during the test. Immediately following exercise, patients were asked to lie down in a supine position. HRR was defined as the difference between the maximal heart rate and 1-minute heart rate following peak exercise. HRR≤18 beats per minute was considered to be abnormal [14].

*Statistical analysis*

Normally distributed values were represented using mean ± SD. A 'p' value < 0.05 was defined as statistically significant. For inter-group comparisons, student's independent-sample t test and $\chi^2$ (Chi-square) test were used for continuous and categorical variables respectively. To examine correlations between HRR and potential predictors, univariate and multivariate analyses were used. SPSS software version 22.0 was utilized for the data analysis.

**Results**

The two groups were similar in their baseline characteristics with the exception of dyslipidemia (Table 1).

The cases with T2DM had a significantly lesser HRR 1 minute after exercise than the controls (p<0.001) (Table 2). Even patients with HRR≤18 were significantly more among cases (n=10, 20%) than the control group (n=1, 2%, p=0.004). The cases also had a significantly higher resting systolic blood pressure (SBP) (p = 0.04) and resting heart rate (p < 0.001). The exercise capacity, metabolic equivalent of task (METS) of cases was also significantly decreased as compared to the control group (p = 0.005).

**Table 1.** Baseline characteristics of cases and controls.

| | Cases | Controls | P value |
|---|---|---|---|
| Age (mean ± S.D.) | 48.9±6.36 | 46.26±7.71 | 0.067 |
| Gender (M / F) | 30/20 | 37/13 | 0.137 |
| Smoking | 8(16) | 6(12) | 0.564 |
| Alcohol | 8(16) | 14(28) | 0.148 |
| Hypertension | 20(40) | 11(22) | 0.052 |
| Dyslipidemia | 43(86) | 25(50) | <0.001* |

*- Statistically significant result; S.D. – Standard deviation; Values are expressed in frequency with percentages in brackets

**Table 2.** A comparison of different parameters during exercise stress test.

| | Cases | Controls | P value |
|---|---|---|---|
| Rest SBP (mmHg) (mean ± S.D.) | 130±7.28 | 125±6.56 | 0.04* |
| Rest DBP (mmHg) (mean ± S.D.) | 80±7.67 | 80±5.37 | 0.471 |
| METS (mean ± S.D.) | 10±2.12 | 10.1±2.86 | 0.005* |
| Rest HR (mean ± S.D.) | 103.8±14.48 | 92.5±15.35 | <0.001* |
| HRR (mean ± S.D.) | 28.62±12.37 | 39.92±9.92 | <0.001* |
| Max HR (mean ± S.D.) | 153.98±12.36 | 155.40±18.32 | 0.651 |
| %PHR (mean ± S.D.) | 91.6±6.25 | 90.9±8.27 | 0.634 |
| Peak SBP (mean ± S.D.) | 179±20.92 | 177.6±23.41 | 0.099 |
| Peak DBP \ (mean ± S.D.) | 90±5.69 | 90±6.67 | 0.830 |

SBP - systolic blood pressure; DBP - diastolic blood pressure; HR - heart rate; S.D. – Standard deviation; HRR – Heart Rate Recovery; METS - metabolic equivalent of task ; PHR – Peak Heart Rate; *- statistically significant result

The reduced HRR was negatively associated with increasing age (r=-.453, p=0.001), duration of diabetes (r=-.354, p=0.012), resting SBP (r=-.434, p=0.002) and peak SBP (r=-.386, p=0.006). Preserved HRR was associated with exercise capacity (METS) (r=.345, p=0.14). There was no correlation between HRR and dyslipidemia. A multiple linear regression model ($R^2$=0.26) revealed the duration of diabetes (β=-0.02, p=0.048) and resting SBP (β=-010, p=0.048) to be the independent predictors of HRR.

## Discussion

Our study showed that HRR, which is a measure of CAN, was significantly lower in T2DM patients. Banthia et al also showed that the subjects with DM had a lower HRR at 1 minute [15]. Even Fang et al showed that HRR after 1 minute of exercise was significantly less in DM patients [16].

Many asymptomatic T2DM patients in our study with no history of coronary artery disease had HRR≤18 which could again increase the propensity of developing an increased cardiovascular mortality in studies [14]. This can explain more mortality in T2DM patients with ischemic heart disease as compared to those without T2DM, but with coronary heart disease [10-12].

The cases in this present study also had significantly higher resting heart rate and SBP. Resting tachycardia is again one of the indicators of diabetic autonomic neuropathy [17,18].

With advancing age, the cardiac autonomic nervous system becomes sluggish [19]. Among the cases within the present study, there was a reduction noted in HRR with advancing age, increased duration of diabetes and high SBP. Fang et al had observed similar results in their study as well [16]. Ko et al also showed that the elderly patients and those with longer duration of diabetes stood a greater chance of developing of cardiovascular autonomic dysfunction [20]. The duration of DM and resting SBP were also revealed to be independent predictors of HRR. Patients with a lesser exercise capacity (METS) had less HRR as well, thereby implying that autonomic dysfunction causes reduced exercise capacity [21]. Fang et al also observed a reduced exercise capacity in patients with an impaired HRR [16].

## Conclusion

HRR may not decisively diagnose a patient but can definitely hint at the presence of the cardiac autonomic dysfunction and thus predict the cardiovascular mortality. As elementary measures like regular exercise trainings have been observed to improve HRR and CAN, therefore early detection and interventions using simple indicators like HRR may help reduce the cardiovascular morbidity and mortality. However more work remains to be done, in light of the ambiguity over the HRR cut-offs for labeling diabetic cardiac autonomic neuropathy.

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