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Variability in Heart Rate Recovery after Tredmill Testing and its Co-Relation with Body Mass Index in Patients with Normal ECG

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Abstract: ***Heart rate variability (HRV) has been established as a specific and sensitive non-invasive tool to study cardiac autonomic activity.[1] AIM - To assess the factors affecting variability in heart rate recovery at one minute (HRR) after Treadmill test (TMT) in individuals with normal ECG and no preexisting cardiovascular diseases. Correlation of impaired HRR (<12) with body mass index (BMI) and association with resting heart rate (RHR) and reserve heart rate (ReHR). Method – The study was conducted in a tertiary care hospital in India over a period of 2 yrs. 138 subjects between age of 18yr to 60yr were taken by simple random sampling. Data was analysed by stata software and chi-square test, multivariate regression analysis was used to find association of variables. Result – Subjects with BMI>25kg/m^2 (overweight and obese) were found to be strongly associated with impaired heart rate recovery (p-value-0.02, adjusted odds ratio-8.233). Conclusion- obesity is strong risk factor for impaired HRR and autonomic dysfunction. As delayed HRR is independent risk factor for coronary artery disease as well as a predisposing factor for arrhythmias and sudden death in obese patients, [2] This study was done to assess the various factors associated with impaired HRR so that preventive measure can be taken for cardiovascular accidents.***

Keywords: Body Mass Index (BMI), heart rate recovery, Treadmill stress test

1. Introduction

HRV is an index of cyclical variations of beat-to-beat (RR) interval that reflects cardiac autonomic function and sympathovagal balance.[1] It is an indicator of the extent of neuronal damage to autonomic nervous system (ANS). Appears to precede the development of cardiovascular disease.[3] Cardiac autonomic function can be assessed by heart rate recovery (HRR) following exercise testing, a slow decline indicating reduced parasympathetic activation. It is through inflammatory states and autonomic nervous system dysfunction that obese patients have a higher risk of morbidity and mortality.[2] Obesity is a **modifiable risk factor** to prevent the occurrence of CHD.

BMI is known to vary with a number of factors, including age, smoking, physical activity, alcohol consumption, and socioeconomic status which are also associated with CHD risk, greatest cumulative CHD risk found for nondrinkers with BMI of 35 kg/m2 or over, and the lowest for drinkers with BMI of less than 25 kg/m2.[3] Present study was intended to find out the risk factors for delayed heart rate recovery, so that preventive measures can be taken and cardiovascular disease taken care on time.

2. Methods

The study was approved by ethical committee of MGM University. Cross sectional observational Study done at tertiary care hospital in Aurangabad over a period of 2 years from nov 2015 to nov 2017. 138 patients were taken by Simple Random Sampling. Individuals aged between 18 to 59 years of both sexes with normal electrocardiogram were taken. Those who had prior abnormal treadmill test, ischemic heart disease, other cardiovascular problems with myocardial dysfunction, chronic obstructive pulmonary disease, asthma, osteoarticular diseases, hypertension or any symptoms suggestive of peripheral or autonomic neuropathy such as giddiness on standing, urinary urgency, tingling sensation of limbs, limb weakness, diarrhea, and constipation were excluded from study. Factors were studied in relation to resting heart rate (RHR), reserve heart rate (ReHR), heart rate recovery (HRR) which were : Age (divided in groups 18yr-30yr, 30yr-40yr, 40yr-50yr, 50yr-60yr), sedentary worker (little or no physical activity), smoker or not (if smoker <1 pack yr, 1 pack yr, 2pack yr, >3 pack yr), alcoholic or not (if yes <30ml/day, 30ml-60ml/day, >60ml/day). BMI was categorized as (18. 5 to <25 kg/m2), Overweight (25 to ≤30 kg/m2), Obese (>30 kg/m2).subjects were advised to abstain from sternous activity, smoking, caffeine 2 hrs prior to test. Baseline heart rate, ECG, blood pressure recorded for all subjects in supine position. Subjects were taken for treadmill testing (TMT) with modified bruce protocol after explaining the procedure, taking informed consent. ECG recordings taken every min during TMT and peak heart rate recorded. After TMT halt heart rate, ECG and blood pressure recorded in supine position. Heart rate at one minute post exercise noted. Monitoring of the patient was done for 6-8 minutes post exercise or until the heart rate, blood pressure, patient symptoms, ST changes. **Heart rate recovery (HRR),** was defined as the difference between maximum HR and HR during the first minute of the active recovery phase, and was classified as **impaired if ≤12 bpm**. **Reserve heart rate (ReHR)** was defined as the difference between the resting HR with the patient supine and maximum HR at peak exercise. And classified as impaired if <80% of predicted for age.

3. Statistical Analysis

The data were analyzed using Stata 12.1 SE software, the distribution of absolute and relative frequencies being used to describe categorical variables, and measures of distribution and dispersion (means and standard deviation) for numerical variables. The three BMI groups and other factors were assessed relation to resting, maximum, reserve and recovery HR. The chi-square test was used to analyze risk factors. The statistical analysis was carried out in two stages, with univariate analysis being used to identify variables with $p \leq 0.50$, which were then included in the multivariate analysis.

4. Results and Observations

138 subjects were recruited and classified as shown in fig no. 1. 21% of subjects were female. 58% of the total, 80% of obese subjects, 54% of overweight and 50% of normal BMI were smokers. All were normotensive. 47% of all subjects were diabetic, 90% of obese subjects, 43% of overweight, and 34% of normal BMI subjects were diabetic. 69% of diabetic were smokers, 80% were alcoholic, 50% had sedentary life style. Physical activity of subjects (classified as sedentary workers and moderate heavy workers, various classes of smoking and alcohol as shown in fig no. 1, 2, 3 were not found to be associated with impaired HRR

Various risk factors were analysed with respect to 3 variables which are RHR, ReHR, HRR. 4.76% subjects in age range of 50yr -60yr had abnormal resting heart rate (RHR) which was highest among the age groups. No association was found between age of subjects and ReHR, RHR, HRR as the p-value for all the three variables were >0.05 (table no. 1, 2). Females were found to have abnormal ReHR in 26.67% of subjects which was higher than male subjects and 35.19% of male subjects had delayed HRR at 1min which was higher than 26.67% in female group, but no association could be established between sex of the subject and 3 variables discussed [p-value>0.05 (table no. 1, 2)]. 45.06% of overweight subjects, 42.86% of obese, 10.87% of normal BMI subjects had impaired heart rate recovery at one minute after TMT.

Among all risk factors studied BMI was found to be associated with impaired HRR in both categories, overweight [BMI-25-30kg/m^2 (unadjusted Odds ratio= 6.7282, C/I=2.3793-19.0261, P-value=0.0003)], obese [BMI-<30kg/m^2 (unadjusted Odds ratio=6..1500, C/I=1.7298-21.8656, P-value=0.0050)] as shown in table no. 1. None of the normal BMI and obese subjects had abnormal RHR. 38.10% of obese subjects, 23.94% of overweight subjects, 2.17% of normal subjects had abnormal ReHR [p-value was 0.001 (table no.2)], obesity was found to be associated with impaired ReHR. None of the normal BMI and obese subjects had abnormal RHR, BMI was not associated with RHR (P-value>0.05). Only variables with p<0.50, and thus potential predictors of impaired HRR, were included in the multivariate analysis: age, sex, sedentary life style, BMI, diabetic, various classes of smoking, various classes of alcohol, ReHR and In the final model the significant variables were BMI and ReHR. BMI was the strongest risk marker [overweight p-value-.002, odds ratio-8.233, 95%C.I.-2.203-30.777, Obese p-value -0.089, odds ratio-3.982, 95% C.I.-808-19.617. ReHR was significant associated with obesity and diabetes [p-value<0.05, (table no. 3)]. Resting heart rate was abnormal in smoker subjects only, none of the other risk factors studied found to be associated with RHR. Impaired ReHR was significantly associated with impaired HRR (P-value-0.00, table no.3).

5. Discussion

Individuals who present impaired HRR after exercise have an almost four-fold greater risk of mortality in ischemic heart disease.[4] Impaired HRR is an indicator of damage to autonomic nervous system (ANS). Decreased HRV reflects an abnormal autonomic sinus node activity characterized by a dominating sympathetic and reduced parasympathetic control.[4] Autonomic nervous system (ANS) activity plays an important role in regulation of body weight.[5] Overweight (BMI between 25-30) and obesity (BMI>30) was strongly associated with impaired HRR in univariate analysis but in multivariate analysis smoking, physical activity, alcohol consumption, sex, age and sedentary behaviour of subjects slightly attenuated the odds ratio and p-value. Overweight subjects had higher risk of abnormal HRR than obese subjects.

Of the parameters assessed during exercise testing, resting HR showed no correlation with ReHR (P-value-0.39), and RHR had no correlation with HRR (p-value -1.00), after adjustment for age, BMI, sex, diabetes, sedentary life style, smoking and alcohol. This is explained by the fact that resting HR is under inhibitory parasympathetic control, while HRR immediately after exercise is modulated by parasympathetic reactivation.[6]

Diabetes was associated with a higher risk of impaired ReHR in our study (P-value<0.05, table no. 2).Smoking can be established as independent factor for abnormal RHR irrespective of BMI of patient but was not associated with abnormal HRR. Obesity was found to be associated with impaired ReHR in present study.

Autonomic nervous system (ANS) activity plays an important role in regulation of body weight. Decreased HRV reflects an abnormal autonomic sinus node activity characterized by a dominating sympathetic and reduced parasympathetic control.[1, 5]

Other cross-sectional and prospective studies have demonstrated a direct or indirect relation between obesity and impaired HRR after exercise, in both the presence and absence of cardiovascular risk factors.[7, 8, 9]

Impaired HRR 1min and ReHR were identified as independent predictor for major cardiovascular events (MACE). [11] In the prediction of the MACE, the patients with impaired HR reserve or impaired HRR 1min were 4.7-fold or 4.4-fold higher than those with normal HR response after adjustment of several factors, respectively. In addition, the patients with both impaired HR reserve and impaired HRR 1min were 7.5-fold higher than those with normal HR response.[10] Impaired HR reserve may indicate disruptions in autonomic balance and an inability of the cardiovascular

system to appropriately respond to the sympathetic discharge and parasympathetic withdrawal that occurs during exercise. Some studies have suggested that impaired HR reserve serves as a protective response in the presence of the CAD to avoid excessively high HR and its associated demands for coronary artery flow.[11]

In a retrospective study conducted by **Yawan et al** comparison of medical record information using a community-practice–based sample of 90 patients undergoing 2 exercise stress tests separated by 18 weeks or less was done. Individual patient's HRR was markedly variable from the first to second stress test. No definition of abnormal HRR provided more than 55% concordance between results from the first and second stress tests.[12] hence treadmill test cant be a gold standard test for impaired HRR and to prognosticate cardiovascular diseases, further studies are needed to evaluate short-term test-retest stability or reproducibility and other tests..[12]

6. Conclusion

A reduced HRV is a powerful and independent predictor of an adverse prognosis not only in patients with heart disease but also in the general population. Obesity is a strong modifiable risk factor for impaired heart rate recovery. Preventive measures taken on time can decrease cardiovascular diseases. Smoking can be established as independent factor for abnormal resting heart rate irrespective of BMI of patient but was not associated with abnormal heart rate recovery.

Ethical disclosures

Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data: We declare that we have followed the protocols of ethical committee on the publication of patient data.

Right to privacy and informed consent: We have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Tables and figures

Table 1: Showing classification of variables and distribution of total subjects among them and their unadjusted odds ratio with respect to HRR and p-value

Total subjects	138	Number of subjects with abnormal HRR	Unadjusted odds ratio (OR) and 95% confidence interval	p-value
Age : • 18yr-30yr • 31yr-40yr • 41yr-50yr • 51yr-60yr	 24 51 42 21	 8 17 17 4	OR 95% C.I. Lower Upper 1.000.357 2.799 1.360.477 3.882 .471.118 1.872	 0.427 1.00 .566 .285
Sex • Male • Female	 108 30	 38 8	OR 95% C.I. for Lower upper .670.272 1.648	 0.259
BMI • 18-24.9 Kg/m^2 • 25-30 kg/m^2 • >30 kg/m^2	 46 71 21	 5 32 9	OR 95% C.I.for Lower Upper **6.728 2.379 19.026** **6.150 1.730 21.865**	 **0.001** **0.000** **0.005**
Physical activity • Sedentary worker • Moderate or heavy worker	 73 65	 23 23	OR 95% C.I.for Lower Upper 1.208.542 2.692 1.159.431 3.120	 0.644 0.770
• Nonsmoker • Smoker <1 pk yr • Smoker 1 pk yr • Smoker 2 pk yr • Smoker >3 pk yr	 59 47 17 11 4	 19 15 6 4 2	OR 95% C.I.for Lower Upper 987.434 2.243 1.148.369 3.572 1.203.314 4.615 2.105.275 16.104	 0.959 0.975 0.811 0.788 0.473
• Diabetic • Non-diabetic	66 72	20 26	OR 95% C.I. for Lower upper 1.300.638 2.649	0.588
• Non-alcoholic • Alcohol <30ml/day • Alcohol 30-60ml/day • Alcohol >60ml	 59 51 17 11	 19 17 6 4	OR 95% C.I. Lower Upper 1.053.474 2.339 1.148.369 3.572 1.203.314 4.615	 0.991 0.900 0.811 0.788

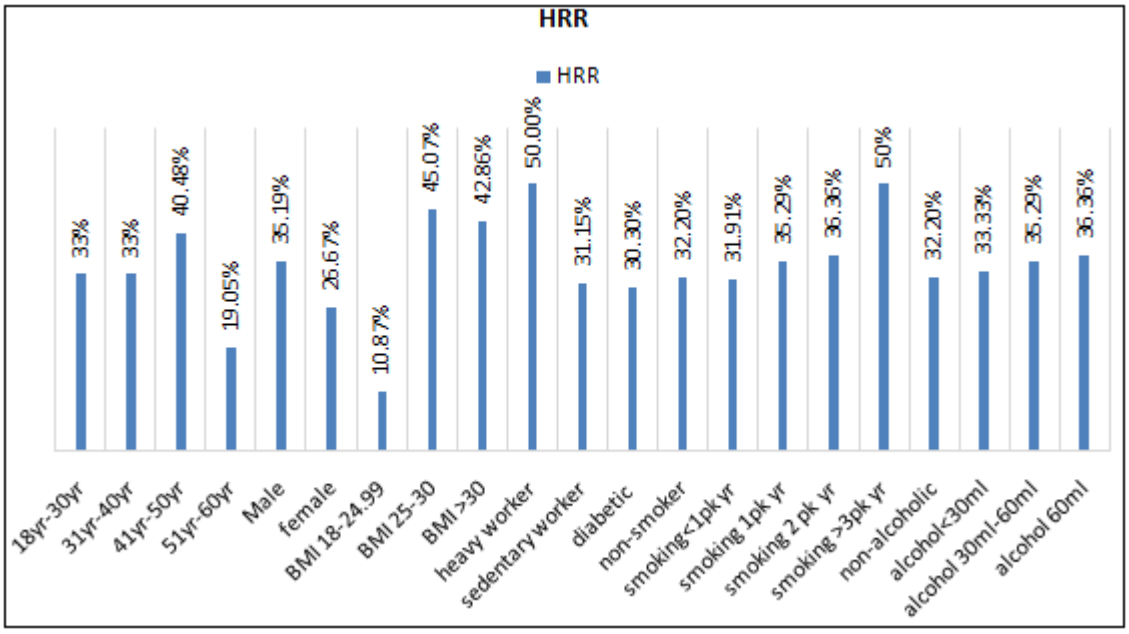

Figure 1: Showing percentage of variables with impaired heart rate recovery.

Table 2: Showing percentage of variables with impaired RHR, ReHR and their p-values

Total subjects	138	Percentage of subject with abnormal RHR	P-value for abnormal RHR	Percentage of subject with abnormal ReHR	P-value for abnormal ReHR
Age :					
• 18yr-30yr	24	4.17%		20.83%	
• 31yr-40yr	51	1.96%	0.561	13.73%	0.692
• 41yr-50yr	42	0.00%		21.43%	
• 51yr-60yr	21	4.76%		23.81%	
Sex					
• Male	108	1.85%	0.623	16.67%	
• Female	30	3.33%		26.67%	0.215
BMI			.		
• 18-24.9 Kg/m^2	46	0%		2.17%	
• 25-30 kg/m^2	71	4.23%	0.235	23.94%	**0.001**
• >30 kg/m^2	21	0%		38.10%	
Physical activity					
• Sedentary worker	73	4.11%		4.11%	
• Moderate or heavy worker	65	0.00%	0.255	25%	0.875
• Nonsmoker	59	1.69%		12.77%	
• Smoker <1 pk yr	47	2.13%	**0.033%**	11.76%	
• Smoker 1 pk yr	17	0%		18.18%	0.261
• Smoker 2 pk yr	11	0%		0%	
• Smoker >3 pk yr	4	25%		27.12%	
(Pk= pack years)					
• Diabetic	66	0.00		25.76%	
• Non-diabetic	72	4.17%	0.094	12.50%	**0.047**
• Non-alcoholic	59	1.69%		11.76%	
• Alcohol <30ml/day	51	3.92%	0.701	11.76%	0.181
• Alcohol 30-60ml/day	17	0.00%		18.18%	
• Alcohol >60ml	11	0.00%		27.12%	

Table 3: Multivariate Regression analysis table of variables against HRR. Variables having p-value <0.5 has been taken. Highlighted portion shows adjusted OR for different variables

		p-value	OR	95% C.I.	
				Lower	Upper
	BMI	.007			
	BMI (1)	**.002**	**8.233**	**2.203**	**30.777**
	BMI (2)	**.089**	**3.982**	**.808**	**19.617**
	Age	.165			
	Age (16yr-30yr)	.328	2.100	.475	9.278
	Age (31-40yr)	.083	4.059	.832	19.810
	Age (41yr-50yr)	.761	.741	.107	5.121
	Sex (51yr-60yr)	.135	.289	.057	1.472
	Reserve_heart_rate	**.000**	**30.873**	**7.060**	**135.001**
	Diabetes_mellitus	.059	2.810	.960	8.227
	Smoking	.595			
	Smoking (<1pack yr)	.699	.768	.202	2.928
	Smoking (1pack yr)	.421	2.027	.363	11.320
	Smoking (2pack yr)	.932	1.095	.136	8.811
	Smoking (3pack yr)	.273	4.410	.311	62.482
	Constant		.000	.015	