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Original Article

Cardiorespiratory Fitness and Heart Rate Recovery in Type-II Diabetic Males : The Effect of Adiposity

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Abstract

The study was done to evaluate cardiorespiratory fitness & heart rate recovery among type-II diabetic males & the influence of adiposity over them. 40 male subjects with history of type-II diabetes (T2D) since 5 years, & without any co-morbidity & addiction were included in the study. 40 healthy males with no addiction history served as controls. Measured obesity indices were BMI, % body fat (%BF), WC (waist circumference) and WHR (waist-hip ratio). Six minute walk test (6MWT) was done to measure HRR-1 & 2 (heart rate recovery at 1st & 2nd min), and to predict VO_2max. The cases had significantly higher %BF, WC, WHR, resting heart rate (rHR) and blood pressure (rBP); and significantly lower HRR-1, HRR-2 & VO_2max. No significant difference was noted in age, physical activity, weight, height & BMI. After controlling for the obesity indices, only difference in VO_2max remained significant, indicating T2D has independent effect on it. Adiposity on the other hand had major contribution for the differences in rHR & rBP. VO_2max was also found as the best classifier for having T2D, followed by WC & HRR-2, with the following respective cut off values: ≤39.82 ml/kg/min; ≥102.75 cm and ≤41.5 bpm.

Introduction

Diabetes mellitus is one of the most common non-communicable diseases, and is among the top five causes of premature death worldwide (1). Excess adiposity has been considered an important factor in the pathogenesis of type-II diabetes (2), and also is known to have negative effect on both cardiorespiratory fitness (3) and heart rate recovery (4).

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Cardiorespiratory fitness is the ability of the circulatory, respiratory and muscular systems to supply oxygen during sustained physical activity (5). It is a strong predictor of type-II diabetes (6), and all-cause mortality for those already having type-II diabetes (7). Maximum oxygen consumption or VO_2max is the gold standard measure of cardiorespiratory fitness (8).

Similarly, heart rate recovery (HRR) has been shown as a valid predictor of type-II diabetes (9), autonomic dysfunction (10) and mortality (9). It is the rate of decline of heart rate following either maximal or submaximal exercise to resting level (11). Heart rate recovery during the first 30 sec or 1 minute (HRR-1) after exercise has been shown to be mediated primarily by activation of parasympathetic nervous system; whereas HRR during first 2 min (HRR-2) and beyond is mediated by both vagal reactivation and sympathetic withdrawal (12).

The present study was planned with the aim to evaluate cardiorespiratory fitness and heart rate recovery among type-II diabetic males, and to find the influence of adiposity over them.

Methodology

The present study was cross sectional & analytical, and was carried out in the Department of Physiology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Swami Ram Nagar, Dehradun. The study was conducted on male volunteers of age group 20-40 years. The control and the case group included 40 subjects in each group. This sample size in each group was obtained using the formula for differences of means for VO_2max at 90% power and α error of 0.05 after rounding up (13). The following inclusion and exclusion criteria were used :

(a) Case group (n=40):

- Inclusion criteria: Diagnosed type-II diabetes with maximum duration since diagnosis of 5 years.
- Exclusion criteria: History of smoking and alcoholism. History of hypertension, respiratory, cardiovascular and skeleto-muscular diseases and disability.

(b) Control group (n=40):

- Inclusion criteria: Healthy.
- Exclusion criteria: Same as the case group.

After explaining the procedure and purpose of the study, a written consent was obtained from the subjects. The study was approved by the Institute ethical committee.

Study Protocol

The subjects were asked to report in the Department of Physiology in the morning around 10 am, after light breakfast. They were instructed prior to avoid tea, coffee, heavy physical activity for atleast 2 hours before the reporting time.

Relevant medical, personal and drug history were taken. Physical activity was assessed by a physical activity recall questionnaire (PAR) scale (14). Anthropometric variables like height (HT in cm) and body weight (BW in kg) were recorded. Following obesity indices were measured:

(a) Indices of general adiposity: body mass index (BMI in kg/m^2) and percentage body fat (%BF) (15, 16). %BF was measured using an impedance body composition analyzer (Omron, model HBF-375).

(b) Indices of abdominal adiposity: waist circumference (WC in cm) and waist-hip ratio (WHR) (15, 17). WHR was calculated as WC divided by HC (hip circumference in cm). WC & HC were measured using a flexible and non-stretching measuring tape.

After a rest of 10 minute in sitting position, resting heart rate (rHR in bpm) using a heart rate monitor (Polar FT1/FT2), and resting systolic blood pressure (rSBP in mmHg) and resting diastolic blood pressure (rDBP in mmHg) using a blood pressure apparatus (model no. EW 254 DC6V) were measured. Six minute walk test (6MWT) was conducted following the standard methodology, and was used to estimate VO_2max for the subjects (14). The subjects were constantly motivated throughout the testing. 6MWT was also used to measure heart rate recovery at 1st min (HRR-1 in bpm) and heart rate recovery at 2nd min (HRR-2 in bpm) after exercise with the subjects sitting passively. HRR-1 and HRR-2 was calculated by subtracting post 6MWT heart rate at 1st minute and 2nd minute from post 6MWT heart rate at 0th

minute respectively. A heart rate monitor (Polar FT1/FT2) was used for the same.

Statistical Analysis

SPSS (Statistical Package for Social Science) version 20 was used for the data analysis. Quantitative data were presented in the form of mean±standard deviation, and ordinal data in median±quartile deviation. Unpaired 't' test was used for comparison of various quantitative parameters between the controls and the cases, and also among case subgroups divided based on various selected cut off values of obesity indices. For the ordinal data, Mann-Whitney test was used. One way ANCOVA (analysis of covariance) was further used for comparison of interested quantitative parameters with significantly different obesity indices as the covariates. Pearson Chi-Square test or Fisher's Exact test, whenever >20% cells of the 2X2 contingency table had expected count <10, with φ (Phi) for estimation of effect size was used for comparison of the frequency or proportion of HRR-1 & 2 between the controls and the cases based on selected cut off values. Zero-order correlation using Kendall tau b and partial correlation after controlling for various obesity indices were used for analyzing the association of type-II diabetes status (0=absent & 1=present) with various variables. Areas under the Receiver Operating Characteristic (ROC) curves were calculated for all the variables so as to assess the best classifiers for having type-II diabetes among the studied subjects. Cut off values with corresponding sensitivity & specificity based on maximum Youden Index were chosen, where Youden Index was calculated as sensitivity+specificity-1. Statistical significance was chosen at α value of ≤5% for all the analyses.

Results

In the present study, the cases have significantly higher values of %BF & WHR; and highly significant higher values of WC as compared to the controls (Table I). However, there are no statistically significant differences in age, PAR scale, HT, BW, BMI & HC between the two groups (Table I).

In our study, there is statistically significant positive correlation between WC & WHR with type-II diabetes (Table II). In addition, they are the only variables among all the obesity indices which are statistically significant classifiers for having type-II diabetes among the studied subjects, with respective cut off values of ≥102.75 cm and ≥.95 (Table III). AUC (area under ROC curve) for the WC is more than that of WHR and next only to that of VO_2max, indicating

TABLE I: Comparison of demographic, anthropometric, cardiovascular & cardiorespiratory fitness parameters between the controls & the cases.

Parameters	*Controls (n=40) Mean±SD*	*Cases (n=40) Mean±SD*	*Unpaired t test p-value (2-tailed)*	*One way ANCOVA#*	
				F value (df=1,75)	*p-value (2-tailed)*
Age (years)	36.95±3.84	38.08±2.25	.115		
PAR Scale	4±0.50^^	3±.50^^	.128^		
HT (cm)	171.24±6.02	170.68±4.59	.640		
BW (Kg)	72.31±10.60	74.70±9.40	.289		
BMI (Kg/m^2)	24.61±2.98	25.62±2.85	.124		
%BF (%)	23.15±6.69	26.27±3.91	.014*		
WC (cm)	99.14±6.97	103.36±3.63	.001**		
HC (cm)	107.35±5.48	108.48±6.08	.387		
WHR	.92±.05	.96±.07	.014*		
rHR (bpm)	83.85±5.03	86.68±4.62	.011*	.645	.424
rSBP (mmHg)	124.9±5.78	128.50±4.81	.003**	2.627	.109
rDBP (mmHg)	81.2±4.72	83.35±3.43	.023*	1.041	.311
HRR-1 (bpm)	19.55±1.80	18.15±2.26	.003**	3.205	.077
HRR-2 (bpm)	40.07±3.02	38.05±2.37	.001**	2.121	.149
VO_2max (ml/kg/min)	41.62±4.67	38.02±4.01	<.001**	5.341	.024*

*p–value ≤0.05: significant; **p–value ≤0.01: highly significant. ^Mann-Whitney Test. ^^Median±Quartile deviation. #Covariates: %BF, WC & WHR. SD=Standard deviation.

TABLE II : Significantly correlated variables with type-II diabetes status among the studied subjects (n=80).

Variables	*Zero-order correlation^ r-value*	*Partial correlation r-value*	
		df=75^^	df=74#
WC (cm)	.285**		
WHR	.230*		
rHR (bpm)	.203*	.092	.085
rSBP (mmHg)	.227*	.184	.178
rDBP (mmHg)	.208*	.117	.115
HRR-2 (bpm)	–.284**	–.166	–.138
VO_2max (ml/kg/min)	–.308**	–.258*	–.541**

*p–value ≤0.05: significant; **p–valued ≤0.01: highly significant. ^Kendall's tau b. ^^Controlling for %BF, WC & WHR; #controlling for BMI, %BF, WC & WHR. Type-II diabetes status, 0=absent & 1=present. df=degree of freedom.

WC to be the best statistically significant classifier of having type-II diabetes among all the studied obesity indices.

The cases also have significantly higher rHR & rDBP, and highly significant higher value of rSBP (Table I). However, they have highly significant lower values of HRR-1 & 2 (Table IV). The frequency of abnormal HRR-1, based on the cut off value of ≤18 bpm (18) is not statistically different between the controls & the cases (Table IV). However, when ≤42 bpm is used as the cut off value for abnormal HRR-2 (19), 100% of the cases have abnormal HRR-2 as compared to 72.5% of the controls. This is statistically highly significant with a medium effect size (Table IV). Unlike HRR-1, HRR-2 is not only a highly significant negative zero-order correlate of type-II diabetes (Table II), but also a highly significant classifier for having type-II diabetes status, with cut off value of ≤41.5 bpm in the present study (Table III).

When the cases are subdivided as per cut off values of obesity indices- BMI: ≥23 Kg/m^2 & ≥25 Kg/m^2 (20), %BF: >25% (21), WC: ≥102 cm and WHR: ≥0.9 (17); the case subgroups with the higher obesity indices also have higher values of resting heart rate and blood pressure, and lower values of HRRs, which are statistically significant, except for rHR for 23 Kg/m^2 BMI cut off subgroups and rDBP for 0.9 WHR cut off subgroups (Table V). This suggests the important influence of increased adiposity over these variables among the studied type-II diabetics.

TABLE III : Statistically significant areas under the ROC curve (AUC) of the classifiers for having type-II diabetes among the studied subjects (n=80).

Classifiers (in descending order of AUC)	*AUC±S.E.*	*p-value (2-tailed)*	*Cut off value at maximum J*	*Sensitivity (%)*	*Specificity (%)*
VO_2max (ml/kg/min)	.716±.058	.001**	≤39.82	75	70
WC (cm)	.696±.061	.003**	≥102.75	65	75
HRR-2 (bpm)	.689±.060	.004**	≤41.5	92.5	37.5
WHR	.661±.061	.013*	≥.95	52.5	75
rSBP (mmHg)	.650±.061	.021*	≥129	40	80
rDBP (mmHg)	.636±.064	.036*	≥79	92.5	40
rHR (bpm)	.636±.062	.036*	≥84	80	40

*p–value ≤0.05: significant; **p–value ≤.01: highly significant. ROC curve=Receiver Operating Characteristic curve, S.E.=Standard Error & J=Youden Index.

TABLE IV : Comparison of the frequency of heart rate recovery at 1st & 2nd min between the controls and the cases based on selected cut off values.

Group	*HRR-1 (bpm) cut off*		*χ^2, df (2-tailed p-value, φ)*	*HRR-2 (bpm) cut off*		*χ^2, df (2-tailed p-value, φ)*
	≤18	*>18*		*≤42*	*>42*	
Controls (n=40)	11 (27.5%)	29 (72.5%)	1.978,1 (.160, –.157)	29 (72.5%)	11 (27.5%)	12.754,1 (<.001**#, –.399)
Cases (n=40)	17 (42.5%)	23 (57.5%)		40 (100%)	0 (0%)	

*p–value ≤0.05: significant; **p–value ≤0.01: highly significant. Pearson Chi-Square test. # Fisher's Exact test. χ^2 = Chi-Square, df=degree of freedom & φ=Phi (effect size).

TABLE V : Comparison of resting heart rate, resting blood pressure, heart rate recovery and cardiorespiratory fitness parameters among the case subgroups divided based on various selected cut off values of obesity indices.

Cut off		Parameters (Mean±SD)					
		rHR (bpm)	*rSBP (mmHg)*	*rDBP (mmHg)*	*HRR-1 (bpm)*	*HRR-2 (bpm)*	*VO_2max (ml/kg/min)*
BMI (Kg/m^2)	≤22.9 (n=8)	84±3.21	125.00±5.95	81.00±3.85	19.75±.89	40.50±1.31	44.09±1.33
	≥23 (n=32)	87.34±4.71	129.38±4.14	83.94±3.11	17.75±2.33	37.44±2.18	36.50±2.81
	p-value (2-tailed)	.066	.019*	.028*	.001**	.001**	<.001**
	≤24.9 (n=15)	84.33±3.46	125.47±4.75	81.47±3.16	19.13±1.64	39.73±1.58	42.15±2.50
	≥25 (n=25)	88.08±4.71	130.32±3.90	84.48±3.12	17.56±2.40	37.04±2.21	35.54±2.31
	p-value (2-tailed)	.011*	.001**	.006**	.019*	<.001**	<.001**
%BF (%)	≤25 (n=17)	84.18±3.57	126.12±4.92	81.53±3.04	19.41±1.66	39.82±1.59	41.66±2.72
	>25 (n=23)	88.52±4.48	130.26±3.97	84.70±3.11	17.22±2.21	36.74±1.98	35.32±2.28
	p-value (2-tailed)	.002**	.005**	.003**	.001**	<.001**	<.001**
WC (cm)	<102 (n=14)	83.57±4.11	125.71±5.54	81.29±3.81	19.14±1.92	39.86±1.79	41.68±3.47
	≥102 (n=26)	88.35±4.02	130.00±3.67	84.46±2.67	17.62±2.28	37.08±2.08	36.04±2.69
	p-value (2-tailed)	.001**	.006**	.004**	.040*	<.001**	<.001**
WHR	<0.9 (n=6)	82.00±2.83	124.33±5.85	81.00±4.34	19.67±.52	40.33±1.63	42.63±3.62
	≥0.9 (n=34)	87.50±4.39	129.24±4.29	83.76±3.14	17.88±2.35	37.65±2.27	37.20±3.52
	p-value (2-tailed)	.006**	.019*	.068	<.001**	.009**	.001**

*p–value ≤0.05: significant; **p–value ≤0.01: highly significant. Unpaired t test.

The negative effect of increased adiposity is also supported by our finding that the statistically significant differences in rHR, rSBP, rDBP, HRR-1 & HRR-2 between the controls and the cases become non-significant once the differences in %BF, WC & WHR are controlled for (Table I). Similarly there are no statistically significant partial correlations between these variables with type-II diabetes status, after controlling for various obesity indices (Table II). Although, zero-order correlations between them are significant (except for HRR-1, which does not have significant zero-order & partial correlation r-values) (Table II). Hence, our finding indicates that increased adiposity has a major contribution to the higher resting heart rate, blood pressure, and lower heart rate recovery observed among the studied type-II diabetics.

The cases also have, on an average, highly significant lower values of VO_2max as compared to the controls (Table I). The values of VO_2max are also significantly lower among the case subgroups with higher obesity indices (Table V), indicating the negative influence of excess adiposity on VO_2max too. Interestingly, the cases still have significantly lower VO_2max, even after statistically controlling for the differences in %BF, WC & WHR (Table I). The cases and the controls already have statistically similar BW & BMI, in addition to age, PAR scale, HT & HC (Table I). This suggests the independent negative effect of type-II diabetes on VO_2max, and hence cardiorespiratory fitness, over and beyond various obesity indices. Also, VO_2max has both highly significant negative zero-order correlation, and significant & highly significant partial correlations with type-II diabetes status, after controlling for various obesity indices (Table II).

Additionally, VO_2max is found to be the best classifier for having type-II diabetes among the studied subjects with the largest statistically highly significant AUC (Table III). The cut off value obtained using ROC curve at maximum Youden Index is ≥39.82 ml/kg/min, at a sensitivity of 75% and specificity of 70% (Table III). Other statistically significant classifiers for having type-II diabetes in decreasing order of AUC are: WC (cut off value: ≥102.75 cm) >HRR-2 (cut off value: ≥41.5 bpm) >WHR (cut off value: ≥.95) >rSBP (cut off value: ≥129 mmHg) >rDBP (cut off value: ≥79 mmHg) >rHR (cut off value: ≥84 bpm) (Table V). However, generalization of these cut off values for increased risk of type-II diabetes should be avoided. As the cut off values obtained are only applicable on these particular studied subjects. Besides, these cut off values which are obtained using the ROC curves are for classifying subjects having type-II diabetes from those not having the disease among the whole studied subjects at a maximum sensitivity &

specificity, and not for assessing increased risk of type-II diabetes in general population.

Discussion

Our findings suggest that the studied diabetic group, on an average, has both more general (%BF) and abdominal adiposity (WC & WHR). The finding of positive association between adiposity and type-II diabetes has been reported earlier (2). WC has also been found to be the best predictor of type-II diabetes by Wang Y et al (22), suggesting that abdominal or android fat distribution carries the highest risk (16).

Similar finding of higher resting heart rate and blood pressure (23), and lower HRR-1 (24) & HRR-2 (19) among type-II diabetics has been reported earlier. Autonomic imbalance with reduction in vagal tone and/or an exaggerated sympathetic activation might be responsible (24). However, obesity per se may also cause autonomic imbalance (25), and hence, negative association between obesity and heart rate recovery has been reported earlier (4). Our findings suggest the major influence of adiposity over resting cardiovascular variables and heart rate recovery among the studied type-II diabetics. Since delayed HRRs and higher rHR are independent indicators of mortality in diabetics (9, 26), our study, therefore, suggests the importance and possible beneficial effect of losing fat among type-II diabetics.

The finding of lower VO_2max among type-II diabetics as compared to healthy controls has been reported earlier (27). Low VO_2max as a strong predictor of type-II diabetes has also been reported earlier (6). In our study, the cut off value obtained for VO_2max for having type-II diabetes among the studied subjects is ≥39.82 ml/kg/min. Low VO_2max and hence cardiorespiratory fitness among the type-II diabetics may be the result of multifactorial causes, including diabetic associated adverse cardiac effects (28), vascular and metabolic alterations (29), high prevalence of pulmonary abnormalities (30) and myopathy (31), in addition to the excess adiposity (2).

Since obesity also has negative effect on VO_2max (3), and type-II diabetes is associated with increased adiposity (2), we try to evaluate the individual effect of type-II diabetes on VO_2max. And our findings clearly suggest that type-II diabetes has independent negative effect on cardiorespiratory fitness over and beyond adiposity. Similar findings of the negative association between type-II diabetes and VO_2max (3), and insulin resistance with VO_2max, independent of obesity (32), have been reported earlier.

Conversely, higher VO_2max was associated with non diabetic state in our study. Enhanced cardiorespiratory fitness has been found to have a protective role in diabetes (33), and is associated with reduced risk of developing diabetes and diabetes-related mortality (3). Besides, evidence from large observational studies have suggested that improving VO_2max could attenuate much, if not all, of the health risk attributed to obesity (34), including obesity-related morbidity and mortality associated with type-II diabetes (35). Hence, endurance training including intermittent and interval training for improving VO_2max would be very beneficial for reducing risk & complications of type-II diabetes, in addition to the fat loss programs.

Conclusion

The studied diabetic group had significantly more general (%BF), and abdominal adiposity (WC & WHR) as compared to the age, physical activity, HT, BW, BMI & HC matched healthy control group. They had significantly higher resting heart rate and blood pressure, but lower heart rate recovery. This was mainly contributed by the excessive adiposity among them. The diabetic group also had significantly lower VO_2max, even after statistically controlling for various obesity indices. This indicated the independent negative effect of type-II diabetes on cardiorespiratory fitness over and beyond adiposity in the present study. VO_2max was also the best statistically highly significant classifier of having type-II diabetes among the studied subjects, followed by WC & HRR-2. The cut off values were: ≥39.82 ml/kg/min; ≥102.75 cm and ≥41.5 bpm respectively.

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