Exercise Capacity and Cardiovascular/Metabolic Characteristics of Overweight and Obese Individuals with Type 2 Diabetes. The Look AHEAD Study

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Running Title: Exercise Capacity in Overweight and Obese Individuals

Exercise Capacity and Cardiovascular/Metabolic Characteristics of Overweight and Obese Individuals with Type 2 Diabetes. The Look AHEAD Study

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Abstract

OBJECTIVE -- We examined associations of cardiovascular, metabolic, and body composition measures with exercise capacity using baseline data from 5145 overweight and/or obese (BMI $\geq$ 25.0) men and women with type 2 diabetes (T2DM) who were randomized participants for the Look AHEAD clinical trial.

RESEARCH DESIGN AND METHODS -- Peak exercise capacity expressed as metabolic equivalents (METs) and estimated from treadmill speed and grade was measured during a graded exercise test (GXT) that was designed to elicit a maximal effort. Other measures included: waist circumference, BMI, T2DM duration, types of medication used, HbA1c, history of cardiovascular disease, metabolic syndrome, beta blockers use, race/ethnicity.

RESULTS -- Peak exercise capacity was higher for males (8.0 ± 2.1 METs) compared to females (6.7 ± 1.7 METs) ($p<0.001$). Exercise capacity also decreased across each decade of age ($p<0.001$) as well as with increasing BMI and waist circumference levels in both genders. Older age, increased waist circumference and BMI, a longer duration of diabetes, increased HbA1c, a history of CVD, having metabolic syndrome, beta blocker use, and being African American compared to white, were associated with a lower peak exercise capacity for both genders. Hypertension and use of diabetic medications were associated with lower peak exercise capacity in females.

CONCLUSIONS -- Among persons with diabetes who are overweight or obese have impaired exercise capacity, which is primarily related to: age, female sex, and race as well as poor metabolic control, BMI, and central obesity.

Obesity is a chronic progressive condition that is increasing worldwide (1) and it has reached epidemic proportions in the United States (2) where currently, in excess of 60 percent of American men and women are either overweight or obese. The health and economic burdens of obesity are substantial (3). Future health burden is of great concern since obesity is a risk factor for both type 2 diabetes and cardiovascular disease (4,5), each of which is responsible for marked increases in health care costs. Overweight and obese individuals have lower fitness levels due to being more sedentary than the general population (6) and having excess weight (7). Similarly, individuals with type 2 diabetes are also more likely to be overweight or obese, sedentary, and unfit (7). While studies in individuals with type 2 diabetes have demonstrated both an impaired cardiovascular response and a reduced aerobic capacity (8-12), the response of overweight and obese individuals with type 2 diabetes to exercise is not well documented and available studies have a relatively small sample size (7, 8). To our knowledge, the Look AHEAD clinical trial has compiled the largest number of graded exercise tests completed on individuals who are overweight and have type 2 diabetes. Understanding the relationship of exercise capacity to risk factors is especially important because fitness level is a strong predictor of future morbidity and mortality in men and women with and without obesity and/or diabetes (10-16)

The aim of the present study is to examine the association demographic, physical, and diabetes- and CVD-related measures with exercise capacity. This analysis was performed on baseline data before any interventions were assigned.

RESEARCH DESIGN AND METHODS -- Look AHEAD (Action for Health in Diabetes) is a 16-center randomized clinical trial of overweight and obese participants, 45-75 yrs, with type 2 diabetes, designed to evaluate the long-term effects (up to 11.5 years) of an intensive weight loss intervention on the time to incidence for major cardiovascular events. (17) A total of 5145 participants between the ages of 45 -75 who had a BMI $\geq$ 25 kg/m^2 ($\geq$ 27 kg/m^2 if on insulin) and type 2 diabetes mellitus were recruited over a 2.5 year period for Look AHEAD. Of these individuals, 59.5% were women, 63.1% were white, 14.0% had a history of CVD, and 15.3% were on insulin.

Assessments

Full details of Look AHEAD design and methods, as well as detailed screening, exclusion criteria, and the randomization process, are reported elsewhere (17); however, measures relevant to this report are described briefly herein. All measurements were taken by staffs that were centrally trained and certified on an annual basis. These measurements were carried out before randomization to the intervention groups.

Waist circumference was measured at the level of the iliac crest to the nearest 0.1 centimeter using the Gulick II Tape Measure (model 67020). Two measurements were obtained with the average of these measurements used to represent the waist circumference.

Exercise capacity was assessed using a symptom-limited graded exercise treadmill test to voluntary exhaustion. The treadmill protocol was individualized to the comfortable walking speed for each participant by having the participant perform a brief walking acclimation procedure that included the following. Participants started walking on the treadmill at 1.5 mph on a level (0%) grade while speed was increased gradually by 0.5 mph units until the subject reached a brisk but comfortable self-selected walking speed, or until 4.0 mph was achieved; this was the treadmill speed that was used for the maximal test.

After a brief rest period, the exercise test was initiated with the speed set at the predetermined level as described above and the grade at 0%. Speed remained constant throughout the test while the grade was increased by 1% each subsequent minute until voluntary exhaustion. During the last 10 seconds of each exercise stage and at the point of test termination, heart rate was measured from a 12-lead ECG and rating of perceived exertion (RPE) was obtained using the 6-20 category Borg Scale (18). For safety, blood pressure was measured during the last 45 seconds of each even minute exercise stage (i.e., stages 2, 4, 6, etc.) and at the point of test termination using a manual sphygmomanometer. Using standard test termination criteria of the American College of Sports Medicine (19), the test was terminated at voluntary exhaustion or if the patient reported signs or symptoms of exercise intolerance (i.e., ischemia, significant ST depression, or complex arrhythmias). For the exercise test to be considered valid, participants not on beta blocker medication had to achieve $\geq$ 85% of age-predicted maximal heart rate and $\geq$4 metabolic equivalents (METs), whereas those participants who were on a beta blocker medication had to achieve a RPE $\geq$18 and $\geq$4 METs. Peak exercise capacity expressed as METs was estimated from treadmill speed and elevation using standardized equations (19, 20) where VO_2 ($mL \cdot kg^{-1} \cdot min^{-1}$) = [0.1 $mL \cdot kg^{-1} \cdot meter^{-1} \cdot S$ ($m \cdot min^{-1}$)] + [1.8 $mL \cdot kg^{-1} \cdot meter^{-1} \cdot S$ ($m.min^{-1}$) $\cdot G$] + 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$; S = speed and G = grade in percent. METs = VO_2 ($mL \cdot kg^{-1} \cdot min^{-1}$)/ 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$.

Metabolic Syndrome was defined as having 3 or more of the following 5 criteria according to Grundy et al (20) 1. Waist circumference ≥102 cm for men or ≥88cm for women. 2. Systolic blood pressure (SBP) ≥130 mmHg or diastolic blood pressure (DBP) ≥85 mmHg or taking antihypertensive medication. 3. Fasting blood glucose (FBG) ≥100 mg/dl or diagnosis of diabetes. 4. Fasting triglycerides ≥150 mg/dl. 5. High Density Lipoprotein (HDL) <40 mg/dl for men or <50 mg/dl for women.

HbA1c. HbA_1c was measured by a dedicated ion exchange, high performance liquid chromatography instrument (Biorad Variant 11). Individuals whose HbA1c exceeded 11% were ineligible; they were thought to require more urgent care and were told to seek treatment. Such individuals could be re-screened after 3 months to re-assess HbA1c eligibility.

Statistical analysis. Analyses were restricted to randomized participants and were performed using SAS version 9.1 (SAS Institute, Cary, NC). Descriptive statistics were presented as mean ± standard deviation for continuous variables and frequency distribution for categorical variables. General linear models were used to examine bivariate relationships of maximum METs with age, BMI, waist circumference, race/ethnicity, HbA1c, diabetes medication, beta blocker use, and the presence of metabolic syndrome, CVD history, and hypertension. Gender-specific models were fitted to generate least square means and p-values with adjustment for either the effects of age, or BMI, or both. Results were tabulated in Table 1. Variables that were significantly related to the maximum METs in bivariate analyses were then entered into gender-specific multiple linear regression models. Age, BMI, waist circumference, duration of diabetes, and HbA1c were included in these models as continuous variables. Backwards selection was used to construct the final models. Residual plots were examined to evaluate the adequacy of models.

RESULTS

Five thousand one hundred forty-five participants (2082 men and 3063 women) met the eligibility criteria and were enrolled in the clinical trial. Participants had a mean age 58.7±6.8 years (59.9±6.7 years for males and 57.9±6.8 years for females). Mean BMI was 35.9±5.9 kg/m² (35.2±5.5 kg/m² for males and 36.5±6.1 kg/m² for females). Mean waist circumference was 118.5 ± 13.4 cm for men and 110.8 ± 13.4 cm for women.

Age, gender, ethnicity, and exercise capacity. Exercise capacity was higher for males (mean METs 8.0 ± 2.1) compared to females (mean METs 6.7 ± 1.7, $p<0.0001$) and exercise capacity decreased across each decade of age ($p<0.0001$). Because of the gender differences, subsequent analyses were performed separately for males and females, and were also adjusted for age. Examination of race/ethnicity demonstrated that when compared to white participants, exercise capacity was lower for African-American participants ($p<0.001$) (Table 1).

Heart rate, RPE, and beta blockade. There were no significant differences between the genders for peak heart rate achieved during the graded exercise test. However, peak heart rate was lower ($p < .01$) for participants using a beta blocker medication (130.6 $\pm$19.2) compared to those not using a beta blocker medication (153.2 $\pm$ 14.0). When expressed as a percent of age-predicted maximum heart rate, similar differences were observed (81.9 $\pm$ 11.6 vs. 94.8 $\pm$ 7.9 for beta blockade and non-beta blockade, respectively; $p< .0001$). Results also demonstrate that the criterion of RPE$\geq$18,which was used as a marker of maximal effort for those on beta blockade, was achieved regardless of beta blocker usage (19.5 $\pm$ 0.8 vs. 19.4 $\pm$ 1.2 for beta blockade and non-beta blockade, respectively).

Body composition, metabolic syndrome and exercise capacity. Exercise capacity expressed as METs was lower for participants with higher BMI and higher waist circumference (Figure 1). BMI and waist circumference were each independently associated with exercise capacity, with participants in the lowest BMI category and lowest quintile of waist circumference having the highest level of fitness (Table 1). After adjusting for both age and BMI, higher waist circumference was still independently associated with lower exercise capacity for both males and females (both $p<0.001$). Exercise capacity (METs) was lower for participants with a history of CVD and/or hypertension as well as those using beta blocker medication (each $p<0.001$; Table 1).

Moreover, participants using medications to control their diabetes had a lower level of fitness than individuals not using these medications, even after adjustment for BMI (p<0.001). Metabolic syndrome was present in 94.0% of participants, and was more prevalent in females (94.8%) than in males (92.9%). Exercise capacity was lower (p<0.0001) in those participants with metabolic syndrome, even after adjustment for BMI (Table 1).

Factors influencing exercise capacity. The gender specific multiple linear regression models of estimated independent mediators of fitness showed that for males, older age, increased waist circumference and BMI, a longer duration of diabetes, increased HbA1c, a prior history of cardiovascular disease (CVD), having metabolic syndrome, use of beta blocker medication, and being African American compared to white, were significant variables in explaining lower exercise capacity (Table 2). For females, older age, increased waist circumference and BMI, a longer duration of diabetes, increased HbA1c, hypertension, prior history of CVD, having metabolic syndrome, use of diabetic medication, use of beta blocker medication, and being African American as compared to being white, were significant variables in explaining lower exercise capacity (Table 2).

CONCLUSIONS

Body composition and exercise capacity.

In this large cohort of overweight/obese individuals with type 2 diabetes, greater impairment of exercise capacity (METs) was associated with increasing levels of general and central obesity. There is further reduction in fitness with increasing age, a longer duration of diabetes, increased HbA1c, a history of CVD, having metabolic syndrome, beta blocker use, and being African American compared to white, in both genders. Additionally, for females there was greater fitness reduction with hypertension and use of diabetic medications. This is supported in a review by Stewart (22) that reported individuals with diabetes have impaired endothelial function, diminished left ventricular diastolic function, and increased arterial stiffness, all of which could contribute to reduced exercise capacity and to an increased risk of future cardiovascular events.

Age and exercise capacity.

The predicted peak exercise capacity in healthy, normal weight populations of males and females declines naturally with age. (23,24) The typical decline in METs with age is approximately 5-10% per decade for both sexes and females are approximately 20% lower than males across the age range. We found these same age and gender trends in Look AHEAD. We also found that when the exercise capacity data are placed into the four categories of Overweight and Class I, II, and III Obesity, there is a corresponding decline of approximately 10-15% per weight category (Table 1). This has been previously demonstrated by Wei and colleagues (11) and others (12). While general and central obesity are independently associated with lower exercise capacity, the synergistic influence of increased fatness is even more dramatic. As shown in Figure 1, individuals in the most favorable quintile of general and central obesity had nearly twice the exercise capacity of those in the least favorable quintile. The importance of fitness over fatness has recently been addressed by Church et al (25) who demonstrated a steep inverse gradient between fitness and mortality in a cohort of men with documented diabetes, an association that was independent of BMI. This suggests that exercise programs that can improve fitness levels, independent of weight loss, have the potential to limit the mortality risk in individuals with type 2 diabetes, although this is yet to be definitively determined.

Metabolic syndrome, HbA_1c, medications, ethnicity, and exercise capacity. Exercise capacity was also lower for those with metabolic syndrome, higher HbA_1c, and those who were on beta blocker therapy and/or using insulin. A recent study by Ugur-Altun et al. (7) examined the relationship between exercise capacity and metabolic variables in 48 men and 42 women with type 2 diabetes and found that a reduced exercise capacity was also associated with increased insulin resistance, lower peak heart rate, and an increased likelihood of an abnormal test. Wong et al. (26) studied 393 individuals with metabolic syndrome without a history of clinical cardiovascular disease, to determine the relationship between myocardial and vascular function and exercise capacity. Their study sample was similar to the Look AHEAD cohort with respect to age, gender, BMI, waist circumference, blood pressure, presence of diabetes (95%) and MET capacity. They found a positive relationship ($P<0.001$) between the number of metabolic syndrome components and impaired echocardiographic indices of left ventricular systolic and diastolic strain, reduced arterial compliance, and a significant decline in exercise capacity. While none of these measures have been collected in the Look AHEAD study, these are likely explanations for the mechanisms behind the impairments seen in this cohort.

We also found that African Americans had a lower exercise capacity compared with whites, which may be a reflection of the lower levels of physical activity reported in African-Americans compared to whites (27-29) This may influence body weight, and in this cohort, African Americans have higher levels of general and central obesity. Moreover, West et al (30) have recently demonstrated that African American women are less responsive to weight loss intervention programs than white women, which may again reflect differences in physical activity.

Central obesity and exercise capacity.

Central obesity is a strong determinant of diabetes and cardiovascular disease risk and is also associated with vascular and autonomic dysfunction and impaired cardiovascular fitness (31). In a 9-yr follow-up study, Koh-Banerjee et al (32) demonstrated that reduced levels of physical activity were associated with increased waist circumference, even after adjustment for BMI. Others (33,34) have found similar results relating fitness and visceral obesity. Our findings highlight the fact that waist circumference, a marker of central obesity, is an important determinant of exercise capacity and warrants further research regarding its independent influence on cardiovascular risk. This point has been made recently by Yusuf et al (35) who revealed that when waist circumference is taken into account, BMI, a marker of general obesity, has little or no relationship to risk of cardiovascular events. This underscores the importance of using physical activity interventions in individuals with type 2 diabetes since improved fitness levels are associated with significant reductions in visceral adipose tissue and, consequently, the associated risks of increased morbidity and mortality from type 2 diabetes and cardiovascular disease independent of BMI (36).

Strengths. A major strength of this study is the large number of individuals (n=5145) included of both sexes and the inclusion of an adequate number of individuals from ethnic groups other than Caucasian (African American: n=803; American Indian/ Native American/ Alaskan Native: n=258; Hispanic: n=677; and Asian/ Pacific Islander/Other/ Mixed: n=161). This is also the largest study of overweight/obese individuals with type 2 diabetes who have undergone graded exercise testing.

Limitations. The results of this study may not be representative of all individuals with type 2 diabetes in this age range due to specific inclusion/exclusion criteria. Since only overweight/obese individuals were included, this will bias the trend towards greater co-morbidities and lower fitness than would be expected. Conversely, each participant also had to meet a minimum fitness level of 4.0 METs, which excluded the very unfit and those with a limited ability to sustain a regular exercise routine, which was a major aspect of the subsequent behavioral intervention.

In summary, among males, having a lower exercise capacity was associated with older age, higher BMI, increased waist circumference, longer duration of diabetes, increased HbA1c, history of CVD, beta blocker use, having metabolic syndrome, and being African American compared to white. Among females, in addition to these same determinants as males, having hypertension and use of diabetes medications also contributed to a lower exercise capacity. In addition to reduced exercise capacity, central obesity is also a risk factor for diabetes and cardiovascular disease. Thus, the present data emphasize the need for interventions to target central obesity rather than just BMI, given the known relationship of increased visceral adipose tissue to both type 2 diabetes and cardiovascular disease.

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Figure 1. Influence of BMI and waist circumference upon METs.

Legend:
Waist Circumference Categories: Males: WC: 1 = < 105 cm; 2 = 105-114.9 cm; 3 = 115-119.9 cm; 4 = 120-129.9 cm; 5 = > 130 cm. Females: WC: 1 = < 100 cm; 2 = 100-104.9 cm; 3 = 105-114.9 cm; 4 = 115-119.9 cm; 5 = > 120 cm.

BMI Categories: S1: 25-29.9; S2: 30-34.9; S3: 35-39.9; S4: ≥40

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Table 1. Influence of BMI, waist circumference, race/ethnicity, diabetes and CVD-related measures, CVD history, and metabolic syndrome upon peak METs

		Overall			Males				Females			
Variable	Subgroup	Mean	SE	P-Value	N	Mean	SE	P-Value	N	Mean	SE	P-Value
Age*	45-49	7.8	0.08	<.0001	149	9.0	0.17	<.0001	403	7.4	0.08	<.0001
	50-59	7.5	0.04		893	8.4	0.07		1481	6.9	0.04	
	60-69	6.8	0.04		846	7.5	0.07		1006	6.2	0.05	
	70-75	6.2	0.10		191	6.8	0.15		171	5.6	0.12	
BMI Category* *	Overweight (25 - 29.9)	8.5	0.06	<.0001	339	9.3	0.10	<.0001	422	7.9	0.07	<.0001
	Class I (30 - 34.9)	7.8	0.04		837	8.5	0.06		979	7.2	0.04	
	Class II (35 - 39.9)	6.9	0.04		531	7.5	0.08		880	6.5	0.05	
	Class III (40 or greater)	5.8	0.05		373	6.2	0.09		776	5.5	0.05	
Waist Circumference***	1	7.5	0.07	<.0001	318	8.9	0.12	<.0001	641	7.1	0.07	<.0001
	2	7.6	0.06		602	8.4	0.08		425	6.8	0.07	
	3	7.0	0.05		282	8.0	0.10		914	6.7	0.05	
	4	7.3	0.06		451	7.7	0.09		371	6.5	0.07	
	5	6.7	0.06		422	6.9	0.12		709	6.2	0.06	
Race**	African American / Black (not Hispanic)	6.7	0.07	<.0001	189	7.6	0.15	0.0283	614	6.4	0.06	<.0001
	American Indian / Native American / Alaskan Native	6.9	0.12		55	8.4	0.27		203	6.5	0.11	
	White	7.3	0.03		1579	7.9	0.05		1664	6.7	0.04	
	Hispanic	7.3	0.07		194	8.1	0.14		483	6.9	0.07	
	Asian/Pacific Islander / Other/Mixed / Missing	7.7	0.15		63	8.3	0.25		98	7.3	0.16	
HbA1c***	< 7.0	7.4	0.03	<.0001	960	8.2	0.06	<.0001	1396	6.8	0.04	<.0001
	7.0+	7.1	0.03		1120	7.8	0.05		1666	6.6	0.03	
Diabetes Medication***	No Diabetic Meds, No Insulin	7.5	0.07	<.0001	228	8.3	0.12	<.0001	413	7.0	0.07	<.0001
	Diabetic Meds Only	7.2	0.03		1444	8.0	0.05		2012	6.7	0.03	

		Overall			Males				Females			
Variable	Subgroup	Mean	SE	P-Value	N	Mean	SE	P-Value	N	Mean	SE	P-Value
	Insulin Only	6.7	0.11		77	7.4	0.20		146	6.3	0.11	
	Insulin and Diabetic Meds	6.9	0.06		308	7.7	0.10		443	6.3	0.07	
Beta Blocker Use**	No	7.3	0.03	<.0001	1619	8.1	0.05	<.0001	2555	6.7	0.03	<.0001
	Yes	6.9	0.06		461	7.4	0.09		507	6.3	0.07	
Metabolic Syndrome***	No	7.9	0.10	<.0001	148	8.5	0.15	<.0001	160	7.2	0.11	<.0001
	Yes	7.1	0.02		1932	7.9	0.04		2902	6.6	0.03	
History of CVD**	No	7.2	0.03	0.0085	1638	8.1	0.05	<.0001	2782	6.7	0.03	0.0001
	Yes	7.0	0.07		442	7.5	0.10		280	6.3	0.10	
History of Hypertension**	No	7.7	0.07	<.0001	300	8.5	0.12	<.0001	512	7.2	0.07	<.0001
	Yes	7.1	0.03		1780	7.9	0.05		2550	6.6	0.03	

Waist Circumference Categories - Males: 1 = < 105 cm; 2 = 105-114.9 cm; 3 = 115-119.9 cm; 4 = 120-129.9 cm; 5 = > 130 cm;
Females: 1 = < 100 cm; 2 = 100-104.9 cm; 3 = 105-114.9 cm; 4 = 115-119.9 cm; 5 = > 120 cm.

*: Means are LS means from model adjusting for BMI; P-values refer to overall significance of variable of interest adjusting for BMI.

**: Means are LS means from model adjusting for age; P-values refer to overall significance of variable of interest adjusting for age.

***: Means are LS means from model adjusting for age and BMI; P-values refer to overall significance of variable of interest adjusting for age and BMI.

Table 2. Multiple linear regression with the maximum METs as the outcome by gender (males and females).

Gender	Variable	β	Standard Error	Test Statistic	P-value
Male	BMI (kg/m^2)	-0.0960	0.01463	-6.56	<.0001
	Waist circumference (cm)	-0.0407	0.00599	-6.79	<.0001
	Age^2 (year)	-0.0009	0.00005	-16.96	<.0001
	Self reported duration of diabetes (year)	-0.0164	0.00637	-2.58	0.0099
	History of CVD	-0.2776	0.10233	-2.71	0.0067
	Metabolic Syndrome	-0.4056	0.15857	-2.56	0.0106
	Beta Blocker Use	-0.3681	0.09557	-3.85	0.0001
	Race/Ethnicity				
	• African American	-0.5214	0.13681	-3.81	0.0001
	• American Indian	-0.0119	0.23663	-0.05	0.9600
	• Hispanic	-0.0534	0.13596	-0.39	0.6946
	• Other/Mixed Race	-0.0731	0.22517	-0.32	0.7453
	HbA1c	-0.1565	0.03422	-4.57	<.0001
Female	BMI (kg/m^2)	-0.1118	0.00692	-16.17	<.0001
	Waist circumference (cm)	-0.0119	0.00320	-3.71	0.0002
	Age (year)	-0.0916	0.00414	-22.13	<.0001
	Self reported duration of diabetes (year)	-0.0141	0.00441	-3.19	0.0014
	Hypertension	-0.1538	0.07698	-2.00	0.0458
	History of CVD	-0.1842	0.09177	-2.01	0.0448
	Metabolic Syndrome	-0.3913	0.12457	-3.14	0.0017
	Use of Diabetes Medications				
	• On Meds but No Insulin	-0.2536	0.07850	-3.23	0.0012
	• Insulin Only	-0.4588	0.14523	-3.16	0.0016
	• On both Diabetic Medication and Insulin	-0.4286	0.10750	-3.99	<.0001
	Beta Blocker Use	-0.2432	0.06713	-3.62	0.0003
	Race/Ethnicity				
	• African American	-0.2473	0.06634	-3.73	0.0002
	• American Indian	-0.1852	0.10640	-1.74	0.0818

Gender	Variable	β	Standard Error	Test Statistic	P-value
	• Hispanic	0.0742	0.07506	0.99	0.3227
	• Other/Mixed Race	0.3449	0.14608	2.36	0.0183
	HbA1c	-0.0587	0.02370	-2.48	0.0133

Reference levels for history of CVD, Metabolic Syndrome, Hypertension, and Beta Blocker Use were the absence of these factors; For race, the reference level was white; For the Use of Diabetes Medication, the reference level was no use.

Appendix is on a different document.

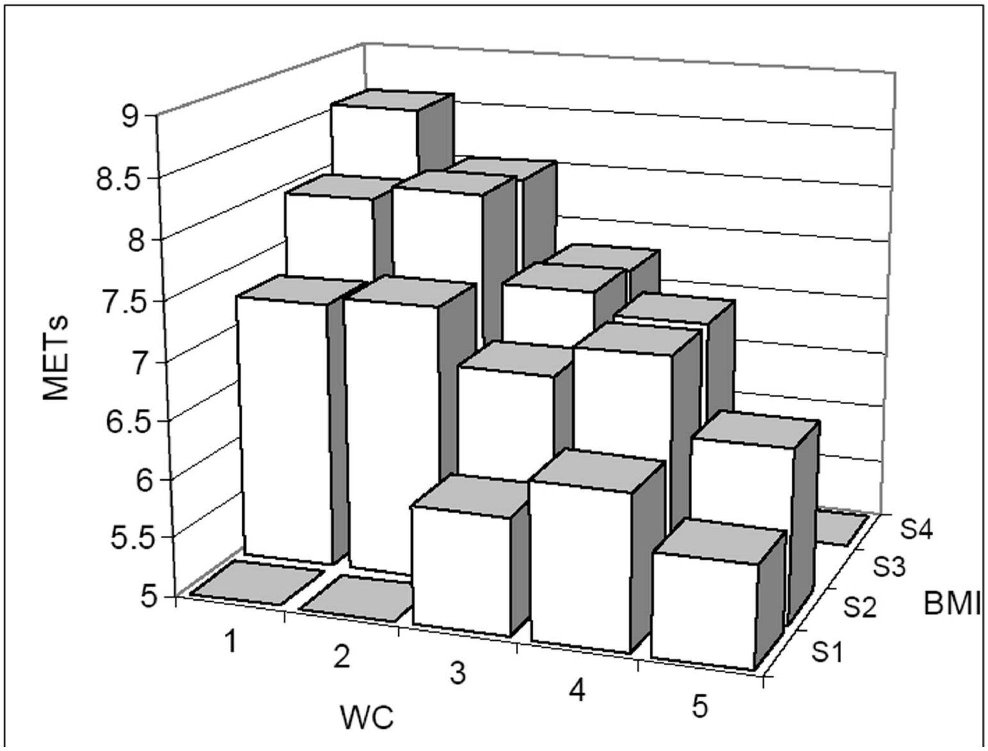

Figure 1. Influence of BMI and waist circumference upon METs. Legend: Waist Circumference Categories: Males: WC: 1 = < 105 cm; 2 = 105-114.9 cm; 3 = 115-119.9 cm; 4 = 120-129.9 cm; 5 = > 130 cm. Females: WC: 1 = < 100 cm; 2 = 100-104.9 cm; 3 = 105-114.9 cm; 4 = 115-119.9 cm; 5 = > 120 cm. BMI Categories: S1: 25-29.9; S2: 30-34.9; S3: 35-39.9; S4: >40