Cardiac function is not associated with glucose control in older women

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ABSTRACT

The present study evaluated the effect of age on glucose tolerance and cardiac function and assessed the relationship between metabolic control and cardiac function and performance. Thirty-four healthy women aged 40 to 81 years were divided into two age groups: younger (≤50 years of age, N=19) and older (≥60 years of age, N=15). Participants performed an oral glucose tolerance test and a graded cardiopulmonary exercise test with non-invasive haemodynamic measurements. Compared to younger, older women demonstrated significantly higher 2-hour glucose (4.67±1.01 vs 6.08±1.54 mmol/l, $p<0.01$), but lower peak exercise O_2 consumption (1.96±0.44 vs 1.38±0.26 l/min, $p<0.01$) and cardiac power output (4.06±0.76 vs 3.35±0.73 Watts, $p=0.01$). When data from all study participants were combined, there was a significant negative relationship between 2-hour glucose and peak cardiac power ($r=-0.39$, $p=0.02$), and peak O_2 consumption ($r=-0.40$, $p=0.02$). The strength of these relationships was affected by age, with moderate negative relationship identified between 2-hour glucose and peak cardiac power output in younger compared to older participants ($r=-0.38$, $p=0.11$ vs. $r=-0.09$, $p=0.75$). Metabolic control and cardiac function decline with age. The lack of relationship between glucose control and cardiac power may suggest that metabolic control does not influence cardiac function and performance in older women.

KEY WORDS: Ageing • Cardiac Function • Cardiopulmonary Exercise Testing • Metabolic Control

INTRODUCTION

Age is the major risk factor for development of chronic diseases. Age-related decline in cardiac and metabolic function increases cardiovascular and metabolic morbidity and mortality in elderly population [1].

In the absence of hypertension or clinically apparent cardiovascular disease, the human heart undergoes structural and functional changes with age that compromise cardiac reserve, lowering the threshold for clinical signs and symptoms [2]. Systolic function at rest i.e. ejection fraction does not seem to change with age but diastolic function progressively declines [3]. Ageing is further associated with changes in myocardial strains, longitudinal shortening, torsion, and cardiac energetics [4].

Impaired metabolic control and abnormal glucose regulation with age lead to increased incidence of diabetes with current estimate suggesting that 74% of people living with diabetes are over the age of 50 [5]. Metabolic dysfunction is associated with an increased risk of cardiovascular diseases i.e. coronary artery disease and heart failure [6].

Currently, a limited number of studies have investigated the association between metabolic control, cardiac function and performance. In particular, no study has reported the effect of age on the relationship between metabolic control, indices of cardiac function and performance including cardiac power output, which has been proposed to be the best indicator of overall function and pumping capability of the heart, and the strongest predictor of mortality [7]. Better understanding of the interaction between body metabolism and function of the heart may lead to development of new strategies to prevent onset of age-related diseases and improve outcomes in elderly population. Therefore, the aim of the present study was twofold; firstly, to define the effect of age on metabolic control and peak cardiac power output, and secondly, to assess the relationship between metabolic control and cardiac function and performance. Based on the previous evidence that individuals with impaired metabolic control are at increased risk

for cardiovascular morbidity and mortality [6] the present study hypothesized that there will be significant relationship between metabolic control and measures of cardiac function regardless of age. This study was designed to address the relationship between metabolic function and performance in women, because of a significant gender difference in age associated changes in cardiac morphology and function [8].

MATERIALS AND METHODS

1. *Participants*

The prospective, single-centre, cross-sectional, observational study recruited 34 healthy women, aged 40 to 81 years. Participants were further stratified according to their age into a younger- (≤50 years old, n=19), and older-age group (≥60 years old, n=15). Study inclusion criteria included (1) no history of cardiovascular disease, pulmonary diseases and other chronic diseases and (2) normal glucose tolerance and lipid profile, normal resting blood pressure, normal electrocardiogram and body mass index ≤30 kg/m2. There exclusion criteria included (1) current or past smokers; (2) participants taking any medication known to affect cardiovascular and or metabolic function; (3) performing regular exercise (≥2 time a week) during the previous 3 years or had been professional or semi-professional athletes; or (4) were not able to perform maximal graded cardiopulmonary exercise stress test. All participants signed an informed consent according to the Declaration of Helsinki, and the study was approved by the National Health Service North East England—Tyne and Wear South.

2. *Study Procedures*

Body composition was measured using air displacement plethysmography method (BodPod, Life Measurement Inc, California). Fasting blood samples were drawn from median

cubital vein for assessment of glucose level. Oral glucose tolerance test was also performed to asses metabolic control [9].

Haemodynamic and gas exchange measurements were performed at rest and in response to maximal graded cardiopulmonary exercise testing using non-invasive gas exchange measurement system (Metalyzer 3B, Cortex, Leipzig, Germany) and the bioreactance method (NICOM, Cheetah Medical, Delaware, USA). The bioreactance method accurately measures frequency of relative phase shift of oscillating electronic current across the thorax, and we have recently reported its validity and reliability to assess cardiac output at rest and during exercise [10-12]. It has greater signal-to-noise ratio by 100-fold compared with the bioimpedance method and is less susceptible to disruption from excessive movements, adipose tissue and electrode placement [12]. Throughout the test, 12-lead electrocardiogram (Custo, CustoMed, GmbH, Ottobrunn, Germany) and blood pressure (Tango, SunTech Medical; Morrisville, North Carolina, USA) were recorded. During the exercise test, participants were asked to cycle at 20 W for 3 min as a warm-up period, followed by increase in workload of 10 W per minute, until volitional exhaustion. Cardiopulmonary exercise test was terminated when (1) subject has reached volitional exhaustion, that is inability to pedal at cadence of 50 revolutions per minute; (2) maximal oxygen consumption was achieved, that is there was no further increase in oxygen utilisation despite increase in exercise intensity (Watts); (3) respiratory exchange ratio >1.15 or (4) subject voluntarily terminated the test. Cardiac power output, expressed in Watts, was calculated as the product of peak exercise cardiac output and mean arterial blood pressure [7]. Peak oxygen consumption, as a measure of metabolic response, was defined as the average oxygen uptake during the last minute of exercise. The arteriovenous oxygen difference (mLO_2/100 mL of blood) was calculated as the ratio between oxygen consumption and cardiac output.

3. Sample Size and Statistical Analysis

It was calculated that a sample size of 30 study participants (≥15 per age group) would be needed to detect a significant difference between the age groups in overall cardiac function i.e. peak cardiac power output of 0.5 Watts with a power of 80%, a two-sided α of 5% [13]. All statistical analysis was carried out using SPSS V.21.0. Prior to statistical analysis, data were tested for univariate and multivariate outliers using standard Z-distribution cut-offs and Mahalanobis distance tests. Kolmogorov-Smirnov test was used to assess normality of distribution. Differences between age groups were assessed using independent t-test. Pearson coefficient of correlation was used to assess the relationship between variables. Statistical significance was indicated if $p<0.05$. Data are presented as mean ± SD unless stated otherwise.

RESULTS

Participant demographic and physical characteristics are presented in Table 1.

The Effect of Age on Metabolic and Cardiac Variables during Rest and Peak Exercise

Metabolic control was significantly reduced in older women as demonstrated with 30% and 13% higher values of 2-hour glucose level and fasting glucose (Table 1). Resting cardiac function was reduced in the older group as demonstrated with significantly lower cardiac output (by 27%), cardiac index (20%), stroke volume (24%), and cardiac power output (21%, Table 1). Heart rate at rest was not significantly different between younger and older women ($p=0.91$). Systolic blood pressure and systemic vascular resistance were 9% and 23% higher in older compared to younger women ($P<0.01$, Table 1).

Exercise tolerance and cardiac performance were significantly reduced in older women. Peak exercise O_2 consumption (ml/kg/min) and cardiac power output were 26% and 17% lower in elderly women (Table 1). Considering that oxygen consumption equals to the product of

cardiac output and arteriovenous oxygen difference, it can be suggested that reduced peak exercise O_2 consumption was secondary to diminished peak cardiac output (by 20%), as the ability of skeletal muscles to extract O_2 (i.e. arteriovenous O_2 difference) was not significantly different between the age groups (p=0.17, Table 1). Despite ability to increase stroke volume from rest to peak exercise by 18%, elderly women demonstrated overall reduced cardiac function (cardiac output) at peak exercise due to significantly reduced heart rate by 30 beats/minute (Table 1). This reduction in peak exercise heart rate is not surprising considering the age difference between the groups and knowing that maximal heart rate is age-dependant. Interestingly, there was no significant difference in peak exercise stroke volume between the two age groups, whereas systolic blood pressure and systemic vascular resistance were significantly higher in elderly group (Table 1).

The Effect of Age on the Relationship between Cardiac Function and Metabolic Control

When all data were combined (young and older women) there was a significant negative relationship between 2-hour glucose level and peak cardiac power output ($r= -0.39$, $P<0.05$, Figure 1A), peak cardiac output ($r= -0.41$, $P<0.05$, Figure 1B), peak oxygen consumption ($r= -0.40$, $P<0.05$, Figure 1D), peak relative oxygen consumption ($r= -0.46$, $P<0.01$, Figure 1E), and systemic vascular resistance ($r= 0.35$, $P<0.05$, Figure 1F). There was no significant relationship between 2-hour glucose and peak mean arterial blood pressure ($r= -0.04$; $P=0.83$, Figure 1C). In addition, a significant negative relationship was identified between fasting glucose and peak cardiac power output ($r= -0.41$, $P<0.05$), peak cardiac output ($r= -0.48$, $P<0.01$) and peak relative oxygen consumption ($r=-0.37$, $P<0.05$).

When data were stratified according to age groups, the following results were revealed. In younger age group there was a negative moderate relationship between 2-hour glucose and peak cardiac power output ($r= -0.38$; $P=0.11$, Figure 2A), peak cardiac output ($r= -0.40$; $P=0.09$,

Figure 2B), peak oxygen consumption (r= -0.31; P=0.20, Figure 2D), peak relative oxygen consumption (r= -0.42; P=0.07, Figure 2E), and systemic vascular resistance (r= 0.38, P=0.10). Conversely, in older women the strength of the relationship between 2-hour glucose and measures of cardiac function and performance was weak (Figure 2A-D).

The Effect of Body Fat on the Relationship between Cardiac Function and Metabolic Control

When data from young and older women were combined there was a significant negative relationship between % body fat and peak oxygen consumption (r= -0.41, P<0.05). On the other hand, there was a significant positive relationship between % body fat and 2-hour glucose level (r= 0.46, P<0.05). However, no significant relationship was identified between % body fat and peak cardiac power output (r- 0.09, P=0.76).

The following results were revealed when data were stratified according to age groups. In younger age group there was a significant negative relationship between % body fat and peak oxygen consumption (r= -0.46, P<0.05), whereas there was a significant positive relationship between % body fat and 2-hour glucose level (r= 0.45, P<0.05). However, no significant relationship was identified between % body fat and peak cardiac power output in younger age group (r- 0.04, P=0.82).

Conversely, in older women % body fat significantly correlated only with a 2-hour glucose (r= 0.36, P<0.05), but not with peak oxygen consumption (r= -0.12, P=0.69) and peak cardiac power (r= -0.15, P=55).

DISCUSSION

The aim of the present study was to define the effect of age on metabolic control and cardiac function, and to assess the effect of age on the relationship between metabolic control and cardiac function and performance in women. The three major findings of the present study are; Firstly, glucose control and cardiac function decline with age. Secondly, moderate negative relationship exists between measures of cardiac function and performance and metabolic control when data from all study participants (i.e. younger and older) were analysed together. Thirdly, there is a lack of the relationship between metabolic control and cardiac function in older women. The present study corroborates the importance to consider the effect of age on interpretation of physiological variables and their relationship.

Women of older age demonstrate impaired metabolic and heart function. The 2-hour blood glucose, a strong predictor of all cause and cardiovascular mortality [14], was significantly higher in women ≥60 than those ≤50 years of age. This finding is in agreement with previous literature suggesting that metabolic control and glucose tolerance decrease with age [19]. It has been proposed that this decline may not be a primary consequence of biological ageing processes but may be secondary to other factors including diseases that disturb glucose metabolism, medications that affect glucose tolerance, and increased obesity [19]. The present study recruited healthy women without history of chronic diseases, not using medication known to affect metabolism, and both age groups demonstrated similar body mass index. Therefore, it can be suggested that observed decline in metabolic control is secondary to biological ageing processes.

Findings of the present study further suggest that cardiac function (i.e. cardiac output and cardiac power output) at rest and response to exercise is significantly reduced in older women. However, it should be noted that both younger and older age women achieved >90%

of their maximal age predicted heart rate suggesting that study participants demonstrated nearly maximal effort during cardiopulmonary exercise stress testing.

The finding of the reduced cardiac function in older age contrast previous suggestion that both resting and peak cardiac function are preserved with ageing in women [8]. Despite suggestion that women, in contrast with men, preserve their full complement of cardiac myocytes during the lifespan [15], concentric remodelling and decline in diastolic function occur due to ventricular stiffening with ageing [4]. In the present study the main difference in overall heart function between the age groups was underlined by significantly reduced resting stroke volume and ability of the heart rate to increase in response to exercise in older women. An interesting observation was a significant increase (by 18%) in stroke volume from rest to peak exercise in elderly but not in younger women. This increase in stroke volume can be seen as a compensatory mechanism contributing to overall cardiac output increase (in order to meet increased metabolic demand during exercise) because of reduced exercise heart rate in elderly women [16]. It was previously suggested that these compensatory mechanisms are in place to prevent decline in exercise cardiac output with age [17]. However, findings from the present study reveal that despite an increase in stroke volume, elderly women demonstrated 20% lower cardiac output at peak exercise.

Exercise tolerance decline with age. In agreement with previous literature [8, 13, 18], the findings from the present study also confirm that peak oxygen consumption, as the gold standard measure of exercise tolerance and cardiorespiratory fitness, was significantly lower in older compared to younger women. The ability of the body to utilise oxygen at rest and during stress (exercise) depends on central and peripheral factors i.e. cardiac function (cardiac output) and ability of skeletal muscles to extract delivered oxygen (arteriovenous oxygen difference). Recent study highlights importance of understanding mechanisms of exercise intolerance in relation to different clinical presentations [19]. According to physiology

principle and Fick equation oxygen consumption equals to product of cardiac output and arteriovenous oxygen difference. Considering that arteriovenous oxygen difference was not significantly different between younger and older women (despite difference in lean body mass), it can be concluded that reduced ability of the heart to respond to stress exercise (heart rate) is a major factor contributing to reduced peak oxygen consumption in older women as previously suggested [14-16, 18, 19]. A decrease in beta adrenergic receptors responsiveness and intrinsic heart rate changes have been used to explain a significant decline in peak exercise heart rate with age [16, 20, 21].

Results of the present study further reveal a significant relationship between metabolic control and measures of cardiac function and performance. In particular, when data from younger and older women were combined there was a significant negative relationship between 2-hour glucose level and peak exercise cardiac power output and oxygen consumption. This finding suggests that those women with better metabolic control are likely to demonstrate better cardiac function and exercise tolerance, therefore reducing susceptibility to development of cardiac and metabolic diseases. Previous studies also report the association between metabolic control and cardiac function [22-24]. However, the present study for the first time show that when study participants are stratified according to the age, a significant relationship between metabolic control and cardiac function and performance remain in younger but not in older participants. This result leads to conclusion that better metabolic control does not suggest better cardiac function in elderly women. This finding was surprising and does not support the study hypothesis. Based on previous evidence suggesting a strong link between impaired metabolic control and risk for development of cardiovascular dysfunction in later life [6], one would expect significant association between 2-hour glucose tolerance and cardiac function in elderly women. This notion however is not confirmed by the findings of the present study. Underlying

molecular and cellular mechanisms that can justify the lack of relationship in older age group remain to be determined in future studies.

Limitations

The following limitations of the present study should be taken into consideration. One may speculate that the number of study participants was limited, particularly when participants were further stratified according to age groups. However, *a priori* sample size calculation suggested that this was a minimum number of participants needed to provide sufficient power to the study to detect significant differences between the two age groups in main variable of interests i.e. cardiac power output. Secondly, considering well-known effect of gender on cardiovascular changes with ageing, the present study recruited only women. Therefore, the main study findings and conclusions may not be applied to male population.

CONCLUSIONS

In conclusion, the main findings from the present study suggest that older women demonstrate significantly reduced metabolic control, cardiac function and exercise tolerance. Findings further reveal lack of the relationship between glucose control and cardiac power output which may indicate that metabolic control does not influence cardiac function and performance in older women.

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REFERENCES

1. Abubakar, I., T. Tillmann, and A. Banerjee, *Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013.* Lancet, 2015. **385**(9963): p. 117-171.

2. Lakatta, E.G., *Age-associated cardiovascular changes in health: impact on cardiovascular disease in older persons.* Heart failure reviews, 2002. **7**(1): p. 29-49.

3. Lakatta, E.G. and D. Levy, *Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part II: the aging heart in health: links to heart disease.* Circulation, 2003. **107**(2): p. 346-354.

4. Hollingsworth, K.G., et al., *Left ventricular torsion, energetics, and diastolic function in normal human aging.* American Journal of Physiology-Heart and Circulatory Physiology, 2011. **302**(4): p. H885-H892.

5. Guariguata, L., et al., *Global estimates of diabetes prevalence for 2013 and projections for 2035.* Diabetes Research and Clinical Practice, 2014. **103**(2): p. 137-149.

6. Halter, J.B., et al., *Diabetes and cardiovascular disease in older adults: current status and future directions.* Diabetes, 2014. **63**(8): p. 2578-2589.

7. Williams, S., et al., *Peak exercise cardiac power output; a direct indicator of cardiac function strongly predictive of prognosis in chronic heart failure.* European heart journal, 2001. **22**(16): p. 1496-1503.

8. Goldspink, D.F., et al., *A study of presbycardia, with gender differences favoring ageing women.* International journal of cardiology, 2009. **137**(3): p. 236-245.

9. Ito, C., et al., *Correlation among fasting plasma glucose, two-hour plasma glucose levels in OGTT and HbA1c.* Diabetes Research and Clinical Practice, 2000. **50**(3): p. 225-230.

10. Perkins, R., et al., *Relationship between bioreactance and magnetic resonance imaging stroke volumes.* British journal of anaesthesia, 2016. **117**(1): p. 134-136.

11. Jones, T., et al., *Bioreactance is a reliable method for estimating cardiac output at rest and during exercise.* British journal of anaesthesia, 2015. **115**(3): p. 386-391.

12. Jakovljevic, D.G., M.I. Trenell, and G.A. MacGowan, *Bioimpedance and bioreactance methods for monitoring cardiac output.* Best Practice & Research Clinical Anaesthesiology, 2014. **28**(4): p. 381-394.

13. Jakovljevic, D.G., et al., *Effect of Physical Activity on Age-Related Changes in Cardiac Function and Performance in WomenCLINICAL PERSPECTIVE.* Circulation: Cardiovascular Imaging, 2015. **8**(1): p. e002086.

14. Borch-Johnsen, K., et al., *Glucose tolerance and cardiovascular mortality-Comparison of fasting and 2-hour diagnostic criteria.* 2001.

15. Olivetti, G., et al., *Gender differences and aging: effects on the human heart.* Journal of the American College of Cardiology, 1995. **26**(4): p. 1068-1079.

16. Gulati, M., et al., *Heart rate response to exercise stress testing in asymptomatic women: the St. James women take heart project.* Circulation, 2010. **122**(2): p. 130-137.

17. Rodeheffer, R.J., et al., *Exercise cardiac output is maintained with advancing age in healthy human subjects: cardiac dilatation and increased stroke volume compensate for a diminished heart rate.* Circulation, 1984. **69**(2): p. 203-213.

18. Fleg, J.L. and E.G. Lakatta, *Role of muscle loss in the age-associated reduction in VO2 max.* Journal of applied physiology, 1988. **65**(3): p. 1147-1151.

19. McCoy, J., et al., *Pathophysiology of exercise intolerance in chronic diseases: the role of diminished cardiac performance in mitochondrial and heart failure patients.* Open heart, 2017. **4**(2): p. e000632.

20. Stratton, J.R., et al., *Cardiovascular responses to exercise. Effects of aging and exercise training in healthy men.* Circulation, 1994. **89**(4): p. 1648-1655.

21. Christou, D.D. and D.R. Seals, *Decreased maximal heart rate with aging is related to reduced β-adrenergic responsiveness but is largely explained by a reduction in intrinsic heart rate.* Journal of applied physiology, 2008. **105**(1): p. 24-29.

22. Kannel, W.B. and D.L. McGee, *Diabetes and cardiovascular disease: the Framingham study.* Jama, 1979. **241**(19): p. 2035-2038.

23. Isomaa, B., et al., *Cardiovascular morbidity and mortality associated with the metabolic syndrome.* Diabetes care, 2001. **24**(4): p. 683-689.

24. Capaldo, B., et al., *Cardiovascular characteristics in subjects with increasing levels of abnormal glucose regulation: the Strong Heart Study.* Diabetes care, 2013. **36**(4): p. 992-997.

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Table 1. Demographic Details of Study Participants,
Metabolic and Haemodynamic Measurements at Rest and During Peak Exercise

	Age Category		*P* value	% difference
	≤50 Years *N*=19	≥60 Years *N*=15		
Age	44±3	71±6	0.01	61
Fat Body Mass, %	32±9	37±9	0.09	16
Lean Body Mass, kg	47±5	41±4	0.01	13
Fat Body Mass, kg	23±10	25±8	0.48	9
Lean Body Mass %	68±9	63±9	0.09	7
Weight, kg	68.9±12.6	65.6±9.6	0.41	5
Body Surface Area, m^2	1.77±0.15	1.68±0.13	0.09	5
Height, cm	166±5	159±5	0.01	4
Body Mass Index, kg/m^2	25.1±4.1	25.9±3.4	0.59	3
Measurements at Rest				
Metabolic				
2 Hour Glucose, mmol/l	4.67±1.01	6.08±1.54	0.01	30
Fasting Glucose, mmol/l	4.64±0.44	5.22±0.31	0.01	13
O_2 Consumption, l/min	0.25±0.04	0.24±0.03	0.19	4
Relative O_2 Consumption, ml/kg/min	3.8±0.8	3.7±0.5	0.63	3
Respiratory Expiratory Exchange Ratio	0.91±0.07	0.90±0.08	0.94	1
Haemodynamic				
Cardiac Index, l/min/m^2	3.50±0.55	2.92±0.39	0.01	20
Cardiac Output, ml/min	6.2±1.2	4.9±0.9	0.01	27
Cardiac Power Output, Watts	1.39±0.32	1.15±0.24	0.03	21
Heart Rate, bpm	69±8	71±9	0.91	0
Stroke Volume, ml/beat	87.8±14.4	70.9±14.1	0.01	24
Systolic Blood Pressure, mmHg	130±16	143±12	0.01	9
Diastolic Blood Pressure, mmHg	87±9	87±10	0.98	0
Mean Arterial Pressure, mmHg	101±10	105±10	0.20	4
Systemic Vascular Resistance, dyne/s/cm^5	1352±273	1765±336	0.01	23
Measurements at Peak Exercise				
Metabolic				
O_2 Consumption, l/min	1.96±0.44	1.38±0.26	0.01	30
Relative O_2 Consumption, ml/kg/min	28.9±8.9	21.5±4.7	0.01	26
Respiratory Expiratory Exchange Ratio	1.19±0.07	1.18±0.12	0.60	1
Haemodynamic				
Cardiac Index, l/min/m^2	8.56±1.50	7.08±1.27	0.01	17
Cardiac Output, ml/min	15±2	12±2	0.01	20
Cardiac Power Output, Watts	4.06±0.76	3.35±0.73	0.01	17
Heart Rate, bpm	170±10	140±15	0.01	18
Stroke Volume, ml/beat	89.4±14.4	85.6±17.5	0.50	4
Systolic Blood Pressure, mmHg	183±21	198±16	0.04	8
Diastolic Blood Pressure, mmHg	90±10	91±9	0.16	4
Mean Arterial Pressure, mmHg	122±12	127±9	0.98	0
Systemic Vascular Resistance, dyne/s/cm^5	667±121	884±175	0.01	33
Arteriovenous Oxygen Difference, ml/100ml	13±3	12±2	0.17	8

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Figure 1. The Relationship Between Metabolic Control and Cardiac Function When Data from All Participants were combined (n=34).

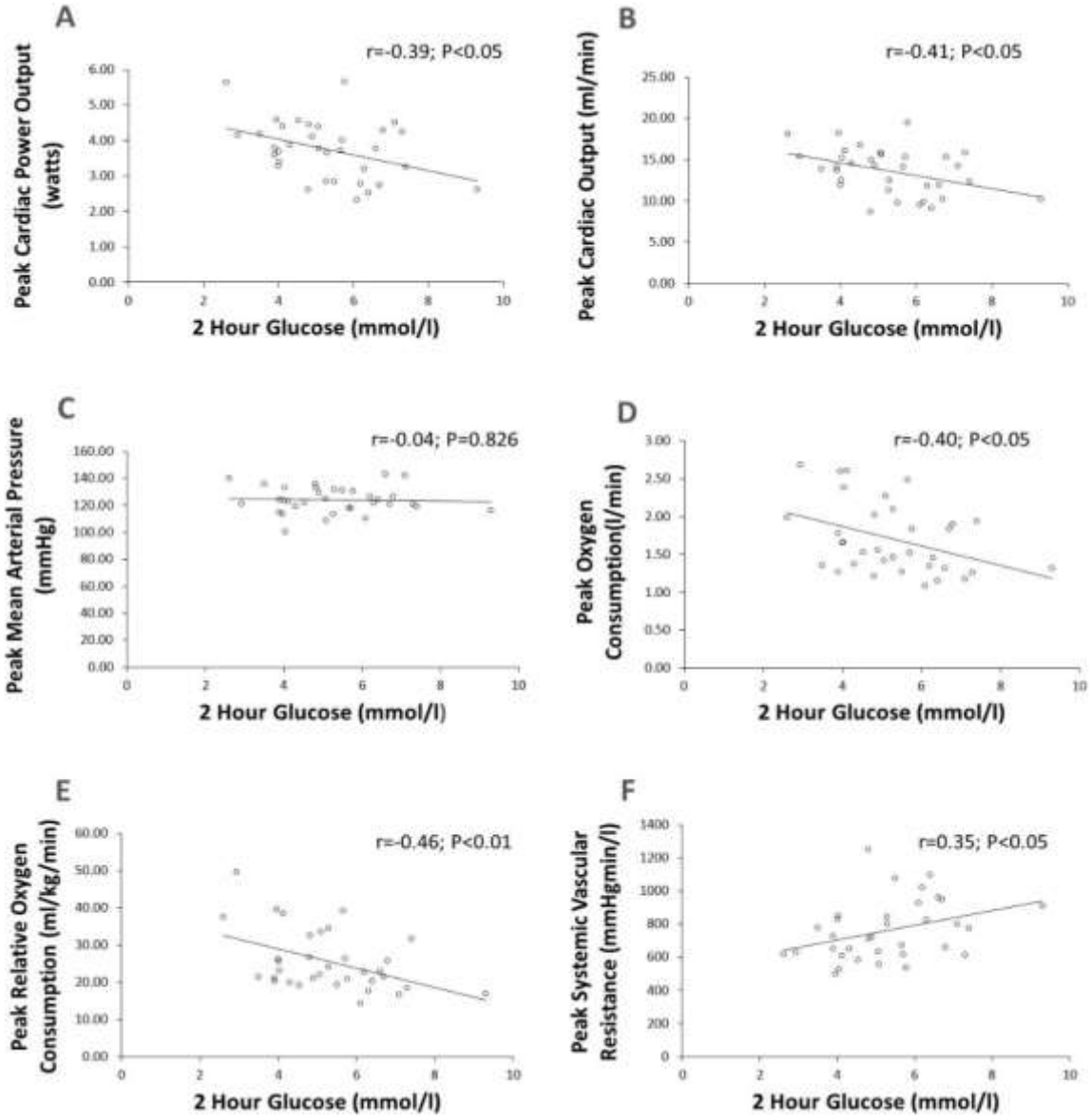

Figure 2. The Relationship Between Metabolic Control and Cardiac Function in Different Age Categories.