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The effect of age on the relationship between cardiac and vascular function

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ABSTRACT

Age-related changes in cardiac and vascular function are associated with increased risk of cardiovascular mortality and morbidity. The aim of the present study was to define the effect of age on the relationship between cardiac and vascular function. Haemodynamic and gas exchange measurements were performed at rest and peak exercise in healthy individuals. Augmentation index was measured at rest. Cardiac power output, a measure of overall cardiac function, was calculated as the product of cardiac output and mean arterial blood pressure. Augmentation index was significantly higher in older than younger participants (27.7 ± 10.1 vs. $2.5 \pm 10.1\%$, $P < 0.01$). Older people demonstrated significantly higher stroke volume and mean arterial blood pressure ($P < 0.05$), but lower heart rate (145 ± 13 vs. 172 ± 10 beats/min, $P < 0.01$) and peak oxygen consumption (22.5 ± 5.2 vs. 41.2 ± 8.4 ml/kg/min, $P < 0.01$). There was a significant negative relationship between augmentation index and peak exercise cardiac power output ($r = -0.73$, $P = 0.02$) and cardiac output ($r = -0.69$, $P = 0.03$) in older participants. Older people maintain maximal cardiac function due to increased stroke volume. Vascular function is a strong predictor of overall cardiac function in older but in not younger people.

1. Introduction

Age-associated changes in cardiac and vascular function are identified as a major risk factor for cardiovascular morbidity and mortality, with older patients having a higher risk of having cardiovascular morbidity and mortality (Westerhof and O'Rourke, 1995; Shih et al., 2011; McEniery et al., 2005; Lakatta, 2002; Franklin, 2005). The age associated changes that occur are present even in the absence of hypertension or clinically apparent cardiovascular disease (Lakatta, 2002). Age-associated cardiovascular changes are the key determinant of the decline in functional capacity in older age (Astrand, 1960; Ogawa et al., 1992). Stiffening of arteries is commonly reported and leads to an increased systolic blood pressure (Takazawa et al., 1996; Jakovljevic et al., 2010). To overcome these vascular changes and increased afterload, the heart needs to impart more energy into the vascular system by generating more pressure. This may lead to an increase in left ventricular wall thickness and mass with ageing, lowering the threshold for clinical signs and symptoms. (Lakatta, 2002). Earlier identification of cardiovascular disease (CVD) may lead to improved prognosis and quality of life in older people. Assessment of vascular function is one commonly used method recognised as an important prognostic index and a potential target for therapeutic intervention in CVD and impact upon clinical care (DeLoach and Townsend, 2008; Weber et al., 2004).

A non-invasive assessment of pulse wave reflection i.e. pulse wave analysis and calculation of augmentation index can be used to determine vascular function and provide information regarding arterial compliance. Central arterial compliance, as measured by augmentation index informs arterial stiffness calculations and overall vascular function (Patvardhan et al., 2011). Augmentation index has been identified as an independent CVD risk factor and is

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strongly correlated with atherosclerosis (Weber et al., 2004). Previous studies have demonstrated a strong relationship between central aortic and radial vascular compliance (Patvardhan et al., 2011; Munir et al., 2008), supporting the use of radial tonometry in vascular function assessment, with a number of studies confirming its reliability (McEniery et al., 2005; Pauca et al., 2001; Fantin et al., 2007; Kohara et al., 2005; Wilkinson et al., 1998; O'Rourke et al., 1999; Takazawa et al., 1996).

Currently, there is limited information on how vascular function impacts on overall cardiac function in older subjects at rest and during peak exercise. This can be demonstrated with assessment of the relationship between augmentation index as a measure of vascular function and cardiac power output, a unique index of cardiac pumping capability and overall cardiac function that integrates both the pressure and flow-generating capacities of the heart (Jakovljevic et al., 2010; Tan, 1986). Considering the strong interaction between vascular and cardiac ageing, we hypothesize that augmentation index can be used to predict maximal cardiac pumping capability which has been shown to be the strongest predictor of mortality in patients with heart failure (Williams et al., 2001). We also aim to evaluate differences in vascular function and cardiac response to exercise between young and older people.

2. Materials and methods

Thirty healthy individuals i.e. 20 young (10 women), aged between 20 and 30 years, and 10 older (6 women) aged between 60 and 71 years participated in the study. All participants performed <60 min of moderate to vigorous activity per week (defined as 3–6 and >6 metabolic equivalent of task, MET), respectively, as defined by the Centers for Disease Control (CDC) and Prevention and the American College of Sports Medicine (ACSM), were non-smokers, normotensive, free from any cardiac and respiratory disorders and no medication 3 months prior to study commencement, as determined during screening and consent. All procedures were according to Declaration of Helsinki and the study was approved by the local research ethics committee. All participants gave their written informed consent. Subjects were instructed to abstain from eating for a >2 h before each test and from vigorous exercise 24 h prior. Subjects were also instructed not to consume alcohol or caffeine containing foods and beverages on test days. All tests were conducting between 9 and 10 am to ensure assessments were consistent and minimise effects of day to day activities. Upon arrival at the laboratory participants were asked to lay in a supine position for 10 min. Blood pressure was measured in duplicate in the brachial-artery of participant's non dominant arm. Mean arterial pressure was calculated as the diastolic pressure plus one third of the pulse pressure.

2.1. Augmentation index measurement

Pulse wave analysis was used to assess vascular function by measuring augmentation index using the SphygmoCor (AtCor Medical, NSW, Australia) under resting condition. As per the manufactures instructions a high fidelity micro-manometer was used to apply pressure and therefore flatten the radial artery in the non-dominant hand at the wrist. The probe was then placed over the vessel at the point where a strong arterial pulse can be ascertained. The probe was pressed down against the artery, ensuring that the artery was not occluded and a signal was produced on the portable computer. Data was collected for a minimum of 20 sequential waveforms into a portable computer with amplitude in excess of 500 mV with accuracy for waveforms of over 85% to ensure validity of measurements. The data were then analysed using the integral software to generate the mean peripheral and corresponding waveform. Augmentation index was then calculated automatically using the SphygmoCor software. Augmentation index was calculated as the difference between the first systolic peak and the second systolic peak of the central arterial waveform, which was expressed as a percentage of pulse pressure.

2.2. Progressive exercise test and cardiac output measurement

Following assessment of arterial stiffness all participants performed maximal graded cardiopulmonary exercise test on an electro-magnetically braked semi-recumbent cycle ergometer (Corival, Lode, Groningen, Netherlands) with simultaneous measurements of respiratory and gas exchange (Cortex metalyser 3B, Leipzig, Germany) and non-invasive cardiac output data using bioreactance method (NICOM®, Cheetah Medical, Deleware, USA), previously detailed (Jakovljevic et al., 2012, 2015; Jones et al., 2015). Briefly, bioreactance estimates cardiac output from analysis of the frequency of relative phase shifts of electrical current applied across the thorax using four dual-surface electrodes. Signals were applied to and recorded from the left and right sides of the thorax; these signals are processed separately and averaged after digital processing. The signal processing unit of the system determines the relative phase shift between the input signal relative to the output signal. The phase shift occurs due to instantaneous changes in blood flow in the aorta. Cardiac output is subsequently estimated as the product of stroke volume and heart rate.

Once participants were connected to the measurement units, 5 min of resting data were recorded. Participants than continued to cycle using graded exercise stress test protocol until volitional exhaustion was reached or were not able to maintain a cadence of 60–70 revolutions per minute. Blood pressure was determined automatically at rest, during and at peak exercise using an automated blood pressure system (SunTech Tango, SunTech Medical, Inc., Morrisville, USA). The graded exercise test was considered maximal if participants achieved any two of the following criteria: no change in oxygen consumption despite further increase in workload, (i) a respiratory exchange ratio of 1.15 or greater, or (ii) ≥90% age predicted maximum heart rate (Winter et al., 2006). Maximal oxygen consumption and cardiac output were defined as the mean values obtained over the last minute of exercise. Anaerobic threshold was automatically calculated using v-slope method (Tan, 1986). Cardiac pumping capability was represented by cardiac power output (expressed in watts) and calculated from the product of cardiac output and mean arterial pressure, as previously described (Tan, 1986; Jones et al., 2015; Goldspink et al., 2009; Fleg et al., 2005). Systemic vascular resistance to blood flow was estimated as the ratio between mean arterial pressure and cardiac output and multiplied by a factor of 80 to convert units to dynes per second per centimeter to the fifth power. Arteriovenous oxygen difference was calculated as the ratio between oxygen consumption and cardiac output.

2.3. Statistical analyses

Statistical analyses were performed using SPSS statistical analysis software (Version 19, IBM, USA). Normality of distribution was assessed using a Kolmogorov–Smirnov test. Relationship between arterial stiffness (i.e. augmentation index) and cardiac pumping capability (i.e. cardiac power output) was assessed using Pearson's product moment coefficient of correlation. Independent sample *t*-tests were used to identify differences between metabolic, gas exchange and haemodynamic data between young and older study participants. Statistical significance was indicated if $P \leq 0.05$. Data are presented as mean ± SD unless otherwise indicated.