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Vascular Health in the Ageing Athlete

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Abstract

The demographics of ageing are changing dramatically such that there will be many more older adults in the near future. This setting likely will produce a new “boomer-driven” epidemic of physiological dysfunction, disability and risk of chronic degenerative disorders, including cardiovascular diseases (CVD). Standing out against this dreary biomedical forecast are Masters athletes, a group of middle-aged and older adults who engage in regular vigorous physical training and competitive sport. Compared with their sedentary/less active (untrained) peers, Masters athletes who perform endurance training-based activities demonstrate a more favorable arterial function-structure phenotype, including lower large elastic artery stiffness, enhanced vascular endothelial function and less arterial wall hypertrophy. As such, they may represent an exemplary model of healthy or “successful” vascular ageing. In contrast, Masters athletes engaged primarily/exclusively in intensive resistance training exhibit less favorable arterial function-structure than their endurance-trained peers and, in some instances, untrained adults. These different arterial properties likely are explained in large part by the different intravascular mechanical forces generated during endurance vs. resistance exercise-related training activities. The more favorable arterial function-structure profile of Masters endurance athletes may contribute to their low risk of clinical CVD.

Keywords

arterial stiffness; endothelium

The world is ageing--the number of older adults is on the rise. This phenomenon comes with serious physiological and health implications including increases in cardiovascular dysfunction and disease (CVD). Indeed, it has been projected that without effective intervention 40% of all U.S. adults will have at least one form of CVD by 2030, with a tripling of attendant medical costs due largely to the ageing of the population (Heidenreich *et al*., 2011).

In the midst of this impending epidemic of age-associated dysfunction and disease stands a physiologically exceptional group of middle-aged and older adults referred to as “Masters athletes”. These individuals exercise vigorously for most, if not all, days of the week, often engaging in athletic competitions and demonstrating enhanced age-normalized physical function and remarkable sports performance (Tanaka & Seals, 2008). Importantly, at least for those performing aerobic exercise-related training and competitions, Masters athletes have greater cardiovascular capacity (e.g., maximal cardiac output and oxygen consumption) (Tanaka & Seals, 2008) and a lower risk of CVD (Laure & Binsinger, 2009) compared with their more sedentary peers.

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Many physiological and/or pathophysiological changes likely contribute to declines in cardiovascular function and increases in CVD risk with ageing. Among the most important are changes to the arterial system including stiffening of the large elastic arteries (aorta and carotid arteries), development of endothelial dysfunction and wall thickening (Lakatta & Levy, 2003). Here we summarize and update recent discussions (Seals *et al.*, 2008; Seals *et al.*, 2009) of evidence suggesting that these adverse vascular changes may be less manifest (or even absent) in certain subgroups of Masters athletes and, therefore, might help explain their more favorable cardiovascular capacity and health.

Large Elastic Artery Stiffness

Large elastic artery stiffness, most commonly assessed by aortic pulse wave velocity (aPWV) or the local compliance of the carotid artery (via ultrasound and tonometry), has emerged as a major independent risk factor for CVD in older adults and is linked to a greater risk of systolic hypertension, left ventricular hypertrophy and other disorders of ageing such as cognitive impairment (Lakatta & Levy, 2003; Mitchell *et al.*, 2010). As reflected by increased aPWV and decreased carotid compliance, large elastic artery stiffness increases with age even in non-hypertensive adults free of clinical CVD (Tanaka *et al.*, 1998; Lakatta & Levy, 2003).

Middle-aged and older male and female Masters endurance athletes (triathletes, cyclists, runners, swimmers) demonstrate lower aPWV (Vaitkevicius *et al.*, 1993; Tanaka *et al.*, 1998) and greater carotid artery compliance (Tanaka *et al.*, 2000; Monahan *et al.*, 2001; Moreau *et al.*, 2003; Moreau *et al.*, 2006a; Nualnim *et al.*, 2011) compared with their non-exercise-trained or sedentary (herein referred to as “untrained”) peers (Figure 1). aPWV in these Masters athletes is similar to those in trained and/or untrained young adults (Vaitkevicius *et al.*, 1993; Tanaka *et al.*, 1998), whereas carotid compliance is lower than that observed in young adult controls (Tanaka *et al.*, 2000; Moreau *et al.*, 2003). The lower large elastic artery stiffness in Masters endurance athletes compared with middle-aged/older untrained adults is associated with other cardiovascular benefits including lower 24-hour systolic and pulse pressures (Seals *et al.*, 1999) and enhanced baroreflex sensitivity (Monahan *et al.*, 2001; Nualnim *et al.*, 2011). Little is known as to the mechanisms by which these Masters athletes maintain lower large elastic artery stiffness with age, but less oxidative stress-related suppression of arterial compliance may play an important role (Moreau *et al.*, 2006a). A lower “subclinical” CVD risk factor burden in the Masters endurance athletes also could contribute, although subjects with major risk factors were excluded in the aforementioned studies.

In contrast to their peers performing endurance training/competitions, Masters athletes engaged in sports requiring intensive resistance training have greater large elastic artery stiffness than untrained adults, as indicated by lower carotid artery compliance (Miyachi *et al.*, 2003). Interestingly, Masters rowers, a group of athletes that perform both intensive resistance and endurance training, demonstrate enhanced carotid artery compliance compared with untrained controls (Cook *et al.*, 2006), suggesting that even some element of endurance training can offset the apparent negative consequences of intensive resistance training. No differences in peripheral large (femoral) artery compliance have been observed among groups of Masters athletes and untrained healthy adults (Cook *et al.*, 2006; Nualnim *et al.*, 2011), suggesting age- and training-specific influences on large elastic arteries.

Vascular Endothelial Function

Vascular endothelial function is most commonly assessed in humans by measuring endothelium-dependent dilation (EDD) using either brachial artery flow-mediated dilation (FMD) or the forearm blood flow responses to brachial artery-infused acetylcholine (Seals *et*

al., 2011). EDD is reduced with advancing age in untrained adults, even in the absence of CVD risk factors/disease (Seals *et al.*, 2011). Unlike their untrained peers, however, male Masters endurance athletes have largely or completely preserved EDD with ageing (Figure 2) (DeSouza *et al.*, 2000; Taddei *et al.*, 2000; Eskurza *et al.*, 2004; Eskurza *et al.*, 2005; Franzoni *et al.*, 2005; Black *et al.*, 2009; Pierce *et al.*, 2011a). These athletes also appear to be at least partially protected from impairments in EDD in response to acute ischemia/reperfusion injury (DeVan *et al.*, 2011).

Reduced vascular oxidative stress is a key mechanism by which EDD is preserved with age in male Masters athletes (Taddei *et al.*, 2000; Eskurza *et al.*, 2004; Franzoni *et al.*, 2005). Indeed, there is now direct evidence of reduced oxidant stress in the vascular endothelial cells of these athletes compared with untrained controls, and this is associated with reduced endothelial cell expression of the oxidant enzyme NADPH oxidase and redox-sensitive transcription factor nuclear factor κ B, as well as increases in the expression the antioxidant enzyme manganese (mitochondrial) superoxide dismutase (SOD) and activity of endothelium-bound SOD (Pierce *et al.*, 2011a). Reduced endothelial oxidative stress in these Masters athletes causes less destruction/greater bioavailability of the endothelium-dependent dilating molecule, nitric oxide (NO), resulting in a greater NO-mediated EDD (Taddei *et al.*, 2000). Greater bioavailability of the critical co-factor for NO production, tetrahydrobiopterin (BH_4), also plays an important role in the maintenance of EDD in these athletes (Eskurza *et al.*, 2005). This could be due to less oxidation of BH_4, increased endogenous BH_4 synthesis or both. Basal NO production also is preserved in male Masters endurance athletes (Seals *et al.*, 2008), perhaps also a result of reduced oxidative stress and enhanced BH_4 bioavailability.

The mechanisms for this endothelial-protective phenotype of male Masters athletes remain to be established, though it is not clearly or consistently related to differences in clinical characteristics (Seals *et al.*, 2008; Seals *et al.*, 2009; Seals *et al.*, 2011). Rather, training-induced increases in intravascular laminar shear (via increases in systemic and active limb blood flow), differences in one or more presently unidentified (protective) circulating humoral factors and/or greater resistance to a given level of potentially endothelium-damageing factors (e.g., plasma LDL cholesterol or glucose) all have been proposed (Seals *et al.*, 2008; Seals *et al.*, 2009; Seals *et al.*, 2011).

In comparison to men, far fewer data are available on vascular endothelial function in female Masters endurance athletes and all of it is based on brachial artery FMD. Initial reports on small groups of women suggested greater EDD in female Masters endurance athletes compared with untrained age-matched controls (Hagmar *et al.*, 2006; Black *et al.*, 2009). A recent study of a much larger sample found no differences brachial FMD in endurance-trained and untrained postmenopausal women, while confirming past observations in men (Pierce *et al.*, 2011b). Extensive analysis revealed no obvious physical or clinical characteristics that could explain the sex-specific differences. However, all of the women were estrogen-deficient and it is possible that a certain critical level of estrogen bioavailability is necessary for exercise-generated physiological signals to modulate vascular endothelial function in this group.

Finally, among Masters endurance athletes, it is possible that vascular endothelial function is influenced by the type of activity performed. A recent investigation found that brachial artery FMD was greater in middle-aged and older Masters runners compared with age- and sex-balanced groups of Masters endurance swimmers and untrained controls (Nualnim *et al.*, 2011). To our knowledge, no cross-sectional studies are available on vascular endothelial function in primarily/exclusively resistance-trained Masters athletes.

Arterial Wall Thickness

Carotid and femoral artery intima-media thickness (IMT) are independent predictors of CVD and increase 2- to 3-fold with adult ageing in the absence of major risk factors or clinical diseases (Lakatta & Levy, 2003; Seals *et al.*, 2008). This large artery wall thickening with age is mediated by hypertrophy of both the intimal and medial layers and likely represents one aspect of a vascular remodeling process in response to changes in intravascular mechanical forces with ageing (Seals *et al.*, 2008). Age-associated increases in IMT also may reflect the development of subclinical or clinical-grade atherosclerotic plaques, although the latter is less likely in healthy adults.

The carotid IMT of male and female Masters endurance athletes does not differ from untrained age- and sex-equivalent untrained adults, nor are the age-related differences in carotid IMT different in endurance athletes compared with untrained adults (Moreau *et al.*, 2002; Tanaka *et al.*, 2002; Moreau *et al.*, 2003). This also is the case in resistance exercise-trained Masters athletes (Miyachi *et al.*, 2003). The absence of an effect likely is explained by the fact that “central” (e.g., carotid artery) blood pressure, a key determinant of IMT among healthy adults, does not differ in Masters athletes and untrained controls.

In contrast, femoral artery IMT is smaller in male and female Masters endurance athletes compared with age- and sex-matched untrained controls, and the age-associated difference is smaller in endurance-trained athletes compared with untrained adults (Figure 3) (Dinenno *et al.*, 2001; Moreau *et al.*, 2002; Moreau *et al.*, 2006b). The smaller femoral IMT and accompanying increase in lumen diameter in Masters endurance athletes are features of “expansive arterial remodeling”, a process presumably aimed at normalizing wall stress in response to exercise-evoked increases in femoral blood flow required to meet the demands of the active muscles in the legs (Dinenno *et al.*, 2001). Rather than smaller, femoral IMT is greater in resistance-trained male Masters athletes compared with untrained age-matched controls (Miyachi *et al.*, 2005). This may be the result of the different intravascular mechanical forces generated in the systemic circulation during resistance compared with endurance training, particularly the marked increases in arterial pressure during weight lifting maneuvers.

Summary and Conclusions

Large elastic artery stiffness, vascular endothelial function and large artery wall thickness are major indicators of arterial health and risk of age-associated CVD (Lakatta & Levy, 2003). Overall, Masters endurance athletes demonstrate a more favorable arterial phenotype compared with untrained middle-aged and older adults, which may explain, at least in part, their greater cardiovascular functional capacity and lower risk of CVD. As such, the Masters endurance athlete may be viewed as a model of “exceptional vascular ageing”. In contrast, Masters athletes for whom training and competitive sport require primarily or exclusively intensive resistance muscle activities exhibit a less favorable arterial function-structure profile than their endurance-trained peers and, in some cases, compared with untrained adults. The differences in arterial properties between Masters athletes engageing in endurance vs. resistance training-requiring sports likely are explained by differences in the intravascular mechanical forces generated during these activities.

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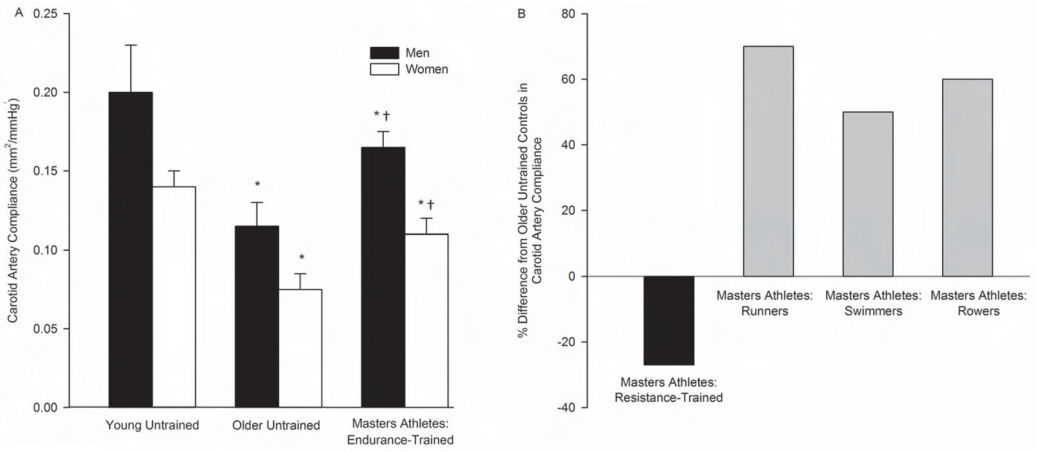

Figure 1.

A) Carotid artery compliance of young untrained adults, older untrained adults and Masters athletes (adapted from Tanaka *et al*., 2000 and Moreau *et al.*, 2003), B) percent difference in carotid artery compliance from study-specific older untrained controls in Masters athletes of different sports (data compiled from Cook *et al.*, 2006, Miyachi *et al.*, 2003 and Nualnim *et al.*, 2011). Values are means ± SEM. *P<0.05 vs. young untrained of same sex; †P<0.05 vs. older untrained of same sex.

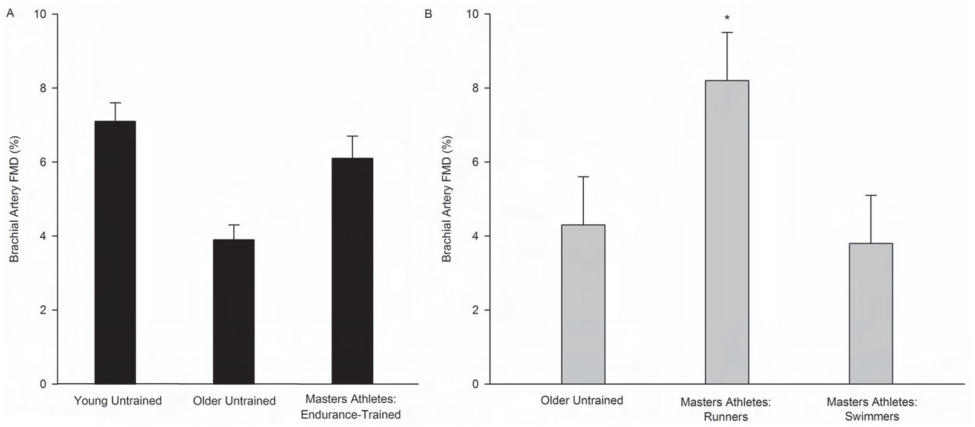

Figure 2.

Brachial artery flow-mediated dilation (FMD) of A) young untrained and older untrained men and male Masters athletes (mean data for each group compiled from Eskurza *et al*., 2004, Eskurza *et al*., 2005, Franzoni *et al.*, 2005 and Pierce *et al.*, 2011a), B) older untrained adults and Masters athletes of different sports (adapted from Nualnim *et al.*, 2011). Values are means ± SEM. *P<0.05 vs. older untrained and swimmers.

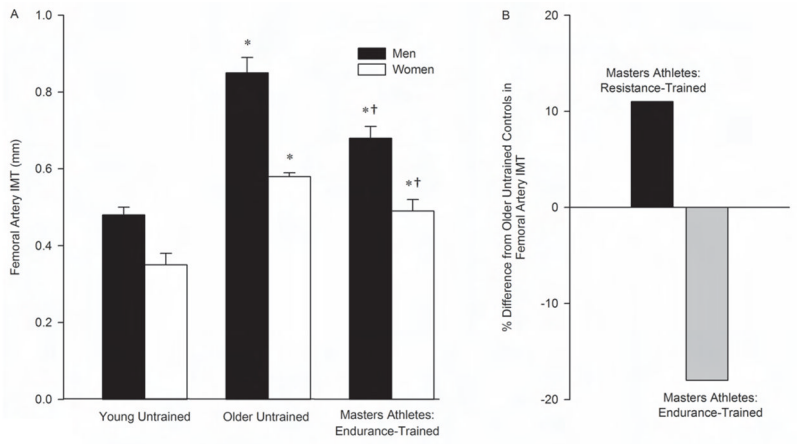

Figure 3.

A) Femoral artery intima-media thickness (IMT) of young untrained adults, older untrained adults and Masters athletes (adapted from Moreau *et al.*, 2006b), B) percent difference in femoral artery IMT from study-specific older untrained controls in resistance-trained male and endurance-trained Masters athletes (adapted from Miyachi *et al.*, 2005 and Moreau *et al.*, 2006b). Values are means ± SEM. *P<0.001 vs. young untrained of same sex; †P<0.001 vs. older untrained of same sex.