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Association between retinal vasculature and muscle mass in older people

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ABSTRACT

Sarcopenia in older people is a major health issue and its early detection could help target interventions and improve health. Evidence suggests that poor muscle mass is associated with greater arterial stiffness and cardiovascular risk. Arterial stiffness in turn is associated with smaller retinal artery width. This study examined the association of muscle mass in older people with retinal vascular width, a non-invasive measure of vascular function.

Methods: Participants >65 years were recruited to a cross-sectional study. Exclusions: Inability to walk independently; diabetes mellitus; stroke (within 6 months), severe macular degeneration, glaucoma, retinal dystrophy; advanced cataract. Digital Retinal images of both eyes were analysed using the VAMPIRE software suite. Central Retinal Artery and Vein Equivalents (CRVE and CRAE) were measured. Body composition was measured using Dual Energy X ray Absorptimetry (DXA). Appendicular Skeletal Muscle Mass/Height^2 was calculated. Physical function was measured: 6-min walk distance, Short Physical performance battery, handgrip strength and quadriceps strength.

Results: 79 participants with mean age 72 (SD 6) years were recruited. 44% were female. Digital Retinal images of sufficient quality for measuring CRAE and CRVE were available for 51/75 (68%) of participants. Regression analysis showed significant association between larger ASMM/H^2 and smaller CRAE ($\beta = -0.20$, $p = 0.001$) and CRVE ($\beta = -0.12$, $p = 0.05$). Handgrip strength, body mass index and sex combined with CRAE explained 88% and with CRVE explained 86% of the variance in ASMM/H^2.

Conclusion: Larger muscle mass was significantly associated with smaller retinal artery size in older people. This unexpected finding needs further investigation.

1. Introduction

Sarcopenia is the age-related loss of skeletal muscle mass and physical function. Sarcopenia is common (estimated to affect 20% of over 60s and >50% of over 80s) and is a major cause of frailty, falls, disability and death. The direct healthcare costs of sarcopenia are enormous, estimated at $18.5 billion per year in 2000 in the United States (Janssen, Shepard, Katzmarzyk, & Roubenoff, 2004). Interventions for sarcopenia are limited and available only for people who already have developed function-limiting sarcopenia. Early detection of sarcopenia and people at risk of sarcopenia would have a major impact on management of the condition.

Emerging evidence suggests a link between cardiovascular disease and muscle mass and physical function (sarcopenia) in old age (Atkins et al., 2014). Arterial stiffness is an established cardiovascular risk factor (Kollias, Stergiou, Dolan, & O'Brien, 2012). Arterial stiffness increases with age (Mitchell et al., 2004) and higher arterial stiffness with age has been demonstrated even in the retinal microcirculation (Kotliar, Baumann, Vilser, & Lanzl, 2010). Arterial stiffness is associated with low muscle mass (Ochi et al., 2010; Abbatecola et al., 2011; Sampaio et al., 2014) and poor leg function in older people, both in those with and without peripheral arterial disease (Watson et al., 2011).

Retinal microvascular changes have been associated, among others, with increased risk of cardiovascular mortality, lacunar

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stroke and diabetes (Liew et al., 2010; Cheung, Sharrett et al., 2007; Cheung, Wang et al., 2007; Doubal et al., 2010). The mechanisms linking microcirculatory changes to macrocirculatory changes are not known but evidence shows that retinal microvascular changes can reflect increases in arterial stiffness independent of measured blood pressure and vascular risk factors (Katsi et al., 2011; Cheung, Sharrett et al., 2007; Cheung, Wang et al., 2007). It is therefore plausible that retinal microvasculature changes could be associated with sarcopenia. Digital retinal imaging provides a non-invasive view of a section of the body vasculature and may therefore provide a convenient method of assessing sarcopenia risk. Our study aimed to examine whether measuring retinal arterial and venular diameters could predict sarcopenia risk.

2. Methods & materials

Participants aged 65 years or over were recruited through the Scottish Primary Care Research Network in a cross-sectional study. Ethical approval was obtained from the East of Scotland Research Ethics Committee.

2.1. Exclusions

Inability to walk independently; past medical history of diabetes mellitus; stroke (within 6 months), severe age related macular degeneration, glaucoma, retinal dystrophy (high rate of retinal changes); advanced cataract (poor retinal images).

2.2. Outcome measurements

Digital retinal images were taken of both eyes by a retinal screening technician. Two field retinal photographs were taken using a digital camera (TOPCON) after dilation of the pupils with 1% tropicamide eye drops. Measurements of retinal vessels were taken with the semi-automatic Vessel Assessment and Measurement Platform for Images of the REtina (VAMPIRE) software suite (Lupascu, Tegolo, & Trucco, 2013; Giachetti, Ballerini, Trucco, & Wilson, 2013; Macgillivray et al., 2012). The assessors were masked to the body composition and physical function measures. Images with insufficient quality to compute reliable central retinal artery equivalent (CRAE)/central retinal vein equivalent (CRVE) estimates were excluded. Following the literature, we used optic disc (OD) centered images for analysis (Wong et al., 2004). The software first located the OD using a validated algorithm (Giachetti et al., 2013) and allowed for manual correction. A reference frame delineating the standard zones A, B and C, i.e., circular sectors (annuli) concentric with the OD, delimited by circles of radii 0.5 and 1 OD diameters (A), 1 and 1.5 (B), 1.5 and 2 (C) was then established. Vessels were manually identified as arteries or veins. CRAE and CRVE were calculated according to the Parr and Hubbard's formula (Knudtson et al., 2003) and allied protocol. Whenever possible, 6 points each on main arteries and veins in Zone B were selected and vessel widths measured using a validated algorithm (Lupascu et al., 2013). The width of a vessel was estimated by taking 7 measures every 3 pixels, and the mean and standard deviation were calculated. Width estimates with high standard deviation (those in the extreme 10 percentiles) were discarded as unreliable. The correlation between right and left eyes was 0.612 for CRAE and 0.631 for CRVE, in line with results reported elsewhere (Patton et al., 2007).

DXA scan for body composition using a Hologic scanner (Discovery W). Body composition was measured using standard procedures by a single technician masked to the retinal and physical function measures. Appendicular muscle mass index was calculated as the sum of muscle mass of both arms and both legs/height^2 (ASMM/H^2) expressed in kg/m^2.

Physical function was measured using the following tests: 6 min walk distance (6MWD), a submaximal test of exercise capacity, which measures the distance walked in 6 min in a standard course. This is a safe, reliable and repeatable measure of functional status in older people (Enright et al., 2003). Handgrip strength using the Takei hand dynamometer was measured in the dominant arm. Quadriceps strength was measured using the Lafayette hand held dynamometer (Lafayette, Ind., USA). Hand held devices have good correlation with the gold standard Biodex dynamometry in older people(Martin et al., 2006). Short physical performance battery

Table 1
Demographic data of those who had measurable digital retinal images vs. those without measurable images. Univariate associations with muscle mass (ASMM/H^2).

	Measurable retinal images $n=51$	Unmeasurable retinal images $n=28$	p value	Univariate associations with ASMM/H^2 ($n=51$)
Age (yrs)	71.7 (5.5)	73.6 (5.7)	0.15	r = 0.06, $p=0.70$
Male (number%)	29 (56.9%)	15 (53.6%)		r = 0.82, $p<0.001$
Number of medications (median IQR)	4 (1-7)	4 (2.3–6.7)	0.76 (Mann whitney U)	r = 0.11, $p=0.45$
Systolic BP (mean	145.6 (26.6)	149.9 (16.6)	0.38	r = −0.21, $p=0.15$
Diastolic BP	76.0 (14.5)	80.6 (9.3)	0.09	r = −0.28, $p=0.04$
Scottish index of multiple deprivation	4.76 (2.57)	4.1 (2.6)	0.31	r = 0.04, $p=0.76$
6 min walk distance	428.2 (95.8)	421.8 (89.7)	0.77	r = −0.03, $p=0.82$
Quadriceps strength	15.89 (6.71)	14.0 (7.8)	0.29	r = 0.47, $p<0.001$
Handgrip strength	28.73 (10.06)	26.9 (8.0)	0.39	r = 0.75, $p<0.001$
SPPB	10.75 (1.62)	10.6 (2.1)	0.70	r = 0.04, $p=0.79$
BMI	27.3 (4.2)	28.3 (4.4)	0.33	r = 0.63, $p<0.001$
ASMM/H^2 kg/m^2	6.83 (1.23)	6.97 (1.11)	0.61	–
CRAE	27.75 (1.34)	–		r = −0.33, $p=0.02$
CRVE	39.98 (2.66)	–		r = −0.23, $p=0.10$
AVR	0.70 (0.03)	–		
Cardiovascular disease	17 (33.3%)	14 (50%)	0.18	r = 0.19, $p=0.18$
COPD	4 (0.1%)	2 (0.1%)	1.00	r = −0.07, $p=0.63$
Osteoarthritis	20 (39.2%)	12 (42.9%)	0.84	r = 0.07, $p=0.63$
Cardiovascular medications	24 (47.1%)	10 (35.7%)	0.32	r = 0.38, $p=0.005$
Poor muscle mass (number%)	18 (35.3%)	9 (32.1%)	0.81	–
EWGSOP sarcopenia (number%)	8 (15.7%)	5 (17.9%)	0.99	–

Values are mean (SD) except where specified
Key: IQR (inter quartile range); BP (blood pressure); SPPB (short physical performance battery); BMI (body mass index); ASMM/H^2 (appendicular skeletal muscle mass/height^2); CRAE (central retinal artery equivalent); CRVE (central retinal vein equivalent); AVR (arteriovenous ratio); ACE (angiotensin converting enzyme).