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### 5.3: HIGH FIT OLDER ADULTS MAINTAIN A SIMILAR ENDOTHELIAL RESPONSE TO ACUTE INFLAMMATION AS YOUNGER ADULTS

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## 5.2 REDUCED SUBLINGUAL ENDOTHELIAL GLYCOCALYX IN TYPE 1 DIABETICS WITH DIABETIC NEPHROPATHY

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**Background:** Glycocalyx is a glycoprotein layer protecting the capillary endothelium. An impaired glycocalyx may precede the development of microvascular complications in diabetes. Capillaroscopy is a new method to estimate the dimensions of the glycocalyx by measuring the perfused boundary region (PBR). We evaluated the glycocalyx thickness in type 1 diabetic patients with different levels of historical and current albuminuria.

**Methods:** Cross-sectional study including 77 type 1 diabetics stratified by history of normoalbuminuria (<30 mg/g; n = 26), microalbuminuria (30–299 mg/g; n = 27) and macroalbuminuria (>300 mg/g; n = 24).

Glycocalyx thickness was assessed by 5 measurements with the GlycoCheck<sup>®</sup> device, a non-invasive hand-held microscope generating video recordings of the sublingual capillaries. Endothelial glycocalyx thickness was estimated from the PBR in capillaries with a diameter range of 5–25  $\mu$ m. Higher PBR indicates smaller glycocalyx width. Urinary albumin-to-creatinine ratio (UACR) was measured in 3 morning samples.

**Results:** In normo-, micro-, and macroalbuminurics PBR was (mean  $\pm$  SD) 2.30  $\pm$  0.22  $\mu$ m, 2.32  $\pm$  0.25  $\mu$ m, and 2.49  $\pm$  0.35  $\mu$ m, respectively. Differences between normo- and macroalbuminurics and micro- and macroalbuminurics were significant (p < 0.05) in an unadjusted model and remained significant after adjustment for age, sex, HbA<sub>1c</sub>, diabetes duration and systolic blood pressure. In pooled (n = 77) multivariate linear regression, higher level of current UACR was associated with a higher PBR (p = 0.0007).

**Conclusion:** In type 1 diabetics with a history of macroalbuminuria, measurements with the non-invasive GlycoCheck<sup>®</sup> device revealed significantly higher PBR, suggesting an impaired glycocalyx, compared to patients with normo- or microalbuminuria.

Moreover, higher current level of albuminuria was associated with higher PBR.

## 5.3 HIGH FIT OLDER ADULTS MAINTAIN A SIMILAR ENDOTHELIAL RESPONSE TO ACUTE INFLAMMATION AS YOUNGER ADULTS

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Inflammation is associated with an increased risk of cardiovascular events and reduced endothelial function. Higher cardiorespiratory fitness is associated with lower risk of cardiovascular events and improved vascular function. Whether fitness plays a role during acute inflammation is unknown.

**Purpose:** Evaluate the role of fitness in the endothelial response to acute inflammation in younger (YA) and older (OA) adults.

**Methods:** Acute inflammation was induced using influenza vaccine in 23 YA (12 male, 26  $\pm$  4 yrs, 24.0  $\pm$  3.5 kg/m<sup>2</sup>) and 60 OA (20 male, 65  $\pm$  5 yrs, 27.8  $\pm$  5.0 kg/m<sup>2</sup>). Blood pressure, flow-mediated dilation (FMD) and inflammatory markers were measured before and 24-hours post-vaccination. VO<sub>2</sub>peak was measured via a treadmill test. A VO<sub>2</sub>peak greater than age- and sex-associated 50th percentile according to the American College of Sports Medicine was defined as Fit.

**Results:** Fit OA reduced FMD more than low fit OA (p = 0.02) 24 h post-vaccination. High and low fit YA similarly decreased FMD at 24 h (p = 0.66). YA and high fit OA had a similar reduction (relative %) in FMD (p < 0.05). Regression analyses indicated no association between VO<sub>2</sub>peak

and change in FMD ( $\beta$  = -0.01, p = 0.98) in YA, but a significant association existed in OA ( $\beta$  = -0.36, p = 0.04) after adjusting for age, sex, BMI and baseline FMD.

	YA-high fit	YA-low fit	OA-high fit	OA-low fit
n	14	9	16	43
VO <sub>2</sub> Max, ml/kg/min	48.4 (5.6)*	35.6 (4.9)	32.3 (4.2)*	21.9 (4.3)
Baseline SBP	113 (13)	115 (13)	125 (14)	125 (14)
Baseline PP	47 (8)	47 (11)	54 (10)	53 (11)
Baseline FMD, %	12.4 (2.7)	11.6 (5.5)	7.5 (3.9)*	5.4 (2.5)
Baseline CRP, mg/l	1.1 (0.7)	0.6 (0.6)	2.4 (3.3)	2.5 (2.2)
Baseline IL-6, pg/ml	1.0 (0.7)	0.8 (0.5)	1.7 (1.4)	1.6 (1.4)
Change SBP, mmHg	-3 (6)	2 (8)	-2 (9)	-2 (11)
Change PP, mmHg	2 (6)	5 (7)	0 (7)	0 (8)
Change FMD, %	-3.2 (4.1)	-2.3 (5.5)	-3.7 (3.8)*	-0.2 (3.5)
Change CRP, mg/l	1.0 (1.5)	0.9 (0.8)	1.1 (2.2)	0.9 (1.4)
Change IL, pg/ml	1.0 (1.5)	1.6 (2.3)	0.8 (2.6)	0.4 (1.0)

FMD: flow mediated dilation, CRP: C-reactive protein, IL-6: interleukin-6, SBP: systolic blood pressure, PP: pulse pressure

\*P < 0.05 vs. low-fit of same age category

**Conclusion:** In OA, higher fitness is associated with a greater decrease in endothelial function during acute inflammation; high fit OA had a similar endothelial response compared to YA. This suggests intact reactivity of the vasculature to inflammatory stress in high fit OA, which may indicate a healthier vessel versus low fit OA.

## 5.4 EFFECT OF ACUTE RESISTANCE EXERCISE ON ARTERIAL HEMODYNAMICS AND CEREBRAL BLOOD FLOW DYNAMICS: DOES SEX MATTER?

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High-intensity resistance exercise (RE) acutely increases arterial stiffness and blood pressure (BP), coupled with reduced cerebral blood flow velocity (CBFv) and greater flow pulsatility in the cerebral circulation, which may be detrimental to cerebral microvasculature. Because females have different CV control mechanisms, it is important to assess potential sex differences in cerebrovascular responses to acute RE.

**Purpose:** To examine the effect of sex on hemodynamics and cerebral vasculature following acute RE.

**Methods:** Men (n = 18, 27 yrs, BMI = 24.2) and women (n = 14, 25 yrs, BMI = 23.8) performed RE (3  $\times$  10, isokinetic knee flexion/extension). Measurements were obtained at baseline and post-exercise (1, 5, 30-minute). Beat-to-beat heart rate (HR), brachial BP, cardiac output (CO), stroke volume and end-tidal CO<sub>2</sub> were collected. CBFv was measured by transcranial Doppler, carotid BP by applanation tonometry and central pulse wave velocity (PWV) by an automated ambulatory BP monitor.

**Results:** Table 1. CBFv pulsatility increased following RE at 1-minute post (p < 0.05) in men and was elevated above baseline 5-minute post-exercise (p < 0.05) in both groups (Figure 1). Mean CBFv increased 1-min post-exercise and decreased below baseline 5-minute post-exercise (p < 0.05) in both sexes. PWV increased 1-minute post-exercise (p < 0.05) in both groups.