Aortic stiffness is associated with less microvascular glycocalyx thickness and lower microvascular perfusion among older adults: role of carotid pressure pulsatility

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Abstract

Introduction: The glycocalyx layer is essential to the maintenance of a healthy microvascular endothelium and diminishes with advancing age. Similarly, the aorta stiffens with aging and increases the risk of cardiovascular disease and target organ damage, possibly through pressure pulsatility-associated microvascular damage. However, the relation between aortic stiffness and the microvascular endothelial glycocalyx in older adults is unknown.

Methods: Sublingual microvessels were assessed using intravital microscopy in older adults (n=24; age 61 ± 6y, 46% women). Perfused boundary region (PBR) and red blood cell (RBC) filling, indices of glycocalyx thickness (larger PBR=smaller thickness) and microvascular perfusion respectively, were determined in vessels between 5-25 µm RBC column width. Aortic stiffness was quantified by carotid-femoral pulse wave velocity (cfPWV) and carotid pulsatility as carotid pulse pressure(PP)/mean arterial pressure(MAP).

Results: Adjusting for age, sex and MAP, cfPWV was independently associated with larger PBR 5-25 (β: 0.08; p=0.001) and lower RBC filling (β: -0.02, p=0.002). Higher carotid pressure pulsatility was associated with lower RBC filling (β: -0.12; p=0.03), which was abolished after adjusting for sex (p=0.11). Upon stratification by sex, higher carotid pulsatility was associated with larger PBR 5-25 (r=0.657, P=0.03) and lower RBC filling (r=-0.729, P=0.01) in females, but not males (P>0.05).

Conclusion: Higher aortic stiffness is associated with less microvascular glycocalyx thickness and lower microvascular perfusion among older adults. Additionally, carotid pressure pulsatility is selectively associated with less glycocalyx thickness and microvascular perfusion in women only. The mechanisms that contribute to sex differences in glycocalyx structure/function in older adults require further study.

Introduction

- Aortic elasticity and endothelial glycocalyx thickness, measures of macrovascular and microvascular function respectively, decline with age (1,4).
- Additionally, aortic stiffening increases pressure and flow pulsatility, causing target organ damage (2).
- However, the relation between aortic stiffness and glycocalyx thickness in older adults in unknown.
- **Hypothesis**: Increased aortic stiffness is associated with less glycocalyx thickness and microvascular perfusion in older adults.

Methods

Subject recruitment and study design:

- Twenty-four healthy older adults (61 ± 6 yrs) free of cardiovascular and metabolic disease were recruited from Iowa City community.
- Subjects were instructed to fast overnight and withhold anti-hypertensive medication and caffeine the morning of vascular measurements and abstain from exercise 24h prior.

Methods (cont.)

Measurement of glycocalyx thickness and microvascular perfusion:

- Glycocalyx thickness and microvascular perfusion were determined non-invasively by Sideview Dark Field imaging of the sublingual microvessels 5-25µm in length (Glycocheck, MicroVascular Health Solutions LLC, Alpine, UT.). Three trials were performed, and values from each trial were averaged. RBC filling was calculated as the percentage of vascular segments with RBC present during all frames (3) and PBR was determined as follows (3): PBR 5-25 = (max RBC flow width – median RBC flow width) ÷ 2.

- ***Measurement of cfPWV wave velocity and carotid pulsatility:***
  - Pulse wave velocity was performed using noninvasive applanation tonometry to determine aortic stiffness (NIHem workstation; Cardiovascular Engineering, Inc., Norwood, MA).
  - A tonometer was used to sequentially collect pressure waveforms from the femoral and carotid artery. The pressure waveform was gated to the R-wave of the ECG to determine the foot-to-foot time delay between the carotid and femoral waveforms.
  - Carotid pressure pulsatility was determined as: $\frac{\text{Carotid PP}}{\text{Carotid MAP}}$

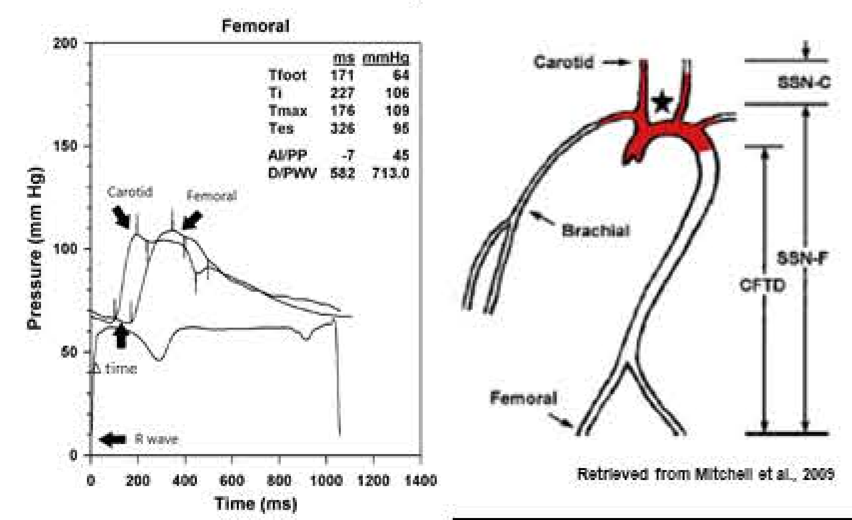

Figure 1 (above). Calculation of cfPWV: A) Example of carotid and femoral pressure waveforms. B) cfPWV distance was determined as: (SSN-F - SSN-C)/Δ time.

Results

Table 1: Subject Characteristics			
Variable	Female (n=11)	Male (n=13)	P value
Age, yrs	63 ± 5	60 ± 6	0.27
BMI, kg/m^2	25.2 ± 4.9	28.3 ± 4.6	0.13
SBP, mmHg	123 ± 16	115 ± 17	0.30
DBP, mmHg	71 ± 9	72 ± 9	0.74
MAP, mmHg	89 ± 11	87 ± 11	0.73
Carotid-femoral PWV, m/s	8.4 ± 1.7	7.2 ± 1.3	0.06
Carotid Pressure Pulsatility	0.57 ± 0.13	0.49 ± 0.13	0.15
RBC column width, µm	8.69 ± 0.84	8.78 ± 0.66	0.79
Perfused diameter, µm	12.72 ± 0.84	12.43 ± 0.61	0.36
PBR 5-25, µm	2.01 ± 0.12	1.83 ± 0.17	**<0.01**
RBC filling %	0.74 ± 0.03	0.77 ± 0.03	**<0.01**

Table 1: Data are mean ± standard deviation. An unpaired t-test was used to test difference in subject characteristics by sex in older adults (n = 24). BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; RBC, red blood cell; PBR, perfused boundary region; P value < 0.05.

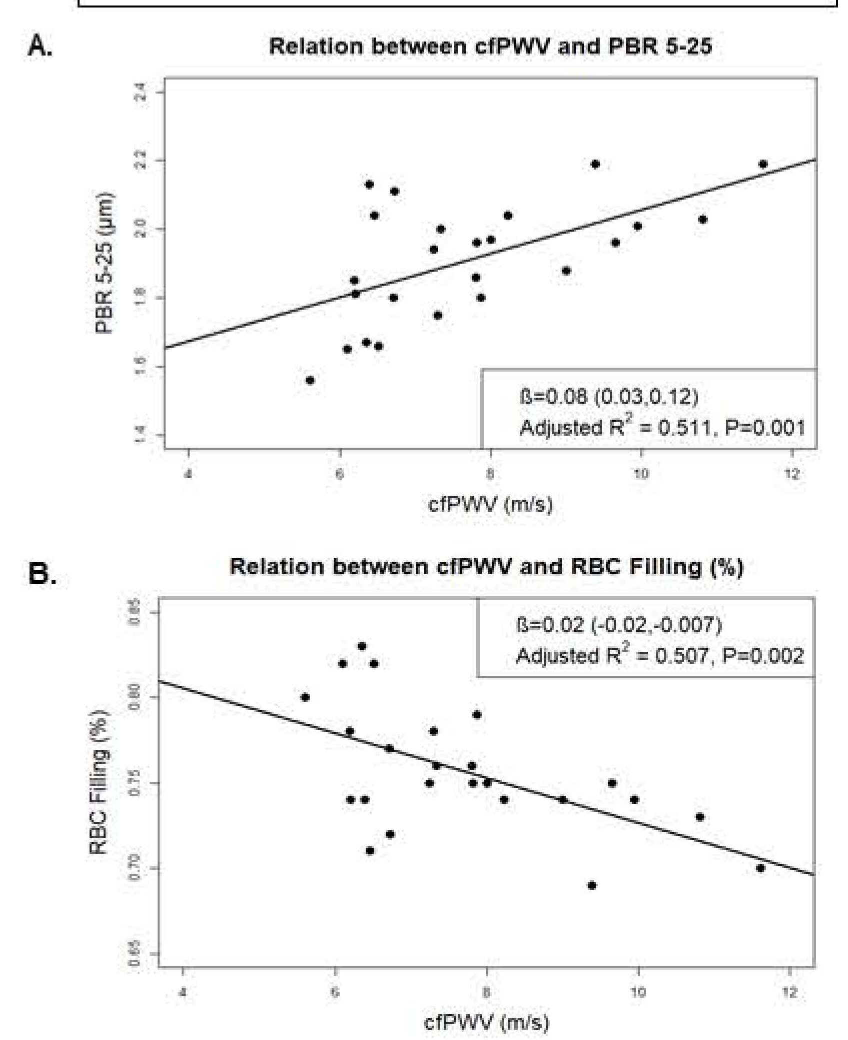

Figure 2A-B (above): Regression analysis between A) cfPWV and PBR 5-25 and B) cfPWV and RBC filling % in older adults (n=24). Multiple regression was used to adjust for age, sex and MAP.

Results (cont.)

Table 2. Linear regression analysis of RBC filling and carotid pressure pulsatility (n=24)					
Model 1			Model 2		
Variable	β (95% CI)	Adjusted R^2	Variable	β (95% CI)	Adjusted R^2
CPP	-0.12 (-0.23,-0.01)*	0.155	CPP Age Sex	-0.10 (-0.02,0.01) 0.001 (-0.001,0.004) 0.03 (0.007,0.06)*	0.315

Table 2. Model 1 is unadjusted. Model 2 is adjusted for age, and sex. CPP = carotid pressure pulsatility. * P < 0.05.

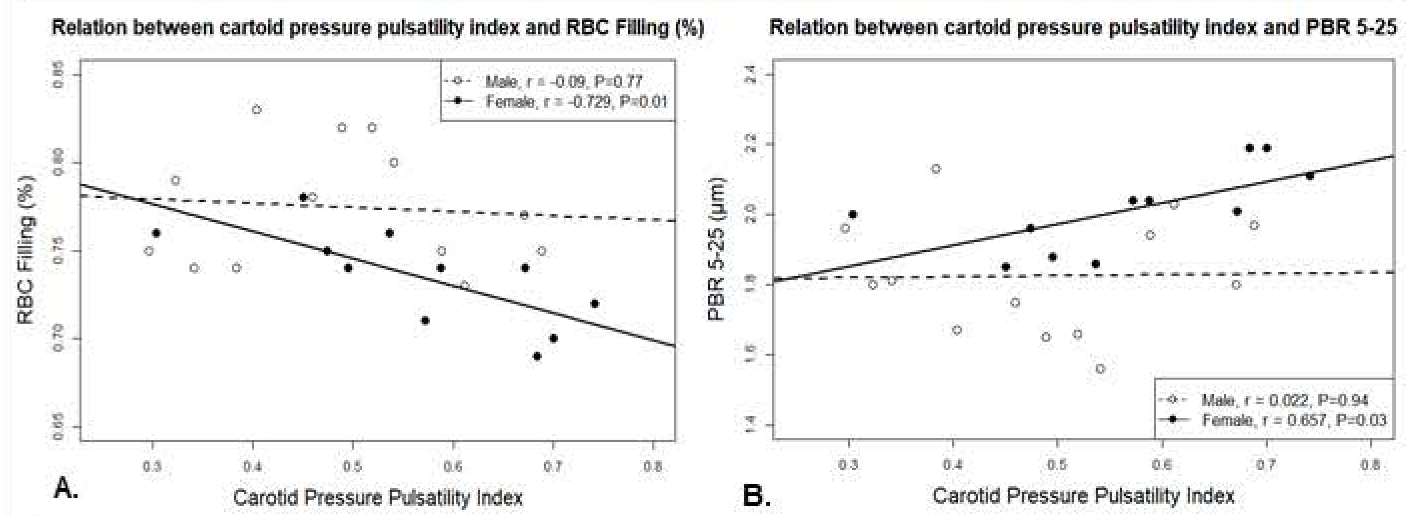

Figure 3A-B (above): Bivariate correlation between A) carotid pressure pulsatility and RBC filling % and B) carotid pressure pulsatility and PBR 5-25 in older adults (n=24).

Summary

- cfPWV is associated with increased PBR 5-25 and reduced RBC filling independent of age, sex, and mean arterial pressure.
- Higher carotid pressure pulsatility is associated with decreased RBC filling %.
- Upon stratification, higher carotid pressure pulsatility is associated with larger PBR 5-25 and lower RBC filling in females, but not males.

Conclusions

- Higher aortic stiffness is associated with decreased microvascular glycocalyx thickness and reduced microvascular perfusion in older adults
- The mechanisms that contribute to sex differences in the glycocalyx structure and function in older adults require further study

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