

Supplemental material

Cerebral Blood Flow and Cerebrovascular Resistance across the Adult Lifespan: A Multimodality Approach

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Table S1. Vascular resistance and pulsatility index measurements using color-coded duplex ultrasonography

Variables	<u>Young</u>		<u>Middle age</u>		<u>Old</u>		<u>P-value</u>		
	Men	Women	Men	Women	Men	Women	Age	Sex	Age × Sex
Vascular resistance (mmHg/mL/min)									
Left-ICA	0.37 ± 0.09	0.34 ± 0.08	0.45 ± 0.13	0.46 ± 0.16*	0.50 ± 0.12	0.50 ± 0.13*	< 0.001	0.814	0.626
Right-ICA	0.38 ± 0.10	0.32 ± 0.06	0.41 ± 0.08	0.46 ± 0.12*	0.47 ± 0.13	0.46 ± 0.13*	< 0.001	0.927	0.026
Left-VA	1.19 ± 0.48	0.98 ± 0.47	1.43 ± 1.16	1.37 ± 0.72*	1.51 ± 1.58	1.95 ± 1.84*	0.013	0.756	0.284
Right-VA	1.66 ± 1.06	1.45 ± 0.86	2.36 ± 1.96	1.86 ± 0.99*	1.79 ± 1.13	1.70 ± 1.02	0.046	0.152	0.617
Pulsatility index (a.u.)									
Left-ICA	0.86 ± 0.15	0.86 ± 0.13	0.86 ± 0.13	0.84 ± 0.14	1.07 ± 0.15	1.05 ± 0.15*†	< 0.001	0.531	0.875
Right-ICA	0.89 ± 0.12	0.85 ± 0.13	0.91 ± 0.11	0.88 ± 0.11	1.09 ± 0.17	1.05 ± 0.16*†	< 0.001	0.072	0.952
Left-VA	1.09 ± 0.19	1.06 ± 0.17	1.06 ± 0.25	1.08 ± 0.20	1.29 ± 0.27	1.31 ± 0.27*†	< 0.001	0.832	0.826
Right-VA	1.04 ± 0.21	1.21 ± 0.26	1.13 ± 0.30	1.13 ± 0.25	1.24 ± 0.26	1.27 ± 0.27*†	0.013	0.106	0.184

ICA: internal carotid artery; VA: vertebral artery. Data are mean ± standard deviation. Bold values represent $p < 0.05$. Results from one-way analysis of variance $p < 0.05$ * vs young; $p < 0.05$ † vs. middle age. $p < 0.05$ * vs young; $p < 0.05$ † vs. middle age.

Table S2. Volumetric blood flow measurements using CDUS and PC-MRI

Variables	Young		Middle age		Old		p-value		
	Men	Women	Men	Women	Men	Women	Age	Sex	Age×Sex
<i>Color-coded duplex ultrasonography (CDUS)</i>									
Volumetric blood flow (mL/min)									
Left-ICA	242 ± 48	242 ± 48	212 ± 42	207 ± 59*	191 ± 38	184 ± 39*†	<0.001	0.566	0.914
Right-ICA	241 ± 52	252 ± 42	229 ± 41	200 ± 47*	205 ± 44	201 ± 46*	<0.001	0.302	0.053
Left-VA	83 ± 31	91 ± 24	86 ± 40	78 ± 30	72 ± 29	66 ± 29†	0.007	0.633	0.330
Right-VA	68 ± 30	69 ± 31	57 ± 30	60 ± 28	65 ± 28	65 ± 30	0.165	0.757	0.977
<i>Phase contrast magnetic resonance imaging (PC-MRI)</i>									
Volumetric blood flow (mL/min)									
Left-ICA	231 ± 43	254 ± 45	205 ± 43	220 ± 48*	193 ± 44	199 ± 45*	<0.001	0.034	0.648
Right-ICA	230 ± 37	260 ± 42	206 ± 43	220 ± 47*	196 ± 45	201 ± 42*	<0.001	0.019	0.346
Left-VA	75 ± 30	99 ± 24	82 ± 44	78 ± 30	64 ± 29	62 ± 30	<0.001	0.246	0.036
Right-VA	67 ± 31	80 ± 28	55 ± 22	60 ± 33*	60 ± 29	59 ± 31*	0.010	0.211	0.434

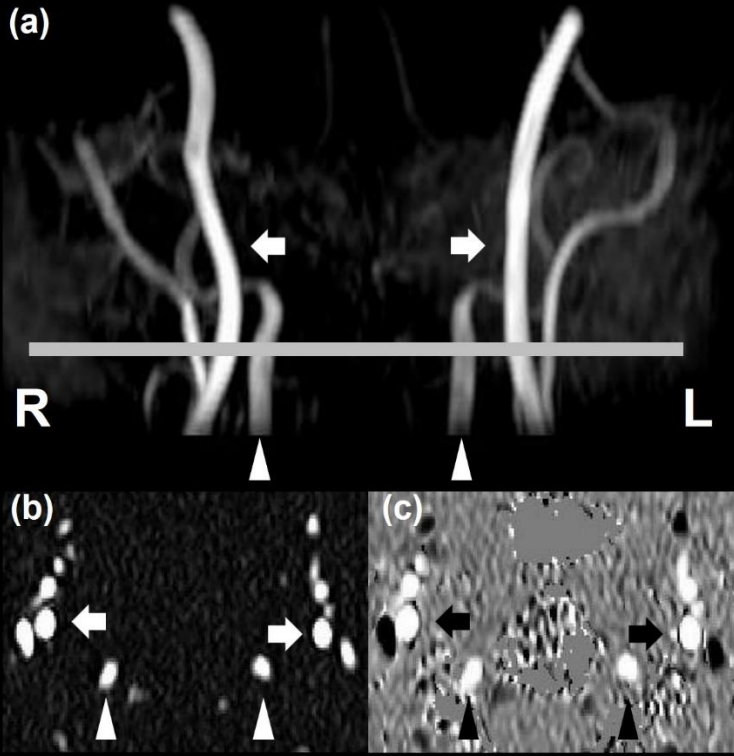
ICA: internal carotid artery; VA: vertebral artery. Data are mean ± standard deviation. Bold values represent $p < 0.05$. Results from one-way analysis of variance $p < 0.05$ * vs young; $p < 0.05$ † vs. middle age. $p < 0.05$ * vs young; $p < 0.05$ † vs. middle age.

Table S3. Mean blood flow velocity, vessel diameter, and volumetric blood flow measured using CDUS and PC-MRI

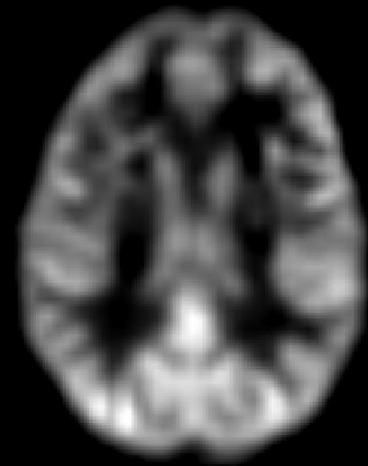
	Velocity (cm/s)				Diameter (mm)				Flow (mL/min)			
	CDUS		PC-MRI		CDUS		PC-MRI		CDUS		PC-MRI	
L-ICA	25.1	± 5.6†	21.2	± 4.6*†	4.2	± 0.5	4.7	± 0.5*†	210.2	± 51.1	216.9	± 48.6
R-ICA	26.0	± 5.8	22.1	± 4.5*	4.2	± 0.5	4.6	± 0.5*	218.1	± 48.6	218.4	± 49.2
L-VA	16.5	± 3.7†	15.3	± 2.8†	3.1	± 0.6†	3.2	± 0.6†	78.2	± 31.4†	76.3	± 33.1†
R-VA	14.7	± 3.4	14.5	± 2.7	3.0	± 0.6	2.9	± 0.6	63.6	± 28.8	63.1	± 30.2
Total									570.1	± 93.4	574.8	± 108.6

CDUS: color-coded duplex ultrasonography; PC-MRI: phase-contrast magnetic resonance imaging; ICA: internal carotid artery; VA: vertebral artery. Data are mean ± standard deviation. Results from paired t-test analysis * P < 0.05 comparisons between the methods of the same vessel. † P < 0.05 comparisons between the left and right side of the vessel using the same methods.

(A) Phase-contrast MRI

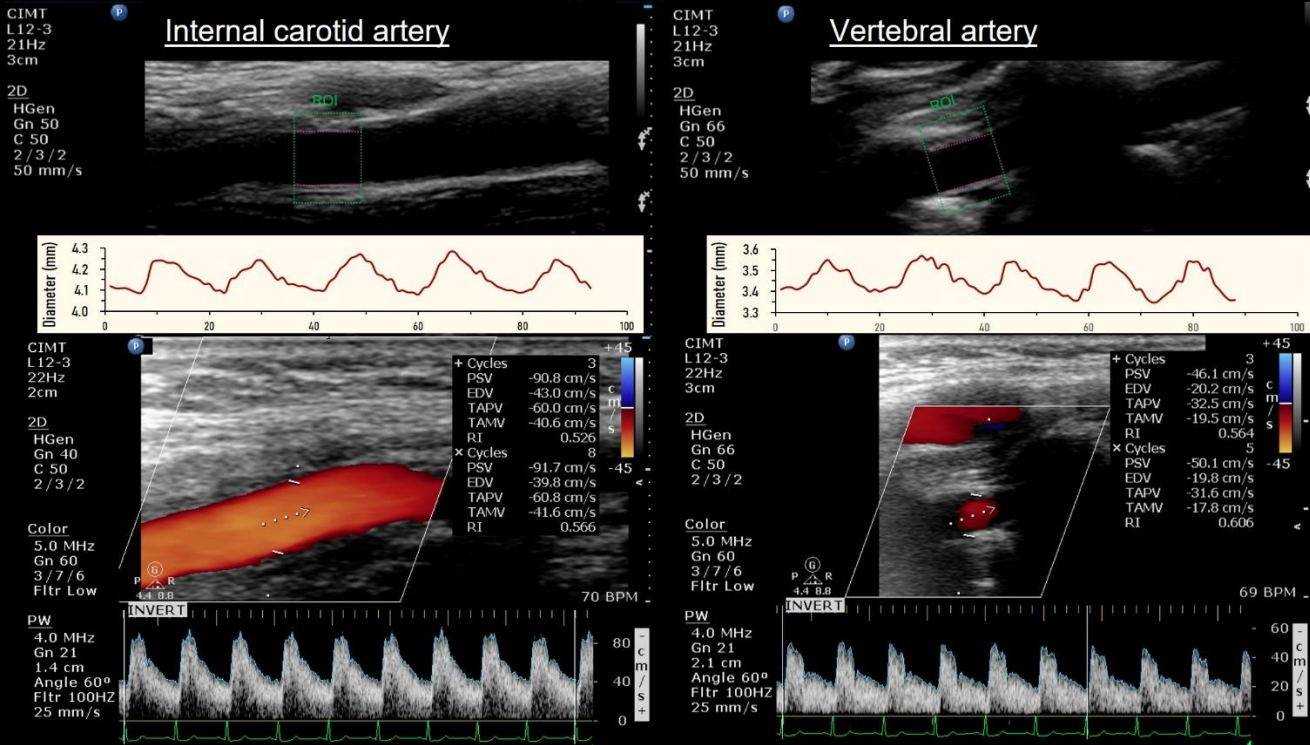


(B) Arterial spin labeling



0 30 60 90 120
Cerebral blood flow (mL/100g/min)

(C) Color-coded duplex ultrasonography



(D) Transcranial Doppler

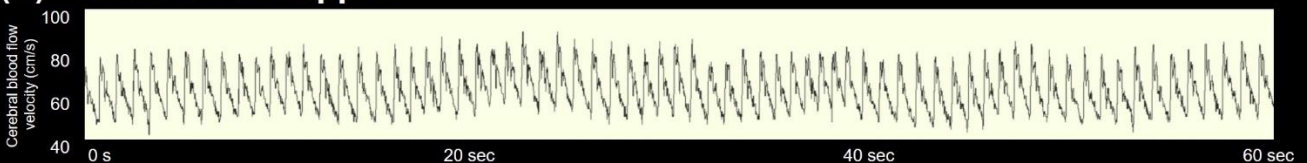


Figure S1: Representation of images of measurement and analysis of cerebral blood flow using phase-contrast MR imaging (A), arterial spin labeling (B), color-coded duplex ultrasonography (C), and transcranial Doppler (D). (A) (a) MR angiography of the right (R) and left (L) internal carotid (ICA: arrows) and vertebral arteries (VA: triangles), and (b) the magnitude and (c) phase velocity maps. The image data were obtained from one subject (30 years old, female). (B) Arterial spin labeling perfusion map from one subject (24 years old, male). (C) Ultrasonography image of measurement of blood flow in the right internal carotid (ICA: left panel) and the right vertebral arteries (VA: right panel) with color-coded duplex ultrasonogram. High-resolution B-mode image of the ICA and VA. Regions of interest, represented by the green rectangles are manually selected to cover a segment of the ICA or VA, the double pink lines are the detected vessel inner walls used to track the wall movements and to measure beat-by-beat pulsatile changes of vessel diameter for the ICA and VA. Beat-by-beat recordings of blood flow velocity at the sites of diameter measurements are presented for the ICA and VA. Image data were obtained from one subject (61 years old, female). (D) Representative illustration of middle cerebral artery blood flow velocity measured using transcranial Doppler. Image data were obtained from one subject (24 years old, male).

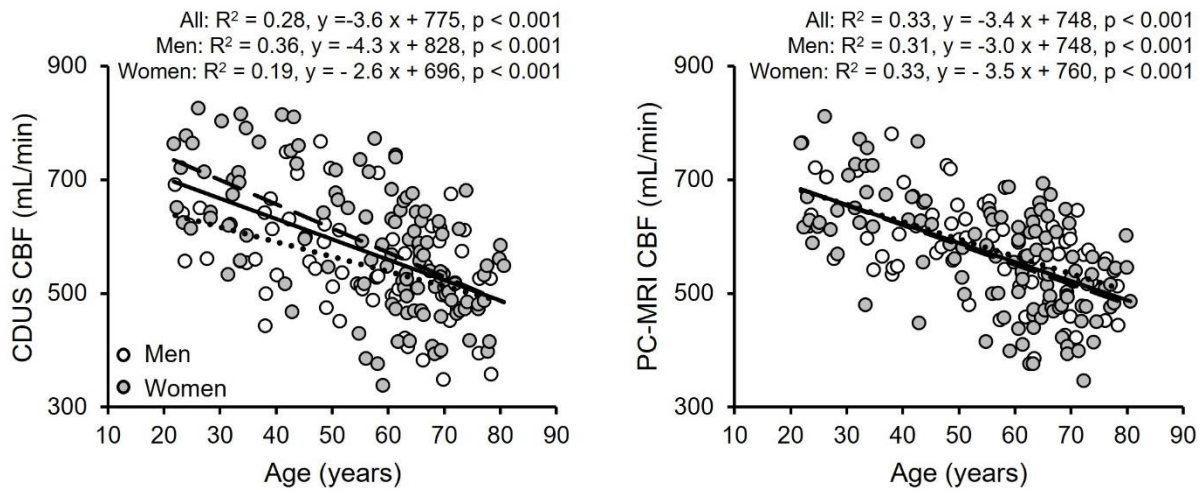


Figure S2: Association of age with total cerebral blood flow (CBF) (not normalized by the brain tissue mass) measured by color-coded duplex ultrasonography (CDUS) and phase-contrast MRI (PC-MRI). Solid line, dotted line, and dashed lines represent the regression equations obtained for all subjects, men, and women, respectively. The rates of decrease in CBF were similar between women and men (p -values of the interaction of age and sex in one-way analysis of covariance: CDUS CBF, $p = 0.565$; PC-MRI CBF, $p = 0.063$).

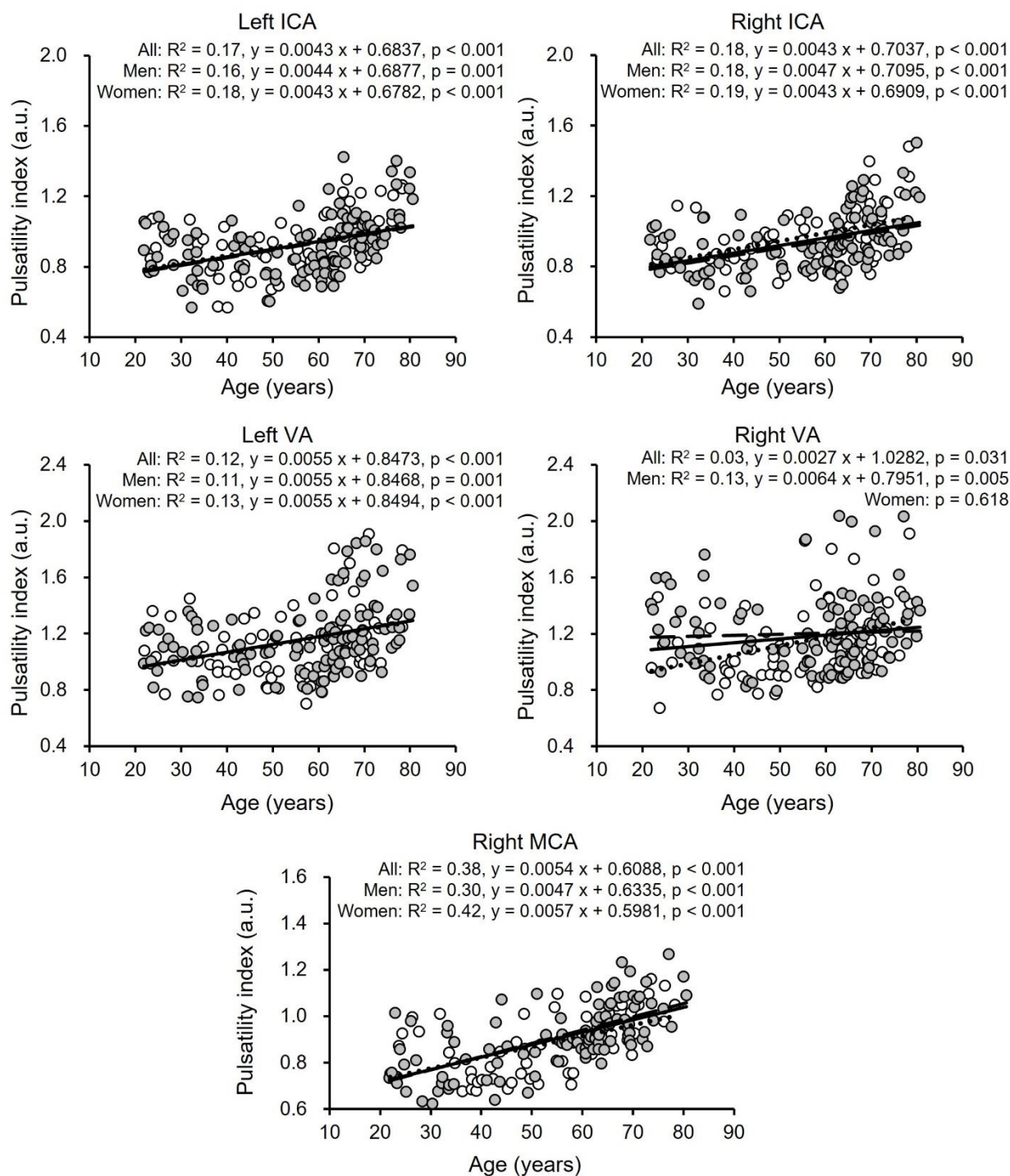


Figure S3: Association of age with pulsatility index (PI) in the left and right internal carotid (ICA) and the vertebral (VA) arteries measured by color-coded duplex ultrasonography (CDUS) and in the right middle cerebral artery (MCA) measured by transcranial Doppler. Solid line, dotted line, and dashed line represent the regression equations obtained for all subjects, men, and women, respectively. The rates of increases in PI were similar between women and men (p -values of the interaction of age and sex in one-way analysis of covariance: left ICA, $p = 0.949$; right ICA $p = 0.777$; left VA, $p = 0.970$; right VA, $p = 0.045$, right MCA, $p = 0.382$).

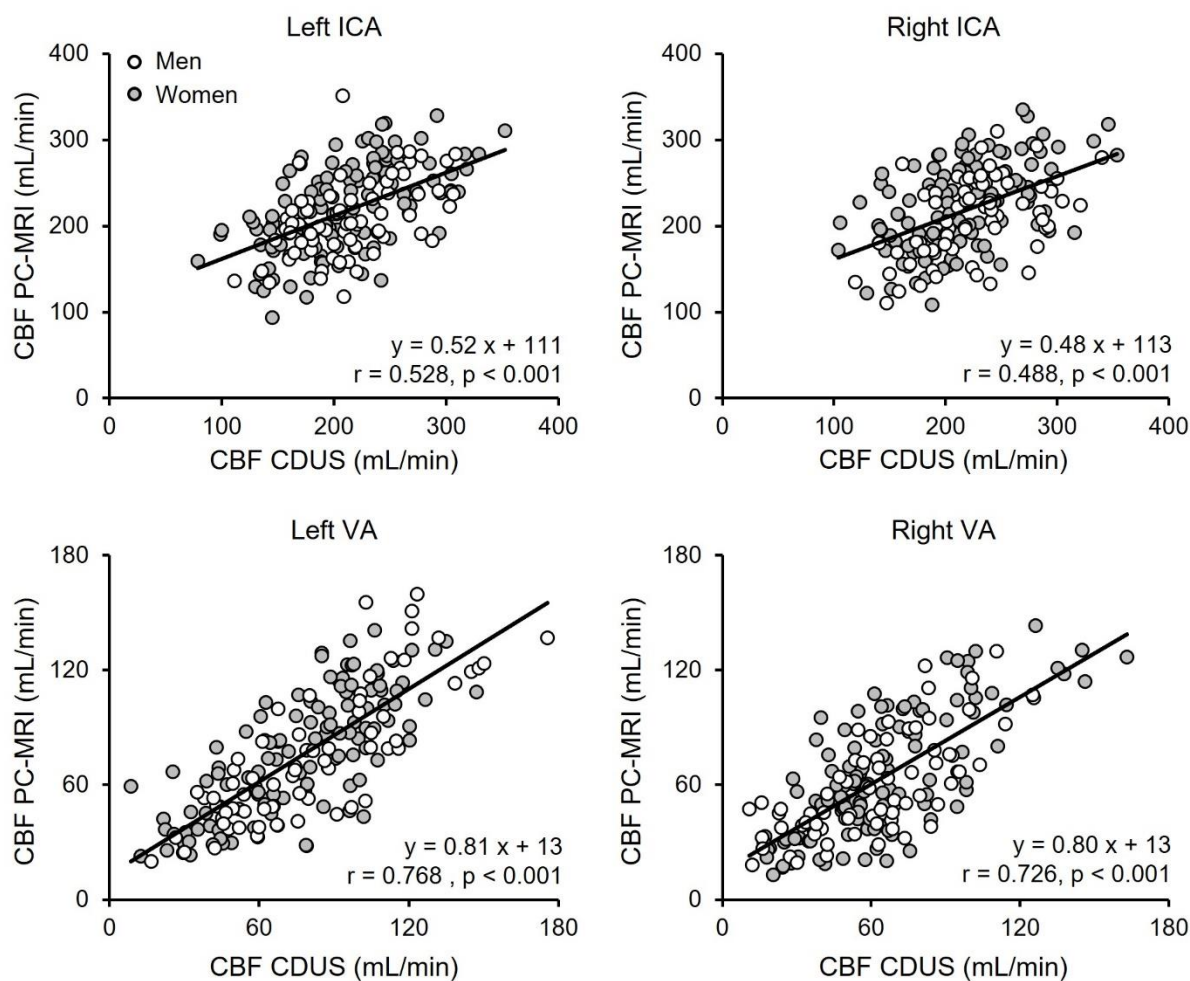


Figure S4: Relationships between CBF measurements using CDUS and PC-MRI at the internal carotid artery (ICA) and the vertebral arteries (VA); CBF: cerebral blood flow; CDUS: color-coded duplex ultrasonography; PC-MRI: phase-contrast magnetic resonance imaging. The correlations between the methods were similar between women and men. (p-values of the interaction of sex and method in one-way analysis of covariance: Left ICA, $p = 0.830$; Right ICA, $p = 0.895$; Left VA, $p = 0.580$; Right VA, $p = 0.244$)

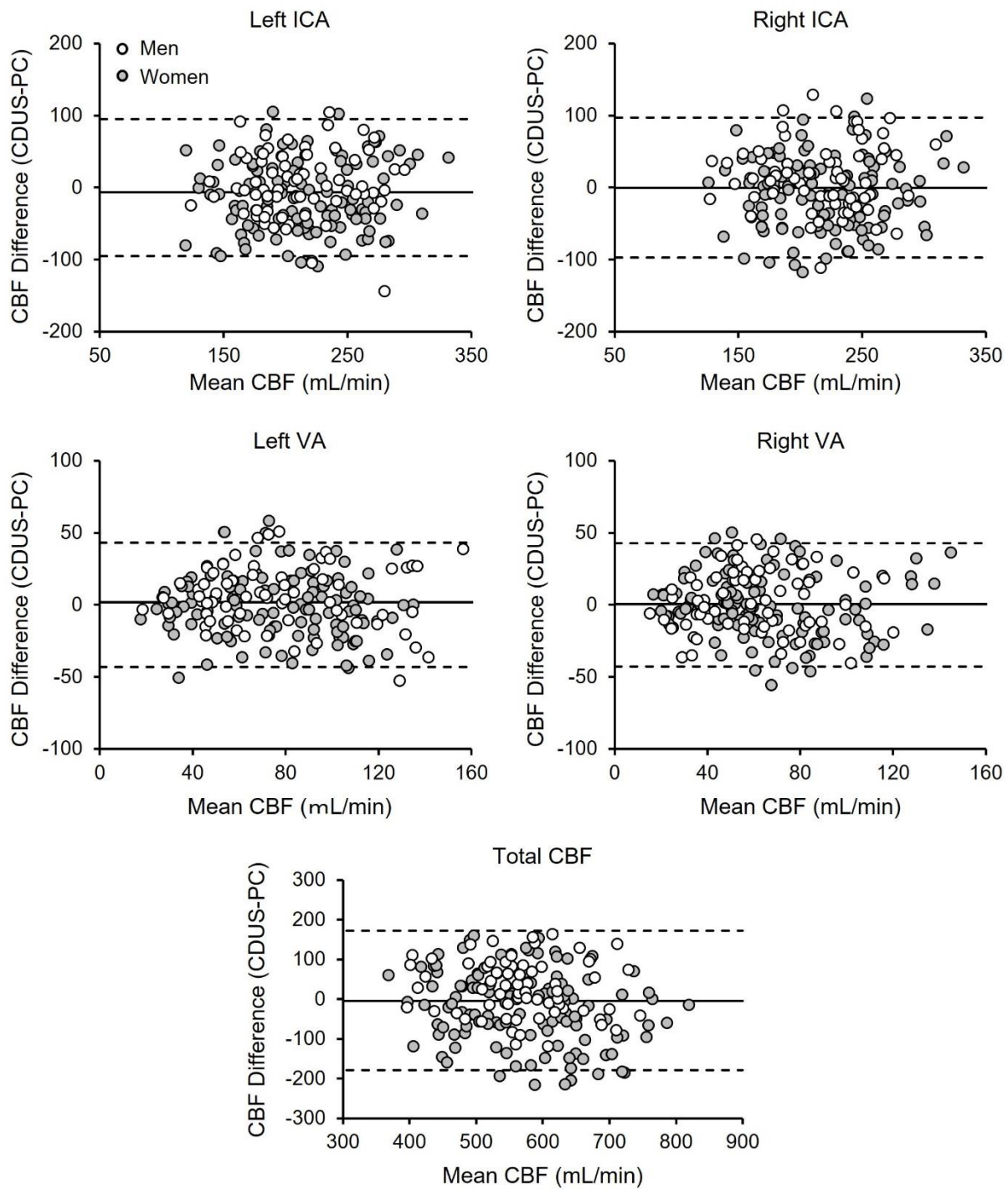


Figure S5: Bland-Altman plots of differences in CBF measurements between CDUS and PC-MRI. Solid line represents mean of difference between CDUs and PC-MRI. Dashed lines represent ± 1.96 of standard deviation. ICA: the internal carotid artery; VA: the vertebral artery; CBF: cerebral blood flow; CDUS: color-coded duplex ultrasonography; PC-MRI: phase contrast magnetic resonance imaging. Bland-Altman plots of differences in CBF measurements between CDUS and PC-MRI were similar between women and men.