

SUPPLEMENTAL DATA

**Physiological determinants of residual cerebral arterial pulsatility on best medical
treatment after TIA or minor stroke**

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Vascular Study Phenotyped Cohort

Supplemental Table 1. Distribution of demographic indices is shown for all patients, for patients undergoing either pulse wave analysis (PWA) or transcranial ultrasound and for patients undergoing both measures, with high quality recordings and not in AF. P-values are presented for patients not included in the analysis with patients with either PWV or TCD performed.

	All Mean (SD)	Had either PWV Or TCD Mean (SD)	p-val
	1013	981	
Age	67 (13.3)	66.9 (13.4)	<0.001
Sex	457 (45.1)	433 (44.1)	<0.001
Hypertension	782 (77.2)	761 (77.5)	0.11
Diabetes	119 (11.7)	112 (11.4)	0.07
Smoking			
- Current	164 (16.2)	158 (16.1)	0.69
- Ever	542 (53.5)	524 (53.4)	0.75
FHx of stroke	303 (29.9)	298 (30.3)	0.07
AF			
- During test	54 (5.3)	50 (5.1)	0.07
- Ever	74 (7.3)	69 (7)	0.07
Dyslipidaemia	819 (80.8)	791 (80.5)	0.33
Heart Failure	16 (1.6)	14 (1.4)	0.031
HTN med			
- CCB	458 (45.2)	444 (45.2)	0.87
- ACE	438 (43.2)	426 (43.4)	0.51
- ARB	133 (13.1)	128 (13)	0.67
- Diuretic	325 (32.1)	314 (32)	0.78
- Beta-blocker	150 (14.8)	147 (15)	0.38
Antiplatelet	857 (84.6)	832 (84.7)	0.30
Anticoagulant	87 (8.6)	82 (8.4)	0.15
Statin	792 (78.2)	764 (77.8)	0.19

Supplemental Table 2. Differences in indices between patients with or without specific demographic characteristics. Results are presented for univariate comparisons, and for estimated marginal means following adjustment for age, sex and cardiovascular risk factors.

	Aortic Measures								Cerebral Measures					
	PWV		SBP		DBP		PP		PSV		EDV		PI	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
<i>Univariate</i>														
Female	9.7	9.7	121.4	124.7	74.6	71.3	46.8	53.5	78.6	85.7	38.5	40.7	0.79	0.83
Diabetes	9.5	11.1	122.8	123.1	73.2	72.7	49.6	50.6	81.2	84.2	39.4	39.2	0.8	0.86
Smoking														
- Ever	9.9	9.6	123.1	122.6	73	73.3	50.1	49.5	82.2	81	39.6	39.2	0.81	0.81
- Current	9.8	9	122.9	122.7	72.8	74.6	50.1	47.9	81.2	83.1	38.9	41.6	0.82	0.75
HTN	8.8	10.6	118.8	126.8	72.6	73.8	46.4	53	82.7	80.3	41.7	36.9	0.75	0.87
Dyslipidaemia	9.0	9.9	120.8	123.4	74.2	72.9	46.6	50.5	82.8	81.2	41.2	39	0.78	0.81
<i>Adjusted</i>														
Female	10.5	10.3	123	125.8	74.5	71.4	48.3	54.5	80.7	88.1	38.2	40.8	0.83	0.87
Diabetes	9.8	11	125	123.8	73.7	72.2	51.1	51.7	82.1	86.7	39.1	39.8	0.82	0.88
Smoking														
- Ever	10.6	10.1	125.1	123.7	73.3	72.5	51.6	51.2	84.7	84.1	39.6	39.4	0.84	0.85
- Current	10.1	10.6	122	126.8	72.4	73.4	49.7	53.2	83.9	84.9	39.7	39.2	0.84	0.85
HTN	9.9	10.8	121.6	127.2	71.6	74.3	50.1	52.8	84.8	84	40.3	38.7	0.82	0.87
Dyslipidaemia	10.4	10.3	124.7	124.1	73.4	72.5	51.2	51.6	84.5	84.3	39.1	39.9	0.86	0.83

Supplemental Table 3. Associations with demographics variables. Results are presented for general linear models as univariate analyses, and following adjustment for age, sex and cardiovascular risk factors. Associations are reported as the unstandardized beta-coefficient and p-values.

	Aortic Measures				Cerebral Measures							
	SBP		DBP		PP		PSV		EDV		PI	
	B	p	B	p	B	p	B	p	B	p	β	p
Univariate												
Age	0.41	<0.001	-0.11	<0.001	0.48	<0.001	-0.17	0.001	-0.35	<0.001	0.008	<0.001
Female Gender	3.74	0.003	-2.95	<0.001	7.68	<0.001	7.08	<0.001	2.26	0.003	0.039	0.008
Diabetes	-0.004	1	-0.545	0.6	1.827	0.28	3.037	0.17	-0.177	0.88	0.061	0.009
Smoking												
- Ever	-0.95	0.45	0.11	0.87	-0.66	0.54	-1.22	0.38	-0.46	0.55	0.002	0.9
- Current	-0.74	0.67	1.95	0.03	-2.6	0.07	1.87	0.32	2.71	0.007	-0.07	<0.001
HTN	5.99	<0.001	0.07	0.93	5.49	<0.001	-5.08	0.002	-6.37	<0.001	0.11	<0.001
MI	-0.32	0.91	-3.64	0.012	1.87	0.44	1.34	0.68	-2.5	0.15	0.099	0.003
Dyslipidaemia	-0.62	0.64	-0.96	0.17	1.43	0.21	-1.93	0.2	-2.91	<0.001	0.06	<0.001
Creatinine	0.009	0.74	-0.012	0.43	0.012	0.63	-0.064	0.06	-0.086	<0.001	0.001	<0.001
Weight	-0.03	0.2	0.02	0.16	-0.04	0.014	-0.02	0.33	0.01	0.66	-0.001	0.028
BMI	-0.18	0.14	0.09	0.19	-0.25	0.022	-0.18	0.21	0.03	0.71	-0.003	0.02
Adjusted												
Age	0.41	<0.001	-0.11	<0.001	0.48	<0.001	-0.17	0.012	-0.35	<0.001	0.008	<0.001
Female Gender	3.74	0.007	-2.95	<0.001	7.68	<0.001	7.08	<0.001	2.26	<0.001	0.039	0.009
Diabetes	-0.004	0.95	-0.545	0.29	1.827	0.14	3.037	0.026	-0.177	0.56	0.061	0.001
Smoking												
- Ever	-0.95	0.33	0.11	0.34	-0.66	0.91	-1.22	0.7	-0.46	0.73	0.002	0.39
- Current	-0.74	0.015	1.95	0.3	-2.6	0.035	1.87	0.63	2.71	0.66	-0.07	0.72
HTN	5.99	0.09	0.07	0.09	5.49	0.95	-5.08	0.021	-6.37	<0.001	0.114	0.08
MI	-0.32	0.44	-3.64	0.003	1.87	0.85	1.34	0.16	-2.5	0.68	0.099	0.1
Dyslipidaemia	-0.62	0.08	-0.96	0.45	1.43	0.33	-1.93	0.86	-2.91	0.55	0.06	0.48
Creatinine	0.009	0.47	-0.012	0.15	0.012	0.73	-0.064	0.3	-0.086	0.6	0.001	0.26
Weight	-0.03	0.74	0.02	0.97	-0.04	0.79	-0.02	0.8	0.01	1	-0.001	0.53
BMI	-0.18	0.74	0.09	0.25	-0.25	0.23	-0.18	0.15	0.03	0.46	-0.003	0.18

Supplemental Table 4. Differences in key indices according to demographic characteristics, limited to patients with both PWA and TCD indices, not in AF. Results are presented for univariate comparisons, and for estimated marginal means following adjustment for age, gender and cardiovascular risk factors.

	Aortic Measures								Cerebral Measures					
	PWV		SBP		DBP		PP		PSV		EDV		PI	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
<i>Univariate</i>														
Female	9.7	9.4	119.1	122.7	74.7	71.2	44.5	51.7	79.4	86.4	38.5	41	0.8	0.83
Diabetes	9.4	11.3	120.7	120.6	73.3	72.5	47.4	48.2	82.1	84.4	39.6	39	0.81	0.88
Smoking														
- Ever	9.6	9.5	120.7	120.7	72.8	73.7	48	47.1	83.3	81.4	39.9	39.2	0.82	0.81
- Current	9.7	9	120.6	120.9	72.7	75.8	48	45.2	82.1	83.5	39.1	41.6	0.83	0.76
HTN	8.7	10.6	116.1	125.5	72.5	74	43.7	51.5	83.5	81.1	41.8	37.1	0.75	0.88
Dyslipidaemia	8.6	9.8	119.5	120.9	74.4	73	45.4	48	83.6	82	41.4	39.1	0.77	0.83
<i>Adjusted</i>														
Female	10.6	10.3	121.3	125.2	74.6	71.4	46.8	53.8	81.3	88.5	37.9	40.6	0.84	0.87
Diabetes	9.6	11.3	123.9	122.6	74	72.1	50	50.7	83	86.8	39.2	39.3	0.83	0.89
Smoking														
- Ever	10.6	10.3	123.5	122.9	73.2	72.8	50.5	50.2	85.6	84.2	39.5	39	0.86	0.86
- Current	10.1	10.7	120.6	125.9	72.1	73.9	48.6	52	84.3	85.5	39.5	39	0.85	0.87
HTN	10	10.8	119.6	126.8	71.6	74.4	48.2	52.5	85.3	84.5	40.1	38.4	0.83	0.89
Dyslipidaemia	10.4	10.4	124.7	121.8	73.4	72.7	51.5	49.1	84.9	84.8	38.7	39.8	0.87	0.84

Supplemental Table 5. Physiological determinants of cerebrovascular indices. Results of general linear models are presented for each cerebral blood flow index (PSV, EDV and PI) for model 1: including aortic pulse wave velocity (PWV), aortic systolic blood pressure (Aor-SBP) and Aortic diastolic blood pressure (Aor-DBP); or for model 2: including all factors in model 1 plus Aortic augmentation index (Aor-Aix) and R-R interval, the inverse of heart rate. Both models are presented unadjusted for clinical characteristics, adjusted for age and gender and adjusted for age, gender and cardiovascular risk factors (diabetes, history of hypertension, current smoking, ever smoking).

	MCA Peak Velocity						MCA Trough Velocity						MCA Pulsatility Index					
	Physiology		Adj Age/Sex		Adj CV RFs		Physiology		Adj Age/Sex		Adj CV RFs		Physiology		Adj Age/Sex		Adj CV RFs	
	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p
Model 1	R ² =	0.01	R ² =	0.06	R ² =	0.07	R ² =	0.12	R ² =	0.24	R ² =	0.25	R ² =	0.37	R ² =	0.42	R ² =	0.43
PWV	-0.08	0.054	0.06	0.221	0.05	0.389	-0.27	<0.001	-0.05	0.297	-0.03	0.559	0.31	<0.001	0.18	<0.001	0.12	0.003
Aor-SBP	0.1	0.028	0.11	0.027	0.12	0.018	-0.16	<0.001	-0.09	0.037	-0.06	0.223	0.41	<0.001	0.32	<0.001	0.29	<0.001
Aor-DBP	-0.11	0.014	-0.12	0.013	-0.12	0.018	0.18	<0.001	0.1	0.024	0.08	0.096	-0.46	<0.001	-0.36	<0.001	-0.34	<0.001
Model 2	R ² =	0	R ² =	0.05	R ² =	0.07	R ² =	0.12	R ² =	0.22	R ² =	0.23	R ² =	0.41	R ² =	0.46	R ² =	0.49
PWV	-0.03	0.471	0.13	0.021	0.12	0.044	-0.26	<0.001	-0.04	0.444	-0.01	0.817	0.38	<0.001	0.25	<0.001	0.19	<0.001
Aor-SBP	0.02	0.668	0.03	0.57	0.04	0.558	-0.13	0.014	-0.09	0.086	-0.06	0.296	0.25	<0.001	0.2	<0.001	0.16	<0.001
Aor-DBP	-0.08	0.111	-0.09	0.116	-0.08	0.166	0.15	0.002	0.08	0.107	0.05	0.331	-0.4	<0.001	-0.32	<0.001	-0.28	<0.001
Aor-Aix	0.07	0.119	0.07	0.192	0.08	0.114	-0.02	0.581	0.02	0.627	0.04	0.416	0.13	<0.001	0.06	0.135	0.07	0.066
R-R int.	0.01	0.906	0.05	0.292	0.06	0.193	-0.09	0.039	-0.04	0.313	-0.05	0.289	0.13	<0.001	0.11	0.001	0.15	<0.001

Supplemental Figure 1: Distributions of cerebral physiological indices per quintile of aortic stiffness or the comparable aortic pressure measure. Results are presented as the mean and confidence interval of each index, split by gender. Results are presented for aortic systolic blood pressure (SBP), aortic diastolic blood pressure (DBP), aortic pulse pressure (PP), MCA peak systolic velocity (PSV), MCA end diastolic velocity (EDV) and MCA pulsatility index (PI).

