

SUPPLEMENTAL MATERIAL

Digital peripheral arterial tonometry and cardiovascular disease events: The Framingham Heart Study

Leroy L. Cooper, PhD, MPH,¹ Na Wang, MA,² Alexa S. Beiser, PhD,^{3,4,5} Jose Rafael Romero, MD,³ Hugo J. Aparicio, MD, MPH,^{3,4} Vasileios-Arsenios Lioutas, MD,⁶ Emelia J. Benjamin, MD, ScM,^{3,7,8,9,10} Martin G. Larson, ScD,^{3,5} Ramachandran S. Vasan, MD,^{3,7,8,9,10} Gary F. Mitchell, MD,¹¹ Sudha Seshadri, MD,^{3,12} and Naomi M. Hamburg, MD, MS^{8,9}

¹Biology Department, Vassar College, Poughkeepsie, NY; ²Biostatistics and Epidemiology Data Analytics Center, Boston University School of Public Health, Boston, MA. ³Boston University and NHLBI's Framingham Study, Framingham, MA; ⁴Department of Neurology, Boston University School of Medicine, Boston, MA; ⁵Department of Biostatistics, Boston University School of Public Health, Boston, MA; ⁶Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; ⁷Cardiology and Preventive Medicine Sections, Department of Medicine, Boston University School of Medicine, Boston, MA; ⁸Evans Department of Medicine, ⁹Whitaker Cardiovascular Institute, Boston University School of Medicine, Boston, MA. ¹⁰Department of Epidemiology, Boston University School of Public Health; and; ¹¹Cardiovascular Engineering, Inc., Norwood, MA; and ¹²Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, University of Texas Health Sciences Center, San Antonio, TX

Supplemental Content:

Table I: Comparison of demographic characteristics and vascular measures between included and excluded participants.

Table II: Individual PAT measures as predictors of incident stroke with further adjustment for presence of left ventricular hypertrophy and atrial fibrillation.

Table III: PAT measures as predictors of incident stroke using generalized propensity scores.

Figure I: Kaplan-Meier estimators of the cumulative probability of an incident stroke when participants were grouped according to quartiles of PAT ratio.

Figure II: Adjusted estimators of the cumulative probability of a CVD event when participants were grouped according to quartiles of PAT ratio.

This supplementary material has been provided by the authors to give the readers additional information about their work.

Table I: Comparison of demographic characteristics and vascular measures between included and excluded participants.

Variable	Included (N=3865)	Excluded (N=varies)*
Clinical variables		
Age, year	55±14	55±20
Women, N (%)	2014 (52.1)	657 (53.3)
Offspring, N (%)	2187 (56.6)	728 (59.1)
Body mass index, kg/m ²	27.7±5.4	27.9±6.0
Heart rate, bpm	62±10	61±11
Mean arterial pressure, mm Hg	95±12	94± 3
Total/HDL cholesterol ratio	3.7±1.2	3.5± 1.2
Hypertension treatment, N (%)	1145 (29.6)	486 (39.6)
Diabetes mellitus, N (%)	301 (7.8)	170 (14.1)
Smoker, N (%)	469 (12.1)	160 (13.0)
Lipid disorder treatment, N (%)	993 (25.7)	414 (33.7)
Left ventricular hypertrophy, N (%) [†]	11 (0.3)	8 (0.7)
Atrial fibrillation, N (%)	103 (2.7)	123 (10.0)
Digital PAT measures		
Baseline pulse amplitude [‡]	5.63±0.89	5.81±0.88
PAT ratio	0.71±0.41	0.57±0.42

Values are mean±standard deviation except as noted. HDL, high-density lipoprotein. PAT, peripheral arterial tonometry. *Since younger individuals (<30 years) did not contribute to events, stratification of excluded participants is not based on age; note that N (656-1232) varies for excluded participants based on availability of data. [†]N=3822 for included participants due to missing data on left ventricular hypertrophy. [‡]arbitrary units. Baseline pulse amplitude and PAT ratio were natural logarithm transformed.

Table II: Individual PAT measures as predictors of incident stroke with further adjustment for presence of left ventricular hypertrophy and atrial fibrillation (N=3822).

PAT Measure	Hazard Ratio (LCL, UCL)	P
Baseline pulse amplitude	1.19 (0.91, 1.56)	0.22
PAT ratio	0.78 (0.62, 0.97)	0.025

PAT, peripheral arterial tonometry. Models consider vascular measures individually, one at a time. Models were adjusted for age, sex, cohort, body mass index, heart rate, mean arterial pressure, total/high-density lipoprotein cholesterol ratio, smoking, diabetes mellitus, lipid disorder treatment, hypertension treatment, left ventricular hypertrophy, and atrial fibrillation. LCL, UCL, lower and upper limits of the 95% confidence intervals. Hazard ratios expressed per 1 standard deviation higher value. With additional exclusions on data for presence of left ventricular hypertrophy, our sample size was reduced to 3822 participants in which we observed 88 (2.3%) stroke events.

Table III: PAT measures as predictors of incident stroke using generalized propensity scores.

PAT Measure	Hazard Ratio (LCL, UCL) using Cox models adjusted for GPS a covariate*	<i>P</i>	Hazard Ratio (LCL, UCL) using the GPS to perform inverse probability weighting	<i>P</i>
Baseline pulse amplitude	1.19 (0.91, 1.55)	0.2	1.38 (1.10, 1.75)	0.007
PAT ratio	0.77 (0.61, 0.98)	0.03	0.74 (0.61, 0.91)	0.005

PAT, peripheral arterial tonometry. GPS, generalized propensity score. Models consider vascular measures individually, one at a time. *Models were also adjusted for age, sex, cohort, body mass index, heart rate, mean arterial pressure, total/high-density lipoprotein cholesterol ratio, smoking, diabetes mellitus, lipid disorder treatment, hypertension treatment, left ventricular hypertrophy, and presence of and atrial fibrillation. LCL, UCL, lower and upper limits of the 95% confidence intervals. Hazard ratios expressed per 1 standard deviation higher value. With additional exclusions on data for presence of left ventricular hypertrophy, our sample size was reduced to 3822 participants in which we observed 88 (2.3%) stroke events.

Figure I: Kaplan-Meier estimators of the cumulative probability of an incident stroke when participants were grouped according to quartiles of PAT ratio (N=3865). Group I (≤ 0.4066 , 33/966 [3.4%]); Group II (> 0.4066 to 0.7258 , 30/966 [3.1%]), Group III (> 0.7258 to 0.9905 , 16/967 [1.7%]); and Group IV (> 0.9905 , 13/966 [1.3%]).

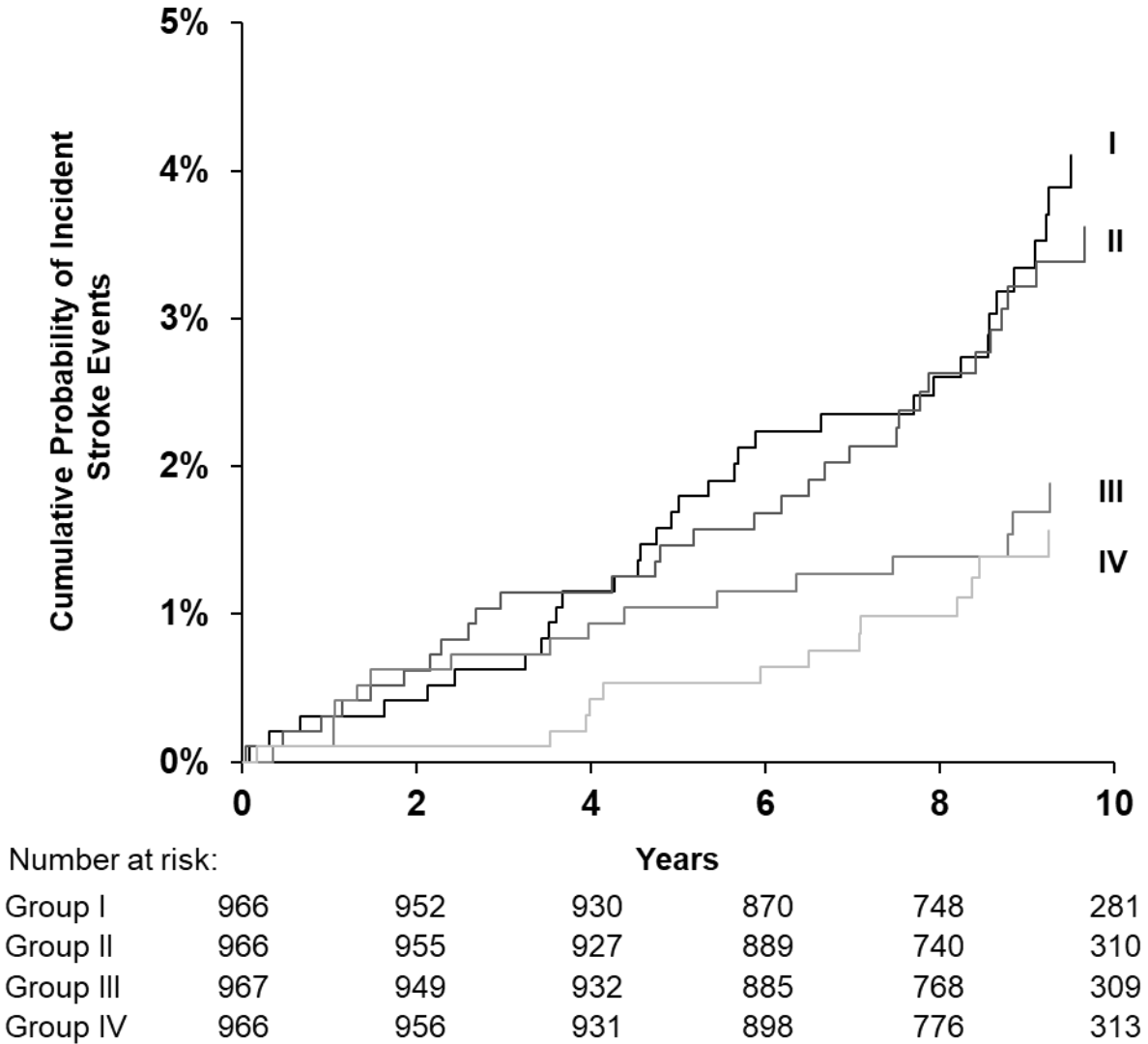


Figure II: Adjusted estimators of the cumulative probability of a CVD event when participants were grouped according to quartiles of PAT ratio (N=3865). Incident CVD event per person for quartile groups of PAT ratio: Group I (≤ 0.4066 , 83/966); Group II (> 0.4066 to 0.7258 , 87/966), Group III (> 0.7258 to 0.9905 , 52/967); and Group IV (> 0.9905 , 48/966). In a model adjusted for age, sex, cohort, body mass index, heart rate, mean arterial pressure, total cholesterol/HDL ratio, smoking, diabetes mellitus, lipid disorder treatment, and hypertension treatment, participants in the lowest PAT ratio group versus participants in the highest PAT ratio group had an adjusted hazard ratio of 0.79 (95% confidence interval, 0.54–1.15; $P=0.22$).

