

Online Supplement

TITLE: Central Pulse Pressure in Chronic Kidney Disease: A CRIC Ancillary Study

Authors: Raymond R. Townsend^a, Julio A. Chirinos^a, Afshin Parsa^b, Matthew A. Weir^b, Stephen M. Sozio^c, James P. Lash^d, Jing Chen^e, Susan P. Steigerwalt^f, Alan S. Go^g, Chi-yuan Hsu^{g,h}, Mohammed Rafeyⁱ, Jackson T. Wright Jr.^j, Mark J. Duckworth^a, Crystal A. Gadegbeku^k, Marshall P. Joffe^{a,l}

On behalf of the Chronic Renal Insufficiency Cohort (CRIC) Investigators

^a-Department of Medicine, University of Pennsylvania, Philadelphia, PA

^b-Department of Medicine, University of Maryland School of Medicine, Baltimore, MD

^c-Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD

^d-Department of Medicine, University of Illinois, Chicago, IL

^e-Tulane University Schools of Medicine and Public Health and Tropical Medicine, New Orleans, Louisiana

^f-Department of Medicine, St John Hospital and Medical Center and Wayne State University School of Medicine, Detroit, MI

^g-Division of Research, Kaiser Permanente of Northern California, Oakland, CA

^h-Division of Nephrology, Department of Medicine, University of California, San Francisco, CA

ⁱ-Department of Nephrology and Hypertension, Cleveland Clinic Foundation, Cleveland, OH

^j-Division of Nephrology and Hypertension, University Hospitals Case Medical Center

^k- University of Michigan Health System, Department of Internal Medicine, Division of Nephrology, Ann Arbor, MI

^l-Center for Clinical Epidemiology & Biostatistics, University of Pennsylvania, Philadelphia, PA

Address for correspondence:

Raymond R. Townsend, MD

University of Pennsylvania

122 Founders Building

3400 Spruce Street

Philadelphia, PA 19104

215-662-4630 Office

215-662-3459 Facsimile

townsend@mail.med.upenn.edu

Supplemental Methods

Central pulse pressure measurements were performed supine after at least 5 minutes of rest using the Sphygmocor PVx System (AtCor Medical, West Ryde, Australia) via the right radial artery at all CRIC sites (1). All personnel were trained and certified to take blood pressure measurements in the dominant arm with a Tyco aneroid sphygmomanometer using American Heart Association standards and to perform the central pressure measurements using radial artery tonometry (2) (3). The operator captured 10 seconds of stable radial artery waveform. Pulse pressure was defined as the difference between the systolic and the diastolic blood pressure in mmHg. When this data was derived from standard blood pressure measurement it was brachial PP; when derived by algorithm from the radial artery waveform it was CPP. The augmentation index (AIX) was derived from the aortic pressure profile. It was defined as the ratio of the contribution of the reflected wave (in mmHg) to the aortic pressure profile divided by the central pulse pressure (and is unitless). The aortic time to wave reflection (Tr) was determined by a transformation algorithm within Sphygmocor PVx software based on detecting the time to an inflection in the aortic systolic upstroke and is presented in milliseconds. The other factors in Table 2 were determined by standard methods and direct participant query as detailed in the primary manuscript.

Supplemental Results

Supplemental Table S1 shows the univariate correlations as presented in the primary manuscript and now supplemented by the addition of the Tr (not significant) and the AIX (statistically significant), shown by gender (\pm SD) (new data lightly shaded for emphasis).

Supplemental Table S2 shows the same analysis as presented in Table 3b of the primary manuscript but now includes both Tr and AIX in the multivariable model. When compared with Table 3b in the primary manuscript Aortic Tr was not significant. However, the incorporation of AIX into the model appeared to account for the contributions of mean arterial pressure, age, gender, diabetes and weight in the primary manuscript.

Supplemental Table S3 shows the same analysis as presented in Table 3c of the primary manuscript. The incorporation of AIX into the model increased the estimation of CPP variability by the model from 0.87 in the primary manuscript to 0.92 in the Supplemental data.

Supplemental References

- (1) Feldman HI, Appel LJ, Chertow GM, Cifelli D, Cizman B, Daugirdas J, Fink JC, Franklin-Becker ED, Go AS, Hamm LL, He J, Hostetter T, Hsu CY, Jamerson K, Joffe M, Kusek JW, Landis JR, Lash JP, Miller ER, Mohler ER, III, Muntner P, Ojo AO, Rahman M, Townsend RR, Wright JT. The Chronic Renal Insufficiency Cohort (CRIC) Study: Design and Methods. *J Am Soc Nephrol*. 2003; 14:S148-S153.
- (2) Perloff D, Grim C, Flack J, Frohlich ED, Hill M, McDonald M, Morgenstern BZ. Human blood pressure determination by sphygmomanometry. *Circulation*. 1993; 88:2460-2470.
- (3) Muntner P, Anderson A, Charleston J, Chen Z, Ford V, Makos G, O'Connor A, Perumal K, Rahman M, Steigerwalt S, Teal V, Townsend RR, Weir M, Wright JT. Hypertension Awareness, Treatment, and Control in Adults with Chronic Kidney Disease: Results from the Chronic Renal Insufficiency Cohort (CRIC) Study. *American Journal of Kidney Diseases*. 2009; 55:441-451.

Supplemental Table S1: Factors associated with Central Pulse Pressure

| Variable | Central Pulse Pressure | | | *Ln Central Pulse Pressure | | |
|--|------------------------|----------------|--------|----------------------------|----------------|--------|
| | Est (StdErr) | R ² | p | Est (StdErr) | R ² | p |
| Female Sex | 3.787 (0.75) | 0.010 | <.0001 | 0.089 (0.02) | 0.012 | <.0001 |
| Race | | | | | | |
| Black | 4.847 (0.79) | 0.020 | <.0001 | 0.106 (0.02) | 0.020 | <.0001 |
| Other | 6.527 (1.28) | 0.020 | <.0001 | 0.128 (0.03) | 0.020 | <.0001 |
| Ethnicity | | | | | | |
| Hispanic | 4.700 (2.12) | 0.025 | <.0001 | 0.091 (0.04) | 0.024 | <.0001 |
| Diabetes | 10.449 (0.72) | 0.076 | <.0001 | 0.227 (0.02) | 0.081 | <.0001 |
| Age (/10 years) | 6.083 (0.33) | 0.123 | <.0001 | 0.147 (0.01) | 0.162 | <.0001 |
| †eGFR (/10 mL/min/1.73m ²) | -2.483 (0.23) | 0.045 | <.0001 | -0.053 (0.00) | 0.046 | <.0001 |
| Weight (/10 Kg) | -0.769 (0.18) | 0.008 | <.0001 | -0.015 (0.00) | 0.006 | <.0001 |
| Body Mass Index (kg/m ²) | 0.032 (0.06) | 0.000 | 0.5666 | 0.002 (0.00) | 0.001 | 0.1590 |
| Waist (/10 cm) | 0.262 (0.23) | 0.001 | 0.2561 | 0.010 (0.00) | 0.002 | 0.0356 |
| ‡MAP (/10 mmHg) | 4.656 (0.26) | 0.118 | <.0001 | 0.093 (0.01) | 0.106 | <.0001 |
| §SBP (/10 mmHg) | 6.160 (0.12) | 0.535 | <.0001 | 0.127 (0.00) | 0.512 | <.0001 |
| DBP (/10 mm Hg) | -1.200 (0.29) | 0.007 | <.0001 | -0.030 (0.01) | 0.009 | <.0001 |
| ¶Aortic Tr (msec) | -0.000 (0.00) | 0.000 | 0.9163 | -0.000 (0.00) | 0.000 | 0.5426 |
| Augmentation Index | 0.673 (0.03) | 0.200 | <.0001 | 0.016 (0.00) | 0.241 | <.0001 |
| Heart Rate (/10 beats/min) | -3.187 (0.33) | 0.037 | <.0001 | -0.073 (0.01) | 0.043 | <.0001 |
| Brachial PP (/10 mmHg) | 8.574 (0.09) | 0.795 | <.0001 | 0.179 (0.00) | 0.778 | <.0001 |
| Hemoglobin (g/dL) | -3.098 (0.21) | 0.083 | <.0001 | -0.069 (0.00) | 0.094 | <.0001 |
| Glucose (/10 mg/dL) | 0.575 (0.08) | 0.021 | <.0001 | 0.012 (0.00) | 0.020 | <.0001 |
| Triglycerides (/10 mg/dL) | -0.060 (0.03) | 0.001 | 0.0754 | -0.002 (0.00) | 0.003 | 0.0159 |
| LDL-Cholesterol (/10 mg/dL) | -0.237 (0.11) | 0.002 | 0.0374 | -0.007 (0.00) | 0.004 | 0.0045 |
| HDL-Cholesterol (/10 mg/dL) | 0.333 (0.24) | 0.001 | 0.1719 | 0.008 (0.01) | 0.001 | 0.1064 |
| Calcium (mg/dL) | -3.709 (0.75) | 0.010 | <.0001 | -0.074 (0.02) | 0.009 | <.0001 |
| #Phosphate (mg/dL) | 1.979 (1.43) | 0.005 | 0.1670 | 0.044 (0.03) | 0.005 | 0.1608 |
| #Calcium-Phosphate (product) | 0.324 (0.06) | 0.011 | <.0001 | 0.007 (0.00) | 0.013 | <.0001 |
| #Parathyroid Hormone (/10 pg/mL) | 0.343 (0.06) | 0.014 | <.0001 | 0.008 (0.00) | 0.016 | <.0001 |
| #Urine Protein (g/day) | 1.439 (0.21) | 0.021 | <.0001 | 0.027 (0.00) | 0.016 | <.0001 |
| #Urine Albumin (g/day) | 1.191 (0.26) | 0.009 | <.0001 | 0.022 (0.01) | 0.007 | <.0001 |
| #HemoglobinA ₁ C (%) | 2.870 (0.24) | 0.054 | <.0001 | 0.063 (0.01) | 0.058 | <.0001 |
| #Uric Acid (mg/dL) | 0.848 (0.20) | 0.007 | <.0001 | 0.017 (0.00) | 0.007 | <.0001 |
| Number of Antihypertensive Drugs | 3.495 (0.24) | 0.083 | <.0001 | 0.078 (0.00) | 0.093 | <.0001 |

*Ln = Natural logarithm transformation of Central Pulse Pressure; †eGFR=estimated Glomerular Filtration Rate; ‡MAP=Mean Arterial Pressure; §SBP=Systolic Blood Pressure; ||DBP=Diastolic Blood Pressure; ¶Aortic Tr = Time to reflected wave in aortic pressure profile; # Available at baseline visit only

Supplemental Table S2: Multivariable regression model for *LnCPP (adjusted for brachial pulse pressure [natural log transformed], and brachial mean arterial pressure, †AIX and Aortic ‡Tr)

| Variable | Estimate (StdErr) | <i>p value</i> |
|-------------------------------|-------------------|----------------|
| §LnBPP (mmHg) | 0.965 (0.009) | <.0001 |
| Mean arterial pressure (mmHg) | 0.002 (0.002) | 0.2242 |
| Age (/10 years) | 0.004 (0.003) | 0.1284 |
| Sex (Male) | -0.009 (0.005) | 0.0805 |
| Diabetes (Yes) | 0.006 (0.005) | 0.2413 |
| Heart Rate (beats/minute) | -0.019 (0.002) | <.0001 |
| Weight (/10 Kg) | -0.001 (0.001) | 0.3554 |
| †AIX | 0.008 (0.000) | <.0001 |
| ‡Aortic Tr | 0.000 (0.000) | 0.3134 |

*=Natural logarithm transformation of Central Pulse Pressure; †= Augmentation Index; ‡ = Time to Aortic reflected wave detection; § = Natural Logarithm transformation of Brachial Pulse Pressure

Supplemental Table S3: Stepwise change in multivariable model R² (from Table S2)

| Variable | Model R ² |
|---|----------------------|
| *LnBPP | 0.820781 |
| LnBPP + Mean Arterial Pressure (/10 mmHg; ‘MAP’) | 0.820817 |
| LnBPP + MAP + Age (/10yrs) | 0.843678 |
| LnBPP + MAP + Age(/10yrs) + Diabetes | 0.843882 |
| LnBPP + MAP + Age(/10yrs) + Diabetes + Heart Rate(/10beats/min) | 0.858931 |
| LnBPP + MAP + Age(/10yrs) + Diabetes + Heart Rate(/10beats/min) + Sex | 0.866866 |
| LnBPP + MAP + Age(/10yrs) + Diabetes + Heart Rate(/10beats/min)+ Sex + Weight (/10kg) | 0.870519 |
| LnBPP + MAP + Age(/10yrs) + Diabetes + Heart Rate(/10beats/min)+ Sex + Weight (/10kg) + †AIX | 0.915581 |
| LnBPP + MAP + Age(/10yrs) + Diabetes + Heart Rate(/10beats/min)+ Sex + Weight (/10kg) + AIX + Aortic Tr | 0.915616 |

*=Natural logarithm transformation of Central Pulse Pressure; †= Augmentation Index; ‡ = Time to Aortic reflected wave detection; § = Natural Logarithm transformation of Brachial Pulse Pressure