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Aortic PWV in Chronic Kidney Disease: A CRIC Ancillary Study

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Abstract

Background—Aortic PWV is a measure of arterial stiffness and has proved useful in predicting cardiovascular morbidity and mortality in several populations of patients, including the healthy elderly, hypertensives and those with end stage renal disease receiving hemodialysis. Little data exist characterizing aortic stiffness in patients with chronic kidney disease who are not receiving dialysis, and in particular the effect of reduced kidney function on aortic PWV.

Methods—We performed measurements of aortic PWV in a cross-sectional cohort of participants enrolled in the Chronic Renal Insufficiency Cohort (CRIC) study to determine factors which predict increased aortic PWV in chronic kidney disease.

Results—PWV measurements were obtained in 2564 participants. The tertiles of aortic PWV (adjusted for waist circumference) were < 7.7 m/sec, 7.7–10.2 m/sec and > 10.2 m/sec with an overall mean (± S.D.) value of 9.48 ± 3.03 m/sec [95% CI = 9.35–9.61 m/sec]. Multivariable regression identified significant independent positive associations of age, blood glucose concentrations, race, waist circumference, mean arterial blood pressure, gender, and presence of diabetes with aortic PWV and a significant negative association with the level of kidney function.

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Conclusions—The large size of this unique cohort, and the targeted enrollment of chronic kidney disease participants provides an ideal situation to study the role of reduced kidney function as a determinant of arterial stiffness. Arterial stiffness may be a significant component of the enhanced cardiovascular risk associated with kidney failure.

Introduction

The velocity of pulse wave travel in the aorta reflects vascular stiffness and predicts coronary heart disease, stroke and death (1). Although such measurements have been performed in the human aorta since the 1920's (2) only in the last few decades has it been possible to non-invasively determine aortic PWV (PWV) and apply such knowledge to the epidemiology of cardiovascular disease (CVD) (3). Studies using aortic PWV measures show that it predicts death and CVD as well as, and in some cases better than, systolic blood pressure in the otherwise healthy elderly (4), diabetics (5), those with hypertension (6) and those receiving hemodialysis (7;8). With regard to those on dialysis, a population with exceptionally high CVD morbidity and mortality, determination of aortic PWV predicted death from CVD even when blood pressure is well controlled (7).

Previous studies of aortic PWV indicate that advancing age, increasing blood pressure and the presence of diabetes are typically associated with increased aortic PWV (9). Although aortic PWV has been well studied in End Stage Renal Disease (ESRD) there is a paucity of knowledge regarding the determinants of PWV in chronic kidney disease before the initiation of dialysis and whether the progressive loss of kidney function is independently associated with higher aortic PWV. Some studies suggest that aortic PWV is not directly related to CKD (10) while other studies have found an association (11). The few studies addressing this relationship have usually analyzed the subset with reduced kidney function from a population recruited for another purpose, and are typically analyzing a relatively homogenous ethnic group. In the current study we analyzed aortic PWV data from the Chronic Renal Insufficiency Cohort (CRIC), a multi-ethnic NIH-funded observational study (12) of people recruited by age-stratified estimated glomerular filtration rate (eGFR) to address further the complex interaction between kidney function, other biochemical and demographic factors in determining the spectrum of aortic PWV in CKD.

Methods

Subjects

Aortic PWV measurements were adopted into the CRIC protocol beginning at the 2nd annual follow-up visit and all participants enrolled in the CRIC study were invited to become part of this ancillary protocol. The procedures were approved by the Institutional Review Boards at the 13 enrolling centers and all subjects provided written informed consent.

Procedures

Aortic PWV measurements were performed supine after at least 5 minutes of rest using the right carotid and right femoral arteries. The Sphygmocor PVx System (AtCor Medical, West Ryde, Australia) device was used at each site. 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 aortic PWV measurements (13). Three electrocardiographic (ECG) leads were attached: one to the right arm, one to the left arm and one to the left lower abdomen or leg providing a standard limb lead II ECG tracing. The head was usually turned to 45 – 60° away from the examiner and the right carotid pulse was gently palpated. The distance from the sternal notch to the

point of the palpable carotid pulse was measured in mm and entered into the computer program. The right femoral pulse was palpated and the distance to the umbilicus from the sternal notch, and then from the umbilicus to the point of femoral palpation was measured in mm and also entered into the program. Next a Millar tonometer attached to an electronic module interface was placed perpendicular to the carotid pulse and repositioned in small increments until a stable wave form was observed (14). The operator captured 10 seconds of stable waveform and repeated the sequence using the femoral artery. After second waveform is capture the computer generates an estimate of aortic PWV with a standard deviation. If the standard deviation was more than 15% of the PWV value the study was repeated.

Laboratory measures

Hemoglobin and hematocrit values were measured directly at the laboratories of each center. Other standard laboratory testing (e.g. creatinine, glucose, etc.) was performed at a central lab in the University of Pennsylvania, as were lipid profiles and urine protein determinations. The eGFR was determined according to the abbreviated MDRD formula using creatinine values calibrated to the Cleveland Clinic Laboratory (15). Certain laboratory values are only available from the baseline visit [see Table 1].

Race

Race was queried for each participant at screening by asking if they consider their racial background as American Indian/Alaskan Native, Asian/Asian American, Black/African American, Native Hawaiian/Other Pacific Islander or White/Caucasian (participants could check more than one box). If a participant checked the box “White” and no other box they were considered as White/Caucasian. If they checked the box for Black/African American either alone or in combination with any other box they were considered Black/African American. If they did not check the White or Black box, or if they preferred not to answer this question they were considered “Other”.

Aortic PWV Data

Enrollment into the PWV ancillary study began in 2005. The data reported here represent aortic PWV measures obtained on subjects whose second annual follow up visit occurred on or before March 31, 2009, representing 79% of the entire eligible CRIC cohort.

Statistical Analyses

Continuous data are presented as mean ± standard deviation (S.D.) or [95% CI]. Categorical variables are expressed as proportions. Certain variables were pre-specified for analyses because other studies showed a relationship to aortic PWV (such as age, systolic blood pressure) or because they are felt to be important in kidney disease (such as calcium, hemoglobin). Univariable regression models for aortic PWV were used to assess the relationship between PWV and the selected variables. To summarize the association between aortic PWV and variables of interest, a multivariable linear regression model was developed. All parameters significant at a $p=0.25$ level in univariable regression were entered into both forward and backward selection algorithms. Where variables were known to be strongly correlated with each other (e.g. serum creatinine and eGFR) the one with the stronger association only was entered. Only those significant at the $p=0.05$ level in the multivariable model were retained in the final model. All multivariable models were adjusted for clinical site. Analyses were executed in SAS 9.1 (SAS Institute, Cary, NC).

We also conducted analyses which used inverse probability of sampling weights to adjust for nonrandom missingness of aortic PWV measurements explainable in terms of other measured covariates (16). These analyses had only trivial effects on the results, which are

presented without the inverse probability weighting adjustment applied. Because PWV required a distance measurement from sternal notch to umbilicus and umbilicus to palpable femoral pulsation site, there may be an artifactual increase in the distance in participants with large waist circumferences. When we compared the femoral distance measurement (within gender) controlling for participant height we found that this distance measurement increased with progressive waist circumference increase. To address this we developed a regression-based method to adjust the femoral distance measurement; the details of this adjustment method are presented in the appendix. Once the adjusted femoral distance measure was obtained, the originally measured sternal-notch to carotid distance was subtracted from it (as per the Sphygmocor method) to determine the adjusted distance aspect of the PWV value.

Results

Demographic characteristics of all participants eligible for aortic PWV measurement at the year 2 follow up visit of the CRIC cohort are shown in Table 1. We anticipated data loss on approximately 20% of participants and we were unable to obtain or use measurements on 716 of 3280 eligible participants (21.8%). Separate columns of data in Table 1 show summary statistics of those within the CRIC cohort who did not have aortic PWV measurements (“WITHOUT PWV”) compared with those who did (“WITH PWV”). In those without aortic PWV measures either poor quality of the data (approximately 30%), or unsuccessful data capture from the femoral site related to obesity or arrhythmia (e.g. atrial fibrillation) (approximately 70%) were the principal reasons. Table 1 reflects the higher weight and larger BMI of those participants in whom we could not successfully perform aortic PWV measurements. In a few cases death or interval ESRD requiring dialysis or a transplant occurred before the second year follow-up visit.

Figure 1 shows the frequency distribution of the waist circumference-adjusted aortic PWV determinations. The tertiles of the adjusted aortic PWV were < 7.7 m/sec, 7.7–10.2 m/sec and > 10.2 m/sec with an overall mean (± S.D.) value of 9.48 ± 3.03 m/sec [95% CI = 9.35–9.61 m/sec].

Figure 2 presents mean aortic PWV values for the cohort by gender and race. In multivariable analyses an interaction was noted between gender and race in that the association of aortic PWV with gender of Whites (men had higher aortic PWV) was significantly different than in Blacks (little difference between men and women).

There was a positive relationship between age and aortic PWV as shown in Figure 3 ($p<0.0001$), which divided each decade into participants without diabetes (open bar) compared to participants with diabetes (solid bars). The mean waist circumference-adjusted aortic PWV in the cohort of those with diabetes (10.6 ± 3.2 m/sec) was significantly greater than those without diabetes (8.6 ± 2.6 m/sec; $p<0.0001$).

The inverse relationship between the estimated glomerular filtration rate (eGFR) and aortic PWV is depicted in Figure 4 ($p<0.001$). This relationship of eGFR to aortic PWV was similar in sub-cohort of subjects who underwent GFR measurement with ^{125}I-iothalamate (1 of 3 participants had this performed; data not shown). Each unadjusted 10 mL/min/1.73m^2 decrement in eGFR was associated with an average increase in aortic PWV of 0.4 m/sec.

Table 2 displays the results of univariable regression of demographic, hemodynamic and laboratory data of our participants on aortic PWV shown three ways. The first group of columns regresses the unadjusted PWV on each independent variable individually. The second group of columns regresses the waist circumference adjusted PWV on the independent variables. The data for the third group of columns was derived by first

performing a regression of the adjusted PWV on the mean arterial pressure and computing the residuals from that regression. Then those residuals were then regressed on each of the other independent variables. The data show the expected relationships of age, blood pressure and diabetes to PWV. In addition, the more novel findings of higher PWV in those of Black race, and the increase in PWV with declining kidney function (and factors associated with reduced kidney function such as increasing phosphorous level and lower hemoglobin level) are also noted.

Table 3 shows the results of the multivariable linear regression. Age, kidney function decrement, serum glucose concentration, Black race, waist circumference, mean arterial pressure, male gender and diabetes had independent and significant associations with aortic PWV. Whereas no distinction based on gender was present prior to waist circumference adjustment, the post-adjustment results produced the significant association with male gender.

Discussion

We performed aortic PWV measurements on a population of 2564 participants recruited specifically with impaired kidney function but not receiving chronic dialysis, of whom approximately one-half were diabetic. Consistent with studies in dialysis patients and other populations, we found that aortic PWV was higher with age, blood pressure and the presence of diabetes. Our investigation notes that in addition to these factors the participant's blood glucose level (irrespective of diabetes presence), estimated kidney function, male gender and African-American ethnicity are independently associated with the aortic PWV value. Our study adds to the literature because it examined a large unique cohort specifically recruited because they have CKD, a patient population hitherto infrequently studied. The large sample size lends robustness to the findings. In addition the reliability of the measurements when done by different operators has been validated in this CKD population (17) supporting the validity of our findings. Other population studies of aortic PWV reported age-associated values similar to those we observed (1;18).

Our concern over waist circumference and its effects on the distance measurement are shared by others. In one study the authors used the carotid to femoral transit time statistically adjusted for height to estimate aortic PWV (10). The increasing prevalence of metabolic syndrome in CKD and the emerging role of obesity in the loss of kidney function indicate that the effect of waist circumference on carotid-femoral distance measurement techniques will need to adjust for this. Despite adjustment, waist circumference remained an independent and statistically significant predictor of PWV, in CKD (19).

The CRIC study was undertaken to enroll a longitudinal CKD cohort that would be ethnically diverse, spanning the ages of 21–74 with approximately 50% of its participants with diabetes to be generalizable to the clinical populations in practice settings (12). The recognition that reduced eGFR is related strongly to CVD morbidity and mortality has stimulated an ongoing search for biologic markers beyond traditional Framingham risk factors since these explain some but not all of the extra CVD burden in CKD (20;21) Thus, the pursuit of non-traditional factors like the determination of aortic PWV may help inform a portion of this challenge. The experience in ESRD suggests strongly that the aortic PWV is an important determinant of survival (7). Aortic PWV determinations have contributed to the epidemiology of CVD outcomes in otherwise healthy elderly people (4), diabetics (5) and those with hypertension (6). However, the influence of PWV on kidney as well as cardiovascular outcomes, and the determinants of aortic PWV in CKD patients not receiving dialysis, is less well studied.

Mourad and colleagues evaluated 1290 subjects, a mixed group composed of those with normal and impaired kidney function, and observed that those with the lowest tertile of kidney function showed an inverse relationship between creatinine clearance and aortic PWV (11). The work of Wang and colleagues in 102 subjects with an eGFR ranging across all 5 stages of CKD also suggested increasing aortic PWV as renal function declined (22). However, Hermans and colleagues in the setting of the Hoorn study examined the relationship between aortic PWV and the degree of kidney function and did not find that reduced renal function independently predicted central artery stiffness (10). Their study was weighted by 755 subjects with stages 2–3 CKD (mean eGFR of 60.6 mL/min/1.73 m^2). They did note an association of PWV with urine albumin to creatinine ratio even after adjustment for age, gender and mean arterial pressure. Our study examined a larger, more ethnically diverse cohort with greater impairment renal function (mean eGFR of 40.7 mL/min/1.73m^2). Our degree of proteinuria was numerically greater, and though univariable regression showed a relationship to PWV this disappeared in the multivariable regression analysis. Our results are in agreement with a study in Japan that followed 71 patients with CKD onto dialysis noting little change in aortic PWV as subjects transitioned onto dialysis (23).

Our data confirm the findings of Chaturvedi who reported higher aortic PWV in those of African descent without CKD and extends these findings to participants with CKD (24). Our data showing the relationship between glucose level and PWV also support the findings of the population-based Hoorn study (25).

Several reasons can be advanced for the progressive stiffness of the aorta as eGFR declines. Accumulation of advanced glycation end-products affecting vessel wall matrix and increase stiffness occurs in both diabetes and in kidney failure and may be related to the glucose findings we report (26;27). Vascular calcification promotes arterial stiffness and occurs in CKD as a result of disordered calcium, phosphorous and vitamin D metabolism, secondary hyperparathyroidism and changes in factors such as fibroblast growth factor 23 and fetuin A (28). Our findings with respect to divalent ion metabolism support this, but failed to show an independent effect since the changes in these variables are known to be strongly related to kidney function. Patients with decreased renal function also demonstrate signs of inflammation, with elevated levels of pro-inflammatory cytokines (29). Several studies show a relation between chronic inflammation, loss of vascular compliance and subclinical atherosclerosis in CKD (30;31). Cytokines affect endothelial function (32) and vascular remodeling (33). TGF-β, a pro-fibrotic cytokine stimulates the synthesis of the vasoconstrictor agent endothelin-1 (34), inhibits the production of nitric oxide (35) and increases renin secretion (36). These inflammatory cytokines are the subject of other CRIC ancillary studies and data regarding their levels in CRIC are still forthcoming.

Important limitations to our study include the distance measurement technique, the loss of data in which subject habitus (obesity) and other factors were not conducive to obtaining successful tracings and the absence of a normal control population. Those in whom we could not obtain suitable PWV readings were different [Table 1] from those with successful measurements which limits the generalizability of our data in CKD patients. The majority of participants in the CRIC study are on multiple antihypertensive medications, and the number of classes of BP medications prescribed was associated with higher mean PWV [Table 2]. The principal effects of antihypertensive drugs on PWV may be mediated through reduction in MAP rather than to non-blood pressure mediated alterations in large artery stiffness (37) and as shown in Table 3 the association between number of BP meds and PWV was not significant in multivariable regression [p=0.213]. Due to the cross sectional nature of our data we cannot infer directionality in the relationship of eGFR and PWV. It may be that reductions in eGFR lead to increases in PWV, or it may be vice versa, in that increases in

PWV may contribute to reductions in eGFR. The longitudinal nature of CRIC, and the use of techniques (e.g. marginal structural models) as longitudinal data accumulates, may inform further the relationship between these variables.

In summary our findings in this large, diverse and unique CKD population show independent associations of age, kidney function, blood glucose concentrations, Black race, blood pressure, male gender and diabetes with aortic PWV. These are important associations in a group with such exceptional CVD burden and we anticipate that they will contribute to the development and pursuit of intervention strategies aimed at reducing both the cardiovascular burden and further kidney function loss in the CKD population which may be mediated substantially through increased aortic stiffness. We anticipate longitudinal data from our and other studies to pursue further the import of these findings.

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Reference List

1. Willum-Hansen T, Staessen JA, Torp-Pedersen C, Rasmussen S, Thijs L, Ibsen H, et al. Prognostic value of aortic PWV as index of arterial stiffness in the general population. Circulation. 2006; 113(5):664–670. [PubMed: 16461839]
2. Bramwell JC, Hill AV. The velocity of the pulse wave in man. Proc Soc Lond (Biol). 1922; 93:298–306.
3. Bramwell JC, Hill A. Velocity of transmission of the pulse wave and elasticity of arteries. Lancet. 1922; i:891–892.
4. Sutton-Tyrrell K, Najjar SS, Boudreau RM, Venkitachalam L, Kupelian V, Simonsick EM, et al. Elevated aortic PWV, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. Circulation. 2005; 111(25):3384–3390. [PubMed: 15967850]
5. Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G, Gosling RG. Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: an integrated index of vascular function? Circulation. 2002; 106(16):2085–2090. [PubMed: 12379578]
6. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, et al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. Hypertension. 2001; 37(5):1236–1241. [PubMed: 11358934]
7. Guerin AP, Blacher J, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness attenuation on survival of patients in end-stage renal failure. Circulation. 2001; 103(7):987–992. [PubMed: 11181474]
8. Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness on survival in end-stage renal disease. Circulation. 1999; 99(18):2434–2439. [PubMed: 10318666]
9. O'Rourke MF, Mancia G. Arterial stiffness. J Hypertens. 1999; 17(1):1–4. [PubMed: 10100086]
10. Hermans MM, Henry R, Dekker JM, Kooman JP, Kostense PJ, Nijpels G, et al. Estimated glomerular filtration rate and urinary albumin excretion are independently associated with greater arterial stiffness: the Hoorn Study. J Am Soc Nephrol. 2007; 18(6):1942–1952. [PubMed: 17460143]
11. Mourad JJ, Pannier B, Blacher J, Rudnichi A, Benetos A, London GM, et al. Creatinine clearance, PWV, carotid compliance and essential hypertension. Kidney Int. 2001; 59(5):1834–1841. [PubMed: 11318954]

12. Feldman HI, Appel LJ, Chertow GM, Cifelli D, Cizman B, Daugirdas J, et al. The Chronic Renal Insufficiency Cohort (CRIC) Study: Design and Methods. J Am Soc Nephrol. 2003; 14(7 Supple 2):S148–S153. [PubMed: 12819321]
13. Perloff D, Grim C, Flack J, Frohlich ED, Hill M, McDonald M, et al. Human blood pressure determination by sphygmomanometry. Circulation. 1993; 88:2460–2470. [PubMed: 8222141]
14. Deloach SS, Townsend RR. Vascular stiffness: Its measurement and significance for epidemiologic and outcome studies. CJASN. 2008; 3(1):184–192. [PubMed: 18178784]
15. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006; 145(4):247–254. [PubMed: 16908915]
16. Robins JM, Rotnitzky A, Zhao L-P. Analysis of semiparametric regression models for repeated outcomes in the presence of missing data. Journal of the American Statistical Association. 1995; 90:106–121.
17. Wimmer NJ, Townsend RR, Joffee MM, Lash JP, Go AS. CRIC Study Investigators. Correlation between PWV and other measures of arterial stiffness in chronic kidney disease. Clinical Nephrology. 2007; 68(3):133–143. [PubMed: 17915615]
18. Shokawa T, Imazu M, Yamamoto H, Toyofuku M, Tasaki N, Okimoto T, et al. PWV predicts cardiovascular mortality: findings from the Hawaii-Los Angeles-Hiroshima study. Circ J. 2005; 69(3):259–264. [PubMed: 15731528]
19. Safar ME, Czernichow S, Blacher J. Obesity, arterial stiffness, and cardiovascular risk. J Am Soc Nephrol. 2006; 17(4 Suppl 2):S109–S111. [PubMed: 16565231]
20. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004; 351(13):1296–1305. [PubMed: 15385656]
21. Collins AJ, Li S, Gilbertson DT, Liu J, Chen SC, Herzog CA. Chronic kidney disease and cardiovascular disease in the Medicare population. Kidney Int Suppl. 2003; (87):S24–S31. [PubMed: 14531770]
22. Wang MC, Tsai WC, Chen JY, Huang JJ. Stepwise increase in arterial stiffness corresponding with the stages of chronic kidney disease. Am J Kidney Dis. 2005; 45(3):494–501. [PubMed: 15754271]
23. Shinohara K, Shoji T, Tsujimoto Y, Kimoto E, Tahara H, Koyama H, et al. Arterial stiffness in predialysis patients with uremia. Kidney Int. 2004; 65(3):936–943. [PubMed: 14871413]
24. Chaturvedi N, Bulpitt CJ, Leggetter S, Schiff R, Nihoyannopoulos P, Strain WD, et al. Ethnic differences in vascular stiffness and relations to hypertensive target organ damage. J Hypertens. 2004; 22(9):1731–1737. [PubMed: 15311101]
25. Henry RM, Kostense PJ, Spijkerman AM, Dekker JM, Nijpels G, Heine RJ, et al. Arterial stiffness increases with deteriorating glucose tolerance status: the Hoorn Study. Circulation. 2003; 107(16): 2089–2095. [PubMed: 12695300]
26. Ueno H, Koyama H, Tanaka S, Fukumoto S, Shinohara K, Shoji T, et al. Skin autofluorescence, a marker for advanced glycation end product accumulation, is associated with arterial stiffness in patients with end-stage renal disease. Metabolism. 2008; 57(10):1452–1457. [PubMed: 18803952]
27. Zieman SJ, Kass DA. Advanced glycation endproduct crosslinking in the cardiovascular system: potential therapeutic target for cardiovascular disease. Drugs. 2004; 64(5):459–470. [PubMed: 14977384]
28. Townsend RR. Vascular compliance and arterial calcification: impact on blood pressure reduction. Curr Opin Nephrol Hypertens. 2008; 17(1):93–98. [PubMed: 18090677]
29. Bolton CH, Downs LG, Victory JG, Dwight JF, Tomson CR, Mackness MI, et al. Endothelial dysfunction in chronic renal failure: roles of lipoprotein oxidation and pro-inflammatory cytokines. Nephrol Dial Transplant. 2001; 16(6):1189–1197. [PubMed: 11390719]
30. London GM, Marchais SJ, Guerin AP, Metivier F, Adda H, Pannier B. Inflammation, arteriosclerosis, and cardiovascular therapy in hemodialysis patients. Kidney Int Suppl. 2003; 84:S88–S93. [PubMed: 12694318]
31. Porazko T, Kuzniar J, Kusztal M, Kuzniar TJ, Weyde W, Kuriata-Kordek M, et al. IL-18 is involved in vascular injury in end-stage renal disease patients. Nephrol Dial Transplant. 2008

32. Nawroth PP, Stern DM. Modulation of endothelial cell hemostatic properties by tumor necrosis factor. J Exp Med. 1986; 163(3):740–745. [PubMed: 3753996]
33. Leibovich SJ, Polverini PJ, Shepard HM, Wiseman DM, Shively V, Nuseir N. Macrophage-induced angiogenesis is mediated by tumour necrosis factor-alpha. Nature. 1987; 329(6140):630–632. [PubMed: 2443857]
34. Kurihara H, Yoshizumi M, Sugiyama T, Takaku F, Yanagisawa M, Masaki T, et al. Transforming growth factor-beta stimulates the expression of endothelin mRNA by vascular endothelial cells. Biochem Biophys Res Commun. 1989; 159(3):1435–1440. [PubMed: 2649101]
35. Roberts AB, Vodovotz Y, Roche NS, Sporn MB, Nathan CF. Role of nitric oxide in antagonistic effects of transforming growth factor-beta and interleukin-1 beta on the beating rate of cultured cardiac myocytes. Mol Endocrinol. 1992; 6(11):1921–1930. [PubMed: 1282674]
36. Antonipillai I, Le TH, Soceneantu L, Horton R. Transforming growth factor-beta is a renin secretagogue at picomolar concentrations. Am J Physiol. 1993; 265(4 Pt 2):F537–F541. [PubMed: 8238382]
37. O'Rourke MF, Hashimoto J. Arterial stiffness: a modifiable cardiovascular risk factor? J Cardiopulm Rehabil Prev. 2008; 28(4):225–237. [PubMed: 18628652]

APPENDIX

Adjustment for waist circumference

An adjustment to account for possible waist-induced error in the sternal notch to femoral artery distance (sternal notch-femoral) was developed by focusing on adjusting the sternal notch-femoral distance and then using this distance to adjust the aortic PWV. A linear regression was run with the distance parameter as the outcome on height, waist, and the height*waist interaction. For each subject, the residual from the estimated regression of aortic PWV on these variables was calculated. This regression was run separately for men and women. Next, for each individual a reference waist was calculated based on the measured height and a reference value of 0.46 for the waist to height ratio (1). This reference waist value was combined with the regression coefficients to generate a predicted value for the distal distance, which is added to the residual to get an adjusted value:

$$\text{DTADJ}=\beta_0+\beta_1{}^*\text{Height}+\beta_2{}^*\text{RefWaist}+\beta_3{}^*\text{Height}{}^*\text{RefWaist}+\text{Residual};$$

The gender-specific beta coefficients and the residual are come from the regression estimates. The regression coefficients for men were 1.903 for β_1, 3.413 for β_2 and −0.005 for β_3. For women the regression coefficients were 4.945 for β_1, 8.932 for β_2 and −0.039 for β_3.

The adjusted distance variable (DTADJ) in turn is used to calculate an adjusted pulse wave velocity (PWV_ADJ):

$$PWV\_ADJ=PWV_{measured}{}^*\left(\frac{DTADJ}{DT\_DIST_{measured}}\right)$$

(Performed using SAS v 9.1, SAS Institute, Cary, NC).

Examples: A man 174.4 cm tall with a waist circumference of 120.5 cm had a sternal notch-femoral distance of 645 mm and an unadjusted aortic PWV of 14.1 m/sec. After applying the regression his sternal notch-femoral distance was reduced to 533 mm and his adjusted aortic PWV was 11.7 m/sec. A man 175.2 cm tall with a waist circumference of 100.5 cm and a sternal notch-femoral distance of 600 mm had an unadjusted aortic PWV of 5.6 m/sec.

Following regression his sternal-notch distance was adjusted to 545 mm and his adjusted aortic PWV was 5.1 m/sec.

Appendix Reference

1. Swiderski, SJ. Thesis (M.S.). Air Force Institute of Technology; 2005 [accessed March 6th 2009]. Fit-To-Fight: Waist vs Waist/Height Measurements to Determine an Individual's Fitness Level - A Study in Statistical Regression and Analysis. Available at: http://www.ntis.gov/search/index.aspx

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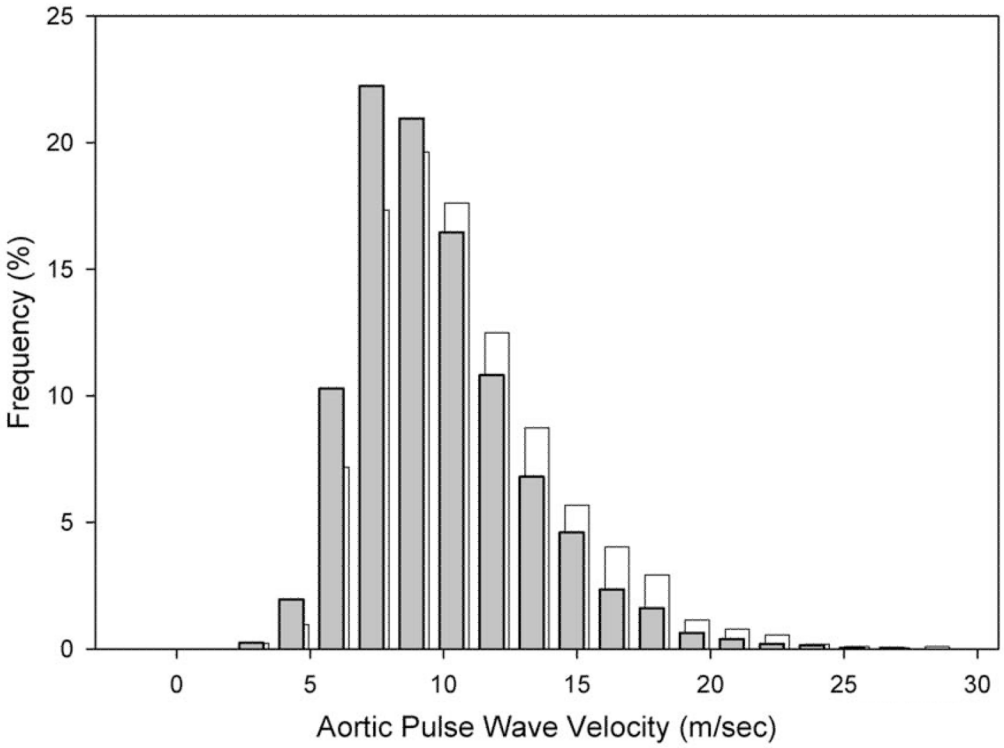

FIGURE 1.

Histogram depicting frequency of ***adjusted*** (for waist circumference) aortic PWV (PWV) in shaded bars (foreground) grouped in units of 1.5 meters/second in the CKD population of the CRIC study. The distribution of the ***unadjusted*** aortic PWV is shown in open bars (background) for reference.

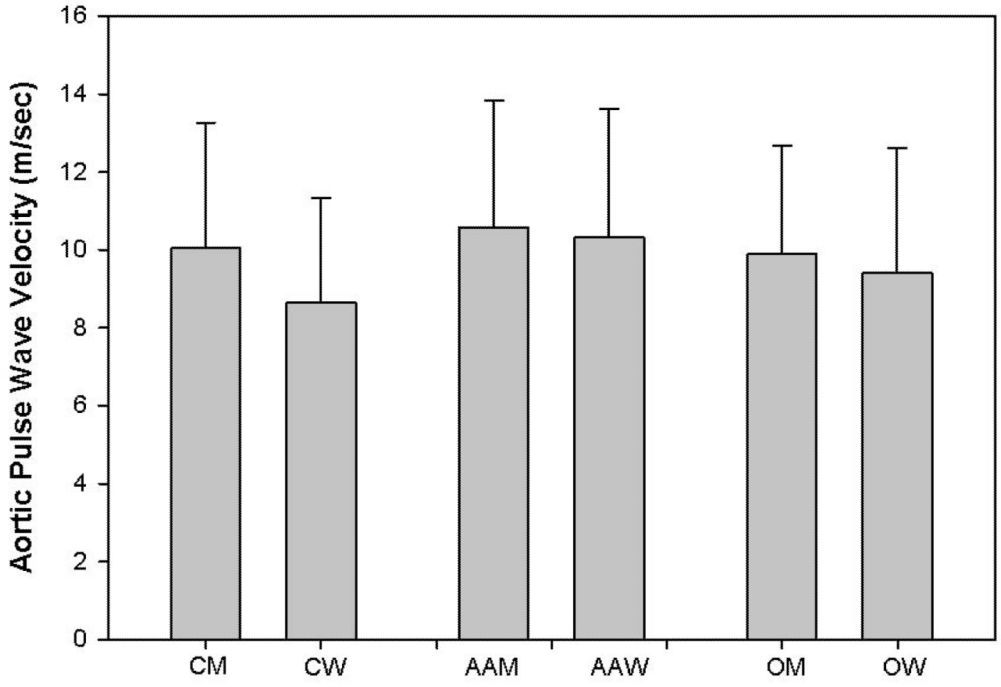

FIGURE 2.
Mean ± S.D. of aortic PWV by race (C=Caucasian; AA=African American/Black; O=Other) and gender (M=Men; W=Women).

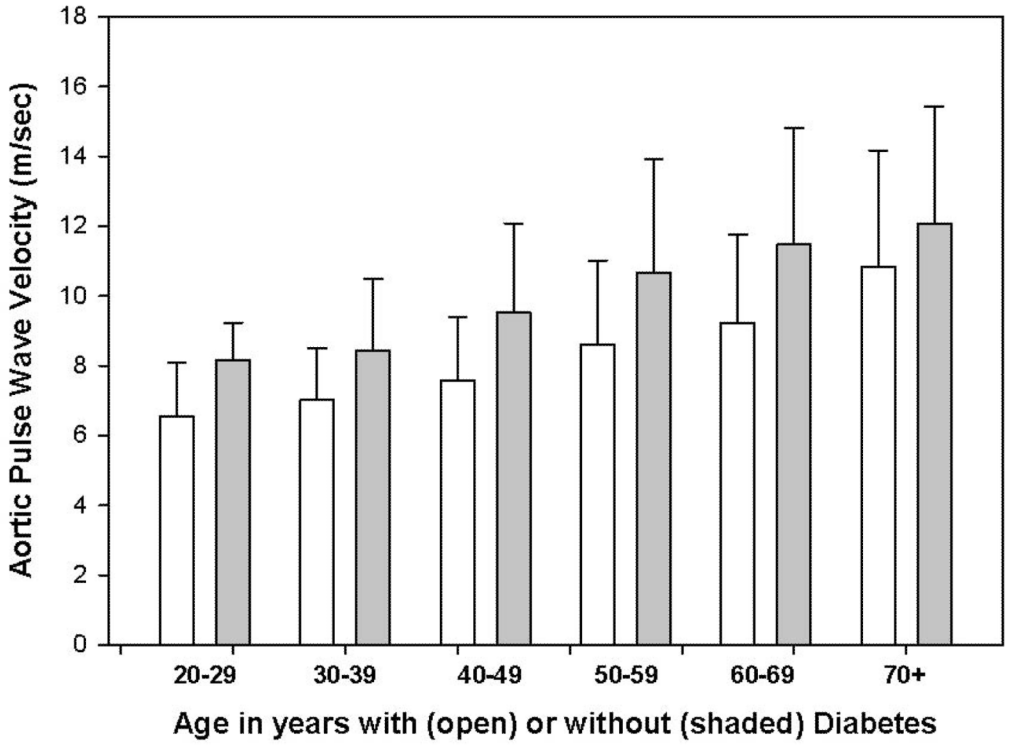

FIGURE 3.
Mean ± S.D. aortic PWV plotted against age in 10 year increments separated within each 10 year interval by the absence (open bar) or presence (shaded bar) of diabetes.

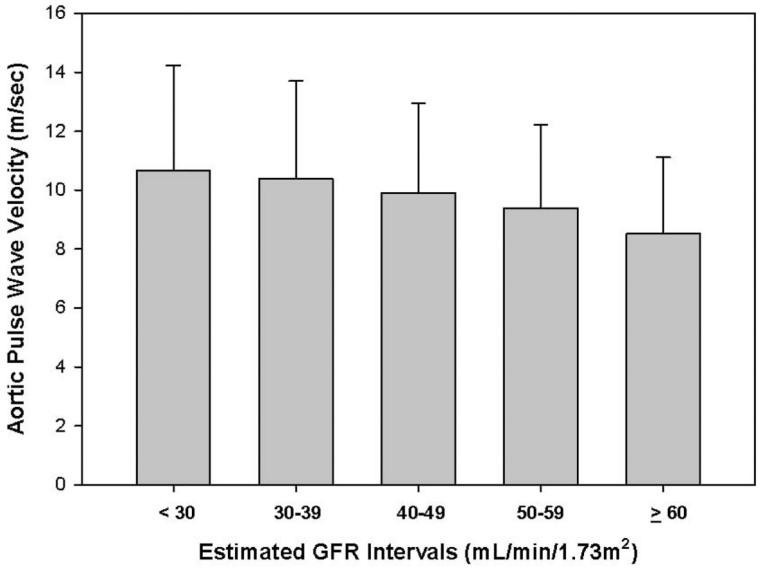

FIGURE 4.

Mean ± S.D. aortic PWV plotted against estimated glomerular filtration rate (eGFR) in 10 mL/min/1.73m^2 increments.

Table 1

Demographic and biochemical profile of PWV cohort

	ALL ELIGIBLE N = 3272	WITHOUT PWV N = 716	WITH PWV N = 2564	P
Male	55.1%	48.5%	57.1%	<.0001
Race				
Black	42%	48.9%	40%	<.0001
Other	9.1%	6%	9.9%	.
White	49.1%	45.1%	50.1%	.
Diabetes at baseline (%=Yes)	46.8%	53.9%	44.9%	<.0001
AGE (years)	60.64 (10.81)	60.5 (10.37)	60.69 (10.99)	0.6932
eGFR (mL/min/1.73m^2)	39.74 (16.02)	37.42 (16.02)	40.68 (15.92)	<.0001
Height (cm)	168.75 (9.49)	167.19 (9.68)	169.36 (9.35)	<.0001
Weight (kg)	91.71 (23.52)	99.45 (27.71)	88.64 (20.87)	<.0001
Body Mass Index (kg/m^2)	32.14 (7.91)	35.51 (9.73)	30.83 (6.64)	<.0001
Systolic BP (mmHg)	127.77 (22.04)	129.1 (22.4)	127.22 (21.87)	0.0613
Diastolic BP (mmHg)	69.86 (12.8)	69.82 (13.11)	69.88 (12.67)	0.9205
Pulse Pressure (mm Hg)	57.89 (19.67)	59.23 (20.09)	57.34 (19.48)	0.0358
Mean Arterial Pressure (mm Hg)	89.13 (13.59)	89.43 (13.79)	89 (13.5)	0.4795
Heart Rate (beats/minute)	67.98 (11.17)	68.56 (10.93)	67.73 (11.27)	0.1045
Hemoglobin (g/dL)	12.67 (1.78)	12.43 (1.81)	12.77 (1.76)	<.0001
Glucose (mg/dL)	113.97 (48.47)	118.2 (51.63)	112.24 (47.03)	0.0075
Creatinine (mg/dL)	2.24 (1.54)	2.38 (1.61)	2.18 (1.51)	0.0055
Triglycerides (mg/dL)	148.74 (105.98)	152.37 (90.44)	147.3 (111.56)	0.3167
Low-density Lipoprotein (mg/dL)	96.97 (33.89)	93.09 (36.1)	98.51 (32.86)	0.0008
High-density Lipoprotein (mg/dL)	47.51 (15.99)	46.02 (16.04)	48.11 (15.94)	0.0063
Calcium (mg/dL)	9.33 (0.52)	9.29 (0.57)	9.34 (0.5)	0.0253
*Phosphate (mg/dL)	3.7 (0.66)	3.81 (0.66)	3.67 (0.65)	<.0001
*Calcium Phosphate Product (Ca*Phos)	33.95 (6.24)	35.05 (6.16)	33.64 (6.23)	<.0001
*Parathyroid Hormone (pg/mL)	73.16 (67.64)	81.43 (75.89)	70.81 (64.94)	0.0003
*Urine Protein (g/day)	1 (2.19)	1.21 (2.67)	0.94 (2.03)	0.0038
*Urine Albumin g/day	0.64 (1.54)	0.77 (1.75)	0.6 (1.47)	0.0114
*Hemoglobin A_1C (%)	6.61 (1.54)	6.77 (1.64)	6.56 (1.51)	0.0020
*Uric Acid (mg/dL)	7.37 (1.9)	7.74 (1.92)	7.27 (1.89)	<.0001

Table 2

Univariable linear regression

Variable	Unadjusted PWV			PWV adjusted for waist circumference			Residual PWVadjusted for MAP		
	Reg coeff(SE)	**R-sq**	**p-value**	**Reg coeff(SE)**	**R-sq**	**p-value**	**Reg coeff(SE)**	**R-sq**	**p-value**
Female (Yes)	−0.320 (0.14)	0.00	0.0259	−0.526 (0.13)	0.01	<.0001	−0.402 (0.12)	0.00	<.01
Black Race	1.105 (0.15)	0.02	<.0001	0.856 (0.13)	0.02	<.0001	0.569 (0.13)	0.01	<.01
Other Race	0.327 (0.24)	0.02	0.1805	0.238 (0.22)	0.02	0.2714	0.141 (0.21)	0.01	0.51
Diabetes (Yes)	2.645 (0.13)	0.13	<.0001	2.045 (0.12)	0.11	<.0001	2.026 (0.12)	0.11	<.01
Age (10 year interval)	1.238 (0.06)	0.14	<.0001	1.008 (0.05)	0.13	<.0001	1.052 (0.05)	0.14	<.01
eGFR (10mL/min/1.73m^2)	−0.463 (0.04)	0.04	<.0001	−0.384 (0.04)	0.04	<.0001	−0.380 (0.04)	0.04	<.01
Height (cm)	−0.011 (0.01)	0.00	0.1353	0.010 (0.01)	0.00	0.1441	0.005 (0.01)	0.00	0.42
Weight (kg)	0.028 (0.00)	0.03	<.0001	0.007 (0.00)	0.00	0.0174	0.005 (0.00)	0.00	0.08
BMI (kg/m^2)	0.111 (0.01)	0.04	<.0001	0.019 (0.01)	0.00	0.0438	0.015 (0.01)	0.00	0.09
Waist circumference (cm)	0.058 (0.00)	0.07	<.0001	0.014 (0.00)	0.01	0.0002	0.014 (0.00)	0.01	<.01
SBP (10 mm Hg)	0.596 (0.03)	0.14	<.0001	0.521 (0.03)	0.14	<.0001	X	X	X
DBP (mm Hg)	−0.016 (0.01)	0.00	0.0047	−0.008 (0.00)	0.00	0.0959	X	X	X
MAP (mm Hg)	X	X	X	0.041 (0.00)	0.03	<.01	−0.000 (0.00)	0.00	1.00
Pulse Pressure (mm Hg)	0.084 (0.00)	0.21	<.0001	0.071 (0.00)	0.20	<.0001	0.060 (0.00)	0.15	<.01
Heart Rate (beats/minute)	0.024 (0.01)	0.01	0.0001	0.014 (0.01)	0.00	0.0104	0.010 (0.01)	0.00	0.08
Number of BP medications	0.786 (0.05)	0.08	<.0001	0.614 (0.05)	0.07	<.0001	0.559 (0.05)	0.06	<.0001
Hemoglobin (g/dL)	−0.345 (0.04)	0.03	<.0001	−0.247 (0.04)	0.02	<.0001	−0.254 (0.04)	0.02	<.01
Glucose (10 mg/dl)	0.162 (0.01)	0.05	<.0001	0.130 (0.01)	0.05	<.0001	0.121 (0.01)	0.04	<.01
Creatinine (mg/dL)	0.733 (0.11)	0.02	<.0001	0.686 (0.10)	0.02	<.0001	0.578 (0.10)	0.01	<.01
Triglycerides (10 mg/dl)	0.017 (0.01)	0.00	0.0069	0.011 (0.01)	0.00	0.0588	0.010 (0.01)	0.00	0.06
LDL (10 mg/dL)	−0.062 (0.02)	0.00	0.0044	−0.049 (0.02)	0.00	0.0106	−0.068 (0.02)	0.01	<.01
HDL (mg/dL)	−0.022 (0.00)	0.01	<.0001	−0.014 (0.00)	0.01	0.0005	−0.013 (0.00)	0.00	<.01
Calcium (mg/dL)	−0.298 (0.14)	0.00	0.0356	−0.259 (0.12)	0.00	0.0374	−0.181 (0.12)	0.00	0.14
*Phosphate (mg/dL)	0.603 (0.11)	0.01	<.0001	0.402 (0.10)	0.01	<.0001	0.416 (0.10)	0.01	<.01
*Calcium*Phosphate Product	0.052 (0.01)	0.01	<.0001	0.033 (0.01)	0.00	0.0013	0.036 (0.01)	0.01	<.01
*PTH (pg/mL)	0.008 (0.00)	0.02	<.0001	0.007 (0.00)	0.02	<.0001	0.006 (0.00)	0.01	<.01
*Urine Protein (g/day)	0.178 (0.04)	0.01	<.0001	0.142 (0.03)	0.01	<.0001	0.099 (0.03)	0.00	<.01

Variable	Unadjusted PWV			PWV adjusted for waist circumference			Residual PWVadjusted for MAP		
	Reg coeff(SE)	R-sq	p-value	Reg coeff(SE)	R-sq	p-value	Reg coeff(SE)	R-sq	p-value
*Urine Albumin (g/day)	0.240 (0.05)	0.01	<.0001	0.189 (0.04)	0.01	<.0001	0.124 (0.04)	0.00	<.01
*Hemoglobin A1C (%)	0.668 (0.05)	0.08	<.0001	0.530 (0.04)	0.07	<.0001	0.502 (0.04)	0.06	<.01
*Uric Acid (mg/dL)	0.254 (0.04)	0.02	<.0001	0.169 (0.03)	0.01	<.0001	0.148 (0.03)	0.01	<.01

Table 3

Multivariable linear regressions for selected variables and aortic PWV*

	Regression 1		Regression 2	
VARIABLE	**As-measured PWV Estimate (SE)**	**p-value**	**Adjusted PWV Estimate (SE)**	**p-value**
Age (per 10 year interval)	1.09 (0.06)	<.0001	0.95 (0.05)	<.0001
eGFR (per 10mL/min/1.73m^2)	−0.27 (0.04)	<.0001	−0.23 (0.04)	<.0001
Glucose (per 10 mg/dl)	0.04 (0.01)	0.0020	0.04 (0.01)	0.0017
Race Black vs. White	0.41 (0.14)	0.0026	0.39 (0.12)	0.0016
Race Other vs. White	0.32 (0.25)	0.2040	0.16 (0.23)	0.4749
MAP (per 1 mm Hg)	0.05 (0.00)	<.0001	0.04 (0.00)	<.0001
Waist Circumference (per 1 cm)	0.03 (0.00)	<.0001	−0.01 (0.00)	0.0007
Diabetes (Yes vs. No)	1.67 (0.14)	<.0001	1.51 (0.13)	<.0001
Female (vs. Male)	−0.04 (0.12)	0.7534	−0.31 (0.11)	0.0054