1.4: PULSE WAVE VELOCITY AND INCIDENT HEART FAILURE IN CHRONIC KIDNEY DISEASE

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We have undertaken an individual participant data (IPD) meta-analysis of carotid-femoral pulse wave velocity (cf-PWV) with all cause mortality, CHD, stroke and combined CVD events using data from 14 studies (2 unpublished). Unlike a previous report, which only used published data, we were able to undertake standardised analyses with and without adjustment for cardiovascular risk factors and test, a priori, for potential interactions between cf-PWV and age group, gender, diabetic or hypertensive status on the various outcomes. We calculated discrimination statistics for models with and without cf-PWV, specifically focussing on individuals at intermediate (25-75th percentile) risk of CVD after adjustment for conventional Framingham risk factors. Fourteen studies provided data on 16,358 subjects with 1700 combined CVD events. We derived within study z-scores of log transformed cf-PWV (pooled SD = 3.3m/s). Risk of all outcomes was associated with increased cf-PWV (Table 1) and was linear across the range of cf-PWV values with no evidence of interaction except for age group (see Figure, p-value for trend = 0.0095). The additional benefit of measuring cf-PWV to reclassify intermediate risk individuals was assessed using the net reclassification index. 18.6% (p<0.001) and 22.4% (p<0.001) were appropriately reclassified into higher or lower quartiles of risk for CHD and stroke outcomes respectively. These findings highlight the added value of cf-PWV as an independent predictor, over and above existing risk factors, in intermediate risk groups and for younger subjects. Assessment of PWV should better identify high risk populations that may benefit from more aggressive risk factor management.

Table 1: Cox Proportional Hazards Models for cf-PWV as Predictor of an Outcome Event During the Follow-Up Period.

Outcome	Model 1*		Model 2^{+}	
	HR (95% CI)	p-value	HR (95% CI)	p-value
All cause mortality	1.21 (1.16, 1.27)	<0.001	1.16 (1.11, 1.23)	<0.001
CHD	1.33 (1.19, 1.48)	<0.001	1.22 (1.09, 1.36)	<0.001
CVD	1.42 (1.27, 1.59)	<0.001	1.28 (1.16, 1.41)	<0.001
Stroke	1.52 (1.30, 1.78)	<0.001	1.25 (1.14, 1.39)	<0.001

*Hazard ratio per 1 SD of log-transformed cf-PWV adjusted for age and sex
$^{+}$ As model 1, further adjustment for Framingham risk factors (systolic blood pressure, cholesterol, HDL-cholesterol, smoking status, baseline diabetes and baseline hypertension, where available).
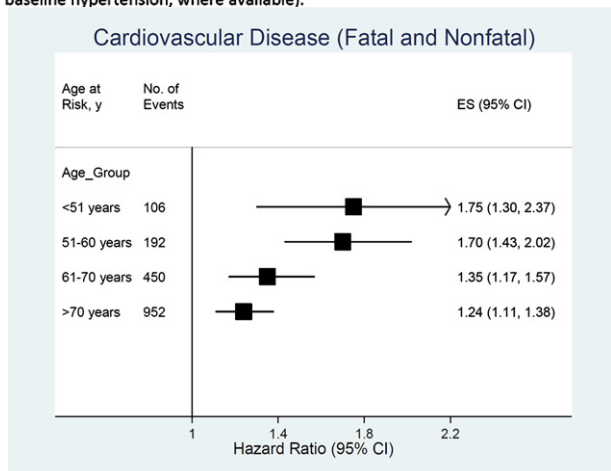

Figure: Pooled hazard ratios for cardiovascular disease for a one standard deviation increase in pulse wave velocity (log transformed) stratified by age group.

1.4

PULSE WAVE VELOCITY AND INCIDENT HEART FAILURE IN CHRONIC KIDNEY DISEASE

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Heart failure (HF) complicates chronic kidney disease (CKD) despite improving medical therapy for co-morbidities like hypertension. We hypothesized that vascular stiffness, (aortic pulse wave velocity [PWV]), predicts incident HF in well controlled CKD participants free of HF at enrollment. We performed aortic (i.e. carotid-femoral) PWV measurements (Sphygmocor) in 1889 participants enrolled in the multicenter Chronic Renal Insufficiency Cohort (CRIC) at their second year follow up visit and followed them prospectively (mean follow-up time of 1.4 years) for incident hospitalized HF events occurring before December 31, 2007 adjudicated by two independent Investigators. Mean age was 60 years, 44% women, 42% black, 6% Hispanic and 47% were Caucasian with mean(SD) blood pressure of 127(22)/70(13) mmHg (more than half of the participants were prescribed >3 antihypertensives) and a mean estimated glomerular filtration rate of 42.6 mL/min/1.73m2. Mean(SD) BMI was 31(6.6) kg/m2. Mean(SD) aortic PWV (adjusted for waist circumference) was 9.5(3.1) m/sec. There were 54 incident HF events. The unadjusted Cox proportional hazard ratio [95% CI] for incident HF for those with PWV >10m/s was 4.71 (2.59, 8.54; censored for deaths / withdrawals); adjusting for age, race, gender and mean arterial pressure it was 3.82[2.02,7.25]. We observed that for each 1 m/sec increase in aortic PWV there was a 11% (unadjusted) and 9% (after adjustment) increase in the hazard for HF.
In summary, aortic PWV independently predicted incident HF in CKD patients with well-controlled BP. Measures to better understand and improve PWV may compliment standard BP control to prevent HF in CKD.

1.5

AORTIC STIFFNESS IS INDEPENDENTLY ASSOCIATED WITH FATAL AND NON-FATAL CARDIOVASCULAR EVENTS IN CHRONIC KIDNEY DISEASE STAGE 2-5

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Objective: Chronic kidney disease (CKD) is characterized by a high cardiovascular risk. Subclinical damage to large arteries has been largely described in CKD and is mostly characterized by an increase in arterial stiffness and an outward remodeling of the carotid artery. However, the predictive value of arterial remodeling and stiffening for cardiovascular events and mortality is still debated in pre-dialysed CKD (stage 2-5).
Methods: 180 patients (mean age 59.6 ± 14 years) with CKD (mean mGFR 32 mL/min/1.73m^2) were included in this longitudinal study. Patients underwent a yearly check-up including arterial evaluation (carotid-femoral pulse wave velocity (SphygmoCor®), carotid thickness, diameter and stiffness (Art-Lab system®) and GFR measurement with the ^{51}Cr-EDTA clearance.
Results: During an average follow-up of 49 ± 16 months, 36 fatal or not fatal cardiovascular events occurred. In COX regression analyses, PWV was significantly associated with fatal and non fatal cardiovascular events (risk ratio for 1 SD 1.46 [1.04-2.04], P=0.02) independently of age, body mass index, proteinuria, measured glomerular filtration rate and mean blood pressure. By contrast carotid intima-media thickness and circumferential wall stress were not significantly associated with fatal and non fatal cardiovascular events.