NORTH AMERICAN ARTERY
Eighth Annual Meeting

ORAL ABSTRACTS

LEVELS OF INACTIVE MATRIX GLYCOPROTEIN ARE INCREASED IN HEART FAILURE AND ARE ASSOCIATED WITH LARGE ARTERY STIFFENING

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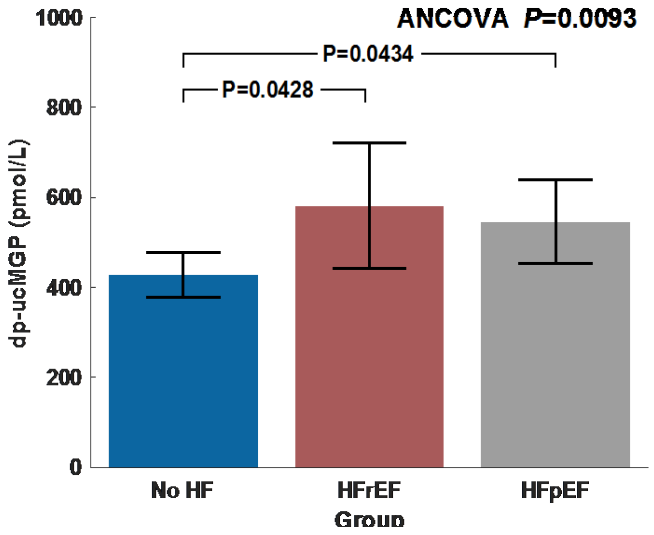
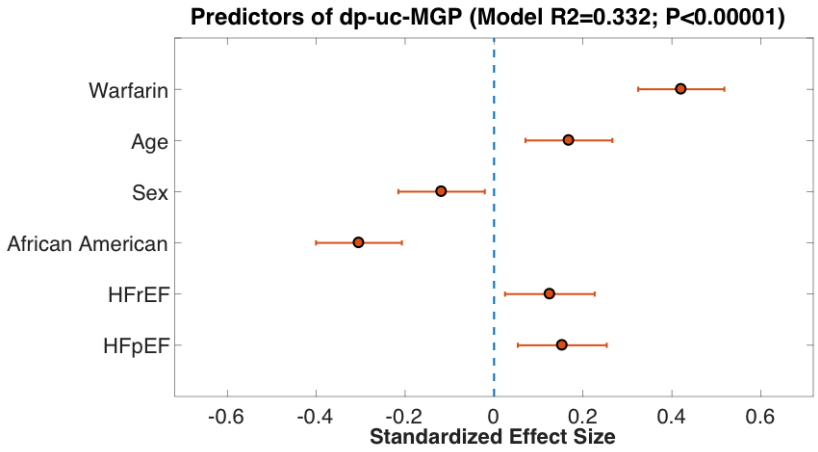
Objectives: Large artery stiffening is increased in heart failure and causes an excessive pulsatile load to the heart and to the microvasculature. Identifying pathways related to arterial stiffness may provide novel therapeutic targets to ameliorate arterial stiffness in heart failure. Matrix Gla-Protein (MGP) is a potent inhibitor of vascular calcification. Activation of MGP is Vitamin-K dependent. We aimed to compare the levels of inactive MGP (dp-ucMGP) in patients without HF, heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF) and to investigate the impact of Vitamin K levels in large artery stiffening.

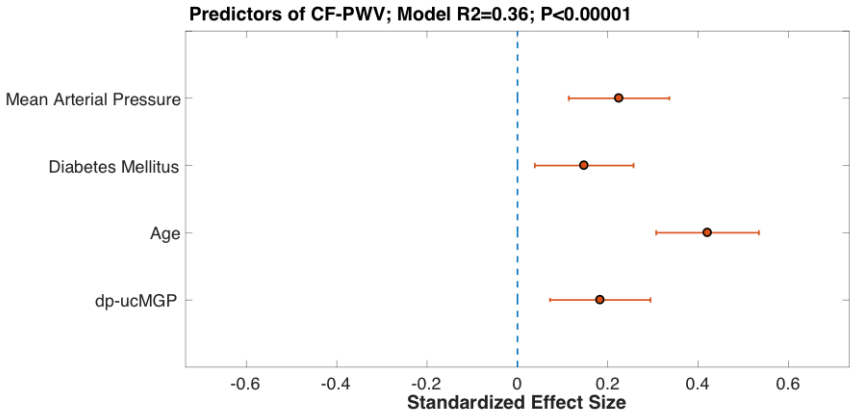
Methods: We enrolled 198 participants without HF, 52 with HFrEF and 96 with HFpEF. Carotid-femoral pulse wave velocity (CF-PWV) was measured with high-fidelity arterial tonometry (Sphygmocor Device). Dp-ucMGP levels were measured with ELISA (VitaK; The Netherlands).

Results: In analyses adjusted for age, gender. ethnicity. and warfarin use, dp-ucMGP levels were significantly greater in both HFrEF and HFpEF compared to controls (720, 639 pmol/L and 427 pmol/L, respectively; ANCOVA *P*=0.009). In multivariable analyses, independent predictors of higher dp-ucMGP levels included the presence of HFpEF or HFrEF, greater age, male gender, and African American ethnicity. Dp-ucMGP predicted CF-PWV (β= 0.17, *P*=0.01), even after adjustment for age, gender, ethnicity, mean arterial pressure, body mass index, a history of hypertension, CAD, diabetes mellitus, mean arterial pressure and warfarin use.

***Conclusions*:** Circulating dp-ucMGP, a marker of vascular vitamin K deficiency, is increased in HFpEF and HFrEF, independently of warfarin use, and is associated with a greater CF-PWV. A deficiency in Vitamin-K dependent activation of MGP, a potent inhibitor of arterial wall calcification, may contribute to large artery stiffening in heart failure. Vitamin K2 supplementation may represent a potential therapeutic strategy to reduce arterial stiffening in patients with HF.


ANCOVA P=0.0093
P=0.0434
P=0.0428
dp-ucMGP (pmol/L)
1000
800
600
400
200
0
No HF
HFrEF
HFpEF
Group


Predictors of dp-uc-MGP (Model R2=0.332; P<0.00001)
Warfarin
Age
Sex
African American
HFrEF
HFpEF
-0.6
-0.4
-0.2
0
0.2
0.4
0.6
Standardized Effect Size


Predictors of CF-PWV; Model R2=0.36; P<0.00001
Mean Arterial Pressure
Diabetes Mellitus
Age
dp-ucMGP
-0.6
-0.4
-0.2
0
0.2
0.4
0.6
Standardized Effect Size

ALTERATIONS IN NOCTURNAL SYSTOLIC BLOOD PRESSURE DIPPING IS ASSOCIATED WITH AORTIC STIFFNESS AND INFLAMMATION AMONG MIDDLE-AGED/OLDER ADULTS WITH OBESITY

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Background: Blood pressure (BP) normally decreases 10-20% at night during sleep. A nocturnal systolic BP decrease of ≤10% ('non-dipping') or a rise in nocturnal BP ('reverse dipping') is associated with increased cardiovascular disease (CVD) risk. However, the mechanisms that contribute to blunted or reverse BP dipping remain unclear. Aortic stiffness, measured by carotid-femoral pulse wave velocity (CFPWV), is an independent predictor of CVD events and is associated with reverse dipping in persons with hypertension. However, no studies have investigated this in middle-aged/older (MA/O) adults with obesity. We hypothesized that blunted and reverse nocturnal systolic BP dipping will be associated with elevated CFPWV in MA/O adults with obesity.

Methods: A total of 107 MA/O adults (40-75 yrs) who were obese (body mass index, BMI ≥ 30 kg/m^2) and had one additional CVD risk factor were analyzed in a retrospective cross-sectional study. CFPWV, 24-hour ABPM, and C-reactive protein (CRP) were measured.

Results: Normal BP dipping (n = 52), non-dipping (n = 43), reverse dipping (n = 5) and extreme dipping (n = 7) groups did not differ by sex, BMI, 24-hour heart rate, or daytime systolic BP, but reverse dippers were slightly older (p = 0.016). Reverse dippers demonstrated higher CFPWV (p = 0.009) compared with normal dippers (p = 0.002) and non-dippers (p = 0.011). After controlling for sex, BMI, BP, and anti-hypertensive medications, the difference in CFPWV between reverse dippers and normal dippers remained significant (p = 0.003), but was abolished after adjustment for age (p=0.196). Furthermore, reverse dippers had significantly elevated CRP compared with the other groups after adjusting for age, sex, BMI, BP and medications (p = 0.007).

Conclusion: These data suggest that alterations in nighttime BP dipping among MA/O adults with obesity are associated with elevated CVD risk perhaps in part to increased aortic stiffness and inflammation.

OBSTRUCTIVE SLEEP APNEA IS ASSOCIATED WITH ARTERIAL STIFFNESS AND PRE-ECLAMPSIA IN A HIGH-RISK PREGNANCY POPULATION

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Objective
To assess the association between obstructive sleep apnea (OSA) and both arterial stiffness and pre-eclampsia throughout pregnancy.

Methods
Women (n=181) with singleton high-risk pregnancies completed the Pittsburgh Sleep Quality Index (PQSI), Restless Leg Syndrome (RLS), and Epworth Sleepiness Scale sleep questionnaires at weeks 10^0-13^6, 21^0-24^6, and 32^0-35^6 gestation. Sleep disordered breathing (SDB; reported or witnessed snoring/hypopnea ≥3 times/week) and both soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PlGF) were evaluated. At 10^6-13^6 weeks and every four weeks thereafter, arterial stiffness and hemodynamics were assessed by applanation tonometry, including carotid-femoral pulse wave velocity (cfPWV), carotid-radial PWV (crPWV), augmentation index (AIx75), and time to wave reflection (T_{1R}).

Results
There were no associations between PSQI nor RLS scores and either arterial stiffness indices or pre-eclampsia. In the first, second, and third trimester, 27 (17%), 28 (17%), and 42 (27%) women, respectively, reported a positive Epworth score, whereas 13 (8%), 26 (15%), and 39 (24%) reported SDB. A minimum clinically important difference in Epworth scores (2 points) and a positive Epworth score (>10) were significantly associated with developing pre-eclampsia. SDB in the third trimester was also associated with pre-eclampsia (Table 1). cfPWV, crPWV, and AIx75 were higher, while T_{1R} was lower at all assessments prior to either positive Epworth scores or reported SDB in the second trimester. These indices were also significantly different in women who subsequently reported SDB in the third trimester (all $p<0.05$). Epworth scores were higher in both the second (6 vs. 9, $p<0.001$) and third trimester (6 vs. 9, $p=0.028$) in women with SDB. No differences in angiogenic markers were found.

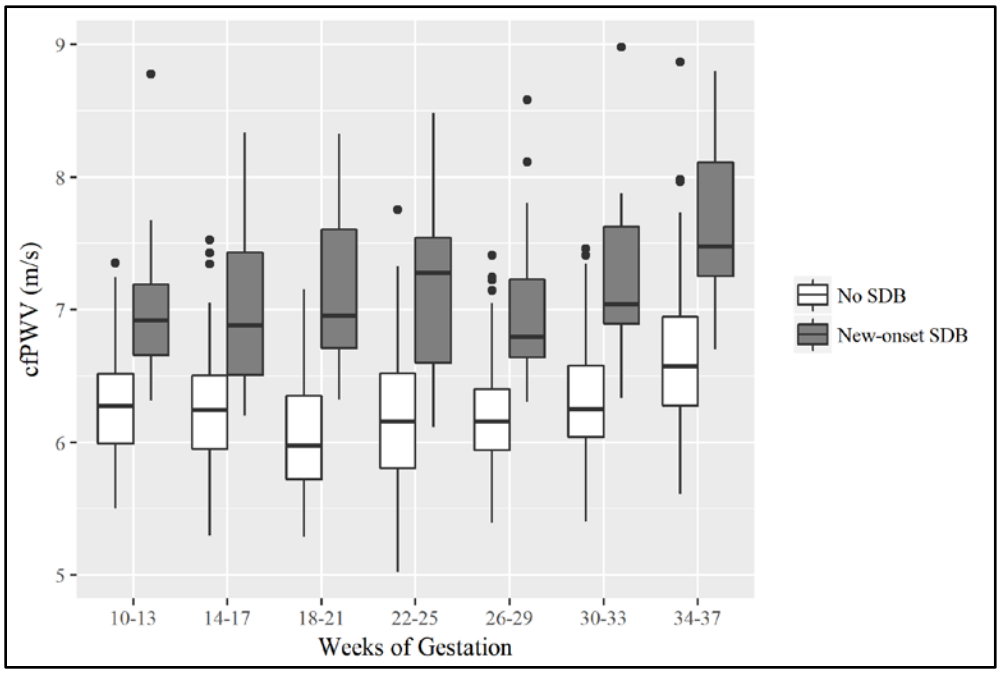
Conclusion
Women with OSA in the second or third trimester had greater arterial stiffness and wave reflection earlier in pregnancy. OSA was associated with pre-eclampsia development. Whether these relationships are causal remains to be investigated.

Table 1 – Adjusted odds for developing pre-eclampsia associated with assessments of obstructive sleep apnea

OSA assessment	OR	95% CI	*p*-value
MCID in 1st trimester Epworth score	1.39	1.01-1.94	0.048
MCID in 2nd trimester Epworth score	1.35	1.04-1.77	0.023
MCID in 3rd trimester Epworth score	1.46	1.10-2.00	0.012
Positive Epworth score (>10) in 2nd trimester	4.90	1.21-19.34	0.021
2nd trimester new-onset positive Epworth score	6.78	1.84-40.71	0.042
3rd trimester new-onset positive Epworth score	6.47	1.39-30.60	0.015
SDB in 3rd trimester	4.69	1.18-18.95	0.025
3rd trimester new-onset SDB	6.07	1.42-25.57	0.012

MCID: Minimum clinically important difference; OSA: obstructive sleep apnea; SDB: sleep-disordered breathing
Analyses adjusted for maternal age at study entry and pre-pregnancy body mass index. 1st, 2nd, and 3rd trimester assessment performed at 10^0-13^6, 21^0-24^0, and 32^0-35^6 weeks of gestation, respectively.

Figure 1 – Carotid-femoral pulse wave velocity across gestation in women with and without 2nd trimester new-onset sleep-disordered breathing (≥3 times/week)



GREATER AORTIC STIFFNESS IS ASSOCIATED WITH LOWER HIPPOCAMPAL CEREBROVASCULAR RESERVE BUT NOT CEREBRAL BLOOD FLOW IN MIDDLE-AGED AND OLDER ADULTS

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Introduction: Recent studies suggest cerebrovascular dysfunction precedes amyloid deposition and cognitive impairment in Alzheimer's disease. Aortic stiffness is an independent risk factor for Alzheimer's disease mediated in part by the development of cerebrovascular dysfunction and reductions in memory recall. However, the degree to which aortic stiffness is associated with functional impairments in the hippocampus as evidenced by measures of cerebral blood flow (CBF) during memory stimulation and cerebrovascular reserve (CVR) (i.e., ability to augment CBF in response to a physiological or pharmacological stimuli) is unknown. Therefore, we hypothesized that elevated aortic stiffness would be associated with 1) lower hippocampal CBF during memory stimulation; 2) reduced hippocampal CVR; and 3) greater amyloid burden in middle-aged and older adults (MA/O).

Methods/Results: Twenty-four MA/O adults (range: 55- 87 years; mean ± SE: 70.0 ± 2.0 years) were recruited to undergo measures of aortic stiffness (carotid-femoral pulse wave velocity, cfPWV) and global and regional CBF using quantitative [^{15}O]water PET imaging. Regional hippocampal CBF (mL/min/100mL) was measured during memory recall of a learned word list and log transformed to normalize the distribution. Hippocampal CVR was calculated as the percent (%) change in CBF in response to the pharmacological vasodilator, acetazolamide. Hippocampal amyloid burden was quantified using distribution volume ratio (DVR) from [^{11}C]PIB PET imaging and normalized to cerebellar gray matter. The following correlations were adjusted for age, MAP (cfPWV only) and education (% word recall only). Elevated cfPWV was associated with reduced hippocampal CVR ($r = -0.59$, $p=0.005$) but not hippocampal CBF ($p= 0.126$) or amyloid deposition ($p= 0.546$). Lower successful word recall trended to be associated with elevated cfPWV ($r= -0.38$, $p=0.097$) and reduced hippocampal CVR ($r= 0.38$, $p= 0.087$) in the present cohort.

Conclusion: Elevated aortic stiffness may impair the ability of the hippocampal cerebrovasculature to augment CBF independent of basal CBF.

Support: NIH 5R01 AG03417, R03 AG047306-01, 1R21 AG043722, U54TR001356

AEROBIC CAPACITY IS ASSOCIATED WITH VASCULAR FUNCTION IN PERSONS WITH MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is a progressive inflammatory disease of the central nervous system resulting in lower physical activity (PA), decreased aerobic capacity ($VO_{2\ peak}$), and impaired vascular function. In a healthy population, $VO_{2\ peak}$ and PA are related to vascular function, however, in persons with MS this association is unclear.

Purpose: To determine the relationship of $VO_{2\ peak}$ and PA with vascular function in people with MS.

Methods: Fifty-eight individuals with MS (Male: 15, 46±12 yrs, 29.0±6.7 kg/m^2, EDSS: 0-4) participated. Measurements of vascular function were obtained after a 10-minute supine rest: carotid intima-media thickness (ultrasound), central pulse wave velocity (cPWV, applanation tonometry) and reactive hyperemia (RH, strain gauge plethysmography). RH was calculated as the change between peak and resting forearm blood flow (FBF). A maximal incremental cycle test was used to assess $VO_{2\ peak}$. An accelerometer was worn for one week to determine moderate/vigorous PA (MVPA; >1722 counts per minute). Stepwise linear regression models included age, BMI, gender and $VO_{2\ peak}$.

Results: $VO_{2\ peak}$ (20.3±5.7 ml*kg-1*min-1) was correlated with cPWV (7.0±1.9 m/s), peak FBF (16.7±6.3 ml/100 ml tissue) and RH (15.0±6.1 ml/100 ml tissue), (p<0.05, Table 1). In stepwise regression analyses, $VO_{2\ peak}$ and BMI were the strongest predictors of peak FBF (β: 0.39 [95% CI; 0.10, 0.68], β: -0.26 [-0.51, -0.01], p<0.05) and RH (β: 0.39 [0.10, 0.67], β: -0.25 [-0.49, -0.01], p<0.05). cPWV was predicted by age and BMI (β: 0.55 [0.02, 0.09], β: 0.11 [0.04, 0.19], p<0.05). MVPA was not a predictor of cPWV, peak FBF or RH.

Conclusion: In individuals with MS, higher $VO_{2\ peak}$ was associated with better vascular function, while MVPA was not. These findings suggest cardiovascular fitness exerts a greater role on vascular function than PA and may have important implications regarding strategies for improving vascular function in persons with MS.

	VO_{2peak} ($ml*kg^{-1}*min^{-1}$)	% MVPA
Age	-.189	-.251
EDSS	-.034	-.164
BMI	**-.526***	-0.088
Brachial SBP (mmHg)	0.005	-.0.035
Brachial DBP (mmHg)	-0.256	-0.142
Aortic SBP (mmHg)	0.085	0.074
cPWV (m/s)	**-0.352***	-0.174
Carotid intima media thickness	-0.150	-0.119
Peak Forearm Blood flow (ml/100ml tissue)	**0.503***	0.113
Reactive Hyperemia (ml/100ml tissue)	**0.506***	0.119

***Significant correlation, p<0.05**

ALTERED VESSEL HEMODYNAMICS AFTER ACUTE MAXIMAL EXERCISE IN ADULTS WITH TYPE 2 DIABETES

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Objective: Adults with type 2 diabetes mellitus (T2DM) have a greater blood pressure (BP) response to acute maximal exercise. The nature of this exaggerated response is likely a function of vascular abnormalities; therefore, we aimed to examine the exercise-induced response of vessel hemodynamics in adults with and without T2DM.

Methods: Adults with (n=105) and without T2DM (n=77) underwent the 'arterial stress test': peripheral BP, heart rate (HR), carotid-femoral pulse wave velocity (cfPWV), and wave reflection parameters were assessed before and immediately after acute maximal treadmill exercise. Linear regression models were used to evaluate between-group differences at rest, and the absolute change of each parameter in response to exercise, adjusting for age, sex, BMI, exercise time, the baseline value, as well as, mean arterial pressure, HR, and height, when relevant.

Results: Mean age was 59.0±11.0 years and BMI 31.5±4.0 kg/m^2 (non-significantly different between groups). All subjects were treated for hypertension (BP 130±14/80±9 mmHg). At rest, subjects with T2DM had higher cfPWV (10.2±2.5 vs. 9.3±1.8 m/s), HR (70±12 vs. 66±10 beats/min), and lower diastolic BP (80±9 vs. 83±9 mmHg), but no significant difference in systolic BP (118±14 vs. 121±12 mmHg). In response to exercise, subjects with T2DM had a greater increase in cfPWV, systolic BP and pulse pressure (PP) (Table 1). A greater number of subjects with T2DM had a hypertensive response to exercise (n=31, 30%) compared to subjects without T2DM (n=14, 18%). No significant differences in corrected augmentation index (AIx75) or reflection index were observed.

Conclusion: Despite no differences in resting systolic BP or PP, we observed an exaggerated systolic BP response in adults with T2DM, and an altered arterial stiffness response to acute exercise.

Table 1: Between-group differences in the absolute change of arterial stiffness, hemodynamics, and wave reflection in response to exercise

Mean (95% CI)	Without T2DM (n=77)	With T2DM (n=105)	Difference
Δ cfPWV (m/s)	3.4 (2.5, 4.3)	4.8 (3.9 , 5.6)	**1.4 (0.1, 2.6)**
Δ Systolic BP (mmHg)	34.1 (29.1, 39.1)	41.3 (37.0, 45.5)	**7.0 (0.7,13.4)**
Δ Diastolic BP (mmHg)	2.6 (0.9, 4.3)	4.6 (3.1, 6.1)	1.0 (-1.2, 3.3)
Δ Pulse Pressure (mmHg)	31.5 (27.2, 35.8)	36.7 (33.0, 40.3)	**5.9 (0.4, 11.4)**
Δ AIx75 (%)	3.0 (1.2, 4.8)	0.5 (-1.1, 2.1)	-2.4 (-4.9, 0.0)
Δ Reflection index (%)	-13.1 (-15.6, -10.6)	-13.5 (-15.7, -11.4)	-0.5 (-3.9, 2.9)

Bolded parameters were significantly different between groups
*Hypertensive response to exercise: systolic BP>210 mmHg in men, and >190 mmHg in women

THE EFFECTS WHEY PROTEIN SUPPLEMENTATION ON AORTIC STIFFNESS AND CENTRAL HEMODYNAMIC LOAD IN COMMUNITY-DWELLING OLDER ADULTS: PRELIMINARY FINDINGS FROM THE ANCHORS-A-WHEY RANDOMIZED CONTROLLED TRIAL

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Dietary and nutraceutical strategies offer promise as a means of improving cardiovascular health with age. Whey protein contains natural ACE-inhibitory properties that have been shown to lower blood pressure. The *Aging, Neurocognitive, and Cardiovascular Health Outcomes Research Study: Add Whey Protein* (ANCHORS A-WHEY) was as 12-week randomized controlled trial (RCT) designed to examine the effect of whey protein on large artery stiffness, cerebral perfusion and cognitive function in older adults. **OBJECTIVE:** to present preliminary findings on the effects of whey protein on aortic stiffness and central hemodynamic load in older adults. **METHODS:** 99 older adults (Mean±SD; age 67±6 yrs, BMI 27.2±4.7kg/m^2, 45% female) participated in this double-blind, RCT (NCT01956994). Participants were randomly assigned to 50g/daily of either whey protein isolate (WPI) or a calorically matched carbohydrate (CHO) placebo for 12-weeks. Aortic stiffness was determined using carotid-femoral pulse wave velocity (cfPWV). Aortic hemodynamics were assessed using radial tonometry and a generalized transfer function (Sphygmocor, Atcor Medical). Aortic rate pressure product (RPP) was calculated as the product of aortic systolic pressure and heart rate (HR) and taken as an index of central hemodynamic load. **RESULTS:** A significant group-by-time interaction was detected for cfPWV. There was a slight increase in PWV in the CHO group with a significant decrease in the WPI group (Table 1, $p<0.05$). A significant group-by-time interaction was detected for aortic RPP ($p<0.05$). There was no change in aortic RPP in the CHO group with a significant decrease in the WPI group ($p<0.05$). Change in cfPWV was associated with change in aortic RPP (r = 0.272, $p = 0.007$). **CONCLUSIONS:** WPI supplementation produces modest reductions in aortic stiffness in community-dwelling older adults. Lower HR and aortic systolic pressure following WPI may result in less cycles of spatial mechanical stress on the artery wall, thus attenuating central hemodynamic load.

Conflicts of Interest: This study was funded by a research grant from the Dairy Research Institute, Dairy Management INC.

Table 1: Changes in aortic stiffness and central hemodynamics pre/post intervention.

	CHO (n=46)		WPI (n=53)				
	Baseline	12 Week	Baseline	12 Week	G	T	GxT
BMI (kg/m^2)	27.0 ± 3.9	27.4 ± 4.1	27.9 ± 5.6	27.8 ± 5.6	0.51	0.26	0.07
Heart rate (b/min)	57 ± 9	56 ± 9	60 ± 9	56 ± 8*	0.39	**0.001**	**0.01**
Brachial							
SP (mmHg)	127 ± 11	128 ± 12	125 ± 13	123 ± 12	0.1	0.42	0.13
DP (mmHg)	79 ± 5	78 ± 6	79 ± 8	76 ± 7	0.24	**0.003**	0.23
MP (mmHg)	95 ± 7	95 ± 7	94 ± 9	92 ± 8	0.12	**0.03**	0.13
Aortic							
SP (mmHg)	117 ± 11	119 ± 12	115 ± 13	112 ± 11	**0.04**	0.48	0.09
DP (mmHg)	80 ± 5	79 ± 6	79 ± 8	77 ± 7	0.22	**0.01**	0.33
RPP (mmHg/min)	6805 ± 1212	6794 ± 1191	6964 ± 1087	6610 ± 1081*	0.96	**0.03**	**0.04**
AIx75 (%)	25 ± 9	25 ± 8	24 ± 10	23 ± 11	0.25	0.5	0.52
cf-PWV (m/s)	9.6 ± 2.5	10.1 ± 2.9	10.1 ± 2.9	9.6 ± 2.7*	0.88	0.88	**0.01**

BMI, body mass index; SP, systolic pressure; DP, diastolic pressure; MP, mean pressure; AIx, augmentation index; cf-PWV, carotid-femoral pulse wave velocity
G, group; T, time; GxT, group-by-time; CHO, carbohydrate; WPI, whey protein isolate
*Significantly different from Baseline ($p<0.05$)

HEMODYNAMIC PATTERNS IDENTIFIED BY IMPEDANCE CARDIOGRAPHY PREDICT MORTALITY IN THE GENERAL POPULATION: THE PREVENCION STUDY

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Background: Blood pressure (BP) is determined by interactions between the heart and arterial properties, and subjects with identical BP may have substantially different hemodynamic determinants.

Objective: To assess whether arterial hemodynamic indices quantified by impedance cardiography (ICG), a simple operator-independent office procedure, independently predict all-cause mortality in adults from the general population, and specifically among those who do not meet criteria for ACC/AHA stage-2 hypertension.

Methods: We studied 1639 adults 18-80 years of age from the general population. We used ICG to measure hemodynamic parameters and metrics of cardiac function. We assessed the relationship between hemodynamic parameters measured at baseline and all-cause mortality over a mean follow-up of 10.9 years.

Results: Several ICG parameters predicted death. The strongest predictors were total arterial compliance index (Standardized HR=0.38; 95%CI=0.31-0.46: $P<0.0001$), and indices of cardiac contractility: velocity index (Standardized HR=0.45; 95%CI=0.37-0.55: $P<0.0001$) and acceleration index (Standardized HR=0.44; 95%CI=0.35-0.55: $P<0.0001$). These remained independently predictive of death after adjustment for age, gender, body mass index, LDL-cholesterol, HDL-cholesterol, triglycerides, fasting plasma glucose, diabetes mellitus, serum creatinine smoking history, as well as systolic and diastolic BP (Figure 1). Among subjects without stage-2 hypertension (n=1,563), indices of cardiac contractility were independently predictive of death, and identified a subpopulation (25% of non-stage-2 hypertensives) that demonstrated a high 10-year mortality risk, equivalent to that of stage-2 hypertensives (Figure 2).

Conclusions: Hemodynamic patterns Identified by ICG independently predict mortality in the general population. The predictive value of ICG applies even in the absence of ACC/AHA stage 2 hypertension and identifies high-risk individuals who are in earlier stages of the hypertension continuum.

Figure 1. Predictors of all-cause mortality in proportional hazards regression models.

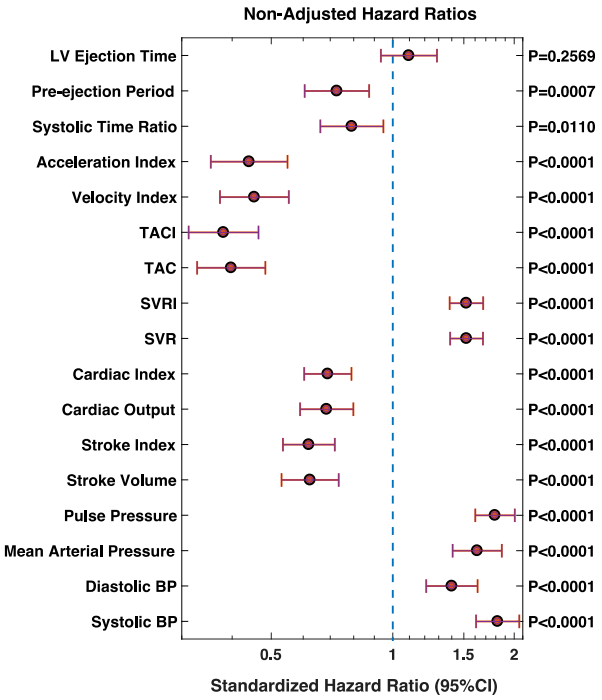
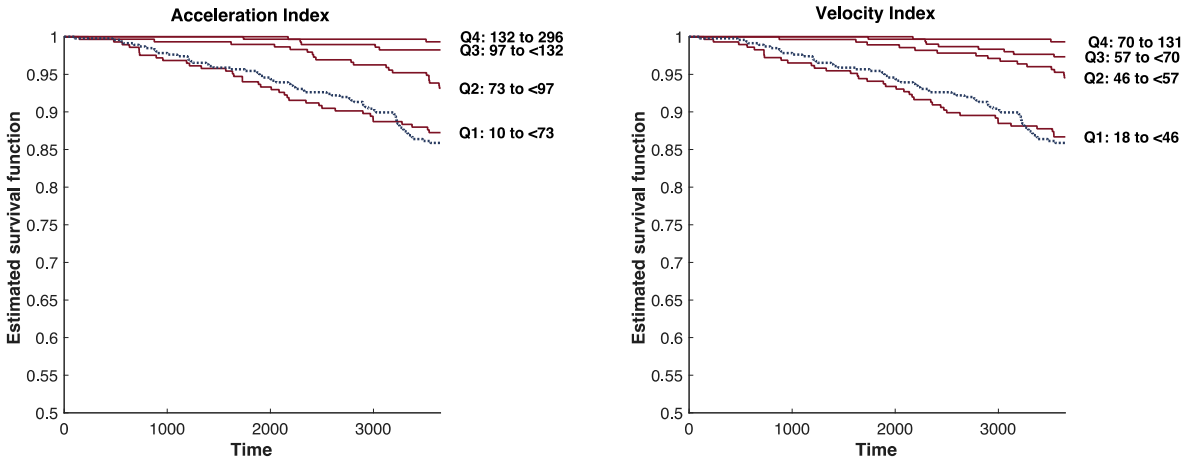


Figure 2. Survival curves (quartiles) of acceleration index and velocity index among subjects without ACC/AHA stage-2 hypertension (red), and among subjects with ACC/AHA stage-2 hypertension (blue).



IS THE MINIMAL RECOMMENDATION OF COMBINED TRAINING ENOUGH TO REDUCE CARDIO-METABOLIC RISK IN HYPERTENSIVE ELDERLY?

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Hypertensive elderly (HYP) are strongly encouraged to incorporate exercise training in their daily routines for health and quality of life improvements. Although both aerobic and resistance exercise training are recommended, the effect of combined aerobic and resistance exercise is not well characterized in this population.

Objectives: To test the effectiveness of combined training on cardio-metabolic risk factors in overweight HYP**.**

Methods: 46 medicated HYP were randomized to either a 16-week combined training program (CT: age 65.5 ± 4y) or a control group (CG: age 65.3 ± 4y), in which both were instructed to maintain their current dietary habits. CT program consisted of moderate intensity resistance exercise twice per week and 50 min moderate intensity (63% VO_2 max.) treadmill exercise three times per week. Subjects underwent assessments of body composition (body plethysmograph), blood biochemical markers, blood pressure, ankle brachial index (ABI) and heart rate variability at baseline and after 16 weeks. Mixed model analyses were performed considering time*group interactions for random subjects with subsequent Bonferroni post hoc. The number of subjects with metabolic syndrome (MS) were compared between groups and between time points by chi-square test. P-value ≤ 0.05 was considered significant.

Results: See table. There was a significant reduction in weight, increase in ABI and lower number of subjects with MS in CT post intervention. There was a trend for HDL to increase after CT (p=0.06), blood pressure reduction (ES -0.5 to -0.3) and cardiac parasympathetic modulation increase in CT (HF ES 0.41).

Conclusions: CT reduced body weight, slightly improved HDL, blood pressure and autonomic control parameters, reduced the number of HYP with MS and increased ABI. Since many cardio-metabolic adaptations are mediated by body composition adaptations, the overweight HYP likely need more volume of exercise and/or some dietary associated intervention to achieve better cardio-metabolic improvements.

Keywords: Aging, Exercise, Hypertension, Obesity, Cardiovascular system, Metabolism.

Table. Effects of 16 weeks of CT and CG on cardio-metabolic variables of hypertensive elderly.

	Combined training (n=23, 7♂/16♀)			Control group (n=23, 8♂/15♀)		
	Pre	Post	ES	Pre	Post	ES
Weight (kg)	79.1 ± 11.8	77.8 ± 12.3*	-0.11	78.4 ± 13.4	78.7 ± 12.8	0.02
BMI (kg/m²)	29.1 ± 4.2	28.8 ± 4.2	-0.07	30.2 ± 3.6	30.3 ± 3.5	0.02
Fat mass (g)	31.4 ± 7.9	30.7 ± 8.5	-0.09	31.4 ± 8.7	32.5 ± 8.7*	0.12
Fat free mass (g) #	47.3 ± 9.6	47.0 ± 9.4	-0.02	46.9 ± 10.8	46.1 ± 10.3	-0.07
MS (subjects)	17	15	-	20	21†	-
Biochemical markers						
Glucose (mg/dL)	106.2 ± 22.2	103.9 ± 21.2	-0.11	107.4 ± 16.2	103.1 ± 17.5	-0.25
TG (mg/dL)	110.2 ± 42.0	118.3 ± 43.3	0.19	115.5 ± 45.8	111.3 ± 48.9	-0.09
TC (mg/dl)	177.1 ± 42.5	180 ± 48.2	0.06	172.8 ± 42.1	165 ± 41.8	-0.19
HDL (mg/dl)	40.4 ± 11.3	43.7 ± 21	0.21	39.6 ± 10.5	38.4 ± 12.8	-0.10
LDL (mg/dl)	107.9 ± 29.2	108.8 ± 31.5	0.03	108.8 ± 34.8	104.3 ± 33.3	-0.13
Insulin (mU/mL)	5.2 ± 5.3	5.0 ± 3.6	-0.04	4.0 ± 2.7	4.8 ± 3.5	0.25
CRP (mg/L)	1.5 ± 1.3	1.2 ± 0.8	-0.22	1.8 ± 1.4	1.5 ± 1.4	-0.22
Blood pressure						
SBP (mmHg) #	133.7 ± 16.5	127.8 ± 13.5	-0.39	134.7 ± 25.1	130.4 ± 13.5	-0.22
DBP (mmHg) #	86.8 ± 9.7	83 ± 9.2	-0.4	82.5 ± 12.7	77.8 ± 9.4	-0.42
MAP (mmHg)	102.5 ± 11.1	97.9 ± 9.6	-0.44	99.9 ± 16.1	95.3 ± 9.5	-0.35
ABI	1.15 ± 0.09	1.24 ± 0.1*	-0.81	1.17 ± 0.1	1.17 ± 0.07†	0.009
Heart rate variability						
RRi (ms)	979.5 ± 145.5	990.5 ± 124.7	0.08	916.5 ± 130.2	903 ± 117.5	-0.11
SDNN (ms)	30.2 ± 14.1	34.5 ± 18.3	0.26	29.4 ± 11.9	28.5 ± 13.2	-0.07
RMSSD (ms)	22.8 ± 11.6	24.7 ± 15.5	0.14	21 ± 12.4	22.3 ± 14.8	0.09
VLF (ms²)	476.1 ± 706.8	747 ± 880.9	0.34	475.3 ± 373.1	428.2 ± 398.6	-0.12
LF (ms²)	215.5 ± 222.4	273.6 ± 333.5	0.21	175 ± 174.4	209.3 ± 309.3	0.14
HF (ms²)	167 ± 138.7	302 ± 504.2	0.41	220.8 ± 301.2	201.9 ± 243.8	-0.07
LF (nu)	55.9 ± 16.9	54 ± 19	-0.10	54.8 ± 20.8	54.5 ± 19.8	-0.02
HF (nu)	44 ± 16.8	46 ± 18.9	0.11	45.1 ± 20.7	45.4 ± 19.8	0.01

Legend: CT: combined training; CG: control group; ES: effect size; BMI: body mass index; MS: metabolic syndrome; TG: triglycerides; TC: total cholesterol; HDL: high density lipoprotein; CRP: C-reactive protein; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; HR: heart rate; RRi: RR interval; SDNN: standard deviation of all RR normal intervals; RMSSD: root mean square standard deviation; VLF: very low frequency; LF: low frequency; HF: high frequency; †: different from CT within same time; *: different from pre within same group; #: time effect.

SYSTOLIC BRACHIAL PRESSURE AND AGE AS DETERMINANTS OF PULSE WAVE VELOCITY DERIVED FROM PULSE WAVE ANALYSIS. JOSEPH E. SCHWARTZ, PhD, STONY BROOK SCHOOL OF MEDICINE, STONY BROOK, NY,

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Objectives: Pulse wave velocity (PWV) as a measure of arterial stiffness is a well-documented risk factor for cardiovascular (CV) morbidity and mortality, independent of other CV risk factors. Given the ease of non-invasive measurement of PWV allowed by recently developed devices, we measured multiple simultaneous risk factors using a brachial cuff-based ambulatory oscillometric device (Mobil-O-Graph, IEM, GmbH and the manufacturer's pulse wave analysis algorithms) to investigate the relationship of PWV to two of its known principal correlates, age and brachial systolic blood pressure (SBP).

Methods: As part of an NIH-funded ancillary study, 234 participants from Phase 2 of the Masked Hypertension Study had their PWV and SBP assessed hourly for up to 40 hours (7,287 valid readings). A multilevel mixed linear model predicting PWV from age and SBP was estimated.

Results: There were 7,182 observations with PWV>5.0 m/sec (the minimum recorded). The participants were 34% male, with mean ± SD age 52.3 ± 9.9 years, SBP 123.8 ± 18.4 mmHg, and PWV 7.6 ± 1.3 m/sec.

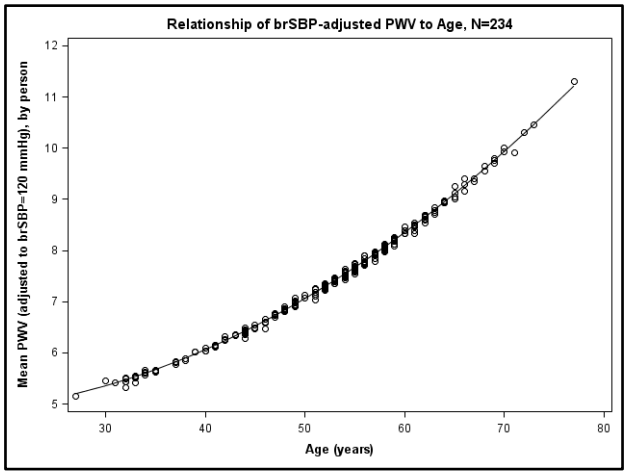
The predicted relationship of PWV to age and SBP was:

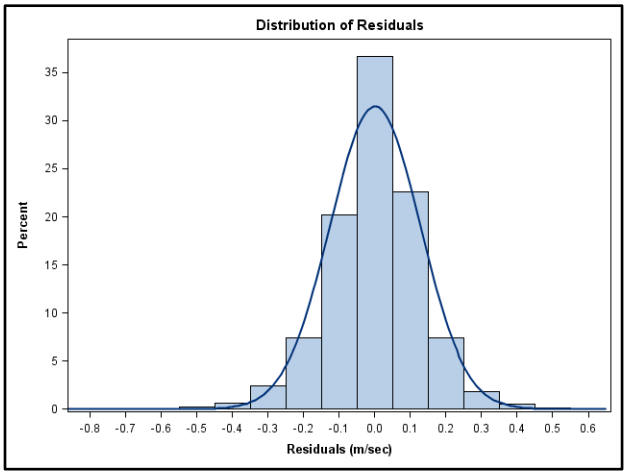
*Predicted PWV = 1.0796 – 0.0317*Age + 0.0015*Age2 + 0.0325*SBP*

Together, age and SBP accounted for 99.1% of the total variance, i.e., less than 1% of the variance in the PWV values was independent of age and SBP.

These findings were confirmed in an external validation dataset with 1,077 valid readings.

Conclusions: These results show that PWV based on this method is nearly completely driven by age and SBP, and therefore provides no additional information beyond age and SBP. This finding does not address the device's other pulse wave analysis parameters such as central BP; nor does it address comparisons to other PWV measurement methods or devices.





CHRONIC KIDNEY DISEASE IS ASSOCIATED WITH INCREASED DP-UC-MGP, A MARKER OF VASCULAR VITAMIN K DEFICIENCY

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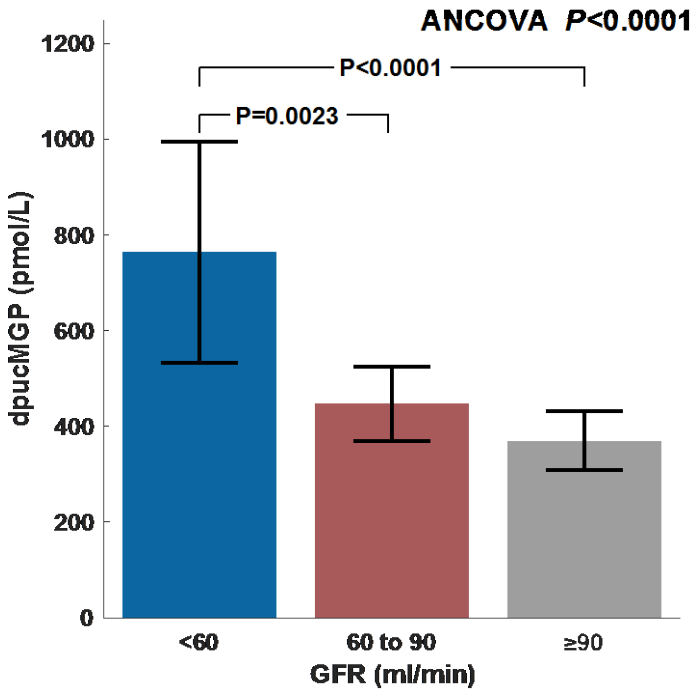
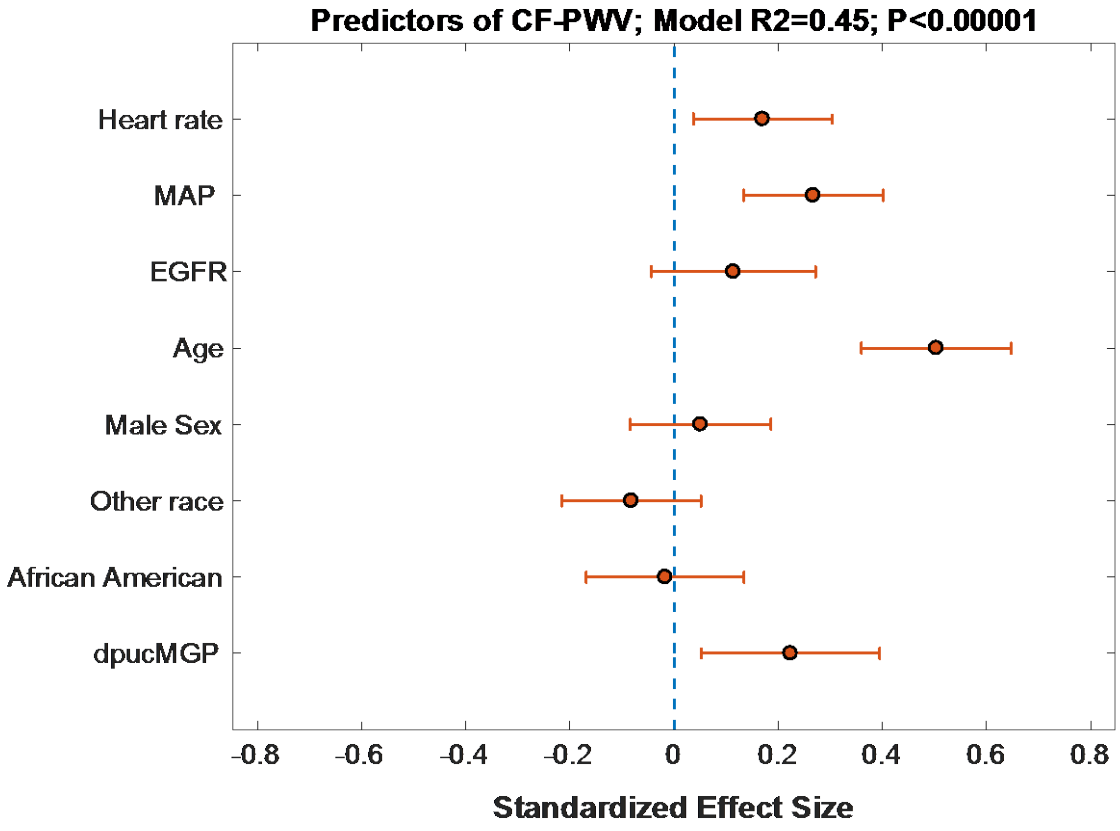
Objective: Large artery stiffening is increased in advanced CKD, but likely develops progressively in earlier stages of CKD. Active matrix Gla-Protein (MGP) is a potent Vitamin-K dependent inhibitor of vascular calcification. A recent animal model demonstrated intrinsic abnormalities in vitamin K metabolism even in early CKD, but whether early human CKD is associated with vascular vitamin K deficiency is unknown. We aimed to investigate how inactive MGP (dp-uc-MGP) levels relate to CKD.

Methods: We enrolled 137 adults without HF with varying degrees of renal function: normal eGFR (>90 mL/min; n=59), mildly reduced eGFR (stage 2 CKD: eGFR = 60-89 mL/min; n=53) or at least moderately reduced eGFR (stage 3-5 CKD; eGFR<60 ml/min; n=25). Carotid-femoral pulse wave velocity (CF-PWV), was measured with carotid and femoral tonometry. Dp-ucMGP levels were measured with ELISA (VitaK; The Netherlands).

Results: Dp-ucMGP levels progressively increased with decreasing renal function (eGFR≥90: 247 pmol/L; eGFR 60-89: 488 pmol/L; eGFR <60: 953 pmol/L; *P*<0.0001). These differences persisted after adjustment for multiple potential confounders (eGFR≥90: 314 pmol/L; eGFR 60-89: 414 pmol/L; eGFR <60: 770 pmol/L; *P*<0.0001). In a multivariable model adjusted for various confounders, dp-ucMGP was a significant independent predictor of CF-PWV (β=0.21; *P*=0.019). In formal mediation analyses, dp-ucMGP mediated a significant relationship between eGFR and higher CF-PWV (β=-0.16; *P*=0.005) whereas no significant dp-ucMGP-independent relationship was present (β=-0.02; *P*=0.80).

Conclusions CKD is associated with increased dp-ucMGP (inactive MGP), a Vitamin-K dependent inhibitor of vascular calcification, which correlates with large artery stiffness. Further studies are needed to assess whether vitamin K2 supplementation represents a suitable therapeutic strategy to prevent or reduce arterial stiffening in CKD.


ANCOVA P<0.0001
P<0.0001
P=0.0023
dpucMGP (pmol/L)
1200
1000
800
600
400
200
0
<60
60 to 90
≥90
GFR (ml/min)


Predictors of CF-PWV; Model R2=0.45; P<0.00001
Heart rate
MAP
EGFR
Age
Male Sex
Other race
African American
dpucMGP
-0.8
-0.6
-0.4
-0.2
0
0.2
0.4
0.6
0.8
Standardized Effect Size

ARTERIAL STIFFNESS RESPONSE TO ACUTE AEROBIC AND RESISTANCE EXERCISE IN OLDER PATIENTS WITH CORONARY ARTERY DISEASE

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Introduction: Arterial stiffness is associated with coronary artery disease (CAD) in older patients. Changes in arterial stiffness have been observed after a single session of aerobic and resistance exercise. While acute aerobic exercise increases arterial compliance, acute resistance exercise decreases arterial compliance. There has not been any data on arterial stiffness response to acute effects of aerobic and resistance sessions, which include older patients or with CAD.

Purpose: We examined arterial stiffness, beta stiffness and central and brachial systolic and diastolic blood pressure's variability after an acute session of aerobic exercise compared to resistance exercise.

Methods: Eighteen male patients with coronary artery disease aged 71.8 ± 10.2 years. Arterial stiffness will be measured by PWV and central and brachial systolic and diastolic blood pressure's, obtained by applanation tonometry and the beta stiffness was obtain with Doppler ultrasound and measured during a 15 minutes rest and 5, 15, 30 minutes after the aerobic and the resistance sessions on different and non-consecutive days. The protocol used for the aerobic session was on the treadmill, performing 10 stages of 2 minutes at high intensity (85-90% heart rate peak) with 1 minute of passive pause between each stage. For the resistance session, they did 6 machines, 3 sets, 8 repetitions at 70% of 1 maximal repetition (45 and 60 seconds pause between exercise and series, respectively).

Results: An interaction effect was detected for central PWV ($p \leq 0.005$), due to an increase in PWV following resistance session and a decrease in PWV following aerobic session. Significant differences were found between sessions after 15 min in brachial systolic blood pressure, beta stiffness ($p \leq 0.005$) who decreased. Controlled for mean arterial pressure and the results were the same ($p \leq 0.005$).

Conclusions: In conclusion, aerobic sessions decreased central arterial stiffness, while the resistance sessions significantly increased central arterial stiffness.

Table. Results before and after which exercise session	PWV, *m/s*	Beta Stiffness, *U*	c MAP, *mmHg*
Variables			
Resistance rest	8.8 ± 2.9	15.5 ± 9.9	82.8 ± 8.1
Aerobic rest	8.8 ± 1.3	12.2 ± 4.9	82.4 ± 7.3
Resistance 5min after	9.4 ± 2.1	15.6 ± 7.8	83.2 ± 10.1
Aerobic 5min after	8.3 ± 1.2	11.3 ± 2.8	84.5 ± 12.5
Resistance 15min after	10.2 ± 2.9	15.1 ± 4.9	81.5 ± 8.3
Aerobic 15min after	8.2 ± 1.1	10.7 ± 3.2	79.5 ± 8.4
Resistance 30min after	10.1 ± 2.6	15.0 ± 5.2	81.2 ± 8.6
Aerobic 30min after	7.8 ± 1.3	10.5 ± 3.2	79.0 ± 8.1

PWV – pulse wave velocity; b MAP – brachial mean arterial pressure