1.4: INCREASED AORTIC STIFFNESS IN YOUNG SUBJECTS WITH MIGRAINE

G. Schillaci, G. Pucci, I. Corbelli, P. Sarchielli, M. Mannarino, M. Pirro, P. Calabresi, E. Mannarino

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1.1 ARTERIAL STIFFNESS IS RELATED TO RENAL FUNCTION IN THE GENERAL POPULATION

L. A. Tomlinson a, Y. Yasmin a, K Maki-Petaja a, S. S. Hickson a, B. J. McDonnell b, C. M. McEniery c, J. R. Cockcroft b, I. B. Wilkinson a

aACCI, Addenbrooke's, Cambridge, United Kingdom
bWales Heart Research Institute, Cardiff, United Kingdom

Introduction: Aortic stiffness is related to renal function in patients with chronic kidney disease and may contribute to the high cardiovascular mortality in this group. However, the relationship between renal function and arterial haemodynamics in the general population has not previously been reported.

Methods: We analysed the relationship between renal function defined by estimated GFR (eGFR) and aortic pulse wave velocity (aPWV), brachial PWV (bPWV) and radial and central wave reflections (rAIx and cAIx) for participants enrolled in the Anglo-Cardiff Collaborative Trial between 2000-2009.

Results: Measurement of eGFR was available for 4795 participants with a mean age of 48.23 years, 45.5% male, BP 130/77, mean eGFR 92.7 ± 38.8 mL/min. Estimated GFR was correlated with aPWV (r = -0.53), bPWV (r = -0.28), rAIx (r = -0.20) and cAIx (-0.25) (all P < 0.001). In multivariate analysis, using a stepwise model including age, mean BP, gender, heart rate, glucose, cholesterol, body mass index and smoking, eGFR remained an independent determinant of aPWV (R² = 0.68, P < 0.001), rAIx (R² = 0.72, P < 0.001) and cAIx (R² = 0.72, P < 0.001) but not bPWV. After exclusion of people with previous CHD, CVA or diabetics (n = 4247), eGFR remained an independent predictor of rAIx and cAIx but not of bPWV.

Conclusion: In the largest analysis of the general population to date, eGFR is independently associated with aortic stiffness and augmentation index but explains little of the variance compared with established determinants. For aortic stiffness, but not wave reflections, this relationship is explained by the coexistence of impaired renal function and vascular disease.

1.2 VASCULAR CALCIFICATIONS AFTER CHRONIC USE OF VITAMIN-K ANTAGONISTS

van Varik BJ a, R. J. M. W. Rennenberg a, A. A. Kroon a, L. J. Schurgers b, P. W. de Leeuw a

aMaastricht University Medical Centre, Maastricht, Netherlands
bMaastricht University, Maastricht, Netherlands

Background: Arterial calcification is commonly observed in cardiovascular disease and is associated with increased arterial stiffness, systolic hypertension and adverse cardiovascular outcome. Arterial calcification is an actively regulated process with several stimulating and inhibiting factors. An important inhibitor of arterial calcification is the Vitamin K-dependent Matrix Gla Protein (MGP). In animal studies, inhibition of Vitamin K by warfarin-treatment was associated with increased arterial calcification. We investigated in this pilot-study whether this effect of Vitamin-K antagonists could also be observed in humans.

Methods: From five different thrombosis services in the Netherlands, we recruited 19 patients that have used oral vitamin-K antagonists for more than 10 years due to an history of cardiac valve replacement or venous thrombo-embolic event. We also recruited 17 control-subjects. We excluded subjects older than 55 years or subjects with a history of diabetes, hyperhomocysteinemia, hyperlipidemia and previous cardiovascular events. To detect arterial calcification, anterior soft-tissue radiographs from the femoral arteries were obtained in all subjects. In addition, the carotid Intima Media Thickness (cIMT) and carotid-femoral Pulse-wave Velocity (PWV) were measured.

Results and conclusion: Femoral radiographs of sufficient quality were obtained for 18 patients and 16 controls. Fourteen (77.8%) patients on vitamin-K antagonists versus 4 (25%) control subjects had femoral artery calcifications (Odds-ratio 10.5; 95%-CI 2.15 – 51.28). Patients had a slightly higher mean cIMT (0.61 ± 0.09 mm) than control subjects (0.56 ± 0.07 mm; P = 0.04). There was no difference in carotid-femoral PWV between the groups. Chronic use of Vitamin-K antagonists is associated with increased arterial calcification.

1.3 IMPACT OF RENAL TRANSPLANTATION ON ARTERIAL STIFFNESS


Addenbrooke's Centre for Clinical Investigation, Cambridge, United Kingdom

Introduction: Risk of a cardiovascular event is known to increase in the period immediately post-transplantation before returning to baseline or lower. We hypothesised that this might be due to changes in arterial stiffness and/or endothelial function.

Methods: We measured aortic pulse wave velocity (aPWV), wave reflections (AIx), and endothelial function in 40 patients undergoing living donor renal transplantation, immediately pre-transplant and at 1 week, 3 and 12 months post-transplant.

Results: 35 patients completed the 12 months follow-up. Mean eGFR increased from 8 ± 3 mL/min pre-transplant to 51 ± 13 mL/min at 1 week post-transplant (P < 0.001) and remained at this level throughout follow-up. aPWV increased from 7.4 ± 1.4 m/s at baseline to 8.1 ± 1.3 m/s at 1 week post-transplant (P < 0.05), but returned to baseline levels after 12 months. A similar trend in mean pressure was observed. AIx was unchanged over the 12 months. Brachial flow mediated dilatation (FMD) was unchanged at 1 week post-transplant but had improved slightly, though significantly at 1 year (4.73 ± 3.76% vs. 6.72 ± 3.22%, P < 0.05). The response to GTN was not altered. In a subset of patients who had plasmapheresis pre and post-transplant, AIx was significantly increased from baseline after 1 year (8.1 ± 11.4% vs. 26.3 ± 11.4%, P < 0.01). Brachial response to GTN was also significantly improved (2.0 ± 1.8% vs. 9.2 ± 4.1%, P = 0.009), although FMD was unchanged.

Conclusion: Arterial stiffness is increased at 1 week post-transplant and returns to baseline by one year reflecting the known changes in cardiovascular risk. Endothelial function appears to improve in the longer term. Therapeutic strategies targeted at minimising arterial dysfunction around the time of transplantation may improve outcomes.

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G. Schillaci a, G. Pucci a, I. Corbelli b, P. Sarchielli b, M. Mannarino a, M. Pirro a, P. Calabresi b, E. Mannarino a

aAddenbrooke's Centre for Clinical Investigation, Cambridge, United Kingdom
bMaastricht University, Maastricht, Netherlands
STIFFNESS: 15-YEAR FOLLOW-UP OF THE EURIDISS COHORT

Intra-aortic balloon pumping augments coronary blood flow, at the expense of diminishing carotid blood flow. This could lead to cerebral insufficiency in patients with obstructive carotid disease.

1.6 DETRIMENTAL EFFECTS ON CAROTID PERFUSION OF INTRA-AORTIC BALLOON PUMP SUPPORT

Introduction: Intra-aortic balloon pumping is widely used to augment diastolic coronary perfusion. However, far less is known about its effects on other large arteries. In this study we assessed the effects of intra-arterial balloon pump pressure support on pressure and flow in the proximal aorta, carotid, coronary and renal arteries.

Methods: Recordings of simultaneous pressure and flow velocity were made using intra-arterial sensor tipped wires. Velocity time integral (VTI) was calculated at each location.

Results: With balloon pump support VTI increased in the coronary arteries (458 to 540 cm, 15%). In contrast, in the carotid arteries VTI markedly decreased (278 to 228 cm, -21%). VTI remained constant in the renal arteries (247 cm) and the aorta (225 cm). The detrimental reduction in carotid VTI was due to the sudden fall in pressure occurring with balloon deflation, which results in carotid velocity transiently becoming negative (Fig. 1).

Conclusion: Intra-arterial balloon pumping augments coronary blood flow, at the expense of diminishing carotid blood flow. This could lead to cerebral insufficiency in patients with obstructive carotid disease.

Figure 1 Pressure and velocity in the carotid artery before (left) and during (right) intra-arterial balloon pump support.