Test-retest reliability of pulse amplitude tonometry measures of vascular endothelial function: Implications for clinical trial design.


Evaluated repeatability of EndoPAT derived measures of endothelial function; (RHI & FRHI), and arterial stiffness; (AI), in 20 healthy adults based on repeated EndoPAT tests (mean interval = 19.5 days) under standardized conditions.

**Results:** PAT-derived measures of endothelial function and arterial stiffness showed strong repeatability (intra-class correlations RHI = 0.74 and AI = 0.83). Authors determined that a crossover design powered at 0.90 requires n=28 to detect a 15% change in RHI.

**Conclusions:** First to show that PAT measurements are repeatable in adults over an interval greater than 1 week and, preliminary evidence suggests that PAT may be more repeatable than FMD.


Carvedilol-lisinopril combination therapy and endothelial function in obese individuals with hypertension.


Hypothesized that carvedilol controlled-release, plus lisinopril combination therapy (C+L) would increase endothelial function and decrease oxidative stress more than hydrochlorothiazide plus lisinopril combination therapy (H+L). Combinations were alternately tested in 25 hypertensive obese patients. Endothelial function (EndoPAT RHI), circulating oxidized low-density lipoprotein (oxLDL), 8-isoprostane, and asymmetric dimethylarginine (ADMA) were obtained at baseline, post-first drug, post-washout, and post second drug.

**Results:** C+L showed significantly improved RHI vs. H+L (P=0.001), including after adjustment for the change in systolic blood pressure. No significant treatment differences were observed for oxLDL, 8-isoprostane, or ADMA.

**Conclusions:** Independent of blood pressure lowering, C+L therapy improves endothelial function more than H+L therapy.


Assessment of endothelial function in atrial fibrillation: utility of peripheral arterial tonometry.


Evaluated EndoPAT in 25 atrial fibrillation, (AF), patients vs. 25 sinus rhythm controls during reactive hyperemia. Hyperemic responses were compared at different durations (5, 10 and 15 beats; 30s; and 1-10min) to determine the optimal measurement duration.

**Results:** Endothelial responses were significantly decreased in AF vs. controls (1.48±0.60 vs 2.05±1.13; P=0.03). Beat-to-beat pulse amplitude was highly variable during AF owing to non-uniform stroke volumes, with limits of agreement being consistently narrower with increasing measurement durations.

**Conclusions:** Methods of determining endothelial function via vessel diameters or blood flow during reactive hyperemia should use measurement durations of at least 1min to ensure accurate and reproducible results.


The endothelin receptor antagonist bosentan improves peripheral endothelial function in patients with type 2 diabetes mellitus and microalbuminuria: a randomised trial.


Tested whether 4 weeks oral administration of the dual endothelin receptor antagonist bosentan improves peripheral endothelial function, in 46 patients with type 2 diabetes and microalbuminuria, randomized to bosentan (n=22), or placebo (n=24). Primary endpoint was change in EndoPAT RHI, secondary endpoint was change in brachial artery FMD.

**Results:** In the bosentan group RHI increased from 1.73 ± 0.43 (mean ± SD) at baseline to 2.08 ± 0.59 at follow-up (p < 0.05), but did not change in the placebo group (1.84± 0.49 to 1.87 ± 0.47). The RHI change was greater in the bosentan group than in the placebo group (p < 0.05). Nitroglycerine-induced hyperemia was not affected. Brachial artery FMD and blood pressure did not change during treatment.

**Conclusions:** Four weeks of bosentan treatment improved peripheral endothelial function in patients with type 2 diabetes and microalbuminuria.

Simultaneous Impairment of Intracranial and Peripheral Artery Vasoreactivity in CADASIL Patients.


Assessed vasoreactivity in intracranial arteries and in peripheral arteries in patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) using quantitative single photon emission computed tomography (SPECT) with the autoradiographic (ARG) method, and the EndoPAT for the peripheral assessment.

Results: Average RHI after post-deflation was lower in CADASIL patients than in normal subjects. RHI correlated significantly with cerebrovascular reactivity in all brain areas in CADASIL patients.

Conclusions: Vasoreactivity is reduced in both peripheral and intracranial arteries in patients with CADASIL.


Endothelial function in children and adolescents with mucopolysaccharidosis.


Evaluated endothelial function using the EndoPAT in 12 youths with mucopolysaccharidosis (MPS), (age 10.3 ± 3.9), and in 9 healthy controls.

Results: Children and adolescents with MPS whether treated by HSCT (hematopoietic stem cell transplantation) (N = 4) or ERT (enzyme replacement therapy ) (N=8) had significantly lower RHI compared to controls (MPS =1.22 ± 0.19 vs. 1.46±0.32, p <0.05).

Conclusions: Children and adolescents with treated MPS have significantly poorer endothelial function than healthy controls. Further study of endothelial function for risk stratification and the long term implications of reduced endothelial function in MPS is warranted.


Evaluation of gender differences in endothelium-independent dilation using peripheral arterial tonometry.


Assessed the EndoPAT response to nitroglycerin (NTG) induced endothelium-independent dilation (EID) in 86 healthy subjects (41 females), following a standard reactive hyperaemia study. Peak reactive hyperaemic index (RHI) and peak NTG-mediated index (NMI) were determined in all subjects.

Results: There were no significant gender differences in RHI, however peak NMI was significantly greater in females than in males (3.11±1.59 versus 2.50±1.34, P= 0.05). Time to peak NMI was not significantly different between genders.

Conclusions: In healthy adults, peak NMI was significantly greater in females than in males, suggesting that gender differences exist in the microvascular vasodilation responses to NTG.


Impact of Vitamin C on Endothelial Function and Exercise Capacity in Patients with a Fontan Circulation.


Evaluated the impact of antioxidant therapy on functional health status in 53 Fontan-palliated patients, randomized to high-dose vitamin C, or placebo for 4 weeks. Peripheral vascular function (EndoPAT) was the primary outcome measure, and exercise capacity the secondary outcome, with both assessed before and after treatment.

Results: Vitamin C therapy was not associated with a significant improvement in either primary or secondary outcome measures. In subjects with abnormal vascular function at baseline, vitamin C therapy more frequently resulted in normalization of the EndoPAT index compared with placebo (45% vs. 17%), and likewise in the PAT ratio (38% vs. 13%).

Conclusions: Short-term therapy with vitamin C does not alter endothelial function or exercise capacity in an asymptomatic Fontan population as a whole. Vitamin C may provide benefit to a subset of Fontan patients with abnormal vascular function.

Effects of nebivolol or irbesartan in combination with hydrochlorothiazide on vascular functions in newly-diagnosed hypertensive patients: The NINFE (Nebivololo, Irbesartan Nella Funzione Endoteliale) study.

Vitale C, Marazzi G, Iellamo F, Spoletini I, Dall’armi V, Fini M, Volterrani M.

Compared effects of 8 weeks of nebivolol to irbesartan, both in association with hydrochlorothiazide, on endothelial function, pulse wave velocity, augmentation index, central and brachial blood pressures in 65 hypertensive patients naive on therapy, at baseline and at the end of the study.

Results: Changes in endothelial function between groups were similar at the end of the study. Significant reductions in pulse wave velocity, central blood pressure, and augmentation index adjusted for heart rate, were found in both groups at the end of the study, without significant differences between groups.

Conclusions: Short-term treatment with nebivolol was not inferior to irbesartan, when both were taken with hydrochlorothiazide.


Polyphenol-rich cranberry juice has a neutral effect on endothelial function but decreases the fraction of osteocalcin-expressing endothelial progenitor cells.


Evaluated effect of daily consumption of Cranberry Juice (CJ) vs placebo in a double blind randomized study over 4 months, on vascular function and on endothelial progenitor cells (EPCs) carrying the osteoblastic marker osteocalcin in 84 subjects with endothelial dysfunction and cardiovascular risk factors. Responses to reactive hyperemia were measured by EndoPAT. Peripheral blood monocytes were stained for EPC markers, and osteocalcin, and counted.

Results: The effect of CJ on peripheral endothelial function and on circulating EPC counts did not change during the study. Compared to placebo, CJ induced a decrease in the fraction of EPCs expressing osteocalcin (p=0.019).

Conclusions: Long-term supplementation of polyphenol-rich CJ did not improve peripheral endothelial function.


Relation between digital peripheral arterial tonometry and brachial artery ultrasound measures of vascular function in patients with coronary artery disease and in healthy volunteers.


Evaluated the relation between EndoPAT and simultaneous brachial artery ultrasonography at baseline and after reactive hyperemia in 99 patients with established coronary artery disease, and 40 healthy controls with low cardiovascular disease risk.

Results: Under basal conditions, the digital pulse volume amplitude demonstrated a significant positive correlation with brachial artery velocity-time integral, independent of arterial diameter, (p<.001), in both cohorts. In contrast, no relation between reactive hyperemia-evoked PAT ratio and either brachial artery flow-mediated dilation or shear stress was observed in either.

Conclusions: EndoPAT measures of vascular function more closely reflected basal blood flow in the brachial artery than reactive hyperemia-induced changes in arterial diameter or flow velocity.


Relationship Among Endothelial Response to Hyperemia, Bone Marrow-Derived Progenitor Cells, and Parathyroid Hormone in Renal Transplantation.

Fatini C, Sticchi E, Cesari F, Gori AM, Cioni G, De Stefano M, Bertoni E, Paudice N, Salvadori M, Zonazzi M, Abbate R.
Transplantation. 2012 Feb 17. [Epub ahead of print]

Evaluated the relationships amongst: endothelial response to hyperemia, circulating progenitor cells (CPCs) and endothelial progenitor cells (EPCs), PTH, and genetic parameters, in 120 renal transplant recipients (RTRs), 107 healthy controls (group A) and 109 patients with cardiovascular risk factors (group B).

Results: Median RHI was lower in RTRs vs. group A (P=0.05). RHI was significantly lower with three or more risk factors (P=0.04) and was positively correlated with EPCs (P=0.04) but not with PTH (P=0.2). Patients under dialysis for > 5 years had lower RHI than those with < 1 year (P=0.08). No relationship between eNOS gene -786T>C, 894G>T, and 4a/4b polymorphisms and RHI. RHI correlated to the expected behavior of EPC’s and PTH levels.

Conclusions: This study shows an altered endothelial response associated with reduced EPCs, and increased PTH in RTRs.

Spotlight on Dr. Aaron Kelly

Dr. Aaron Kelly is an Assistant Professor of Pediatrics at the University of Minnesota Medical School. Dr. Kelly’s research focuses on the prevention of cardiovascular disease and type 2 diabetes in children and adults, with a particular emphasis on obesity and vascular health, and is supported by the NIH, the Thrasher Research Fund, and industry. He is the principal investigator of an NIH-funded study seeking to characterize endothelial function/activation, arterial stiffness, and carotid intima-media thickness in children and adolescents with severe obesity, and a member of the American Heart Association Committee on Atherosclerosis, Hypertension, and Obesity in the Young.

Dr. Kelly and his colleagues have published a number of articles using the EndoPAT in children and adults, significantly contributing to the scientific base and clinical acceptance of the EndoPAT, as evidenced by the following publications:


