Effect of Lifestyle Modifications on Endothelial Function in Metabolic Syndrome Patients


Investigated the utility of the lifestyle modification self-assessment score (Self-AS) in the improvement of endothelial function by office-based counseling in 207 patients with metabolic syndrome (MetS), 70 of whom participated in a prospective interventional study received simple office-based lifestyle modification counseling that was accompanied by Self-AS questionnaire after 10 months, and 124 age- and sex-matched controls without MetS. Endothelial function was assessed by EndoPAT-RHI.

RESULTS: MetS patients had significant endothelial dysfunction compared with controls (P < 0.001). RHI was significantly improved following lifestyle modifications (P < 0.001), whereas reductions in waist circumference (P = 0.01) and increased high-density lipoprotein cholesterol (P < 0.001) independently correlated with improved RHI. Self-AS significantly correlated with changes in waist circumference (P = 0.001) and RHI (P = 0.02). Patients with a good achievement of lifestyle modifications (higher Self-AS) had significant improvement in endothelial function compared with those with lower scores (P < 0.001).

CONCLUSION: Good achievement of lifestyle modifications as evaluated on Self-AS, significantly improved endothelial function with concomitant reductions in waist circumferences in MetS patients.


Latest PAT Publications

Non-invasive endothelial function testing and the risk of adverse outcomes: a systematic review and meta-analysis.


Eur Heart J Cardiovasc Imaging. 2014 Jan 7. [Epub ahead of print]

Systematically reviewed and meta-analysed articles relating flow-mediated dilatation (FMD) of the brachial artery or EndoPAT, to CV events, to understand their roles in predicting adverse events, including cardiovascular (CV) events and all-cause mortality, and to determine whether they are independent risk factors for future CV events and mortality. Data were extracted on study characteristics, study quality, and outcomes. Relative risks (RRs) from individual studies were combined and a pooled multivariate RR was calculated.

RESULTS: For FMD, 32 studies (15,191 individuals), were meta-analysed. The pooled RR of CV events and all-cause mortality per 1% increase in FMD, adjusting for potential confounders, was 0.90 (0.88-0.92). Three studies (865 individuals), evaluated the prognostic value of EndoPAT for CV events, and the pooled RR per 0.1 increase in reactive hyperaemia log-index (Ln-RHI), was 0.85 (0.78-0.93).

CONCLUSION: FMD and EndoPAT are independent predictors of CV events and all-cause mortality. Further evaluation of the prognostic utility of PAT is necessary to compare it with FMD as an endothelial function test in clinical practice.


The Effects of Dipeptidyl Peptidase-4 Inhibitors on Cardiovascular Disease Risks in Type 2 Diabetes Mellitus (Review Article).

Yousefzadeh P, Wang X.


Review of the current literature investigating the effects of dipeptidyl peptidase-4 (DPP-4) inhibitors on the risk factors of cardiovascular disease (CVD).

RESULTS: The majority of the recent clinical studies have demonstrated that DPP-4 inhibitors have beneficial effects on the cardiovascular (CV) system. These agents may have the potential to lower blood pressure, improve lipid profile and endothelial dysfunction (as demonstrated with EndoPAT measurements, among others), decrease the macrophage-mediated inflammatory response, and prevent myocardial injury.

CONCLUSION: DPP-4 inhibitors have some CV protective effects in type 2 diabetes mellitus (T2DM) in addition to their antidiabetic actions. Long-term outcome clinical trials are under way to investigate the effects of the DPP-4 inhibitors on the elevated CV risks in patients with T2DM. Further investigation in a large cohort is warranted to assess the exact mechanisms of CV protective effects of DPP-4 inhibitors.


Successful Diet and Exercise Therapy as Evaluated on Self-Assessment Score Significantly Improves Endothelial Function in Metabolic Syndrome Patients.


Investigated the utility of the lifestyle modification self-assessment score (Self-AS) in the improvement of endothelial function by office-based counseling in 207 patients with metabolic syndrome (MetS), 70 of whom participated in a prospective interventional study received simple office-based lifestyle modification counseling that was accompanied by Self-AS questionnaire after 10 months, and 124 age- and sex-matched controls without MetS. Endothelial function was assessed by EndoPAT-RHI.

RESULTS: For FMD, 32 studies (15,191 individuals), were meta-analysed. The pooled RR of CV events and all-cause mortality per 1% increase in FMD, adjusting for potential confounders, was 0.90 (0.88-0.92). Three studies (865 individuals), evaluated the prognostic value of EndoPAT for CV events, and the pooled RR per 0.1 increase in reactive hyperaemia log-index (Ln-RHI), was 0.85 (0.78-0.93).

CONCLUSION: FMD and EndoPAT are independent predictors of CV events and all-cause mortality. Further evaluation of the prognostic utility of PAT is necessary to compare it with FMD as an endothelial function test in clinical practice.


Effects of atorvastatin and ezetimibe on endothelial function in dyslipidemic patients with chronic kidney disease.

Ishimitsu T, Ohno E, Ueno Y, Onoda S, Nagase A, Ohira T, Nakano N, Satonaka H.


Compared the effects of a statin and an intestinal cholesterol transporter inhibitor in 20 dyslipidemic patients with Chronic kidney disease (CKD) presenting with proteinuria and/or pathological glomerular filtration rate. Either 5-10 mg atorvastatin or 10 mg ezetimibe was given for 3 months each in a randomized crossover manner and the parameters of oxidative stress, inflammation and EndoPAT-RHI were compared.

RESULTS: Atorvastatin lowered serum LDL cholesterol more than ezetimibe (P < 0.001), while serum -glutamyl tranpeptidase was higher in atorvastatin than in ezetimibe (P = 0.013). On the other hand, serum oxidized LDL and high-sensitivity C-reactive protein were lower in atorvastatin treatment than in ezetimibe treatment (P=0.002 & P=0.003). Although serum adiponectin was not significantly different between the two drugs, RHI was higher in atorvastatin than in ezetimibe (P = 0.023).

CONCLUSION: Atorvastatin is more potent than ezetimibe in improving the serum lipid profile, reducing oxidative stress, suppressing inflammation and preserving endothelial function, while ezetimibe may be advantageous in reducing the hepatic lipid load.


A randomized pilot study of L-arginine infusion in severe falciparum malaria: preliminary safety, efficacy and pharmacokinetics.

Yeo TW, Lampah DA, Rooslamiati I, Gitawati R, Tjitra E, Kenangalem E, Price RN, Duffull SB, Anstey NM.

Assessed the safety, efficacy and pharmacokinetics of L-arginine to improve NO bioavailability in an open-label pilot study of L-arginine in adults with severe malaria (ARGISM-1 Study). Patients randomized to 12 g L-arginine hydrochloride (n=6), or saline, (n=2), over 8 hours together with intravenous artesunate. Vital signs, blood lactate, L-arginine and EndoPAT-RHI were assessed serially. Pharmacokinetics of L-arginine determined using NONMEM.

RESULTS: No deaths in either group. Following L-arginine, no changes in blood pressures or other vital signs, nor significant changes in mean potassium, glucose, bicarbonate, or pH, lactate clearance, or RHI, with transient mean maximal increases in plasma potassium of 0.3 mmol/L, and mean maximal decreases in blood glucose of 0.8 mmol/L and bicarbonate of 2.3 mEq/L. Pharmacokinetic modelling (n=4) showed L-arginine concentrations 40% lower than predicted.

CONCLUSION: The first clinical trial of an adjunctive treatment aimed at increasing NO bioavailability in severe malaria. L-arginine 12 g over 8 hours was safe, but did not improve lactate clearance or endothelial NO bioavailability. Future studies may require increased doses of L-arginine.

Test-retest reliability of peripheral arterial tonometry in the metabolic syndrome.

Sauder KA, West SG, McCrea CE, Campbell JM, Jenkins AL, Jenkins DJ, Kendall CW.

Assessed the test-retest reliability of EndoPAT-RHI in adults with the metabolic syndrome (n = 20) and determined the sample size and power estimates for study design. Participants completed five EndoPAT tests each separated by 1 week.

RESULTS: RHI showed robust repeatability (intra-class correlation = 0.74). A parallel-arm study powered at 0.90 would require 22 participants to detect an absolute change in RHI of 0.40 units (equal to ~25% change in this sample), whereas a crossover study would require 12 participants.

CONCLUSION: Demonstrated that EndoPAT can be used to assess endothelial dysfunction in adults with the metabolic syndrome as reliably as in healthy samples.


Coffee polyphenols improve peripheral endothelial function after glucose loading in healthy male adults.


Investigated the vascular effects of coffee polyphenols (CPPs), and tested the hypothesis that a single ingestion of CPP during glucose loading would improve EndoPAT-RHI in a randomized intervention study with crossover design of the effects of a 75-g glucose load with or without CPP, in healthy, nondiabetic adult men.

RESULTS: Blood glucose and insulin levels were similarly elevated after glucose loading with and without CPP. RHI did not significantly decrease after glucose loading without CPP, but significantly increased with CPP (P < .05) relative to baseline, and between treatments (P < .05). No significant changes were observed in an oxidative stress marker after glucose loading, with or without CPP.

CONCLUSION: These findings suggest that a single ingestion of CPP improves RHI after glucose loading in healthy subjects.


Adolescent blood pressure hyperreactors have a higher reactive hyperemic index at the fingertip.

Radtke T, Eser P, Kriemler S, Saner H, Wilhelm M.

Examined the impact of blood pressure hyperreactivity (BPhyp), on EndoPAT-RHI, amongst 52 healthy, normotensive adolescents, mean age 14.5 ± 0.7 years, 16 of whom had BPhyp identified according to their cardiovascular response to a cold pressor test, and 16 matched normal responders. RHI was assessed at rest and after exhaustive cycling exercise. Indices of autonomic tone were assessed by ambulatory electrocardiograph, and physical activity was measured using accelerometry.

RESULTS: At rest, BPhyp had a significantly higher RHI than normal reactors (2.1 ± 0.4 vs. 1.6 ± 0.4, P<0.003). After exhaustive cycling exercise, these differences were abolished. No differences between groups existed in physical activity levels, exercise capacity and indices of autonomic tone.

CONCLUSION: Normotensive hyperreactors have a markedly higher RHI compared to normal reactors. Future studies using Endo-PAT should consider the large effect of vascular hyperreactivity.

Impaired endothelial function after aneurysmal subarachnoid haemorrhage correlates with arginine:asymmetric dimethylarginine ratio.


Prospective observational study of 48 aneurysmal subarachnoid haemorrhage (SAH) subjects, and 23 controls examining associations between EndoPAT-RHI and plasma concentrations of S-100B protein, nitrite/nitrate, arginine, and asymmetric dimethyl arginine (ADMA), middle cerebral artery flow velocity (VMCA), angiographic vasospasm, delayed neurological deficit, and 30 day survival. Measurements were obtained at days 0-2, 3-5, 6-8, 9-11, and 12-15.

RESULTS: RHI was 1.67 (±0.46) at days 0-2 after SAH but increased at days 3-15 to the same levels as in controls (P<0.05 vs. days 0-2), and both arginine and ADMA increased after SAH compared with days 0-2 controls (P<0.05). RHI was lower in subjects who died before day 30 (P=0.07), but no trends were observed in relation to angiographic vasospasm or delayed neurological deficit. S-100B was highest in non-survivors (P<0.01) and in subjects with neurological deficit (P<0.01). RHI was positively correlated with arginine:ADMA ratio (r=0.43, P<0.005), but not with nitrite/nitrate, VMCA, or S-100B.

CONCLUSION: EndoPAT-RHI is attenuated in the first days after SAH indicating acute systemic endothelial dysfunction, and correlates with imbalance of the arginine/ADMA pathway.

Endothelial function and Cardiovascular Events in Chronic Kidney Disease.


Stratified cardiovascular risk in 383 chronic kidney disease (CKD) patients with at least one coronary risk factor, and determined if EndoPAT-RHI was associated with angiographically determined CAD, and was predictive of cardiovascular events during a mean 30 month follow-up.

RESULTS: Ln-RHI was significantly lower in CKD than in 323 risk factor-matched non-CKD controls (0.53 ± 0.19 vs. 0.58 ± 0.22, p=0.001). Amongst CKD patients, Ln-RHI was significantly lower in CAD (0.50 ± 0.18, n=262) vs. non-CAD (0.58 ± 0.21, n=121) (p<0.001). Multivariate logistic regression analysis identified Ln-RHI as an independent factor associated with the presence of CAD (p=0.001). During follow up, CKD patients had 90 cardiovascular events, and low Ln-RHI was an independent predictor of cardiovascular events (p<0.001). C-statistics for the predictive value of combined Ln-RHI and Framingham risk score (FRS), were 0.49 for FRS, and 0.62 for FRS + Ln-RHI (p<0.005), with 22% reclassification index improvement (p<0.001).

CONCLUSION: EndoPAT-RHI was significantly impaired in CKD patients and correlated with the presence of CAD. Severe endothelial dysfunction was an independent and incremental predictor of cardiovascular events in CKD.


Reactive Hyperaemia Index as a marker of endothelial dysfunction in children with Crohn’s disease is significantly lower than healthy controls.


Determine the extent of premature atherosclerosis in paediatric Crohn’s disease (CD) by measuring EndoPAT-RHI as a functional marker of endothelial dysfunction (ED), in 21 CD children and 12 matched controls.

RESULTS: RHI was significantly lower in CD vs. controls (p<0.05). E-selectin (p<0.05), asymmetric dimethylarginine (p<0.01) and high-sensitive CRP (p<0.05), but not vascular cells adhesive molecule-1 values, were significantly increased in CD vs. controls.

CONCLUSION: Significantly decreased RHI and elevated plasma levels of specific biochemical parameters seems to be related to systemic inflammation and ED in CD children. This combined method assessment might be a useful tool for detection of ED and stratification of cardiovascular risk in CD patients.

Association between lowered endothelial function measured by peripheral arterial tonometry and cardio-metabolic risk factors -- a cross-sectional study of Finnish municipal workers at risk of diabetes and cardiovascular disease.


Determined the association between endothelial function measured by EndoPAT-FRHI, and cardio-metabolic risk factors, anthropometry, levels of total cholesterol, HDL cholesteral, triglycerides, fasting glucose, glyctated haemoglobin, and high sensitivity C-reactive protein taken from the blood samples, in a middle aged population of 312, at risk of diabetes or cardiovascular disease.

RESULTS: In the linear regression model, male sex was associated with lower F-RHI. In sex-adjusted linear regression models, waist circumference, fasting glucose, glyctated hemoglobin, triglycerides, body fat percentage, body mass index, current smoking, and impaired fasting glucose or diabetes were separately associated with lower F-RHI, and HDL cholesterol and resting heart rate were associated with higher F-RHI. HDL, sex, body mass index, and current smoking entered a stepwise multivariable regression model, in which HDL cholesterol was associated with higher F-RHI, and smoking, male sex and body mass index were associated with lower F-RHI, explaining 28.3% of FRHI variability.

CONCLUSION: Main predictors of a lowered FRHI include low level HDL, male sex, overweight and smoking. FRHI remains largely accounted for by unknown factors.

Professor Chim Lang, MD.

Professor Chim Lang is a consultant cardiologist and clinical pharmacologist and Professor of Cardiology at Ninewells Hospital and Medical School, University of Dundee, United Kingdom. He trained in both cardiology and clinical pharmacology in the UK and in the USA, where he was a Merck International Fellow in Clinical Pharmacology at Vanderbilt University, Nashville and a Fulbright Scholar at Columbia University, New York. He is a Fellow of the Royal College of Physicians of Edinburgh and of London, a Fellow of the American College of Cardiology, and sits on the editorial boards of several scientific journals. He leads an integrated cardiovascular research laboratory dedicated and equipped to the study of cardiac and vasomotor regulation. These techniques are applied towards translational research and in the development of biomarkers and novel treatment strategies in patients with cardiovascular diseases, ranging in scope from the clinical physiology and pharmacology of neurohormones in cardiovascular diseases, to the pathophysiology of the peripheral and coronary endothelia. Prof. Lang and colleagues have contributed significantly to the scientific base and clinical acceptance of the EndoPAT, as evidenced by the following publications:


In the management of CV risk
Prof. Michael Shechter, Chaim Sheba Medical Center, Tel Hashomer, Israel

As an Additional Marker to Target in Secondary Prevention
Prof. Amir Lerman, Mayo Clinic, Rochester, MN, USA

Sleep Apnea Endothelial Dysfunction Association – Targeting the Two makes it Even Better
Prof. Giora Pillar, Carmel Medical Center, Haifa, Israel

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World Anti-Aging Congress & Exposition
May 15th - 17th, 2014
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Booth # 1028

AADSMA
American Academy of Dental Sleep Medicine 23rd Annual Meeting
May 29th – 31st, 2014
Minneapolis, MN, USA
Booth # 316

EAS
European Atherosclerosis Society 82nd Congress
May 31st – June 3rd, 2014
Madrid, Spain
Booth # 15

SLEEP 2014
28th Annual Meeting of the Associated Professional Sleep Societies
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