Examined the effects of erythritol on vascular function in 24 patients with type 2 diabetes mellitus, who consumed erythritol 36 g/day as an orange-flavored beverage for 4 weeks and a single dose of 24 g during the baseline and final visits. Determined vascular function, including Endo PAT-log RHI, before and after acute (2 h) and chronic (4 weeks) erythritol consumption.

RESULTS: Acute erythritol improved lnRHI (0.52 ± 0.48 to 0.87 ± 0.29, P = 0.005). Chronic erythritol decreased central pulse pressure (47 ± 13 to 41 ± 9 mmHg, p=0.02) and tended to decrease carotid-femoral pulse wave velocity (p=0.06).

CONCLUSION: Erythritol consumption acutely improved lnRHI, and chronic treatment reduced central aortic stiffness. Erythritol may be a preferred sugar substitute for patients with diabetes mellitus.


Studied the effects of 6 months of plant stanol esters (staest) on arterial stiffness and endothelial function (Endo PAT-RHI), in 92- asymptomatic adults, (35 men) who had prehypertension or stage 1 hypertension, mean age 54.5 y, tested before and after intervention staest group serum total, LDL, and non-HDL cholesterol concentrations declined significantly vs. controls (p<0.001 for all).

RESULTS: Post intervention staest group serum total, LDL, and non-HDL cholesterol concentrations declined significantly vs. controls (p<0.001 for all). Both CAVI and AI were unchanged in staest, but increased in control men and difference in the changes between groups was significant (p=0.023, p=0.046 respectively). The reductions in LDL and non-HDL cholesterol were related to improvement in RHI (r=-0.452, p=0.006 and -0.436, p=0.008).

CONCLUSION: LDL and non-HDL cholesterol lowering with 6 months staest reduced arterial stiffness in small arteries and had a beneficial effect on large arterial stiffness and on RHI.


Compared the effects of 5 weeks of low-fat dairy vs. low-fat nondairy products on systolic and diastolic blood pressures (SBP and DBP), plasma lipids and Endo PAT-RHI, and augmentation index (AI), in 62 men and women with untreated prehypertension or stage 1 hypertension, mean age 54.5 y, tested before and after a standard breakfast challenge at the end of each treatment period.

RESULTS: No significant differences between dairy and nondairy treatments in SBP or DBP in the resting postprandial state or from premeal to 3.5 hours postmeal, or in RHI or AI from premeal to 2 hours postmeal. Among 14 subjects with endothelial dysfunction (RHI ≤ 1.67), premeal RHI was significantly higher in the dairy versus nondairy condition (2.32 versus 1.50, p=0.002). Fasting plasma lipoproteins were not significantly different between treatments.

CONCLUSION: No significant effects of consuming low-fat dairy vs. low-fat nondairy products were observed for blood pressures, RHI, AI, or plasma lipids in the overall sample, however dairy foods might improve RHI in those with endothelial dysfunction.


AUTHORS’ ABSTRACT - Atherosclerosis underlies the major causes of death in the Western World. Our main goal is to detect early changes of atherosclerosis and to identify subjects at highest cardiovascular risk that may aid in the development of prevention approaches and better management that will decrease cardiovascular morbidity and mortality. The new methods that are of interest include the advanced vascular ultrasound methods, the infra red and near infra red imaging techniques, the Endo PAT device that reflects peripheral arterial tone, the electron beam computed tomography, the magnetic resonance imaging, and the molecular imaging techniques. In this review we will focus on the future of advanced imaging techniques that are being developed to detect early (pre-clinical) development of atherosclerosis.
Investigated the effect of orthostasis on endothelial function using Endo PAT-RHI in 11 males and 20 females, and further examined effects of steroid hormones on the RHI response to orthostasis in females at different menstrual phases (n=11), and on oral contraceptives (n=9). Subjects were tested twice, two weeks apart; (menstruating females first tested on either days 1-7 or 14-21 of cycle). RHI was assessed at baseline and following a 20-min active orthostatic challenge.

**RESULTS:** In females, baseline RHI 1.71 ± 0.09 (mean ± SEM) increased to 2.07 ± 0.09 following orthostasis (p<0.001), and from 1.60 ± 0.08 to 1.94 ± 0.13 (p<0.001) in males. There were no significant differences between females and males, nor in menstrual cycle phases and the usage of oral contraceptive.

**CONCLUSION:** Increased vasodilatory endothelial response followed orthostasis in males and females; the effect of gender and sex hormones appears limited. Further studies indicated to determine the role of post orthostasis endothelial response in the pathophysiology of orthostatic intolerance.


**EDITOR’S note:** An inter-test interval of at least 60 minute between repeat Endo PAT studies is required. The apparently short time period between tests in this study may possibly have contributed to the observed increase in RHI following orthostasis.

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**Methodological considerations and practical recommendations for the application of peripheral arterial tonometry in children and adolescents.**


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Authors allude to Endothelial dysfunction’s recognition as the prime mover in the development of atherosclerosis and hence its pivotal role in both cardiovascular morbidity and mortality, and review the clinical utility of invasive and non-invasive means for assessing it. They conclude that Endo PAT which assesses microvascular function provides a non-invasive method which avoids the user dependence of flow-mediated dilatation (FMD), which evaluates nitric oxide dependent vasodilation in large vessels. Authors further observe that in children and adolescents there is no consensus with regard to either measuring protocol or data analysis of Endo PAT, with most studies applying the conventional adult methodology, which may not be appropriate.

**CONCLUSION:** While providing a detailed description of Endo-PAT’s methodology and use, authors allude to differences between children, adolescents and adults and provide recommendations for a standardized application of Endo PAT in children and adolescents, as well as for population-specific data analysis methodology.


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**Automated preoperative assessment of endothelial dysfunction and risk stratification for perioperative myocardial injury in patients undergoing non-cardiac surgery.**

_McIlroy DR, Chan MT, Wallace SK, Symons JA, Koo EG, Chu LC, Myles PS._


Measured preoperative Endo PAT-RHI in 238 subjects before intermediate or high-risk surgery to determine whether RHI could provide effective risk stratification for Myocardial injury after non-cardiac surgery (MINS).

**RESULTS:** Myocardial injury (serum troponin ≥0.04 μg/l within 3 postoperative days) occurred in 35 subjects (14.7%). Using adjusted for age Lee index, and a composite measure of the extent of surgery, an RHI threshold of ≤1.22, was associated with MINS [odds ratio 10.1, 95% confidence interval (CI) 3.3-30.9, p=0.001] and increased time to discharge ([hazard ratio 0.39, 95% CI 0.23-0.65, p=0.001]). RHI identified MINS with a sensitivity of 31%, a specificity of 96%, and a positive diagnostic likelihood ratio of 8.0. Risk classification for MINS was improved by adding RHI to the Lee index (χ² statistic increased from 0.69 to 0.77, p=0.003), but prognostic utility varied widely between sites.

**CONCLUSION:** Assessment of RHI may enhance preoperative risk stratification for MINS. A large inter-site variation in prognostic utility needs to be further understood.


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**Obesity, hyperglycemia and endothelial function in inner city Bronx adolescents: a cross-sectional study.**

_Agarwal C, Cohen HW, Muzumdar RH, Heptulla RA, Renukuntla VS, Crandall J._


Investigated if childhood obesity is associated with endothelial dysfunction (Endo PAT-RHI), and if obesity plus impaired glucose regulation further lowers RHI; in 14 lean and 37 obese 12-18 year olds. The obese group was subdivided into normal (NCT, n = 22) and impaired glucose regulation (IGR, n = 15).

**RESULTS:** RHI was lower in obese vs. lean (1.70 +/- 0.02 vs. 1.98 +/- 0.09, p=0.02), and remained so when adjusted for age, sex and ethnicity (p=0.02). RHI worsened with increasing metabolic burden in the lean, obese-NCT and obese-IGR groups, respectively (p trend = 0.03). Obese subjects were significantly more insulin resistant (p=0.03), had higher levels of leptin (p=0.004), hsCRP (p=0.0004), and TNF-alpha (p=0.03) vs. lean. Adjusting for insulin resistance and adipocytokines substantially attenuated the obesity association with RHI.

**CONCLUSION:** Risk factors for adult cardiovascular disease, including impaired RHI, insulin resistance and inflammation, are evident in obese adolescents, and insulin resistance and inflammation may mediate worsening RHI in obesity.

Nitrosylated Hemoglobin Levels in Human Venous Erythrocytes Correlate with Vascular Endothelial Function Measured by Digital Reactive Hyperemia.


Tested whether erythrocyte levels of nitrosylated hemoglobin (HbNO-heme) may reflect vascular endothelial function (Endo PAT-RHI), in 50 healthy volunteers. Erythrocyte HbNO levels were measured at baseline and at the peak of hyperemia.

RESULTS: Overall mean baseline erythrocyte HbNO concentration was 219+/−12 nmol/L, with HbNO levels and RHI higher in contraceptive pill users than in males. HbNO levels increased at 1-2 min post-occlusion (120+/−8% of baseline); post-occlusion HbNO levels were correlated with basal levels. Both basal and post-occlusion HbNO levels were significantly correlated with RHI, (r=0.58; P<0.0001 for basal HbNO).

CONCLUSION: Demonstrates quantitative measurements of 5-coordinate α-HbNO in human venous erythrocytes, its dynamic physiologic regulation and correlation with Endo PAT-RHI. This opens the way to further understanding of in vivo determinants of NO bioavailability in human circulation.

http://www.ncbi.nlm.nih.gov/pubmed/24130774

Impaired Digital Reactive Hyperemia and the Risk of Restenosis after Primary Coronary Intervention in Patients with Acute Coronary Syndrome.


Investigated whether impaired Endo PAT-RHI is associated with restenosis (>50% at eight months), after percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS), in 86 ACS patients who underwent successful primary PCI of native vessels for de novo lesions. RHI was calculated at three weeks and eight months after ACS.

RESULTS: Restenosis was detected in 17 patients (20%). There were no differences in RHI at three weeks between patients with and without restenosis, but RHI at eight months was significantly attenuated in patients with restenosis (p=0.03). Univariate logistic regression analysis showed that eight-month RHI<2 was a significant risk factor for restenosis (p=0.02).

CONCLUSION: Impairment of RHI at eight months is associated with restenosis after primary intervention in patients with ACS, suggesting the potential of Endo PAT-RHI as a noninvasive test for identifying patients with a high risk of restenosis.

We were deeply saddened by the untimely passing of Professor Joseph A Vita M.D., a most esteemed colleague and friend, a professor at Boston University, a renowned cardiologist and scientist, one of the leading investigators in the area of endothelial function with over 200 peer-reviewed publications and on the editorial boards of the foremost journals in the cardiovascular field.

Joe was one of the Framingham Heart Study key investigators and was instrumental in introducing non-invasive endothelial function testing into this prestigious study.

His pioneering work in this field has been extensive and broached a wide span of clinical and basic research areas in vascular biology and inflammation, and particularly on endothelial dysfunction in atherosclerosis and associated risk factors.

Joe's publications employing EndoPAT were also broad ranging; from mitochondrial dysfunction in the impairment of endothelial dysfunction in T2DM, to clinical intervention studies, and to large community based epidemiological studies.

The seminal contributions of Joe's work has indelibly enriched the scientific base and clinical acceptance of testing endothelial function, and will stand as an enduring and shining legacy of this great man.

We extend our condolences to his wife and family.