**Latest PAT Publications**

### Ticagrelor improves peripheral arterial function in patients with a previous acute coronary syndrome.


Compared EndoPAT-RHI in 127 patients with a previous acute coronary syndrome (ACS) within 3 months to 3 years, on maintenance dose of; (1) aspirin only (controls; n = 35), (2) clopidogrel 75 mg (n = 35), (3) prasugrel 10 mg (n = 32), or (4) ticagrelor 90 mg twice daily (n = 25).

**RESULTS:** Ticagrelor significantly improved RHI compared to aspirin only controls (p < 0.01), clopidogrel (p < 0.01), and prasugrel (p < 0.001). There were fewer patients with RHI <1.67 in the ticagrelor group (12%) compared to aspirin (51%), clopidogrel (46%), and prasugrel (53%) (p < 0.01).

**CONCLUSION:** Treatment with ticagrelor improves RHI compared to no ADP blocker, clopidogrel, or prasugrel treatment.


### Acute Consumption of Walnuts and Walnut Components Differentially Affect Postprandial Lipemia, Endothelial Function, Oxidative Stress, and Cholesterol Efflux in Humans with Mild Hypercholesterolemia.


Evaluated the effects on postprandial lipemia, endothelial function (EndoPAT-RHI), and oxidative stress of consumption of whole walnuts (85 g), separated nut skins (5.6 g), de-fatted nutmeat (34 g), and nut oil (51 g) respectively, in a 4-period, four-way crossover trial in 15 healthy overweight and obese adults.

**RESULTS:** Walnut skin decreased RHI compared with baseline (P = 0.02) and a difference persisted between the skin and oil treatments (P = 0.01), while the Framingham RHI was maintained with the oil treatment compared with the skins and whole nut. Ferric reducing antioxidant potential (FRAP), and mean FRAP was greater with oil and skin treatments compared with the nutmeat (P < 0.01). Cholesterol efflux increased following whole walnut consumption vs. fasting baseline (P = 0.02).

**CONCLUSION:** Walnut oil favorably affected endothelial function and whole walnuts increased cholesterol efflux. These 2 novel mechanisms may explain in part the cardiovascular benefits of walnuts.


### Weight Loss by Multidisciplinary Intervention Improves Endothelial and Sexual Function in Obese Fertile Women.


Investigated two 8 week weight loss programs on female sexual dysfunction complaints (6FSFI-6 scores), and endothelial function (EF, EndoPAT-RHI) in 44 premenopausal, obese females, allocated to: (A) intensive residential diet plus controlled exercise program with lifestyle modifications (n=23), or (B), non-intensive outpatient diet and exercise (n=21), both followed by 8 weeks outpatient controlled diet plus home exercise.

**RESULTS:** After 16 weeks, FSFI-6 score, frequency of sexual activity, arousal, lubrication, satisfaction scores, and RHI were significantly improved in (A) vs. (B) (all P<0.01), with likewise marked improvements in insulin resistance (IR), (P<0.001), weight (P<0.01), body mass index (P<0.01), fat mass (P<0.0001), and percentage of fat mass (P<0.005). FSFI-6 scores were related to peak insulin (P<0.0001) and RHI (P<0.001).

**CONCLUSION:** A multidisciplinary approach to female obesity was superior to conventional outpatient clinic for weight loss and improvement of sexual dysfunction. Such changes might be related to persistent improvements in EF and IR.


### Drug attrition during pre-clinical and clinical development: Understanding and managing drug-induced cardiotoxicity.


This article summarizes the clinical manifestations of drug-induced cardiotoxicity by various cancer chemotherapies and novel drugs for the treatment of other diseases. Furthermore, it presents an overview of biomarker and imaging techniques for the detection of drug-induced cardiotoxicity, and noninvasive assessment of endothelium-dependent vasorelaxation as a reflection of the functional status of the endothelium and vasculature and the impact of drugs on it. Article cites EndoPAT as an appropriate means to this end.

**CONCLUSION:** Guidelines for the management of patients exposed to drugs with cardiotoxic potential are presented as well as a checklist for collecting information when a safety signal is observed in clinical trials to more effectively assess the risk of cardiotoxicity and manage patient safety.

Self-Esteem Variability Predicts Arterial Stiffness Trajectories in Healthy Adolescent Females.


Explored the self-esteem of adolescent females over a 2.5-year period, and how it covaries with trajectories of vascular function (EndoPAT–RHI and EndoPAT–AI), in 130 adolescent females who completed the Rosenberg Self-Esteem scale every 6 months and RHI and AI were measured three times over the a 2.5-year period.

RESULTS: Hierarchical Linear Modeling revealed an association between self-esteem variability and EndoPAT–AI trajectories, (β = 9.0 × 10⁻³, SE = 4.4 × 10⁻³, p = .04). Neither trait self-esteem nor self-esteem variability was related to EndoPAT–RHI.

CONCLUSION: These findings suggest that fluctuating self-esteem may accelerate the early stages of vascular stiffening in young women, regardless of whether self-views are generally positive or negative.  

Investigation of changes in body composition, metabolic profile and skeletal muscle functional capacity in ischemic stroke patients: the rationale and design of the Body Size in Stroke Study (BoSSS).


The Body Size in Stroke Study (BoSSS) is a prospective, longitudinal observational study that will explore associations between the metabolic profile, body tissue wasting and particular metabolic and functional changes in skeletal muscle tissue in 150 consecutive stroke patients after 12 and 24 months, compared to matched healthy subjects and patients with chronic heart failure of similar age as controls.

The main objective is to study changes in body composition in stroke patients, and secondarily, changes in insulin sensitivity of adipose tissue and skeletal muscle and endothelial function (EndoPAT–RHI), and peripheral blood flow to provide insight in the vascular regulation in stroke patients.

CONCLUSION: This study will be the largest observational study providing insights into the metabolic and functional changes of muscle tissue in patients with acute ischemic stroke, and will increase our understanding of the pathophysiological tissue wasting in stroke disease, and help to develop new therapeutic strategies.

The Singapore Heart Failure Outcomes and Phenotypes (SHOP) Study and Prospective Evaluation of Outcome in Patients With Heart Failure With Preserved Left Ventricular Ejection Fraction (PEOPLE) Study: Rationale and Design.


Describes the Singapore Heart Failure Outcomes and Phenotypes (SHOP) study and Prospective Evaluation of Outcome in Patients with Heart Failure (HF), with Preserved Left Ventricular Ejection Fraction (PEOPLE) studies; parallel prospective studies using identical protocols to enroll 2,500 patients with HF, and over 2,000 matched controls without HF, in multiple centers in Singapore and New Zealand, to determine the relative prevalence, characteristics, and outcomes of patients with HF and preserved EF (EF 50%) vs. HF and reduced EF, and to determine initial data on ethnic differences within and between these countries.

Participants will undergo detailed clinical assessment, echocardiography, and blood biomarker measurements at baseline, 6 weeks, and 6 months, and be followed over 2 years for death or hospitalization. Substudies include vascular assessment (EndoPAT–RHI), cardiopulmonary exercise testing, retinal imaging, and cardiac magnetic resonance imaging.

CONCLUSION: The first prospective multicenter studies defining the epidemiology and interethnic differences among patients with HF in the Asia-Pacific region. Will provide unique insights into the pathophysiology and outcomes for these patients.

The Use of Digital Peripheral Artery Tonometry to Detect Endothelial Dysfunction in Pregnant Women Who Smoke.


Determined and compared endothelial function (EndoPAT–RHI), and serum cotinine and high-sensitivity C-reactive protein (CRP) levels in 29 smoker and 31 nonsmoker women with singleton pregnancies between 16 and 23 weeks.

RESULTS: Demographics including age, race, and parity were similar between groups. Mean RHI was not significantly different between smokers and nonsmokers (1.43 ± 0.32 versus 1.53 ± 0.39, p = 0.27). No correlation was noted when cotinine values were plotted against RHI or CRP values in smokers, but RHI did correlate with diastolic blood pressure (p = 0.002), systolic blood pressure (p = 0.006), and heart rate (p = 0.004).

CONCLUSION: Endothelial dysfunction was associated with systolic and diastolic blood pressure but both endothelial dysfunction and CRP values were not associated with smoking status in the mid-trimester of pregnancy.


Simultaneously assessed flow-mediated dilation (FMD) and EndoPAT-RHI in 454 women (age 40.4±16.1 years) and 100 men (mean age 44.7±15.3 years). Plasma estradiol, progesterone, luteinizing hormone, and follicle stimulating hormones were measured, and menstrual cycle and reproductive history were recorded.

RESULTS: Vascular function was blunted in men vs. women irrespective of menopausal status and adjustment for classical cardiovascular risk factors and hormones. FMD was positively correlated with estradiol during the menstrual cycle, while pulse amplitude and brachial artery diameter were negatively correlated with progesterone. Multivariable-adjusted regressions showed a relation of estradiol, and of age at menarche, with FMD, (P = 0.025 and P = 0.039 respectively), age at menopause status and adjustment for classical cardiovascular risk factors and hormones.

CONCLUSION: Better FMD and RHI vascular reactivity in women is not fully explained by female sex hormones and menopausal status. Age at menarche and duration of breastfeeding were also related to vascular function and need further investigation.


Peripheral artery disease is associated with severe impairment of vascular function.


Investigated whether peripheral artery disease (PAD) is associated with greater vascular dysfunction than established coronary artery disease (CAD), in subjects aged > 45 years with combined PAD and CAD (n = 198), PAD alone (n = 179), CAD alone (n = 466), and controls without CAD or PAD (n = 477); using non-invasive tests (brachial artery flow-mediated dilation (FMD) and EndoPAT-RHI, to evaluate endothelial function.

RESULTS: Patients with PAD had lower FMD vs. patients with CAD alone and no PAD or CAD (p < 0.0001). In multivariable models, adjusting for clinical covariates and the presence of CAD, PAD remained associated with FMD (p < 0.0001). PAD was associated also with lower nitroglycerin-mediated dilation and reactive hyperemia. Patients with both PAD and CAD had a lower RHI in unadjusted models but not in adjusted models. FMD was modestly associated with RHI in atherosclerotic patients with disease (r = 0.23, p < 0.0001) but not among control participants.

CONCLUSION: Patients with PAD have greater vascular function impairment, consistent with endothelial dysfunction, possibly contributing to adverse cardiovascular prognosis in PAD.


Lack of predictive correlation between peripheral arterial tone and colour flow Doppler parameters in men with erectile dysfunction.


Determined whether EndoPAT-RHI, or EndoPAT-AI, can predict the results of penile colour flow Doppler after pharmacological erection with prostaglandin E1, to identify both arterial insufficiency (abnormal peak systolic velocity (PSV)) and veno-occlusive disease (abnormal end diastolic velocity (EDV)) using colour flow Doppler in the evaluation of erectile dysfunction (ED) in 50 men presenting to an ED clinic.

RESULTS: Using Doppler analysis, 58% of patients were found to have arterial insufficiency (abnormal PSV) and 48% had veno-occlusive disease (abnormal EDV). Using EndoPAT-AI, 44% of patients were found to have increased arterial stiffness, and 54% had an abnormal RHI. Neither AI nor RHI were correlated with PSV or EDV.

CONCLUSION: In this cohort, EndoPAT- RHI and EndoPAT-AI did not reliably predict the results of penile Doppler. The two tests appear to measure different although potentially complementary aspects of the local and systemic vasculature.


Endothelial Dysfunction and Arterial Stiffness in Ischemic Stroke: The Role of Sleep-Disordered Breathing.


Evaluated endothelial function (EndoPAT-RHI), and arterial stiffness (EndoPAT-AI), in 37 post acute patients who had experienced an ischemic event 3 months before, in relation to sleep-disordered breathing (SDB), sleep disruption, and nocturnal oxygenation parameters, determined by full polysomnography.

RESULTS: AI was significantly different between patients with apnea-hypopnea index, (AHI) <20 and AHI index ≥20 (22.4±15.6% versus 34.6±21.6%; P=0.042), whereas RHI was not (2.02±0.65 versus 2.31±0.61; P=0.127). Patients with AHI ≥20 showed an increased risk for arterial stiffness (odds ratio, 5.98 [95% CI, 1.11-41.72]) even when controlling for age, sex, body mass index, hypertension, and diabetes mellitus. AI was correlated with the arousal index (P=0.010) and with mean O₂ saturation (P=0.043).

CONCLUSION: Post-stroke patients with moderate to severe SDB were more prone to have an increased AI, which was also correlated with sleep disruption (arousal index) and mean O₂ saturation.

Philipp Wild, Univ.-Prof. Dr. med., MSc., serves as Head of Preventive Cardiology and Preventive Medicine, Head of Clinical Epidemiology at the Center for Thrombosis and Hemostasis, Coordinating Investigator, Gutenberg Health Study, and Principal Investigator, German Center of Cardiovascular Research, Johannes-Gutenberg University, Medical Center Mainz Germany.

Professor Wild’s main research interests are in cardiovascular and genetic epidemiology with a special focus on subclinical, intermediate phenotypes of the cardiac and vascular disease, interaction between coagulation, inflammation and cardiovascular disease, implementation, conduct and analysis of epidemiological and clinical trials as well as health care research in the field of cardiovascular diseases including large-scale biobanking, and in preventive medicine. Professor Wild has published prolifically, with over 80 publications to date.

Professor Wild, together with his colleagues, are making significant contributions to the scientific base and clinical acceptance of the EndoPAT, as evidenced by the following publications:


