**Endothelial Progenitor Cells in Acute Myocardial Infarction and Sleep Disordered Breathing.**


Compared endothelial progenitor cells (EPCs), numbers and functions in 40 male acute myocardial infarction (AMI) patients with sleep disordered breathing, (AMI-SDB, n=19), and 21 matched patients without SDB- (AMI-only), to determine the effects of intermittent hypoxia (IH) in-vitro on EPCs proliferative and angiogenic properties. SDB status was determined using WatchPAT. Effects of IH in-vitro were studied in twelve healthy subjects.

**RESULTS:** Circulating EPCs, vascular endothelial growth factor (VEGF) in monocytes, EC-CFUs numbers, and EC-CFUs paracrine effects on endothelial tube formation were significantly higher in AMI-SDB patients, while plasma stromal cell-derived factor (SDF)-1 levels were significantly decreased. EC-CFUs numbers and their paracrine effects on endothelial tube formation were increased after exposure to IH in-vitro, compared to normoxia.

**CONCLUSION:** Co-existent mild-moderate SDB in AMI patients increased the mobilization, proliferative and angiogenic capacities of EPCs. IH in-vitro had similar effects on healthy EPCs functions.


**Bax/Mcl-1 balance affects neutrophil survival in intermittent hypoxia and obstructive sleep apnea: effects of p38MAPK and ERK1/2 signaling.**


Investigated the potential contribution of the intrinsic stress-induced mitochondrial pathway in extending neutrophil survival under intermittent hypoxia conditions, using neutrophils of healthy individuals under in-vitro IH and those of OSA patients (SH) in-vivo, based on the balance between pro-apoptotic Bax and anti-apoptotic Mcl-1 protein expression, and the potential involvement of p38MAPK and ERK1/2 signaling pathways in the control of Mcl-1 expression. Sleep disordered breathing was quantified by either WatchPAT or PSG.

**RESULTS:** Compared to normoxia, IH and SH up-regulated Mcl-1 by about 2-fold, and down-regulated Bax by 41% and 27%, respectively. IH induced ERK1/2 and p38MAPKs phosphorylation, whereas SH induced only p38MAPK. In both IH, and OSA neutrophils, Bax/Mcl-1 ratios were lower than normoxic controls (p=0.015), and Bax did not co-localize with mitochondria.

**CONCLUSION:** Findings suggest that decreased Bax/Mcl-1 balance promotes neutrophil survival in in-vitro IH and in OSA patients, Bax/Mcl-1 protein function in IH and SH might be regulated by different signal transduction pathways, highlighting a novel regulatory function through ERK1/2 signaling in IH.


**Evaluation of Watch PAT as a diagnosing test for patients with obstructive sleep apnea hypopnea syndrome.** [Article in Chinese]


Evaluated the accuracy of obstructive sleep apnea hypopnea syndrome (OSAHS) detection and its influencing factors, of Watch PAT versus simultaneous polysomnography (PSG) in 35 snoring patients.

**RESULTS:** Apnea hypopnea indices (AHI) were correlated (R= 0.955, P < 0.001), but values trended higher in PSG, with a linear regression of AHI (PSG) = 0.944 + 1.030AHI Watch PAT, (P = 0.06). Using ROC analysis (cut point ≥ 8.65), the AUC reached 0.953 (P < 0.001), sensitivity 92.3% and specificity 100.0%. BMI in patients who had an absolute values of differences (AVID ≥ 5) trended higher than in those with AVID < 5 (P = 0.077).

**CONCLUSION:** Watch PAT is highly sensitive in the diagnosis of OSAHS, and can be used as a simple and reliable screening method for suspected OSAHS, but accuracy may be relatively low in those with a great BMI.

Sleep-disordered breathing in acute ischemic stroke and transient ischemic attack: effects on short- and long-term outcome and efficacy of treatment with continuous positive airways pressure--rationale and design of the SAS CARE study.


Describes the SAS CARE 1 study on the effects of sleep-disordered breathing (SDB), on clinical evolution, vascular functions, and markers within the first three-months after an acute cerebrovascular event (CE), and the SAS CARE 2 study to assess the effect of continuous positive airways pressure (CPAP), on clinical evolution, cardiovascular events, and mortality as well as vascular functions and markers at 12 and 24 months after acute CE, in 200 acute CE patients. Vascular functions and markers (blood pressure, heart rate variability, endothelial function (EndoPAT RHI) and specific humoral factors will be assessed in the acute phase and at three-months follow-up. SAS CARE 2 will include a sample of patients with acute CE in the previous 60-90 days, receiving CPAP as appropriate.

CONCLUSION: These studies will improve our understanding of the role of clinical SCB in patients with acute cerebrovascular event and the feasibility/efficacy of CPAP in selected patients with SDB.


Gender-Dependent Impact of Obstructive Sleep Apnea on Digital Vascular Function.


Assessed whether OSA is associated with endothelial dysfunction (EndoPAT RHI), and if this association is influenced by gender, in 479 subjects drawn from a large population-based cohort of 30,000 subjects aged 30-65 years.

RESULTS: OSA was diagnosed in 55.5% (n = 266) of subjects. The RHI was significantly lower in subjects with severe OSA than in those without OSA (p = 0.002). In the multivariate model for RHI, a significant interaction between OSA and gender was found. In gender-specific multivariate linear regression models, adjusting for conventional cardiovascular risk factors, OSA was an independent predictor of a low RHI in women (p = 0.006) but not in men. The association between OSA and low RHI in women was independent of post-menopausal status.

CONCLUSION: In a large population-based sample of middle-aged subjects, OSA was independently associated with impaired digital vascular function in women only.


Ambulatory Models of Care for Obstructive Sleep Apnea: Diagnosis and Management.


An Invited Review, overviewing the status of ambulatory devices in the diagnosis and management of Obstructive Sleep Apnea (OSA). Authors describe the increasing interest in the use of simplified, ambulatory models of care involving clinical prediction tools, portable sleep monitoring and home auto-titrating continuous positive airway pressure (CPAP), in view of the ever mounting, and increasingly unmet pressure on laboratory-based sleep services. Authors summarized six randomised controlled studies evaluating the clinical effectiveness of ambulatory management strategies versus traditional laboratory-based care for patients with OSA. Amongst these is the Watch PAT based study by Berry et al (Sleep 2008; 31: 1423–31), regarding which the reviewers surmised that compared to full split night lab PSG and CPAP titration, Watch-PAT 100 diagnosis followed by autotitrating CPAP for pressure determination, showed no significant differences in CPAP compliance, change in Epworth Sleepiness Scale, change in functional outcomes of sleep questionnaire, patient satisfaction with CPAP or mean residual AHI on CPAP, between the two groups.


Habitual flavonoid intake and endothelial function in healthy humans.


Examined the relationship between endothelial function (EF), and dietary flavonoids in 19 healthy adults (mean age 72 years). Flavonoid intake was assessed via a focused food frequency questionnaire. EF was determined by EndoPAT RHI, both before and after a dose of flavonoid-rich cocoa.

RESULTS: Background flavonoid intake and baseline RHI were significantly positively correlated (r = 0.7, p = 0.001), and the RHI response to cocoa was also significantly correlated with simultaneous blood flavanol concentration, (r = 0.5, p = 0.03).

CONCLUSION: Individual variation in EF in healthy older people, measured as the RHI response to flavonoid-rich cocoa, is highly dependent upon usual daily flavonoid consumption. Raises the possibility that fruit and vegetable related flavonoid consumption dictates basal endothelial function.

Examined the impact of physical activity (PA), level based on accelerometry in 52 healthy adolescents (28 females, age 14.5 ± 0.7 y), on surrogate markers of cardiovascular health, including endothelial function (EF, by EndoPAT-RHI), vagal activity (VA), based on 24 h heart rate analysis, blood pressure (BP), peak oxygen uptake and maximum power output. The cohort was divided into equal groups based on daily moderate-to-vigorous (MVPA) and vigorous PA (VPA), PA intensity levels respectively.

**RESULTS:** MVPA was an independent predictor for VA (P = 0.010), and VPA was associated with maximum power output (P = 0.016). Higher MVPA exhibited a higher VA, (P = 0.006) and a lower systolic BP (P = 0.046). Higher VPA had higher maximum power output (P = 0.012). No significant differences were observed for RHI between groups.

**CONCLUSION:** PA intensity was associated with beneficial effects on VA, systolic BP, and exercise capacity, but not EF.


Evaluated endothelial function (EndoPAT RHI) in 58 diabetic and 36 non-diabetic patients without CAD, mean age 63 +/- 9 years, undergoing coronary angiography.

**RESULTS:** Prevalence of cardiovascular risk factors was similar between groups. RHI was significantly lower in diabetic patients compared to non-diabetics (1.72 +/- 0.34 vs 2.00 +/- 0.44; p < 0.005) and they correlated with levels of glycosylated hemoglobin (p = 0.05; r = -0.266).

**CONCLUSION:** Despite similar level of other risk factors, RHI was much more impaired in diabetic patients than in non-diabetics, further supporting the impact of DM on cardiovascular risk.


Determined whether endothelial dysfunction measured by log transformed EndoPAT RHI (L_RHI) could predict the prognosis of 159 patients with heart failure with preserved ejection fraction (HfPdEF). Patients were followed-up for 300 days for HF-related events, which including HF-related death and re-hospitalization due to congestive heart failure.

**RESULTS:** A total of 32 HF-related events occurred during follow-up, including 4 deaths due to HF and 28 cases of re-hospitalization due to acute decompensated HF. Cox regression analysis indicated that L_RHI (HR 0.56, 95% CI: 0.39-0.80 for an increase of 0.1) was an independent predictor of HF-related events. By receiver operating characteristic analysis, the area under the curve was for prediction of adverse events at a cut point value of 0.49, was 0.73 (95% CI: 0.62-0.83).

**CONCLUSION:** EndoPAT L_RHI is a predictor of poor prognosis in patients with HfPdEF.


Measured vascular reactivity in 48 non diabetic hemodialysis patients (HD) subjects in comparison with 55 age and gender matched healthy controls. Arterial stiffness (radial artery), Pulse Wave Velocity (PWV), and endothelial function (EndoPAT RHI), were assessed.

**RESULTS:** Arterial stiffness was significantly higher in HD patients than controls (p < 0.05). HD subjects had an increased pulse wave velocity (p < 0.05), and RHI, was significantly lower in male patients only, (p< 0.01).

**CONCLUSION:** Noninvasive assessment of peripheral vascular function may be useful for the identification of patients at risk for late cardiac events.

Lena Lavie PhD, Associate Professor at the Lloyd Rigler Sleep Apnea Research Laboratory in the Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel. Prof. Lavie’s research in the areas of leukocyte biology, oxidative stress and inflammatory-atherogenic processes in sleep apnea, is aimed at elucidating the pathophysiological mechanisms leading to cardiovascular morbidity in sleep apnea patients, based upon an understanding of basic mechanisms by which intermittent hypoxia alters the function of various leukocytes subpopulations towards an inflammatory and atherogenic phenotype, including endothelial progenitor cells, dendritic cells, and neutrophils.

Professor Lavie and colleagues have contributed significantly to the scientific base and clinical acceptance of PAT technology, in particular in the area of angiogenic properties of endothelial progenitor cells increase in acute myocardial infarction, which may potentially benefit patients with MI and ischemic heart disease; as evidenced by the following publications:


