Clinical Studies Compendium

Endothelial Function Assessment is a clinically proven functional biomarker in all major cardiovascular disease states, adding prognostic value beyond commonly used tools.

Endothelial Function
The Best Patient Management Indicator for CAD/Symptomatic Patients
Secondary and Tertiary Prevention

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Identify post-stenting patients at 4-times higher-risk for near-future events

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Identify Heart Failure patients at high-risk for readmissions
EndoPAT™ Identifies CAD Patients at Risk for Near-Future Cardiac Events

Peripheral Endothelial Function and Cardiovascular Events in High-Risk Patients

J Am Heart Assoc. 2013;2:e000426

This landmark study is an extension of previous studies and demonstrates the importance of assessing endothelial health for the prediction of cardiac events in treated patients.

Method: 528 High-risk patients referred to diagnostic angiography and tested with the EndoPAT™ for RHI (Reactive Hyperemia Index) before the angiography procedure. Patients diagnosed were treated as follows:
- Stenting in 344
- CABG in 21
- Medical therapy in 77

Follow up mean 2.8 years for CV adverse events (CV death, MI or unstable angina, revascularization, HF, Stroke, Aortic disease or PAD).

Results: In the low RHI group* there were 4 times more CV events (see Figure A). The EndoPAT™ is shown to be an independent predictor of adverse events, achieving CV Risk net reclassification of 49% beyond FRS (Framingham Risk Score).

Clinical Application: Endothelial function measured with the EndoPAT™ gives additional prognostic information for near-future cardiovascular events in high-risk patients. The EndoPAT™ will reclassify risk better than standard tools even after optimal medical treatment or revascularization procedures are provided.

*Low RHI: Ln_(RHI)=0.531 (RHI≤1.7)
Identifying Residual Risk in Well Treated CAD Patients (Statin treatment)

Method: 213 CAD patients, already well treated with statin therapy (achieved LDL<100), were followed-up for secondary CAE (Coronary Artery Events) for a median of 2.7 years.

Results: During follow-up, CAE occurred in 4 (4%) patients in the Ln_RHI ≥ 0.54 group and 18 (15.8%) patients in the Ln_RHI<0.54 group (P=0.006). traditional risk score for secondary CAE, or after taking into account eGFR.

Clinical Application: Even after achieving target LDL-C with statin therapy, residual secondary CAE risk remains significant. The EndoPAT™ may help in stratifying residual risk of secondary CV events in successfully treated CAD patients and in improving prognosis.

Atherosclerosis 2014
*Low RHI: Ln_RHI<0.54 (RHI<1.72)
EndoPAT™ Assessment in Symptomatic Patients with Chest Pain

Method: 270 symptomatic outpatients with unexplained chest pain (low-risk at stress test, no new obstructive lesions by an invasive coronary angiogram) were tested using the EndoPAT™. The patients were then followed for CV adverse events (AE): death, myocardial infarction, revascularization or cardiac hospitalization during a mean follow-up of 5.8 years.

Results: In the group of patients with a low EndoPAT® score the adverse events rate was 48%, whereas in the group achieving a higher EndoPAT™ score AE rate was 28%. A low Ln_RHI* score on the EndoPAT™ test, indicating endothelial dysfunction, was correlated with a higher Adverse Events rate. Statistical analysis showed Ln_RHI was an independent predictor of adverse events.

Clinical Application: Non-invasive assessment of endothelial function using the EndoPAT™ may assist in identifying risk factors for CV adverse events in patients with unexplained chest pain, allowing timely treatment and prevention of CVD progression.
EndoPAT™: Identifying High-Risk Women with Chest Pain by Assessing Endothelial Function

Method: 140 post-menopausal women experiencing symptoms of chest pain were tested with the EndoPAT™. They were later tested with coronary angiography to diagnose obstructive CAD. In case of non-obstructive or normal angiography - they were then tested with an invasive Acetylcholine provocation test, adenosine reduced coronary flow reserve, and stress thallium test to further diagnose ischemic heart disease.

Results: Among 112 women the EndoPAT™ non-invasively diagnosed endothelial dysfunction, which was consistent with the invasive test methods and predicted the presence of IHD, especially NOCAD (non-obstructive) which was not diagnosed by angiography. The EndoPAT™ successfully identified both obstructive CAD and NOCAD (non-obstructive coronary artery disease). Among 30 patients with normal EndoPAT™ results, no indication for heart disease was found in any other test.

Clinical Application: The EndoPAT™ is a useful and safe clinical test which can effectively help identify high-risk women with chest pain prior to invasive tests. In cases of normal angiography, the EndoPAT™ may be used to rule out microvascular disease (MVD).

Predicts Ischemic Heart Disease in Post-Menopausal Woman

Figure 3. RHI and Ischemic Heart Disease (IHD)

*Low RHI: Ln_RHI<0.6 (RHI<1.82)
The Prognostic Value of Endothelial Function Assessment in Heart Failure Patients

Incremental Prognostic Significance of Peripheral Endothelial Dysfunction in Patients with Heart Failure with Normal Left Ventricular Ejection Fraction


Journal of the American College of Cardiology 2012 Oct 30;60(18):1778-86

Method: 321 patients with heart failure HFNEF (normal left ventricular ejection fraction) were tested with the EndoPAT™ and then followed up for a mean of 20 months for CV adverse events.

Results: Adverse events occurred at a rate almost 4 times greater in the group of endothelial dysfunction than in the normal function group (28.1% vs. 8.8%).

Multivariate Cox hazard analysis identified the RHI EndoPAT™ score as an independent predictor of cardiovascular events. The C-statistic for CVD events increased with the addition of RHI (EndoPAT™ score) to the heart failure prognostic 5 factors - age, diabetes, NY heart association classification, hospitalization history and left ventricular ejection fraction (even beyond BNP).

Clinical Application: Peripheral endothelial dysfunction measured with the EndoPAT™ may independently predict future cardiovascular events, and may improve risk stratification in patients with HF.
**Endothelial Function - a Key Indicator of Successful Treatment**

**Persistent Impairment of Endothelial Vasomotor Function Has a Negative Impact on Outcome in Patients with Coronary Artery Disease**

Yoshinobu Kitta, Jyun-pei Obata, Takamitsu Nakamura, Mitsumasa Hirano, Yasushi Kodama, Daisuke Fujioka, Yukio Saito, Ken-ichi Kawabata, Keita Sano, Tsuyoshi Kobayashi, Toshiaki Yano, Kazuto Nakamura, Kiyota Kugiyama

*Journal of the American College of Cardiology 2009;53;323-330*

**Method:** 251 patients recently diagnosed with CAD were also diagnosed with impaired endothelial function measured by respective diameter changes of the brachial artery in ultrasound (flow-mediated dilation - FMD <5.5%). After the first FMD measurement, all patients received optimal therapy including medications and lifestyle changes to reduce risk according to the AHA/ACC guidelines. Measurement of FMD was repeated after 6 months. After the second test, patients were followed up for 36 months or until an adverse event (cardiac death, nonfatal myocardial infarction, recurrent and refractory angina pectoris requiring coronary revascularization or ischemic stroke).

**Results:** FMD was persistently impaired (<5.5%) in 104 (41%) patients after 6 months of optimized therapy, and in the second group of 147 patients (59%) it improved (FMD ≥ 5.5%). During 36 months of follow-up, events occurred in 27 (26%) patients with persistently impaired endothelial function and in 15 (10%) patients with improved endothelial function (p<0.01). Multivariate Cox hazards analysis showed that persistent impairment of endothelial function independently predicted adverse events (hazard ratio: 2.9, 95% confidence interval: 1.5 to 6.2, p<0.01)

**Clinical Application:** Persistent impairment of endothelial vasomotor function despite optimized therapy to reduce risk factors indicates that further CAD treatment is necessary to reduce risk for cardiac adverse events.

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**Targeting Endothelial Dysfunction for Treatment in CAD Patients Improves Outcomes**

![Cumulative event-free probability graph showing improved and persistent endothelial dysfunction outcomes](image)
Both physicians and patients take heart disease very seriously and treat symptoms aggressively. Yet, for patients who survived a heart attack the probability of sudden cardiac death is 4-6 times greater than that of the general population*

The EndoPAT™, giving simple and fast results, helps to easily identify responders to therapy, and personalize your efforts at Secondary Prevention to help ensure treatment is as effective as possible for the particular patient.

*AHA Heart Disease and Stroke statistics, 2013 update, Go et al, Circulation 127, 2013