

DVA3.0

Measurement of endothelial function in the microcirculation (retinal dynamic vessel analysis)





ESC

European Society
of CardiologyCardiovascular Research (2020) 0, 1–14
doi:10.1093/cvr/cvaa085

REVIEW

Endothelial Function in Cardiovascular Precision Medicine: A Consensus Paper of the European Society of Cardiology Working Groups on Atherosclerosis and Vascular Biology, Aorta and Peripheral Vascular Diseases, Coronary Pathophysiology and Microcirculation, and Thrombosis

(3) Newer techniques to measure endothelial dysfunction that are relatively easy to perform, such as finger plethysmography and the **retinal flicker test**, have the potential for increased clinical use provided a consensus is achieved on the measurement protocol used. In addition, larger clinical studies are needed to establish reference values and to assess their clinical utility.

Imedos DVA 3.0

Flickerlight-induced dilatation (FID)
(mikrozirkulatorische EF)



Marker of endothelial function



Reproducibility of results



**Endorsement of leading
medical societies**



Predictivity of events



Norm values



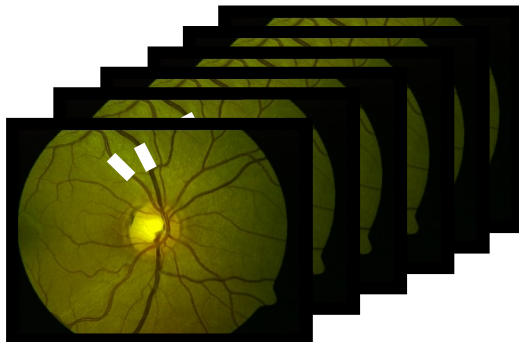
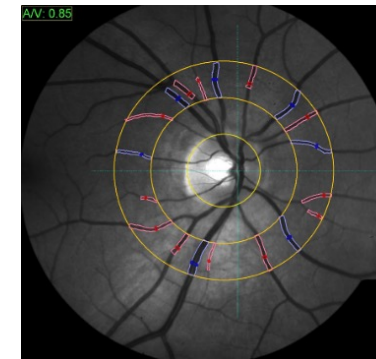
Imedos DVA 3.0 – Dynamic vessel analysis

Flickerlight-induced dilatation (FID)
(microcirculatory EF / Vessel function)



Static vessel analysis

Vessel structure (via single picture)

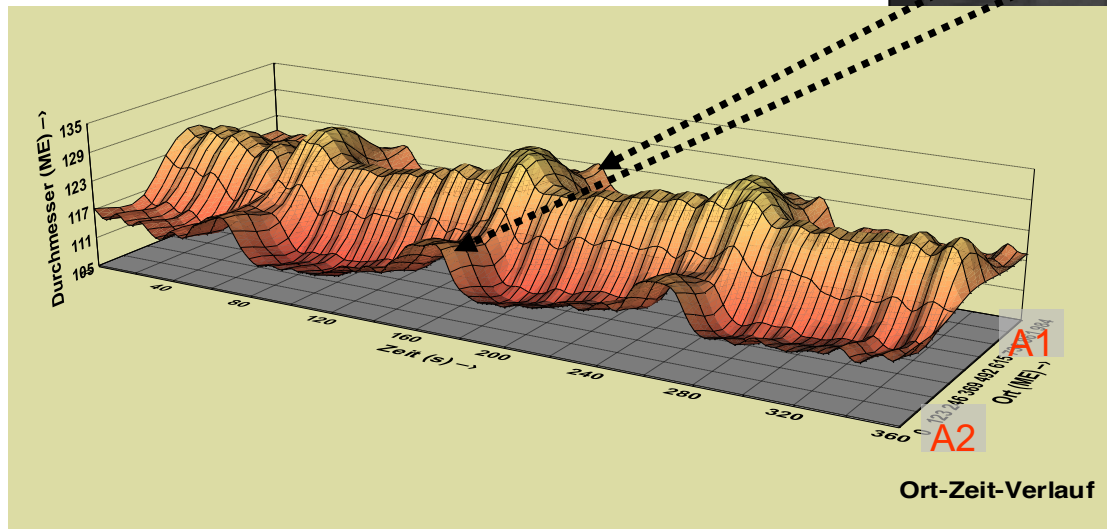
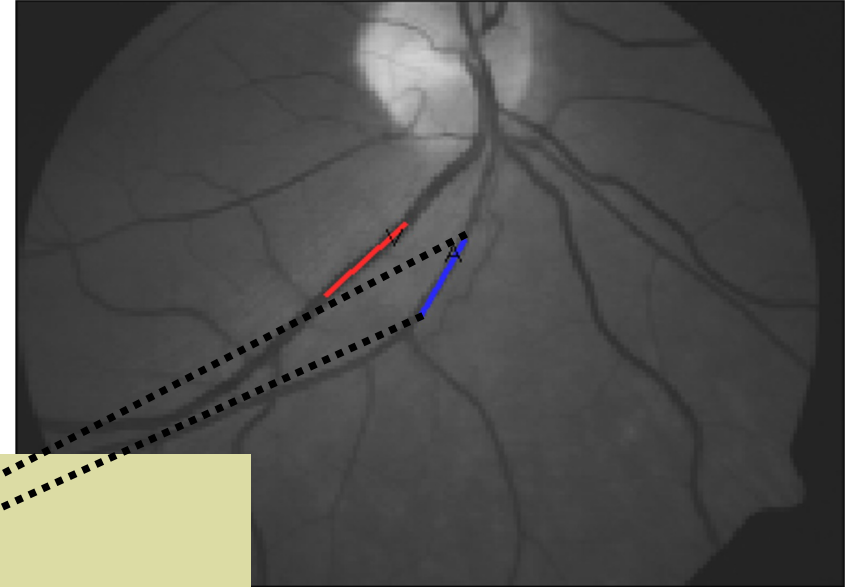


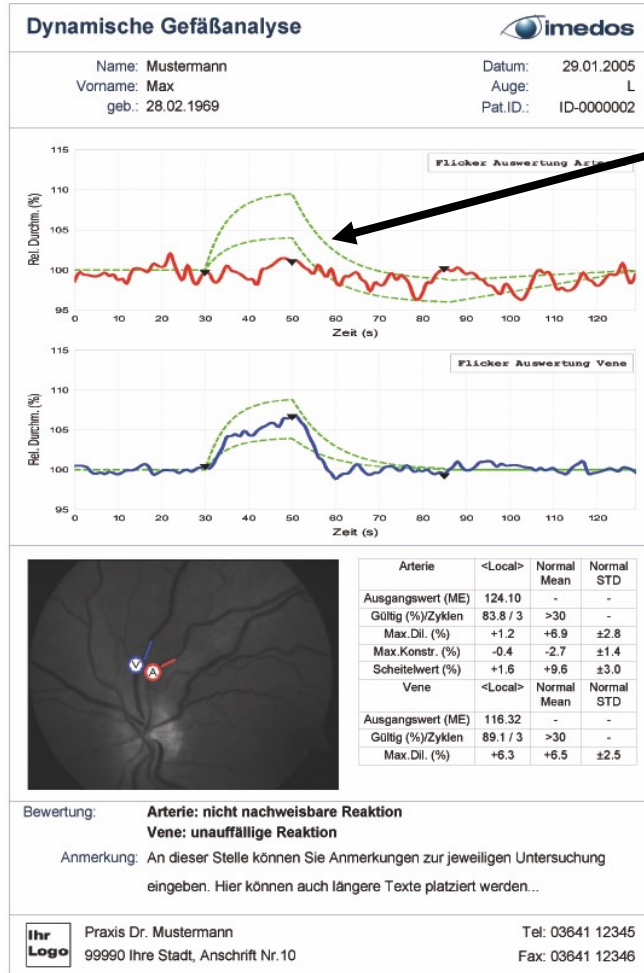
Vessel function
(over time)

Vessel function (over time)

Three cycles of stimulus (Flickerlight) change of vessel diameter

NO-induced dilation of retinal vessels





Reduced response to Flickerlight stimulation



Microvascular dysregulation (endothelial dysfunction)

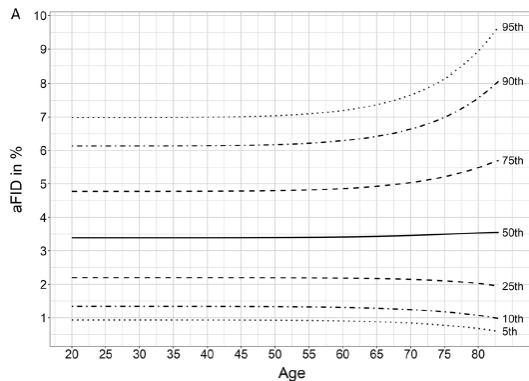


Reduced autoregulatory reserve

Normative data and standard operating procedures for static and dynamic retinal vessel analysis as biomarker for cardiovascular risk

scientific reports

Lukas Streese¹, Giulia Lona¹, Jonathan Wagner¹, Raphael Knaier¹, Andri Burri¹, Gilles Nève¹, Denis Infanger¹, Walthard Vilser², Arno Schmidt-Trucksäss¹ & Henner Hanssen^{1✉}



Conclusion

Retinal vessel analysis is a non-invasive, reproducible, and easily applicable diagnostic tool which offers a micro-vascular window to the heart. Our findings allow for a better understanding of retinal vessel physiology and differentiation of pathophysiology. The presented normative data are milestones towards clinical implementation of static and dynamic retinal vessel imaging in daily clinical routine. We recommend and define use of standardized operating procedures and normative values to pave the way for improvement of clinical decision making and CV risk stratification in a personalized medicine approach.

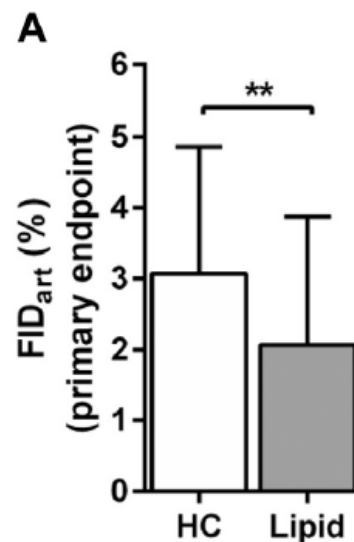
Retinal microvascular dysfunction in hypercholesterolemia

Matthias P. Nägele, MD¹, Jens Barthelmes, MD¹, Valeria Ludovici, MD, Silviya Cantatore, RN, Michelle Frank, MD, Frank Ruschitzka, MD, Andreas J. Flammer, MD¹, Isabella Sudano, MD, PhD^{*,1}

Conclusion

This observational study on RVA in hypercholesterolemia found a significant degree of retinal microvascular dysfunction in patients with hypercholesterolemia, evidenced by a significant reduction in FID_{art}. LDL, but not HDL, cholesterol was a significant negative predictor of FID_{art}, highlighting the adverse effect of hypercholesterolemia on the retinal microcirculation. Dynamic RVA may be a promising method for the noninvasive study of microvascular endothelial dysfunction in populations at risk for cardiovascular disease.

Journal of
Clinical
Lipidology

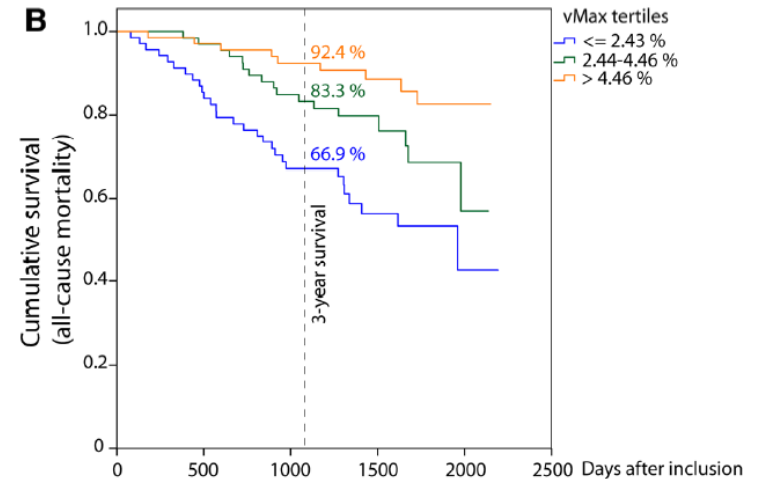


J Clin Lipidol. Nov-Dec 2018;12(6):1523-1531.e2.

Clinical Track

Impaired Retinal Vessel Dilation Predicts Mortality in End-Stage Renal Disease

Roman Günthner,* Henner Hanssen,* Christine Hauser, Susanne Angermann, Georg Lorenz, Stephan Kemmner, Julia Matschkal, Matthias C. Braunisch, Claudius Küchle, Lutz Renders, Philipp Moog, Siegfried Wassertheurer, Marcus Baumann, Hans-Peter Hammes, Christopher C. Mayer, Bernhard Haller, Sarah Stryeck, Tobias Madl, Javier Carbajo-Lozoya, Uwe Heemann, Konstantin Kotliar,† Christoph Schumacher†



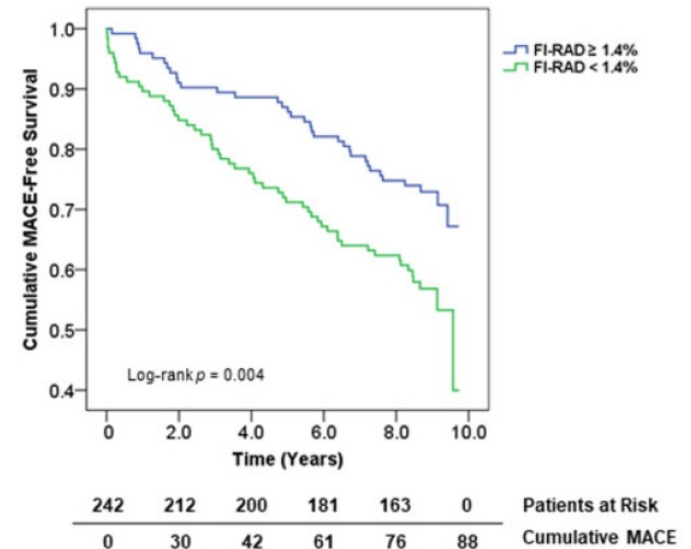
Methods and Results: In the multicenter prospective observational ISAR study (Risk Stratification in End-Stage Renal Disease), data on dynamic retinal vessel analysis were available in a subcohort of 214 dialysis patients (mean age, 62.6±15.0; 32% women). Microvascular dysfunction was quantified by measuring maximum arteriolar dilation and maximum venular dilation (vMax) of retinal vessels in response to flicker light stimulation. During a mean follow-up of 44 months, 55 patients died, including 25 cardiovascular and 30 noncardiovascular fatal events. vMax emerged as a strong independent predictor for all-cause mortality. In the Kaplan-Meier analysis, individuals within the lowest tertile of vMax showed significantly shorter 3-year survival rates than those within the highest tertile (66.9±5.8% versus 92.4±3.3%). Univariate and multivariate hazard ratios for all-cause mortality per SD increase of vMax were 0.62 (0.47–0.82) and 0.65 (0.47–0.91), respectively. Maximum arteriolar dilation and vMax were able to significantly predict nonfatal and fatal cardiovascular events (hazard ratio, 0.74 [0.57–0.97] and 0.78 [0.61–0.99], respectively).

Impaired retinal microvascular function predicts long-term adverse events in patients with cardiovascular disease

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5 Conclusion

The present study is the first to confirm that an uncomplicated measurement of retinal arteriolar endothelial dysfunction, as measured by FI-RAD at a single time point, is a strong and independent predictor of long-term MACE in patients with CAD and cardiovascular risk factors. Our results demonstrate promising utility for dynamic retinal vascular analysis in risk stratifying and predicting patients at high risk of cardiovascular disease. Additional clinical studies and validation of this novel marker of microvascular dysfunction are required to establish the applicability of this method to the clinical arena.



Cardiovasc Res. 2021 Jul 7;117(8):1949-1957

Retinal microvascular dysfunction in heart failure

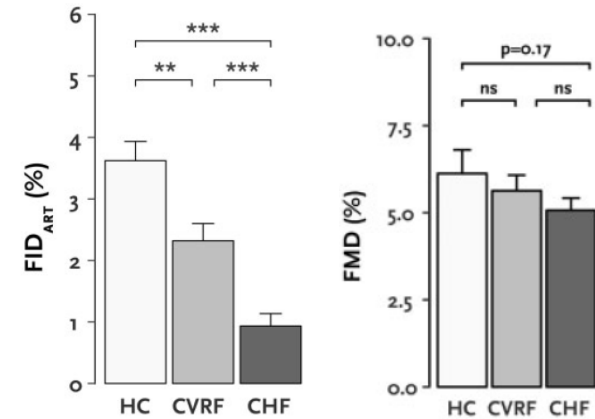
Matthias P. Nägele¹, Jens Barthelmes¹, Valeria Ludovici^{1,2}, Silviya Cantatore¹, Arnold von Eckardstein¹, Frank Enseleit¹, Thomas F. Lüscher¹, Frank Ruschitzka¹, Isabella Sudano¹, and Andreas J. Flammer^{1*}

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Received 12 March 2017; revised 19 May 2017; editorial decision 24 August 2017; accepted 27 September 2017

Methods and results

In this prospective, single-centre, observational study, 74 patients with compensated CHF (mean age 63.5 ± 11.2 years, 32% female, mean left-ventricular ejection fraction $37 \pm 12.8\%$), 74 patients with cardiovascular risk factors (CVRF; 64.1 ± 12.7 years, 34% female), and 74 healthy controls (HC; 57.8 ± 14.2 years, 35% female) were included. The primary endpoint, flicker-induced dilatation of retinal arterioles (FID_{art}), was significantly reduced in patients with CHF compared to CVRF and HC (mean FID_{art} 0.9 ± 0.2 vs. 2.3 ± 0.3 and vs. $3.6 \pm 0.3\%$, respectively, both $P < 0.001$ before and after propensity score-weighted analysis). Similar differences were seen for venular FID. FID_{art} was less impaired in patients with dilated compared to ischaemic cardiomyopathy. No significant differences were observed for arteriovenous ratio and flow-mediated dilatation. Impaired FID_{ven} was associated with echocardiographically estimated systolic pulmonary artery pressure and left atrial volume index.





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