Data article

Title: *Assessing the perceived quality of brachial artery Flow Mediated Dilation studies for inclusion in meta-analyses and systematic reviews: description of data employed in the development of a scoring tool based on currently accepted guidelines.*

Authors: Arno Greyling [a, b], Anke C.C.M van Mil [a, c, d], Peter L. Zock [b, c], Daniel J. Green [e], Lorenzo Ghiadoni [f], Dick H. Thijssen [a, g *] on behalf of the TIFN International Working Group on Flow Mediated Dilation

Affiliations: [a)] Department of Physiology, Radboud University Medical Centre, Nijmegen, The Netherlands

[b)] Unilever R&D Vlaardingen, Vlaardingen, The Netherlands

[c)] TI Food and Nutrition, Wageningen, The Netherlands

[d)] Maastricht University Medical Centre, Maastricht, The Netherlands

[e)] School of Sports Science, Exercise and Health, The University of Western Australia, Crawley, Australia

[f)] University of Pisa, Pisa, Italy

[g)] Research institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, United Kingdom

Contact email: Dick.Thijssen@radboudumc.nl

Keywords

Cardiovascular disease; Atherosclerosis; Endothelial function; Reproducibility; Methodology

Abstract

Brachial artery flow mediated dilation (FMD) is widely used as a non-invasive measure of endothelial function. Adherence to expert consensus guidelines on FMD measurement has been found to be of vital importance to obtain reproducible data. This article lists the literature data which was considered in the development of a tool to aid in the objective judgement of the extent to which published studies adhered to expert guidelines for FMD measurement. Application of this tool in a systematic review of FMD studies (http://dx.doi.org/10.1016/j.atherosclerosis.2016.03.011)[1] indicated that adherence to expert consensus guidelines is strongly correlated to the reproducibility of FMD data.

Specifications Table

Subject area	*Medicine*
More specific subject area	*Vascular Physiology*
Type of data	*Table*
How data was acquired	*Systematic literature survey and expert consensus*
Data format	*Processed*
Experimental factors	*Methodological parameters related to valid measurement FMD*
Experimental features	*Assessment tool based on 33 studies pertaining to the most appropriate methods to assess FMD in humans identified from literature and expert guidelines for FMD measurement*
Data source location	*Nijmegen, The Netherlands*
Data accessibility	*Data is within this article*

Value of the data

- The literature data provided here establishes an evidence base and a physiological background rationale for the individual components included in the Adherence Score, aiding in the improvement of the practical guidance and technical approaches to FMD measurement and analysis.
- This “Adherence Score” which ranges between 0 (i.e. no adherence) and 10 (i.e. full adherence) can conceivably be employed to evaluate the perceived quality of studies reporting FMD data, with a higher outcome of this measure being strongly related to better reproducibility of the FMD data.
- This tool may prove useful additional information when pooling, contrasting and comparing different studies, e.g. for the purpose of meta-analyses or systematic reviews.

Data

A tool to enable objective assessment of the level adherence to the FMD guidelines was developed. Table 1 presents the 19 different factors that make up the *"Adherence Score"* tool along with citations to the literature data which justify the inclusion of each factor in question.

Table 1. Scoring tool based on currently accepted guidelines for the assessment of the perceived quality of FMD studies

Characteristic	Score	Reference
Subject preparation		
Fasting state (>6h)	Yes ☐ 0.2; No ☐ 0	2-4
No smoking or any tobacco consumption prior to measurement (>6h)	Yes ☐ 0.2; No ☐ 0	5-7
No habitual exercise prior to measurement (>48h)	Yes ☐ 0.2; No ☐ 0	8-10
No food/beverages that contain alcohol and/or caffeine for >12 h	Yes ☐ 0.2; No ☐ 0	11, 12
No food/beverages that are rich in polyphenols (cocoa, tea, fruit juices) for >18 h	Yes ☐ 0.2; No ☐ 0	13
No vitamins for at least 72h	Yes ☐ 0.2; No ☐ 0	14-16
Vasoactive medications withheld on the morning of the study if possible for single measurements; Careful noting of the use and timing of any drugs in the case repeated measurements	Yes ☐ 0.2; No ☐ 0	17, 18
Supine position; Rest for at least 15 min prior to measurements in a quiet, temperature controlled room	Yes ☐ 0.2; No ☐ 0	19-21
In female subjects, repetitive measurement should be made at the same time of the menstrual cycle (ideally on days 1–7)	Yes ☐ 0.2; No ☐ 0	22, 23

Characteristic	Score	Reference
Repeated measurements done in fixed time windows (same time of day)	Yes ☐ 0.2; No ☐ 0	24-26
Image acquisition		
Diameter measurements recorded continuously + over the heart cycle OR;	Yes ☐ 2; No ☐ 0	27, 28
Diameter measurements obtained during end diastole only	Yes ☐ 1; No ☐ 0	
Simultaneous acquisition of pulse-wave Doppler velocity signal for quantification of shear stimulus	Yes & insonation angle ≤60° ☐ 2; Yes & insonation angle >60°/not reported ☐ 1; No ☐ 0	29-31
Image analysis		
Analysis using automated edge detection and wall tracking software	Yes & continuous (i.e. time bins of ≤5 seconds) ☐ 2; Yes & fixed time points ☐ 1; No ☐ 0	32-34
Laboratory information		
Use of experienced sonographers reported	Yes ☐ 1; No ☐ 0	
Same sonographers paired to same subjects for repeated measurements	Yes ☐ 1; No ☐ 0	

Experimental Design, Materials and Methods

Based on previous expert-consensus guidelines,[35] we devised a scoring system reliant on the reporting of 19 different methodological factors related to FMD measurement. These factors were identified after critical review and appraisal of published physiological studies pertaining to the most appropriate methods to assess FMD in humans. Values were assigned to each component proportional to its perceived importance for valid assessment of the FMD. This was done through expert consensus discussion within the Working Group (AG, LG and DHJT). The *"Adherence Score"* that any given study can be assigned ranges from 0 to 10 points depending on how many of the 19 different factors that are reported or referred to in the text of the paper in question.

Acknowledgements

Ms Anke van Mil is financially supported by a Top Institute for Food and Nutrition-grant.

Dr. Dick Thijssen is financially supported by the Netherlands Heart Foundation (E Dekker-stipend, 2009T064). Professor Green receives Fellowship and grant funding from the National Heart Foundation of Australia (APP1045204).

References

[1] Greyling, A, van Mil, AC, Zock, PL, et al., Adherence to guidelines strongly improves reproducibility of brachial artery flow-mediated dilation, Atherosclerosis, 2016;248:196-202.

[2] Padilla, J, Harris, RA, Fly, AD, et al., The effect of acute exercise on endothelial function following a high-fat meal, Eur.J.Appl.Physiol, 2006;98:256-262.

[3] Vogel, RA, Corretti, MC and Plotnick, GD, Effect of a single high-fat meal on endothelial function in healthy subjects, Am.J.Cardiol., 1997;79:350-354.

[4] Ceriello, A, Cavarape, A, Martinelli, L, et al., The post-prandial state in Type 2 diabetes and endothelial dysfunction: effects of insulin aspart, Diabet.Med., 2004;21:171-175.

[5] Kato, T, Inoue, T, Morooka, T, et al., Short-term passive smoking causes endothelial dysfunction via oxidative stress in nonsmokers, Can.J.Physiol Pharmacol., 2006;84:523-529.

[6] Karatzi, K, Papamichael, C, Karatzis, E, et al., Acute smoke-induced endothelial dysfunction is more prolonged in smokers than in non-smokers, Int J Cardiol, 2007;120:404-406.

[7] Neunteufl, T, Priglinger, U, Heher, S, et al., Effects of vitamin E on chronic and acute endothelial dysfunction in smokers, J Am Coll Cardiol, 2000;35:277-283.

[8] Tjonna, AE, Rognmo, O, Bye, A, et al., Time course of endothelial adaptation after acute and chronic exercise in patients with metabolic syndrome, J.Strength.Cond.Res., 2011;25:2552-2558.

[9] Tinken, TM, Thijssen, DH, Hopkins, N, et al., Impact of shear rate modulation on vascular function in humans, Hypertension, 2009;54:278-285.

[10] Dawson, EA, Whyte, GP, Black, MA, et al., Changes in vascular and cardiac function after prolonged strenuous exercise in humans, J Appl Physiol (1985), 2008;105:1562-1568.

[11] Hijmering, ML, de Lange, DW, Lorsheyd, A, et al., Binge drinking causes endothelial dysfunction, which is not prevented by wine polyphenols: a small trial in healthy volunteers, Neth.J.Med., 2007;65:29-35.

[12] Papamichael, CM, Aznaouridis, KA, Karatzis, EN, et al., Effect of coffee on endothelial function in healthy subjects: the role of caffeine, Clin.Sci.(Lond), 2005;109:55-60.

[13] Kay, CD, Hooper, L, Kroon, PA, et al., Relative impact of flavonoid composition, dose and structure on vascular function: a systematic review of randomised controlled trials of flavonoid-rich food products, Mol Nutr Food Res, 2012;56:1605-1616.

[14] Harris, RA, Nishiyama, SK, Wray, DW, et al., The effect of oral antioxidants on brachial artery flow-mediated dilation following 5 and 10 min of ischemia, Eur.J.Appl.Physiol, 2009;107:445-453.

[15] Richardson, RS, Donato, AJ, Uberoi, A, et al., Exercise-induced brachial artery vasodilation: role of free radicals, Am.J.Physiol Heart Circ.Physiol, 2007;292:H1516-H1522.

[16] Eskurza, I, Monahan, KD, Robinson, JA, et al., Effect of acute and chronic ascorbic acid on flow-mediated dilatation with sedentary and physically active human ageing, J.Physiol, 2004;556:315-324.

[17] Magen, E, Viskoper, JR, Mishal, J, et al., Effects of low-dose aspirin on blood pressure and endothelial function of treated hypertensive hypercholesterolaemic subjects, J.Hum.Hypertens., 2005;19:667-673.

[18] Zhang, L, Gong, D, Li, S, et al., Meta-analysis of the effects of statin therapy on endothelial function in patients with diabetes mellitus, Atherosclerosis, 2012;223:78-85.

[19] Dyson, KS, Shoemaker, JK and Hughson, RL, Effect of acute sympathetic nervous system activation on flow-mediated dilation of brachial artery, Am.J.Physiol Heart Circ.Physiol, 2006;290:H1446-H1453.

[20] Widlansky, ME, Vita, JA, Keyes, MJ, et al., Relation of season and temperature to endothelium-dependent flow-mediated vasodilation in subjects without clinical evidence of cardiovascular disease (from the Framingham Heart Study), Am.J.Cardiol., 2007;100:518-523.

[21] Ghiadoni, L, Donald, AE, Cropley, M, et al., Mental stress induces transient endothelial dysfunction in humans, Circulation, 2000;102:2473-2478.

[22] Hashimoto, M, Akishita, M, Eto, M, et al., Modulation of endothelium-dependent flow-mediated dilatation of the brachial artery by sex and menstrual cycle, Circulation, 1995;92:3431-3435.

[23] Williams, MR, Westerman, RA, Kingwell, BA, et al., Variations in endothelial function and arterial compliance during the menstrual cycle, J.Clin.Endocrinol.Metab, 2001;86:5389-5395.

[24] Jones, H, Green, DJ, George, K, et al., Intermittent exercise abolishes the diurnal variation in endothelial-dependent flow-mediated dilation in humans, Am.J.Physiol Regul.Integr.Comp Physiol, 2010;298:R427-R432.

[25] Jarvisalo, MJ, Jartti, L, Marniemi, J, et al., Determinants of short-term variation in arterial flow-mediated dilatation in healthy young men, Clin.Sci.(Lond), 2006;110:475-482.

[26] ter Avest, E, Holewijn, S, Stalenhoef, AF, et al., Variation in non-invasive measurements of vascular function in healthy volunteers during daytime, Clin Sci (Lond), 2005;108:425-431.

[27] Kizhakekuttu, TJ, Gutterman, DD, Phillips, SA, et al., Measuring FMD in the brachial artery: how important is QRS gating?, J Appl Physiol (1985), 2010;109:959-965.

[28] Gemignani, V, Bianchini, E, Faita, F, et al., Ultrasound measurement of the brachial artery flow-mediated dilation without ECG gating, Ultrasound Med Biol, 2008;34:385-391.

[29] Padilla, J, Johnson, BD, Newcomer, SC, et al., Normalization of flow-mediated dilation to shear stress area under the curve eliminates the impact of variable hyperemic stimulus, Cardiovasc Ultrasound, 2008;6:44.

[30] Padilla, J, Johnson, BD, Newcomer, SC, et al., Adjusting flow-mediated dilation for shear stress stimulus allows demonstration of endothelial dysfunction in a population with moderate cardiovascular risk, J.Vasc.Res., 2009;46:592-600.

[31] Pyke, KE and Tschakovsky, ME, Peak vs. total reactive hyperemia: which determines the magnitude of flow-mediated dilation?, J.Appl.Physiol, 2007;102:1510-1519.

[32] Sonka, M, Liang, W and Lauer, RM, Automated analysis of brachial ultrasound image sequences: early detection of cardiovascular disease via surrogates of endothelial function, IEEE Trans Med Imaging, 2002;21:1271-1279.

[33] Woodman, RJ, Playford, DA, Watts, GF, et al., Improved analysis of brachial artery ultrasound using a novel edge-detection software system, J Appl Physiol, 2001;91:929-937.

[34] Gemignani, V, Faita, F, Ghiadoni, L, et al., A system for real-time measurement of the brachial artery diameter in B-mode ultrasound images, IEEE Trans Med Imaging, 2007;26:393-404.

[35] Thijssen, DH, Black, MA, Pyke, KE, et al., Assessment of flow-mediated dilation in humans: a methodological and physiological guideline, Am J Physiol Heart Circ Physiol, 2011;300:H2-12.