

RESEARCH

Feasibility of 3D4D echocardiography for the detection of colour-coded flow in the left anterior descending artery

Stephan Stoebe, Dietrich Pfeiffer and Andreas Hagendorff

Division of Cardiology and Angiology, Department of Internal Medicine, Neurology and Dermatology, University of Leipzig, Liebigstr. 20, 04103 Leipzig, Germany

Correspondence should be addressed to S Stoebe
Email
stephan.stoebe@gmx.de

Abstract

The aim of this study was to test the feasibility of the visualisation of 3D4D coronary flow in detectable segments of coronary arteries. Regarding the feasibility of this new approach, the hypothesis was proposed that the flow signals of the course of detectable coronary arteries can be better visualised by 3D4D echocardiography than by the conventional 2D approach. A total of 30 consecutive patients with sinus rhythm, in whom the distal left anterior descending artery (LAD) was visualised by 2D colour-coded Doppler echocardiography, were selected for 3D4D scanning procedures. All measurements were performed using a Vivid 7 or E9. All segments visualised by 2D colour-coded Doppler echocardiography were also examined by 3D4D echocardiography. Using defined settings, the width of the colour-coded flow signal differs significantly between 2D- and 3D4D echocardiography. The length of larger segments of the visualised colour-coded flow signal of the coronary flow could be better detected with 2D imaging. Small segments of coronary artery flow (<11 mm), however, could be significantly better visualised by 3D4D echocardiography. The main advantage of 3D4D echocardiography of the coronary artery flow is the visualisation of the proportions of vessels with complex morphology. 3D4D echocardiography of LAD flow by colour-coded Doppler echocardiography raises new possibilities for the direct flow visualisation of the detectable segments of coronaries. With its sufficiently high spatial and temporal resolution, this new method has the potential to be implemented in clinical scenarios. The possible application to the quantification of stenoses by the flow visualisation has to be evaluated in further studies.

Key Words

- ▶ transthoracic echocardiography
- ▶ 3D4D echocardiography
- ▶ coronary flow imaging
- ▶ left anterior descending artery

Introduction

The visualisation of specific parts of coronary artery branches with 2D echocardiography is generally possible, but not very common in the clinical scenario. The left anterior descending coronary artery (LAD) is located in the anterior interventricular sulcus, which is relatively close to the chest wall. Owing to these anatomical circumstances, the distal part of the LAD can be well detected by

conventional 2D transthoracic colour-coded Doppler echocardiography in almost all cases (1, 2, 3). It is well-known in the literature that the detection of other parts of the coronary artery tree is feasible in 50–100% of patients (4, 5, 6, 7, 8, 9, 10). The middle part of the LAD as well as the distal part of the right coronary artery is also detectable by 2D colour-coded Doppler echocardiography in 50–75%

of patients (11, 12, 13). The main problem for transthoracic detection of the coronaries is the circumflex territory in the lateral left ventricular region, where colour-coded flow signals of segments of the marginal branches can only be detected in 25–50% of patients (14).

In contrast to the direct morphological visualisation by 2D echocardiography, the visualisation of the coronary artery flow by transthoracic colour-coded Doppler echocardiography is established in clinical practice for the detection of coronary artery disease by determining the coronary flow reserve (CFR) during adenosine or dipyridamole stress (4, 5, 11, 15, 16, 17, 18). However, the visualisation of coronary artery flow by colour-coded Doppler echocardiography is primarily used to detect and target the vessel branches for subsequent quantification of coronary artery flow by pulsed-wave Doppler echocardiography. The quantification of coronary artery flow is not established by colour-coded Doppler flow, this assessment is performed by the pulsed-wave Doppler, comparing coronary flow signals at rest and during vasodilator stress (4, 5). In addition, CFR is established for estimating the prognosis in patients with coronary artery disease (7, 9, 19, 20, 21, 22, 23, 24, 25).

This study was carried out to introduce a new approach of visualisation of 3D4D coronary flow of the LAD. Regarding the feasibility of this new approach, the hypothesis was proposed that a longer course of the LAD

could be better visualised and better quantitatively analysed by the colour-coded flow signal using 3D4D echocardiography than 2D echocardiography with respect to the length and the curvatures of the vessels.

Patients and methods

In 33 patients (19 males, 14 females; mean age 55±17) with sinus rhythm adenosine stress, echocardiography was performed to detect coronary artery disease. Only three patients were excluded from the study due to limited image quality during rest and vasodilator stress. In 30 patients who entered the study, a normal CFR was determined and no wall motion abnormalities were observed during vasodilator stress. Thus, on the basis of the results of the normal non-invasive stress test, normal function of coronary arteries was assumed in this cohort of patients. In all 30 patients examined during the study, the distal LAD flow could be well visualised using 2D colour-coded Doppler echocardiography. Then, 3D scanning procedures were also performed in these patients. Because 3D colour-coded scanning requires a biplane preview, the 2D evaluation of coronary flow was always performed before the 3D approach. In all patients, attempts were made to visualize proportions of the right and circumflex artery by colour-coded imaging. Owing to the frequent unsuccessful attempts at visualizing these regions in the far field, the distal LAD territory was

Table 1 Settings of the ultrasound systems (Vivid 7 and Vivid E9, GE Healthcare), which were used for 2D (M4S- and M5S-probe) and 3D4D (3V- and 4V-probe) colour-coded imaging of the LAD.

GE Vivid system	Vivid 7	Vivid E9	Vivid 7	Vivid E9
Parameter	M4S-probe	M5S-probe	3V-probe	4V-probe
Grey scale imaging				
Frequency (MHz)	1.7/3.4	1.7/3.3	2.0/4.0	2.0/4.0
Gain (dB)	0	0	4	0
Compression	11	12	11	12
Reject	2	2	2	2
Dynamic range	6	6	6	10.7
Data-dependent processing	0.2	0.1	0.1	0.2
Performance (dB)	0	0	0	0
FPS (/s)	18–37	47–60	12–14	41–55
Colour imaging				
Gain (dB)	6	4	–4	–4
PRF (kHz)	1.25	1.75	1.00	4.00
Frequency (MHz)	3.0	3.1	2.9	3.1
Sample volume (mm)	1.2	1.1	1.1	1.1
Low velocity reject (cm/s)	3.22	6	5.32	2
Performance (dB)	0	0	0	0
FPS (/s)	18–29	51–73	12–17	29–63

PRF, pulse repetition frequency; FPS, frames per second.

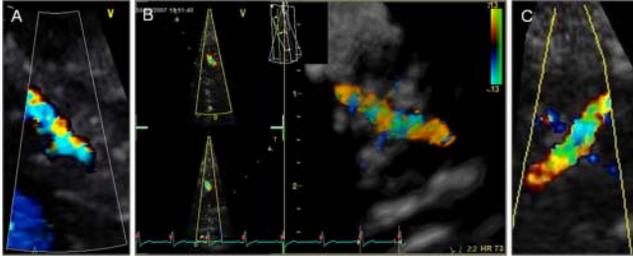


Figure 1
Comparison of the spatial resolution of the colour-coded flow of the distal LAD using the M4S-probe ((A) conventional 2D approach) and using the 3V-probe ((B) biplane scan and 3D4D visualisation of the LAD and (C) 2D plane acquired by post-processing of the 3D near real-time full volume data set).

focused. However, in five patients additionally, segments of the right coronary artery flow were well visualised. No ultrasound contrast agents were used in order to improve Doppler signal quality.

All measurements were performed using ultrasound systems of one vendor (Vivid 7 or a Vivid E9; GE Healthcare, Vingmed Ultrasound AS, Horten, Norway). 2D echocardiography was performed using a M4S-probe (Vivid 7) or M5S-probe (Vivid E9). 3D4D echocardiography was performed using a 3V-probe (Vivid 7) or 4V-probe (Vivid E9). In addition, the algorithm of the EchoPac Software version 12.0.1 (GE Healthcare) was used. In all 30 patients, the distal part of the LAD flow was acquired by the apical approach using an oblique long-axis view. The middle part of the LAD was acquired by the caudal parasternal short-axis view or by the subcostal view. The settings, which were used for 2D and 3D4D colour-coded echocardiography of the LAD, are given in Table 1.

For 3D4D echocardiography a near real-time volume data set was acquired within seven consecutive heart beats during breath hold of the patients. For the detection of the colour-coded signal by 3D4D echocardiography, the LAD was scanned in a biplane preview. Then, the detected LAD flow signal was centred in the 3D data set during the near

real-time acquisition. The angle of the colour-coded sector for 3D imaging of the flow was 18° in both biplane previews using the Vivid 7 and 30–40° using the Vivid E9. 3D4D echocardiography was performed under resting conditions in all patients. With respect to the cooperation of the patient and the additional time duration for acquisition during adenosine infusion, it was only possible to get 3D data sets of the colour-coded flow signals at stress in seven of the 30 patients, with a sufficiently high image quality.

The acquisition of the colour signals of coronary artery flow by colour-coded Doppler echocardiography obviously depends on the Doppler angle. Thus, it was focused on the optimal transducer position to get reliable proportions or parts of the branches of the coronary arteries. Thus, it was not differentiated between different distal parts of the LAD territory.

In addition to the qualitative 3D4D visualisation of distal segments of the LAD, the width and the length of the flow segments in these LAD regions were measured and compared with the detected parameters using 2D colour-coded echocardiography with respect to the predefined settings. In every patient, the measurable maximum longitudinal length was assessed. Proportions of curved parts of the coronaries were measured by the addition of multiple detectable straight distances of the vessels to obtain the total length of the visible region. For measurements of the widths of the coronary segments, the maximum diameter was used, which could be visualised by the colour-coded signal. To improve the visualisation of the colour-coded flow signal, the tissue gain was adjusted in each patient.

Statistical analyses

Data are expressed as mean ± s.d. paired Student's *t*-test and Wilcoxon's signed-rank sum test were applied to compare values of vessel width and length for 2D with those for 3D

Table 2 Parameter of the vessel width and length of the distal LAD, which could be visualised by colour-coded 2D and colour-coded 3D4D echocardiography.

	Width 2D (mm)	Length 2D (mm)	Width 3D (mm)	Length 3D (mm)
Mean values				
All vessels	4.0 ± 1.4*	16.4 ± 7.9	2.9 ± 2.1*	18.5 ± 16.1
Vessels < 11 mm length	2.9 ± 0.6*	8.4 ± 2.1*	2.1 ± 0.4*	13.1 ± 4.6*
Vessels > 12 mm length	4.5 ± 1.4*	19.3 ± 7.2	3.2 ± 2.4*	20.5 ± 18.3

A *P value < 0.05 was considered as statistically significant.

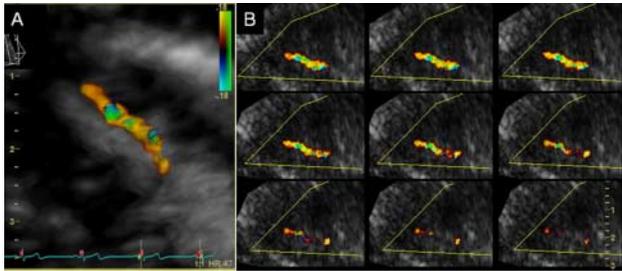


Figure 2
Documentation of the 3D4D colour-coded LAD flow ((A) 3D visualisation). The nine-slices view through the longitudinal course of the vessel ((B) nine different planes of the LAD signal within a distance of 2 mm) documents a high spatial resolution of the colour-coded LAD flow signal using the new technique.

colour-coded Doppler echocardiography. *P* values <0.05 were considered statistically significant. All analyses were performed using the SPSS Software version 17.0.

Results

In all 30 patients, the LAD signal was detectable by 2D colour-coded imaging and the pulsed Doppler spectrum was suitable for evaluation of the coronary flow at rest and during vasodilator stress. The length of the LAD obtained by 2D colour-coded echocardiography was

between 5 and 34 mm. All LAD flow segments, which were imaged by 2D colour-coded Doppler echocardiography, were also visualised by 3D4D echocardiography at rest. The detected length of the colour-coded LAD flow signal using 3D4D echocardiography was between 7 and 95 mm. However, the corresponding 3D images have a lower spatial and temporal resolution of the colour-coded LAD signal due to technical factors (Fig. 1a and b). Whereas the width of the detected colour-coded flow signal was significantly different for the two imaging modalities, the length of the distal LAD, which could be visualised, was not significantly different in any of the patients (Table 2). However, if a length of the LAD of less than 11 mm (in eight of 30 patients; 27%) was visualised by 2D echocardiography, the detected length of the LAD using 3D4D echocardiography was significantly increased in comparison to the 2D technique (Table 2). Despite the technical limitation regarding the spatial resolution of the colour-coded LAD flow signal using 3D4D echocardiography, the 3D4D colour-coded LAD flow signal was well visualised. Quantifications of the vessel diameters and of the possibly suspected stenoses actually cannot be performed by the analysis of the colour-coded flow signal, mostly due to the fact that tissue- and colour-gain settings markedly influence the width and the length of the colour-coded flow signal. However, the spatial resolution

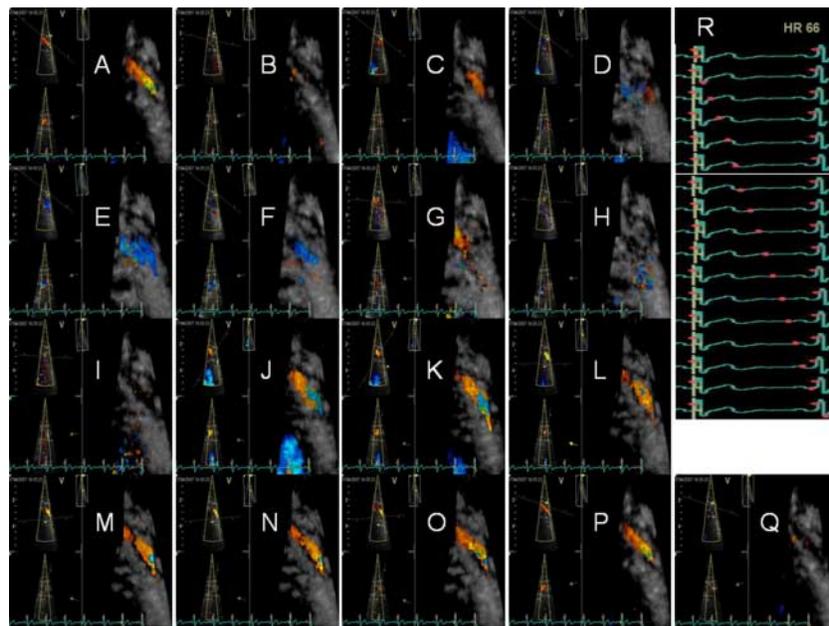


Figure 3
Visualisation of the colour-coded distal LAD flow by 3D4D echocardiography ((A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P and Q) 17 consecutive frames of the 3D4D visualisation and (R) the corresponding trigger of each frame is documented within the ECG of one heart cycle at a heart rate of 66/min).

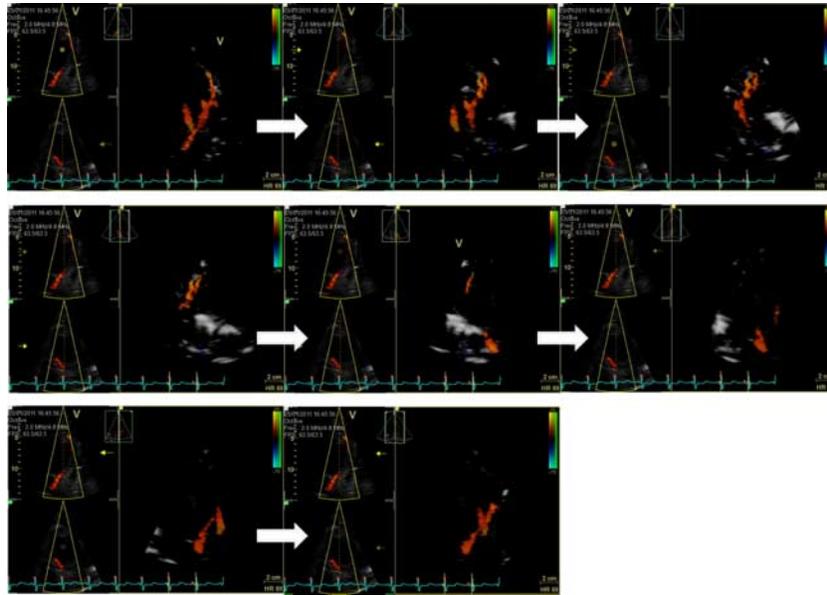


Figure 4

Qualitative visualisation of the coronary artery tree. A large course of the vessel is documented from different views. The images show a birds-eye view onto the coronary colour-coded flow signal of the LAD with rotation

of the 3D data set clockwise. Between each view there is an angle difference of about 20° (arrows indicate the order starting with the upper left view).

was high enough to get six to nine different slices of the colour-coded LAD flow signal in the longitudinal direction (Fig. 2). The visualisation of a larger segment of the LAD flow by a 3D4D echocardiography – especially if only small regions were detected – is due to the fact that 3D4D echocardiography of the vessel shows its complete course in contrast to 2D echocardiography which enables only the view of one sectional plane. The temporal resolution for colour-coded 3D4D echocardiography using a near real-time volume data set is up to 17 frames per second using the Vivid 7 system (Fig. 3) and up to 63 frames per second using the Vivid E9 system. Depending on the heart

rate, 5–12 frames/diastole were acquired using the Vivid 7. However, up to 18–29 diastolic frames could be acquired for visualisation of the diastolic LAD flow using the Vivid E9. The advantage of 3D4D echocardiography of the coronary artery flow is the direct visualisation of the vessel tree, including bifurcations and possibly curved courses of the vessels from multiple different views (Fig. 4).

In four patients, the distal LAD was visualised by 3D4D echocardiography at rest and during adenosine infusion (140 µg/min per kg). Using identical settings for the visualisation of the colour-coded flow signals of the coronary arteries at rest and during adenosine stress,

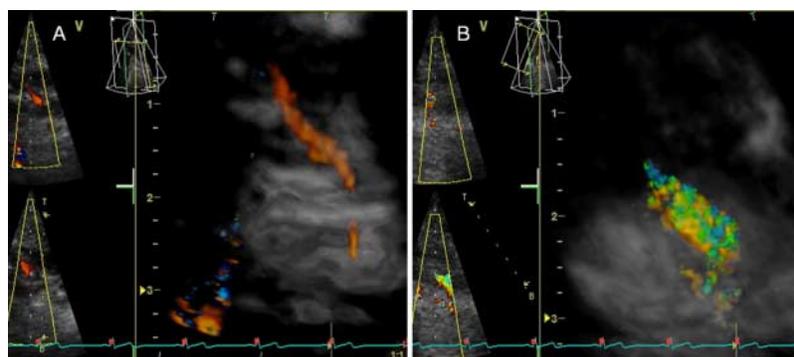


Figure 5

3D4D visualisation of the distal colour-coded LAD flow signal at rest (A) and during adenosine infusion (B) using identical ultrasound applications.

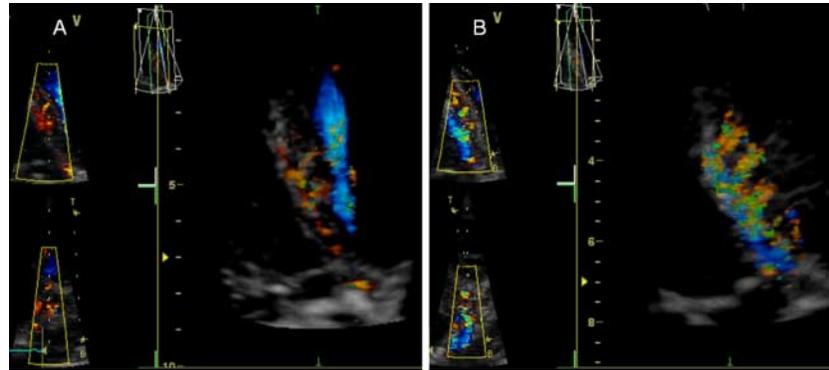


Figure 6
3D4D visualisation of the distal colour-coded right coronary artery (RCA) flow signal at rest (A) and during adenosine infusion (B) using identical ultrasound applications.

the increase in the width was documented between rest and stress (Figs 5 and 6).

Discussion

Conventional transthoracic echocardiography is currently used for the detection of coronary artery disease by the presence of regional wall motion defects at rest or during stress-induced ischaemia. Fibrosis and inflammation can be further reasons for wall-motion abnormalities. The determination of CFR by transthoracic Doppler echocardiography enables the analysis of coronary vascular response. Significant coronary artery stenoses can be revealed by a pathological CFR (6, 8, 18, 23, 26).

The assessment of CFR by pulsed-wave Doppler echocardiography was the primary reason to try the visualisation of coronary artery flow by 3D4D echocardiography in this study. Thus the main focus is to demonstrate that colour-coded 3D4D visualisation of the coronary artery flow is possible and feasible, whilst pointing out advantages and disadvantages of this new approach.

With respect to 3D data acquisition, the colour-coded 3D4D flow visualisation of the LAD can be facilitated. It is shown, that smaller courses of the distal LAD can be better and more easily visualised within a 3D data set than in only one sectional plane. Thus, the detection of smaller segments by 3D4D echocardiography enables new possibilities for the visualization of coronary arteries in more distal segments of the coronary artery tree.

The colour-coded 3D4D echocardiography of the flow signals within detectable segments of coronary arteries possibly enables further diagnostic options. The colour-coded flow signals could be used to visualise the lumen itself. Therefore a distinct separation between intracoronary

blood flow and vessel wall is necessary. If this modality is optimised, intrastenotic flow velocities will be distinguished from plaque lesions and post-stenotic low flow velocities of post-stenotic dilated vessels. If this issue can be solved, colour-coded flow signals will have the potential to be used non-invasively for intraluminal flow visualisation. With respect to this future technical development of 3D4D visualisation of the coronary flow, coronary stenoses could be detected by improving the spatial resolution and by optimising the gain settings. Further studies are needed to evaluate the vessel width of the 3D4D colour-coded Doppler signal in comparison with the angiographic dimensions of the vessel lumen.

A further advantage of 3D4D echocardiography of coronary artery flow by colour-coded Doppler echocardiography is the possibility of creating multiple views of the coronary artery flow by post-processing (Fig. 4). However, currently the spatial resolution of 2D images is still better in comparison with the 3D4D approach.

The main focus of this paper is the basic methodological aspect showing the potential of this new approach and the new possibilities with commercially available high-end echo machines. The potential of this approach may be relevant in the future if 3D4D assessment of coronary artery flow can be improved by further technical developments.

Limitations

The main limitation of this study is the selected cohort of patients, because patients with limited image quality were excluded. It is obvious that a good acoustic window facilitates the acquisition of a near real-time volume data set. In addition, the 3D image quality is influenced by the

cooperation of the patient during breath-holding, which is limited under adenosine-stress conditions, as well as by arrhythmias.

A further limitation is due to the ultrasound penetration during 3D4D echocardiography, which is correlated with the depth of the sector. In comparison with distal branches of the right coronary artery, which are much more far away from the transducer, imaging of the distal LAD flow is possibly better with higher frequencies. The visualisation of the vessel flow is also limited by the angle of colour-coded 3D4D echocardiography. It is obvious that the larger the angle the larger the part of the vessel, that can be detected.

The limitation of lower temporal resolution seems to be solved, because the increase in the frame rate in new ultrasound settings will enable 3D real-time imaging of coronary flow with sufficient temporal resolution. The quantification of the colour-coded LAD flow signal has to be standardised in further studies. One possible proposal to evaluate this new technique of 3D4D coronary flow visualisation by echocardiography is to analyse changes in the 3D4D colour-coded flow signals in comparison with LAD Doppler spectra at rest and during vasodilator stress. With respect to the visualised segments of the distal LAD territory, there is no proof of validation by angiography, whether the segments are really the LAD or diagonal side branches. Nevertheless, on the basis of the normal stress findings, normal flow conditions of the visualised segments can be assumed.

In summary, the 3D4D visualisation of coronary artery flow is not an easy procedure and is based on two main prerequisites. Firstly, the cooperation of the patient with respect to breath-holding is necessary due to the near real full volume acquisition over seven heart cycles. Secondly, an absolutely stereotactic mode of positioning the transducer is necessary to get convincing 3D4D data sets. Thus, the challenge regarding technical skills is marked for this procedure and training is absolutely necessary.

Conclusions

The results of this study demonstrate that imaging of the colour-coded LAD flow signals by 3D4D echocardiography is feasible in patients, in whom 2D colour-coded LAD flow signals are detectable. The spatial and temporal resolution of this new method is sufficiently high to introduce 3D4D coronary flow detection into the clinical scenario. Small and curved courses of the distal colour-coded LAD flow will be visualised more easily within a 3D data set than in 2D sectional planes. The potential for quantification of

stenoses by direct visualisation has to be evaluated in further studies.

Declaration of interest

I, S Stoebe, declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

References

- 1 Chammas E, Dib C, Rahhal M, Helou T, Ghanem G & Tarcha W 2007 Noninvasive assessment of coronary flow reserve in the left anterior descending artery by transthoracic echocardiography before and after stenting. *Echocardiography* **24** 789–794. (doi:10.1111/j.1540-8175.2007.00478.x)
- 2 Pizzuto F, Voci P, Mariano E, Puddu PE, Sardella G & Nigri A 2001 Assessment of flow velocity reserve by transthoracic Doppler echocardiography and venous adenosine infusion before and after left anterior descending coronary artery stenting. *Journal of the American College of Cardiology* **38** 155–162. (doi:10.1016/S0735-1097(01)01333-X)
- 3 Pizzuto F, Voci P, Mariano E, Puddu PE, Chiavari PA & Romeo F 2003 Noninvasive coronary flow reserve assessed by transthoracic coronary Doppler ultrasound in patients with left anterior descending coronary artery stents. *American Journal of Cardiology* **91** 522–526. (doi:10.1016/S0002-9149(02)03298-8)
- 4 Dimitrow PP & Krzanowski M 2005 Coronary flow reserve assessment. *European Heart Journal* **26** 849. (doi:10.1093/eurheartj/ehi211)
- 5 Lambert H, Tries HP, Stein T & Lethen H 1999 Noninvasive assessment of coronary flow reserve with transthoracic signal-enhanced Doppler echocardiography. *Journal of the American Society of Echocardiography* **12** 186–195. (doi:10.1016/S0894-7317(99)70134-3)
- 6 Iwata S, Hozumi T, Matsumura Y, Sugioka K, Yoshitani H, Murata E, Takemoto Y, Kobayashi Y, Yoshiyama M & Yoshikawa J 2006 Cut-off value of coronary flow velocity reserve by transthoracic Doppler echocardiography for the assessment of significant donor left anterior descending artery stenosis in patients with spontaneously visible collaterals. *American Journal of Cardiology* **98** 298–302. (doi:10.1016/j.amjcard.2006.01.100)
- 7 Ikonomidis I, Tzortzis S, Paraskevaidis I, Triantafyllidis H, Papadopoulos C, Papadakis I, Trivilou P, Parissis J, Anastasiou-Nana M & Lekakis J 2012 Association of abnormal coronary microcirculatory function with impaired response of longitudinal left ventricular function during adenosine stress echocardiography in untreated hypertensive patients. *European Heart Journal Cardiovascular Imaging* **13** 1030–1040. (doi:10.1093/ehjci/jes071)
- 8 Hyodo E, Hirata K, Hirose M, Sakanoue Y, Nishida Y, Arai K, Kawarabayashi T, Shimada K, Hozumi T, Muro T *et al* 2012 Detection of restenosis after percutaneous coronary intervention in three major coronary arteries by transthoracic Doppler echocardiography. *Journal of the American Society of Echocardiography* **23** 553–559. (doi:10.1016/j.echo.2010.03.007)
- 9 Meimoun P, Boulanger J, Luyckx-Bore A, Zemir H, Elmekies F, Malaquin D, Doutrelan L & Tribouilloy C 2010 Non-invasive coronary flow reserve after successful primary angioplasty for acute anterior myocardial infarction is an independent predictor of left ventricular adverse remodelling. *European Journal of Echocardiography* **11** 711–718. (doi:10.1093/ejehocardi/jeq049)

- 10 D'Andrea A, Severino S, Mita C, Riegler L, Cocchia R, Gravino R, Castaldo F, Scarafile R, Salerno G, Pirone S *et al* 2009 Clinical outcome in patients with intermediate stenosis of left anterior descending coronary artery after deferral of revascularization on the basis of noninvasive coronary flow reserve measurement. *Echocardiography* **26** 431–440. (doi:10.1111/j.1540-8175.2008.00807.x)
- 11 Voci P & Pizzuto F 2001 Imaging of the posterior descending coronary artery. The last frontier in echocardiography. *Italian Heart Journal* **2** 418–422.
- 12 Lethen H, Tries HP, Kersting S & Lambertz H 2003 Validation of noninvasive assessment of coronary flow velocity reserve in the right coronary artery. A comparison of transthoracic echocardiographic results with intracoronary Doppler flow wire measurements. *European Heart Journal* **24** 1567–1575. (doi:10.1016/S0195-668X(03)00284-7)
- 13 Cortigiani L, Rigo F, Sivari R, Gherardi S, Bovenzi F & Picano E 2009 Prognostic correlates of combined coronary flow reserve assessment on left anterior descending and right coronary artery in patients with negative stress echocardiography by wall motion criteria. *Heart* **95** 1423–1428. (doi:10.1136/hrt.2009.166439)
- 14 Auriti A, Pristipino C, Cianfrocca C, Granatelli A, Guido V, Pelliccia F, Greco S, Richichi G & Santini M 2007 Distal left circumflex coronary artery flow reserve recorded by transthoracic Doppler echocardiography: a comparison with Doppler-wire. *Cardiovascular Ultrasound* **5** 22. (doi:10.1186/1476-7120-5-22)
- 15 Krzanowski M, Bodzoń W & Dimitrow PP 2003 Imaging of all three coronary arteries by transthoracic echocardiography. An illustrated guide. *Cardiovascular Ultrasound* **1** 1–16. (doi:10.1186/1476-7120-1-16)
- 16 Murata E, Hozumi T, Matsumura Y, Fujimoto K, Sugioka K, Takemoto Y, Watanabe H, Yamagishi H, Yoshiyama M, Iwao H *et al* 2006 Coronary flow velocity reserve measurement in three major coronary arteries using transthoracic Doppler echocardiography. *Echocardiography* **23** 279–286. (doi:10.1111/j.1540-8175.2006.00206.x)
- 17 Tries HP, Lambertz H & Lethen H 2002 Transthoracic echocardiographic visualisation of coronary artery blood flow and assessment of coronary flow reserve in the right coronary artery: a first report of 3 patients. *Journal of the American Society of Echocardiography* **15** 739–742. (doi:10.1067/mje.2002.118525)
- 18 Cortigiani L, Rigo F, Gherardi S, Bovenzi F, Molinaro S, Picano E & Sicari R 2013 Prognostic implication of Doppler echocardiographic derived coronary flow reserve in patients with left bundle branch block. *European Heart Journal* **34** 364–373. (doi:10.1093/eurheartj/ehs310)
- 19 Lethen H, Tries HP, Brechtken J, Kersting S & Lambertz H 2003 Comparison of transthoracic Doppler echocardiography to intracoronary Doppler guidewire measurements for assessment of coronary flow reserve in the left anterior descending artery for detection of restenosis after coronary angioplasty. *American Journal of Cardiology* **91** 412–417. (doi:10.1016/S0002-9149(02)03235-6)
- 20 Ruscazio M, Montisci R, Colonna P, Caiati C, Chen L, Lai G, Cadeddu M, Pirisi R & Iliceto S 2002 Detection of coronary restenosis after coronary angioplasty by contrast-enhanced transthoracic echocardiographic Doppler assessment of coronary flow velocity reserve. *Journal of the American College of Cardiology* **40** 896–903. (doi:10.1016/S0735-1097(02)02055-7)
- 21 Meimoun P, Benali T, Elmekies F, Sayah S, Luyckx-Bore A, Doutrelan L, Hamdane Z, Boulanger J & Tribouilloy C 2009 Prognostic value of transthoracic coronary flow reserve in medically treated patients with proximal left anterior descending artery stenosis of intermediate severity. *European Journal of Echocardiography* **10** 127–132. (doi:10.1093/ejehocard/jen190)
- 22 Rigo F, Gherardi S, Galderisi M, Pratali L, Cortigiani L, Sicari R & Picano E 2006 The prognostic impact of coronary flow-reserve assessed by Doppler echocardiography in non-ischaeamic dilated cardiomyopathy. *European Heart Journal* **27** 1319–1323. (doi:10.1093/eurheartj/ehi795)
- 23 Rigo F, Sicari R, Gherardi S, Djordjevic-Dikic A, Cortigiani L & Picano E 2007 Prognostic value of coronary flow reserve in medically treated patients with left anterior descending coronary disease with stenosis 51% to 75% in diameter. *American Journal of Cardiology* **100** 1527–1531. (doi:10.1016/j.amjcard.2007.06.060)
- 24 Rigo F, Sicari R, Gherardi S, Djordjevic-Dikic A, Cortigiani L & Picano E 2008 The additive prognostic value of wall motion abnormalities and coronary flow reserve during dipyridamole stress echo. *European Heart Journal* **29** 79–88. (doi:10.1093/eurheartj/ehm527)
- 25 Ascione L, Carlomagno G, Sordelli C, Iengo R, Monda V, Severino S, Merenda R, D'Andrea A & Caso P 2013 Dipyridamole coronary flow reserve stratifies prognosis in acute coronary syndrome patients without left anterior descending disease. *European Heart Journal Cardiovascular Imaging* **14** 858–864. (doi:10.1093/ehjci/jes305)
- 26 Wild PS & Zotz R 2002 Fragment reconstruction of coronary arteries by transesophageal echocardiography. A method for visualizing coronary arteries with ultrasound. *Circulation* **105** 1579–1584. (doi:10.1161/01.CIR.0000012548.11483.C9)

 Received in final form 21 July 2014

Accepted 23 July 2014