Fragment reconstruction of coronary arteries using transesophageal echocardiography for coronary diagnostics

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Aims Ultrasound differs procedurally from the established methods for non-invasive coronary visualization and is therefore an interesting alternative for non-invasive diagnostics. In this study, fragment reconstruction of coronary arteries by transesophageal echocardiography (FRC-TEE) was investigated for the first time in a patient population being evaluated for coronary angiography.

Methods and results Ultrasonic and angiographic findings were compared visually and using quantitative measurements in 50 patients. One hundred and seventy-one vessels were examined by FRC-TEE. The total lengths visualized were 9.6±1.7 cm for the right coronary artery, 7.0±1.1 cm for left circumflex, 3.9±1.2 cm for left anterior descending (LAD), and 1.5±0.8 cm for the left main coronary artery. There was high concordance between results of both procedures. Sixty-three stenoses were detected using FRC-TEE. The mean difference in degree of stenosis between techniques was 0.2±5.1%. Stents could be visualized in 19 segments. FRC-TEE detected distal stenoses of the coronary arteries to only a limited extent: 14 stenoses and 2 stents, predominantly in the LAD artery (n=13), were not identified.

Conclusions FRC-TEE is a potential method for diagnosing coronary artery disease. FRC-TEE and angiography yield comparable findings during the evaluation of coronary lesions. Further investigations are needed to verify the encouraging findings and define FRC-TEE’s applications.

KEYWORDS Transesophageal echocardiography; Coronary artery; Coronary artery disease; Non-invasive visualization; Coronary diagnostics

Introduction

Multislice computer tomography, electron beam tomography, and magnetic resonance imaging (MRI) predominate the current literature on non-invasive technologies for coronary visualization and diagnostics.1–3 Although non-invasive imaging has undergone an extensive evolution, with steady improvements in the quality of the images produced, these current technologies have disadvantages and limitations. Ultrasound represents an interesting alternative approach to these technologies for coronary visualization, having different procedural characteristics.

To obtain the best image quality for heart and coronary artery visualization by ultrasound, transesophageal echocardiography (TEE) is necessary. TEE is appropriate for both inpatients and outpatients. It is broadly available in health facilities, as it requires little in the way of technical infrastructure. It exposes neither patient nor examiner to radiation; nor does it require use of a contrast agent, which is associated with certain side effects and higher cost. Also, radiation-based techniques are hardly conceivable in primary prevention or periodic follow-up examinations in secondary prevention. With TEE, the independence of contrasting the lumen allows visualization of the vessel wall and the dimensions and morphology of occluded vessel segments. TEE is less invasive than conventional angiography, and therefore presents fewer risks and complications.4 A large-scale multicenter trial by Daniel et al. (1991), to the time the technique established itself in clinical routine, established that TEE can be performed with low risk.5,6 TEE appears to be less expensive than the imaging technologies named above, although economic evaluation is somewhat unreliable during the development phase, due to scarcity of data.
Fragment reconstruction of coronary arteries by means of transesophageal two-dimensional (2D) echocardiography (FRC-TEE) is a newly developed ultrasound method. This technique enables the generation of images from successive vessel fragments based on theoretical and mathematical principles. Hence, by assembling the single 2D images of vessel fragments, the coronary artery can be reconstructed in one summation image. The assembled 2D images follow the vessel course in the third dimension, visualizing the entire vessel over its actual length in a modified 3-dimensional (3D) view. This enables a view perpendicular to all parts of the vessel and thus artery evaluation using just one image, reducing the risk of misinterpretation and the time required.

In its initial application, this technique has considerably improved the imaging of coronary artery length and quality. In the current study we prospectively investigated for the first time FRC-TEE in a patient population being evaluated for coronary angiography in order to assess its clinical potential.

Methods

Study group

The study collective included 51 subjects (33 men, 18 women) that had been admitted with an indication for heart catheterization. The trial protocol has been approved by the local ethics committee. Informed written consent for study participation was obtained from all subjects. Patients were evaluated for anthropometric data, heart insufficiency (the NYHA-stadium), presence and duration of diabetes mellitus, lipid disorder, and respiratory disease. Previous thorax or heart surgery and existence of a prosthetic heart valve were documented.

Fragment reconstruction of coronary arteries by transesophageal echocardiography

FRC-TEE examinations were performed using a HP Sonos 5500 (Philips Medical Systems) with a multiplane probe (Omni II) in harmonic fusion mode. Generation of successive vessel fragments and fragment reconstruction of the coronaries was accomplished using the same algorithms as previously described. Image data were transferred to a computer connected to the ultrasound system. Fragment reconstruction was carried out during the transesophageal ultrasound examination by an assistant examiner using USIP II software. This software was developed according to the specific requirements of the method by our group and allows a sequential recording and cataloguing of images or loops and the subsequent reconstruction during the examination. The programming was carried out in C++ with a platform independent open source framework (wxWidgets) and a high performance image processing library from Intel (Santa Clara, CA, USA).

Standard conditions for a conventional TEE examination were used. Examinations were performed after a fasting period of at least 4 h. The upper pharyngeal region was locally anaesthetized with lidocaine spray. Sedation with midazolam (Dormicum®) was offered and, if favoured, administered at a dose of 0.04 mg/kg body weight. Examinations were performed in quiet conditions with the subject in a comfortable position. Subjects were asked to perform controlled, shallow breathing and avoid any movement. The examination time was limited to 20 min; after this time the examination was terminated irrespective of its progress. The right and left coronary artery (RCA and LCA) were evaluated in arbitrary order.

Heart catheterization

All patients underwent heart catheterization. For coronary angiography, a conventional single-plane heart catheter system was used (Siemens, Erlangen, Germany), together with the nonionic, water-soluble contrast agent Levovist®. For visualization of stenoses, care was taken to display the vessel segment vertically to the line of vision. Angiographic results were used as the reference examination for evaluation of ultrasound findings.

Image analysis

Ultrasound examination conditions for each subject were evaluated by the examiner subsequent to the examination. The ultrasound image quality for each visualized coronary artery was retrospectively evaluated by a blinded reviewer. The quality was rated as 'good', 'middle', or 'poor'. All measurements were performed independently by the examiner and the reviewer in order to consider the intra- and interobserver variance. The lengths of the reconstructed vessels were determined by measuring an assumed centreline between the two vessel-wall segments. The ostium served as the proximal measuring point, and the point at which the curves of both vessel walls were still identifiable served as the distal measuring point. Each measurement was performed twice and the mean calculated.

All stenoses detected by FRC-TEE were compared with the corresponding angiography findings visually and using quantitative measurements. Quantitative measurements were performed on lesions that impressed visually with a lumen obstruction of >20%. The minimal diameter of each stenosis and the prestenotic diameter 2 cm proximal to the lesion were measured from endothelium to endothelium in triplicate by each examiner. The respective degree of stenosis was determined subsequently. The average absolute difference between the degree of stenosis determined with angiographic and echocardiographic techniques and the intra- and interobserver variance for each procedure were calculated. Stents were localized using both procedures, the stent status documented, and in the case of an in-stent stenosis the degree of stenosis determined. In addition, stenoses and stents visualized by angiography but not FRC-TEE were documented. All measurements in both procedures were carried out using USIP II software.

Data analysis

One female subject was excluded from the data analyses due to inability to perform the FRC-TEE. Intubation was not possible due to a pronounced defence reaction in spite of adequate intravenous sedation. Ninety-five percent confidence intervals (CI) were determined. Absolute lengths of the visualized arteries and their means were calculated. The degree of stenosis was calculated as a percentage: (minimum diameter in the stenosis/prestenotic diameter) × 100%. Correlations between image quality and both individual anamnesis and physical status were calculated.

Results

Patient characteristics

The mean patient age was 64.0 ± 13.6 years (range 18–90 years), and the mean body mass index was 28.2 ± 3.9 kg/m² (range 21.8–36.9). Table 1 shows the patient characteristics that were evaluated for their impact on ultrasound examination conditions and image quality. Angiography showed a distribution over all stenosis of coronary artery disease (CAD): no CAD: n = 11, 1-vessel disease: n = 13, 2-vessel disease: n = 9, 3-vessel disease: n = 17.

Examination conditions, imaging rates, and image quality

All FRC-TEE investigations were carried out without complications and provided evaluable results. As shown in Table 2, the FRC-TEE examination conditions were predominantly
judged to be good or middle (n = 42, 84%). One hundred and seventy-one of 203 vessels (84%) were investigated with FRC-TEE within the 20-min examination time limit. The difference in imaging rates across the single coronaries (see Table 2) is accounted for by the free examination order, with most examinations starting with imaging of the left main coronary artery (LM) and left circumflex coronary artery (LCX) and concluding with the left anterior descending artery (LAD).

Ratings of image quality for the RCA, LM, and LCX showed a similar distribution to that of examination conditions: 86, 88, and 98% of the images, respectively, were rated to be of good or middle quality (Table 2). Review of the LAD images revealed an opposite trend, with only 25% having good or middle image quality. Anamnestic and anthropometric factors were found to have no influence on examination conditions or image quality.

Visualized lengths of coronary arteries

The lengths of the coronary arteries visualized with FRC-TEE are shown in Figure 1. The average difference in length between the two reviewers was -0.6 ± 2.4 mm (95% CI -5.3 to 4.1).

Table 1  Characteristics of the study sample (n = 50)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n = 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>64.0 ± 13.6 (18; 90)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.2 ± 3.9 (21.8; 37)</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>67.1 ± 17.5 (15; 89)</td>
</tr>
<tr>
<td>NYHA-stadium</td>
<td></td>
</tr>
<tr>
<td>Stadium 0 and I, %</td>
<td>54</td>
</tr>
<tr>
<td>Stadium II, %</td>
<td>26</td>
</tr>
<tr>
<td>Stadium III, %</td>
<td>20</td>
</tr>
<tr>
<td>Stadium IV, %</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>32</td>
</tr>
<tr>
<td>IDDM, %</td>
<td>10</td>
</tr>
<tr>
<td>NIDDM, %</td>
<td>22</td>
</tr>
<tr>
<td>Lipid disorder, %</td>
<td>70</td>
</tr>
<tr>
<td>Respiratory disease, %</td>
<td>26</td>
</tr>
<tr>
<td>Thorax or heart surgery, %</td>
<td>8</td>
</tr>
<tr>
<td>Existing prosthetic heart valve, %</td>
<td>4</td>
</tr>
</tbody>
</table>

BMI indicates body mass index, IDDM insulin-dependent diabetes mellitus and NIDDM non-insulin-dependent diabetes mellitus. Data presented are percentages for categorical variables and mean ± SEM for normal continuous variables.

Table 2  Imaging rate, image quality, and examination conditions of fragment reconstruction of coronary arteries using transesophageal echocardiography (n = 50)

<table>
<thead>
<tr>
<th></th>
<th>Total n (%)</th>
<th>RCA n (%)</th>
<th>LM n (%)</th>
<th>LCX n (%)</th>
<th>LAD n (%)</th>
<th>IM n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging ratea</td>
<td>171/203 (84)</td>
<td>42/50 (84)</td>
<td>49/50 (98)</td>
<td>49/50 (98)</td>
<td>28/50 (56)</td>
<td>3/3 (100)</td>
</tr>
<tr>
<td>Image qualityb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>42 (25)</td>
<td>06/42 (14)</td>
<td>16/49 (33)</td>
<td>18/49 (37)</td>
<td>02/28 (07)</td>
<td>0/3 (0)</td>
</tr>
<tr>
<td>Middle</td>
<td>93 (54)</td>
<td>30/42 (71)</td>
<td>27/49 (55)</td>
<td>30/49 (61)</td>
<td>05/28 (18)</td>
<td>1/3 (33)</td>
</tr>
<tr>
<td>Poor</td>
<td>36 (21)</td>
<td>06/42 (14)</td>
<td>06/49 (12)</td>
<td>01/49 (02)</td>
<td>21/28 (75)</td>
<td>2/3 (66)</td>
</tr>
<tr>
<td>Examination conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td></td>
<td>10/50 (20)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Middle</td>
<td></td>
<td>32/50 (64)</td>
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<td></td>
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</tr>
<tr>
<td>Poor</td>
<td></td>
<td>08/50 (16)</td>
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</tr>
</tbody>
</table>

a The imaging rates resulted from a given examination time limit of 20 min.

b Image quality was evaluated by a reviewer that was not present during the examination.

RCA, right coronary artery; LA, left main coronary artery; LCX, left circumflex artery; LAD, left anterior descending artery; IM, ramus intermedius.

Visualization of coronary artery stenoses and stents

FRC-TEE detected 63 coronary artery stenoses meeting the stenosis definition (degree of stenosis visually estimated to be 20–100%) in the visualized vessel segments. All of these stenoses had a correlate in angiography images (Figure 2). In contrast, coronary angiography had no lesion without a correlate in FRC-TEE in the vessel segments visualized by ultrasound. The average degree of stenosis was 51.9 ± 18.7% for FRC-TEE and 51.9 ± 19.6% for angiography. As Figure 3 shows the difference in absolute degree of stenosis between the procedures was -0.1 ± 4.8% (95% CI -9.4 to 9.2) with comparable results between the different coronary vessels. The absolute difference in the degree of stenosis between reviewers was -0.2 ± 3.3% for FRC-TEE and -0.3 ± 4.2% for angiography. Nineteen stents were detected using FRC-TEE (Figure 4). Six were located in the RCA, 3 in the LAD, and 10 in the LCX. Only one stent showed a 30% in-stent restenosis; all others appeared open, so that no further evaluation was performed. Fourteen stenoses (stenosis degree ≥50%) and two stents were
identified with angiography but could not be detected using FRC-TEE. They were located distal to the vessel parts visualized by ultrasound and were found predominantly in the LAD (stenoses: LAD: 11, RCA: 2, LCX: 1, stents: LAD 2).

Discussion
Results of this prospective single-centre study show for the first time that FRC-TEE can visualize longer segments of the coronary arteries from their ostial origin in a patient population being evaluated for coronary angiography. The results exceed the previous quantitative and qualitative delineation of coronary arteries by ultrasound. The dimensions of the artery lengths that were visualized and the presentability of vessels are comparable to those of the MRI technique. This work showed that localization and assessment of pathologic vessel findings such as vessel remodelling with arterial wall thickening, stenoses, and stents is realizable using FRC-TEE (Figure 4). The study results show acceptable concordance between the degree of stenosis determined by ultrasound and coronary angiography. Even the visualization of small vessels was found to be moderately feasible (Figure 5A). The technique also assists differential diagnostics for lesion localization (Figure 5B) and—not requiring a contrast agent—FRC-TEE enables visualization of vessel segments that are distal to a total vessel occlusion (Figure 5C).

The literature justifies use of coronary angiography as a reference examination when determining ultrasound accuracy. However, despite the good correlation in the current study between ultrasound and angiography, for coronary diagnostics it must be considered that quantitative analysis of vessel obstruction using diameter measurement is only a morphological interpretation. Previous work showed this to be a deficient estimator of the functional significance of a single coronary lesion.

In light of these facts, use of FRC-TEE to image the vessel wall seems an interesting option. The evaluation of a lesion by coronary angiography is often confounded by the

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**Figure 2** Visualization of stenoses in fragment reconstruction of coronary arteries using transesophageal echocardiography with corresponding angiography. (A) Fragment reconstruction of coronary arteries using transesophageal echocardiography showing a right coronary artery with proximal stenosis. (B) Corresponding angiography to (A). (C) Angiography visualizing a left circumflex artery with stenosis of the middle segment. (D) Corresponding FRC-TEE to (C). In multiplane transesophageal probes, image generation always demonstrates the ultrasound picture from the same side. Thus, reconstructions from the left coronary artery show mirror images of vessel.

**Figure 3** Absolute difference in stenosis degree between stenoses in fragment reconstruction of coronary arteries using transesophageal echocardiography and cath (n = 63). 95% CI, 95% confidence interval of the mean.
phenomenon of coronary ‘remodelling,’ first described in 1987 by Glagov. The remodelling process is observed histologically as the outward displacement of the external vessel wall overlying the atheroma. The adventitial enlargement opposes luminal encroachment, thereby concealing the presence of disease. Although remodelled lesions do not restrict blood flow, clinical studies have demonstrated that these low-grade lesions represent the most important source of acute coronary syndromes. Figure 6 shows exemplarily the ultrasound image of a LCX with visualization of the vessel wall and its thickening. Compared with angiography, the ultrasound image gives a modified impression of the local atherosclerotic process. However, future investigations have to evaluate the potential of ultrasound further, especially in comparison to the morphology shown by the gold standard, the intravascular ultrasound.

Beyond this, FRC-TEE could also be of interest for monitoring the development of low to middle grade lesions by periodical follow-up examinations, especially in the case of important prognostic localizations of stenoses. The procedure might also impact the evaluation of coronary arteries in research investigating the hereditary origin of CAD, as hereditable patterns have been found in particular for proximal CAD. Recent efforts to use marker-coupled ultrasound contrast agents to detect ‘hot’ arteriosclerotic lesions in instable plaques are exciting. Further technical advances in this field would inaugurate another field of development for coronary artery visualization by ultrasound and would allow the implementation of the evolution from direct morphological to direct functional imaging.

FRC-TEE is a potential imaging alternative for patients with adipositas per magna, contrast agent allergies, renal insufficiency, hyperthyreosis, and in selected circumstances, patients with pacemakers, implants, tattoos, and claustrophobia.

The difficulties visualizing distal parts of vessels, in general, and the middle-distal and distal segments of the LAD, in particular, are a limitation of FRC-TEE. Technical modifications of the transesophageal probe are needed to address this limitation. The results of this study suggest that evaluation of the LAD is underrepresented due to methodological reasons. However, measurement of coronary flow reserve can complement coronary diagnostics by transesophageal ultrasound: Doppler-TEE of the LAD has been used to reliably evaluate coronary flow reserve and the functional significance of coronary artery stenosis. Furthermore, Doppler-TEE can be used for visualization and measurement of flow velocity and flow reserve in aortocoronary saphenous vein grafts. Non-invasive assessment of left and right internal mammary artery graft patency with ultrasound technique is also possible, but restricted to transthoracic colour Doppler echocardiography.

With further automatization of the method, the FRC-TEE examination time could be shortened. The possibilities of visualizing the fourth dimension and determining the functional significance of coronary lesions should be pursued. In view of the current developments in conventional 3D ultrasound and the innovations to come, the experiences with FRC-TEE—a modified 3D technique—and the imaging possibilities of ultrasound, are also a valuable basis for conventional 3D volume reconstructions of the coronary tree.

**Limitations and perspectives**

The study findings are limited in their significance by virtue of the limited number of examinations and single-centre
design. A multi-centre trial is needed to establish the variance between examiners. Data from larger collectives must be assembled in order to define diagnostic measures and provide information about influencing factors for examination conditions and image quality. With respect to the clinical development of FRC-TEE, further trials should focus on use for secondary prevention follow-up examinations for stenoses identified in prognostically important locations and after coronary intervention with stent implantation. Use of FRC-TEE to obtain prognostic information by evaluating local changes of the vessel wall may also be worthy of further investigation.

Generally FRC-TEE and TEE are semi-invasive procedures, against which provisos might arise. Cierpka et al. showed that patients subjectively tolerate the method well. Short-acting benzodiazepine premedication improves patient comfort during and after TEE. Our experience has confirmed these facts, especially when the exams are performed routinely and by experienced hands.

In conclusion, in this single-centre study FRC-TEE demonstrated potential for diagnostic use in CAD showing good comparability to angiography for the evaluation of coronary lesions. FRC-TEE differs procedurally from other non-invasive methods. Further investigations are needed to verify the encouraging results of this study, to determine the technique’s diagnostic parameters, and to define its applications.

Conflict of interest: none declared.

References