Coronary artery diameter can be assessed reliably with transthoracic echocardiography

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Kiviniemi, Tuomas O., Markku Saraste, Juha W. Koskenvuo, K. E. Juhani Airaksinen, Jyrir O. Toikka, Antti Saraste, Jussi Pärkkä, and Jaakko J. Hartila. Coronary artery diameter can be assessed reliably with transthoracic echocardiography. Am J Physiol Heart Circ Physiol 286: H1515–H1520, 2004.—We studied whether diameters of coronary arteries can be measured accurately with the use of transthoracic echocardiography (TTE). By knowing the anatomic diameter of the coronary artery together with coronary flow velocity it is possible to measure coronary flow volume more precisely by TTE. However, the suitability of TTE for measurement of diameters of all main epicardial coronary arteries has not been systematically validated. We measured the diameters of the left main (LM), left anterior descending (LAD), left circumflex (LCX), and right coronary arteries (RCA) with the use of TTE [manual two-dimensional (2D), color-Doppler, and automated 2D analysis] in 30 patients who had normal coronary anatomy. We compared these diameters to those measured with quantitative coronary angiography (QCA). We could measure diameters of LM, LAD, LCX, and RCA by TTE in up to 37%, 63%, 7%, and 60% of patients, respectively. The overall correlation coefficients between TTE and QCA measurements were 0.83 (P < 0.01) with manual 2D analysis, 0.82 (P < 0.01) with automated 2D analysis, and 0.94 (P < 0.01) with a color-Doppler-based analysis. Interobserver variability of TTE measurements was low (coefficient of variation 5.4 ± 4.6–7.5 ± 8.8%). TTE is an accurate method to evaluate coronary artery diameter in patients with healthy coronary arteries.

angiography; circulation; Doppler analysis

IT HAS BEEN SHOWN that transthoracic echocardiography (TTE), which is noninvasive and widely used in clinical practice, can be used to visualize the left main artery (LM) (25, 32) and left anterior descending coronary artery (LAD) (9, 13, 16, 21, 23, 26, 31). It has been possible to detect stenoses and aneurysms of these coronary arteries by changes of arterial lumen diameter with the use of TTE (23, 25, 31, 32). Moreover, segmental thickening in the walls of these coronary arteries as seen by TTE has been shown to predict the presence of coronary artery disease (10, 12, 21).

Previously, good agreement has been demonstrated between coronary artery diameter measurements by TTE and quantitative coronary angiography (QCA) (13) or epicardial echocardiography (16) in the middle or distal segments of the LAD. However, the suitability of TTE for assessment of diameter of other coronary arteries has not been systematically validated. Therefore, we studied whether TTE-derived coronary artery diameters of the LM, LAD, left circumflex artery (LCX), and right coronary artery (RCA) are comparable to corresponding values in angiography.

METHODS

We studied 30 consecutive patients who had undergone QCA because of chest pain. All patients had normal coronary arteries. The study group consisted of 16 men and 14 women (average age 57 ± 8.2 yr, weight 77 ± 13 kg, and body mass index 26 kg/m2).

The Ethics Committee of Turku University Hospital approved the study protocol. All patients gave their written informed consent.

Echocardiography. We performed TTE studies with a Sequoia C 256 ultrasound apparatus (Acuson, Mountain View, CA) with a 3.5-MHz transducer with harmonic imaging properties. A single sonographer carried out all TTE studies. Both B-mode and color-Doppler mapping were used to identify coronary arteries. Coronary arteries appeared as linear tubular structures demonstrating mainly diastolic color-Doppler flow signal. Because of better resolution in the axial direction, only the coronary arteries lying as perpendicularly as possible to the ultrasound beam were included in this study. Images of coronary arteries were stored in a digital network (KinetDX WS3000, Acuson) for later analysis. The duration of a single TTE study varied from 25 to 60 min. TTE studies were done on average 121 ± 158 days after coronary angiography.

The diameter of the LM was measured from the left parasternal view when patients were lying in the left lateral decubitus position. The imaging plane was oriented in parallel with the short-axis view of the aortic root slightly above the aortic valve. The proximal LAD was measured with the same view, except with slight lateral angulation and rotation. If a patient’s proximal LAD was not seen, we measured the distal LAD from the apical two-chamber view by aiming the ultrasound beam superiorly in parallel with the epicardial surface of the heart and scanning the interventricular sulcus. The part of the LAD that was apical to the papillary muscle level was considered as its distal part. In some patients, the diagonal branch between the middle and distal parts of the LAD could be visualized by TTE. The LCX was measured from its middle part with an apical long-axis view focusing on the tissue adjacent to the lateral side of the mitral ring. The RCA was measured from the end of its proximal part or the beginning of its middle part with either left or right parasternal views or a subcostal short-axis view. The ultrasound beam was focused on the anterior tricuspid ring.

For comparison with QCA, the sonographer marked the distance between the ostium and the point of measurement in the LM, LAD, and RCA. In the distal LAD the point of measurement was estimated by using papillary muscles and diagonal branches as a landmark. In the LCX the point of measurement was estimated by using the mitral ring as a landmark.

Images were analyzed with Image software (ImageJ 1.30, National Institutes of Health, Bethesda, MD). First, all the TTE images
were browsed by two observers independently of the sonographer. Usually the coronary artery is only partially visible on a single longitudinal imaging plane. Thus, to avoid angle interrogation error diameter was measured from the largest distance between the luminal edges. If both independent observers found the same echogenic lines in the same area of an image to represent arterial walls and the image quality was sufficient, the image was approved for later analysis. Color-Doppler images were included if the echogenic lines representing arterial walls were seen and steady colored edges of the coronary flow were inside these lines. Finally, the two observers made measurements in parallel independently of each other to assess the intra- and interobserver variability of the results.

All measurements were made from end-diastolic images. We measured the diameter manually and semiautomatically with gray-scale intensity plots from two-dimensional (2D) images and manually with color-Doppler images. In the manual 2D method, we measured the lumen from the black-white interface of near and far walls. In the automated 2D method, we cropped an area representing the arterial lumen and its walls from an echocardiographic image to obtain an image for analysis. A rectangular region of interest was then set on the image, and specific software (RoiZoom 1.0, Turku University Hospital, Turku, Finland) recognized two points on the opposite walls where the intensity was 80–90% of the maximum and the distance between the points resembled the lumen. The software automatically defines intensity curves pixel by pixel and calculates the average diameter of these curves. In the color-Doppler method images were measured manually from one colored edge to another. Each artery diameter was calculated as an average of six consecutive measurements with each method.

In addition, the effect of 0.5 mg of sublingual nitroglycerin on coronary artery diameter was assessed in seven healthy volunteers (proximal LAD in 4 and RCA in 3 subjects) with TTE. Coronary artery diameter was measured before and 1–5 min after the administration of nitroglycerin with the manual 2D method as described above. Mean diameters at rest and after the administration of nitroglycerin were calculated from three separate cardiac cycles, and the percent change of coronary artery diameter was calculated.

**Coronary angiography.** Coronary angiography was performed via the femoral artery with the Judkins technique after an intravenous injection of 3,750 IU of heparin and 0.5 mg of sublingual nitroglycerin. Angiography was performed with 5-Fr catheters (Cordis, Johnson & Johnson).

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**Fig. 1.** Transthoracic echocardiography (TTE) images of the lumen of the left main artery (LM; A), left anterior descending artery (LAD; B), left circumflex artery (LCX; C), and right coronary artery (RCA; D). Coronary arteries appeared as 2 linear echogenic lines. The lumen is between these lines (*). Measurements were done from 1 luminal edge of the vessel wall to the other (arrowheads). Diastolic color-Doppler flow signal in the LAD is also demonstrated in B. Color-Doppler measurements were done from margins of flow signal. Imaging properties are on right. HR, heart rate; Δ, contrast resolution.
A single operator analyzed coronary artery diameters with QCA software (Quantcor stenosis evaluation software, Siemens). Images were calibrated with the catheter. Luminal diameter was calculated from an average of five measurements. Care was taken that coronary artery diameters were measured as close as possible to each other by TTE and QCA.

Data analysis. Data are presented as means ± SD unless stated otherwise. Pearson’s correlation and intraclass correlation coefficients were calculated for TTE and QCA measurements. The difference between the TTE and QCA measurements and the difference in intra- and interobserver measurements were calculated as mean difference ± 2SD. Coefficients of variation were calculated as (SD/mean) × 100 of means of the diameters measured by the two methods. All statistical tests were performed with the Statistical Analysis System (SAS).

RESULTS

TTE images of the LM, LAD, LCX, and RCA are shown in Fig. 1. In TTE, only the coronary arteries lying as perpendicularly as possible to the ultrasound beam were included in the study because diameter measurements are more accurate in the axial direction. In this way, the LM, LAD, LCX, and RCA could be identified in 20 (67%), 25 (83%), 7 (23%), and 21 (70%) patients, respectively. However, all images were not sufficient for evaluation of the anatomic diameter because of noise and inaccurate projection. Therefore, we selected the applicable images as described in METHODS for later analysis. Thus, with manual analysis of 2D images, the anatomic diameter of the LM, LAD, LCX, and RCA could be satisfactorily measured in 11 (37%), 19 (63%), 2 (7%), and 18 (60%) patients, respectively. With the automated 2D method the LM, LAD, LCX, and RCA were measurable in 11 (37%), 18 (60%), 0, and 18 (60%) patients, respectively. Color-Doppler images could be obtained from the LM, LAD, LCX, and RCA in 6 (20%), 17 (57%), 5 (17%), and 12 (40%) patients, respectively. We approved for analysis 1 (3%), 8 (27%), 0, and 2 (7%) color-Doppler images in the LM, LAD, LCX, and RCA, respectively. Together, the diameters of the LAD and RCA could be measured in most of the patients with TTE, whereas the LCX was detected in only a few patients.

The diameters and correlation between coronary artery diameters measured with the use of TTE and QCA are shown in Tables 1 and 2. With the manual analysis of 2D images the Pearson’s and the intraclass correlation coefficients between TTE and QCA in all coronary arteries were 0.83 (P < 0.01) and 0.82, respectively (Fig. 2). The Pearson’s correlation coefficient in the proximal part of the LAD alone was 0.78 (P < 0.01), and the intraclass correlation coefficient was 0.77.

With the automated 2D analysis the Pearson’s correlation coefficient of all coronary arteries was 0.82 (P < 0.01) and the intraclass correlation coefficient was 0.74 (Fig. 2). With the color-Doppler method the Pearson’s and intraclass correlation coefficients of all coronary arteries were 0.94 (P < 0.01) and 0.94, respectively (Fig. 2). The mean difference between the two techniques in the manual 2D, automated 2D, and color-Doppler methods was 0.0 (~0.8 to 0.7), 0.2 (~0.7 to 1.0), and ~0.1 (~0.7 to 0.6) mm, respectively. Thus TTE provided accurate measurements of coronary artery diameter compared with QCA.

Intraobserver and interobserver variability are shown in Table 3. In manual 2D, automated 2D, and color-Doppler analyses, coefficients of variation for intraobserver variability were as low as 6.1 ± 7.5%, 3.3 ± 2.9%, and 4.9 ± 5.3%, respectively. Pearson’s correlation coefficient between two observers was 0.91 with the manual 2D method, 0.90 with the automated 2D method, and 0.96 with the color-Doppler method. Coefficients of variation for interobserver variability

Table 1. Correlations of coronary artery diameter measurements between QCA and manual 2D, automated 2D, and color-Doppler TTE

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>LM</th>
<th>LAD Proximal</th>
<th>RCA</th>
</tr>
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<tbody>
<tr>
<td>Pearson correlation</td>
<td>0.83, P &lt; 0.01</td>
<td>0.58, P = 0.08</td>
<td>0.78, P &lt; 0.01</td>
<td>0.46, P = 0.02</td>
</tr>
<tr>
<td>Intraclass coefficient</td>
<td>0.82</td>
<td>0.52</td>
<td>0.77</td>
<td>0.46</td>
</tr>
<tr>
<td>Automated 2D TTE</td>
<td></td>
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<tr>
<td>Pearson correlation</td>
<td>0.82, P &lt; 0.01</td>
<td>0.33, P = 0.38</td>
<td>0.83, P &lt; 0.01</td>
<td>0.25, P = 0.30</td>
</tr>
<tr>
<td>Intraclass coefficient</td>
<td>0.74</td>
<td>0.37</td>
<td>0.76</td>
<td>0.10</td>
</tr>
<tr>
<td>Color-Doppler 2D TTE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson correlation</td>
<td>0.94, P &lt; 0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraclass coefficient</td>
<td>0.94</td>
<td></td>
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</tbody>
</table>

Table 2. Results of measurements of diameters of each coronary artery with QCA and manual 2D, automated 2D, and color-Doppler TTE

<table>
<thead>
<tr>
<th></th>
<th>LM</th>
<th>LAD Proximal</th>
<th>LAD Distal</th>
<th>LCX</th>
<th>RCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiography</td>
<td>4.1 ± 0.38 (n=11)</td>
<td>3.4 ± 0.46 (n=17)</td>
<td>1.9 ± 0.30 (n=3)</td>
<td>2.9 ± 0.58 (n=2)</td>
<td>3.6 ± 0.42 (n=22)</td>
</tr>
<tr>
<td>Manual 2D TTE</td>
<td>4.0 ± 0.39 (n=11)</td>
<td>3.6 ± 0.61 (n=17)</td>
<td>1.8 ± 0.11 (n=3)</td>
<td>2.8 ± 0.53 (n=2)</td>
<td>3.6 ± 0.30 (n=22)</td>
</tr>
<tr>
<td>Automated 2D TTE</td>
<td>4.2 ± 0.39 (n=10)</td>
<td>3.6 ± 0.67 (n=15)</td>
<td>2.2 ± 0.41 (n=3)</td>
<td>2.8 ± 0.47 (n=2)</td>
<td>3.8 ± 0.43 (n=21)</td>
</tr>
<tr>
<td>Color-Doppler TTE</td>
<td>4.2 (n=1)</td>
<td>3.4 ± 0.22 (n=3)</td>
<td>1.8 ± 0.32 (n=6)</td>
<td>3.4 ± 0.46 (n=3)</td>
<td></td>
</tr>
</tbody>
</table>

Values (in mm) are means ± SD. QCA measurements are from patients who were analyzed by TTE. LCX could not be measured by color-Doppler TTE in any patient.
were also low, namely, 5.4 ± 4.6%, 6.0 ± 4.9%, and 7.5 ± 8.8%, respectively. The mean epicardial nitroglycerin-induced vasodilatation was 7.4 ± 5.7%.

**DISCUSSION**

This study provides evidence that TTE can be used to measure diameters of the LM, LAD, and RCA in patients with angiographically healthy coronary arteries. Compared with QCA, TTE provides accurate measurements of diameters of these coronary arteries. Moreover, low intraobserver and interobserver variability suggest good reproducibility of TTE-derived diameter measurements.

The fact that certain parts of the coronary arteries can be visualized with TTE has been recognized for several years (32). 2D TTE has been used to study the LM (25, 32), the proximal LAD (21, 23, 31), as well as the middle and distal LAD (10, 12, 13, 16, 26). In previous studies, the measurements of distal LAD diameter by TTE and QCA provided highly similar results (13) and a good correlation was shown between measurements of middle LAD diameter by epicardial echocardiography and TTE (11). Moreover, moderate correlation in measurement of LM diameter by TTE and QCA was recently found (7). Our results extend the previous findings in that, in addition to the LM and the LAD, we were able to measure the diameter of the RCA in most study subjects. Moreover, we found a significant and good correlation between TTE and QCA in the LM, RCA, and proximal LAD. This provides evidence that 2D TTE is an accurate method for measuring diameters of these coronary arteries. It appeared that definition of coronary artery walls by the color-Doppler method increased the accuracy of diameter measurement. However, the intensity of the color-Doppler flow signal was usually weak and it was only possible to measure coronary diameter in a few patients by this approach. This was due to the fact that the coronary arteries were measured perpendicular to the ultrasound beam to achieve the best possible axial resolution.

There are several potential applications for our results. By knowing the anatomic diameter of the coronary artery together with the coronary flow velocity it would be possible to measure coronary flow volume by TTE; that is, coronary flow rate (ml/min) can be calculated as flow rate = π(D/2)^2 × HR × VTI × 1/cosθ, where D is coronary artery diameter (mm), HR is heart rate (min⁻¹), VTI is velocity time integral (mm), and θ is the angle between the ultrasound transducer and the artery (8, 20). Indeed, TTE has been used to assess LAD flow in children, and a difference between children with cardiomyopathy (20) or ventricular septal defect (34) and healthy children has been found. In another study, transesophageal Doppler echocardiography appeared to overestimate absolute coronary flow volume when compared with epicardial Doppler echocardiography and electromagnetic flow assessment in dogs (4).

Coronary flow reserve (CFR) is an important index of coronary artery function and myocardial blood flow. It is defined as a ratio of coronary blood flow during maximal pharmacologically induced vasodilatation to baseline flow. Decreased CFR values are associated with coronary artery disease, hypertension, diabetes mellitus, smoking, hypercholesterolemia, and hypertrophic cardiomyopathy (1). CFR can be measured noninvasively by PET (22, 24) and MRI (17).
CORONARY ARTERY DIAMETER AND ECHOCARDIOGRAPHY

Table 3. Intraobserver and interobserver variability of coronary artery diameter measurements by manual 2D, automated, and color-Doppler methods in 10 subjects

<table>
<thead>
<tr>
<th></th>
<th>CV (mean ± SD), %</th>
<th>Mean difference (range)</th>
<th>CV (mean ± SD), %</th>
<th>Mean difference (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual 2D</td>
<td>6.1±7.5</td>
<td>−0.2 (−0.8 to 0.4)</td>
<td>5.4±4.6*</td>
<td>0.0 (−0.4 to 0.3)*</td>
</tr>
<tr>
<td>Automated</td>
<td>3.3±2.9</td>
<td>−0.1 (−0.5 to 0.2)</td>
<td>6.0±4.9</td>
<td>0.0 (−0.7 to 0.7)</td>
</tr>
<tr>
<td>Color-Doppler</td>
<td>4.9±5.3</td>
<td>0.0 (−0.6 to 0.6)</td>
<td>7.5±8.8</td>
<td>0.1 (−0.7 to 0.8)</td>
</tr>
</tbody>
</table>

Coefficient of variation (CV) = SD/mean × 100. Mean difference is a mean of (measurement 1 − measurement 2). *30 Subjects.

However, these methods are expensive and scarcely available for clinical use. In addition, PET involves exposure to ionizing radiation. Thus there is a need for an inexpensive, safe, repeatable, and accurate method suitable for evaluation of CFR. Transthoracic Doppler echocardiography has been used to measure CFR in several studies (2, 3, 14, 15, 28). These studies, however, have measured coronary flow velocity alone. This may underestimate the actual CFR (1) because diameter of the coronary artery increases during pharmacological stimulation. It is likely that flow volume could provide more accurate estimates of CFR than coronary flow velocity alone. Assessment of coronary flow velocity was not included in our study protocol because artery diameters were measured perpendicularly to obtain the best axial resolution. However, when measuring coronary flow velocity the angle between flow and the ultrasound beam should be kept minimal. It remains to be studied whether both coronary artery diameter and flow can be accurately measured from some parts of the coronary artery tree.

Other potential applications for analysis of coronary artery diameter and structure by 2D TTE include direct detection of coronary stenosis and aneurysms (23, 25, 31, 32), assessment of thickening of the adventitia of the coronary artery wall as an index of atherosclerotic changes (10, 12, 21), assessment of impaired coronary artery reactivity to physiological stimuli (29), and localization of coronary artery stents (18).

Study limitations. Some limitations of our study should be pointed out. First, we were able to measure the LCX in only a few patients and correlation to QCA could not be studied because of the small number of observations. As LCX was visualized from the apical long-axis view it was far from the transducer, which may have resulted in poor image resolution. Second, the number of color-Doppler measurements was low in our study for the reasons discussed above. Third, it is likely that we measured the diameter of an artery from slightly different places by TTE and QCA, which may have reduced the correlation between these methods.

There are several factors, including axial and lateral resolution, geometric error, and the use of nitroglycerin, that may affect the measurements. Our phantom study (CIRS, model 40) indicated that axial resolution is <0.5 mm in a 25-mm depth when the ultrasound frequency is 3.5 MHz. In previous studies, axial resolution was even 0.25 mm at the depth of 50 mm when an 8-MHz transducer was used (12). By increasing the ultrasound frequency it would be possible to have better axial resolution, but at the expense of penetration depth of the ultrasound beam. Furthermore, if there is a sufficient difference in acoustic impedance, even small structures far below resolution limits produce an echo and can be detected (33). Although we could visualize both anatomic and color-Doppler images of almost all parts of the three coronary arteries, image quality was affected by inaccurate projection plane and false echoes. We chose only those images that unambiguously represented a longitudinal cross section of a coronary artery and its lumen lying as perpendicularly as possible to the ultrasound beam. Color-Doppler technique adjustments including color-Doppler gain and frequency were found too difficult to standardize.

Geometric error affected the QCA measurements. In QCA the three-dimensional anatomy of the human heart is displayed on a two-dimensional picture and all tissues lie on each other. Therefore, objects far from the calibration point may be in a different plane. Objects closer to the camera than the catheter plane seem to be bigger on the screen, and vice versa. Before QCA, patients were given sublingual nitroglycerin to prevent coronary artery spasms during the procedure. The effect of nitroglycerin on coronary artery diameter is vasodilatation. In previous studies, the degree of vasodilatation in angiographically normal left coronary arteries was 3–12% after sublingual nitroglycerin (5, 6, 19, 27). We assessed the nitroglycerin-mediated vasodilatation in seven healthy volunteers by TTE. In this study, the mean epicardial vasodilatation was 7.4 ± 5.7%. Thus nitroglycerin is likely to have a minor effect on our measurements.

We conclude that TTE is a feasible and accurate method in the evaluation of coronary artery diameter in a majority of patients with healthy coronary arteries. In cases with optimal image quality, TTE-derived anatomic coronary artery diameter measurements correlated well with corresponding values from QCA. However, the measurements were made at rest. More studies are needed to evaluate the change of coronary artery diameter after drug-induced maximal vasodilatation to measure CFR accurately. Previously, TTE has been used in the evaluation of immediate effects of intravenous medical therapy on coronary flow velocity (30). In the future, there is a possibility for more detailed data of coronary flow volume. Precise non-invasive CFR measurements would be useful in interventional studies and in the detection of stenosis of epicardial arteries or dysfunction of the microcirculation.

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GRANTS

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