Original Studies

Comparison Between Three-Dimensional Angiographic Reconstruction and Intravascular Ultrasound: Imaging of the Left Main Coronary Artery

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Objectives: The purpose of this study was to evaluate the left main (LM) coronary artery anatomy using three-dimensional (3D) quantitative coronary angiography (QCA) software as compared to intravascular ultrasound (IVUS). Background: Percutaneous intervention of the LM coronary artery is becoming more common in selected patients with LM coronary artery disease (CAD). Quantification of LM CAD by conventional angiography can be difficult. IVUS is considered the gold standard to evaluate LM anatomy and severity of CAD but entails additional steps, catheters, and expertise. Our objective was to compare a novel quantitative angiographic analysis system with IVUS for LM anatomy. Methods: Fifty five patients underwent both coronary angiography and IVUS of the LM. LM measurements were analyzed with 3D QCA (IC-PRO, Paieon, Israel) software using IVUS as the reference standard. The measurements included proximal, middle, distal minimal luminal diameter (MLD) and area. Additionally, lesion MLD, minimal luminal area were recorded by both systems. Bland–Altman plots were used to investigate agreement between the two imaging systems. Results: Of the 55 patients in our cohort, average age was 66 ± 11 years (25% female). By Bland-Altman analysis there was very good agreement between 3D QCA and IVUS for measures of MLD and minimal lumen area (MLA). However, there was poor concordance in the estimation of plaque burden between the two methods. Conclusions: Our data demonstrate that 3D QCA software has fair agreement when compared with IVUS for imaging of LM MLD and MLA. These results suggest that 3D QCA could potentially be helpful to guide intervention of the LM. © 2012 Wiley Periodicals, Inc.

Key words: intravascular ultrasound; three-dimensional quantitative coronary angiography (3D QCA); percutaneous coronary intervention; left main coronary artery

INTRODUCTION

Historically left main (LM) coronary artery disease (CAD) has been treated primarily with coronary artery bypass surgery. Over the last decade, evidence has accumulated which supports percutaneous coronary intervention (PCI) for treatment of LM CAD in selected patients [1–5]. Because of accumulating favorable data and experience, PCI is more commonly becoming a therapeutic option in selected patients with LM CAD. However, PCI of the LM may be challenging and requires optimal imaging to allow accurate assessment of LM dimensions and severity of CAD.

A variety of imaging modalities currently exist to evaluate the coronary arteries including the LM.

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Conventional invasive two-dimensional (2D) coronary angiography remains the most commonly used diagnostic modality for CAD assessment but it has been shown to be suboptimal for the evaluation of LM lesions [6–8]. Intravascular ultrasound (IVUS) has proven to be an accurate method to evaluate LM anatomy and severity of CAD but has limitations such as the inability to evaluate the 3D shape of the LM including its bifurcation angle [9–13]. 3D quantitative coronary angiography (3D QCA) is a novel, adjunctive analytical tool that has been developed to assist with planning and guidance of PCI and importantly does not require additional invasive catheterization beyond conventional 2D angiography. This relatively new imaging technique utilizes data derived from different views during 2D angiography and provides measurements of luminal diameter and area [14–18]. More recently, we and others have shown that 3D QCA is useful in the assessment of the LM and especially its bifurcation angle before and after PCI [18,19].

The goal of this study was to determine whether cross sectional area and minimal luminal diameter (MLD) measurements of the LM obtained using 3D QCA correlate with those obtained with IVUS (used as the reference standard).

METHODS

Patient Selection

This was a single center retrospective study. The study cohort consisted of consecutive patients who underwent both coronary angiography and IVUS of the LM. Exclusion criteria were: age <18 years, lack of authorization for medical records research, and inadequate image quality for analysis. Baseline clinical and demographic characteristics were recorded. The study was approved by the Mayo Clinic Institutional Review Board.

Analysis Method

3D reconstruction was performed off line by an experienced observer, blinded to individual patient data and clinical outcome, with an advanced version of a validated program for 3D QCA (IC-PRO, Paieon Medical, Rosh Ha’ayin, Israel) [15]. The sequence of a single 3D reconstruction has been thoroughly described elsewhere [20–22] and involves a catheter calibration phase, and an analysis of two different views (with at least 30° angulation difference). The software algorithm rendered a 3D image as well as quantitative information. An example of the model created by the software is shown in Fig. 1 along with cross-sectional and longitudinal IVUS images. IVUS analysis was performed according to the methods described in the consensus document on IVUS studies by the American College of Cardiology [23]. The quantitative and qualitative analyses were conducted off-line by a trained investigator unaware of the individual patient data or the treatment of the patient, using the recorded CDs. This investigator was also blinded to the 3D QCA measurements.

RESULTS

Patients

The study included 55 patients. Mean age was 66 ± 11 years, and 25% were female. Baseline characteristics are presented in Table I.
Comparison of Paieon 3D QCA Measurements with IVUS

The measurements obtained by 3D QCA and IVUS are shown in Table II. Overall, 3D QCA MLD measurements seemed to be well calibrated to IVUS as the mean difference between the two was generally small. The range of difference between the two was generally 1.5-mm under to 2.0-mm over for 3D QCA vs. IVUS.

For minimal lumen area (MLA), 3D QCA and IVUS were again well calibrated. The range of differences was approximately 10 mm$^2$ under to 10 mm$^2$ over for 3D QCA versus IVUS for the proximal, middle, and distal measures, but was only 6 mm$^2$ under to 5 mm$^2$ over for the lesion measure. However, for plaque burden the 3D QCA measure was typically much smaller than the IVUS measure (median difference of $34\%$).

Bland-Altman plots for MLD are shown in Fig. 2 and for MLA in Fig. 3. These generally show very good agreement between the two imaging systems. Delta values for MLD were $0.11 \pm 0.61$ mm (proximal LM), $0.22 \pm 0.76$ mm (mid LM), $0.04 \pm 0.60$ mm (distal LM), and $-0.06 \pm 0.53$ mm (lesion site) and for MLA, $-0.89 \pm 3.84$ mm$^2$ (proximal LM), $+0.63 \pm 4.25$ mm$^2$ (mid LM), $-0.01 \pm 3.24$ mm$^2$ (distal LM), and $-0.04 \pm 2.59$ mm$^2$ (lesion site). In contrast, there was poor agreement between the two systems for plaque burden (delta: $-33.50 \pm 16.45$ mm$^2$, Fig. 4). These plots did not reveal any patterns

### TABLE II. Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (N = 55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td>66.2 ± 11.2</td>
</tr>
<tr>
<td>Female, No. (%)</td>
<td>14 (25%)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>86.4 ± 16.1</td>
</tr>
<tr>
<td>Body surface area</td>
<td>2.0 ± 0.2</td>
</tr>
<tr>
<td>Hypertension, No. (%)</td>
<td>43 (78%)</td>
</tr>
<tr>
<td>Hyperlipidemia, No. (%)</td>
<td>49 (89%)</td>
</tr>
<tr>
<td>Diabetes mellitus, No. (%)</td>
<td>16 (29%)</td>
</tr>
<tr>
<td>Smoker, No. (%)</td>
<td>34 (62%)</td>
</tr>
<tr>
<td>Family Hx of CAD, No. (%)</td>
<td>20 (36%)</td>
</tr>
<tr>
<td>PVD, No. (%)</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>Known CAD, No. (%)</td>
<td>48 (87%)</td>
</tr>
<tr>
<td>Previous PCI, No. (%)</td>
<td>12 (22%)</td>
</tr>
<tr>
<td>Previous CABG, No. (%)</td>
<td>7 (13%)</td>
</tr>
</tbody>
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PVD = peripheral vascular disease; CAD = coronary artery disease; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft.

### TABLE II. Difference Between 3D QCA and IVUS Measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Paieon Median (Min, Max)</th>
<th>IVUS Median (Min, Max)</th>
<th>Average Median (Min, Max)</th>
<th>Paieon-IVUS Median (Min, Max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLD Proximal (mm)</td>
<td>3.3 (2.08, 5.93)</td>
<td>3.4 (2.30, 5.60)</td>
<td>3.3 (2.34, 5.77)</td>
<td>$-0.2 (-1.52, 1.69)$</td>
</tr>
<tr>
<td>MLD Middle (mm)</td>
<td>3.4 (1.83, 6.74)</td>
<td>3.3 (2.00, 4.70)</td>
<td>3.3 (2.07, 5.72)</td>
<td>$0.1 (-1.52, 2.04)$</td>
</tr>
<tr>
<td>MLD Distal (mm)</td>
<td>2.9 (1.76, 5.10)</td>
<td>2.8 (1.80, 5.10)</td>
<td>2.8 (1.83, 5.10)</td>
<td>$0.0 (-1.45, 1.90)$</td>
</tr>
<tr>
<td>MLD Lesion (mm)</td>
<td>2.6 (0.92, 3.73)</td>
<td>2.5 (1.60, 3.60)</td>
<td>2.5 (1.62, 3.62)</td>
<td>$0.0 (-1.59, 0.89)$</td>
</tr>
<tr>
<td>MLA Proximal (mm$^2$)</td>
<td>9.6 (4.20, 28.68)</td>
<td>10.9 (4.70, 30.30)</td>
<td>10.3 (4.81, 29.49)</td>
<td>$-1.3 (-7.91, 12.02)$</td>
</tr>
<tr>
<td>MLA Middle (mm$^2$)</td>
<td>10.2 (3.63, 36.42)</td>
<td>9.8 (3.60, 24.80)</td>
<td>9.9 (4.29, 30.61)</td>
<td>$0.3 (-8.46, 13.06)$</td>
</tr>
<tr>
<td>MLA Distal (mm$^2$)</td>
<td>7.9 (3.49, 24.14)</td>
<td>7.3 (3.30, 25.10)</td>
<td>7.5 (3.99, 24.62)</td>
<td>$0.3 (-12.44, 6.39)$</td>
</tr>
<tr>
<td>MLA Lesion (mm$^2$)</td>
<td>6.7 (1.11, 24.24)</td>
<td>6.1 (2.50, 15.00)</td>
<td>6.0 (3.11, 12.83)</td>
<td>$0.1 (-5.94, 5.44)$</td>
</tr>
<tr>
<td>Plaque Burden (%)</td>
<td>28 (12.0, 74.0)</td>
<td>65.2 (32.6, 85.5)</td>
<td>47.2 (31.3, 77.0)</td>
<td>$-33.9 (-63.9, 5.20)$</td>
</tr>
</tbody>
</table>

MLD = minimal luminal diameter; MLA = minimal luminal area.
of systemic differences, such as greater variability at larger values.

As 3D QCA is a 3D reconstruction derived from two different views, its accuracy may be theoretically compromised when the views are non-orthogonal, especially for the assessment of highly eccentric lesions. To investigate this, we identified the angle between the two views used for each 3D reconstruction as well as the plaque eccentricity index in patients with a LM lesion. We did not find that intermodality agreement (represented by the difference between 3D QCA and IVUS measurements) was affected by either the angulation or eccentricity index (data not shown).

**DISCUSSION**

The major findings of the current study are: (1) there is fair agreement for measurements of MLD as well as MLA using 3D QCA software as compared to IVUS; (2) there was poor concordance in the estimation of plaque burden between the two modalities. The current study supports the potential role for 3D QCA in replacing IVUS for measurements of size and severity of CAD for guided PCI of LM disease.

LM CAD is a significant angiographic and clinical finding as the LM provides blood flow to the majority of the left ventricular myocardium. Thus, patients with obstructive LM CAD are at high risk for cardiovascular events resulting in significant morbidity and mortality [25]. Some of the debate surrounding treatment of LM CAD revolves around the unreliability of conventional 2D angiography in obtaining an accurate diagnosis of significant LM narrowing. Previous studies have shown that there is a high percentage of patients with angiographically normal LM coronary arteries who are found to have disease by IVUS and that there is significant interobserver and intraobserver variability in the assessment of LM lesion severity by conventional 2D angiography [26–30]. In addition, data have shown that the presence of equivocal stenosis of the LM demonstrated by conventional 2D angiography may not allow for appropriate decision making about the need for revascularization and often results in underestimation of the functional significance of the stenosis [31].

IVUS has proven to be a useful adjunct in the evaluation and diagnosis of LM CAD and its role is well established. Fractional flow reserve (FFR) has also been established as an important component in the evaluation of LM CAD and has been shown to be a strong predictor of survival and event rates in patients with indeterminate LM disease [32–35]. The use of IVUS and FFR comes with an increased risk to the patient and adds additional costs and time to the interventional procedure. Because of these factors, alternative imaging strategies that are less invasive and less expensive but similarly accurate are needed to
complement what is currently available for the diagnosis and treatment of patients with LM CAD.

3D QCA uses images obtained from two views taken during conventional 2D angiography to calculate MLD and MLA, which previously needed to be determined by IVUS, especially in lesions of intermediate severity. The very good agreement found in our study between IVUS and 3D QCA is promising and indicates that measurements of MLA and MLD may be obtainable by conventional 2D angiography and processing by 3D QCA using a unique algorithm. Moreover, we also found that even in the setting of non-orthogonal angiographic views and eccentric lesions, 3D QCA performed comparably with IVUS, indicating that the use of two different views separated by at least 30° is sufficient, to overcome most of the foreshortening inherent in single views from 2D angiography. If replicated in larger scale trials, 3D QCA may then allow the interventional cardiologist to avoid a more invasive, time consuming, and costly method (i.e., IVUS) for the accurate assessment of LM MLD and MLA.

The poor agreement between 3D QCA and IVUS for lesion size is not surprising as IVUS can clearly demonstrate the vessel lumen, along with plaque characteristics and burden. In contrast, 3D QCA utilizes a dedicated algorithm to anticipate the “funnel shape” nature of the vessel in stenotic segments. Moreover, 3D QCA is a product of the 2D angiographic views. It is reasonable to expect correlation in measurement of the vessel lumen which is shown in clarity during 3D angiography. However, 2D angiography is primarily a “lumenographic” study and has inherent inferiority in the assessment of the vessel wall which is required for plaque burden calculations.

The most significant clinical implications from this study are that we have demonstrated for the first time the reliability of a new noninvasive method of determining the severity of LM lesions in terms of MLA and MLD. While 3D QCA is not a physiologic method, its benefits come from the fact that it is noninvasive and can be calculated online during the interventional procedure without the time and cost of additional catheters. Having a secure understanding of the true degree of LM stenosis is paramount to the effective treatment of LM CAD. Our results are therefore important and may have a significant impact on clinical practice if validated in a larger scale study.

Limitations

This study has limitations inherent to a retrospective cohort study. The small size of the study group may limit the generalizability and reliability of the findings. Also, it is important to point out that three out of 55 patients had a large difference in luminal-CSA which significantly overestimated the real lumen size. This will need to be addressed by future studies and possible refinements to the software.

CONCLUSION

Our data demonstrate that 3D QCA software has fair agreement when compared with IVUS for the imaging of LM MLD and MLA. These results suggest that 3D QCA could potentially be helpful to guide intervention of the LM without the additional risks or cost associated with intravascular imaging.

REFERENCES


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