

Evaluating Left Main Severity

Making the case for IVUS as a valuable imaging modality in addition to angiography.

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Although angiography continues to be the gold standard for the assessment of coronary artery stenoses, it has significant intraobserver and interobserver variability. When facing an intermediate and/or ambiguous left main disease, detailed anatomic information may be obtained with intravascular ultrasound (IVUS), as well as physiologic assessment with fractional flow reserve (FFR), providing useful additional and complementary information to angiographic images. In this article, we present a case in which the IVUS assessment was a valuable imaging tool for making decisions, and we further discuss some available data in the context of this topic.

CASE PRESENTATION

An 82-year-old woman with hypertension and moderate chronic obstructive pulmonary disease was admitted because of unstable angina. Coronary angiography revealed a 30% distal left main, a 45% ostial left anterior descending (LAD) artery, a 50% mid LAD, a 70% proximal right coronary artery (RCA), a 90% mid RCA, and 70% posterior descending artery (PDA) stenoses. To further evaluate the LAD lesion and plan the revascularization strategy (percutaneous coronary intervention [PCI] vs coronary artery bypass grafting), FFR assessment was performed. Upon a result of 0.81, PCI of the RCA and PDA with bare-metal stents was performed. However, 6 months later, the patient was readmitted for a non-ST elevation myocardial infarction. Coronary angiography revealed patent RCA stents, with doubtful “ring-like” images at the distal left main-ostial LAD portion (Figure 1A and B, arrows). IVUS was performed to better assess this lesion. The IVUS

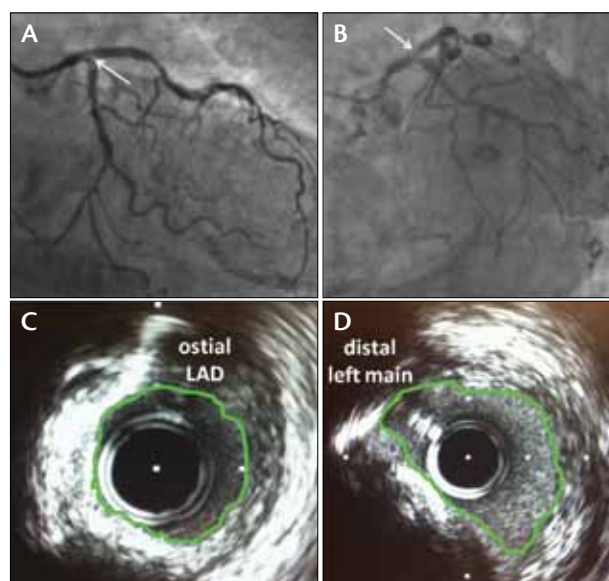


Figure 1. What you see with angiography is not what you get with intravascular imaging. Angiographic pictures show a doubtful “ring-like” image (arrow) located at the distal left main and ostial left descending artery (LAD): right oblique caudal view (A); left oblique caudal view (B). Intravascular ultrasound image showing an eccentric, severely calcified plaque involving the ostial LAD, with a minimal lumen area of 3.82 cm² (C), and the distal left main coronary artery with a minimal lumen area of 5.94 cm² (D). The green line area highlights the minimal lumen area.

assessment showed an eccentric and severely calcified plaque, involving the distal left main up to the ostial LAD and exhibiting a minimal lumen area (MLA) of

3.82 cm² and 5.94 cm² for the ostial LAD and the distal left main coronary artery, respectively (Figure 1C and D). Therefore, unprotected left main-LAD PCI was successfully performed.

DISCUSSION

Angiographic and IVUS Correlation

There is a large body of evidence showing the lack of correlation between angiographic and IVUS measurements. Hermiller and colleagues¹ showed by IVUS that as many as 89% of patients with angiographically normal left main had disease; they also reported the absence of a correlation between IVUS and quantitative coronary analysis (QCA) lumen dimensions in patients with evident angiographic left main stenosis. Abizaid et al² also showed a poor correlation ($r = 0.36$; $P < .001$) in minimal lumen diameter (MLD) measurements by IVUS and QCA, the latter overestimating the degree of left main disease in some patients. Recently, the findings reported by de la Torre Hernandez and colleagues³ further support the lack of correlation between angiography and IVUS. Patients exhibiting an MLA < 9 mm² showed a mean angiographic stenosis of $35\% \pm 10\%$, whereas those exhibiting an MLA between 6 to 9 mm² showed a mean angiographic stenosis of $37\% \pm 8\%$ ($P = .1$).³ In addition, 17% of the patients showed quantitative stenosis of 30%, and 33% of this subgroup of patients had an MLA < 6 mm².³ In 43% of the patients with angiographic stenosis over 50%, the MLA was > 6 mm².³ Therefore, this work showed a wide overlap and scatter of angiographic stenoses and MLD relative to an MLA cutoff of 6 mm², correlation coefficients for angiographic stenosis and MLA ($r = -0.18$; $P = .0015$), and for angiographic MLD and MLA ($r = 0.34$; $P = .0001$).³

Sano and colleagues⁴ added information showing that the correlation between angiography and IVUS may also vary depending on left main location lesion. Whereas distal lesions showed better correlations, lesions located at the ostium showed worse correlation. This issue may be related to the fact that ostial left main lesions had the greatest interobserver discrepancy when assessed by coronary angiography.⁵

Anatomical Information Provided by IVUS

IVUS can accurately assess and therefore classify left main disease based on plaque conformation characteristics and distribution along the left main shaft, up to its bifurcation.^{4,6,7} Maehara et al⁶ reported that nonostial lesions are more calcified than ostial lesions. Sano and colleagues⁴ have shown that distal lesions were calcified in approximately 50% of the patients and had the largest plaque burden, whereas ostial lesions were mostly fibrotic

(75% of the patients) with the smallest plaque burden. Oviedo et al⁷ showed that contrary to the well-known angiographic classifications, IVUS showed that left main bifurcation disease is rarely focal and that both the LAD and left circumflex (LCX) sides of the carina are usually spared. Moreover, the investigators demonstrated the presence of a continuous plaque involvement from the distal left main into the proximal LAD in 90% of the cases, from the left main into the LCX artery in 66% of the cases, and from the left main into both LAD and LCX arteries in 62% of the evaluated patients.⁷ In addition, plaque distribution was not influenced by the LAD/LCX angiographic angle, lesion severity, left main length, or remodeling.⁷

IVUS Assessment and the Impact on Long-Term Follow-Up

Abizaid et al² studied 122 patients with ambiguous left main angiograms. As mentioned, this study showed discrepancies between angiographic and IVUS measurements. Although no differences were found in MLD assessed by QCA (2.32 ± 0.83 vs 2.00 ± 0.72 ; $P = .11$), the mean MLA among those who have had any event was 6.8 ± 4.4 mm² versus 10.0 ± 5.3 mm² among those who did not have events ($P = .0127$).² The presence of diabetes, any untreated coronary stenosis $> 50\%$, and an IVUS-driven MLD were found to be independent predictors of major adverse cardiac event at 1-year follow-up; of note, the plaque burden was not associated with a worse outcome. According to these results, Ricciardi and colleagues⁸ showed that despite being angiographically silent, left main disease detected by IVUS (IVUS MLA assessment), was found to be a predictor of late cardiac events (hazard ratio, 0.59; $P = .015$). More recently, Okabe and colleagues⁹ (same research group as Abizaid) reported clinical outcomes in 100 patients with moderate or ambiguous left main disease who were followed for a period of 5 years. The mean MLA among those who have had any event was 7.2 ± 2.2 mm² versus 10.6 ± 3.4 mm² among those who did not have events ($P = .006$).⁹ It is interesting to point out that, despite the fact that the patients who had events were more than 10 years older, and that IVUS plaque burden was not associated with worse outcome at 1-year follow-up, the plaque burden at the minimum luminal area site remained the only predictor of worse outcomes at 5-year follow-up (odds ratio, 1.34; $P = .025$).⁹

IVUS-Guided Treatment for Angiographically Intermediate and/or Ambiguous Left Main Stenosis

Fassa and coworkers¹⁰ performed IVUS on 121 patients with angiographically normal left main coro-

nary arteries to determine the lower range of normal MLA (defined as the mean -2 standard deviations, estimated at 7.5 mm^2). Afterward, the authors studied 214 patients with intermediate left main stenoses, and a deferral revascularization strategy was proposed to those patients with an $\text{MLA} \geq 7.5 \text{ mm}^2$, whereas patients having an $\text{MLA} < 7.5 \text{ mm}^2$ underwent revascularization. At a mean time of 3.3 ± 2.0 years of follow-up, no significant differences were found in major adverse cardiac events (target vessel revascularization, acute myocardial infarction, and death) between patients with an $\text{MLA} < 7.5 \text{ mm}^2$ who underwent revascularization and those with an $\text{MLA} \geq 7.5 \text{ mm}^2$ who were deferred from revascularization ($P = .28$), demonstrating that an IVUS-guided treatment strategy is safe. More recently, de la Torre and colleagues³ prospectively evaluated 354 patients with intermediate left main stenoses. Of the 186 patients with an $\text{MLA} \geq 6 \text{ mm}^2$, 179 (96.2%) did not receive any revascularization (deferred group). Of the 168 patients with an $\text{MLA} < 6 \text{ mm}^2$, 152 (90.5%) underwent left main revascularization (revascularized group).³ A total of 351 patients (99%) completed 2-year follow-up. Clinical outcomes from both groups (deferred and revascularized) showed similar results; cardiac death-free survival was 97.7% in the deferred group versus 94.5% in the revascularized group ($P = .5$), and survival free from cardiac death, myocardial infarction, and any revascularization was 87.3% versus 80.6%, respectively ($P = .3$).³ The investigators concluded that an IVUS $\text{MLA} > 6 \text{ mm}^2$ seems to be a safe value for deferring revascularization of ambiguous left main disease.

IVUS or FFR for the Assessment of Intermediate, Ambiguous Left Main Disease

The frequent concomitant presence of lesions in the LAD (approximately 90%), LCX, or both,⁷ may interfere with the accurate evaluation of the left main stenosis/severity by FFR. In the previously presented case, the patient had a 50% mid LAD lesion that was initially evaluated by a negative (0.81) FFR. One advantage of IVUS over the pressure wire is that this tool can help evaluate for the diagnosis and treatment of left main disease. It should be noted, however, that a single IVUS MLA cutoff is limited to the fact that the hemodynamic effects of a lesion not only depend on MLA , but also on numerous other factors, including lesion length, eccentricity, entrance and exit angles and forces, reference vessel dimensions, the amount of myocardium subtended by the lesion, as well as the presence of serial lesions in the assessment path.¹¹ Discrepancies often exist between IVUS MLA of 4.5 to 6 mm^2 and FFR

findings;^{12,13} physiological assessment with FFR may add precious additional information in ambiguous IVUS findings.

CONCLUSIONS

Based on the available data, in the presence of angiographically ambiguous left main disease, an IVUS $\text{MLA} < 6 \text{ mm}^2$ identifies patients who are likely to benefit from revascularization (coronary bypass or PCI). In patients exhibiting an IVUS $\text{MLA} > 6 \text{ mm}^2$ (6 to 7.5 mm^2), the results must be evaluated within the clinical context and/or be further assessed with a physiological test on the table (FFR), but revascularization can be deferred in most of these cases. For patients presenting with an IVUS $\text{MLA} > 7.5 \text{ mm}^2$, revascularization should definitely be deferred. ■

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