Validation of Intravascular Ultrasound–Derived Parameters With Fractional Flow Reserve for Assessment of Coronary Stenosis Severity

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Background—We assessed optimal intravascular ultrasound (IVUS) criteria for predicting functional significance of intermediate coronary lesions.

Methods and Results—Overall, 201 patients with 236 coronary lesions underwent IVUS and invasive physiological assessment before intervention. Fractional flow reserve (FFR) was measured at maximal hyperemia induced by intravenous adenosine infusion. FFR <0.80 at maximum hyperemia was seen in 49 (21%) of the overall 236 lesions. The independent determinants of FFR were minimal lumen area (MLA; β=0.020; 95% confidence interval [CI], 0.008 to 0.031; P=0.032), plaque burden (β=−0.002; 95% CI, −0.003 to 0.001; P=0.001), lesion length with a lumen area <3.0 mm^2 (β=−0.003; 95% CI, −0.005 to −0.001; P=0.005), and left anterior descending artery location (β=−0.035; 95% CI, −0.055 to −0.016; P=0.001). The best cutoff value (with a maximal accuracy) of the MLA to predict FFR <0.80 was <2.4 mm^2, with a diagnostic accuracy of 68% (90% sensitivity, 60% specificity, and area under the curve=0.800; 95% CI, 0.742 to 0.848; P<0.001). The cutoff value of plaque burden to predict FFR <0.80 was ≥79% (69% sensitivity, 72% specificity, and area under the curve=0.756; 95% CI, 0.696 to 0.810; P<0.001). The cutoff value of lesion length with a lumen area <3.0 mm^2 was 3.1 mm (84%sensitivity, 63%specificity, and area under the curve=0.765; 95% CI, 0.706 to 0.818; P<0.001). Among 117 lesions with an MLA ≥2.4 mm^2, 112 (96%) had an FFR ≥0.80,; and all but 1 showed FFR ≥0.75. Conversely, 44 (37%) lesions with an MLA <2.4 mm^2 had an FFR <0.80.

Conclusions—IVUS-derived MLA ≥2.4 mm^2 may be useful to exclude FFR <0.80, but poor specificity limits its value for physiological assessment of lesions with MLA <2.4 mm^2. Thus, FFR or stress tests may be necessary to accurately identify ischemia-inducible intermediate stenoses. **(*Circ Cardiovasc Interv*. 2011;4:65-71.)**

Key Words: intravascular ultrasound ■ fractional flow reserve

Although percutaneous coronary intervention (PCI) for ischemia-inducing coronary stenosis can improve clinical outcome, medical therapy alone may be preferable for lesions without inducible ischemia.[1–5] Fractional flow reserve (FFR) <0.80 identifies ischemia-inducing stenoses with an accuracy of >90%.[6–8] Recent studies have suggested that FFR-guided PCI is associated with reduced major adverse cardiac events in patients with multivessel coronary artery disease.[9–11] Although FFR is the standard tool for physiological assessment, there have been attempts to find intravascular ultrasound (IVUS) measurements, especially of the minimum lumen area (MLA), corresponding to the functional significance of a stenosis and to integrate both morphological and physiological data.[12–15] Nevertheless, the accuracy of IVUS criteria to predict an abnormal FFR remains debatable.[16,17] The aims of this study are (1) to assess the optimal IVUS criteria for predicting FFR in 236 unselected intermediate coronary lesions that underwent functional assessment to decide the treatment strategy and (2) if possible, to devise an algorithm that would accurately relate IVUS measurements to an abnormal FFR.

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Methods

Study Population

Between July 2009 and May 2010, 201 consecutive patients with 236 coronary lesions underwent IVUS and invasive physiological assess-

Received July 16, 2010; accepted November 24, 2010.

From the Department of Cardiology (S.-J.K., J.-Y.L., J.-M.A., W.-J.K., D.-W.P., S.-W.L., Y.-H.K., C.W.L., S.-W.P., S.-J.P.) and the Department of Biostatistics (S.-C.Y.), University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea; and the Cardiovascular Research Foundation (G.S.M.), New York, NY.

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Circ Cardiovasc Interv **is available at http://circinterventions.ahajournals.org** **DOI: 10.1161/CIRCINTERVENTIONS.110.959148**

ment preintervention; all 201 patients were included in the current analysis. All patients were 35 to 85 years of age and had at least 1 target vessel with a mild to intermediate de novo lesion (30% to 75% of diameter stenosis on visual estimation). Exclusion criteria were multiple stenoses (>30% of diameter stenosis on visual estimation) within a single target vessel, bypass graft lesions, significant left main coronary disease, side branch lesions, in-stent restenosis, previous PCI at the target vessel, culprit vessels in the setting of a myocardial infarction, and thrombi-containing lesions. This study was approved by the institutional review board, and all patients provided written informed consent.

Angiographic Analysis

Qualitative and angiographic analysis was done by standard techniques with automated edge-detection algorithms (CASS-5, Pie-Medical, Maastricht, Netherlands) in the angiographic analysis center of the CardioVascular Research Foundation, Seoul, Korea.

FFR Measurement

"Equalizing" was performed with the guide wire sensor positioned at the guiding catheter tip. Then the 0.014-inch pressure guide wire (Radi, St Jude Medical, Uppsala, Sweden) was advanced distal to the stenosis. FFR was measured at maximal hyperemia induced by intravenous adenosine infusion, administered at 140 μg/kg/min through a central vein. Hyperemic pressure pull-back recordings were performed as described previously.[5,6] The stenosis was considered functionally significant when the FFR was <0.80.

IVUS Imaging and Analysis

After FFR assessment, IVUS imaging was performed after intracoronary administration of 0.2 mg nitroglycerin using motorized transducer pullback (0.5 mm/s) and a commercial scanner (Boston Scientific/SCIMED, Minneapolis, MN) consisting of a rotating 40-MHz transducer within a 3.2F imaging sheath. Using computerized plannimetry (EchoPlaque 3.0, Indec Systems, MountainView, CA), off-line quantitative IVUS analysis was performed as previously described[11,12] in a core laboratory at the Asan Medical Center. The proximal and distal reference segments were selected within 5 mm proximal and distal to the lesion. Averaged proximal and distal reference external elastic membrane (EEM) and reference lumen areas and the mean reference lumen diameter were obtained. At the site of the smallest lumen, MLA and EEM area were measured. Plaque burden (PB) at the MLA site was calculated as (EEM area−lumen area)/EEM area×100 (%). Percent of area stenosis was also calculated as (reference lumen area−MLA)/reference lumen area×100 (%). Lesion length was measured using the motorized pullback device.

Statistical Analysis

All statistical analyses were performed using SAS release 9.1 (SAS Institute Inc, Cary, NC) or SPSS (version 10.0, SPSS Inc, Chicago, IL). Data were analyzed on a per-patient and per-lesion basis for the corresponding calculations. All values are expressed as mean±1 standard deviation (continuous variables) or as counts and percentages (categorical variables). For the per-patient data, continuous variables were compared by use of the unpaired *t* test or nonparametric Mann-Whitney test; categorical variables were compared with the χ^2 statistics or Fisher exact test. For the per-lesion data, a logistic generalized estimated equation model with robust standard errors that accounted for the clustering between lesions in same subject were created. To ascertain independent predictors of FFR as continuous and binary variable (FFR <0.8), linear mixed model and multivariable logistic generalized estimated equation model with robust standard errors were used, respectively.

To see the variability of the IVUS measurements and FFR at maximal hyperemia, intraobserver and interobserver coefficients of variation were calculated in 30 patients with 30 lesions. Receiver-operating curves (ROCs) were analyzed to assess the best cutoff values of IVUS parameters to determine FFR <0.80 with a maximal accuracy, using MedCalc (MedCalc Software, Mariakerke, Belgium). The optimal cutoff was calculated by using Youden index. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with 95% confidence intervals (CI) were obtained. Multivariable logistic regression analysis was also performed to the independent determinants to predict FFR <0.8. A probability value <0.05 was considered statistically significant.

Table 1. Baseline Clinical Characteristics in 201 Patients

	FFR <0.80 (n=39)	FFR ≥0.80 (n=162)	Total (n=201)
Age, y	60±11	62±9	61±9
Male	31 (80%)	113 (70%)	144 (72%)
Ejection fraction, %	62±6	61±6	61±6
Diabetes, n (%)	15 (39%)	46 (28%)	61 (30%)
Hypertension, n (%)	22 (56%)	101 (62%)	123 (61%)
Smoking, n (%)	25 (64%)	74 (45%)*	99 (49%)
Hyperlipidemia, n (%)	26 (67%)	110 (68%)	136 (68%)
Previous PCI, n (%)	6 (15%)	24 (15%)	30 (15%)
Renal failure, n (%)	0 (0%)	3 (2%)	3 (2%)
Clinical manifestation			
Stable angina, n (%)	33 (85%)	112 (69%)	145 (72%)
Unstable angina, n (%)	5 (13%)	35 (22%)	40 (20%)
Non–ST-elevation MI, n (%)	1 (2%)	15 (9%)	16 (8%)

MI indicates myocardial infarction.
*P=0.029 versus lesions with FFR <0.8.

Results

Baseline Characteristics

The baseline clinical characteristics in 201 patients with 236 coronary lesions are summarized in Table 1. FFR <0.80 at maximum hyperemia was seen in 49 (21%) lesions (Table 2). There was no significant difference in FFR between acute coronary syndrome versus non–acute coronary syndrome presentation (0.86±0.07 versus 0.84±0.09, P=0.344) or patients with diabetes mellitus (DM) versus without DM (0.85±0.08 versus 0.85±0.09, P=0.697). FFR in 157 left anterior descending artery (LAD) lesions was significantly lower compared with 79 non-LAD lesions (0.83±0.09 versus 0.88±0.07, P<0.001).

IVUS Determinants for FFR

FFR at maximum hyperemia significantly correlated with IVUS-measured MLA (r=0.507, P<0.001), plaque burden (r=−0.387, P<0.001), area stenosis (r=−0.388, P<0.001), length of the lesion with a lumen area <3.0 mm^2 (r=−0.472, P<0.001), and length of the lesion with a lumen area <4.0 mm^2 (r=−0.453, P<0.001, Figure 1). FFR showed a weak correlation with the reference lumen area (r=0.211, P=0.002).

Multivariable linear and logistic regression analysis included age, male sex, DM, reference lumen diameter, LAD lesion location, MLA, PB, area stenosis, and lesion length with a lumen area <3.0 mm^2. In the overall cohort of 236 lesions, the independent determinants of FFR as a continuous variable were MLA (β=0.020; 95% CI, 0.008 to 0.031; P=0.032), PB (β=−0.002; 95% CI, −0.003 to 0.001;

Table 2. FFR and IVUS Findings in 236 Intermediate Lesions

	Total (n=236)	FFR <0.80 (n=49)	FFR ≥0.80 (n=187)
Vessel			
LAD artery, n (%)	157 (67%)		
Left circumflex artery, n (%)	26 (11%)		
Right coronary artery, n (%)	53 (22%)		
Preadenosine FFR	0.95±0.06	0.89±0.09	0.96±0.03*
Postadenosine FFR	0.85±0.09	0.72±0.08	0.88±0.05*
Proximal reference segment			
MLA, mm^2	8.3±3.0	7.9±2.3	8.4±3.1
Mean lumen diameter, mm	3.2±0.6	3.2±0.5	3.2±0.6
Mean P+M area, mm^2	6.3±2.7	6.4±2.3	6.2±2.8
Mean plaque burden, %	42.3±11.4	44.3±10.4	41.8±11.6
Mean EEM area, mm^2	14.6±4.6	14.3±3.5	14.7±4.9
Mean EEM diameter, mm	4.3±0.7	4.3±0.5	4.3±0.7
Distal reference segment			
MLA, mm^2	7.0±2.7	6.2±2.4	7.2±2.8*
Mean lumen diameter, mm	3.0±0.6	2.8±0.5	3.0±0.6*
Mean P+M area, mm^2	4.4±2.9	4.2±2.8	4.4±2.9
Mean plaque burden, %	36.3±11.7	37.4±12.3	36.0±11.6
Mean EEM area, mm^2	11.3±5.0	10.4±4.6	11.6±5.0
Mean EEM diameter, mm	3.7±0.8	3.6±0.8	3.8±0.8
Average of proximal and distal references			
Averaged EEM area, mm^2	12.9±4.5	12.2±3.6	13.1±4.6
Averaged EEM diameter, mm	4.0±0.7	3.9±0.6	4.0±0.7
Averaged lumen area, mm^2	7.6±2.5	7.0±2.0	7.8±2.6
Averaged lumen diameter, mm	3.1±0.5	3.0±0.4	3.1±0.5
At MLA site			
MLA, mm^2	2.6±1.0	1.8±0.5	2.8±1.0*
EEM area, mm^2	11.1±4.3	10.5±4.1	11.2±4.4
Mean EEM diameter, mm	3.7±0.7	3.6±0.7	3.7±0.7
Area stenosis, %	64.9±12.2	73.1±9.3	62.8±12.0*
PB, %	74.8±10.1	81.2±7.7	73.2±10.0*
Lesion length, mm			
Length with lumen area <4.0 mm^2, mm	9.3±9.0	14.7±10.7	8.1±8.2*
Length with lumen area <3.0 mm^2, mm	4.6±6.0	9.0±7.7	3.4±4.7*
Length with lumen area <2.4 mm^2, mm	2.4±3.8	4.9±4.4	1.7±3.3*

P+M indicates plaque plus media.
*P<0.05 versus lesions with FFR <0.80.

P=0.001), lesion length with a lumen area <3.0 mm^2 (β=−0.003; 95% CI, −0.005 to −0.001; P=0.005), and LAD location (β=−0.035, 95% CI, −0.055 to −0.016; P=0.001). The independent determinants for FFR <0.80 were age (odds ratio [OR], 0.238; 95% CI, 0.090 to 0.629; P=0.003), MLA (OR, 0.206; 95% CI, 0.100 to 0.424; P<0.001), PB (OR, 1.062; 95% CI, 1.014 to 1.111; P=0.010), and LAD lesion location (OR, 4.371; 95% CI, 0.755 to 10.885; P=0.002).

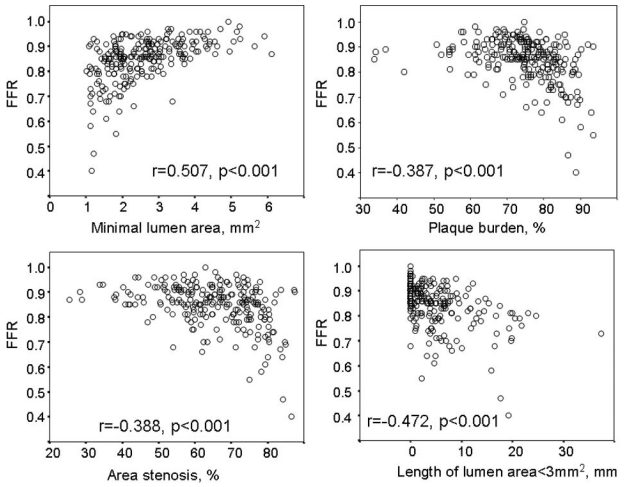


Figure 1. Relationship between FFR and IVUS parameters. FFR significantly correlated with MLA (r=0.507, P<0.001), PB (r=−0.387, P<0.001), area stenosis (r=−0.388, P<0.001), and length with a lumen area <3.0 mm^2 (r=−0.472, P<0.001).

In the overall group of 236 lesions, the best cutoff value (with a maximal accuracy) of the IVUS-measured MLA to predict FFR <0.80 was <2.4 mm^2 (90%sensitivity, 60% specificity, and area under the curve (AUC)=0.800; 95% CI, 0.742 to 0.848; P<0.001). The overall diagnostic accuracy was 68% (Figure 2), with a confidence interval for the cutoff value of MLA of 1.8 to 2.6 mm^2. In addition, the cutoff value of PB to predict FFR <0.80 was ≥79% (69% sensitivity, 72% specificity, AUC=0.756; 95% CI, 0.696 to 0.810; P<0.001). For the prediction of FFR <0.80, the cutoff value of lesion length with a lumen area <3.0 mm^2 was 3.1 mm (84% sensitivity, 63%specificity, AUC=0.765; 95% CI, 0.706 to 0.818; P<0.001).

Among 117 lesions with an MLA ≥2.4 mm^2, 112 (96%) had an FFR ≥0.80; and all but 1 showed FFR ≥0.75. Conversely, 44 (37%) of 119 lesions with an MLA <2.4 mm^2 had an FFR <0.80. Therefore, we performed a second multivariable analysis using the remaining 119 lesions with an MLA <2.4 mm^2 (with the same variables as listed above) in an attempt to further refine this cutoff in predicting an abnormal FFR. In this subgroup of 119 lesions with an MLA <2.4 mm^2, the independent predictors for FFR were age (β=2.955; 95% CI, 1.152 to 7.580; P=0.019) and PB (OR, 2.955; 95% CI, 1.028 to 1.164; P=0.001). However, in lesions with an MLA <2.4 mm^2, there was no IVUS parameter that improved on the accuracy to predict an FFR <0.80 (Figure 3).

Among 92 lesions with an IVUS MLA between 2.4 mm^2 and 4.0 mm^2, 87 (95%) showed FFR ≥0.80. An MLA <4.0 mm^2 predicted FFR <0.80 with a sensitivity of 100% but a specificity of only 13%. The cutoff value of lesion length with a lumen area <4.0 mm^2 was 10.4 mm (56% sensitivity, 76% specificity, AUC=0.698; 95% CI, 0.615 to 0.772; P=0.001).

Effect of Vessel Size, Diabetes, and Lesion Location

Figure 4 shows the subgroup analysis according to reference lumen diameter and LAD versus non-LAD lesion location,

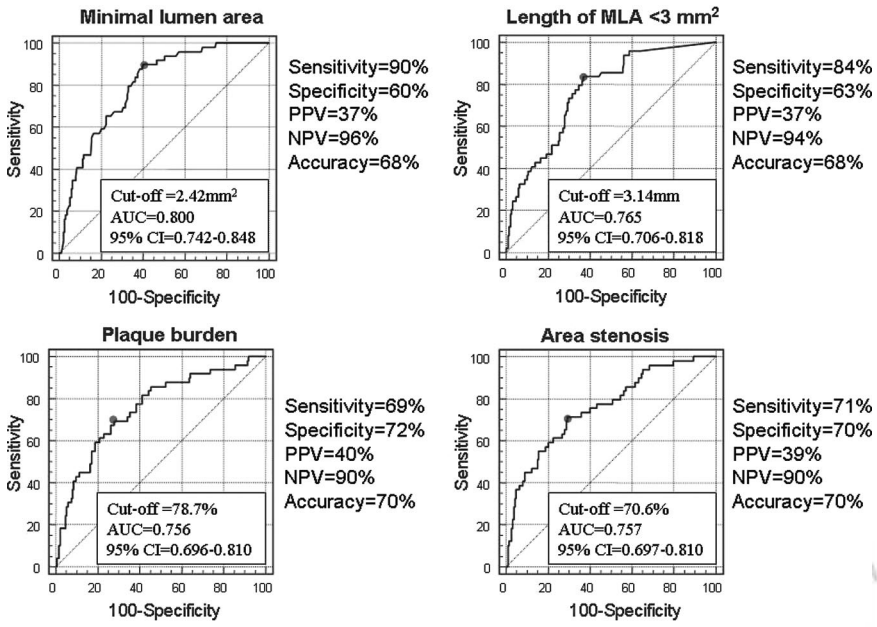


Figure 2. Cutoff values and diagnostic accuracies of IVUS-derived predictors for FFR <0.80.

When the cutoff value of an MLA <2.4 mm^2 was applied to the 27 lesions with reference lumen diameter <2,5 mm, the diagnostic accuracy was markedly reduced to 44% (sensitivity of 100% and specificity of 25%). Comparing patients with DM versus without DM, there was no significant difference in sensitivity (94% versus 88%, P=0.468) or specificity (57% versus 61%, P=0.389) of MLA <2.4 mm^2 for the detection of FFR <0.80. The predictive value of the plaque burden did not differ among the subgroups. Table 3 presents the optimal cutoff values of the 4 main IVUS parameters—MLA, lesion length with a lumen area <3.0 mm^2, PB, and area stenosis—in predicting FFR <0.80 in subgroups classified by reference lumen diameter and LAD versus non-LAD lesion location.

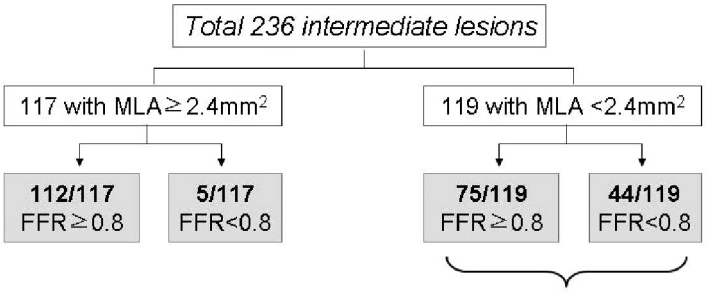
Reproducibility

In 30 lesions, interobserver and intraobserver coefficients of variation were 0.19 and 0.13 in the IVUS-measured MLA. The coefficient of variation of 2 measurements of FFR at maximal hyperemia was 0.04.

Discussion

The major findings of this study are the following: (1) IVUS-measured MLA, PB, and lesions length were the independent determinants for FFR at maximal hyperemia in intermediate lesions. (2) Although an MLA <2.4 mm^2 was the best cutoff value to predict FFR <0.80 with a high sensitivity and NPV, the specificity and PPV were poor. (3) In lesions with an MLA <2.4 mm^2, there was no IVUS-derived anatomic parameter that improved on the prediction of a significance stenosis (FFR <0.80).

A few studies have validated an IVUS-measured MLA <3.0 mm^2 or <4.0 mm^2 as an anatomic predictor for physiological lesion significance such as an abnormal FFR.[12–15] However, these studies were performed in a small number of lesions and reported only a fair ROC cut-point and



119 with MLA <2.4mm²	Cut-off	Sensitivity	Specificity	Accuracy	AUC	95% CI
Length with lumen area <3.0mm²	11.7mm	36%	84%	66%	0.567	0.473-0.657
Length with lumen area <2.4mm²	4.1mm	55%	68%	63%	0.609	0.516-0.697
Plaque burden	81.2%	66%	68%	67%	0.686	0.595-0.768
Area stenosis	77.2%	50%	81%	69%	0.647	0.554-0.732

Figure 3. Identification of FFR <0.80 using IVUS-derived predictors. Cutoff and predictive values of IVUS parameters versus FFR <0.80 in 119 lesions with MLA <2.4 mm^2 are shown (FFR <0.80, n=44).

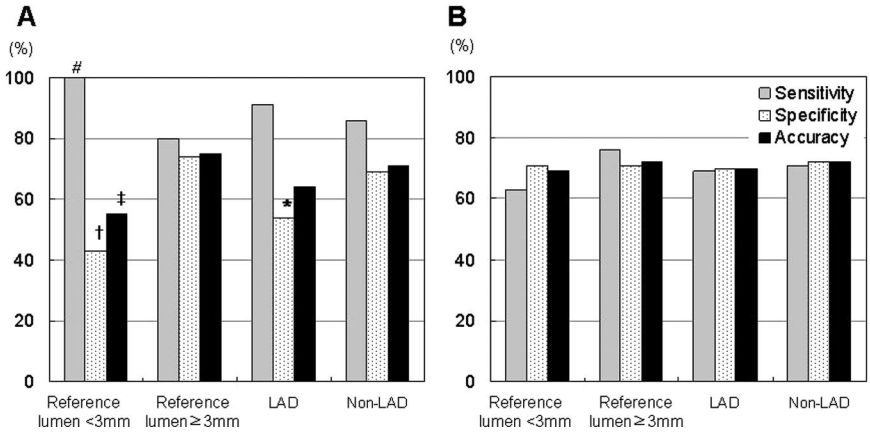


Figure 4. Subanalysis according to reference lumen diameter and LAD versus non-LAD, lesion location for the cutoff values of MLA <2.4 mm^2 (A), and PB $\geq 79\%$ (B) to identify FFR <0.80. *$P=0.025$ versus non-LAD (54% versus 69%). #$P=0.028$ versus reference lumen ≥ 3 mm, (100% versus 80%). †$P<0.001$ versus reference lumen ≥ 3 mm, (43% versus 74%). ‡$P<0.001$ versus reference lumen ≥ 3 mm (55% versus 75%).

modestly wide confidence intervals. Furthermore, there is concern of the trivial effect of an MLA threshold <4.0 mm^2 or even <3.0 mm^2 in small vessels such as those with a diameter <2.5 mm as well as the simplicity of relating a single anatomic measurement such as the MLA to the complexity of hemodynamic lesion significance.[16,17] Nevertheless, in this study an MLA measured by IVUS before PCI provided the largest AUC on ROC analysis for the prediction of an FFR <0.80. An MLA ≥ 2.4 mm^2 excluded the possibility of FFR <0.80 with a high NPV of 96%. Conversely, an MLA <2.4 mm^2 was less specific for predicting an abnormal FFR, suggesting that using this criterion 40% of lesions without functional significance might be a target for unnecessary PCI.

Takagi et al[12] first reported IVUS parameters to predict FFR <0.75 in 42 patients with 51 lesions. Although MLA <3.0 mm^2 predicted FFR <0.75 with a sensitivity 83% and specificity 92%, the main limitation was that only 26 (51%) lesions were intermediate lesions. Lee et al[18] recently reported an MLA <2.0 mm^2 as the best cutoff values to predict FFR <0.75 with sensitivity of 82% and a specificity of 81% in lesions with a reference segment lumen diameter <3 mm. Briguori et al[15] evaluated 53 lesions, all of which had intermediate stenosis. Their cutoff value of MLA <4.0 mm^2 had a good sensitivity (92%) and NPV (96%) for detecting FFR <0.75. However, it showed poor specificity (56%) and PPV (46%), similar to our data. Furthermore, using the scatterplot of their data, an MLA <2.4 mm^2 may be better cutoff than MLA <4.0 mm^2, improving the diagnostic accuracy from 64% to 76%.

Although the cutoff value of FFR 0.75 to 0.80 has been used to identify ischemia-inducing lesions, we decided to use

Table 3. Cutoff and Predictive Values of IVUS Parameters for Detecting FFR <0.80 in the Subgroups

	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC	95% CI
LAD (n=157), FFR <0.8 (n=42)								
MLA, mm^2	2.32	88	57	43	93	65	0.772	0.698–0.835
Length with lumen area <3.0 mm^2, mm	3.76	79	62	43	88	66	0.738	0.662–0.805
PB, %	75.1	86	57	42	92	64	0.746	0.670–0.812
Area stenosis, %	70.2	67	73	48	86	71	0.747	0.671–0.813
Non-LAD (n=79), FFR <0.8 (n=7)								
MLA, mm^2	1.92	86	81	30.	98	82	0.863	0.767–0.930
Length with lumen area <3.0 mm^2, mm	1.42	100	63	21	100	66	0.804	0.699–0.884
PB, %	86.6	71	97	71	97	95	0.833	0.733–0.908
Area stenosis, %	74.6	86	86	38	94	86	0.905	0.818–0.959
RLD <3.0 mm (n=110), FFR <0.8 (n=24)								
MLA, mm^2	2.32	100	45	34	100	57	0.769	0.679–0.844
Length with lumen area <3.0 mm^2, mm	4.92	92	62	40	96	68	0.810	0.724–0.879
PB, %	75.2	83	55	34	92	62	0.729	0.636–0.809
Area stenosis, %	58.4	96	47	34	98	58	0.742	0.650–0.821
RLD ≥3.0 mm (n=126), FFR <0.8 (n=25)								
MLA, mm^2	2.42	80	75	44	94	76	0.839	0.763–0.899
Length with lumen area <3.0 mm^2, mm	0.52	92	59	34	97	66	0.762	0.678–0.834
PB, %	78.9	76	74	42	93	74	0.783	0.701–0.852
Area stenosis, %	74.5	76	77	45	93	77	0.815	0.736–0.879

RLD indicates reference lumen diameter.

the upper limit of that small transition zone to minimize the number of ischemic lesions left untreated as was done in the FAME study.[11,19] Nevertheless, the current data demonstrated that the sensitivity of MLA <2.4 mm^2 to predict FFR <0.80 was as high as 90%; and this cutoff value also predicted FFR <0.75, with a sensitivity of 96%. On the other hand, the previously suggested cutoff MLA value of 4.0 mm^2 was beyond the 95% confidence interval range of the current data (1.8 to 2.6 mm^2), and the specificity was only 13% for the prediction of FFR <0.80.

Limitations

In this current study, FFR <0.80 was seen in only 21% of the intermediate lesions, which is relatively lower than previously reported. The predictabilities of MLA <2.4 mm^2 were poor in the lesions with small reference lumen diameter <3.0 mm compared with ≥ 3.0 mm. Moreover, this cutoff could not be applied to small vessels with reference lumen diameter <2.5 mm. In some individual cases with diffuse disease and small reference vessels, a small lumen area may not necessarily cause physiologically significant flow limitation. Although MLA ≥ 2.4 mm^2 may rule out the possibility of functionally significant stenosis with a good NPV, we were not able to develop a satisfactory algorithm for discriminating FFR ≥ 0.80 from FFR <0.80 using IVUS parameters due to low specificity and PPV of the cutoff values. IVUS provides only a few anatomic parameters among numerous factors potentially affecting FFR. There were differences in the cutoff values of MLA and PB between LAD and non-LAD lesion location, which may be due to much larger myocardial mass to be supplied by LAD compared with other coronary arteries. However, because of the small number of the lesions with FFR <0.80 among the various subgroups, we were not able to identify subgroup-specific cutoff values for the various IVUS measurements to predict FFR <0.80.

Conclusion

IVUS-measured MLA is only one of many factors affecting coronary flow hemodynamics. Although IVUS-derived MLA ≥ 2.4 mm^2 may be a useful criterion for excluding intermediate lesions with an FFR <0.80, an MLA <2.4 mm^2 does not always equate with functional significance. Thus, physiological assessment such as direct FFR measurement or stress tests may be necessary for identifying the ischemia-inducible stenosis that require PCI to reduce unnecessary procedures, especially in lesions with MLA <2.4 mm^2 or small-vessel disease.

Acknowledgments

We thank The Korea Health 21 R&D Project, Ministry of Health & Welfare, Republic of Korea (A090264).

Disclosures

None.

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CLINICAL PERSPECTIVE

We assessed optimal intravascular ultrasound (IVUS) criteria for predicting functional significance of intermediate coronary lesions. Overall, 201 patients with 236 coronary lesions underwent IVUS and invasive physiologic assessment pre-intervention. Fractional flow reserve (FFR) was measured at maximal hyperemia induced by intravenous adenosine infusion. FFR <0.80 at maximum hyperemia was seen in 49 (21%) of the overall 236 lesions. The independent determinants of FFR were minimal lumen area (MLA; $\beta=0.020$; 95% confidence interval [CI], 0.008 to 0.031; $P=0.032$), plaque burden ($\beta=-0.002$; 95% CI, -0.003 to 0.001; $P=0.001$), lesion length with a lumen area <3.0 mm^2 ($\beta=-0.003$, 95% CI, -0.005 to -0.001; $P=0.005$), and LAD location ($\beta=-0.035$; 95% CI, -0.055 to -0.016; $P=0.001$). The best cutoff value (with a maximal accuracy) of the MLA to predict FFR <0.80 was <2.4 mm^2 with a diagnostic accuracy of 68% (90% sensitivity, 60% specificity, and area under the curve=0.800; 95% CI, 0.742 to 0.848; $P<0.001$). The cutoff value of plaque burden to predict FFR <0.80 was $\geq$79% (69% sensitivity, 72% specificity, and area under the curve=0.756; 95% CI, 0.696 to 0.810; $P<0.001$). Among 117 lesions with an MLA ≥ 2.4 mm^2, 112 (96%) had an FFR ≥ 0.80, and all but 1 showed FFR ≥ 0.75. Conversely, 44 (37%) lesions with an MLA <2.4 mm^2 had an FFR <0.80. IVUS-derived MLA ≥ 2.4 mm^2 may be useful to exclude FFR<0.80, but poor specificity limits its value for physiologic assessment of lesions with MLA <2.4 mm^2. Thus, FFR or some other functional assessment may be necessary to accurately identify ischemia-inducible intermediate stenoses.