

Usefulness of combined intravascular ultrasound parameters to predict functional significance of coronary artery stenosis and determinants of mismatch

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KEYWORDS

- fractional flow reserve
- interventional
- myocardial
- predictive value of tests
- ultrasonography

Abstract

Aims: Efficacy of combined intravascular ultrasound (IVUS) parameters in functional significance prediction and discrepancy between IVUS and fractional flow reserve (FFR) have not been well defined. This study therefore aimed to: 1) evaluate the diagnostic accuracy of combined IVUS parameters, namely minimal lumen area (MLA) and percent plaque burden (%PB), in functional significance prediction of coronary artery stenosis; and 2) define factors that affect the relation between FFR value and IVUS parameters.

Methods and results: At 11 international centres, IVUS and FFR measurements were concurrently performed in 945 major epicardial coronary artery lesions (886 patients). Functional significance was defined as FFR ≤ 0.8 . MLA and FFR correlated weakly ($r=0.289$, $p<0.001$). Diagnostic accuracy of MLA ≤ 4.0 mm², %PB $>70\%$ and their combination were 50%, 47% and 51%, respectively, with similar area under the curve (AUC) of 0.561, 0.511 and 0.516, respectively. The best cut-off values (BCV) were MLA ≤ 3.0 mm² and %PB $>75\%$, with accuracy of 60% for MLA, 50% for %PB and 56% for their combination, and AUC of 0.618, 0.511 and 0.533, respectively. MLA BCV ≤ 3.0 mm² had higher predictive power than %PB BCV $>75\%$ or their combination. Independent predictors of functional significance were male gender (odds ratio 1.76 [95% confidence interval: 1.19-2.62]), left ventricular ejection fraction (LVEF, 0.98 [0.96-0.99]), LAD lesion (2.52 [1.73-3.67]), reference vessel diameter (0.60 [0.41-0.86]), lesion length (1.04 [1.02-1.06]) and MLA (0.79 [0.69-0.92]). False negative lesion incidence was 24.4% in association with race (for Asians, 0.391 [0.219-0.698]), LAD lesion (2.677 [1.709-4.191]) and LVEF (0.977 [0.957-0.997]). False positive lesion incidence was 17.0% in association with non-LAD lesion (2.444 [1.620-3.686]).

Conclusions: Combined IVUS parameters did not improve the accuracy of functional significance prediction. Discrepancy between IVUS and FFR, which was not rare, should be taken into account in clinical decision making.

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Introduction

Although determination of the severity of coronary artery stenosis is the first step in coronary artery disease diagnosis, the accuracy of the available diagnostic tools remains under debate¹. The inherent limitation of two-dimensional quantitative coronary angiography (QCA) to define functional severity has propelled the use of other modalities such as intravascular ultrasound (IVUS) which has become one of most popular imaging techniques to assess angiographically ambiguous stenosis²⁻⁴. Although IVUS more accurately assesses lesions than QCA alone, there is no agreement on the accuracy of historical cut-off values for individual IVUS parameters such as minimal lumen area (MLA), percent plaque burden (%PB) and lesion length regardless of patient or lesion characteristics⁵⁻⁹. There have been recent attempts to clarify the IVUS parameter cut-off values that best define haemodynamically significant lesions using fractional flow reserve (FFR)¹⁰. Although the combination of MLA and %PB by IVUS appeared to predict functional significance better in small studies^{11,12}, this has not been validated in a larger one. This study therefore aimed to: 1) evaluate the diagnostic accuracy of combined IVUS parameters, namely MLA and %PB, in functional significance prediction of coronary artery stenosis; and 2) define the factors which affect the relation between FFR value and IVUS parameters.

Methods

STUDY POPULATION

This international multicentre registry was performed at 11 centres (four in Korea, two in Japan, one in China, one in Singapore, two in the USA and one in Europe), all with ample experience in IVUS and FFR. This registry included previously published^{5,6,13,14} and unpublished data. All patients had *de novo* lesions with visual intermediate stenosis (30% to 70%) in non-left main major epicardial coronary arteries. IVUS and FFR measurements were simultaneously obtained in the lesion of interest. Lesions were excluded if any of the following conditions were present: left main disease, prior coronary artery bypass graft surgery, additional stenosis (>30% by visual estimation) in the same vessel, left ventricular ejection fraction <35%, primary myocardial or valvular disease, and culprit vessel in the setting of acute myocardial infarction. The study protocol was approved by each institutional review board and all patients provided written informed consent.

Data analysis

The target vessel was engaged using a 5 Fr-7 Fr guiding catheter. QCA data were analysed by an independent technician blinded to the result. After acquiring optimal projections, QCA analysis including reference vessel diameter, minimal lumen diameter, lesion length and percent diameter stenosis was performed at each participating centre by computer-assisted analysis. IVUS imaging was obtained in a standard fashion using an automated motorised pullback system (0.5 mm/s) with either of two commercially available imaging catheters (Boston Scientific/SCIMED, Minneapolis, MN, USA, or Volcano Corp., Rancho Cordova, CA, USA). MLA

was measured by a skilled specialist at each centre and obtained at the site of the smallest lumen, and %PB was calculated as: $(100 \times [\text{vessel area at MLA site} - \text{MLA}] / \text{vessel area at MLA site})^{15}$.

FFR was measured using a 0.014 inch pressure guide-wire (St. Jude Medical, St. Paul, MN, USA, or Volcano Corp.). Maximum hyperaemia was induced according to the standard protocol of each individual centre. Hyperaemia was induced with adenosine in 92.1% and papaverine in 7.9% of cases using: intravenous continuous infusion of adenosine (140-220 µg/kg/min) via central or antecubital vein; intracoronary continuous infusion of adenosine (240 µg/min); intracoronary bolus injection of adenosine (12-80 µg into the left coronary artery, 8-40 µg into the right coronary artery); or intracoronary bolus injection of papaverine (20 µg)¹⁶. The lesion was considered functionally significant when FFR was ≤ 0.8 ^{17,18}. In addition to IVUS and FFR analysis, detailed data on baseline demographic and clinical characteristics were submitted to the data management core laboratory at Seoul National University Cardiovascular Centre.

Statistical analysis

Data are presented as means±standard deviations for continuous variables and frequencies for categorical variables. Student's t and chi-square tests were used to compare continuous and categorical variables, respectively. Correlations between IVUS parameters and FFR were assessed by Pearson correlation analysis.

Receiver operating characteristic (ROC) curve analysis was used to determine the best cut-off values (BCV) of the IVUS parameters predicting the functional significance of a lesion. Diagnostic accuracy including sensitivity, specificity, and positive and negative predictive values was calculated using best new cut-off values as well as the historical cut-off values of ≤ 4.0 mm² and %PB >70%. Independent predictors for functional significance were identified by multivariate logistic regression analysis. All statistical analyses were performed using SPSS, Version 19.0.0 (IBM Corp., Armonk, NY, USA), and a p-value of <0.05 was considered statistically significant.

Results

BASELINE CHARACTERISTICS

Eight hundred and eighty-six patients (945 lesions) were enrolled in this pooled analysis from 11 centres, each with a different enrolment period ranging overall from 2004 to 2010. Among them, 64 patients (64 lesions) were excluded (incomplete clinical information, <18 years old, left ventricular ejection fraction <35%, or incomplete angiographic data). Data from 822 patients were finally included in this study. Data on a total of 881 lesions with 881 MLA and 701 %PB values were available.

Patient baseline characteristics are presented in **Table 1**. Mean FFR value was 0.81 ± 0.11 . FFR was ≤ 0.80 in 353 lesions (40.1%). Mean MLA was 3.1 ± 1.3 mm². MLA was ≤ 4.0 mm² in 689 lesions (78.2%). Mean %PB was $72.1 \pm 11.6\%$. The correlation between MLA and %PB was -0.594 ($p < 0.001$). Functionally significant lesions were longer, more frequently located in the left anterior

Table 1. Baseline clinical characteristics.

	All patients (n=822)
Age, years	63.2±10.3
Male gender, n (%)	580 (70.6)
Asian ethnicity, n (%)	580 (70.6)
Diabetes mellitus, n (%)	279 (33.9)
Hypertension, n (%)	578 (70.3)
Hyperlipidaemia, n (%)	541 (65.8)
Smoking, n (%)	243 (29.6)
ACS, n (%)	191 (23.2)
BMI ≥30, n (%)	129 (15.7)
LVEF, %	60.9±9.1
ACS: acute coronary syndrome; BMI: body mass index; LVEF: left ventricular ejection fraction	

descending artery, and had smaller reference vessel diameter and minimal lumen diameter, higher percent diameter stenosis, and smaller MLA (Table 2). In analysis of the relationship between IVUS parameters and FFR, MLA showed a statistically significant but very weak correlation ($r=0.289$, $p<0.001$), and there was no correlation between %PB and FFR ($r=0.001$, $p=0.970$) (Figure 1). For LAD lesions, the correlation between MLA and FFR value was

0.321 ($p<0.001$) and that between %PB and FFR value was -0.224 ($p<0.001$). Similarly, in proximal lesions, the correlation with FFR was 0.348 for MLA ($p<0.001$) and -0.193 for %PB ($p=0.001$) (Table 3).

Table 3. Correlation between FFR and IVUS parameters.

Lesion subsets	Variables	FFR	
		Correlation coefficient	p-value
All lesions	MLA	0.289	<0.001
	%PB	0.001	0.970
LAD lesions	MLA	0.321	<0.001
	%PB	-0.224	<0.001
Proximal lesions	MLA	0.348	<0.001
	%PB	-0.193	0.001
LAD: left anterior descending artery; MLA: minimal lumen area; %PB: percent plaque burden			

HISTORICAL IVUS CUT-OFF VALUES TO PREDICT FUNCTIONAL SIGNIFICANCE

Three hundred and two (43.8%) out of 689 lesions with $MLA \leq 4.0 \text{ mm}^2$ and 185 lesions (42.2%) out of 438 lesions with %PB >70% had functionally significant stenosis. Three hundred and

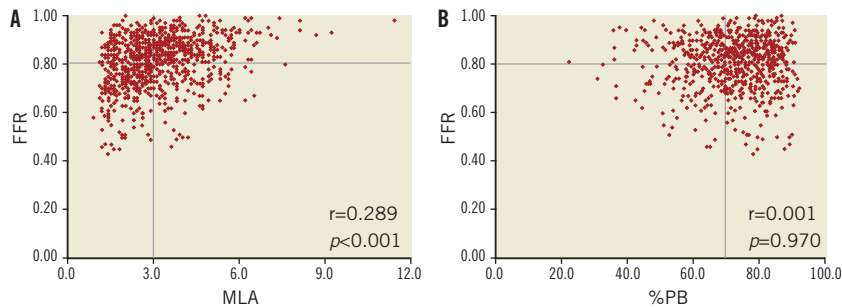


Figure 1. Relationship between FFR and IVUS MLA/%PB. There was a positive correlation between IVUS MLA and FFR ($r=0.289$, $p<0.0001$) and no correlation between IVUS %PB and FFR ($r=0.001$, $p=0.970$).

Table 2. Lesion characteristics.

		All lesions (n=881)	FFR ≤0.80 (n=353)	FFR >0.80 (n=528)	p-value
Angiographic variables	LAD lesion, n (%)	576 (65.4)	275 (77.9)	301 (57.0)	<0.001
	Proximal lesion site, n (%)	395 (44.8)	152 (43.1)	243 (46.0)	0.407
	Reference diameter, mm	3.0±0.5	2.9±0.5	3.1±0.5	<0.001
	Minimal lumen diameter, mm	1.5±0.4	1.3±0.4	1.7±0.4	<0.001
	Diameter stenosis, %	49.6±12.7	54.2±12.8	46.4±11.6	<0.001
	Lesion length, mm	14.5±7.9	16.5±8.2	13.2±7.4	<0.001
Pressure wire variable	Fractional flow reserve	0.81±0.11	0.71±0.08	0.88±0.05	<0.001
IVUS variables	MLA, mm ²	3.1±1.3	2.7±1.2	3.4±1.4	<0.001
		(n=701)	(n=302)	(n=399)	
	Vessel area at MLA site, mm ²	11.5±4.0	11.0±3.6	11.9±4.3	0.003
	% plaque burden, %	72.1±11.6	71.8±11.9	72.3±11.4	0.564
LAD: left anterior descending artery; MLA: minimal lumen area					

fifty-four lesions (50.5%) satisfied the combined cut-off values of $MLA \leq 4.0 \text{ mm}^2$ and $\%PB > 70\%$ (Figure 2). Diagnostic performance of historical cut-off values of IVUS is shown in Figure 3.

The area under the curve (AUC) of $MLA \leq 4.0 \text{ mm}^2$ to define functional significance was 0.561 (95% confidence interval [CI]: 0.528-0.594) and that of $\%PB > 70\%$ was 0.511 (95% CI: 0.473-0.548). The AUC of combined IVUS criteria was 0.516 (95% CI: 0.478-0.554). When the ROC curves were compared, there were no significant differences between $MLA \leq 4.0 \text{ mm}^2$, $\%PB > 70\%$ and both ($p=0.285$ between MLA and $\%PB$; $p=0.217$ between MLA and both; and $p=0.716$ between $\%PB$ and both).

RENEWED IVUS BEST CUT-OFF VALUES TO PREDICT FUNCTIONAL SIGNIFICANCE

BCV of IVUS MLA to predict the presence of functional significance ($FFR \leq 0.8$) in this pooled analysis was 3.0 mm^2 (AUC 0.646, 95% CI: 0.609-0.684) and that of $\%PB$ was 75% (AUC 0.523, 95% CI: 0.479-0.567) (Figure 4).

Two hundred and forty-three lesions (50.4%) among 482 lesions with $MLA \leq 3.0 \text{ mm}^2$, and 129 lesions (41.9%) among 308 lesions with $\%PB > 75\%$ showed functional significance; 187 lesions (26.7%) fulfilled the combined $MLA \leq 3.0 \text{ mm}^2$ and $\%PB > 75\%$ (Figure 5). Diagnostic performance of new BCVs for individual and combined IVUS parameters is shown in Figure 3.

In ROC curve comparisons, new MLA BCV $\leq 3.0 \text{ mm}^2$ (AUC 0.618, 95% CI: 0.585-0.650) had higher predictive power than new $\%PB$ BCV $> 75\%$ (AUC 0.511, 95% CI: 0.473-0.548) or combined criteria (AUC 0.533, 95% CI: 0.496-0.571). However, $\%PB$ cut-off was not superior to combined criteria ($p=0.0045$ between MLA and $\%PB$; $p=0.0045$ between MLA and both; and $p=0.196$ between $\%PB$ and both).

DETERMINANTS OF FUNCTIONAL SIGNIFICANCE

Univariate analysis of predictors of functional significance is shown in Table 4. Male gender, Asian race, left anterior descending artery (LAD) lesion and lesion length showed positive correlation

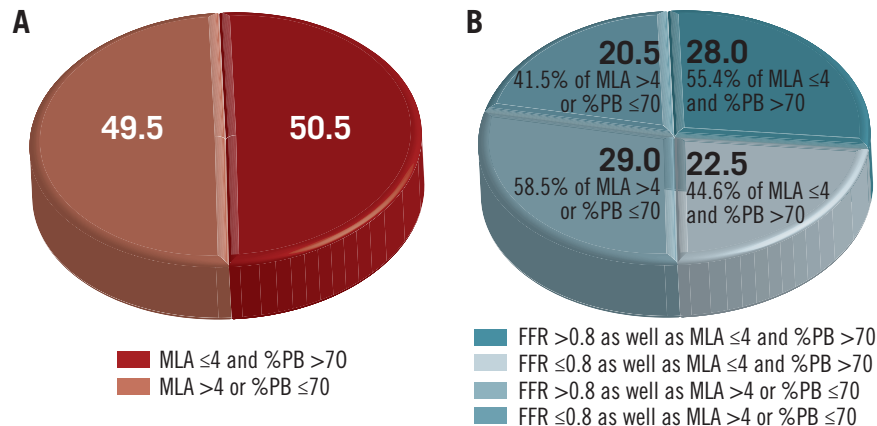


Figure 2. Historical IVUS cut-off. Distribution of study population according to: A) historical IVUS cut-off, and B) combination of IVUS and FFR cut-off. Among lesions with $MLA \leq 4.0 \text{ mm}^2$ and $\%PB > 70\%$, only 44.6% had $FFR \leq 0.80$.

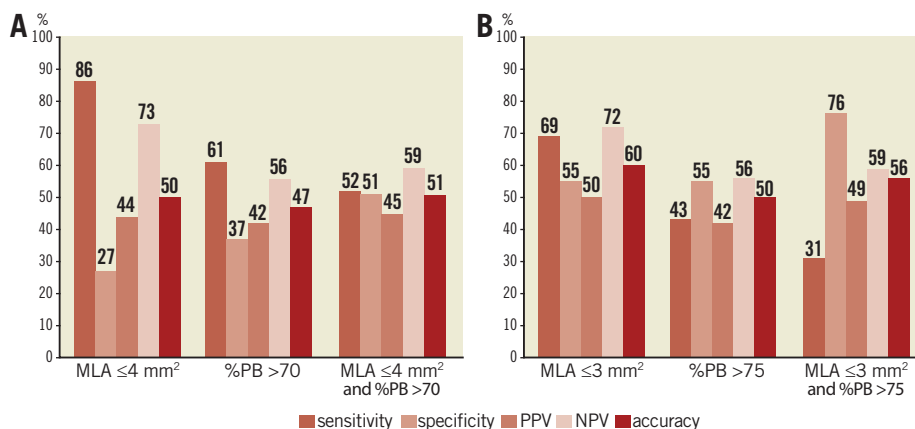


Figure 3. Diagnostic accuracy of IVUS criteria. Diagnostic accuracy according to historical (A) and new (B) IVUS criteria. Adaptation of new IVUS criteria improved specificity but decreased sensitivity. Consequently, accuracy did not vary much from that of historical IVUS criteria.

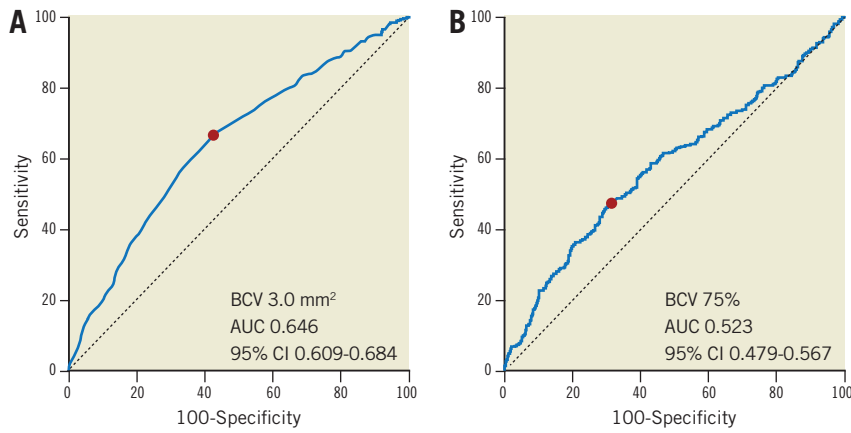


Figure 4. Receiver-operating characteristic curves for new IVUS criteria to predict FFR ≤ 0.80.

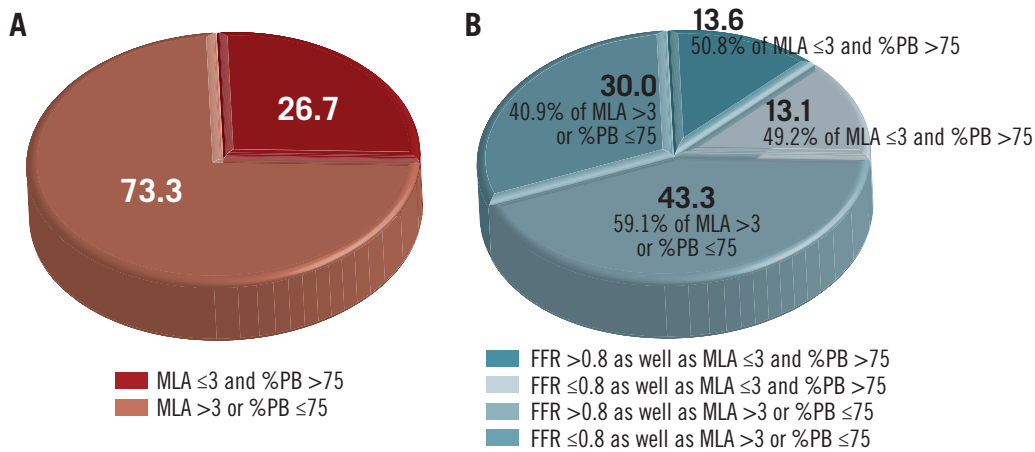


Figure 5. New IVUS cut-off. Distribution of study population according to: A) new IVUS cut-off, and B) combination of new IVUS and FFR cut-off. Among lesions with MLA ≤ 3.0 mm² and %PB > 75%, only 49.2% had FFR ≤ 0.80.

Table 4. Multivariate analysis of functional significance.

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value
Gender (male)	1.53	1.12-2.07	0.007	1.76	1.19-2.62	0.005
Race (Asian)	1.54	1.13-2.08	0.006			
Age	0.99	0.98-1.01	0.215			
BMI	0.97	0.94-1.00	0.084			
LVEF	0.98	0.96-0.99	0.002	0.98	0.96-0.99	0.010
LAD lesion	2.66	1.96-3.61	<0.001	2.52	1.73-3.67	<0.001
RVD	0.45	0.34-0.59	<0.001	0.60	0.41-0.86	0.006
Lesion length	1.06	1.04-1.08	<0.001	1.04	1.02-1.06	<0.001
MLA	0.67	0.59-0.75	<0.001	0.79	0.69-0.92	0.002
%PB	1.00	0.98-1.01	0.563			
Diabetes	1.10	0.83-1.46	0.506			
Smoking	1.02	0.76-1.37	0.902			
ACS	1.09	0.79-1.50	0.591			

ACS: acute coronary syndrome; BMI: body mass index; CI: confidence interval; LAD: left anterior descending artery; LVEF: left ventricular ejection fraction; MLA: minimal lumen area; %PB: percent plaque burden; RVD: reference vessel diameter

with functional significance, while left ventricular ejection fraction (LVEF), reference vessel diameter (RVD) and MLA had negative correlation. Multivariate analysis showed the independent predictors of functional significance were male gender (odds ratio [OR] 1.76, 95% CI: 1.19-2.62), LVEF (OR 0.98, 95% CI: 0.96-0.99), LAD lesion (OR 2.52, 95% CI: 1.73-3.67), RVD (OR 0.60, 95% CI: 0.41-0.86), lesion length (OR 1.04, 95% CI: 1.02-1.06) and MLA (OR 0.79, 95% CI: 0.69-0.92).

FACTORS TO PREDICT FUNCTIONAL AND ANATOMICAL MISMATCH

In terms of diagnostic accuracy of new BCV, incidence of false positive (mismatch) lesion, i.e., $MLA \leq 3.0 \text{ mm}^2$ and $\%PB > 75\%$ and $FFR > 0.80$, was 17.0%, in association with non-LAD lesion (OR 2.444, 95% CI: 1.620-3.686, $p < 0.001$). For false negative lesion (reverse mismatch), i.e., $MLA > 3.0 \text{ mm}^2$ or $\%PB \leq 75\%$ and $FFR \leq 0.80$, the incidence was 24.4% in association with race (OR 0.391, 95% CI: 0.219-0.698, $p = 0.001$ in the case of Asians), LAD lesion (OR 2.677, 95% CI: 1.709-4.191, $p < 0.001$) and LVEF (OR 0.977, 95% CI: 0.957-0.997, $p = 0.023$) (Table 5).

Table 5. Predictors of “mismatch” and “reverse mismatch” between IVUS parameters and FFR.

	Odds ratio	95% CI	p-value
Predictor for “mismatch”			
Non-LAD lesion	2.444	1.620-3.686	<0.001
Predictors for “reverse mismatch”			
Race (Asian)	0.391	0.219-0.698	0.001
LAD lesion	2.677	1.709-4.191	<0.001
LVEF	0.977	0.957-0.997	0.023
CI: confidence interval; LAD: left anterior descending artery; LVEF: left ventricular ejection fraction			

Discussion

The major findings of this large international multicentre pooled analysis were: 1) addition of $\%PB$ to MLA did not improve diagnostic performance of IVUS criteria to predict the functional significance of coronary lesions; 2) anatomical and functional mismatch occurred frequently; and 3) the predictors of mismatch were race, LAD lesion and LVEF.

IVUS CUT-OFF VALUES TO DEFINE FUNCTIONAL SIGNIFICANCE

Based on the study by Abizaid et al¹⁹, $MLA \leq 4.0 \text{ mm}^2$ has been accepted as the standard cut-off to determine functional significance. However, several recent studies have proposed different ischaemic thresholds of MLA between 2.0 mm^2 and 3.1 mm^2 according to vessel size or lesion location^{5,7,13,20}. The current large international multicentre study showed that ischaemia-predictable MLA is smaller than the historical value, and varies according to anatomical factors and the amount of myocardium supplied by the target segment.

In contrast to MLA, $\%PB$ reflects difference in vessel size (or amount of myocardium) and has been utilised to improve the accuracy of functional significance prediction²¹. However, the benefit of $\%PB$ to define the functional significance of coronary stenosis has been inconsistent in previous studies. Waksman et al found that $\%PB$ was not an independent predictor for identifying $FFR < 0.8$ (OR 1.03, 95% CI: 0.99-1.06, $p = 0.110$)²². Likewise, when Yang et al evaluated the relationship between various IVUS parameters and FFR, $\%PB$ was not an independent predictor²³. In our study, the accuracy of $\%PB > 70\%$ alone to predict functional significance was similar to that of $MLA \leq 4.0 \text{ mm}^2$. Moreover, there was inferiority in newly determined $\%PB$ BCV of $> 75\%$ compared with new MLA BCV of $\leq 3.0 \text{ mm}^2$. Although the diagnostic accuracy of $\%PB$ to predict functional significance could be lower than that of other anatomical parameters, $\%PB$ as a prognostic factor should not be undervalued as validated in a recent study²⁴.

Because the accuracy of individual IVUS values was challenged, that of their combination was evaluated. Briguori et al (43 patients, 53 lesions) found that the combined use of $MLA \leq 4.0 \text{ mm}^2$ and $\%PB > 70\%$ greatly improved specificity compared to the MLA criterion alone²¹. However, these criteria are no longer valid because MLA cut-off value varies according to lesion conditions. Although Chen SL et al suggested different cut-off values of MLA and $\%PB$ to predict functional significance according to clinical presentation, vessel size and lesion location, the combination of MLA and $\%PB$ increased the diagnostic value only for LAD lesion¹². Similar results were obtained in our study. Although the correlation between FFR and IVUS variables was poor, its value improved after lesion was subdivided into only LAD lesion or proximal lesion. The correlation between MLA and FFR value was 0.321 ($p < 0.001$), and that between $\%PB$ and FFR value was -0.224 ($p < 0.001$) when only LAD lesion was selected. Similarly, the correlation in proximal lesion was 0.348 in MLA ($p < 0.001$) and -0.193 in $\%PB$ ($p = 0.001$). Therefore, the accuracy of anatomical lesion assessment to predict functional significance can be affected by the affected myocardium.

The combination of IVUS criteria in the present study also failed to increase diagnostic accuracy in predicting functional significance, for which there might be several explanations. First, as discussed above, $\%PB$ might have a lower diagnostic value than MLA. Second, although $\%PB$ increased, positive remodelling of a vessel can compensate for luminal loss during early atherosclerosis, thereby affecting the correlation between MLA and $\%PB$ with FFR. Third, contingent upon its definition, $\%PB$ can be affected by change in vessel area evoked by spasm or stretch during IVUS examination. Fourth, the use of combined criteria improved specificity but decreased sensitivity because of a higher possibility of false negatives. Consequently, there was almost no change in diagnostic accuracy.

FACTORS ASSOCIATED WITH FFR VALUE

The current study suggested that gender affects functional severity. Compared with females, males generally have higher body

mass index and larger coronary arteries which might account for the gender difference seen. A similar explanation can be used for the observed effect of race. Because lower LVEF is associated with higher left ventricular end-diastolic pressure (LVEDP), and in turn LVEDP is positively associated with FFR, LVEF has a negative correlation with functional significance²⁴. LAD also influenced functional significance. This could be explained by the larger extent of myocardium supplied by LAD compared to non-LAD arteries⁹. Larger reference vessel diameter is also related to a greater extent of affected myocardium, and therefore functional severity varies with vessel diameter²². Not surprisingly, lesion length and MLA affect lesion severity. Iguchi et al (165 patients, 199 lesions) suggested that lesion length >16 mm was the BCV to predict functional significance for intermediate lesions (AUC: 0.940)²⁵.

The variety of factors which affect coronary physiology renders it more difficult to pinpoint anatomical parameters to predict physiology. Even with the most widely used historical parameters, a single anatomical value could not appropriately reflect specific physiologic conditions (different resting flow, myocardial bed size, and achievable hyperaemic flow capacity, among others) in individual patients. Each imaging modality is limited by its own resolution on a geometric measurement, which in turn limits the usefulness of such measurement.

Limitations

First, this is a pooled analysis which has the possibility of selection bias. Second, various hyperaemic methods were used with different hyperaemic agents, routes of administration and dosages. However, the efficacy of all hyperaemic methods has previously been validated in several studies. Third, IVUS and QCA analysis was performed at each centre without common core lab analysis; however, data were obtained from skilled and validated analysts. Fourth, although the FFR cut-off value to define functional significance is a continuum spanning from 0.75 to 0.80, we decided to use the upper limit as was done in the FAME study. Therefore, the IVUS cut-off value would change if FFR <0.75 was defined as standard. Fifth, FFR analysis was performed based on cross-sectional information without pullback evaluation. Although serial stenosis was excluded in this study, mild plaque beyond the lesion of interest might affect FFR value.

Conclusion

Because of the various factors that affect FFR, IVUS parameters such as MLA and %PB, either alone or in combination and at different thresholds, have limited ability to predict functional significance in intermediate coronary artery stenosis. This limitation of IVUS should always be taken into account in clinical decision making. Therefore, it is no longer reasonable to use IVUS alone to inform decisions on stent implantation. When evaluating the relationship between functional and anatomical parameters, more careful consideration is warranted to avoid frequent mismatch between FFR and IVUS.

Impact on daily practice

Although IVUS can provide various anatomical information on coronary artery disease, inherent limitations to define the functional significance of coronary artery stenosis need to be taken into account in clinical decision making. Our study showed that the addition of percent plaque burden to minimal lumen area did not improve diagnostic performance of IVUS to predict the functional significance of coronary stenosis. False positive results (IVUS+, FFR-) were more common in non-LAD lesions and false negative results (IVUS-, FFR+) were more common in LAD lesions, Westerners and low left ventricular ejection fraction.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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