## Review Article Critical analysis of the correlation between optical coherence tomography versus intravascular ultrasound and fractional flow reserve in the management of intermediate coronary artery lesion

Yan-Feng Ma<sup>1</sup>, Jiang-Ming Fam<sup>2</sup>, Bu-Chun Zhang<sup>1</sup>

<sup>1</sup>Department of Cardiology, The Affiliated Hospital of Xuzhou Medical College, Jiangsu, China; <sup>2</sup>National Heart Centre Singapore, Singapore

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**Abstract:** The appropriate assessment of intermediate coronary artery stenosis continues to be a challenge for cardiologists. Several studies have shown that anatomic parameters obtained by intravascular ultrasound (IVUS) and optical coherence tomography (OCT) showed a correlation with fractional flow reserve (FFR) values in identifying hemodynamically severe coronary stenoses. However, the efficacy of IVUS/OCT versus FFR integration in intermediate coronary lesions is still debated. This review will allow for an independent analysis of research data and outlines the diagnostic efficiency of IVUS and OCT derived-anatomical parameters in identifying the hemodynamic significance of an angiographically intermediate stenosis as determined by FFR.

Keywords: Intravascular ultrasound, optical coherence tomography, fractional flow reserve, co-registration, intermediate lesions

#### Introduction

An intermediate coronary lesion on angiography is defined by a diameter stenosis of 40% to 70%. Clinical decision making in patients with intermediate coronary stenosis is still being debated. Conventional two-dimensional coronary angiography could not provide the anatomic information in detail [1].

Fractional flow reserve (FFR) is the well-established physiological index to assess the functional significance of a coronary stenosis [2]. Earlier studies showed that FFR <0.75 is an accurate predictor of ischemia [3]. http://eurheartj.oxfordjournals.org/content/32/3/345. long-ref-6Recent studies however, have used FFR  $\leq$ 0.80 as the optimal cut-off point to guide revascularisation [4]. Although clinical decision making based on FFR can be safely made with a good predictive value, it does not provide morphological and anatomical information. In order to find a good predictor of the hemodynamic severity of an intermediate coronary lesion, and provide morphological information, more recent studies have suggested that hybrid imaging modalities seem favorable. Several investigators have reported different multimodality imaging by combining IVUS and FFR [5], OCT and FFR [6-8]. They found a correlation between FFR values and anatomical parameters (minimum lumen area (MLA) and minimal lumen diameter (MLD)) derived from IVUS or OCT [5-7].

However, the differences in inclusion criteria and anatomical variables resulted in the different cut-off values of MLA and MLD for ischemic FFR. Thus, the purpose of this systematic review is to summarize the studies regarding the role of anatomic assessment obtained by IVUS versus OCT and physiological assessment provided by FFR in identifying intermediate coronary artery stenosis. We hope that this article can permit more accurate decisions in the management of patients with intermediate coronary lesions.

Study	Number of lesions (subjects)	Percentage diameter stenosis (%)	FFR cut-off value
Stefano GT et al, 2011 [6]	18 (14)	40-70	0.80
Shiono Y et al, 2012 [8]	62 (59)	58.2±17.0	0.75
Gonzalo N et al, 2012 [9]	61 (56)	50.9±7.7	0.80
Pawlowski T et al, 2013 [10]	71 (48)	40-70	0.80
Pyxaras SA et al, 2013 [11]	55 (36)	34±13	0.80
Reith S et al, 2014 [12]	142 (100)	56.08±10.75	0.80
Zafar H et al, 2014 [13]	41 (30)	45±10.7	0.80

Table 1. Correlation between OCT and FFR study characteristics

FFR, fractional flow reserve.

### Methods

#### Study design

This review included all available original studies reporting the use of OCT or IVUS versus FFR for the evaluation of intermediate coronary lesions. Review articles and animal studies were excluded.

### Literature search and data extraction

The online MEDLINE and EMBASE database were searched for literature in December 2014. The search strategy was "optical coherence tomography", "optical frequency domain imaging", "intravascular ultrasound", "intracoronary ultrasound", "fractional flow reserve", "intermediate coronary stenosis", and "coronary stenosis". No time restriction for publication date was used. All titles and abstracts of the articles were evaluated. After exclusion based on the title and abstract, full articles were evaluated, and articles meeting the inclusion criteria were identified. In addition, a manual search of the reference lists of the identified studies was performed, and references were evaluated. Selected studies were reviewed and relevant patient characteristics and parameters obtained by OCT or IVUS and FFR values were registered. Extracted parameters were the number of included coronary lesions, degree of stenosis, OCT/IVUS derived-MLA or MLD cut-off value, FFR ischemic threshold. In addition, sensitivity/specificity value for OCT or IVUS-derived MLA/MLD in predicting ischemic FFR values were also extracted.

### Results

A total number of 191 articles were found from which 25 studies [6, 8-31] were included for

final data analysis. Among these, seven articles [6, 8-13] investigating OCT, 19 IVUS [9, 14-31], and 1 study [9] investigated both OCT and IVUS. All studies used FFR to identify hemodynamically coronary stenoses.

# Correlation between OCT measurements and FFR

Seven studies [6, 8-13] evaluated the relation between OCT-derived lumen measurements and FFR. Table 1 summarise the baseline patient and lesion characteristics of the study population. These 7 studies included a total of 343 patients (450 nonobstructivelesions). Quantitative measures of intermediate coronary stenosis by angiography that arise from 40% to 70%. Six studies used FFR ≤0.80 as a cut-off value [6, 9-13], one study [8] showed that FFR <0.75 is the threshold for diagnosing functionally significant stenosis. Table 2 provides detailed data on sensitivity, specificity, accuracy and other selected characteristics from published articles. MLD sensitivity ranged from 70% to 90.3%, MLA sensitivity ranged from 70% to 93.5%. Whereas MLD specificity ranged from 67% to 87%, MLA specificity ranged from 63% to 97%. A good correlation was found between OCT derived MLD/MLA and FFR ischemic threshold based on the results of diagnostic accuracy except for Stefano GT et al. [6].

Stefano GT *et al.* [6] were the first to determine the correlation between FFR and OCT derived lumen measurements in 14 patients with 18 stenoses. They found a potential complementary role of physiological and anatomical assessment to guide decision making in the evaluation of intermediate coronary artery stenosis. Since then, more researches found OCT combined with FFR has the potential to become

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Study	Cut-off value	AUC	Diagnostic accuracy	Sensitivity	Specificity	Main outcome
Stefano GT et al, 2011 [6]	NP	NP	NP	NP	NP	This is the first description of a potential complementary role of FD-OCT and FFR to guide decision making in the evaluation of intermediate coronary artery stenosis.
Shiono Y et al, 2012 [8]	MLD: 1.35 mm MLA: 1.91 mm²	MLD: 92% MLA: 90%	MLD: 85.5% MLA: 85.4%	MLD: 90.3% MLA: 93.5%	MLD: 80.6% MLA:77.4%	Anatomical measurements of coronary stenosis obtained by OCT show significant correlation with FFR.
Gonzalo N et al, 2012 [9]	MLD: 1.34 mm MLA: 1.95 mm²	MLD: 74% MLA: 73%	MLD: 73% MLA: 72%	MLD: 82% MLA: 82%	MLD: 67% MLA: 63%	OCT has a moderate diagnostic efficiency in identifying coronary stenosis with an associated FFR <0.80 and OCT is slightly more efficient than IVUS, particularly in vessels <3 mm.
Pawlowski T et al, 2013 [10]	MLD: 1.28 mm MLA: 2.05 mm <sup>2</sup>	MLD: 90% MLA: 91%	MLD: 87% MLA:87%	MLD: 71% MLA: 75%	MLD: 84% MLA: 90%	OCT-derived MLA have a significant correlation with FFR ( $r^2$ =0.63, P<0.05). Vessel size influenced the OCT cut-off value.
Pyxaras SA et al, 2013 [11]	MLD: 1.53 mm MLA: 2.43 mm <sup>2</sup>	MLD: 88% MLA: 89%	MLD: 80% MLA: 87%	NP	NP	Correlation coefficients between OCT and FFR data were weak ( $r^2$ =0.28, P=0.001 for MLD and $r^2$ =0.23, P=0.003 for MLA).
Reith S et al, 2014 [12]	MLD: 1. 305 mm MLA: 1.64 mm <sup>2</sup>	MLD: 83% MLA: 84%	NP	MLD: 86.3% MLA: 78.8%	MLD: 69.4% MLA: 75.8%	OCT-derived MLA, MLD and percent area stenosis show a significant correlation with FFR measurements in both diabetic and non-diabetic patients.
Zafar H et al, 2014 [13]	MLD: 1. 23 mm MLA: 1.62 mm <sup>2</sup>	MLD: 76% MLA: 80%	NP	MLD: 70% MLA: 70%	MLD: 87% MLA: 97%	The FFR values and FD-OCT anatomical parameters MLA ( $r^2$ =0.4, P<0.001), MLD ( $r^2$ =0.28, P<0.001) were found to be significantly correlated. The diagnostic efficiency of MLA in identifying significant stenosis in vessels <3 mm washigh.

### Table 2. Relation between OCT-derived lumen measurements and FFR ischemic threshold

OCT, optical coherence tomography; FFR, fractional flow reserve; MLD, minimal lumen diameter; MLA, minimal lumen area.

Study	Number of lesions (subjects)	Percentage diameter stenosis (%)	FFR cut-off value
Takagi A et al, 1999 [14]	51 (42)	46.16±21.8	0.75
Briguori C et al, 2001 [15]	53 (43)	52±11	0.75
Jasti V et al, 2004 [16]	55 (55)	49±15	0.75
Costa MA et al, 2007 [17]	800 (60)	45.40±9.80	0.75
Lee CH et al, 2010 [18]	94 (94)	54.1±14.0	0.75
Kang SJ et al, 2011 [19]	236 (201)	30-75	0.80
Koo BK et al, 2011 [20]	315 (300)	50.4±11.4	0.80
Ben-Dor I et al, 2012 [21]	205 (185)	48.3±9.4	0.80
Gonzalo N et al, 2012 [9]	47 (47)	50.9±7.7	0.80
Kang SJ et al, 2012 [22]	784 (692)	51.0±11.8	0.80
Cui M et al, 2013 [23]	165 (141)	59.63±11.29	0.80
Waksman R et al, 2013 [24]	367 (350)	45.3±8.7	0.80
Lopez-Palop R et al, 2013 [25]	61 (61)	40±70	0.80
Kang SJ et al, 2013 [26]	700 (700)	51.6±12.5	
Han JK et al, 2014 [27]	881 (822)	49.6±12.7	0.80
Naganuma T et al, 2014 [28]	132 (109)	50.7±13.7	0.80
Voros S et al, 2014 [29]	85(85)	55.3±19.5	0.75
Yang HM et al, 2014 [30]	206 (206)	54.3±8.3	0.80
Park SJ et al, 2014 [31]	112 (112)	46.9±11.4	0.80

Table 3. Correlation between IVUS and FFR study characteristics

FFR, fractional flow reserve.

a valuable tool for the assessment of coronary artery stenosis. However, the variation of MLA threshold to identify ischemia lesions is quite wide, from 1.62 mm<sup>2</sup> to 2.43 mm<sup>2</sup> among these published studies. We also found that the value of MLA to identify ischemia lesions has an excellent specificity (63-97%) and high accuracy (72-87%) in these studies. Reith S *et al.* study [12] demonstrated that the correlation between OCT-derived intraluminal parameters and FFR values appear to be reliable in both diabetic and non-diabetic patients with intermediate coronary lesions.

Despite the heterogeneity of the patients studied, five of these seven studies [8-10, 12, 13] reported OCT-derived anatomical parameters and FFR values have a moderate or significant correlation in the evaluation of intermediate coronary artery stenosis. Pyxaras SA *et al.* [11] conduct a comparison study between 3-dimensional quantitative coronary angiography (3D-QCA) with OCT and FFR in the assessment of intermediate coronary lesions. They found that stronger correlation between FFR and 3D-QCA, as opposed to OCT. Correlation coefficients between OCT and FFR data were weak ( $r^2$ =0.28, *P*=0.001 for MLD and  $r^2$ =0.23, *P*=0.003 for

MLA). The author analysed the vessel bending angle cause inaccurate lumen dimensions may explain why correlation coefficients with FFR were significantly higher for 3D-QCA than for OCT. In order to enhance the accuracy of OCT in predicting FFR values, Guagliumi G established a new method for evaluating lesion severity, vascular resistance ratio (VRR), a measure of blood flow resistance derived from volumetric FD-OCT lumen profiles. The VRR-FFR relationship was evaluated in 21 patients, the results showed VRR have a stronger linear correlation with FFR measurements in evaluating lesion severity [7]. Thus, OCT-derived lumen parameters may be a useful criterion for excluding hemodynamically significant stenosis.

# Correlation between IVUS measurements and FFR

Nineteen studies [9, 14-31] including a total of 4,305 patients (5,349 non-obstructive lesions), provided IVUS measurements (MLA, MLD) with FFR. The majority of the studies used FFR ≤0.80 as a cut-off value except for six studies [14-18, 29]. Nineteen studies [9, 14-31] evaluated the relation between IVUS-measured MLA and FFR ischemic threshold, the sensitivity

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Study	Cut-off value	AUC	Diagnostic accuracy	Sensitivity	Specificity	Main outcome
Takagi A et al, 1999 [14]	MLA: 2.36 mm <sup>2</sup>	NP	NP	MLA: 83.0%	MLA: 92.3%	MLA measured by IVUS showed a significant correlation with the FFR values.
Briguori C et al, 2001 [15]	MLD: 1.9 mm MLA: 3.9 mm <sup>2</sup>	MLD: 79% MLA: 79%	NP	MLD: 100.0% MLA: 92.0%	MLD: 66% MLA: 56%	MLA ${\leq}4.0$ mm², MLD ${\leq}1.8$ mm reliably identified functionally critical intermediate coronary stenosis.
Jasti V et al, 2004 [16]	MLD: 2.8 mm MLA: 5.9 mm <sup>2</sup>	NP	MLD: 96% MLA: 94%	MLD: 93% MLA: 93%	MLD: 98% MLA: 94%	Strong correlations between FFR and MLD ( $r^2$ =0.79, P<0.0001) and MLA ( $r^2$ =0.54, P<0.0001) among patients with left main coronary artery stenosis.
Costa MA et al, 2007 [17]	MLA: 3.33 mm <sup>2</sup>	NP	NP	NP	NP	There was no correlation between IVUS and FFR in small coronary disease (Reference diameter ${\rm <2.8\ mm}$ ).
Lee CH et al, 2010 [18]	MLA: 2.0 mm <sup>2</sup>	NP	NP	MLA: 82.35%	MLA: 80.77%	IVUS-derived MLA predicted a FFR of <0.75 with good sensitivity and specificity in small coronary disease (Reference diameter <3 mm).
Kang SJ et al, 2011 [19]	MLA: 2.42 mm <sup>2</sup>	MLA: 80%	MLA: 68%	MLA: 90%	MLA: 60%	MLA <2.4 $\rm mm^2$ was the best cut-off value to predict FFR <0.80 with a high sensitivity.
Koo BK et al, 2011 [20]	MLD: 1.5 mm MLA: 2.75 mm <sup>2</sup>	NP	NP	MLD: 69% MLA: 69%	MLD: 63% MLA: 65%	IVUS diagnostic criteria varied according to lesion location and anatomic variation of the coronary artery.
Ben-Dor I et al, 2012 [21]	MLA: 3.09 mm <sup>2</sup>	MLA: 73%	NP	MLA: 69.2%	MLA: 79.5%	There was moderate correlation between FFR and IVUS-derived MLA ( $r^2$ =0.36, P<0.001), and MLD ( $r^2$ =0.25, P<0.001). The correlation was better for larger-diameter vessels.
Gonzalo N et al, 2012 [9]	MLD: 1.59 mm MLA: 2.36 mm <sup>2</sup>	MLD: 67% MLA: 63%	MLD: 66% MLA: 66%	MLD: 67% MLA: 67%	MLD: 65% MLA: 65%	No significant correlation between FFR value and IVUS measurements (MLA: $r^{2}$ =0.01, P=0.4; MLD: $r^{2}$ =0.03, P=0.2).
Kang SJ et al, 2012 [22]	MLA: 2.4 mm <sup>2</sup>	MLA: 77%	MLA: 69%	MLA: 84%	MLA: 63%	IVUS-derived MLA poorly predicted FFR < 0.80 with an overall diagnostic accuracy 69%.
Cui M et al, 2013 [23]	MLD: 1.88 mm MLA: 3.27 mm <sup>2</sup>	MLD: 64.8% MLA: 70.9%	MLD: 69% MLA: 73.6%	MLA: 71.4%	MLA: 67.0%	There was a moderate correlation between IVUS parameters (MLA: r²=0.442, P<0.001; MLD: r²=0.372, P<0.001) and FFR.
Waksman R et al, 2013 [24]	MLA: 3.07 mm <sup>2</sup>	MLA: 65%	NP	MLA: 64%	MLA: 64.9%	Anatomic measurements by IVUS show a moderate correlation with the FFR values.
Lopez-Palop Z et al, 2013 [25]	MLA: 3.1mm <sup>2</sup>	MLA: 77%	NP	MLA: 96%	MLA: 53.6%	The correlation between MLA and FFR is weak ( $r^2=0.4$ ; P=0.003) in long coronary lesions.
Kang SJ et al, 2013 [26]	MLA: 2.51 mm <sup>2</sup>	MLA: 76.2%	NP	MLA: 82%	MLA: 62%	The MLA correlated with FFR ( $r^2$ =0.463, P<0.001).
Han JK et al, 2014 [27]	MLA: 2.75 mm <sup>2</sup>	MLA: 64.6%	MLA: 62%	MLA: 61%	MLA: 63%	Best cut-off value of MLA to define the functional significance was 2.75 $mm^2$ in Asians and 3.0 $mm^2$ in Westerners.
Naganuma T et al, 2014 [28]	MLA: 2.70 mm <sup>2</sup>	MLA: 82.2%	MLA: 77.3%	MLA: 79.5%	MLA: 76.3%	A significant correlation between MLA (cut-off value was 2.84 mm <sup>2</sup> in reference diameter vessel (RVD) $\geq$ 3.0 mm; and 2.59 mm <sup>2</sup> in those with RVD <3.0 mm) and FFR.
Voros S et al, 2014 [29]	MLD: 1.73 mm MLA: 2.68 mm <sup>2</sup>	MLD: 71% MLA: 75%	MLD: 61% MLA: 78%	MLD: 80% MLA: 70%	MLD: 57% MLA: 80%	IVUS parameters (MLA: $r^2$ =0.25, P=0.04; MLD: $r^2$ =0.29, P=0.02) correlated with FFR.
Yang HM et al, 2014 [30]	MLA: 3.2 mm <sup>2</sup>	MLA: 78%	NP	MLA: 85.1%	MLA: 66.7%	IVUS parameters correlated with functional significance.
Park SJ et al, 2014 [31]	MLD: 1.9 mm MLA: 4.5 mm <sup>2</sup>	MLD: 75% MLA: 83%	NP	MLD: 64% MLA: 77%	MLD: 75% MLA: 82%	MLA ${\leq}4.5~\text{mm}^2$ is a useful index correlated with FFR value ${\leq}0.80$ in intermediate left main coronary artery stenosis.

### Table 4. Relation between IVUS -derived lumen measurements and FFR ischemic threshold

IVUS, intravascular ultrasound; FFR, fractional flow reserve; MLD, minimal lumen diameter; MLA, minimal lumen area; AUC, area under the curve; NP, not reported.

ranged from 61% to 93%, the specificity ranged from 53.6% to 94%. Seven studies [9, 15, 16, 20, 23, 29, 31] investigated IVUS-measured MLD and FFR, the measured sensitivity ranged from 64% to 100%, the specificity ranged from 57% to 98%. Overall, the regression analysis showed significant correlation between FFR value and IVUS measurements except for three studies [9, 17, 22]. A summary of these studies is provided in **Tables 3, 4**.

Of the IVUS-derived measurements, MLA cutoff values to predict FFR had been widely reported. The correlation between MLA cut-off points and ischemic FFR threshold ranged from 2.0 mm<sup>2</sup> to 3.9 mm<sup>2</sup> in non-left main coronary artery (LMCA) intermediate stenosis and from 4.5 mm<sup>2</sup> to 5.9 mm<sup>2</sup> in LMCA stenosis. One of the main reasons for the wide variation of the IVUS-derived MLA that correlates with ischemic FFR value among published studies reflects the great spectrum of anatomical variations of the intermediate coronary artery disease and makes it difficult to determine a single cut-off point to guide decision making in the revascularization.

Takagi *et al.* [14] first reported IVUS-derived MLA <3.0 mm<sup>2</sup> predicted FFR <0.75 with a sensitivity 83% and specificity 92%. The combination of the MLA and area stenosis had 100% sensitivity and 90% specificity to predict FFR. Ten studies [9, 14, 18-20, 22, 26-29] reported smaller MLA cut-off points ranged from 2.36 mm<sup>2</sup> to 2.75 mm<sup>2</sup>. With regard to IVUS-MLD, the cut-off values stable compared with MLA. Six studies [9, 15, 20, 23, 29, 31] reported the MLD <2.0 mm at the lesion site in predicting functional ischemia.

The FIRST (Fractional Flow Reserve and Intravascular Ultrasound Relationship) study, based on a multicenter, prospective registry in the USA and Europe proposed 3.07 mm<sup>2</sup> as a best cut-off value to define the presence of myocardial ischemia [24]. Han JK et al. study [27] is the largest sample-size up to date and an international multicenter study with 822 patients (881 lesions), the pooled analysis found that best cut-off value of IVUS-MLA to define the functional significance (FFR <0.8) was 2.75 mm<sup>2</sup>, further subgroup analysis showed that ethnicity influenced on the cut-off value of MLA, it was 2.75 mm<sup>2</sup> in Asians and 3.0 mm<sup>2</sup> in Westerners. However, another study revealed that there is no significant correlation

between FFR value and IVUS measurements on the regression analysis. In this study, MLA optimal cut-off values in identifying stenoses with FFR ≤0.80 was 2.36 mm<sup>2</sup> (67% sensitivity, 65% specificity, diagnostic accuracy 66%) [9]. We carefully reviewed this study and found important reasons in the diagnostic efficiency of IVUS to assess hemodynamic stenotic relevance was low, which include the following: (1) this is a head-to-head comparison with OCT and IVUS in identifying hemodynamically severe coronary stenosis study, the results showed OCT is slightly more efficient than IVUS in the assessment of functional stenosis severity, particularly in vessels <3 mm; (2) IVUS was not performed in all cases compared with OCT; (3) It is also important to notice that luminal diameter between OCT and IVUS are not necessarily equivalent, luminal areas measured by IVUS have been shown to be larger than those measured by OCT systems. All these could contribute to a low sensitivity of IVUS for stenosis detection in this study.

Among these included studies, a study by Costa MA et al. [17] indicated that IVUS anatomical parameters are limited in determining the hemodynamic significance of small coronary disease. While Gonzalo N et al. study [9] suggested that OCT is slightly more efficient than IVUS in the assessment of functional stenosis severity, particularly in vessels <3 mm. Kang SJ et al. [22] found that age, gender, target vessel, lesion location, lesion length, and plaque rupture affected IVUS-measured MLA criterion and diagnostic accuracy. A meta-analysis of 11 studies comparing IVUS-MLA versus FFR for assessment of intermediate lesions showed that the weighted overall mean MLA cut-off was 2.61 mm<sup>2</sup> in non-LMCA and 5.35 mm<sup>2</sup> in LMCA to predict a functional stenosis [32]. Several trials have evaluated IVUS has a relatively strong correlation with FFR in evaluating intermediate LMCA stenosis [16, 31]. Limited variability in LMCA length, diameter, and amount of supplied myocardium might explain the better correlation in LMCA than non-LMCA stenosis.

### When to use IVUS or OCT with FFR in the management of intermediate coronary lesions

At present, there is no single intravascular imaging modality defined as "gold-standard" for the assessment of atherosclerotic plaques. Both IVUS and OCT can be used to visualize MLD, MLA, lesion length, calcium, fibrosis and lipids. IVUS or OCT have unique features and intrinsic shortcomings. According to the literature, when it comes to evaluation of left main and bifurcation lesions, IVUS tends to be better. OCT is an advanced imaging technique that enables ultra-high resolution evaluation of vascular biology. For this reason, previously difficult to image neointimal hyperplasia, plaque composition, thin-cap fibroatheromas (TCFA), intraluminal thrombus or plaque vulnerability can be seen with OCT [33].

### Clinical outcomes

To date, no prospective randomized studies have been performed to demonstrate the superiority of IVUS/OCT versus FFR integration is associated with improved clinical outcomes in comparison with FFR or coronary angiography alone. However, the authors acknowledge these combined anatomic-functional assessments could be complementary techniques to be used in the catheterization laboratory to provide additional information that permit more accurate decisions in the management of intermediate artery stenosis and identify patients with ischaemia-causing stenosis who may benefit from revascularization. Therefore, an integrated anatomic-physiologic-based revascularization in intermediate lesions results in avoiding unnecessary procedures, reducing medical costs, and improving each patient's clinical outcomes.

### Future directions and conclusions

The management of patients with angiographically intermediate coronary lesions is a major clinical issue, the present study represents the first structured review focusing on anatomic versus physiologic assessment of intermediate coronary lesions, and indicates that a good correlation between FFR and OCT versus IVUS from currently available evidence. FFR provides validated functional insights, while OCT versus IVUS provides image-based lesion assessment, both techniques representing the gold standard for functional and anatomical definition of coronary stenosis severity. Their use may improve the decision making process in patients with angiographically intermediate coronary lesions.

The guidelines recommended that coronary intervention should be preceded by objective

evidence of myocardial ischemia [34]. Nevertheless, the present cost of imaging catheters sometimes do not allow for the use of multimodalities. Clinical co-registration of FFR pull back and intracoronary imaging modalities may be an important tool to reduce the risk of myocardial ischemia.

Although most studies indicate that FFR and OCT/IVUS-derived intraluminal measurements are significantly correlated and OCT/IVUS predicts hemodynamically relevant coronary stenosis with moderate diagnostic efficiency. However, intraluminal anatomic parameters influenced by vessel sizes, lesion location, plaque severity, and ethnicity. In addition, catheter-based imaging in coronary arteries may be sensitive to cardiac motion artifacts and wire tension movements also account for the intraluminal anatomic parameters variation. In order to solve the above problems, a series of solutions should be developed, including combined IVUS and OCT with FFR in a single catheter, which allows integration of coronary anatomy and physiologic information. Moreover, IVUS/ OCT integrated systems but also motorized FFR pullback and non-invasive imaging modalities should be connectable. Thus, the operator should be able to see the corresponding information of the complementary imaging modality just by pointing at any region of interest.

In conclusion, the correlation between FFR and cross-section information on vascular elements provided by OCT and IVUS in identifying intermediate coronary artery stenosis is promising based on the published evidence. A further randomized controlled study with a large sample and long follow-up is warranted to provide more evidence to support the strategy.

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### Disclosure of conflict of interest

None.

Address correspondence to: Dr. Bu-Chun Zhang, Department of Cardiology, The Affiliated Hospital of Xuzhou Medical College, 99 West Huai-Hai Road, Xuzhou 221002, Jiangsu Province, China. Tel: 086-561-85806997; Fax: 086-561-85802753; E-mail: zhangbc138@sina.com.cn

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