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Impact of Lesion Length on Functional Significance in Intermediate Coronary Lesions

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Abstract

Introduction: The present study aimed at assessing the role of lesion length in predicting Fractional Flow Reserve (FFR) value for physiological evaluation of intermediate coronary lesions.

Methods: In the current study, 68 patients with 83 coronary lesions were enrolled. All of the patients in this study underwent routine coronary angiography, according to appropriate indications. To evaluate physiologically significant intermediate coronary stenosis (defined between 40% and 70% on visual estimation), the Fractional Flow Reserve (FFR) study was performed and the Quantitative Coronary Angiography (QCA) data were also assessed for measurement of lesion length. The correlation between QCA data and FFR values was also examined.

Results: Eighty-three lesions were evaluated from 68 patients. Stenosis was considered physiologically significant when FFR was lower than 0.75. The FFR was significant in twelve lesions (14.5%). There was a negative correlation between FFR value and lesion length (r = -0.294 and P = 0.013). Moreover, lesion length in physiologically significant FFR group (21.07 ± 6.9) was greater than that of the non-significant FFR group (15.23 ± 6.5) (P value < 0.05). Furthermore, the correlation between QCA data and FFR values was also investigated, yet, there was only a positive correlation between FFR and Minimum Luminal Diameter (MLD) values (r = 0.248 and P value = 0.04). The Receiver Operating Characteristic (ROC) curve analysis for predicting the significant FFR value demonstrated that a lesion length greater than 17.5 mm was the best cut-off point for prediction of the significant FFR value with acceptable sensitivity and specificity of 83.3% and 68.8%, respectively.

Conclusions: There is a negative correlation between lesion length and FFR value in intermediate coronary lesions. In addition, a lesion length greater than 17.5 mm is the best cut- off point for prediction of significant FFR values.

INTRODUCTION

The benefits of Percutaneous Coronary Intervention (PCI) are mainly due to the reduction of myocardial ischemia; therefore, clinical practice guidelines currently recommend performing PCI only when symptoms and/ or myocardial ischemia are identified [1-3]{Brueren, 2002 #2;Levine, 2011 #3;Wijns, 2010 #1}. The assessment of a coronary lesion with intermediate severity (defined as luminal narrowing with 40% to 70% diameter stenosis) continues to be a challenge for cardiologists. This has resulted in inappropriate stenting of functionally non-significant lesions, because they were deemed non-significant based on angiographic data as well as inappropriate deferral of physiological significant lesion only based on visual angiographic assessment. In order to overcome these limitations, physiological testing is often conducted before proceeding with coronary interventions [1, 4]. The functional significance of coronary stenotic lesions is governed by the degree of stenosis as well as features such as shape, length, eccentricity of the lesion, collateral routes of perfusion, and vasomotor tone among others. These physical constraints and the resultant flow characteristics contribute

to the disparity between angiographic and corresponding physiologic assessment of disease severity [5]. The accuracy of Fractional Flow Reserve (FFR) for assessment of functional significance of a coronary stenosis has been well established. Improved clinical outcomes have been demonstrated in clinical trials when the decision to perform PCI was based on FFR [5]. Coronary angiography often underestimates or overestimates the functional severity of the lesions. Although such a "visual-functional mismatch" is frequently encountered, the mechanism of this phenomenon is poorly understood. This issue has important implications for many physicians attempting to overcome angiography-dependent decision-making to avoid unnecessary revascularization procedures [4-8]. There are studies suggesting a correlation between lesion length and FFR values [9]; and have indicated that employing this parameter in the setting of inability to access FFR for prediction of significant stenosis could be useful [10]. There are various lesion lengths from 10 mm to 28 mm, which were considered as cut-off points for prediction of physiologically significant FFR (< 0.75) in multiple studies [9-12]. Thus, this study aimed at investigating the correlation between lesion length and FFR values.

METHODS

This study was a prospective single center observational study (Modarress Hospital), and the study protocol was approved by the institutional review board of Cardiovascular Research Center of Shahid Beheshti University of Medical Sciences. All patients, who were enrolled in the present research, provided a written informed consent. All patients in this study underwent routine coronary angiography due to appropriate indications. To evaluate physiologically significant intermediate coronary stenosis (defined between 40% and 70% on visual estimation) the FFR study was carried out, and Quantitative Coronary Angiography (QCA) data were also assessed for measurement of lesion length. In this study, the correlation between QCA indices and FFR values was appraised. Some lesions and patient characteristics were excluded from the study. The exclusion criteria were as follow, multiple stenosis within a single target vessel (the lesions were considered separate if they were more than 3 reference vessel diameters apart), bypass graft lesions, left main lesions, side branch lesions, in-stent restenosis, previous percutaneous coronary intervention in the target vessel, culprit vessels in the setting of a myocardial infarction, previous history of myocardial infarction in target vessel territory, Thrombolytic in Myocardial Infarction (TIMI) flow grade < 3 and angiographic thrombi-containing lesions.

Fractional Flow Reserve (FFR)

"Equalizing" was performed with the guide wire sensor positioned at the guiding catheter tip. A 0.014-inch pressure guide wire (Radi, St. Jude Medical, Uppsala, Sweden) was then advanced distal to the stenosis. The FFR was measured at the maximal hyperemia induced by the intra-coronary administration of 200 micrograms of nitroglycerin, and intra-coronary adenosine was infused (200 micrograms for right coronary artery and 300 micrograms for Left Anterior Descending (LAD) or Left Circumflex Artery (LCX)). Stenosis was considered significant when FFR was < 0.75.

Quantitative Coronary Angiography

The patients initially underwent routine coronary angiography. The angiographic cine images were acquired at 15 frames per second (Axiom ArtisII, Siemens, Germany). Two-dimensional quantitative coronary angiography was performed off-line (using standard commercial software, SYNGO, Siemens). All analyses were conducted during electrocardiography-gated end-diastolic frame. The angiographic views with the least foreshortening and yielding the best depiction of stenosis were utilized. Edge detection correction was conducted whenever required. Minimum Luminal Area (MLA), percentage area of stenosis, Minimum Luminal Diameter (MLD), percentage diameter of stenosis and lesion length was measured, using 2D-QCA. All measurements were performed twice and were averaged by a single experienced cardiologist blinded to the FFR results. The intra-observer variability was determined as 0.91 (0.79 to 0.96)). For data analysis, the SPSS 20 software was applied and the correlation between the quantitative variables was evaluated by Pearson's correlation coefficient and Spearman rank correlation. In order to define the cut-off points for prediction of FFR, the Receiver Operator Characteristic (ROC) curve analysis was employed.

RESULTS

In this study, 83 lesions in 68 eligible patients, who underwent coronary angiography, were assessed, and the FFR and QCA parameters were measured. The baseline characteristics of the patients are provided in Table 1.

Table 1: Baseline Characteristics of the Patients

Patients characteristics	Mean (SD) or N (%)
Age, y	59.7 (8.9)
Male, n	45(66.2)
Diabetes mellitus, n	24 (35.5)
Hypertension, n	35 (51.5)
Dyslipidemia, n	32(47.1)
Smoking, n	8 (11.8)
Positive familial history, n	8(11.8)
Chronic stable angina	46 (56.8)
Unstable angina	33(42.2)
NSTEMI	1 (1.1)
LAD	55 (66.3)
LCX	15 (18)
RCA	13 (15.6)

NSTEMI: Non-ST Segment Elevation Myocardial Infarction; LAD: Left Anterior Descending; LCX: Left Circumflex Artery; RCA: Right Coronary Artery;

The average age was 60.6 years. Forty-five (66%) patients were male and twenty-three were female. Hypertension was the most prevalent risk factor (51.5%) in the patients. The LAD artery was the most common culprit vessel evaluated in this study, which was involved in 55 cases (66%), while the LCX artery and RCA were involved in 15(18%) and 13 (16%) patients, respectively. The mean lesion length was 16.8 ± 6.9 mm.

Table 2: Correlation between Fractional Flow Reserve and Quantitative Coronary Angiography Data

	MLD	Ref D	MLD per	MLA circ	MLA dens	Length
FFR						
Correlation	.248*	.173	-.053	-.130	-.058	-.294*
Significance	.043*	.172	.668	.304	.646	.013*

FFR: fractional flow reserve; QCA: Quantitative Coronary Angiography; MLD: minimal luminal diameter; Ref D: reference diameter; MLD per: minimal luminal diameter percent; MLA circ: minimal luminal circular area, MLA dens: minimal luminal area density

Fractional Flow Reserve was significant in twelve lesions (14.5%). There was a negative correlation between the FFR value and lesion length (r = -0.294, P = 0.013). Furthermore, the lesion length in physiologically significant FFR group (21.07 ± 6.9) was greater than that of then non-significant ones (15.23 ± 6.5) (P value < 0.05), Table 2.

This study also evaluated the correlation between the QCA data and the FFR values, yet there was only a positive correlation between the FFR and the MLD values (r = 0.248 and P value = 0.04). The Receiver Operating Characteristic (ROC) curve analysis for predicting significant FFR value (FFR ≤ 0.75) demonstrated that a lesion length greater than 17.5 mm is the best cut-off point for prediction of a significant FFR value with acceptable sensitivity and specificity of 83.3% and 68.8%, respectively (Fig 1).

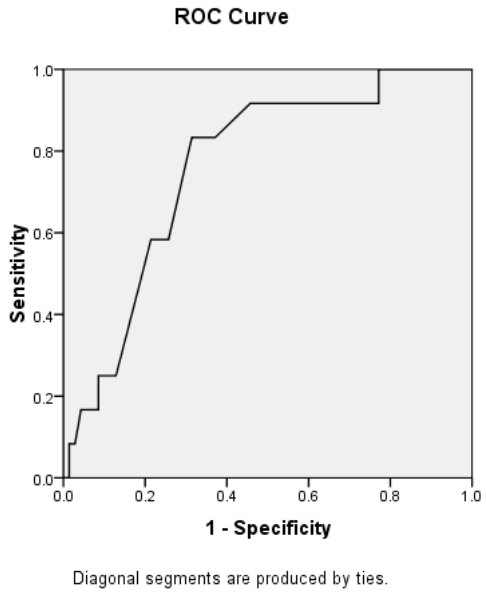

Figure 1: Receiver Operating Characteristic Curve Analysis for Predicting Significant Fractional Flow Reserve (FFR) Value (FFR ≤ 0.75).

The figure demonstrates that a lesion length greater than 17.5 mm is the best cut-off point for prediction of significant FFR value with an acceptable sensitivity and specificity of 83.3% and 68.8%, respectively.

DISCUSSION

The present study showed that the lesion length had a significant effect on intermediate stenosis. The present study proved that lesion length of more than 17.5 mm was the best cut off value for predicting physiologically significant FFR. In the DEFER study, non-significant stenosis was randomly allocated to groups to be treated either medically or by stenting. After a follow-up of 5 years, the prognosis of lesions treated medically was excellent with a mortality and myocardial infarction rate that was < 1% per year and was not improved by stenting. In the FFR-guided arm of the Fractional Flow Reserve versus Angiography for Multi vessel Evaluation (FAME) study, the lesions with an FFR of < 0.80 were stented, while PCI was deferred in lesions with FFR of > 0.80. After a follow-up of 2 years, outcome of the deferred lesions was excellent with medical treatment yielding at a rate of < 1% myocardial infarction or death [7]. The FFR-guided PCI reduced the need for revascularization for many intermediate lesions [6]. Moreover, FFR-guided Coronary Artery Bypass Grafting (CABG) was associated with a lower number of graft anastomoses and lower rate of on–pump surgery compared with angiography-guided CABG without a higher event rate during the follow up, and a lower rate of angina [8]. A sub-analysis of the FAME trial demonstrated that two-thirds of the coronary lesions with a diameter stenosis of > 50% were not ischemia producing. Conversely, for left main coronary artery lesions, approximately one-fifth of the lesions with a diameter stenosis of < 50% were producing ischemia [5-8, 13]. Thus far, only a few studies have emphasized on the lesion length in coronary stenosis. In a relatively small sample size (17 lesions) study, Takayama and Hodgson reported a positive correlation between lesion length and pressure gradient; in addition, they stated that the MLA or the lesion length measured by 3D Intravascular Ultrasound (IVUS) was the only significant independent determinant of FFR [14]. In another study, Briguri et al. reported a weak negative correlation (r = -0.41) between the FFR values and lesion length in intermediate coronary lesions. They also claimed that the ROC analysis revealed that a 10-mm lesion length was the best IVUS cutoff value for predicting the FFR values of less than 0.75 [15]; however, this cut-off value had high specificity (80%) and low sensitivity (41%), as compared to the current study. The research findings were approximately similar to those of by Igu Chi et al., indicating that a lesion length more than 16.1 mm in intermediate lesion was the predictor of FFR<80; additionally, another study in Singapore demonstrated that lesion length of >20mm was the best cut-off point for FFR < 0.75 [9-12].

The linear correlation between lesion length and coronary flow was previously demonstrated by parameters of quantitative angiography and classical fluid dynamic equations. The functional influence of length in critical stenosis could be less than that of moderate stenosis. Focal critical narrowing in shorter lesions would be the most relevant factor for blood flow impairment with the independence of lesion length. On the other hand, in longer lesions, as determined by fluid dynamic equation, the blood turbulence increases in the coronary lumen by frequent presence of irregularities, curves,

angulations, and bifurcations [12]. As defined by Poiseuill's law of fluid dynamics, the pressure gradient is influenced by coronary blood flow and viscosity, radius, and lesion length. In effect, the pressure gradient is inversely proportional to the forth power of lesion radius and disproportional to the lesion length. The current findings are consistent with this equalization. The current study revealed that a 17.5-mm lesion length cutoff value could be an indicator of functionally significant intermediate coronary lesion; however, it does not supersede the FFR whenever possible and could be a clue for functional prediction of intermediate coronary lesion with relative acceptable accuracy. This study had a number of limitations. First, the number of the included subjects was relatively small. Second, due to the fact that this study excluded the IVUS data, it was not possible not assess the relationship between the FFR and IVUS data, especially for measurement of vessel and lesion sizes. It is undeniable that the current investigation with such a sample size could not answer all the questions; however, it can be a helpful guide for future studies with large sample size and powerful meta-analyses. Lesion length evaluation is useful for prediction of physiologically significant intermediate coronary lesion with partial accuracy. Furthermore, it could be beneficial when it is impossible to access FFR.

AUTHORS' CONTRIBUTION

Conception or design of the work: Safi, Eslami
Data collection: Eslami, Safi
Data analysis and interpretation: Khaheshi, Naderian
Drafting the article: Khaheshi, Naderian, Beheshtian
Critical revision of the article: Eslami
Final approval of the version to be published: Safi, Eslami

CONFLICTS OF INTERESTS

The authors of this article declared no conflicts of interest.

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