

## UTILITY OF NON-INVASIVE CORONARY FLOW PATTERN VERSUS FRACTIONAL FLOW PRESSURE DROP FOR LEFT ANTERIOR CORONARY ARTERY STENTING

Ragab Abdelsalam mahfouz, Magdy Mohamad Abdelsemei, Tamer Mohamed Moustafa, Elsayed kamal Mohammed\*

Cardiology Department, Faculty of Medicine-Zagazig University, Egypt

### ABSTRACT

**Background and Aim:** To assess the usefulness of coronary flow reserve as a guide in patient with left anterior descending coronary artery lesion during percutaneous coronary intervention in comparison with fractional flow reserve.

**Methods:** The study included 80 patients with left anterior descending artery stenotic lesions, proved by coronary angiography, in the cardiac catheterization laboratory of the Faculty of Military Hospital, during the period from November 2012 to June 2014. All patients were subjected to all of the following: Complete history taking, full general and local examination, ECG analysis. All our patient were assessed by Doppler wire to measure pressure drop at LAD lesion and also by non-invasive coronary flow pattern utilizing transthoracic echo-Doppler study. Then we compare the results of both values on the basis of the improvement in left ventricular ejection fraction( by biplane Simpson rule) to find the cut point at which we can document that this LAD lesion deserve stenting .

**Results:** FFR was negatively correlated with significant correlation with EF improvement with R value of -0.575 and P-value of 0.008,figure. Also there is strong inversed relation with lesion percent with R-value of -0.468 and P-value of 0.01. The correlation between FFR and improvement in wall motion score was significantly inversed with R-value of -0.519 and P-value of 0.03. Also there was strong correlation between FFR and CFR ,P-value was 0.00 and R-value was +0.436.

CFR has strong reciprocal correlation with FFR (P-value was 0.00 and R-value was. inve+0.436. There is significant correlation of CFR with EF improvement with R value of -0.583and P-value of 0.002. Also there is significant correlation of CFR with lesion percent with R-value of -0.585and P-value of 0.001, figure. The correlation between CFR and wall motion score was significant with R-value of -0.393 and P-value of 0.03.

The optimal cutoff values for coronary flow reserve of <1.75 was the best value for indication of stenting of an intermediate coronary lesion. A sensitivity of 92% and a specificity of 87%. On the other hand the best cut-of value of fractional flow reserve was <0.75 for indication of stenting for an intermediate coronary artery lesion with a sensitivity of 94% and specificity of 86%.

**Conclusions:** The current study showed Coronary flow reserve measurements by TTE in the distal to mid LAD were feasible in most patients with an optimal cut-off value < 1.75 showed high accuracy to detect angiographically significant stenoses in the LAD. This is comparable to <0.75 as an optimal cut-off value of FFR to detect angiographically significant stenoses. CFR measurement utilizing TTE might be considered as a simple non-invasive tool for functional status of an intermediate coronary artery lesion for stenting.

**Key Words:** LAD (left anterior descending artery ), coronary flow reserve, fractional flow reserve.

### INTRODUCTION

Coronary flow depends on a complex multifactorial regulation mechanism that acts on the small vessels compromising microcirculation (1). The state of microcirculation is especially important in the context of revascularization after acute myocardial infarction (AMI) since it defines the quality of myocardial perfusion once the lesion responsible for the infarction has been revascularized (2).

The use of intracoronary sensor-tipped pressure and Doppler ultrasound guidewires in the interventional cardiology makes it possible to apply the findings of coronary physiology to the resolution of clinical problems. In particular, these devices have been used to diagnose myocardial viability within AMI (3) or progressive recovery

of coronary flow reserve following initial impairment after an infarction have been associated with the preservation of myocardial viability (4). In addition, the analysis of phasic coronary flow characteristics with Doppler ultrasound guidewire has been related to the degree of myocardial perfusion in AMI(5) , as well as to the recovery of postinfarction contractile function(6) and , thus, to patient prognosis(7).

The evaluation of coronary pressure by fractional flow reserve (FFR) provide direct physiological and functional significance of coronary stenosis complementary to angiographic characterization (8). In fact, it has been shown that the correlation between FFR and diameter stenosis is weak, with large overlap particularly in patients with intermediate coronary stenosis, particularly

disabling the prediction of functional significance of coronary stenosis on the basis of coronary angiography(9)

#### MATERIALS AND METHODS

Our study was conducted in Department of cardiology, Zagazek university and military hospital in Saudi Arabia and included 80 patients with documented significant left anterior descending coronary disease on the basis of coronary angiography at military hospitals during the period from 1/5/2011 to 1/9/2013.

The following patients were excluded from our study: Patients in whom CABG is the preferred treatment, patients with left main disease, patients with recent STEMI, patients with LV EF < 30%, patients with tortuous and calcific LAD precluding FFR measurement, elderly patients, patients with dyskinetic LV segments on echocardiographic assessment and patient planned for concomitant cardiac surgery.

Complete history taking, full general and local examination, ECG analysis, our patient were assessed by Doppler wire to measure pressure drop at LAD lesion and also by non-invasive coronary flow pattern utilizing transthoracic echo-Doppler study. Then we compare the results of both values on the basis of the improvement in left ventricular ejection fraction to find the cut point at which we can document that this LAD lesion deserve stenting .

#### Statistical Analysis

Continuous variables are summarized as mean  $\pm$  standard error. Analysis of variance was used to analyze the data and assess any significant linear correlations, summarized using both the Pearson ( $r$ ) and Spearman ( $\rho$ ) correlation coefficients among EF improvement, FFR, and CFR. Multiple linear regression analysis was also

conducted to compare simultaneous correlations among hemodynamic parameters.

Sensitivity and specificity estimates for each analysis are independently combined across all the studies using random effects that allow for the possibility that sensitivity and specificity estimates may differ across studies.

#### RESULTS

FFR was negatively correlated with significant correlation with EF improvement with R value of -0.575 and P-value of 0.008. Also there is strong inversed relation with lesion percent with R-value of -0.468 and P-value of 0.01. The correlation between FFR and improvement in wall motion score was significantly inversed with R-value of -0.519 and P-value of 0.03. Also there was strong correlation between FFR and CFR, P-value was 0.00 and R-value was +0.436 .

CFR has strong reciprocal correlation with FFR (P-value was 0.00 and R-value was +0.436). There is significant correlation with EF improvement with R value of -0.583 and P-value of 0.002. Also there is significant correlation with lesion percent with R-value of -0.585 and P-value of 0.001. The correlation between CFR and wall motion score was significant with R-value of -0.393 and P-value of 0.03.

the optimal cutoff values for coronary flow reserve of <1.75 was the best value for indication of stenting of an intermediate coronary lesion. A sensitivity of 92% and a specificity of 87% while the best cut-of value of fractional flow reserve was <0.75 for indication of stenting for an intermediate coronary artery lesion with a sensitivity of 94% and specificity of 86%.

**Table(1)** demographic data.

Parameter	Value		
AGE	Mean	SD	0.16
	57.28	15.4	
SEX	Male: 48	60%	0.5
	Female: 32	40%	
Current Smoking	Value	Percent	0.6
	35	43.75%	
Dyslipidemia	Value	Percent	0.01
	50	62.5%	
D.M	Value	Percent	0.2
	43	53.75%	
HTN	Value	Percent	0.01
	52	65%	
FH	Value	Percent	0.1
	46	57.5%	

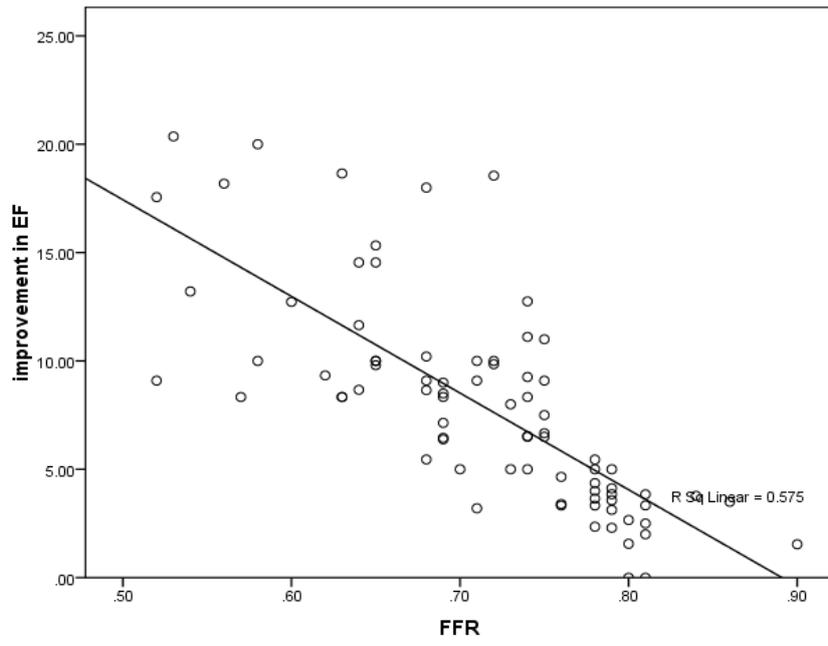


Figure (1): Correlation between FFR and EF improvement

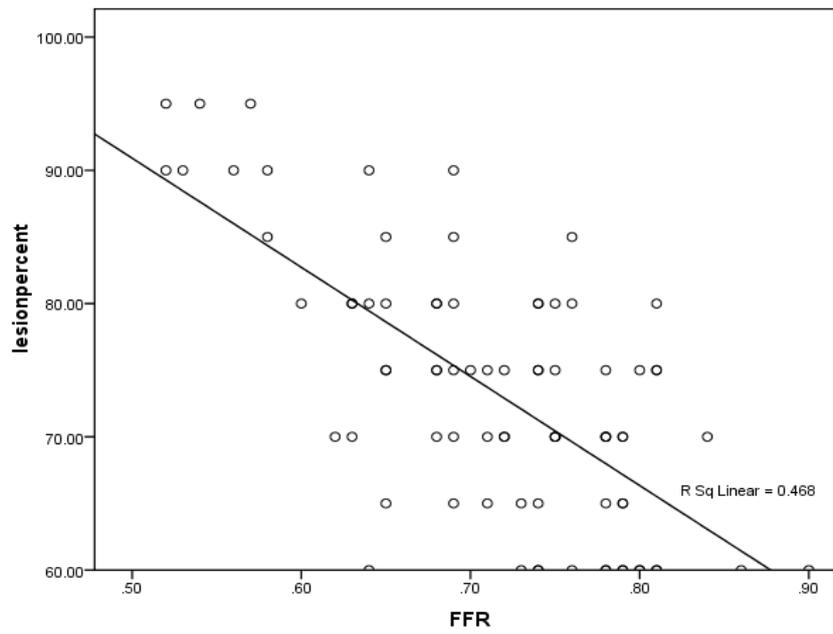


Figure (11): Correlation between FFR and lesion percent

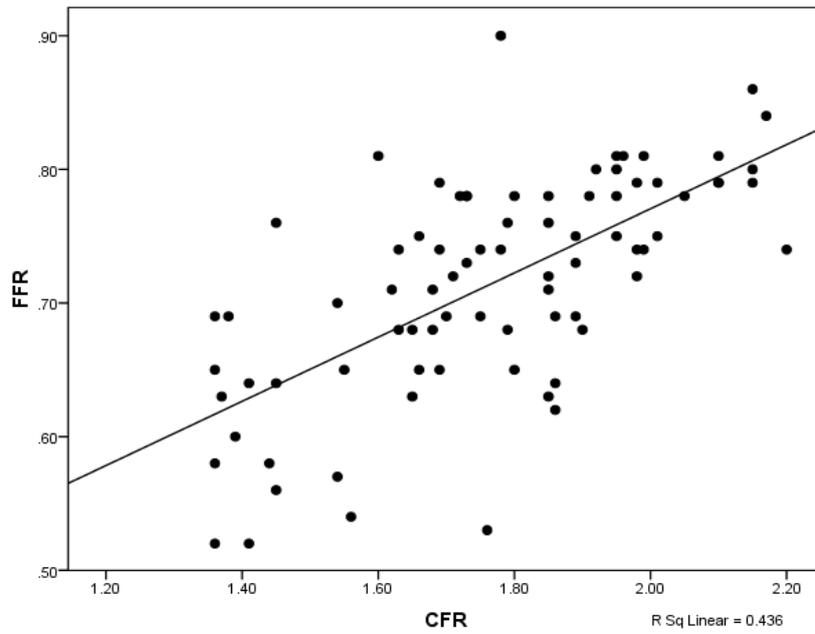


Figure (111): correlation between FFR and CFR.

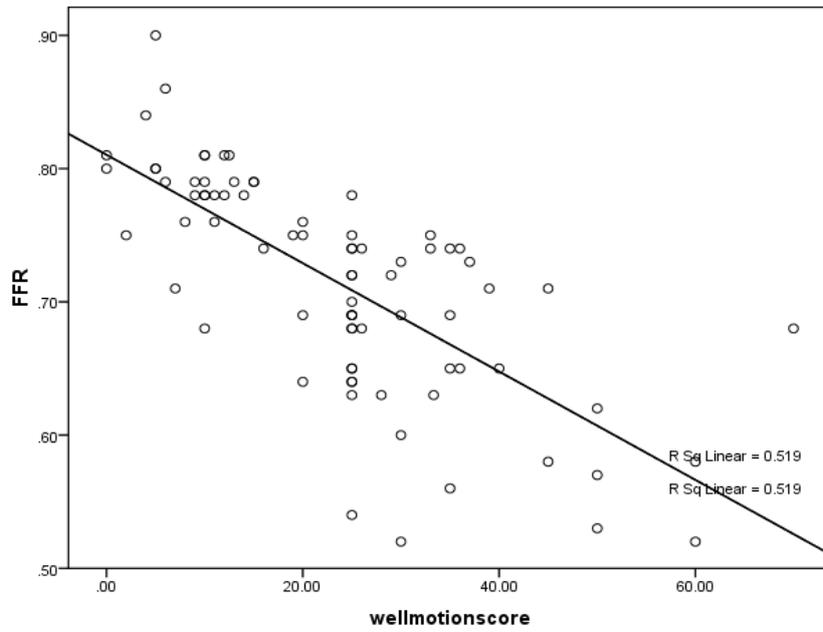
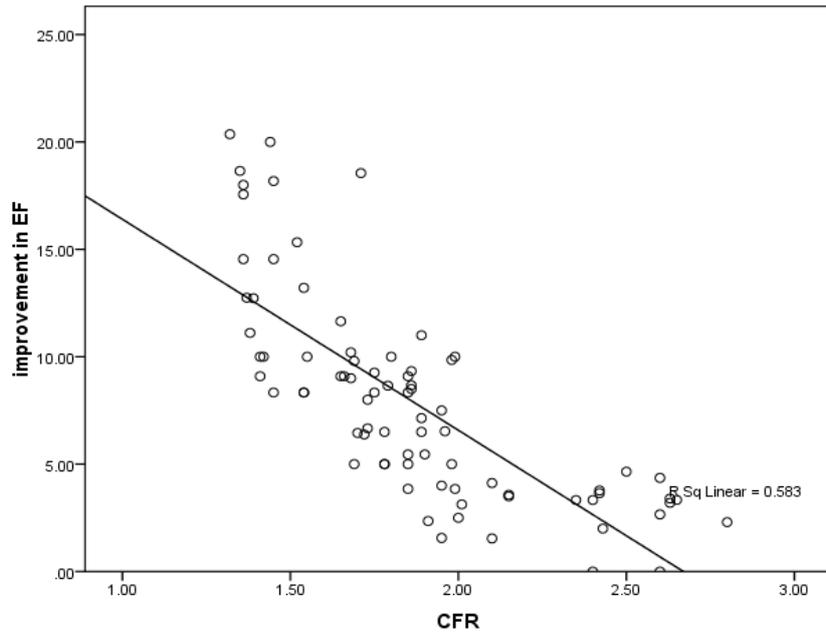
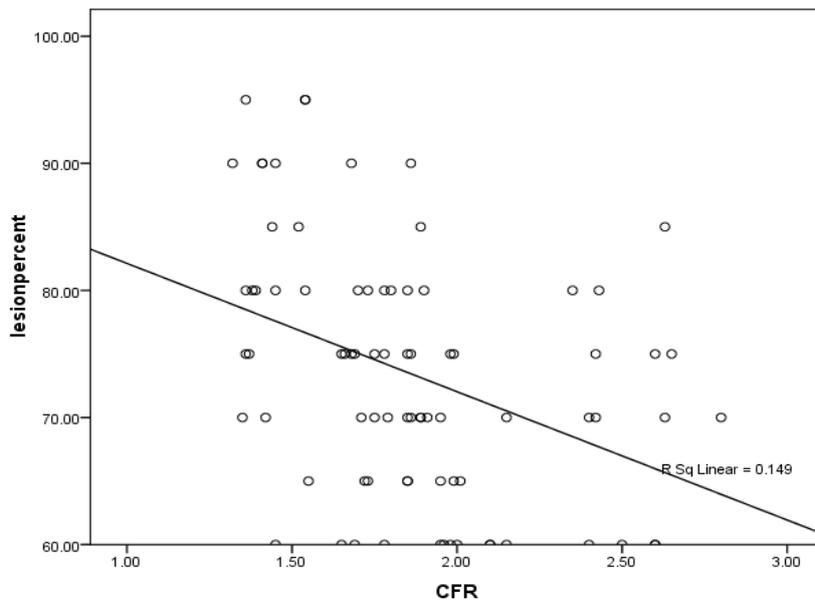


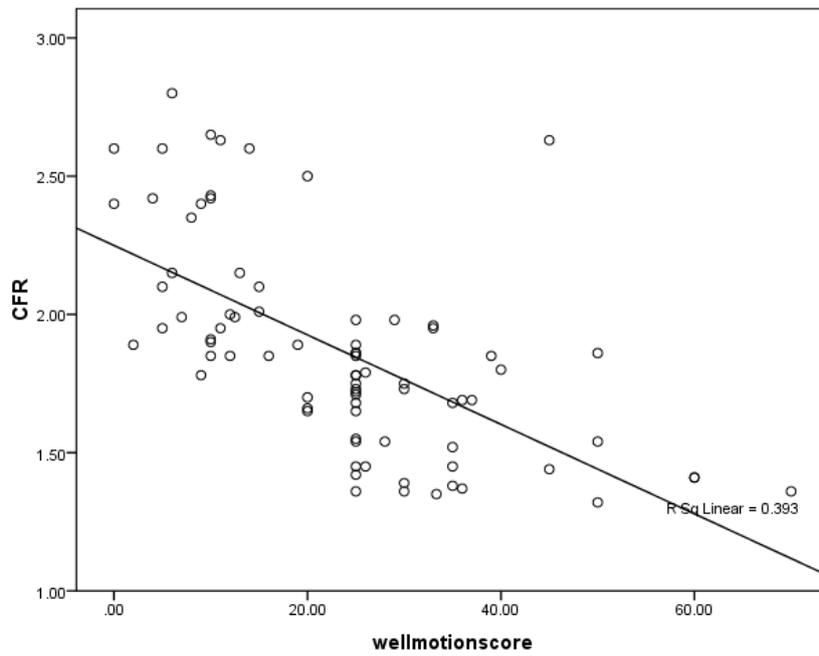
Figure (1V): correlation between FFR and wall motion score improvement



Figure(V):correlation between CFR and improvement of EF.



Figure(V1):correlation between CFR and lesion percent.



Table( V11): correlation between CFR and wall motion score improvement.

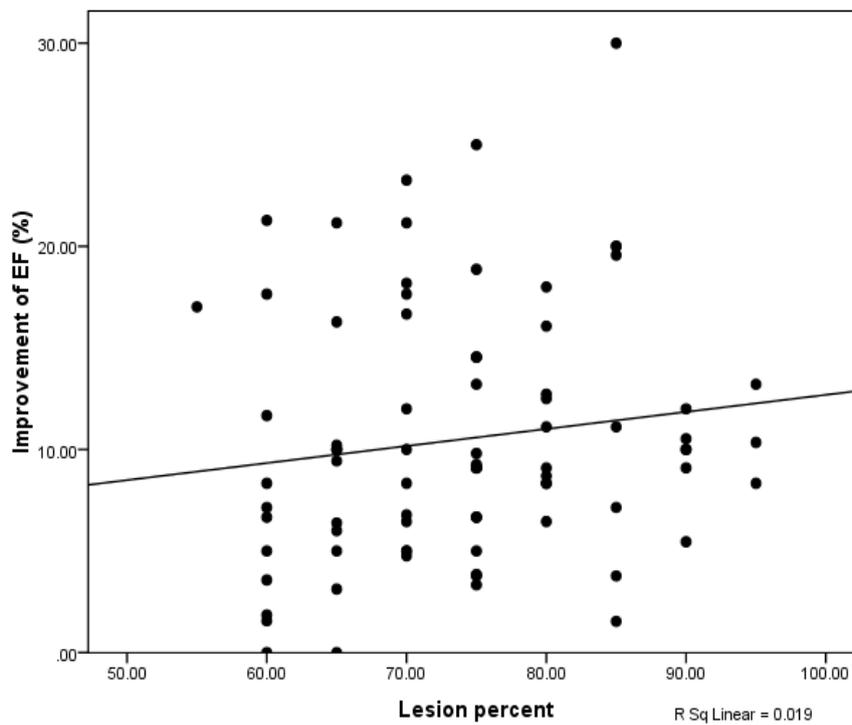
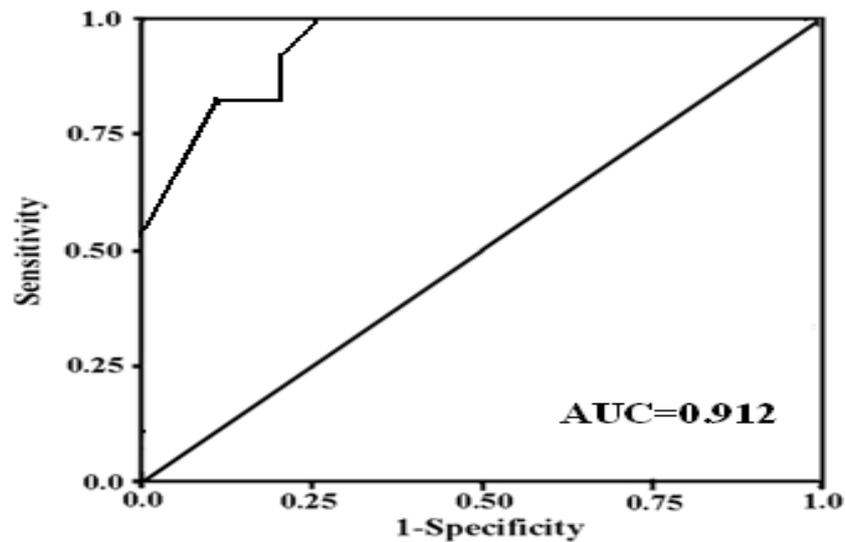
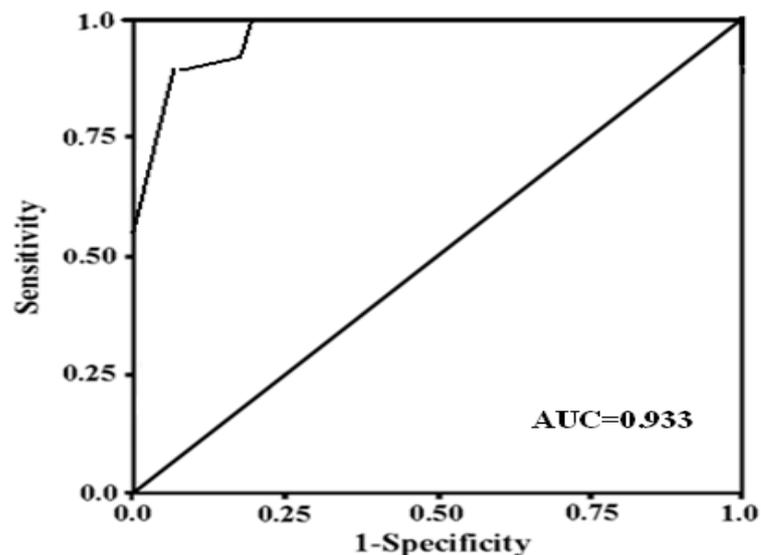


Figure (V111):correlation between lesion percent and EF improvement.



**Figure ( X ):** The receiver-operating characteristic curve of CFR with a cut-off value of  $\leq 1.62$  for indication of coronary intervention. (AUC=0.912)



**Figure ( XI ):** The receiver-operating characteristic curve of FFR with a cut-off value of  $\leq 0.75$  for indication of coronary intervention. (AUC=0.933)

## DISCUSSION

In this study of consecutively included patients with angiographically documented left anterior descending coronary artery disease, the feasibility and accuracy of diagnosing significant stenosis in the LAD, using CFR measurements on TTE and compared with findings by FFR. The main findings were that, (1) Coronary flow reserve measurements in the distal to mid LAD were feasible in the majority of patients; (2) coronary flow reserve  $< 1.75$  had high accuracy for the detection of diameter stenosis  $\geq 70\%$  as defined by CA in the LAD; (3) FFR  $< 0.75$  had high accuracy for detection of significant stenoses, as

defined by CA, and (4) CFR  $< 1.75$  was comparable to FFR  $< 0.75$  in accuracy for the detection of diameter stenosis  $> 70\%$ .

Both CFR and FFR showed positive correlations with lesion severity, with no correlations with other baseline characteristics (including diastolic blood pressure, heart rate, and rate-pressure product).

**Cortigiani et al., 2011(10)** reported that CFR  $\leq 1.91$  was the best value for diagnosing coronary stenosis of  $\geq 75\%$  in hypertensive and normotensive patients (including diabetics) with known or suspected CAD.

Miller et al., 1994 (11) found a strong correlation between CFR ( $\leq 2.0$ ) measured by the Doppler guide wire and technetium-99m sestamibi myocardial perfusion imaging results (89%). Likewise, Tron et al. 20 also found that CFR  $\leq 2.0$ , as measured by the Doppler guide wire, was a stronger predictor of abnormal myocardial perfusion (89%) than angiographic variables, such as percent lumen stenosis and minimal lumen diameter. Thus, CFR measurement by TTDE should correlate more strongly with the results of myocardial perfusion imaging than with angiographic results

Overall, our study demonstrated that CFR-derived measurements perform relatively well for the prediction of anatomic assessment of coronary stenosis. The optimal ROC-derived cut-point was  $< 1.75$  and comparable to the FFR historical cut-points  $< 0.75$  with a sensitivity and specificity of 96% and 82% and an accuracy of 89% in prediction of coronary artery stenosis  $> 75\%$ . The main novel findings of our study was that transthoracic measurements of CFR performed comparably to FFR assessment in prediction of significant coronary artery lesions, suggesting that CFR may be used as an alternative to assess functional coronary artery stenosis and to serve as gatekeeper to invasive coronary angiography in patients presenting with chest pain syndromes.

Recent studies have reported that TTDE successfully permits visualization and measurements of coronary flow velocity in the distal LAD. Furthermore, contrast-enhanced Doppler recording was recently reported to improve blood flow detection in the LAD and to increase the rate of success in obtaining spectral Doppler signals (12). In the present study, we measured CFR in the distal LAD with a high rate of success (92%), sufficiently applicable for clinical practice, using these color flow mapping and contrast-enhanced Doppler recording. A previous study has demonstrated the clinical usefulness of CFR measured by TTDE for physiologic assessment of coronary lesion severity. But they compare CFR with exercise thallium-201 single-photon emission computed tomography (13). The present study demonstrated, for the first time, to our knowledge, head to head comparison between CFR and FFR in assessment of functional coronary artery stenosis and showed that CFR measured by TTDE enables accurate physiologic assessment of the severity of LAD stenosis and predicts the results of QCA (96% sensitivity, 90% specificity). This higher accuracy may reflect its value as a physiologic index of LAD stenosis severity, as

compared with the findings of the previous study that each peak and mean CFR  $< 2.0$ , as determined by TTDE, had sensitivities of 92% and 92% and specificities of 82% and 86%, respectively, for the presence of significant angiographic stenosis. (14) Coronary flow reserve, as measured by TTDE, was reported to be clinically useful for noninvasive assessment of significant stenosis in the LAD, as compared with CFR obtained by quantitative coronary angiography (14). However, coronary angiography, even with quantitative methods, has limited reliability in predicting the physiologic significance of coronary artery stenosis (15,16,17). Many studies have demonstrated that there is a good correlation between the results of myocardial perfusion scintigraphy and intracoronary Doppler flow velocity variables, and CFR determined by the Doppler guide wire is a reliable marker of the physiologic significance of coronary artery stenosis and predicts the presence of myocardial ischemia (18). Miller et al., 1994 found a strong correlation between CFR ( $\leq 2.0$ ) measured by the Doppler guide wire and technetium-99m sestamibi myocardial perfusion imaging results (89%). Likewise, Tron et al. 20 also found that CFR  $\leq 2.0$ , as measured by the Doppler guide wire, was a stronger predictor of abnormal myocardial perfusion (89%) than angiographic variables, such as percent lumen stenosis and minimal lumen diameter. Thus, CFR measurement by TTDE should correlate more strongly with the results of myocardial perfusion imaging than with angiographic results

#### Limitations:

Our study has several limitations. First, it was a single-center study. Second, CFR can't be obtained in all studied population, and third, the small sample. In addition, our method of physiologic assessment of coronary artery stenosis with TTDE is currently restricted to the LAD, for anatomic reasons.

#### CONCLUSION

Coronary flow reserve measurements by TTE in the distal to mid LAD were feasible in most patients with an optimal cut-off value  $< 1.75$  showed high accuracy to detect angiographically significant stenoses in the LAD. This is comparable to  $< 0.75$  as an optimal cut-off value of FFR to detect angiographically significant stenoses. CFR measurement utilizing TTE might be considered as a simple non-invasive tool for functional status of an intermediate coronary artery lesion for stenting.

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