

## DIAGNOSTIC ACCURACY OF FRACTIONAL FLOW RESERVE IN DIAGNOSING STENTABLE INTERMEDIATE STENOSIS IN PATIENTS OF CORONARY ARTERY DISEASE KEEPING ANGIOGRAPHY AS A GOLD STANDARD

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### ABSTRACT

**Objective:** To determine diagnostic accuracy of fractional flow reserve in diagnosing stentable intermediate stenosis in patients of coronary artery disease keeping angiography as gold standard.

**Study Design:** Cross sectional validation study.

**Place and Duration of Study:** Cardiology ward and Coronary Care Unit of PIMS Islamabad, from Jun 2015 to Nov 2015.

**Methodology:** This study included 130 patients with coronary artery disease. General physical examination and systemic examination was done for all subjects as per protocol of inclusion and exclusion criteria. All the patients underwent Conventional angiography followed by fractional flow reserve in intermediate coronary artery disease. Diagnostic accuracy of fractional flow reserve was detected by determining sensitivity, specificity and accuracy.

**Results:** The mean age of the patients was  $56 \pm 8.790$  years, ranging from 31 to 72 years. There were 88 (67.7%) male patients and 42 (32.3%) female patients in the study. There were 31 true positive, 3 false negative and 92 were found true negative. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of fractional flow reserve for diagnosis of stentable intermediate stenosis was 91.2%, 95.8%, 88.6%, 96.8% and 94.6%, respectively.

**Conclusions:** Fractional flow reserve is a reliable test for detection of stentable intermediate stenosis among patients with coronary artery disease and should be done in every case of coronary artery disease.

**Keywords:** Coronary artery disease, Conventional angiography, Fractional flow reverse.

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### INTRODUCTION

Ischemic heart disease is emerging as one of the leading cause of death worldwide. A large number of deaths are being caused by heart diseases. An estimated 17 million deaths occur each year due to cardiovascular disease globally. Heart diseases are the most prevalent cause of death<sup>1,2</sup>. Coronary artery disease can be labeled as a shocking disease because it can cause sudden dis-ability or death in life of a person living healthy life, without any warning signs<sup>3</sup>. The treatment of coronary artery disease has many challenges involved for the physicians for better prognosis of the disease. There is a need for

making prompt diagnosis and deliver appropriate therapy expeditiously.

The coronary artery disease is equally prevalent in developed and developing countries but it has highest susceptibility in the world among Asian population of Indo-Pak region. According to some estimates, coronary artery disease is becoming leading cause of death among the Indo-Pakistan subcontinent. Its prevalence has increased almost 2.5 times from 3.6% in 1970 to 9.5% in 1990 in people of >35 years old based upon the meta-analysis of previous studies<sup>5</sup>. Ischemic changes can be monitored effectively by electrocardiography, which is a safe and operational investigation method. The electrocardiography can be very helpful in identifying the occlusive thrombus at initial stages. In such patients early percutaneous

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intervention has better results as a therapeutic option<sup>4</sup>.

There is no evidence of improvement in complaints with stenting among the patients of hemodynamically non-significant stenosis. Similarly no data is available which can favour the better prognosis with stenting among these patients, therefore a method is required to identify the patient for efficient stenting. The functional significance of angiographically equivocal stenosis can be determined competently through fractional flow reserve (FFR), because it is considered as accurate invasive index in catheterization laboratory. The revascularization of an intermediate coronary stenosis based upon FFR has excellent short term results and a better prognosis<sup>5</sup>.

The pressure behind a stenosis relative to the pressure prior to stenosis is defined as fractional flow reserve and this procedure is performed during the coronary angiography. The normal value of FFR is  $\geq 0.8$  and any value between the ranges of 0.75 to 0.80 is considered in gray zone which do not clearly indicate the decision for revascularization and require clinical verdict for final decision. Some studies have demonstrated that in patients with FFR under 0.80, the postponement of PCI can be harmful. Some recent studies have shown efficacy of using the 0.80 upper limit of this zone as threshold value to perform the PCI in order to minimize the hazard of ischemic lesion to be left untreated<sup>6,7</sup>.

The sensitivity of FFR in the identification of reversible ischemia is 90.3 percent, the specificity 82.9%, the positive predictive value 82.4 percent, the negative predictive value 90.6%, and the accuracy 86.4%. While the coronary angiography has sensitivity of 96%, specificity of 92%. Prevalence of CAD (Coronary artery disease) is 27%<sup>8-10</sup>.

In this study we did FFR of the patients who underwent angiography. We selected the patients of intermediate stenosis suitable for percutaneous coronary intervention which can't be proven just on conventional angiography whether it is stentable or not. If FFR value comes to be 0.80 or

more than 0.80 it is functionally non significant stenosis and stenting will not be done that will prevent unnecessary angioplasties and will reduce economic burden over patients.

## METHODOLOGY

In this cross sectional validation study, a total of 130 admitted patients of Cardiology ward and CCU were included. The study was started by taking ethical approval from hospital ethical review board. All the patients in the study were briefly described about the study and informed written consent was taken prior to include in the study. The sample size was calculated with help of WHO sample size calculator using 95% confidence level, Sensitivity of 90.3%, and Specificity of 82.9%, Prevalence of 27%, and absolute precision of 10%. All the patients were selected by non-probability consecutive sampling method.

The inclusion criteria for this study was male and female patients of age above 30 years admitted with Coronary artery disease having USAP (Unstable angina pectoris) or NSTEMI (Non ST elevation Myocardial Infarction). The patients having renal failure (Serum creatinine  $>1.6$  mg/dl) were excluded from the study.

The demographic information and patient history was taken along with general physical examination and systemic examination. Subjects as per protocol of inclusion and exclusion criteria underwent FFR followed by Conventional angiography by Interventional Cardiologist. Result of both procedures was compared independently and finally data was entered on performa by researcher. Data was analyzed by using SPSS version 21. Mean  $\pm$  SD was calculated for age and FFR. Frequency and percentage was presented for gender. The sensitivity, specificity, positive predictive value and negative predictive value were calculated with the help of 2x2 cross table taking Angiography as gold standard.

## RESULTS

In this validation study a total of 130 patients were included whose mean age was  $56 \pm 8.79$  years. The minimum age of the participants was 31 years and maximum was 79 years. Majority 45

(34.6%) of the patients in study had age of 61-70 years, followed by 36 (27.7%) patients in 51-60 years age group and 26 (20%) patients had age in the interval of 41-50 years as elaborated in (table-I). There were 88 (67.7%) male patients and 42 (32.3%) female patients in the study.

In our whole study sample, 35 (26.92%) patients had FFR positive and 31 (88.57%) out

**Table -I: Distribution of patients by age (n=130).**

Age (Years)	Frequency	Percentage
31-40	11	8.5
41-50	26	20
51-60	36	27.7
61-70	45	34.6
>70	12	9.2
Mean $\pm$ SD	56 $\pm$ 8.79 years	
Range	31-73 years	

**Table-II: Comparison of fractional flow reserve versus conventional angiographic findings (n=70).**

Fractional Flow Reserve	Intermediate Stenosis on Conventional Angiography (Gold Standard)	
	(Yes) Positive	(No) Negative
(<0.8) Positive	31	4
(>0.8) Negative	3	92

**Table-III: The diagnostic accuracy of fractional flow reserve.**

Validation Parameters	Value
Sensitivity	91.2%
Specificity	95.8%
Positive Predictive value	88.6%
Negative Predictive value	96.8%
Accuracy	94.6%

of these 35 were also proved to be positive on conventional angiography, that is were true positive and remaining 4 (11.43%) were labeled as false positive. The results of FFR were negative for 95 (73.08%) patients, and out of these 3/95 (3.16%) patients had positive findings on conventional angiography that is why were labeled as false negative and remaining 92 had both results on FFR and conventional angiography as negative, and were called as true negative (table-II).

The overall diagnostic accuracy of FFR for stentable intermediate stenosis was found 94.6% in our study. The sensitivity was 91.2%, speci-

ficity 95.8%, positive predictive value 88.6% and negative predictive value was found to be 96.8% (table-III).

## DISCUSSION

The prognosis of coronary artery disease patients has a strong relationship with manifestation and extent of myocardial ischemia. The revascularization is dependent upon coronary atherosclerotic plaques, which are responsible for myocardial ischemia and the coronary atherosclerotic plaques influence can be determined efficiently by the interventional cardiologists through fractional flow reserve (FFR). The atherosclerotic plaques intensity can be identified more efficiently with FFR as compare to angiography alone<sup>11-16</sup>.

The importance of therapeutic decision making based upon angiography is decreasing now a days because in some cases its results are not so reliable to make treatment decision. The angiographic assessment of coronary lesions become more challenging in cases presented with intermediate severity of lesions, the lesions having diameter stenosis of 50-70% are called intermediate severity lesions. This present study was conducted in 130 patients with coronary artery disease to determine the diagnostic accuracy of FFR in determining the stentable disease and the results were in favor of FFR which showed a high diagnostic accuracy of 94.6% at a cut off value of 0.8.

Angiography is considered as gold standard for the management of patients with coronary artery disease (CAD). It describes the areas of stenosis but cannot describe that which stenotic lesion is stentable. Fractional flow reserve (FFR) provides a functional evaluation, by measuring the pressure decline caused by a vessel narrowing. In this study diagnostic performance of FFR of patients was assessed by determining the patients of intermediate stenosis suitable for percutaneous coronary intervention which could not be proven just on conventional angiography whether it is stentable or not.

A study was performed by Koo BK, et al<sup>17</sup>, which was conducted on 159 vessels to determine the diagnostic performance of FFR in vessels with intermediate stenosis by comparing it with CT angiography. In a study of 47 vessels having 50% to 69% stenosis on the basis of coronary computed tomography angiography, ischemic FFR was noted in 25.5% cases, that is ischemia FFR. On the basis of these stenosis 83.0% diagnostic accuracy was found with 66.7% sensitivity, 88.6% specificity, 66.7% positive predictive value and 88.6% negative predictive value. Like our study, the definitions for ischemia was identical to those used in the FAME study for ischemia by FFR (<0.80) and obstructive stenosis by angiography (50%)<sup>18</sup>.

In another study the diagnostic performance of FFR was determined in 60 patients with coronary artery disease. The FFR values were compared to conventional angiographic findings taken as gold standard<sup>19</sup>. In a study of FFR a high accuracy of 86.4% was noted at a cut off value of  $FFR \leq 0.80$  for lesion-specific ischemia, with a high sensitivity of 90.3%, specificity of 82.9%, positive predictive value of 82.4% and negative predictive value of 90.6%. Like our study, the diagnostic accuracy was found to be high. They also used the similar cut off value as used in our study i.e. 0.8<sup>14</sup>. The studies that have worked on the diagnostic performance of FFR in detection of stentable disease are low and have shown a high accuracy. So, it can be used as a reliable indicator for stentable stenotic disease.

In this study, there were 35 patients who underwent coronary artery stenting based on FFR findings. This is a very important observation that it saved a majority of patients from unnecessary coronary artery stenting which costs around Rs. 100,000. The results of this study are also very important as it saved the cost of stenting in many patients which is very important in a country where the majority of the patients belong to poor socioeconomic groups. However, it raises the issue of safety of not doing the angioplasty on basis of the FFR. Some previous studies have demonstrated that in patients who were

evaluated for PCI to be performed or not, on the basis of FFR, the deferred patients have better outcome as compared to patients in which PCI was performed<sup>20</sup>.

FFR has become the gold standard for defining the functional significance of coronary stenosis. Routine use of FFR in daily clinical practice will reduce unnecessary intervention and improve the outcomes of patients with CAD. Novel hyperemic stimuli and novel physiologic indices without hyperemia will reduce the current procedural barriers and expand the clinical application of physiologic assessment in the cardiac catheterization laboratory. Further-more, noninvasive assessment of the functional significance of coronary stenosis such as FFRCT can be helpful in predicting the functional significance of coronary lesions and in planning the treatment strategy before the invasive procedures actually take place. Future developments in this technological realm will continue to improve clinical outcomes for patients with CAD<sup>21</sup>.

The results of FAME study have revealed that use of FFR for PCI decision making has given wonderful results, that the use of FFR for PCI can save cost by reducing stent use, reducing re-hospitalization and MACE. 22 Therefore, the FFR-guided treatment could have been more economical in daily practice if decision making for PCI relies more strictly on FFR value.

## CONCLUSION

FFR is a reliable investigation for detection of stentable intermediate stenosis in patients of coronary artery disease. Its use is recommended in all patients of intermediate coronary artery disease. The overall diagnostic accuracy of FFR for stentable intermediate stenosis was found quite high at 94.6% in our study with sensitivity of 91.2%, specificity of 95.8% for detection of stentable disease. So, a patient with positive FFR should be subjected to coronary artery stenting.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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