Kardiologia Polska 2017; 75, 6: 545–553; DOI: 10.5603/KP.a2017.0037 ISSN 0022–9032

ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Comparison between fractional flow reserve and visual assessment for moderate coronary artery stenosis

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Abstract

Background: Fractional flow reserve (FFR) is an interventional diagnostic method, based on intracoronary pressure measurement, used for the assessment of the severity of coronary artery stenoses.

Aim: Our study aimed to compare visual measurements made by multiple observers with FFR measurement in the assessment of angiographically moderate coronary artery stenosis.

Methods: The angiographic images of moderate coronary artery lesions of 359 patients enrolled in the study were interpreted independently by three interventional cardiologists assigned as observers (O1, O2, O3).

Results: In FFR, 37.9% were haemodynamically significant, while 62.1% were insignificant. 40.3% of the lesions were considered severe by O1, 39.9% by O2, and 44.4% by O3. When we compare the FFR results to the observers' decisions about lesion severity, the serious lesion percentages of all three observers were different both from each other and from the FFR result, at a statistically significant level (respectively, $p < 0.001$, $p < 0.001$). The kappa analysis performed to check the agreement between the observers' decisions and FFR revealed significant difference between FFR results and the decisions made by all observers ($p < 0.001$). The kappa agreement analysis performed by matching observers' decisions in pairs revealed a good agreement between O1 and O2 and a moderate agreement between O2 and O3 as well as O1 and O3, although there was still a significant disagreement between all pairs of observers ($p < 0.001$).

Conclusions: Visual assessment, even when performed by experienced interventional cardiologists, does not yield similar results with FFR procedure in the process of determination of the functional importance of moderately severe coronary artery stenoses.

Key words: fractional flow reserve, visual assessment, moderate coronary artery stenosis

Kardiol Pol 2017; 75, 6: 545–553

INTRODUCTION

Cardiovascular diseases are one of the leading causes of morbidity and mortality all over the world [1]. The clear majority of deaths due to cardiovascular diseases arise from deaths linked to coronary artery disease (CAD). For more than 30 years, invasive coronary angiography has been used to assess the presence and prevalence of obstructive CAD [2]. Coronary angiography (CAG), which is being used at an ever-increasing rate, has some handicaps in assessing the severity of CAD. The major cause of this is because in clinical practice, after CAG, the lesions are assessed only visually. Visual assessment of the coronary arteries can yield to high rate of inter-observer variations, even when performed by expert observers [3]. Fractional flow reserve (FFR) was developed in the 1990s to assess the severity of epicardial coronary artery stenosis by means of intracoronary pressure. Due to the fact that haemodynamic parameters such as heart rate and blood pressure are not affected [4], FFR is considered the gold standard for physiological assessment of coronary artery stenosis. However, in developing countries it may not be possible to implement FFR to each patient due to intense workload and technical difficulties. An assessment of the data obtained with a single

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Received: 13.08.2016 **Accepted:** 29.12.2016 **Available as AoP:** 03.03.2017

operator is clearly not as objective as FFR. In the literature, variable inter-observer and even intra-observer [5] comments can be found. However, it is a matter of ongoing curiosity and research whether multiple observers could yield results that are more consistent with FFR.

Therefore, regarding the assessment of angiographically moderate coronary artery stenosis, in our study we aimed to compare FFR and visual assessments conducted by multiple observers.

METHODS

This study included all patients who were diagnosed with moderate coronary artery lesions and studied by FFR, among those who presented to our hospital between 2011 and 2014. Patients with stable and unstable CAD and those who presented with ST elevation myocardial infarction (STEMI) and who had undergone FFR measurement for non-culprit lesion after primary percutaneous intervention of culprit artery were enrolled. The indications of CAG were determined based on the current guideline recommendations. As such, non-invasive stress and imaging tests were used for all stable patients with an intermediate pre-test probability. Our hospital's database was screened retrospectively regarding the FFR procedures, and 30 of the 400 patients were excluded from the study because only FFR was administered without the recording of angiographic images, and 11 patients were excluded due to lack of sufficient demographic data. Ethics Board Committee approval was obtained for the study protocol.

With regard to the 359 patients who were included in the study, their age, gender, risk factors (hypertension, diabetes mellitus, hyperlipidaemia, smoking history), history of CAD (previous coronary artery bypass grafting, myocardial infarction, stent implantation), clinical status (stable angina pectoris, unstable angina pectoris, non-ST elevation myocardial infarction [NSTEMI] or STEMI), laboratory parameters, drugs used, New York Heart Association functional class (NYHA), and Canadian Cardiac Society (CCS) angina classification was recorded upon archive scanning.

Regarding the 359 patients who were included in the study, their coronary angiographic imaging was performed in accordance with conventional standard techniques, using the Judkins technique through femoral percutaneous access with a Siemens Artis Zee Floor (Siemens AG Healthcare, Germany) angiographic X-ray system located in our catheter laboratory. Coronary arteries were scanned with a speed of 12 frames per second with cranial and caudal perspectives, at the right and left oblique planes. As opaque substance, iopromide (Ultravist-370) was used. They were recorded to CDs in the digital environment in the DICOM^R format. Data was collected for the assessed arteries (left anterior descending artery [LAD], circumflex artery [Cx], right coronary artery [RCA]) and for the number of recorded exposures.

All coronary angiographies were interpreted by three experienced interventional cardiologists who work in our clinic (observer O1, O2, O3), independently from each other, by using Philips Inturis Suite Lite 2.1.1 DICOM imaging version, on a high resolution 19-inch flat screen. All observers were selected from among cardiologists who had conducted at least 1000 interventional procedures and who had experience in procedures such as FFR, intravascular ultrasound (IVUS) imaging, atherectomy, rotablation, and intracoronary pressure measurements. Significant left main disease (diameter stenosis > 50%), multiple lesions in the same vessel, angiographic evidence of collateral flow distally to the assessed lesion, significant valvular disease, and bypass graft lesions were considered as the exclusion criteria.

No information was given to the observers regarding the patients' demographic information, risk factors, clinical features, FFR results, and the decisions taken after the FFR procedure. The observers interpreted the lesions as "significant", "not significant", and "unsure". Later, their decisions were recorded as "medical follow-up", "PCI" (percutaneous coronary intervention), or "CABG" (coronary artery bypass surgery).

Fractional flow reserve measurement

After diagnostic catheterisation had been performed a 6 French guiding catheter without side holes was advanced into the ostium of the left coronary artery or RCA. Following the intravenous systemic heparinisation (2000–5000 bolus dose ACT to be 250–350 s) a pressure recorder wire with 0.014-inch sensor tip (Pressure-Wire Certus, the St. Jude medicalsystems AB, Uppsala, Sweden) was reset and calibrated. The pressure wire (Pd) and coronary catheter (Pa) were aligned to make sure that the same pressure was measured, and then the transducer end (the pressure sensor located in the first 3 cm of pressure wire) was moved immediately to the distal stenosis. To verify that we were at the right position before taking measurements, images were taken with contrast material. Prior to the baseline measurements, 200-μg isosorbide dinitrate was applied as a regular procedure. Basal heart rate, phasic and mean aortic pressure, and phasic and mean coronary pressure at distal stenosis were recorded. After taking measurements at rest, to obtain maximal hyperaemia, measurements were recorded 15 s after administration of intracoronary 100–150 μg bolus adenosine. Considering that maximal hyperaemia was not provided, adenosine administration was repeated after 30 s. The FFR value, which is also named as the maximal trans-stenotic gradient, was calculated by dividing the average distal intracoronary pressure by average aortic pressure, during maximal hyperaemia. All haemodynamic data was recorded offline in the computer system (St. Paul, Minn., St. Jude Medical). In the patients whose FFR values were detected to be > 0.80, the lesion was considered to be

haemodynamically insignificant, whereas < 0.80 was considered as haemodynamically significant.

Statistical analysis

Study data was recorded on the computer, and the SPSS (Statistical Package for Social Sciences) for Windows 20.0 package was used for the evaluation of data. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as a percentage. For the comparison of descriptive statistical methods (mean, SD), comparison of quantitative data, as well as the intra-group comparison of parameters showing normal distribution, the Student t test was used. On the other hand, for the intra-group comparison of parameters that did not show normal distribution, the Wilcoxon test was used. In categorical data, cross tables and χ^2 analysis was used. Kappa analysis was performed for compliance with the FFR in terms of lesion severity of observers. Results were evaluated at the 95% confidence interval and at a $p < 0.05$ significance level.

RESULTS

In our study, 73.6% of patients who underwent FFR process were male. The mean age of the patients was 62.6 ± 10.1 years. 61.1% of patients were hypertensive, 36.4% were diabetics, 36.4% were smokers, 66.1% had stable angina, 17.2% had unstable angina, 8.1% were admitted to NSTEMI, and 4.2% were admitted to STEMI clinics. 65% were asymptomatic, 58.1% had CCS class 1 angina, 39.2% had class 2, and 2.8% had class 3 angina. 32.5% of patients had previously known CAD (PCI or CABG). Table 1 shows the demographic characteristics of the patients. After diagnostic CAG, critical stenosis was detected in one coronary artery of 43.6% of patients, in two coronary arteries of 32.5%, and in three coronary arteries of 23.9% (Table 1).

Most of the lesions that were administered FFR measurement were in the LAD (68.7%). 17.5% of lesions were ostial, 58.5% proximal, 15.5% were shaft lesions, and 8.5% were located distally. 5.3% of all lesions were in-stent lesions. 37.9% of lesions were haemodynamically significant when assessed by FFR, and 62.1% were not significant. Lesions undergoing FFR were judged to be PCI in 22.2% of patients and CABG in 17.2% of patients. The characteristics of the FFR process are shown in Table 2.

As shown in Table 3, when the observers' evaluations were viewed one by one, we can see that the first observer found 40.3% of lesions to be significant, the second observer found 39.9% significant to significant, and the third observer found 44.4% to be significant. When we compare the observers' decisions about lesion severity with the FFR results, all three observers' percentages for guessing severe lesions were statistically different, both from each other and from the FFR result ($p < 0.001$). In the kappa analysis conducted for FFR compliance in terms of the assessment of lesions severity, statistically significant differences were present separately between the FFR results and observers 1, 2, and 3 ($p < 0.001$). In the kappa agreement analysis conducted by matching the observers' decisions in pairs, there was substantial agreement between observer 1 and observer 2, and moderate agreement between observer 2 and observer 3, and between observer 1 and observer 3; however, the differences continued at a statistically significant level ($p < 0.001$) (Tables 3, 4).

Table 1. Clinical, angiographic, and physiological data of the patients

Male/female	73.6%/26.4%
Age [years]	62.6 ± 10.1
Body mass index [kg/m^2]	26.6 ± 3.1
Heart rate [bpm]	77.8 ± 12.2
NYHA class:	
I	65%
II	30.3%
III	4.7%
CCS class:	
I	58.1%
II	39.2%
III	2.8%
Clinical status:	
SAP	66.1%
USAP	17.2%
NSTEMI	8.1%
STEMI	4.2%
Others	4.4%
Hypertension	61.1%
Diabetes mellitus	36.4%
Hyperlipidaemia	29.7%
Smoking	36.4%
Family history	16.7%
LVEF [%]	56.3 ± 11.5
LDL [mg/dL]	108.7 ± 37.6
Blood urea nitrogen [mg/dL]	19.6 ± 9.8
Creatinine [mg/dL]	1.0 ± 0.9
Haemoglobin [g/dL]	13.8 ± 2.1
Angiographically significant lesions:	
One vessel	43.6%
Two vessels	32.5%
Three vessels	23.9%

NYHA — New York Heart Association; CCS — Canadian cardiovascular society; SAP — stable angina pectoris; USAP — unstable angina pectoris; NSTEMI — non-ST segment elevation myocardial infarction; STEMI — ST segment elevation myocardial infarction; Others — includes: patients undergoing coronary angiography for the identification of heart failure aetiology, during a preoperative evaluation before a non-cardiac surgery, and for assessment of coronary anatomy prior to planned valvular surgery; LVEF — left ventricular ejection fraction; LDL — low-density lipoprotein

Table 2. Fractional flow reserve (FFR) results

Index coronary artery:	
LMCA	2.6%
LAD	68.7%
Cx	11.4%
RCA	11.4%
IM	1.8%
Diagonal	4.1%
FFR lesion segments:	
Ostial	17.5%
Proximal	58.5%
Shaft	15.5%
Distal	8.5%
In-stent lesion	5.3%
FFR:	
Significant	37.9%
Not significant	62.1%
Treatment:	
Medical follow-up	38.6%
PCI	22.2%
CABG	17.2%
PCI for other lesion	21.9%

LMCA — left main coronary artery; LAD — left anterior descending artery; Cx — circumflex artery; RCA — right coronary artery; IM — intermediate artery; PCI — percutaneous coronary intervention; CABG — coronary artery bypass grafting

Table 3. Each observer's and fractional flow reserve (FFR) results

	FFR	O1	O2	O3
Significant	37.9%	40.3%	39.9%	44.4%
Not-significant	62.1%	58.9	60.1%	52.8%
Unsure		0.8%	1.4%	2.8%
Treatment:				
Medical follow-up	38.6%	59.4%	60.4%	56.0%
PCI	22.2%	34.7%	34.6%	37.7%
CABG	17.2%	5.9%	5.1%	6.3%

CABG — coronary artery bypass grafting; O — observer; PCI — percutaneous coronary intervention

Table 4. Inter-observer agreement

	Kappa value
Observer 1–2	0.673
Observer 1–3	0.570
Observer 2–3	0.468

When we examine the observers' agreement with FFR in terms of significant and insignificant lesions, the fact that the lesions that were considered significant haemodynamically with FFR were found to be significant by the observers, was different at a statistically significant level. Regarding haemodynamically significant lesions as for FFR, the first observer considered 73.3% of the mentioned lesions to be significant, the second observer considered 85.9% of the mentioned lesions to be significant, and the third observer considered 71.9% of the mentioned lesions to be significant. When we examined the observers' agreement with FFR separately, there was substantial agreement only between the second observer and FFR, and the statistically significant difference persisted (Table 5).

In the kappa agreement analysis conducted by matching the observers' decisions in pairs, there was substantial agreement between observer 1 and observer 2, and moderate agreement between observer 2 and observer 3, and between observer 1 and observer 3; however, differences continued at a statistically significant level (Table 6). When we examined the results in which all three of the observers gave the same decision, the "significant lesion" guessing rate was 58.9% and the "not significant lesion" guessing rate was 61.6%. In the kappa agreement analysis conducted for these results, there was agreement at a moderate level, and the statistically significant difference persisted ($p < 0.05$) (Table 6).

DISCUSSION

When we examine the results obtained from our study, the FFR measurement was administered primarily to the lesions at the LAD. 37.9% of the FFR-administered lesions had been found to haemodynamically significant. When we examined the observers' interpretation regarding the same lesions, the first observer found 40.3% to be significant, the second observer found 39.9% to be significant, and the third observer found 44.4% to be significant. For the observers' guessing rates regarding the severity of the lesions, the percentages of all three observers were different both from each other, and from the FFR result, with a statistically significant level. There was slight agreement between FFR and the observers, and moderate to good agreement between the observers. Regarding haemodynamically significant lesions for FFR, the first observer considered 73.3% of the mentioned lesions to be significant, the second observer considered 85.9% of the mentioned lesions to be significant, and the third observer considered 71.9% of the mentioned lesions to be significant.

In daily practice, coronary angiographies are almost always read visually at the time of recording. When compared to quantitative measurement, it is a well-known fact that stenosis percentages are higher in visual assessments. Even when expert observers perform the visual assessment of the coronary arteries, inter-observer variabilities can be quite high [3]. Despite the fact that this is very well known, the most recent

Table 5. Fractional flow reserve (FFR) measurement versus visual assessment for each observer

FFR		Significant (%)	Non-significant (%)	Total (%)	Kappa	p
Observer 1	Significant	73.3	20.7	40.3	0.500	< 0.001
	Non-significant	26.7	77.9	58.7		
Observer 2	Significant	85.9	11.3	39.2	0.707	< 0.001
	Non-significant	14.1	86.5	59.3		
Observer 3	Significant	71.9	28.4	44.5	0.406	< 0.001
	Non-significant	24.4	69.4	52.6		

Table 6. Fractional flow reserve (FFR) measurement versus visual assessment for multiple observers

FFR		Significant (%)	Not significant (%)	Kappa	p
Observer 1 and 2	Significant	68.1	7.8	0.532	0.035
	Non-significant	9.9	76.7		
Observer 1 and 3	Significant	63.1	12.3	0.393	0.034
	Non-significant	13.5	63		
Observer 2 and 3	Significant	64.5	6.4	0.454	0.031
	Non-significant	4.3	66.2		
For all observers (joint decision)	Significant	58.9	5.5	0.399	0.029
	Non-significant	5	61.6		

studies on this subject were made in the early 1990s, and to reveal the current status of this issue, Nallamothu et al. [6] carried out a project called the "Assessing Angiography (A2) Project" as follows: In seven large hospitals in the United States, coronary angiographies of PCI-administered patients were selected randomly, the intervened stenosis was measured with quantitative methods (quantitative coronary angiography [QCA]) and compared to the visual assessment of the physician who carried out the process. In the study, the stenosis percentage of the physicians who read the lesions visually was found to be 84.2 ± 10.1 on average, and lesion severity was evaluated as ≥ 70% in 213 of the 216 evaluated patients. However, when measured as QCA the stenosis percentage was found to be 76.1 ± 10.9% on average. There were an average of 8.2 ± 8.4 differences between QCA and visual assessment ($p < 0.001$). Regarding the 213 lesions, the operating physician interpreted them as ≥ 70% stenosis; it was found that 56 (26.3%) were read as < 70% in QCA. Regarding the 58 patients whose stenosis percentage was 50–70% as per QCA, 50 of the mentioned patients were visually read as 70–90%, and six patients as in the group of 90–< 100%. Regarding the 134 patients who were 70–< 90% in QCA, 70 of them were read in the 90–< 100% group in QCA. These numbers indicate that we make the most mistakes with regard to the group of people who have moderate coronary artery stenosis.

In assessing the haemodynamic significance of stenosis determined as angiographically moderate (between 40% and 70%), FFR is an important invasive diagnostic tool. Regarding percutaneous interventions guided by FFR, its benefits have been shown in moderate stenosis [7], during intervention to side branches [8, 9], in left main coronary artery (LMCA) lesions [10], in bypass graft anastomosis regions [11], and in in-stent restenosis [12].

The first of the studies in relation to FFR, and the study that popularised this method for our daily practice, is the Percutaneous Coronary Intervention of Functionally Non-significant Stenosis (DEFER) study and its five-year results [13]. The DEFER study has shown that, in the patients who do not have any objective evidence of ischaemia, if the FFR value is above 0.75, then they can be medically followed-up with safety, without PCI. It has been shown through the Flow reserve versus Angiography for Multivessel Evaluation (FAME) I and II studies that percutaneous intervention performed under the guidance of the FFR is superior to both single optimal medical therapy and angiographic evaluation [5, 14]. In the FAME study, 1005 patients with multivessel disease were randomised into PCI arms under the guidance of angiography and FFR. Unlike the DEFER study, the FFR limit value was taken as 0.80. The most important conclusion to be drawn from the FAME study is as follows: regarding the lesions the coronary artery stenosis severity of which is angiographically

assessed as 50–70%, when the mentioned reassessed with FFR, only 35% were found to be functionally significant, and 65% non-significant. Results that match these results have been found also in our study: 37.9% of lesions were haemodynamically significant when assessed by FFR, and 62.1% were not significant. On the other hand, the observers found, respectively, 40.3%, 39.9%, and 44.4% of all lesions to be significant. The two-year follow-up results of the FAME study also support the FFR-guided revascularisation in multivessel disease patients. With this study, it is recommended that if myocardial ischaemia evidence cannot be obtained by non-invasive methods, the use of FFR to determine the functional significance of coronary lesions during coronary angiography is recommended as Class 1 [15].

A Comparison of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention and Coronary Artery Bypass Graft Surgery in Patients with Multivessel Coronary Artery Disease (FAME 3) study was designed as a randomised controlled trial comparing a study that compares CABG to PCI in patients with multivessel disease through FFR [16]. By the Heart Team, patients with multivessel disease who do not have LMCA lesions that are suitable both for CABG and PCI, are taken into the study; these patients are assessed with classic and functional SYNTAX scores, and the hypothesis of the study is to prove that PCI carried out with FFR is at least as good as CABG. One-month, one-, three-, and five-year follow-up are carried out, and long-term results are expected for this study regarding the new generation of drug-eluting stents.

As we can understand from these studies, the functional severity of coronary artery lesions is estimated by CAG as less or more than the actual. The cause of this 'visual-functional incompatibility' has not yet been clearly identified. In the Natural History of FFR-Guided Deferred Coronary Lesions (IRIS FFR-DEFER) study published in 2012 by Park et al. [17], with stenosis of coronary artery measured with quantitative methods, 1000 patients and 1219 lesions were compared in terms of the lesion's functional significance with IVUS and FFR. The lesions causing to narrowing of more than 50% in luminal diameter, but whose FFR value is > 0.80 and which are considered "mismatches", were detected in 35% of LMCA lesions, and in 57% of non-LMCA lesions. On the other hand, the lesions causing to narrowing of less than 50% in luminal diameter, but whose FFR value is < 0.80 were detected in 40% of LMCA lesions, and in 16% of non-LMCA lesions, which is identified as a reverse mismatch. In this study, the following were expressed as independent predictors of mismatch: age, non-LAD lesion localisation, the lack of a plaque rupture, short lesions, wide minimum lumen area, and less plaque burden. This study shows that the contradictions between the CAG and FFR are dependent on many clinical and anatomical factors. When assessing ischaemia with FFR, an ischaemia index should be developed which takes into consideration multiple local factors.

Current guidelines and extensive studies that have been conducted recommend the use of FFR in the case that non-invasive tests are not diagnostic or are unreachable. The current guidelines for myocardial revascularisation reaffirm the diagnostic value of FFR and that FFR-guided PCI with medical therapy has been shown to decrease the need for urgent revascularisation compared with optimal medical therapy alone [15, 18]. Nevertheless, the use of FFR is still not as common as expected. First, some cardiologists think of this process as a waste of time, and they decide on the severity of the coronary lesions with conventional angiography. The second reason is the cost of the FFR process. In a conducted study, it has been shown that $1795 less cost is incurred per patient when administered PCI under the guidance of FFR, compared to the application of PCI after the application of nuclear imaging method; and $3830 less cost is incurred compared to PCI conducted with conventional CAG [19]. Thirdly, regarding patients with coronary artery stenosis at the border, some clinicians think that PCI avoids adverse clinical events by providing plaque stabilisation. However, in the DEFER study it was shown that performing interventional procedures does not provide additional benefit for coronary artery stenosis that does not cause ischaemia, and that it may be harmful because of the complications that can occur due to interventional procedures. According to the 15-year outcome data of the DEFER study, which is the first randomised study on FFR, no significant differences existed between stenting and deferred PCI groups with respect to clinical outcomes among patients with stable CAD having non-ischaemic lesions. Furthermore, the deferred PCI group even had a slight advantage regarding the incidence of myocardial infarction over long-term follow-up [20].

However, in developing countries it is not possible to perform FFR for each patient under the heavy workload and due the technical difficulties. Clearly the data obtained by the evaluation of a single operator are not as objective as FFR, and this situation has been shown with QCA as mentioned above. Nevertheless, by thinking of the possibility that independent and experienced multiple observers could yield results that are more consistent with FFR by reducing their error rates, in our study, in the assessment of the severity of secondary lesions in CAD, we aimed to determine whether results similar to FFR can be obtained with assessment conducted by multiple observers. However, our results indicate that, in the assessment conducted with three observers independently from each other, statistically significant differences exist between the individual results of observers and the FFR result, as was well as the differences between two-pair and three-pair joint decisions of the observers.

In the literature, four studies of significantly similar work draw our attention. In the study conducted by Brueren et al. [21], including 52 patients, visual assessment with FFR values were considered to be consistent only in 69.2% of

the patients. In our study, these percentages are: maximum 68.1% for severe lesions as per the double and joint decisions of the observers; and maximum 76.7% for the not-significant lesions, and the percentages match between the studies. Again in this study, the haemodynamic severity of the lesions was assessed as less than the real value in six patients, and more than the real value in 10 patients. As a result, visual assessment for FFR was found to have 63% positive and 76% negative prediction, and it was highlighted that for moderate coronary artery stenosis correct interpretations cannot be made even by experienced observers. However, the study does not cover multiple observers, and the study population is small compared to our study.

In the second study in the literature, which includes 51 patients, moderate and severe lesions in coronary lesions were assessed [22]. The lesions were interpreted by four independent observers from different hospitals, and separated into three groups as: serious, not serious, and undesirable. Regardless of whether the threshold value was taken as 0.75 or 0.80, the correct prediction rate by observers did not exceed 50%. Upon the intersection of the two observers' data, an increase of only 16% was detected. In the case where the joint decision of three observers was taken as a basis due to the significant differences between the observers, the accuracy rate fell to 29%. It was observed that there was no significant improvement in the decision taken with the data of two observers; moreover, it was found that the decisions made using the joint decision of three observers were inconsistent with FFR at a statistically significant level, and that the rate of agreement fell in agreement analysis (kappa value: 0.399).

In the study by Fischer et al. [23], including 83 patients, moderately severe coronary lesions were assessed visually and quantitatively concurrently with FFR. Because of the evaluation made by the observers, the observers' assessments and FFR matched only in half of the patients. The sensitivity and negative predictive value were detected as high (80–91%), whereas the specificity and positive predictive value quite were low (from 47% to 25%).

Another conducted study was published by Berilgen et al. [24]. The results of the study, in which the patients were examined retrospectively, does not coincide with the previously reported data in the literature. Differently from the other studies, in the assessments made with three observers, the prediction rate of "non-severe lesions" was reported as 90.5%; however, the lesions that were assessed as severe in the joint decision of all three observers were reported as 50.5%, which is low, and the intra-observer consistency for predicting non-severe lesions was quite low (kappa value: 0.370). In our study, higher consistency rates were detected in the assessments made with a single observer. In the assessment made with observer 2, the prediction rate for "significant" lesions was 85.9%, and a substantial rate of agreement was present; however, despite this agreement, statistically significant correlation with FFR was not achieved.

The question of the situations in which FFR should be used, based on the results of these studies, is a very important question for clinicians because, when we consider the cost effectiveness of regular use of the expensive method of FFR prior to PCI, it would be a logical approach to determine the lesion group in which the FFR procedure can yield important results. The DILEMMA score, which is a new rating score, is created by using minimum lumen area obtained by quantitative angiography, lesion length, and myocardium at risk (BAR-MJI (Bypass Angioplasty Revascularisation Investigation [BARI] Myocardial Jeopardy Index [MJI]) variables, and it has been designed to determine the necessity of the FFR procedure in patients with moderate coronary artery stenosis [25]. In this new scoring system, the total score is 12, and in patients with DILEMMA score ≤ 2, the FFR value has been determined as > 0.80 with $> 95\%$ sensitivity, and for patients whose DILEMMA score is ≥ 9, the FFR value has been detected as < 0.80 with $> 95\%$ sensitivity. The most important results to come from this study are that the lesion severity can be predicted for persons whose DILEMMA score is low (≤ 2) or high (≥ 9), whereas it may be beneficial to apply the FFR procedure for persons whose score is between ≤ 2 and ≥ 9. Instead of performing FFR procedure to each lesion, it would increase the cost–effectiveness to use FFR for lesions in which we have difficulty predicting the lesion severity.

As is the case in our study, in the study conducted by Biasco et al. [26] the artery localisation where the FFR is applied is usually the LAD, and they specified five angiographic parameters as independent predictors that restrict the flow in moderate stenosis [26]. The independent predictors were shown as follows: the presence of a mild-to-moderate tandem lesion (30–50%) proximal to the lesion of interest, lesion length > 20 mm, distal take-off of all diagonal branches ≥ 2 mm, "apical wrap" of LAD, and collaterals to an occluded Cx or RCA. The risk score of P20-DAC2 was created with these parameters, and it is expected that this to be improved and published upon more extensive studies.

Our study contains the broadest patient population to date, which compares multiple observers to the visual assessment conducted by FFR. Considering this information, in studies in the literature, constantly, all the assessments conducted with one observer, the ones conducted with two observers, and those conducted with multiple observers are not consistent with FFR. It should be noted that anatomical assessment and haemodynamic importance are not the same. It is a cost-effective approach to use the FFR procedure in the scope of new technological developments and in the scope of indications with randomised clinical trials.

CONCLUSIONS

As a result, for determination of the functional significance of angiographically moderate coronary artery stenosis, conducting visual observations does not yield results similar to those of the FFR process, even if experienced interventional cardiologists conduct the observation. In visual assessment, especially in lesions of moderate severity, the haemodynamic effect of the lesion cannot be detected, and even when conducted by expert observers, intra-observer variations can be high. Consequently, we believe functional assessment methods must be applied to make the right decision in terms of treatment, especially in angiographically moderate coronary artery lesions.

Conflict of interest: *none declared*

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Cite this article as: Duran Karaduman B, Akçay M, Ayhan H, et al. Comparison between fractional flow reserve and visual assessment for moderate coronary artery stenosis. Kardiol Pol. 2017; 75(6): 545–553, doi: 10.5603/KP.a2017.0037.

Porównanie pomiaru cząstkowej rezerwy przepływu i oceny wzrokowej umiarkowanych zwężeń tętnic wieńcowych

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Streszczenie

Wstęp: Cząstkowa rezerwa przepływu (FFR) to interwencyjna metoda diagnostyczna polegająca na wewnątrznaczyniowym pomiarze ciśnienia w tętnicach wieńcowych, która jest stosowana w celu oceny stopnia ciężkości zwężenia tętnic wieńcowych.

Cel: Badanie przeprowadzono w celu porównania pomiarów wizualnych wykonanych przez wielu obserwatorów z pomiarem FFR w ocenie umiarkowanego, wg badania angiograficznego, zwężenia tętnicy wieńcowej.

Metody: Angiograficzne obrazy umiarkowanie zwężonych tętnic wieńcowych 359 chorych włączonych do badania zostały zinterpretowane niezależnie przez trzech kardiologów interwencyjnych określonych jako obserwatorzy (O1, O2, O3).

Wyniki: W badaniu FFR 37,9% zmian było hemodynamicznie istotnych, natomiast 62,1% zmian uznano za nieistotne. Obserwator O1 zakwalifikował jako ciężkie 40,3% zmian, obserwator O2 — 39,9% zmian, a obserwator O3 — 44,4% zmian. Porównując wyniki FFR z ocenami obserwatorów, stwierdzono statystycznie istotne różnice w zakresie odsetka zmian określonych jako ciężkie zarówno między obserwatorami, jak i w odniesieniu do pomiarów FFR (odpowiednio, $p < 0,001$, $p < 0,001$). Analiza kappa przeprowadzona w celu sprawdzenia zgodności między oceną obserwatorów a badaniem FFR wykazała istotne różnice między wynikami FFR a decyzjami wszystkich obserwatorów ($p < 0,001$). Analiza zgodności kappa, w której zestawiono pary decyzji obserwatorów, ujawniła dużą zgodność między obserwatorami O1 i O2, a także umiarkowaną zgodność między obserwatorami O2 i O3 oraz O1 i O3, chociaż nadal występowały istotne niezgodności między wszystkimi parami obserwatorów ($p < 0,001$).

Wnioski: Ocena wzrokowa, nawet jeśli jest przeprowadzona przez doświadczonego kardiologa interwencyjnego, nie pozwala uzyskać takich samych wyników jak pomiar FFR w procesie ustalania czynnościowego znaczenia umiarkowanie ciężkich zwężeń tętnic wieńcowych.

Słowa kluczowe: cząstkowa rezerwa przepływu, ocena wzrokowa, umiarkowane zwężenie tętnicy wieńcowej

Kardiol Pol 2017; 75, 6: 545–553

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Praca wpłynęła: 13.08.2016 r. **Zaakceptowana do druku:** 29.12.2016 r. **Data publikacji AoP:** 03.03.2017 r.