# Quantitative Flow Ratio identifies Non-Culprit Coronary Lesions requiring Revascularization in Patients with ST-segment Elevation Myocardial Infarction and Multivessel Disease.

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**ABSTRACT**

**Background:** The non-culprit lesion (NCL) management in ST-segment elevation myocardial infarction (STEMI) patients with multivessel disease is debated. We sought to assess if quantitative flow ratio (QFR), a non-invasive tool to identify potentially flow limiting lesions, may be reliable in this scenario.

**Methods and Results:** The present proof-of-concept study is based on a 3-step process: i) identification of the QFR reproducibility in NCLs assessment (cohort A, n=31); ii) prospective validation of QFR diagnostic accuracy in respect to fractional flow reserve (FFR) (cohort B, n=45); iii) investigation of long-term clinical outcomes of NCLs stratified according to QFR (cohort C, n=110). A blinded core-lab computed QFR values for all NCLs. Cohort A showed a good correlation and agreement between QFR values at index (acute) and at staged (subacute, 3-4 days later) procedures (r=0.98, 95%CI 0.96-0.99; mean difference 0.004 [-0.027-0.34]). The inter-rater agreement was k=0.9. In cohort B, FFR and QFR identified 16 (33%) and 17 (35%) NCLs potentially flow limiting. Sensitivity, specificity, negative and positive predictive values were 88%, 97%, 94% and 94%. The area under the ROC curve was 0.96 (95% CI 0.89-0.99). Finally, in cohort C we identified 110 STEMI patients where at least one NCL was left untreated. Patients with NCLs showing a QFR value ≤0.80 were at higher risk of adverse events (HR 2.3, 95%CI 1.2-4.5, p=0.01).

**Conclusions:** In a limited and selected study population, our study showed that QFR computation may be a safe and reliable tool to guide coronary revascularization of NCLs in STEMI patients.

**KEYWORDS**

Non culprit lesion, quantitative flow ratio, fractional flow reserve, ST-segment elevation myocardial infarction

## INTRODUCTION

Primary percutaneous coronary intervention (PCI) of the culprit coronary lesion is currently considered the best treatment option for patients with ST-segment elevation myocardial infarction (STEMI). Nevertheless, in approximately 50% of these patients, additional, severe (>50% of the vessel diameter) stenotic lesions are located in the non–infarct related coronary arteries [1-3]. The optimal reperfusion strategy in STEMI patients with multivessel disease (MVD) is highly debated [3]. Recently, several studies suggested a shift from a conservative approach to complete revascularization [4-5]. Whether fractional flow reserve (FFR) –guided treatment of non-culprit lesions (NCLs) may further improve clinical outcomes compared to angiography-guided treatment is still unclear [6-7]. In addition, although FFR has the highest recommendations in the guidelines, it is still underused also in patients with stable coronary artery disease [8]. The FFR underuse may be caused by the lengthening of the procedural time and the potential side effects related to adenosine use which has led to the introduction of more straightforward indices such as instantaneous wave-free ratio (iFR) [9-10]. To further expand the use of physiological lesions assessment, a quick, reliable and non-invasive tool to assess the functional role of NCLs may be helpful in the daily clinical practice. Quantitative flow ratio (QFR) could be an attractive solution for this unmet clinical need. QFR is a novel approach for the evaluation of coronary stenosis significance based on 3-dimensional quantitative coronary angiography (3D QCA) and contrast frame counting. QFR has shown good agreement with pressure wire-determined FFR measurements in patients with stable coronary artery disease [11].

In the present study, we sought to perform the first validation of the QFR as a tool to identify NCLs requiring revascularization in patients with STEMI and MVD.

## METHODS

### *Study design*

The present is a proof-of concept study based on a 3-step process (Figure 1). Firstly, we investigated the reproducibility and agreement of QFR values of NCLs (and subsequent correlation with FFR) between acute and subacute scenario using STEMI patients from a retrospective, multi-center, observational study (cohort A). Secondly, we prospectively evaluated in consecutive STEMI patients with MVD the diagnostic accuracy of QFR in respect to the gold standard FFR, assessing both in the primary PCI immediately after culprit lesion revascularization (cohort B). Thirdly, we established the long-term clinical outcomes of NCLs according to QFR result (cohort C). Each study was approved by the corresponding Ethics Authority. All patients gave their written informed consent.

### *Cohort A*

Cohort A included STEMI patients from a retrospective, multi-center, observational study (Figure 1) [12]. Detailed methods have been previously described [12]. Briefly, from January 2009 to December 2012, patients with acute coronary syndromes who underwent coronary angiography and FFR assessment of at least one borderline coronary stenosis were selected [12]. STEMI patients were included in the study as long as FFR assessment was performed 3–4 days after primary PCI in a coronary artery different from the infarct-related one [12]. Angiograms of both primary PCI and staged procedure were accurately reviewed. Starting from images of the NCL(s) routinely acquired for diagnostic purpose, QFR values were computed. We included patients in whom QFR computation for NCL(s) was feasible for both procedures (Figure 1).

***Cohort B***

Cohort B included STEMI patients prospectively enrolled in the ARYOSTO registry (prospective registry of acute coronary syndromes in Ferrara, NCT02438085) from December 2016 to June 2017 (Figure 1). Patients ≥18 years old who presented with STEMI within 12 hours after symptom onset and who had an indication for primary PCI were eligible for enrolment if the non–infarct related (IRA) coronary arteries (or their major side branches of at least 2.0 mm in diameter) showed lesions with stenosis of 50% or more (quantitative coronary angiography or visual assessment). During primary PCI, the operator identified the culprit lesion and treated it with PCI and stent implantation. If the treatment was successful and the patient hemodynamically stable, the operator acquired the two angiographic projections for QFR computation of the NCL(s). Angiographic projections were acquired at 15 frames/sec during a single injection of 6 ml of radiographic contrast medium at a flow of 4 ml/sec and at a pressure of 300 psi using a power injector system (MEDRAD Avanta®; Bayer HealthCare, Warrendale, PA, USA). Immediately after the FFR measurement was performed (Figure 1 and 2).

***Cohort C***

Cohort C included STEMI patients of the clinical Evaluation of the Xience-V stent in Acute Myocardial INfArcTION (EXAMINATION) trial (NCT00828087) who were enrolled in the following three centers: i) Azienda Ospedaliero-Universitaria S.Anna, Ferrara, Italy; ii) Ospedale Bolognini, Seriate (BG), Italy; iii) Hospital Universitari Clinic, Barcelona, Spain (Figure 1) [13]. Briefly, the EXAMINATION was an international, multicenter, prospective clinical trial involving STEMI patients randomized to receive bare metal stent or everolimus eluting stent for the treatment of coronary stenosis [13]. Post-procedural angiograms (index procedure and staged PCI, if done) were reviewed to identify NCL(s) that were left untreated.

Finally, their QFR value was calculated to obtain the non-invasive functional syntax score (NI-FSS) (Figure 1).

***Quantitative flow ratio***

Computation of QFR was performed offline, using the software package QAngio XA 3D (Medis Medical Imaging System, Leiden, the Netherlands). In the first step, 2 angiographic projections, at least 25° apart, were selected and 3D reconstruction of the interrogated vessel without its side branches was performed, as previously described [11]. 3D quantitative coronary analysis (QCA) data were readily available. Then, the software computed the fixed and contrast QFR [11]. As compared to fixed QFR (fQFR) value, contrast QFR (cQFR) value was obtained integrating the frame count analysis in the computation. In the pivotal study, cQFR showed a better diagnostic accuracy as compared to fQFR [11]. Thus, in the present analysis we used cQFR values. In addition, to be consistent across the three cohorts, we considered the QFR value of the entire vessel until its diameter became less than 1.5 mm (vessel cQFR). A lesion was considered potentially flow limiting if QFR was 0.80 or less. QFR computation was done in the core laboratory of the University Hospital of Ferrara. Study angiograms were anonymized and submitted to the core lab. Two independent operators (GS, MT), blinded to FFR and outcome, performed the QFR computation. Both operators are certified operator for QFR computation. The inter-rater agreement between operators was very high in all cases ($k>0.95$). The median time to calculate cQFR was 5.2 [4-6.5] minutes. NCLs involving left main and/or right coronary artery ostium, segments with severe tortuosity or with diffuse and distal disease were excluded (Figure 1). Similarly, for cohort A and C, patients without at least 2 angiographic projections ≥25° apart of the same NCL were not eligible for QFR computation.

***Fractional flow reserve***

FFR was measured with a coronary pressure guidewire (cohort A: St. Jude Medical Systems, Uppsala, Sweden; cohort B: Comet guidewire, Boston Scientific, USA) at maximum hyperemia induced by intravenous adenosine (140 μg per kilogram of body weight per minute) [12,14]. FFR was defined as the ratio between the mean distal coronary pressure and the mean aortic pressure, during steady-state maximum hyperemia, and was considered potentially flow limiting if 0.80 or less [12,14].

***Non invasive functional syntax score***

The detailed methodology for functional SYNTAX score (FSS) has already been described [15]. Briefly, each untreated coronary lesion producing ≥50% diameter stenosis in vessels ≥1.5 mm by visual estimation, was identified. In the original FSS, lesions with a FFR value ≤0.80 were scored. FSS was then calculated using the SYNTAX score algorithm from its website, by separately adding the individual scores of lesions with an actual value of FFR ≤0.80 and ignoring lesions with FFR >0.80 [15]. In our model of NI-FSS, functional assessment was done with QFR and not with FFR [16]. An independent reviewer (GS), who was blinded to outcomes, identified all untreated lesions (considering final angiographic results after index or planned staged procedures, if performed). QFR value was calculated for these lesions and those showing a QFR value ≤0.80 were considered potentially flow-limiting and were scored in the NI-FSS. Accordingly, we identified two subgroups of patients: i) those receiving functional complete revascularization (NI-FSS =0, absence of NCLs with QFR value ≤0.80); ii) those receiving incomplete revascularization (NI-FSS >0, at least one NCL with QFR value ≤0.80 and left untreated).

***Endpoints***

The objective of Cohort A was to verify the reproducibility of QFR computation between index and staged procedures (acute vs. subacute scenario). The numerical agreement between QFR and FFR and the diagnostic accuracy of QFR with pressure wire derived FFR as reference standard was the endpoint of the cohort B. As suggested by Petraco et al. [17], FFR values were divided in 0.05 quantiles, from 0.4 to 1, and the agreement (diagnostic accuracy) between QFR and FFR measurements was calculated in each quantile. Agreement between values was considered when both values were below (or equal to) or above the established cut-off of 0.80 [17]. For cohort C, the objective was the relationship between NI-FSS calculated with QFR and 5-year occurrence of patient-oriented cardiac events (POCE, cumulative occurrence of all-cause death, any myocardial infarction, and any coronary revascularization). The definition of singular adverse events has been previously reported and followed Academic Research Consortium (ARC) criteria [18].

***Statistical analysis***

Continuous data were tested for normal distribution with the Kolmogorov-Smirnov test. Normally distributed values were presented as mean±SD and compared by *t* test and 1-way ANOVA. Otherwise, median [interquartile range], Mann-Whitney *U* and Kruskal-Wallis tests were used. Categorical variables were summarized in terms of number and percentages and were compared by using two-sided Fisher's exact test. Correlation and agreement between QFR and FFR was determined by Pearson's correlation coefficient (r) and Bland and Altman plot. Kappa coefficient was used to measure the inter-rater agreement between QFR values from images collected during primary PCI vs. staged procedure (cohort A). To explore the cQFR ability to identify NCL(s) potentially flow limiting (as identified by FFR) sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were

reported and receiver operating characteristics (ROC) curves whit their area under the curve (AUC) were constructed. ROC curve was used to identify the best cut-off, defined as the one that maximized both sensitivity and specificity. Kaplan-Meier method was used to derive the event rates at follow-up and to plot time-to-event curves; differences were evaluated using the log-rank test. A 2-sided value of $p<0.05$ was considered significant. All analyses were performed with STATISTICA 8 (Statsoft Inc, Tulsa, Okla, USA) and MedCalc 11.2.1 (MedCalc Software, Mariakerke, Belgium).

## RESULTS

The overall study population included 304 STEMI patients with MVD (Figure 1). Primary PCI of the culprit lesion was successful in 301 (98%) patients. In all patients, culprit lesion was treated with stent implantation. As reported in Figure 1, 111 (37%) patients were excluded due to several reasons. Thus, the final study population included 186 STEMI patients with MVD (Table 1).

### *Reproducibility of QFR assessment (cohort A)*

Cohort A included 31 patients for a total of 34 NCLs (Table 1). For each of the 34 NCLs, cQFR values at index and staged procedures were available. cQFR values were normally distributed. Mean cQFR was 0.86±0.08 at both procedures. The correlation between cQFR values at primary PCI and at staged procedure was r=0.98 (supplemental online). Bland and Altman plot showed a mean difference of 0.004 [-0.027-0.034] (supplemental online). The inter-rater agreement was k=0.9. Additional data about correlation and agreement between cQFR and FFR values were available in the supplemental online.

### *Diagnostic accuracy of QFR in respect to FFR (cohort B)*

Cohort B included 45 patients for a total of 49 NCLs where both cQFR and FFR were measured during primary PCI (Table 1). Both cQFR and FFR values were normally distributed. Mean cQFR was 0.82±0.1. Mean FFR value was 0.84±0.11. Overall, cQFR values showed good correlation with FFR (r=0.90) (Figure 3A). Bland and Altman plot showed a mean difference of -0.011 [-0.106-0.084] (Figure 3B). FFR identified 16 (33%) NCLs potentially flow limiting. These were 17 (35%) according to cQFR. Diagnostic accuracy was 94%. It was excellent (100%) at extremes (Figure 3C). Close to established 0.80

cut-off, QFR-FFR classification agreement decreased (Figure 3C). Sensitivity, specificity, NPV and PPV were 88%, 97%, 94% and 94% for cQFR. The area under the ROC curve for cQFR was 0.96 (95% CI 0.89-0.99), with a best cut-off ≤0.81 (supplemental online). The cut-off value yielded a sensitivity of 93% (95%CI 70-99) and a specificity of 91% (95%CI 76-98).

***Long-term clinical outcome according to NI-FSS (cohort C)***

Cohort C included 110 patients in whom at least one NCL was left untreated (Table 1). After calculation of NI-FSS, we distinguished 54 (50%) patients with functional complete revascularization (NI-FSS=0) and 56 (50%) with incomplete revascularization (NI-FSS>0) (Table 2). Baseline characteristics did not differ significantly among groups (Table 2). At 5-year follow-up, 39 (35%) patients experienced an adverse event (supplemental Table 1). The cumulative incidence of POCE was significantly higher in the incomplete revascularization group as compared to the functional complete revascularization group (46% vs. 24%, p=0.01, respectively). Figure 4 shows the cumulative occurrence of POCE in the 2 subgroups (log-rank p=0.01). Patients with incomplete revascularization experienced a 2.3-fold increase in the risk of POCE (HR 2.3, 95%CI 1.2-4.5, p=0.01). Of note, patients with functional complete revascularization showed a long-term outcome like those receiving angiographic complete revascularization (supplemental online).

## DISCUSSION

This is the first study to assess the diagnostic performance of QFR in STEMI patients with MVD. Firstly, we demonstrated a good reproducibility of QFR computation, independently of the fact that images of NCLs were acquired during primary PCI or few days later during staged procedure. Furthermore, we found that QFR had a good diagnostic accuracy and diagnostic performance with standard FFR measurement as reference. Finally, we presented initial results that prove the potential prognostic value of QFR as incorporated in the FSS which safely defers NCLs.

The optimal revascularization strategy for patients admitted for primary PCI with MVD is often discussed [3-7]. Although unequivocal evidences are missing, it is generally accepted that complete revascularization should be preferred compared to solely treating the culprit lesion [3-7]. Nevertheless, it is well established that NCL treatment based on eyeballing tends to overestimate the need for revascularization and thus increases the number of stents implanted, contrast media administrated and finally the rate of complications [19]. Despite early doubts on the reliability of FFR in the acute setting, recent randomized clinical trials showed the beneficial effects of a FFR-guided revascularization strategy for NCLs [6-7]. However, it appears to be hard to gain a global penetration of this strategy in a real-world setting. We designed this proof-of concept study to assess whether QFR could be considered as an alternative solution to identify NCLs requiring revascularization in STEMI patients with MVD. We showed that QFR computation has a good correlation and agreement with FFR to define the hemodynamic significance of NCLs. In addition, QFR values were reproducible, independently of the timing of image acquisition. QFR is a novel computer-based diagnostic tool that was recently introduced for the evaluation of the functional significance of coronary stenosis by combining 3D reconstruction of the target vessel and the contrast flow velocity

[11]. Recently, a good correlation and agreement between QFR and FFR was documented in patients with stable coronary artery disease [11]. Its application in the context of STEMI patients is particularly appealing since QFR does not require drug administration or wiring of non-infarct-related arteries and the off-line analysis can be done immediately after primary PCI. In addition, we added a first small clinical validation of this application. We found that functional complete revascularization (as evaluated by QFR) showed a favourable 5-year outcome. As compared to patients with at least one NCL flow limiting left untreated, those with NCLs resulted not flow-limiting at QFR assessment displayed a lower risk of adverse events, despite the absence of revascularization. In a sub-study from the FAME trial, Nam et al. introduced the concept of FSS, which was calculated by adding to the syntax score (SS) the individual scores of lesions with an actual value of FFR <0.80 and ignoring lesions with FFR >0.80 [15]. They demonstrated that this score was an independent predictor of 1-year MACE and that FSS had better predictive accuracy for MACE compared with SS [15]. At the state of the art, this is the first study using FSS with QFR to quantify residual coronary artery disease, and showing that STEMI patients with functional incomplete revascularization (NI-FFS>0), after the primary PCI or the planned staged procedure, had a higher 5-year occurrence of adverse events. On the contrary, those with functional complete revascularization showed the same rate of adverse events of patients where each NCL has been treated with stent implantation.

Therefore, our findings indicate that QFR computation of NCLs is feasible in the STEMI setting where the advantages of FFR-guided revascularization are not fully documented and where the penetration of FFR may be hampered by several factors. Future and larger trials are needed to confirm our preliminary findings. Especially, it would be amenable to plan a randomized clinical trial comparing an FFR-based complete revascularization vs. a QFR-based complete functional revascularization.

### *Study limitations*

This is a small proof-of concept analysis with inherent limitations. Firstly, our study population is relatively small. QFR analysis requires a learning curve both in images acquisition and subsequent computation. Thus, the true translation of our findings in clinical practice should be verified with a multicentre design. Moreover, QFR was computed off-line in this study. On-line computation may improve the feasibility, because a second operator should provide direct feedback on the image quality to the operator. At the same time, before of the QFR implementation in the daily clinical practice, it is required a validation of the technique in studies where it is measured in a timely fashion. In addition, some anatomical issues (e.g. ostial lesion, severe vessel tortuosity, diffuse long disease) remain exclusion criteria for QFR computation. Finally, it is important to note that the prognostic role of QFR should be prospectively validated. Our data are only hypothesis-generating and only future randomized clinical trials may confirm or not that the revascularization of coronary lesion can be safely deferred based on QFR value.

### *Conclusions*

Our small proof-of concept study showed, for the first time, that QFR computation may be a safe and reliable tool to identify the ischemic role of NCLs in STEMI patients presenting MVD. If confirmed in future studies, QFR computation based on diagnostic images of primary PCI could guide a functional complete revascularization.

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**DISCLOSURES**

None.

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**FIGURE LEGEND**

**Figure 1. Study population and procedures**

ST-segment elevation myocardial infarction. PCI: percutaneous coronary intervention. QFR: quantitative flow ratio. FFR: fractional flow reserve. NCL: non-culprit lesion. IRA: infarct related artery. ACS: acute coronary syndromes. RCA: right coronary artery. FSS: functional syntax score. POCE: patient-oriented cardiac events. Pts: patients.

**Figure 2. Example of combined assessment with FFR and QFR of a non culprit lesion**

Red arrow: culprit lesion of STEMI. Panels B and C: non culprit lesions in the mid portion of left anterior descending (LAD) and right coronary artery (RCA). Panels D-G orthogonal projections and border detection of LAD and RCA. Panel H: contrast quantitative flow ratio (QFR) of LAD. Panel I: fractional flow reserve (FFR) of LAD. Panel L: contrast QFR of RCA. Panel M: FFR of RCA.

**Figure 3. Agreement between QFR and FFR in cohort B**

A: scatter plot of QFR and FFR values. B: Bland-Altman plot of contrast QFR and FFR. C: level of agreement (diagnostic accuracy) between the QFR and FFR for each range of disease (from 0.4 to 1 in bands of 0.05). Black dots mark the centre of each 0.05 quantile. Agreement between QFR and FFR values was considered when both tests were below (or equal to) or above their established cut-off. The QFR value in the 3 cases of disagreement is shown. QFR: quantitative flow ratio. cQFR: contrast QFR. FFR: fractional flow reserve.

**Figure 4. 5-year cumulative occurrence of POCE stratified according to functional complete or not revascularization**

POCE: patient-oriented cardiac events.

Continue black line: functional complete revascularization. Dotted black line: functional incomplete revascularization.

**Figure 1**

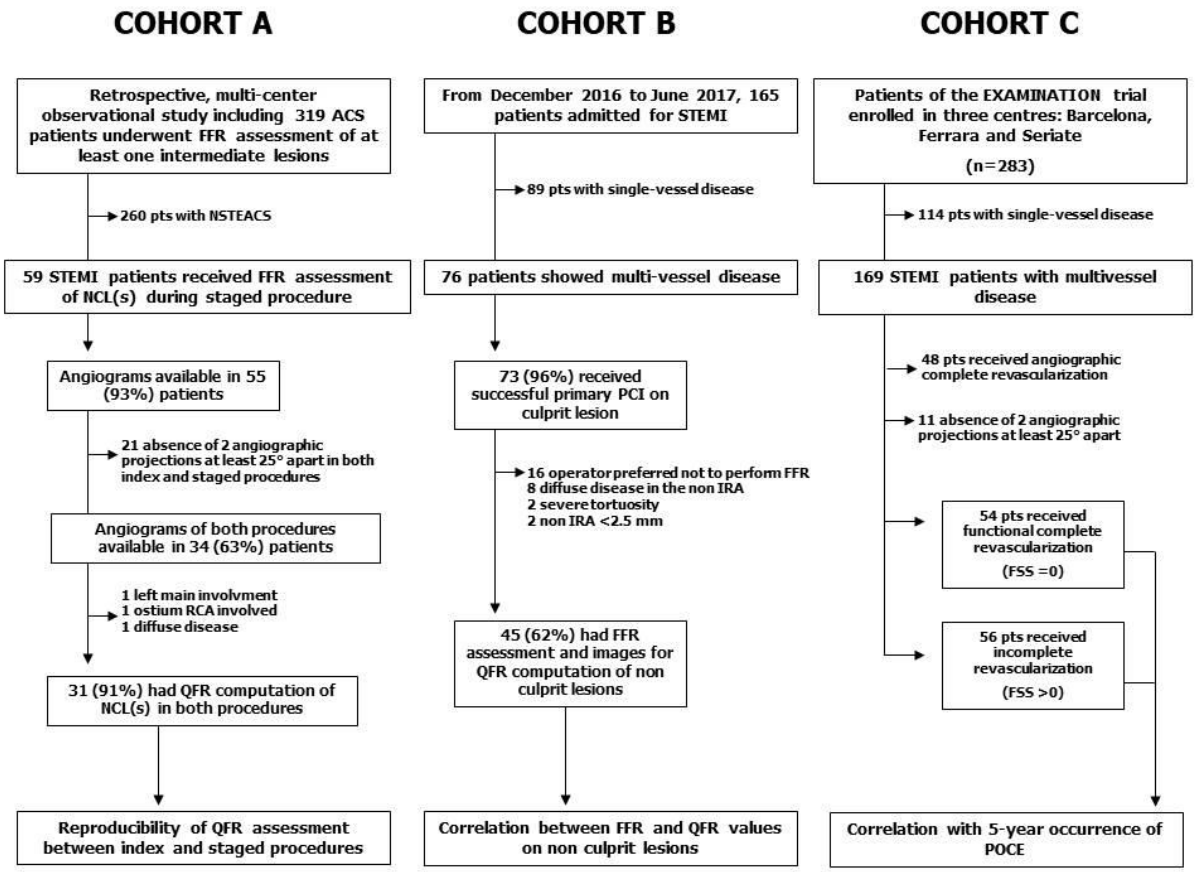
COHORT A
COHORT B
COHORT C
Retrospective, multi-center observational study including 319 ACS patients underwent FFR assessment of at least one intermediate lesions
260 pts with NSTEACS
59 STEMI patients received FFR assessment of NCL(s) during staged procedure
Angiograms available in 55 (93%) patients
21 absence of 2 angiographic projections at least 25° apart in both index and staged procedures
Angiograms of both procedures available in 34 (63%) patients
1 left main involvment
1 ostium RCA involved
1 diffuse disease
31 (91%) had QFR computation of NCL(s) in both procedures
Reproducibility of QFR assessment between index and staged procedures
From December 2016 to June 2017, 165 patients admitted for STEMI
89 pts with single-vessel disease
76 patients showed multi-vessel disease
73 (96%) received successful primary PCI on culprit lesion
16 operator preferred not to perform FFR
8 diffuse disease in the non IRA
2 severe tortuosity
2 non IRA <2.5 mm
45 (62%) had FFR assessment and images for QFR computation of non culprit lesions
Correlation between FFR and QFR values on non culprit lesions
Patients of the EXAMINATION trial enrolled in three centres: Barcelona, Ferrara and Seriate
(n=283)
114 pts with single-vessel disease
169 STEMI patients with multivessel disease
48 pts received angiographic complete revascularization
11 absence of 2 angiographic projections at least 25° apart
54 pts received functional complete revascularization
(FSS =0)
56 pts received incomplete revascularization
(FSS >0)
Correlation with 5-year occurrence of POCE

**Figure 2**

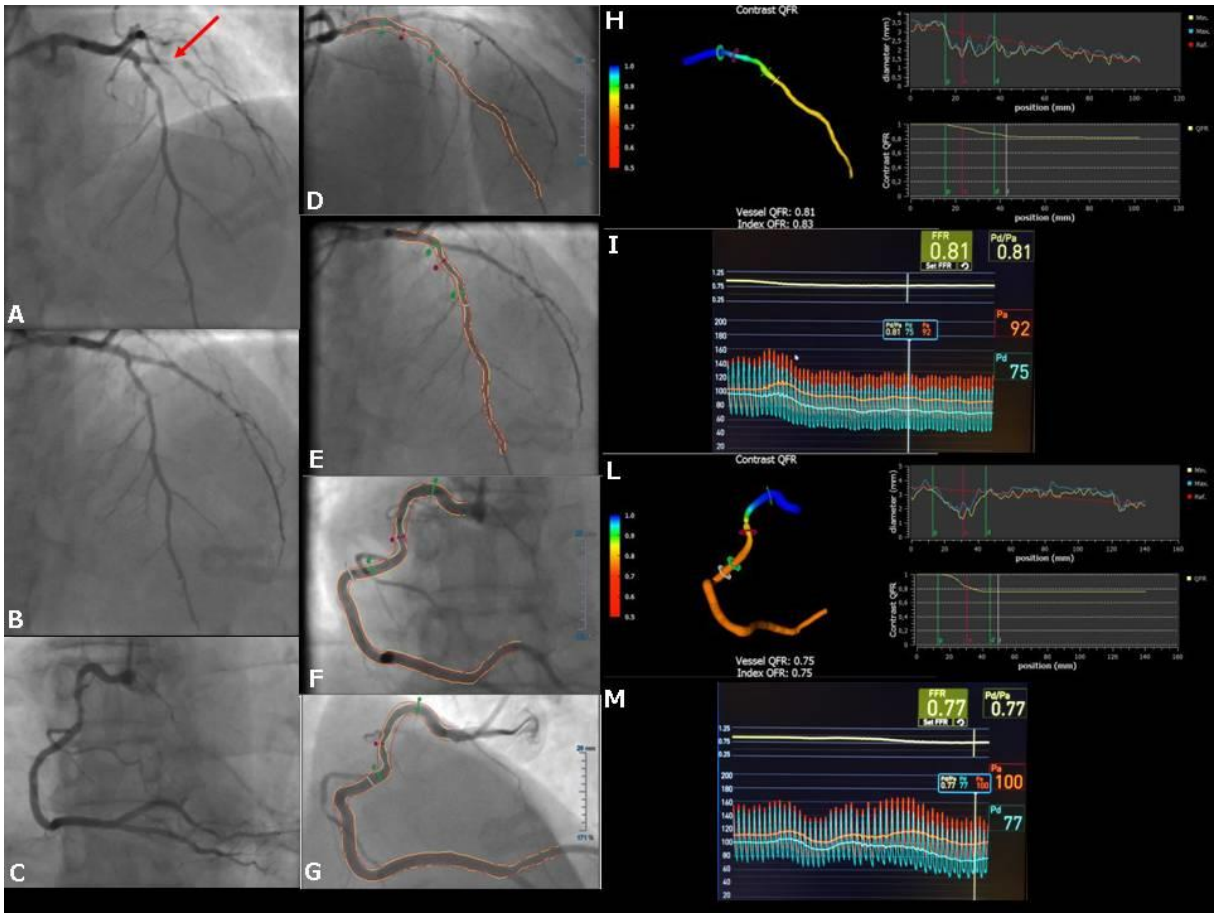
A
B
C
D
E
F
G
H
Contrast QFR
Vessel QFR: 0.81
Index QFR: 0.83
I
FFR
0.81
Pd/Pa
0.81
Pa
92
Pd
75
L
Contrast QFR
Vessel QFR: 0.75
Index QFR: 0.75
M
FFR
0.77
Pd/Pa
0.77
Pa
100
Pd
77

**Figure 3A**

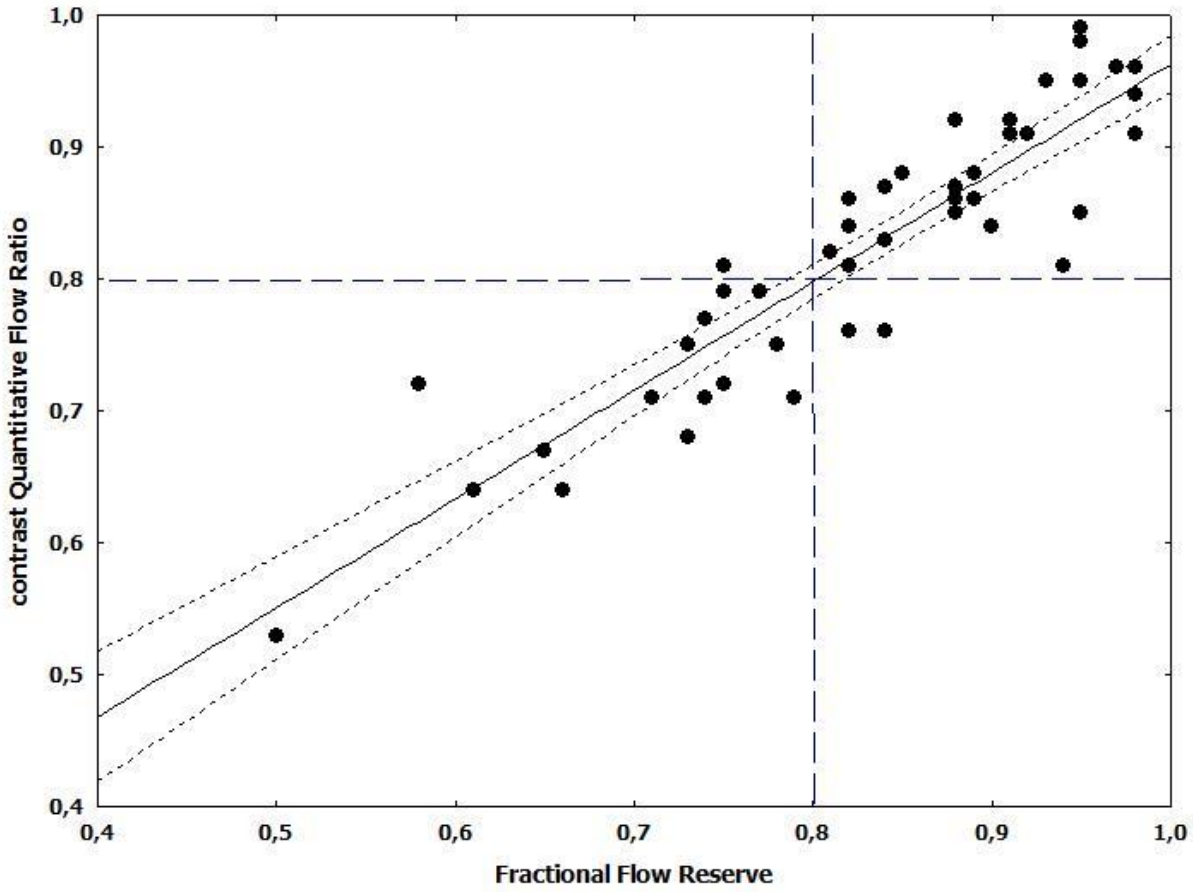
1,0
0,9
0,8
0,7
0,6
0,5
0,4
contrast Quantitative Flow Ratio
0,4
0,5
0,6
0,7
0,8
0,9
1,0
Fractional Flow Reserve

**Figure 3B**

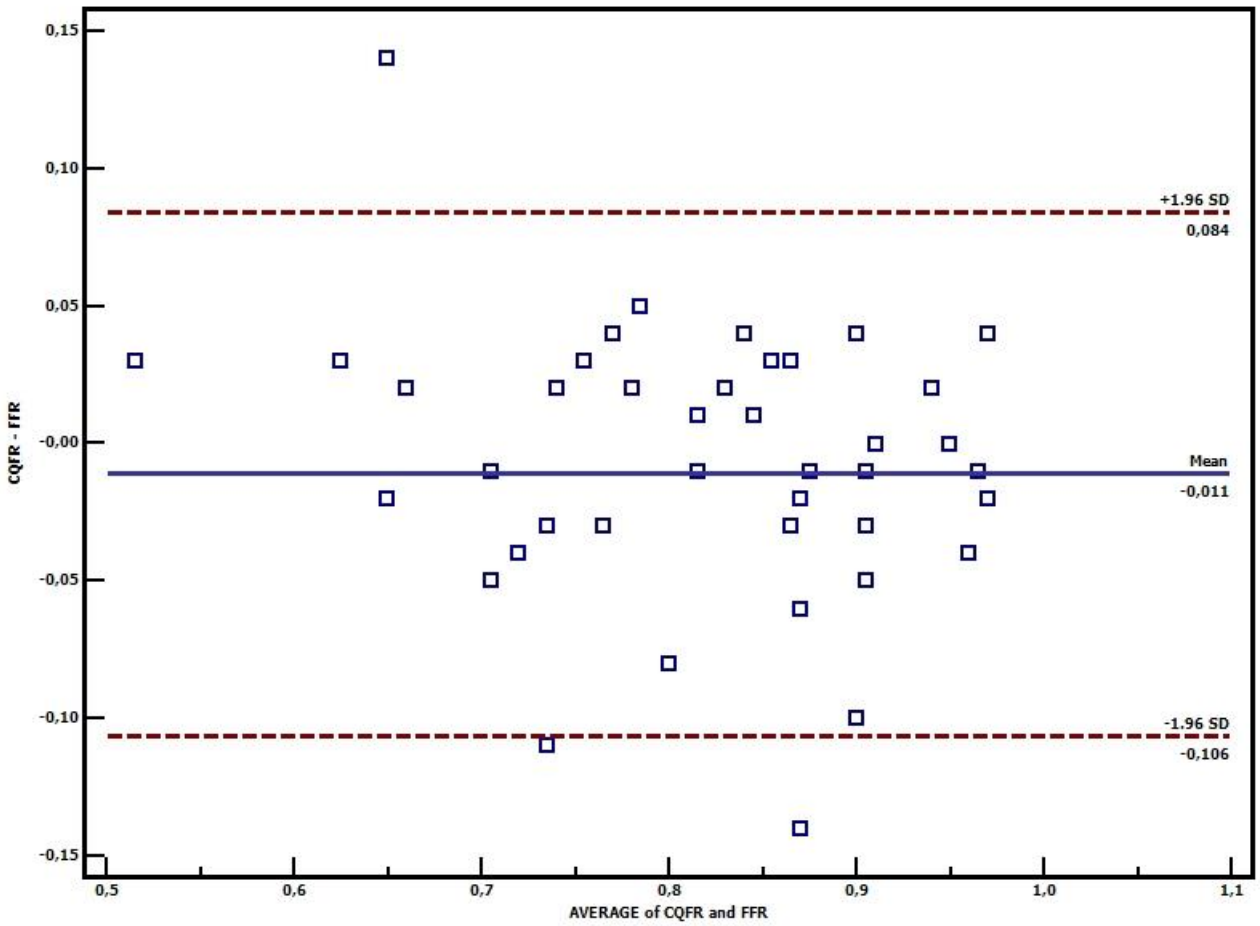
0,15
0,10
0,05
-0,00
-0,05
-0,10
-0,15
CQFR - FFR
+1.96 SD
0,084
Mean
-0,011
-1.96 SD
-0,106
0,5
0,6
0,7
0,8
0,9
1,0
1,1
AVERAGE of CQFR and FFR

**Figure 3C**

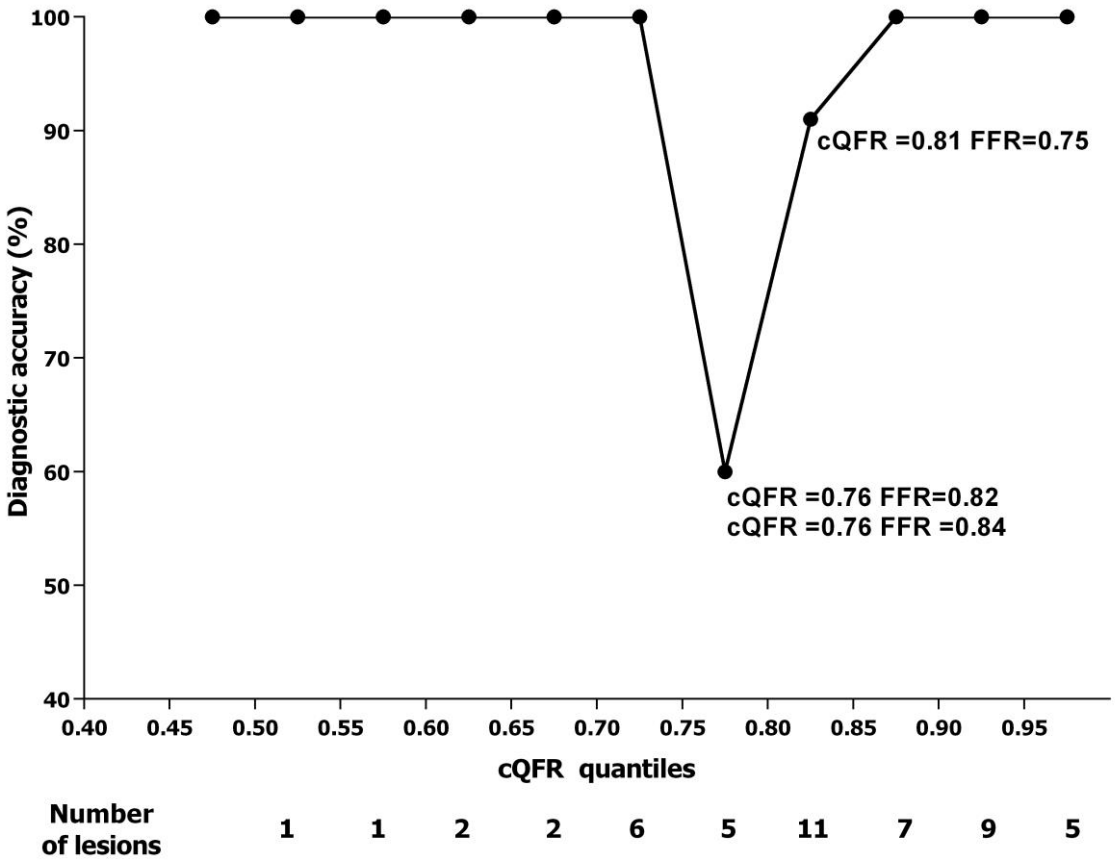
100
90
80
70
60
50
40
Diagnostic accuracy (%)
cQFR =0.81 FFR=0.75
cQFR =0.76 FFR=0.82
cQFR =0.76 FFR =0.84
0.40
0.45
0.50
0.55
0.60
0.65
0.70
0.75
0.80
0.85
0.90
0.95
cQFR quantiles
Number of lesions
1
1
2
2
6
5
11
7
9
5

**Figure 4**

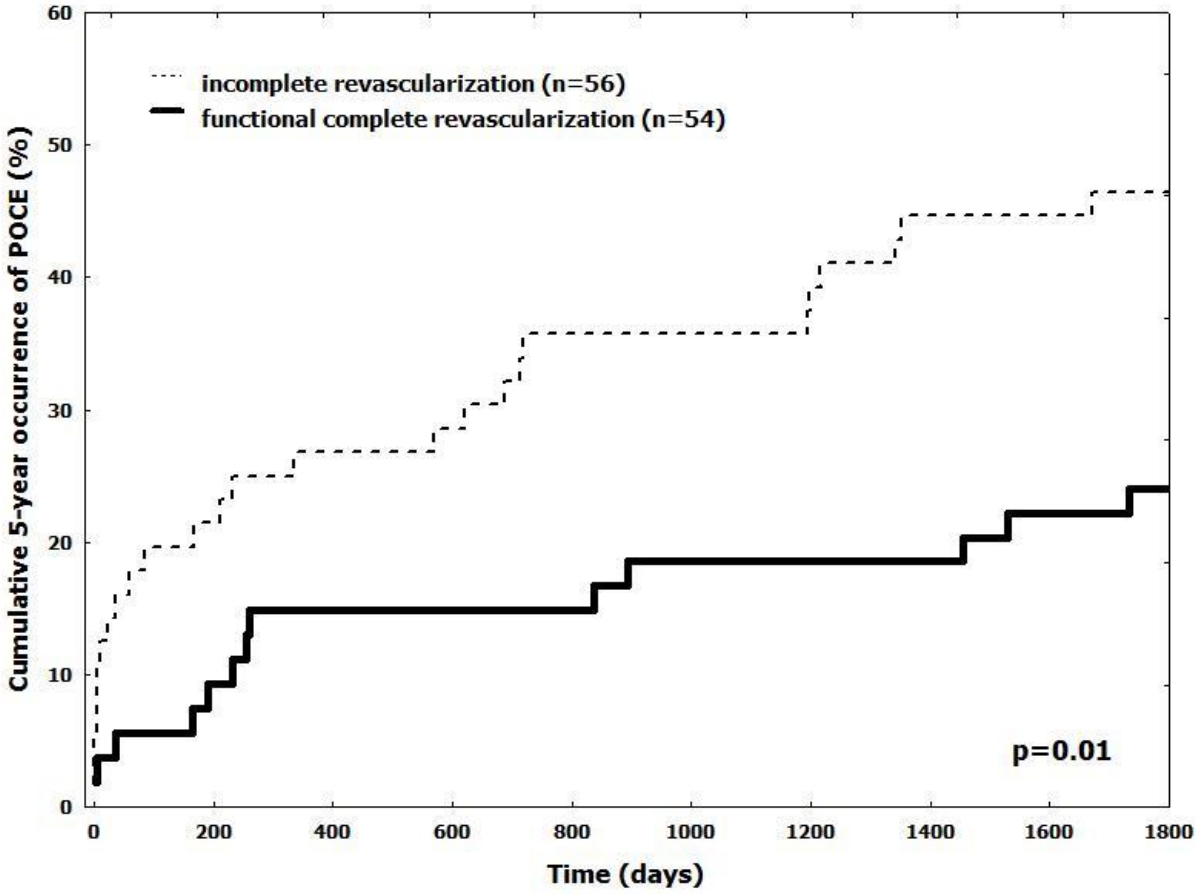
incomplete revascularization (n=56)
functional complete revascularization (n=54)
Cumulative 5-year occurrence of POCE (%)
Time (days)
p=0.01
0
10
20
30
40
50
60
0
200
400
600
800
1000
1200
1400
1600
1800

**Table 1. Baseline characteristics of study population**

| | Cohort A (n=31) | Cohort B (n=45) | Cohort C (n=110) |
|---|---|---|---|
| Age, years | 64±12 | 62±11 | 64±12 |
| Male sex, no. % | 25 (31) | 36 (80) | 89 (81) |
| BMI, Kg/m2 | 26±4 | 28±5 | 27±4 |
| **CV risk farctors, no. (%)** | | | |
| Previous or current smoker | 16 (31) | 19 (45) | 60 (54) |
| Diabetes | 3 (10) | 4 (9) | 24 (22) |
| Arterial hypertension | 20 (65) | 29 (64) | 55 (50) |
| Dyslipidemia | 15 (48) | 23 (51) | 47 (43) |
| **CV medical history, no. (%)** | | | |
| MI | 3 (10) | 2 (4) | 9 (8) |
| PCI | 6 (19) | 2 (4) | 7 (6) |
| CABG | 1 (2) | 0 (0) | 5 (4) |
| Stroke | 1 (2) | 1 (2) | 5 (4) |
| **General data** | | | |
| Troponin peak, ng/dl | 5.5 [2.7-20] | 5.1 [2.5-15] | 5.9 [3-18.5] |
| Heart rate at admission, bpm | 75 [60-85] | 72 [60-80] | 73 [60-85] |
| Systolic blood pressure at admission, mmHg | 132 [110-150] | 130 [115-155] | 133 [110-155] |
| Killip class $\geq$2, no. (%) | 2 (6) | 5 (11) | 2 (2) |
| Ejection fraction at discharge, (%) | 51±15 | 47±7 | 49±10 |
| Drug eluting stent, no. (%) | 31 (100) | 44 (98) | 59 (53) |
| Two vessel disease, no. (%) | 28 (90) | 40 (89) | 89 (81) |
| Three vessel disease, no. (%) | 3 (10) | 5 (11) | 21 (19) |
| **Infarct related artery, no. (%)** | | | |
| Left anterior descending | 11 (35) | 16 (36) | 35 (32) |
| Left circumflex | 8 (25) | 11 (24) | 23 (21) |
| Right coronary artery | 11 (35) | 18 (40) | 52 (47) |
| **Non infarct related artery, no. (%)** | | | |
| Left anterior descending | 16 (51) | 25 (56) | 63 (57) |
| Left circumflex | 8 (26) | 8 (18) | 40 (36) |
| Right coronary artery | 10 (32) | 16 (37) | 28 (25) |
| Reference vessel diameter, mm | 3±0.5 | 3±0.4 | 3±0.5 |
| Diameter stenosis, (%) | 59±13 | 66±10 | 62±11 |

BMI: body mass index. CV: cardiovascular. MI: myocardial infarction. PCI: percutaneous coronary intervention. CABG: coronary artery bypass graft. bpm: beats per minute.

**Table 2. Baseline characteristics of cohort C stratified according to NI-FSS**

| | Functional complete revascularization (n=54) | Incomplete revascularization (n=56) | p |
|---|---|---|---|
| Age, years | 64±11 | 64±13 | 0.6 |
| Male sex, no. % | 46 (85) | 43 (77) | 0.8 |
| BMI, Kg/m2 | 27±3 | 28±4 | 0.7 |
| **CV risk farctors, no. (%)** | | | |
| Previous or current smoker | 27 (50) | 33 (59) | 0.6 |
| Diabetes | 10 (18) | 14 (25) | 06 |
| Arterial hypertension | 24 (44) | 31 (55) | 0.6 |
| Dyslipidemia | 23 (41) | 24 (43) | 0.9 |
| **CV medical history, no. (%)** | | | |
| MI | 5 (9) | 4 (7) | 0.7 |
| PCI | 5 (9) | 2 (4) | 0.4 |
| CABG | 1 (2) | 4 (7) | 0.3 |
| Stroke | 4 (7) | 1 (2) | 0.3 |
| **General data** | | | |
| Killip class ≥2, no. (%) | 1 (2) | 1 (2) | 0.8 |
| Ejection fraction at discharge | 50±10 | 49±11 | 0.5 |
| Drug eluting stent, no. (%) | 30 (56) | 29 (52) | 0.9 |
| Two vessel disease, no. (%) | 44 (81) | 45 (80) | 0.8 |
| Three vessel disease, no. (%) | 10 (19) | 11 (20) | |
| **Infarct related artery, no. (%)** | | | |
| Left anterior descending | 17 (31) | 18 (32) | |
| Left circumflex | 11 (20) | 12 (21) | 0.6 |
| Right coronary artery | 26(48) | 26 (46) | |
| **Non infarct related artery, no. (%)** | | | |
| Left anterior descending | 32 (59) | 31 (55) | |
| Left circumflex | 19 (35) | 21 (38) | 0.3 |
| Right coronary artery | 13 (24) | 15 (27) | |

NI-FSS: non-invasive functional syntax score. BMI: body mass index. CV: cardiovascular. MI: myocardial infarction. PCI: percutaneous coronary intervention. CABG: coronary artery bypass graft.