Fractional Flow Reserve or Optical Coherence Tomography to Guide Management of Angiographically-Intermediate Coronary Stenosis: A Single-Center Trial

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Running Title: FFR or OCT in Patients with Intermediate Stenoses

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**ABSTRACT**

**Background:** Fractional flow reserve (FFR) and optical coherence tomography (OCT) may help both in assessment of angiographically-intermediate coronary lesions (AICL) and in percutaneous coronary interventions (PCI) optimization.

**Objectives:** To compare OCT-guidance and FFR-guidance in patients with AICL in a single-center, prospective, 1:1 randomized trial (acronym: FORZA, NCT01824030).

**Methods:** Patients with AICL were randomized to FFR or OCT. In the FFR arm, PCI was performed if FFR was ≤0.80. In the OCT arm, PCI was performed if area stenosis was ≥75% or 50%-75% with minimal lumen area <2.5 mm² or plaque rupture. Angina (evaluated by Seattle Angina Questionnaire, SAQ), major adverse cardiac events (MACE) and cost were assessed at the end of follow up. Predefined primary end point was the composite of MACE or significant angina (defined as SAQ frequency scale<90) at 13-month.

**Results:** A total of 350 patients (with 446 AICL) were enrolled (176 randomized to FFR and 174 to OCT). The primary end point of MACE or significant angina at 13-month occurred in 14.8% patients of FFR arm and in 8.0% of OCT arm (P=0.048). This result was driven by a not statistically significant lower occurrence of all primary end-point components. Up to 13-month, rate of medically managed patients was significantly higher (p<0.001) and total cost significantly lower (P<0.001) with FFR in comparison to OCT.

**Conclusions:** In patients with AICL, OCT-guidance is associated with lower occurrence of the composite of MACE or significant angina. FFR-guidance is associated with a higher rate of medical management and lower costs.

**KEY WORDS:** Fractional Flow Reserve; Optical Coherence Tomography; FFR; OCT; Percutaneous Coronary Interventions; PCI; Personalized Medicine

**CONDENSED ABSTRACT**

Fractional flow reserve (FFR) and optical coherence tomography (OCT) may help both in assessment of angiographically-intermediate coronary lesions (AICL) and in percutaneous coronary interventions (PCI) optimization. We conducted a single-center, prospective, 1:1 randomized trial comparing FFR or OCT in 350 patients with AICL. Patients randomized to FFR, as compared with OCT, were significantly more commonly managed by medical therapy. The primary end point of MACE or significant angina at 13-month occurred in 14.8% patients of FFR arm and in 8.0% of OCT arm (P=0.048). This result was driven by a (not statistically significant) lower occurrence of all primary end-point components.

**ABBREVIATIONS AND ACRONYMS**

PCI: percutaneous coronary interventions
AICL: angiographically intermediate coronary lesions
FFR: fractional flow reserve
OCT: optical coherence tomography
MLA: minimal lumen area
AS: area stenosis
RLA: reference lumen area
MI: myocardial infarction
MACE: major adverse cardiac events
SAQ: Seattle angina questionnaire
INTRODUCTION
The decision whether to perform percutaneous coronary interventions (PCI) in patients with angiographically intermediate coronary lesions (AICL) is a daily clinical challenge. Once decision to perform PCI is taken, PCI results may be optimized by adjunctive devices, but their possible clinical impact is debated. Both functional assessment by fractional flow reserve (FFR) or intracoronary imaging techniques, such as optical coherence tomography (OCT), may be considered for lesion severity evaluation and PCI optimization. Major international clinical guidelines on myocardial revascularization support the use of physiological assessment to guide revascularization in patients with AICL (1,2). Yet, intracoronary imaging techniques are raising growing interest (1,2). Since head-to-head comparisons between FFR and OCT are lacking, we designed a prospective randomized trial aimed at assessing the clinical (and economic) implications associated with FFR or OCT use in patients with AICL (3). The results obtained up to one month of follow-up were previously reported (4) and documented that FFR, as compared with OCT, increased the rate of patients treated with initial medical therapy, reduced asymptomatic renal injury and costs. In the present paper, we report the pre-defined analyses at 13-month follow-up.

METHODS
Study design
The Fractional Flow Reserve vs Optical Coherence Tomography to Guide RevasculariZAtion of Intermediate Coronary Stenoses (FORZA, ClinicalTrials.gov Identifier: NCT01824030 URL: https://clinicaltrials.gov/ct2/show/NCT01824030 ) study is an open-label, single-center prospective randomized trial comparing the clinical outcome and the costs in patients with at least one AICL, randomized to FFR- or OCT-guidance. Rationale and study design have been published as full paper (3). Briefly, patients with stable ischemic heart disease or stabilized (culprit lesion treated previously) acute coronary syndrome and evidence of at least one
AICL were 1:1 randomized to either FFR-guidance or OCT-guidance for both PCI performance and, in the case of revascularization, PCI optimization. AICL was defined as a coronary lesion with a visually estimated percentage diameter stenosis ranging from between 30% and 80% in the (non-distal segment) of a major epicardial vessel. To be eligible for the study, patients had to have single vessel disease with AICL or multivessel disease with AICL only or multivessel disease with at least one AICL and previously treated angiographic critical stenoses. The full list of exclusion criteria is reported in the Supplementary Table 1. The randomization process was previously described (3,4). Both the operator and the patient were unblinded to the technique used.

The study flow chart is summarized in Figure 1. The study was approved by the Ethics Committee of our Institution (internal code: 6261/13) and all patients signed a dedicated informed consent form.

**FFR-guidance protocol**

In the FFR arm (after intracoronary administration of nitroglycerin) a 0.014-inch pressure monitoring guidewire (Pressure Wire Certus or Aeris, Abbott Vascular, Abbott Park, Illinois, U.S.A) was advanced beyond the AICL under radioscopic examination. Then, FFR was defined as the lowest ratio of distal coronary pressure (Pd) divided by aortic pressure (Pa) after achievement of hyperemia using intravenous administration of 140 μg Kg-1 min-1 adenosine. When FFR value was >0.80, PCI was not performed. In contrast, when FFR value was ≤0.80, PCI was performed with the aim of achieving a post-stenting FFR ≥0.90. If post-stenting FFR was <0.90, a further post-dilation of the stent could be performed. If FFR remained <0.90, a pullback of the wire to identify another possible pressure drop and/or a subsequent stent implantation at least 5 mm from the stent was performed according to physician’s preference (5). The final achievement of an FFR≥0.90 was defined as an “optimal FFR result”.
**OCT-guidance protocol**

In OCT arm, OCT images were acquired (after intracoronary administration of nitroglycerin) at the site of AICL with commercially available systems (C7 System; LightLab Imaging Inc/St Jude Medical, Westford, Massachusetts, U.S.A. and, after its availability, Optis System; Abbott Vascular, Abbott Park, Illinois, U.S.A.) after the OCT catheter (C7 Dragonfly; LightLab Imaging Inc/St Jude Medical, Westford, Massachusetts, U.S.A. and Dragonfly Optis; Abbott Vascular, Abbott Park, Illinois, U.S.A.) was advanced to the distal end of the target lesion. The entire length of the region of interest was scanned collecting the following measures: minimal lumen area (MLA, defined as cross section area at the smallest lumen area level), proximal reference lumen area (pRLA, defined as cross section at the frame with largest lumen within 10 mm proximal to MLA and before any major side-branch), distal reference lumen area (dRLA, defined as cross section at the frame with largest lumen within 10 mm distal to MLA and before any major side-branch) and mean reference lumen area (mRLA, defined as pRLA + dRLA)/2). Based on these parameters, percentage of area stenosis (AS) was calculated using the following formula: (mRLA-MLA)/mRLA × 100.

Plaque rupture (also called ulceration) was defined as a recess in the plaque beginning at the luminal-intimal border (6).

PCI was performed when at least one of the following criteria was present:

1) AS ≥ 75%,

2) AS between 50% to 75% and MLA <2.5 mm²,

3) AS between 50% to 75% and plaque rupture.

In patients who underwent revascularization, OCT was used also to guide PCI and optimize PCI results. Further interventions, following stent implantation, were performed in the presence of major stent malapposition (defined as distance between strut and vessel wall greater than 350 μm or < 350>200 μm for a length > 600 μm), major under-expansion (in-
stent minimal cross-section area <75% of the RLA) or major edge dissection (defined as length > 600 µm). Absence of any of the above-mentioned abnormalities was defined as “optimal OCT result”.

*Treatment cost estimation*

Estimated cost to treat each patient was obtained by assessing the costs of the index procedure, the costs of first hospitalization duration and the costs related with any unplanned hospitalization occurring after discharge, due to the occurrence of major adverse events (3). Details for procedural and hospitalization cost evaluation have been previously reported (4). Costs for unplanned hospitalizations were calculated using the standard National Health System reimbursement rates (based on discharge diagnosis and revascularization procedure performed).

*Clinical outcome assessment and definitions*

Clinical data (risk factors, medical history) and procedure details of enrolled patients were prospectively collected in a dedicated electronic database at the time of patient enrolment. Clinical data recording and clinical follow-up was performed by physicians not involved in the study procedures. In the case of suspected adverse clinical events, patient’s records and angiographic studies were carefully reviewed by two senior cardiologists blinded to treatment adopted.

The clinical events were defined as follows:

- Death (the cause of death was ascertained by reviewing of the available clinical records and all deaths without clear non-cardiac causes were considered as cardiac death)

- Myocardial Infarction (MI) was defined according to the third universal definition of myocardial infarction (7)
- Target vessel revascularization was defined as clinically driven revascularization by either PCI or coronary-aortic bypass grafting on the vessel evaluated by FFR or OCT regardless the fact that it was initially treated by PCI (3).

- Major adverse cardiac events (MACE): death or MI or target vessel revascularization.

- Target vessel failure: any MACE not clearly related with another vessel or cause.

Each enrolled patient completed a Seattle Angina Questionnaire (SAQ) before treatment, at 1- and 13-month follow up. SAQ consists of a questionnaire of eleven questions grouped into five main scales (physical limitation, angina stability, angina frequency, treatment satisfaction, and disease perception) specifically developed for patients with coronary artery disease (8). Scale scores were then transformed to a 0 to 100 visual analog scale and higher scores indicated better health status (8). Due to the evidence of overlaps between the five assessment scales, ‘significant residual angina’ was defined as a value < 90 on the angina frequency scale (3).

**Primary end point of the study**

Details of primary end-point selection and sample size calculations were reported in the trial design paper (3). Briefly, the study was designed to test the hypothesis of possible superiority of OCT over FFR in the clinical management of patients AICL after 13 months of follow-up. According to the study design (3), the primary end point had to be selected after observations of MACE occurring up to the 13th month. In particular, in the case of MACE rate absolute difference >1% across the study arms, the primary end point was pre-specified to be the composite of significant residual angina (<90 score at SAQ angina frequency scale) and MACE at 13-month (3). Sample size was estimated assuming a 50% reduction of the primary end point in the OCT arm (as compared with FFR) with an alpha error of 5% and power of 80% (3).

**Statistical analyses**
All analyses were performed according to the intention to treat. Continuous variables were tested for normality using the Kolmogorov-Smirnov test, and compared by the Student’s t or Mann-Whitney U tests, as appropriate. Categorical variables were expressed as counts (percentages), and analyzed by chi-square or Fisher’s exact tests, as appropriate. Combined adverse events were evaluated on a per-patient hierarchical basis. The incidence of MACE, medical management and target vessel failure over time was studied with the use of the Kaplan-Meier method and compared by the log-rank test. All the 13-month rates referenced in the results are Kaplan-Meier estimates at 13 months.

A multivariate Cox regression analysis including potential confounding demographic and clinical variables (risk factors, clinical presentation and discharge therapy) was carried out in order to identify independent predictors of the primary endpoint and to determine their adjusted hazard ratios.

A 2-tailed p value <0.05 was established as the level of statistical significance for all tests. Analyses were carried out using SPSS v. 21.0 (SPSS, Chicago, IL, USA). Statistical significance was defined by two-tailed P<0.05.

RESULTS

Baseline characteristics of the study population and procedure conduction

A total of 350 patients entered the study and were randomized to FFR (n= 176) or OCT (n=174). The baseline clinical and angiographic characteristics of the patients enrolled in the study are reported in Table 1 and were extensively discussed previously (4). Briefly, cardiovascular risk factors were highly prevalent and included 35.4% of diabetes and 17.7% of chronic kidney disease. Most patients were stable with a preserved left ventricular ejection fraction. Multivessel coronary disease was common and more than one lesion was often investigated (mean investigated lesion per patient: 1.27 in both arms). As shown in the table 1, all baseline characteristics were comparable between the two study groups (with the
exceptions of significantly higher prevalence of previous MI in OCT arm and higher prevalence of left anterior descending artery involvement in the FFR arm).

The comparison of procedures and the clinical outcomes up to one month have been described previously in a dedicated report (4). In particular, 29.3% of the lesions in FFR arm and 50.7% of the those in OCT arm were managed by PCI (4) and this translated into a statistically significant higher rate of patients referred to initial medical management with FFR (67.7% vs. 41.1% with OCT, P<0.001) (4). Procedural characteristics have been reported previously and showed remarkable differences between study arms that included lower use of balloons/stents, lower contrast dose administration, lower occurrence of acute kidney injury in the FFR-guidance arm (4). Details on PCI procedures are reported in the Supplementary Table 2 showing a significant larger implanted stent diameter in the OCT group compared with FFR (3.2 ±0.5 mm vs. 2.9±0.3 mm; p=0.009).

All patients were discharged alive and their clinical outcome up to 1 month was previously reported (4).

13-month clinical outcomes

All patients completed the 13-month follow up. The primary end point of MACE or significant angina at 13-month occurred in 14.8% patients of FFR arm and in 8.0% of OCT arm (P=0.048). This result was driven by a not statistically significant lower occurrence of all components of the primary end point (Figure 2). At multivariate analysis, randomization to OCT was confirmed to independently predict the primary end point (adjusted hazard ratio: 0.40, 95% confidence intervals 0.19-0.85, p=0.018).

The MACE rate observed at 13-months was 5.7%, with a not significant lower incidence in OCT arm as compared to FFR (3.4% vs. 8.0%, p=0.064, Figure 3). Of note, target vessel failure occurred significantly less commonly in patients randomized to OCT.
(2.3% vs. 7.4% with FFR; P= 0.027 Figure 3). Details of clinical adverse events noticed during the study are provided in Supplementary Table 3.

Data on the SAQ frequency scale in patients randomized to FFR or OCT are reported in the Supplementary Figure 1. At 13 months, a steady improvement in angina status was observed in both arms (P<0.001 vs. baseline for FFR and OCT), without statistically significant differences across study arms.

As shown in Figure 4, the rate of patients that continued to be managed by medical therapy over 13 months was higher with FFR (62.5% vs. 44.8% with OCT; P<0.001). Similarly, up to 13 months, the mean estimated cost per patient continued to be significantly lower with FFR (2577 Euro, 95%CI: 2038-3470 vs. 3750 Euro, 95%CI: 2734-4503, in OCT arm; P<0.001, Figure 4).

DISCUSSION

The optimal management of ischemic heart disease patients with AICL represents an unmet clinical need. The use of adjunctive techniques at the end of coronary angiography is appealing since it may help taking decisions during the same invasive procedure. Functional evaluation by FFR is actually regarded as the most valuable tool in the decision-making of AICL. On the other hand, intracoronary imaging techniques evolved over last years. Contemporary OCT is able to accurately characterize the coronary lesions and (in the case of PCI) to easily detect suboptimal stent results. In such context, head-to-head comparisons of different adjunctive technique selections may provide clinically meaningful insights. The present randomized study conducted in patients with AICL suitable for invasive evaluation by either OCT or FFR showed that:

- the use of OCT is safe, causes higher number of PCIs, but is associated with lower occurrence of the combined endpoint of MACE or significant angina after 13 months (central illustration)
the use of FFR is associated with higher rate of medically managed patients and lower costs up to 13 months (central illustration).

These results are original, should be regarded as hypotheses generating (due to the limitations of stemming from a small, single-center study) and call for further comparisons between functional and imaging invasive techniques.

Patients with AICL, of difference with tight coronary lesions, may have no need of myocardial revascularization. Different pressure-wire derived functional data proven their ability in predicting stenosis-related myocardial ischemia and safety for revascularization deferral. As a result, current guidelines on PCI recommend the use of FFR (or instantaneous wave-free ratio) to assess the haemodynamic relevance of intermediate-grade coronary stenoses (1,2). Nevertheless, FFR is still strongly underused (9) and invasive imaging techniques are often adopted since they are able to both define coronary anatomy and guide eventual PCI (10). Among different techniques, OCT represents a cutting-edge imaging modality since it offers, as compared with intravascular ultrasound, improved image quality. Recent data started highlighting the possible clinical impact for OCT findings in different clinical settings like natural history of untreated coronary lesions (11) and post-PCI outcome (12). In the present study, we compared FFR-guidance with OCT-guidance in patients with AICL. The early-follow up results showed that the selection of FFR was associated with a significantly higher number of conservatively treated lesions. This translated into a higher number of medically managed patients and initial benefit in terms of renal preservation and costs as compared with OCT (4). The later clinical course could help assess the clinical implications associated with these differences in the initial management. We set at 13-month the primary end-point evaluation since it allowed to cover the higher risk of major stent complications (thrombosis and restenosis) and most of patients eventually treated by PCI completed their 12-month double antiplatelet therapy one month before. We focused on a
composite end point of MACE or residual angina since we expected in FFR arm a low rate of hard adverse events together with a not negligible rate of persistent angina (13). To estimate residual angina, we used a quality of life tool like SAQ that has been specifically developed (8), that has been extensively validated and that continues to be adopted in contemporary clinical trials (14). Such assumptions were confirmed by the results observed in the FFR arm since the MACE rate at 13-month (8%) was comparable with that observed in the recent DEFINE FLAIR trial (7% MACE rate at 12-month in FFR group) (15) and significant angina (SAQ angina frequency <90) was present in 6.8% of patients.

In the OCT arm, despite their borderline angiographic severity, AICLs were often revealed by OCT as tight (area stenosis ≥75% or with MLA <2.5%) and sometimes with complicated morphology (4). Such findings fit with recent data (16,17) and reinforce the interest on the results of the present study. Of note, to take into account vessel size (an indirect measure of myocardial territory supplied) and to rule out the possibility of overtreating smaller vessels, we set as cut-off for treatment the presence of relevant lumen reduction (>50%) as compared with reference segments and treated severe lumen reductions (≥75%) regardless MLA value. For instance, these criteria were also recently found in a small retrospective study to be significantly associated with hemodynamic significance (18). When PCI was required, in the OCT arm we used imaging to select the initial treatment strategy but also to check stent result and optimize PCI result by treating OCT-detected stent complications. Yet, since large studies like CLI-OPCI II (12) were lacking at the time of study design, the PCI optimization protocol aimed only at reducing major stent malapposition, major stent underexpansion (cut-off 75%) and edge dissections. In other words, the OCT guidance protocol applied was conceived, based on the few data available at the time of study design, at limiting overtreatment during the PCI conduction. For instance, a large multicenter prospective randomized trial (ILUMIEN IV, NCT03507777) has been
designed to test the hypothesis of superiority for OCT guidance during PCI optimization. It should be underlined that the “conservative” OCT criteria adopted in the present trial might have led not to revascularize some plaques at potential increased risk (11) and to leave some stents not expanded at best (19). Besides these considerations, the OCT-guidance protocol applied in our study was feasible and did not increase periprocedural major adverse events. At 13-month, the OCT arm, as compared with FFR, showed a significantly lower occurrence of the primary composite endpoint of MACE or residual angina. Notably, all adverse events were numerically higher with FFR and the more device-specific endpoint of target vessel failure was significantly improved by OCT.

The present study also demonstrated that the efficacy of FFR in limiting revascularizations and costs, extensively documented in comparison with angiographic guidance (19), is maintained in comparison with imaging guidance. Indeed, as compared with OCT, estimated cost per patient were strikingly lower with FFR and the numerically higher occurrence of unplanned revascularizations during the follow-up was far from fulfilling the marked difference in medically managed patients determined during the initial evaluation. As a final remark, both FFR and OCT deserve specific (and completely different) knowledge, learning curve and operator’s experience. From such perspective, the environment of the present study was particularly favorable since it has been conducted in a high-volume center by few operators daily practicing both techniques and with documented internal performance review for both FFR (20) and OCT (21).

Study Limitations

The present study was a non-sponsored single center trial. As consequence of limited funds, it had small sample size and was conducted locally without both structured clinical research organization and independent clinical events committee. The primary composite end point of the study comprised occurrence of angina which represents a weak end point.
Furthermore, like other trials with similar design, patients and physicians were not blinded and this (especially in the presence of untreated lesions) may determine management biases, especially for target vessel revascularization and medical treatment. In particular, the significantly lower rate of dual antiplatelet therapy and the trend to lower rate of statin therapy in the FFR arm may have led to a significant disadvantage with respect to medical therapy.

As a consequence of such important recognitions, the results observed in the FORZA trial don’t allow drawing firm conclusions and, on the opposite, call for further evaluations of the implications associated with the different management strategies of patients with AICL.

CONCLUSIONS

In patients with AICL suitable for invasive evaluation by either OCT or FFR, the choice of one technique instead of the other, may significantly affect the clinical course. In particular, FFR guidance is associated with a higher rate of medical management and lower costs up to 13-month, while OCT-guidance causes more initial elective revascularizations but a lower occurrence of the combined endpoint of MACE or significant angina after 13 months.

PERSPECTIVES

WHAT IS KNOWN?

The decision whether to revascularize patients with coronary lesions of intermediate severity at angiography may benefit from adjunctive invasive techniques. Among different options, functional evaluation by FFR (or instantaneous wave-free ratio) is considered as the gold standard.

WHAT IS NEW?

In patients with angiographically-intermediate coronary lesions, OCT (a cutting-edge high resolution intracoronary imaging technique) can be used to both guide revascularization and PCI optimization since it may improve (as compared with FFR) the combined end-point of
MACE or significant angina at 13-month. Nevertheless, OCT-guidance, as compared with FFR, increases the number of revascularizations and the costs.

**WHAT IS NEXT?**

The observed results open the door for further evaluations of imaging-guidance in the management of coronary artery disease patients presenting with different angiographic or clinical features.
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FIGURE LEGENDS

Figure 1. Study flow chart.

FFR, fractional flow reserve; OCT, optical coherence tomography; AS, area stenosis; MLA, minimal lumen area; PCI, percutaneous coronary intervention; RLA, reference lumen area; MACE, major adverse cardiac events.

Figure 2. Primary study end point and its individual components at 13-month follow-up.

MI, myocardial infarction; SAQ, Seattle Angina Questionnaire.

Figure 3. Major adverse cardiac events (A) and target vessel failure (B) occurring in the FFR and OCT group.

Results are expressed as Kaplan-Meier curves, and p values are log-rank estimates. MACE, major adverse cardiac events; TVF, target vessel revascularization; FFR, fractional flow reserve; OCT, optical coherence tomography.

Figure 4. Rate of patients managed with medical therapy alone (A) and costs (B) in the FFR and OCT groups. Results in panel A are expressed as Kaplan-Meier curves, and p values are log-rank estimates. Results in panel B are expressed as box plots with median and interquartile ranges. FFR, fractional flow reserve; OCT, optical coherence tomography.

Central Illustration. Schematic representation of FORZA trial design and main trial findings.

FFR, fractional flow reserve; OCT, optical coherence tomography; PCI, percutaneous coronary interventions; MACE, major adverse cardiac events.
Patients with (one or more) angiographically-intermediate coronary stenosis (n = 350)

1:1 Randomization

FFR-guidance (n = 176)
- FFR ≤ 0.80
  - YES: PCI with FFR optimization
    - PCI aimed at achieving FFR ≥ 0.90
  - NO: NO PCI (Optimal Medical Therapy)

OCT-guidance (n = 174)
- NO
  - AS ≥75% or
  - AS >50% <75% plus MLA < 2.5 mm² or
  - AS >50% <75% plus plaque rupture
  - YES: PCI with OCT optimization
    - PCI aimed at minimizing major stent malapposition (>350 μm, or <350 μm >200 μm for a length >600 μm), major stent under-expansion (<75% of the RLA), or major edge dissection (length >600 μm)

Clinical follow-up at 13 months
- MACE; target vessel failure; angina status assessed by the Seattle Angina Questionnaire
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<th>13-month follow-up</th>
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<td>Medical therapy → PCI ↑ Contrast medium use ↓</td>
<td>Costs ↓ MACE or significant angina ↓</td>
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<td></td>
<td>Kidney injury</td>
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Table 1. Baseline clinical, angiographic, and procedural characteristics

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<td><strong>CLINICAL PRESENTATION</strong></td>
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<td>LVEF (%)</td>
<td>60±8</td>
<td>56±9</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>BASELINE ANGIOGRAPHIC FEATURES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>92 (52.3%)</td>
<td>83 (47.7%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Investigated lesion location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>150 (66.7%)</td>
<td>134 (60.6%)</td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td>37 (16.4%)</td>
<td>27 (12.2%)</td>
<td>0.02</td>
</tr>
<tr>
<td>RCA</td>
<td>38 (16.9%)</td>
<td>60 (27.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>MANAGEMENT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients treated with PCI</td>
<td>57 (32.4%)</td>
<td>92 (52.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of balloons per patient</td>
<td>0.74±1.48</td>
<td>1.45±1.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of stents per patient</td>
<td>0.33±0.57</td>
<td>0.64±0.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Optimal result (according to study protocol) obtained</td>
<td>19 (47.5%)</td>
<td>55 (64.7%)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>DISCHARGE THERAPY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>166 (94.3%)</td>
<td>163 (93.6%)</td>
<td>0.83</td>
</tr>
<tr>
<td>P2Y12 inhibitors</td>
<td>115 (65.3%)</td>
<td>133 (76.4%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>137 (77.8%)</td>
<td>144 (82.7%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>56 (31.8%)</td>
<td>55 (31.6%)</td>
<td>0.97</td>
</tr>
<tr>
<td>Statins</td>
<td>152 (86.3%)</td>
<td>161 (92.5%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Nitrates</td>
<td>25 (14.2%)</td>
<td>19 (10.9%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Ranolazine</td>
<td>31 (17.6%)</td>
<td>24 (13.7%)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Data are expressed as counts (percentage) or mean ± standard deviation.
FFR, fractional flow reserve; OCT, optical coherence tomography; BMI, body mass index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; MI, myocardial infarction; LVEF, left ventricular ejection fraction; LAD, left anterior descending artery; LCX, left circumflex; RCA, right coronary artery; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.