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Evolving Routine Standards in Invasive Hemodynamic Assessment of Coronary Stenosis

The Nationwide Italian SICI-GISE Cross-Sectional ERIS Study

Matteo Tebaldi, MD,[a] Simone Biscaglia, MD,[a] Massimo Fineschi, MD,[b] Giuseppe Musumeci, MD,[c] Alfredo Marchese, MD,[d] Antonio Maria Leone, MD,[e] Marco Luciano Rossi, MD,[f] Giulio Stefanini, MD,[f] Antongiulio Maione, MD,[g] Alberto Menozzi, MD,[h] Fabio Tarantino, MD,[i] Veronica Lodolini, BSc,[a] Francesco Gallo, MD,[a] Emanuele Barbato, MD, PhD,[j] Giuseppe Tarantini, MD, PhD,[k] Gianluca Campo, MD[a,l]

ABSTRACT

OBJECTIVES The aims of the ERIS (Evolving Routine Standards of FFR Use) study are to describe the current use of invasive coronary physiology assessment and discern the reasons for its nonuse in daily practice.

BACKGROUND Adoption of coronary physiology guidance in the catheterization laboratory varies among countries, centers, and operators.

METHODS ERIS is an investigator-driven, nationwide, prospective, cross-sectional study involving 76 Italian catheterization laboratories. Each center had a 60-day window to include consecutive cases that fulfilled the inclusion and exclusion criteria. Two pre-specified groups were enrolled: 1) patients who had operators apply fractional flow reserve or instantaneous wave-free ratio assessment (physiology assessment group); and 2) patients who had operators decide not to perform fractional flow reserve or instantaneous wave-free ratio assessment, although the patients met the inclusion and exclusion criteria (visual estimation group).

RESULTS Overall, 1,858 cases were included (physiology assessment group, n = 1,177; visual estimation group, n = 681). Physiology-based guidance was used in 7% and 13% of the total volume of angiographic and percutaneous coronary interventions, respectively. Its use was in line with European and American guidelines in 48% of the cases (n = 569). Physiology guidance was used in a consistent number of patients with acute coronary syndromes (n = 529 [45%]). The main reason for not using physiology guidance was the operator's confidence that clinical and angiographic data alone were sufficient.

CONCLUSIONS Use of coronary physiology assessment in daily practice meets the current guideline indications in approximately 50% of cases. The major limiting factor for the adoption of physiology guidance was the operator's confidence in visual assessment alone. (Evolving Routine Standards of FFR Use [ERIS]; NCT03082989) (J Am Coll Cardiol Intv 2018;11:1482–91) © 2018 by the American College of Cardiology Foundation.

From the [a]Cardiovascular Institute, Azienda Ospedaliero-Universitaria di Ferrara, Cona, Italy; [b]Department of Cardiovascular Diseases, University Hospital Santa Maria alle Scotte, Siena, Italy; [c]S.C. Cardiologia, A.O. Santa Croce e Carle, Cuneo, Italy; [d]Interventional Cardiology Unit, Anthea Hospital, Bari, Italy; [e]Institute of Cardiology, Catholic University of the Sacred Heart, Rome, Italy; [f]Division of Cardiology, Cardio Center, Humanitas Research Hospital, Rozzano, Milan, Italy; [g]Department of Medicine and Surgery, University of Salerno, Salerno, Italy; [h]Unità Operativa di Cardiologia, Azienda Ospedaliero-Universitaria, Parma, Italy; [i]Cardiology Unit, Ospedale G.B. Morgagni, Forlì, Italy; [j]Division of Cardiology, Department of Advanced Biomedical Sciences, Federico II University, Naples, Italy; [k]Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy; and the [l]Maria Cecilia Hospital, GVM Care & Research, E.S: Health Science Foundation, Cotignola, Italy. This study was an investigator-driven clinical trial conducted by Società Italiana di Cardiologia Interventistica. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Over the past 2 decades, several randomized clinical trials have clearly shown that coronary revascularization driven by intracoronary pressure measurement (i.e., coronary physiology assessment), namely, fractional flow reserve (FFR), is superior in terms of adverse event reduction compared with angiographic guidance alone (1,2). On the basis of these data, intracoronary pressure measurements have been widely supported in both European and American guidelines (3–5). Nevertheless, the penetration of physiology-based guidance varies significantly across continents, countries, centers, and operators, ranging from 3% to 30% of the total volume of coronary revascularizations (6–9). In addition, the recent introduction of resting index assessment, such as instantaneous wave-free ratio (iFR), has not translated into a significant increase in physiology-based guidance (10,11). Several factors have been proposed to explain the variability in physiology assessment adoption, such as differences in equipment, reimbursement policies, and operator choice. The latter was the factor most commonly cited in a recent survey, even in the ideal scenario of no budget limits (12). Other investigators have suggested concerns regarding adenosine side effects, costs, and time (7). However, no study has investigated systematically and prospectively the actual reasons for avoidance of physiology-based guidance in a real-world clinical setting. Starting from this background, Società Italiana di Cardiologia Interventistica designed and conducted the ERIS (Evolving Routine Standards of FFR) project.

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The aims of the ERIS study were as follows: 1) to assess how, where, and why physiology-based guidance is applied in daily practice through a large, real-life, prospective cohort of consecutive cases; 2) to evaluate agreement between current guideline recommendations and routine use of physiology-based guidance; and 3) to clarify the reasons that lead operators to avoid functional evaluation.

METHODS

The ERIS study was a prospective project based on a 2-step process. First, all Italian catheterization laboratories at which at least 20 functional assessments were performed in 2015 were invited to participate in a survey focused on the management of intermediate coronary lesions (from October 2016 to January 2017). Second, catheterization laboratories that responded to the survey were involved in the nationwide, multicenter, prospective, cross-sectional study (from March 2017 to September 2017).

SURVEY FOR CENTER SELECTION. On the basis of the findings of the International Survey on Interventional Strategy (12), a Web-based platform for the survey was built (a detailed description is provided in the Online Appendix) (Advice Pharma Group, Milan, Italy). The link for the survey was sent by e-mail to the contact at the catheterization laboratory. The survey contained specific questions regarding the center, operators, and 4 clinical cases. Cases were selected by independent interventional cardiologists (M.T. and S.B.) from a database in which both quantitative coronary analysis and FFR assessment had been performed for each stenosis (with the true values concealed). The participants were asked to identify relevant stenosis (location and visual estimation of percentage diameter stenosis [DS]) and to describe their management. Participants were asked to make their decisions as in their usual clinical practice. Finally, agreement between the strategy suggested by the participants and the result obtained by the application of physiology-based guidance was calculated.

PROSPECTIVE STUDY DESIGN. After the collection of all answers to the survey, the nationwide, multicenter, prospective, cross-sectional study was started in March 2017. The Institutional Review Board of the coordinating center approved the study on February 21, 2017. The protocol was registered at ClinicalTrials.gov (NCT03082989). Each participating catheterization laboratory had a 60-day window to include consecutive cases that fulfilled the inclusion and exclusion criteria. Each participating center obtained approval from the corresponding Institutional Review Board. All patients provided written informed consent. The study included 2 pre-specified groups of patients. The first was patients who had operators decide to use invasive physiology-based assessment to guide the decision to perform coronary intervention (physiology assessment group). The second included patients who met the protocol eligibility criteria for invasive functional assessment, but the operators decided not to perform FFR or iFR assessment (visual estimation group).

INCLUSION AND EXCLUSION CRITERIA FOR THE PHYSIOLOGY ASSESSMENT GROUP. Patients ≥18 years of age who underwent coronary artery angiography for a diagnosis of ischemic heart disease were eligible if FFR and/or iFR assessment was performed in at least 1 coronary lesion with ≥50% DS (visual estimation or quantitative coronary analysis).

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

DS = diameter stenosis

FFR = fractional flow reserve

iFR = instantaneous wave-free ratio

NSTEACS = non-ST-segment elevation acute coronary syndrome(s)

PCI = percutaneous coronary intervention

SCAD = stable coronary artery disease

Refusal to provide informed consent was the only exclusion criterion. The decision to perform FFR and/or iFR assessment was left to the operator.

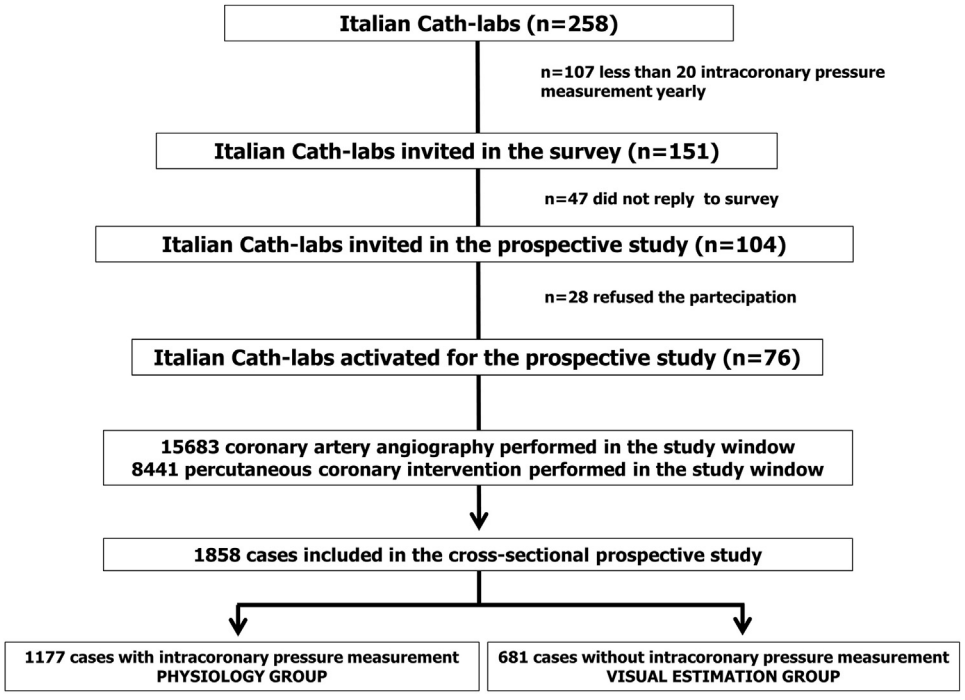
INCLUSION AND EXCLUSION CRITERIA FOR THE VISUAL ESTIMATION GROUP. On the basis of the current guidelines and consensus documents (3-7), the steering committee identified 3 clinical indications for which FFR or iFR assessment should be considered before coronary revascularization. The following 2 clinical indications are based on the current European (European Society of Cardiology) and American (American College of Cardiology/American Heart Association) guidelines (indications as per the guideline) (3-5): 1) patients with stable coronary artery disease (SCAD) showing at least 1 coronary lesion with 50% to 90% DS and nondiagnostic and/or unavailable stress test results; and 2) patients with SCAD showing coronary lesions with 50% to 70% DS and available stress test results. The following third indication was based on the consensus of the committee (indication per protocol): 3) patients with non-ST-segment elevation acute coronary syndromes (NSTEACS) and at least 1 nonculprit lesion with 50% to 70% DS. The steering committee decided to expand the current guideline indication considering that the trials that tested the prognostic role of physiology assessment were based on the presence of intermediate stenosis and decision for revascularization, independently from the availability of noninvasive stress test results. All consecutive patients ≥18 years who met these criteria were considered eligible. Denied informed consent was the only exclusion criterion. The protocol required operators to clearly describe and report the reasons for not performing FFR or iFR assessment. It was possible to select a pre-specified item or to fill in a free-text box. For each lesion analyzed, >1 answer could be selected. To better categorize the reasons, we applied the classification suggested by Cabana et al. (13) regarding barrier categories.

DATA COLLECTION AND DATA QUALITY. The following data were collected: baseline characteristics (including demographics, risk factors, and medical history), information on cardiac procedures (coronary angiography, percutaneous coronary intervention [PCI], and functional assessment), coronary anatomy and lesions, functional assessment type (FFR and/or iFR), route of adenosine administration, result (value) of the coronary physiology examination, and the subsequent revascularization decision and procedures. To assess the concordance (or discordance) between the coronary physiology assessments and the operator's decision, an abnormal invasive functional result was defined as FFR ≤0.80 and iFR ≤0.89 (1,2,10,11). In cases in which the functional assessment was performed after stent implantation (with FFR determined in all such cases), we defined positive FFR as ≤0.88 (14). The study was focused on procedure-related data. Follow-up (in- and out-of-hospital) was not required. At each site, the principal investigator was responsible for screening consecutive patients admitted to the catheterization laboratory. The principal investigator was responsible for the collection of all cases that met the inclusion and exclusion criteria in the study period, regardless of the operator who performed the procedure. Data were collected using a Web-based electronic case report form, with the central database located at the Advice Pharma Group. Data were checked for missing or contradictory entries and for values outside the normal range by using a validation plan, integrated in the data entry software. Random controls to confirm the consistency of the data reported on case report forms and the inclusion of consecutive cases were performed by the sponsor (Società Italiana di Cardiologia Interventistica).

OBJECTIVES. The main objectives of the ERIS study were as follows: 1) to describe the characteristics of patients and lesions subjected to FFR and iFR assessment; 2) to compare the use of coronary physiology assessment and the current European and American guideline recommendations; and 3) to investigate the operators' reasons for not using coronary physiology-based guidance. According to the current guidelines (5-7), appropriate physiology guidance use was defined in the following cases: 1) coronary lesions (50% to 90% DS) among patients with SCAD when the stress test result is unavailable, nondiagnostic, or discordant; and 2) intermediate coronary lesions (50% to 70% DS) among patients with SCAD.

STATISTICAL ANALYSIS. Continuous data were tested for normal distribution using the Kolmogorov-Smirnov test. Normally distributed values are presented as mean ± SD and were compared using the Student's *t*-test and 1-way analysis of variance. Otherwise, the median (interquartile range), Mann-Whitney *U* test, and Kruskal-Wallis test were used. Categorical variables are summarized in terms of number and percentage and were compared using the 2-sided Fisher exact test. A 2-sided p value < 0.05 was considered to indicate statistical significance. All analyses were performed using STATISTICA version 10 (StatSoft, Tulsa, Oklahoma).

FIGURE 1 Flowchart of the Selection of the Study Centers



RESULTS

Among 151 catheterization laboratories performing at least 20 intracoronary pressure measurements yearly, 104 (69%) replied to the survey for the selection of centers (**Figure 1**). Of these, 76 confirmed their willingness to participate in the prospective cross-sectional study; therefore, they were activated for the data collection (**Figure 1**, Online Figures 1 to 3 and online available ERIS project organization).

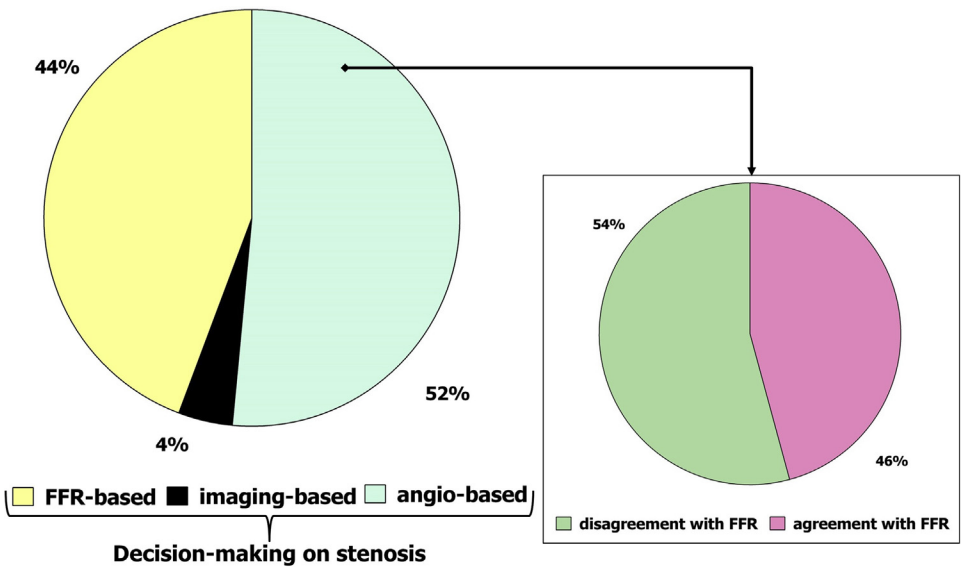
SURVEY FOR CENTER SELECTION: MAIN FINDINGS. Overall, 140 operators provided 1,400 decisions about stenosis significance (detailed in the Online Appendix, Online Table 1). About one-half of the decisions regarding stenosis management (52%) were based on visual assessment only (**Figure 2**). These decisions were concordant with the intracoronary pressure measurement in 46% of cases (**Figure 2**). In the remaining 48% of cases, the operators acknowledged the need for an additional diagnostic tool, mostly intracoronary pressure measurement (91% of the cases) (Online Appendix, Online Table 2).

PROSPECTIVE CROSS-SECTIONAL STUDY: GENERAL INFORMATION. The study population included 1,858 consecutive cases (**Figure 1**). In 1,177 cases, intracoronary pressure measurement was performed (physiology assessment group). Physiology-guided procedures represented 7% and 13% of coronary angiography and PCI total volume, respectively (**Figure 1**). In 681 cases, although the invasive functional assessment was indicated by the guideline or protocol, the operator decided against its performance (visual estimation group; **Table 1**).

PHYSIOLOGY ASSESSMENT GROUP: PATIENT CHARACTERISTICS. Functional assessment was performed in 648 patients (55%) with SCAD (**Table 1**). A more detailed analysis of their characteristics can be found in the Online Appendix, Online Table 3, and Online Figure 4. The remaining 529 patients (45%) in the physiology group received functional evaluation in an acute coronary syndrome (ACS) setting, among whom 169 (32%) had ST-segment elevation myocardial infarction and 360 (68%) had NSTEACS. Considering the patients with ST-segment elevation myocardial infarction, only 4 (0.3%) underwent functional assessment during primary PCI. More than two-thirds of the patients with NSTEACS (n = 251 [70%]) were troponin positive.

PHYSIOLOGY ASSESSMENT GROUP: LESION DESCRIPTION. Overall, 1,398 coronary lesions were investigated with intracoronary pressure measurement. FFR was performed in the majority (n = 1,251 [89%]), and iFR was preferred in the remaining cases (n = 147 [11%]). The most used route of administration

FIGURE 2 Distribution of the Different Decisions in the Survey and Appropriateness of Angiography-Based Decisions



Decisions about the significance of stenosis were based on visual estimation (angiography based) or on intracoronary pressure measurement (fractional flow reserve [FFR] based) or on an additional imaging assay (intravascular ultrasonography, optical coherence tomography, or noninvasive stress test with imaging). Among the angiography-based decisions, the proportions of concordance and discordance with the known functional metric are depicted at the right.

of adenosine was intravenous (n = 808 [64%]). The description of the angiographic and physiology data can be found in the Online Appendix and Online Tables 4 and 5. In 1,263 lesions (90.5%), the functional assessment was performed during the diagnostic phase to guide the decision to perform coronary revascularization. It was performed both before and after coronary revascularization in 126 lesions (9.4%) and only after stent implantation in 9 (0.1%). **Figure 3** shows the results of the functional assessment and revascularization strategy. The functional assessment result before coronary revascularization was negative in 875 coronary lesions (63%) (**Figure 3**). In 61 of these cases (7%), despite the negative functional assessment result, the operator decided to proceed with PCI and stent implantation (**Figure 3**). In contrast, in 82 of 514 coronary lesions (16%) with positive functional assessment results, the operator decided not to perform revascularization (**Figure 3**). Overall, the disagreement between the physiology-based guidance result and the subsequent revascularization strategy was approximately 9%. The functional assessment result after stent implantation was positive in 42 cases (31%) (**Figure 3**). In most (89%) of the cases, the functional assessment result was not followed by any further intervention (**Figure 3**).

PHYSIOLOGY ASSESSMENT GROUP: AGREEMENT WITH CURRENT GUIDELINES. In the physiology assessment group, FFR or iFR was performed in agreement with current guideline recommendations in 569 cases (48%), including 281 patients with SCAD without stress test results (49%), 44 patients with SCAD with inconclusive stress test results (8%), and 244 patients with SCAD with positive stress test results (43%) but with intermediate-severity coronary lesions (50% to 70% DS).

VISUAL ESTIMATION GROUP: PATIENT CHARACTERISTICS. Overall, 681 patients met the inclusion criteria for the visual estimation group (**Table 1**). The operators' mean age in the visual estimation group was higher than that in the physiology group (48 ± 9 years vs. 44 ± 8 years; $p < 0.0001$).

VISUAL ESTIMATION GROUP: LESION DESCRIPTION. As shown in **Figure 4**, FFR or iFR assessment was not performed in 398 cases (544 lesions) despite indication by the guidelines and in 283 cases (392 lesions) despite indication by the protocol. Overall, the visual estimation group included 936 coronary lesions (detailed description in the Online Appendix and Online Tables 4 and 6). In the visual estimation group, the DS of the coronary lesions was more severe

than that in the physiology assessment group ($p < 0.0001$) (Online Appendix, Online Figures 5 and 6). The clinical management of these lesions is shown in **Figure 4**. PCI was performed in 52% of the lesions (n = 488).

VISUAL ESTIMATION GROUP: OPERATOR RATIONALE FOR FUNCTIONAL ASSESSMENT AVOIDANCE. A detailed list of the operators' reasons for avoiding coronary physiology-based assessment is reported in **Table 2**. The most frequently cited reason (39%) was the operator's confidence that the clinical and angiographic data were sufficient to achieve the correct decision for the patient.

TABLE 1 Baseline Characteristics of the Study Population

	Physiology Assessment Group (n = 1,177)	Visual Estimation Group (n = 681)	p Value
Age, yrs	68 ± 10	68 ± 11	0.69
Male	859 (73)	500 (73)	0.87
CV risk factors			
Previous smoker	332 (28)	196 (29)	0.81
Current smoker	252 (21)	189 (28)	<0.01
Diabetes	292 (25)	190 (28)	0.16
Arterial hypertension	905 (77)	527 (77)	0.85
Dyslipidemia	806 (68)	449 (66)	0.28
CV medical history			
MI	246 (21)	164 (24)	0.12
PCI	387 (33)	245 (36)	0.19
CABG	31 (3)	33 (5)	0.01
COPD	83 (7)	56 (8)	0.41
LVEF <40%	287 (24)	83 (12)	<0.01
CrCl <45 ml/min	150 (13)	94 (14)	0.56
Clinical indication			
STEMI	169 (14)	–*	–
NSTEACS	360 (30)	273 (40)	
SCAD	648 (55)	408 (60)	
Angiography			
Lesions >50%	1.8 ± 0.9	1.9 ± 1.0	0.01
Lesions with FFR/iFR	1.2 ± 0.5	–	–
Lesions eligible for FFR/iFR	–	1.4 ± 0.7	–
Lesions treated with PCI	0 (0–1)	0 (0–1)	0.85

Values are mean ± SD, n (%), or median (interquartile range). *STEMI as clinical presentation was not considered an inclusion criterion for patients in the visual estimation group.

CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; CrCl = creatinine clearance; CV = cardiovascular; FFR = fractional flow reserve; iFR = instantaneous wave-free ratio; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NSTEACS = non-ST-segment elevation acute coronary syndrome; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease; STEMI = ST-segment elevation myocardial infarction.

DISCUSSION

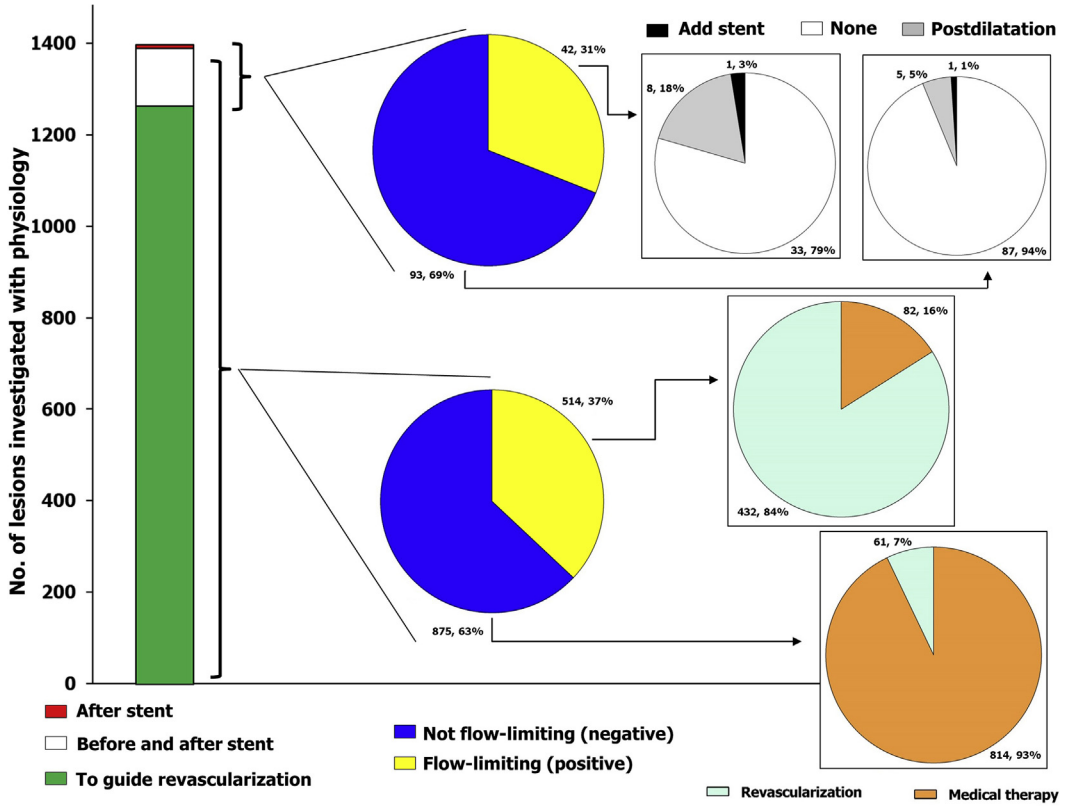
The application of intracoronary pressure measurements to guide the decision to perform revascularization in catheterization laboratories varies widely worldwide (6–9). This trend is confirmed in Italy, where the mean physiology/PCI ratio is approximately 7%, ranging from 0% to 30% among catheterization laboratories (from the annual report of the Italian Society of Interventional Cardiologists, available at https://gise.it). The ERIS project has been promoted with the aim of clarifying the underlying reasons for the variability through a nationwide, cross-sectional, prospective study. The major strengths of the study are the large number of centers involved and the large number of representative consecutive cases. In addition, for the first time, we collected the operators' rationale for not performing the physiology assessment at the time of the clinical decision-making process in real-life cases.

To recruit centers, we initiated the ERIS program, with a survey similar to the one conducted by Toth et al. (12) in 2012 and 2013. Compared with the findings of the International Survey on Interventional Strategy, we observed increased awareness that FFR and iFR are gold-standard tools to discriminate flow-limiting lesions (from 21% to 44%) (12). Nevertheless, the occurrence of an angiography-based decision in cases of intermediate DS is still high (approximately 50%) and led to an arguably "wrong" decision in approximately one-half of the cases.

The analysis of prospective data showed that physiology assessment was applied in agreement with the current European and American guidelines in approximately one-half of cases. A relevant number of patients with SCAD with a Class I recommendation in the current guidelines did not receive functional assessment. This is counterbalanced by relatively high use of physiology-based guidance in the ACS setting. The operators involved in the ERIS study were confident in using FFR or iFR assessment for nonculprit lesions, especially in patients with NSTEMI. This approach is interesting because, though feasible, it is not supported by adequately powered randomized data. In fact, most of the data regarding physiology assessment of nonculprit lesions are from patients with STEMI (15,16), whereas fewer data are available in patients with NSTEACS (17). Randomized clinical trials are ongoing and will provide crucial information to better define the application of physiology assessment in this clinical subset (NCT02892903, NCT02862119, and NCT01881555).

As might be expected, FFR and iFR assessment was used more often in intermediate lesions of the left anterior descending coronary artery to guide the decision to perform revascularization. The association between intermediate stenosis and functional assessment seems to be a well-established concept in

FIGURE 3 Physiology Assessment Group: Functional Assessment Result and Clinical Management

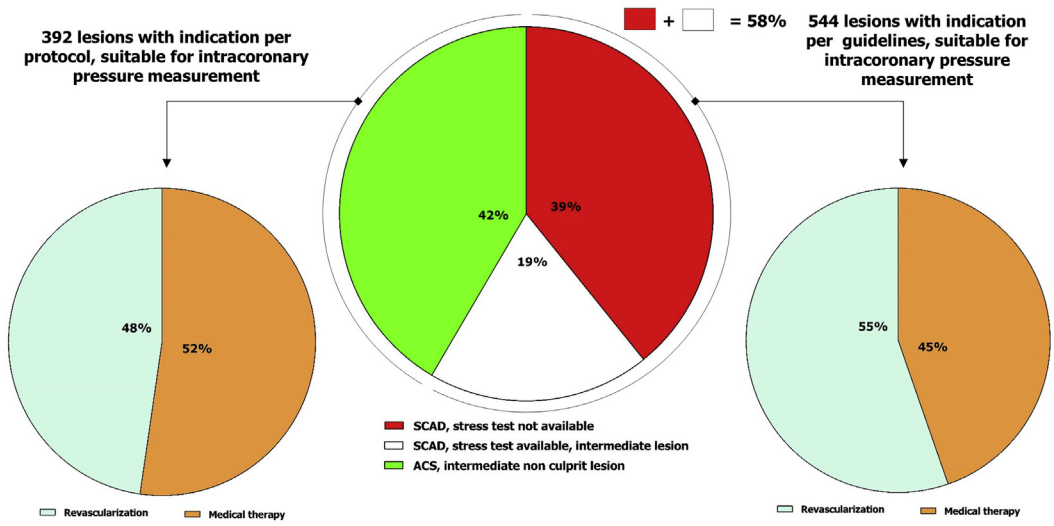


Each pie chart represents the number of lesions and the percentage. When functional assessment was performed to guide the decision to perform revascularization, fractional flow reserve (FFR) ≤0.80 or instantaneous wave-free ratio (iFR) ≤0.89 was considered positive. When FFR assessment was performed after stent placement, FFR ≤0.88 was defined as positive.

the operators' thinking, and this link is indirectly confirmed by the finding that the DS of the coronary lesions in the visual estimation group was more severe. However, it is important to note that nearly 20% of stenoses visually estimated to have DS between 71% and 90% were not functionally significant when evaluated using FFR. This indicates that physiology-based guidance can be useful in assessing lesions deemed to be angiographically severe (18).

The major novelty of the present study is the detailed description of the reasons for not performing FFR or iFR assessment even when indicated by guidelines or protocol. Recent reviews and consensus documents have speculated that the main potential reasons for the low frequency of physiology-based guidance could be adenosine costs, limited availability, side effects, and contraindications, as well as lack of time or reimbursement (7). Our study did not confirm these speculations. In most cases, the operator was confident that clinical history and angiographic data were sufficient to guide the decision to perform coronary revascularization. This finding has been suggested by the International Survey on Interventional Strategy (12). Our survey and especially our prospective data confirmed this also in consecutive real-life cases. Adenosine, procedural time, and cost related to adenosine and pressure wire were considered limitations only in a small proportion of cases and operators. This finding is consistent with the observation that the introduction in the market of resting index (e.g., iFR) did not meaningfully change the number of intracoronary pressure measurements. Our data strongly show that the true constraint limiting the use of physiology guidance is the cultural barrier of the oculostenotic reflex. Despite several studies that showed disagreement between physiology and visual estimation, most operators continue to consider angiography superior to physiology. This is not necessarily driven by the operator's desire to perform PCI,

FIGURE 4 Visual Estimation Group: Clinical Presentation and Clinical Management



ACS = acute coronary syndrome(s); SCAD = stable coronary artery disease.

because approximately 50% of the lesions were not treated. Obviously, physiology assessment does not substitute for clinical judgment and should always be interpreted in the clinical context of each patient. However, a merely angiography-based approach results in a higher rate of discordant decisions with respect to the true functional importance of the stenosis and thus in unnecessary stenting or inappropriate deferral in approximately 30% to 50% of all cases (12,15).

The mean age of the operators who performed intracoronary pressure measurement tended to be less than that of operators who preferred visual estimation. Younger operators could be more prone to seek help in the decision-making process by functional assessment than older, more experienced operators. Noteworthy is the fact that the technical limitations of the available pressure wires were indicated as causes of physiology-based guidance avoidance. Accordingly, the development of newer wires with better performance may significantly contribute to overcome these barriers. Finally, some operators signaled a preference for intracoronary imaging or noninvasive stress tests in follow-up. Indeed, intravascular ultrasonography and optical coherence tomography provide anatomic, rather than physiology, information; therefore, they are not as suitable for determining coronary stenosis functional significance.

STUDY LIMITATIONS. Although our findings are consistent with those of previous studies (6–9,12,19), the ERIS study is a nationwide Italian project; thus, our findings may not be generalizable to other countries. In addition, we cannot exclude selection bias and interference in the list of reasons for physiology-based guidance avoidance due to the study design (because of the inclusion of patients in the visual

TABLE 2 Operator Rationale for Not Performing a Physiology Assessment When Indicated

Attitudes (lack of agreement and inertia of previous practice)	
Clinical and angiographic data are sufficient	455 (39.3)
Certainly significant lesion	223
Certainly not significant lesion	164
FFR/iFR does not improve my ability to stratify lesions	68
I prefer to achieve a complete revascularization	102 (8.8)
Co-culprit lesion in a patient with ACS	67 (5.7)
I will monitor the patient's symptoms during follow-up	56 (4.5)
Knowledge (lack of awareness and familiarity)	
FFR/iFR not feasible (e.g., wire does not cross the lesion and myocardial bridge)	129 (11.1)
Lesion >50% in the proximal LAD or left main coronary artery	120 (10.3)
Intracoronary imaging (IVUS/OCT) is better	82 (7.5)
Stratification in the follow-up with stress test	40 (3.4)
Behavior (external barriers)	
Time constraint	47 (4.1)
Adenosine side effects or cost	30 (2.6)
Costs	28 (2.5)

Values are n (%) or n.

ACS = acute coronary syndrome(s); IVUS = intravascular ultrasonography; LAD = left anterior descending coronary artery; OCT = optical coherence tomography; other abbreviations as in Table 1.

estimation group who met the criteria indicated by the steering committee). Likewise, clinical follow-up was not available. Nevertheless, the assessment of differences in adverse events between the physiology assessment and visual estimation groups was beyond our scope. Finally, the operators were aware that their practice was audited during the study period. Thus, we cannot exclude a consequent bias between the reported findings and the real-world situation and bias due to the exclusion of centers that performed a limited number of intracoronary pressure measurements (<20 per year).

CONCLUSIONS

The prospective, cross-sectional ERIS study observed that functional coronary assessment follows the current guideline recommendation in 48% of cases, and operator confidence in lesion severity on the basis of visual evaluation alone is the most frequent reason for not using physiology-based guidance. Educational programs focused on the advantages and disadvantages of invasive coronary physiology assessment should be implemented to fill the gap between guideline indications and daily practice.

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ADDRESS FOR CORRESPONDENCE: Dr. Gianluca Campo, Cardiovascular Institute, Azienda Ospedaliera Universitaria S. Anna, Via Aldo Moro 8, Cona (FE) 44124, Italy. E-mail: cmpglc@unife.it.

PERSPECTIVES

WHAT IS KNOWN? The use of physiology-based guidance to assist coronary revascularization decisions in real life varies among countries, centers, and operators, and the barriers causing this variability are unknown.

WHAT IS NEW? Intracoronary physiology assessment follows the current European and American guideline recommendations in approximately 50% of cases because it is frequently applied in nonculprit lesions among patients with ACS. The operator's confidence in visual estimation of lesion severity is the most frequent reason for not performing functional assessment.

WHAT IS NEXT? More data supporting the use of physiology-based guidance among patients with ACS with multivessel disease and educational programs focused on advantages and disadvantages of invasive coronary physiology assessment may fill the gap between guideline indications and daily practice.

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KEY WORDS acute coronary syndrome(s), fractional flow reserve, instantaneous wave-free ratio, percutaneous coronary intervention, stable coronary artery disease

APPENDIX For supplemental Methods, figures, and tables, please see the online version of this paper.