Changes in the treatment strategy following intracoronary pressure wire in a contemporaneous real-life cohort of patients with intermediate coronary stenosis. Results from a nationwide registry

Oriol Rodriguez-Leor, Beatriz Toledano, Ramón López-Palop, Fernando Rivero, Salvatore Brugaletta, José Antonio Linares, Tomás Benito, Pilar Carrillo, Martí Puigfel, German Cediel, Mario Sadaba, Beatriz Vaquerizo, Juan Rondán, Iván Gómez, Fernando Alfonso, Roberto Sáez, Ana Planas, Fernando Lozano, Felipe Hernández, Manel Sabaté, José Ramón Ruíz-Arroyo, Francisco Torres, José María de la Torre Hernández, Enrique Gutiérrez, Ana Belén Cid-Álvarez, José Luís Díez, Luis Fernández, José Moreu, Soledad Ojeda, Pablo Cerrato, Valeriano Ruiz-Quevedo, Juan Sanchis, Antonio Gómez-Menchero, Raymundo Ocaranza, Mohsen Mohandes, José María Hernández, Miren Maite Alfageme, Pablo Aguiar, José Ramón López Mínguez, Armando Pérez de Prado, REGIPRES investigators

PII: S1553-8389(23)00029-5

DOI: https://doi.org/10.1016/j.carrev.2023.01.027

Reference: CARREV 2933

To appear in: *Cardiovascular Revascularization Medicine*

Received date: 21 July 2022

Revised date: 27 December 2022

Accepted date: 30 January 2023

Please cite this article as: O. Rodriguez-Leor, B. Toledano, R. López-Palop, et al., Changes in the treatment strategy following intracoronary pressure wire in a contemporaneous real-life cohort of patients with intermediate coronary stenosis. Results from a nationwide registry, *Cardiovascular Revascularization Medicine* (2023), https://doi.org/10.1016/j.carrev.2023.01.027

Changes in the treatment strategy following intracoronary pressure wire in a contemporaneous real-life cohort of patients with intermediate coronary stenosis. Results from a nationwide registry

Oriol Rodriguez-Leor[1,2,3] MD PhD, Beatriz Toledano[1] MD, Ramón López-Palop[4] MD PhD, Fernando Rivero[5] MD PhD, Salvatore Brugaletta[6] MD PhD, José Antonio Linares[7] MD PhD, Tomás Benito[8] MD PhD, Pilar Carrillo[4] MD PhD, Martí Puigfel[9] MD PhD, German Cediel[1] MD PhD, Mario Sadaba[10] MD PhD, Beatriz Vaquerizo[11] MD PhD, Juan Rondán[12] MD PhD, Iván Gómez[13] MD PhD, Fernando Alfonso[5] MD PhD, Roberto Sáez[14] MD PhD, Ana Planas[15] MD PhD, Fernando Lozano[16] MD PhD, Felipe Hernández[17] MD PhD, Manel Sabaté[6] MD PhD, José Ramón Ruíz-Arroyo[7] MD PhD, Francisco Torres[18] MD PhD (28) José María de la Torre Hernández[19] MD PhD, Enrique Gutiérrez[20] MD PhD, Ana Belén Cid-Álvarez[21] MD PhD, José Luís Díez[22] MD PhD, Luis Fernández[23] MD PhD, José Moreu[24] MD PhD , Soledad Ojeda[25] MD PhD, Pablo Cerrato[26] MD PhD, Valeriano Ruiz-Quevedo[27] MD PhD, Juan Sanchis[28] MD PhD, Antonio Gómez-Menchero[29] MD PhD, Raymundo Ocaranza[30] MD PhD, Mohsen Mohandes[31] MD PhD, José María Hernández[32] MD PhD, Miren Maite Alfageme[33] MD PhD, Pablo Aguiar[34] MD PhD, José Ramón López Mínguez[35] MD PhD and Armando Pérez de Prado[8] MD PhD

In representation of the REGIPRES investigators

[1] Institut del Cor, Hospital Universitari Germans Trias i Pujol, Badalona, España

[2] CIBER de Enfermedades CardioVasculares (CIBERCV) Instituto de Salud Carlos III, Madrid, España

[3] Institut de Recerca en Ciències de la Salut Germans Trias i Pujol, Badalona, España

[4] Servicio de Cardiología, Hospital de Sant Joan, Alacant, España

[5] Servicio de Cardiología, Hospital de la Princesa, Madrid, España

[6] Servicio de Cardiología, Hospital Clínic i Provincial de Barcelona, Barcelona, España

[7] Servicio de Cardiología, Hospital Clínico Lozano Blesa, Zaragoza, España

[8] Servicio de Cardiología, Hospital de León, León, España

[9] Servicio de Cardiología, Hospital Josep Trueta de Girona, Girona, España

[10] Servicio de Cardiología, Hospital de Galdakao, Galdakao, España

[11] Servicio de Cardiología, Hospital del Mar, Barcelona, España

[12] Servicio de Cardiología, Hospital de Cabueñes, Gijón, España

[13] Servicio de Cardiología, Hospital Universitario 12 de Octubre, Madrid, España

[14] Servicio de Cardiología, Hospital de Basurto, Basurto, España

[15] Servicio de Cardiología, Hospital de Castellón, Castellón de la Plana, España

[16] Servicio de Cardiología, Hospital de Ciudad Real, Ciudad Real, España

[17] Servicio de Cardiología, Clínica Universitaria de Navarra, Madrid, España

[18] Servicio de Cardiología, Hospital del Vinalopó, Elx, España

[19] Servicio de Cardiología, Hospital Universitario Marqués de Valdecilla, Santander, España

[20] Servicio de Cardiología, Hospital Universitario Gregorio Marañón, Madrid, España

[21] Servicio de Cardiología, Hospital Clínico de Santiago, Santiago de Compostela, España

[22] Servicio de Cardiología, Hospital Universitari de la Fe, Valencia, España

[23] Servicio de Cardiología, Hospital de Cruces, Barakaldo, España

[24] Servicio de Cardiología, Hospital de Toledo, Toledo, España

[25] Servicio de Cardiología, Hospital Universitario Reina Sofía, Córdoba, España

[26] Servicio de Cardiología, Hospital de Mérida, Mérida, España

[27] Servicio de Cardiología, Complejo Hospitalario Navarra, Pamplona, España

[28] Servicio de Cardiología, Hospital Clínico Universitario de Valencia, Valencia, España

[29] Servicio de Cardiología, Hospital de Huelva, Huelva, España

[30] Servicio de Cardiología, Hospital Lucus Augusti, Lugo, España

[31] Servicio de Cardiología, Hospital Universitari Joan XXIII, Tarragona, España

[32] Servicio de Cardiología, Hospital Virgen de la Victoria, Málaga, España

[33] Servicio de Cardiología, Hospital Universitario Araba, Vitoria, España

[34] Servicio de Cardiología, Hospital San Pedro de Logroño, Logroño, España

[35] Servicio de Cardiología, Hospital Universitario de Badajoz, Badajoz, España

Contributorship statement:

Planning: ORL, BT, RLP, APP

Conduct: all authors

Reporting: ORL, RLP, FA, GC, APP

Brief title: Change in treatment strategy after pressure wire

Word count: Manuscript 2,972 words

Corresponding author

Oriol Rodriguez-Leor

Institut del Cor, Hospital Universitari Germans Trias i Pujol

Carretera de Canyet SN, 08916 Badalona, España

oriolrodriguez@gmail.com

@oriolrodriguez5

Role of the sponsors

The registry was endorsed by the Intracoronary Diagnostic Techniques Working Group of the Interventional Cardiology Association of the Spanish Society of Cardiology. The study was supported by an unconditional grant from Philips-Volcano, Abbott Vascular, and Boston Scientific. The sponsors did not have access to the database or the final results until the preparation of this manuscript. None of them participated in the preparation or review of this manuscript.

Conflict of interest

Dr. Perez de Prado has received personal fees from iVascular, Boston Scientific, Terumo, Bbraun and Abbott Vascular. All other authors have reported that they have no relationship relevant to the contents of this paper to disclose.

Abstract

Background

Intracoronary pressure wire is useful to guide revascularization in patients with coronary artery disease.

Aims

To evaluate changes in diagnosis (coronary artery disease extent), treatment strategy and clinical results after intracoronary pressure wire study in real-life patients with intermediate coronary artery stenosis.

Methods

Observational, prospective and multicenter registry of patients in whom pressure wire was performed. The extent of coronary artery disease and the treatment strategy based on clinical and angiographic criteria were recorded before and after intracoronary pressure wire guidance. 12-month incidence of MACE (cardiovascular death, non-fatal myocardial infarction or new revascularization of the target lesion) was assessed.

Results

1414 patients with 1781 lesions were included. Complications related to the procedure were reported in 42 patients (3.0%). The extent of coronary artery disease changed in 771 patients (54.5%). There was a change in treatment strategy in 779 patients (55.1%) (18.0% if medical treatment; 68.8% if PCI; 58.9% if surgery ($p < 0.001$ for PCI vs medical treatment; $p = 0.041$ for PCI vs CABG; $p < 0.001$ for medical treatment vs CABG). In patients with PCI as the initial strategy, the change in strategy was associated with a lower rate of MACE (4.6% vs 8.2%, $p = 0.034$).

Conclusions

The use of intracoronary pressure wire was safe and led to the reclassification of the extent of coronary disease and change in the treatment strategy in more than half of the cases, especially in patients with PCI as initial treatment.

Key words

Pressure wire, FFR, coronary artery disease, non-hyperemic diastolic indices, registry.

Abbreviations

CABG: coronary artery bypass graft

CAD: coronary artery disease

ICPW: intracoronary pressure wire

iFR: instantaneous wave-free ratio

FFR: fractional flow reserve

NHPR: non-hyperemic pressure ratio

PCI: percutaneous coronary intervention

MACE: major adverse cardiovascular event

Introduction

Intracoronary pressure wire (ICPW) is recommended to guide revascularization in patients with coronary artery disease (CAD) who present intermediate stenoses at coronary angiography. It has been shown that both the hyperemic indices - fractional flow reserve (FFR) - and the new non-hyperemic pressure ratios (NHPR) - instantaneous wave-free ratio (iFR, Volcano Corporation, Rancho Cordova, CA, USA), diastolic hyperemia-free ratio (DFR, Boston Scientific, Marlborough, MA, USA), diastolic pressure ratio (dPR, Opsens Inc, Quebec, Canada) and resting full-cycle ratio (RFR, Abbott Vascular, Santa Clara, CA, USA) - are able to identify coronary lesions whose treatment can be safely deferred (1-3). In addition, the clinical outcomes of percutaneous coronary intervention (PCI) under ICPW guidance are better than when guidance is limited to coronary angiography, in both patients with stable CAD and acute coronary syndrome (4-7).

Several studies have suggested that the use of ICPW in intermediate lesions is associated to a high rate (up to 44%) of change in treatment modality (medical treatment, PCI or coronary artery bypass graft [CABG] surgery)(8,9). Furthermore, ICPW studies allow reclassification of the extent of CAD and, in patients with multivessel disease, can modify the revascularization strategy (increase or reduce the number of lesions to be treated through either PCI or CABG). At present there is little information available on the reclassification of the extent of CAD and changes in revascularization strategy.

The Spanish Pressure Wire Registry (REGIPRES) was designed to evaluate the changes in the extent of CAD and in the specific treatment strategy following ICPW, including the new non-hyperemic indices, in a contemporary real-life cohort of non-selected patients, and to assess the impact upon the clinical outcomes after one year.

Method

Patients

A prospective, observational multicenter study was carried out involving consecutive patients over 18 years of age with CAD in which following coronary angiography, and based on clinical and/or angiographic criteria, it was decided to perform ICPW to assess the functional repercussion of at least one coronary stenosis lesion. A total of 32 Spanish centers participated in the study between January 2017 and January 2018. The only exclusion criterion was the impossibility of completing the study. The basal angiographic and clinical parameters were recorded on a prospective basis.
The study protocol was approved by a reference Ethics Committee. This study was conducted in abidance with the principles of the Declaration of Helsinki.

Objectives

The primary objectives were: (a) to describe the incidence of reclassification of the extent of CAD after ICPW; (b) to describe the incidence of change in treatment modality and in coronary revascularization strategy of the patient after ICPW; and (c) to evaluate the safety of the treatment strategy per patient over 12 months of clinical follow-up.

Coronary angiography procedure

Coronary angiography was carried out according to the standard practice in each center. Each center performed a quantitative angiography-based analysis of the evaluated lesions (reference diameter, minimum luminal diameter, length, percentage stenosis according to diameter and percentage stenosis according to area). Diffuse coronary artery disease was defined as either a lesion longer than 20 mm or an artery that had several narrowed sections (greater than or equal to 70% narrowed) separated by relatively healthy portions of the artery.

Intracoronary pressure wire procedure

ICPW evaluation was performed after recording the angiographic parameters, and was made according to the local standard practice, with measurement of FFR and/or NHPR, according to operator criterion. Functional evaluation of all lesions with intermediate stenosis was recommended.
There was no specific recommendation regarding the use of FFR or NHPR, or both. The method for obtaining hyperemia was left to the criterion of the operator. Likewise, there was no specific recommendation regarding the use of any of the cut-off values validated

in clinical trials (0.75 or 0.80 for FFR; 0.89 or a hybrid approach for NHPR) for deciding the indication of revascularization. However, the operator was required to record whether the final decision was based only on the result of ICPW or whether other clinical and/or angiographic parameters were also considered.

Reclassification of the extent of CAD and changes in revascularization strategy

As part of the inclusion algorithm, operators were required to establish a management strategy for each lesion based on all the information available after coronary angiography and before and after the ICPW study. The concordance between the initial and the final strategy was recorded for each patient. In patients with revascularization as treatment modality after ICPW, changes in revascularization strategy (more or fewer lesions to be treated through either PCI or CABG) were also documented. Clinical decisions were left entirely to the criterion of the operators.

Clinical follow-up and definition of assessment criteria

The patients were followed-up on for 12 months after the index procedure for appearance of the primary composite endpoint (major adverse cardiovascular event [MACE]) corresponding to death of cardiovascular causes, non-fatal myocardial infarction or repeat and non-scheduled revascularization of the target lesion. Myocardial infarction over follow-up was defined by the presence of at least two of the following three criteria: (a) clinical manifestations consistent with myocardial ischemia; (b) electrocardiographic changes consistent with ST-segment elevation acute myocardial infarction; and (c) elevation of myocardial necrosis markers to above the reference levels of each center. An independent committee reviewed the coherence of each reported event before final classification.

Statistical analysis

Continuous variables were reported as the mean ± standard deviation (SD) in the case of data with a normal distribution, or as median and interquartile range (IQR) in the case of data with a non-normal distribution. Categorical variables were reported as numbers (percentages). The groups and subgroups were compared using the Student t-test or Wilcoxon rank sum test for continuous variables, while the chi-squared test or Fisher's exact test was used to compare categorical variables. The MACE-free survival data were represented and analyzed using Kaplan-Meier curves and Cox regression analysis.

Statistical significance was considered for $p \leq 0.05$. The data were analyzed using the Stata IC 15.1 package (Stata Corp., College Station, TX, USA).

Results

Patients

The registry included 1414 patients with intermediate coronary stenosis in which ICPW was performed in at least one lesion, with a total of 1781 evaluated lesions. **Figure 1** shows the patient flow chart according to the change in treatment strategy following the ICPW study. **Table 1** summarizes the clinical characteristics of the two groups.

Reclassification of the extent of coronary disease following the intracoronary pressure wire study

The diagnosis of the extent of CAD changed after the ICPW study in 771 patients (54.5%). **Figure 2** shows the extent of CAD based on the initial coronary angiography study, and the extent of CAD following the ICPW study.

Change in treatment strategy following the intracoronary pressure wire study

In relation to the initial treatment strategy, ICPW led to a change in treatment in 18.0% of the patients with medical treatment, 68.8% of the patients with PCI, and 58.9% of the patients with CABG ($p < 0.001$ for PCI versus medical treatment; $p = 0.041$ for PCI versus CABG; $p < 0.001$ for medical treatment versus CABG). **Figure 3** shows the change in treatment strategy following the ICPW study.

Intracoronary pressure wire procedure

The procedure could be completed in all the patients included in the registry. Complications related to the procedure were reported in 42 patients (3.0%), with no significant sequelae in any of them: syncope secondary to paroxysmal atrioventricular block related to adenosine administration in 19 patients (1.3%), coronary artery dissection related to wire manipulation in 6 patients (0.4%), atrial fibrillation in 4 patients (0.4%), ventricular tachycardia in 1 patient (0.1%) and other non-pre-specified minor complications in 12 patients (0.8%).

Hyperemia was not induced in 25.1% of the patients, with NHPR being the only calculated index in these cases. In patients with induced hyperemia, intracoronary adenosine was used in 69.2% of the cases, peripheral venous adenosine in 26.8%,

central venous adenosine in 0.9%, and peripheral venous regadenoson in 2.9%. **Table 2** shows the basal characteristics of the lesions and the result of the ICPW study in the 1781 evaluated lesions.

A total of 26.8% of evaluated lesions were regarded as the culprit lesion and 37.6% as a non-culprit lesion, while in 35.6% of the cases the culprit or non-culprit status of the lesion could not be established. Among the 451 patients in which the final decision was based on NHPR, the decision was based on iFR in 443 cases, on RFR (resting full-cycle ratio) in four cases, on dPR (diastolic pressure ratio) in two cases, and on DFR (diastolic hyperemia-free ratio) in two cases. Thus, iFR was used in over 98% of the cases. The operators reported that in 7% of the patients the decision regarding the revascularization strategy was not only based on the ICPW result but that other clinical and/or angiographic factors were also considered.

Intracoronary pressure wire in patients with acute vs chronic coronary syndrome

There were 1310 patients with information about clinical status previous to ICPW study; 604 (46.1%) had acute coronary syndrome while 706 (53.9) had chronic coronary syndrome. Both populations are described in table 3. Patients with acute coronary syndrome were younger, more frequently male, and had less prevalence of diabetes and hypercholesterolemia but were more frequently smokers and had better renal function. Number of lesions evaluated, use of NHPR and change in treatment strategy were similar between both groups, but there were differences regarding initial and final treatment strategy. When the results of FFR and NHPR were compared according to whether the patient had acute or chronic coronary syndrome, there were no differences in the rate of deferral (58.9% for FFR vs. 63.7% for NHPR, p=0.26, in acute coronary syndrome; 64.2% for FFR vs. 64.0% for NHPR, p=0.95, in chronic coronary syndrome).

Clinical outcomes at 12 months of follow-up

Data at 12 months of clinical follow-up were available in 92% of the patients. The incidence of MACE after 12 months of follow-up was 5.4%. There were no differences in MACE on comparing the patients with a change in treatment strategy versus those with no change in treatment strategy (6.0% versus 4.9%, respectively; p = 0.42). **Table 4** shows the events at 12 months of follow-up in both groups. The incidence of MACE at 12 months of follow-up in the patients with medical treatment as the initial

strategy was 4.2%, with no differences on comparing the patients with a change in treatment strategy versus those with no change in treatment strategy (4.7% versus 4.0%, respectively; p = 0.81). The incidence of MACE at 12 months of follow-up in the patients with PCI as the initial strategy was 5.7%, though the patients with no change in treatment strategy had a significantly higher incidence of MACE (4.6% versus 8.2%, respectively; p = 0.034). The incidence of MACE at 12 months of follow-up in the patients with CABG as the initial strategy was 8.0%, with no differences on comparing the patients with a change in treatment strategy versus those with no change in treatment strategy (9.4% versus 5.7%, respectively; p = 0.53). **Figure 4** shows the Cox regression curves for MACE in the general population and according to the initial treatment strategy.

Discussion

The results of the REGIPRES have shown that in a non-selected, contemporaneous real-life cohort of patients with CAD in which following coronary angiography, and based on clinical and/or angiographic criteria, ICPW was performed to assess the functional repercussion of at least one coronary stenosis lesion, the use of ICPW proved safe and: (1) it led to a high incidence of reclassification of the extent of CAD and to a change in treatment strategy in up to 55% of all cases (more frequent in those patients in which the initial intention was to perform PCI); (2) it avoided revascularization in 44.5% of patients with an initial indication for PCI and 15.4% for CABG without an increase in events at one-year follow-up, and (3) it induced revascularization in 17.1% of the patients considered who were initially candidates for medical treatment.

Despite the fact that the physiological assessment of coronary stenosis has received class IA recommendation for guiding revascularization when there is no evidence of ischemia, and class IIaB recommendation in patients with multivessel disease subjected to PCI (10), intracoronary physiological evaluation had remained a relatively limited practice (11). However, in recent years, and particularly following publication of the DEFINE-FLAIR and iFR-SWEDEHEART studies (2,3), there has been a significant increase in its use. Thus, in Spain, the number of ICPW studies increased from 4614 (6.8% of all PCI procedures) in 2014 to 9191 (12.1% of all PCI procedures) in 2019 (12).

In our study, the use of ICPW resulted in a change in the diagnosis of the extent of CAD in 54.5% of the patients. A study carried out by López-Palop et al. in a center with great experience in the use of ICPW demonstrated a discrepancy between the prediction of the result of the functional study based on angiography and the clinical data and the final result of the functional study of over 30%, with an overestimation of FFR in 11.3% and an underestimation of FFR in 18.8% (13). Another study published by Park et al. showed that outside the left main coronary artery, up to 57% of the lesions with angiographic stenosis > 50% presented FFR > 0.80, while 16% of the lesions with angiographic stenosis < 50% presented FFR ≤ 0.80 - with the identification of clinical factors associated to this discrepancy, such as the length of the lesion, its morphology, its degree of eccentricity, or the presence of lesions with an acute appearance (14).

Change in treatment modality following the intracoronary pressure wire study. Comparison with previous studies

The use of ICPW as a guide to deciding the modality of coronary revascularization has been investigated in a number of earlier studies that have demonstrated a rate of change of between 26% and 44% (8,9,15,16). In our case, following ICPW, we recorded an increase in the number of patients that were treated on a conservative basis, without revascularization (from 27% to 53.8%), and a decrease was moreover observed in the number of lesions treated with PCI and CABG. These data clearly differ from those of the French R3F registry, where the proportion of patients subjected to revascularization decreased from 45% to 42% (8), and even more so from the Portuguese POST-IT registry, where following FFR an increase was recorded in the number of patients subjected to revascularization, percutaneous or surgical, from 34.8% to 44.0%(9). These differences probably can be explained by the fact that the populations included in the studies were different (80.5% of the patients with stable CAD in R3F versus 65% in POST-IT and 53.9% in our own study). This circumstance very likely implied that prior ischemia testing also differed (61.4% in R3F versus 42.7% in POST-IT and 29% in our study), and that the incidence of positive prior ischemia testing differed as well (48% in R3F versus 36% in POST-IT and 21% in our registry). The DEFINE REAL trial, including only patients with multivessel disease and ICPW study, reported a change in treatment modality in 27% of the cases and a change in treatment strategy in 30% - these figures likewise being lower than in our study (17).

FFR or NHPR in non-culprit lesion evaluation in patients with acute coronary syndrome

In our series, 706 patients had acute coronary syndrome. The evaluation of non-culprit lesions in patients with acute coronary syndrome remains controversial. Van der Hoeven et al evaluated NHPR, FFR, CFR and IMR in non-culprit lesions in patients with ST elevation myocardial infarction, comparing values in the acute phase versus 1-month follow-up; their results suggested a transient change in microcirculation that led to an overestimation of lesion severity for NHPR and an underestimation in case of FFR (18). Escaned et al. published an analysis of 4486 patients enrolled in the DEFINE-FLAIR and the iFR-SEWEDEHEART trials comparing safety of revascularization deferral with HNPR and FFR in patients with acute coronary syndrome or stable angina. This analysis showed that deferral of revascularization was safe with both NHPR and FFR, with low MACE, but lesions were more frequently deferred when NHPR was used to assess lesion significance, without an impact on events during follow-up (19). Similarly, our study showed, in patients with acute coronary syndrome, a trend toward a greater deferral with NHPR, that didn't reach statistical significance, probably due to the small sample size.

Prognostic implications of ICPW. Considerations in relation to previous studies

In coincidence with our own findings, the French R3F registry and the Portuguese POST-IT registry evidenced no differences in MACE after 12 months between the patients with a change in treatment modality and those in which no change was made (8,9). However, on analyzing the influence of the change in strategy according to the initial treatment option, our study has shown that in those patients who were going to undergo PCI, the change in strategy was effectively associated to a lesser incidence of MACE. This difference has not been previously reported, and may be due to the facts that there was a low previous ischemia test rate, and that there were far fewer revascularizations among the patients with a change in strategy (17.7% versus 44.9% in the patients with no change in strategy). This finding must be interpreted with caution and may be viewed as a possible generator of hypotheses. Nevertheless, if confirmed, it would reinforce the safety of ICPW guided management, at least over 12 months of follow-up - particularly in those cases in which PCI is considered as treatment option.

Study limitations

This is a prospective observational study, and as such it is adequate for assessing patient changes - though it has some inherent limitations regarding interpretation of the outcome events. In particular, it is not possible to rule out possible treatment bias in deciding whether or not to perform repeat revascularization during follow-up. During the follow-up, the patient, the clinician and the interventionalist are aware of the existence of coronary lesions and the results of the ICPW study, which may condition the treatment. Furthermore, we cannot discard the potential role of other non-measured confounding factors. Nevertheless, a number of measures were adopted to limit this risk. Firstly, the a priori revascularization decision was recorded immediately before ICPW, based on the clinical and angiographic information. Secondly, the final revascularization decision was recorded immediately after the ICPW study. Therefore, the only additional significant information between the two decisions was the availability of the results of the ICPW study.

Centers performing high-volume ICPW in Spain were invited to participate in the registry. Although the sample is probably representative, center participation rate was approximately 60%. The centers that participated in the study routinely use ICPW in their decision making. The a priori revascularization decision was probably made according to a prediction of the ICPW outcome based on the experience of the operator in the functional study of lesions of this kind - not only considering angiography or the clinical condition of the patient. In centers less used to performing ICPW, a higher percentage of changes in treatment strategy could be expected. Coronary angiography and the results of ICPW were evaluated at each center without the intervention of a core laboratory, and this could have given rise to some heterogeneity among the participating centers - though this problem was minimized by including centers experienced in the use of both techniques. Although MACE incidence in patients with PCI as first treatment option was almost double in patients with no change in treatment strategy, this finding should be taken with caution as it comes from a non-prespecified secondary analysis. The absence of significant differences in the patients referred to surgery could be explained by the few number of individuals in this subgroup. Clinical follow-up was conducted over a period of 12 months; as a result, possible clinical events occurring beyond this period are not reflected in our study.

Conclusions

The REGIPRES study has shown that in a non-selected, contemporaneous real-life cohort of patients with intermediate coronary stenosis, the use of ICPW proved safe and led to reclassification of the extent of CAD and to a change in treatment strategy in over half of the patients, mainly in the form of a decrease in PCI. The change in strategy was more frequent in those patients in which the initial intention was to perform PCI, and in these individuals the change in strategy was related to a decrease in clinical events at one year of follow-up. These findings reinforce the role of ICPW as a guide for the indication of revascularization in patients with intermediate coronary stenosis.

What is known

Previous observational registries have assessed pressure wire use in a non-controlled setting. These registries had low representation of patients with acute coronary syndrome. In these studies, up to 44% of patients had individual change in treatment modality, but the impact of change in treatment modality was modest overall.
It is noteworthy that the use of pressure guidewire was associated with an increased revascularization rate, and only included FFR without non-hyperemic indexes use.

What the study adds

(1) Our study describes the complications related to the pressure wire procedure in a very large number of patients and outside a controlled setting.
(2) Our study describes the change in diagnosis of the extent of coronary disease following pressure wire use.
(3) Our study integrates non-hyperemic indices, in addition to FFR.
(4) In our study population, practically 50% of the patients presented acute coronary syndrome, versus only 20% and 35% in the previous registries. The distribution of patients between stable and unstable cases in our study is much more consistent with the daily situation found in interventional cardiology units.
(5) Our study not only reflects the change in treatment modality (medical versus percutaneous coronary intervention [PCI] versus coronary artery bypass graft [CABG]) but moreover for the first time also reflects the change in treatment strategy when revascularization is performed in patients with multivessel disease (treatment of more or fewer lesions after pressure wire).
(6) In our study, and in contrast to the previous publications, a decrease in the number of patients subjected to revascularization was observed after pressure

wire use, with good safety outcomes after 12 months of clinical follow-up in the non-revascularized patients. This observation is particularly remarkable, since it is more consistent with what would be expected in real life on analyzing the results of the randomized studies, i.e., DEFER, FAME or FAME2.

(7) In our study, in those patients in which the initially contemplated treatment modality based on the clinical and angiographic data was PCI, utilization of the pressure wire reduced the number of treated lesions very significantly, and the clinical course moreover proved better in those patients subjected to a change in strategy.

REFERENCES

1. Zimmermann FM, Ferrara A, Johnson NP, Van Nunen LX, Escaned J, Albertsson P, Erbel R, Legrand V, Gwon HC, Remkes WS, Stella PR, van Schaardenburg P, Beg GJW, De Bruyne B, Pijls NH. Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial. Eur Heart J 2015;36:3182-88
2. Davies JE, Sen S, Dehbi HM, Al-Lamee R, Petraco R, Nijjer SS, Bhindi R, Lehman SJ, Walters D, Sapontis J, Janssens L, Vrints CJ, Khashaba A, Laine M, Van Belle E, Krackhardt F, Bojara W, Going O, Härle T, Indolfi C, Niccoli G, Ribichini F, Tanaka N, Yokoi H, Takashima H, Kikuta Y, Erglis A, Vinhas H, Canas Silva P, Baptista SB, Alghamdi A, Hellig F, Koo BK, Nam CW, Shin ES, Doh JH, Brugaletta S, Alegria-Barrero E, Meuwissen M, Piek JJ, van Royen N, Sezer M, Di Mario C, Gerber RT, Malik IS, Sharp ASP, Talwar S, Tang K, Samady H, Altman J, Seto AH, Singh J, Jeremias A, Matsuo H, Kharbanda RK, Patel MR, Serruys P, Escaned J. Use of the instantaneous free-wave ratio versus fractional flow reserve in PCI. N Engl J Med 2017;376:1824-34
3. Gotberg M, Christiansen EH, Gudmunsdsdottir IJ, Sandhall L, Danielewicz M, Jakobsen L, Olsson SE, Öhagen P, Olsson H, Omerovic E, Calais F, Lindroos P, Maeng M, Tödt T, Venetsanos D, James SK, Kåregren A, Nilsson M, Carlsson J, Hauer D, Jensen J, Karlsson AC, Panayi G, Erlinge D, Fröbert O; iFR-SWEDEHEART Investigators. Instantaneous free-wave ratio versus fractional flow reserve to guide PCI. N Engl J Med 2017;376:1813-23
4. Tonino PA, De Bruyne B, Pijls N, Siebert U, Ikeno F, van' t Veer M, Klauss V, Manoharan G, Engstrøm T, Oldroyd KG, Ver Lee PN, MacCarthy PA, Fearon

WF; FAME Study Investigators. Fractional flow reserve versus angiography for guiding percutaneous coronary interventions. N Engl J Med 2009;360:213-24

5. De Bruyne B, Fearon WF, Pijls NH, Barbato E, Tonino P, Piroth Z, Jagic N, Mobius-Winckler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engström T, Oldroyd K, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Limacher A, Nüesch E, Jüni P; FAME 2 Trial Investigators. Fractional flow reserve-guided PCI for stable coronary artery disease. N Engl J Med 2014;371:1208-17
6. Smits PC, Abdel-Wahab M, Neumann FJ, Boxma-de Klerk BM, Lunde K, Schotborgh CE, Piroth Z, Horak D, Wlodarczak A, Ong PJ, Hambrecht R, Angerås O, Richardt G, Omerovic E; Compare-Acute Investigators. Fractional flow reserve-guided multivessel angioplasty in myocardial infarction. N Engl J Med 2017;376:1234-44
7. Layland J, Oldroyd KG, Curzen N, Sood A, Balachandran K, Das R, Junejo A, Ahmed N, Lee MMY, Shaukat A, O'Donnell A, Nam J, Briggs A, Henderson R, McConnachie A, Berry C, FAMOUS-NSTEMI investigators. Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: the British Heart Foundation FAMOUS-NSTEMI randomized trial. Eur Heart J 2015;36:100-11
8. Van Belle E, Rioufol G, Pouillot C, Cuisset T, Bougrini K, Teiger E, Champagne S, Belle L, Barreau D, Hanssen M, Besnard C, Dauphin R, Dallongeville J, El Hani Y, Sideris G, Bretelle C, Lhoest N, Barnay P, Leborgne L, Dupouy P; Investigators of the Registre Français de la FFR–R3F. Outcome impact of coronary revascularization with fractional flow reserve at time of diagnostic angiography; insights from a large French multicenter fractional flow reserve registry. Circulation 2014;129:173-85
9. Baptista SB, Raposo L, Santos L, Ramos R, Calé R, Jorge E, Machado C, Costa M, Infante de Oliveira E, Costa J, Pipa J, Fonseca N, Guardado J, Silva B, Sousa MJ, Silva JC, Rodrigues A, Seca L, Fernandes R. Impact of routine fractional flow reserve evaluation during coronary angiogiography on management strategy and clinical outcome: one-year results of the POST-IT. Circ Cardiovasc Interv 2016;9:e003288
10. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Jüni P, Kastrati A, Koller A, Kristensen

SD, Niebauer J, Richter DJ, Seferović PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO. 2018 ESC/EACTS guidelines on myocardial revascularization. Eurointervention 2019;14:1435-1534

11. Götberg M, Cook CM, Sen S, Nijjer S, Escaned J, Davies JE. The evolving future of instantenous wave-free ration and fractional flow reserve. J Am Coll Cardiol 2017;70:1379-1402
12. Ojeda S, Romaguera R, Cruz-Gonzalez I, Moreno Raul. Spanish Cardiac Catheterization and Coronary Intervention Registry. 29th Official Report of the Interventional Cardiology Association of the Spanish Society of Cardiology (1990-2019). Rev Esp Cardiol 2020;73:927-936
13. López-Palop R, Carrillo P, Agudo P, Cordero A, Frutos A, Mashlab S, Martínez R, El Amrani A, Ramos D. Factors associated with errors in visual estimation of the functional significance of coronary lesions. Rev Esp Cardiol 2016;69:657-663
14. Park SJ, Kang SJ, Ahn JM, Shim EB, Kim YT, Yun SC, Song H, Lee JY, Kim WJ, Park DW, Lee SW, Kim YH, Lee CW, Mintz GS, Park SW. Visual-functional mismatch between coronary angiography and fractional flow reserve. JACC Cardiovasc Interv 2012;5;1029-1036
15. Curzen N, Rana O, Nicholas Z, Golledge P, Zaman A, Oldroyd K, Hanratty C, Banning A, Wheatcroft S, Hobson A, Chitkara K, Hildick-Smith D, McKenzie D, Calver A, Dimitrov BD, Corbett S. Does routine pressure wire influence management strategy at coronary angiography for diagnosis of chest pain? The RIPCORD Study. Circ Cardiovasc Interv 2014;7:248-255
16. Van Belle E, Baptista SB, Raposo L, Henderson J, Rioufol G, Santos L, Pouillot C, Ramos R, Cuisset T, Calé R, Teiger E, Jorge E, Belle L, Machado C, Barreau D, Costa M, Hanssen M, Oliveira E, Besnard C, Costa J, Dallongeville J, Pipa J, Sideris G, Fonseca N, Bretelle C, Guardado J, Lhoest N, Silva B, Barnay P, Sousa MJ, Leborgne L, Silva JC, Vincent F, Rodrigues A, Seca L, Fernandes R, Dupouy P; PRIME-FFR Study Group. Impact of routine fractional flow reserve on management decision and 1-year clinical outcome of patients with acute coronary syndromes. Circ Cardiovasc Interv 2017; 0(6):e004296
17. Van Belle E, Gil R, Klauss V, Balghith M, Meuwissen M, Clerc J, Witzenbichler B, Cercek M, Vlachojannis M, Lang I, Commeau P, Vincent F, Testa L, Wasek W, Debry N, Kische S, Gabrielli G, Sardella G. Impact of

routine invasive physiology at time of angiography in patients with multivessel coronary artery disease on reclassification of revascularization strategy. J Am Coll Cardiol Intv 2018;11:354-365

18. van der Hoeven NW, Janssens GN, de Waard GA, Everaars H, Broyd CJ, Beijnink CWH, van de Ven PM, Nijveldt R, Cook CM, Petraco R, ten Cate T, von Birgelen C, Escaned J, Davies JE, van Leeuwen MAH, van Royen N. Temporal changes in coronary hyperemic and resting hemodynamic indices in nonculprit vessels of patients with ST segment elevation myocardial infarction. JAMA Cardiol 2019;4: 736–744.
19. Escaned J, Ryan N, Mejía-Rentería H, Cook CM, Deb i H-M, AlegriaBarrero E, Alghamdi A, Al-Lamee R, Altman J, Ambrosia A, Baptista SB, Bertilsson M, Bhindi R, Birgander M, Bojara W, Brugaletta S, Butler C, Calais F, Silva PC, Carlsson J, Christiansen EH, Danielewicz M, Di Mario C, Doh J-H, Erglis A, Erlinge D, Gerber RT, Going O, Gudmundsdottir I, Härle T, Hauer D, Hellig F, Indolfi C, Jakobsen L, Janssens L, Jensen J, Jeremias A, Karegren A, Karlsson A-C, Kharbanda RK, Khashaba A, Kikuta Y, Krackhardt F, Koo B-K, Koul S, Laine M, Lehman SJ, Lindroos P, Malik IS, Maeng M, Matsuo H, Meuwissen M, Nam C-W, Niccoli G, Nijjer SS, Olsson H, Olsson S-E, Omerovic E, Panayi G, Petraco R, Piek JJ, Ribichini F, Samady H, Samuels B, Sandhall L, Sapontis J, Sen S, Seto AH, Sezer M, Sharp ASP, Shin E-S, Singh J, Takashima H, Talwar S, Tanaka N, Tang K, Van Belle E, van Royen N, Varenhorst C, Vinhas H, Vrints CJ, Walters D, Yokoi H, Fröbert O, Patel MR, Serruys P, Davies JE, Götberg M. Safety of the deferral of coronary revascularization on the basis of instantaneous wave-free ratio and fractional flow reserve measurements in stable coronary artery disease and acute coronary syndromes. JACC Cardiovasc Interv 2018;11:1437–1449.

Figure 1. Patient flow chart according to the change in treatment strategy following the intracoronary pressure wire study.
Figure legend: ICPW: intracoronary pressure wire; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft.

Figure 2. Extent of coronary artery disease based on coronary angiographic analysis (2A) and following intracoronary pressure wire study (2B).
Figure legend: Figure 2A shows the extent of coronary artery disease based on coronary angiographic analysis and its reclassification following intracoronary pressure wire study. Figure 2B shows the extent of coronary artery disease following pressure wire study and its classification when only considering the coronary angiographic analysis.

Figure 3. Change in treatment strategy following intracoronary pressure wire study.
Figure legend: PCI: percutaneous coronary intervention; MT: medical treatment; CABG: coronary artery bypass graft.

Figure 4. Cox regression curves for MACE according to whether there had been a change in treatment strategy following intracoronary pressure wire study.
Figure legend: (A) All patients; (B) patients with medical treatment as therapeutic option based on initial coronary angiography; (C) patients with PCI as therapeutic option based on initial coronary angiography; (D) patients with CABG as therapeutic option based on initial coronary angiography.
PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft.

Changes in the treatment strategy following intracoronary pressure wire in a contemporaneous real-life cohort of patients with intermediate coronary stenosis. Results from a nationwide registry

CREDIT AUTHOR STATEMENT

Oriol Rodriguez-Leor: Conceptualization, Methodology, Data curation, Formal analysis, Writing original draft preparation.
Beatriz Toledano: Methodology, Data curation, Writing-Reviewing and editing
Ramón López-Palop: Data curation, Writing-Reviewing and editing
Fernando Rivero: Data curation, Writing-Reviewing and editing
Salvatore Brugaletta: Data curation, Writing-Reviewing and editing
José Antonio Linares: Data curation, Writing-Reviewing and editing
Tomás Benito: Data curation, Writing-Reviewing and editing
Pilar Carrillo: Data curation, Writing-Reviewing and editing
Martí Puigfel: Data curation, Writing-Reviewing and editing
German Cediel: Data curation, Formal analysis
Mario Sadaba: Data curation, Writing-Reviewing and editing
Beatriz Vaquerizo: Data curation, Writing-Reviewing and editing
Juan Rondán: Data curation, Writing-Reviewing and editing
Iván Gómez: Data curation, Writing-Reviewing and editing
Fernando Alfonso: Data curation, Writing-Reviewing and editing
Roberto Sáez: Data curation, Writing-Reviewing and editing
Ana Planas: Data curation, Writing-Reviewing and editing
Fernando Lozano: Data curation, Writing-Reviewing and editing
Felipe Hernández: Data curation, Writing-Reviewing and editing
Manel Sabaté: Data curation, Writing-Reviewing and editing
José Ramón Ruíz-Arroyo: Data curation, Writing-Reviewing and editing
Francisco Torres: Data curation, Writing-Reviewing and editing
José María de la Torre Hernández: Data curation, Writing-Reviewing and editing
Enrique Gutiérrez: Data curation, Writing-Reviewing and editing
Ana Belén Cid-Álvarez : Data curation, Writing-Reviewing and editing
José Luís Díez: Data curation, Writing-Reviewing and editing

Luis Fernández: Data curation, Writing-Reviewing and editing

José Moreu: Data curation, Writing-Reviewing and editing

Soledad Ojeda: Data curation, Writing-Reviewing and editing

Pablo Cerrato: Data curation, Writing-Reviewing and editing

Valeriano Ruiz-Quevedo: Data curation, Writing-Reviewing and editing

Juan Sanchis: Data curation, Writing-Reviewing and editing

Antonio Gómez-Menchero: Data curation, Writing-Reviewing and editing

Raymundo Ocaranza: Data curation, Writing-Reviewing and editing

Mohsen Mohandes: Data curation, Writing-Reviewing and editing

José María Hernández: Data curation, Writing-Reviewing and editing

Miren Maite Alfageme: Data curation, Writing-Reviewing and editing

Pablo Aguiar: Data curation, Writing-Reviewing and editing

José Ramón López Mínguez: Data curation, Writing-Reviewing and editing

Armando Pérez de Prado: Conceptualization, Methodology, Data curation, Writing-Reviewing and editing

Table 1. Clinical characteristics of the patients according to modification of treatment strategy after ICPW.

	Change in treatment strategy N = 779	**No change in treatment strategy N = 635**	**P-value**	**All patients N = 1414**
Age, years	66.9 ± 11.0	66.5 ± 10.7	0.72	66.7 ± 10.8
Male gender, n (%)	586 (75.2)	481 (75.8)	0.82	1067 (75.5)
Hypertension, n (%)	550 (70.6)	432 (68.0)	0.30	982 (69.5)
Diabetes, n (%)	282 (36.2)	221 (34.8)	0.59	503 (35.6)
Dyslipidemia, n (%)	460 (59.1)	374 (58.9)	0.95	834 (59.0)
Active smoker, n (%)	304 (39.0)	246 (38.7)	0.91	550 (38.9)
Creatinine, mg/dl	1.07 ± 0.70	1.03 ± 0.56	0.82	1.05 ± 0.64
Clinical condition, % - ACS - Stable CAD	 348 (44.8) 402 (55.2)	 278 (47.8) 304 52.2	 0.28	 604 (46.1) 706 (53.9)
Previous ischemia test, n (%) • Positive test • Negative test • Indeterminate test	231 (29.7) 169 (73.2) 31 (13.4) 31 (13.4)	185 (29.1) 133 (71.9) 20 (10.8) 32 (17.3)	0.71	416 (29.4) 302 (72.6) 51 (12.3) 63 (15.1)
>1 lesion assessed, n (%)	239 (30.7)	103 (16.2)	<0.001	342 (24.2)

NHI to guide decision, n (%)	271 (34.8)	180 (28.4)	0.010	451 (31.9)
Initial strategy, n (%)				
- MT	69 (8.9)	313 (49.2)	<0.001	382 (27.0)
- PCI	656 (84.2)	285 (44.9)		941 (66.6)
- CABG	54 (5.8)	54 (6.9)		91 (6.4)
Final strategy, n (%)				
- MT	433 (55.6)	314 (49.5)	0.06	747 (52.8)
- PCI	303 (38.9)	284 (44.7)		587 (41.5)
- CABG	43 (5.5)	37 (5.8)		80 (5.7)
Decision according to ICPW, n (%)				
- Deferred in concordance	547 (70.2)	292 (46.0)	<0.001	839 (59.3)
- Treated in concordance	138 (17.7)	285 (44.9)		423 (29.9)
- Independent of ICPW	94 (12.1)	58 (9.1)		152 (10.8)

ACS: acute coronary syndrome; CAD: coronary artery disease; MT: medical treatment; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; ICPW: intracoronary pressure wire. Deferred in concordance refers to patients in which treatment of all the evaluated lesions was deferred in concordance with the ICPW results (FFR > 0.80 or NHI > 0.89). Treated in concordance refers to patients subjected to revascularization of at least one lesion in concordance with ICPW (FFR ≤ 0.80 or NHI ≤ 0.89). Independent of ICPW refers to patients in which at least one lesion with FFR ≤ 0.80 or NHI ≤ 0.89 was left untreated, or in which at least one lesion with FFR > 0.80 or NHI > 0.89 underwent revascularization.

Table 2. Baseline characteristics of the evaluated lesions and results of the pressure wire study.

	NHI n = 891	FFR n = 1247	All n = 1781
Location of the lesion			
Left main coronary artery	24 (2.7)	50 (4.0)	66 (3.7)
Left anterior descending coronary artery	458 (51.4)	681 (54.6)	919 (51.6)
Ramus	21 (2.4)	15 (1.2)	32 (1.8)
Circumflex artery	203 (22.8)	254 (20.4)	386 (21.7)
Right coronary artery	185 (20.8)	246 (19.7)	377 (21.2)
Mammary artery graft	0 (0)	1 (0.1)	1 (0.1)
Characteristics of the lesion			
Bifurcation lesion	80 (9.0)	128 (10.3)	175 (9.8)
Ostial lesion	49 (5.5)	92 (7.4)	131 (7.4)
Diffuse coronary disease	76 (8.5)	96 (7.7)	143 (8.0)
Quantitative angiographic analysis			
Stenosis by diameter, %	48±13	48±12	48±13
Minimum luminal diameter, mm	1.50±0.49	1.50±0.47	1.51±0.49
Reference diameter, mm	2.94±0.70	2.90±0.67	2.93±0.69
Lesion length, mm	13.2±9.5	13.6±9.0	13.7±9.4
Physiological indices			
NHI, mean±SD	0.90±0.10	-	-

NHI, median [IQR]	0.93 [0.88-0.97]	-	-
FFR, mean±SD	-	0.83±0.08	-
FFR, median [IQR]	-	0.84 [0.78-0.89]	-

FFR: fractional flow reserve; NHI: non-hyperemic diastolic index; SD: standard deviation; IQR: interquartile range.

Table 3. Clinical characteristics of the patients according to clinical status (acute coronary syndrome versus chronic coronary syndrome)

	Acute Coronary Syndrome N = 706	**Chronic Coronary Syndrome N = 604**	**P-value**	**All patients N = 1310**
Age, years	65.4 ± 11.3	67.9 ± 10.3	0.001	66.7 ± 10.8
Male gender, n (%)	473 (78.3)	509 (72.1)	0.010	982 (75.0)
Hypertension, n (%)	405 (67.1)	508 (72.0)	0.054	913 (69.7)
Diabetes, n (%)	190 (31.4)	285 (40.4)	0.001	475 (36.3)
Dyslipidemia, n (%)	336 (55.6)	441 (62.5)	0.012	777 (59.3)
Active smoker, n (%)	281 (46.5)	231 (32.7)	<0.001	512 (39.1)
Creatinine, mg/dl	0.99 ± 0.40	1.08 ± 0.71	0.007	1.04 ± 0.59
Change in treatment strategy, n (%)	326 (54.0)	402 (56.9)	0.28	728 (55.6)
Previous ischemia test, n (%) • Positive test • Negative test	46 (7.6) 33 (71.7) 6 (13.0)	334 (47.3) 240 (71.9) 39 (11.7)	<0.001	380 (29.0) 273 (71.8) 39 (11.7)

• Indeterminate test	7 (15.2)	55 (16.5)		55 (16.5)
>1 lesion assessed, n (%)	142 (23.5)	180 (25.5)	0.41	3422 (24.6)
NHPR to guide decision, n (%)	193 (32.0)	225 (31.9)	0.97	418 (31.9)
Initial strategy, n (%)				
- MT	147 (24.3)	203 (28.7)	0.012	350 (26.7)
- PCI	429 (71.0)	451 (63.9)		880 (67.2)
- CABG	28 (4.6)	52 (7.4)		80 (6.1)
Final strategy, n (%)				
- MT	286 (47.6)	400 (56.7)	<0.001	686 (52.4)
- PCI	291 (48.2)	264 (37.4)		555 (42.4)
- CABG	27 (4.5)	42 (6.0)		69 (5.3)
Decision according to ICPW, n (%)				
- Deferred in concordance	347 (57.4)	426 (60.3)	0.53	773 (59.0)
- Treated in concordance	186 (30.8)	207 (29.3)		393 (30.0)
- Independent of ICPW	71 (11.8)	73 (10.3)		144 (11.0)

ACS: acute coronary syndrome; CAD: coronary artery disease; MT: medical treatment; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; ICPW: intracoronary pressure wire. Deferred in concordance refers to patients in which treatment of all the evaluated lesions was deferred in concordance with the ICPW results (FFR > 0.80 or NHI > 0.89). Treated in concordance refers to patients subjected to revascularization of at least one lesion in concordance with ICPW (FFR ≤ 0.80 or NHI ≤ 0.89). Independent of ICPW refers to

patients in which at least one lesion with FFR ≤ 0.80 or NHI ≤ 0.89 was left untreated, or in which at least one lesion with FFR > 0.80 or NHI > 0.89 underwent revascularization.

Table 4. Clinical events over 12 months of follow-up according to whether there had been a change in treatment strategy following intracoronary pressure wire study.

	Change in treatment strategy N = 779	**No change in treatment strategy N = 635**	**P-value**	**All patients N = 1414**
MACE, n (%)	35 (4.9)	35 (6.0)	0.42	70 (5.4)
Cardiovascular mortality, n (%)	6 (0.9)	10 (1.7)	0.16	16 (1.2)
Non-fatal myocardial infarction, n (%)	21 (3.0)	19 (3.2)	0.78	40 (3.1)
Recurrent chest pain, n (%)	33 (4.7)	28 (4.8)	0.92	61 (4.7)
Non-cardiovascular mortality, n (%)	6 (0.9)	19 (1.7)	0.16	16 (1.2)
Revascularization over follow-up, n (%)			0.81	
• No revascularization	690 (96.6)	561 (96.1)		1241 (96.4)
• TLR	16 (2.3)	14 (2.4)		30 (2.3)
• Non-TLR	8 (1.1)	9 (1.5)		17 (1.3)

MACE: major adverse cardiovascular event; TLR: target lesion revascularization; Non-TLR: non-target lesion revascularization.

HIGHLIGHTS:

(8) In a non-controlled, real-life setting, the pressure wire is safe, with an extremely low complications rate.

(9) Following pressure wire use, we have demonstrated a very significant change in assessment of the extent of coronary disease.

(10) Following pressure wire use, we have evidenced a very significant change not only in treatment modality (medical, PCI or CABG) but also in management strategy.

(11) We have shown that the change in treatment modality and/or strategy has prognostic implications, particularly in those patients in which the intention of the operator prior to utilization of the pressure wire was to perform PCI.

(12) These results are clearly different from those observed in previous studies conducted in clearly different populations (with a very limited representation of patients with acute coronary syndrome, which nowadays represent most of all treated cases) and in reimbursement-based healthcare systems. For these two reasons, we believe that the data of our study come much closer to the reality of what the management of these patients should be.

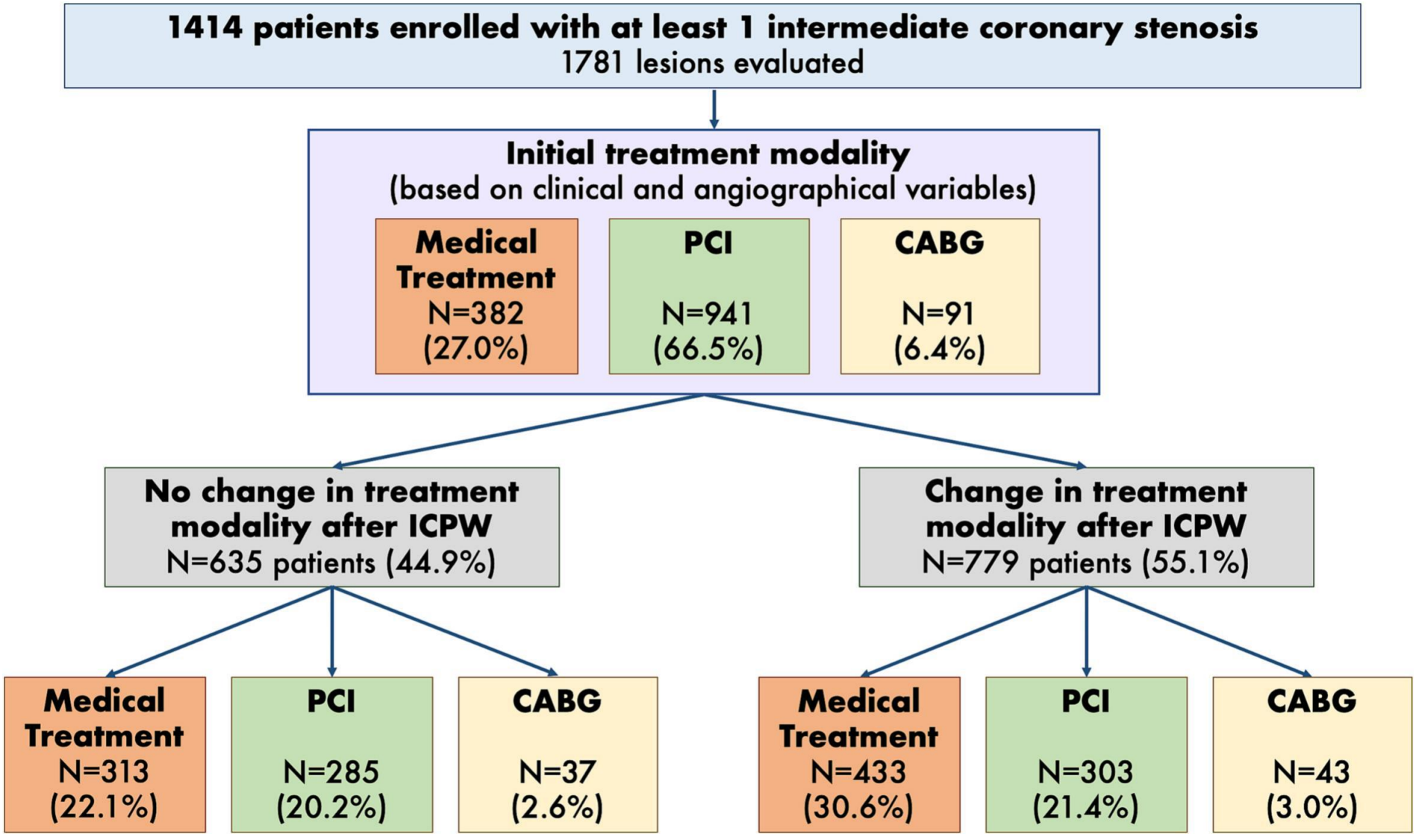
1414 patients enrolled with at least 1 intermediate coronary stenosis
1781 lesions evaluated
Initial treatment modality
(based on clinical and angiographical variables)
Medical Treatment
N=382
(27.0%)
PCI
N=941
(66.5%)
CABG
N=91
(6.4%)
No change in treatment modality after ICPW
N=635 patients (44.9%)
Change in treatment modality after ICPW
N=779 patients (55.1%)
Medical Treatment
N=313
(22.1%)
PCI
N=285
(20.2%)
CABG
N=37
(2.6%)
Medical Treatment
N=433
(30.6%)
PCI
N=303
(21.4%)
CABG
N=43
(3.0%)

Figure 1

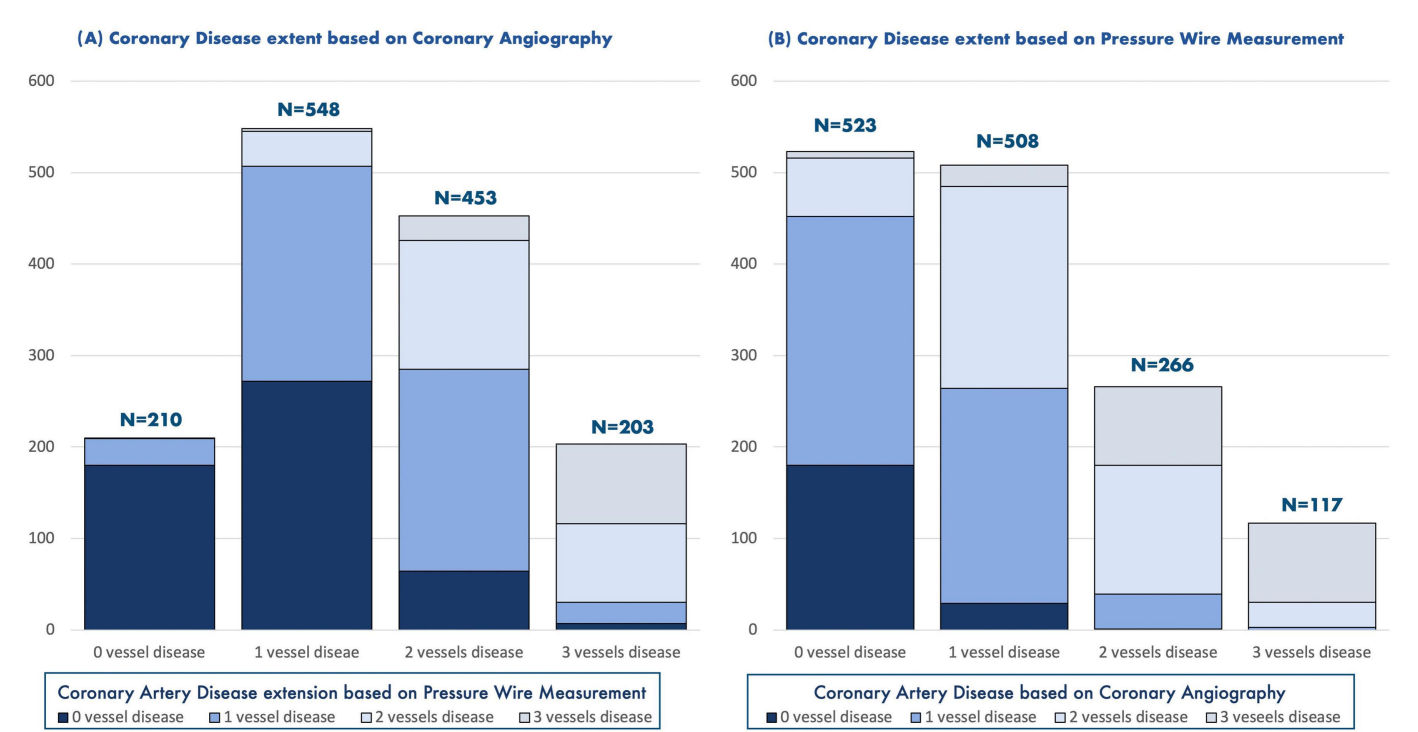
(A) Coronary Disease extent based on Coronary Angiography
600
500
400
300
200
100
0
N=210
N=548
N=453
N=203
0 vessel disease
1 vessel diseae
2 vessels disease
3 vessels disease
Coronary Artery Disease extension based on Pressure Wire Measurement
0 vessel disease
1 vessel disease
2 vessels disease
3 vessels disease
(B) Coronary Disease extent based on Pressure Wire Measurement
600
500
400
300
200
100
0
N=523
N=508
N=266
N=117
0 vessel disease
1 vessel disease
2 vessels disease
3 vessels disease
Coronary Artery Disease based on Coronary Angiography
0 vessel disease
1 vessel disease
2 vessels disease
3 veseels disease

Figure 2

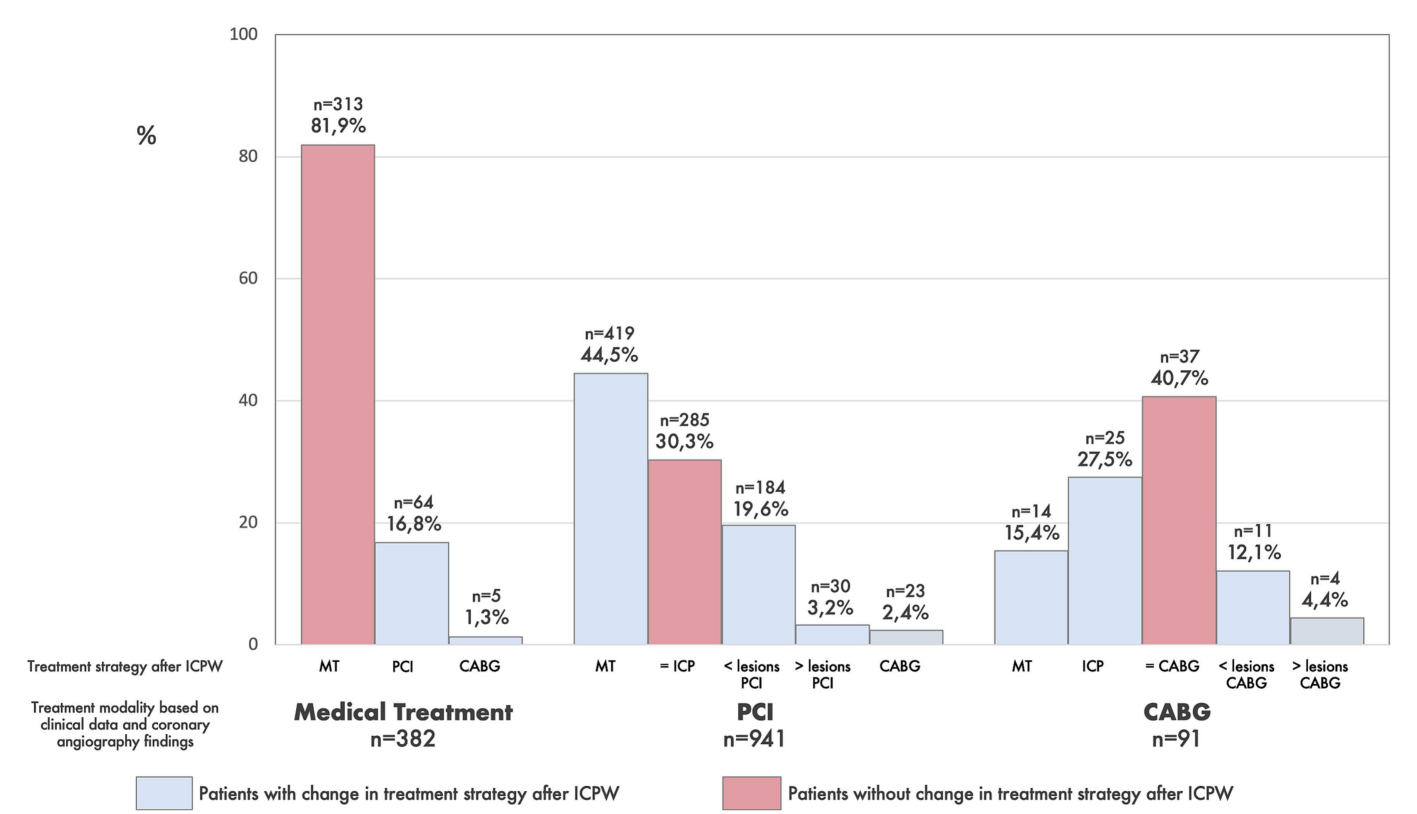
%
100
80
60
40
20
0
n=313
81,9%
n=64
16,8%
n=5
1,3%
n=419
44,5%
n=285
30,3%
n=184
19,6%
n=30
3,2%
n=23
2,4%
n=14
15,4%
n=25
27,5%
n=37
40,7%
n=11
12,1%
n=4
4,4%
Treatment strategy after ICPW
MT
PCI
CABG
MT
= ICP
< lesions PCI
> lesions PCI
CABG
MT
ICP
= CABG
< lesions CABG
> lesions CABG
Treatment modality based on clinical data and coronary angiography findings
Medical Treatment
n=382
PCI
n=941
CABG
n=91
Patients with change in treatment strategy after ICPW
Patients without change in treatment strategy after ICPW

Figure 3

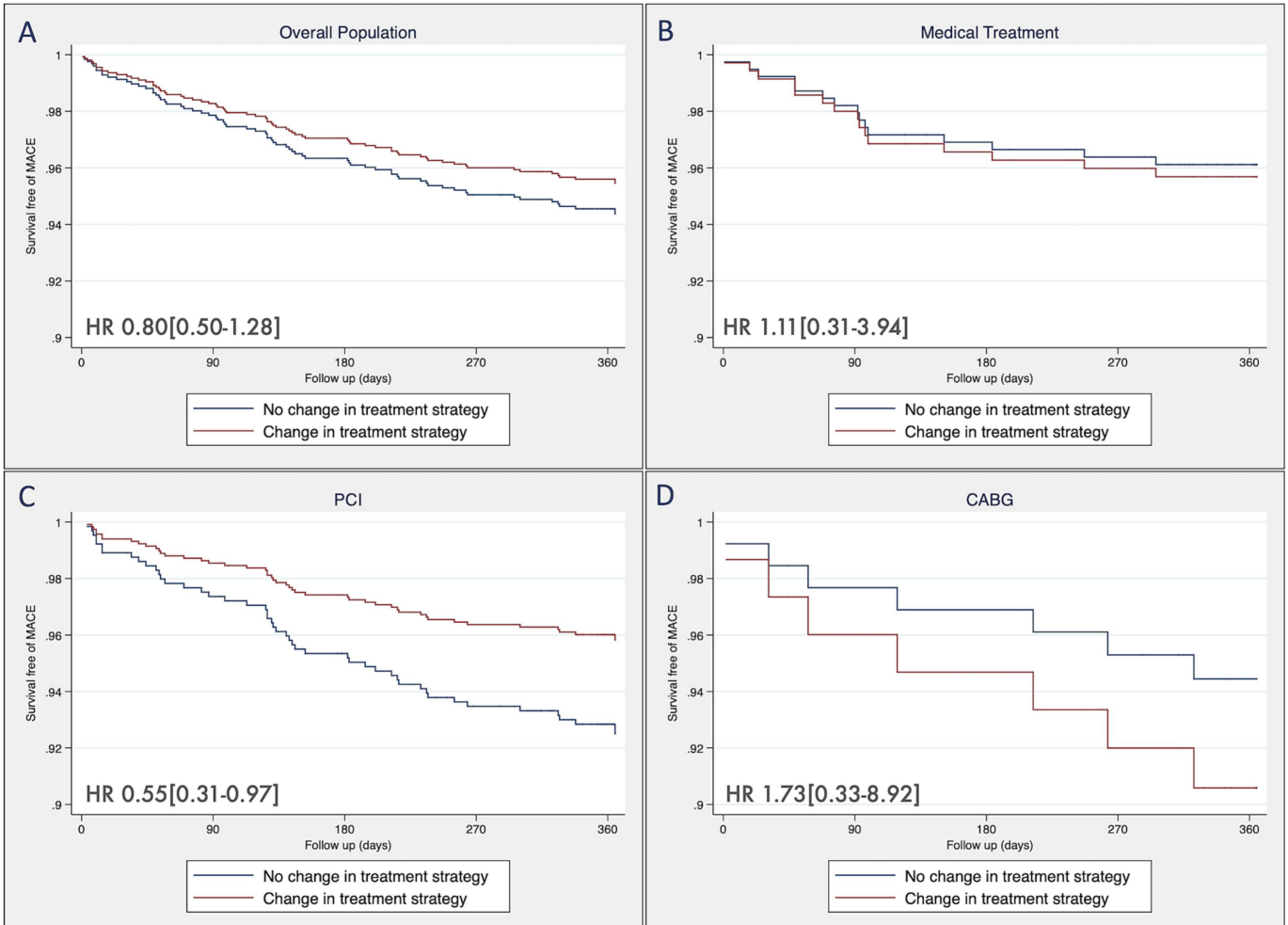
A
Overall Population
Survival free of MACE
1
.98
.96
.94
.92
.9
HR 0.80[0.50-1.28]
0
90
180
270
360
Follow up (days)
No change in treatment strategy
Change in treatment strategy
B
Medical Treatment
Survival free of MACE
1
.98
.96
.94
.92
.9
HR 1.11[0.31-3.94]
0
90
180
270
360
Follow up (days)
No change in treatment strategy
Change in treatment strategy
C
PCI
Survival free of MACE
1
.98
.96
.94
.92
.9
HR 0.55[0.31-0.97]
0
90
180
270
360
Follow up (days)
No change in treatment strategy
Change in treatment strategy
D
CABG
Survival free of MACE
1
.98
.96
.94
.92
.9
HR 1.73[0.33-8.92]
0
90
180
270
360
Follow up (days)
No change in treatment strategy
Change in treatment strategy

Figure 4