with cardiovascular risk factors, namely, *risk factors*, *diabetes mellitus*, *epidemiology*, *cardiovascular disease*, *obesity*, *cardiovascular risk*, and *metabolic syndrome*.

Three distinct blocks reflecting changes in the field of cardiovascular research between the periods 1997 to 2006 and 2007 to 2016 were observed. The first was a block showing a trend toward consolidation featuring keywords indicative of a relatively stable connection between the 2 periods, such as *acute myocardial infarction, heart failure, coronary disease, and acute coronary syndrome: echocardiography*, *electrophysiology*, *arrhythmias*, and *atrial fibrillation*. These terms were related to the knowledge domains of cardiomyopathies/ischemic heart disease, heart disease/heart failure and echocardiography, and electrophysiology/arrhythmias. The second block showed a decreasing trend for the domain of interventional cardiology, which, based on the keywords used by authors, was more prominent between 1997 and 2006. The third block showed a greater impact for the domain of epidemiology/risk factors and preventive cardiology in the second period. One of the most significant findings shown by the map was the increase in the frequency of occurrence and interconnections between keywords associated with cardiovascular risk factors, such as *diabetes mellitus*, *obesity*, and *metabolic syndrome*. This rise in frequency provides evidence that epidemiology/risk factors and preventive cardiology is an emerging knowledge domain in the field of cardiovascular research.

The main limitation of this study is that our results are based on data from a single journal, *Revista Española de Cardiología*. Nonetheless, we believe that the large number of articles analyzed provides a sufficiently representative picture of the field of cardiovascular research in Spain.

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Selection of the Best of 2017 on Percutaneous Treatment of Chronic Occlusions

Selección de lo mejor del año 2017 en el tratamiento percutáneo de la oclusión crónica

To the Editor,

Chronic occlusion is currently the most complex setting for percutaneous treatment of coronary lesions. Until recently, this type of intervention had a success rate of about 50% to 60%, and the main limiting step was the crossing of the coronary guidewire to the distal true lumen. Despite these poor results, the international interventional cardiologist community was not discouraged and continued to perform new procedures while incorporating new techniques and new materials[1]; the current success rates in specialized units are about 85% to 90%. Notably, during the 30-year history of this type of procedure,[2] no randomized study has compared its outcomes with those of medical therapy. However, 3 such articles have been published in the last year: EXPLORE,[3] DECISION-CTO (NCT01078051), and EURO CTO (NCT01760083). Each of these studies has completely different inclusion criteria, primary endpoints, and results (Table). Crucially, none found a significant reduction in "hard" endpoints such as cardiac mortality, which is why these results have caused some pessimism in the international scientific community about the use of percutaneous revascularization in patients with chronic occlusions. However, before changing our clinical practice, we need to discuss some general and specific aspects that may have influenced the results of these studies. First, there are 3 situations of interest: *a)* the procedural success rate is variable (73%-91%) and lower than that of other types of coronary revascularizations and, of course, if it is low, it greatly penalizes the intervention group; *b)* the number of patients that cross from one group to another, if high, affects the validity of the comparison; and *c)* a long inclusion period in high-volume centers means that many patients eligible for the study have not been included. Therefore, the findings cannot be generalized and are applicable only to a selected group of patients who are often the least symptomatic.

The EXPLORE study[3] randomized 304 patients with AMI treated with primary angioplasty and with chronic occlusion of a vessel in a second stage to medical therapy or percutaneous revascularization of the chronic occlusion. The primary endpoint was an improvement in ejection fraction and ventricular volumes on magnetic resonance imaging at 4 months. In the general study, there were no differences in the ejection fraction between the groups (44.1% ± 12.2% versus 44.8% ± 11.9%; P = not significant). However, in the subgroup of patients with chronic occlusion of the left anterior descending artery, the differences were significant in favor of the group of patients who underwent percutaneous coronary intervention (47.2% ± 12.3% versus 40.4% ± 11.9%; $P < .02$). One of the major limitations was the low rate of primary success (73%), which was below the current standards. The main features of this study are summarized in the Table.

In the DECISION-CTO study, 834 patients with chronic occlusion were randomized to medical therapy or percutaneous intervention. The primary endpoint was the composite of death from any cause, myocardial infarction, stroke, or repeat revascularization at 3 years. Although there were no significant differences between the groups, this study also suffers from some limitations. For example, the predetermined sample size (1284 patients) was not reached due to slow inclusion (6.5 years) in high-volume centers, meaning that a methodological deficit can be added to the above limitation regarding the applicability of the results. In addition, the crossover rate from the medical therapy group was relatively high (18%).

Table
Randomized Studies of Chronic Occlusions: Percutaneous Revascularization Versus Medical Therapy

Study	EXPLORE	DECISION-CTO	EURO CTO
Patients/hospitals, n	304/14	834/19	396/26
Published in peer-reviewed journal	Yes[3]	No	No
Enrollment period, mo	89	78	36
Predetermined sample size	Reached	Not reached	Not reached
Crossover rate of medical therapy to revascularization		18%	7.3%
Procedural success	73%	91.1%	86.6%
Primary endpoint	Improved ejection fraction and ventricular volumes on magnetic resonance at 4 months	The primary endpoint was a composite of death from any cause, myocardial infarction or stroke, or repeat revascularization at 3 years	Efficacy: improved quality of life according to the SAQ at 1 year Safety: incidence of myocardial infarction or death at 3 years
Results	Without differences in the primary endpoint Subgroup with LAD occlusion: differences in favor of the revascularization group	Without differences in the primary endpoint	Efficacy endpoint: differences in favor of the revascularization group Safety endpoint: data not available

LAD, left anterior descending artery; SAQ, Seattle Angina Questionnaire.

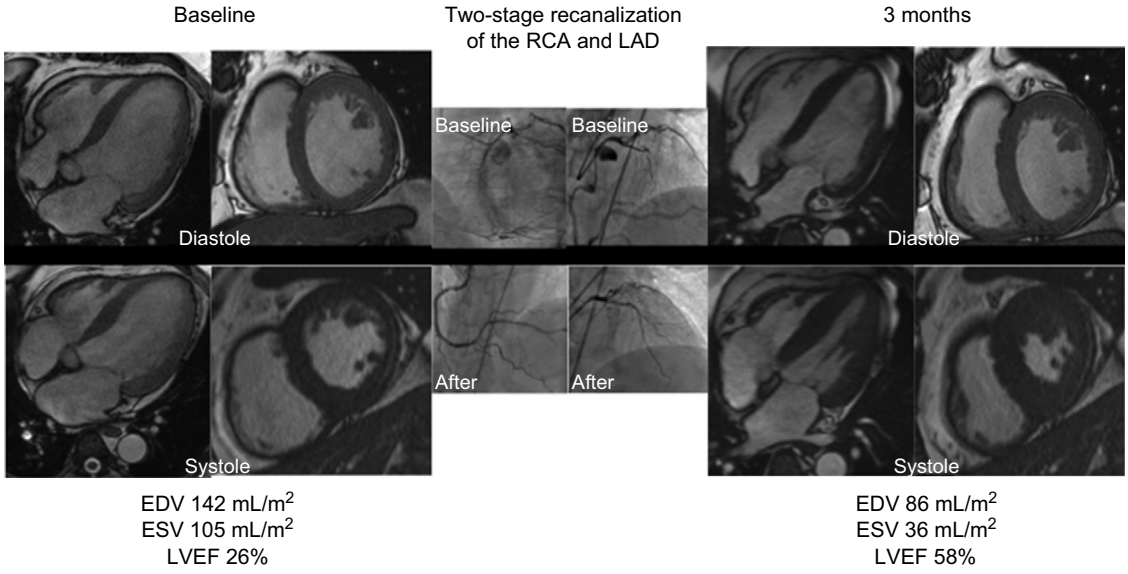

Figure. Changes in ejection fraction on magnetic resonance imaging 3 months after the procedure in a patient with chronic occlusion of the RCA and LAD, which were recanalized in 2 stages. EDV, end-diastolic volume; ESV, end-systolic volume; LAD, left anterior descending artery; LVEF, left ventricular ejection fraction; RCA, right coronary artery.

Finally, the EURO CTO study included 396 patients with chronic occlusion who were randomized 2:1 to percutaneous intervention or medical therapy. The primary efficacy endpoint was an improvement in quality of life according to the Seattle Angina Questionnaire (SAQ) at 1 year; the safety endpoint was the incidence of myocardial infarction or death at 3 years. The study was positive with regard to the efficacy endpoint; however, the 3-year follow-up data are not available. Because this study also failed to reach the predetermined sample size (600 patients for the efficacy endpoint and 1200 for the safety), it also has methodological limitations similar to those already mentioned.

Hoping that a randomized study with sufficient statistical power and without major limitations can demonstrate reduced mortality, the scientific community will continue to be divided between those who believe that there is some evidence for its usefulness based on observational studies[4,5] and clinical experience (Figure) and those who maintain that there is no evidence to systematically recommend the interventionist strategy. In the meantime, the latest North American and European clinical guidelines for revascularization both confer the percutaneous treatment of chronic occlusion in experienced centers a IIA level of evidence, grade of recommendation B.

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Selection of the Best of 2017 in Interventional Cardiology: Revolution in the Study of Coronary Physiology and New Parameters

Selección de lo mejor del año 2017 en cardiología intervencionista: revolución en el estudio de la fisiología coronaria y nuevos parámetros

To the Editor,

The use of coronary physiology as an invasive method for identifying hemodynamically significant coronary stenosis in stable patients dates back to the 1990s. However, following the results of the DEFER trial[1] and particularly the FAME trial,[2] which demonstrated that the use of fractional flow reserve (FFR) to guide revascularization reduced major adverse cardiac events (MACE) compared with angiography-guided revascularization, the technique has gained importance in clinical decision-making regarding patients with multivessel coronary disease.

Against this background, the emergence in recent years of a new invasive index for assessing coronary disease severity at rest without the need for induction of hyperemia has revolutionized the scientific community. Specifically, the instantaneous wave-free ratio (iFR) (Figure 1) shows a similar or even better ability than FFR to precisely detect myocardial ischemia. However, until 2017, there were no clinical studies that compared the use of iFR-guided vs FFR-guided revascularization. The DEFINE-FLAIR trial[3] included more than 2000 patients with intermediate coronary stenosis, with questionable severity, who were randomized to receive FFR-guided or iFR-guided revascularization. That trial was a noninferiority study for MACE at 1 year of follow-up. The cutoff values for indication for revascularization were FFR $\leq$ 0.80 and iFR $\leq$ 0.89.

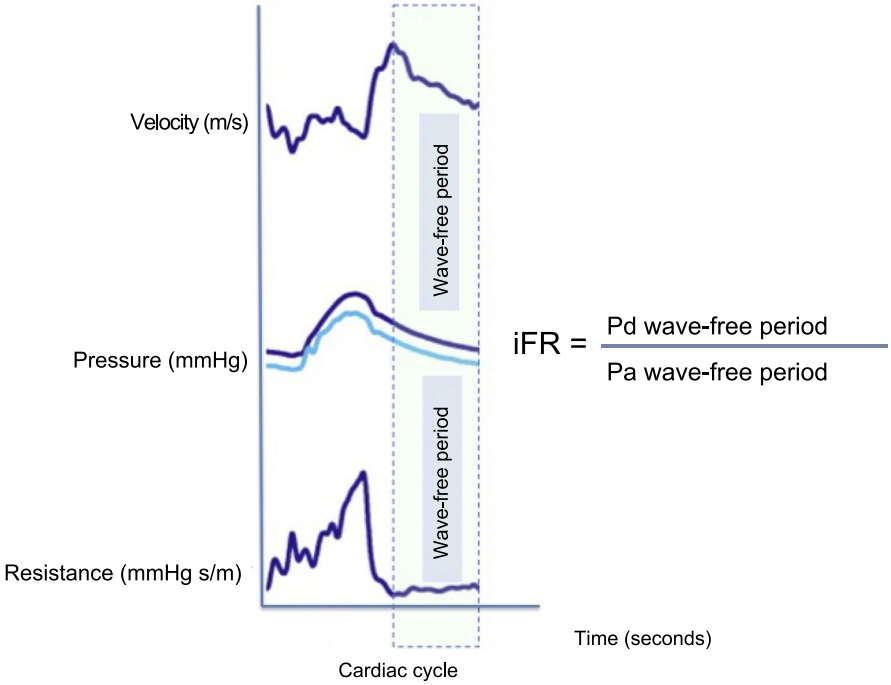

Figure. Illustration of microvascular flow velocity, pressure and resistance waves during the cardiac cycle. There is a period during diastole when flow velocity is high and pressure is low. This leads to lower microvascular resistance during the wave-free period. The iFR is calculated using an automatic algorithm that calculates the ratio at rest between the distal coronary pressure and the aortic pressure during the wave-free period. iFR, instantaneous wave-free ratio; Pa, aortic pressure; Pd, distal coronary pressure.