

# Elective Coronary Revascularization Procedures in Patients With Stable Coronary Artery Disease



## Incidence, Determinants, and Outcome (From the CORONOR Study)

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### ABSTRACT

**OBJECTIVES** The authors sought to describe the incidence, determinants, and outcome of elective coronary revascularization (ECR) in patients with stable coronary artery disease (CAD).

**BACKGROUND** Observational data are lacking regarding the practice of ECR in patients with stable CAD receiving modern secondary prevention.

**METHODS** The authors analyzed coronary revascularization procedures performed during a 5-year follow-up in 4,094 stable CAD outpatients included in the prospective multicenter CORONOR (Suivi d'une cohorte de patients CORONariens stables en région NORd-Pas-de-Calais) registry.

**RESULTS** Secondary prevention medications were widely prescribed at inclusion (antiplatelet agents 96.4%, statins 92.2%, renin-angiotensin system antagonists 81.8%). A total of 481 patients underwent  $\geq 1$  coronary revascularization procedure (5-year cumulative incidences of 3.6% [0.7% per year] for acute revascularizations and 8.9% [1.8% per year] for ECR); there were 677 deaths during the same period. Seven baseline variables were independently associated with ECR: prior coronary stent implantation ( $p < 0.0001$ ), absence of prior myocardial infarction ( $p < 0.0001$ ), higher low-density lipoprotein cholesterol ( $p < 0.0001$ ), lower age ( $p < 0.0001$ ), multivessel CAD ( $p = 0.003$ ), diabetes mellitus ( $p = 0.005$ ), and absence of treatment with renin-angiotensin system antagonists ( $p = 0.020$ ). Main indications for ECR were angina associated with a positive stress test (31%), silent ischemia (31%), and angina alone (25%). The use of ECR had no impact on the subsequent risk of death, myocardial infarction, or ischemic stroke (hazard ratio: 1.04; 95% confidence interval: 0.76 to 1.41).

**CONCLUSIONS** These real-life data show that ECR is performed at a rate of 1.8% per year in stable CAD patients widely treated by secondary medical prevention. ECR procedures performed in patients without noninvasive stress tests are not rare. Having an ECR was not associated with the risk of ischemic adverse events. (J Am Coll Cardiol Intv 2018;11:868-75)  
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The management of patients with coronary artery disease (CAD) has been substantially modified during the last decades by the increasing use of revascularization procedures and the effective evidence-based secondary prevention therapies including antiplatelet agents, statins, and/or renin-angiotensin system inhibitors (1-4). Although invasive strategies are unanimously accepted in the acute setting (3,4), uncertainty largely persists regarding elective coronary revascularization (ECR) procedures when performed in stable CAD outpatients treated with contemporary secondary prevention therapies (1,2,5,6). There are limited recent data in the literature on the real life practice of ECR in cohorts of patients with stable CAD (7,8). We thus designed the present analysis to describe the incidence, determinants, and outcome of ECR procedures performed during a 5-year follow-up period in 4,184 stable CAD outpatients included in the CORONOR (Suivi d'une cohorte de patients CORONariens stables en région NORd-Pas-de-Calais) registry.

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## METHODS

**STUDY POPULATION.** The CORONOR study is a prospective multicenter registry that included 4,184 consecutive outpatients with stable CAD. The study population has been previously reported in detail (9,10). The patients were included by 50 cardiologists from the region Nord-Pas-de-Calais in France between February 2010 and April 2011. Patients were considered eligible if they had evidence of CAD defined by at least 1 of the following: previous myocardial infarction (MI) (>1 year ago), previous coronary revascularization (>1 year ago), and/or obstruction of  $\geq 50\%$  of the luminal diameter of at least 1 native coronary vessel on coronary angiography. The sole exclusion criterion was hospitalization for MI or coronary revascularization within the last year. This study was approved by the French medical data protection committee and authorized by the Commission Nationale de l'Informatique et des Libertés for the treatment of personal health data. All patients consented to the study after being informed through a written document of the objectives of the study and on the treatment of data, as well as on their rights to object, of access, and of rectification.

**STUDY DESIGN AND DEFINITIONS.** A case record form, which contained information regarding demographic and clinical details of the patients including usual cardiovascular risk factors and treatments, was

prospectively completed at the initial visit by the investigators (i.e., the treating cardiologists). The patients were then followed up by their treating cardiologists. The number of outpatient visits as well as the practice and/or the type of noninvasive stress tests during follow-up was at the discretion of the treating cardiologists. Protocol-specified follow-up was performed at 2 years and at 5 years, using a standardized case record form to report coronary revascularizations. When coronary revascularization was reported, all related documents (reports of outpatient visits, reports of noninvasive stress tests, discharge summaries, percutaneous coronary intervention [PCI] and/or coronary artery bypass [CABG] reports) were collected. We also collected follow-up data on death, MI, and ischemic stroke. Missing information was completed by contacting either their general practitioners and/or the patients themselves. All clinical events were adjudicated by 4 investigators (T.M., O.T., N.L., and C.B.) blinded to each other. A third investigator joined the adjudication in case of disagreement according to pre-specified definitions. Coronary revascularization procedures were adjudicated as elective or acute. Acute coronary revascularizations were defined as those performed in a setting of an acute coronary syndrome, including all myocardial infarctions (ST-segment elevation and non-ST-segment elevation myocardial infarction) as well as unstable angina. Coronary revascularizations not performed in a setting of an acute coronary syndrome were defined as ECR. In patients with ECR, data on: 1) type of procedure (PCI, CABG); 2) use of bare-metal stent (BMS) or drug-eluting stent (DES) when stents were used; 3) the practice of fractional flow reserve (FFR)-guided procedures; 4) anginal symptoms or equivalent before revascularization; 5) the practice of noninvasive stress tests before revascularization, as well as the type of test if performed (electrocardiogram [ECG] exercise test, nuclear stress test, stress echocardiography); and 6) antianginal medication modification before revascularization were retrospectively collected. The cause of death was determined after a detailed review of the circumstances of death and classified as cardiovascular or noncardiovascular (11). Deaths from unknown cause were considered as cardiovascular. MI was defined according to the universal definition (12,13). Ischemic stroke was defined as a sudden onset of focal neurological symptoms with the presence of cerebral infarction in the appropriate territory on brain imaging.

## ABBREVIATIONS AND ACRONYMS

<b>ACE</b>	= angiotensin-converting enzyme
<b>ARB</b>	= angiotensin receptor blocker
<b>BMS</b>	= bare-metal stent(s)
<b>CABG</b>	= coronary artery bypass
<b>CAD</b>	= coronary artery disease
<b>CI</b>	= confidence interval
<b>DES</b>	= drug-eluting stent(s)
<b>ECG</b>	= electrocardiogram
<b>ECR</b>	= elective coronary revascularization
<b>FFR</b>	= fractional flow reserve
<b>HR</b>	= hazard ratio
<b>LDL-C</b>	= low-density lipoprotein cholesterol
<b>MI</b>	= myocardial infarction
<b>PCI</b>	= percutaneous coronary intervention
<b>SHR</b>	= subhazard ratio

**TABLE 1** Baseline Characteristics in the Overall Study Population and According to ECR During the 5-Year Follow-Up

	All Patients (N = 4,094)	No Elective Revascularization (n = 3,733)	Elective Revascularization (n = 361)	p Value
Age, yrs	67 ± 12	67 ± 12	66 ± 10	0.013
Males	78.0	77.8	80.1	0.338
History of hypertension	60.1	60.1	59.8	0.922
Diabetes mellitus	31.0	30.4	38.0	0.003
LDL-C, mg/dl	89 ± 28	89 ± 28	94 ± 34	0.001
Current smoker	11.3	11.4	10.3	0.564
Prior MI	62.4	63.2	53.7	<0.0001
Multivessel CAD	57.8	57.0	65.4	0.002
Prior stent implantation	68.8	67.8	78.7	<0.0001
Prior coronary bypass	21.4	21.5	19.7	0.430
LVEF, %	58 ± 11	57 ± 11	59 ± 10	0.041
Treatment at inclusion				
Antiplatelet therapy	96.4	96.3	97.2	0.362
β-Blockers	79.2	79.6	74.8	0.030
ACE inhibitor or ARB	81.8	82.3	77.0	0.013
Statins	92.2	92.3	90.6	0.228
Nitrates	14.8	14.5	17.5	0.141
Calcium antagonists	25.0	24.6	29.4	0.047
Nicorandil	11.5	11.0	16.3	0.002
Ivabradine	4.3	4.1	6.1	0.083
Antianginal drugs, n*	1.3 ± 0.7	1.3 ± 0.7	1.4 ± 0.8	0.011

Values are mean ± SD or %. \*β-Blockers, nitrates, calcium antagonists, nicorandil, ivabradine.  
ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CAD = coronary artery disease; ECR = elective coronary revascularization; LDL-C = low-density lipoprotein cholesterol; LVEF = left ventricular ejection fraction; MI = myocardial infarction.

**STATISTICAL ANALYSIS.** Continuous variables were described as the mean ± SD or as median with 25th and 75th percentiles. Categorical variables were presented as absolute numbers and percentages. Cumulative incidence is from the estimated cumulative incidence functions. Univariate and multivariate assessments of baseline variables associated with ECR were performed using competitive risk regression with death as the competing event according to the method of Fine and Gray (14). Patients with acute revascularization were not excluded from the dataset and were not censored at time of acute revascularization. Subhazard ratios (SHRs) and 95% confidence intervals (CIs) were calculated. The proportional hazards assumption was tested and satisfied by including interaction time-dependent terms in the multivariable regression analysis. Variables with a p value <0.05 in univariate analysis were entered into the final model. Collinearity was excluded by means of a correlation matrix between candidate predictors. Differences in categorical variables were assessed using chi-square analysis. Differences in the number of antianginal medications were assessed by the paired Student's *t*-test. The association of ECR with subsequent outcome was assessed by Cox analysis

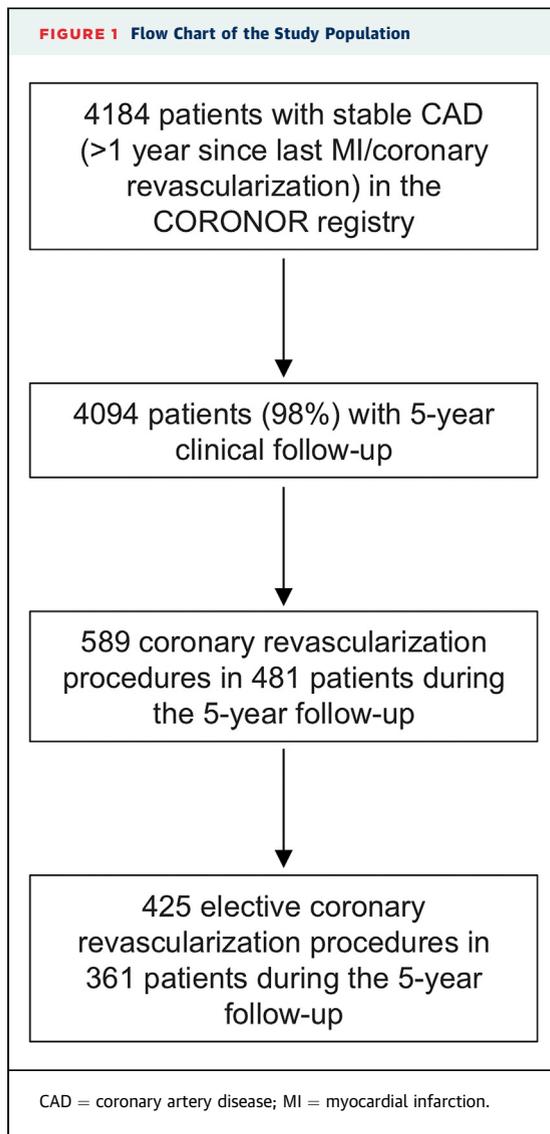
with ECR as a time-dependent variable. We assessed the association with the combined endpoint of cardiovascular death, MI, or ischemic stroke, and with all-cause mortality. Hazard ratios (HRs) and 95% CI were calculated. All statistical analyses were performed using the STATA version 14.1 software (STATA Corporation, College Station, Texas). Statistical significance was assumed at a p value <0.05.

## RESULTS

**STUDY POPULATION.** A clinical follow-up was obtained at a median of 4.9 (interquartile range: 4.3 to 5.2) years in 4,094 (98%) of the 4,184 patients with stable CAD included in the CORONOR study; 90 patients were lost to follow-up at the 5-year time point. As shown in **Table 1**, most patients were male (78%), with a mean age of 67 ± 12 years and with 31% of patients being diabetic. A history of MI was documented in 62.4% of cases, with 68.8% of the patients having had prior coronary stent implantation and 21.4% prior CABG. Secondary preventative medications were widely prescribed (antiplatelet agents 96.4%, statins 92.2%, angiotensin-converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARB] 81.8%, β-blockers 79.2%). In addition to β-blockers, medications with antianginal effect included nitrates (14.8%), calcium antagonists (25.0%), nicorandil (11.5%), and ivabradine (4.3%). At inclusion, the mean number of antianginal drugs (β-blockers, nitrates, calcium antagonists, nicorandil, ivabradine) was 1.3 ± 0.7 per patient.

**CORONARY REVASCUARIZATION PROCEDURES DURING FOLLOW-UP.** Of the 4,094 patients, 481 underwent ≥1 coronary revascularization procedures during the follow-up (5-year cumulative incidence of 11.8%) (**Figure 1**). As shown in **Figure 2**, the risk appeared constant over time (2.4% per year). In total, there were 589 coronary revascularization procedures (518 [88%] PCIs and 71 [12%] CABGs) in the 481 patients. DES alone were implanted in 371 PCI procedures, BMS alone in 96 procedures, DES and BMS in 4 procedures, and balloon angioplasty alone in 47 procedures. Coronary revascularization was performed in a setting of an acute coronary syndrome in 28% of the cases, whereas 72% were ECR procedures. Five-year cumulative incidences were 3.6% (0.7% per year) for acute revascularizations and 8.9% (1.8% per year) for ECR.

Baseline characteristics of patients with versus patients without ECR are summarized in **Table 1**. By competitive risk regression, 7 baseline variables were independently associated with ECR during follow-up: prior coronary stent implantation (SHR: 1.93; 95% CI: 1.47 to 2.53), no prior MI (SHR: 1.60; 95% CI: 1.27 to 2.02), low-density lipoprotein-cholesterol (LDL-C)



(SHR: 1.06 per 10-mg/dl increase; 95% CI: 1.03 to 1.09), age (SHR: 0.85 per 10-year increase; 95% CI: 0.78 to 0.93), multivessel CAD (SHR: 1.42; 95% CI: 1.12 to 1.81), diabetes mellitus (SHR: 1.39; 95% CI: 1.10 to 1.76), and baseline treatment with ACE inhibitors or ARB (SHR: 0.73; 95% CI: 0.56 to 0.95) (Table 2). Antianginal therapy at baseline was not independently associated with ECR during follow-up.

**INDICATIONS FOR ECR.** The indications for ECR are illustrated in Figure 3. The 3 main indications were angina associated with a positive stress test (134 procedures), silent ischemia (130 procedures), and angina alone (104 procedures). In addition, 27 ECR procedures were performed in a context of clinical manifestations of heart failure and/or left ventricular dysfunction. Other indications were revascularization before or during aortic valvular intervention (n = 15),

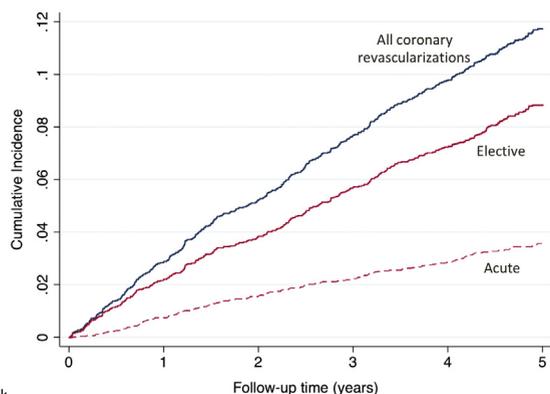
revascularization in a context of ventricular arrhythmia (n = 7), revascularization before aortic aneurysm intervention (n = 2), and revascularization following systematic coronary angiography (n = 3).

In patients with angina and a positive stress test and in patients with silent ischemia, the type of noninvasive stress test was an ECG exercise test in 107 cases, a nuclear stress test in 72 cases, and a stress echocardiography in 68 cases; in 17 patients, there was documentation of a positive stress test, but the type of test was not specified. The proportion of FFR-guided procedures was low: 2.2%, 7.7%, and 4.8%, in the angina and positive stress test group, the silent ischemia group, and the angina alone group, respectively (p = 0.121).

Table 3 summarizes the antianginal treatment at time of ECR for the angina and positive stress test group, the silent ischemia group, and the angina alone group. The mean number of antianginal medications per patient increased from  $1.4 \pm 0.7$  at inclusion to  $1.7 \pm 0.9$  (p < 0.0001) before revascularization in the angina and positive stress test group, and from  $1.6 \pm 0.8$  to  $1.9 \pm 0.9$  (p = 0.0001) in the angina alone group; by contrast, the number of antianginal medications was unchanged in the silent ischemia group (from  $1.4 \pm 0.7$  at inclusion to  $1.3 \pm 0.6$  before revascularization; p = 0.319).

**TEMPORAL TRENDS IN ECR.** A further analysis was performed to determine whether practice patterns regarding ECR may have evolved over time. We compared 2 periods of time: February 2010 to December 2012 (period 1; 9,298 patient-years) versus January 2013 to July 2016 (period 2; 9,301 patient-years). There were 200 (2.1/100 patient-years) and 225 (2.4/100 patients-year) ECR procedures, in periods 1 and 2, respectively. The proportions of ECR procedures performed for angina and a positive stress test, silent ischemia, and angina alone were similar during the 2 periods of time: 33%, 28.5%, and 26%, respectively, during period 1, and 30.2%, 32.4%, and 23.1%, respectively, during period 2 (p = 0.707). In patients with documentation of ischemia by noninvasive testing before ECR, the proportions of ECG exercise test, nuclear stress test, and stress echocardiography, were similar during the 2 periods of time: 45.9%, 30.3%, and 23.8%, respectively, during period 1, and 41.3%, 28.9%, and 30.4%, respectively, during period 2 (p = 0.513).

**OUTCOME AFTER ELECTIVE CORONARY REVASCULARIZATION.** During the follow-up period, there were 677 deaths, 170 MIs, and 96 ischemic strokes in the overall population. The composite endpoint of death, MI, or ischemic stroke occurred in 869 patients (21.2%). When used as a time-dependent variable, the use of

**FIGURE 2** Cumulative Incidence of All Coronary Revascularizations, ECRs, and Acute Coronary Revascularizations During the 5-Year Follow-Up

Number at risk	0	1	2	3	4	5
All revascularizations	4094	3857	3628	3384	3119	1500
Elective	4094	3881	3674	3453	3204	1540
Acute	4094	3942	3774	3598	3381	1639

ECR = elective coronary revascularization.

ECR was not associated with the risk of the composite endpoint (HR: 1.04; 95% CI: 0.76 to 1.41;  $p = 0.803$ ). Similar results were observed for all-cause mortality (HR: 0.82; 95% CI: 0.56 to 1.20;  $p = 0.298$ ). **Figure 4** shows the incidence rates for both the composite endpoint and all-cause mortality according to ECR. In an analysis taking into account the indications, ECR for angina and positive stress test, ECR for silent ischemia, and ECR for angina alone were not associated with the composite endpoint (HR: 0.57 95% CI: 0.29 to 1.15;  $p = 0.117$ ; HR: 0.88 95% CI: 0.49 to 1.55;  $p = 0.657$ ; and HR: 1.31 95% CI: 0.77 to 2.23;  $p = 0.306$ , respectively; patients without ECR as reference).

## DISCUSSION

International guidelines unanimously recommend coronary revascularization as an integral part of management in patients with acute coronary syndromes (3,4). By contrast, the role of coronary revascularization for the treatment of patients with stable manifestations of CAD remains a matter of intense debate, and there is still important research ongoing in this area (6).

There is an abundant amount of literature on the prognostic impact of coronary revascularization when performed in patients with stable CAD (5,6,15). By contrast, there is much less information on the real-life practice of coronary revascularization (i.e., incidence, indications, predictors) in populations of patients with stable CAD. Data from randomized studies that have specifically targeted this population (16,17) are useful but may be subject to selection bias related to their

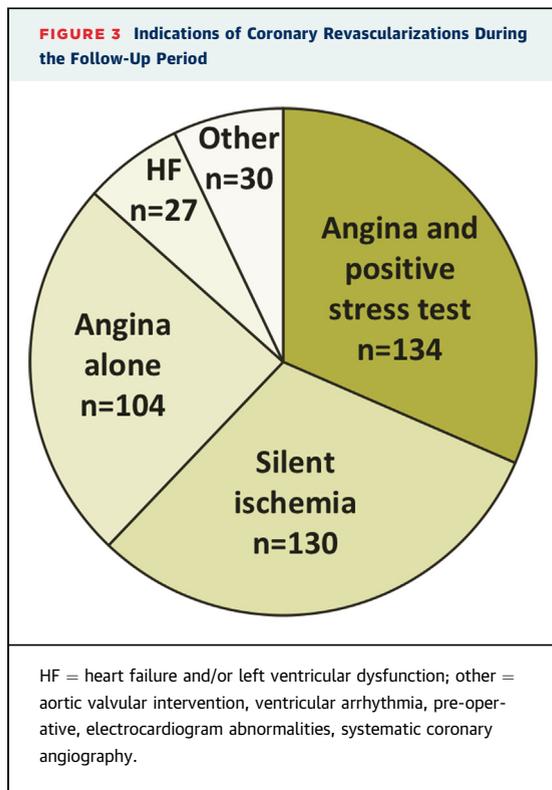
**TABLE 2** Multivariate Analysis: Independent Predictors of ECR During the 5-Year Follow-Up

	SHR	95% CI	p Value
Prior coronary stent implantation	1.93	1.47-2.53	<0.0001
No prior MI	1.60	1.27-2.02	<0.0001
LDL-C, per 10 mg/dl	1.06	1.03-1.09	<0.0001
Age, per 10-yr increase	0.85	0.78-0.93	<0.0001
Multivessel CAD	1.42	1.12-1.81	0.003
Diabetes mellitus	1.39	1.10-1.76	0.005
ACE or ARB at inclusion	0.73	0.56-0.95	0.020

CI = confidence interval; SHR = subhazard ratios by competitive risk regression; other abbreviations as in **Table 1**.

specific inclusion-exclusion criteria. Patient cohorts and registries focusing on stable CAD are rare (7,18) and were often performed at a time when secondary prevention was not as stringent as in contemporary practice. In the recent international CLARIFY registry (Registry to Provide Contemporary Information Regarding Characteristics, Management and Outcomes of Outpatients With Stable Coronary Artery Disease) (8), the rate of coronary revascularization at 1-year follow-up was 2.5% overall.

Our result of a yearly rate of coronary revascularization of 2.4% is in line with the data from the CLARIFY registry (8). It has to be underlined that this was in a context of a high prescription of secondary prevention medications, including a nearly systematic use of statins, which have been shown to reduce the use of coronary revascularization by about one-quarter per mmol/l reduction in LDL-C (19). Moreover, our study highlights that elective procedures account for three-quarters of coronary revascularizations performed in stable CAD patients. At the end of the 5-year follow-up, nearly 1 of 10 stable CAD patients had undergone ECR, with most of the procedures being PCIs. The design of our study also allows us to determine the baseline profile of stable CAD patients that are more likely to undergo ECR during follow-up (**Table 2**). Although speculative, there might be different explanations linking these variables to revascularization. A history of prior stent implantation identifies a group of patients who are by definition suitable for revascularization and for whom restenosis may lead to recurrent procedures; the greater amount of viable myocardium in patients with no prior MI may be an incentive for revascularization; residual risk factors (LDL-C, diabetes mellitus) or insufficient prescription of ACE inhibitors and/or ARB may have an impact on plaque progression; finally, younger patients are probably more likely to undergo noninvasive testing and/or revascularization when ischemia is suspected and/or



detected. Other unexplored factors, such as the financial impact for institutions and/or physicians, might also have played a role in the decision to perform ECR.

One strength of our study is the provision of detailed information on the indications for ECR in stable CAD. To the best of our knowledge, this type of data has not been reported in previous reports on cohorts of stable CAD patients. Even in recent clinical trials of coronary revascularization (PCI and/or CABG), the indications

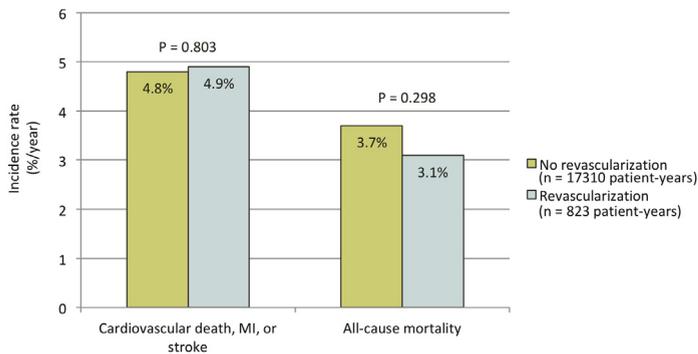
are rarely detailed and very often reported as “stable CAD” (20) or “stable angina” (21,22). Our data show that the main indications of ECR can be divided into approximately 3 thirds: angina and positive stress test, angina alone, and silent ischemia. Information on the symptomatic status of CAD patients should be interpreted considering ongoing antianginal therapy. Indeed, recent appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease take account of the number of antianginal drugs (23). In the present study, medical therapy was intensified in symptomatic patients, with a mean number of antianginal drugs per patient close to 2. There were, however, a significant number of patients receiving no or minimal antianginal treatment at the time of ECR (Table 3), leaving room for further optimization. In addition, although it has been shown that a systematic attempt to document myocardial ischemia before coronary revascularization may be lacking in current practice (24), the number of patients who underwent coronary revascularization for stable symptoms alone (without documentation of ischemia by noninvasive testing) was surprisingly high. Coronary revascularization in this context would be considered appropriate if guided by FFR (23), but this was not the case in our study, where almost all procedures were angiographically guided. It should, however, be noted that FFR guidewires were not reimbursed in France during most of the study period. This apparent aggressive use of ECR in stable CAD patients should be pointed out, and this demonstration of a gap between consensus and/or guidelines and real-world practices supports continued education with a particular emphasis on the indications for ECR. Moreover, the results of a recent randomized trial that failed to demonstrate an improvement in symptoms by PCI when compared with optimal medical management will have to be taken into account (25). The large number of revascularizations performed for silent ischemia also has to be underlined. It is stated in recent guidelines that patients with extensive ischemia may derive benefits from revascularization even in the absence of symptoms (26). However, our dataset did not include a quantification of the extent of ischemia before revascularization, and this issue could not be examined. Finally, we found no evidence of change in practice patterns regarding ECR of stable CAD patients between 2010 and 2012, and between 2013 and 2016. This may be related to the fact that the results of major randomized trials on coronary revascularization in stable CAD were already known when inclusions in the CORONOR registry started in 2010 (5,27).

Whether or not coronary revascularization of stable CAD patients may decrease the risk of death or MI is

**TABLE 3** Antianginal Treatment at Time of ECR

	Angina and Positive Stress Test (n = 134)	Silent Ischemia (n = 130)	Angina Alone (n = 104)
β-Blockers	79.8	86.1	70.2
Nitrates	19.4	4.6	33.6
Calcium antagonists	33.6	28.5	37.5
Nicorandil	21.6	8.5	27.9
Ivabradine	16.4	4.6	22.1
Antianginal drugs, n*			
0-1	44.0	69.2	35.6
2-3	52.0	30.8	59.6
4-5	3.0	—	4.8
Mean ± SD	1.7 ± 0.9	1.3 ± 0.6	1.9 ± 0.9

Values are % mean ± SD. \*β-Blockers, nitrates, calcium antagonists, nicorandil, ivabradine.  
ECR = elective coronary revascularization.

**FIGURE 4** Prognostic Impact of ECRs

Incidence rates for the composite end point (cardiovascular death, myocardial infarction [MI], or ischemic stroke) and for all-cause mortality according to elective coronary revascularization during 5-year follow-up. Elective coronary revascularization (ECR) was used as a time-dependent variable. No revascularization indicates the before/no revascularization states; revascularization indicates the post-revascularization state. p Value is by the Cox model.

still largely debated (6). Although both the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) and the BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) trials failed to demonstrate a benefit from an early invasive approach in this population (5,27), large-scale nonrandomized studies have reported improved prognosis with revascularization (28-30). In the present study, the use of ECR was not associated with a different risk of subsequent clinical events, and our results therefore suggest that medical treatment optimization should be promoted in such patients. Our study is, however, limited by its observational design, and whether or not revascularization is needed in stable CAD will have to be determined by randomized studies. The ongoing ISCHEMIA trial (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) is currently addressing this important and timely question (6). One strength of the ISCHEMIA study versus the COURAGE and BARI 2D studies is the inclusion of patients before coronary angiography; a blinded computed tomography angiogram is performed to exclude left main disease and to confirm the presence of obstructive CAD before randomization.

**STUDY LIMITATIONS.** Information on the class of angina at time of ECR was not available. In addition, information on quality of life after ECR was not available. Regarding the association of ECR with subsequent clinical events, it should be emphasized that our study was not powered enough to detect

small differences. The present data should be considered as hypothesis-generating, and further studies are needed. In addition to randomized trials directly addressing the prognostic impact of revascularization as discussed earlier in the text, large observational studies on the real-life practice of ECR in stable CAD with long-term follow-up will also be useful. Because the data reflect the practices in a regional area, it will have to be determined whether our findings are representative of practices in other parts of the world. Our study has, however, several strengths: it is based on a large prospective cohort, all included patients were CAD established patients with high rates of previous coronary revascularization and evidence-based secondary prevention therapies, and all the outcome events were blindly adjudicated.

## CONCLUSIONS

ECR procedures are performed at a rate of 1.8% per year in patients with stable CAD and are mostly PCIs. In one-quarter of the cases, ECR is performed for angina alone without documentation of ischemia. Having an ECR is not associated with the risk of subsequent adverse events. Whether or not ECR can improve patient outcome is, however, beyond the scope of our analysis and will require further studies.

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## PERSPECTIVES

**WHAT IS KNOWN?** Observational data are lacking regarding the practice of ECR in patients with stable CAD receiving modern secondary prevention.

**WHAT IS NEW?** ECR procedures are performed at a rate of 1.8% per year in patients with stable CAD. Main indications are angina and positive stress test, silent ischemia, and angina alone. Having an ECR is not associated with the risk of subsequent adverse events.

**WHAT IS NEXT?** Randomized studies are currently investigating the role of ECR in patients with stable CAD.

## REFERENCES

1. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2012;60:e44-164.
2. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013;34:2949-3003.
3. Levine GN, Bates ER, Blankenship JC, et al. 2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention and the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction. *J Am Coll Cardiol* 2016;67:1235-50.
4. Roffi M, Patrono C, Collet JP, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2016;37:267-315.
5. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;356:1503-16.
6. Stone GW, Hochman JS, Williams DO, et al. Medical therapy with versus without revascularization in stable patients with moderate and severe ischemia: the case for community equipoise. *J Am Coll Cardiol* 2016;67:81-99.
7. Daly C, Clemens F, Lopez Sendon JL, et al. Gender differences in the management and clinical outcome of stable angina. *Circulation* 2006;113:490-8.
8. Steg PG, Greenlaw N, Tardif JC, et al. Women and men with stable coronary artery disease have similar clinical outcomes: insights from the international prospective CLARIFY registry. *Eur Heart J* 2012;33:2831-40.
9. Bauters C, Deneve M, Tricot O, Meurice T, Lamblin N. Prognosis of patients with stable coronary artery disease (from the CORONOR study). *Am J Cardiol* 2014;113:1142-5.
10. Hamon M, Lemesle G, Tricot O, et al. Incidence, source, determinants, and prognostic impact of major bleeding in outpatients with stable coronary artery disease. *J Am Coll Cardiol* 2014;64:1430-6.
11. Bauters C, Tricot O, Meurice T, Lamblin N. Long-term risk and predictors of cardiovascular death in stable coronary artery disease: the CORONOR study. *Coron Artery Dis* 2017;28:636-41.
12. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *J Am Coll Cardiol* 2012;60:1581-98.
13. Lemesle G, Tricot O, Meurice T, et al. Incident myocardial infarction and very late stent thrombosis in outpatients with stable coronary artery disease. *J Am Coll Cardiol* 2017;69:2149-56.
14. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competitive risk. *J Am Stat Assoc* 1999;94:496-509.
15. Trikalinos TA, Alsheikh-Ali AA, Tatsioni A, Nallamothu BK, Kent DM. Percutaneous coronary interventions for non-acute coronary artery disease: a quantitative 20-year synopsis and a network meta-analysis. *Lancet* 2009;373:911-8.
16. Braunwald E, Domanski MJ, Fowler SE, et al. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. *N Engl J Med* 2004;351:2058-68.
17. Poole-Wilson PA, Lubsen J, Kirwan BA, et al. Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with stable angina requiring treatment (ACTION trial): randomised controlled trial. *Lancet* 2004;364:849-57.
18. Steg PG, Bhatt DL, Wilson PW, et al. One-year cardiovascular event rates in outpatients with atherothrombosis. *JAMA* 2007;297:1197-206.
19. Baigent C, Keech A, Kearney PM, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005;366:1267-78.
20. Genereux P, Giustino G, Witzensbichler B, et al. Incidence, predictors, and impact of post-discharge bleeding after percutaneous coronary intervention. *J Am Coll Cardiol* 2015;66:1036-45.
21. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;360:961-72.
22. Bona KH, Mannsverk J, Wiseth R, et al. Drug-eluting or bare-metal stents for coronary artery disease. *N Engl J Med* 2016;375:1242-52.
23. Patel MR, Calhoon JH, Dehmer GJ, et al. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2017;69:2212-41.
24. Desai NR, Bradley SM, Parzynski CS, et al. Appropriate use criteria for coronary revascularization and trends in utilization, patient selection, and appropriateness of percutaneous coronary intervention. *JAMA* 2015;314:2045-53.
25. Al-Lamee R, Thompson D, Dehbi HM, et al. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. *Lancet* 2018;391:31-40.
26. Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2014;35:2541-619.
27. Frye RL, August P, Brooks MM, et al. A randomized trial of therapies for type 2 diabetes and coronary artery disease. *N Engl J Med* 2009;360:2503-15.
28. Hannan EL, Samadashvili Z, Cozzens K, et al. Comparative outcomes for patients who do and do not undergo percutaneous coronary intervention for stable coronary artery disease in New York. *Circulation* 2012;125:1870-9.
29. Min JK, Berman DS, Dunning A, et al. All-cause mortality benefit of coronary revascularization vs. medical therapy in patients without known coronary artery disease undergoing coronary computed tomographic angiography: results from CONFIRM (CORonary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter Registry). *Eur Heart J* 2012;33:3088-97.
30. Wijeyesundera HC, Bennell MC, Qiu F, et al. Comparative-effectiveness of revascularization versus routine medical therapy for stable ischemic heart disease: a population-based study. *J Gen Intern Med* 2014;29:1031-9.

**KEY WORDS** coronary artery disease, elective revascularization, follow-up, outcome, outpatient