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Original article

Economic evaluation of complete revascularization versus stress echocardiography-guided revascularization in the STEACS with multivessel disease

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A B S T R A C T

Introduction and objectives: Economic studies may help decision making in the management of multivessel disease in the setting of myocardial infarction. We sought to perform an economic evaluation of CROSS-AMI (Complete Revascularization or Stress Echocardiography in Patients With Multivessel Disease and ST-Segment Elevation Acute Myocardial Infarction) randomized clinical trial.
Methods: We performed a cost minimization analysis for the strategies (complete angiographic revascularization [ComR] and selective stress echocardiography–guided revascularization [SelR]) compared in the CROSS-AMI clinical trial (N = 306), attributable the initial hospitalization and readmissions during the first year of follow-up, using current rates for health services provided by our health system.
Results: The index hospitalization costs were higher in the ComR group than in SelR arm (19 657.9 ± 6236.8 € vs 14 038.7 ± 4958.5 €; $P < .001$). There were no differences in the costs of the first year of follow-up rehospitalizations between both groups for (ComR 2423.5 ± 4568.0 vs SelR 2653.9 ± 5709.1; $P = .697$). Total cost was 22 081.3 ± 7505.6 for the ComR arm and 16 692.6 ± 7669.9 for the SelR group ($P < .001$).
Conclusions: In the CROSS-AMI trial, the initial extra economic costs of the ComR versus SelR were not offset by significant savings during follow-up. SelR seems to be more efficient than ComR in patients with ST-segment elevation acute coronary syndrome and multivessel disease treated by emergent angioplasty.
Study registred at ClinicalTrial.gov (Identifier: NCT01179126).

Evaluación económica de revascularización completa y revascularización guiada por ecocardiografía de estrés en el SCACEST con enfermedad multivaso

Palabras clave:
Evaluación económica
Cardiopatía isquémica
Síndrome coronario agudo
Infarto agudo de miocardio
Enfermedad multivaso
Revascularización
Intervención coronaria percutánea
Angioplastia primaria

R E S U M E N

Introducción y objetivos: Los estudios económicos pueden ayudar a tomar decisiones en el tratamiento de la enfermedad multivaso en el infarto. Se planteó realizar una evaluación económica del ensayo clínico CROSS-AMI *(Complete Revascularization or Stress Echocardiography in Patients With Multivessel Disease and ST-Segment Elevation Acute Myocardial Infarction).*
Métodos: Se realizó un análisis de comparación de costes económicos de las estrategias (revascularización angiográfica completa [RCom] y revascularización selectiva guiada por isquemia en ecocardiograma de estrés [RSel]) comparadas en el ensayo clínico CROSS-AMI (N = 306), derivados de la hospitalización inicial y del primer año de seguimiento, según las tarifas oficiales vigentes en nuestro sistema de salud.

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Resultados: El coste de la hospitalización inicial resultó superior en el grupo de RCom que en la rama de RSel (19.657,9 ± 6.236,8 frente a 14.038,7 ± 4.958,5 euros; p < 0,001). No hubo diferencias entre ambos grupos en el coste del primer año de seguimiento (RCom, 2.423,5 ± 4.568,0 euros; Rsel, 2.653,9 ± 5.709,1 euros; p = 0,697). El coste total fue 22.081,3 ± 7.505,6 euros en la rama de RCom y 16.692,6 ± 7.669,9 euros en la rama de RSel (p < 0,001).

Conclusiones: En el ensayo clínico CROSS-AMI, el sobrecoste inicial de la RCom frente a la RSel no se vio compensado por un ahorro significativo en el seguimiento. La RSel parece ser una estrategia más eficiente que la RCom para los pacientes con síndrome coronario agudo con elevación del segmento ST y enfermedad multivaso tratados mediante angioplastia emergente.

Estudio registrado en ClinicalTrials.gov (Identificador: NCT01179126).

Abbreviations

ComR: complete revascularization
PCI: percutaneous coronary intervention
SelR: selective stress echocardiography–guided revascularization
STEMI: ST-segment–elevation myocardial infarcation

INTRODUCTION

Cardiovascular disease is the leading cause of mortality in Western countries, with acute myocardial infarction occupying the top position.[1,2] Percutaneous coronary intervention (PCI) is the reperfusion therapy of choice for patients with acute ST–segment-elevation acute myocardial infarction (STEMI).[3] Approximately 40% to 60% of patients with STEMI have multivessel coronary artery disease and a worse clinical prognosis.[4,5]

The current recommendation for treating multivessel disease in patients with STEMI is to consider revascularizing nonculprit lesions, above all to reduce the need for revascularization and the risk of death or infarction following discharge.[3,6] The conservative arms in trials conducted so far, however, have been excessively conservative, as the only artery revascularized is the infarct-related artery (IRA), with no consideration given to the potential functional impact of nonculprit lesions. The true benefits of complete revascularization, therefore, may be overestimated.[7]

While decision-making should be guided by the patient's clinical profile and the safety and effectiveness of proposed interventions, economic evaluations reflecting the cost of various procedures are helpful for complex decision-making scenarios, particularly when resources are limited.[8,9]

Multivessel disease in patients with STEMI provides an ideal setting for economic evaluations, as treatment is both complex and costly, and several aspects, such as how best to select nonculprit lesions, remain to be clarified before systematic complete revascularization can be recommended.[7]

The aim of this study was to conduct an economic evaluation nested in the CROSS-AMI (Complete Revascularization or Stress Echocardiography in Patients With Multivessel Disease and ST-Segment Elevation Acute Myocardial Infarction) clinical trial.

METHODS

CROSS-AMi trial design

As previously reported,[10] the CROSS-AMI trial was a multicenter randomized clinical trial of patients with STEMI and multivessel disease comparing complete anatomic revascularization of all nonculprit coronary lesions during initial hospitalization (ComR) with selective revascularization based on stress echocardiography-guided detection of ischemia (SelR).[10] The trial received ethics committee approval and was conducted in accordance with the principles of the Declaration of Helsinki (reference 2010/160). It was registered at ClinicalTrials.gov under identifier number NCT01179126.

A total of 306 patients from our hospital were recruited for the trial between October 2010 and October 2015. They all provided signed informed consent. In brief, patients with STEMI who had undergone emergency PCI to treat an infarct-related artery (IRA) were eligible for inclusion if they had significant stenosis (70% by visual estimation) in at least 1 coronary artery other than the IRA (see inclusion and exclusion criteria of the supplementary data). They were randomized to the ComR or SelR arm using a pseudorandom number system within 48 hours of the index PCI. Patients in the ComR group (n = 154) were scheduled for a second PCI to treat all significant lesions prior to discharge. A pressure wire was not used to select which lesions to treat. Patients in the SelR group (n = 152) underwent an exercise or dobutamine stress echocardiogram during the index admission. As per protocol, PCI was indicated for nonculprit lesions in patients with recurrent spontaneous myocardial ischemia, coronary lesions with evidence of low-load ischemia (≥ 120 beats per minute), or ischemia in more than 2 coronary segments (figure 1).

Cost analysis

We performed a cost minimization analysis comparing the ComR and SelR strategies from the CROSS-AMI trial. The assumption in such analyses is that the strategies being compared are of similar effectiveness. The aim is thus to estimate and compare respective costs.

Index admission costs were estimated from the perspective of the public health care system in the autonomous community where our hospital is based. They were calculated as the sum of costs attributable to the emergency PCI, coronary angiography, repeat PCIs, and any diagnostic cardiology tests performed during the index admission. Follow-up costs were calculated as the sum of costs attributable to hospital stays during readmissions for a cardiac or noncardiac cause in the 12 months following discharge and any diagnostic cardiology tests or additional revascularization procedures performed during admission.

To estimate costs, we analyzed lengths of stay for the index admission and readmissions during follow-up. We also calculated the number of diagnostic and therapeutic cardiology procedures performed during these hospital stays. The costs were derived from official rates established for health care services provided by

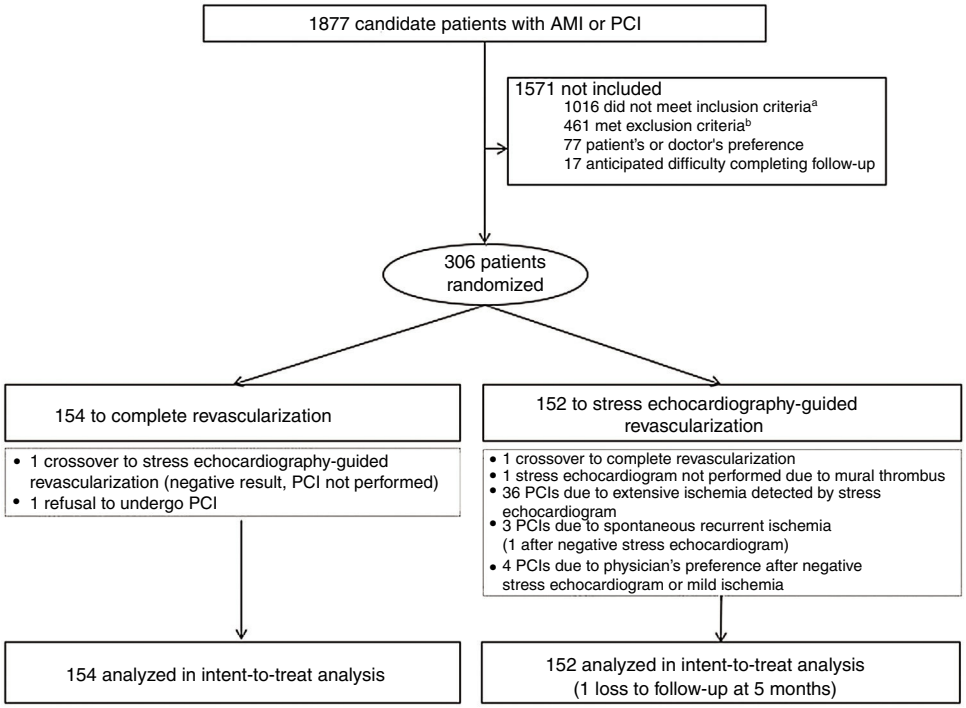

Figure 1. Flow diagram of the CROSS-AMI trial design. AMI, acute myocardial infarction; IRA, infarct-related artery; PCI, percutaneous coronary intervention. [a]Due to single-vessel coronary artery disease (n = 904), multivessel index PCI (n = 82), and suboptimal index PCI (n = 30). [b]Inadequate anatomy for PCI in lesions other than the IRA (n = 245), significant disease in left truncus arteriosus (n = 70), cardiogenic shock (n = 73), severe comorbidity (= 57), previous revascularization surgery (n = 4), and AMI due to coronary stent thrombosis (n = 12).

hospitals belonging to the public health care system in our autonomous community[11] (table 1).

We also performed a detailed analysis of disposable material used. The rate system used in our health care system is generic and covers staffing costs, maintenance costs, and average material costs. It does not cover the cost of all the devices used for PCI (eg, sheaths, catheters, guidewires, balloons, stents). As per the trial protocol, a prospective record was made of all material used for PCIs performed during the index admission. The cost of this material, obtained from the purchasing department, was the price paid by the hospital (table 2).

Statistical analysis

Quantitative variables are expressed as mean ± standard deviation (SD), while categorical variables are described as absolute and relative frequencies. Costs are expressed as mean ± SD costs per

Table 1
Hospitalization and cardiological procedure costs[11]

	Cost, €
Hospitalization	
Cardiac or intensive care unit (per d)	1142.47
Conventional hospital ward (per d)	528.95
Noninvasive procedures	
Echocardiography	321.64
Exercise stress test	310.76
Exercise or pharmacological stress echocardiography	377.67
Myocardial perfusion with SPECT	294.32
Invasive procedures	
Coronary angiography	1055.38
Coronary angiography and balloon angioplasty	3325.31
Coronary angiography, balloon angioplasty, and stent placement	6856.31

SPECT, single photon emission computed tomography.

Table 2
Disposable material costs

Procedure	Cost, €
Arterial sheath	29
Diagnostic catheter	13
Contract injector syringe (ACIST system)	29
ACIST contrast injector connection system	44
Inflator with pressure monitoring	43
Guiding catheter	91
Coronary guidewire	128
Angioplasty balloon	484
Conventional stent	624
Drug-eluting stent	1100
Thrombus aspiration catheter	496
Vascular closure devices	180
Hemostatic patch	66

patient. Categorical variables were compared using the chi-square test or, where appropriate, the Fisher exact test, while quantitative variables were compared using the *t* test or, in the case of nonnormally distributed data, the Mann-Whitney U test. Statistical analyses were performed in SPSS version 24.0 (IBM). A *P* value of less than .05 was considered statistically significant for 2-tailed comparisons.

RESULTS

Participants

The baseline characteristics of the 306 patients randomized to the 2 trial arms are shown in table 3. There were no significant differences between the groups in terms of cardiovascular risk factors, medical history, or clinical presentation of myocardial infarction.

Of the 154 patients in the ComR arm, 152 (99%) underwent PCI for nonculprit lesions (147 required just 1 procedure, while 5 needed an additional 2). One patient requested to be switched to the SelR arm. The stress echocardiogram was negative and the patient was discharged without undergoing PCI. Another patient refused to undergo this procedure (figure 1).

Of the 152 patients in the SelR arm, one was switched to the ComR arm and treated with PCI, while another did not undergo a stress echocardiogram due to a mural thrombus. Two patients developed spontaneous recurrent ischemia before the stress echocardiogram and were treated with PCI as per protocol. Stress echocardiography was thus performed in 148 patients and showed extensive ischemia in 36, all of whom were treated with a second PCI. Of the remaining patients (64 with negative stress echocardiography results, 25 with inconclusive results, and 23 with results suggestive of mild ischemia), 1 underwent a second PCI before discharge because of spontaneous recurrent ischemia and 4 were referred for PCI by their cardiologists (figure 1).

Events

The primary endpoint in the CROSS-AMI trial, a composite measure consisting of cardiovascular death, acute myocardial infarction, coronary revascularization, and readmission due to heart failure, occurred in 22 patients (14%) in the ComR group and 21 (14%) in the SelR group (hazard ratio, 0.95; 95% confidence interval [95%CI], 0.52-1.72; *P* = .85). There were no differences in

Table 3
Patients' baseline characteristics

	Complete revascularization (n = 154)	Ischemia-guided revascularization (n = 152)	*P*
Age, y	61.3 ± 10.4	62.0 ± 11.8	.607
Height, cm	168.1 ± 7.3	167.4 ± 8.0	.419
Weight, kg	79.8 ± 13.9	79.3 ± 13.4	.726
BMI	28.1 ± 3.9	28.2 ± 3.8	.900
Female	19 (12.3)	29 (19.1)	.105
Hypertension	74 (48.1)	61 (40.1%)	.163
Dyslipidemia	73 (47.4)	73 (48.0)	.913
Diabetes	21 (13.6)	23 (15.1)	.709
Active smoking	70 (45.5)	63 (41.4)	.733
Family history of ischemic heart disease	14 (9.1)	19 (12.5)	.336
Previous AMI	8 (5.2)	8 (5.3)	.979
Previous PCI	8 (5.2)	8 (5.3)	.979
Noncardiac atherosclerosis	9 (5.8)	8 (5.3)	.824
Index PCI	149 (98)	148 (98.7)	1
Rescue PCI	3 (2)	2 (1.3)	1
Radial access artery (emergency PCI)	147 (96)	139 (91%)	.156
SBP, mmHg	137.9 ± 31.5	135.4 ± 28.0	.477
DBP, mm Hg	83.0 ± 18.0	80.0 ± 16.4	.116
HR, bpm	72.1 ± 17.0	70.8 ± 16.2	.496
Killip class			.370
I	151 (98.1)	150 (98.7)	
II	3 (1.9)	1 (0.7)	
III	0	1 (0.7)	
IRA			.982
LADA	55 (36)	54 (36)	
Cx	24 (15)	24 (15)	
RCA	75 (49)	74 (49)	
Triple-vessel disesae	65 (42)	68 (45)	.655
LVEF, %	57.6 (10.3)	56.3 (7.8)	.232
Diseased vessels, No.	2.42 ± 0.50	2.45 ± 0.50	.657
Significant lesions, No.	3.54 ± 1.30	3.63 ± 1.42	.580

AMI, acute myocardial infarction; BMI, body mass index; Cx, circumflex artery; DBP, diastolic blood pressure; HR, heart rate; IRA, infarct-related artery; LADA, left anterior descending artery; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; RCA, right coronary artery; SBP, systolic blood pressure.
Values are expressed as No. (%) or mean ± standard deviation.

Table 4
Procedures performed during index admission and readmissions during first year of follow-up

	Complete revascularization (n = 154)	Ischemia-guided revascularization (n = 152)	*P*
Hospitalization			
Hospital stay, d	8.46 ± 10.32	7.28 ± 3.35	.182
Time to stress echocardiography, d	—	5.48 ± 4.50	—
Time from stress echocardiography to revascularization of lesions other than IRA, d	—	4.13 ± 2.59	—
Time to revascularisation of lesions other than IRA, d	5.85 ± 2.96	9.16 ± 3.51	< .001
Coronary angiography	152 (98.7)	45 (29.6)	< .001
PCI in nonculprit lesion	152 (98.7)	44 (28.9)	< .001
Echocardiography	147 (95.5)	26 (17.1)	< .001
Stress echocardiography	2 (1.3)	148 (97.4)	< .001
First year of follow-up			
Readmission	36 (23.4)	34 (22.4)	.471
Cardiac cause	21 (13.6)	22 (14.5)	.830
Noncardiac cause	17 (11.0)	16 (10.5)	.890
Hospital stay, d	2.14 ± 5.25	2.58 ± 7.93	.575
Coronary angiography	5 (3.2)	4 (2.6)	1.000
Complete revascularization (PCI)	16 (10.4)	18 (11.8)	.700
IRA	10 (6.5)	4 (2.6)	.120
Lesions other than IRA	9 (5.8)	15 (9.9)	.190
Stent restenosis	8 (4.7)	3 (2.0)	.130
Stent thrombosis	8 (4.7)	2 (1.3)	.080
Echocardiogram	80 (51.9)	75 (49.3)	.366
Stress echocardiogram	21 (13.6)	21 (13.8)	.548
SPECT	3 (1.9)	3 (2.0)	.652
Conventional exercise stress test	4 (2.6)	5 (3.3)	.749

IRA, infarct-related artery; PCI, percutaneous cutaneous intervention; SPECT, single photon emission computed tomography.
Values are expressed as No. (%) or mean ± standard deviation.

risk for any of the components of the composite endpoint (table 1 of the supplementary data).[10]

Cost comparison

Details of lengths of stay and procedures and tests performed during the index admission and readmissions are shown for the ComR and SelR groups in table 4. The estimated costs are provided in table 5.

Index admission

No significant differences were observed between the ComR and SelR groups for length of stay during the index admission (8.46 ± 10.32 vs 7.28 ± 3.35 days, *P* = .182). Time to revascularization of nonculprit lesions was shorter in the ComR group than in the SelR group (5.9 vs 9.1 days, *P* < .001). In the SelR group, mean time from randomization to stress echocardiography was 5.5 days, while mean time from stress echocardiography to PCI was 4.13 days.

As mentioned, 98.7% of patients allocated to the ComR group underwent elective PCI for nonculprit lesions, compared with just 28.9% in the SelR group (*P* < .001). By contrast, stress echocardiography was performed in 97.4% of patients in SelR group but in just 1.3% of those in the ComR group (*P* < .001).

Transthoracic echocardiography was performed in 95.5% of ComR patients but in just 17.1% of SelR patients (*P* < .001).

Although the cost of emergency PCI during the index admission was similar for both groups (€6856.3 for ComR vs €6833 for SelR, *P* = .319), the cost of elective PCIs was significantly higher in the ComR group (€6856.3 vs €1975.4, *P* < .001). The cost of stress echocardiography, by contrast, was higher in the SelR group (€377.7 vs €4.9, *P* < .001).

The total estimated cost for the index admission was €19 657.9 in the ComR group vs €14 038.7 in the SelR group (*P* < .001). In other words, the SelR strategy yielded an estimated mean savings of €5619.13 (95%CI, €4350.6-€6887.7) per patient.

First year of follow-up

Readmission rates in the 12 months following discharge were similar in the 2 groups (23.4% for ComR vs 22.4% for SelR, *P* = .471). The reasons for readmission included cardiac conditions (13.6% vs 14.5%, *P* = .830) and noncardiac conditions (11.0% vs 10.5%, *P* = .890). There were no significant differences between the groups in terms of readmission length of stay (2.14 vs 2.58 days, *P* = .575).

A comparable proportion of patients in both groups underwent noninvasive cardiological tests (eg, transthoracic echocardiography [51.9% vs 49.3%, *P* = .366] and stress echocardiography [13.6% vs 13.8%, *P* = .548]) and coronary revascularization (10.4% vs 11.8%, *P* = .700).

Costs attributable to readmission stays (€1088.8 vs €1329.3, *P* = .553), additional tests such as echocardiography, stress echocardiography, and coronary angiographies, and new PCIs were also similar in the 2 groups.

The total estimated cost of readmission in the first year of follow-up was €2423.5 for the ComR group and €2653.9 for the SelR group (*P* = .697). The overall cost of the ComR strategy was

Table 5
Costs (€) during index admission and readmissions during first year of follow-up

	Complete revascularization (n = 154)	Ischemia-guided revascularization (n = 152)	*P*
Hospitalization			
Hospital stay, d	5631.22 ± 6076.1	4807.52 ± 2690.5	.127
Emergency PCI	6856.31 ± 0	6833.08 ± 286.4	.319
Elective revascularization	6856.31 ± 1108.6	1975.38 ± 3188.9	< .001
Transthoracic echocardiography	309.11 ± 62.4	55.02 ± 121.5	< .001
Stress echocardiography	4.90 ± 42.9	377.73 ± 74.6	< .001
Total cost of index admission	19 657.85 ± 6236.8	14 038.72 ± 4958.5	< .001
First year of follow-up			
Readmission	10 88.81 ± 2778.1	1329.33 ± 4173.8	.553
New coronary angiography	41.11 ± 237.8	27.77 ± 169.5	.573
Coronary angoigraphy and PCI	756.86 ± 2155.6	766.82 ± 2168.1	.968
Transthoracic echocardiography	183.79 ± 200.9	165.05 ± 173.6	.384
Conventional exercise stress test	8.07 ± 49.6	10.22 ± 55.6	.721
Stress echocardiography	51.5 ± 130.03	57.15 ± 149.1	.724
SPECT	7.64 ± 57.8	5.81 ± 41.19	.749
Other tests following discharge	189.24 ± 771.1	216.52 ± 725.9	.774
Total cost of follow-up	2423.49 ± 4568.0	26 53.85 ± 5709.1	.697
Total final cost	22 081.3 ± 7505.6	16 692.57 ± 7669.9	< .001

PCI, percutaneous cutaneous intervention; SPECT, single photon emission computed tomography.
Values are expressed as No. (%) or mean ± standard deviation.

therefore significantly higher than that of the SelR strategy (€22 081.3 vs €16 692.6, $P < .001$).

Cost of disposable material

No significant differences were observed between the ComR and SelR groups for the cost of disposable material used in the index PCI (€1643 vs €1687) (table 6). The cost of elective PCI material, however, was significantly higher in the ComR group (€3166 vs €896, $P < .001$). The total cost of disposable material was therefore €4810.4 in the ComR group vs €2557.0 in the SelR group (difference of €2253 [95%CI, €1794.2-€2712.2] per patient).

DISCUSSION

In this economic evaluation of data from the CROSS-AMI trial from the perspective of the public health care service in our autonomous community, the mean cost of the ComR strategy during the index admission was significantly higher than that of the SelR strategy (€19 658 vs €14 039). In other words, the SelR strategy yielded an estimated mean savings of €5619 per patient, attributable to the performance of fewer PCIs during the index admission. No differences, by contrast, were detected for readmission costs in the 12-month follow-up period analyzed. When admission and readmission costs were combined, the ComR strategy cost an estimated €5388 more than the SelR strategy.

The differences in costs are largely due to differences in the proportion of patients treated with PCI for nonculprit lesions during the index admission (just 29% of patients in the SelR group compared with 99% of those in the ComR group). This observation is supported by our complementary analysis of the cost of disposable material for elective PCIs (nonculprit lesions), which was significantly higher in the ComR group than the SelR group (€3166 vs €869, $P < .001$). No differences were observed for disposable material used for emergency PCIs.

One of the main benefits claimed for complete revascularization in patients with STEMI and multivessel disease is that it reduces the likelihood of future clinical events, thus offsetting the initially higher costs of revascularization.[4] No significant differences, however, were observed between the ComR and SelR groups for the occurrence of clinical events during the 12-month follow-up period.[10] Readmission costs were thus similar for the 2 strategies, tipping the balance in favor of the less costly SelR strategy based on

Table 6
Cost (€) of disposable material

	Complete revascularization (n = 154)	Ischemia-guided revascularization (n = 152)	*P*
Cost of disposable material for index PCI	1643.76 ± 931.9	1687.59 ± 924.3	.680
Cost of disposable material for second PCI during index admission	3166.68 ± 1771.2	869.38 ± 1617.0	< .001
Total cost of disposable material	4810.44 ± 2026.1	2556.96 ± 2051.7	< .001

PCI, percutaneous coronary intervention.
Values are expressed as No. (%) or mean ± standard deviation.

ischemia detection testing and against the more costly ComR strategy involving PCIs. Our findings show that the higher initial costs of the ComR strategy were not offset by savings expected from a reduction in clinical events during follow-up.

Times to stress echocardiography and revascularization in the CROSS-AMI trial[10] can clearly be improved and may have influenced our results. The trial, however, was a pragmatic trial designed to reflect routine clinical practice, and therefore certain delays, influenced by multiple factors beyond the researchers' control, were to be expected. Mean time to revascularization was significantly shorter in the ComR group than in the SelR group (5.85 vs 9.1 days, $P < .001$), but lengths of hospital stay and associated costs were comparable. In addition, the possible impact of delays was minimized because the mean time from randomization to performance of stress echocardiography in the SelR group was 5.5 days (similar to the time to revascularization in the ComR group) and just 29% of patients required a second PCI.

Numerous studies have analyzed the treatment of multivessel disease in STEMI,[12,13] but just 1 of these—the Complete versus Culprit-Only Primary PCI trial (CvLPRIT)[14]—includes an economic evaluation.[15] It is very difficult, however, to compare the results of this evaluation with ours due to differences in revascularization strategies, outcomes, and cost analysis methods. It could, however, be speculated that the results of the economic evaluation of the CvLPRIT trial might have been influenced by the inclusion of ischemia testing in the conservative arm. In addition, the findings of that evaluation raise numerous doubts. The authors estimated a 72% likelihood of complete revascularization being cost-effective at a willingness-to-pay threshold of £20 000 per quality-adjusted life year (QALY), raising questions about the effectiveness of this procedure in almost one-third of patients. In addition, QALYs were assessed using an indirect survey (EuroQoL 5-dimensional survey) administered to just 70% of patients. An additional drawback is the high percentage of missing values requiring multiple imputation, which carries a risk of bias and lack of precision.[16] The authors detected no significant differences in the cost of the 2 treatment strategies during the index admission (£4890 in the complete revascularization group vs £4668 pounds in the IRA-only treatment group, $P = .654$). Based on our findings, higher costs would be expected in the former.

The CROSS-AMI trial, unlike the Compare-Acute[17] and DANAMI-3-PRIMULTI[18] trials, did not use invasive pressure-wire assessment of nonculprit lesions. We cannot compare costs between the trials, however, as no economic evaluations have been conducted for these 2 trials. This is unfortunate, as pressure wire measurement has been shown to be cost-effective in the setting of stable coronary disease.[19,20] Invasive fractional flow reserve is a more costly technique than noninvasive stress echocardiography, and in addition, the cost of revascularization where necessary must also be considered. In the Compare-Acute trial, 55% of nonculprit lesions were treated, compared with just 28% of those in the CROSS-AMI SelR arm.

While complete revascularization has been shown to be superior to the treatment of culprit lesions only, [12] when it comes to "serious" events (death and myocardial infarction[6]), its true impact may have been overestimated due to the overly conservative treatment of nonculprit lesions.[7] One recent proposal calls for an individualized approach to the treatment of multivessel disease in patients with STEMI, with decisions guided by clinical profile (age, frailty, comorbidities) and the severity, complexity, and relevance of nonculprit lesions. Economic considerations are also important.[21] Our results show that SelR, based on elective revascularization only, is a more cost-effective strategy than ComR. It was associated with lower PCI costs during the index admission and similar costs during follow-up as the patients in both groups experienced a similar number of clinical events.

The optimal timing for the assessment and revascularization of nonculprit lesions in patients with STEMI and multivessel disease remains a matter of debate.[7] In the CROSS-AMI trial, stress echocardiography and PCIs were performed during the index admission. Nonetheless, noninvasive assessment and revascularization within 4 to 6 weeks of discharge is a valid alternative for most patients with uncomplicated myocardial infarction, particularly considering that infarction causes physiological changes in coronary circulation.[22] In the COMPLETE trial, the benefit of complete revascularization was independent of the timing of nonculprit lesion PCI.[23]

Limitations

One of the main limitations of this study is the inclusion of just 306 patients (77% of the planned study population) due to the premature interruption of the CROSS-AMI.[10] Nonetheless, based on the sensitivity analyses performed and the assumption of a similar rate of events, even if they all occurred in the same group, the likelihood of observing significant differences for the main endpoint with a full sample is remote.[10]

Selection bias due to exclusion criteria or analysis of baseline characteristics (eg, high frequency of Killip class I) cannot be ruled out. In all, 31% of candidates assessed for inclusion in the trial were finally recruited. While this may have affected the external validity of the trial, this inclusion rate of 31% is similar to rates reported for major clinical trials.[13]

Stress echocardiography provides more prognostic information than a conventional exercise stress test,[24] but its interpretation may be more difficult and depends on the operator. That said, the hospitals that participated in the CROSS-AMI trial have extensive experience with stress echocardiography.[25]

Our findings might have varied with a longer follow-up period. This is unlikely, however, as no significant differences were observed between the 2 groups after 3 years in an extended follow-up evaluation. Nonetheless, it cannot be completely ruled out that differences would not have been detected after a follow-up period of more than 5 years.

Our use of current health care service rates limits the applicability of our findings to health care systems with comparable cost estimates. It should be noted that autonomous communities in Spain use different rate systems, making comparisons difficult. Another consideration is that potential cost variations in the future would alter our results.

The costs calculated for the follow-up period included cardiology procedures and treatments administered during readmissions, but not primary care visits, emergency room care, or other outpatient tests. Nonetheless, these costs would be unlikely to have a significant bearing as in the CvLPRIT15 trial, medical visits accounted for less than 10% of total costs.[15]

CONCLUSIONS

In this economic evaluation nested within the CROSS-AMI clinical trial and conducted from the perspective of our health care system, the ComR strategy was significantly more expensive than the SelR strategy during the index admission. No significant differences were observed between the 2 groups for costs attributable to diagnostic and therapeutic procedures performed during hospital readmissions in the first year of follow-up.

The higher costs of the ComR strategy during the index admission were not thus offset by lower costs during the 12-month follow-up, probably due to the similar incidence of clinical events in the 2 groups.

In brief, in patients with STEMI and multivessel disease who undergo emergency PCI for an IRA, SelR would appear to be a more cost-effective strategy than ComR (treatment of all nonculprit lesions) for a follow-up period of 12 months, as it yielded similar clinical outcomes at a lower cost during this period.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest in relation to this publication.

WHAT IS KNOWN ABOUT THE TOPIC?

- Multivessel disease is common in STEMI, has a worse prognosis, and is difficult to treat.
- Current recommendations call for consideration of complete revascularization of nonculprit lesions based on the findings of studies comparing this option with a conservative strategy involving the revascularization of nonculprit lesions.
- The CROSS-AMI trial, however, is the only clinical trial to date to compare 2 revascularization strategies.
- Economic evaluation studies are useful in complex situations such as this, particularly when resources are limited.

WHAT DOES THIS STUDY ADD?

- The higher cost of complete revascularization compared with selective stress echocardiography–guided revascularization during the index admission was not offset by significant savings in a 12-month follow-up because the 2 groups experienced a similar number of clinical events.
- Selective stress echocardiography-guided revascularization in patients with STEMI and multivessel disease treated with emergency PCI of an IRA appears to be more cost-effective than complete revascularization during a 1-year follow-up period, as it achieved similar clinical outcomes at a lower cost.

APPENDIX. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.1016/j.rec.2020.09.028

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