Scientific letters

Addition of Antiangina Drugs and Recurrent Cardiovascular Events Associated With Incomplete Revascularization in Acute Coronary Syndrome

Adición de antianginosos y complicaciones cardiovasculares recurrentes asociadas a la revascularización incompleta en el síndrome coronario agudo

To the Editor,

Coronary revascularization is a crucial part of the treatment of acute coronary syndrome (ACS) due to its survival benefit.[1] However, numerous studies have shown that between 30% and 60% of patients receive incomplete coronary revascularization (ICR), which is associated with worse cardiovascular prognosis.[2] While some of the drugs available for treating angina have failed to show any change in cardiovascular prognosis, they have been shown to reduce the degree of angina and improve the patient's quality of life, making them widely used in clinical practice.[3]

Here we present a retrospective study conducted in all consecutive patients admitted with ACS over a 24-month period. ICR was defined as lesions > 70% remaining untreated in the main vessels or in the secondary branches with diameter > 1.5 mm^2. The endpoints analyzed during the follow-up period were the addition of any antianginal drug and the cumulative incidence of cardiovascular complications (readmissions due to any cardiovascular cause and/or death due to cardiovascular cause). The antianginal drugs evaluated during the follow-up period were beta-blockers, dihydropyridine calcium-channel blockers, nitrates, ivabradine, and ranolazine. A multivariate analysis of the addition of antianginal drugs was carried out using a Cox regression model with hazard ratios; recurrent events were analyzed using negative binary logistic regression, with the IRR (incidence rate ratio), which has been postulated as a more precise way of analyzing the actual prognosis of cardiovascular disease.[4]

As shown in Table, 28.7% of the patients received ICR, and these patients had a higher mean age, prevalence of risk factors and comorbidities, as well as a higher score on the GRACE (Global Registry of Acute Coronary Events) scale. Patients with ICR

Table
General Characteristics of the Original Cohort According to the Degree of Revascularization

	Total	ICR	CCR	*P*
Patients	557 (100.0)	160 (28.7)	397 (71.3)	
Age, y	67.5 ± 13.0	72.5 ± 12.3	65.5 ± 12.8	< .01
Age > 75 y, %	31.9	47.8	25.6	.01
Men, %	73.8	77.4	72.7	.25
Diabetes mellitus, %	30.0	37.1	26.6	.01
Hypertension, %	65.4	74.8	61.3	< .01
Active smoker, %	34.1	23.3	38.7	.01
Dyslipidemia, %	49.6	56.6	46.6	.03
Previous HF, %	2.7	6.9	0.8	< .01
Previous IHD, %	22.6	38.4	16.2	< .01
Previous PTCA, %	11.7	16.4	9.9	.03
Previous CABG, %	3.8	8.2	1.8	.01
PAD, %	5.0	11.3	2.5	< .01
AF, %	7.7	10.1	6.6	.16
Previous stroke, %	7.7	10.7	6.6	.10
COPD, %	7.5	8.8	7.1	.49
STE-ACS, %	37.5	23.9	43.3	< .01
GFR, 60 mL/min/1.72 m^2	78.4 ± 25.3	72.5 ± 24.5	80.7 ± 25.2	.01
GFR < 60 mL/min/1.72 m^2, %	22.8	29.2	20.2	.02
GRACE score	139.6 ± 41.0	149.4 ± 47.8	135.6 ± 37.3	< .01
GRACE score > 140, %	46.9	48.8	46.1	.32
No. of diseased vessels	1.7 ± 0.9	2.4 ± 0.8	1.4 ± 0.8	< .01
No. of treated vessels	1.1 ± 0.6	0.9 ± 0.7	1.2 ± 0.6	< .01
Drug-eluting stents, %	57.4	38.4	65.1	< .01
Bioabsorbable stents, %	1.6	0.6	2.0	.24
Total No. of stents	1.3 ± 1.1	1.0 ± 1.2	1.4 ± 1.0	< .01
No. of stents, %	19.7	41.3	11.1	< .01
Charlson comorbidity index	2.1 ± 2.0	2.6 ± 2.4	1.9 ± 1.8	< .01
Charlson comorbidity index ≥ 4, %	16.0	23.9	12.9	.01
LVEF, %	54.0 ± 12.2	50.8 ± 13.8	55.1 ± 11.3	< .01

Table *(Continued)*
General Characteristics of the Original Cohort According to the Degree of Revascularization

	Total	ICR	CCR	*P*
Treatments at discharge, %				
Antiplatelet agents	98.3	98.0	98.5	.68
Dual antiplatelet therapy	82.8	72.8	88.3	< .01
Oral anticoagulants	6.3	8.8	5.3	.14
Beta-blockers	87.1	82.8	89.1	.02
Statins	94.1	91.9	94.9	.18
ACE/ARB inhibitors	80.4	83.8	79.2	.23
Calcium-channel blockers	14.9	23.6	11.7	.01
Nitrates	7.6	18.2	3.6	< .01
Ranolazine	1.3	3.4	0.5	.01
Ivabradine	1.7	4.7	0.5	.01

ACE, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; CABG, coronary artery bypass graft; CCR, complete coronary revascularization; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; ICR, incomplete coronary revascularization; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; PAD, peripheral artery disease; PTCA, percutaneous transluminal coronary angioplasty; STE-ACS, ST-segment elevation acute coronary syndrome.
Unless otherwise indicated, data are expressed as no. (%) or mean ± standard deviation.

received a lower number of stents, and the use of drug-eluting stents was less common. The most common reasons for receiving ICR were advanced age (28.8%), the presence of chronic occlusions (25.0%), renal failure (20.6%), and diffuse lesions (13.1%). Antianginal drugs (except beta-blockers) were more commonly recommended at discharge in patients with ICR, although they received less dual antiplatelet therapy. During the follow-up period (median, 19 months), mortality due to any cause was 10.6%, and mortality due to cardiovascular cause was 8.9%. An antianginal drug was added in 12.9% of the patients and, as shown in Figure, this was much more common in the patients with ICR (24.5% vs 7.1%; $P < .01$); mortality and recurrence of cardiovascular

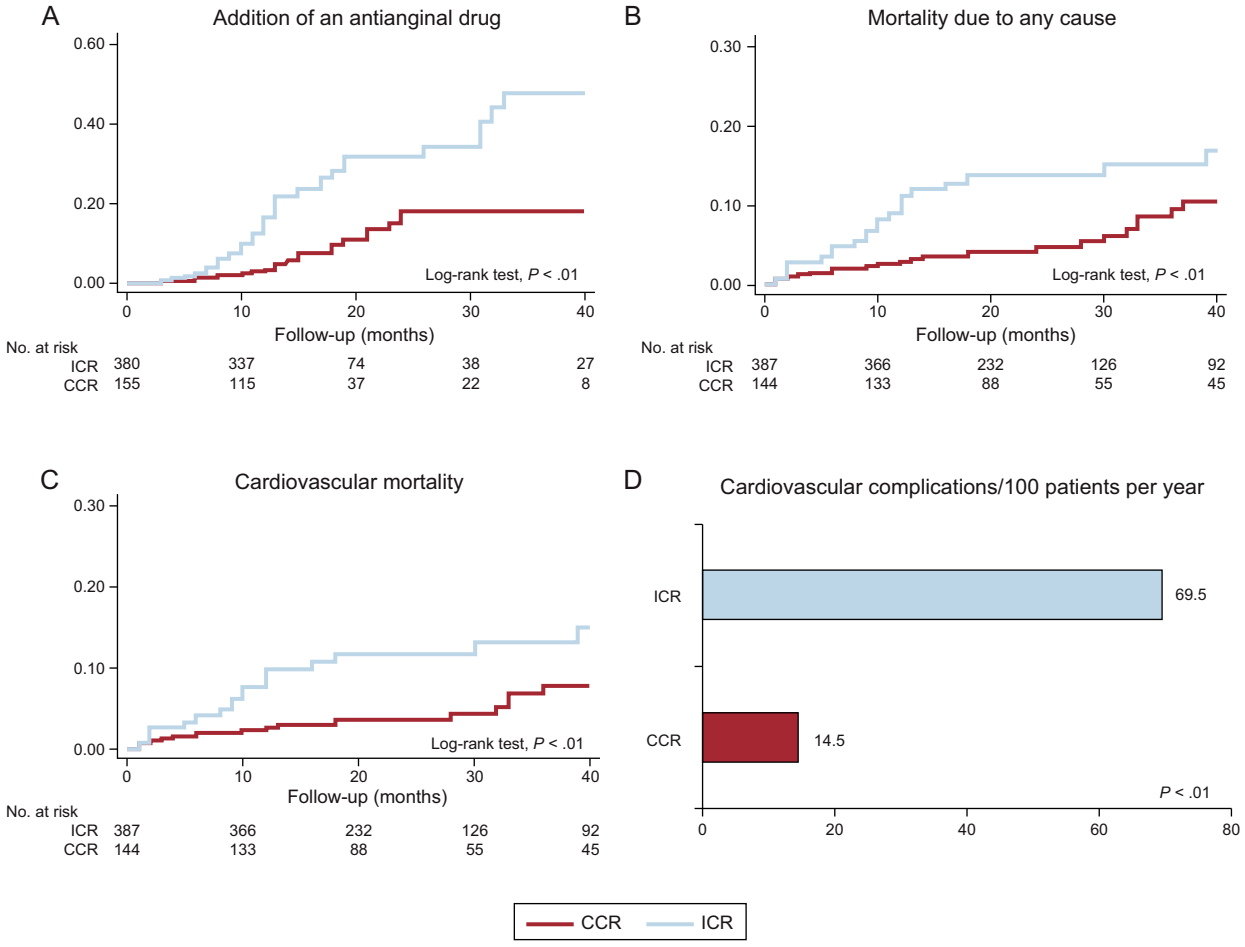

Figure. Kaplan-Meier curves showing addition of antianginal drugs (A); mortality due to any cause (B); mortality due to cardiovascular cause (C); and adjusted recurrence rates (D) during follow-up. CCR, complete coronary revascularization; ICR, incomplete coronary revascularization.

complications were also higher (Figure). The multivariate analysis (adjusted for age, sex, ACS type, risk factors, previous cardiovascular disease, GRACE score, and treatment at discharge) showed an independent association between the ICR and the addition of antianginal drugs (odds ratio, 2.62; 95% confidence interval, 1.34-5.14; $P < .001$) as well as with recurrent cardiovascular complications (IRR, 1.49; 95% confidence interval, 1.10-2.01; $P = .01$).

The analysis of this cohort of patients with ACS reflects aspects of ICR that have not been widely studied to date. Coronary revascularization has become one of the pillars of ACS treatment, but ICR is a reality that generates a high-risk patient group in which medical treatment is highly relevant.[5] The patients with ICR in this series received a lower number of stents and fewer drug-eluting stents, indicating that the percutaneous revascularization was less aggressive, both quantitatively and qualitatively. Some antianginal drugs are widely used in clinical practice due to the improvement observed in quality of life,[3] despite the lack of evidence to support an improvement in prognosis. The patients with ICR in this series received more antianginal drugs at discharge, and others were added during the follow-up period. This is partly related to the treatment by the professionals involved in this phase, and may also be related to demand among patients who generally have more frequent angina, which impairs their quality of life to varying degrees.[3]

In conclusion, a significant percentage of patients with ACS undergo ICR, which is associated with an increased addition of antianginal drugs and the adjusted recurrence of cardiovascular complications during the follow-up period. The 2 priority objectives to be taken into account in the treatment of patients with ACS are maximum optimization of the degree of revascularization, and pharmacological treatment.

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REFERENCES

1. Cordero A, López-Palop R, Carrillo P, et al. Cambios en el tratamiento y el pronóstico del síndrome coronario agudo con la implantación del código infarto en un hospital con unidad de hemodinámica. *Rev Esp Cardiol.* 2016;69:754–759.
2. Garcia S, Sandoval Y, Roukoz H, et al. Outcomes after complete versus incomplete revascularization of patients with multivessel coronary artery disease: A meta-analysis of 89,883 patients enrolled in randomized clinical trials and observational studies. *J Am Coll Cardiol.* 2013;62:1421–1431.
3. Borras X, Garcia-Moll X, Gomez-Doblas JJ, Zapata A, Artigas R. Estudio de la angina estable en España y su impacto en la calidad de vida del paciente. Registro AVANCE. *Rev Esp Cardiol.* 2012;65:734–741.
4. Rogers JK, Pocock SJ, McMurray JJ, et al. Analysing recurrent hospitalizations in heart failure: A review of statistical methodology, with application to charm-preserved. *Eur J Heart Fail.* 2014;16:33–40.
5. Iqbal J, Zhang YJ, Holmes DR, et al. Optimal medical therapy improves clinical outcomes in patients undergoing revascularization with percutaneous coronary intervention or coronary artery bypass grafting: Insights from the synergy between percutaneous coronary intervention with taxus and cardiac surgery (syntax) trial at the 5-year follow-up. *Circulation.* 2015;131:1269–1277.

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Mapping the Conceptual Structure of Cardiovascular Research: An Analysis Based on *Revista Española de Cardiología*

Mapas de la estructura conceptual del campo de investigación cardiovascular: un análisis basado en Revista Española de Cardiología

To the Editor,

Database unit processing is used in bibliometric studies to visualize scientific activity in a given knowledge domain via scientific or bibliometric maps. These maps are constructed from the analysis of co-occurrence relations, ie, relationships between 2 co-occurring units of analysis.[1] Bibliometric indicators of relatedness have been used to build bibliometric networks based on cocitation analysis (to measure intellectual structure) coauthorship analysis (to measure social structure), and coword analysis (to measure knowledge or conceptual structure). The conceptual structure of the field of cardiovascular research has been previously analyzed using predictors of knowledge domains.[2]

To visualize the conceptual structure and development over time of cardiovascular research in Spain, we analyzed articles published in *Revista Española de Cardiología* between 1997 and 2006 and 2007 and 2016. The articles were extracted from Science Citation Index Expanded, a scientific and medical index that is available through the Web of Science platform.[3] In total, 2197 documents were retrieved. From these, we selected 202 keywords with a frequency of occurrence of 7 or more: 111 from the period 1997 to 2006 and 94 from the period 2007 to 2016. The method employed consisted of the following stages[4]: selection of keywords used by the authors of the articles, calculation of keyword co-occurrence frequency, clustering analysis, and visualization of results in density or heat maps. The maps were constructed using the VOSviewer software tool.[5] In bibliometric density maps, areas with the highest density of co-occurrence relations between keywords are shown by a color close to red, while those with a lower density are shown by a color closer to yellow or green.

The conceptual structure of cardiovascular research between 1997 and 2006 is reflected in the bibliometric map shown in Figure 1. The keywords with the highest impact were related to 3 knowledge domains: cardiomyopathies/ischemic heart disease, heart disease/heart failure and echocardiography, and interventional cardiology. The domains related to the keywords with the lowest impact were electrophysiology/arrhythmias and epidemiology/risk factors and preventive cardiology. There were 2 very dense areas in the center of the map: *a*) an area related to the knowledge domain of cardiomyopathies (labeled with the keywords *myocardial infarction*, *prognosis*, and *unstable angina*), which was closely connected to the domain of interventional cardiology (labeled with *coronary angioplasty*, *stent*, and *restenosis*) and *b*) an area related to the domains of heart disease/heart failure and echocardiography (labeled with the keywords *heart failure*, *echocardiography*, and *surgery*).

The bibliometric map corresponding to the second period, 2007 to 2016, is shown in Figure 2. The knowledge domains with the highest keyword impact were heart disease/heart failure and echocardiography, cardiomyopathies/ischemic heart disease, and epidemiology/risk factors and preventive cardiology. The domains