

## Diffuse Coronary Artery Disease Not Amenable to Revascularization: Long-term Prognosis



### Enfermedad difusa no revascularizable de los tres vasos coronarios: pronóstico a largo plazo

#### To the Editor,

Although percutaneous and surgical revascularizations have been shown to be beneficial in coronary artery disease, these procedures are not always feasible because of diffusely diseased vessels. There is little information on patients not eligible for revascularization because the inclusion criteria are usually expressed in subjective terms such as “refractory angina”, “severe diffuse disease”, or “anatomy not amenable to revascularization”, which results in wide heterogeneity. Even Medicare has no classification code for these patients, and the United States Task Force addressing this situation stresses the urgent need for studies.<sup>1</sup>

We analyzed the outcome of a cohort of patients with highly diffuse coronary artery disease who, on the basis of anatomic criteria, were not eligible for any type of revascularization. In December 2004, we selected all the patients who had been diagnosed as having 3-vessel disease since January 1999 in a hemodynamic referral center for 9 other hospitals. The coronary angiograms were reviewed by an interventional cardiologist and a cardiac surgeon, and those patients who were not considered candidates for any type of complete or incomplete revascularization constituted the study cohort. Those patients with valve disease that might have caused the symptoms were excluded. The clinical and angiographic data were collected from the database of the cardiac catheterization laboratory and the follow-up consisted of annual telephone calls made from December 2005 to December 2013. Information on patients who had died was obtained from their families or medical records.

Between January 1999 and December 2004, coronary angiography was performed in 16 215 patients with suspected coronary artery disease; 3672 (22.6%) had 3-vessel disease. Of these, 220 were considered to be ineligible for complete or incomplete revascularization on the basis of anatomic criteria (5.9% of the patients with 3-vessel disease and 1.3% of the overall sample). The Table shows the clinical characteristics of these 220 patients and their medication.

Follow-up information was obtained for 217 patients (98.6%); after 45.1 [interquartile range, 8.3–67.9] months, the overall mortality rate was very high (61.1% at 5 years). The Figure shows the survival curve according to age group. On Cox analysis, the predictors of 5-year mortality were age, previous myocardial infarction,  $\geq 50\%$  left main coronary artery disease, ejection fraction, mitral regurgitation  $\geq 2$ , and hemoglobin concentration. The variables sex, creatinine clearance, diabetes mellitus, previous stroke, atrial fibrillation, and left bundle branch block were excluded from the final model. The area under the receiver operating characteristic (ROC) curve was 0.77 (0.70–0.84;  $P < .001$ ).

This report analyzed the outcome of a cohort of patients with different clinical manifestations of ischemic heart disease in whom the common denominator was an anatomy not amenable to revascularization. Mortality was notably higher than that in the general population, according to age groups provided by the Spanish National Institute of Statistics. For example, at the age of 70 years, the mean survival in the general population is 16.49 years and at age 80 years, 9.3%, clearly longer than the  $4.47 \pm 0.45$  years recorded in the 70- to 80-year-old patients in our series.<sup>2</sup>

The disparity in survival among the published series may be due to the differences in patient characteristics. In the series of Henry

et al,<sup>3</sup> in which the inclusion criterion was refractory angina or myocardial ischemia not amenable to revascularization, mortality was 3.9% at 1 year, 17.5% at 5 years, and 28.4% at 9 years, whereas in series in which the point of departure was the coronary anatomy, encompassing different clinical signs of ischemic heart disease, the mortality rate was much higher. In a series of 2776 patients with multivessel disease and an anatomy that made them ineligible for revascularization, the 5-year mortality was 37%.<sup>4</sup> In another study involving patients with 3-vessel or left main coronary artery disease and ventricular function  $< 50\%$ , 41% of the patients did not undergo revascularization and, 2.2 years later, 38% had died.<sup>5</sup> Different inclusion criteria result in highly marked differences among the patients in the series. In that of Henry et al,<sup>3</sup> in which the mean age was 63.5 years, 36.6% of the patients had diabetes, and 14.8% had chronic kidney disease, the cohort had a lower risk profile than the patients in our study, only 34.1% of whom had refractory angina.

#### Table

Clinical Characteristics of the Patients and Medication Received (n=220)

Age, years	70.1 $\pm$ 8.6
Women	72 (32.7)
Diabetes mellitus	128 (58.2)
Hypertension	135 (61.4)
Hypercholesterolemia	132 (60)
Smoking	101 (45.9)
Previous myocardial infarction	118 (53.6)
$\geq 50\%$ left main coronary artery disease	67 (30.5)
Previous PCI	1 (0.5)
Ejection fraction $\leq 30\%$	41 (18.7)
Mitral regurgitation $\geq 2$	22 (10)
Indication for coronary angiography	
Stable angina	75 (34.1)
Unstable angina	46 (20.9)
Non-ST-segment elevation acute coronary syndrome	53 (24.1)
ST-segment elevation acute coronary syndrome	9 (4.1)
Sudden death	5 (2.3)
Heart failure	32 (14.5)
Previous stroke	45 (20.5)
Chronic kidney disease	
Stage 3	88 (40.9)
Stage 4	23 (10.5)
Stage 5	1 (0.5)
Hemoglobin $< 12$ g/dL	72 (32.9)
Medication	
Beta-blockers	100 (45.5)
Digoxin	44 (20)
Aspirin	155 (70.5)
Clopidogrel	78 (35.5)
Oral anticoagulation	35 (15.9)
Statins	122 (55.5)
ACE inhibitors/ARB	143 (65)
Nitrates	184 (83.7)
Calcium channel blockers	83 (37.8)
Spironolactone	28 (12.7)
Diuretics	117 (53.2)
Amiodarone	20 (9.1)
Ivabradine	8 (3.7)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; PCI, percutaneous coronary intervention.

Data are expressed as no. (%) or mean  $\pm$  standard deviation.

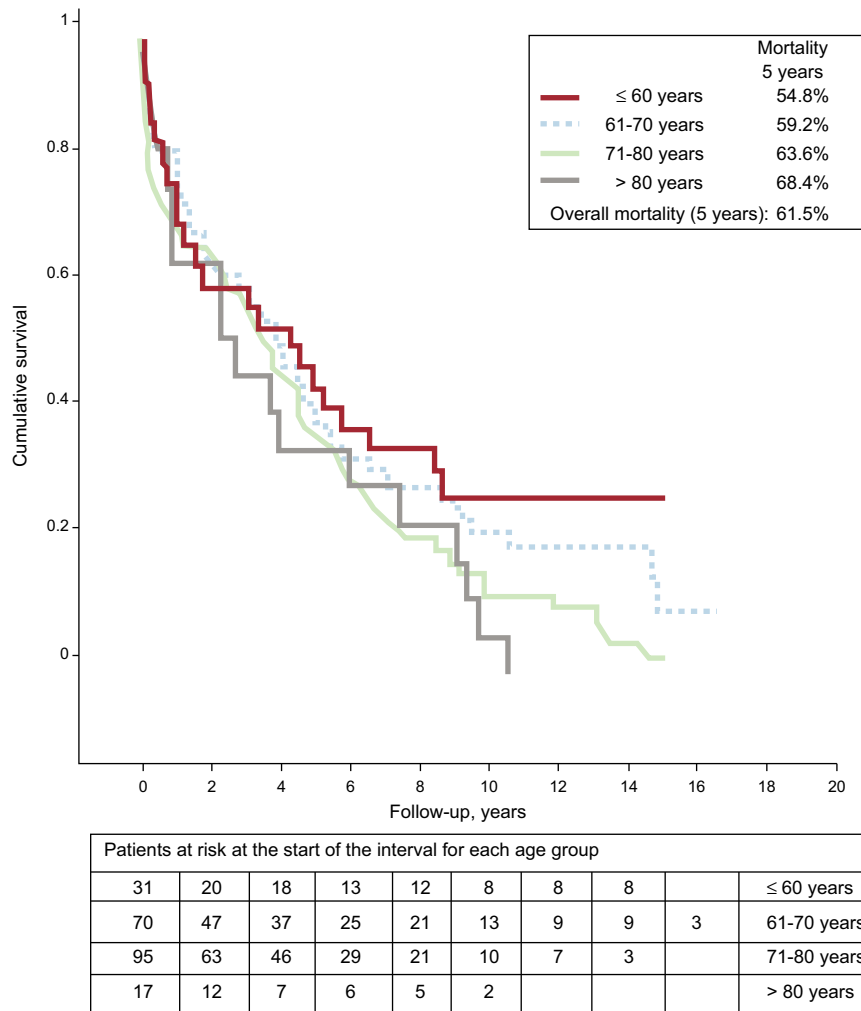


Figure. Survival analysis.

The predictive variables identified in our report have been described in previous series. Diabetes mellitus and chronic kidney disease showed no statistically significant association, although an association would probably have been observed with a larger sample size. The lack of significance of these 2 variables could also be due to the inclusion criteria: in other series, both entities may have affected the prognosis because of their role in the progressive deterioration of the coronary anatomy. All the patients in our series, whether or not they have diabetes mellitus or chronic kidney disease, had a markedly deteriorated anatomy from the start.

As limitations, we cannot rule out possible subjectivity in the evaluation of the coronary angiographies. Secondly, analysis of medication is complex because of changes made during follow-up and modifications in the guidelines. However, despite the under-use of certain drugs, this series reflects daily practice during the study period, as the patients were referred from 9 different hospitals. Finally, we cannot exclude the possibility that the variables considered included features that were associated with prognosis in previous series.

In conclusion, patients with severe diffuse coronary artery disease and an anatomy that is not amenable to revascularization

represent a subgroup of patients with a very high mortality rate who all too seldom receive optimal medical treatment.

Iñigo Lozano,<sup>a,\*</sup> Esmeralda Capin,<sup>b</sup> Jesús M. de la Hera,<sup>b</sup> Juan C. Llosa,<sup>b</sup> Amelia Carro,<sup>b</sup> and Ramón López-Palop<sup>c</sup>

<sup>a</sup>Servicio de Cardiología, Hospital de Cabueñes, Gijón, Asturias, Spain

<sup>b</sup>Servicio de Cardiología, Hospital Central de Asturias, Oviedo, Asturias, Spain

<sup>c</sup>Servicio de Cardiología, Hospital de San Juan, San Juan de Alicante, Alicante, Spain

\* Corresponding author:

E-mail address: [inigo.lozano@gmail.com](mailto:inigo.lozano@gmail.com) (I. Lozano).

Available online 27 April 2015

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<http://dx.doi.org/10.1016/j.rec.2015.02.013>

**Organization of Heart Failure Care in Spain: Characteristics of Heart Failure Units**



**Organización de la atención a la insuficiencia cardiaca en España: unidades existentes y características**

**To the Editor,**

Heart failure (HF) is a major health problem, and the burden it places on health care systems and society in general has increased in recent years and is expected to continue to grow.<sup>1</sup> Due to the wide diversity of patients with very different prognoses and therapeutic options, current guidelines recommend a multidisciplinary approach and the establishment of organizational structures to guarantee its implementation (recommendation class I A).<sup>2</sup>

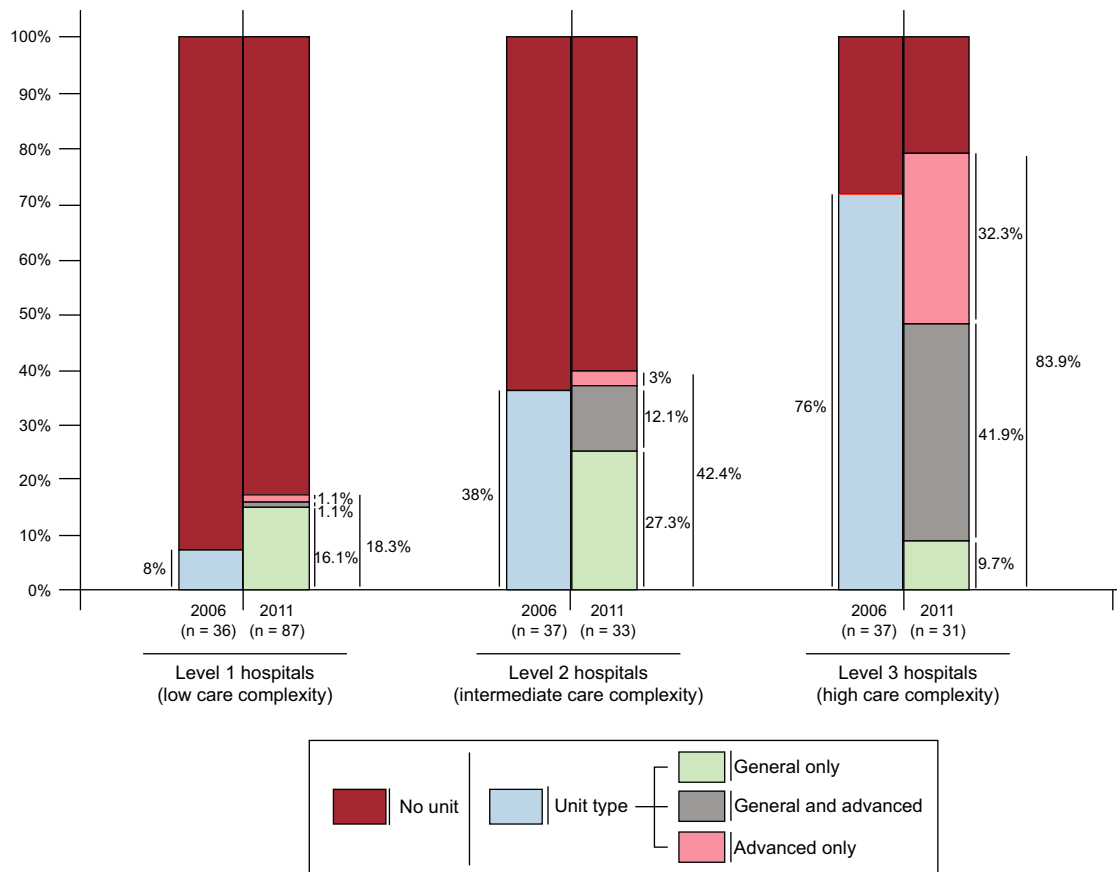
Here we present the results of the MOSAIC (*Mapa de la Organización de la Insuficiencia Cardiaca en España* [Map of Heart Failure Organization in Spain]) project, which updates and expands the information available about resources and organizational structures in Spain for the care of patients with HF<sup>3</sup> and complements the data from other recent studies conducted by the Spanish Society of Cardiology.<sup>4</sup>

We contacted 219 of the 246 hospitals listed (89%) in the general catalog of the Spanish Ministry of Health, Social Services, and Equality (*Ministerio de Sanidad, Servicios Sociales e Igualdad* [MSSSI])<sup>5</sup>; 60 hospitals declined to participate, and 8 were excluded due to insufficient data. We thus present information from 151 hospitals, obtained by an online and telephone survey in the last quarter of 2011.

The hospitals were classified into 3 groups according to the complexity of health care provision: level 1 (no hemodynamic monitoring, electrophysiology, or cardiac surgery), level 2 (hemodynamic monitoring and/or electrophysiology, but no surgery), and level 3 (hemodynamic monitoring, electrophysiology, and surgery).

The study examined 2 types of HF unit. A general unit is a designated hospital service with an assigned manager and a specific protocol for the care of HF patients. An advanced unit has resources for the treatment of critically ill patients, including the management of advanced HF, pretransplant evaluation, hemodynamic monitoring, and ability to recommend implantation of an automated implantable cardioverter defibrillator or cardiac resynchronization device.

The survey included hospitals from all 17 Spanish autonomous regions and Melilla, with a total assigned catchment population of 34.2 million people. Of these centers, 87 (57.6%) are level 1



**Figure.** Heart failure units by type and hospital complexity.