

## Special article

## Update on Ischemic Heart Disease and Intensive Cardiac Care

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## ABSTRACT

This article summarizes the main developments reported in 2014 on ischemic heart disease, together with the most important innovations in intensive cardiac care.

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## Actualización en cardiopatía isquémica y cuidados críticos cardiológicos

## RESUMEN

Se revisan los principales avances publicados en el año 2014 sobre cardiopatía isquémica, junto con las novedades más relevantes acerca de cuidados críticos cardiológicos.

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## Abbreviations

CAD: coronary artery disease

PCI: percutaneous coronary intervention

FFR: fractional flow reserve

ACS: acute coronary syndrome

NSTEMACS: non–ST-segment elevation acute coronary syndrome

## EPIDEMIOLOGY AND PATHOGENESIS

## Epidemiology

According to data from the RECALCAR registry,<sup>1</sup> 31.2% of the total number of deaths in 2010 in Spain were due to cardiovascular diseases. Nevertheless, Spain has one of the lowest mortality rates

for coronary artery disease (CAD) in Europe for both sexes. Recent data indicate that Spanish mortality rates for cardiovascular diseases have dropped 36% in men and 40% in women since the mid-1970s.

This year, results from the DIOCLES<sup>2</sup> study have been published for the management and prognosis of acute coronary syndrome (ACS) in Spain. This is part of an ongoing project by the Coronary Artery Disease and Acute Cardiac Care Group to promote periodical ACS registries. These registries provide valuable information about the prognosis and management of ACS over time in our country.<sup>3–5</sup> The DIOCLES study included 2557 patients who were hospitalized between January and June, 2012, with suspected ACS in 44 randomly-selected Spanish hospitals. Hospital mortality was 4.1%, which is significantly lower than the rate reported in the latest MASCARA<sup>6</sup> registry (5.7%), as seen in the Table.<sup>7–28</sup> Among the 1602 patients with non–ST-segment elevation ACS (NSTEMACS) included in the registry (62.7% of the total), the use of p2y12 inhibitors increased (from 42%–91%), the use of glycoprotein IIb/IIIa inhibitors decreased (from 21% to 4%, respectively), and the use of angiography during hospitalization increased (from 63% to 81%) as did percutaneous coronary intervention (PCI) rates (from 34% to 53%). These data confirm the gradual incorporation of clinical practice guideline recommendations in Spain; at the same time, ACS-related in-hospital mortality had significantly decreased.

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**Table**  
Relevant Molecular Biomarkers in Studies Published in Recent Months

Molecule	Use/association	Reference
Proinflammatory cytokine/nuclear protein HMGB1	Levels proportional to coronary atherosclerosis	Haghjooy-Javanmard, et al <sup>7</sup>
Serum choline plasmalogens (phospholipids)	Markers of coronary atherosclerosis	Nishimukai et al <sup>8</sup>
GDF 15	Association with ischemic heart disease severity; better than ischemia-modified albumin and PAPP-A	Fan et al <sup>9</sup>
HBA <sub>1c</sub> in nondiabetic patients	Independent predictor of coronary artery disease and its severity	Garg et al <sup>10</sup>
Serum tryptase	Prognostic relationship between tryptase levels and the SYNTAX score in acute coronary syndrome	Pastorello et al <sup>11</sup>
Adiponectin and derivatives	Development of coronary disease	Wang et al <sup>12</sup> Kawagoe et al <sup>13</sup>
Circulating adipokines	Ischemia confirmed with SPECT	Hung et al <sup>14</sup>
Apelin	Plasma levels correlated inversely with severity and directly with plaque stability in patients with acute coronary syndrome	Zhou et al <sup>15</sup>
Serum adiponin	Low levels related with infarction in coronary patients	Yu et al <sup>16</sup>
FGF23	Cardiovascular prognosis and influence in response to treatment with ACE inhibitors	Udell et al <sup>17</sup>
Circulating osteoglycin and NGAL/MMP9	Predictors of 1-year events after angiography; expressed in vulnerable plaques	Cheng et al <sup>18</sup>
S100A9 (platelet protein)	Elevated in patients with infarction; involved in the pathway of thrombosis	Wang et al <sup>19</sup>
Serum TGF-β1 and SMAD3	Associated with coronary disease; useful for risk stratification and diagnosis	Chen et al <sup>20</sup>
sST2 soluble	Predictor of long-term mortality in stable coronary disease, complementary to NT-proBNP and TnT	Dieplinger et al <sup>21</sup>
Levels of HDL-C	Prognostic after acute coronary syndrome (Spanish cohort) and in stable patients (COURAGE substudy)	Fácila et al <sup>22</sup>
PSA and fPSA	Related with extension and prognosis in acute coronary syndrome	Acharjee et al <sup>23</sup> Durmaz et al <sup>24</sup>
BNP/NT-proBNP	Detection of ischemia after exercise; prognostic over the long term in stable coronary heart disease (meta-analysis)	Lee et al <sup>25</sup>
Monocyte chemoattractant protein-1, galectin-3	Associated with cardiovascular events	Wei et al <sup>26</sup> Tuñón et al <sup>27</sup>
Copeptin (carboxyl-terminus of the vasopressin prohormone secreted stoichiometrically with arginine-vasopressin from the neurohypophysis)	As a dual marker strategy, combining myocardial damage (cTn) and endogenous stress (copeptin); early diagnostic accuracy for AMI	Rubini Gimenez et al <sup>28</sup>

ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; BNP, brain natriuretic peptide; cTn: cardiac troponin; FGF23, fibroblast growth factor 23; fPSA, free prostate-specific antigen; GDF 15, growth differentiation factor 15; HBA<sub>1c</sub>, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; HMGB1, high-mobility group protein B1; MMP-9, matrix metalloproteinase 9; NGAL, neutrophil gelatinase-associated lipocalin; NT-proBNP, N-terminal pro-brain natriuretic peptide; PAPP-A, pregnancy-associated plasma protein A; PSA, prostate-specific antigen; SMAD3, decapentaplegic homolog 3; SPECT, single-photon emission computed tomography; sST2, soluble suppression of tumorigenicity 2; TGF-β1, transforming growth factor β1; TnT, troponin T.

Interesting data have also been provided by the EURHOBOP registry,<sup>29</sup> which shows important differences among European countries in ACS management. The study included 12 231 consecutive ACS patients who had been admitted to hospital from 2008 to 2010 in 7 European countries (Germany, Spain, Finland, France, Greece, Italy, and Portugal). There was a higher prevalence of smokers in Greece, France and Spain, and there were more diabetic patients in Spain and Portugal. In patients with NSTEMI (67.2% of the total), the most notable difference was fewer angiographies and coronary revascularizations in southern European countries: 66.1% in France, 57.4% in Germany, 44.1% in Finland, 37.3% in Spain, 33.4% in Portugal, and 19.6% in Greece. It should be remembered that these data are from 2010 and, as shown by the DIOCLE study data from 2012, these differences have been decreasing in recent years in Spain.

The differences in CAD prognosis according to sex are still controversial. In the recently published RESCATE II study,<sup>30</sup> mortality was similar in women and in men 28 days after an initial ACS (5.57% and 4.46%, respectively;  $P = .39$ ), but 7-year

mortality was higher in men (hazard ratio [HR] = 1.93; 95% confidence interval [95%CI], 1.46-2.56;  $P < .001$ ).

### Pathogenesis

There is a growing interest in understanding which underlying mechanisms lead to atherosclerotic plaque destabilization and the subsequent appearance of ACS. Local and systemic inflammation play a fundamental role in the pathophysiology of ACS. A related review by Libby et al<sup>31</sup> merits attention as it offers a global perspective of the mechanisms by which inflammation can lead to the appearance of ACS. These observations have important potential therapeutic implications for the prevention of ACS and its recurrence.

### CARDIOVASCULAR PREVENTION

The RECALCAR registry<sup>1</sup> has demonstrated a high prevalence of classic cardiovascular risk factors in Spain, which is disproportionate

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