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Special article

Ischemic Heart Disease and Acute Cardiac Care 2015: A Selection of Topical Issues

Selección de temas de actualidad en cardiopatía isquémica y cuidados agudos cardiológicos 2015

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EPIDEMIOLOGY, PREVENTION, AND CARDIOVASCULAR RISK FACTORS

From an epidemiological point of view, new data have been obtained from the EUROASPIRE IV registry.[1] This 24-country registry included 16 426 patients younger than 80 years who were admitted for acute coronary syndrome (ACS) or underwent a coronary, surgical, or percutaneous intervention with at least 6 months' follow-up.

The results were unmistakably negative. Although the patients were in secondary prevention, with a consequently more intensive follow-up and risk factor treatment, 48.6% of smokers continued to smoke, 37.6% were still obese (body mass index $\geq$ 30), 42.7% had blood pressure $\geq$ 140/90 mmHg, 26.8% were diabetic, 80.5% showed a low-density lipoprotein-cholesterol level $\geq$ 70 mg/dL, and less than half had been referred to a cardiac rehabilitation program.

In the field of cardiovascular prevention, the most important study of 2015 was probably the IMPROVE-IT trial.[2] This study randomized 18 144 ACS patients to either simvastatin 40 mg or simvastatin 40 mg plus ezetimibe 10 mg. Patients had to have been admitted for ACS in the 10 days before their randomization, be older than 50 years, and have one of the following: new ST-segment alteration, elevated troponins, diabetes mellitus (DM), previous infarction, peripheral arterial disease, cerebrovascular disease, or bypass surgery more than 3 years prior to entry. The mean follow-up duration was 57 months.

The primary composite end point of cardiovascular death, nonfatal myocardial infarction, unstable angina, and coronary revascularization showed an absolute risk reduction of 2.0%. At the European Society of Cardiology (ESC) congress of 2015, different subanalyses were presented showing that ezetimibe treatment did not increase the risk of diabetes mellitus or cancer during follow-up and might even have an added benefit in diabetic patients. Thus, the study showed that lower low-density lipoprotein-cholesterol levels (even $<$ 50 mg/dL) lead to fewer cardiovascular events.

In the ODYSSEY LONG TERM study,[3] alirocumab, a member of the family of new lipid-lowering PCSK-9 inhibitors, significantly decreased low-density lipoprotein-cholesterol after 24 weeks of treatment (–62%; $P < .001$). In post-hoc analysis, the rate of cardiovascular events was lower in the alirocumab group (1.7% vs 3.3%; $P = .02$). These good results were even seen after comparison with the combination of maximum dose statins + ezetimibe and in patients with heterozygous familial hypercholesterolemia.[4,5]

In the area of DM, the TECOS study[6] included 14 671 patients with type 2 diabetes mellitus and established cardiovascular disease and showed that addition of sitagliptin to standard antihyperglycemic therapy did not increase the number of cardiovascular events (cardiovascular death, nonfatal infarction or stroke, hospitalization for unstable angina) during a median follow-up of 3 years (11.4% with sitagliptin vs 11.6% with placebo). In the ESC congress, a preplanned subanalysis was presented that concluded that this approach did not increase the rate of admissions for heart failure (7.4% vs 7.0%). Similarly, lixisenatide (the ELIXA study[7]) did not increase the number of cardiovascular events.

BIOMARKERS AND DIAGNOSTIC TECHNIQUES

Two contributions have to be highlighted regarding biomarkers of ischemic heart disease. First, new data on their usefulness, but also a difficulty caused by the widespread use of troponin measurement in patients admitted to the emergency room. The problem arises when elevated troponins are detected and the clinical history permits an alternative diagnosis to infarction. This aspect and its serious repercussions on the prognosis of patients with elevated troponin who are not classified as having ACS are discussed in the article by Bardají et al,[8] which presents a consecutive series of 1032 patients admitted to the emergency room and with a follow-up of 1 year.

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Abbreviations

AMI: acute myocardial infarction
ACS: acute coronary syndrome
CT: computed tomography
DAPT: dual antiplatelet therapy
PCI: percutaneous coronary intervention
STEACS: ST-segment elevation acute coronary syndrome

Second, new biomarkers could be useful for patients with infarction. Peroxisome proliferator-activated receptor gamma coactivator 1-alfa is a metabolic regulator induced during ischemia that prevents cardiac remodeling in animal models. In humans, the baseline expression of this coactivator and an attenuated systemic response after acute myocardial infarction (AMI) are associated with greater myocardial salvage and predict less ventricular remodeling.[9]

Highlights related to ischemic heart disease imaging include new contributions from the SCOT-HEART study,[10] involving 9847 patients with chest pain indicative of angina pectoris. These patients were randomized to the standard evaluation of suspected ischemic heart disease vs additional computed tomography (CT) coronary angiography. The use of CT coronary angiography changed the planned investigations (15% vs 1%; $P < .0001$) and treatments (23% vs 5%; $P < .0001$) but failed to decrease 6-week symptom severity or subsequent rehospitalizations for chest pain. After 1.7 years, the use of CT coronary angiography was nonsignificantly associated with a 38% reduction in fatal and nonfatal AMI.

A similar study was PROMISE,[11] which randomized 10 003 patients with chest pain to a strategy of initial anatomical testing with CT coronary angiography or a strategy of functional testing (exercise electrocardiography, nuclear stress testing, or stress echocardiography). The CT coronary angiography strategy failed to improve the clinical results at a median follow-up of 2 years vs functional testing. These 2 studies are complemented by a publication by a group from *Hospital Clínic* in Barcelona.[12] This study compared the usefulness of coronary CT with that of stress echocardiography in patients with acute chest pain, normal troponins, and normal electrocardiography. Both techniques showed excellent sensitivity and acceptable specificity, although the study did not evaluate the impact of more simple strategies such as conventional stress testing in terms of avoiding significant clinical events. Finally, stress cardiac magnetic resonance imaging was shown to be a useful technique for prognosis determination in patients with reduced ventricular function,[13] with only a perfusion defect predicting clinical events in a multivariate regression model.

STABLE CHRONIC ISCHEMIC HEART DISEASE

Another recent publication was that of the OFRECE study.[14] One of its objectives was to estimate the prevalence of stable angina in the Spanish population ≥ 40 years. In a representative sample of 8400 people, the prevalence of stable angina in Spain was low (definite angina according to the Rose questionnaire, 2.6%; confirmed angina, 1.4%) (Table), but increased with age, reaching 7.1% in individuals aged between 70 and 80 years (Figure). This figure is lower than previous estimates made more than 15 years ago in Spain and than European data as a whole and thus agrees with the lower cardiovascular mortality seen in Spain and other Mediterranean countries. The study found that 4.9% of the Spanish population had a history of acute ischemic heart disease that became chronic.[14] Thus, there are about 1 100 000 patients with chronic coronary disease in Spain, although only 24% would have clinically overt disease; the rest, more than 850 000, would require health care centered on secondary prevention.

In the 3 main congresses held in the last year, various clinical trials were published on the duration of dual antiplatelet therapy (DAPT) in patients with coronary heart disease. Three studies provided the most important information on this subject. The first was the DAPT study,[15] a clinical trial of almost 10 000 patients who had received a stent (most stents were covered and only 26% of the patients had a history of ACS) and had completed the first year with DAPT without problems. The DAPT consisted of with clopidogrel (65%) or prasugrel (35%). In the follow-up from the end of the first year to 30 months after stenting, there were fewer stent thrombosis incidents (0.4% vs 1.4%) and major adverse

Table
Prevalence of Stable Angina (Definite Angina According to the Rose Questionnaire and Confirmed Angina) by Sex and Age Group*

	Men		Women		Total	
	No. (%)	95%CI	No. (%)	95%CI	No. (%)	95%CI
Definite angina (Rose questionnaire)						
40–49 y	939 (0.5)	0.0–1.0	1192 (0.9)	0.3–1.5	2131 (0.7)	0.3–1.1
50–59 y	912 (2.2)	1.2–3.2	1090 (1.2)	0.5–2.0	2002 (1.7)	1.1–2.4
60–69 y	909 (1.5)	0.5–2.5	885 (2.0)	1.0–3.0	1794 (1.8)	1.1–2.5
70–79 y	706 (5.2)	2.3–8.1	879 (8.6)	4.9–12.3	1585 (7.1)	4.9–9.3
≥ 80 y	373 (6.1)	2.1–10.2	493 (5.3)	2.9–7.7	866 (5.6)	3.5–7.7
Total	3839 (2.2)	1.6–2.9	4539 (2.9)	2.2–3.7	8378 (2.6)	2.1–3.1
Confirmed angina						
40–49 y	939 (0.3)	0.0–0.8	1192 (0.2)	0.0–0.5	2131 (0.3)	0.0–0.6
50–59 y	912 (1.5)	0.7–2.3	1090 (0.6)	0.1–1.0	2002 (1.0)	0.6–1.5
60–69 y	909 (0.8)	0.1–1.6	885 (0.7)	0.2–1.2	1794 (0.8)	0.3–1.2
70–79 y	706 (4.5)	1.6–7.3	879 (4.2)	1.9–6.5	1585 (4.3)	2.6–6.1
≥ 80 y	373 (2.9)	0.3–5.6	493 (2.1)	0.5–3.8	866 (2.4)	1.0–3.8
Total	3839 (1.5)	1.0–2.1	4539 (1.3)	0.8–1.7	8378 (1.4)	1.0–1.8

95%CI, 95% confidence interval.
* The OFRECE study. Reproduced with the permission of Alonso et al.[14]