Theoretical Impact on Coronary Disease of Using a Computerized Clinical Decision Support System in the Prescription of Lipid-lowering Treatment

Impacto teórico en la enfermedad coronaria de usar un sistema informatizado de ayuda en la prescripción del tratamiento hipolipemiante

To the Editor,

Low-density lipoprotein cholesterol (LDL-C) is a strong cardiovascular risk factor, especially for coronary artery disease. However, in Spain, there is plenty of room for improvement in increasing the number of patients at very high cardiovascular risk who attain lipid goals. Recently, our group published the results of the first validation study of the computerized European clinical decision support system (CDSS) specific to lipid-lowering therapy (designated in Spanish as HTE-DLP). The study shows that the number of patients who reach the treatment goal of LDL-C < 70 mg/dL increases 4.4 times with use of the HTE-DLP by experts in vascular risk. The objective of the present study was to assess the theoretical impact on the frequency of coronary artery disease of using the HTE-DLP throughout Spain with the CASSANDRA-REGICOR methodology.

The CASSANDRA-REGICOR system permits an estimate of the number of fatal and nonfatal coronary events that would occur in the Spanish population in the next 10 years in different scenarios according to trends in prevalence of cardiovascular risk factors. The system uses incidence data on coronary disease and risk factor prevalence from the REGICOR study. Extrapolation to Spain is based on data from the IBERICA study (incidence) and the DARIOS study (risk factor prevalence). The number of coronary events was predicted for 2010 to 2020 in patients aged between 35 and 75 years old. Population projections were provided by the Catalan Statistics Institute (IDESCAT) and Spanish National Statistics Institute (INE). The application enables an assessment of the impact of different scenarios of risk factor prevalence.

The HTE-DLP is the first CDSS for lipid-lowering treatment developed in Spain (RTA88/09) (Figure). It is based on the 2011 European guidelines for lipid-lowering treatment. Taking

**Table (Continued)**

Principals Characteristics of Patients Diagnosed With Coronary Artery Disease Who Answered the MEDAS–14 Screener

<table>
<thead>
<tr>
<th>Duration of CAD</th>
<th>Cardiologist</th>
<th>Cardiology nurse</th>
<th>Cardiology accident and emergency services</th>
<th>Admitted to cardiology</th>
<th>Treated with cardioprotective drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–2 years</td>
<td>53 (48)</td>
<td>8 (7)</td>
<td>11 (10)</td>
<td>9 (8)</td>
<td>Statins: 104 (95) ACE-inhibitors or ARA-II: 78 (71) Beta-blockers: 80 (73) Antiplatelet agents: 105 (95) MEDAS-14, mean (SD) score: 8.9 (2.3) &lt; 9 points: 41 (37) ≥ 9 points: 69 (63)</td>
</tr>
<tr>
<td>3–5 years</td>
<td>40 (36)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6–12 years</td>
<td>20 (18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 or more years</td>
<td>10 (9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACE-inhibitors, angiotensin converting enzyme inhibitors; ACS, acute coronary syndrome; ARA-II, angiotensin II receptor antagonist; CAD, coronary artery disease; CVRF, cardiovascular risk factors; MEDAS-14, 14-point Mediterranean diet adherence screener.

* Some patients suffered angina and ACS. The values express No. (%) or mean (standard deviation).

MedD, as key elements for the superior efficacy of this diet compared with a low-fat diet. It is likely that the MedD will be clearly reinforced as an intervention to be included in nonpharmacological treatment for preventing cardiovascular disease thanks to the possibility of new studies backing the results published by de Lorigeril et al. The data from this study show that a majority of patients with CAD (63%) had acceptable adherence to the MedD. The application of the MEDAS–14 screener makes it possible to identify which aspects require improvement and provides the opportunity to focus and adapt a dietary intervention.

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Figura. Ejemplo de la interfaz del sistema informatizado de ayuda en la toma de decisiones del tratamiento hipolipemiante (HTE-DLP).
Table

Effect of Using HTE-DLP on the Incidence Rate and Number of Fatal and Nonfatal Coronary Events in Individuals Aged 35 to 74 Years and Health Expenditure Extrapolated to 2020 According to Estimates Based on the CASSANDRA-REGICOR System

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Use of HTE-DLP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated male population</td>
<td>12 502 843</td>
<td>12 951 521</td>
</tr>
<tr>
<td>Estimated female population</td>
<td>12 951 521</td>
<td>12 951 521</td>
</tr>
<tr>
<td>Incidence rate/100 000 men</td>
<td>234.5-238.4</td>
<td>220.5-220.7</td>
</tr>
<tr>
<td>Incidence rate/100 000 women</td>
<td>50.3-50.5</td>
<td>49.4-49.5</td>
</tr>
<tr>
<td>Number of expected cases of coronary artery disease in men</td>
<td>29 139-29 807</td>
<td>27 569-27 594</td>
</tr>
<tr>
<td>Number of expected cases of coronary artery disease in women</td>
<td>6515-6541</td>
<td>6398-6411</td>
</tr>
<tr>
<td>Estimated cost of coronary artery disease in men, millions of Euros</td>
<td>409 956 391</td>
<td>387 868 261</td>
</tr>
<tr>
<td>Number of coronary events avoided in men</td>
<td>1570-2213</td>
<td>1570-2213</td>
</tr>
<tr>
<td>Number of coronary events avoided in women</td>
<td>117-130</td>
<td>117-130</td>
</tr>
<tr>
<td>Reduction in costs due to coronary events avoided in men, millions of Euros</td>
<td>22 088 330</td>
<td>30 815 343</td>
</tr>
<tr>
<td>Reduction in costs due to coronary events avoided in women, millions of Euros</td>
<td>1 646 673</td>
<td>1 838 970</td>
</tr>
</tbody>
</table>

HTE-DLP, computerized clinical decision support system for lipid-lowering treatment.

Values presented with upper and lower 95% CI for the mean total cholesterol.

into account patients’ cardiovascular risk, comorbidities, and concomitant drugs, the application presents all lipid-lowering therapeutic options for a specific patient, ordered from best to worst according to criteria of efficacy, safety, and cost-effectiveness.3

The mean (SD) value of total cholesterol in HTE-DLP users after 12 weeks was 156.6 (44) mg/dL,3 which in the CASSANDRA-REGICOR system would be equivalent to the effect of the theoretical maximum reduction of 23% for men and 24% for women. To calculate the effect of health costs, a mean cost per coronary event of 14 069 Euros was applied; 87% of this sum corresponds to direct costs and 13% to loss of productivity.5

Use of the HTE-DLP throughout Spain in 2020 would lead to a decrease in fatal and nonfatal coronary events in individuals aged 35 to 74 years of between 5.4% and 7.4% in men and 1.8% and 2.0% in women. This would correspond to a decrease in health costs for coronary disease of between 4.7% and 6.4% (Table).

Of the studies published to date on CDSS for lipid-lowering treatment, only the study by Gilutz et al8 in 7448 patients has found a decrease (2.1% in this case), in the number of readmissions to hospital per year for coronary artery disease in the intervention group.

The use of CDSS for lipid-lowering treatment may have an impact not only on direct costs of lipid-lowering medication, which were 19% lower in the case of HTE-DLP for every 1 mg decrease in LDL-C,5 but also on indirect costs of these events.

The limitations of the study include the fact that the estimates are approximations to reality based on clinical practice, risk factor prevalence, degree of control, and current demographic trends. In the future, this figure may turn out to be an underestimate, particularly for women, in view of possible variations in the prevalence of risk factors, such as increased prevalence of obesity, hypertension, and diabetes mellitus, and a greater than expected survival of the population, with more individuals aged 75 years or greater. On the other hand, the availability of new drugs and improvements in clinical practice may increase the number of patients who attain their treatment goals, and the findings may be an overestimate. Finally, we should bear in mind that the study data have been extrapolated from the HTE-DLP validation study in a small sample. It is important to highlight that the data used were subject to quality control to guarantee their internal and external validity. However, large prospective studies would be needed in real clinical practice to measure the true effect and safety of CDSS.

In conclusion, the general use in clinical practice of a computerized system for prescribing supervision of lipid-lowering treatment may have a positive impact on coronary artery disease and help to optimize the use of health resources.

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CONFLICTS OF INTEREST

A. Zamora and F. Fernández de Bobadilla have intellectual property protection for HTE-DLP.

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**Predicting the Risk of Systemic Septic Embolism in Patients With Infective Endocarditis**

**Predicción del riesgo de embolia sistémica séptica en pacientes con endocarditis infecciosa**

To the Editor,

Despite the progress made over the past decades in the management of infective endocarditis, the mortality rate is still high. Embolic events (EE) are the most frequent extracardiac complication, with an incidence of symptomatic EE ranging from 10% to 50%, affecting mainly the central nervous system and therefore worsening prognosis.

The possibility of EEs also affects treatment options, as surgery is indicated to prevent them; a recent study showed that early surgery significantly reduces EE occurrence. As they are early-onset phenomena in infective endocarditis, it is essential to quantify the embolic risk at the time of diagnosis in order to avoid this complication and help in the therapeutic decision-making process.

Two systems for predicting embolic risk in infective endocarditis were designed recently, one French and one Italian. Our objective was to test and compare the clinical utility of both systems.

We studied 153 consecutive patients admitted to a tertiary care center between January 2009 and April 2014 with a diagnosis of infective endocarditis according to the modified Duke criteria. In the first 24 hours of admission, all patients underwent a transthoracic echocardiogram and 90% took a transesophageal one.

The embolic risk was calculated using the French system, which gives 1 point to each of the following covariates: diabetes mellitus, atrial fibrillation, vegetation > 10 mm, embolism prior to antibiotic therapy and Staphylococcus aureus. Age was added as a continuous variable to the sum of the above points, as per the French system, to estimate EE risk. The risk was also calculated using the Italian system, assigning 1 point to vegetation ≥ 13 mm and 1 point to S. aureus. Patients were classified as being at high risk of embolism if they had a probability > 7.5% according to the French system and of 2 points using the Italian system.

The performance of both systems in predicting EEs based on diagnosis and having started antibiotic therapy was evaluated using a Cox regression model. Embolic events based only on clinical suspicion or cutaneous manifestations were not considered.

The clinical, echocardiographic, and microbiological data are shown in the Table. The Charlson comorbid index was 4 (SD, 2). The length of the vegetation was 8 (SD, 7) mm on the transesophageal echocardiogram. While in hospital, 27 (17.6%) EEs were recorded, 16 (59.9%) affecting the central nervous system. In-hospital mortality was 3 times higher (12/27; 44.4%) in patients with EE than in patients without EE (11.9%).

The estimations generated with the French system showed a significant association with embolic risk (hazard ratio [HR] = 2.7; 95% confidence interval [95%CI], 1.37-5.46). However, of the 27 patients who suffered an EE, 12 (44.4%) had been classified as low risk. The occurrence of EE was better predicted by this system than by chance (P = .03), although its discrimination was moderate (C-statistic = 0.66; 95%CI, 0.54-0.77).

The estimations from the Italian model were also associated with embolic risk: HR = 2.2 (95%CI, 1.28-3.92) and C = 0.62 (95%CI, 0.49-0.74; P = .05). In this model, 85.2% (n = 23) of patients who suffered an EE had been classified as low risk.

Calibration of both models was adequate (P ≥ .2). Compared with the Italian system, the French one showed a net reclassification improvement index of 7.4% (P = .5).

Therefore, although both models have a similar predictive power, the French system better classifies patients who are at low embolic risk than the Italian one. The main advantage of the Italian system is that it is easier to use, requiring only two variables, whereas the French system, apart from using a greater number of variables, requires software for its calculation. In our cohort, only 1 patient had a right-sided embolism. Excluding her from the analysis did not affect the general results; therefore, in essence our results refer to left-sided embolisms.

In conclusion, in this contemporaneous series of infective endocarditis, approximately 1 in 6 patients had EE after their diagnosis or start of antibiotic therapy. The unadjusted excess risk of in-hospital death of patients with EE is around 30%. It is possible to predict the embolic risk with a simple clinical tool. In our population, the French system was shown to be more useful; therefore, including it as part of the clinical judgement should help to improve the therapeutic decision-making process, making it