Selection of the Best of 2016 in Acute Cardiovascular Care

Selección de lo mejor del año 2016 en cuidados agudos cardiovasculares

To the Editor:

A new guideline on life support and cardiopulmonary resuscitation was published by the European Resuscitation Council in late 2015. The main changes in this guideline are detailed in a recent article by Fernández-Lozano et al. Some of these changes are worth highlighting, such as the recommended frequency of chest compressions, which is now 100-120 bpm (in 2010 it was 100 bpm), keeping interruptions in compressions to a minimum (10-12 ventilations/min; compression:ventilation, 30:2). The depth of compressions for adults should be 5 cm without exceeding 6 cm. Vasopressin has been removed from the cardiac arrest algorithm in adults and all comatose adult patients should now have their temperature measured on return of spontaneous circulation, with a target range between 32 and 36 °C (in 2010 it was between 32 and 34 °C).

Kudenchuk et al. randomized 3026 patients with out-of-hospital refractory ventricular fibrillation or pulseless ventricular tachycardia to amiodarone, lidocaine, or placebo. No significant differences in prognosis were detected among the 3 study arms in terms of survival or neurological outcomes (Table).

A retrospective study of the Japanese Utstein registry in 282,183 adult patients with out-of-hospital cardiac arrest showed that prehospital cardiopulmonary resuscitation maneuvers initiated by bystanders should continue for at least 40 minutes from notification of the emergency medical services, with at least 33 minutes of resuscitation maneuvers after arrival on the scene. Prior action for the above duration achieved an improvement in survival and neurological outcomes at 30 days.

According to the United States National Cardiovascular Data Registry, in patients in cardiogenic shock (CS) resulting from acute myocardial infarction who survived hospitalization (n = 5555 [4.9%]), deaths attributable to CS occurred mainly in the first 60 days after discharge (9.6% versus 5.5%; adjusted hazard ratio [HR], 1.62; 95% confidence interval [CI], 1.46-1.80). In contrast, once the first 60 days had elapsed, mortality did not differ significantly between the 2 groups (taking patients without CS as the reference group, adjusted HR = 1.08; 95% CI, 1.00-1.18).

The results of 2 clinical trials on renal replacement therapy for critically ill patients with acute kidney injury (AKI) have been published: ELAIN and AKIKI. The ELAIN study enrolled 231 patients with AKI at a German site and randomized them to early or delayed renal replacement therapy. Early therapy was defined as therapy initiated within 8 hours of diagnosis of stage 2 AKI according to the Kidney Disease: Improving Global Outcomes (KDIGO) classification. Delayed replacement therapy was indicated within 12 hours of diagnosis of stage 3 AKI. Significant differences in favor of early therapy compared with delayed therapy were found in terms of lower mortality (primary outcome measure) at 90 days (39.3% versus 52.7%; P = .03).

Unlike the results of the ELAIN study, the multicenter French clinical trial AKIKI reported a similar mortality rate with both early and delayed strategies, although the design of this study differed substantially from that of the ELAIN study. In the AKIKI study, 620 patients with invasive mechanical ventilation, perfusion of adrenaline/noradrenaline, or both who developed AKI during their stay in the intensive care unit were randomized 1:1 to an early or delayed strategy. The early strategy consisted of hemodialysis sessions (continuous or intermittent) within 6 hours of documentation of stage 3 AKI according to the KDIGO classification. In the delayed strategy, renal replacement therapy was initiated in the event that AKI persisted for more than 72 hours with at least 1 of the following conditions: blood urea nitrogen > 112 mg/dL (equivalent to 240 mg/dL serum urea), serum potassium > 5.5 mmol/L despite medical treatment, metabolic acidosis, oliguria, or pulmonary edema. The primary outcome measure, survival at 60 days, did not differ significantly between the 2 groups (48.5% versus 49.7%; P = .79).

Table

Efficacy and Safety of Parenteral Use of Amiodarone, Lidocaine, and Placebo (Saline Solution) in Nontraumatic Cardiac Arrest (Refractory Ventricular Fibrillation or Pulseless Ventricular Tachycardia). Results the Resuscitation Outcomes Consortium Study

<table>
<thead>
<tr>
<th>Outcome Measures</th>
<th>Placebo n = 1059</th>
<th>Amiodarone n = 974</th>
<th>Lidocaine n = 993</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival, %</td>
<td>21</td>
<td>.08</td>
<td>24.4</td>
<td>.70</td>
</tr>
<tr>
<td>Secondary outcome measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Return of spontaneous circulation, %</td>
<td>34.6</td>
<td>.52</td>
<td>35.9</td>
<td>.07</td>
</tr>
<tr>
<td>Modified Rankin scale ≤ 3 points</td>
<td>16.6</td>
<td>.19</td>
<td>18.8</td>
<td>.44</td>
</tr>
<tr>
<td>Admitted to hospital, %</td>
<td>39.7</td>
<td>.01</td>
<td>45.7</td>
<td>.55</td>
</tr>
<tr>
<td>Adverse Events, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>0.2</td>
<td>0.1</td>
<td>0.3</td>
<td>.61</td>
</tr>
<tr>
<td>Anaphylaxis within 24 hours</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Clinical seizure</td>
<td>3.7</td>
<td>3.2</td>
<td>5.1</td>
<td>.07</td>
</tr>
<tr>
<td>Temporary cardiac pacing</td>
<td>2.7</td>
<td>4.9</td>
<td>3.2</td>
<td>.02</td>
</tr>
<tr>
<td>Death before discharge</td>
<td>78.8</td>
<td>75.3</td>
<td>75.7</td>
<td>.16</td>
</tr>
<tr>
<td>Any adverse events within first 24 hours or death before discharge</td>
<td>80.4</td>
<td>78.3</td>
<td>78.0</td>
<td>.20</td>
</tr>
</tbody>
</table>

a Placebo compared with amiodarone.
b Amiodarone compared with lidocaine.
c Placebo compared with lidocaine.
CONFLICTS OF INTEREST

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Selection of the Best of 2016 in Vascular Risk and Cardiac Rehabilitation

Selección de lo mejor del año 2016 en riesgo vascular y rehabilitación cardíaca

To the Editor,

Various studies with considerable impact in the field of cardiovascular prevention and cardiac rehabilitation have been published in 2016. Three of these studies are relevant due to their positive results in patients with type 2 diabetes mellitus (T2DM) and cardiovascular disease. The renal substudy of the EMPA-REG trial,1 designed with a prespecified analysis to determine the effects of empagliflozin on microvascular complications in patients with T2DM at high cardiovascular risk or with established cardiovascular disease found a significant reduction of 39% in the primary outcome of incident or worsening nephropathy (hazard ratio [HR], 0.61; 95% confidence interval [95%CI], 0.53–0.70). There was also a doubling of the serum creatinine level in 1.5% of the empagliflozin group vs 2.6% in the placebo group, with a relative risk reduction of 44%, and a need for renal-replacement therapy of 0.3% vs 0.6% in the placebo group, with a relative risk reduction of 55%; however, there were no differences in albuminuria development. The composite outcome of death from cardiovascular causes or worsening of the creatinine level was significantly less frequent in the empagliflozin group: 0.61 (0.55–0.69; P < .001). The reduction in cardiovascular events found in the EMPA-REG trial was maintained in this renal failure population.

The second study, the LEADER trial,2 evaluated the effect of liiraglutide in patients with T2DM and cardiovascular disease or at high cardiovascular risk vs placebo. There were fewer cardiovascular events in the liiraglutide group: 13.0% vs 14.8% (HR, 0.87; 95%CI, 0.78–0.97; P = .007). This decrease was mainly driven by a reduced mortality rate (8.2% vs 9.6% with placebo; HR, 0.85; 95%CI, 0.74–0.97; P = .02). The rates of the other components of the primary outcome were not significantly different vs the placebo group (myocardial infarction, stroke, hospitalization due to congestive heart failure).

Thus, LEADER is the first study of glucagon-like peptide-1 (GLP1) analogs to show a mortality reduction. The results of the SUSTAIN-6 trial3 were presented 3 months later. This study was conducted in a very similar population to those of the previous studies of patients with T2DM. The results showed a reduction in the primary composite outcome of death, nonfatal stroke, or nonfatal myocardial infarction of 26%, caused by a 39% reduction in acute stroke and with no significant differences in myocardial infarction and death. There was a notable 35% reduction in the rate of coronary or peripheral revascularization. Vitreous hemorrhage, blindness, or conditions requiring treatment with an intravitreal agent or photocoagulation were significantly more frequent in patients receiving semaglutide: 3% in patients receiving the active compound vs 1.8% of the placebo group, representing a 76% increase (P = .02).

The SPRINT hypertension trial4 was prematurely interrupted due to a 30% decrease in the risk of cardiovascular events, including death from cardiovascular causes, as well as a 25% reduction in death from any cause, in the intensive treatment group who had a blood pressure target of less than 120/80 mmHg. These benefits were more evident in 3 subgroups of patients: those without renal failure or previous cardiovascular disease, those older than 75 years, and those with prehypertension.

The CLARIFY registry5 was subsequently published. Its results suggested caution with blood pressure target values in hypertensive patients with stable coronary heart disease. Although a reduction in systolic blood pressure to 120 to 139 mmHg or in diastolic blood pressure to 70 to 79 mmHg reduced both fatal and nonfatal events, greater reductions were accompanied by myocardial infarction and heart failure (the stroke risk was decreased, however). These findings thus indicate the presence of a J-curve phenomenon in the control of blood pressure levels in patients with stable ischemic heart disease.

The European guidelines, such as that for cardiovascular prevention,6 insist on preventive policies, lifestyle changes, and adherence and recommend a low-density lipoprotein-cholesterol (LDL-C) target that varies according to patients’ vascular risk: a) very high risk, <70 mg/dl or a reduction of 50% in the LDL-C if the baseline is between 70 and 135 mg/dl; b) high risk, LDL-C < 100 mg/dl or a reduction of 50% in the LDL-C if the baseline is between 100 and 200 mg/dl; and c) others, LDL-C < 115 mg/dl.

The therapeutic recommendations are as follows: first step, high-intensity statin therapy (IA); second step, combination with ezetimibe (IB); and third step, PCSK9 inhibitors (IB).