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 cardiaca

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 liraglutide in patients with T2DM and cardiovascular disease or at high cardiovascular risk vs placebo. There were fewer cardiovascular events in the liraglutide group: 13.0% vs 14.9% (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 trial[3] 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 trial[4] 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 registry[5] 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 (IIB); and third step, PCSK9 inhibitors (IIB).

Studies of cardiac rehabilitation still show disagreements in the relative merits of interval and continuous training. The push for telerehabilitation and electronic health care continues, both in phase 2 and phase 3. Alarming results are being published on the long-term maintenance of the benefits of rehabilitation. Finally, more and more evidence supports the value of rehabilitation in patients with heart failure.

In conclusion, the current policy in the fight against smoking continues: modified packets, reduced cigarette size, and less attractive packaging. The use of varenicline, even during hospitalization for an acute coronary syndrome, has been shown to be safe, with no associated cardiovascular risk, and to effectively promote smoking cessation.

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