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Selection of the Best of 2017 in Vascular Risk and Cardiac Rehabilitation

Selección de lo mejor del año 2017 en riesgo vascular y rehabilitación cardiaca

To the Editor,

2017 has been a prolific year for high-impact publications in this discipline. In the field of nutrition, the clinical practice guidelines recommend replacing the intake of fats, especially saturated fats, with unsaturated fats and carbohydrates to avoid increasing low-density lipoprotein cholesterol (LDL-C) and consequently the occurrence of cardiovascular (CV) events. Recent randomized clinical trials and metanalyses of observational studies contradict these recommendations. One such study is the PURE[1] cohort study, with 135 335 individuals from 18 countries, in which it was observed that a high intake of carbohydrates (> 60%) increased the risk of total mortality, whereas intake of fats (including saturated fats) reduced this risk, with no association found between total fat intake and CV disease or CV mortality, and there was even an inversely proportional relationship between saturated fats and stroke. It is without doubt a study that raises new questions and will require, at least, revision of the current recommendations on the appropriate dietary proportion of the different macronutrients.

Regarding lipids, the Fourier[2] trial has been the real protagonist and has provided data on the CV benefits of treatment with evolocumab. In this trial, 27 567 patients with atherosclerotic disease (acute myocardial infarction, nonhemorrhagic stroke, or symptomatic peripheral arterial disease) and with LDL-C > 70 mg/dL (or non—high-density lipoprotein cholesterol > 100 mg/dL) were randomized to receive evolocumab 140 mg or placebo every 2 weeks. LDL-C decreased by 59% in the evolocumab group and reached a mean of 30 mg/dL. The reduction in relative risk for the primary outcome (CV death, acute myocardial infarct or stroke) in the evolocumab group was 15% at 36 months, with the greatest benefit occurring after the first 12 months. There were no significant differences regarding serious side effects. This study demonstrated that inhibition of proprotein convertase subtilisin-kexin type 9 (PCSK9) with evolocumab reduces LDL-C and translates to CV benefits.

For diabetes, the most noteworthy study was the CANVAS[3] trial, in which 10 142 diabetic patients with high CV risk were randomized to receive canagliflozin or placebo. The canagliflozin group achieved a 14% reduction in the primary outcome (composite outcome of CV mortality, nonfatal myocardial infarction and nonfatal stroke), 26.9 vs 31.5 events/1000 patients/year (hazard ratio [HR] = 0.86; 95% confidence interval [95%CI], 0.75-0.97; $P = .02$ for superiority). There was an increase of almost double the number of amputations in the treated group (6.3 vs 3.4/1000 patients/year; HR = 1.97). This study provides evidence that the CV benefits of SGLT2 inhibitor oral antidiabetics are a class effect. It also supports the focus of treatment of diabetes being based not only on lowering glucose levels, but also on more general effects in an aim to reduce CV events and improve prognosis, similar to what was seen last year with the GLP1 agonists liraglutide and semaglutide.

Another publication was the first study to demonstrate that a CV screening program can be associated with a reduction in mortality. The Viborg Vascular[4] (VIVA) trial is a prospective randomized trial conducted in 50 156 Danish men aged between 65 and 74 years, assigned to triple screening for abdominal aortic aneurysm (AAA), peripheral vascular disease (PAD), and hypertension versus standard care. Those diagnosed with PAD or AAA received smoking cessation therapy, aspirin (75 mg/day), simvastatin (40 mg/day) and an antihypertensive, and those with AAA > 50 mm were referred to vascular surgery. More than 20% of participants received a diagnosis: 3% with AAA, 11% with PAD, and 11% with untreated hypertension. There was a 7% reduction in 5-year mortality, and 1 life was saved for every 169 participants assessed, making it more cost-effective than the European cancer screening programs. A substudy of the VIVA trial[5] also showed an inverse association between AAA growth and glycated hemoglobin concentration in individuals with and without known diabetes.

The inflammatory hypothesis of atherothrombotic disease is based on inflammation playing a role in the formation, progression and rupture of the atheromatous plaque and in the generation of acute coronary events. Canakinumab is a monoclonal antibody against interleukin 1β that produces an anti-inflammatory effect. The CANTOS trial[6] compared subcutaneous 3-monthly administration of canakinumab vs placebo in patients with a history of acute myocardial infarction and high levels of C-reactive protein, with a combined primary outcome of CV death, nonfatal acute myocardial infarction, and nonfatal stroke at 48 months.

The main results were a significant reduction in the primary outcome in the treatment group due to a reduction in nonfatal acute myocardial infarction. There was also a reduction in C-reactive protein levels, no differences in LDL-C levels, and a lower risk of cancer in the canakinumab group vs placebo group, although this was at the expense of an increase in fatal infections. The most relevant result of this study was that it demonstrated the inflammation theory, paving the way in the search for promising new lines of treatment.

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Selection of the Best of 2017 on the Usefulness of Cardiac Stimulation in the Treatment of Vasovagal Syncope

Selección de lo mejor del año 2017 sobre la utilidad de la estimulación cardiaca en el tratamiento del síncope vasovagal

To the Editor,

During 2016 and 2017, 5 papers have been published on recurrent vasovagal syncope with cardioinhibitory response to the tilt table test (TTT) and treatment with pacemaker implantation.

The first paper reported on a single center, retrospective, observational study of 24 patients with recurrent syncope. An in-depth diagnostic protocol was applied, including a TTT and exclusion of any other cause for syncope, followed by insertion of an implantable loop recorder (ILR). When patients then had a first syncope recurrence accompanied by asystole longer than 3 seconds or asystole longer than 6 seconds irrespective of syncope recurrence, they received a dual-chamber pacemaker with rate drop response (RDR). In the 35-month follow-up, syncope recurred in 7 patients, 4 of whom were TTT-positive. However, of the 17 patients without syncope recurrence, the TTT was positive in only 2.[1]

The second paper described a prospective, multicenter study with 281 patients older than 40 years who underwent a diagnostic study starting with carotid sinus massage (CSM). Of these patients, 78 had asystole and were given an implantable PM. The remaining 203 patients underwent a TTT. A VASIS type 2B response with asystole was induced in 38 patients, who were then given an implantable PM. The remaining 165 patients received an ILR. Asystole was recorded in 21 of these patients, who were then given an implantable PM. All 137 patients treated with a PM received a dual-chamber device with rate drop sensing to allow minimal ventricular pacing time. Syncope recurred in 25 of the 281 patients (18%), and there were no differences according to the test (CSM, TTB or ILR) that indicated PM requirement. At 3 years of follow-up, 20% of the 137 patients with a PM had had syncope recurrence, which was significantly lower than the 43% in the 142 patients who received no PM ($P = .01$). Among the patients who had asystole during the TTT, syncope recurrence was 3% at 12 months and 17% at 21 months. Among the patients with a negative TTT, syncope recurrence was only 5% at 3 years.[2]

The third paper reported on a multicenter, prospective, single-blind, randomized study that enrolled 30 patients with a dual-chamber PM with closed-loop stimulation (CLS) implanted at least 6 months prior to enrolment, with a history of recurrent syncopes and cardioinhibitory response to the TTT. At the initial visit, patients were randomized 1:1 by a central system into 1 of 2 pacing groups, DDD-CLS first or DDD first (at a fixed rate of 60 bpm), and they underwent a first TTT with the PM activated. At the end of the test, the PM was reprogrammed and 1 week later, the test was repeated with the other pacing mode, i.e., with crossover from DDD-CLS to DDD and from DDD to DDD-CLS. Compared with DDD, the DDD-CLS mode significantly reduced the occurrence of syncope in the TTT (30.0% vs 76.7%; $P < .001$). Among the patients who had a syncope in both TTTs and with both pacing modes, DDD-CLS significantly delayed the onset of syncope during TTT. The maximum fall in blood pressure recorded during the TTT was significantly lower in DDD-CLS than in DDD.[3]

The fourth paper described the SPAIN study, with a multicenter, prospective, randomized, double-blind design, that enrolled 54 patients with recurrent syncope and TTT cardioinhibitory response. A total of 46 patients completed the protocol. All patients received a DDD-CLS PM and were randomized 1:1 to 2 groups: group A first received DDD-CLS for 12 months and then DDI for 12 months; group B first received DDI and then DDD-CLS for the same periods of time as group A. During 22 months of follow-up, in group A, 72% of patients receiving DDD-CLS therapy had $\geq$ 50% reduction in syncopes versus 28% of patients receiving DDI; and in group B, all patients had $\geq$ 50% reduction in syncopes after switching from DDI mode to DDD-CLS in the second year ($P = .0003$). Just 4 patients (8.7%) had a syncope when in DDD-CLS mode, versus 21 (45.65%) who had one when in DDI mode (hazard ratio = 6.72; odds ratio = 0.11; $P < .0001$). The Kaplan-Meier analysis showed significantly longer time to first syncope in group A versus group B and the same finding was also observed in the 46 patients in DDD-CLS mode versus DDI mode ($P < .0001$). Therefore, DDD-CLS pacing significantly reduces syncope burden, lowers syncope recurrence 7-fold, and significantly prolongs time to first recurrence.[4,5] The BIOSync study,[6] the fifth paper referred to here, aims to confirm our results.

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