other lipid-lowering agents such as statins and ezetimibe that need to be taken every day. Finally, although these agents might not seem cost-effective in some health care systems due to their current price, they might be the only therapeutic alternative for certain patient groups to attain the recommended target LDL-C levels.[6]

We conclude with the polypill, which is a therapeutic approach of considerable interest for clinical cardiology, particularly in patients with treatment adherence problems. The advantages of these compounds are discussed in greater detail in another scientific letter.

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Available online 2 January 2017

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1885-5857/

Selection of the Best of 2016 in Diabetes and Heart

Selección de lo mejor del año 2016 en diabetes y corazón

To the Editor,

Recent data published by the World Health Organization confirm that the prevalence of diabetes mellitus (DM) continues to increase, from 4.7% in 1980 to 8.5% in 2014.[1] DM caused more than 1.5 million deaths in 2012, with most of them occurring in individuals older than 70 years. In addition, a recent study of a large population of patients with DM2 showed that, despite acceptable preventive treatment, cardiovascular (CV) deaths were 33% more frequent in patients with DM2 than in controls, and that CV conditions were the most frequent cause of death in patients with DM.[2] These figures, along with the fact that at least one third of patients seen in cardiology departments have DM, should make clinical cardiologists aware of the importance of diabetic treatments for patients with cardiac disease, particularly given the reduction in the rate of CV events that can be achieved with some hypoglycemic agents. We also know, however, that hypoglycemic agents can be harmful to patients with cardiac disease because part of our job when attending these patients involves discontinuing potentially harmful treatments that may increase the risk of heart failure or even mortality in certain patient subgroups (Table). Three trials have recently been published and their results should be disseminated to maximize the benefit to patients with CV disease and DM2.

The EMPA-REG OUTCOMES study[3] reported that, after a mean follow-up of 3.1 years, empaglifozin reduced the primary outcome (composite of nonfatal myocardial infarction, nonfatal stroke, and CV death) by 14% in 7020 patients with DM2 and CV disease. This reduction was driven mainly by a 38% decrease in CV deaths. Empaglifozin also reduced hospitalization for heart failure by 35% and overall mortality by 32%. The number of patients needed to treat to avoid 1 admission for heart failure or CV death was 35 in 3 years. Of note, the reduction in the risk of admission for heart failure occurred both in patients with a history of heart failure and in those without. Possible mechanisms to explain these benefits include decreases in blood pressure, body weight

Table
Effects of the Hypoglycemic Therapeutic Groups on Cardiovascular Mortality and Admissions for Heart Failure

Therapeutic group	Cardiovascular mortality	Admissions for heart failure
Insulin	Neutral	Neutral (harmful)
Metformin	Neutral (beneficial)	Neutral
Sulfonylureas	Neutral (harmful)	Neutral (harmful)
Glitazones	Neutral	Harmful
SGLT2 inhibitors	Empaglifozin, beneficial	Empaglifozin, beneficial
DPP4 inhibitors	Neutral	Neutral; saxagliptin, harmful
GLP-1 agonist	Lixisenatide and semaglutide, neutral; liraglutide, beneficial	Neutral

Data from small studies and registries are shown in parentheses.

(including visceral adiposity), albuminuria, glycemia, arterial rigidity, sympathetic nervous system activation, oxidative stress, and uric acid resulting from empaglifozin use. However, the rapid onset of the beneficial effect (the curves already separated after 2 to 3 months) and the low likelihood that the benefit was mediated by an antithrombotic effect (given there was no decrease in the rates of myocardial infarction and stroke) suggest that most of the benefit was derived from an amelioration of worsening of heart failure and a reduction in sudden cardiac death mediated by a hemodynamic effect (osmotic diuresis and improvement in cardiac function due to afterload reduction) or from antiarrhythmic effects.

The randomized LEADER trial,[4] with administration of subcutaneous liraglutide 1.8 mg/d to more than 9000 patients with high CV risk (81% with prior CV disease) followed up for 42 to 60 months, reported a 13% decrease in the primary outcome measure (CV death, nonfatal myocardial infarction, or nonfatal stroke), driven mainly by a 22% decrease in CV deaths. The all-cause mortality rate was also lower in the liraglutide group (hazard ratio, 0.85; 95%CI, 0.74-0.97; P = .02), whereas the rate of myocardial infarction, stroke, and hospitalization for heart failure showed no differences.

Finally, the SUSTAIN-6 trial[5] in 3297 patients with diabetes, most of whom had CV disease, showed that active treatment with either 0.5 mg or 1.0 mg of once-weekly subcutaneous semaglutide (another glucagon-like peptide type 1 [GLP-1]) reduced the risk of the primary composite outcome by 26%. This reduction was due mainly to a significant decrease (39%) in the rate of nonfatal stroke and a nonsignificant decrease (26%) in nonfatal myocardial infarction, with no difference in CV death. On the negative side, the complications related to diabetic retinopathy increased. Unlike the EMPA-REG study,[3] the benefits in the 2 aforementioned studies with GLP-1 agonists[4,5] appeared later, and there was a trend toward a lower incidence of myocardial infarction and stroke. This trend may indicate that the benefit of these GLP-1 agonists is mediated by a beneficial effect on atherosclerosis progression.

With regard to coronary intervention, in recipients of stents with diabetes (whether controlled or not), the use of everolimus-eluting stents significantly decreased the risk of myocardial infarction, stent thrombosis, repeat revascularization, and a composite of adverse cardiac events compared with the use of paclitaxel-eluting stents.[6]

With all these results, which for the first time have demonstrated a clear decrease in CV events with different treatments for DM2, clinical cardiologists can no longer look the other way and pass up the opportunity to improve the CV prognosis of patients through the appropriate use of these drugs.

CONFLICTS OF INTEREST

J.C.S has participated in audits and presentations funded by the Boehringuer-Lilly alliance.

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Available online 7 December 2016

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1885-5857/

Selection of the Best of 2016 in Ischemic Heart Disease

Selección de lo mejor del año 2016 en cardiopatía isquémica

To the Editor,

From 2015 to 2016, several important studies have been published on ischemic heart disease. The present article will mention some of the most salient studies.

In chronic ischemic heart disease, a notable publication was the report of the long-term results of the COURAGE[1] trial. In this trial, 2287 stable patients were randomized to initially receive optimal medical treatment or additional coronary angioplasty. The data from 1211 patients (53% of the original sample) with a median follow-up of 6.2 years are in line with those of the original study; that is, no differences were found in mortality between the 2 treatment groups (24% vs 25%; P = .76).[1]

Several recent studies have reported that control of cardiovascular risk factors is inadequate, even in secondary prevention. The EVITA[2] trial analyzed the efficacy of varenicline in achieving smoking cessation in patients with a recent acute coronary syndrome. In this multicenter, controlled, double-blind trial, 302 patients hospitalized for an acute coronary event (mean age, 55 years; 75% males; ST-segment elevation in 56%; mean number of cigarettes smoked, 21/d) were randomized to receive varenicline or placebo for 12 weeks. The primary aim was abstinence at 24 weeks, confirmed by determination of exhaled carbon dioxide. Patients who received the drug smoked significantly less than the control cohort (abstinence, 47.3% vs 32.5%), with a similar rate of adverse events at 30 days after treatment discontinuation.[2]

Beyond cardiovascular risk, a Swedish group has confirmed the importance of periodontal disease in the genesis of myocardial infarction. The PAROKRANK[3] trial researchers analyzed 805 patients aged < 75 years with a first myocardial infarction