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Internal Medicine

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ABSTRACT & COMMENTARY

Statins After an MI: Does it Happen?

By Martin S. Lipsky, MD

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Dr. Lipsky is a retained consultant for Health Solutions & Strategies.

SYNOPSIS: Following hospital discharge for a heart attack, the majority of Medicare patients do not get recommended high-intensity statin therapy.

SOURCE: Rosenson RS, Kent SJ et. a l. Underutilization of high-intensity statins therapy after hospitalization for coronary artery disease. *J Am Coll Cardiol* 2015;65:270-275.

Following a hospitalization for coronary heart disease (CHD) or acute coronary syndrome (ACS), randomized trials demonstrate that high-intensity atorvastatin is more effective than either placebo or low- to moderate-intensity therapy with either pravastatin or atorvastatin.[1-3] Based on this evidence, the American College of Cardiology and the American Heart Association guidelines recommend high-intensity therapy in cases of an acute cardiac event, and recommend therapy be initiated before discharge.

Previous studies indicate that more than 80% of patients receive a statin after a myocardial infarction (MI) or coronary revascularization.[4-5] However, few studies examined the percentage of individuals who met guidelines and were prescribed and filled a script for high-intensity statins. One previous study demonstrated that only about 1 in 3 patients filled a high-intensity statin script,[6] and that the only correlation with taking a high-intensity statin after 1 year was being prescribed a high-intensity statin at discharge.

The authors used a random sample of Medicare beneficiaries between ages 65-74 who filled a statin script after being hospitalized for a MI or for bypass surgery from 2007-2009. Of the more than 8000 patients who filled a statin script, only 27% of the first post-discharge scripts were for a high-intensity

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[INSIDE]

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statin such as 40-80 mg of atorvastatin or 80 mg of simvastatin. The percentage that filled a high-intensity statin post-discharge was 23.1%, 9.4%, and 80.7% for beneficiaries not taking statins pre-hospitalization, taking low- to moderate-intensity statins, and taking high-intensity before the CHD event, respectively. Only 11.5% of beneficiaries whose first post-discharge statin fill was for a low- or moderate-intensity statin eventually filled a high-intensity statin within 365 days of discharge.

The authors conclude that the majority of Medicare beneficiaries do not fill high-intensity statin scripts after hospitalization for CHD.

■ COMMENTARY

Despite evidenced-based guidelines supporting the use of high-intensity statins in a high-risk population, Rosenson and colleagues found that only about 1 in 4 individuals hospitalized for a coronary event receive high-dose statins. To no great surprise, the greatest predictor of who fills a high-intensity statin was being on one before hospitalization. Even though one might argue that physicians are reluctant to use a high dose initially and prefer to titrate the dose up if tolerated, by years end, the percentage on high-intensity therapy only increased to about 35%. Unfortunately, the Medicare dataset used did not allow for an analysis of characteristics such as liver disease, dose intolerance, or renal disease that may account for such low compliance with the guidelines.

So why are doctors reluctant to use these medicines as recommended? One explanation may be that physicians are unaware of the recommendation, although physicians participating in the care of patients with MIs or bypass surgery likely would be familiar with this recommendation. It is possible that despite their physician's recommendation, patients might be reluctant to fill these scripts. However, in the face of a significant cardiac event, most patients will at least follow their physician's initial advice.

So what explains such a low level of compliance with a recommended guideline? It likely relates to concerns about the risk of using high-dose statins in an older population who are the most vulnerable to side effects. Statins may have gotten a bad rap early on, with some early studies reporting the risk of adverse effects as high as 20%; however, a recent Johns Hopkins study reviewing 20 years of research concluded that the risks linked to statins, including muscle toxicity, diabetes, and dementia, are very low and far outweighed by a statin's benefits. The authors found little evidence of significant myalgias and only a modest increase in myositis. Rhabdomyolysis was primarily associated with regimens that are no longer recommended. Regarding blood sugar elevations, this evidence-based review found only a modest increase in the risk of type 2 diabetes with statins.

This association was found only among people with other risk factors for diabetes, raising the question of whether diabetes might have inevitably developed even without statin use. Another meta-analysis by Macedo et al found an increase in muscle complaints and creatine phosphokinase levels with statin use, but also concluded that the absolute excess risk of side effects with statins is very small compared to its beneficial effects in patients whose risks exceed a certain threshold of cardiovascular risk. The findings by Rosenson suggest that physicians might be underestimating the benefit:risk ratio for high-intensity statins in those with a coronary event.

So what is the take home message for the primary care physician? Consider reviewing how well you adhere to the guidelines regarding high-dose statin therapy. If you are not prescribing these medications as recommended, then perhaps the next step is to determine why not. If it is because of the concern about adverse effects, then I would encourage you to review the cited meta-analyses and decide if you agree with their assessments. If it is because you want to use the strategy in older patients of "start low, go slow," then consider a tracking system to allow you to remember to increase the dose in patients without significant side effects. ■

REFERENCES

1. Cannon CP, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;350:1495-1504.
2. LaRosa JC, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med* 2005;352:1425-1435.
3. LaRosa JC, et al. Safety and efficacy of atorvastatin-induced very low-density lipoprotein cholesterol levels in patients with coronary heart disease (a post-hoc analysis of the treating to new targets [TNT] study). *Am J Cardiol* 2007;100:747-775.
4. Roe MT, et al. Treatments, trends, and outcomes of acute myocardial infarction and percutaneous coronary intervention. *J Am Coll Cardiol* 2010;56:254-263.
5. Peterson ED, et al. Trends in quality of care for patients with acute myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006 *Am Heart J* 2008;156:1045-1050.
6. Arnold SV, et al. Beyond medication prescription as performance measures: Optimal secondary prevention medication dosing after acute myocardial infarction. *J Am Coll Cardiol* 2013;62:1791-1801.

ABSTRACT & COMMENTARY

Does a Link Exist Between OSA and CAD?

By Barbara A. Phillips, MD, MSPH

Professor of Medicine, University of Kentucky; Director, Sleep Disorders Center, Samaritan Hospital, Lexington

Dr. Phillips serves on the speakers bureau for PotomaCME.

SYNOPSIS: Obstructive sleep apnea is associated with coronary artery calcification in non-obese individuals, but the effect is largely attenuated by body mass index.

SOURCE: Luyster FS, et al. Relation of obstructive sleep apnea to coronary artery calcium in non-obese versus obese men and women aged 45-75 years. *Am J Cardiol* 2014;114:1690-1694.

This report results from a secondary analysis of the Pittsburgh-based Heart Strategies Concentrating on Risk Evaluation (Heart SCORE) study. For this analysis, the investigators used the baseline data on a subset (n = 252) of participants who had computed tomography and home sleep testing within 24 months of each other and whose weight was fairly constant. The final group was largely white (56%), male (61%), and the mean age was 61 years. Most of these participants (76%) had significant coronary artery calcification (CAC) and 37% had sleep apnea, as it was defined in this study. The main finding of the study was that the odds ratio for the presence of CAC was 2.33 (1.01-5.38) for participants with sleep apnea, compared to those without ($P < 0.05$) after adjustment for age, gender, race and ethnicity, smoking status, diabetes, hypertension, and dyslipidemia. However, after adjustment for body mass index (BMI), the relationship was no longer statistically significant. Furthermore, there was no association between severity of sleep-disordered breathing and CAC in those whose BMIs were over 30 kg/m^2.

■ COMMENTARY

This study adds to the growing body of evidence that suggests a link between obstructive sleep apnea and coronary artery disease (CAD). However, based on these data alone, one might conclude that the relationship is mediated by obesity, which is common to both conditions. I suspect that this lackluster finding is largely due to the definition of sleep apnea that was used here, which was based on flow signals from portable studies. Measures of apnea and hypopnea (used to calculate the apnea plus hypopnea index [AHI]) that are based on measures of flow alone are not particularly reproducible, predictive, or reliable; interscorer reliability and predictive value are greatly improved by the use of some measure of oxygen desaturation (either 3% or 4%) to define respiratory events.[1-3] Indeed, relationships between AHI and CAC have been demonstrated to be quite robust when based on definitions of sleep apnea in which the criteria for apnea and/or hypopnea include some measure of oxygen desaturation.[4,5] Data are accumulating that the degree and duration of oxygen desaturation appear to be the primary predictors of most adverse outcomes, including even cancer, in patients with sleep-disordered breathing.[6] We simply don't have that data in the current study.

More compelling evidence that sleep apnea is associated with CAD comes from studies in which sleep apnea had been treated and markers or predictors of CAD are improved. One such trial was a randomized trial on the effects of 4 months of continuous

positive airway pressure therapy on early markers of atherosclerosis, which demonstrated decreases in intima-media thickness, C-reactive protein, and catecholamines, strongly suggesting that sleep apnea is an independent risk factor for atherosclerosis.[7]

In conclusion, it appears that sleep apnea is a risk factor for CAD, but the effect is confounded by obesity and likely related to oxygen desaturation. ■

REFERENCES

1. Lin CL, et al. Comparison of the indices of oxyhemoglobin saturation by pulse oximetry in obstructive sleep apnea hypopnea syndrome. *Chest* 2009;135:86-93.
2. Redline S, et al. The scoring of respiratory events in sleep: Reliability and validity. *J Clin Sleep Med* 2007;3:169-200.
3. Whitney CW1, et al. Reliability of scoring respiratory disturbance indices and sleep staging. *Sleep* 1998;21:749-757.
4. Arik B, et al. Advanced age and apnea-hypopnea index predict subclinical atherosclerosis in patients with obstructive sleep apnea syndrome. *Multidiscip Respir Med* 2013;8:9.
5. Jung HH, et al. Sleep apnea, coronary artery disease, and antioxidant status in hemodialysis patients. *Am J Kidney Dis* 2005;45:875-882.
6. Campos-Rodriguez F1, et al; Spanish Sleep Network. Association between obstructive sleep apnea and cancer incidence in a large multicenter Spanish cohort. *Am J Respir Crit Care Med* 2013;187:99-105.
7. Drager LF, et al. Effects of continuous positive airway pressure on early signs of atherosclerosis in obstructive sleep apnea. *Am J Respir Crit Care Med* 2007;176:706-712.

ABSTRACT & COMMENTARY

B-type Natriuretic Peptides (BNP) Values Improve CVD Risk Prediction

By Harold L. Karpman, MD, FACC, FACP

Clinical Professor of Medicine, UCLA School of Medicine

Dr. Karpman reports no financial relationships relevant to this field of study.

SYNOPSIS: Elevated BNP values in a large cohort of women with numerous CV events modestly improved measures of CVD risk prediction.

SOURCES: Everett BM, et al. B type natriuretic peptides improve cardiovascular disease risk prediction in a cohort of women. *J Am Coll Card* 2012;64:1789-1797; Iwanga Y, et al. B type natriuretic peptide strongly reflects diastolic wall stress in patients with chronic heart failure: Comparison between systolic and diastolic heart failure. *J Am Coll Cardiol* 2006;47:742-748.

Measurement of B-type natriuretic peptides (BNP) values have gained acceptance as a tool for diagnosis and risk stratification in patients experiencing shortness of breath and chest pain.[1-3] Elevated BNP levels have demonstrated a consistent association with adverse cardiovascular outcomes in stable patients with and without established cardiovascular disease (CVD),[4] but only a few studies have examined whether BNP levels improve clinical risk prediction in the general population.[5-8]

Recognizing that women have a higher level of BNP values than do men,[5] and yet have a lower absolute risk for CVD than men of similar age and risk factor burden,[9] Everett and colleagues decided to evaluate the relationship between BNP values and incident CVD in women. They analyzed a prospective case cohort within the Women's Health Initiative (WHI) observational study, which is a multi-ethnic cohort of 93,676 postmenopausal women ages 50-79 who were enrolled between 1994 and 1998 at 40 sites across the United States. BNP levels were obtained at baseline in 1821 women who subsequently had a major cardiovascular event, and the BNP value in this group was compared to BNP values obtained from a reference cohort of 1992 women. The results of the study determined that the BNP values modestly improved measures of CVD risk prediction.

■ COMMENTARY

Data supporting BNP values as a cardiovascular risk predictor have been predominantly derived from male cohorts.[4] Two randomized, controlled trials[10,11] that were recently published demonstrated the efficacy of primary prevention strategies focused on patients with elevated BNP levels, thereby demonstrating the potential utility of BNP-based risk predictions. Recognizing that women were under-represented in the current cardiovascular risk prediction literature, Everett and colleagues

carefully analyzed the data from the WHI, which is a large, carefully characterized cohort with a high prevalence of events providing tremendous power to investigate risk prediction among women who were otherwise under-represented in the current literature. The "hard" endpoints that they used were a composite of cardiovascular death, myocardial infarction, and stroke (congestive heart failure was not included). Although the present study results contribute important information to help refine risk prediction, many important clinical questions remain unanswered, including those related to pathophysiology and clinical translation. Our current understanding of BNP levels is that they are primarily related to ventricular wall stress, and it remains unclear why BNP values should be predictive of the primary endpoint components utilized in this study. Further investigation into the underlying mechanism of why elevated BNP values are associated with an increased frequency of CVD may eventually shed some light on cardiovascular event pathogenesis.

In summary, the results of the Everett study may prove to be clinically useful because recent studies have suggested that targeting intensified cardiovascular care on the basis of multiple clinical measurements, including BNP levels, can reduce cardiovascular events,[10,11] at least in high-risk populations. Adding BNP measurements to the growing list of risk factors may, therefore, prove to be quite beneficial in the long term. ■

REFERENCES

1. Maisel AS, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002;347:161-167.
2. Januzzi JL, et al. The N-terminal pro-BNP investigation of dyspnea in the emergency department (PRIDE) study. *Am J Cardiol* 2005;95:948-954.
3. Thygesen K, et al. Recommendations for the use of natriuretic peptides in acute cardiac care: A position statement from the Study Group on Biomarkers in Cardiology of the ESC Working Group on Acute Cardiac Care. *Eur Heart J* 2012;33:2001-2006.
4. Di Angelantonio E, et al. B-type natriuretic peptides and cardiovascular risk: Systematic review and meta-analysis of 40 prospective studies. *Circulation* 2009;120:2177-2187.
5. Olson MH, et al. N-terminal pro- brain natriuretic peptide, but not high-sensitivity C-reactive protein improves cardiovascular risk prediction in the general population. *Eur Heart J* 2007;28: 1374 -1381.
6. Zethelius B, et al. Use of multiple biomarkers to improve the prediction of death from cardiovascular causes. *N Engl J Med* 2008;358:2107-2116.
7. Melander O, et al. Novel and conventional biomarkers for prediction of incident cardiovascular events in the community. *JAMA* 2009;302:49-57.
8. Blankenberg S, et al. Contribution of 30 biomarkers to 10-year cardiovascular risk estimation into population cohorts: The MONICA, risk, genetics, archiving and monographs (MORGAM) biomarker project. *Circulation* 2010;121:2388-2397.
9. National Heart, Lung, and Blood Institute. Incidence and Prevalence: 2006 Chart Book on Cardiovascular and Lung Diseases. Available at:http://wwwnhlbi.nih.gov/resources/docs/06_ip_chtbk.pdf. Accessed August 14, 2013.
10. Ledwidge M, et al. Natriuretic peptide-based screening and collaboration care for heart failure: The STOP-HF randomized trial. *JAMA* 2013;310:66-74.
11. Huelsmann M, et al. PONTIAC (NT-proBNP selected prevention of cardiac events in population of diabetic patients without a history of cardiac disease): A prospective randomized controlled trial. *J Am Coll Card* 2013;62:1365-1372.

PHARMACOLOGY UPDATE

Secukinumab Injection (Cosentyx™)

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; and Assistant Professor of Medicine, University of California, San Francisco. Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA

Drs. Elliott and Chan report no financial relationships relevant to this field of study.

A recombinant, fully humanized monoclonal antibody to interleukin-17 has been approved for the treatment of moderate-to-severe plaque psoriasis. Secukinumab is marketed by Novartis as Cosentyx.

INDICATIONS

Secukinumab is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.[1]

DOSAGE

The recommended dose is 300 mg (two injections) given subcutaneously weekly for five doses (week 0, 1, 2, 3, and 4). This is followed by 300 mg every 4 weeks.[1] Some patients may only require 150 mg per dose. Secukinumab is available as a single-use 150 mg Senso-ready pen or prefilled syringe for self injection. It is also available as single-use (150 mg) lyophilized powder for health care professional use.

POTENTIAL ADVANTAGES

Secukinumab targets a different cytokine in the pathogenesis of psoriasis.[2]

POTENTIAL DISADVANTAGES

Increased infection rates have been associated with secukinumab treatment.[1,2] Most common adverse events reported were nasopharyngits, diarrhea, and upper respiratory tract infections.[1] These ranged from 3-12%.

COMMENTS

The safety and efficacy of secukinumab were evaluated in four clinical trials.[1,3,4] These adult participants (n = 2403) had plaque psoriasis (minimum 10% body surface involvement and Psoriasis Area and Severity Index [PASI] ≥ 12) and were candidates for phototherapy or systemic therapy. Patients were randomized to secukinumab 150 mg, 300 mg, an active control, or placebo.[1,2] Secukinumab was administered at weeks 0, 1, 2, 3, and 4, followed by dosing every 4 weeks. The active control was etanercept 50 mg twice weekly for 12 weeks, then once weekly to week 51. Two trials were 12 weeks in duration and two were 52 weeks, with assessment at 12 weeks.

The primary endpoints were proportion of participants who achieved a reduction in PASI of at least 75% (PASI75), and treatment success was based on the modified Investigator's Global Assessment (IGA). PASI is a composite instrument for psoriasis severity (i.e., erythema, induration, scaling, and percent body-surface affected). IGA is a 5-point clinician assessment of overall disease severity (0 = clear, 1 = almost clear, 4 = severe). PASI75 at week 12 for the four studies ranged from 67-71% for secukinumab 150 mg, 75-87% for 300 mg, and 0-5% for placebo. IGA for clear or almost clear ranged from 51-53% for 150 mg, 62-73% for 300 mg, and 0-3% for placebo. Eighty-one percent to 84% of responders at week 12 maintained PASI75 for 52 weeks on 300 mg and 72-82% on 150 mg. The percentage maintaining IGA of clear or almost clear were 74-80% and 59-68%, respectively. In the study with an active control, etanercept, PASI75 was 44% and IGA 27%. The median times for 50% reduction of baseline PASI score was 3 weeks for the 300 mg dose and 3.9 weeks for the 150 mg dose vs 7 weeks for etanercept. The adverse drug reaction profiles were similar between secukinumab and etanercept;[3] however, Candida infections were more frequent with secukinumab (2.3-4.7%) compared to 1.2% for etanercept.[3]

CLINICAL IMPLICATIONS

Secukinumab is the first in the class monoclonal antibody to interleukin-17A, which is regarded as an important cytokine in the pathogenesis of psoriasis.[2,4] Previous drugs have targeted TNF and IL23. Secukinumab provides another effective treatment for plaque psoriasis. It appears to be more effective than etanercept but similar in magnitude to other biological agents (e.g., adalinumab and ustekinumab.[6,7] The wholesale cost is $3420 per 300 mg dose. ■

REFERENCES

1. Cosentyx Prescribing Information. Novartis Pharmaceuticals. January 2015.
2. Kirham BW et al. *Immunology* 2013;141:133-42.
3. Langley RG et al. Secukinumab in plaque psoriasis — results of two phase 3 trials. *N Engl J Med* 2014;37:326-338.
4. Blauvelt A et al. Secukinumab administration by pre-filled syringe: Efficacy, safety and usability results from a randomized controlled trial in psoriasis. *Br J Dermatol* 2014;172:484-493.
5. Martin DA et al. The emerging role of IL-17 in the pathogenesis of psoriasis: Preclinical and clinical findings *J Invest Dermatol* 2013;133:17-26.
6. Humira Prescribing Information. AbbVie Inc. December 2014.
7. Stelare Prescribing Information. Janssen Biotech. March 2014.

Clinical Briefs

By Louis Kuritzky, MD

Modifying the Home Environment to Prevent Falls

SOURCE: Keall MD, et al. *Lancet* 2015;385: 231-238.

Falls in the home setting are a commonplace source of serious injury. In the recent past, most studies on falls have addressed children, disabled persons, or the very elderly. There is little information on more general populations, or whether a standardized set of environmental modifications — not designed to address any specific disability — would reduce falls and their consequences.

Keall et al studied households (n = 842) in New Zealand, including persons of all ages. Subjects were identified as holders of what is called a "community services card," which indicates that either the person is low income, unemployed, a student, over the age of 65 years, or receives governmental health benefits related to illness.

Half of the homes in the study received no intervention. The other half received home modifications, including handrails for steps and stairs (inside and out), repairs to window catches, tub and toilet grab-rails, good quality outside lighting, high-visibility slip resistant edging for outside steps, securing of carpet edges, non-slip bathmats, slip-resistant resurfacing for decks/patios, and a pamphlet on home safety. All modifications were provided free of charge by a qualified builder.

Compared to non-intervention homes (control) over the 3-year period of observation, home modification reduced falls by 26% per year and all injuries by 39% per year (both statistically significant). The average cost of the intervention was $564 New Zealand dollars, which by current currency conversion charts is $423 U.S. ■

Every Other Day Tadalafil for Lower Urinary Tract Symptoms and Erectile Dysfunction

SOURCE: Choi H, et al. *J Int Impot Res* 2014;27: 33-37.

Although the incidence of erectile dysfunction (ED) and lower urinary tract symptoms (LUTS) both increase with age, there is an as-yet ill-explained independent association of LUTS with ED. That is, within each age decile, more severe LUTS is associated with more severe ED.

The PDE-5 inhibitor tadalafil is approved for treatment of LUTS or ED. The dose used to treat LUTS is less than the usually effective dose for ED, but men treating LUTS with low-dose tadalafil (5 mg daily) also report improvements in sexual function.

Tadalfil has the longest half-life of currently available PDE5 inhibitors: 18.5 hours. Based on this long half-life, might tadalafil provide similar symptom improvement in LUTS and ED if provided every other day? Choi et al performed a trial in men (n = 144) with symptom scores consistent with LUTS and ED to compare 5 mg tadalafil daily vs every other day. LUTS symptoms and sexual dysfunction symptoms improved to a similar degree with both regimens. Although there were some differences in outcomes that were statistically significant in favor of the daily regimen, differences were generally small and of doubtful clinical significance. Men may achieve comparable symptom improvement for ED and LUTS using tadalafil 5 mg every other day as with every day dosing. ■

Reassuring Safety Data about Incretins and CHF

SOURCE: Yu OH, et al. *Diabetes Care* 2015;38: 277-284.

The class of medications used to treat diabetes (and obesity), known as "the incretins," includes several DPP4 inhibitors and GLP1 agonists. These agents have achieved a favorable status in prescribing algorithms because of the combination of their low risk of hypoglycemia, impact on weight (neutral for DPP4, weight loss for GLP1), and effects on postprandial glucose attributed to glucagon blunting.

Nonetheless, analysis of the SAVOR-TIMI trial, in which a 27% increased risk of congestive heart failure (CHF) was found in persons taking saxagliptin compared to placebo, spurred concerns that incretins might worsen risk for CHF. Other trials with other DPP4 inhibitors did not find a statistically significant increased CHF risk (e.g., the EXAMINE trial with alogliptin).

Yu et al performed a nested case-control analysis of diabetic patients who received new prescriptions for antidiabetic drugs and were free of CHF at that time. They compared the incidence of CHF in patients who had been prescribed incretins vs two or more other oral agents for their diabetes.

Among a population of 57,737 diabetics, 1118 incident cases of CHF were identified. Incident CHF was not more common in persons prescribed incretins; to the contrary, there was a trend toward less CHF in incretin-treated patients (odds ratio = 0.85; confidence interval, 0.62-1.16). These data are reassuring about the safety profile of incretins in regards to CHF. ■

CME INSTRUCTIONS

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CME QUESTIONS

1. Following an acute coronary event, the benefits of high-intensity statins outweigh their risk in a 70-year-old woman.

a. True

b. False

2. The incidence of myositis in patients older than age 65 taking a high-intensity statin:

a. is high and requires monitoring with creatine phosphokinase levels.

b. is high and usually indicates a high likelihood of rhabdomyolysis.

c. is low and not a reason to avoid prescribing a high-dose statin in someone with high CV risk.

d. is high and rhabdomyolysis is heralded by myalgias, and the statin should be discontinued if a patient complains of myalgia.

3. Sleep apnea is associated with coronary artery disease:

a. never.

b. only in obese people younger than the age of 35.

c. with regard to degree of oxygen desaturation.

d. and there is no evidence that CPAP can reduce the risk.

4. With respect to CVD risk prediction in women, elevated BNP values:

a. are of no value.

b. modestly improve risk prediction.

c. are of greater value than in men.

d. are of greater value than were other CVD risk factors.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.

[IN FUTURE ISSUES]

The Accelerating Cost of Generic Drugs