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ABSTRACT & COMMENTARY

Statins, Cognitive Decline, and Dementia

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis of the ASPREE database showed that with almost five years of follow-up, statins are not associated with cognitive decline or dementia in a large group of elderly subjects in whom multiple tests of cognition were performed serially.

SOURCE: Zhou Z, Ryan J, Ernst ME, et al. Effect of statin therapy on cognitive decline and incident dementia in older adults. *J Am Coll Cardiol* 2021;77:3145-3156.

There is little evidence supporting a connection between taking statins and experiencing cognitive decline and dementia. Zhou et al analyzed the systematically collected comprehensive cognitive data in the Aspirin in Reducing Events in the Elderly (ASPREE) trial to determine the association of statin use with incident dementia and mild cognitive impairment (MCI), to assess the influence of statin lipophilicity on neurocognitive effects, and to identify factors that may modify statin effects on cognition.

ASPREE was a large prospective, randomized, placebo-controlled study of daily low-dose aspirin in subjects > age 70 years or > age 65 years in U.S. minorities. Subjects presented with no prior cardiovascular (CV) disease events or dementia and scored > 78 on the Modified Mini-Mental State Examination (3MS). Investigators recruited participants between 2010 and 2014 in Australia and the United States.

Taking a closer look at ASPREE, Zhou et al grouped subjects by their baseline statin use, resulting in 12,948 not on statins and 5,898 on statins for closer examination. The mean age was 74 years, and 56% were women. More subjects in the statin group were diabetic or hypertensive and were on more concomitant medications. Cognitive function was assessed at baseline; at one, three, and five years; and after the final visit (maximum seven years). Multiple covariates were assessed that could affect neurocognitive function or could interact with statins.

During the median follow-up of 4.7 years, Zhou et al identified 566 cases of dementia. Using statins was not associated with the risk of dementia (HR, 1.16; 95% CI, 0.97-1.40; *P* = not significant). MCI developed in 380 subjects and also was not associated with statin use (HR, 1.44; 95% CI, 0.90-2.29; *P* = not significant). Although statin users recorded lower global cognition scores at baseline, there

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was no significant difference between statin users and no use of statins groups over the follow-up period. There were no differences in outcomes among those using lipophilic vs. hydrophilic statins. There were interactions between baseline cognitive scores and statin therapy for the development of dementia. No other interaction effects were found, including baseline LDL cholesterol levels. In addition, sensitivity analyses of the various comorbidities did not alter the results. The authors concluded that in older adults, there was no association between statin use and the development of MCI or dementia.

■ COMMENTARY

In 2012, the FDA issued a warning indicating statins had been reported in their adverse events reporting system as causing short-term cognitive impairment.[1] This caused quite a stir, and it was hard to convince older patients to take statins. Since then, other investigators reviewed the evidence on which the FDA based its decision, drawing different conclusions.[2-4]

ASPREE focused on patients > age 65 years who completed several cognitive function tests over about five years. Also, the outcomes were adjudicated by a committee, sensitivity analyses were conducted, and researchers explored whether lipophilicity of the statin was of importance. Zhou et al showed statin use was not associated with incident MCI or dementia or that cognitive function declines over time on statins. In addition, they did not find that lipophilicity influenced the results, and sensitivity analyses did not show that comorbidities affected the results. However, in those in the lowest quartile of normal cognitive function at baseline, there was an interaction suggesting a potential statin effect on dementia risk. For this reason, the investigators urged caution in interpreting their data until randomized, controlled trials in progress are completed.

There were other weaknesses to the Zhou et al study. It was a post-hoc analysis of an observational study conducted for other reasons, so there could be residual confounding. There could be an indication bias since the statin group exhibited more CV disease at baseline. Reverse causality is another consideration as declining cognition within the normal range could have been an indication for statins to prevent any CV components to cognitive dysfunction. Also, these were highly selected subjects with few comorbidities, less frailty, and who were taking fewer drugs than an older general population would have been. In addition, there were no data on LDL cholesterol levels, dosage of the statins, and the length of statin use before the study. Finally, this was a relatively short-term study.

The main issue is whether the risk of statins outweighs the benefits for older patients. In this regard, some believe heart failure outweighs CV events in older subjects, making statin use more problematic. Since their introduction, the adverse effects of statins have been of great interest. The most serious, rhabdomyolysis, is rare. Early on, liver function was a concern, but routine testing of liver function is no longer recommended since serious liver disease also is rare. There seems to be a real association with diabetes, but it is believed the benefits of statins outweigh this small risk. Muscle symptoms have become the biggest reason patients quit taking statins, but recent controlled studies have shown most of these symptoms are not reproducible. There has been fear that too low cholesterol levels could adversely affect the nervous system, but studies of the PCSK9 inhibitors, which can lower LDL cholesterol to < 20 mg/dL, have not borne this out. Thus, cognitive dysfunction is the new big worry with statins. The Zhou et al study is reassuring in that over five years, no significant deterioration in cognitive function was observed in a higher-risk elderly population studied serially by multiple cognition tests. ■

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ABSTRACT & COMMENTARY

Important Lessons About Edge-to-Edge Repair

By Jeffrey Zimmet, MD, PhD

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SYNOPSIS: This analysis of mitral surgery after failed transcatheter edge-to-edge repair demonstrates high rates of valve replacement as opposed to repair. Surgical mortality was higher than predicted but was significantly lower in high-volume centers.

SOURCE: Chikwe J, O'Gara P, Fremes S, et al. Mitral surgery after transcatheter edge-to-edge repair: Society of Thoracic Surgeons database analysis. *J Am Coll Cardiol* 2021;78:1-9.

In 2013, the FDA approved transcatheter edge-to-edge repair (TEER) to treat severe degenerative mitral regurgitation in patients at high and prohibitive risk for surgery. In 2019, this approval expanded to include a subset of patients with heart failure and significant functional mitral regurgitation despite optimal medical therapy. The use of the MitraClip system has grown; to date, approximately 15,000 of these procedures have been performed in the United States. As a minimally invasive approach, TEER can be remarkably effective in the treatment of mitral disease. Yet, recent real-world retrospective analyses have shown between 20% and 30% of patients are left with residual or recurrent moderate or severe mitral regurgitation within a year of the procedure. In addition, some fraction of patients trade regurgitation for stenosis.

Some patients with unsatisfactory results ultimately go to surgery. Considering patients gain entry to TEER partially by being judged as high risk for surgery, one would assume this would remain true for surgery after a failed transcatheter approach. Chikwe et al mined the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database to identify and characterize patients who have undergone surgical reintervention after TEER. During the period from June 2014 to July 2020, 524 such patients were confirmed. After exclusion of emergencies and patients with prior mitral surgery, a cohort of 463 patients was available for analysis.

The average age of patients was 76 years, and half were women. The annual number of such surgeries increased year over year, with 32 procedures in 2015 and 126 in 2019. One of the most striking results was that only 22 patients underwent mitral valve repair; the remainder underwent valve replacement, with a bioprostheses in most cases. Just over half of patients underwent extra procedures in addition to mitral valve surgery. The remainder (48.8%) underwent isolated mitral valve surgery. Add-on procedures included concomitant tricuspid repair or replacement in 152 patients for moderate or severe tricuspid regurgitation, and coronary artery bypass grafting in 57 patients. In the overall cohort of patients undergoing reintervention for failed MitraClip, the mortality rate within 30 days was 10.6%. Among the subset of patients undergoing isolated mitral valve surgery, the median STS predicted risk of mortality was 6.5%, while the observed mortality was 10.2%.

A total of 357 different surgeons performed the included procedures at 227 unique hospitals. An analysis of mortality by operative case volume revealed only centers in the highest quintile of volume (> 10 cases) recorded a significantly lower operative mortality rate (2.6%, or two of 76). Operative mortality was 12.4% (n = 64 of 515) in centers that performed fewer procedures.

Notably, 177 patients were labeled with underlying degenerative mitral valve disease. Successful mitral valve repair in this group was similar (n = 12) to the entire cohort. Although the predicted risk of mortality was 7.3% in this group, the observed mortality was somewhat lower at 6.2% (n = 11 of 175). Mortality was significantly lower in those surgeries that were labeled as elective (n = 3 of 108, 2.8%) as opposed to urgent. The authors concluded surgery after failed MitraClip was uncommon but increased steadily during the study period and was associated with low rates of successful mitral repair. The highest-volume centers achieved significantly lower mortality than others.

■ COMMENTARY

It should come as no surprise that observed mortality was high after surgical reintervention for patients who, in theory, were at high risk for surgery in the first place. The data collection from the STS database leaves many gaps that would be pertinent to this analysis. For example, no data are available on the timing of surgery relative to the TEER procedures, the number of clips involved, or whether the surgical treatment was for mitral regurgitation or stenosis. Most patients who were classified with non-degenerative mitral regurgitation had no further information as to the etiology of the regurgitation. Importantly, only patients who underwent surgery were included, so no conclusions can be drawn about the presumably larger population of patients with failed TEER who were turned down for surgery.

Also notable was the rate of successful valve repair, as opposed to replacement, was extremely low. This was true in patients whose initial valve pathology was listed as degenerative, as well as in the entire population. Surgery as the upfront treatment (not after unsuccessful TEER) for degenerative mitral regurgitation should be expected, in experienced centers, to be successful about 95% of the time. This is considered the gold standard for treatment of this subset of mitral regurgitation patients. The relatively low operative mortality (2.8%) seen in the subset of degenerative regurgitation patients undergoing elective procedures certainly calls into question whether these patients were characterized correctly as high surgical risk to begin with. The low rate of subsequent repair reminds us that even successful surgery after failed TEER results in a second-best outcome of valve replacement. It is in this context that the current data can inform patient selection for TEER and may play a role in patient consent. For patients with failed TEER who do require surgery, strong consideration should be given to referral to experienced centers. ■

ABSTRACT & COMMENTARY

Anticoagulation Plus Antiplatelet Therapy in Chronic Atherosclerosis

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis of the COMPASS trial for the secondary endpoint of mortality showed the combination of low-dose rivaroxaban and aspirin significantly lowered the all-cause mortality rate vs. low-dose aspirin alone.

SOURCE: Eikelboom JW, Bhatt DL, Fox KAA, et al. Mortality benefit of rivaroxaban plus aspirin in patients with chronic coronary or peripheral artery disease. *J Am Coll Cardiol* 2021;78:14-23.

The Cardiovascular Outcomes for People Using Anticoagulant Strategies (COMPASS) trial compared rivaroxaban 2.5 mg twice a day plus aspirin 100 mg/day (RA group) to aspirin alone (AA group) in patients with known coronary or peripheral vascular disease. The combined primary endpoint was cardiovascular (CV) death, stroke, or myocardial infarction (MI). After 1,323 events, the trial ended early because of favorable outcomes in the RA group.

Subsequently, it was approved for this secondary prevention goal in more than 100 countries, including the United States. The components of the combined primary endpoint constituted the three secondary endpoints of the trial. One was mortality, both all-cause and CV. COMPASS mortality and the factors that influenced mortality were the subject of this report by Eikelboom et al. Mortality was classified as CV when no other clear cause of death was discovered. The potential risk factors for death considered were the extent of polyvascular disease, chronic kidney disease (estimated GFR less than 60 mL/minute), mild to moderate heart failure (EF > 30% or New York Heart Association class I or II), and diabetes.

There were 18,278 patients enrolled in COMPASS at 602 sites in 33 countries who were followed for a mean of 23 months. All-cause mortality was reduced significantly (1.8 for RA vs. 2.2% for AA; HR, 0.82; 95% CI, 0.71-0.96; $P = 0.01$). CV mortality was reduced by 18% in the RA group compared to the AA group (3.4% vs. 4.1%, respectively; HR, 0.82; 95% CI, 0.71-0.96; $P = 0.01$). Coronary heart disease mortality was reduced (0.5% for RA vs. 0.7% for AA; HR, 0.73; 95% CI, 0.55-0.96; $P = 0.03$). There was no appreciable effect on non-CV mortality (1.7% for RA vs. 1.9% for AA; HR, 0.87; 95% CI, 0.71-1.08; $P = 0.20$).

When analyzing specific causes of death, there was no observed effect on non-cerebral bleeding, MI, stroke, heart failure, or sudden death. The overall

number needed to treat (NNT) to prevent one death in 30 months was 81. Patient subgroups with risk factors that reduced this NNT included chronic kidney disease (NNT = 59), diabetes (NNT = 53), polyvascular disease (NNT = 47), and heart failure (NNT = 23). In those with more than one of these risk factors, the more that were present the lower the NNT: two risk factors (NNT = 40); three risk factors (NNT = 19). The authors concluded the combination of low-dose rivaroxaban and aspirin vs. low-dose aspirin alone reduced all-cause mortality, mainly because of significant reductions in CV mortality. The authors also observed that the magnitude of the mortality benefit was greater in patients at the highest risk for a CV event.

■ COMMENTARY

The combined endpoint of mortality, stroke, and MI in the overall COMPASS trial was reduced by 24% in the RA group compared to the AA group. The secondary endpoint analysis by Eikelboom et al demonstrated this was caused mainly by a reduction in CV mortality since non-CV mortality was not affected. This reduction in CV mortality coincided with a decrease in all CV events except stroke and heart failure death. This lack of effect on heart failure death is not surprising since heart failure deaths probably are caused by arrhythmias or pump failure. These would not be expected to be influenced by rivaroxaban or aspirin. Cerebral vascular disease probably caused stroke deaths in these patients, not atrial fibrillation. Also of interest is the fact rivaroxaban alone was not superior to aspirin in COMPASS. This suggests ischemic events drive the reduction in CV mortality. The finding that higher-risk patients benefitted more from the rivaroxaban/aspirin combination suggests patients with more advanced disease are those in whom plaque rupture more likely would result in thrombus formation. Whereas in patients with milder disease, antiplatelet drugs would be sufficient, and the increased risk of an anticoagulant would not result in net clinical benefit.

In the overall COMPASS trial, major bleeding was more common in the RA group compared to the AA group, but intracranial hemorrhage and fatal bleeding were not. Also, in the mortality analysis by Eikelboom et al, fatal bleeding other than that caused by hemorrhagic stroke was rare and not different between the RA and AA groups. Although rarely fatal, major bleeding is a concern of patients and physicians. This represents a major obstacle to recommending RA for secondary prevention. The message of the Eikelboom et al analysis is patients with demonstrated atherosclerosis and two or more risk factors for a CV event are those who should be targeted for RA therapy. The authors believe the mortality benefit they have shown should tip the equilibrium between benefits and risks in such patients. ■

ABSTRACT & COMMENTARY

Iron Therapy for Acute Heart Failure

By Michael H. Crawford, MD, Editor

SYNOPSIS: Giving intravenous ferric carboxymaltose to stabilized post-acute heart failure patients with iron deficiency improved quality of life vs. placebo-treated patients within four weeks, which persisted during subsequent therapy for up to 24 weeks.

SOURCE: Jankowska EA, Kirwan BA, Kosiborod M, et al. The effect of intravenous ferric carboxymaltose on health-related quality of life in iron-deficient patients with acute heart failure: The results of the AFFIRM-AHF study. *Eur Heart J* 2021 Jun 3;ehab234. doi: 10.1093/eurheartj/ehab234. [Online ahead of print].

AFFIRM-AHF showed that for patients who were hospitalized with acute heart failure caused by reduced left ventricular ejection fraction (HFrEF) and iron deficiency (ID), treatment with intravenous (IV) ferric carboxymaltose (FCM) was safe and reduced the risk of HF rehospitalizations, but did not reduce cardiovascular death.[1] One of the prespecified secondary outcomes was health quality of life (QOL), which is the subject of the Jankowska et al report.

ID was defined as a serum ferritin < 100 ng/mL, or 100 ng/mL to 299 ng/mL if the transferrin saturation was < 20%. IV FCM was administered just before discharge from a hospitalization for acute HFrEF and at six weeks after discharge, then at 12 and 24 weeks (if necessary). Health QOL was assessed before randomization in the hospital and repeated at weeks 2, 4, 6, 12, 24, 36, and 52. Health QOL was determined by the 12-item Kansas City Cardiomyopathy Questionnaire (KCCQ-12), from which the overall summary score (OSS) and the clinical summary score (CSS) were derived for up to 52 weeks.

The 1,108 patients included in the intention to treat analysis were a mean age of 71 years, recorded a

mean EF of 33%, and 55% were men. Completion of the KCCQ-12 was 96% at week 2 and 73% at week 52. Most of this decline was because of mortality. KCCQ-12 scores ranged from 0-100, where 100 is the best QOL. The baseline OSS for the FCM group was 38 and 37 for the placebo group; the corresponding CSS were 41 and 40, respectively.

After week 4 post-discharge, FCM patients exhibited significantly greater improvements in OSS and CSS vs. placebo patients. The adjusted mean difference at week 4 was 2.9 (95% CI, 0.5-5.3; $P = 0.018$) for OSS and 2.8 (95% CI, 0.3-5.3; $P = 0.029$) for CSS. At 24 weeks, the mean difference was 3.0 for OSS (95% CI, 0.3-5.6; $P = 0.028$) and 2.9 for CSS (95% CI, 0.2-5.6; $P = 0.035$). At 52 weeks, the effect had attenuated but still favored FCM patients (OSS mean difference = 1.44 and CSS = 0.63). Sensitivity analyses that incorporated mortality and the effect of COVID-19 on QOL showed similar results to the main analysis. The authors concluded that in patients hospitalized for acute HFrEF with ID and treated with IV FCM, clinically meaningful improvements in health QOL were observed as early as four weeks after discharge and lasted up to 24 weeks.

■ COMMENTARY

The AFFIRM-AHF study led to fewer hospitalizations, but showed no effect on mortality. Staying out of the hospital could mean one feels better, but a formal analysis of QOL is preferable. Thus, this analysis of the QOL data in AFFIRM-AHF is of interest. Jankowska et al showed treatment with IV FCM started in the hospital just before discharge and continued intermittently if ID persisted for 24 weeks improved QOL by about three points on the KCCQ-12 score vs. placebo. With a score range of 0-100, a three-point advantage over placebo seems modest at best. However, as the authors argued, this is a relevant change, which correlates with subjective well-being. This is like the changes observed for other pharmacological agents, such as the gliflozins and sacubitril/valsartan, and interventions, such as exercise training. To put this in perspective, the change in KCCQ-12 scores seen with cardiac resynchronization therapy is about 10 points in "good responders" to this device therapy where overall responses are heterogeneous. The KCCQ-12 focuses on symptom frequency, physical and social limitations, and QOL impairments. The KCCQ-23 features better psychometric properties but takes more time to complete, which reduces compliance. Also, the 12-question version correlates well with the 23-question version. The attenuation in effect after 24 weeks is not entirely surprising considering no further FCM was given after 24 weeks by protocol.

ID is associated with a poor prognosis in HFrEF regardless of the presence of anemia. It is largely underdiagnosed and undertreated. One reason is the diagnosis of ID in HF is problematic. Ferritin levels are affected by inflammatory stress, renal dysfunction, malnutrition, and the catabolic state seen in severe HF. Also, volume shifts during the treatment of HF may increase or decrease ferritin levels. Interestingly, after the treatment of acute HF, ferritin levels tend to rise for six weeks without any therapy, perhaps because of lower plasma volume. Thus, to see changes in QOL at six weeks in the FCM group is remarkable.

Treating frank anemia in HF is known to improve outcomes, especially if the hemoglobin is lower than 8 g/dL. Why would iron therapy improve outcomes in the absence of frank anemia? Presumably because iron is a key component of muscle energetics. Based on the Jankowska et al study, after hemodynamic stabilization of acute HFrEF, if ID is identified, give FCM before discharge and reassess at six weeks and every three to four months after, with further administration of FCM as indicated. ■

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ABSTRACT & COMMENTARY

When in Doubt, Take It Out: Left Atrial Appendage Occlusion

By Joshua D. Moss, MD

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SYNOPSIS: In a randomized trial of patients with atrial fibrillation, left atrial appendage occlusion during elective cardiac surgery was associated with lower rates of ischemic stroke or systemic embolism after 30 days.

SOURCE: Whitlock RP, Belley-Cote EP, Paparella D, et al. Left atrial appendage occlusion during cardiac surgery to prevent stroke. *N Engl J Med* 2021;384:2081-2091.

Atrial fibrillation (AF) is a common cause of ischemic stroke, with emboli thought to originate most frequently from the left atrial appendage (LAA). Whitlock et al sought to determine whether LAA occlusion performed at the time of cardiac surgery would reduce the risk of stroke or systemic embolism when added to routine anticoagulation therapy.

A total of 4,811 patients (mean age 71 years, 67.5% male) from 105 centers in 27 countries were randomly assigned to undergo LAA occlusion or no occlusion during their scheduled surgical procedure. Patients were eligible if they were older than age 18 years, presented with a history of AF with a CHA_2DS_2-VASc score of at least 2, and were scheduled for cardiac surgery for another indication. Patients undergoing off-pump surgery, mechanical valve implantation, surgery for complex congenital heart disease, or isolated implantation of a left ventricular assist device were excluded.

Amputation and closure of the LAA was the preferred technique, used in 56% of patients. A stapler or approved surgical occlusion device also were used commonly (about 26% of patients). Percutaneous closure and purse-string closure were not permitted. Patients and all treating clinicians were blinded to the randomization assignment, while the surgeons and intraoperative teams were not involved in the post-surgical anticoagulation management or data collection. The median CHA_2DS_2-VASc score was 4. At hospital discharge, just over 80% of patients in both groups were on oral anticoagulation, decreasing slightly to between 75% and 80% at the three-year visit. Mean follow-up was 3.8 years, with follow-up completed by 98% of participants.

The primary outcome measured was first occurrence of ischemic stroke, transient ischemic attack (TIA) with positive neuroimaging, or noncerebral systemic embolism. In the first 30 days after surgery, primary outcome events were similar in the two groups: 2.2% in the LAA occlusion group and 2.7% in the no occlusion group, a statistically non-significant difference. However, a primary outcome event occurred in 2.7% of the occlusion group after 30 days vs. 4.6% in the no occlusion group, for a hazard ratio of 0.58 (95% CI, 0.42-0.80). Primary outcome results were similar using intention-to-treatment, per-protocol, and as-treated analyses. In a secondary analysis, ischemic stroke occurred in 4.6% of the occlusion group and 6.9% of the no occlusion group (HR, 0.66; 95% CI, 0.52-0.84). Mortality rates, hospitalization for heart failure, and incidence of major bleeding or myocardial infarction were not significantly different between groups.

In a further analysis of the primary outcome, point estimates favored LAA occlusion for all predefined subgroups and remained statistically significant in men; patients older than age 72 years; patients with CHA_2DS_2-VASc score ≤ 4; patients with ejection fraction $\geq 50\%$; and patients with no prior stroke, TIA, or systemic embolism. The authors concluded LAA occlusion at the time of cardiac surgery in patients with AF, most of whom continued to receive antithrombic therapy, was associated with a lower risk of ischemic stroke or systemic embolism vs. those who did not undergo this extra procedure.

■ COMMENTARY

Presented as a late-breaking trial at this year's American College of Cardiology Scientific Session, the Left Atrial Appendage Occlusion (LAAOS III) trial results are noteworthy for both the practice changes they should encourage and those they should not. Randomization was robust, with care taken to keep patients and those managing their anticoagulation blinded to group assignment. The study population was diverse, with well-distributed proportions of paroxysmal, persistent, and permanent AF and a variety of indications for cardiac surgery. Results likely are broadly applicable. The primary endpoint was simple, leaving little room for misinterpreting outcomes. A subgroup analysis suggested consistent effects across

the spectrum of patients enrolled. Barring perhaps those patients who would have been excluded from enrolling in the trial (and who generally would have been indicated for permanent anticoagulation regardless), it seems difficult to argue against LAA occlusion during cardiac surgery in just about any patient with a history of AF.

However, clinicians must take care not to mistakenly extrapolate the results as evidence for LAA occlusion to replace therapeutic anticoagulation. Considering blinding to whether LAA occlusion was performed, management of antithrombotic therapy was meant to continue as it would have otherwise. Indeed, by three years postoperation, more than 75% of patients in both groups remained on anticoagulation. Therefore, it remains unknown whether LAA occlusion alone is as protective as anticoagulation (or as protective as LAA occlusion plus anticoagulation). The study also offers no specific insight into LAA occlusion devices implanted percutaneously, such as the WATCHMAN device. The presence of endovascular hardware and potentially incomplete LAA occlusion might reduce the positive effect seen.

From an electrophysiologist's standpoint, two questions naturally arise. First, did the type and burden of AF affect the rate of stroke or systemic embolism? That would help inform future studies on potentially stopping anticoagulation or using "as-needed" anticoagulation for patients with low arrhythmia burden who undergo surgical LAA occlusion. Second, what was the efficacy of concomitant surgical ablation of AF, which about one-third of the patients underwent? That patient population also could represent a group for whom holding anticoagulation after LAA occlusion might be safe, but this would require additional study. Secondary analyses and additional studies are sure to follow the well-designed and executed LAAOS III trial. Meanwhile, it seems clear patients with AF referred for cardiac surgery are likely to benefit from concomitant LAA occlusion. ■

CME/CE QUESTIONS

1. **In the COMPASS trial, mortality analysis, the risk factor associated with the lowest number needed to treat to prevent one death using rivaroxaban plus aspirin compared to aspirin alone in vascular disease patients was:**
   a. diabetes.
   b. polyvascular disease.
   c. heart failure.
   d. all three factors combined.

2. **For patients with systolic heart failure and iron deficiency, treatment with ferric carboxymaltose resulted in significant improvements in quality of life by:**
   a. two weeks.
   b. four weeks.
   c. 12 weeks.
   d. 24 weeks.

3. **Which factor likely increases the risk of cognitive decline with long-term statin use?**
   a. Very low baseline cognitive function
   b. Use of lipophilic statins
   c. Higher baseline LDL cholesterol levels
   d. Multiple comorbidities

4. **Surgery to correct a failed transcatheter edge-to-edge repair of the mitral valve carries a 30-day mortality rate of:**
   a. 2.5%.
   b. 5%.
   c. 10%.
   d. 15%.

5. **Surgical occlusion of the left atrial appendage at the time of cardiac surgery in patients with atrial fibrillation reduced the risk of systemic embolism by what percent compared to those without it?**
   a. 6%
   b. 12%
   c. 25%
   d. 42%