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ABSTRACT & COMMENTARY

Stenting Nonculprit Lesions After STEMI: Long-Term Data Support Complete Revascularization

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: Data from the CvLPRIT trial of complete vs. culprit-only percutaneous coronary intervention in ST-segment elevation myocardial infarction (MI) show a significantly lower rate of major adverse cardiovascular events, all-cause mortality, and lower composite MI in the complete revascularization group at a median follow-up of 5.6 years.

SOURCE: Gershlick AH, Banning AS, Parker E, et al. Long-term follow-up of complete versus lesion-only revascularization in STEMI and multivessel disease: The CvLPRIT Trial. *J Am Coll Cardiol* 2019;74:3083-3094.

In recent years, investigators have published several randomized trials concerning culprit-only percutaneous coronary intervention (PCI) vs. complete revascularization (CR) in ST-segment elevation myocardial infarction (STEMI). After Complete versus Culprit-Only Revascularization Strategies to treat Multivessel Disease after early PCI for STEMI (COMPLETE), a trial that included more than 4,000 patients, it is difficult at first to know what significance to attribute to the Complete versus Lesion-only Primary PCI Trial (CvLPRIT). CvLPRIT creators randomized patients with STEMI and multivessel disease to CR or infarct-related, artery-only (IRA) PCI. CR was completed during the index procedure or prior to hospital discharge. The original CvLPRIT publication reported results at 12 months, with the primary endpoint a composite of all-cause death, recurrent MI, heart failure, and ischemia-driven revascularization. In the recent publication, long-term follow-up data were complete for 91.8% of the CR group and 92% of the IRA group.

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At a median follow-up of 5.6 years, the composite major adverse cardiovascular event (MACE) rate was significantly lower in the CR group vs. IRA group (24% vs. 37.7%; hazard ratio [HR], 0.57; 95% confidence interval [CI], 0.37-0.87; *P* = 0.0079). Although the trial was not powered for individual endpoints, the secondary composite endpoint of death or MI also favored CR, occurring in 10% of the CR group vs. 18.5% of the IRA group (HR, 0.47; 95% CI, 0.25-0.89; *P* = 0.0175).

In a landmark analysis from the 12-month time point to the end of follow-up, there was a trend toward a lower composite event rate in the CR group, but this did not meet statistical significance. The authors concluded the significantly lower rate of MACE in STEMI previously seen at one year in patients undergoing CR vs. culprit lesion-only PCI is sustained at long-term follow-up to a median of 5.6 years. At the longer-term follow-up, the composite of death and MI also was significantly lower among CR patients, with a relative risk reduction of nearly 50%.

■ COMMENTARY

There were some shortcomings associated with this investigation. CvLPRIT was not large. The authors of the original trial recruited only 296 patients, with 150 randomized to PCI of all angiographically significant lesions and 146 randomized to IRA PCI.

Investigators did not use hemodynamic tests of lesion significance (fractional flow reserve [FFR] or instantaneous wave-free ratio), which in other contexts have led to improved outcomes. Instead, the authors relied on angiographic definitions of significance only (lesion estimates of greater than 70% or 50% in two orthogonal views), which would be predicted to lead to overtreatment compared with an FFR-based approach. Finally, cardiovascular events in this trial were not adjudicated, but rather relied on site-level reporting. In the wake of the recent controversy over the EXCEL trial, it is important to recognize that even different definitions of MI as an endpoint can affect the overall results significantly.

In trials like CvLPRIT, the fact that a central clinical events committee did not adjudicate the occurrence of endpoints such as MI could lead to incorrect conclusions. Still, there were strengths. In addition to confirming a sustained effect of complete revascularization on MACE over time, longer-term results were positive (where the original 12-month report was not) in terms of the hard outcomes of death and MI. When added to the positive results of other trials, this provides compelling evidence for a benefit of CR in patients presenting with STEMI.

[In the wake of the recent controversy over the EXCEL trial, it is important to recognize that even different definitions of myocardial infarction as an endpoint can affect the overall results significantly.]

These results also are a reminder that patients presenting with acute coronary syndromes are fundamentally different than those with stable angina and demand a different approach. In the wake of the ISCHEMIA trial, this point is worth discussion with both patients and medical providers alike.

Nonetheless, take each case on an individual basis. For each patient, ask what achieving CR will require in terms of risks. Is the nonculprit PCI straightforward or a complex chronic total occlusion? Is the patient frail? Did he or she present with advanced chronic kidney disease or poor vascular access? Complete revascularization following STEMI should be considered in every case, but a patient-centered approach is required. Going forward, expect other investigators to elucidate the remaining uncertainties in this space, including the most optimal timing of additional revascularization. ■

ABSTRACT & COMMENTARY

Subclinical Atrial Fibrillation Detected By Implanted Loop Recorders: Common, But How Burdensome?

By Joshua Moss, MD

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Dr. Moss reports he is a consultant for Abbott, Biosense Webster, and Boston Scientific.

SYNOPSIS: In older patients with risk factors for stroke drawn from the general population, previously undiagnosed and asymptomatic episodes of atrial fibrillation are detected frequently via implantable loop recorder monitoring, allowing for early initiation of anticoagulation therapy.

SOURCE: Diederichsen SZ, Haugan KJ, Brandes A, et al. Natural history of subclinical atrial fibrillation detected by implanted loop recorders. *J Am Coll Cardiol* 2019;74:2771-2781.

There is evidence to suggest subclinical episodes of atrial fibrillation (AF) — those detected only incidentally — are associated with a higher risk of stroke. Diederichsen et al sought to characterize burden, progression, symptoms, and heart rates associated with subclinical AF.

Subjects enrolled in the LOOP study (Atrial Fibrillation Detection by Continuous ECG Monitoring Using Implantable Loop Recorder to Prevent Stroke in High-risk Individuals) were invited to participate from the general population. Eligible subjects had no history of AF, were at least 70 years of age, and presented with at least one additional risk factor for stroke: hypertension, diabetes, heart failure, or prior stroke. Subjects were randomized in a 1:3 ratio to receive an implantable loop recorder (ILR) or be assigned to a control group. Arrhythmia monitoring continued until end of ILR battery life (minimum three years), device explanation, initiation of antiarrhythmic treatment, or death. Subjects with AF episodes detected by the ILR and adjudicated by two cardiologists were offered oral anticoagulation and clinical follow-up. The primary endpoint was cumulative AF burden, including all episodes lasting at least six minutes.

A total of 590 individuals with day-to-day data retrieval from an ILR were monitored for a median of 40.2 months. Thirty subjects died during that period, with mortality attributed to cancer in 53% and cardiovascular disease in 33%. More than one-third experienced adjudicated AF episodes lasting at least six minutes, 92% of whom then started oral anticoagulation. However, median overall AF burden was only 0.13%, and only 18 of the 205 subjects with AF had a burden > 5%. Anticoagulation initiation rates did not differ significantly relative to arrhythmia burden detected. Mortality was higher in subjects with AF detected during the first year of follow-up, with a hazard ratio of 4.51 (95% confidence interval, 2.08-9.58).

In a multivariate model, older age and higher NT-proBNP were independently associated with significantly higher odds of AF detection (the odds ratio was 1.33 for every five-year increment in age). However, in the subset of participants with newly detected AF, younger age was associated with higher overall arrhythmia burden, as well as male gender and history of hypertension.

Regarding arrhythmia progression, 55.1% of subjects in whom AF was detected showed an overall decrease in AF burden over the subsequent monitoring period, and 22% exhibited complete remission of AF over the last six months of monitoring. Only 16% developed episodes of AF lasting > 24 hours, the vast majority of whom initially experienced shorter episodes (many at least six months before the first 24-hour episode). Only 6.3% of subjects experienced episodes lasting longer than seven days. Many patients with newly detected AF reported no symptoms (90% denied symptoms upon initial diagnosis, and few went on to trigger symptom-episode recordings on the ILR thereafter). Those who did report symptoms at the time of the initial episode tended to record higher heart rates in AF (median 122 beats per minute vs. 95 beats per minute in subjects without symptoms).

■ COMMENTARY

In the era of wearable and direct-to-consumer devices for heart rate and rhythm monitoring, detection of

AF in the absence of any symptoms undoubtedly will become more common. The data gathered and presented thus far as part of the LOOP study are valuable in helping clinicians understand what to expect in older, asymptomatic patients with risk factors for stroke who start some form of long-term arrhythmia monitoring (whether self-motivated or on the advice of a physician). Chances are good that AF will be detected within several years in these patients, as it was in 35% of study subjects monitored with an ILR.

There were multiple limitations to this study, well described by the authors in their manuscript, related to specific statistical techniques, possible selection bias introduced by the inclusion criteria, and the likelihood of inconsistent symptom reporting. Perhaps more important is a crucial unanswered question: Will the therapies typically used for symptomatic AF (and/or AF detected by intermittent routine monitoring such as in-office ECGs) lead to more harm or good overall? Other researchers have demonstrated that even short, subclinical episodes of AF detected by a cardiac implantable electronic device (CIED) are associated with higher risk of stroke. Still, the population studied here was different from other populations with AF in several ways. First, subjects did not have an indication for a CIED (nor necessarily the comorbidities associated with such patients). Second, subjects did not exhibit the symptoms that brought most previously studied AF patients to medical attention. Third, subjects' overall arrhythmia burden remained low, with more than one in five demonstrating complete spontaneous regression by the end of the monitoring period. Additionally, overall heart rates were not dramatically higher in patients diagnosed with AF, and remained, on average, slower than 100 beats per minute, even during AF in the few patients with higher (> 5%) arrhythmia burden.

Therefore, it is conceivable that automatic initiation of therapeutic anticoagulation when AF is detected in such a way might fail to significantly reduce stroke risk while still increasing risk of bleeding complications disproportionately. Similar dilemmas exist for initiation of rate-controlling medications, antiarrhythmic drugs, or ablation therapy. Until longer-term outcomes comparing the ILR group to the control group in the LOOP study are published, it still makes sense to favor anticoagulation for patients with incidentally diagnosed (and self-diagnosed) AF with other stroke risk factors. But more than ever, it will be crucial for clinicians to understand and convey relative risks and benefits about potential downstream tests, medications, and procedures. ■

ABSTRACT & COMMENTARY

Aggressive Afterload Reduction Does Not Improve Outcomes in Acute Decompensated Heart Failure

By Jamie L. W. Kennedy, MD, FACC

Associate Professor, Division of Cardiology, Advanced Heart Failure & Transplant Cardiology, University of California, San Francisco

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

SYNOPSIS: The authors of the GALACTIC trial found no benefit from an aggressive vasodilation approach for patients hospitalized with acute decompensated heart failure.

SOURCE: Kozhuharov N, Goudev A, Flores D, et al. Effect of a strategy of comprehensive vasodilation vs usual care on mortality and heart failure rehospitalization among patients with acute heart failure: The GALACTIC randomized clinical trial. *JAMA* 2019;322: 2292-2302.

Acute decompensated heart failure is exceedingly common. Still, evidence to guide management is scant. The authors of three recent large trials studied novel vasodilating compounds: nesiritide in ASCEND-HF, ularitide in TRUE-AHF, and serelaxin in RELAX-AHF-2. Unfortunately, all three produced disappointing results. In the GALACTIC trial, Kozhuharov et al sought to examine the benefit of a treatment approach emphasizing aggressive vasodilation in the first three days of heart failure hospitalization.

The authors enrolled patients hospitalized with acute decompensated heart failure (systolic or diastolic). The median time from presentation to study enrollment was five hours. The intensive vasodilation

treatment algorithm included transdermal nitrates and hydralazine on the day of admission, followed by gradual transition to angiotensin-converting enzyme/angiotensin receptor blocker/angiotensin receptor-neprilysin inhibitors (ACE/ARB/ARNI) over the following days. Diuretics, beta-blockers, and other medical management was at the discretion of the treating physician. The primary endpoint was a combination of mortality and heart failure rehospitalization at 180 days.

Investigators enrolled 789 patients at 10 centers in five European countries between December 2007 and February 2018 (386 in the treatment arm, 402 usual care). The average age was 78 years, and 37% were female. A little more than half of the patients presented with systolic heart failure with left ventricular ejection fraction (LVEF) < 40%. The mean LVEF overall was 37%. Comorbid conditions were common: 60% had coronary disease, half had atrial fibrillation, and one-third had diabetes. Symptoms were New York Heart Association class III in 55% of patients and class IV in 45%.

The primary endpoint (death or rehospitalization for heart failure) occurred in 30.6% of the treatment arm vs. 27.8% usual care. Death occurred in 14.4% of the treatment arm vs. 15.3% usual care. The results of a subgroup analysis suggested women fared better with usual care than aggressive vasodilation; no differences were seen based on chronicity of heart failure, LVEF, age, renal function, coronary disease, baseline blood pressure, or BNP. There was no difference between the groups in patient-reported dyspnea on days 2 or 6, and no difference in NT-proBNP at enrollment or discharge.

The treatment assignments were not blinded, and the medications used in the intervention arm are widely available. Thus, it is possible there was not much difference between the intervention and usual care arms. To investigate this, the authors reported the average doses of medications received by treatment arm and hospital day. As prescribed by the intervention algorithm, high doses of nitroglycerin and hydralazine were used during hospital days 1 through 3 in the treatment group, but not the usual care group.

As expected, blood pressure was significantly lower in the treatment group on hospital day 2, and hypotension occurred in 8% of the intervention patients vs. 2% usual care. At the time of discharge, blood pressure was similar in both groups, with systolic levels about 10 mmHg lower than at admission. Similar diuretic doses were used, with similar weight loss during the hospitalization. On discharge, the treatment arm was prescribed a higher average dose of ACE/ARB/ARNI; this difference had disappeared at 180 days. Headache and dizziness were more common in the intervention arm; otherwise, adverse events were similar between groups. The authors concluded that treating acute decompensated heart failure with aggressive vasodilation does not improve the composite of mortality and heart failure hospitalization at 180 days.

■ COMMENTARY

The duration of enrollment speaks to the difficulty in studying this patient population. The patients enrolled are representative of heart failure patients clinicians treat regularly. The 15% mortality at 180 days confirms a "sick" population. The authors achieved aggressive vasodilation in the first few days of the hospital stay, as seen in lower blood pressure and more hydralazine and nitroglycerin used in the intervention arm. Sadly, this did not translate to better outcomes. Perhaps enrolling patients with both preserved and reduced ejection fraction contributed to the observed outcome. Interventions with proven benefit in systolic heart failure have failed to demonstrate benefit in heart failure with preserved ejection fraction trials (ACE inhibitors, ARBs, and, recently, ARNIs). The authors attempted to address this concern with a LVEF subgroup analysis, which did not suggest heterogeneity.

[The authors concluded that treating acute decompensated heart failure with aggressive vasodilation does not improve the composite of mortality and heart failure hospitalization at 180 days.]

The GALACTIC trial highlights two areas in heart failure that warrant further investigation: the management of acutely decompensated patients, and the integration of multiple evidence-based therapies. Unfortunately, the long duration of the trial and the final negative outcome may deter investigators from pursuing additional trials of this nature. Going forward, my inpatient management of heart failure will focus on adequate diuresis and initiation/uptitration of evidence-based heart failure therapies, including sacubitril/valsartan based on the results of PIONEER-HF. I will continue to use short-acting vasodilators, such as hydralazine, nitroglycerin, and nitroprusside, for significantly hypertensive patients and for acutely dyspneic patients who are trending toward intubation and mechanical ventilation. ■

ABSTRACT & COMMENTARY

The Risk of Endocarditis With Bacteremia

By Michael H. Crawford, MD, Editor

SYNOPSIS: Interrogation of the Danish National Patient Registry revealed bacteremia due to *Enterococcus faecalis* was most likely to be associated with infective endocarditis; thus, echocardiography is warranted in these patients.

SOURCE: Østergaard L, Bruun NE, Voldstedlund M, et al. Prevalence of infective endocarditis in patients with positive blood cultures: A Danish nationwide study. *Eur Heart J* 2019;40:3237-3244.

To decide which patients with bacteremia need an echocardiogram, knowledge of the risk of infective endocarditis (IE) with various blood stream infections is needed. Danish researchers interrogated the Danish National Patient Registry for patients with bacteremia typically associated with IE (*Enterococcus faecalis*, *Staphylococcus aureus*; *Streptococcus* spp., and coagulase-negative staphylococci [CoNS]) from 2010 to 2017.

The study outcome was a diagnosis of IE and a hospitalization of at least 14 days (unless the patients died earlier). The 69,021 patients identified were collected into four groups of two contiguous years. The highest prevalence of IE was in patients with *E. faecalis* (17%), followed by *S. aureus* (10%), *Streptococcus* spp. (7%), and CoNS (2%). The prevalence of IE in *E. faecalis* patients significantly increased over time (12% in 2011 vs. 19% in 2015; $P = 0.0005$) and in those with *Streptococcus* spp. (6% in 2010 vs. 8% in 2017; $P = 0.03$). Overall, the rates of IE were higher in men with *E. faecalis*, *Streptococcus* spp., and CoNS ($P < 0.0001$), but not for *S. aureus*. Also, all but *S. aureus* showed a higher prevalence of IE with advancing age ($P < 0.0001$). The authors concluded that the overall prevalence of IE was one in six for *E. faecalis* bacteremia, one in 10 for *S. aureus*, and one in 14 for *Streptococcus* spp. These results suggest echocardiographic screening for bacteremia caused by these three organisms is clinically warranted.

■ COMMENTARY

Considering the high in-hospital mortality of IE (about 20%), early identification of patients at high risk for IE is desirable. The four bacteria species investigated in this study account for 75-85% of cases of IE in reported series. Thus, assessing the prevalence of IE in patients with bacteremia from these organisms makes sense. Interestingly, all four are gram-positive bacteria, which are known to be superior at adhering to the endothelium.

The most surprising result of the study was the higher IE rate for *E. faecalis* than *S. aureus* (17% vs. 10%). However, the study also showed an increase in *E. faecalis* IE with age, which could be attributed to colon cancer and other diseases increasing the prevalence of *E. faecalis* bacteremia. The higher overall prevalence of *E. faecalis* IE probably is due in part to the aging of the population. At age 70-80 years, the *E. faecalis* IE rate was 20% vs. 12% for *S. aureus*. Whereas at age 40-50 years, the authors observed a rate of 13% for both. *E. faecalis* IE also is much more prevalent in men for reasons that are poorly understood, but may be due more to underlying epidemiologic characteristics than biologic ones.

Current major organizational guidelines recommend consideration of echocardiography, especially transesophageal echocardiography (TEE) for *S. aureus* bacteremia (class IIa). The results of this study suggest this recommendation should be extended to *E. faecalis*. However, the systematic application of echocardiography, especially TEE, for a disease with a ≤ 20% prevalence in the at-risk population may not be feasible or cost effective. In most series, the use of echo is about 50-65%. Many have suggested using a risk score such as NOVA, PREDICT, VIRSTA, or AANDOC to cull the highest-risk bacteremia patients for echoes. The Duke score is not recommended because studies have shown that it is largely driven by the echo results. These scores are highly sensitive and carry a negative predictive value of > 95% (but specificity is lower). This may be acceptable for such a high mortality disease.

There were several limitations to the Østergaard et al study. First, as it was an administrative database study, there was limited clinical information, such as echo results. Second, the authors used ICD-10 codes to diagnose IE. Prior validation studies revealed this approach carried a positive predictive value of 90%. Third, the increase in the prevalence of IE over time may have been because of an increased use of echo and nuclear imaging. Fourth, echoes were not performed systemically; the estimates of IE rates may be conservative. Finally, the differences in the incidence rates for various organisms may vary geographically; these results may not reflect all areas in the world. I believe the main message of this paper is the increased prevalence of *E. faecalis* IE and the corresponding need to consider echoes earlier in the course of *E. faecalis* bacteremia. ■

ABSTRACT & COMMENTARY

Optimal Antithrombic Therapy After PCI for Atrial Fibrillation Patients

By Michael H. Crawford, MD, Editor

SYNOPSIS: In three subgroups of coronary artery disease patients with atrial fibrillation, apixaban plus a $P2Y_{12}$ inhibitor provided superior safety and similar efficacy outcomes as treatment with warfarin, aspirin, or both for six months.

SOURCE: Windecker S, Lopes RD, Massaro T, et al. Antithrombotic therapy in patients with atrial fibrillation and acute coronary syndrome treated medically or with percutaneous coronary intervention or undergoing elective percutaneous coronary intervention: Insights from the AUGUSTUS trial. *Circulation* 2019;140:1921-1932.

When patients with atrial fibrillation (AF) undergo percutaneous coronary intervention (PCI), the ideal antithrombic therapy would be an oral anticoagulant and aspirin plus a $P2Y_{12}$ inhibitor. However, such regimens have increased bleeding risk compared to an oral anticoagulant plus a $P2Y_{12}$ inhibitor without aspirin. This so-called dual therapy approach has not been shown to increase ischemic events. Still, the optimal regimen for different subgroups of patients with AF and coronary artery disease (CAD) is unclear.

The AUGUSTUS trial investigators specified three mutually exclusive subgroups to explore the safety and efficacy of antithrombic regimens. The patient subgroups were: acute coronary syndrome (ACS) treated medically, ACS undergoing PCI, and stable CAD undergoing PCI. The antithrombic regimen comparisons used a unique 2 × 2 factorial design wherein apixaban was compared to warfarin and aspirin was compared to placebo in patients taking a $P2Y_{12}$ inhibitor. The primary outcome was major or clinically significant bleeding. Secondary outcomes were death or hospitalization and the composite of death, myocardial infarction (MI), stroke, stent thrombosis, or urgent revascularization. Patients were randomized for up to 14 days after ACS or PCI and treated for six months. From 492 sites in 33 countries, 4,614 patients were randomized, 2,811 with ACS and 1,784 with elective PCI. Among ACS patients, 1,714 were treated by PCI and the rest medically. For the entire cohort, the mean CHA_2DS_2-VASc score was 4, and the mean HAS-BLED score was 3, with no significant differences among the three groups.

The apixaban-treated cohort experienced less major bleeding compared to the warfarin cohort in the medically treated ACS patients (hazard ratio [HR], 0.44; 95% confidence interval [CI], 0.28-0.68), PCI-treated ACS patients (HR, 0.68; 95% CI, 0.52-0.89), and elective PCI patients (HR, 0.82; 95% CI, 0.64-1.04), but with similar death and ischemic events in all three groups (P = 0.71). The authors concluded that in the three subgroups of CAD patients with AF, apixaban plus a $P2Y_{12}$ inhibitor provides superior safety and similar efficacy outcomes as treatment with warfarin, aspirin, or both for six months.

■ COMMENTARY

The authors of this prespecified subgroup analysis of the AUGUSTUS trial used a unique 2 × 2 factorial technique to compare antithrombic regimens in patients taking a $P2Y_{12}$ inhibitor: apixaban vs. warfarin and aspirin vs. placebo. They demonstrated that the apixaban plus a $P2Y_{12}$ inhibitor without aspirin was safer and equally efficacious as warfarin, aspirin, or both in ACS patients managed medically and PCI patients with ACS or stable CAD. In comparing apixaban vs. warfarin, the number needed to treat to prevent one significant bleed was 16 for the ACS medical group, 23 for the ACS-PCI group, and 39 for the elective PCI group. Also, the endpoint of death or hospitalization was reduced with apixaban vs. warfarin, with no difference in death or ischemic events across all three patient groups. In comparing aspirin to placebo, the number needed to harm (NNH) with aspirin was 33, 13, and 11 in the three groups, respectively. Further, the death or hospitalization and death or ischemic events endpoints were not different on aspirin vs. placebo. In the two PCI subgroups, the endpoint of stent thrombosis or MI was numerically lower in the aspirin group. However, this was offset by the higher bleeding rate, resulting in no net clinical benefit.

Other recent trials of DOACs vs. warfarin in PCI patients, such as PIONEER AF-PCI (rivaroxaban) and RE-DUAL PCI (dabigatran), also revealed lower bleeding rates with a DOAC plus a $P2Y_{12}$ inhibitor vs. warfarin, $P2Y_{12}$, and aspirin therapy, without an increase in ischemic events. However, it was unclear whether the results were driven by lower doses of DOAC (dabigatran) or the omission of aspirin. This AUGUSTUS trial substudy helps clarify these issues because the authors used the recommended stroke prevention doses of apixaban and employed a unique factorial technique that allowed for comparing

aspirin to placebo. Interestingly, in the lower-dose dabigatran arm of RE-DUAL PCI, patients exhibited higher rates of stent thrombosis and MI. This AUGUSTUS data cannot establish the efficacy of not using aspirin in PCI patients, and there may be high-risk subgroups of post-PCI patients in whom triple therapy for some period is warranted.

There were limitations to this analysis. Although the safety of apixaban plus a $P2Y_{12}$ inhibitor therapy in the total trial population was replicated, the subgroups were underpowered for bleeding risk. Also, since patients were randomized for up to 14 days after PCI, many received aspirin during their initial management of ACS. In addition, the study ended at six months after enrollment, so the ideal therapy after six months is unknown. The strongest feature was the inclusion of medically managed ACS patients, which can be up to one-third of all ACS patients. In this group, the NNH on aspirin was 11 vs. 33 in ACS PCI patients. Thus, there may be a stronger case for aspirin in PCI patients, especially those with ACS. In addition to other trials, AUGUSTUS suggests that dual antithrombic therapy without aspirin can be considered for six months after PCI or in medically treated ACS patients with AF to reduce bleeding risk. The challenge is identifying PCI patients who are at higher risk of ischemic events and also may need aspirin therapy for some period. ■

CME/CE QUESTIONS

1. **A strength of the CvLPRIT study was:**
   a. the large number of patients enrolled.
   b. the use of fractional flow reserve to confirm lesion severity.
   c. the independent adjudication of events.
   d. the confirmation of the results of other studies.

2. **Patients older than age 70 years with atrial fibrillation (AF) detected by long-term implantable loop recorders:**
   a. are rare.
   b. have high AF burdens.
   c. are more likely to die.
   d. are symptomatic.

3. **In a recent randomized, controlled trial of acute decompensated heart failure, aggressive use of which agents failed to improve on usual care?**
   a. Nitrates and hydralazine
   b. Neprilysin inhibitors and angiotensin receptor blockers
   c. Beta-blockers
   d. Diuretics

4. **Newer data suggest the prevalence of infective endocarditis is highest in bacteremia because of:**
   a. coagulase-negative staphylococci.
   b. *Enterococcus faecalis*.
   c. *Streptococcus* spp.
   d. *Staphylococcus aureus*.

5. **Recent studies have shown the enhanced safety, with equal efficacy, of dual antithrombic therapy without aspirin in patients with AF undergoing percutaneous interventions. A substudy of the AUGUSTUS trial showed similar results in which new clinical group?**
   a. Type 2 diabetes patients
   b. Medically treated acute coronary syndrome patients
   c. Patients with HAS-BLED scores > 4
   d. Patients with CHA_2DS_2-VASc scores > 4

CME/CE OBJECTIVES

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

- discuss the most current information related to cardiac illness and the treatment of cardiac disease;
- explain the advantages and disadvantages, as well as possible complications, of interventions to treat cardiac illness;
- discuss the advantages, disadvantages, and cost-effectiveness of new and traditional diagnostic tests in the treatment of cardiac illness; and
- discuss current data regarding outpatient care of cardiac patients.