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Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Keep Calm and Compress On, But Do Not Hold Your Breath Too Long

By Joshua Moss, MD

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

SYNOPSIS: In a recent analysis, using any CPR was associated with significant improvement in 30-day survival, with slightly better outcomes associated with standard CPR over compression-only CPR.

SOURCE: Riva G, Ringh M, Jonsson M, et al. Survival in out-of-hospital cardiac arrest after standard cardiopulmonary resuscitation or chest compressions only before arrival of emergency medical services. *Circulation* 2019; Apr 1. doi: 10.1161/CIRCULATIONAHA.118.038179. [Epub ahead of print].

In 2000, the American Heart Association first recommended compression-only CPR (CO-CPR) when bystander rescuers were unwilling or unable to perform mouth-to-mouth rescue breathing. By 2010, efficacy of CO-CPR was supported by two randomized studies. The guideline update that year reoriented the universal sequence of assessment and care from A-B-C (Airway, Breathing, Compressions) to C-A-B. Untrained rescuers were advised to provide CO-CPR or follow EMS dispatcher instructions. In the 2015 guidelines, dispatchers were advised to provide CO-CPR instructions to callers for adults with suspected cardiac arrest. The Swedish national CPR guidelines were modified similarly in 2006, 2011, and 2016. Riva et al analyzed data from three guideline "eras," 2000-2005, 2006-2010, and 2011-2017, to evaluate frequency and type of CPR delivered and association with 30-day survival. The authors used data from the Swedish Register for Cardiopulmonary Resuscitation, a national quality registry of out-of-hospital cardiac arrest (OHCA) events to which all EMS organizations in Sweden report. A total of 30,445 bystanders witnessed OHCA events between 2000 and 2017, with registry information on type of CPR performed and 30-day survival included in the analysis. Cases were excluded if they were unwitnessed, EMS-witnessed, or treated with rescue breath-only CPR. Otherwise, type of

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CPR was classified as standard (S-CPR, including rescue breathing), CO-CPR, or NO-CPR (none delivered before EMS arrival).

Patients were more likely to receive NO-CPR or CO-CPR when EMS response time was shorter (median response time seven minutes in the NO-CPR group, eight minutes in the CO-CPR group, and 10 minutes in the S-CPR group). Responders delivering S-CPR were more likely to be medically educated (25.1% of the S-CPR group vs. 15.3% of the CO-CPR group). Over the three eras analyzed, rates of CPR received before EMS arrival increased from about 41% (2000-2005) to 59% (2006-2010) to 68% (2011-2017). The proportion of patients receiving CO-CPR also increased, from 13% of CPR recipients (2000-2005) to 24% (2006-2010) to 44% (2011-2017).

Interestingly, survival at 30 days, always poor for OHCA, nearly doubled over the study period, regardless of whether CPR was delivered or what type of CPR was used. In the most recent era (2011-2017), 30-day survival was best for patients who received standard CPR (16.2% vs. 14.3% for CO-CPR and 7.1% for NO-CPR). When data were adjusted for patient age, sex, cause of arrest, location, EMS response time, and year, the odds of survival were 2.6 times higher with S-CPR and two times higher with CO-CPR compared with NO-CPR. The authors concluded that future CPR guidelines should continue to endorse CO-CPR as an option.

■ COMMENTARY

The current data, while limited by their observational nature, provide some important insights into CPR patterns and efficacy. Bystander CPR delivery increased dramatically between 2000 and 2017. Well over half of CPR delivered was CO-CPR between 2014 and 2017 (compared to less than 20% of the CPR delivered in 2000). Those observations suggest one of two things: either the emphasis on CO-CPR has contributed to an increase in willingness and/or ability to perform CPR, or that willingness and ability increased independently, and people are simply following guideline recommendations. We can only speculate about which explanation accounts for these findings, but data from other studies certainly suggest that bystanders are more likely to participate when CO-CPR is accepted and expected.

For witnesses of OHCA without medical training, the publication of data such as these hopefully will encourage even more to participate in providing CPR until EMS arrives (in addition to ensuring the rapid arrival of EMS). However, for cardiologists and other medically trained responders, a few take-home messages should not be lost. S-CPR, including rescue breathing, was associated with improved 30-day survival compared with CO-CPR, with an adjusted odds ratio of 1.2 (95% confidence interval, 1.1-1.4). S-CPR appeared slightly superior to CO-CPR (and both were significantly superior to NO-CPR) across all subgroups analyzed, except when EMS response time was longer than 10 minutes. With an EMS response time between 10 and 14 minutes, only S-CPR was associated with improved survival over NO-CPR. No form of CPR was associated with improved survival when EMS response time was > 14 minutes. While not proof of direct causation, the data suggest that CO-CPR without rescue breathing could become inadequate before S-CPR. The prognosis for prolonged arrest without EMS support is unsurprisingly grim.

Importantly, there are insufficient data to support CO-CPR for children and infants (for whom asphyxia may be the cause of their cardiac arrest), and rescue breathing still is recommended. From these data, it is unknown whether patients who are alive at 30 days after S-CPR and CO-CPR experience equivalent neurologic outcomes.

Further, it is unknown whether CO-CPR is similarly effective for victims of unwitnessed cardiac arrest. Overall, it is unknown whether this robust Swedish data set can be completely generalized to all populations, considering the potential for variations in causes of OHCA, response time and efficacy of EMS systems, and education and awareness of bystanders. With these points in mind, it is notable that the 2015 Guidelines for Basic Life Support, the most recent update, still

recommend chest compressions and rescue breaths in a ratio of 30:2 when administered by a healthcare provider or a trained lay rescuer (if able). Emphasis should be placed on timely and effective chest compressions, but healthcare providers should not forget to breathe. ■

ABSTRACT & COMMENTARY

Do Antianginal Agents Prevent Revascularization Procedures?

By Michael H. Crawford, MD, Editor

SYNOPSIS: For patients with stable ischemic heart disease, adding either ranolazine or calcium channel blockers to nitrate or beta-blocker therapy reduced the incidence of subsequent revascularization and costs vs. beta-blocker or nitrate therapy alone or in combination.

SOURCES: Meyer N, Tran O, Hartsfield C, et al. Revascularization rates and associated costs in patients with stable ischemic heart disease initiating ranolazine versus traditional antianginals as add-on therapy. *Am J Cardiol* 2019;123:1602-1609.

Rasalingam R, Boden WE. Role of ranolazine in reducing angina, subsequent revascularization, and healthcare expenditures in stable ischemic heart disease. *Am J Cardiol* 2019;123:1729-1731.

In patients with documented stable ischemic heart disease (SIHD), if symptoms are not controlled by antianginal (AA) therapy, guidelines recommend considering coronary artery revascularization, which increases the cost of managing such patients. Meyer et al analyzed a large group of insured patients in the United States.

SIHD patients treated with beta-blockers, calcium channel blockers, nitrates, or ranolazine were identified. They were divided into four groups: ranolazine added to one to three other AAs, beta-blockers as second or third AA, calcium channel blockers added, or long-acting nitrate added. The authors assessed revascularization, hospitalizations for revascularization, hospital length of stay, and total healthcare costs. The groups were adjusted for differing clinical characteristics, such as age, sex, and comorbidities. From 2008 through June 2016, the authors identified 108,741 patients with SIHD on AAs (18% were on ranolazine, 21% beta-blockers, 24% calcium channel blockers, and 37% long-acting nitrates). At baseline, 85% of patients were taking one AA and 15% were taking two AAs.

During follow-up (12 months), revascularization rates were lowest for the ranolazine group (11%) compared to the beta-blocker (16%) group and the nitrate group (14%; $P < 0.001$ for both) and were similar to the calcium channel blocker group (10%). In addition, compared to the beta-blocker and nitrate groups, ranolazine-treated patients were less likely to be hospitalized and stayed fewer days if they were admitted ($P < 0.001$). Mean healthcare costs were higher for beta-blocker ($4,465) and nitrate ($3,609) subjects vs. ranolazine ($2,933) or calcium channel blocker ($2,753) subjects ($P < 0.001$). The authors concluded that for SIHD patients, ranolazine and calcium channel blocker therapy was associated with fewer revascularization procedures and lower healthcare costs than treatment with beta-blockers or long-acting nitrates.

■ COMMENTARY

This study was designed to show the superiority of ranolazine as the second-choice agent for treating angina in SIHD patients whose symptoms are not controlled by one of three standard therapies for angina; it did. However, Meyer et al also showed that ranolazine was no better than calcium channel blockers for this purpose, a point glazed over in this pharmaceutical company-sponsored study. This does not surprise me, as earlier studies with calcium channel blockers showed their superiority over beta-blockers and nitrates for controlling angina. This fact seems to have been lost on my younger colleagues. I am continually surprised by how few of them put their patients on calcium channel blockers for angina control. When asked why, younger physicians usually respond that they thought the calcium channel blockers were only used for hypertension. Granted, calcium channel blockers can produce adverse effects. Dihydropyridine calcium channel blockers can cause tachycardia — but are a good addition to beta-blockers for this reason. Non-dihydropyridine calcium channel blockers can precipitate heart failure in patients with left ventricular ejection fractions < 35% — but are good at controlling heart rate. One major advantage of ranolazine as a second-choice agent for angina is that it does not affect heart rate or blood pressure. All three standard agents can reduce blood pressure to unacceptable levels at higher doses. The other interesting point: the preponderance of SIHD patients with angina were treated with only one agent (almost always a beta-blocker). This may be because U.S. guidelines recommend using a beta-blocker first in a stepwise algorithm for pharmacologic therapy. There are no solid data

supporting this recommendation, and it may be an extrapolation from beta-blocker use after myocardial infarction and for heart failure. This undertreatment may be fueled by the ready availability and relatively low risk of percutaneous revascularization (PCI). However, revascularization does not prevent myocardial infarction or extend life. If symptom relief is the goal, it makes sense to try optimal medical therapy that includes not only more than one AA but risk factor control and lifestyle alterations. This approach was quite effective in the COURAGE trial.[1]

There were limitations to the Meyer et al study. It was retrospective and based on administrative data. There is a lack of granularity in the data. For example, we do not know which calcium channel blockers the patients were taking, the doses of any drugs, or compliance. Also, administrative databases may misclassify outcomes compared to medical records review. Despite the study's flaws, Meyer et al emphasized that angina control with optimal medical therapy (which should include a calcium channel blocker or ranolazine) is preferable from a cost perspective and perhaps for patient safety than proceeding to PCI on suboptimal therapy. ■

REFERENCE

1. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;356:1503-1516.

ABSTRACT & COMMENTARY

Reducing Mortality in Stable Ischemic Heart Disease Patients

By Michael H. Crawford, MD, Editor

SYNOPSIS: A multivariate analysis of a large registry of patients with stable ischemic heart disease revealed that beta-blocker use was associated with lower mortality only when prescribed in the first year after acute myocardial infarction.

SOURCES: Sorbets E, Steg PG, Young R, et al. Beta-blockers, calcium antagonists, and mortality in stable coronary artery disease: An international cohort study. *Eur Heart J* 2019;40:1399-1407.

Nissen SE, Reed GW. Can we trust observational data for clinical decision-making? *Eur Heart J* 2019;40:1408-1410.

The European Society of Cardiology recommends both beta-blockers and calcium channel blockers as first-line treatment for symptomatic patients with stable ischemic heart disease (SIHD). However, there are little data on whether such therapy improves outcomes. In the absence of randomized, controlled trials (RCTs), Sorbet et al examined the association between beta-blockers or calcium channel blockers and clinical outcomes.

Patients were enrolled between November 2009 and June 2010 in 45 countries and followed for five years. The primary outcome was all-cause mortality. Other outcomes included cardiovascular mortality, myocardial infarction, and stroke. Beta-blocker and calcium channel blocker therapy and their doses were ascertained annually. The total study population was 32,378, of which a complete data set was available for 68%. At baseline, 78% of patients were on beta-blockers. Multivariate adjusted hazard ratios (HR) showed no relationship between beta-blockers and any primary or secondary outcome.

In patients ≤ 1 year post-myocardial infarction (MI), beta-blocker use was associated with a lower risk of all-cause mortality (HR, 0.68; 95% confidence interval [CI], 0.50-0.91; $P = 0.01$) and cardiovascular mortality (HR, 0.52; 95% CI, 0.37-0.73; $P = 0.0001$). In patients > 1 year post-MI, there were no differences in outcomes for those on beta-blockers, and there was no difference in outcomes with beta-blockers after categorization by presence of angina. At baseline, 27% of patients were on calcium channel blockers, most of which were long-acting dihydropyridines (80%). There was no association with calcium channel blockers and outcomes. The authors concluded that in a contemporary population of SIHD patients, beta-blocker use was associated only with lower mortality if patients were ≤ 1 year following an acute MI. Calcium channel blocker use was not associated with lower mortality or MI.

■ COMMENTARY

The recommendation to use beta-blockers in almost all SIHD patients is an abstraction from RCTs conducted decades ago in acute MI patients. These trials were performed before the extensive use of reperfusion and revascularization and prior to the widespread use of secondary prevention therapies such as statins. The potential benefits of calcium channel blockers were extrapolated from their demonstrated efficacy for relieving angina and small,

randomized, post-MI trials.[1] Considering the absence of RCTs showing a benefit of beta-blockers and calcium channel blockers in SIHD patients, Sorbets et al conceived the prospective, observational CLARIFY study (prospeCtive observational LongitudinAl RegIstry oF patients with stable coronary arterY disease). Its strengths included its large, international design and the fact that the authors recruited SIHD patients with a spectrum of characteristics from whom data were collected prospectively. Also, this was a contemporary study, with high rates of revascularization and proven secondary prevention therapies. In addition, the authors chose relatively hard endpoints: all-cause and cardiovascular mortality, MI, and stroke. They showed that beta-blockers significantly reduced mortality only in patients who were within one year of an acute MI. Further, their findings suggest calcium channel blockers do not reduce mortality. These results are consistent with those of smaller studies and post hoc analyses of larger trials. Further, a subgroup analysis showed that the results were robust across all subgroups analyzed. Since no harm was discovered, Sorbets et al stated that it was acceptable to use beta-blockers and calcium channel blockers for symptom relief and other indications (e.g., hypertension in SIHD patients), but not as secondary prevention agents).

Sorbets et al, along with Nissen and Reed in an accompanying editorial, noted the study's weaknesses. Like any observational study, there may be residual confounders that were not accounted for in Cox models. The authors did not employ the more rigorous propensity score adjustments. Although patients were enrolled prospectively, the data analysis was not prespecified, so this was essentially a post hoc analysis, which is inherently biased. Also, the study was not blinded, and the outcomes were not adjudicated.

Further, patients were not enrolled at the time of drug initiation, which biases the study toward those who can tolerate the therapy. Finally, patients with clear indications for beta-blockers, such as severe heart failure and life-threatening ventricular arrhythmias, were excluded.

Considering these weaknesses, Nissen and Reed opined that size alone does not guarantee accuracy. They pointed out that the HRs in the study did not meet the more rigorous criteria beyond statistical significance (> 2.0 or < 0.5). Thus, they consider this study only hypothesis-generating. However, since no RCT is likely to be conducted on this issue and considering the consistency of this study with others, I do not plan on recommending beta-blockers purely for secondary prevention in SIHD patients. ■

REFERENCE

1. Gibson RS, Boden WE, Theroux P, et al. Diltiazem and reinfarction in patients with non-Q-wave myocardial infarction. *N Engl J Med* 1986;315:423-429.

ABSTRACT & COMMENTARY

Positive Outcomes With One Month of Dual Antiplatelet Therapy After PCI

By Jeffrey Zimmet, MD, PhD

Associate Professor of Medicine, University of California, San Francisco; Director, Cardiac Catheterization Laboratory, San Francisco VA Medical Center

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

SYNOPSIS: In this randomized trial that included more 3,000 patients, one month of dual antiplatelet therapy (DAPT) followed by single antiplatelet therapy with clopidogrel was noninferior to 12 months of DAPT following percutaneous coronary intervention with drug-eluting stents.

SOURCE: Watanabe H, Domei T, Morimoto T, et al. Effect of 1-month dual antiplatelet therapy followed by clopidogrel vs 12-month dual antiplatelet therapy on cardiovascular and bleeding events in patients receiving PCI: The STOPDAPT-2 randomized clinical trial. *JAMA* 2019;321:2414-2427.

The introduction of drug-eluting stents (DES) brought a promise of low restenosis rates, but at the apparent expense of delayed arterial healing with the first-generation devices. The specter of late stent thrombosis, first recognized in earnest in 2006, led to recommendations for dual antiplatelet therapy (DAPT) regimens lasting one year or longer. However, subsequent advances in stent technology have resulted in improved safety and faster endothelialization following stent deployment. Indeed, the results of

multiple trials of later-generation DES have suggested that these devices carry equivalent or even lower risk of stent thrombosis vs. their bare-metal counterparts. Although current U.S. guidelines recommend a minimum of six months of DAPT following DES deployment in elective procedures, retrospective data suggest that more recent iterations of these devices heal more quickly still, and that patients who require discontinuation of DAPT as early as one month can experience favorable outcomes.

Enter the STOPDAPT-2 trial, a multicenter, randomized study of the safety of short-duration DAPT. Watanabe et al enrolled 3,045 patients at 90 centers in Japan between late 2015 and 2017. Patients were eligible for inclusion if they had undergone successful PCI with the Xience series of everolimus-eluting stents and had not experienced major in-hospital complications. Enrolled patients were, on average, 68.6 years of age; 78% were male. Most procedures were performed for stable angina, but a substantial proportion (approximately 38%) were for acute coronary syndromes (ACS). Of these ACS patients, approximately half presented with ST-elevation myocardial infarction (STEMI), with the remainder represented by non-STEMI and unstable angina.

Enrolled patients were randomized 1:1 to receive either one month of DAPT followed by 11 months of clopidogrel monotherapy or 12 months of DAPT. During the first month, all patients received aspirin in addition to a thienopyridine (either clopidogrel or prasugrel) that was chosen by the attending physician. Clopidogrel was used in 62% of patients and prasugrel was used in the remaining 38%. After the first month, patients in the short DAPT group stopped taking aspirin and were continued on clopidogrel as a single agent. The control group received aspirin and clopidogrel for 12 months; those initially managed on prasugrel were switched to clopidogrel at the one-month mark. The primary endpoint was a composite of cardiovascular death, MI, stent thrombosis, stroke, and bleeding. Cardiovascular and bleeding events were analyzed separately as major secondary endpoints.

At 12 months, the primary endpoint occurred in fewer one-month DAPT patients compared with the control group (2.36% vs. 3.70%; hazard ratio [HR], 0.64; 95% confidence interval [CI], 0.42-0.98; P = 0.04 for superiority). Bleeding was the main driver of this difference. The major secondary cardiovascular endpoint was not significantly different between the two groups, while the major secondary bleeding endpoint (a composite of major and minor bleeding) occurred in just 0.41% of one-month DAPT patients vs. 1.54% of 12-month DAPT patients (HR, 0.26; 95% CI, 0.11-0.64; P = 0.004 for superiority). Definite or probable stent thrombosis, while numerically higher in the short DAPT group (four events vs. one event in the control group), was not statistically different between the groups. The authors concluded that in this large, randomized study of patients following successful PCI with everolimus-eluting stents, patients treated with just one month of DAPT followed by clopidogrel monotherapy experienced a net clinical benefit compared with those treated with DAPT for 12 months.

■ COMMENTARY

The main message of this trial is clear: Converting to a regimen of single antiplatelet therapy with clopidogrel only one month following PCI with the Xience DES platform appears to be safe regarding ischemic outcomes. Further, such a move confers a lower risk of bleeding events. But how generalizable are these results?

In most everyday clinical practice, patients completing their required DAPT regimen pare down to aspirin alone. In contrast, clopidogrel was the agent chosen for single antiplatelet therapy in this trial. Overall, clopidogrel is more effective as a single antiplatelet agent than aspirin and may be less likely to cause upper gastrointestinal bleeding. Significantly, the known variability in clopidogrel responsiveness did not hinder the Watanabe et al study, even though genetic polymorphisms resulting in reduced conversion of the clopidogrel prodrug to its active metabolite are known to be more prevalent in Asian populations.

Does it matter that all patients in the trial were treated with Xience stents? Would the same result hold for other DES? Maybe. Although the current-generation DES models are similar, we cannot exclude the possibility that the use of other platforms might have generated different results. More than half of eligible patients were not enrolled, many because the attending physician declined to participate, presumably due to a lack of clinical equipoise. Certainly, one could suggest this led to the selection of lower-risk patients for this trial. Overall, the non-enrolled patients were more complicated than the enrolled population, with older age, more STEMI and prior MI, more target vessels treated, and a greater proportion involving the left main. It is unclear that more complex patients could be treated safely with the very short DAPT duration used in STOPDAPT.

Another important point was the exceedingly high use of intravascular imaging (85% of the short DAPT group used intravascular ultrasound, and nearly the entire remainder was performed with optical coherence tomography). Using intravascular imaging to optimize stenting results has been reported to decrease ischemic outcomes in multiple prior

studies. Whether the results of STOPDAPT can be extrapolated to the United States, where a minority of PCI procedures (fewer than 7% of all PCI, in one recent study) are performed with intravascular imaging, is an open question. The results of the STOPDAPT trial suggest that a one-month duration of DAPT followed by clopidogrel monotherapy is safe and may be beneficial for a subset of lower ischemic risk patients. Further studies will be required to demonstrate whether this approach may be extrapolated to the general population of post-PCI patients. ■

ABSTRACT & COMMENTARY

Treating Infective Endocarditis in Moderate-Risk Patients

By Michael Crawford, MD, Editor

SYNOPSIS: There are patients with a moderate risk of infective endocarditis who may warrant consideration of antibiotic prophylaxis.

SOURCE: Østergaard L, Valeur N, Wang A, et al. Incidence of infective endocarditis in patients considered at moderate risk. *Eur Heart J* 2019;40:1355-1361.

U.S. guidelines recommend antibiotic prophylaxis for patients at high risk for infective endocarditis (IE). The authors of recent studies have identified patients at moderate risk, but the magnitude of this risk is unclear. Investigators analyzed Danish national patient registries to determine the incidence of IE in patients considered moderate risk.

Moderate-risk patients were defined as those with acyanotic congenital heart valve disease, acquired valve disease, hypertrophic cardiomyopathy (HCM), mitral valve prolapse or regurgitation, and those with implanted cardiac electrical devices. Each diagnostic category was compared to matched controls without any of these conditions. Researchers also examined patients with prosthetic heart valves as a high-risk comparator group. Patients were followed until another moderate- or high-risk condition developed or 10 years passed. The primary outcome was hospital admission for IE.

Østergaard et al identified 83,453 patients with a left-sided valve disorder, 50,828 with an implanted electrical device, and 3,620 with HCM for a total of 137,901 patients. The median follow-up was 3.7 years. There was a 0.9% incidence of IE in left heart valve disorders, 1.3% in electrical devices, and 0.5% in HCM. Compared to controls, these three conditions led to a higher risk of IE (hazard ratio [HR], 8.75, 6.63, and 6.57, respectively), but were lower than the risk in high-risk patients (HR, 0.27, 0.28, and 0.13, respectively). Further, the 10-year mortality rate was higher in these three groups vs. controls ($P < 0.0001$). Similar findings were present when those with acyanotic congenital heart valve defects were analyzed. The authors concluded that the cumulative risk of IE in moderate-risk patients at 10 years was about 1%, which was higher than controls but lower than the high-risk population (4.8%).

■ COMMENTARY

The authors of a recent paper from England[1] identified patient groups at moderate risk for IE, which Østergaard et al corroborated in this study. However, Østergaard et al quantitated the risk as compared to an age- and sex-matched control population and included considerably more clinical details, making comorbidity adjustments more robust. In addition, these authors compared the incidence rates to those of a high-risk subgroup with prosthetic valves. They identified the following moderate-risk groups: left heart valve disease, HCM, and implanted electrical devices. They provided robust data on the these conditions, which showed incidence rates of about 1% (one-fifth to one-quarter the rate in patients with prosthetic valves). Thus, these were truly moderate-risk groups.

Is a 1% risk of IE enough to give antibiotic prophylaxis to everyone in these groups? The authors of the current guidelines thought not, but perhaps there are subgroups who would benefit. For this question, Østergaard et al provided some granularity that could be helpful. For example, they found that implanted defibrillators led to higher rates of IE compared to pacemakers. However, those with any device with more than one lead were at higher risk than those with single-lead devices. Other studies have shown that bicuspid aortic valves and moderate or more regurgitation of a left-sided valve increases the risk of IE. Østergaard et al did not provide these data. Also, other studies have shown that HCM with obstruction is higher risk than without obstruction; again, these authors could not confirm this. There were other limitations to the Østergaard et al study. The authors

lacked autopsy data, which could have reduced IE incidence rates. They did not have data on whether IE was left- or right-sided, nor was there any bacteriologic data. Of course, since this was a retrospective database study, there could have been unmeasured confounders. Does this study inform my decisions on antibiotic prophylaxis to prevent IE? Yes, it does. It reinforces the prior studies that showed there were moderate-risk patients at significant risk, such as those with left heart valve disease, HCM, and implanted electrical devices. However, it probably is not reasonable to prophylax all these patients. As other studies have shown, those with moderate or more regurgitation, bicuspid aortic valves, or obstructive HCM (who probably also have significant mitral regurgitation) are certainly worth considering for antibiotic prophylaxis. The electrical device situation is more complex, as few single-lead devices are placed in the United States now. Most pacemaker patients could be candidates for prophylaxis. Also, lead-related IE is difficult to diagnose, and the consequences of lead IE could be dire for the patient. Thus, I am inclined to recommend prophylaxis for multilead defibrillator and biventricular pacemaker patients, but perhaps not dual-chamber pacemaker patients who are uncomplicated. ■

REFERENCE

1. Thornhill MH, Jones S, Prendergast B, et al. Quantifying infective endocarditis risk in patients with predisposing cardiac conditions. *Eur Heart J* 2018;39:586-595.

CME/CE QUESTIONS

1. In stable ischemic heart disease patients requiring more than one antianginal agent, which added drug reduces subsequent revascularization rates?

a. Long-acting nitrates

b. Beta-blockers

c. Ranolazine or calcium channel blockers

d. Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers

2. In stable ischemic heart disease patients, beta-blockers for secondary prevention are efficacious in:

a. almost all patients.

b. those within one year of an acute myocardial infarction.

c. post-stroke patients.

d. those with heart failure and preserved left ventricular ejection fraction.

3. The highest risk of infective endocarditis is in patients with:

a. a prosthetic heart valve.

b. left-sided valve disease.

c. hypertrophic cardiomyopathy.

d. an implanted electrical device.

4. The 30-day survival rate after witnessed cardiac arrest is best with:

a. compression-only CPR.

b. no CPR.

c. respiration support only.

d. standard CPR.

5. In a recent study of switching from dual therapy to monotherapy after percutaneous coronary intervention with the latest generation stents, which monotherapy showed outcomes similar to dual therapy for one year?

a. Aspirin

b. Clopidogrel

c. Prasugrel

d. Ticagrelor