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Critical analysis of the latest clinical research in cardiovascular medicine [ALERT]

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ABSTRACT & COMMENTARY

Research Provides More Support for Antiplatelet Therapy De-escalation

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: The authors of a single-center study randomized post-acute coronary syndrome patients either to remain on higher-potency antiplatelet agents or to change to clopidogrel after one month. The results showed a benefit to de-escalation in terms of both bleeding and ischemic events, regardless of initial platelet reactivity.

SOURCE: Deharo P, Quilici J, Camoin-Jau L, et al. Benefit of switching dual antiplatelet therapy after acute coronary syndrome according to on-treatment platelet reactivity: The TOPIC-VASP pre-specified analysis of the TOPIC randomized study. *JACC Cardiovasc Interv* 2017;10:2560-2570.

Antiplatelet therapy plays a central role in the treatment of acute coronary syndrome (ACS) patients post-percutaneous coronary intervention (PCI), reducing the risk of recurrent ischemic events and stent thrombosis. The newer $P2Y_{12}$ inhibitors prasugrel and ticagrelor have demonstrated superiority over clopidogrel in this population, albeit with significant costs, both financially and in terms of clinically significant bleeding. In response to this data, the European Society of Cardiology relegated clopidogrel to second-line status several years ago. The 2014 American College of Cardiology/American Heart Association guidelines for non-ST elevation ACS similarly gave a class IIa recommendation to the strategy of choosing ticagrelor or prasugrel over clopidogrel for ACS patients undergoing PCI. Although the usual practice is to continue the same drug for the duration of the guideline-recommended 12 months of dual antiplatelet therapy (DAPT), switching from the more potent agents to clopidogrel also is relatively common in everyday practice. Whether this happens for reasons of cost or for bleeding, the obvious concern has been that the benefits of the highly potent agents on ischemic outcomes would be lost.

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This activity is intended for the cardiologist. It is in effect for 36 months from the date of the publication.

Enter the Timing Of Platelet Inhibition after acute Coronary Syndrome (TOPIC) study, a single-center, open-label trial that included patients with ACS who had undergone successful coronary stenting and who were treated with either ticagrelor or prasugrel. One month after the ACS episode, patients were randomized to either remain on the more potent $P2Y_{12}$ agent or to switch to clopidogrel. All patients underwent platelet function testing by platelet reactivity index vasodilator-stimulated phosphoprotein (PRI-VASP) to assess response to the initial high-potency regimen. The primary endpoint of the trial assessed a composite of ischemic and bleeding events, including cardiovascular death, unplanned coronary revascularization, and Bleeding Academic Research Consortium bleeding episodes.

In the overall group of 646 patients, those who switched from DAPT to a clopidogrel-based regimen demonstrated a significant reduction in the primary composite endpoint (9.3% vs. 23.5%; $P < 0.01$), driven almost entirely by a reduction in bleeding events. This occurred without a significant difference in ischemic events (9.3% vs. 11.5%; $P = 0.36$). Forty-seven percent of the total were classified based on platelet function testing as exhibiting low on-treatment platelet reactivity (LTPR), which has been described as "hyper-responsiveness" and is a marker for increased bleeding risk on the potent antiplatelet agents. Separating patients by platelet reactivity status showed that LTPR patients who switched from DAPT exhibited an even greater reduction in the primary endpoint at one year (11.9% vs. 33.1%; $P < 0.01$) compared with the overall group, and that this was related to decreased rates of both bleeding and ischemic complications. In patients without LTPR, rates of bleeding were similarly reduced by switching from DAPT, but the composite endpoint was not statistically different.

The authors concluded that switching from DAPT to a less-potent clopidogrel-based regimen at one month was associated with reduced bleeding, regardless of patients' individual responses to the newer $P2Y_{12}$ inhibitors. The benefits were greater in patients who experienced LTPR, in whom the hazard of remaining on the newer agents was especially pronounced.

■ COMMENTARY

The story of DAPT after stenting for ACS appears at first glance to become more complicated with each additional trial result. The use of the more potent $P2Y_{12}$ inhibitors prasugrel and ticagrelor in this population has been shown to result in improved overall ischemic outcomes, leading to their adoption as first-line agents in some settings. However, with more rapid healing of current-generation drug-eluting stents, clinicians have observed a push toward shorter DAPT durations than the guideline-directed 12 months. For example, the authors of the ISAR-SAFE trial demonstrated non-inferiority of six vs. 12 months of DAPT in 1,601 ACS patients treated with aspirin and clopidogrel. The authors of the COMBO trial came to a similar conclusion. This trial included nearly 1,500 patients with ACS receiving a novel sirolimus-eluting stent in whom a three-month duration of DAPT was noninferior to 12 months (although nonsignificant trends toward higher all-cause mortality and stent thrombosis were reported with shorter duration of DAPT).

The concept of de-escalating antiplatelet therapy from the more potent agents to clopidogrel is not new, driven not by a push for improved outcomes but rather primarily by economic concerns, whereby off-patent clopidogrel is much more affordable that other drugs. This trend was well-illustrated in the PRAGUE-18 study. The authors randomized acute myocardial infarction patients to ticagrelor vs. prasugrel and found no significant difference in efficacy or safety between the two. Patients in this trial were informed prior to discharge about the out-of-pocket costs of prasugrel and ticagrelor, as well as the expected advantages of those drugs compared to clopidogrel. An unexpected finding of the trial was that a substantial proportion of the subjects switched drugs, primarily because of cost considerations, with nearly 50% of patients switching from prasugrel to clopidogrel and 60% switching from ticagrelor to clopidogrel. Although patients who switched medications exhibited lower risk profiles overall, the authors found

that the (nonrandomized) de-escalation to clopidogrel resulted in a lower risk of major cardiovascular events as well as a lower risk of bleeding. In our own environment, we have seen similar issues, with some patients treated with ticagrelor switched to clopidogrel at the first post-discharge clinic visit, usually as a result of reduced cost. The authors of TOPIC set out to systematically study patients' existing real-world habits. This trial goes beyond demonstrating the safety of this practice and suggests a clear benefit in terms of bleeding. Although this was a relatively small study, the positive results of making the switch one month after the ACS event certainly are plausible. Although these data likely are insufficient to change guidelines, the information provides reassurance about the safety of this growing practice and should prompt its consideration, at least in patients with higher bleeding risk. ■

ABSTRACT & COMMENTARY

Assessing Device-assisted CPR Safety

By Michael H. Crawford, MD, Editor

SYNOPSIS: A randomized, prospective, noninferiority study of the safety of two automated CPR devices (LUCAS and AutoPulse) against the standard manual chest compressions in cardiac arrest victims showed that in cases of severe or life-threatening complications, the LUCAS device was noninferior to standard CPR, but more organ damage with the AutoPulse cannot be excluded.

SOURCES: Koster RW, Beenen LF, van der Boom EB, et al. Safety of mechanical chest compression devices AutoPulse and LUCAS in cardiac arrest: A randomized clinical trial for non-inferiority. *Eur Heart J* 2017;38:3006-3013.

Lamhaut L, Hutin A. Looking at the force beyond the dark side of mechanical message. *Eur Heart J* 2017;38:3014-3016.

It is difficult for all members of a healthcare team to perform consistent CPR chest compressions. Automated devices have become more popular and have demonstrated improvements in aortic blood pressure and coronary perfusion compared to manual chest compressions. However, no study has shown increased survival with these devices. Further, some observers have suggested using automated devices causes increased chest wall damage.

Investigators from the Netherlands conducted a randomized, controlled trial of two devices widely available in the United States to test the hypothesis that these devices may cause more chest wall or visceral damage than manual compressions. The study population consisted of in-hospital cardiac arrest patients or those arriving in the ED with the need for ongoing CPR. Patients < 18 years of age with traumatic arrest and those treated with a device by emergency medical personnel in the ambulance were excluded. Patients were randomized 1:1:1 to manual compressions, the LUCAS device, or the AutoPulse device. The depth and rate of manual compressions were calibrated by displacement of a Philips HeartStart MRx defibrillator. All arrests were handled for study purposes by a cardiac arrest team that received appropriate training every six months. The team was not blinded to the device used. Either autopsy or postmortem CT scans were used to identify any injuries in those who didn't survive. The primary endpoint was damage to visceral organs, large blood vessels, and vertebrae. Secondary endpoints included rib or sternal damage. The study was not powered to analyze survival or compare the two devices. The authors designed this study as a noninferiority investigation.

A total of 1,697 patients were randomized, but after applying the exclusion criteria, AutoPulse was employed in 115, LUCAS in 122, and manual compressions in 137. Serious or life-threatening visceral organ damage was seen in 12% of AutoPulse patients, 7% of LUCAS patients, and 6% of control patients, which was not statistically different ($P = 0.75$). Investigators observed the secondary outcome in 46% of AutoPulse patients, 40% of LUCAS patients, and 41% of control patients ($P = 0.82$). The death of three patients was clearly related to CPR. Two patients experienced liver rupture with the LUCAS device and exsanguinated, and one patient on AutoPulse experienced a tension pneumothorax and developed an air embolism in the brain. The authors concluded that the LUCAS device does not cause more serious or life-threatening harm than manual compressions, but more damage cannot be excluded with the AutoPulse device.

■ COMMENTARY

The LUCAS device did not exceed the 95% confidence intervals for non-inferiority, but the AutoPulse device did, so the authors could not confirm noninferiority for the AutoPulse device. Interestingly, the first AutoPulse trial ended early because of an increasing mortality trend, and previous trials of the LUCAS device have not shown improved outcomes. However, current guidelines recommend the use of these devices during patient transport and during coronary interven-

tions. Thus, it is pertinent to make sure these devices are not harmful. The LUCAS device did not increase serious organ damage, but did lead to more sternal fractures, which are rarely life-threatening. There were two cases in which the use of the LUCAS device seemed to be lethal. This was due to liver rupture, but surely the device could not have been properly placed to cause this complication. The AutoPulse device raises intrathoracic pressure and in one instance resulted in a tension pneumothorax with lethal air embolism to the brain. This cannot be ascribed to improper device use and may be a small but serious risk of the AutoPulse device.

The main strength of this study is that 90% of the patients underwent autopsy, CT scans, or extensive clinical evaluation of complications. However, there are several weaknesses. The patients were randomized before exclusion criteria were applied, which could have introduced biases. Placement of either device took three to five minutes. During this time, there could have been more return of spontaneous circulation. Everyone was subjected to usual chest compressions before the devices were placed, resulting in a device use time of only about 20 minutes. One would expect more time if the device was used in the catheterization laboratory. Ventilation use specifics were not provided, which could be an issue with the AutoPulse device in particular. Finally, the devices were compared to CPR enhanced by measurement devices, which provided instant feedback of rate and depth. The results compared to regular CPR could have been different.

How does this study inform clinical practice? Clearly, the LUCAS device, when deployed properly, is not harmful when compared to optimized CPR. Therefore, using this device in situations in which CPR is challenging (during coronary interventions) or unsafe for the operators (patient transport), as recommended in the guidelines, is reasonable. Other situations may be appropriate, too. When there is a large size difference between the patient and the operator, device use could be more effective. In this study, even with measured feedback, sternal depression was less than recommended with CPR. One of my colleagues, who is an above-average-sized man, hopes that when he arrests, healthcare providers use the LUCAS device rather than relying on a 90-pound intern to resuscitate him. ■

ABSTRACT & COMMENTARY

A Closer Look at the Effects of NSAIDs on Blood Pressure

By Michael H. Crawford, MD, Editor

SYNOPSIS: An ambulatory blood pressure monitoring substudy of the PRECISION trial showed that ibuprofen use significantly increased mean 24-hour systolic blood pressure compared to celecoxib. Further, naproxen produced intermediate results despite equivalent pain relief in patients with arthritis.

SOURCES: Ruschitzka F, Borer JS, Krum H, et al. Differential blood pressure effects of ibuprofen, naproxen, and celecoxib in patients with arthritis: The PRECISION-ABPM (Prospective Randomized Evaluation of Celecoxib Integrated Safety Versus Ibuprofen or Naproxen Ambulatory Blood Pressure Measurement) trial. *Eur Heart J* 2017;38:3282-3292.

Weintraub WS. Safety of non-steroidal anti-inflammatory drugs. *Eur Heart J* 2017;38:3293-3295.

Selective and nonselective nonsteroidal anti-inflammatory drugs (NSAIDs) are used often and on a regular basis in osteoarthritis patients, many of whom present with concomitant hypertension. However, the relative effect of various agents on blood pressure (BP) is unclear. Thus, the ambulatory blood pressure measurements (ABPM) substudy of the Prospective Randomized Evaluation of Celecoxib Integrated Safety vs. Ibuprofen or Naproxen (PRECISION) study of patients with osteoarthritis with or at increased risk of cardiovascular (CV) disease is of interest. Patients were randomized to three NSAIDs at a low dose that could be increased as needed (celecoxib 100-200 mg twice per day vs. ibuprofen 600-800 mg three times per day vs. naproxen 375-500 twice per day). ABPMs were performed every 20 minutes during awake times and every 30 minutes during sleep times. The primary endpoint was the change from baseline in mean systolic BP (SBP) at four months. Also, the relationship between the change in BP and subsequent major CV events were analyzed. Successful completion of the study was accomplished in 374 of the 545 subjects enrolled at 60 centers in the United States. The change in mean SBP was significant for ibuprofen (3.7 mmHg; $P < 0.001$) but not for celecoxib (-0.3 mmHg) or naproxen (1.6 mmHg). Clinic SBP showed similar results (5.2

mmHg with ibuprofen, 1.0 mmHg with celecoxib, and 3.2 mmHg with naproxen). During the 2.5-year follow-up, few patients experienced major CV events (nine with ibuprofen, seven with celecoxib, and six with naproxen). The authors concluded that the nonselective NSAID ibuprofen compared to the selective NSAID celecoxib showed a significant increase in mean SBP on ABPM.

■ COMMENTARY

Celecoxib is the only selective COX-2 inhibitor left on the market in most of the world. Thus, it was reassuring to see in the full PRECISION trial that hard CV endpoints were not significantly different with celecoxib compared to ibuprofen or naproxen (2.3% vs. 2.7% vs. 2.5%, respectively) as we reported last year in *Clinical Cardiology Alert*. Also, there were no differences in arthritis quality-of-life measures, but there were less observed gastrointestinal and renal adverse effects on celecoxib. It is well known that NSAIDs can increase BP. Small increases in SBP can increase the likelihood of adverse CV events significantly. Indeed, the observed adverse CV effects of NSAIDs may be more due to BP changes than their effect on endothelial function. Hence, this substudy of PRECISION patients undergoing ABPM is pertinent.

PRECISION-ABPM demonstrated several important points. Mean SBP/24 hours increased only by the nonselective NSAIDs. Also, hospitalizations for hypertension were 69% higher for patients on ibuprofen than those on celecoxib. Among subjects with normal BP at baseline, new hypertension was diagnosed in 10% on celecoxib, 23% on ibuprofen, and 19% on naproxen. The odds ratio for new hypertension on celecoxib was 0.39 (P = 0.004). These results were consistent across all subgroups, including factors such as race, diabetes, chronic kidney disease, and aspirin use. This more favorable effect on BP was accomplished at equivalent efficacy with arthritis relief.

The major limitation of this study was that the FDA limited the dose of celecoxib that could be used to a maximum of 400 mg/day. Most patients were on 200 mg/day. Previous studies that used higher doses showed increased CV adverse events with celecoxib vs. placebo. Also, there was not a placebo group in PRECISION, although it would have been difficult to conduct such a study in patients with symptomatic arthritis. However, the study was blinded and randomized. It is reassuring that low-dose celecoxib is reasonably safe. However, it is not completely safe, as a COX-2 inhibitor reduces prostacyclin and increases thrombosis risks. Finally, the results of PRECISION cannot be extrapolated to intermittent use of these drugs for arthritis flares. ■

ABSTRACT & COMMENTARY

Searching for a Connection Between Silent Myocardial Infarction and Heart Failure

By Van Selby, MD

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

SYNOPSIS: In a large community-based cohort, the development of silent myocardial infarction on ECG was associated with increased risk of future heart failure.

SOURCE: Qureshi WT, Zhang ZM, Chang PP, et al. Silent myocardial infarction and long-term risk of heart failure: The ARIC study. *J Am Coll Cardiol* 2018;71:1-8.

Approximately one-half of myocardial infarctions (MI) are silent, appearing as new Q waves on the ECG of a patient with no clinical evidence of MI. Although silent MI has been associated with increased all-cause mortality and other adverse outcomes, no one has conducted a large study to determine an association between silent MI and the risk of developing heart failure (HF).

Qureshi et al analyzed data from the Atherosclerosis Risk in Communities (ARIC) study. They retrospectively evaluated 9,243 patients determined to be free of cardiovascular disease during a baseline visit between 1987 and 1989. All patients underwent three follow-up evaluations, including an ECG, approximately once every three years. Silent MI was defined as ECG evidence of MI (appearance of a

major Q/QS wave or minor Q/QS wave plus major ST-T abnormalities) that was not present at baseline but was identified during any follow-up ECG in the absence of clinical evidence of MI. The primary outcome was new HF, defined as the first occurrence of HF hospitalization.

During a median follow-up of 13 years, 10.6% of participants experienced a first hospitalization for HF. In a multivariate analysis adjusted for age, sex, hypertension, and other risk factors, the development of silent MI was associated with an increased risk of HF (hazard ratio [HR], 1.35; $P = 0.035$). The risk of HF associated with silent MI was strongest in younger patients (HR, 1.66 in patients < 53 years of age compared to HR, 1.19 in patients > 53 years of age). The risk of silent MI was similar in men and women. The development of clinical MI (with compatible symptoms and biomarkers) was an even stronger predictor of HF (HR, 2.85; $P < 0.001$). The authors concluded that silent MI is associated with HF and provides an opportunity to identify a new HF risk factor.

■ COMMENTARY

This large, well-conducted cohort study showed that > 3% of patients with no cardiovascular disease at baseline developed silent MI during the follow-up period. Given the frequency with which ECGs are obtained in routine clinical practice, it is important to understand the clinical significance of this finding. By demonstrating that silent MI is associated with increased risk of future HF, Qureshi et al built on previous work to show an association between silent MI and other adverse outcomes.

These findings are not particularly surprising, as the relationship between myocardial damage and subsequent dysfunction is well known. Similarly, it is not surprising the risk of HF associated with clinical MI was stronger than that associated with silent MI. Clinically apparent MIs may represent larger infarct size, and, therefore, are more likely to cause myocardial dysfunction. But while guidelines provide clear recommendations for management following clinical MI, there are no strong data to inform the management of patients with silent MI. Although identifying silent MI as a risk factor is important, the next obvious step is to find a solution.

Based on the findings of this study, patients with silent MI but no evidence of cardiomyopathy or clinical HF could be considered American College of Cardiology/American Heart Association Stage A HF ("at risk for HF"). Management of these patients focuses on a heart-healthy lifestyle, prevention of vascular and coronary disease, and prevention of left ventricular (LV) structural abnormalities. The finding of silent MI could (and should) be used to encourage patients to increase exercise or quit smoking. In patients with silent MI and hypertension, treating with drugs that have been shown to prevent LV remodeling, such as ACE inhibitors, seems like a logical choice, although this strategy has not been evaluated in large clinical trials.

ARIC is a well-organized study with much strength. However, several limitations are worth noting. Approximately 40% of patients were missing an ECG and were excluded from the analysis. The diagnosis of HF was based purely on ICD-9 codes, without validation by physician review.

Despite these limitations, based on the strength of their findings and our knowledge of cardiovascular pathophysiology, the association between silent MI and HF seems valid. Qureshi et al have identified a new HF risk factor that is cheap and easy to treat. For now, the presence of silent MI should alert the treating clinician to treat other cardiovascular risk factors aggressively. As the prevalence of HF continues to increase, future studies hopefully will provide specific interventions to decrease progression to HF in at-risk patients. ■

ABSTRACT & COMMENTARY

Noninvasive Ablation of Ventricular Tachycardia: A Paradigm Shift?

By Joshua D. Moss, MD

Associate Professor of Clinical Medicine, Cardiac Electrophysiology, Division of Cardiology, University of California, San Francisco

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

SYNOPSIS: In five patients with recurrent ventricular tachycardia refractory to conventional therapies, relatively short treatments with electrophysiology-guided stereotactic body radiation therapy were highly effective at reducing arrhythmia burden.

SOURCE: Cuculich PS, Schill MR, Kashani R, et al. Noninvasive cardiac radiation for ablation of ventricular tachycardia. *N Engl J Med* 2017;377:2325-2336.

Although catheter mapping and ablation techniques advance, ventricular tachycardia (VT) remains a difficult problem to manage in many patients with cardiomyopathy. Arrhythmogenic substrate that is mid-myocardial and not easily targeted with radiofrequency energy delivered from either the endocardial or epicardial surface of the heart poses a particular challenge. Additionally, catheter ablation procedures often take many hours to complete, and complications, while infrequent, can be serious or life-threatening.

Cuculich et al sought to demonstrate an entirely noninvasive technique for both identifying arrhythmogenic substrate and delivering ablation energy to eliminate refractory VT. To identify target areas for ablation, patients underwent multielectrode body-surface electrocardiography using a 256-electrode vest while VT was induced via noninvasive programmed stimulation (NIPS) using their existing implantable cardioverter defibrillators (ICD). The electrocardiographic data, combined with chest CT imaging, were used to identify sites of earliest electrical activation during VT (the "exit sites"). Additionally, single-photon emission CT or MRI was used to identify areas of anatomic scarring. A volumetric target for ablation was identified, targeting the exit site of the VT and the full myocardial thickness of any associated ventricular scar. Patients underwent a specialized planning CT scan to expand the target ablation area, accounting for respiratory and cardiac motion as well as uncertainty in radiation delivery. Once an electrophysiologist and radiation oncologist determined the planned target volume, a single total dose of 25 Gy was delivered using a stereotactic body radiation therapy (SBRT) device, an off-label clinical use.

During an eight-month period, nine patients were evaluated for this novel therapy, and five underwent treatment. Of those five, the mean left ventricular ejection fraction was 23%, all demonstrated New York Heart Association class III or IV heart failure symptoms, all were taking multiple antiarrhythmic drugs, and three had failed prior invasive catheter ablation. Patients experienced between five and 4,312 VT episodes in the three months prior to SBRT (6,577 total episodes for all five patients). The actual radiation treatment required only 11-18 minutes and targeted between 17 and 81 mL of tissue. Patients left the hospital one to two days after treatment. The authors instituted a six-week "blanking period" after radiation therapy to account for expected arrhythmias arising from post-ablation inflammation. One elderly patient with severe cardiomyopathy, a very high VT burden, atrial fibrillation, and contraindications to anticoagulation suffered a fatal stroke three weeks after treatment. In the remaining four patients, there were four episodes of VT in 46 patient-months after the six-week blanking period, a 99.9% reduction in arrhythmia burden from baseline. Only one ICD shock was delivered during that follow-up period, compared with 55 shocks prior to treatment.

■ COMMENTARY

Although small, this study is remarkable in several ways. First, it represents a completely novel approach to the treatment of VT that relies on neither antiarrhythmic drugs (and their associated toxicities) nor invasive catheter mapping and ablation (with lengthy procedure times, limitations in delivering transmural energy, and risk of acute complications). After careful, noninvasive, and relatively low-risk planning procedures, the actual radiation therapy required an average of < 15 minutes. The reduction in arrhythmia burden far exceeded nearly all prior studies of invasive catheter ablation for VT, although to be fair, the actual recurrence rate was technically 50%. Of the four patients who survived past the six-week blanking period and onward to one year of follow-up, one experienced three episodes of recurrent VT during follow-up (compared to 30 in the three months pre-treatment), and another patient experienced one episode during follow-up (compared to five in the three months pre-treatment). Nevertheless, all patients discontinued antiarrhythmic medication, with one patient restarting amiodarone at nine months.

The authors wisely cautioned against considering the procedure suitable for clinical use based on these initial data alone. Serial CT scans at three months showed inflammatory changes in the lung tissue adjacent to the target ablation area, although there was near-complete resolution by 12 months. That said, late toxic effects to the heart and adjacent structures from high-dose focal SBRT are feasible and will require longer-term follow-up in a larger study population to fully assess. The one patient who suffered a fatal stroke three weeks after radiation treatment presented with multiple risk factors for thromboembolism, including atrial fibrillation without ongoing anticoagulation, but an unanticipated risk of SBRT cannot be ruled out completely.

For now, this procedure likely will be reserved for participants in research trials at limited centers or for compassionate use. However, with further refinement and study, noninvasive cardiac radiation carries the potential to represent a true paradigm shift in the treatment of refractory ventricular tachycardia. ■

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CME QUESTIONS

1. **Which of the following is most likely to significantly elevate systolic blood pressure in patients with arthritis?**
   a. Celecoxib
   b. Ibuprofen
   c. Naproxen
   d. Acetaminophen

2. **Mid-wall origin ventricular tachycardia has been treated successfully in a few cases with:**
   a. high-frequency ultrasound.
   b. targeted microwave energy.
   c. stereotactic radiation therapy.
   d. All of the above

3. **Major organ damage with CPR is least likely to occur with the deployment of:**
   a. a LUCAS device.
   b. an AutoPulse device.
   c. standard CPR.
   d. a LUCAS device and standard CPR.

4. **A silent myocardial infarction detected on ECG is a harbinger of:**
   a. more infarcts.
   b. atrial fibrillation.
   c. heart failure.
   d. stroke.

5. **Switching from prasugrel or ticagrelor to clopidogrel 30 days after stenting for acute coronary syndromes resulted in:**
   a. fewer bleeding complications.
   b. higher mortality.
   c. more stent thrombosis episodes.
   d. fewer strokes.

CME 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.