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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

FDA Approves Ivabradine for Systolic Heart Failure

By Van Selby, MD

Assistant Professor of Medicine, UCSF Cardiology Division, Advanced Heart Failure Section

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

SOURCES: Böhm M, et al. Twenty-four-hour heart rate lowering with ivabradine in chronic heart failure: Insights from the SHIFT Holter substudy. *Eur J Heart Fail* 2015;17:518-526.
Swedberg KS, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): A randomized placebo-controlled study. *Lancet* 2010;376:875-885.

On April 15, the FDA approved ivabradine for reducing the risk of hospitalization in stable symptomatic heart failure (HF), sinus rhythm, and a resting heart rate of ≥ 70 bpm on a maximally tolerated dose of beta-blocker. Ivabradine is a selective I_f ("funny current") inhibitor that lowers heart rate by acting primarily on the sinoatrial node.

The primary data supporting approval come from the Systolic Heart Failure Treatment with the I_f inhibitor Ivabradine Trial (SHIFT), which randomized 6558 patients with symptomatic heart failure, ejection fraction ≤ 35%, sinus rhythm with a heart rate of ≥ 70 beats per minute, and at least one hospitalization for HF within the previous year to ivabradine vs placebo. During a median 23 months of follow-up, patients randomized to ivabradine had a significantly lower rate of the primary endpoint of cardiovascular death or hospitalization for worsening heart failure (hazard ratio, 0.82; $P < 0.0001$). The positive result was driven primarily by a reduction in hospitalization for heart failure, with no significant effect on all-cause mortality. The drug was well tolerated overall with relatively few serious side effects.

In a recently published substudy from SHIFT, 602 patients wore 24-hour Holter monitors while randomized to ivabradine or placebo. Over 8 months, average heart rate decreased by 9.5 ± 10.0 bpm in patients randomized to ivabradine compared to 1.2 ±

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8.9 bpm in the placebo group ($P < 0.0001$). There were no significant differences in the rate of ventricular or supraventricular arrhythmias. Patients randomized to ivabradine had a higher risk of experiencing heart rate < 40 bpm ($P < 0.0001$), but no patient in either group had an episode of heart rate < 30 bpm. The authors concluded that ivabradine effectively lowers heart rate in patients with systolic HF without significant adverse effects.

■ COMMENTARY

The approval of ivabradine introduces heart rate as a target for treatment of systolic HF. Several findings from SHIFT support this concept. In the placebo arm of the trial, baseline heart rate was proportionally related to adverse outcomes. Furthermore, in subjects randomized to ivabradine there was an association between the heart rate achieved on therapy and subsequent outcomes, and the beneficial effects of ivabradine were mostly explained by heart rate reduction. The Holter study clearly demonstrates the ability of ivabradine to effectively lower the heart rate throughout the day.

SHIFT met the primary endpoint and makes a compelling argument for aggressive heart rate reduction. However, there are several important points to keep in mind. When the original SHIFT trial was published, many heart failure experts raised concerns regarding the generalizability to the U.S. heart failure population. No patients were enrolled from sites in the United States, with the majority from Eastern Europe. While 90% of patients were on some beta-blocker at randomization, only 49% were taking at least 50% of the target dose and only 23% were at the target dose. Hypotension was the most commonly cited reason for not achieving target doses of beta-blocker, but the average systolic blood pressure was 122 mmHg, suggesting there may in fact have been room to increase the dose. Whether patients would have seen similar benefit with ivabradine had they already been taking guideline-recommended doses of beta-blockers is unknown. In SHIFT, patients taking at least 50% of guideline-recommended doses of beta-blockers at randomization did not experience a significant benefit with respect to the primary outcome, although there was a mild reduction in HF hospitalizations. Given the overwhelming evidence from clinical trials showing benefit with beta-blockers in the treatment of systolic heart failure (including mortality benefit), it is imperative that clinicians strive to attain guideline-recommended doses of beta-blockers before considering ivabradine. In the real world, with aggressive use of guideline-based beta-blockers the number of patients eligible for ivabradine may prove to be relatively small. For now, in HF patients with a heart rate above 70 bpm despite truly maximum-tolerated doses of beta-blockers, ivabradine is a reasonable option. ■

ABSTRACT & COMMENTARY

Valve Thrombosis After TAVR: Is It as Rare as We Thought?

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.

SOURCES: Leetmaa T, et al. Early aortic transcatheter heart valve thrombosis: Diagnostic value of contrast-enhanced multidetector computed tomography. *Circ Cardiovasc Interv* 2015;8:e001596.
Latib A, et al. Treatment and clinical outcomes of transcatheter heart valve thrombosis. *Circ Cardiovasc Interv* 2015;8:e001779.

Several years ago, before we began performing transcatheter aortic valve replacement (TAVR) at our own institution, one of my patients came for a 1-month follow-up visit after having TAVR elsewhere. We were alarmed to discover

that his transvalvular gradients had quadrupled since his procedure. Ultimately we hit upon case reports of early transcatheter aortic valve thrombosis, and began systemic anticoagulation. Now, two new reports in shed new light on this phenomenon.

In the study by Leetmaa et al, a series of 140 patients receiving the Edwards Sapien valve at a single center underwent multidetector CT 1-3 months after TAVR. Valve thrombosis was identified in five patients, which was 4% of the sample. Four of the five patients were asymptomatic, and in these patients echocardiography showed no structural abnormality and no abnormal gradients. Three of the five had ejection fractions below 35%, and two did not receive the standard post-TAVR dual antiplatelet therapy. No structural issues (underexpansion, non-circularity) were noted with the valves in the affected patients.

Latib et al looked at retrospective data from 4266 patients undergoing transcatheter aortic valve replacement at 12 centers between 2008 and 2013. Thrombosis events were defined as: 1) valve dysfunction secondary to thrombosis diagnosed based on response to anticoagulation therapy or imaging, or 2) mobile mass detected on the valve suspicious for thrombus in the absence of infection, irrespective of dysfunction. By these criteria, 26 (0.61%) valve thromboses were reported, of which 20 came from the Edwards Sapien/Sapien XT cohort and six from the Medtronic CoreValve cohort. Seventeen patients (65%) presented with exertional dyspnea, while eight (31%) had no specific symptoms. Only one of the patients had discontinued the recommended antiplatelet regimen.

Echocardiography demonstrated increased transvalvular gradients in the majority (92% had mean gradients > 20 mmHg), with an average mean gradient of 40.5 mmHg. Thickened leaflets or thrombotic apposition of leaflets was seen by echo in 77% of cases, while only six (23%) showed a thrombotic mass. None of the identified patients had stroke or other evidence of thromboembolic phenomena. Of the 26 identified patients, 23 were treated with systemic anticoagulation. This resulted in a significant decrease of the trans-valve gradient or disappearance of the thrombotic mass in all 23 patients. The authors concluded the following:

- Valve thrombosis occurred in 0.61% of TAVR patients in this registry. Patients most often presented with dyspnea and increased transvalvular gradient.
- All thrombosis cases occurred within 2 years from transcatheter aortic valve implantation and were not associated with discontinuation of antiplatelet therapy.
- Thrombosis should be suspected in cases of premature valve dysfunction, even if a thrombotic mass is not clearly detected.
- Anticoagulation resulted in restoration of normal valve function within 2 months of treatment, and should be considered the treatment of choice when transcatheter valve thrombosis is suspected.

■ COMMENTARY

With TAVR now making its way into the mainstream of treatment options for patients with severe aortic stenosis, we are seeing increasing numbers of patients who have undergone this procedure in all settings, and, therefore, we need to be aware of less-common complications. The CT study demonstrates that valve thrombosis may be more common than earlier thought, although the meaning of asymptomatic thrombus formation without valve dysfunction is far from clear. There are no data to guide us when presented with evidence of an asymptomatic thrombosis. While CT may be more sensitive than echo for detection of such issues, CT is not indicated as a routine screening tool post-TAVR.

On the other hand, the registry study highlights only the subset of valve thrombosis events that came to clinical attention, and here the advice is more clear. Dual antiplatelet therapy, although recommended as a standard therapy, is not fully effective at preventing this outcome. Transcatheter valve thrombosis should be considered in all cases of transcatheter valve dysfunction and should be treated with anticoagulation — in most cases with vitamin K antagonists. Echocardiography will usually show increased gradients, but may not reveal any structural abnormality. Advice from experienced valve centers should be sought in equivocal cases. ■

ABSTRACT & COMMENTARY

Endovascular Intervention Takes Center Stage in Treatment of Acute Stroke

By Jeffrey Zimmet, MD, PhD

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

SOURCES: Jovin TG et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med* 2015 Apr 17. [Epub ahead of print].
Saver JL et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015 [Epub ahead of print].

Not long ago, the relative merits of interventional therapy vs thrombolytics were in doubt in acute myocardial infarction. Today, primary PCI is the clear standard of care. In a similar vein, data for endovascular intervention in acute stroke have historically been equivocal, with multiple prior studies failing to show a clear benefit. With more recent trials, however, using up-to-date technology and careful patient selection, the tide appears to have turned. Two recent randomized trials, published online April 17 in the *New England Journal of Medicine*, illustrate the direction this field is taking.

The REVASCAT trial enrolled acute ischemic stroke patients with evidence of proximal anterior circulation occlusion and the absence of a large infarct on neuroimaging who presented early enough to be treated within 8 hours of symptom onset. The patients randomized to thrombectomy who received alteplase were required to have evidence of ongoing occlusion 30 minutes after initiation of infusion (to exclude those with complete response to tPA). The primary outcome was the severity of disability at 90 days, as assessed by the modified Rankin scale (mRS).

Although the REVASCAT trial was initially intended to enroll 690 patients, recruitment stopped after only 25% of patients had completed their 90-day follow up (206 patients) at the recommendation of the data and safety monitoring board, because of loss of equipoise. At 90 days, there was a greater reduction in severity of disability with thrombectomy vs medical therapy alone based on the distribution of mRS points. After adjustment, the odds ratio for improving 1 mRS point was 1.7 (95% confidence interval, 1.05-2.80). Secondary outcomes, including functional independence and infarct volumes by imaging, also favored thrombectomy.

The SWIFT PRIME trial was a multicenter study conducted at 39 centers in the United States and Europe. One hundred ninety-six patients were randomized to tPA plus thrombectomy vs tPA alone. The study used iterations of a specific stent retriever thrombectomy device (the Solitaire device), and was funded by its manufacturer, Covidien. As in the REVASCAT trial, all subjects had confirmed occlusion of the intracranial internal carotid artery, the first segment of the middle cerebral artery, or both on vessel imaging and an absence of large infarct at the time of intervention. The primary outcome measure was, similarly, disability at 90 days, as assessed by means of the mRS.

Thrombectomy treatment met the primary endpoint, with an impressive number needed to treat (NNT) of only 2.6 for one additional patient to have a less-disabled outcome. The proportion of patients who were functionally independent at 90 days was higher in the intervention group than in the control group, with an absolute difference of 25 percentage points.

In both studies, the authors conclude that mechanical thrombectomy in patients presenting early with acute ischemic stroke due to large vessel occlusion is both safe and effective in reducing disability at 90 days.

■ COMMENTARY

These two studies join a growing body of recent evidence (MR CLEAN, ESCAPE, EXTEND IA) supporting improved clinical outcomes with interventional treatment of acute stroke. This comes on the heels of a slew of negative trials from just 2 years ago, IMS, MR RESCUE, and SYNTHESIS, which had suggested that invasive therapy was no more effective than intravenous tPA alone. What accounts for the change?

The REVASCAT manuscript points out four major issues that differentiate the positive from the negative trials: 1) limiting enrollment to patients with imaging-confirmed occlusion of the proximal portion of the middle cerebral artery with or without concomitant occlusion of the internal carotid artery; 2) imaging-based exclusion of patients who have already sustained a large infarct at the time of presentation; 3) use of a stent retriever to optimize technical success; and 4) optimization of reperfusion times.

In viewing these results, we must recognize that a minority of patients with acute stroke meet these stringent entry criteria; an accompanying editorial by Anthony J. Furlan quotes an estimate of 10%. Identifying these patients requires the rapid performance and interpretation of structural and perfusion imaging in advance of proceeding to intervention, which requires a significant infrastructure in addition to what is required for the intervention itself. Nonetheless, with such striking results suggesting a low NNT to reduce disability, we are sure to see the further development of interventional stroke systems in years to come. ■

ABSTRACT & COMMENTARY

Antibiotic Prophylaxis Guidelines and Endocarditis Rates

By Michael Crawford, MD, Editor

SOURCE: Dayer MJ, et al. Incidence of infective endocarditis in England, 2000-13: A secular trend, interrupted time-series analysis. *Lancet* 2015;385:1219-1228.

Because no randomized, clinical trials of antibiotic prophylaxis for the prevention of infective endocarditis (IE) have ever been done, between 2007 and 2009, guidelines from the American Heart Association and the European Society of Cardiology recommended antibiotic prophylaxis (ABP) for high-risk patients only, and the United Kingdom National Institute for Health and Clinical Excellence recommended complete cessation of ABP in 2008. The latter afforded an opportunity to study ABP vs no ABP in the UK. Thus, these investigators performed a retrospective, interrupted time series study comparing ABP from 2004-2013 and IE hospital records from 2000-2013. ABP in the United Kingdom consisted of a unique prescription of a single-dose of amoxicillin or clindamycin. Episodes of IE were only counted once, excluding hospital transfer and readmission cases. The incidence of IE was corrected for changes in the UK population. High-risk patients were identified if they had prior IE, a predisposing cardiac condition, or a prior cardiac operative procedure that put them at risk.

After 2008, the number of prescriptions for ABP fell from about 11,000/month to about 1300/month by 2013. Prior to 2008, there was an upward trend in IE incidence, but afterward the slope of the line increased significantly, so that by 2013, there were 35 more cases per month than expected. The increase in IE affected both high- and low-to-moderate-risk individuals. The incidence of IE associated death also trended upward, but was not statistically significant. The authors concluded that the incidence of IE in the United Kingdom has increased significantly since the introduction of the new guidelines.

■ COMMENTARY

Smaller U.S. studies with a 2-year follow up have not shown an increase in IE after the new guidelines were published. This study is much larger with almost 20,000 cases of IE and it has a 5-year follow-up. The data are convincing that the incidence of IE is rising in the UK. The other big difference is that ABP was still allowed in the United States for high-risk cases. The new UK guidelines recommended complete cessation of ABP. Thus, it may be that ABP for higher-risk patients may outweigh any risks or costs associated with this strategy, but not for low-risk individuals. Perhaps the U.S. guideline got it right by recommending ABP for patients with prior IE, prosthetic valves, cyanotic congenital heart disease, and certain repaired congenital lesions. However, these new data raise the question of whether intermediate-risk patients would benefit from ABP. Such patients would include those with repaired valve lesions, known rheumatic valve disease, and ventricular assist device patients. I have been most uncomfortable excluding ABP from known valve disease, especially mitral regurgitation, and repaired valves or repaired congenital lesions with residual valve disease or shunts. More disturbing in this UK study was the trend toward a high death rate in IE, which was not statistically significant. This could be because most ABP is for dental procedures, and IE from oral flora is less likely to be fatal. Also, there may have been too few deaths to have the statistical power for this analysis.

The major issue with this study is that it is observational and, thus, does not prove a cause-effect relationship. However, the investigators tried to find other explanations, such as the increased use of electrical leads in the heart, but could not. There are weaknesses in this study. It was based on hospital coding which can be unreliable. The diagnosis of IE can be challenging and some patients may have been treated empirically without a definite diagnosis. There are no data on the types of organisms causing IE. One would expect mouth flora cases to increase, which would support the lack of ABP hypothesis. There is no information on the type or frequency of dental care. In the United Kingdom, most ABP prescriptions are written by dentists. Finally, there is no information on potential demographic changes in the population. For example, more immigrants with rheumatic heart disease could change the risk pool.

Despite the limitations of this type of study, it supports the U.S. view of treating high-risk patients with ABP. We should not go back to treating low-risk patients, such as those with mild mitral valve prolapse and mild mitral regurgitation. However, this study does encourage me to broaden my indications into more moderate-risk patients, such as those with significant mitral regurgitation. ■

ABSTRACT & COMMENTARY

Insights into the Association of Atrial Fibrillation and Myocardial Infarction

By Cara Pellegrini, MD

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

SOURCE: Soliman EZ, et al. Atrial fibrillation and risk of ST-segment elevation versus non-ST segment elevation myocardial infarction: The atherosclerosis risk in communities (ARIC) study. *Circulation* 2015 Apr 27. pii: CIRCULATIONAHA.114.014145. [Epub ahead of print].

Atrial fibrillation (AF), a condition that affects more than 5 million people in the United States alone, has long been recognized to have implications beyond its obvious effect on heart rhythm. A diagnosis of AF quickly triggers discussions of appropriate stroke prevention, given the associated five-fold risk of stroke in persons with AF. It has also been found to portend other poor outcomes, such as a three-fold risk of heart failure, and a doubling of risk of dementia and death. Most recently, the relationship of AF and myocardial infarction (MI) has been a focus of study, with large cohorts finding prevalent AF to be associated with increased risk of incident MI.

Soliman and colleagues sought to confirm that association and, more interestingly, shed some light on a potential mechanism in utilizing the atherosclerosis risk in communities (ARIC) cohort of 14,462 participants without coronary heart disease at baseline. The ARIC study investigated the variation in cardiovascular risk factors, medical care, and disease by race and sex; more than half the study population was female and a quarter were African American. Only 31 patients had known AF at baseline. Incident AF came from intermittent electrocardiograms and review of discharge records, and MI data came from hospitalization records. AF was investigated as a time-varying variable with overall incident MI and by type of MI, ST elevation MI (STEMI) or non-ST elevation MI (NSTEMI). AF events occurring after an MI were not included.

Over a median follow-up of 21.6 years, 1374 MI events occurred, 80% of which were NSTEMIs. AF was associated with a 63% increased risk of MI after adjustment for potential confounders (hazard ratio [HR] 1.63; 95% confidence interval [CI], 1.32-2.02). Notably, AF was only associated with NSTEMI risk, (HR, 1.80; 95% CI, 1.39-2.31), and not STEMI risk. With adjustment for age, those with AF had an almost three-fold incidence of MI as compared to those without an AF diagnosis. Among women and blacks, the risk of MI in the setting of AF was disproportionately high, with women incurring an almost four-fold risk of MI with a diagnosis of AF (incidence rate ratio 3.75; 95% CI, 3.14-4.47) and blacks a more than three-fold risk (incidence rate ratio 3.26; 95% CI, 2.57-4.14).

■ COMMENTARY

The relationship between AF and MI is complex. AF may predispose to MI due to an increase in oxygen demand with higher heart rates and sympathetic activation. Alternatively, the mechanism may be less direct, occurring in part due to the endothelial dysfunction, pro-inflammatory state, and prothrombotic effects of AF. The lack of association between AF and STEMIs, typically vaso-occlusive events, suggests that direct coronary thromboembolism is a less likely mechanism. Coronary artery disease is also known to increase AF risk, but those with coronary heart disease were excluded at baseline.

The elevated risk in women and African Americans may be due to genetic differences or differences in AF-associated morbidities. As previous data have shown, these groups are less likely to be treated with anticoagulation or even be aware of their AF; under-treatment may play a role. Though adjustment for warfarin use did not do much to narrow the gap between women and men or whites and blacks in this study, the absolute number of those treated with anticoagulation, how tight their INR control was, and the effect of novel anticoagulants were not studied.

Given the mounting evidence suggesting that stroke, MI, and AF have pathophysiologic mechanisms in common, the presence of any one should at a minimum heighten suspicion for the others. Other data have suggested that CHADS-Vasc scores predict stroke incidence outside the context of AF, though with a lower absolute risk. Particularly with the options provided by the novel anticoagulants, I suspect that our threshold for anticoagulation of a cohort deemed to be at risk for cardiovascular disease in general will continue to drop. Special attention to seeking and treating AF in women and blacks should be encouraged, as the complications of this rhythm appears higher for them. ■

ABSTRACT & COMMENTARY

The Echo Calcium Score

By Michael Crawford, MD, Editor

SOURCES: Gaibazzi N, et al. Prognostic value of echocardiographic calcium score in patients with a clinical indication for stress echocardiography. *JACC Cardiovasc Imaging* 2015;8:389-396.

Gardin JM. Can calcium supplementation improve stress echocardiography? *JACC Cardiovasc Imaging* 2015;8:397-939.

Aortic valve sclerosis and mitral annular calcification detected by echocardiography are known to be associated with atherosclerosis and are predictive of cardiovascular (CV) morbidity and mortality. These investigators from Italy hypothesized that an echo calcium score (eCS) could predict CV events in subjects without known coronary artery disease (CAD). They retrospectively selected 1303 subjects from five European and one U.S. institution without known CAD, significant valvular disease, or chronic kidney disease, who had stress echoes done by either pharmacologic stress (60%) or exercise stress for clinical reasons (40%). Transthoracic echoes were evaluated for evidence of calcium in the aortic valve, mitral annulus, ascending aorta, and papillary muscles, which was scored as a range from 0 to 8. Outcomes were determined by chart review or patient or primary physician phone calls. Mean subject age was 63 years, and 57% were men. Scores of 0 were present in 58%, and 98% of the subjects had scores between 0 and 4. Positive stress tests were found in 12%, and they were more likely to have an eCS > 0 ($P < 0.001$). During the median follow-up of 27 months, 58 patients experienced the primary endpoint of death (n = 37) or myocardial infarction (n = 21). In addition to age and diabetes, eCS and a positive stress echo were multivariate predictors of the combined endpoint, but only stress echo demonstrated incremental discrimination over clinical variables. Subjects with eCS > 0 and a positive stress echo had the worst prognosis with a 3-year event rate of 24% vs 2% in those with no calcium and a negative stress test ($P < 0.001$). The authors concluded that eCS has significant independent prognostic value for predicting CV events.

■ COMMENTARY

The detection of coronary artery calcium by CT scan has been known to have considerable predictive and prognostic value for CAD. The detection of cardiac and vascular calcification by echocardiography has also been shown to be associated with atherosclerosis. So the concept that cardiac and proximal aortic calcium detected on echo may be of value in the evaluation of patients suspected of having CAD is an interesting idea that was tested in this study.

Unlike CT scans, echo does not expose the patient to radiation and costs much less. Also, if a stress echo has been deemed clinically indicated, one can more or less evaluate calcium in the heart and aorta for little or no incremental cost. This study demonstrated that eCS does have independent predictive value for death and myocardial infarction at any level of calcium detected. The sensitivity and specificity of eCS for these hard events was 74% and 60%, respectively. However, as the authors stated, eCS "failed to demonstrate incremental value on top of clinical and stress wall motion data." Consequently, it is difficult to know how to use this information clinically from this study.

The strengths of this study are that the reproducibility of the eCS was good (correlation coefficient 0.80) and any calcium detected was equally good, a predictor compared to no calcium, so there is no need to calculate a score. Unfortunately, there are important weaknesses in this study. The study population is biased toward subjects with suspected CAD undergoing clinically indicated stress testing. However, few had a positive stress test (12%), and few had eCS scores > 3 out of 8, so many were lower risk. Also, it is not clear if the patients at each of the six centers were similar, especially since many centers used pharmacologic stress echo, which is rarely used in the United States. In addition, the distinction between calcium and fibrosis on echo is not always accurate. Finally, in this retrospective study, the blinding of the stress results from the eCS value would be difficult to do.

Despite these caveats and limitations, I believe this study demonstrates that there is some value to making a note of what appears to be calcium on an echocardiogram, as it is probably evidence of an atherosclerotic process. The echo images in this paper are shown side by side with CT images, and there is remarkable similarity. Of course, these are undoubtedly the best images they have. Nevertheless, although not a game changer, calcium in the heart and aorta on echo is worth adding to the evidence for vascular disease in a patient. ■

QUESTIONS & COMMENTS:
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CME QUESTIONS

1. **Since new guidelines recommending cessation of antibiotic prophylaxis in the UK were published, the incidence of infective endocarditis has:**
   a. stayed the same.
   b. increased.
   c. decreased.
   d. increased in high-risk patients.

2. **Atrial fibrillation increases the risk of:**
   a. stroke.
   b. heart failure.
   c. myocardial infarction.
   d. All of the above

3. **Mechanical thrombectomy treatment for stroke is indicated in patients with:**
   a. proximal middle cerebral artery occlusion.
   b. negative head CT scan for large infarct.
   c. presentation within 2 hours of symptom onset.
   d. Both A and B

4. **Ivabradine is indicated in heart failure patients with:**
   a. hypotension on ACEI/ARB therapy.
   b. rising creatinine on diuretics.
   c. a heart rate > 70 beats/min after maximum tolerated beta blocker therapy.
   d. evidence of hepatic hypoperfusion.

5. **Evidence of cardiac or aortic calcium on echocardiography suggests:**
   a. coronary atherosclerosis.
   b. rheumatic heart disease.
   c. Marfan's syndrome.
   d. syphilis.

6. **Which of the flowing is most correct concerning valve thrombosis after TAVR?**
   a. It occurs in 10%.
   b. It is associated with antiplatelet therapy cessation.
   c. It can occur without a visible thrombus on echo.
   d. Anticoagulation therapy is ineffective.

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.