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ABSTRACT & COMMENTARY

What Device-Detected Atrial Fibrillation Burden Reveals About Stroke Risk

By Joshua Moss, MD

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

SYNOPSIS: In a retrospective analysis of electronic health record data matched with remote pacemaker and implantable cardioverter-defibrillator recordings of atrial fibrillation episodes, a threshold daily arrhythmia burden portending higher stroke risk was determined over a range of CHA_2DS_2-VASc scores.

SOURCE: Kaplan RM, Koehler J, Ziegler PD, et al. Stroke risk as a function of atrial fibrillation duration and CHA_2DS_2-VASc score. *Circulation* 2019;140:1639-1646.

Multiple studies have demonstrated a correlation between stroke risk and the burden and duration of atrial fibrillation (AF) episodes detected by implantable pacemakers and defibrillators. Kaplan et al sought to explore further this correlation and its interaction with traditional stroke risk factors, as assessed by the CHA_2DS_2-VASc score, in a large, retrospective study cohort. The Optum electronic health record (EHR) database, with deidentified data from patients collected between 2007 and 2017, was used in conjunction with linked data from a Medtronic CareLink database.

A total of 28,032 patients met the assigned inclusion criteria: an implanted device with an atrial lead capable of detecting AF, at least six months of CareLink device data before an assigned index date from which to calculate AF burden, at least 12 months of EHR data before that assigned index date from which to calculate a CHA_2DS_2-VASc score, and at least six months of EHR data after the assigned index date from which to assess rates of ischemic stroke and systemic embolism. Average patient age was 69 years, and 63% were male. Diagnoses of transient ischemic attack (TIA) were excluded, given the more ambiguous definition in the EHR. Burden

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of AF was classified into three groups based on maximum daily AF duration in the six months before the index date: no AF (< 6 minutes), 6 minutes to 23.5 hours, and > 23.5 hours.

In patients not on anticoagulation, both longer AF duration and a higher CHA_2DS_2-VASc score were significantly associated with an increased rate of stroke and systemic embolism (SSE). The rate was slightly higher in the subset of those patients with a clinical history of AF at baseline (and also recorded a higher mean CHA_2DS_2-VASc score). Patients with a CHA_2DS_2-VASc score ≥ 2 with AF detected (but not on anticoagulation) tended to be slightly older and were more likely to be female, but clinical contraindications for anticoagulation were unavailable.

There was a clear interaction between AF duration and CHA_2DS_2-VASc score when assessing stroke risk in patients not on anticoagulation. In patients with a CHA_2DS_2-VASc score of 2, SSE risk was less than 1% per year when maximum AF daily duration was < 23.5 hours, and 1.52% per year with duration > 23.5 hours. On the other hand, in patients with a CHA_2DS_2-VASc score of 3-4, SSE risk was less than 1% per year only when maximum AF daily duration was < 6 minutes, and 1.28-1.77% per year when > 6 minutes. Patients with a CHA_2DS_2-VASc score ≥ 5 had a stroke risk > 1.5% per year, regardless of AF duration (or even whether they were on anticoagulation).

The authors concluded a combination of AF duration and CHA_2DS_2-VASc score can be used to make more informed decisions about initiation of anticoagulation. Using a 1% yearly stroke rate as the "actionable threshold" (the threshold at which the risk of ischemic stroke exceeds the risk of intracranial hemorrhage on oral anticoagulation), Kaplan et al hypothesized a favorable effect of anticoagulation in patients with a CHA_2DS_2-VASc score of at least 2 when maximum AF duration exceeded 23.5 hours/day, and in patients with a CHA_2DS_2-VASc score of 3-4 when maximum AF duration exceeded six minutes/day.

■ COMMENTARY

This large study, with its robust rhythm-monitoring data, was strong in several ways, making it useful for informing discussions with patients about the risks and benefits of therapeutic anticoagulation. The criteria used to define stroke were fairly strict, which should improve the overall specificity, but might underestimate actual SSE rates. Patients and clinicians alike often wonder whether brief episodes of AF lasting less than a day truly increase stroke risk. These data provide information that is more nuanced than yes/no and that is both clinically plausible and simple to convey in layman's terms.

There also are some caveats that must be considered. First, regarding accuracy and applicability of the data, a study of EHR and CareLink databases comes with all the usual pitfalls of a retrospective analysis. Outcomes in patients with pacemakers and implantable cardioverter-defibrillators may not be directly generalizable to the entire population. Interestingly, the overall rate of SSE in patients not on anticoagulation (615 strokes in 21,768 patients, about 2.8%) was similar to that of patients who were on anticoagulation (175 strokes in 6,264 patients, about 2.8%). Events in patients on anticoagulation were clustered in those with a CHA_2DS_2-VASc score ≥ 5, while more than 15% of events in the absence of anticoagulation occurred in patients with a CHA_2DS_2-VASc score of 0-1 (and more than one-third recorded a score of ≤ 2).

Additionally, calculated stroke risks would have favored anticoagulation based on the hypothesized "actionable threshold" of 1% in all patients with a CHA_2DS_2-VASc score ≥ 5, regardless of whether they experienced AF (the event rate was 1.51% in anticoagulated patients with a high risk score and no AF). All this raises the question of whether the AF is predominantly a causative factor of SSE, or simply another marker of risk. That question will be particularly relevant when thinking about how much anticoagulation reduces stroke in high-risk patients, and deciding whether episodic rhythm-guided use of anticoagulation is ever appropriate (since

events may not be temporally related to episodes of AF). Prospective trials that may help answer these questions are ongoing.

Finally, Kaplan et al stated that patients "at intermediate clinical risk may benefit from continuous AF burden monitoring to refine their individualized stroke risk." Inevitably, there will be attempts to extrapolate these findings to commercially available devices, such as the Kardia monitor and Apple Watch. However, considering their inferior sensitivity and specificity when compared to an implanted device with an atrial lead, such extrapolation must be performed with caution. ■

ABSTRACT & COMMENTARY

Warfarin or DOACs for Atrial Fibrillation in Chronic Kidney Disease?

By Michael H. Crawford, MD, Editor

SYNOPSIS: A large outpatient observational study of patients with atrial fibrillation and chronic kidney disease who were anticoagulated revealed that, compared to warfarin, direct oral anticoagulants exhibited less all-cause mortality and major bleeding with at least equivalent efficacy at preventing stroke.

SOURCE: Makani A, Saba S, Jain SK, et al. Safety and efficacy of direct oral anticoagulants versus warfarin in patients with chronic kidney disease and atrial fibrillation. *Am J Cardiol* 2020;125:210-214.

Although atrial fibrillation (AF) is common in patients with chronic kidney (CKD), the relative safety and efficacy of warfarin vs. direct oral anticoagulants (DOACs) is unclear. The seminal trials of DOACs in AF excluded patients with advanced renal disease. However, DOACs were approved for use in CKD patients based on small pharmacokinetic studies.

To clarify this issue, Makani et al studied patients seen in the University of Pittsburgh clinics between 2010 and 2017 who received a diagnosis of nonvalvular AF and a CHA_2DS_2-VASc score of ≥ 2 who were treated with anticoagulants. They were stratified into three groups based on their estimated glomerular filtration rate (GFR): > 60, 30-60, or lower than 30 mL/min. The primary endpoints were all-cause mortality, major bleeding, and stroke. Among the 21,733 patients included, 10,794 were on DOACs and 10,939 on warfarin. Baseline characteristics were similar between the two treatment arms. There was no difference in the two arms in the distribution of the three CKD groups.

During a mean follow-up of 3.4 years, the adjusted risk of death for all three CKD groups was lower in the DOAC arm: GFR > 60 mL/min (hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.70-0.84; $P < 0.001$), GFR 30-60 mL/min (HR, 0.74; 95% CI, 0.68-0.81; $P < 0.001$), and GFR < 30 mL/min (HR, 0.76; 95% CI, 0.63-0.93; $P = 0.005$).

Major bleeding also occurred much less in the DOAC arm: GFR > 60 mL/min (HR, 0.93), GFR 30-60 mL/min (HR, 0.83), and GFR < 30 mL/min (HR, 0.69). Embolic stroke rates were lower in the DOAC arm: GFR > 60 mL/min (HR, 0.86), GFR 30-60 mL/min (HR, 0.87), and GFR < 30 mL/min (HR, 0.60), as was hemorrhagic stroke: GFR > 60 mL/min (HR, 0.58), GFR 30-60 mL/min (HR, 0.41), and GFR lower than 30 mL/min (HR, 0.55). However, only the rates of hemorrhagic stroke in the two groups with GFR > 30 mL/min were statistically significant. Also, patients who suffered a stroke were more likely to die. The authors concluded that, compared to warfarin, DOACs were equivalent regarding stroke prevention, with lower all-cause mortality rates and fewer major bleeds in nonvalvular AF patients at all levels of CKD.

■ COMMENTARY

Current guidelines state that in AF patients with advanced CKD or who are on dialysis, treatment with warfarin or a DOAC might be reasonable (IIb, B-NR). Although such patients were excluded from large trials, in those patients who developed CKD during those studies, there were no safety issues with DOACs. This large, nonrandomized study confirms these observations and the conclusions of pharmacokinetic studies. This investigation reveals that the efficacy is at least no different from warfarin and perhaps better, especially if hemorrhagic stroke is considered. Also, there was a trend for lower embolic stroke rates with DOACs, which was not statistically significant.

There were several limitations to this study. It was a large, retrospective database study with little detail. The authors chose not to evaluate cardiovascular mortality due to the difficulty of adjudicating cause

of death in this type of observational outpatient study. We do not know the causes of death, as the study data lacked this granularity. Also, compliance with medications and international normalized ratio levels on warfarin are unknown. In addition, there are no data on antiplatelet therapy because the authors could not determine the duration of therapy. It would have been useful to know the type and doses of the DOACs used. Presumably, Makani et al followed the manufacturer's recommended doses for patients with various levels of CKD. Finally, although included in the study, a separate analysis of hemodialysis patients would have been of interest. Those with GFR < 30 mL/min made up 7% of the study population. Perhaps there were too few dialysis patients to analyze. With these new data, it seems reasonable to consider DOACs rather than warfarin in AF patients with CKD, especially if their CHA_2DS_2-VASc score is ≥ 2. This is a situation in which shared decision-making with the patient is important because of the risks involved with therapy and the paucity of data. ■

ABSTRACT & COMMENTARY

Anatomic vs. Functional Testing in Older Coronary Artery Disease Patients

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis of the PROMISE trial by age showed that cardiovascular death or myocardial infarction was predicted by a positive stress test in patients with symptoms suggesting myocardial ischemia who were >age 65 years, but only CT angiography or a calcium score was predicted in symptomatic patients < age 65 years.

SOURCE: Lowenstern A, Alexander KP, Hill CL, et al. Age-related differences in the noninvasive evaluation for possible coronary artery disease: Insights from the prospective multicenter imaging study for evaluation of chest pain (PROMISE) trial. *JAMA* 2020;5:193-201.

The Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) showed that patient outcomes were no different overall with an initial functional stress test compared to coronary CT angiography (CTA). While digging deeper into PROMISE, Lowenstern et al hypothesized that patient age may alter this finding.

In this analysis, 8,966 patients were included, of whom 71% were < age 65 years, 23% were between age 65 and 74 years, and 6% were > age 75 years. Patients were randomized to a strategy of an initial functional test (exercise ECG, stress echo, or stress nuclear perfusion) or coronary CTA and coronary artery calcium (CAC) score. The primary endpoint was a composite of cardiovascular (CV) death or myocardial infarction (MI) over a median follow-up of 25 months.

Older patients produced more positive tests of either type. A positive functional test was associated with CV death and MI in older patients: age 65-74 years (hazard ratio [HR], 3.2; 95% confidence interval [CI], 1.4-7.0) and ≥ age 75 years (HR, 6.6; 95% CI, 1.5-29.4), but not in patients < age 65 years (HR, 1.1; 95% CI, 0.4-2.8).

On the other hand, a positive CTA was associated with CV death or MI in patients < age 65 years (HR, 3.0; 95% CI, 1.5-6.3), but not in older patients: age 65-74 years (HR, 0.7; 95% CI, 0.2-2.9) and ≥ age 75 years (HR, 1.1; 95% CI, 0.2-5.3). A CAC > 100 (Agatston score) was associated with CV death or MI in those < age 65 years (HR, 2.7; 95% CI, 1.3-5.7), but not in older patients: age 65-74 (HR, 0.4; 95% CI, 0.1-1.4) and > age 75 years (HR, 1.3; 95% CI, 0.3-6.9).

The authors concluded older patients with stable symptoms suggestive of episodic myocardial ischemia are more likely to produce a positive stress test and more CAC, but only a positive functional stress test was associated with an increased risk for CV death or MI. Conversely, in younger patients, only a positive CTA or CAC was predictive of the primary endpoint. The authors suggested age should be considered in choosing the initial diagnostic evaluation of patients with stable symptoms suggestive of myocardial ischemia.

■ COMMENTARY

The PROMISE authors reported no difference in patient outcomes with either testing strategy, and positive tests of both types were more common in older patients: < age 65 years (10%), age 65-74 years (15%), and ≥ age 75 years (20%). However, when the results were stratified for age, there was a difference between the two types of tests. Lowenstern et al noted the extent of CAC increases with age, but is not related to outcome. Since all the patients

studied exhibited symptoms suggestive of myocardial ischemia, presumably the majority of them had coronary artery disease (CAD). Others have shown with serial CT imaging that increasing calcium over the years in those with baseline CAC detected is the norm despite risk factor control. Lowenstern et al suggested this may be part of the plaque stabilization process and not necessarily a bad thing. For this reason, serial CT scans in those positive for calcium are not recommended. Thus, the results of the Lowenstern et al study, which showed the lack of predictive value of CT scans for CAD events in older individuals, is not surprising. Also, CTA is limited by dense calcium and atrial fibrillation, which are more common in older patients.

On the other hand, a positive functional stress test did predict events in older patients, but not younger patients; this dichotomy is unclear. Perhaps younger symptomatic patients have a lower prevalence of CAD, which could lead to more false-positive functional tests. That CTA and CAC were predictive of events in younger patients may be related to the higher certainty of the diagnosis of coronary artery atherosclerosis. These results are important because the next step in the evaluation of the symptomatic patient with a positive test usually is invasive coronary angiography and possibly a percutaneous coronary intervention or bypass surgery. Thus, it is important to pick the most accurate test for each patient.

This analysis of PROMISE by age suggests that in those < age 65 years, a coronary CT may be a good test if the resting heart rhythm is sinus with a rate < 70 beats per minute. In those > age 65 years, a functional test would be better. Since the type of functional test was selected by each physician and not randomized, no recommendation on the type of test can be made based on this study.

There were limitations. Although this analysis by age was a prespecified subgroup, age was not included in the randomization scheme; technically, these results are hypothesis-generating. Also, the group of patients > age 75 years was small. The follow-up was short and there were few events: 1% in the < age 65 years patients, 2% in age 65-74 years patients, and 3% in the ≥ age 75 years group. The distribution of stress test type by age was not uniform, since nuclear perfusion studies, especially with pharmacologic stress, were deployed more commonly in the elderly. The guidelines recommend CT studies in intermediate risk patients, but this study suggests stratification by age is important with functional stress tests preferred in those > age 65 years. ■

ABSTRACT & COMMENTARY

Role of Cardiac MRI in Recurrent Pericarditis

By Michael H. Crawford, MD, Editor

SYNOPSIS: This multicenter study revealed cardiac MRI may be useful in the diagnosis of difficult pericarditis cases, especially if pericardial edema and late gadolinium enhancement are found. Pericardial thickening and elevated C-reactive protein were found to be predictive of recurrent pericarditis and other complications.

SOURCE: Imazio M, Pivetta E, Palacio Restrepo S, et al. Usefulness of cardiac magnetic resonance for recurrent pericarditis. *Am J Cardiol* 2020;125:145-151.

In situations where clinical, electrocardiographic, and echocardiographic criteria cannot establish the diagnosis of pericarditis, cardiac MRI has been recommended. Diagnosis may be especially challenging in recurrent pericarditis.

Investigators from Italy conducted a multicenter observational study of consecutive patients with suspected recurrent pericarditis who were evaluated by cardiac MRI. The diagnosis of acute pericarditis was made when two or more of four clinical criteria were met. Also, C-reactive protein (CRP) was measured to assess its value. These patients were followed for at least 18 months for the adverse events of recurrences, tamponade, and constriction. Cardiac MRI was performed as soon as possible after the onset of symptoms to assess pericardial thickness, pericardial edema/inflammation, myocardial and pericardial fibrosis by late gadolinium enhancement (LGE), and pericardial effusion. In addition, all cardiac MRI cases were matched with patients without pericarditis who had undergone cardiac MRI on the same day.

Inclusion criteria were met in 128 patients who underwent a cardiac MRI a mean of 12 days after the onset of symptoms. In 92 of the 128 patients, two or more of the four cardiac MRI diagnostic findings were found. Pericardial edema and LGE had an area under the curve (AUC) for diagnosing pericarditis of

0.80 and 0.76, respectively. Pericardial thickening and effusion were less predictive at AUCs of 0.64 and 0.71, respectively. The combination of pericardial edema and LGE had a sensitivity of 73% and a specificity of 99%. During a mean follow-up of 34 months, 52% of the patients had a recurrence, 6% tamponade, and 11% constriction. In a multivariate model, an elevated CRP (hazard ratio [HR], 11.7; 95% confidence interval [CI], 5-27.2) and cardiac MRI pericardial thickening (HR, 2.6; 95% CI, 1.6-4.4) were predictors of adverse events during follow-up. LGE predicted a lower risk (HR, 0.3; 95% CI, 0.1-0.7). A prognostic model using sex, age, CRP, and all four cardiac MRI variables had a C-index of 0.84. The authors concluded cardiac MRI has a high diagnostic accuracy for the diagnosis of acute pericarditis and may identify patients at risk for complications during follow-up.

■ COMMENTARY

Acute and recurrent pericarditis can be difficult to diagnose, and pharmacologic treatment can produce considerable side effects. Consequently, accurate diagnosis is desirable. Currently, diagnosis is based on four clinical criteria, with two of four required to make the diagnosis. Chest pain is present in 40% of cases, but it is nonspecific. Only one-third of patients have pericardial rubs auscultated and < 60% have classical ECG changes. Many do not exhibit detectable pericardial effusions by echocardiography. CRP often is elevated, but also is nonspecific and not considered a key diagnostic finding. Thus, another diagnostic technique such as CMR could be useful.

In this study, all cardiac MRI criteria showed a high specificity (90-100%) and positive predictive value (84-100%). However, their sensitivity (30-73%) and negative predictive value (58-78%) were lower. However, these cardiac MRI criteria are better than almost all the clinical criteria. Also, cardiac MRI pericardial thickening plus an elevated CRP was the best cardiac MRI-clinical combination for identifying future complications due largely to enhanced prediction of pericardial constriction. Pericardial thickening was observed in 80% of those destined to experience pericardial constriction. Interestingly, the combination of older age and pericardial LGE were associated with less complications.

The major limitation of this study was the delay in obtaining cardiac MRI. The mean time from first symptoms to cardiac MRI was 12 days, which may have mitigated some of the diagnostic features. Cardiac MRI was most helpful for diagnosis and prognosis if performed within two weeks. However, this was a real-world study, and cardiac MRI is expensive, time-consuming, and unpleasant. It often is avoided unless really needed or indicated. At this time, the classic four clinical plus echocardiographic findings make up the initial evaluation of suspected pericarditis, with the possible addition of CRP. Cardiac MRI should be considered early if the diagnosis is unclear or if recurrent pericarditis is suspected. Cardiac MRI can help make the diagnosis and is predictive of complications. In classic cases that respond well to therapy, cardiac MRI probably is unnecessary. ■

ABSTRACT & COMMENTARY

Heart Failure Confers Increased Risk of Venous Thromboembolic Events

By Jamie L. W. Kennedy, MD, FACC

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

SYNOPSIS: In the Atherosclerosis Risk in Communities (ARIC) cohort, incident heart failure hospitalization with either preserved or reduced ejection fraction was associated with long-term increased risk of venous thromboembolic events.

SOURCE: Fanola CL, Norby FL, Shah AM, et al. Incident heart failure and long-term risk for venous thromboembolism. *J Am Coll Cardiol* 2020;75:148-158.

Heart failure (HF) is recognized as a risk factor for a venous thromboembolic event (VTE), although the magnitude of this risk is not well-defined. Hospitalized HF patients routinely receive prophylactic measures, either pharmacological or mechanical. It is rare to continue prophylaxis following discharge, although a sizable number of HF patients are chronically anticoagulated for indications such as atrial fibrillation. Fanola et al sought to understand the risk of VTE conferred

by a new diagnosis of HF in a large prospective population-based study.

The authors of the Atherosclerosis Risk in Communities (ARIC) study recruited 15,792 men and women between 1987 and 1989, ranging in age from age 45 to 64 years. Participants primarily were African American and Caucasian. Participants have been followed via phone calls at least annually, along with periodic in-person exams. These data have provided a wealth of information on the development of HF, coronary disease, and other cardiovascular diseases.

The authors of the VTE analysis nested three separate analyses in their work, differentiated by increasingly robust information available about the ARIC participants over time. The first analysis concerned the rate of VTE in patients following an incident HF hospitalization compared to patients not diagnosed with HF, starting with enrollment in the ARIC study. They found the incidence of VTE in patients with HF was 11.8 per 1,000 patient-years compared to 2.3 per 1,000 patient-years for patients without HF, for a hazard ratio (HR) of 3.13. Understandably, this risk was highest in the month following HF hospitalization, but remained significantly elevated over long-term follow-up. Interestingly, the risk for African Americans with HF was increased 4.4 fold, compared to 2.4 fold for whites with HF.

The second analysis, starting in 2005, concerned the rate of VTE in patients with HF with preserved ejection fraction (HFpEF) vs. HF with reduced ejection fraction (HFrEF). As before, the rate of VTE was substantially higher in HF patients, 21.8 per 1,000 patient-years, vs. 3.04. The rates were similar between HFrEF and HFpEF (24.4 vs. 23.1 per 1,000 patient-years; HR, 5.53 vs. 4.71). The subset of patients with unknown EF had a VTE rate of 19.0 per 1,000 patient-years. Similar to the first analysis, VTE occurred most frequently in the month following hospitalization, but the excess risk persisted over the long term. In this analysis, race was no longer associated with increased VTE risk.

The final analysis, starting in 2011, examined the relationship between a variety of echocardiographic markers associated with the development of HF and risk of VTE in patients without documented HF. Increased left ventricular (LV) relative wall thickness and mean LV wall thickness both conferred elevated risk of subsequent VTE (HR, 1.25 and 1.32, respectively). Interestingly, left atrial volume index, perhaps the best indicator of chronically elevated filling pressures, was associated with VTE in the univariate analysis, but the association became insignificant after correction for comorbid conditions. HF with either reduced or preserved EF carries a significantly higher risk for VTE. Furthermore, patients with echocardiographic findings conferring increased risk of developing HF also carry a higher risk of VTE, suggesting a prothrombotic state is an early development in the pathway to symptomatic HF. The ARIC analysis was limited by the requirement for hospitalization for both HF and VTE diagnosis. The true VTE rate may be somewhat higher than reported.

■ COMMENTARY

How do we use these data? Would HF patients benefit from prophylactic anticoagulation following discharge? There have been several studies of extended (four- to six-week) courses of prophylactic anticoagulation in acutely ill medical patients following discharge: EXCLAIM (enoxaparin), MAGELLAN (rivaroxaban), ADOPT (apixaban), and APEX (betrixaban). HF patients were well-represented in these studies, ranging from 18-44% of enrolled subjects. These studies have produced, at best, mixed results. Only the MAGELLAN study met its primary endpoint demonstrating a reduction in VTE, although at the expense of significantly more bleeding complications. Based on these data, four to six weeks of pharmacological prophylaxis following discharge from a HF hospitalization does not seem to be helpful.

The ARIC data reveal the persistently elevated VTE risk; perhaps long-term prophylactic anticoagulation would be beneficial. There are no studies directly addressing this question, but the COMMANDER HF trial may shed some light on the subject. Those authors examined the long-term use of low-dose rivaroxaban (2.5 mg twice daily) vs. placebo in patients with systolic HF and coronary artery disease. The addition of rivaroxaban did not affect the primary composite endpoint of death, myocardial infarction, or stroke over a median follow-up of 21.1 months. Of these three components, the stroke rate was significantly lower in the rivaroxaban group. It is worth noting the mortality rate in this study was high at 22%.

Symptomatic deep vein thrombosis (DVT) and pulmonary embolism (PE) were two secondary endpoints in this study. There was no difference between the treatment and control arms. Interestingly, the rates were much lower than reported in the ARIC analysis (0.10 to 0.15 per 100 patient-years for DVT vs. 0.19 to 0.23 for PE). Based on this study, long-term prophylaxis does not appear beneficial, although it does seem that COMMANDER HF captured advanced stage HF patients, while the ARIC cohort represents a wider

range of HFrEF severity as well as HFpEF patients.

I have to admit I have scoffed frequently at the seemingly requisite emergency room lower extremity ultrasound in decompensated HF patients with symmetric bilateral lower extremity edema. But perhaps a higher index of suspicion is one takeaway from the ARIC data. Patients with somewhat atypical symptoms, out of proportion pulmonary hypertension, or significant right heart dysfunction, and those who fail to improve with HF management, should prompt consideration of VTE. Another lesson is to review VTE prophylaxis protocols, update them if needed, assess implementation rates, and explore any barriers to implementation. ■

CME/CE QUESTIONS

1. **In patients who are > age 75 years and who have possible angina pectoris, the best initial test is:**
   a. invasive coronary angiography.
   b. CT angiography.
   c. CT coronary calcium score.
   d. stress testing.

2. **The best confirmatory cardiac MRI finding in patients with suspected acute pericarditis is pericardial:**
   a. edema.
   b. late gadolinium enhancement.
   c. effusion.
   d. thickening.

3. **In a large, community-based study, subjects who developed heart failure also had a higher risk of:**
   a. pneumonia.
   b. deep venous thrombosis.
   c. stroke.
   d. peripheral vascular disease.

4. **For a patient with an implanted device and in whom atrial fibrillation (AF) is detected, what information would lead to considering anticoagulation?**
   a. CHA_2DS_2-VASc = 2; AF maximum daily duration > 6 minutes, < 23 hours
   b. CHA_2DS_2-VASc = 2; AF duration < 6 minutes
   c. CHA_2DS_2-VASc = 3-4; AF duration < 6 minutes
   d. CHA_2DS_2-VASc = 3-4; AF duration > 6 minutes, < 23 hours

5. **In patients with AF and advanced kidney disease (glomerular filtration rate < 30 mL/min), the best treatment is:**
   a. no anticoagulation.
   b. aspirin.
   c. a direct oral anticoagulant.
   d. a vitamin K antagonist.

CME/CE OBJECTIVES

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

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