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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Left Ventricular Diastolic Function in the Elderly

By Michael H. Crawford, MD, Editor

SYNOPSIS: Analysis of the ability of echo Doppler measures of diastolic function to predict heart failure and death in community subjects > 65 years of age was improved by applying age-adjusted normal values for e', which are considerably lower than those recommended in the American Society of Echocardiography guidelines.

SOURCE: Shah AM, Claggett B, Kitzman D, et al. Contemporary assessment of left ventricular diastolic function in older adults: The Atherosclerosis Risk in Communities study. *Circulation* 2017;135:426-439.

Measures of diastolic function on echocardiography change with age, yet little is known about where values consistent with normal aging transition to pathological diastolic dysfunction. Thus, investigators from the Atherosclerosis Risk in Communities (ARIC) study, which enrolled 15,792 subjects between 1987 and 1989, analyzed those who returned for a fifth study visit between 2011-2013, which included an echocardiogram. This analysis included 5,801 of these subjects, mean age 75 years, who were free of heart failure. Also, a low-risk group of 401 subjects (7%) free of cardiovascular disease or risk factors for it was identified. In addition, the findings were validated by using the participants in the Copenhagen City Heart Study who were > 65 years of age. Six measures of diastolic function were assessed: tissue Doppler e', septal, and lateral; mitral valve early diastolic velocity E to e' ratio (E/e') septal and lateral; left atrial (LA) width and volume index.

All diastolic measures were associated robustly with NT-proBNP and incident heart failure hospitalization or death ($P < 0.001$). Based on the low-risk group, the lower limits of e', septal, and lateral were 4.6 and 5.2 cm/s, respectively. These values are considerably lower than the American Society of Echocardiography (ASE) guideline, which calls for lower limits of 7 and 10, respectively. The E/e' upper limits for the low-risk group were 14.4 and 12.7, respectively, which are similar to guideline limits of 15 and 13. Similarly, the upper limit for low-risk LA diameter and volume of 3.7 cm and 30 mL/m² were similar to the guideline values of 4.0 cm and 34 mL/m².

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In the total ARIC study sample free of prevalent heart failure, e' (using the new reference limits) was abnormally low in 29%, E/e' was high in 31%, and LA volume was higher in 23%. Using ARIC normal limits as compared to the guidelines, 42% of the ARIC population was reclassified to normal diastolic function.

These findings were replicated in the Copenhagen City Heart Study age > 65 years population, in which 46% exhibited normal diastolic function and demonstrated a low risk of heart failure hospitalization or death (1%/year over 1.7 years). Those with one or two abnormal measures of diastolic function were at moderate risk (2.4%/year) and those with all three measures abnormal, which occurred in 5% of this population, were at high risk (7.5%/year).

The authors concluded that tissue Doppler e' velocity normally declines with healthy aging and is benign. Thus, age-based normal values improve the risk prediction of measures of diastolic function.

■ COMMENTARY

When the new ASE measurement of diastolic dysfunction guidelines came out, I was dismayed to see that an e' of < 10 cm/s was considered abnormal and a point toward the diagnosis of diastolic dysfunction. I thought this was going to be like the E/A of mitral valve inflow velocity, where almost every older person was abnormal.

Shah et al must have felt my pain because they undertook this analysis of the echo data in the ARIC population. This represents the largest database of normative data in older adults. They found a group that was low risk by traditional factors who exhibited a lower limit of e' of 5. When this criterion was applied to the larger ARIC database and the Copenhagen study, those with normal diastolic function (no abnormal echo measures) experienced a heart failure hospitalization and death rate of 1%. Analysis of two other large databases (ENGAGE AF-TIMI 48, TOPCAT) also confirmed these findings.

As I suspected, when the guideline e' values were used, 95% of the ARIC population exhibited abnormal values, but when the new lower cut points were used, only 28% were abnormal. Clearly, 10 is too high of a lower limit of e' for elderly subjects.

The investigators' low-risk group's E/e' upper limit ranged from 12-15 depending on whether septal or lateral measurements were used and whether the subjects were male or female. The guideline range is 13-15. LA volume upper limit was 30 mL/m², vs. 34 by the guidelines. Race and sex minimally influenced these measures.

The authors recommended using the e' lower limit of 5cm/s in subjects > 65 years of age. For the other measures, clinicians can use whichever number they are comfortable with, since there is very little difference between the ARIC values and the guidelines.

But how do clinicians treat patients 50-65 years of age? The jump from an e' lower limit of 5-10 is large. It is likely that patients 50-65 years of age would exhibit a lower normal limit between these two points, but we don't know that for sure.

Obviously, we need more robust age-based normal values for e'. ■

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ABSTRACT & COMMENTARY

Diastolic Stress Testing Improves Diagnostic Accuracy in Evaluation of Heart Failure with Preserved Ejection Fraction

By Van Selby, MD

Assistant Professor of Medicine, University of California, San Francisco, Cardiology Division, Advanced Heart Failure Section

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

SYNOPSIS: Adding echocardiographic assessment of diastolic function during exercise improves the accuracy of current algorithms for evaluating suspected heart failure with preserved ejection fraction.

SOURCE: Obokata M, Kane GC, Reddy YN, et al. Role of diastolic stress testing in the evaluation for heart failure with preserved ejection fraction: A simultaneous invasive-echocardiographic study. *Circulation* 2017;135:825-838.

Confirming a diagnosis of heart failure with preserved ejection fraction (HFpEF) can be challenging when classic signs are not present. Algorithms from major societies often recommend including natriuretic peptide levels and data from resting echocardiography to evaluate suspected HFpEF. However, the accuracy of these algorithms has not been evaluated rigorously. Furthermore, many patients who present with HFpEF only demonstrate hemodynamic abnormalities during exercise, and, therefore, incorporating exercise echocardiography may increase sensitivity.

The authors studied consecutive patients referred to the Mayo Clinic catheterization laboratory for simultaneous exercise right heart catheterization (RHC) and echocardiography to evaluate exertional dyspnea of unclear etiology. All patients exhibited left ventricular ejection fraction (EF) ≥ 50%. Patients were diagnosed with HFpEF based on the combination of clinical symptoms and elevated pulmonary capillary wedge pressure (PCWP), either at rest (> 15 mmHg) or with cycle ergometer exercise (≥ 25 mmHg). Patients with normal PCWP and no other clear hemodynamic abnormality were diagnosed with non-cardiac dyspnea (NCD).

Of 74 patients who completed the study, 24 (32%) were found to have NCD and 50 (68%) met criteria for HFpEF based on invasive data. Among patients with confirmed HFpEF, 18% had an N-Terminal pro-B-type natriuretic peptide (NT-proBNP) < 125 pg/mL, the level most frequently used to rule out HFpEF. Using guideline-recommended algorithms based on rest echocardiography alone, only 60% of subjects with confirmed HFpEF met diagnostic criteria, demonstrating poor sensitivity.

All patients were then reclassified after including exercise echocardiographic data. Patients were classified as HFpEF if the average ratio of transmitral E to mitral annular e' velocities (E/e') at peak exercise was > 14 lateral or the septal E/e' > 15. Using this added criteria, the sensitivity increased to 90%, although the false positive rate also was higher at 29%.

The authors concluded that algorithms based solely on echocardiographic assessment of diastolic function at rest are not sensitive for diagnosing HFpEF in patients with unexplained dyspnea, and including measurement of exercise E/e' improves diagnostic accuracy.

■ COMMENTARY

When clear signs and symptoms of heart failure are not present, right heart catheterization with exercise is considered the gold standard for diagnosing HFpEF in patients with unexplained dyspnea. The majority of patients with suspected HFpEF are not referred for invasive testing, so guidelines for the diagnosis of HFpEF generally require evidence of elevated left ventricular filling pressure as measured by either echocardiography (i.e., an elevated E/e' ratio) or natriuretic peptide levels.

The authors conducted an important study that highlights the limitations of noninvasive testing performed at rest only. Depending on the exact algorithm used, 40-66% of all patients who met invasive criteria for HFpEF would not have been diagnosed based on resting echocardiography alone. This is explained partly by the fact that 44% of subjects who met invasive criteria for HFpEF actually demonstrated PCWP < 15 at rest. Therefore, the problem with relying on the E/e' ratio at rest

is not inaccuracy, but rather the fact that it misses exercise-induced abnormalities.

Although sensitivity of current algorithms was poor, this study confirmed the specificity of standard echocardiographic criteria for diagnosis of diastolic dysfunction and HFpEF. Patients with high E/e' at rest are likely to exhibit elevated PCWP at rest as well, and in these cases, exercise testing often is unnecessary. It is patients who present with suspected HFpEF but normal E/e' at rest in whom exercise echocardiography should be considered. Also, it is worth noting that natriuretic peptide levels, often used in the evaluation of suspected heart failure, were normal in 18% of patients with HFpEF.

Exercise echocardiography can be technically challenging. This was a single-center study with all echocardiograms performed in a highly experienced research laboratory. Even in this setting, many of the echocardiographic studies were technically limited. E/e' only could be obtained in 80% of subjects at peak exercise, and the tricuspid regurgitant velocity only could be measured in 50% of subjects at peak exercise.

The specific diagnostic algorithm proposed by the authors will require prospective validation before it can be recommended widely. However, the argument that exercise often is required for a thorough evaluation of suspected HFpEF is valid and should encourage practitioners to use exercise testing more frequently in the evaluation of dyspnea of unclear etiology. Exercise echocardiography may be particularly well-suited for patients with an intermediate pre-test probability of HFpEF in whom adequate echocardiographic windows can be obtained. In patients with normal diastolic function on resting echocardiography and an average E/e' at peak exercise < 14 lateral and septal E/e' < 15, a diagnosis of HFpEF is unlikely. It is important to remember that including exercise improves sensitivity, but also increases the false positive rate. Therefore, patients with abnormal E/e' may require exercise RHC to confirm the diagnosis. ■

ABSTRACT & COMMENTARY

Study Challenges Orthodoxy of IV Hydration for Prevention of Contrast Nephropathy

By Jeffrey Zimmet, MD, PhD

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

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

SYNOPSIS: This trial randomized 660 patients with chronic kidney disease and a planned procedure requiring intravascular iodinated contrast to prophylactic hydration or to no hydration. No hydration was found to be non-inferior for prevention of contrast-induced nephropathy and saved significant costs.

SOURCE: Nijssen EC, Rennenberg RJ, Nelemans PJ, et al. Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): A prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. *Lancet* 2017 Feb 20. pii: S0140-6736(17)30057-0. doi: 10.1016/S0140-6736(17)30057-0. [Epub ahead of print].

The number of diagnostic and therapeutic procedures requiring intravascular iodinated contrast continues to grow year after year, and with this has come an increase in patients at risk for contrast-induced acute kidney injury. Although no specific treatment exists for this problem, the number of preventive measures studied to date is impressive. Many treatments have shown early promise in small studies only to fail to show consistent and reproducible results. N-acetylcysteine (Mucomyst) is the archetype of such treatments, but other examples include statins, sodium bicarbonate-containing IV fluid, calcium channel blockers, vitamin C, vitamin E, dopamine, fenoldopam, and remote ischemic preconditioning. However, experts and guidelines have recommended adequate hydration for patients at risk for contrast-induced nephropathy, usually with IV saline administered before and after the procedure.

The near-universal agreement on the value of pre- and post-hydration obscures the relative lack of randomized trial evidence supporting its value. The majority of trials in the literature compare one form of prophylaxis with another, and only three trials have included a group randomized to receive no hydration. No investigators had looked at periprocedural hydration

vs. no hydration in the high-risk groups targeted by the guidelines.

Enter the AMACING study. In this prospective, randomized, open-label study, consecutive patients referred for procedures requiring iodinated contrast at Maastricht University Medical Centre in the Netherlands were eligible for enrollment if they had an estimated glomerular filtration rate (eGFR) between 45 and 59 mL per minute combined with a second risk factor, or if they had an eGFR between 30 and 45 mL per minute. Patients with eGFR < 30 were excluded. Patients were assigned 1:1 to either receive IV hydration or to receive no hydration. The specific hydration protocol used in most cases was that recommended by current local guidelines — namely, normal saline at a rate of 3-4 mL/kg per hour for four hours before and four hours after contrast administration. As a standard, patients received pre-warmed iopromide (Ultravist), which is a low-osmolar, non-ionic contrast medium. All patients were subjected to serum creatinine measurements immediately before, two to six days after, and 26-35 days after their contrast procedure. The primary outcome measure was the incidence of contrast-induced nephropathy as determined by rise in serum creatinine at the two-to-six-day blood draw.

Of the 660 consecutive patients who were enrolled, 328 were assigned to receive prophylactic hydration, while 332 received no prophylaxis. In the analysis of day two to six creatinine administration (available in approximately 90% of subjects), contrast-induced acute kidney injury occurred in eight (2.6%) of 307 non-hydrated patients and in eight (2.7%) of 296 hydrated patients. Similarly, there was no significant difference between groups in the day 26-35 creatinine values. No instances of renal failure or requirement for dialysis were recorded. On the other hand, 18 patients in the prophylaxis group (5.5%) experienced complications from hydration, including 13 cases of symptomatic heart failure.

Partly due to the relatively long hydration protocols involved, the hydration group incurred greater hospital costs, and skipping hydration led to significant financial savings.

The authors concluded that forgoing periprocedural hydration in this moderate-risk group of patients was non-inferior to hydration for the prevention of contrast-induced nephropathy. They further reported that using no hydration was less expensive, and was associated with fewer complications than IV hydration.

■ COMMENTARY

Given that the use of IV hydration is the only measure that has maintained near-universal approval for prevention of contrast nephropathy, it is interesting to note that this recommendation is based as much on expert consensus as on trial data. The AMACING study meets this challenge head on, enrolling patients identified as high risk for CIN and comparing guideline-directed IV hydration with no prophylactic therapy. Doing this took some guts, and the results were striking. Against expectations, the results suggested a cost to this therapy in terms of resource utilization and complications, without apparent benefit. But while some lower-risk patients may benefit from abstaining from IV hydration, it is too early to write off this therapy for many cardiac procedure patients.

Editorialists have criticized the unusual non-inferiority design of the trial and have questioned the method of calculation of the non-inferiority margin. More important is the low reported event rate, which was far lower than comparable studies, and results in loss of discriminatory power. Although a mix of IV and intra-arterial contrast procedures was represented, primarily diagnostic procedures were included, consequently, with relatively low contrast volumes (compared with coronary interventional procedures, for which typical contrast volumes are higher). Patients with eGRF < 30, who are likely at the highest risk of CIN, were specifically excluded from this trial. No knowledge is gained about this group of patients.

Patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention have been studied in two randomized trials that compared no hydration with IV hydration with normal saline. The authors of these trials reported much higher rates of CIN (11-35%) compared with AMACING, and found a significant positive effect of hydration on this outcome.

The idea that IV fluid at a fixed rate and dose is beneficial for every patient without regard to individual volume status is overly simplistic. Hypovolemia is to be avoided, but volume overload, with resulting high renal venous pressure and decreased renal perfusion, can be just as detrimental. For cardiac procedures in particular, the opportunity to individualize prescribed hydration based on measured volume status typically is present. This was the basis of the 2014 POSEIDON trial, which modulated hydration based on measured left ventricular end-diastolic pressure and found a significant beneficial effect on prevention of contrast nephropathy.

More and larger trials are needed to definitively settle this issue. For now, at-risk patients undergoing invasive cardiac procedures should continue receiving peri-contrast hydration, guided by evaluation of volume status. ■

ABSTRACT & COMMENTARY

Uncertainties in Assessing Stroke Risk in Atrial Fibrillation

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis of 34 randomized trials in atrial fibrillation patients not on anti-coagulation showed considerable variation in stroke rates corresponding to their predicted risk by the CHA_2DS_2-VASc scores. When these scores are 2 or less, stroke rates are low enough to question the benefit versus risk of anti-coagulation therapy.

SOURCES: Quinn GR, Severdija ON, Chang Y, Singer DE. Wide variation in reported rates of stroke across cohorts of patients with atrial fibrillation. *Circulation* 2017;135:208-219.

Nielsen PB, Lip GY. Adding rigor to stroke rate investigations in patients with atrial fibrillation. *Circulation* 2017;135:220-223.

Studies show that the adoption of oral anti-coagulant (OAC) use in atrial fibrillation (AF) patients is underutilized, largely because of concerns about bleeding risk. The stroke and bleeding risks vary in patients with AF, and popular clinical risk scores such as CHA_2DS_2-VASc do not define a fixed stroke risk for all. Investigators reviewed stroke rates in AF patient cohorts not on OACs from randomized trials worldwide to further refine the relationship between the CHA_2DS_2-VASc score and the actual stroke risk. Anti-platelet use was allowed but was not analyzed. To include the maximum number of patients, only one year follow-up data was used. Patients undergoing procedures or who exhibited high-risk comorbidities, such as hypertrophic cardiomyopathy, end-stage renal disease, myocardial infarction, or prior stroke, were excluded. Two groups of studies are reported: an overall stroke risk group, and a group in which CHA_2DS_2-VASc scores were used to stratify the data. There were 17 studies in the overall group, two in the CHA_2DS_2-VASc score-stratified group and 15 in both for 34 total studies. The total study population was > 500,000 AF patients not on OACs. Stroke rates for each study ranged from 0.45%/year to 9.28%/year. Stroke rates also varied by region, with the North American rate less than one-third the European rate. Also, stroke rates were lower in prospective vs. retrospective studies. In the 17 studies using the CHA_2DS_2-VASc score, with a score of 1, 76% of the studies showed stroke rates < 1%/year, and 18% exhibited rates > 2%/year. With a CHA_2DS_2-VASc score of 2, 27% of the studies demonstrated a stroke rate of < 1%/year, 49% showed a rate of 1-2%/year, and 33% exhibited rates > 2%/year. Notably, all North American studies showed stroke rates of < 1%/year for patients with CHA_2DS_2-VASc scores between 0 and 2. The authors concluded that considerable variation in stroke rates corresponding to the patients' CHA_2DS_2-VASc scores is seen between studies of patients with AF who are not on OACs. Most studies did not show stroke rates that would justify anticoagulant therapy at CHA_2DS_2-VASc scores of 1 or 2.

■ COMMENTARY

One approach to OAC use in AF is finding the equipoise between stroke vs. bleeding risk. This is the point at which stroke risk equals bleeding risk, and the so-called net clinical benefit is zero. Scores above or below this point would inform OAC prescription decisions. However, the authors noted that the use of formal bleeding risk scores, such as HAS-BLED, doesn't contribute much to this equation, and that the OAC decision is driven by the stroke risk in 90% of cases. Also, guidelines do not recommend the use of formal bleeding scores. Hence, Quinn et al focused on the variation in stroke risk across studies in patients with the same CHA_2DS_2-VASc scores. An editorial accompanying the article noted that this variation is not surprising given the international distribution of the studies. Also, it is known that the CHA_2DS_2-VASc score is only of modest predictive value (c index of about 0.60).

Quinn et al and the editorialists from Europe disagree on the stroke risk above which OAC is beneficial (1-2% and > 0.9%, respectively). This difference in opinion influences the interpretation of the study results, with the Europeans favoring OAC at CHA_2DS_2-VASc scores ≥ 1 for men and ≥ 2 for women. The study authors thought their findings only support OAC for scores > 2 in either sex. Basically, both approaches mean that once a clinician identifies one to three risk factors beyond female sex, OACs should be prescribed. So, there is no reason to calculate the score; one must remember what the risk factors are. Of course, not all the CHA_2DS_2-VASc risk factors are of equal weight. For example, having known vascular disease is not equal to being a woman, yet each is worth 1 point. Thus, some have recommended a more holistic approach considering the weighting of risk factors and other factors not in the CHA_2DS_2-VASc score, such as race. We know Asians are at a higher risk for stroke, for example. Also, risk is not static and can change over time, so the anticoagulant or not decision is not good forever.

Why stroke rates differ so widely in various studies probably is mainly due to study methodology. An analysis of the Swedish AF study showed that changing patient

enrollment criteria could alter the stroke risk from 2.7% to 9.3% per year. However, the difference in stroke rates between North America and Europe is harder to explain and must color the editorialists' opinion of who needs OACs. No clear trend related to time was found, and factors such as anti-platelet therapy and warfarin vs. new OACs were not investigated. At this point, one must acknowledge that stroke rates for specific CHA_2DS_2-VASc scores are uncertain, especially in the critical 1-2 range in which the tipping point for anti-coagulation therapy lies. Thus, other factors must be considered in this decision and well-documented in the medical record. ■

ABSTRACT & COMMENTARY

Another Good Reason to Consider Early Ablation for Ventricular Tachycardia

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 a retrospective cohort of patients with structural heart disease and ventricular tachycardia, amiodarone often could be safely reduced or discontinued after ablation.

SOURCE: Liang JJ, Yang W, Santangeli P, et al. Amiodarone discontinuation or dose reduction following catheter ablation for ventricular tachycardia in structural heart disease. *J Am Coll Cardiol* 2017. Published online while in press.

Ventricular tachycardia (VT) is common in patients with left ventricular (LV) dysfunction and often is treated with antiarrhythmic drugs, in part to prevent the discomfort and morbidity associated with ICD shocks. Amiodarone is the most effective and widely used medication but is associated with significant toxicities.

Cardiologists at the University of Pennsylvania sought to determine whether VT ablation could facilitate safe reduction or discontinuation of amiodarone. In a cohort of 231 patients with structural heart disease referred between 2008 and 2011, VT ablation was performed using standard techniques. Many patients (55%) were on amiodarone shortly before the ablation procedure; of the rest, 33% had amiodarone discontinued remotely for toxicity. Ablation success was judged in part by attempts to induce VT at the end of the procedure with programmed stimulation (if the patient was believed to be medically stable). Many patients also were subject to repeated testing for inducible VT performed via their implanted ICD several days later (non-invasive programmed stimulation, or NIPS). Treating clinicians made decisions about post-procedure antiarrhythmic drug therapy, including amiodarone, based on these results and other factors.

The authors divided patients into three groups retrospectively: those who had pre-procedure amiodarone dosing reduced or discontinued after ablation (n = 99), those who had pre-procedure amiodarone dosing maintained or increased after ablation (n = 29), and those who were not on amiodarone immediately pre-procedure (n = 103). Patients who had pre-procedure amiodarone dosing maintained or increased after ablation tended to be both older and sicker, with lower ejection fraction (EF), more heart failure medications, more biventricular ICDs, and more inducible VT — even after ablation. There was no significant difference in one-year VT-free survival among the three groups despite the differences in post-procedure amiodarone use. A multivariate analysis was performed, incorporating a wide variety of clinical factors, including EF, severity of heart failure symptoms, common comorbidities, medications, arrhythmia characteristics, and procedural findings. The only independent, significant predictor of shorter time to VT recurrence post-ablation was whether a clinically important VT could be induced during post-procedure NIPS. Mortality was 80% in the group with maintained or increased amiodarone dosing over a mean of 1.8 years, significantly higher than in the other groups. The authors concluded that after successful VT ablation, as confirmed by noninducibility at the end of ablation and NIPS, amiodarone may be safely reduced or discontinued without an unacceptable increase in VT recurrence.

■ COMMENTARY

The risks of long-term amiodarone use are well-known and dose-dependent. There also is evidence that it may be independently associated with higher mortality in some groups, though it can be difficult to prove it is not simply a marker of more advanced disease. Nevertheless, it can be effective for suppression of ventricular arrhythmias, and once a patient starts a course of medication for VT, it can be difficult for his or her clinicians to consider reducing or discontinuing it. Although it seems inherently logical that VT ablation should facilitate decreased amiodarone use, this hypothesis had not been formally studied. If a patient undergoes complex VT ablation at

a tertiary care center and is referred to their primary cardiologist for post-ablation management, the appropriateness and timing of amiodarone dose reduction may be ambiguous. Fear of recurrent arrhythmia and ICD therapy undoubtedly leads both providers and patients to err on the side of caution.

This study adds valuable evidence to support a more aggressive approach to reducing the use of this potentially toxic medication after ablation at an experienced VT treatment center. Patients were not at higher risk for recurrent VT or, importantly, appropriate ICD shocks in the year after their ablation procedure, regardless of whether amiodarone was maintained, reduced, or discontinued. Patients who were maintained on a stable or higher dose of amiodarone experienced significantly higher mortality.

There are important limitations that must be considered when drawing conclusions from the data. Despite careful efforts to perform multivariate analysis, in a retrospective, observational study such as this, there are almost certainly other unmeasured confounders that influenced post-procedure amiodarone dosing and mortality. Only a prospective, randomized trial of amiodarone dosing after an ablation procedure with strict pre-defined endpoints for success will help clinicians answer the question.

For now, cardiologists should carefully consider with their patients the potential risks and benefits of ablative therapy (including the potential for reducing amiodarone exposure) for any episode of VT. It has been demonstrated that patients referred for ablation later in their arrhythmia course tend to take higher doses of amiodarone than those referred earlier, and even a single arrhythmia episode should prompt a discussion of VT ablation. Also, electrophysiologists performing these often-complex procedures should maintain an open dialogue with the cardiologists charged with the patients' long-term care, so that procedural success and medication strategies post-procedure are understood and agreed upon. Efforts to stop amiodarone or transition to another antiarrhythmic drug with less toxicity such as sotalol may pay significant dividends in the long term. ■

CME/CE QUESTIONS

1. **Which of the following echo Doppler measures of diastolic left ventricular function is most affected by aging?**
   a. E/e'
   b. e'
   c. Left atrial volume
   d. All of the above

2. **After ventricular tachycardia ablation, which of these factors would favor reduction or discontinuation of amiodarone?**
   a. Failure to induce VT at the end of the procedure
   b. Negative non-invasive programmed ICD stimulation
   c. Amiodarone toxicity
   d. All of the above

3. **Stoke rates in patients with a CHA_2DS_2-VASc score of 1 or 2 are:**
   a. high enough to warrant anti-coagulation.
   b. constant between different studies.
   c. uncertain.
   d. higher in North America.

4. **Which proposed prophylactic therapy for contrast-induced nephropathy has not been well-studied?**
   a. IV saline hydration
   b. IV sodium bicarbonate
   c. N-acetylcysteine
   d. Calcium channel blockers

5. **Which of the following has the highest sensitivity for detecting right heart catheterization confirmed HFpEF?**
   a. NT-proBNP < 125 pg/mL
   b. Exercise echo Doppler E/e' > 14
   c. Resting E/e' > 14
   d. Resting e' < 10