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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Heart Rate and Diastolic Blood Pressure in Chronic Aortic Regurgitation Patients

By Michael H. Crawford, MD, Editor

SYNOPSIS: A retrospective observational study of patients with moderate to severe aortic regurgitation showed the independent predictive value of diastolic blood pressure and resting heart rate for all-cause mortality under medical management.

SOURCES: Yang LT, Pellikka PA, Enriquez-Sarano M, et al. Diastolic blood pressure and heart rate are independently associated with mortality in chronic aortic regurgitation. *J Am Coll Cardiol* 2020;75:29-39.

Chambers J. Aortic regurgitation: The value of clinical signs. *J Am Coll Cardiol* 2020;75:40-41.

Current guidelines caution against using drugs that lower heart rate or diastolic blood pressure (DBP) in patients with chronic aortic regurgitation (AR). However, these cautions are really hypotheses since there are little data to support them.

Investigators from the Mayo Clinic retrospectively identified 820 patients with chronic moderate to severe AR without significant concomitant valve or myocardial disease from 2006 to 2017. Routine follow-up echocardiograms included measurement of heart rate and BP. The severity of AR was determined by a combination of parameters approach on echocardiography. The primary endpoint was all-cause mortality under medical management. Aortic valve surgery was a secondary endpoint. For their multivariate logistic regression analysis, the hazard ratios (HR) were plotted using a resting heart rate (RHR) of 60 beats per minute (bpm) and a DBP of 70 mmHg as the reference points. The mean age of patients was 59 years, and 82% were men.

The mechanisms of AR were annular or aortic root dilation in 26%, cusp prolapse in 13%, and cusp restriction in 10%. In 43% of patients, there was a mixed mechanism, and it was indeterminate in 7%. Baseline characteristics showed those with lower DBP and higher heart rates often were more symptomatic and had more severe AR. During the mean follow-up of 5.5 years, 49% underwent aortic valve surgery (AVS) and 19% died, about one-third of the latter after AVS. Survival under medical

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management was 94% at one year, 79% at five years, and 63% at 10 years.

A multivariate model adjusting for baseline characteristics and the presence of guideline triggers for AVS demonstrated the independent predictive value of DBP and RHR for all-cause death under medical management: DBP HR, 0.79; 95% confidence interval (CI), 0.66-0.94 per 10 mmHg increase; $P <$ 0.01, and RHR HR, 1.23; 95% CI, 1.03-1.45 per 10 beat increase; $P = 0.01$. These results persisted after further adjustment for hypertension, medications, and timing of AVS. Systolic BP was not predictive, but pulse pressure per 10 mmHg increase was weakly predictive: HR, 1.1; 95% CI, 1.01-1.24; $P = 0.02$.

Further analysis of DBP showed a J-shaped curve with mortality starting to increase at < 70 mmHg and peaking at 55 mmHg. For RHR, there was a linear relationship to mortality, increasing after RHR was > 60 bpm. The authors concluded that in patients with chronic moderate to severe AR, DBP and RHR are robustly associated with all-cause death independent of comorbidities, guideline-based surgical triggers, hypertension, and medications. These measures should be considered in decision-making for AVS.

■ COMMENTARY

In patients without heart valve disease, a rapid pulse has been associated with mortality. This finding in AR patients is unsurprising, but the lack of a J-shaped curve perhaps is. In this observational study, there was no discernable adverse effects of pulses down to 40 bpm, although the number of patients with RHR < 50 bpm was small. The authors advanced the theory that the large stroke volume associated with chronic stable AR activates baroreceptors, resulting in increased vagal tone. Investigators observed about 40% of patients who recorded heart rates > 60 bpm. As the left ventricular begins to fail and stroke volume drops, sympathetic tone increases, leading to an acceleration in RHR. The concept that a slower heart rate increases diastolic filling and makes AR worse may not be correct. Thus, avoiding drugs to slow the heart rate may not be necessary unless they also decrease the contractile state of the left ventricle.

Significant AR will lower the aortic diastolic pressure, and the resultant large stroke volume will increase systolic and pulse pressures. This phenomenon is one of the hallmarks of significant AR and is associated with classic physical findings in this condition. The finding that lower DBP values are associated with higher mortality may just reflect more severe AR. However, low DBP was a predictor of mortality independent of markers of AR severity, such as left ventricular size and function.

Pulse pressure was weakly associated with mortality, but systolic BP was not. This is probably because systolic pressure is more related to arterial stiffness in this age group. This weakens the relationship with pulse pressure.

Considering the strong association of mortality with DBP, one must question the recommendation to aggressively treat hypertension in significant AR. In my experience, aggressive treatment of systolic BP in such patients is not well tolerated. If one is considering treating systolic hypertension in such patients, think about AVS. Aggressive treatment of systolic pressure often lowers DBP, too, which reduces coronary artery perfusion pressure. This may help explain why low DBP predicts mortality.

There were limitations to this study, including selection bias (about half the patients underwent AVS). Also, there are no data on the specifics of medical therapy or non-echo parameters such as BNP. Most patients were white men. Cardiovascular death was not analyzed, and patients with coronary artery disease were included. However, current thinking suggests clinicians may be waiting too long to operate on these patients.

Consideration of factors other than symptoms, left ventricular size, and function such as exercise hemodynamic response, global strain, and BNP, should be analyzed. Clearly, DBP and RHR should be added to this list. ■

ABSTRACT & COMMENTARY

Rivaroxaban After Transcatheter Aortic Valve Replacement

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: In this randomized trial of post-transcatheter aortic valve replacement patients without a separate indication for anticoagulation, a rivaroxaban-based approach was associated with a higher risk of death and thromboembolic complications compared with dual antiplatelet therapy.

SOURCE: Dangas GD, Tijssen JGP, Wöhrle J, et al. A controlled trial of rivaroxaban after transcatheter aortic-valve replacement. *N Engl J Med* 2020;382:120-129.

The optimal antithrombotic regimen for routine post-procedure management of transcatheter aortic valve replacement (TAVR) patients is unknown. Dual antiplatelet therapy was used in early TAVR trials, based on expert opinion rather than on comparative data. This remains the most common post-procedure pharmacologic treatment. Although clinically evident thrombosis affecting valve function is relatively rare, imaging studies dating back to 2015 have revealed a substantial rate of subclinical leaflet thrombosis in the months after TAVR: highly variable, but accounting for more than 15% of patients in most studies, resulting in leaflet thickening or reduced leaflet motion. The relationship of this imaging-defined leaflet thrombosis to either short-term thromboembolic events or to downstream valve degeneration is unknown.

Based on the observation that patients on oral anticoagulation show reduced rates of subclinical leaflet thrombosis, Dangas et al sought to study how a rivaroxaban-based approach compares with standard antiplatelet therapy in post-TAVR care. To this end, patients without an established indication for oral anticoagulation who had undergone successful TAVR were randomized one-to-one to either rivaroxaban-based treatment (aspirin plus rivaroxaban 10 mg/day for three months, followed by rivaroxaban monotherapy) or to an antiplatelet regimen consisting of aspirin plus clopidogrel for three months, followed by aspirin monotherapy.

The design of the trial designated a primary efficacy endpoint: the composite of death and all thromboembolic complications, including myocardial infarction, stroke, valve thrombosis, and both arterial and venous thromboembolism. The authors also reported major bleeding as a primary safety endpoint and used these data in combination with the efficacy endpoint to report a net benefit outcome.

Over the 30-month trial period, 1,644 patients were enrolled at 136 centers in 16 countries. The mean age was 80.6 years, just fewer than half were women, and most were recruited from centers in Western Europe. A total of 826 patients were randomly assigned to the rivaroxaban group and 818 to the antiplatelet group. At a median follow-up of 17 months, death or first thromboembolic event (the primary efficacy outcome) occurred in 105 patients in the rivaroxaban group and in 78 patients in the antiplatelet group (incidence rates, 9.8 and 7.2 per 100 person-years, respectively; hazard ratio [HR] with rivaroxaban, 1.35; 95% confidence interval [CI], 1.01-1.81; $P = 0.04$). Notably, stroke and myocardial infarction were not different between the groups. However, mortality alone was significantly more common in the rivaroxaban group: 64 vs. 38 (HR for rivaroxaban, 1.69; 95% CI, 1.13-2.53). The primary safety outcome of life-threatening, disabling, or major bleeding increased in the rivaroxaban group, consistent with expectations (46 vs. 31 patients; HR, 1.5, 1.50; 95% CI, 0.95-2.37; $P = 0.08$). The data safety monitoring board halted the trial early in response to this information, suggesting overall harm of the treatment approach.

The authors concluded that in post-TAVR patients without an indication for oral anticoagulation, treatment with a regimen including rivaroxaban was associated with higher risks of death and thromboembolic complications and an increased risk of bleeding compared with the current antiplatelet standard of care.

■ COMMENTARY

GALILEO started with a good idea. Subclinical leaflet thrombosis as defined by imaging is quite common after TAVR. Prevention of this development might reasonably be expected to decrease thromboembolic complications. This idea

is so logical that many practitioners in recent years have discussed adding oral anticoagulation to the routine post-TAVR regimen, even in the absence of efficacy data. The fact that the results have shown harm for this particular approach is a cautionary tale and highlights the need for meticulous randomized, controlled trials.

The rare outcome of symptomatic valve thrombosis was numerically lower in the rivaroxaban group (3 vs. 7 events), although this did not meet statistical significance. In the imaging substudy of the trial that included 231 patients, rivaroxaban treatment was associated with a significant reduction in subclinical leaflet thrombosis, as defined by leaflet thickening and reduced leaflet motion. In this case, rivaroxaban at the dose prescribed was effective at preventing the target surrogate outcome, but led to worse clinical outcomes anyway. At this point, we do not understand the clinical significance of subclinical leaflet thrombosis. The idea that it may be associated with earlier valve degeneration remains a viable concept. Whether the natural history of this process, and the longevity of these valves, may be altered for the better through anticoagulant medications is unknown. Future trials may give more insight into this process.

Notably, most of excess deaths in the rivaroxaban arm of GALILEO did not also experience severe bleeding. Most of these deaths occurred long after the study drug was discontinued. Hence, the cause of the observed increase in death with the rivaroxaban approach is unknown and will require further study. For now, what is known after this trial is routine treatment of post-TAVR patients with direct-acting oral anticoagulants is not indicated in the absence of a traditional indication for these drugs. Even in those cases of a clear anticoagulation indication (e.g., the TAVR patient with atrial fibrillation), the best regimen remains unknown, and further trials in this arena are ongoing. ■

ABSTRACT & COMMENTARY

Home Oral Factor Xa Inhibitor Treatment for Pulmonary Embolism

By Michael Crawford, MD, Editor

SYNOPSIS: Low-risk pulmonary embolus patients discharged in < 48 hours on rivaroxaban recorded a nominal three-month rate of recurrent emboli or major bleeding, suggesting such patients do not need to be hospitalized for treatment of pulmonary emboli.

SOURCE: Barco S, Schmidtmann I, Ageno W, et al. Early discharge and home treatment of patients with low-risk pulmonary embolism with the oral factor Xa inhibitor rivaroxaban: An international multicenter single-arm clinical trial. *Eur Heart J* 2020;41:509-578.

Prior studies of using vitamin K antagonists to treat low-risk pulmonary embolism (PE) patients at home have been controversial due to study design limitations, including the definition of low risk. Recently, direct oral anticoagulants (DOAC) have been used successfully to treat acute PE patients.

Barco et al conducted a multicenter, single-arm study of early discharge and ambulatory treatment with rivaroxaban in low-risk PE patients to determine its efficacy and safety (HOT-PE trial). The identification of low-risk PE patients employed the European Society of Cardiology clinical criteria, plus the presence of normal right ventricular (RV) size and function and the absence of mobile thrombi in the right heart on echocardiograms. Treatment with heparin or an oral anticoagulant was allowed before enrollment. Researchers cut off prior treatment, and started subjects on rivaroxaban less than two hours later. The doses of rivaroxaban followed the manufacturer's recommendations. Patients were discharged within 48 hours of the diagnosis of PE, and treatment continued for three months. The primary efficacy outcome was recurrent PE or PE-related death. The safety outcomes were major bleeding, clinically relevant nonmajor bleeding, and serious adverse events.

An interim analysis was conducted after 525 patients had completed their three-month visit to determine if premature study discontinuation was warranted for clear efficacy or harm. In 49 centers in seven countries, 2,854 patients with PE were screened and 525 were enrolled (2,329 were excluded). The enrolled patients' average age was 57 years, and 46% were women. The median length of initial hospitalization was 37 hours. Only three of the 525 enrolled patients experienced the primary outcome of recurrent nonfatal PE, so the study ended prematurely based on prespecified statistical criteria. The primary safety outcome of major bleeding occurred in six patients, clinically significant bleeding in 31, and serious adverse events in 58. Two patients died of cancer. The authors concluded that selected

low-risk PE patients can be treated effectively and safely with early discharge on rivaroxaban therapy.

■ COMMENTARY

Since the efficacy and safety of DOAC vs. warfarin in outpatients with deep vein thrombosis (DVT) has been demonstrated, the investigators in HOT-PE believed it was unnecessary to include a conventionally treated control group. Exclusion criteria were straightforward: serious comorbidities, another condition requiring hospitalization, and a social environment not conducive to ambulatory anticoagulation management. In fact, 21% of patients recorded a simplified pulmonary embolism severity index (sPESI) score of ≥ 1 (a score of 0 is low risk), but the authors excluded patients with right heart dysfunction and thrombi, which clinical indices such as sPESI do not consider. Also, in their multivariate analysis, neither age nor a history of cancer (both in sPESI) affected the results.

The study ended early at 50% of the planned enrollment because the primary endpoint of recurrent PE was 0.6%, so the null hypothesis was rejected early. The authors of similar studies with warfarin observed PE recurrence rates of 0.6-2.0%. The safety outcome of major bleeding was 1.2% in the Barco et al study and 0.7-1.8% in prior trials with warfarin. In previous trials of rivaroxaban in DVT, the major bleeding rates were 0.5-2.0%. Thus, efficacy and safety are similar to PE trials with warfarin and DVT studies with DOACs.

The decision to discharge a patient early after PE is important because PE can be fatal. In this study, three patients experienced recurrent PE, and there were no PE-related deaths over the three months of the study. These results are compelling for triaging more patients to ambulatory care, but how many are going to meet the inclusion criteria for early discharge? In this trial, it was 20% — significant enough to reduce costs and make some patients happy. Of course, it does require initial hospitalization and treatment with heparin, enoxaparin, or other anticoagulants, along with an echocardiogram to cull the highest-risk patients with right ventricular dysfunction or mobile thrombi. However, this would be standard protocol for most other hospitalized patients. The next step is identifying low-risk patients at the point of first encounter with immediate triage of low-risk patients to ambulatory care. The key to this step is the availability of echocardiography. ■

ABSTRACT & COMMENTARY

Heart Failure-Exacerbating Medications

By Michael H. Crawford, Editor

SYNOPSIS: In a large, diverse cohort of Medicare patients hospitalized for heart failure exacerbations, almost half were on medications known to exacerbate heart failure; more than one-third were on these agents at discharge.

SOURCE: Goyal P, Kneifati-Hayek J, Archambault A, et al. Prescribing patterns of heart failure exacerbating medications following a heart failure hospitalization. *JACC Heart Fail* 2020;8:25-34.

Hospital admissions and readmissions due to heart failure (HF) exacerbations are common. Considerable national efforts have been invested in preventing them. However, little attention has been paid to concomitant therapy known to exacerbate HF.

The authors of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study identified Medicare beneficiaries > age 65 years with an adjudicated HF hospitalization between 2003 and 2014. In this diverse cohort, only hospitalizations > 90 days after eligible hospitalizations were included since earlier hospitalizations were likely to feature few medication changes. The HF-exacerbating medications were taken from the 2016 American Heart Association (AHA) Scientific Statement list of directly toxic medications and those that exacerbate underlying myocardial dysfunction.[1] Only those medications classified as major exacerbating agents due to the potential for life-threatening effects were studied.

A total of 558 unique patients with 723 unique hospitalizations were included. Their median age was 76 years; 44% were women, and 34% were black. The prevalence of HF-exacerbating medications was 41% at hospital admission and 36% at discharge. These patients were more likely to exhibit several comorbid conditions. The most frequently prescribed concerning medications were albuterol, metformin, nonsteroidal anti-inflammatory drugs (NSAIDs), and diltiazem. During hospitalization, 17% reduced intake of HF-exacerbating drugs, 19% took the same amount, 12% took more, and 51% were not taking any of these medications at admission or discharge. A multivariate analysis showed the factors most associated with potentially harmful prescribing were

diabetes (odds ratio [OR], 1.8; 95% confidence interval [CI], 1.18-2.75) and small hospital size (OR, 1.93; 95% CI, 1.18-3.16). The authors concluded that HF-exacerbating medications are frequently initiated or continued in Medicare patients admitted for HF.

■ COMMENTARY

The emphasis in HF management programs has been on guideline-based optimal medical therapy, not on avoiding drugs that could exacerbate HF. Thus, it is perhaps not surprising that almost half of older patients admitted for HF are on such medications. What is perhaps surprising is that potentially harmful drugs often are continued or even added during hospitalizations such that 36% are discharged on such drugs. When I teach trainees about why patients experience HF exacerbation, I usually mention the five most common reasons: ischemia, arrhythmias, dietary indiscretion, medication noncompliance, and stress (e.g., infection). Now, we should add potentially harmful medications.

The AHA document lists dozens of agents with evidence for a casual role in HF exacerbations. Goyal et al focused on 22 such agents with the highest risk for harm. However, the level of evidence was not the same for each. For example, trastuzumab (Herceptin), a chemotherapy agent, carries level A evidence, NSAIDs level B, and metformin level C. Diabetes was one of the most common comorbidities leading to the prescription of potentially harmful drugs. Fortunately, there are newer drugs for diabetes that may help prevent HF (e.g., sodium-glucose transporter inhibitors). Obstructive airway disease was another common comorbidity, occurring in 30% of the Goyal et al cohort. Most drugs used for these pulmonary conditions can exacerbate heart failure (e.g., steroids, albuterol, antibiotics). These considerations point out one downside of disease-specific guidelines: therapeutic competition.

The strengths of this study were that the results are generalizable due to the diversity of the patients and the 380 hospitals studied. Weaknesses included the consideration of only standing medication orders, which may have underestimated the number of patients receiving bronchodilators and NSAIDs. Some drugs, such as citalopram, are only toxic at extremely high doses or with significant renal dysfunction; their significance may be overestimated.

Clearly, this study shows that medication list management in hospitalized HF patients is suboptimal. This may be an area where the electronic medical record could help by flagging potentially harmful drugs if HF is on the admitting diagnoses list. All we need is another warning signal on the computer, so maybe there is a better way. There are pharmacists on our inpatient teams, and I am going to see if they can help me with this. ■

REFERENCE

1. Page RL, O 'Bryant CL, Cheng D, et al. Drugs that may cause or exacerbate heart failure: A scientific statement from the American Heart Association. *Circulation* 2016;134:e32-e69.

ABSTRACT & COMMENTARY

Efficacy of Class I vs. Class III Antiarrhythmic Drugs in Obese Patients

By Joshua Moss, MD

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

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

SYNOPSIS: In an observational cohort of patients with atrial fibrillation, obese patients were less likely than nonobese patients to avoid symptomatic recurrence on sodium channel blocking agents in contrast to a roughly equivalent response in both groups to potassium channel blocking agents.

SOURCE: Ornelas-Loredo A, Kany S, Abraham V, et al. Association between obesity-mediated atrial fibrillation and therapy with sodium channel blocker antiarrhythmic drugs. *JAMA Cardiol* 2020;5:57-64.

In a recent Mendelian randomization study, a causal relationship between obesity and atrial fibrillation (AF) was demonstrated. Emerging evidence implicates modulation of the cardiac sodium channel as a potential mechanism. However, little is known about whether obesity-related abnormalities in the cardiac sodium channel affect the response to class I (sodium channel blocking) antiarrhythmic drugs (AADs). Ornelas-Loredo et al conducted an observational cohort study of 311 adults with

documented AF and attempted maintenance of sinus rhythm with either class I or class III AADs. Obesity was defined as a body mass index (BMI) > 30 kg/m^2. Patients were deemed to have a symptomatic response to an AAD when the same AAD was continued for at least three months. Discontinuation of an AAD within three months because of recurrent symptomatic AF necessitating change in therapy was considered nonresponse. Additionally, a parallel animal study was conducted with 10 mice with diet-induced obesity (DIO) and 10 control mice. Inducibility of AF via rapid transesophageal pacing, as well as suppression of inducibility with either flecainide (class I AAD) or sotalol (class III AAD), were determined.

In the observational cohort, the mean age was 65 years; 39% were women, and 54% were obese. Symptomatic nonresponse to class I AAD occurred more frequently in obese patients than in nonobese patients (30% vs. 6%; P = 0.001). Most obese nonresponders were switched to a class III AAD, and several underwent ablation. In contrast, nonresponse rates to class III AADs was similar in both groups (9% vs. 5%), and most of those patients were either switched to amiodarone therapy or underwent ablation. In a multivariate analysis, obesity remained a significant factor associated with nonresponse to class I agents vs. class III agents. The odds ratio (OR) of nonresponse was 4.5 in obese patients (95% confidence interval [Cl], 1.84-11.2) vs. 1.34 in nonobese patients (95% CI, 0.28-6.36). Female sex also was associated with a higher likelihood of nonresponse to AADs (OR, 2.3; 95% CI, 1.07-4.99), as was hyperthyroidism (OR, 4.95; 95% CI, 1.23-20).

In mice, pacing-induced AF was achieved in 100% of DIO mice vs. 30% of nonobese mice (P < 0.001). The DIO mice showed a greater reduction in AF burden when treated with the class III agent sotalol vs. the class I agent flecainide (85% vs. 25%; P < 0.01). The authors concluded the human and mice data supported the hypothesis that obesity differentially mediates response to AAD in subjects with AF, with a relative reduction in the effectiveness of sodium channel blockers (class I AAD).

■ COMMENTARY

The study adds additional valuable data to our growing body of knowledge about the effects of obesity and AF. Previous clinical trials have demonstrated slowing and even reversal of AF progression with weight-loss management and aggressive risk factor modification (REVERSE-AF, discussed in the April 2019 issue, available at this link: http://bit.ly/2uskkmO), as well as reduced incidence of AF in obese patients who undergo bariatric surgery (discussed in the March 2017 issue, available at this link: http://bit.ly/39jCvKx). It now appears obesity also may be associated with reduced efficacy of sodium channel blockers (or even proarrhythmia); Ornelas-Loredo et al hypothesized this to be related to obesity-mediated modulation of the cardiac sodium channel.

If additional prospective data confirms this, these findings carry important implications for medical management of AF. The sodium channel blocking agents, specifically class Ic medications, such as flecainide and propafenone, often are first-line AADs for rhythm control in patients with AF. They have the advantage of safe outpatient initiation and a generally well-tolerated side effect profile. In contrast, class III drugs often require inpatient hospitalization for initiation, more drug-drug interactions, and arguably more proarrhythmia. However, they were effective for at least six months in 14 of 19 obese patients who failed class I therapy and were switched to them. If nearly one-third of obese patients will experience symptomatic AF recurrence within three months of maximum-tolerated class I doses, clinicians may wish to consider modifying their initial drug therapy discussions to favor a class III agent.

That said, there were multiple limitations to this study, many of which the authors described well. Principally, significant effects of confounding cannot be ruled out despite extensive efforts to account for them statistically. The reasoning for why some patients in the observational cohort were initially treated with class I agents and others with class III agents initially are not explored, and other comorbidities found commonly in obese patients (and that might affect medication response) still may play a role.

Furthermore, while obesity as a dichotomous variable (with BMI cutoff at 30 kg/m^2) proved a significant risk factor for nonresponse to class I drugs, BMI as a continuous variable was not. In the mouse cohort, the authors never specifically discussed the response to sotalol vs. flecainide in the few control mice with inducible AF. Thus, it is difficult to prove whether the differential response seen in DIO mice is an effect of obesity or simply a characteristic of these mice.

For now, I would suggest these findings be applied in two principal ways. First, maintain a lower threshold to use a class III AAD as first-line drug therapy or transition to one sooner in obese patients with AF. Second, continue to encourage weight loss and risk factor modification above all in the management of AF in obesity. ■

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CME/CE QUESTIONS

1. **A study of mice and human subjects showed obesity may impair the response to which drugs for atrial fibrillation?**
   a. Class I
   b. Class II
   c. Class III
   d. Class IV

2. **About what percent of older patients admitted for heart failure exacerbations are on medications known to exacerbate heart failure?**
   a. 10%
   b. 25%
   c. 50%
   d. 65%

3. **An independent predictor of all-cause mortality in patients followed medically for chronic moderate to severe aortic valve regurgitation is:**
   a. resting bradycardia.
   b. diastolic blood pressure < 70 mmHg.
   c. systolic blood pressure > 140 mmHg.
   d. pulse pressure < 40 mmHg.

4. **Which tool enhances the clinical identification of low-risk pulmonary embolism patients for ambulatory care who are taking a direct oral anticoagulant?**
   a. CT angiography
   b. Ventilation perfusion scan
   c. Electrocardiogram
   d. Echocardiography

5. **The GALILEO study showed that adding an oral anticoagulant to antiplatelet therapy after transcatheter aortic valve replacement results in:**
   a. less valve thrombi.
   b. fewer systemic emboli.
   c. less aortic regurgitation.
   d. lower mortality.

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.