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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

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SPECIAL FEATURE

Late-breaking Clinical Trials from the Heart Rhythm Society May 2017 Scientific Sessions

By Joshua D. Moss, MD

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

SYNOPSIS: Late-breaking findings of several important clinical trials were presented at this year's Heart Rhythm Society Scientific Sessions in Chicago. A selection particularly relevant to the general cardiology community is presented here.

SOURCE: Late-Breaking Clinical Trials I; Late-Breaking Clinical Trials II. *Heart Rhythm* 2017;14:940-947.

THE S-ICD POST-MARKET APPROVAL STUDY(Gold MR, et al.)

A prospective registry of the totally subcutaneous ICD (S-ICD) was created following FDA approval of the device in 2013. The reported findings included an average of two years of follow-up data for 1,637 patients implanted at 86 U.S. centers, 77% for primary prevention and 23% for secondary prevention. Patients had similar co-morbidities to those typically implanted with a more traditional transvenous ICD: 74% had heart failure with an overall mean ejection fraction of 32%, and 34% had diabetes. Additionally, 13% of patients were on hemodialysis. The device was effective at implant, with successful conversion of induced VT/VF achieved in 98.7% (first shock conversion in 95.6%). There were few complications, with an infection rate of 1.2% and 30-day complication-free rate of 96.2%. Registry follow-up is scheduled to continue to five years for all patients.

■ COMMENTARY

The subcutaneous ICD offers an important tool in our armamentarium for treating ventricular arrhythmias, with the advantage of requiring no intravascular hardware (particularly ideal in younger patients and those with more risk factors for infection). Procedural time is similar to that for implanting a sin-

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gle-lead transvenous ICD, and implants can be performed without fluoroscopy. This registry data further affirms the low 30-day complication rate and high rate of defibrillation success at implant. We await important information about "real-world" success rates of terminating clinical arrhythmias, incidence of inappropriate ICD shocks, and proportion of arrhythmias that potentially could be treated with transvenous overdrive pacing rather than a shock.

THE NODE-I TRIAL
(Stambler B, et al.)

Etripamil is a short-acting L-type calcium channel blocker with rapid onset of action, designed for intranasal administration and being developed as a self-administered outpatient therapy for paroxysmal supraventricular tachycardia (PSVT). NODE-1 is a Phase II, multicenter, randomized, controlled study of 104 patients undergoing electrophysiology studies.

After SVT (AV reentrant tachycardia or AV nodal reentrant tachycardia) was induced and sustained for at least five minutes, either a dose of etripamil ranging from 35-140 mg or placebo was administered intranasally. Conversion rates to sinus were as high as 95% within 15 minutes of administration of the highest dose of etripamil, compared with 35% in the placebo group (mean time to conversion ranged from 2.6-3.4 minutes).

Nasal congestion occurred in up to 45% of etripamil patients, compared with 0% who received placebo, and transient second-degree AV block (Mobitz type I) was seen in one patient who received the highest dose of the study drug. There were two cases of hypotension reported as adverse events.

■ COMMENTARY

Etripamil eventually may offer a new treatment approach for patients with paroxysmal SVT, particularly those who do not wish to take daily medications or undergo an ablation procedure. The next step will be a trial of patient self-administration to terminate PSVT in the ambulatory setting.

THE POWDER-AF MULTICENTRE RANDOMISED TRIAL
(Duytschaever M, et al.)

This three-center randomized trial included patients who underwent a standard pulmonary vein isolation procedure for paroxysmal AF and who continued a previously ineffective antiarrhythmic drug therapy (ADT) for the three-month post-ablation blanking period. Of 153 patients who were free of AF at the end of the blanking period, half were randomly assigned to continue the ADT, and half were told to stop the medication. Assessment of recurrent AF was based on a seven-day Holter monitor and quality of life questionnaires at six and 12 months post-procedure. Sustained atrial arrhythmia was documented in 2.7% of the group on ADT, significantly less than in the group off medication (21.9%; $P < 0.001$). Patients on continued ADT also had a lower rate of repeat ablations and unscheduled visits; quality-of-life scores were similar.

■ COMMENTARY

These findings may have important implications for the clinician managing patients with AF after an ablation procedure, often the cardiologist who originally referred the patient. Continuation of an antiarrhythmic drug for up to one year after the ablation procedure, even if that drug was ineffective at controlling the arrhythmia, resulted in significantly fewer atrial arrhythmias, repeat ablations, and unscheduled visits. Although quality-of-life scores were similar, the potential for reduced cost and burden to the medical system may warrant consideration of this strategy.

THE REVEAL AF STUDY
(Reiffel JA, et al.)

In this single-arm, multicenter study, 385 patients with risk factors for AF, $CHADS_2$ score ≥ 3 (or = 2 with an additional risk factor), and no AF detected on ≥ 24 hours of external monitoring received an insertable cardiac monitor (ICM). By 30 days (the longest typical duration of monitoring when using an external device) the incidence of adjudicated AF ≥ 6 minutes was 6.2%. However, that incidence increased to 27.1% by 12 months and 40.0% by 30 months.

Oral anticoagulation was prescribed in 56.3%.

■ COMMENTARY

Several studies have demonstrated that a higher incidence of AF can be detected with longer-term continuous ambulatory monitoring. In CRYSTAL AF (*N Engl J Med 2014;370:2478-2486*), an insertable cardiac monitor detected AF in 12.4% of patients with cryptogenic stroke by 12 months, compared with 2.0% of patients undergoing conventional monitoring. The REVEAL AF study went a step further by including all patients with risk factors for AF, not just those with stroke. The authors did not comment on whether any specific risk factor vs. compatible symptoms predicted AF more reliably, nor on what proportion of patients may have been diagnosed otherwise (via symptom-based monitoring or routine screening). Nevertheless, the impressively high incidence of previously undiagnosed AF, which resulted in anticoagulation therapy in the majority of cases, suggests there may be a public health benefit to more rigorous AF screening in high-risk patients. The risks and benefits of anticoagulating asymptomatic patients once AF is detected incidentally by monitoring will require further studies. ■

ABSTRACT & COMMENTARY

Antiplatelet Therapy After TAVR: More ARTE Than Science

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: The current clinical standard of dual antiplatelet therapy following transcatheter aortic valve replacement (TAVR) is controversial. The authors of the ARTE trial randomized post-TAVR patients to single or dual antiplatelet therapy and found that single antiplatelet therapy was associated with a lower risk of major bleeding events.

SOURCE: Rodés-Cabau J, Masson JB, Welsh RC, et al. Aspirin versus aspirin plus clopidogrel as antithrombotic treatment following transcatheter aortic valve replacement with a balloon-expandable valve: The ARTE (Aspirin Versus Aspirin + Clopidogrel Following Transcatheter Aortic Valve Implantation) randomized clinical trial. *JACC Cardiovasc Interv* 2017 May 11. pii: S1936-8798(17)30812-9. doi: 10.1016/j.jcin.2017.04.014. [Epub ahead of print].

Current practice calls for between three and six months of dual antiplatelet therapy (DAPT) following transcatheter aortic valve replacement (TAVR). This recommendation has its origin in the major trials leading to TAVR approval in the United States (the PARTNER Trial and the CoreValve US Pivotal Trial). It is clear that the origin of this practice comes from expert opinion rather than from randomized trials. The traditional TAVR population includes primarily patients of advanced age and high frailty, with comorbidities that bring an elevated bleeding risk along with high surgical risk. In this group of patients, the use of higher intensity antiplatelet regimens may come with additional hazards beyond what we see in a surgery-eligible population.

The ARTE trial was a prospective, randomized, open-label clinical trial conducted at nine centers in Canada, Europe, and South America. A total of 222 patients presenting for TAVR with the Edwards balloon-expandable valve (initially the SAPIEN XT, and later the SAPIEN 3) were randomized 1:1 to receive either aspirin alone or aspirin plus clopidogrel following the TAVR procedure. Patients who had an indication for chronic anticoagulation were excluded, as were patients with recent drug-eluting stent implantation who already had an indication for DAPT. Patients with a recent history of serious bleeding or any history of intracranial hemorrhage, as well as patients with allergy to either drug, also were excluded. Patients were evaluated clinically at one month, three months, six months, and 12 months. The primary endpoint was the rate of death, myocardial infarction (MI), ischemic stroke or transient ischemic attack (TIA), or major bleeding at the three-month point.

To no one's surprise, the aspirin alone group showed a trend toward lower occurrence of the primary endpoint (15.3% DAPT vs. 7.2% aspirin alone; $P = 0.065$), with non-significant trends in mortality (6.3% vs. 3.6%; $P = 0.37$), MI (3.6% vs. 0.9%; $P = 0.18$), and stroke or TIA (2.7 vs. 0.9%; P

= 0.31). DAPT was associated with a higher rate of major or life-threatening bleeding events (10.8% vs. 3.6%; *P* = 0.038).

The authors concluded that aspirin alone, when compared with DAPT, was associated with lower rates of major bleeding following TAVR without increasing the hazard for death or thrombotic complications, including MI and stroke.

■ COMMENTARY

The story of anticoagulant choice in routine TAVR patients is an interesting tale whose final chapters have yet to be written. Initial trials of TAVR were performed with DAPT after valve deployment, in part as a reflex equating the stent-mounted valve prostheses with other vascular stent implants.

Although there is no evidence to suggest that higher levels of antiplatelet activity (or of any antiplatelet activity at all) are important with TAVR valves, evidence has mounted in recent years that a significant percentage of such valves can be plagued by subclinical leaflet thrombosis (with as-yet-unclear clinical implications). In the recently-reported RESOLVE and SAVORY registries, approximately 15% of patients on antiplatelet therapy alone showed reduced leaflet motion suggesting thrombus, with no significant difference between dual and single antiplatelet therapy regarding this outcome. Anticoagulants, including warfarin and new oral anticoagulant drugs, reduced this frequency to approximately 3%.

Despite these data, guidelines continue to recommend DAPT as standard of care post-TAVR. ARTE is the latest in a string of modest-sized trials concluding that single antiplatelet therapy is not only as safe, but actually may be safer than DAPT in this population. At our center, we have little hesitation in simplifying the post-TAVR regimen to single antiplatelet therapy in patients who have thrombocytopenia or are otherwise at elevated risk of bleeding. Guidelines are unlikely to change until larger trials are published. POPular-TAVI and CLOE are examining similar questions with a cumulative total of thousands of patients planned. More interesting yet will be the forthcoming trials of anticoagulant vs. antiplatelet therapy post-TAVR, of which the AUREA (vitamin K antagonist), GALILEO (rivaroxaban), and ATLANTIS (apixaban) trials are the most widely anticipated. ■

ABSTRACT & COMMENTARY

Distinguishing Ischemic from Non-ischemic Cardiomyopathy Clinically

By Michael H. Crawford, MD, Editor

SYNOPSIS: This cardiac catheterization-based study of patients with newly diagnosed reduced left ventricular ejection fraction of unknown etiology showed that 15% had ischemic cardiomyopathy and they could be identified by clinical characteristics and an ECG-based risk score.

SOURCE: Smilowitz NR, Devanabanda AR, Zakhem G, et al. Comparison of clinical and electrocardiographic predictors of ischemic and nonischemic cardiomyopathy during the initial evaluation of patients with reduced (≤ 40%) left ventricular ejection fraction. *Am J Cardiol* 2017;119:1650-1655.

In newly discovered reduced left ventricular ejection fraction (LVEF), it is considered appropriate to perform invasive coronary angiography to identify ischemic cardiomyopathy (ICM), which is potentially treatable by revascularization. However, are angiograms always necessary? Investigators from New York University retrospectively identified patients referred for left heart catheterization with a new diagnosis of LVEF < 40% by echocardiography between 2010 and 2014 to see if they could develop a clinical risk score to predict the likelihood of obstructive (> 70% diameter reduction) coronary artery disease (CAD). Patients were excluded if the etiologic diagnosis was obvious, such as those admitted with acute coronary syndrome, previous revascularization or myocardial infarction, severe left heart valve disease, right ventricular pacing for conduction disease, or had an established non-ischemic cardiomyopathy diagnosis.

Inclusion criteria were met in 273 of the 5,030 patients referred for coronary angiography, and ischemic cardiomyopathy (ICM) was found in 41 patients (15%). Patients with ICM were older, more likely to have diabetes, peripheral arterial disease, and use tobacco. Also, ICM patients were more

likely to have ECG evidence of Q wave infarction (34% vs. 13%; $P < 0.001$) and ischemic ST-T changes (22% vs. 9%; $P = 0.02$), but left bundle branch block was less likely (2% vs. 15%; $P = 0.03$). A risk model including all clinical and ECG data was highly predictive of ICM (C statistic = 0.81). A simplified model that only included age, hypertension, diabetes, tobacco, Q wave infarction, and ST-T changes on ECG also was highly predictive (C = 0.80). When the risk score (range -1 to 9 points) was dichotomized at 3.5, the negative predictive value was 95%. The authors concluded that specific clinical and ECG abnormalities could be used to estimate which patients with reduced LVEF were at low risk of having ICM.

■ COMMENTARY

The issue of performing an invasive evaluation of the coronary arteries in patients with newly diagnosed LV systolic dysfunction of unclear etiology is important because myocardial ischemia is potentially treatable. Many centers, such as the one where this study was performed, have had a policy that all such patients undergo a left heart catheterization. This study hypothesized that clinical and ECG features of the patient may be able to identify a low-risk group in which catheterization is not mandatory. They found that four clinical factors (age, hypertension, diabetes, and tobacco use) and two ECG abnormalities (Q waves and ischemic ST-T changes) could be used to calculate a point score that would identify a low risk of ICM group. The feature with the highest points assigned was age > 65 years (3 points). Age 55-64, diabetes, and Q waves all were assigned 2 points each. All the rest were 1 point, except for hypertension, which was scored as a -1. The maximum score was 9, but any score < 3.5 was considered a low risk for ICM. The up to 3.5-point cutoff for the low risk of ICM group had a negative predictive value of 95%. From a qualitative approach, if a patient is < 65 years of age and does not have diabetes or Q waves, their score will not be > 3.5, even if they have all the other factors in the score, so invasive angiography could be avoided in such patients. Since the false-negative rate is not zero perhaps in those with low scores, a non-invasive test for coronary disease should be used, such as stress testing or CT angiography. Other interesting findings were that 12% of non-ICM patients had ECG Q waves and only 2% of ICM patients had left bundle branch block. Both these findings have been found in other studies, and the paucity of left bundle in ICM is well-known.

There are several weaknesses to this study. It is a single-center retrospective study and suffers from the selection bias of catheterization-referred patients. However, at this center the policy was to perform invasive coronary angiography in this type of patient. CAD was defined as significant obstructive disease, but this is the disease most likely to be amenable to revascularization. Right ventricular dysfunction on echocardiography also is known to be associated with non-ICM, but wasn't considered in this study. Also, the authors didn't look at segmental left ventricular wall motion abnormalities either, perhaps because previous studies have not shown this to be a useful discriminator.

I believe many clinicians are using clinical judgment based on the characteristics of the patient, the ECG, and the echocardiogram to cull the low likelihood group and not performing invasive angiography on them. However, this paper provides a more systematic approach, which would promote more uniformity in decision-making. ■

ABSTRACT & COMMENTARY

B-type Natriuretic Peptide Is Less Useful in Elderly Patients with Dyspnea

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: Among patients ≥ 80 years of age presenting with acute dyspnea, B-type natriuretic peptide level was not useful for differentiating cardiac vs. respiratory etiologies when added to a model of clinical predictors.

SOURCE: Plichart M, Orvoën G, Jourdain P, et al. Brain natriuretic peptide usefulness in very elderly dyspnoeic patients: The BED study. *Eur J Heart Fail* 2017;19:540-548.

B-type natriuretic peptide (BNP) is used frequently to identify cardiac vs. respiratory etiologies in patients presenting with dyspnea. However, many factors influence BNP level, limiting its usefulness in certain populations. The diagnostic accuracy of BNP concentration in the assessment of dyspnea in very elderly (> 80 years of age) patients has not been studied adequately. The authors of the BNP Usefulness in Elderly Dyspneic Patients (BED) study enrolled 383 patients ≥ 80 years of age who were evaluated for acute dyspnea. All patients had BNP levels measured in addition to other clinical testing, including echocardiography. Independent cardiologists blinded to the BNP result evaluated each case according to standard guidelines to determine whether the cause of dyspnea was cardiac vs. respiratory.

Sixty-two percent of patients had cardiac dyspnea, and 38% had respiratory dyspnea. BNP levels were significantly higher among patients with cardiac vs. respiratory etiologies (median level 385.5 vs. 172.0 ng/L; $P < 0.001$). However, BNP was not a good test for discriminating cardiac vs. respiratory etiologies (area under the curve [AUC] = 0.68). The authors created a multivariate model of clinical predictors that discriminated cardiac vs. respiratory dyspnea with high accuracy (AUC = 0.915). When added to this model, BNP was independently associated with cardiac etiology but did not improve the AUC significantly ($P = 0.16$). No single BNP cutoff value was found that diagnosed or excluded cardiac etiologies with adequate reliability. Clinical predictors associated with a cardiac etiology included higher body mass index, history of heart failure (HF), X-ray findings consistent with pulmonary edema, and lower ejection fraction. History of chronic respiratory disease, rhonchi, and higher white blood cell count all were associated with a respiratory etiology. The authors concluded that BNP is not a useful diagnostic tool among very elderly patients with acute dyspnea, but noted that it may be of interest for prognosis in heart failure.

■ COMMENTARY

Both American and European guidelines give a class IA recommendation for the use of natriuretic peptide biomarkers such as BNP to support or exclude heart failure in patients presenting with dyspnea. A cutoff level of 100 ng/L is recommended often to rule out cardiac dyspnea, regardless of age. However, guidelines also acknowledge that comorbidities can influence BNP levels and recommend they be taken into account when interpreting a given patient's BNP. Elderly patients are more likely to present with comorbidities, and age alone can influence BNP level. Therefore, it is important to understand how this changes the utility of BNP as a diagnostic test.

The Breathing Not Properly Multinational Study was one of the first and largest to evaluate the utility of BNP measurement in patients presenting with dyspnea. A post-hoc subanalysis of this study found that BNP was a weaker predictor in subjects > 70 years of age. BNP levels tended to be higher in elderly subjects, and this decreased the specificity for any given cutpoint. Several smaller studies subsequently found that BNP remained useful in elderly patients, though higher cut-points were needed.

Plichard et al now add the largest study to date specifically evaluating the utility of BNP in elderly patients. Their primary finding is that a clinical model consisting of age, body mass index, gender, and other covariates discriminated cardiac vs. respiratory etiologies with high accuracy. Although BNP levels were higher in patients with cardiac dyspnea, adding BNP levels to their clinical model did not improve the discriminative ability of their model significantly.

Although the findings of this study weaken enthusiasm for BNP use in elderly patients, there are a few important aspects to keep in mind. The baseline multivariable model already had an impressive ability to discriminate cardiac vs. respiratory dyspnea, and it would be difficult for the addition of BNP to improve on this model significantly. The model these authors used involved many variables and was not practical for routine use in clinical settings. BNP levels were clearly higher in patients with cardiac etiologies, and perhaps if a simpler, more realistic baseline model were used, then adding BNP would improve the diagnostic accuracy. Another limitation is the lack of a "gold standard" for the diagnosis of cardiac (as opposed to respiratory) dyspnea. Instead of abandoning BNP testing in elderly patients, it may be better to continue using it to differentiate cardiac vs. respiratory causes of dyspnea while taking into consideration its limitations. Elderly patients have higher BNP levels than younger patients, and a higher BNP level cannot "rule in" cardiac dyspnea with the same accuracy as it can in younger patients. BNP levels should be used along with all other available clinical data when determining the etiology of acute dyspnea in elderly patients. ■

ABSTRACT & COMMENTARY

Left Ventricular Volume Affects Function in Chemotherapy Patients

By Michael H. Crawford, MD, Editor

SYNOPSIS: Reductions in left ventricular ejection fraction in patients receiving potentially cardiotoxic chemotherapy may be because of significant decreases in left ventricular volume in up to 20% of these patients. In such patients, a trial of volume repletion may be appropriate before stopping chemotherapy or adding cardioprotective drugs.

SOURCE: Meléndez GC, Sukpraphrute B, D'Agostino RB Jr, et al. Frequency of left ventricular end-diastolic volume-mediated declines in ejection fraction in patients receiving potentially cardiotoxic cancer treatment. *Am J Cardiol* 2017;119:1637-1642.

Left ventricular ejection fraction (LVEF) is followed in patients receiving potentially cardiotoxic chemotherapy frequently. However, EF is preload-dependent, and little attention has been paid to changes in LV volume with chemotherapy. Investigators from Wake Forest University prospectively studied 112 patients receiving potentially cardiotoxic chemotherapy by cardiac magnetic resonance (CMR) imaging before and three months after chemotherapy. The patients received an admixture of agents: alkylating agents (74%), anthracyclines (72%), and tyrosine kinase inhibitors (51%). Exclusion criteria included contraindications to CMR and if they had an EF < 50% at baseline. Chemotherapy-induced LV dysfunction was defined as an EF decline of > 10% or to an absolute value of < 50%. Significant declines in LV end-diastolic volume (EDV) were defined as > 19mL (25th percentile) and increases in LV end-systolic volume (ESV) as > 10mL (75th percentile).

Chemotherapy-related decreases in LVEF were seen in 26 of the 112 patients (23%). Of these 26 patients, six exhibited significant drops in LVEDV, and only one of these had an increase in ESV. In 15 of the 26, ESV increased significantly without a change in EDV, which suggests a true decrease in contractility. Five of the 26 had minor changes in EDV and ESV. Thus, about 20% of the patients who experienced a significant decrease in EF had isolated reductions in EDV, suggesting that they moved downward on the Frank-Starling curve rather than experiencing a reduction in contractility. The authors concluded that nearly one-fifth of patients experiencing significant reductions in LVEF with chemotherapy have isolated reductions in EDV, which could be treated with volume repletion. They recommended paying more attention to LV volumes when assessing the imaging results of patients with large drops in EF associated with potentially cardiotoxic chemotherapy.

■ COMMENTARY

A reduced LVEF after chemotherapy is a common reason for an outpatient cardiology consultation, and many of these patients have their chemotherapy stopped, which might not be good for their long-term survival. Also, most end up on cardioprotective drug therapy, which no one knows how long to continue. This study suggests that nearly one-fifth of these patients may have a reduced EF solely due to reduced LVEDV, with the patient moving down the Frank-Starling curve. This is not surprising given that chemotherapy often causes emesis and nausea that could suppress oral intake. The tip-off is that the EDV is

reduced, and the ESV is not increased. Usually with reduced contractility, the ESV increases. Of course, this requires accurate LV volume measurements, which you don't get from a multiple gated acquisition scan, if your oncologists are still using that antiquated technology. Echocardiography should be more than adequate, and you can analyze diastolic function and LV strain rate, which will augment the assessment of LV performance. Not all echo labs provide a quantitative report, so you may have to make your own measurements or use another technique. This study used CMR, which is quite accurate but also expensive and not available everywhere.

The major weakness of this study is that the authors didn't volume-replete the low EDV, low EF patients to see how many would recover their EF. However, it would seem worth trying in stable patients, before stopping chemotherapy or adding cardioprotective drugs that may lower blood pressure. ■

CME/CE QUESTIONS

1. **In patients with newly diagnosed reduced left ventricular ejection fraction (LVEF) of unknown etiology, ischemic cardiomyopathy is:**
   a. rare.
   b. uncommon.
   c. common.
   d. frequent.

2. **In chemotherapy-associated LVEF reduction, what is the least common cause?**
   a. Reduced LV end-diastolic volume (LVEDV) and increased end-systolic volume (ESV)
   b. Increased LVESV
   c. Decreased LVEDV
   d. Minor changes in LV volumes

3. **Etripamil is a new drug for converting supraventricular tachycardia to sinus rhythm that is given:**
   a. intravenously.
   b. subcutaneously.
   c. intranasally.
   d. orally.

4. **A recent trial comparing aspirin alone to aspirin plus clopidogrel post-transcatheter aortic valve replacement showed that aspirin alone significantly reduced:**
   a. the primary combined endpoint.
   b. major bleeding.
   c. stroke.
   d. mortality.

5. **B-type natriuretic peptide levels are of less use for diagnosing cardiac dyspnea in patients:**
   a. < age 40 years.
   b. age 40-60 years.
   c. age 60-80 years.
   d. > age 80 years.

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.