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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Valve Disease and Thromboembolic Risk

By Michael Crawford, MD, Editor

SOURCES: Philippart R, et al. Prognostic value of CHA_2DS_2-VASc score in patients with 'non-valvular atrial fibrillation' and valvular heart disease: The Loire Valley Atrial Fibrillation Project. *Eur Heart J* 2015;36:1822-1830.

Breithardt G, Baumgartner H. Valvular heart disease among non-valvular atrial fibrillation: A misnomer, in search of a new term. *Eur Heart J* 2015;36:1794-1797.

The CHA_2DS_2-VASc score (CVS) for the prediction of stroke and other thromboembolism risk in patients with atrial fibrillation (AF) has been validated in patients with non-valvular AF (*see Table 1*). AF patients with mitral stenosis or a prosthetic left heart valve are known to have a high risk of thromboembolism, and vitamin K antagonists are recommended for them regardless of their CVS. However, little data are available on how to manage AF patients with native, non-rheumatic valve disease. Thus, investigators from France and the United Kingdom tested the hypothesis that the CVS would work well in such patients. The hypothesis was tested in the echocardiography database of a large hospital in Tours, France, to identify 8053 AF patients without valve disease (n = 6851) and those with either aortic stenosis (AS) or regurgitation (AR) and mitral regurgitation (MR) (n = 1202) between 2000 and 2010. Thromboembolic events were identified after a mean follow-up of 868 days in 627 patients. The AF patients with valve disease (61% MR, 24% AR, 32% AS) had a higher risk of events (hazard ratio [HR], 1.39; 95% confidence interval, 1.14-1.69; $P = 0.001$), even after adjustment for anticoagulant and antiplatelet use. The severity of valve disease was not associated with more events, but patients with aortic valve disease had higher event rates than those with MR. The event rate per year increased with increasing CVS in those with and without valve disease, and the predictive value of the CVS was the same in both groups. Comparing a CVS of 0-1 to 2-3, the event rate/year not on anticoagulants increased from 1.62% to 6.19% in AF patients without valve disease and from 1.90% to 5.98% in those with valve disease. The authors concluded that in "non-valvular AF" patients (no mitral stenosis or valve prostheses) the presence of left ventricular valve disease increased the risk of thromboembolic events and that this

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Table 1. The CHA_2DS_2-VASc Score

Factor	Points
Congestive heart failure	1
Hypertension history	1
Age 65-74 years	1
Age > 74 years	2
Diabetes	1
Stroke, TIA thromboembolism	2
Vascular disease history	1
Sex, female	1
Scores >1 favor anticoagulant therapy.	

result correlated with higher CVS scores.

■ COMMENTARY

Almost all the research on anticoagulants and AF has been in so-called "non-valvular AF." It is now clear that this terminology was imprecise. What was really meant was "AF patients with no other high-risk condition for thromboemboli," such as rheumatic mitral stenosis and prosthetic valves. The latter patients had clear indications for anticoagulation if they developed AF. Patients with non-rheumatic mitral valve disease and patients with aortic valve disease fell into a gray zone in which there wasn't much data. Thus, this retrospective observational study focusing on AF patients with and without gray zone valve disease is of interest. In their traditional non-valvular AF patients, 22% had left heart valve disease (LHVD), 60% of which was non-rheumatic MR. This LHVD subgroup of the "non-valvular" AF patients had a higher incidence of thromboembolic events. However, they were older and had more comorbidities than the group with absolutely no valve disease, which was reflected in higher CVSs. On multivariate analysis, only age, female sex, and the CVS were predictive of events. Of course, the first two are included in the CVS. In fact, in this study the CVS had the same predictive value in both groups, which suggests that it can be used for all AF patients without rheumatic mitral stenosis or a prosthetic valve.

These distinctions are important for choosing an oral anticoagulant. We know that the new oral anticoagulants (NOAC) are at least as good as vitamin K antagonists (VKA) in "non-valvular AF," but not in prosthetic valves. There are no comparative data in mitral stenosis, but most would favor VKA in these patients. Can we use NOACs in the AF patients with non-rheumatic, non-prosthetic LHVD? This study suggests that if we use the CVS we can. Other studies comparing the NOACs to VKAs have included some LHVD patients (e.g., ROCKET AF), and the results were similar. Thus, the available data suggest NOACs are adequate in LHVD patients with AF.

Clearly, the term "non-valvular AF" is confusing. The American College of Cardiology/American Heart Association/European Society of Cardiology guidelines define "non-valvular AF" as the absence of rheumatic disease, mitral stenosis, prosthetic valves, or valve repair. That leaves a lot of LHVD on the table. Perhaps we need new terminology in this area as the editorial accompanying this article suggests. The immediate practical conclusion of this study is that the CVS score can be used to determine who needs oral anticoagulant therapy in "non-valvular AF" patients with LHVD with confidence. ■

ABSTRACT & COMMENTARY

Doppler Echo Risk Stratification in Aortic Stenosis

By Michael H. Crawford, MD, Editor

SOURCES: Rusinaru D, et al. Relation of dimensionless index to long-term outcome in aortic stenosis with preserved LVEF. *JACC Cardiovasc Imaging* 2015;8:766-775.

Zoghbi WA. Velocity acceleration in aortic stenosis revisited. *JACC Cardiovasc Imaging* 2015;8:776-778.

The accurate estimation of the severity of aortic stenosis (AS) by Doppler echocardiography is hampered by the need for left ventricular outflow tract (LVOT) area in the continuity equation. LVOT area is estimated from LVOT diameter, which is difficult to measure and assumes a circular subvalvular channel, which it probably isn't. The dimensionless index (DI) is the ratio of LVOT time velocity integral (VTI) to the aortic VTI, with severe AS defined as a DI of < 0.25. It is basically the continuity equation without LVOT area. The purpose of this study was to test the hypothesis that DI predicts outcome after AS diagnosis. They enrolled 488 patients from two tertiary hospitals in France and defined more than mild AS as having a valve area of < 2 cm^2 and a left ventricular ejection fraction (LVEF) > 50%. Patients with more than mild left heart valve regurgitation, non-native valve AS, angina, heart failure, or syncope were excluded. Patients were managed by their own physicians. The mean age of the population was 76 years and 57% were men. All had no or minimal symptoms and were followed for a mean of 32 months (range 8-58). The primary outcome was all-cause death or aortic valve replacement (AVR). The secondary outcome was cardiac death. Receiver operating curve analysis showed that a DI of 0.25 was the best cutoff for predicting a peak aortic jet velocity of > 4 m/s and a DI of 0.20 for a jet velocity of > 5 m/s. There were 241 primary events (117 death and 124 AV replacements). The 5-year event-free survival was 56% for a DI > 0.25, 41% for a DI between 0.20-0.25, and 22% for a DI < 0.20. Multivariate analysis showed that at DIs > 0.25 there was no increase in risk with decreasing DI, but with DIs < 0.25 decreasing DI showed increased risk. Also, using DI as compared to AV area and peak jet velocity improved the prediction of events (C-statistic 0.714 vs 0.674 and vs 0.667, respectively, $P = 0.002$). DI was not associated with all-cause death, but did predict cardiac death (hazard ratio, 2.08; 95% confidence interval, 1.06-4.11; $P = 0.034$). The authors concluded that DI is an accurate indicator of AS severity of clear prognostic value, and a cutoff of < 0.25 should be used for decision making.

■ COMMENTARY

The determination of the severity of AS by Doppler echo is the standard approach, but it does have pitfalls. Using peak velocity can underestimate the severity if the Doppler beam isn't within 20 degrees of the jet or if the patient has a low-flow state, such as reduced LV function. It can also overestimate the severity of AS if the ascending aorta is small because of the phenomenon of pressure recovery. Since the traditional gold standard is the invasive determination of valve area by the Gorlin equation, Doppler echo has been used to calculate aortic valve area by the continuity of flow equation. One must remember that flow is the product of the velocity multiplied by the cross-sectional area of the flow channel. The difficulty in determining the cross-sectional area of the LVOT flow accurately has hampered the estimation of aortic valve area by Doppler echo. Hence, there has been interest in using the continuity equation without the LVOT area, which becomes the ratio of the LVOT VTI divided by the aortic valve VTI or the DI. The DI has not been used extensively because of a paucity of data, especially with regard to outcomes.

This study is the first large study of the utility of the DI to predict death or AVR in mainly asymptomatic patients with more than mild AS and LVEF > 50%.

[Dimensionless index is an accurate indicator of aortic stenosis severity of clear prognostic value, and a cutoff of < 0.25 should be used for decision making.]

In other words, these patients had significant AS, but did not meet criteria for immediate AVR. They found that DI in this population predicts AVR or cardiac death during follow-up, regardless of other co-morbidities. Additionally, there is an abrupt change in the slope of this relationship at a DI < 0.25 or when the aortic flow velocity is more than four times the LVOT flow velocity. They propose that a DI < 0.25 defines severe AS. This cutoff is in agreement with previous studies. Also, the DI is not affected by LVOT diameter, body surface area, or stroke volume. However, these were patients with relatively normal stroke volumes. DI does not solve the problem of low-flow, low-gradient AS patients. In addition, as Dr. Zoghbi's editorial points out, DI could be affected by extremes in LVOT size as might be seen in those with very dilated LVs or very small LVs due to extreme hypertrophy. In the average patient with an LVOT diameter around 2 cm (1.8-2.2 cm) there should be no problem. However, both the authors and Dr. Zoghbi recommend a multi-measurement approach considering valve anatomy, peak velocity, AV area, and the DI in patients with normal LV function to estimate the severity of AS. ■

ABSTRACT & COMMENTARY

RITA-3 Reports 10-year Mortality Outcomes: Time to Rethink the Guidelines, or Much Ado About Nothing?

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.

SOURCE: Henderson RA, et al. Ten-year mortality outcome of a routine invasive strategy vs a selective invasive strategy in non-ST-segment elevation acute coronary syndrome: The British Heart Foundation RITA-3 randomized trial. *J Am Coll Cardiol* 2015;66:511-520.

Current U.S. and European guidelines assign a class I indication to a routine early invasive strategy for evaluation and treatment of non-ST elevation acute coronary syndromes (NSTEACS). This is based on the outcomes of a bevy of randomized clinical trials comparing routine invasive with selective invasive strategies. One of these trials, RITA-3, enrolled 1810 moderate-risk NSTEACS patients and randomized them to a planned invasive strategy, usually with coronary angiography within 72 hours, or to a conservative strategy where cardiac cath was reserved for patients with ongoing or recurrent ischemia. The publication of the 1-year results in *The Lancet* in 2002 assigned a significant advantage to the planned invasive strategy in terms of the composite endpoint, driven primarily by a nearly 50% reduction in refractory angina. Death and myocardial infarction (MI) were similar between the two groups at 1 year. However, the mortality curves separated over time, such that by the planned 5-year follow up, not only were revascularization, MI, and angina lower in the invasive group, but there was also a 24% relative reduction in all-cause mortality. Because all surviving patients were prospectively entered into a national registry in the United Kingdom, national mortality data are now available for this cohort at the 10-year mark.

What the authors report appears surprising. At 10 years, the mortality advantage earlier assigned to the routine invasive strategy had dissipated, with the death of approximately 25% of patients in each group. The usual suspects emerged as independent predictors of death in a multivariate analysis: age, previous MI, heart failure, smoking status, diabetes, heart rate, and ST-segment depression. Patients were further stratified into low-risk, medium-risk, and high-risk groups based on a post-discharge Global Registry of Acute Coronary Events (GRACE) score. And while mortality at 10 years was markedly different between the low-risk (14.4%) and high-risk (56.2%) groups, there was no difference in within-group mortality based on the treatment strategy.

The authors conclude that the mortality benefit of the routine early invasive strategy seen at 5 years is attenuated at later follow-up, and suggest that further trials of more contemporary treatment strategies in NSTEACS are needed.

■ COMMENTARY

NSTEACS patients are a heterogeneous group, and treatment must be individualized without trying to heed absolutes (e.g., all patients must go to cath within 72 hours). Certain groups of high-risk patients should nearly always take an early-invasive approach (e.g., the patient with positive biomarkers and ongoing ischemia despite maximal medical therapy). Such high-risk patients for whom there is a lack of clinical equipoise were excluded from trials such as RITA. Other patients are decidedly low-risk, and the same trials have consistently failed to demonstrate benefit of the early-invasive strategy for this group, even in terms of softer outcomes, such as recurrent ischemia.

Several points are worth noting about the trial itself. Because the data from this study are derived from a national registry rather than from the follow-up mechanisms of the trial, there are no data beyond 5 years for other important endpoints, including recurrent angina, revascularization, and MI. The trial included a relatively modest-risk population, and the revascularization rate during the initial hospitalization in the early invasive group (~55%) was significantly lower than in other contemporary NSTEACS trials such as ACUITY and ICTUS. It is certainly worth asking whether the previously

reported 5-year mortality benefit was a plausible result in this trial.

How important is the purported intermediate-term mortality benefit in the current guideline recommendations for routine early intervention? The various trials in this space (TACTICS TIMI 18, FRISC II, ISAR-COOL, etc.) have been relatively consistent in terms of reduction in recurrent MI, recurrent ischemia, and revascularization in the short and intermediate terms. The RITA-3 trial did not examine these outcomes past 5 years, and therefore, the longer-term effects of this strategy remain unknown. However, the known positive effects are important to both patients and clinicians, and clearly support early intervention.

The RITA-3 10-year results should certainly prompt a re-evaluation of the mortality data associated with the early interventional strategy in NSTEACS. A more contemporary trial, as suggested by the study authors, would certainly be welcome. Significant changes have occurred in ACS management since these trials were performed — DES, radial access, newer antiplatelet agents, etc. Until then, however, I do not expect my own practice to change very much. Medium- and high-risk patients who are good candidates for cardiac cath will continue to go early to planned coronary angiography. And for low-risk patients, both conservative and planned invasive strategies remain viable alternatives. ■

ABSTRACT & COMMENTARY

New Study Calls for Caution in Use of Triple Anticoagulant Therapy

By Jeffrey Zimmet, MD, PhD

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

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

SOURCES: Hess CN, et al. Use and outcomes of triple therapy among older patients with acute myocardial infarction and atrial fibrillation. *J Am Coll Cardiol* 2015;66:616-627.

Valle JA, Messenger JC. Triple therapy…can we replace more with better? *J Am Coll Cardiol* 2015;66:628-630.

Patients presenting with acute myocardial infarction (MI) who undergo coronary stenting require treatment with dual antiplatelet therapy, typically for 12 months or more following the event. For patients who also have indications for systemic anticoagulation, most commonly those with atrial fibrillation (AF) and elevated CHA_2DS_2-VASc scores, choosing the most beneficial anticoagulant regimen is difficult. Combining oral anticoagulants with dual antiplatelet therapy, often referred to as triple therapy, comes with well-described bleeding hazards but uncertain benefit.

In this study, Hess et al used a national registry database to identify older patients with a history of AF or flutter who presented with acute MI and underwent in-hospital percutaneous coronary intervention (PCI) with stenting. Longitudinal data from such patients presenting between Jan. 1, 2007 and Dec. 31, 2010 were obtained by linking registry information with data from the Centers for Medicare & Medicaid Services. Medicare Part D data were used to identify warfarin and P2Y12 antagonist use. Notably, warfarin was the only oral anticoagulant available for clinical use in the United States during this period.

The study identified 4959 MI patients older than 65 years of age who had a history of AF and were treated with PCI during this time. Of those patients, 27.6% (n = 1370) were discharged on triple therapy, and 72.4% (n = 3589) were discharged on dual antiplatelet therapy (DAPT) without an additional anticoagulant. Those discharged on triple therapy were most often already on warfarin prior to the index hospitalization. Compared with dual antiplatelet therapy patients, those discharged with triple therapy were more often male and more frequently had a history of PCI or coronary artery bypass graft (CABG), prior stroke, and recent AF or atrial flutter. On the other hand, patients discharged on antiplatelet agents alone were more likely to have experienced an in-hospital major bleeding event. As would be expected, patients prescribed triple therapy had higher predicted stroke risk compared with DAPT patients; however, use of triple therapy

was not associated with predicted bleeding risk (*P* for trend = 0.18). Patients given triple therapy were more likely to have presented with non-ST segment elevation myocardial infarction (NSTEMI) rather than ST segment elevation myocardial infarction (STEMI), more often had a left ventricular ejection fraction ≤ 40%, and were more likely to have received bivalirudin during their PCI procedures. Although use of drug-eluting stents (DES) was similar between groups for patients who suffered STEMI, DES use was lower among triple therapy patients as compared to DAPT patients presenting with NSTEMI.

At 2 years post-discharge, rates of major adverse cardiac events (MACE) were similar between the DAPT and triple therapy groups (32.7 vs 32.6%). Of the individual components, only the unadjusted rate of ischemic stroke was lower in the triple therapy group (3.2% vs 4.7%; *P* = 0.02). All-cause mortality, MI readmission, and stroke readmission were all similar. After adjustment for patient, treatment, and hospital characteristics, the adjusted hazard ratio (HR) for ischemic stroke was no longer statistically significant.

Unsurprisingly, the incidence of serious bleeding requiring hospitalization within 2 years post-discharge was significantly higher for triple therapy patients compared with those on DAPT (17.6% vs 11.0%; *P* < 0.0001). This hazard was evident from shortly after discharge, and remained significant throughout the follow-up period. Triple therapy was also associated with a higher incidence of intracranial hemorrhage (adjusted HR, 2.04; 95% confidence interval, 1.25-3.34; *P* < 0.01).

The authors concluded that approximately one in four older patients with AF undergoing PCI for acute MI were discharged on triple therapy, and that this therapy was associated with higher rates of major bleeding without a measurable benefit in terms of major adverse cardiac events, including stroke.

■ COMMENTARY

Patients with concomitant needs for anticoagulant and antiplatelet therapies are, and are likely to remain, a particularly challenging group to treat. In this large retrospective study, triple therapy was associated with a significant bleeding hazard without a detectable benefit.

As pointed out in the accompanying editorial by Drs. Valle and Messenger, when it comes to anticoagulant regimens in these patients, "'more' does not appear to be 'better' … Although the question of whether triple therapy is beneficial for MACE remains troublingly uncertain, the data are convincing for bleeding." Clearly, we should use caution when taking this approach. And yet, there are subsets of patients at higher risk of ischemic stroke or other thrombotic events for whom combination therapy still appears to be worth considering. Few trials have addressed the question of whether a better alternative exists. One exception is the WOEST trial, published in 2013, which reported a bleeding advantage to use of clopidogrel plus warfarin as compared to triple therapy, without an associated ischemic cost. WOEST was relatively small (573 patients), however, and was underpowered for events such as stent thrombosis.

Whether we are likely to have better data in the near future is uncertain. Many of the trials that are currently in the works, such as REDUAL-PCI and PIONEER AF-PCI, focus on the potential of the newer oral anticoagulants as compared to warfarin in this arena. For now, it is clear clinicians should carefully consider the potential benefits and fully assess bleeding risks in each such patient, and should employ triple therapy only after careful consideration. ■

ABSTRACT & COMMENTARY

Serum Chloride Level Predicts Mortality in Acute Heart Failure

By Van Selby, MD

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

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

SOURCE: Grodin JL, et al. Prognostic role of serum chloride levels in acute decompensated heart failure. *J Am Coll Cardiol* 2015;66:659-666.

The association between serum sodium level and outcomes in acute decompensated heart failure (ADHF) is well-established. Serum chloride levels are also routinely obtained with basic chemistry panels, but the clinical significance of hypochloremia in ADHF has not been studied.

Grodin and colleagues reviewed data from 1318 patients hospitalized at the Cleveland Clinic with a discharge diagnosis of ADHF. They examined the association between the admission serum chloride level and all-cause mortality, and compared the prognostic significance of serum chloride and sodium levels. The relationship between serum chloride, sodium, and mortality was also evaluated in a validation cohort of 876 patients admitted to the Hospital of the University of Pennsylvania for heart failure (HF). Patients in both cohorts had predominantly systolic HF.

In univariate analyses, each unit increase in chloride was associated with a 6% decrease in mortality (hazard ratio [HR] per unit increase, 0.94; 95% confidence interval [CI], 0.92-0.95; $P < 0.001$). Admission serum sodium level was also associated with mortality (HR per unit increase, 0.95; 95% CI, 0.93-0.97; $P < 0.001$). In multivariate analyses adjusted for other clinical variables, the chloride level remained predictive of mortality (HR per unit increase, 0.93; $P < 0.001$), whereas serum sodium level was no longer independently associated with mortality (HR per unit increase, 1.03; $P = 0.18$). Of note, mortality risk was strongly associated with changes in serum chloride levels < 96 mEq/L, but did not vary significantly at values > 96.

The findings were similar in the cohort from Pennsylvania; serum chloride remained predictive in multivariate models adjusted for other clinical predictors (HR, 0.95; $P = 0.01$), while serum sodium was not (HR, 0.99; $P = 0.58$). The authors conclude that serum chloride levels measured during hospitalization for ADHF are independently and inversely associated with long-term mortality, independent of serum sodium levels.

■ COMMENTARY

The authors should be commended for challenging the long-held assumption that sodium is the key electrolyte in the pathophysiology of heart failure. Furthermore, in an era where the search for novel biomarkers often leads to increasingly complex and costly laboratory techniques, they chose to study a parameter that has been measured as part of standard care for decades. The pathophysiological role of chloride in heart failure is not well understood, mainly because it has not been studied in detail. Many of the same maladaptive responses that reduce serum sodium in HF also impact chloride levels. These include elevated levels of both arginine vasopressin and angiotensin II. Yet, these similarities alone cannot explain why chloride would be an even stronger prognostic marker than sodium. The authors suggest chloride plays a broader homeostatic role, serving as a buffer for cations and helping the kidney eliminate salt and water. This argument is further supported by the important role of chloride in a wide variety of other bodily functions, including maintenance of osmotic balance and muscle function. Regardless of the mechanism, the strong statistical association between chloride levels and mortality suggests further investigation may yield new insights that help shape our understanding of HF.

This study does have several limitations. The cohorts studied were obtained from two large, tertiary academic centers, and not necessarily representative of the broader ADHF population. The multivariate models did not include many well-known prognostic markers in HF, such as systolic blood pressure and natriuretic peptide levels. Furthermore, it must be emphasized that adding chloride levels to the multivariate predictive model had a very modest effect on the overall predictive ability. The C-statistic, a marker of discriminative ability, only increased from 0.68 to 0.69 with the addition of chloride level. The cohorts studied in this analysis were comprised of patients with primarily systolic HF, so we cannot conclude that chloride levels maintain their prognostic utility in those with preserved ejection fraction (unlike sodium, whose association with mortality has been proven in both preserved and reduced ejection fraction).

There is still a lot of work to be done on this topic. Future studies will need to validate the prognostic role of chloride in broader HF cohorts and elucidate the pathophysiological role of chloride in HF. Eventually, interventions that specifically target hypochloremia may improve the care of patients with ADHF, a condition for which we have yet to identify a therapy that meaningfully improves outcomes. Despite the limitations and further work needed, for now we have a new prognostic marker that is widely available and possibly more useful than serum sodium level for estimating prognosis in ADHF. ■

QUESTIONS & COMMENTS:
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CME QUESTIONS

1. Which of the following is associated with mortality in acute decompensated heart failure in a multivariate model?

a. Sodium
b. Potassium
c. Chloride
d. Carbon dioxide

2. Which of the following echo Doppler measures is strongest at predicting outcomes in patients with aortic stenosis?

a. Peak aortic jet velocity
b. Mean aortic gradient
c. Aortic valve area
d. The dimensionless flow velocity index

3. The RITA-3 trial compared a conservative vs invasive approach to NSTEMI patients and demonstrated a mortality benefit in the invasive group at __?

a. 1 year
b. 3 years
c. 5 years
d. 10 years

4. Post-percutaneous intervention patients with atrial fibrillation on dual antiplatelet therapy and oral anticoagulants show which of the following?

a. Increased major bleeding
b. Reduced stroke risk
c. Fewer major adverse cardiovascular events
d. All of the above

5. The CHA_2DS_2-VASc score is useful for estimating the risk of thromboembolic events in patients with which of the following?

a. Rheumatic valve disease
b. Non-rheumatic valve disease
c. No valve disease
d. Both b and c

CME OBJECTIVES

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

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