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Clinical Cardiology

Critical analysis of the latest clinical research in cardiovascular medicine [ALERT]

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ABSTRACT & COMMENTARY

Is Sodium Restriction Detrimental in Chronic Heart Failure?

By Van Selby, MD

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

SYNOPSIS: In an observational study of outpatients with NYHA class II or III heart failure, dietary sodium restriction (< 2500 mg/day) was associated with increased risk of death or heart failure hospitalization.

SOURCE: Doukky R, et al. Impact of dietary sodium restriction on heart failure outcomes. *JACC Heart Fail* 2016 2016;4:24-35.

Dietary sodium restriction is perhaps the most common self-care recommendation patients with chronic heart failure (HF) receive. However, data evaluating the effectiveness of sodium restriction are sparse, and the few studies that do exist have shown conflicting results.

To evaluate the relationship between dietary sodium restriction and clinical outcomes in chronic HF, Doukky et al analyzed data from the HF Adherence and Retention Trial (HART), a multicenter study of 902 patients with New York Heart Association (NYHA) functional class II or III systolic or diastolic HF. Patients were followed for a median of 36 months, and sodium intake was assessed using a food frequency questionnaire. Patients were classified as either sodium restricted (< 2500 mg/d) or unrestricted (≥ 2500 mg/d), and propensity score matching was used to address possible confounders. The primary outcome was the composite of death or HF hospitalization.

Sodium restriction was associated with a significantly higher risk of death or HF hospitalization (42.3% vs 26.2%; hazard ratio [HR], 1.85; $P = 0.004$). The difference was primarily due to higher rates of HF hospitalization (HR, 1.82; $P = 0.015$), though there was also a nonsignificant increase in the rate of death ($P = 0.074$). Subgroup analyses found the increased risk associated with sodium restriction was particularly high in patients not taking angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers

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(HR, 5.78; P = 0.002) and patients with milder NYHA class II symptoms (HR, 2.36; P = 0.003). Sodium restriction was not associated with any significant effect on quality of life, 6-minute walk distance, or symptom severity. The authors concluded that dietary sodium restriction may have a detrimental effect on outcome in patients with symptomatic chronic HF. They stress that a randomized clinical trial is warranted to resolve the issue.

■ COMMENTARY

Excessive sodium intake is associated with fluid retention, and many episodes of acute decompensated HF are often attributed to "sodium binges" in patients with stable chronic HF. For decades, sodium restriction has been a cornerstone of appropriate HF management, and the benefits of sodium restriction were so obvious that a trial evaluating its effectiveness seemed unnecessary. Current U.S. guidelines recommend patients with symptomatic HF restrict sodium intake to between 2000-3000 mg/day.

More recently, investigators are evaluating the effectiveness of sodium restriction more rigorously, and the results have been mixed. Several small studies have shown a clear benefit, with decreased signs and symptoms of HF as well as improved event-free survival. However, other studies have shown no clear benefit associated with sodium restriction, especially in patients with milder (class I-II) HF. The Doukky study is important for two reasons. First, the patients were recruited from a large, multicenter clinical trial. Second, the study evaluated an objective clinical outcome and found increased adverse outcomes among sodium-restricted patients.

Why would sodium restriction be harmful? Small studies have shown that sodium restriction increases neurohormonal activation by worsening intravascular volume depletion. Sodium restriction may also worsen hemodynamics, with a decrease in cardiac index and increase in systemic vascular resistance. In the Doukky study, patients not receiving angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers showed an especially high risk of adverse events with sodium restriction, suggesting the effect is mediated through neurohormonal pathways. Interestingly, sodium restriction was associated with a greater increase in adverse outcomes among patients with milder, class II symptoms. This is similar to what has been reported in other studies. It is possible that more symptomatic (class III) patients are particularly prone to hypervolemia, and, therefore, sodium restriction is beneficial for preventing worsening fluid overload. Class II patients, on the other hand, experience the detrimental neurohormonal activation from sodium restriction without seeing the benefits related to hypervolemia.

Limitations include the retrospective design, small sample size, and use of a food frequency questionnaire to measure dietary sodium intake. The authors used propensity matching to eliminate confounders, but it is still possible the sodium-restricted patients comprised a sicker group overall. This study offers no information regarding the utility of sodium restriction during hospitalization for acute HF.

Despite these limitations, the Doukky study adds to a growing body of research suggesting dietary sodium restriction may not be beneficial, perhaps even harmful in chronic HF. In response to this increasing evidence, the most recent European guidelines have removed any formal recommendation regarding sodium restriction, and the 2013 American Heart Association/American College of Cardiology guidelines downgraded the strength of their longstanding recommendation regarding dietary sodium restriction from class I (recommended) to class IIa (reasonable). Given the prevalence of chronic HF and the widespread use of recommendations regarding dietary sodium intake, many in the field echo the authors' call for a randomized trial to rigorously evaluate the effectiveness of these recommendations. Until then, there is no clear evidence to support aggressive sodium restriction in chronic HF, especially in patients with mild disease. ■

ABSTRACT & COMMENTARY

Blood Transfusion in Cardiac Disease Patients

By Michael Crawford, MD, Editor

SYNOPSIS: An observational study confirms the hypothesis that ischemic heart disease patients may do better with higher hemoglobin levels as compared to ICU patients without heart disease.

SOURCES: Ding YY, et al. Hemoglobin level and hospital mortality among ICU patients with cardiac disease who received transfusions. *J Am Coll Cardiol* 2015;66:2510-2518.

Rao SV, Vora AN. Transfusion in ischemic heart disease: Correlation, confounding, and confusion. *J Am Coll Cardiol* 2015;66:2519-2521.

The threshold hemoglobin (Hgb) level for red blood cell transfusion in hospitalized patients with cardiac disease is controversial. Thus, investigators from Boston University studied the Veterans Affairs (VA) electronic database to determine the Hgb level at which blood transfusion was associated with lower hospital mortality in medical ICU patients with cardiac disease. ICU admissions who had at least one transfusion in the first 30 days were the transfusion group; all others were the no transfusion group. The Hgb nadir was the lowest level before transfusion, or if not transfused the lowest level in the first 30 days in the ICU. Other variables included ICU admission diagnoses, comorbid conditions, and demographic characteristics. Researchers used adjusted linear regression analyses to analyze more than 5 years of ICU admissions data. Among the 258,826 ICU admissions, hospital death occurred in 12% and transfusions were noted in 12% during the first 30 days in the ICU. In addition to being older and sicker, those who died were twice as likely to have received a transfusion. In patients without cardiac disease, transfusion was associated with reduced adjusted hospital mortality when Hgb was < 7.7 g/dL. Above this level, transfusion was associated with higher mortality. In patients with cardiac disease, the corresponding level was 8.7 g/dL and 10 g/dL when the ICU admission diagnosis was acute myocardial infarction (MI). Sensitivity analyses in a smaller subset with more complete data showed that the Hgb levels below which mortality was reduced by transfusion could be about 1 g/dL lower than that for the total population. The authors concluded that in patients admitted to the ICU with comorbid cardiac disease, the Hgb level below which transfusion was associated with lower hospital mortality was < 8-9 g/dL and < 9-10 g/dL if the admitting diagnosis was acute MI.

■ COMMENTARY

Since the 1999 publication of the Transfusion Requirements in Critical Care (TRICC) randomized trial, critical care physicians and hospitals have pushed to restrict blood transfusions to those with a Hgb < 7 g/dL because this group showed lower mortality vs the comparison < 10 g/dL group. Cardiologists were concerned when this advice was applied to patients with acute ischemic heart disease (IHD) because the myocardium extracts nearly all the oxygen to it from the blood. The only way to deliver more oxygen to the myocardium is to deliver more oxygen, and a low Hgb would limit this. Some small observational studies supported this belief that higher Hgb thresholds for transfusion in IHD patients lowered mortality, but not all. Randomized, controlled trials (RCT) in acute coronary syndrome patients were called for. Two small pilot RCTs with a total of 155 patients showed conflicting results. It now seems unlikely that a large RCT will ever be conducted on this topic.

Given this background, this mega-observational analysis of more than 250,000 ICU admissions in the VA health system is of interest. It confirmed the TRICC study by showing that in ICU patients with no cardiac disease, the beneficial threshold was 7-8 g/dL, but in patients with cardiac comorbidities it was 8-9 g/dL and with acute MI it was 9-10 g/dL. Interestingly, both the American Association of Blood Banks and the American College of Cardiology/American Heart Association guidelines recommend a threshold of < 8 g/dL for patients with IHD. Thus, the weight of evidence and opinion seems to support higher Hgb thresholds for transfusion in IHD patients. The authors wisely suggested that there is probably a continuum of risk in ICU patients different from those with isolated medical disease, those with cardiac comorbidities, and those admitted with acute coronary syndrome. Also, some acute coronary syndrome patients may have severe medical illnesses, such as septic shock and pneumonia. Thus, considerable clinical judgment is required, and Hgb threshold levels are just guidelines.

There are significant limitations to this study. The accompanying editorial points out that the statistical techniques used are somewhat novel for an observational study and not fully vetted. Of course, the larger the study, the less likely all the details one would desire are present. For example, we do not know the do-not-resuscitate status of the patients.

Also, only 3% of the study population is women, but that represents about 7000 individuals. In addition, the data analyzed is from 2001-2005. Newer concepts and therapies may have altered ICU care in the last 10 years. Finally, this study does not shed any light on heart failure patients, which is an even more complex situation. For now, the transfusion Hgb threshold for IHD patients should increase at least 1 g/dL to < 8 and perhaps higher, especially for acute MI patients. ■

ABSTRACT & COMMENTARY

Selecting Patients for Statin Primary Prevention

By Michael Crawford, MD, Editor

SYNOPSIS: The new vascular disease risk calculator discriminates who will experience a vascular event in the near future better than using a trial entry criteria approach or a hybrid approach.

SOURCES: Mortensen MB, et al. Primary prevention with statins: ACC/AHA risk-based approach versus trial-based approaches to guide statin therapy. *J Am Coll Cardiol* 2015;66:2699-2709.

Bittner V. Selecting patients for statin therapy in primary prevention: If we could only predict the future. *J Am Coll Cardiol* 2015;66: 2710-2712.

The new American College of Cardiology/ American Heart Association (ACC/AHA) risk assessment equation was based on decades-old cohort studies and may overestimate risk in modern cohorts. Accordingly, a trial-based approach, which uses statin trial population characteristics rather than a risk assessment, has been recommended. Also, a hybrid approach combining both methods has advocates. Investigators compared these three methods for statin allocation in the Copenhagen General Population Study (CGPS). CGPS enrolled randomly selected Danish adults between 40-75 years of age. The study excluded diabetics, those with vascular disease, statin users, and patients with an LDL-cholesterol > 189 mg/dL or an estimated 10-year risk of atherosclerotic cardiovascular disease (ASCVD) of < 7.5%. Trial-based statin allocation was based on the entry criteria of five primary prevention trials. The hybrid approach required a risk assessment of > 7.5% and meeting criteria for inclusion in one of the five trials demonstrating statin benefit. Of the total population of 57,892 eligible patients (57% women), more were statin eligible using the trial-based approach vs the risk equation (59% vs 42%). The hybrid approach reduced the number of eligible patients vs the risk equation (21% vs 42%). Of those eligible for statin therapy, the ASCVD rate per 1000 person years was 9.8 with the risk equation, 6.8 with trial-based approach, and 11.2 with the hybrid approach. The ACC/AHA risk equation discriminated better than the other two approaches who would and would not have an ASCVD event (area under receiver operating characteristic curve 0.68 for the risk equation, 0.57 for the trial-based approach, and 0.61 for the hybrid approach). The authors concluded that use of the ACC/AHA risk equation approach will prevent more ASCVD deaths than the other two approaches while treating fewer patients than the trial-based approach.

■ COMMENTARY

Ever since the introductions of the new risk calculator and the concept that we should treat risk instead of lipid levels, there has been controversy, with concerns at both ends of the spectrum. Age heavily influences the new risk calculator. It is possible that younger patients with mildly elevated lipids and a bad family history (which isn't part of the formula) will not be treated, yet should be. More likely is the concern that older individuals with reasonable lipid levels will be treated unnecessarily. This would translate into higher healthcare costs and potential adverse effects in this group, which is why the trial-based and hybrid approaches were advanced.

Dr. Bittner asks whether this study will resolve the primary prevention dilemma of who to treat with statins. Unfortunately, the answer is no. The risk calculator approach was best at identifying those destined to experience an event. However, we don't know if these are the same individuals who will benefit from statin therapy. We would need a randomized trial to answer that question, but it is unlikely we will ever see such a trial. Also, the 8% of the population who had events, but were not identified by any of the three approaches, are a concern. Data only presented in the online data tables show that this 8% had higher Lp(a) levels than the rest of the population, so perhaps we should add Lp(a) as a treatment indicator. Also, none of these methods consider family history, yet other studies have shown it is important in risk prediction.

There are limitations to this study. First, they studied a largely white, European population; however, the lipid-lowering trials had the same weakness. Also, clinical trials tend to exclude more people. In fact, some enrolled < 10% of those screened. Thus, the trial approach may not represent a real patient population, whereas this large population study would. One advantage of the risk equation is that it can be adjusted over time as new data are generated, but trial results are frozen in time. The follow-up period in this study was only 5 years, so 10-year risk had to be extrapolated. In addition, treatment was not evaluated in this study and some higher-risk patients, who were not on statins at baseline (an exclusion criteria), may have been put on statins during the study period.

What should we do? Using the risk calculator as a first step makes sense and if statin therapy is indicated, deploy them. For those with a 10-year ASCVD event rate < 7.5%, individual judgment should be used. For example, if there is a family history of coronary artery disease at young ages, I would start statins regardless of the risk calculator. In the elderly with a risk > 7.5%, a discussion of the pros and cons of statin therapy would be beneficial, especially in those > 75 years of age in whom we have little data, but don't expect them to be different than younger patients. Finally, the whole patient should be considered and attention given to other risk factors besides lipid values, smoking, hypertension, and age (all in the risk formula), such as diet and exercise. ■

ABSTRACT & COMMENTARY

Five-year EVEREST II Results Allay Long-term Safety and Durability Concerns About MitraClip

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: MitraClip is the only approved percutaneous mitral device, which is currently indicated in the United States for repair of moderate-to-severe degenerative mitral regurgitation in patients at high surgical risk. Although MitraClip patients had higher rates of re-operation in the first year, adverse event rates in the 1- to 5-year range were reassuringly low and were comparable with surgery.

SOURCE: Feldman T, et al. Randomized comparison of percutaneous repair and surgery for mitral regurgitation: 5-year results of EVEREST II. *J Am Coll Cardiol* 2015;66:2844-2854.

Percutaneous repair of mitral regurgitation (MR) remains a challenging endeavor, for which there is currently a single approved device: the MitraClip system. MitraClip was approved in the United States in October 2013, in large part based on the randomized EVEREST II trial. This study, although flawed, was a well-executed trial for which follow-up data collection has been exceptional. EVEREST II randomized 279 patients with moderate to severe (3+ or 4+) MR and high surgical risk in a 2:1 fashion to either percutaneous (n = 184) or surgical (n = 95) treatment. The original analysis included imaging and clinical outcomes at 12 months and demonstrated several key points. The MitraClip procedure itself is safe, and as expected had fewer procedural complications than open surgery. It is less effective than surgical repair, however, with a greater proportion of patients during that first year registering 3+ or 4+ MR and a higher percentage requiring re-operation. Both surgical and percutaneously treated patients showed improvements in symptoms and in parameters of left ventricular remodeling.

MitraClip is fundamentally different from surgical repair. For example, the percutaneous procedure does not include the stabilizing annuloplasty ring, which is central to surgical repair. This, along with greater residual MR observed in the early time points among MitraClip patients, led to obvious concerns regarding the durability of both symptomatic and functional benefits.

At the 5-year time point, 24 patients in each arm had been excluded from the analysis (the majority due to withdrawn consent), leaving 154 patients in the percutaneous arm and 56 in the surgical arm, respectively. The primary outcome was freedom from a composite of death, repeat mitral surgery, or 3+ or 4+ MR. At 5 years, this occurred in 44.2% of MitraClip patients vs 64.3% of surgical patients (*P* = 0.01). Mortality was not different between groups. The composite outcome was driven by higher rates of

moderate-to-severe MR (12.3% vs 1.8%; $P = 0.02$) and mitral surgery (27.9% vs 8.9%; $P = 0.03$) in the percutaneous group. Looking at the data over time, however, we see that the majority (78%) of mitral surgeries occurred during the first 6 months. Between 6 months and 5 years, however, there was no difference between the percutaneous and surgical groups in the incidence of surgery for mitral dysfunction.

At the previously reported 12-month time point, a larger percentage of the device-treated patients had 3+ or 4+ MR — none of the surgical patients vs 17.9% of the percutaneous repair patients. This difference persisted at 5 years. However, fears that larger numbers of MitraClip patients would subsequently develop moderate-to-severe MR proved to be unfounded (2.5% vs 18.8%; $P = 0.01$). Despite the lack of annuloplasty, measurements of septal-lateral annular dimension (both systolic and diastolic) remained stable from 1-5years in patients who received MitraClip.

The authors reported that the primary finding of this follow-up study was the positive durability of MR reduction with MitraClip, with rates of worsening MR and surgery for mitral dysfunction in the 1- to 5-year range being low and comparable to the surgical group.

■ COMMENTARY

Lest we get too caught up in the positive findings, we should first remember that both at the 1- and 5-year time points, surgery was more effective than MitraClip in terms of freedom from MR and repeat mitral surgery. MitraClip is not a replacement for surgery, but rather is a viable option for selected patients who are thought to be at prohibitive surgical risk. Relative efficacy, however, tracked with the etiology of mitral dysfunction. Surgery was clearly superior in degenerative MR, while efficacy of the device was comparable to surgery in functional MR patients. The device is approved only for degenerative MR in the United States, while functional MR is the indication for more than half of such procedures in Europe. This simply highlights the uncertainty surrounding the benefit of any interventional therapy for functional MR patients, who overall have worse outcomes and survival rates. The ongoing COAPT trial seeks to define a potential role for MitraClip in this difficult patient subset.

MitraClip device technique has only improved since its commercial launch, due in large part to superior imaging technology (such as the general availability of 3D TEE) and more-focused patient selection. In the trial, a little more than 38% of patients were treated with two or more clips, and 11% had no clips deployed. In modern clinical practice, multiple clips are more commonly deployed to achieve better MR reduction, and failure of the procedure to deploy any clips is clearly lower than that observed in EVEREST.

From a safety perspective, single leaflet device detachment was reported in nine patients within the first year and in a single patient at 14 months. No further episodes were detected, and no cases of device embolization or late mitral stenosis were found. In the 1- to 5-year time period, the benefits of MitraClip therapy were maintained in terms of MR reduction, favorable left ventricular remodeling, and symptom improvement. For those patients who are appropriate for MitraClip, these data are very reassuring and support continued use. ■

ABSTRACT & COMMENTARY

Prescient Warning Symptoms: A New Target for Sudden Cardiac Death Prevention

By Cara Pellegrini, MD

Assistant Professor of Medicine, UCSF; Cardiology Division, Electrophysiology Section, San Francisco VA Medical Center

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

SYNOPSIS: Typical cardiac symptoms frequently precede sudden cardiac arrest and are frequently unheeded, but when acted on are associated with decreased mortality.

SOURCE: Marijon E, et al. Warning symptoms are associated with survival from sudden cardiac arrest. *Ann Intern Med* 2016;164:23-29.

By definition, sudden cardiac death (SCD) is an unexpected loss of pulse without obvious cardiac cause. Affecting more than 550,000 Americans and accounting for more than half the cardiovascular deaths in the United States, SCD has traditionally confounded efforts to predict its victims beyond broad strokes. Few variables outside of depressed left ventricular ejection fraction really affect prediction meaningfully. Perhaps it is not surprising that despite continued research and clinical efforts, the survival

after sudden cardiact arrest remains very low and stable around 7%.

Against this backdrop Marijon et al hypothesized that there might be a warning signal in the form of symptoms in the hours to days prior to an arrest that, if heeded, might improve outcomes. They performed a large prospective, community-based study of survivors and decedents of SCD in the Portland, OR, area. SCD cases were canvassed from the EMS system, the medical examiner's office, and EDs of all local hospitals. Utilizing EMS reports, hospital records, and outpatient community physician charts, the authors collected data on 839 patients 35-65 years of age with symptoms reported during the 4 weeks prior to SCD. They compared patient characteristics and mortality among those who "acted on" these symptoms (called 911) and those who did not.

They found that 51% of patients had reported symptoms prior to their SCD. Of note, symptoms immediately prior to collapse were not included. Eighty percent of symptoms started more than 1 hour before SCD, including 34% of patients who had more than 1 day from symptom onset to ultimate SCD. (Ninety-three percent of these patients had recurrent symptom episodes during the 24 hours prior to the arrest.) The most common symptom was chest pain (46%) and this was mostly typical angina. Only 19% of those with symptoms called 911. Older patients and those with a history of heart disease or continuous chest pain were more likely to seek help. Survival was significantly higher among those who did call 911. While multiple known factors that predict survival — witnessed arrest, bystander cardiopulmonary resuscitation, and initially shockable rhythm — were all more common in those who called 911, after adjustment for these and other suspected confounders, those who called 911 retained a nearly five-fold survival benefit. The authors concluded that warning symptoms frequently occur before SCD but are unfortunately mostly ignored, suggesting a new target for awareness.

■ COMMENTARY

This study is provocative in suggesting that SCD occurrence could be specifically predicted and potentially prevented, albeit likely with only 1 day or perhaps 1 week of lead time. Still, in this era of rapid data sharing, near-instant automated electrogram interpretations, and geolocalization, even a brief warning period could prove sufficient to be life-saving. Rather than continuing to focus so much of our effects on defining risk predictors (with minimal success), perhaps we'd be better served educating the public on the importance of symptom recognition and preparing more rapid response capabilities to actual (near) events. The merits of this approach are both highlighted and detracted by the knowledge that 12% of patients in this study had consulted a physician within 30 days of their SCD and received a "systemic work-up." Is recognition of the soon-to-be-afflicted still hazy only 1 month prior to the event? After all, symptoms such as chest pain and shortness of breath are not so unusual, and the denominator of those with such symptoms to view the numerator of those who ultimately had an arrest is not known. On the other hand, maybe this statistic simply underscores that the most important preventive action is that most proximate to the event, i.e., calling 911 and performing CPR.

In concert with data from myocardial infarction literature, women were less likely to experience chest pain and more likely to report shortness of breath prior to SCD. Notably, symptom prevalence was very similar between men and women. Also interesting was that overall symptom occurrence was similar between survivors and non-survivors, suggesting that the difference in outcome was not wholly related to disparate etiologies, such as stuttering ischemia leading to ventricular fibrillation and asystolic arrest, which might be expected to have a worse outcome.

About one-quarter of patients did not have symptom data, and the potential bias of this large proportion of missing data must be considered. The observational nature of the study obviously makes causal interpretation of the association between calling 911 and lower mortality fraught. The authors noted that this ongoing long-term study might have led to some recall and response bias on part of the EMS staff. Conversely, by including only those who actually did sustain a SCD, the positive effects of early symptom alert may be underestimated. Finally, it remains unproven that, even if there were greater recognition of symptoms and responsive action, lives would be saved. Nonetheless, I believe that these results warrant renewed public awareness efforts regarding the importance of careful attention to cardiac symptoms (including shortness of breath, particularly among women) and the need to seek emergent help when they occur. ■

QUESTIONS & COMMENTS:
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CME/CE QUESTIONS

1. **Which statement concerning warning symptoms prior to sudden cardiac death is true?**

   a. Half the victims experience warning symptoms.

   b. Most symptoms occurred > 1 hour prior to the event.

   c. The most common symptom was chest pain.

   d. All of the above

2. **The new risk of vascular disease equation compared to the criteria for entry into randomized cholesterol treatment trial studies showed:**

   a. more people were statin-eligible.

   b. the observed event rate was higher.

   c. it better discriminated who would experience an event.

   d. None of the above

3. **At 5 years follow-up in high-risk surgical patients with moderate-to-severe mitral regurgitation (MR), use of the percutaneous mitral clip compared to surgery showed:**

   a. greater freedom from death, re-operation, or moderate-to-severe MR.

   b. higher rates of moderate to severe MR.

   c. lower mortality.

   d. All of the above

4. **Recent studies suggest that dietary sodium restriction in chronic systolic heart failure patients may be:**

   a. of no benefit (neutral).

   b. harmful.

   c. beneficial.

   d. substituted for diuretics.

5. **A very large database study of ICU patients suggests that the threshold hemoglobin level for considering blood transfusion in comorbid heart disease patients should be:**

   a. 8.7 g/dL.

   b. 7.0 g/dL.

   c. 10 g/dL.

   d. 7.7 g/dL.

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.