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ABSTRACT & COMMENTARY

Choosing a Vasopressor in Cardiogenic Shock: Is There a Difference?

By Van Selby, MD

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

SYNOPSIS: When studying cardiogenic shock after acute myocardial infarction, these investigators found using epinephrine compared to norepinephrine produced similar effects on blood pressure and cardiac index, but resulted in a higher incidence of refractory cardiogenic shock.

SOURCE: Levy B, Clere-Jehl R, Legras A, et al. Epinephrine versus norepinephrine for cardiogenic shock after acute myocardial infarction. *J Am Coll Cardiol* 2018;72:173-182.

Among patients with acute myocardial infarction (AMI), the development of cardiogenic shock (CS) is associated with high mortality. Vasopressors are used to raise blood pressure and maintain end-organ perfusion, with epinephrine and norepinephrine the two most commonly used agents. However, data directly comparing the effects of epinephrine and norepinephrine in CS are lacking.

In a multicenter, prospective, double-blind study, Levy et al randomized 57 patients with CS after AMI to epinephrine vs. norepinephrine. All patients underwent successful revascularization by percutaneous coronary intervention (PCI) and met pre-specified criteria for CS (hypotension, cardiac index < 2.2 L/min/m^2, wedge pressure > 15 mmHg, and left ventricular ejection fraction < 40% before inotropic support). In both groups, the study drug was titrated for a target mean arterial pressure (MAP) of 65-70 mmHg. The primary efficacy outcome was the change in cardiac index at 72 hours. The primary safety endpoint was the incidence of refractory CS, which the authors defined as CS with major cardiac dysfunction according to echocardiography, elevated serum

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lactate level, and acute deterioration of end-organ function as well as sustained hypotension.

For the primary outcome, there was no significant difference in cardiac index between the two groups ($P = 0.43$), although cardiac index was transiently higher in the epinephrine group at hours two and four. Similarly, there was no significant difference in mean arterial pressure ($P = 0.80$).

The incidence of refractory CS was significantly higher in the epinephrine group compared to the norepinephrine group (37% vs. 7%; $P = 0.008$), leading to early termination of the study. Epinephrine also was associated with significantly higher increases in heart rate ($P < 0.0001$), cardiac double product ($P = 0.0002$), and lactic acidosis ($P < 0.0001$). Death at 60 days occurred in 52% of patients in the epinephrine group and 37% of patients in the norepinephrine group ($P = 0.25$). Epinephrine was associated with a trend toward increased death at day seven and a significantly higher risk of death or need for extracorporeal circulatory support at day seven ($P = 0.031$).

The authors concluded that among patients with CS secondary to AMI, epinephrine use compared to norepinephrine use is associated with similar effects on cardiac index and arterial pressure, with a higher incidence of refractory shock.

■ COMMENTARY

Data from well-conducted, randomized trials in CS are scarce, and multiple expert panels have stressed the need for more clinical trials to inform treatment decisions. In one of the only previous randomized trials comparing two vasopressors for shock, dopamine was associated with higher mortality compared to norepinephrine in the subgroup of patients with CS. Although small, the Levy et al study is important because it directly compares the two most commonly used vasopressors.

The observed hemodynamic differences between the two agents mostly make sense. Both drugs successfully raised and maintained arterial pressures. However, it seems epinephrine does this at a higher metabolic cost. Epinephrine significantly increases heart rate and the cardiac double product (meaning higher myocardial oxygen consumption). These changes are likely related to the higher ß activity with epinephrine and may be particularly harmful in CS patients with pre-treatment tachycardia, ischemia, or increased risk of arrhythmias.

Although the study was relatively small and not powered to detect changes in clinical endpoints, the available data suggest the unfavorable physiologic effects of epinephrine translate into worse clinical outcomes. Epinephrine was associated with increased risk of refractory cardiogenic shock, and showed nonsignificant trends toward decreased survival.

Levy et al also switched two patients from epinephrine to norepinephrine due to sustained ventricular tachycardia. By contrast, the only possible advantage seen with epinephrine is a shorter duration of additional inotropic support (e.g., dobutamine).

There were significant limitations. Of 163 patients screened, 106 were excluded from the study, which may limit generalizability to the broader CS population. The definition of refractory shock used in this study is not a widely accepted one, and included elevated serum lactate in the diagnostic criteria. Epinephrine use is associated with excess lactic acid production (known as type B lactic acidosis); therefore, lactate may not perfectly reflect tissue perfusion. It is also important to remember that CS develops because of a wide variety of cardiac pathology, with varying hemodynamics. The Levy et al study only included post-AMI CS.

Until larger trials are performed in CS, we have to rely on the available data. Based on the findings of Levy et al, it seems that epinephrine is associated with unfavorable hemodynamic effects and *may* be associated with worse clinical outcomes in post-AMI CS. ■

ABSTRACT & COMMENTARY

Invasive Procedures and the Risk of Infective Endocarditis

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: This large study suggests that several invasive, nondental medical procedures may be triggers for subsequent infective endocarditis, reopening the debate regarding prevention and management.

SOURCE: Janszky I, Gémes K, Ahnve S, et al. Invasive procedures associated with the development of infective endocarditis. *J Am Coll Cardiol* 2018;71:2744-2752.

Infective endocarditis (IE) is a condition that occurs in relatively low absolute numbers, but confers a very high risk for morbidity and mortality. U.S. guidelines for the prevention of IE have focused on bacteremia following dental procedures, with less coverage devoted to gastrointestinal (GI) and genitourinary (GU) tract procedures. It seems likely that the 2007 American Heart Association IE guideline update, along with its European counterpart, was well-received by dentists, for it removed the recommendation for prophylactic antibiotics prior to dental work for all but the highest-risk patients (those with a prosthetic heart valve, with a prior history of IE, for certain patients with complex congenital heart disease, and for cardiac transplant recipients with valvulopathy). Likewise, this update deleted the recommendation of the use of antibiotic prophylaxis for procedures involving the GI and GU tracts. Other invasive procedures, including so-called "clean" invasive procedures such as coronary angiography, receive no mention.

Much of the change in guidelines was based on the lack of convincing evidence for the efficacy of prophylactic antibiotics for prevention of IE. Clinicians often assume that the risk for endocarditis with medical procedures is negligible as well, but data addressing this point are missing from the debate. To address this shortfall, Janszky et al analyzed all cases of endocarditis in Sweden over a 14-year period following the 1997 adoption of a standardized classification system for coding of medical procedures. To avoid confounding, the authors used a case-crossover design in which each patient serves as his or her own control. For each case, the occurrence of medical procedures in the 12-week period preceding the endocarditis diagnosis was compared with the 12-week period one year earlier. Over the course of the study period, 7,013 cases of IE in adult patients were identified. Researchers found multiple invasive procedures were associated with an increased risk of endocarditis. Among outpatient procedures, this included not only GI and GU procedures such as colonoscopy (relative risk [RR], 2.89; 95% confidence interval [CI], 1.35-6.17) and cystoscopy (RR, 1.59; 95% CI, 0.98-2.58), but also coronary angiography (RR, 4.75; 95% CI, 1.61-13.96), bone marrow puncture (RR, 4.33), and bronchoscopy (RR, 5.0), as well as transfusion and hemodialysis. The same procedures performed on an inpatient basis appeared to have similar or stronger associations with subsequent endocarditis, with the RR for bronchoscopy, for example, rising to 16. Coronary artery bypass grafting had an especially strong association (RR, 13.8), as well as a conglomeration of other major and minor cardiovascular therapeutic procedures, including aortic surgery and pacemaker insertion (RR, 9.75). Phacoemulsification, a common procedure that would not be expected to lead to transient bacteremia, was not associated with elevated risk. The study included no information about antibiotic prophylaxis, and the authors did not have access to microbiological data on the pathogens involved in endocarditis. The authors concluded that multiple invasive medical procedures appear to contribute to the subsequent development of IE. They argued for a potential reconsideration of prophylactic antibiotics for certain high-risk patients and procedures. However, more strongly, the authors contended that this knowledge supports a renewed focus on aseptic technique in procedures, and that increased awareness of the risk following certain procedures could lead to earlier diagnosis and improved outcomes.

■ COMMENTARY

This is the largest study to date linking invasive procedures to an increased risk of endocarditis. The

completeness and high reported accuracy of the Swedish National Patient Register add to the strength of the study, and the case-crossover design represents an improvement over traditional case-control studies.

A range of invasive procedures, including but by no means limited to dental procedures, could lead to a transient bacteremia, which is a necessary condition for the formation of an infective vegetation. Transient bacteremia always will be a frequent outcome of certain procedures; cystoscopy and colonoscopy come to mind. However, for others, varying levels of sterile technique can lead to different results. For example, in cardiac catheterization, there is significant variability in sterile technique from institution to institution, with variable use of hats and masks. It is rare that the cath lab is considered a completely sterile environment exactly like the OR. Because of the variable time delay between transient bacteremia and development of clinically evident IE, the inciting procedure may well not be identified as causative on a case-by-case basis. There is room for improved aseptic technique in this procedure, as in others identified in the study, including bone marrow biopsy and basic vascular access for hemodialysis.

The stratified analysis suggested that the risk of invasive inpatient procedures was higher in the latter half of the study period than in the earlier period. Whether this is at all attributable to the newer guidelines restricting prophylactic antibiotics surely will add to the debate. Based on their analysis, the authors estimated that 476 high-risk patients would need to receive prophylactic antibiotics to prevent one case of IE, assuming that prophylaxis was 100% effective. This number was considerably lower for certain high-risk procedures (83 for bronchoscopy, for example). This will add information for future guidelines and, if confirmed, could result in altered prophylaxis recommendations for certain patients and procedures. However, it is more likely that the overall approach will be less about antibiotic prophylaxis and more about improving sterility, where possible, while developing system-based approaches to management of procedure-related bacteremia. ■

ABSTRACT & COMMENTARY

Tailored Anticoagulation for Paroxysmal Atrial Fibrillation

By Joshua D. 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 Biosense Webster and Abbott.

SYNOPSIS: Intermittent anticoagulation guided by continuous assessment of arrhythmia status in patients with low-to-moderate risk did not result in any strokes or thromboembolic events over a relatively short follow-up period. Such a strategy may be an alternative to chronic anticoagulation but requires further study.

SOURCE: Waks JW, Passman RS, Matos J, et al. Intermittent anticoagulation guided by continuous atrial fibrillation burden monitoring using dual chamber pacemakers and implantable cardioverter-defibrillators-Results from the Tailored Anticoagulation for Non-Continuous Atrial Fibrillation (TACTIC-AF) pilot study. *Heart Rhythm* 2018 Jul 5. pii: S1547-5271(18)30593-9. doi: 10.1016/j.hrthm.2018.06.027. [Epub ahead of print].

Anticoagulation with warfarin or direct oral anticoagulants (DOACs) for prevention of stroke and other thromboembolic events is a cornerstone of therapy for atrial fibrillation (AF). Whether AF is associated with symptoms, and regardless of episode duration and frequency, anticoagulation is recommended based on presence of risk factors such as age, hypertension, diabetes, and congestive heart failure. However, chronic anticoagulation therapy comes with the cost of elevated bleeding risk. Waks et al hypothesized that in patients with low arrhythmia burden and relatively low thromboembolic risk, the continuous monitoring afforded by modern implantable pacemakers and defibrillators could facilitate "tailored anticoagulation." Patients could start and stop anticoagulation based on AF burden, enabling protection from stroke and other thromboembolic events while reducing bleeding risks. This multicenter pilot study initially was designed as a randomized trial, with 1:1 assignment to standard therapy vs. tailored anticoagulation and 12 months follow-up. However, the control arm was removed after about two years to facilitate enrollment, and the trial continued as a single-arm prospective trial. Ultimately,

61 patients with a $CHADS_2$ score ≤ 3 and a St. Jude pacemaker or ICD with a functioning atrial lead and capability for remote monitoring were enrolled at 10 centers in the United States. Patients had to have experienced at least one episode of AF but a "low" overall burden: < 30 minutes of total AF per day, and no continuous episodes lasting > 6 minutes.

For 48 patients, tailored anticoagulation therapy was used. After one month of mandatory anticoagulation, their DOAC was discontinued if no significant AF burden was present. Anticoagulation was restarted if biweekly remote monitoring revealed an episode of continuous AF > 6 minutes or a total burden of > 6 hours over a 24-hour period. Automatic transmissions for AF also were programmed for atrial rates > 200 bpm lasting > 30 minutes, and for total AF burden > 6 hours over a 24-hour period. For 13 patients who remained in a control arm, anticoagulation was continued, regardless of AF burden. Patients in the tailored therapy group averaged 71 years of age, 52% demonstrated a $CHADS_2$ score of 2, and 35% a $CHADS_2$ score of 1. During follow-up, these patients logged 3,763 total days on DOAC therapy after the first 30 days, out of 14,826 total monitored days. Due to protocol violations, 1,777 of those days on anticoagulation actually were "unnecessary." There were two gastrointestinal bleeds in patients on anticoagulation and one fatal intracranial hemorrhage in a patient not on anticoagulation at the time. No strokes or transient ischemic attacks (TIAs) occurred. There were two episodes of epistaxis in the smaller control group. The authors concluded that this approach could certainly improve patient compliance and decrease cost and bleeding risk compared with continuous DOAC therapy.

■ COMMENTARY

In many ways, anticoagulation for thromboembolic prophylaxis in patients with AF has become considerably easier with the advent of DOACs. With fewer dietary and drug interactions than warfarin and no need for regular monitoring of therapeutic levels, the threshold for physicians to prescribe the medications and patients to take them has decreased. Nevertheless, anticoagulation for AF remains underused, and the added expense of DOACs compared with warfarin can be an obstacle. Additionally, bleeding risks remain an important consideration. It is possible that a tailored approach to anticoagulation could reduce the risk of thromboembolic events in a select group of patients to the same degree as daily chronic anticoagulation, while simultaneously reducing both bleeding risks and costs. This pilot study represents an important step toward demonstrating the feasibility of such an approach. Although it was underpowered to detect thromboembolic events, with an average of only 309 days of follow-up per patient, the lack of any strokes or TIAs was reassuring. There also were minimal adverse events and a dramatic reduction in the use of anticoagulation, despite protocol violations at one study site, resulting in many days of unnecessary therapy.

The principal weaknesses of the study are the sample size, the limited follow-up, and the lack of a true control group. Additionally, patients were required to have an implanted pacemaker or defibrillator with an atrial lead and remote monitoring capabilities, which limits the population for which this approach is currently applicable. Other studies have demonstrated the use of an implantable loop recorder to assess AF burden. However, additional data will be needed to test whether the cost of invasive monitoring is offset by the savings on drug therapy, confirm whether thromboembolic risk is adequately addressed, and assess whether there are less bleeding events or improved quality of life with tailored therapy.

Additionally, some prior studies have shown strokes and TIAs can occur without an apparent temporal relationship to periods of AF, suggesting that other nonarrhythmic factors (such as left atrial size and/or function) may play a role. For now, the safest approach for paroxysmal AF in patients with stroke risk factors likely remains chronic, uninterrupted anticoagulation, particularly considering the relatively low rates of serious or fatal bleeding events in trials of DOACs. However, as further trials are conducted and additional safety data gathered, tailored therapy may eventually prove to be a viable or even superior alternative. ■

ABSTRACT & COMMENTARY

When Can Surgeons Perform Aortic Valve Replacement Safely After a Stroke?

By Michael H. Crawford, MD, Editor

SYNOPSIS: Interrogation of Danish administrative registry data demonstrated that a stroke within three to four months of aortic valve surgery was associated with a higher rate of perioperative stroke.

SOURCES: Andreasen C, Jørgensen ME, Gislason GH, et al. Association of timing of aortic valve replacement surgery after stroke with risk of recurrent stroke and mortality. *JAMA Cardiol* 2018;3:506-513.

Mullen MT, Messé SR. Aortic valve surgery after recent stroke: Patience is a virtue. *JAMA Cardiol* 2018;3:514-515.

Prior stroke is a risk factor for perioperative stroke with surgical aortic valve (AV) replacement, but little is known about this risk in relation to time since stroke. Andreasen et al interrogated Danish administrative registry data for patients undergoing AV replacement between 1996 and 2014. Those with multivalve surgery or infective endocarditis within one year prior to surgery were excluded. The primary outcome was major adverse cardiovascular events (MACE) 30 days post-operative. The study population was divided into four groups: no prior stroke, prior stroke < 3 months, three to 12 months prior, and > 12 months prior.

[The authors concluded prior stroke is a major risk factor for perioperative stroke in patients undergoing surgical AV replacement.]

Of the 14,030 patients identified, 616 had prior stroke and 13,414 did not. Most patients were men with a mean age of about 70 years and had received bioprosthetic valves. Patients with prior stroke had more comorbidities such as atrial fibrillation and carotid artery disease. MACE occurred in 5.7% of patients without compared to 23% in those with prior stroke < 3 months before surgery (adjusted odds ratio [OR], 4.57; 95% confidence interval [CI], 3.24-6.44). Also, ischemic stroke was more frequent in the latter group (OR, 14.7; 95%CI, 9.7-22.3), but not 30-day, all-cause mortality (OR, 1.45; 95% CI, 0.83-2.54). The risk of all adverse outcomes declined with time and was stable after two to four months. The authors concluded that prior stroke is a major risk factor for perioperative stroke in patients undergoing surgical AV replacement, especially if it occurred < 3 months prior to surgery.

■ COMMENTARY

It is not surprising that prior stroke is a risk factor for adverse outcomes with cardiac surgery since it is part of the STS and EuroScore risk calculators. What is unclear was the time frame of the prior stroke regarding the surgery. The risk of recurrent stroke was highest when the prior stroke was < 3 months ago, but declined after that and reached a nadir at four months. Andreasen et al considered it reasonable to consider surgery three months after a stroke. However, since this was an observational study with no control group, the results have to be considered hypothesis-generating.

There are some interesting aspects of the study. The overall stroke rate was about 1% for the entire group, but increased to 2% if coronary bypass was performed in addition to AV replacement. Also, neither atrial fibrillation nor carotid artery disease was related to the occurrence of perioperative stroke, but atrial fibrillation did increase the risk of MACE, as has been shown before. Few patients had transcutaneously delivered valves, but their results were similar.

There are weaknesses to this study beyond its observational nature. The number of patients with prior stroke was small relative to the total population. Perhaps this was because prior stroke would increase the preoperative risk score and remove some patients from surgery consideration. Since this was an administrative database study, key clinical details are unavailable, and adverse events likely were underestimated. Those who underwent surgery despite a recent stroke were probably sicker, in need of urgent surgery, and probably higher-risk patients in general. The study period spanned almost two decades, so it may not accurately reflect today's practice.

Despite these limitations, waiting to perform AV replacement surgery for at least three, preferably four, months after stroke probably will result in fewer perioperative strokes. ■

ABSTRACT & COMMENTARY

Anticoagulation Management After Intracerebral Hemorrhage in Mechanical Heart Valve Patients

By Michael H. Crawford, MD, Editor

SYNOPSIS: An observational study of patients with mechanical heart valves on oral anticoagulants who had an intracranial hemorrhage demonstrates that it generally is safe to resume anticoagulants after 14 days. However, in high-risk-for-thromboembolism patients, such as those with atrial fibrillation, restarting anticoagulants six to 13 days postoperative may be considered.

SOURCES: Kuramatsu JB, Sembill JA, Gerner ST, et al. Management of therapeutic anticoagulation in patients with intracerebral haemorrhage and mechanical heart valves. *Eur Heart J* 2018;39:1709-1723.

Verheugt FWA. Anticoagulation resumption after intracranial haemorrhage with mechanical valves: A data-free zone. *Eur Heart J* 2018;39:1724-1725.

The optimal time to resume oral anticoagulation (OAC) in patients with mechanical heart valves who have suffered an intracerebral hemorrhage (ICH) is controversial. Kuramatsu et al performed a nationwide observational cohort study of patients on OAC who suffered an ICH and identified 137 patients with mechanical heart valves out of 2,504 collected between 2006 and 2015 from 22 centers (RETRACE I and II studies). Only those with an initial international normalized ratio (INR) > 1.5 who survived at least 72 hours were included. Patients were divided into two groups: no therapeutic anticoagulation (TA) during the hospitalization or only venous thromboembolism (TE) prophylaxis (n = 71) and TA (n = 66). The primary safety outcome was major hemorrhage (expanding ICH or extracranial) during hospitalization. Secondary outcomes included thromboemboli, 90-day mortality, functional status, and when TA resumed.

Optimal INR reversal (< 1.3 within four hours) was achieved in 25% of patients, but this was not associated with subsequent TE. Hemorrhagic complications were noted in 15% of patients and were higher in those restarted on TA after 72 hours (26%) vs. those not (5.6%; $P = 0.001$). There was a trend toward lower TE in those restarted on TA (1.5% vs. 9.9%; $P = 0.06$). A propensity score matching analysis showed that restarting TA increased the incidence rate of hemorrhagic complications (likelihood ratio, 8.0; 95% confidence interval, 2.73-28.54; $P < 0.01$). TA patients demonstrated an increased risk of hemorrhage until day 13 post-ICH and an increased risk of hemorrhage plus TE until day six. TA was not associated with mortality or functional outcome at discharge or at 90 days post-ICH. Patients with concomitant atrial fibrillation (AF) exhibited an increased rate of hemorrhagic and TE complications (34% vs. 16%; $P = 0.02$). AF patients restarted on TA did not show increased hemorrhage, but those not started on TA demonstrated higher rates of TE, which increased their combined endpoint (33% vs. 8%; $P = 0.01$). The authors concluded that optimal timing of the resumption of TA after ICH was 14 days, but the earliest starting point was six days in those at high risk of TE, such as those with concomitant AF.

■ COMMENTARY

This is the largest study so far of this issue, for which a randomized trial would be unethical. Although rare (0.5% per year), ICH is a serious complication of OAC therapy for mechanical heart valves and a complication that often proves fatal. Currently, mechanical heart valves must be anticoagulated by vitamin K antagonists and rapid reversal of their effects is difficult to achieve. Even in this study, which almost exclusively used prothrombin complex concentrates, complete reversal within four hours was achieved in only 25% of patients. Despite this, ICH expansion was reduced significantly through reversal of anticoagulation without an increase in TE. A unique feature of the study was a 72-hour hold before anticoagulants could be administered to prevent confusing disease outcomes with treatment effects. The main thrust of the study: When could anticoagulants be restarted safely? Kuramatsu et al demonstrated that complete safety from major hemorrhage did not start until > 13 days after ICH. But with every day off anticoagulants, the risk of TE rose such that after six days, the risk of the combined endpoint of hemorrhage or TE was higher. Thus, the authors concluded that

in those at high risk of TE, anticoagulation could be considered at six days. Such patients would include those with AF, with a prosthetic mitral valve, or with a caged-ball valve prosthesis. Interestingly, other studies of AF alone have shown that the optimal time for restarting anticoagulants is seven or eight *weeks* following ICH.

The major limitation of the study, besides its retrospective and observational nature, is that there was no common protocol between the 22 centers. Further, each patient was treated according to the practice of the physicians taking care of him or her. Still, we are not likely to obtain better information than the data collected in this careful analysis. This study can inform our decision-making, but probably won't change the current guidelines (European Society of Cardiology 2017, which state that heparin can be started on day three and vitamin K antagonists at day seven after ICH).[1] The Kuramatsu et al study suggests this may be too aggressive. ■

REFERENCE

1. Halvorsen S, Storey RF, Rocca B, et al; ESC Working Group on Thrombosis. Management of antithrombotic therapy after bleeding in patients with coronary artery disease and/or atrial fibrillation: Expert consensus paper of the European Society of Cardiology Working Group on Thrombosis. *Eur Heart J* 2017;38:1455-1462.

CME/CE QUESTIONS

1. The results of a recent large observational study suggest that, if feasible, aortic valve replacement surgery should be delayed for how long after a stroke?

a. One month

b. Three months

c. Six months

d. Nine months

2. In patients with mechanical heart valves and oral anticoagulant-associated intracranial hemorrhage, how many days should one wait before restarting anticoagulants?

a. Two days

b. Five days

c. 10 days

d. 14 days

3. Which of the following is most correct concerning the use of epinephrine vs. norepinephrine in acute myocardial infarction-associated cardiogenic shock?

a. Cardiac index was higher on epinephrine.

b. Mean arterial pressure was higher on epinephrine.

c. Refractory shock incidence was higher on epinephrine.

d. The death rate was significantly higher on epinephrine.

4. Which of the following procedures carries a high risk of subsequent infective endocarditis?

a. Bronchoscopy

b. Colonoscopy

c. Cystoscopy

d. All of the above

5. A randomized trial of intermittent oral anticoagulants guided by device detected atrial fibrillation exhibited:

a. no gastrointestinal bleeding.

b. no intracranial hemorrhage.

c. no strokes.

d. All of the above

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.