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Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Methamphetamine-associated Pulmonary Hypertension and Cardiomyopathy Are Distinct Diseases

By Van Selby, MD

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

SYNOPSIS: In a large study of methamphetamine users, female sex was associated with presence of pulmonary hypertension, whereas male sex, hypertension, and alcoholism were associated with cardiomyopathy. Both pulmonary hypertension and cardiomyopathy patients exhibited substantially increased mortality.

SOURCE: Zhao SX, Kwong C, Swaminathan A, et al. Clinical characteristics and outcome of methamphetamine-associated pulmonary arterial hypertension and dilated cardiomyopathy. *JACC Heart Fail* 2018;6:209-218.

Methamphetamine (MA) use has been associated with both cardiomyopathy (CMP) and pulmonary arterial hypertension (PAH). However, both conditions remain understudied and little is known about the similarities and differences between these conditions regarding risk factors, morbidity, and mortality.

Zhao et al retrospectively identified all patients with either a MA-related diagnosis or positive toxicology screen at a large public hospital in Northern California between 2010 and 2017. MA-PAH was defined as an estimated right ventricular systolic pressure > 45 mmHg by transthoracic echocardiography (TTE) in the absence of an alternative cause for pulmonary hypertension. MA-CMP was defined as a left ventricular ejection fraction (LVEF) persistently < 40% without an alternative explanation such as valvular or coronary artery disease. The control group consisted of patients who reported MA use but showed no evidence of cardiovascular disease on TTE. Of 4,662 MA users identified during the study period, 296 were included in the MA-CMP group, 50 in the MA-PAH group, and 356 in the control group.

Financial Disclosure: *Clinical Cardiology Alert*'s Physician Editor Michael H. Crawford, MD, Peer Reviewer Susan Zhao, MD, Nurse Planner Aurelia Macabasco-O'Connell, PhD, ACNP-BC, RN, PHN, FAHA, Editor Jonathan Springston, Editor Jesse Saffron, and Editorial Group Manager Terrey L. Hatcher report no financial relationships relevant to this field of study.

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Patients with MA-PAH were more likely to be female (58%), and when compared to the control group, sex was the only significant predictor of MA-PAH (odds ratio [OR] for male sex, 0.49; $P = 0.023$). The MA-CMP group was predominantly male (86%). In a multivariate regression analysis, male sex (OR, 3.8; $P < 0.001$), alcohol abuse (OR, 3.0; $P < 0.001$), and hypertension (OR, 2.1; $P < 0.001$) all were strongly associated with MA-CMP compared to controls.

Among MA-CMP patients, median EF was 25.2 ± 6.5%, with biventricular dilation in many patients, and 57% demonstrated New York Heart Association functional class III or IV symptoms. The MA-PAH group also exhibited evidence of advanced disease. In those who underwent right heart catheterization, the median pulmonary vascular resistance was 11.8 Wood units (interquartile range, 9.0-15.3). Most patients demonstrated reduced cardiac index and elevated right atrial pressure.

Over a median follow-up of 20 months, both MA-CMP and MA-PAH were associated with increased mortality (18.0% and 15.2%, respectively, compared to 4.5% mortality in the control group; $P < 0.001$ for the overall comparison). There was no statistically significant difference in survival between the MA-CMP and MA-PAH groups ($P = 0.697$).

The authors concluded that MA-CMP and MA-PAH carry distinct risk factors, with female sex associated with MA-PAH, whereas male sex, hypertension, and alcoholism are associated with MA-CMP. Both conditions are associated with increased mortality.

■ COMMENTARY

MA use is increasing across the United States. The association between MA abuse and cardiovascular disease is widely recognized, although the exact pathophysiology is not understood completely. Increased catecholamine levels, with resulting hypertension, tachycardia, and vasoconstriction, contribute to the development of cardiomyopathy, and direct cell injury may play a significant role, too. Both cardiomyopathy and PAH are recognized complications of long-term MA use, although most current literature about these conditions is limited to case series with small sample sizes. In the largest published cohort of MA-related cardiovascular disease, Zhao et el clearly showed MA-CMP and MA-PAH are two distinct diseases, with different risk factors and patient profiles. However, both conditions are associated with substantial morbidity and increased mortality.

In both MA-CMP and MA-PAH, the disease severity was remarkable. The median EF of 25% in CMP, with most patients reporting functional class III or IV symptoms, as well as the marked hemodynamic and echocardiographic abnormalities in the MA-PAH group, speak to the profoundly detrimental effects of MA on the cardiovascular system. It also likely reflects delays in seeking care and medication nonadherence, two of the many factors that make MA users a particularly challenging population to treat.

This was a retrospective study with the usual limitations, including confounding. The authors could not address the important question of how the disease trajectory and outcomes are influenced by whether a patient can quit using MA. Despite these basic limitations, this study represents a crucial step toward better understanding of the risk factors, patient characteristics, and outcomes associated with the two main cardiovascular complications of chronic MA abuse.

No therapy has specifically been shown to improve outcomes in MA-CMP or MA-PAH, but providers should use standard guideline-based therapies for chronic heart failure and pulmonary hypertension as appropriate. Probably the most important lesson is that everyone who treats cardiovascular disease needs at least basic familiarity with MA and to keep it in mind during the workup of PAH or cardiomyopathy.

As a cardiologist in a region with particularly high rates of MA use, I ask about MA use and order toxicology screens in nearly all new patients with PAH or nonischemic cardiomyopathy routinely. Many patients are unaware of the link

between MA use and their declining health, and explaining the association as well as the high mortality associated with these conditions can be very helpful for motivating patients to quit. ■

ABSTRACT & COMMENTARY

Coffin Nail for Omega-3 Fatty Acids?

By Michael H. Crawford, MD, Editor

SYNOPSIS: A meta-analysis of 10 randomized, controlled trials of omega-3 fatty acids for the prevention of coronary heart disease and major vascular events showed no significant effect on fatal and non-fatal coronary heart disease or any major vascular event. These results do not support the use of omega-3 fatty acids supplements in patients with prior coronary heart disease.

SOURCE: Aung T, Halsey J, Kromhout D, et al. Associations of omega-3 fatty acid supplement use with cardiovascular disease risks: Meta-analysis of 10 trials involving 77,917 individuals. *JAMA Cardiol* 2018;3:225-233.

The authors of observational population studies have reported that increased fish or omega-3 fatty acid (FA) consumption reduces the risk of dying from coronary heart disease (CHD). However, studies in patients with CHD or at high risk for it have shown mixed results.

Thus, the omega-3 treatment trialists collaboration performed a meta-analysis of 10 randomized, controlled trials of omega-3 FA supplements for the prevention of cardiovascular disease. The primary endpoints were fatal CHD, non-fatal myocardial infarction (MI), stroke, major vascular events, and all-cause mortality in prespecified subgroups. Data were obtained directly from the principal investigator in nine of the 10 trials. The prespecified subgroups included age, sex, prior CHD, prior stroke, diabetes, blood lipids, statin use, and trial design (blinded or open-label). A total of 77,917 individuals participated in the 10 trials. Eight trials were blinded and two were open-label. Men comprised 61% of the participants and the mean age was 64 years. Two-thirds reported a prior history of CHD, 28% experienced a prior stroke, and 37% were diabetic. Major vascular events occurred in 16% (3% MI, 3% CHD deaths, 2% stroke, 8% revascularization).

Randomization to omega-3 FA supplementation resulted in no significant associations with CHD death (relative risk [RR], 0.93; 95% confidence interval [CI], 0.83-1.03; $P = 0.05$), non-fatal MI (RR, 0.97; 95% CI, 0.87-1.08; $P = 0.43$), any CHD event (RR, 0.96; 95% CI, 0.90-1.01; $P = 0.12$), or major vascular events (RR, 0.97; 95% CI, 0.93-1.01; $P = 0.10$) in any subgroups. Also, there was no effect noted on all-cause mortality (RR, 0.96; 95% CI, 0.92-1.01; $P = 0.16$). The authors concluded that this meta-analysis of 10 randomized, controlled trials of omega 3-FA treatment fails to support the use of these supplements in patients with CHD.

■ COMMENTARY

Although a properly designed and powered randomized, controlled trial is preferable, a well-conducted meta-analysis of smaller randomized, controlled trials generally is better than observation studies. Given the tremendous public interest in omega-3 FA, this meta-analysis of 10 randomized, controlled trials is of interest. This analysis featured several strengths. First, in all but one trial, study level data were obtained from the principal investigator. For the last trial, the published data were detailed enough for inclusion, and when this study was eliminated the results did not change. Second, the authors excluded studies in which the intervention was dietary advice or fish consumption. Third, Aung et al excluded trials with < 500 participants and with less than one-year follow-up. The mean follow-up for the 10 trials chosen was 4.4 years. Finally, these investigators evaluated prespecified subgroups of clinical importance such as diabetics, statin use, various lipid levels, and prior cardiovascular diseases. All but one trial used a combination of omega-3 FA with doses up to 1,800 mg/day for each ingredient. These doses are not high enough to reliably decrease triglycerides, but there are trials underway to evaluate this. One weakness of this analysis is that there were not prespecified subgroups for smoking and cancer history. However, there was no adverse cancer signal observed. Generally, the trials were markedly consistent. There was some weak heterogeneity in three subgroups. No history of prior stroke favored therapy, as did age > 65 years and an open-label study design. Hopefully, these nuances will be addressed in larger randomized, controlled trials underway. At this time, the European Society of Cardiology does not recommend omega-3 FA supplementation (2016), but the American Heart Association (AHA) does for those with prior CHD or heart failure with reduced left ventricular function (2017). This meta-analysis does not support the AHA recommendation. ■

ABSTRACT & COMMENTARY

Risk of Endocarditis Revisited

By Michael H. Crawford, MD, Editor

SYNOPSIS: The authors of a population-wide study of hospitalizations and deaths from infective endocarditis (IE) in England confirmed the high risk of IE in certain cardiac conditions, but showed that other conditions thought to be low risk also are at higher risk and found new higher-risk categories not previously identified. Investigators suggested these data should be considered when the antibiotic prophylaxis guidelines are revised.

SOURCES: Thornhill MH, Jones S, Prendergast B, et al. Quantifying infective endocarditis risk in patients with predisposing cardiac conditions. *Eur Heart J* 2018;39:586-595.

Sun YP, O'Gara PT. Cardiovascular conditions predisposing to infective endocarditis: Time to reconsider the current risk classification system? *Eur Heart J* 2018;39:596-598.

Data on the relative risks of developing infective endocarditis (IE) or dying from IE with different predisposing cardiac conditions in a large population cohort are lacking. Thus, investigators from England surveyed all patients admitted to English hospitals between 2000 and 2013 with a condition associated with an increased risk of IE and followed them for five years to assess subsequent admissions for IE. This information was compared to a reference group of the entire population of England (> 51 million). The incidence of IE in the whole English population was 36.2 cases/million/year with an admission-related mortality of 6.3 cases/million/year. The incidence was highest in those with a previous history of IE and prosthetic valves or repaired valves (14,359, 4,637, and 4,710 cases/million/year, respectively). IE admission deaths also were highest in these groups (2,940, 1,092, and 907 cases/million/year, respectively). Admissions for IE and subsequent deaths were high in patients with congenital heart conditions (CHC) with a shunt or conduit, but lower in those with unrepaired cyanotic CHC and considerably lower in those post repair using prosthetic material. In fact, the incidence of IE or death on admission for IE was higher in those with rheumatic fever or non-rheumatic valve disease compared to those with cyanotic CHC repaired with prosthetic material.

Among conditions in which the risk of IE has not been characterized, hypertrophic cardiomyopathy had a significantly higher risk of IE than the controls (odds ratio [OR], 33; 95% confidence interval [CI], 23-45; $P < 0.0001$) but an insignificant risk of IE death (OR, 4; 95% CI, 0.2-18; $P = 0.17$). Whereas implanted electrophysiology (EP) devices had a relatively high incidence of IE (OR, 10; 95% CI, 9-11; $P < 0.0001$) and a higher risk of IE death (OR, 10; 95% CI, 9-12; $P < 0.001$) compared to controls. The authors concluded that some conditions considered at moderate risk of IE and not candidates for antibiotic prophylaxis should be re-evaluated.

■ COMMENTARY

After consideration of the lack of quality data and with pressure from the dental industry, the guidelines were changed in 2007 to state that the use of prophylactic antibiotics for traumatic procedures in areas of the body not amenable to sterilization should be restricted to a few very high-risk conditions. Subsequent studies on the effect of these changes on the incidence of IE have shown conflicting results. This study was designed to use the National Health Service data from England to establish the incidence of IE and hospital death from IE in the English population from 2000 until 2013 with a minimum five-year follow-up and to relate these data to the patient's cardiac conditions that put them at risk for IE. The results confirm the high-risk status of prior IE, valve surgery (replacement, repair), or CHC with shunts or conduits, but not unrepaired cyanotic CHC and repaired CHC with prosthetic material.

There were too few heart transplant patients to accurately assess IE incidence (considered high risk if they have valve regurgitation). Unrepaired cyanotic CHC had a risk of IE similar to rheumatic fever, non-rheumatic valve disease, and congenital valve abnormalities (e.g., bicuspid valve). Repaired CHC with prosthetic material had a lower risk than these valve diseases. The surprise was the moderate risk of IE in hypertrophic cardiomyopathy (HCM). However, many patients with HCM have mitral valve regurgitation. Not surprising was the moderate risk of IE with implanted EP devices.

There were limitations to this study. The authors used ICD-10 codes to categorize the patients rather than the actual medical records. There are no data on comorbidities, the infecting organisms, therapy, or surgery. Also, non-rheumatic valve disease is a broad category that could have subgroups with different results. Finally, the authors only examined hospital admissions and deaths, so the incidence estimates

probably are underestimated. There always has been a proviso that the antibiotic prophylaxis guidelines were just that, and clinical judgment regarding individual patients should be employed. These data from England will help inform which patient considerations outside the restrictive guidelines would be appropriate. Clearly, high risk (OR, > 76) are patients with prior IE, valve replacement/repair, and CHC with shunts/conduits. Intermediate risk patients (OR, 10-66) would include (in decreasing order by OR): congenital valve abnormalities, unrepaired cyanotic CHC, rheumatic fever, non-rheumatic valve disease, HCM, CHC repaired with prosthetic material, and EP devices.

Whether the next edition of the antibiotic prophylaxis guidelines will alter the recommendations based on these data is unknown, but clinicians should be aware that many believe we have been too restrictive and the patient categories requiring prophylaxis should be revised. ■

ABSTRACT & COMMENTARY

The Pulmonary Embolism Rule-out Criteria in Low-risk Patients

By Michael H. Crawford, MD, Editor

SYNOPSIS: A cluster randomized trial of the pulmonary embolism rule-out criteria (PERC) compared to usual care for patients estimated to be at low risk of pulmonary embolus (PE) in EDs showed that PERC was non-inferior to usual care at identifying patients who would be free of symptomatic PE at three months, resulting in less use of healthcare resources.

SOURCES: Freund Y, Cachanado M, Aubry A, et al. Effect of the pulmonary embolism rule-out criteria on subsequent thromboembolic events among low-risk emergency department patients: The PROPER Randomized Clinical Trial. *JAMA* 2018;319:559-566.

Kline JA. Utility of a clinical prediction rule to exclude pulmonary embolism among low-risk emergency department patients reason to PERC up. *JAMA* 2018;319:551-553.

The pulmonary embolism rule-out criteria (PERC) for use in EDs consists of eight clinical criteria that are used to identify a population at low risk of PE in whom further testing would be associated with an unfavorable risk-benefit ratio. Observational studies have demonstrated its usefulness, but the lack of prospective randomized trials have hampered its adoption. Thus, investigators from 14 EDs in France conducted a multicenter, non-inferiority, randomized, clinical trial to test the hypothesis that a PERC score of 0 would identify patients in whom the diagnosis of PE can be excluded safely. Patients who presented with new onset or worsening dyspnea or chest pain and a low clinical gestalt of PE (likelihood < 15%) were included. Patients were excluded if another diagnosis was obvious, if they were in severe distress (e.g., hypotensive), receiving anticoagulants, or had contra-indications to contrast CT of the pulmonary arteries (CTPA). The PERC criteria were: O_2 saturation < 94%, pulse > 100 bpm, age > 50 years, unilateral leg swelling, hemoptysis, recent trauma or surgery, prior PE or deep venous thrombosis, and estrogen use. Seven EDs used PERC, and seven did not. At six months, there was a two-month break. Then, the EDs switched to the opposite strategy. In the PERC groups, if the score was 0, no further testing was conducted. If the PERC was ≥ 1 (maximum of 8), the usual strategy measuring D-dimer, if positive, was followed by CTPA. In the control group, the usual strategy was applied to all. If CTPA was inconclusive, pulmonary ventilation perfusion (VQ) scanning or lower leg ultrasound was performed. All patients were followed for three months. The primary outcome of the study was the occurrence of a symptomatic thromboembolic event. After excluding protocol violations, 1,749 patients were included in the per-protocol population (902 controls and 847 PERC). The mean age was 44 years, and 51% were women. In the PERC groups, there were 459 PERC-negative patients. PE was diagnosed in 2.7% of the control patients and 1.5% of the PERC group. The proportion of patients undergoing CTPA was less in the PERC group (13% vs. 23%; $P < 0.001$). ED length of stay also was lower in the PERC group (mean reduction, 36 minutes). Only one PE was missed by the PERC rule initially, but due to ongoing pain and a positive D-dimer, a CTPA was conducted, which was negative, but a VQ scan showed small defects. There was no difference in mortality at three months. The non-inferiority of PERC was confirmed. The authors concluded that in low-risk ED patients, undergoing evaluation for possible PE, randomization to a PERC strategy vs. usual care did not result in an inferior rate of thromboembolic events over

three months, confirming that this is a safe strategy in such patients.

■ COMMENTARY

Many believe that with the development of D-dimer and CTPA at the turn of this century, ED patients are over-tested for PE in the United States. Given that CTPA can result in renal injury (14%), a false-positive diagnosis of PE (5%), and possibly later breast cancer in women, various clinical scores were developed to help identify low-risk patients who probably didn't need further testing. The PERC rule has the advantage of first using the clinicians' gestalt that the patient has a < 15% chance of developing a PE. Then, if all eight PERC criteria are negative, the person is at such a low risk of PE that more harm than good is likely to result from further testing. Observational studies in the United States and elsewhere have confirmed the utility of the rule, but two retrospective studies in Europe did not. Hence, these investigators from France designed and carried out this real-world randomized, clinical trial of the use of PERC vs. usual care. Both strategies employed D-dimer and CTPA if deemed necessary. The endpoint was symptomatic PE in the three months after the ED visit. In the PERC group, only one clinically apparent PE was missed, albeit a small one only detected by VQ scanning. Thus, the criteria for non-inferiority were met.

Since the PERC strategy identified PE in 1.5% and usual care in 2.7%, PERC probably missed some small sub-segmental PEs. Whether such small PEs require treatment or not is unresolved. Clearly, no clinically significant PEs were missed by the PERC strategy. Studies have shown that usual care detects PE in 5% of patients, so the rate of 2.7% in the control group is low, which speaks to the value of clinical gestalt for initial screening. If the risk is low, then PERC can be applied. In the United States, most EDs would also perform a D-dimer in almost all patients, but if PERC and D-dimer are negative, CTPA or other imaging tests could be avoided. This strategy was not tested in the French study.

There were limitations to this study. It was not a randomized trial at the patient level, which would have been challenging to conduct, but rather a cluster randomization of EDs. Also, 54 patients were lost to follow-up, which could have influenced the results. No cost data were presented, although there was clearly less testing, shorter ED stays, and fewer hospital admissions in the PERC group. However, a negative PERC could have led to more testing for other conditions. Despite these shortcomings, this trial adds considerable weight to the use of the PERC rule in low-risk patients undergoing evaluation for possible PE. ■

ABSTRACT & COMMENTARY

Real-world Study of Left Atrial Appendage Occluder Devices Raises New Concerns

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: A large observational study from France of two devices used commonly for occlusion of the left atrial appendage in patients with atrial fibrillation showed that device-related thrombus was not uncommon and was associated with subsequent stroke.

SOURCE: Fauchier L, Cinaud A, Brigadeau F, et al. Device-related thrombosis after percutaneous left atrial appendage occlusion for atrial fibrillation. *J Am Coll Cardiol* 2018;71:1528-1536.

The use of oral anticoagulation to prevent stroke and other thromboembolic events is an important principle in the treatment of patients with atrial fibrillation (AF). Based on the concept that most left-sided thrombus in AF develops in the left atrial appendage (LAA), occlusion of the LAA by mechanical devices has emerged as an alternative to long-term anticoagulation. In Europe, most of these procedures are performed with either the Watchman nitinol cage device, which has been studied in two large randomized, clinical trials and is approved for use in the United States, or with a version of the Amplatzer Amulet or Cardiac Plug devices, which has data from large European registries. Clinical trials have primarily enrolled AF patients who are fully eligible for anticoagulation to allow for randomization. Trials of the Watchman device have used a post-implant regimen of 45 days of aspirin and warfarin, followed

by 4.5 months of dual antiplatelet therapy (DAPT). Most patients in these trials have undergone post-implant imaging by transesophageal echo to look for both device leak and for device-related thrombus (DRT). Clinical trials of these devices have consistently reported low DRT rates — 20 of 478 implants in the combined PROTECT-AF trial and the CAP registry, for example. Additionally, the consequences of DRT have been downplayed both in the literature and in the device packaging, with very low reported rates of embolic events associated with DRTs.

In real-world use, LAA occlusion often is applied to patients who have contraindications to long-term anticoagulation and who are at higher risk of thromboembolism than patients studied in the approval trials. Regimens of post-implant anticoagulation vary, as do follow-up imaging. Fauchier et al examined data from eight centers in France to evaluate clinical outcomes in patients using the two main LAA closure systems, differences in antithrombotic management at discharge from hospital, and the incidence and prognosis of thrombus formation on the device after LAA occlusion.

In their cohort, 469 consecutive patients underwent LAA closure with either the Watchman (n = 272) or ACP-Amulet (n = 197) devices. Mean follow-up was 13 months, and post-implant imaging with either transesophageal echo or CT scans was available in 339 patients an average of 2.8 months post-procedure. DRT was found in 26 of these patients, giving an incidence of 7.7%. While older age and history of stroke were found to be independent predictors of DRT, use of oral anticoagulation or DAPT at discharge were protective. Importantly, DRT was found to convey a significantly higher risk of stroke compared with patients without associated thrombus, with a hazard ratio > 4. The authors concluded that thrombus formation on LAA occluder devices is not uncommon, and that this finding is strongly associated with a higher risk of ischemic stroke during intermediate-term follow-up.

■ COMMENTARY

The main findings of this study were that thrombus development on LAA occluder devices in real-world use is higher than what has previously been reported, and that this is associated with increased rates of thromboembolic complications.

Although some would note that this study was limited by its retrospective nature and incomplete imaging, its relatively large size and independent nature (no industry support) make its findings highly relevant to clinical practice. Industry has promoted the concept that DRT is a relatively benign finding, which defies logic. As one would expect from basic principles, this study suggests that thrombus on a device in the LAA confers an increased risk of thromboembolism.

Real-world LAA occluder patients generally are at higher thromboembolic risk compared with those studied in the randomized trials, and often include patients without options for systemic anticoagulation. These patients are problematic, as those who are not treated with oral anticoagulants or with DAPT post-implant clearly are at higher risk for DRT, with subsequent increased risk for stroke. Remember that the Watchman device is considered to be contraindicated when the use of warfarin, aspirin, or clopidogrel are not possible. As noted in the accompanying editorial, a DRT does not represent a failure of LAA occlusion as a preventive strategy, but is instead an iatrogenic complication.

Real-world patients also clearly undergo lower rates of post-implant imaging than what is recommended, whether because they are too frail, or because they refuse post-implant imaging. Follow-up imaging, most often by TEE, is an important part of care after LAA occluder implantation. Anticoagulation should be prescribed in response to a diagnosis of DRT.

Those caring for patients with atrial fibrillation should remember that LAA occlusion is not a complete substitute for anticoagulation, and short-circuiting the recommended post-implant regimen of anticoagulation results in higher rates of DRT. LAA occlusion remains a viable option for many, but patients and their medical providers should be aware of the associated issues. ■

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CME/CE QUESTIONS

1. A meta-analysis of 10 randomized, controlled trials of omega-3 fatty acid supplementation to prevent atherosclerotic cardiovascular disease showed a reduction in:

a. fatal myocardial infarction.

b. stroke.

c. all-cause mortality.

d. None of the above

2. An observational study of patients with left atrial appendage occlusion devices for atrial fibrillation undergoing left atrial imaging showed:

a. device-related thrombus in almost 8%.

b. device dehiscence in 4%.

c. no subsequent strokes.

d. All of the above

3. A population-based study in England showed that which of the following conditions was associated with a low risk of infective endocarditis?

a. Congenital heart disease with a shunt or conduit

b. Repair of congenital heart disease with prosthetic material

c. Unrepaired cyanotic congenital heart disease

d. Prosthetic heart valve

4. Methamphetamine-dilated cardiomyopathy is associated with:

a. alcohol abuse.

b. male sex.

c. systemic hypertension.

d. All of the above

5. The pulmonary embolism rule-out criteria include all of the following *except*:

a. hemoptysis.

b. age ≥ 50 years.

c. current oral anticoagulant use.

d. heart rate ≥ 100 bpm.

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.