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Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Withdrawal of Medical Therapy Associated With Relapse in Recovered Dilated Cardiomyopathy

By Van Selby, MD

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Dr. Selby reports he is a consultant for Alnylam Pharmaceuticals and Akcea Therapeutics.

SYNOPSIS: In patients with dilated cardiomyopathy and recovered ejection fraction, discontinuation of heart failure medical therapies was associated with a 44% risk of relapse within six months.

SOURCE: Halliday BP, Wassall R, Lota AS, et al. Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): An open-label, pilot, randomized trial. *Lancet* 2019;393:61-73.

With advances in medical therapy for heart failure with reduced ejection fraction (HFrEF), many patients with dilated cardiomyopathy will obtain normalization of left ventricular ejection fraction (LVEF) and volumes, with resolution of heart failure symptoms. Patients and providers are left to decide whether to continue medical therapy once a patient appears to be "cured" of heart failure. No prospective, randomized trial has been conducted to evaluate medication withdrawal in patients who are thought to have recovered dilated cardiomyopathy.

Halliday et al conducted an open-label, randomized trial that included 101 patients with prior dilated cardiomyopathy who demonstrated evidence of recovery. This recovery was defined as an LVEF that had improved from < 40% to ≥ 50% with normalization of left ventricular volume and N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentration < 250 ng/L with no signs or symptoms of heart failure. Patients were randomized to continuation of heart failure medical therapy or a phased withdrawal of medical therapy (starting with diuretics, then mineralocorticoid

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receptor antagonists, beta-blockers, and finally ACE inhibitors or ARBs) over 16 weeks. The primary endpoint was relapse of dilated cardiomyopathy, defined as any of the following: a reduction in LVEF of at least 10% to a value < 50%, an increase in LV volume by > 10%, a two-fold rise in NT-proBNP to a concentration > 400 ng/L, or clinical evidence of heart failure.

During six months of follow-up, 44% of patients randomized to withdrawal met criteria for relapse, compared to none of the patients who continued medical therapy ($P = 0.0001$). At the end of the six-month study period, patients in the control arm crossed over and discontinued medical therapy, with a similar (36%) rate of relapse. There were no deaths in either group. All patients with relapse were asymptomatic at the time relapse was identified.

The authors concluded that many patients with recovered dilated cardiomyopathy are at a high risk for relapse following discontinuation of medical therapy. Therefore, drug withdrawal usually should not be attempted in these patients.

■ COMMENTARY

As any provider who treats dilated cardiomyopathy can attest, patients often are eager to discontinue medical therapy as soon as their heart failure has "recovered," often determined by improvement in LVEF. The authors have addressed an important clinical question and demonstrated a high risk of cardiomyopathy recurrence shortly after withdrawal of medical therapy. This provides clinicians with valuable data to support a recommendation to continue medical therapy after cardiac function appears to have normalized.

One of the primary messages from this study is that dilated cardiomyopathy often has not truly "recovered." As the study authors suggested, it may be more appropriate to describe these patients as "in remission" to emphasize the fact that risk of recurrence persists after the LVEF and LV volumes have normalized and requires ongoing maintenance therapy to prevent relapse. There may be some patients who truly recover. However, our current tools for assessment (echocardiography, BNP levels, clinical exam) were unable to identify these patients in the Halliday et al study. Perhaps newer techniques such as cardiac MRI, strain imaging, and novel biomarkers will facilitate identification of patients with ongoing, subtler cardiac dysfunction or hormonal activation that was not identified using more standard techniques.

When relapse occurred, it generally happened quickly (within eight weeks of drug discontinuation in more than half of those who did relapse). All patients with relapse were immediately restarted on medical therapy. This helps explain why there were no deaths, unplanned cardiovascular hospitalizations, or other major cardiac events during the study period despite the high rate of relapse. This finding emphasizes the importance of early re-evaluation any time a patient with recovered cardiomyopathy discontinues medical therapy for any reason, with prompt re-initiation of heart failure therapies if cardiac function has deteriorated.

This was a small, open-label study with several limitations. Considering the small size, the authors could not explore predictors of successful drug withdrawal. For example, certain etiologies of dilated cardiomyopathy may tolerate discontinuation of medical therapy better than others when the underlying cause of the cardiomyopathy has been removed. It is also possible that withdrawal of some, although not all, medical therapy may be safe in some patients. Hopefully, larger studies will help identify a subset of patients in whom dilated cardiomyopathy has truly recovered and medical therapy can be discontinued safely.

Despite these limitations, patients with dilated cardiomyopathy and recovered ejection fraction should stay on medical therapy indefinitely at this time. Patients often are disappointed to hear this news, but sharing these data with them will help demonstrate the high risk associated with discontinuation. ■

ABSTRACT & COMMENTARY

Medication First? Ablation First? Either Way, Make Weight Loss a Priority

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 Abbott, Boston Scientific, and Medtronic.

SYNOPSIS: Weight loss management and aggressive risk factor modification associated with slowing or even reversal of atrial fibrillation progression.

SOURCE: Middeldorp ME, Pathak RK, Meredith M, et al. PREVEntion and regReSsive Effect of weight-loss and risk factor modification on Atrial Fibrillation: The REVERSE-AF study. *Europace* 2018;20:1929-1935.

Atrial fibrillation (AF) is known to be a progressive disease, often starting as paroxysmal episodes that become increasingly frequent and/or sustained, then evolving into persistent, long-standing persistent, and "permanent" forms. Prior research has clearly shown lower AF burden and fewer symptoms with sustained weight loss, as well as fewer episodes of new onset AF after bariatric surgery. Middeldorp et al sought to characterize the impact of weight loss and risk factor management on progression (or regression) of AF.

Data from the previously published LEGACY study cohort[1] were analyzed retrospectively. Of 825 patients with symptomatic AF and BMI > 27 kg/m^2 referred to a single center in Australia, 355 patients who had not undergone AF ablation and who had at least 24 months of follow-up were included in the final cohort. Other exclusion criteria were terminal cancer, severe medical illness, or permanent AF. Patients participated in a dedicated physician-led clinic focused on weight loss and risk factor modification, with a structured program that included one-on-one individualized counseling. Goals included an initial target of > 10% weight loss, resting home blood pressures < 130/80 mmHg on at least 80% of readings, cholesterol and glucose intolerance management (with lifestyle measures and pharmacotherapy as needed), treatment of sleep apnea, smoking cessation, and alcohol reduction. Patients were seen in a separate dedicated AF clinic for arrhythmia management, with rate and rhythm control tactics at the discretion of the treating physician.

For outcomes analysis, the 355 patients in the final cohort were divided by the extent of weight loss achieved: < 3% (group 1 = 116 patients), 3-9% (group 2 = 104 patients), and ≥ 10% (group 3 = 135 patients). Baseline characteristics of the three groups were similar, with mean BMI around 33 kg/m^2, although group 3 patients were slightly older (mean age, 65 years vs. 63 years in group 2 and 61 years in group 1). All groups were followed for a mean of about four years. The type of AF and burden for each patient were assessed with at least annual clinical review, 12-lead ECG, device interrogation, and seven-day Holter monitoring.

After controlling for a multitude of risk factors, the extent of weight loss achieved was significantly associated with AF progression. More than 40% of patients in group 1 (with < 3% weight loss) saw progression of their AF from paroxysmal to persistent. Only 25% were free of AF at final follow-up; most of the remaining patients saw no change. In marked contrast, 36% of patients in group 3 (with ≥ 10% weight loss) showed reversal of AF from persistent to paroxysmal, and 52% were free of AF over the final year of follow-up; only 3% of patients progressed and 9% showed no change. All groups lowered antiarrhythmic drug use rates by the end of follow-up, with the greatest change by far in group 3. Other notable findings associated with greater weight loss in group 3 were a reduction in AF burden (including 85% of patients with paroxysmal episodes lasting two to seven days initially, regressing to ≤ 48-hour episodes) and lower mean systolic blood pressure readings and less use of antihypertensive medications compared to groups 1 and 2.

■ COMMENTARY

The importance of focused weight loss efforts and risk factor modification in the prevention of AF has become increasingly clear. These data add dramatic new evidence to support such treatment to prevent disease progression. Eighty-eight percent of overweight patients who achieved ≥ 10% weight loss via a goal-directed, motivational, structured program with one-on-one individualized counseling experienced either a regression of their disease

from persistent to paroxysmal or were free of AF at follow-up.

The primary limitation of the study is its observational nature, with all the biases inherent in the absence of randomization and prospective evaluation. Patients who can lose weight more easily also may be less likely to have progressive disease or perhaps had been overweight for a shorter period and had less attendant atrial remodeling. A direct causative effect of weight loss on AF regression cannot be inferred; still, the association is striking.

The primary difficulty in applying the results of the study to clinical practice is actually achieving the kind of weight loss results seen in this single center's dedicated clinic. Busy internists, cardiologists, and electrophysiologists are unlikely to have time to provide comparable, individualized weight loss and risk factor management. However, a strong argument could be made in investing in such a dedicated stand-alone clinic, as long-term healthcare costs would undoubtedly be lower. Data on ablation procedures from this study serve as a good example. More patients in group 3 were arrhythmia-free at the time of final follow-up than patients who were arrhythmia-free in groups 1 and 2 combined, and most were without ablation. Arrhythmia-free patients in group 1 most often required multiple ablations, while those in group 2 most often required one ablation.

Clinicians will continue to offer patients all options for management of AF, including rate-control (if appropriate and effective at mitigating symptoms), antiarrhythmic drug therapy, and ablation. Some electrophysiologists defer offering a first ablation procedure until a certain goal weight is achieved, both to minimize procedural risks and maximize chances for long-term success. No matter what route is chosen, aggressive weight loss efforts and risk factor modification for overweight patients undoubtedly should be a principle component of the treatment plan. ■

REFERENCE

1. Pathak RK, Middeldorp ME, Meredith M, et al. Long-term effect of goal-directed weight management in an atrial fibrillation cohort: A long-term follow-up study (LEGACY). *J Am Coll Cardiol* 2015;65:2159-2169.

ABSTRACT & COMMENTARY

Who Needs a TEE Prior to Atrial Fibrillation Cardioversion?

By Michael H. Crawford, MD, Editor

SYNOPSIS: A study of patients with atrial fibrillation or flutter undergoing transesophageal echocardiography (TEE) showed a left atrial appendage thrombus in 8% overall and 4% in those appropriately anticoagulated. Repeat TEE after anticoagulation for a mean of 96 days showed resolution of thrombus in only 59% of subjects.

SOURCE: Niku AD, Shiota T, Siegel RJ, Rader F. Prevalence and resolution of left atrial thrombus in patients with nonvalvular atrial fibrillation and flutter with oral anticoagulation. *Am J Cardiol* 2019;123:63-68.

Embolic stroke after electric cardioversion of atrial fibrillation (AF) or flutter (AFI) is a catastrophic complication that potentially can be prevented by warfarin or direct oral anticoagulant (DOAC) therapy. Often, transesophageal echocardiography (TEE) is used to assess for left atrial appendage (LAA) thrombus before cardioversion, even if patients have been on warfarin or DOAC therapy. However, there are few data to support this practice.

Investigators from Cedars-Sinai Medical Center in Los Angeles performed a retrospective observational study of more than 2,000 TEE studies performed on 1,485 patients with AF or AFI between 2013 and 2017 to gain insight into the utility of TEE prior to cardioversion. LAA thrombus included discrete masses and viscid echo densities distinct from spontaneous echo contrast. Patients with LAA occluder or past LAA ligation were excluded. The initial TEE in the 1,485 patients exhibited LAA thrombus in 117. Among these 117 patients, 61 were on antiplatelet therapy, and all but one were on an anticoagulant. Fifty-six patients were considered adequately anticoagulated by taking warfarin with an international normalized ratio (INR) > 2.0 or on a DOAC. The thrombus rate in this group was 4%. In 63 of 117 patients with LAA thrombus, a repeat TEE was performed within one year (mean, 96 days) of being on continuous anticoagulant therapy. Thrombus resolution was observed in 37 of those 63 patients. The only clinical variable associated with LAA thrombus persistence on anticoagulation was the presence of

diabetes. Resolution rates were not influenced by the configuration of the LAA. Resolution did not vary by anticoagulation type. Among the 117 patients with LAA thrombus, eight suffered a thromboembolic event, and only two were noncompliant with oral anticoagulants. The authors concluded that LAA thrombus persistence on anticoagulant therapy is common and not clinically predictable. Thus, they recommended TEE prior to cardioversion in all patients with a history of LAA thrombus, regardless of anticoagulation therapy.

■ COMMENTARY

Increasingly, my institution's electrophysiology section is requesting TEEs on all patients who are undergoing electrical or chemical cardioversions or who might cardiovert in association with therapy for AF or AFI, despite taking (presumably) adequate anticoagulant therapy. However, very few of the TEEs performed for this purpose reveal LAA thrombus. Thus, this study caught my attention. This analysis of the authors' five-year experience with TEEs conducted on patients with AF or AFI reached several conclusions: Eight percent of the patients had LAA thrombus, yet almost all were on oral anticoagulants. In those thought to be appropriately anticoagulated, it still was 4%. Forty percent of those with LAA thrombus who underwent a repeat TEE after about three months of appropriate anticoagulant therapy still showed LAA thrombus. There was no difference in thrombus incidence or resolution between warfarin or DOAC therapy. The only clinical predictor of persistent LAA thrombus was diabetes.

It is common practice to perform cardioversion of AF/AFI without a TEE if the patient has been on adequate oral anticoagulation for more than three weeks. This study suggests this practice runs the risk of cardioverting four out of 100 patients with a thrombus. Whether these thrombi would embolize and hit a vital organ is unknown. Other studies of TEE prior to cardioversion have shown embolism rates in those with negative TEEs of 1-2%. The risk of TEE is minimal in well-selected patients, but there are patients in whom the risk of TEE is competitive with these embolism rates. Thus, if almost complete avoidance of thromboembolism with cardioversion is the goal, then a routine TEE regardless of anticoagulant status is reasonable. The authors noted that the ascertainment of who is compliant with DOAC therapy is challenging since there is no INR-type test for these agents. In particular, I worry about patients on DOACs that have to be taken twice a day (dabigatran and apixaban).

There are limitations to this study. There could be a selection bias toward performing TEEs on higher-risk patients. Most patients recorded CHA_2DS_2-VASc scores of ≥ 3. Three-dimensional echo was not performed routinely, so the sensitivity for detecting thrombi may be less if 3D echo was not conducted. No robust analysis of medication noncompliance beyond INR was performed. Also, there were no data on the persistence or recurrence of AF/AFI and how this may have affected the results. Finally, the number of patients in this one center study was relatively small.

Clearly, patients with known prior LAA thrombus should undergo TEE-guided cardioversion based on the poor resolution rates reported in this study. Whether everyone with AF/AFI undergoing elective cardioversion or any procedure or medication that might lead to cardioversion needs TEE is uncertain. Still, the data in this study support the trend in this direction that I have observed. ■

ABSTRACT & COMMENTARY

Impact of Atrial Fibrillation on Survival in Patients With Severe Mitral Regurgitation

By Michael H. Crawford, Editor

SYNOPSIS: A large observational study of patients with severe mitral valve regurgitation due to flail leaflets revealed that atrial fibrillation at entry was associated with excess mortality. Surgery to correct regurgitation was associated with better survival vs. medical therapy; however, atrial fibrillation negatively influenced post-surgical outcomes.

SOURCE: Grigioni F, Benfari G, Vanoverschelde JL, et al. Long-term implications of atrial fibrillation in patients with degenerative mitral regurgitation. *J Am Coll Cardiol* 2019;73:264-274.

Atrial fibrillation (AF) complicating the course of degenerative mitral regurgitation (DMR) is unwelcome but not a clear indication for mitral valve (MV) repair or replacement due to inadequate knowledge. Investigators from the Mitral Regurgitation International Database (MIDA) sought to define the prevalence, clinical context, and prognostic implications of AF in patients with

DMR and a documented flail leaflet(s). Patients with functional MR or significant comorbidities were excluded. The primary endpoint of this prospective, observational study was all-cause mortality. The secondary endpoint was death from cardiovascular (CV) causes. The database included 2,425 patients (mean age, 67 years), of whom 1,646 were in sinus rhythm at entry, 317 had paroxysmal AF (pAF), and 462 had persistent or chronic AF (cAF). Entry left ventricular ejection fraction (EF) was 64 ± 10%. Most patients had a normal EF, were asymptomatic initially, and had severe MR (94%).

Over a mean follow-up of nine years, there were 933 deaths, of which 64% were CV-related. New AF and pAF were 24% and 36% at 10 years and were predictive of 10-year survival: sinus rhythm, 74%; pAF, 59%; and cAF, 46% ($P < 0.0001$) and were independent of all baseline characteristics. Surgery (88% repair) was associated with improved survival independent of baseline characteristics and rhythm (adjusted hazard ratio [HR], 0.26; 95% confidence interval, 0.23-0.30; $P < 0.001$). However, post-surgical survival was related to AF: 10-year survival in sinus rhythm was 82%; pAF, 70%; and cAF, 57% ($P < 0.0001$). The authors concluded that detection of AF of any type should prompt consideration of surgery in patients with severe DMR.

■ COMMENTARY

Mitral valve surgery for severe DMR with new onset AF is a class IIa-B recommendation if repair at a low risk is highly feasible. The lack of data has kept AF from attaining a class I indication. The results of this study suggest that a class I indication may be warranted now in patients with severe DMR due to a flail leaflet who develop AF. The results of previous observational studies have suggested that flail leaflets alone with significant MR carry a high mortality that can be mitigated by surgery. Indeed, this MIDA registry study confirmed this. Those who underwent surgery (88% repair) exhibited improved survival independent of baseline characteristics and rhythm. However, even after surgery, AF before or after surgery increased 10-year mortality. Perioperative mortality was low at 2% but seemed to be related to AF, too: sinus rhythm HR, 1.67; pAF, 2.1; and cAF, 3.3% ($P = 0.16$). In aggregate, these data suggest that early surgery before cAF develops should be considered in patients with severe MR and a flail leaflet and that pAF should strengthen this decision. In the MIDA registry, no systematic hunt for AF was performed, but it raises the question of whether there should be one. Since pAF can be asymptomatic, perhaps ambulatory ECG monitoring should be performed in all patients with severe MR and a flail leaflet, especially if there is a reluctance to advise or accept surgery.

There were limitations to the MIDA database analysis beyond its observational nature, where residual confounding cannot be excluded completely. The enrollment period spanned from 1980 to 2005. Certainly, there were advances in surgical techniques during this period. There was a high incidence of systemic hypertension in these patients (40%), which raises the question of what role blood pressure plays in such patients. Also, there were very few ablations or Maze procedures performed (5%), which raises the issue of whether more invasive approaches to AF pre- and post-operation would have altered the results favorably. In addition, fewer patients with AF preoperatively underwent MV repair, which certainly decreased the operative and long-term survival of the ones who underwent valve replacement. Finally, it is unclear whether the presence of AF in patients without flail leaflet(s) and with more moderate MR would affect outcomes. At this time, I am going to add ambulatory ECG monitoring to my evaluation of patients with moderate to severe MR. I will use its presence to bolster my argument for earlier surgery in appropriate patients. ■

ABSTRACT & COMMENTARY

Management of Spontaneous Coronary Artery Dissection

By Jeffrey Zimmet, MD, PhD

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

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

SYNOPSIS: In the largest study to date about patients with spontaneous coronary artery dissection who underwent follow-up angiography, 95% of those who underwent repeat cath more than 30 days later showed spontaneous angiographic healing.

SOURCE: Hassan S, Prakash R, Starovoytov A, Saw J. Natural history of spontaneous coronary artery dissection with spontaneous angiographic healing. *JACC Cardiovasc Interv* 2019; Feb. 22. pii: S1936-8798(18)32479-8. doi: 10.1016/j.jcin.2018.12.011. [Epub ahead of print].

Although it is uncommon, spontaneous coronary artery dissection (SCAD) is an increasingly recognized cause of acute myocardial infarction (MI). Because of underdiagnosis, the true prevalence is unknown. The authors of prior studies have reported this condition in 0.1-4.0% of patients presenting with acute coronary syndrome. However, the authors of a more recent study of MI in women < 60 years of age with improved angiographic recognition of SCAD reported that this condition was the cause of MI in up to 24-35% of such cases. Currently, upon recognition of an acute SCAD event, medical therapy is recommended as first-line therapy, except in the cases involving ongoing ischemia, hemodynamic instability, or dissection of the left main coronary artery. Prior studies of angiographic follow-up in SCAD have been small and have used inconsistent definitions of angiographic healing.

Hassan et al examined patients in two prospective SCAD registries (the Non-Atherosclerotic Coronary Artery Disease registry and the Canadian SCAD study) who had undergone repeat invasive coronary angiography. Of 404 total SCAD patients, 202 underwent repeat angiograms after the initial event. Forty-six of these had undergone percutaneous coronary intervention (PCI), leaving 156 conservatively managed patients for the analysis, with a total of 182 noncontiguous SCAD lesions. Characteristics of the patients mirrored prior reports of SCAD. Most patients were younger (mean age, 51.5 ± 8.7 years), 88.5% were women, and 75.6% also had received diagnoses of extra-coronary fibromuscular dysplasia. All had presented with MI, with 77.6% represented by non-ST-segment elevation MI. Nearly 70% of cases involved type 2 angiographic SCAD, defined as diffuse smooth narrowing that can vary in severity. A little more than one-quarter of patients exhibited the more-classic appearance of type 1 SCAD, showing contrast dye staining of the arterial wall with multiple lumens. A total of 46.7% of lesions had less than TIMI grade 3 flow, with 40 cases showing TIMI grade 0 flow. The median angiographic stenosis severity was 79%.

All patients in this study underwent repeat invasive angiography, with median time to repeat imaging of 154 days (interquartile range, 70-604 days). Spontaneous angiographic healing was observed in 157 of 182 lesions. Of the 25 lesions that did not meet criteria for healing, 17 underwent the repeat angiographic study < 30 days from the index SCAD event. At follow-up, only 10 of the 182 lesions had less than TIMI grade 3 flow. Of the 40 lesions with initial TIMI grade 0 flow, 35 had improved to TIMI grade 3 flow at follow-up. The authors concluded that in conservatively managed SCAD lesions, the overwhelming majority heal spontaneously when imaged more than 30 days from the index event.

■ COMMENTARY

In this largest-yet retrospective cohort of SCAD patients with available angiographic follow-up, more than 95% of lesions examined more than 30 days after the index event met criteria for spontaneous angiographic healing. This supports the current recommendations for conservative first-line management of SCAD patients (when clinically feasible). It is interesting to note that so many patients in this study were successfully managed this way. For example, the 22% of patients in this cohort who presented with ST elevation MI were successfully treated without revascularization. Likewise, although nearly half of included lesions and vessels had less-than-normal flow (and 40 of them had TIMI grade 0 flow), conservative management still was undertaken based on the patient's clinical status at the time, with PCI undertaken only for cardiogenic shock, ongoing ischemia, sustained ventricular arrhythmia, or left main involvement.

The recommendation for conservative management comes in part from the complexity of PCI in patients with SCAD, including a historically high complication rate that can include failure to wire the true lumen and propagation of the dissection proximally and distally. The findings of this study support this general recommendation, showing that patients who complete successful conservative management most often also demonstrate spontaneous healing of the artery over time.

However, this recommendation comes with caveats. Cardiologists should examine each case individually and manage in the most appropriate manner. Among the current cohort of patients, all of whom were treated at a high-volume center with significant experience with SCAD, 46 of the 202 with repeat angiograms were excluded because they had undergone clinically indicated PCI. Follow-up information shows that clinical event rates were high even among patients who showed evidence of angiographic healing (35% had recurrent MIs, 6.7% underwent revascularization, 2% suffered stroke, and 1.5% died). Although the upfront recommendation is for conservative therapy when possible, these patients are complex, and management requires an open mind. ■

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CME/CE QUESTIONS

1. **In overweight patients with atrial fibrillation, what percent reduction in weight is associated with fewer atrial fibrillation events?**
   a. 3%
   b. 5%
   c. 7%
   d. 10%

2. **For repeat angiography performed more than 30 days after conservatively managed spontaneous coronary artery dissection, what percentage of dissections have healed?**
   a. 100%
   b. 95%
   c. 90%
   d. 85%

3. **In a study of patients with dilated cardiomyopathy and recovered left ventricular function, approximately what percent of patients experienced a decline in left ventricular function after heart failure medication withdrawal?**
   a. 55%
   b. 45%
   c. 30%
   d. 20%

4. **In patients with left atrial appendage thrombus identified on transesophageal echocardiogram, after appropriate anticoagulant therapy, approximately what percent of patients showed thrombus resolution?**
   a. 50%
   b. 60%
   c. 70%
   d. 80%

5. **In patients with severe degenerative mitral regurgitation with flail leaflet, the presence of atrial fibrillation significantly increased:**
   a. overall 10-year mortality.
   b. surgical mortality.
   c. perioperative stroke.
   d. mitral valve replacement rates.

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.