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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Spironolactone for Resistant Hypertension

By Michael Crawford, MD, Editor

SYNOPSIS: A randomized, double-blind, placebo-controlled study in resistant hypertension patients on three drugs, including a diuretic, showed that the addition of spironolactone was superior to doxazosin and bisoprolol for lowering blood pressure and it was well tolerated.

SOURCES: Williams B, et al. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): A randomised, double-blind, crossover trial. *Lancet* 2015;386:2059-2068.

Sternlicht H, Bakris GL. Spironolactone for resistant hypertension-hard to resist? *Lancet* 2015;386:2032-2034.

Resistant hypertension is common, and the choice of additional drug therapy in this condition is not clear. Investigators tested three drug classes as additional therapy beyond the recommended angiotensin-converting-enzyme inhibitor (ACEI)/angiotensin II receptor blocker (ARB), calcium blocker plus diuretic. An alpha-blocker to further reduce peripheral resistance (doxazosin), a beta-blocker to reduce renin (bisoprolol), and additional diuresis with spironolactone were tested in a randomized, double-blind, placebo-controlled, crossover trial. The study included patients on maximally tolerated doses of the recommended three classes of drugs who had a clinical blood pressure (BP) of > 140 mmHg systolic or > 135 for diabetics and average home BP measures > 130 over 4 days (18 measurements). After 1 month of single-blind placebo, patients were rotated through four regimens for 6 weeks at the lower dose and 6 weeks at the higher dose: spironolactone 25-50 mg/day, doxazosin 4-8 mg/day, bisoprolol 5-10 mg/day, and placebo. The primary endpoint was the average of three home systolic BP twice a day for 4 days (24 measurements). Plasma renin was measured at baseline, and serum electrolytes were measured at each visit. Researchers screened 436 patients 18-79 years of age, randomized 335 patients (mean age 61 years), and placed 314 patients in the intention-to-treat analysis. Two hundred thirty patients completed the entire protocol. The average decrease in systolic BP on spironolactone was significantly greater than on placebo (-8.7 mmHg, $P < 0.0001$) and the response to doxazosin (-4.0 mmHg, $P < 0.0001$) and bisoprolol (-4.5 mmHg, $P < 0.0001$). Spironolactone's superiority persisted across all measured renin levels except the very highest, where

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it was equally as efficacious the other two drugs. Adverse events were not different with the three drugs, and only six patients on spironolactone had a potassium > 6.0 mmol/L on one occasion only (maximum 6.5). The authors concluded that spironolactone was the most efficacious fourth drug for patients with drug-resistant hypertension.

■ COMMENTARY

Resistant hypertension is defined as levels above the patients target on maximally tolerated doses of three drugs, one of which is a diuretic, and afflicts about 10% of treated hypertensives. Current guidelines suggest adding a fourth drug, but do not specify which one. It has been suggested that resistant hypertension is a result of non-compliance, not necessarily with drug therapy but rather lifestyle modifications such as reduced salt intake, alcohol consumption, and weight loss. The most important of these is probably salt intake. In this study, 24-hour urine-sodium excretion on placebo was 8 g. Thus, the concept of additional diuresis has arisen. Some believe that switching to a longer-acting diuretic, such as chlorthalidone or indapamide, works, but this has not been systematically studied. Another concept is that those treated with long-term ACEI/ARB develop aldosterone escape, leading to salt and water retention. Therefore, previous observational studies suggest aldosterone antagonists may be efficacious in resistant hypertension. This study tested this hypothesis and compared spironolactone to two other classes of agents: beta-blocker and alpha-blocker.

In this population of predominantly white subjects, spironolactone was remarkably effective. It was twice as effective as bisoprolol and doxazosin. Also, about 60% achieved target BP (< 135 systolic) on spironolactone vs about 40% on the other two drugs. Although bisoprolol and doxazosin were better than placebo, only spironolactone showed a dose response relationship, suggesting that higher doses, if tolerated, would produce better results. The authors suggested that the use of spironolactone in resistant hypertension may reduce the fuel for non-pharmacologic approaches such as renal denervation. Also, the study raises the question as to whether the earlier use of spironolactone would be beneficial. In the past, combination pills with hydrochlorothiazide and spironolactone were popular to reduce the incidence of hypokalemia. Perhaps these agents should receive another look in light of these data.

This study has several strengths. The authors used average home BP, which is always lower, as their endpoint measure. There was a big placebo effect noted in clinic BP (-10 mmHg) but not with average home BP. The population was relatively large for this type of study and several biochemical measures were taken, which will be reported later.

There are also weaknesses. The trial was of short duration and has no outcome data. The patients were predominantly white and had glomerular filtration rates (GFR) > 45.

There were remarkably few adverse events and they were not different between the three drugs (all < 3%). Hyperkalemia was infrequent and resulted in no serious events. The authors noted that serum sodium decreased 1.2 mmol/L on average, and potassium increased 0.5 mmol/L. Estimated GFR decreased, but no more than you would expect while administering another diuretic. Whether this has long-term consequences is unknown. The authors did not observe gynecomastia, but the length of exposure to spironolactone is probably too short to see this side effect.

The editorial by Sternlicht and Bakris concluded that despite the imperfections in this study, using spironolactone for resistant hypertension is "hard to resist." Future studies should clarify general applicability and whether a more aggressive thiazide diuretic approach would be just as effective. ■

ABSTRACT & COMMENTARY

Remote Hemodynamic Monitoring Shows Long-term Benefit in Heart Failure Patients

By Van Selby, MD

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

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

SYNOPSIS: Remote pulmonary artery pressure monitoring in NYHA class III heart failure patients resulted in fewer subsequent hospitalizations and was well tolerated.

SOURCE: Abraham WT, et al. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: Complete follow-up results from the CHAMPION randomized trial. *Lancet* 2015 Nov 6 pii: S0140-6736(15)00723-0. doi: 10.1016/S0140-6736(15)00723-0. [Epub ahead of print].

Remote hemodynamic monitoring is a novel strategy for treating chronic heart failure (HF). The CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in New York Heart Association (NYHA) Class III Heart Failure Patients (CHAMPION) trial enrolled 550 patients with class III heart failure and at least one HF hospitalization in the previous year. Most the patients had a reduced left ventricular ejection fraction and about 20% had an ejection fraction > 40%. All patients had a wireless pulmonary artery pressure sensor (CardioMEMS) implanted. Of those implanted, 270 patients were randomized to CardioMEMS-guided management while the other 280 were randomized to standard guideline-based therapy, with treating clinicians blinded to the hemodynamic data. After 6 months of follow-up, there was a 33% reduction in HF hospitalizations among patients randomized to CardioMEMS-guided therapy.

Following the 6-month randomization period, the remaining 347 patients were transitioned to a 13-month open-access period. During this time, hemodynamic data became available to the treating clinician for all patients, and there was no communication with the study sponsor related to patient management.

During the open-access period, the CardioMEMS-guided therapy group experienced a 48% reduction in the rate of HF hospitalization (hazard ratio [HR], 0.52; 95% confidence interval [CI], 0.40-0.69; $P < 0.0001$) and a 47% decreased risk of death or first HF hospitalization (HR, 0.53; 95% CI, 0.38-0.73; $P < 0.0001$). Among patients originally randomized to guideline-based management alone, making hemodynamic data available to the treating clinician was associated with a similar 48% reduction in HF hospitalizations ($P < 0.0001$). The CardioMEMS-guided strategy was also associated with improvements in quality of life scores.

There were eight device-related or system-related complications and seven procedure-related adverse events, all occurring within the original 6-month period. No sensor failures occurred over an average 31 months of follow-up. The authors concluded that management of functional class III heart failure using home transmission of pulmonary artery pressure measurements has significant long-term benefit in reducing hospital admission rates.

■ COMMENTARY

Based on the results of the CHAMPION trial randomization period, the FDA approved the CardioMEMS device in May 2014 for patients with NYHA class III HF and at least one HF hospitalization in the previous year. At the time, the CHAMPION trial was criticized for communication between the study sponsor and individual sites regarding management of patients in the treatment group. To better evaluate the effects of remote hemodynamic monitoring in the "real world," there was no communication between the sponsor and the treating clinicians during the open-access period reported in this follow-up publication. Although a clinical trial cannot perfectly reproduce real-world clinical care, these findings provide strong evidence that using an implantable hemodynamic monitor to guide therapy leads to a sustained reduction in HF hospitalizations. The magnitude of the reduction observed in CHAMPION is greater than what has been reported for nearly any other HF treatment available today.

For providers considering the CardioMEMS device for a patient, it is important to understand the reality

of managing patients post-implant. Remote monitoring generates substantial new patient data. Providers and office staff must be ready to receive these data, use the information to make medication adjustments, and communicate these changes to patients, all in a timely manner. Patients who receive hemodynamic-guided therapy have better outcomes, in part, because knowledge of hemodynamic data leads to more frequent adjustments (during the initial randomization period, patients in the CardioMEMS group had more than twice as many HF medication adjustments compared to those in the medical-therapy arm). As remote monitoring becomes more widespread, healthcare payers will need to determine how best to reimburse for this extra workload. Patient selection is equally important. The successful use of the technology requires that patients transmit pressure measurements regularly and adhere to the recommended medication adjustments.

The additional information from this open access extension period strengthens the evidence supporting remote hemodynamic monitoring for patients with NYHA class III HF and a recent HF hospitalization, and suggests this technology can be successfully used in real world clinical practice. Importantly, the CardioMEMS device is effective regardless of ejection fraction, making it one of the few interventions with proven efficacy in HF with preserved ejection fraction. With careful patient selection and a clear plan for ongoing patient follow-up, remote hemodynamic monitoring is a promising option for patients with HF and prior hospitalizations. ■

ABSTRACT & COMMENTARY

Management of Functional Mitral Regurgitation

By Michael Crawford, MD, Editor

SYNOPSIS: In symptomatic patients with coronary artery disease, left ventricular ejection fraction < 30%, and significant mitral valve regurgitation, coronary bypass graft surgery (CABG) or CABG plus mitral valve repair should be considered.

SOURCES: Samad Z, et al. Management and outcomes in patients with moderate or severe functional mitral regurgitation and severe left ventricular dysfunction. *Eur Heart J* 2015;36:2733-2741.

Vahanian A, Iung B. Severe secondary mitral regurgitation and left ventricular dysfunction: A 'deadly combination' against which the fight is not over! *Eur Heart J* 2015 Oct;36:2742-2744.

Symptomatic moderate-to-severe mitral regurgitation (MR) and a left ventricular ejection fraction (LVEF) < 30% is considered a class IIb indication for surgical correction, but with little supporting evidence (level C). Thus, investigators from Duke University queried their database from 1995-2000 to identify such patients and determine their long-term outcomes with different treatment strategies. They excluded patients with primary or organic MR and prior mitral valve surgery. Follow-up visits occurred 6 months after surgery and yearly thereafter. Survival data were available on 99% of patients. The primary endpoint was death, left ventricular assist device placement, or cardiac transplant. The median follow-up of the 1441 patients was 4.7 years. The median age was 64 years, and 39% were women. MR was moderate in 70% and severe in 30%. Most had heart failure symptoms (83%). Physicians pursued medical therapy in 75% at 1 year, percutaneous coronary intervention (PCI) in 8%, coronary bypass graft surgery (CABG) in 6%, CABG plus mitral surgery in 7%, and mitral surgery alone in 4%. Surgeons performed mitral valve repair in 95% of those who had surgery. Among the 52% of patients who had coronary artery disease (CAD), those who had CABG (hazard ratio [HR], 0.56; 95% confidence interval [CI], 0.42-0.76) and CABG plus mitral valve surgery (HR, 0.58; 95% CI, 0.44-0.78) had improved event-free survival. PCI was of borderline benefit (HR, 0.78; 95% CI, 0.61-1.00), but isolated mitral valve surgery was not beneficial (HR, 0.64; 95% CI, 0.33-1.27; $P = 0.2$). Propensity score adjustments for baseline differences in the treatment groups showed that mitral valve surgery was associated with better event-free survival (HR, 0.69; 95% CI, 0.53-0.88), and among the CAD patients, mitral valve surgery was superior to medical therapy (HR, 0.71; 95% CI, 0.52-0.95). The authors concluded that in symptomatic patients with moderate-to-severe MR and severe left ventricular dysfunction, those who had mitral valve surgery experienced higher event-free survival.

■ COMMENTARY

The management of significant MR in symptomatic patients with an LVEF < 30% is controversial. This retrospective observational study from Duke University attempted to shed light on the decision process in such patients. In this series, three-fourths of patients

received medical therapy and one-fourth underwent a procedure. Those who underwent a procedure had more severe MR, higher LVEFs, and were more likely to have CAD. One-third of the procedures were PCI, which was of borderline benefit. The rest underwent surgery and after propensity score adjustments, mitral valve surgery was associated with better survival. However, a subgroup analysis showed that only those who had CABG or CABG plus mitral valve surgery benefitted. Isolated mitral valve surgery did not increase survival. The issue is whether any of the patients on medical therapy would have benefited from surgery. Clearly, if they had CAD and myocardial ischemia or viable myocardium, they probably would have. If not, they may not have.

The strengths of this study included the large number of patients, 5 years of follow-up, a homogeneous population of functional MR, and a skilled team. Weaknesses included the retrospective, nonrandomized study and the exclusive use of visual estimation of MR severity in this age of echo Doppler quantitation. Also, this was a study of predominantly surgical repair vs medical therapy. There is no description or standardization of such medical therapy. Finally, in many ways, the study is dated because there are no viability assessments, and mitral clipping and transcutaneous valve delivery are only used in a handful of patients.

The approach to symptomatic patients with significant (moderate to severe) MR and an LVEF < 30% should be as follows. First, optimize medical therapy for heart failure with maximally tolerated doses of the standard medications and resynchronization therapy, if indicated. Second, quantitate the severity of MR. If moderate-to-severe or severe, consider a procedure if the patient remains symptomatic on maximal medical therapy. If ischemic or viable myocardium is demonstrated, then consider CABG with mitral valve repair. If the heart valve team deems this not feasible or too risky, then consider PCI with mitral valve clipping or transcutaneous replacement. Fortunately, there are several prospective trials underway concerning these issues that should help refine our approach to these difficult patients. ■

ABSTRACT & COMMENTARY

FAME Data Shows Durability of Fractional Flow Reserve Strategy at 5 Years

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: The 5-year results of the FAME study did not show any late catch up in major adverse cardiac events in the fractional flow reserve-guided (FFR) group, supporting the long-term safety of the FFR-guided approach to percutaneous coronary interventions.

SOURCE: van Nunen LX, et al, Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial. *Lancet* 2015;386:1853-1860.

Although coronary angiography is the gold standard for the diagnosis of coronary atherosclerotic disease, it presents difficulties in identifying targets for percutaneous coronary interventional (PCI) therapies. The visual estimation of coronary stenosis severity by coronary angiography, besides being relatively subjective, in many cases is not the optimal means of determining the presence or absence of myocardial ischemia. In the cardiac catheterization laboratory, that title goes to the measurement of fractional flow reserve (FFR), which allows the quantitative assessment of ischemic capacity in a lesion or series of lesions in a single artery.

The Fractional Flow Reserve Versus Angiography for Guidance of PCI in Patients with Multivessel Coronary Artery Disease (FAME) trial, first published in 2009, was a multicenter trial in which more than 1000 patients with multivessel coronary disease were randomized to having their PCI guided either by angiography or by FFR. In the angiography group, stenting was performed in all angiographically identified lesions. The FFR group had physiologic assessment of all lesions, with PCI performed only if the FFR value was ≤ 0.80. The results are well-known. Patients in the FFR group, on average, had fewer stents placed, as some of the lesions identified by angiography were not significant by FFR. After 1 year, patients in the FFR had fewer major adverse cardiac events and greater freedom

from angina. At 2 years, the FFR group had significantly lower rates of death and nonfatal myocardial infarction. The long-term safety of this strategy has not been reported. Specifically, some have expressed concern that medical rather than interventional treatment of less-severe lesions might be susceptible to a catch-up phenomenon.

In August 2015, FAME investigators reported the 5-year results of their study. Major adverse cardiac events (MACE) at 2 and 5 years, defined as a composite of death, myocardial infarction, and any repeat revascularization, were prespecified endpoints of the study. Notably, although events up to the 2-year mark were adjudicated by an independent clinical events committee, the 5-year events were reported by individual sites and were verified by available source documentation. Regardless, completeness of follow-up data was excellent. At 5 years, only 67 of the original angiography-guided patients and 73 of the 509 FFR patients had been lost to follow-up. MACE occurred in 154 of 496 patients in the angiography-guided group vs 143 of 509 patients in the FFR-guided group (relative risk [RR], 0.91; 95% confidence interval [CI] 0.75-1.10; P = 0.31). All-cause mortality was also not significantly different between groups, with 10% mortality (49 of 496 patients) in the angiography-guided group, and 9% (44 of 509 patients) in the FFR-guided group (RR, 0.88; 95% CI, 0.59-1.29; P = 0.50).

Interestingly, there was a positive interaction between patient sex and treatment strategy, with FFR-guided PCI favoring men (P = 0.027). Male patients had a persistently significant difference in MACE at 5 years that was not seen in the female patients, who represented 26% of the total.

The investigators noted that while the absolute difference in MACE between angiography and FFR-guided groups persisted at 5 years, this difference was no longer significant as compared with the 1- and 2-year data. The authors said this result is due to the smaller number of patients at risk and the similar incidence of events in both groups beyond 2 years. Their interpretation is that the benefits of using FFR guidance occur mainly in the first 2 years, with subsequent similar risk increases in both groups. The authors concluded that these results confirm the long-term safety of FFR-guided PCI in multi-vessel disease.

■ COMMENTARY

The results of the FAME trial have already substantially changed the practice of clinical cardiology. Patients in the FFR-guidance group, on average, had fewer lesions treated and received fewer stents than those in the angiography group. Despite this less aggressive treatment, these patients actually showed superior hard outcomes in the first 2 years, with lower resource use. Although guidelines reflect the findings, multiple studies have shown that FFR remains relatively underutilized. Some have expressed a concern that the 1- and 2-year benefits of FFR-guided PCI might be undermined by a late catch-up phenomenon, with an excess of events in patients provided FFR-guided therapy. These 5-year results, although imperfect, should do much to allay these fears and pave the way for more consistent use of this technology in clinical decision making. ■

ABSTRACT & COMMENTARY

Echo Diagnosis of Left Ventricular Non-compaction

By Michael Crawford, MD, Editor

SYNOPSIS: The echocardiographic diagnosis of left ventricular non-compaction is difficult, and experienced readers disagree frequently. Careful attention to suggested criteria and the use of other imaging modalities in difficult cases resolves most diagnostic disagreements.

SOURCES: Stöllberger C, et al. Interobserver agreement of the echocardiographic diagnosis of LV hypertrabeculation/noncompaction. *JACC Cardiovasc Imaging* 2015;8:1252-1257.

Pinto FJ. When and how to agree in disagreeing on the diagnosis of noncompaction by echocardiography? *JACC Cardiovasc Imaging* 2015;8:1258-1259.

The diagnosis of left ventricular (LV) non-compaction has profound implications for patients, yet no uniform criteria for its diagnosis by echocardiography exist. Investigators from Austria and Germany studied the interobserver agreement in two laboratories using the same criteria. Potentially afflicted patient echoes were mixed with controls who were age- and LV systolic function-matched. Three readers from two labs were blinded to the identity of the echoes and the other readers' initial opinion.

Patients with other congenital cardiac conditions, recent myocardial infarction, and aortic valve disease were excluded. In brief, the criteria were: more than three prominent trabecular formations; two layered myocardiums with a heavily trabeculated endocardial layer and a dense epicardial layer; a non-compacted to compacted myocardium ratio of > 2:1; and contrast or color flow evidence of perfusion in the intratrabecular spaces. The three reviewers discussed discordant opinions. Echoes from 100 patients, of which 51 had received the diagnosis of LV non-compaction (NC), were reviewed. LV ejection fraction ranged from 4-88%. Agreement between the three reviewers occurred in 65% of the cases. Review of the 35 discordant cases resulted in agreement in 24 while 11 remained questionable. In those with an initial clinical diagnosis of LVNC (51 patients), only 27 had agreement between the three observers. Of the remaining 24, all agreed there was no LVNC in three, there was LVNC in eight, and 10 remained questionable. Among the 49 not diagnosed as LVNC, only in 33 did all three observers agree there was no LVNC. Of the remaining 16, all agreed that two had LVNC. The remaining 14 were reviewed and LVNC was excluded in 13 and one remained questionable. The authors concluded that there is considerable interobserver disagreement in the diagnosis of LVNC using uniform criteria, which can be reduced by mutual review, but in 11% of cases, the diagnosis remains questionable.

■ COMMENTARY

Since it was first described in 1984, the diagnosis of this rare condition has increased. Some believe it is being overdiagnosed now. This is an important issue, because this condition has been associated with malignant arrhythmias, sudden death, and heart failure. It may affect patients' careers, e.g., competitive athletes and their subsequent management or, e.g., defibrillator placement. Even in those with mild cases with normal global LV function, there can be psychological harm with this diagnosis.

Small studies in single labs have suggested considerable variability between observers in the diagnosis of LVNC. These investigators sought to assess the variability between two experienced labs in different countries who used the same criteria. They found that in those in whom LVNC was diagnosed on their routine clinical echo, the reviewers agreed with the diagnosis in 53%. Even more disturbing, there was only 67% agreement with the diagnosis of the absence of LVNC. After a re-review and discussion among the reviewers, 11% remained questionable. Agreement was hampered by poor images, small LVs with normal function, aberrant bands, false chordae, and unusual papillary muscles. Not only is it difficult to distinguish from normal variants, LVNC can be seen in any cause of LV hypertrophy or dilatation. In this study, the authors excluded patients with aortic valve disease and recent myocardial infarction.

There were limitations to this study. The reviewers only had access to the recorded studies, so they couldn't request additional views, contrast use, or 3-D images. There are no data on intraobserver reproducibility. Also, the anatomical location of the observed abnormalities was not considered. In addition, other imaging modalities use was not reported and could have improved diagnostic accuracy. However, there is no accepted gold standard for the diagnosis of LVNC and there are insufficient pathological data to validate imaging methods.

[Since LVNC was first described in 1984, the diagnosis of this rare condition has increased. Some believe it is being overdiagnosed now. This is an important issue, because this condition has been associated with malignant arrhythmias, sudden death, and heart failure.]

European Society of Cardiology President Faust Pinto's accompanying editorial suggests that in questionable cases, contrast echo, 3-D transesophageal echo, or MRI should be used to help clarify. However, there are no universally accepted criteria for LVNC by these studies. One MRI study of normal subjects found LVNC in 91% at the apex and 78% at the mid-wall. This suggests that there is a spectrum from normal variants to severe LVNC. The latter subjects usually have low LV systolic performance, so clinical decisions are easier in them. The subject with normal LV systolic function is a greater challenge, and care must be taken not to overdiagnose this condition. ■

QUESTIONS & COMMENTS:
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CME/CE QUESTIONS

1. **The 5-year follow-up of the FAME trial showed that fractional flow reserve (FFR) guided as compared to usual percutaneous coronary intervention resulted in:**

   a. more major adverse cardiac events (MACE) in the FFR group.

   b. less MACE in the FFR group.

   c. equivalent MACE in both groups.

   d. more MACE with FFR in men.

2. **Remote monitoring of pulmonary artery pressures in NYHA class III heart failure patients vs usual care resulted in:**

   a. reduced hospitalization.

   b. a 5% incidence of pulmonary embolism.

   c. a 6% procedural complication rate.

   d. All of the above

3. **The best fourth drug for hypertension resistant to three drugs including a diuretic is:**

   a. bisoprolol.

   b. doxazosin.

   c. spironolactone.

   d. minoxidil.

4. **Which of the following statements is correct regarding the diagnosis of left ventricular non-compaction by echocardiography?**

   a. There is considerable intraobserver disagreement.

   b. Further review reduces questionable cases to about 10%.

   c. Other imaging modalities can help resolve questionable cases.

   d. All of the above

5. **In symptomatic patients with left ventricular ejection fraction < 30% and moderate-to-severe mitral regurgitation, which treatments are associated with increased survival?**

   a. Maximum medical therapy

   b. Coronary bypass surgery

   c. Coronary bypass surgery plus mitral valve repair

   d. Both B and C

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.