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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

ABSTRACT & COMMENTARY

Metoprolol Prior to Primary PCI: An Old Drug Gets Some New Data

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

SOURCE: Pizarro G, et al. Long term benefit of early pre-reperfusion metoprolol administration in patients with acute myocardial infarction: Results from the METOCARD-CNIC trial. *J Am Coll Cardiol* 2014; Mar 24. doi: 10.1016/j.jacc.2014.03.014. [Epub ahead of print.]

Beta-blockers have long been considered a cornerstone of therapy for patients with acute myocardial infarction (MI). The optimal timing of beta-blocker administration has been a question, however, and the most recent American College of Cardiology Foundation/American Heart Association guidelines give a class I indication only to the use of oral beta-blockers in the first 24 hours in ST-segment elevation myocardial infarction (STEMI) patients who do not have contraindications. The Effect of Metoprolol in Cardioprotection During an Acute Myocardial Infarction (METOCARD) trial was a multicenter, randomized trial of early intravenous metoprolol administration in hemodynamically stable anterior STEMI patients who were going for primary percutaneous coronary intervention (PCI). Patients assigned to the metoprolol arm received the drug prior to reperfusion. This was based on the hypothesis that early beta-blocker therapy would attenuate reperfusion injury. During the trial, 270 patients were randomized to pre-PCI metoprolol (139 patients) or to no metoprolol (131 patients). All patients without exclusions subsequently received oral metoprolol within 24 hours. The primary endpoint of the trial was infarct size, measured by MRI at 5-7 days. In the initial publication of the trial results, the authors reported that the mean infarct

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size by MRI was lower in the metoprolol group as compared with controls, and that the left ventricular ejection fraction (LVEF) was higher.[1] Interestingly, this effect was shown primarily in patients who had a completely occluded artery prior to intervention (26.7 ± 15.0 g in metoprolol patients vs 34.4 ± 20.0 g in the control group, adjusted difference, –8.13; 95% confidence interval [CI], –13.10 to –3.16; *P* = 0.0024), while no significant effect was revealed in patients with an already open infarct artery at the time of initial angiography (20.7 ± 16.4 g in the metoprolol group vs 22.2 ± 28.3 g in the control group, *P* = 0.6).

The authors now report on the longer-term results of the study, with some intriguing findings. All patients had at least 12 months of clinical follow-up. In addition, 101 patients per group had follow-up MRI at 6 months post-MI. At the 6-month time point, fewer patients in the early metoprolol group had severely depressed LVEF (≤ 35%) compared with the control group (11% vs 27%, *P* = 0.006). With a median follow-up of 2 years, the prespecified endpoint of a composite of death, heart failure admission, reinfarction, and malignant arrhythmia occurred less often in the IV metoprolol group compared with controls (10.8% vs 18.3%; adjusted hazard ratio [HR], 0.55; 95% CI, 0.26-1.04, *P* = 0.065). Heart failure readmission was significantly reduced in the treatment group (2.2% in IV metoprolol vs 6.9% in controls; HR, 0.32; 95% CI, 0.015-0.95; *P* = 0.046). In addition, fewer patients in the intervention group had a class I indication for implantable cardioverter-defibrillator (ICD) at 6 months, compared with controls. The number needed to treat to avoid one ICD indication was 8 (95% CI, 4.5-31; *P* = 0.015). In patients undergoing primary PCI for STEMI, pre-procedure IV metoprolol resulted in higher long-term LVEF, less major adverse effects, fewer readmissions for heart failure, and reduced indications for ICD placement.

■ COMMENTARY

The METOCARD trial was a relatively modest-sized trial, powered to look primarily at a surrogate endpoint — infarct size by MRI. That the long-term secondary clinical endpoints also showed a significant effect is remarkable, especially given that the study was not powered for clinical endpoints. The hypothesized chain of effects here is simple and elegant: Pre-PCI metoprolol reduces reperfusion injury, resulting in decreased in infarct size, which translates downstream into less ventricular remodeling, higher LVEF, and a reduction in clinical events.

It is worth commenting on the differences between this study population and that of prior trials. Much of the tempered enthusiasm for early IV beta-blocker in STEMI comes from the 2005 COMMIT/CCS2 trial, which studied early IV followed by oral metoprolol in a population of 45,852 patients with acute MI.[2] In that trial, the effect of metoprolol on the combined endpoint of death, recurrent MI, or cardiac arrest was neutral. Although recurrent MI and VT were lower in the treated group, this was counterbalanced by a significant increase in the occurrence of early cardiogenic shock. Thus, the class IIa recommendation: "It is reasonable to administer intravenous beta blockers at the time of presentation to patients with STEMI and no contraindications to their use who are hypertensive or have ongoing ischemia." The METOCARD trial was comparatively selective in enrolling patients with anterior MI, who were likely to have a large region of myocardium affected, but excluded patients with SBP < 120 mmHg, AV block, or heart rate < 60, as well as patients with prior infarction. Notably, in the COMMIT trial, certain subgroups were more likely to develop cardiogenic shock, including patients of advanced age, systolic BP < 120 mmHg, presenting heart rate > 110 beats per minute, or increased time since onset of symptoms. With the addition of the METOCARD data to the knowledge base, pre-reperfusion IV beta-blocker appears worth considering for patients who do not fit into these high-risk subgroups. ■

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ABSTRACT & COMMENTARY

Accuracy of ECG Localization of the Culprit Artery in STEMI

By Michael H. Crawford, MD, Editor

SOURCE: Noriega FJ, et al. Influence of the extent of coronary atherosclerotic disease on ST-segment changes induced by ST elevation myocardial infarction. *Am J Cardiol* 2014;113:757-764.

The early ECGs are the mainstay of predicting the culprit coronary artery in ST-segment elevation myocardial infarction (STEMI). However, in patients with multivessel coronary artery disease (CAD), other significant lesions may affect the accuracy of culprit artery prediction. Thus, these investigators from Spain reviewed the clinical records, ECGs, and acute angiograms of 289 patients with STEMI. Patients with left bundle branch block or ventricular-paced rhythm were excluded. On angiography, single vessel disease occurred in 149 patients (51%) and multivessel disease in 140. The patients were divided into three groups based on their culprit artery: 140 left anterior descending (LAD), 118 right coronary artery (RCA), and 31 left circumflex (LCx). With LAD occlusion, the overall pattern of ST segment changes was the same for single vessel and multivessel disease. However, only proximal LAD occlusion exhibited reciprocal ST depression in the inferior leads. With RCA occlusion, the ST segment pattern was similar for single and multivessel disease and included reciprocal ST depression in leads I, aVL, and V_2, but in those with multivessel disease, ST depression often extended to leads $V_{3\text{-}4}$. LCx occlusion resulted in ST elevation in the inferior leads and often V_6 and reciprocal changes in $V_{2\text{-}3}$ or even V_4 in multivessel disease. In fact, ST elevation in V_6 was highly predictive of LCx infarction. The authors concluded that patients with either single vessel or multivessel CAD have similar coronary artery-related ST changes on the admission ECG and that reciprocal changes in LAD occlusion patients predict a proximal culprit lesion.

■ COMMENTARY

Controversy has surrounded the interpretation of reciprocal ST segment changes on admission ECGs in patients with clear STEMI. Three major hypotheses have been advanced to explain them. The first is mirror ECG changes in opposing leads. This electrical phenomenon has been confirmed in animal studies where a single coronary is ligated and is supported by their study since reciprocal changes were present in both single vessel and multivessel disease patients in equal numbers in all three territories. Second is that reciprocal changes represent the ischemic zone around a large infarct that extends into adjacent leads. This study supports this hypothesis, especially in the LAD territory where proximal lesions exhibited reciprocal changes and more distal lesions did not. Presumably the proximal lesions subtended a larger infarct. Finally, there is the hypothesis of ischemia at a distance. This theory supposes that the occlusion of an artery may render an adjacent area with a significant coronary lesion ischemic when collaterals from the culprit vessel are lost. The data in this study did not support this theory as a major mechanism, but cannot totally exclude it either, since this level of analysis was not performed. However, the investigators conclude that reciprocal changes do not require the presence of multivessel disease.

Also of interest is that this study has added another criterion for distinguishing RCA from LCx occlusion as a cause of inferior lead ST elevation. ST elevation in V_6 was 71% sensitive and 83% specific for LCx occlusion. Three other criteria have been proposed in previous studies that demonstrated similar accuracy: 1) ST elevation in lead III > II suggests RCA occlusion; 2) ST depression in lead I supports RCA occlusion; and 3) ST depression in leads V_1, V_2, and V_3 summed divided by the ST elevation summed in leads II, III, and aVF is < 1, or the simpler ST depression in lead V_3 divided by the ST elevation in lead III < 1 supports an RCA lesion. ■

ABSTRACT & COMMENTARY

Beta-Blockers in CAD Patients Undergoing Non-Cardiac Surgery

By Michael H. Crawford, MD, Editor

SOURCES: Andersson C, et al. Association of beta-blocker therapy with risks of adverse cardiovascular events and deaths in patients with ischemic heart disease undergoing noncardiac surgery: A Danish nationwide cohort study. *JAMA Intern Med* 2014;174:336-344.
Whelton SP, Bansal S. Perioperative beta-blockers revisited: Good for what ails you? *JAMA Intern Med* 2014;174:345-346.

Recent controversy has erupted concerning the use of prophylactic beta-blockers in patients with known or suspected coronary artery disease (CAD) undergoing non-cardiac surgery. Thus, these investigators from Stanford University and Denmark analyzed the Danish National Patient Registry for patients with a history of ischemic heart disease who underwent non-cardiac surgery from 2004-09. Two cohorts were identified, those with and without heart failure. Among those without heart failure, patients were further grouped as to whether they had a myocardial infarction (MI) or not. Of the 28,263 surgeries included in this analysis, 7990 (28%) were in patients with heart failure, 12,601 (45%) who had a prior MI, 3964 (14%) who had prior coronary bypass surgery, and 6760 (24%) who had a percutaneous intervention. Orthopedic surgery was most common (40%), and 20% had abdominal surgery and 33% were urgent or emergent. Beta-blockers were prescribed for 41% of the patients. Sophisticated statistical techniques were used: multivariate analysis, propensity matching, and sensitivity analyses. Five percent of the patients experienced a major adverse cardiac or cerebral event (MACCE). Among those with a MACCE, death occurred in 75%, stroke in 3.5%, and MI in 22%. MACCE were more common in the heart failure patients (10% vs 3%). Beta-blocker use overall did not significantly affect outcomes (adjusted MACCE hazard ratio [HR], 0.90; 95% CI, 0.79-1.02). In heart failure patients, beta-blocker use reduced MACCE (HR, 0.78; 95% CI, 0.66-0.91). Among the patients without heart failure, a recent MI (< 2 years) favored beta-blocker therapy (MACCE HR, 0.54; 95% CI, 0.37-0.78). Patients with a history of revascularization did not benefit from beta-blocker therapy. The type of surgery did not influence the results of beta-blocker therapy. The authors concluded that among those with ischemic heart disease, 30-day MACCE was only improved by beta-blockers in those with heart failure or recent MI.

■ COMMENTARY

The concept that excess adrenergic tone during and after surgery could lead to cardiac events in susceptible individuals such as those with ischemic heart disease and that beta-blocker therapy in the perioperative period may abrogate this risk is attractive. Early randomized trials, although small, supported this hypothesis and beta-blockers quickly became the go-to intervention for preventing perioperative MI and death, especially in known CAD patients undergoing moderate-to-high risk surgery. The 2009 European Society of Cardiology (ESC) Guidelines recommend beta-blockers for all CAD patients and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines from the same year recommend beta-blockers in CAD patients undergoing high-risk surgery (class IIa), and if a patient is already on beta-blockers to continue them (class I). Newer studies have shown an increased risk of bradycardia and hypotension with beta-blockers and no consistent reduction in adverse cardiovascular events. This raises the question of whether we have pushed this concept too far (into lower-risk individuals) or whether it is no longer of value with modern anesthesia and surgical care.

This study addresses these issues by analyzing a large registry database from Denmark of patients with ischemic heart disease undergoing non-cardiac surgery. They found that beta-blockers were only beneficial in those with heart failure or recent MI. Neither prior revascularization nor the type of surgery influenced the results. The results make sense in that heart failure and recent MI are strong indications for beta-blockers in all patients. This would support the ACC/AHA class I indications for beta-blockers in those who already have an indication for them, but not the class IIa and ESC recommendation for all CAD patients undergoing major surgery. Also, prior revascularization seems to be protective as beta-blockers were ineffective in these patients.

The strengths of this study are the large population of unselected patients and the sophisticated analyses that were done to offset the non-

randomized study design limitation. These registry studies are becoming more popular and complex as we realize that many clinical questions, such as the ones studied here, will never be subjected to a randomized trial. Other weaknesses of this study are the lack of information on drug doses, compliance, and adverse effects. Also, we don't know how ischemic heart disease and heart failure were diagnosed.

This study adds to the body of literature on this topic and supports the ACC/AHA class I medication for perioperative beta-blockers in those who already have an indication for their use. It does not support beta-blockers for all CAD patients undergoing major surgery, but doesn't preclude the judicious use of them in selected high-risk patients. Selective therapy fits the new mantra of personalized medicine. ■

ABSTRACT & COMMENTARY

Pharmacologic Rate Control in Atrial Fibrillation

By Michael H. Crawford, MD, Editor

SOURCE: Ulimoen SR, et al. Calcium channel blockers improve exercise capacity and reduce N-terminal Pro-B-type natriuretic peptide levels compared with beta-blockers in patients with permanent atrial fibrillation. *Eur Heart J* 2014;35:517-524.

Current guidelines recommend monotherapy with either beta-blockers or rate lowering calcium blockers for heart rate control in patients with permanent atrial fibrillation (AF). However, few comparative data exist on these therapies. Thus, this group of investigators from Norway report on a prespecified substudy of the RATe control in Atrial Fibrillation (RATAF) study of four different once-daily drug regimens for rate control in permanent AF. They included 80 patients with non-valvular, non-ischemic AF without heart failure who after a 2-week drug washout were started on metoprolol succinate 100 mg, diltiazem SR 360 mg, verapamil SR 240 mg, or carvedilol 25 mg once daily in randomly determined 3-week intervals in a blinded fashion. Cardiopulmonary exercise testing and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels were done at baseline and on the last day of each treatment period.

One-quarter of the patients dropped out of the study, half because of adverse effects of the drugs, leaving 60 analyzable patients. All four treatments significantly decreased resting and maximum exercise heart rates compared to baseline. At peak exercise, carvedilol resulted in the lowest heart rate. The mean peak oxygen uptake (peak VO_2) was significantly lower during metoprolol and carvedilol compared to baseline (21 and 20 vs 23 mL/kg/min, $P < 0.001$), whereas diltiazem (24) and verapamil (23) were unchanged. Diltiazem and verapamil treatment significantly reduced NT-proBNP at rest and peak exercise (831 and 897 pg/mL at rest vs 1039) and (985 and 1063 at peak vs 1262 pg/mL). Metoprolol and carvedilol increased these levels (1332 and 1205 at rest vs 1039 pg/mL) and (1634 and 1440 at peak vs 1262 pg/mL). The authors concluded that when diltiazem and verapamil are used for heart rate control in permanent AF, they preserve exercise capacity and reduce NT-proBNP levels, whereas beta-blockers do the opposite.

■ COMMENTARY

Beta-blockers are often considered first-line therapy for heart rate control in AF. In hospitalized patients, especially those with ischemic heart disease or heart failure, this approach makes sense and this study appropriately excluded such patients. Also, in patients with paroxysmal AF, which may be triggered by increases in adrenergic tone, beta-blockers would be a logical first pick. In this study of outpatients with permanent AF, calcium antagonists were equally efficacious as beta-blockers in controlling rest and exercise heart rate, but unlike beta-blockers, they increased exercise performance and reduced NT-proBNP.

Patients with permanent AF may be particularly vulnerable to the negative lusitropic effects of beta-blockers. Since beta-blockers impair early diastolic left ventricular (LV) relaxation, lack of atrial contraction to compensate may explain the raised BNP and reduced exercise tolerance on beta-blockers despite similar heart rate control as calcium blockers. Also, calcium blockers decrease isovolumic LV relaxation time and improve diastolic filling.

There are some limitations to this study. It is small and one-quarter of the enrolled patients dropped out. About half dropped out for reasons unrelated to the study and the rest experienced adverse drug effects, mostly when on beta-blockers. Also, it is unclear whether the drug doses chosen were equivalent. In addition, we have no LV function data to help understand the mechanism of the differences in responses to treatments. Finally, the resting heart rate targets in this study were an aggressive 60-80 beats/minute, whereas the newest studies suggest that heart rates up to 110 beats/minute are acceptable. Whether this more lenient heart rate target would have changed the results of the study is unknown. However, many patients have symptoms with heart rates over 90 beats/minute, so symptom relief has to be considered in treatment goals. At this time, my take away from this study is that unless there are other indications for beta-blockers, calcium antagonists should be tried first in patients with permanent AF who need heart rate control. ■

ABSTRACT & COMMENTARY

Should Dialysis Patients with Atrial Fibrillation Be Treated with Warfarin?

By Edward P. Gerstenfeld, MD

Professor of Medicine, Chief, Cardiac Electrophysiology, University of California, San Francisco

Dr. Gerstenfeld does research for Biosense Webster, Medtronic, and Rhythmia Medical.

SOURCE: Shah M, et al. Warfarin use and the risk for stroke and bleeding in patients with atrial fibrillation undergoing dialysis. *Circulation* 2014;129:1196-1203.

This was a retrospective cohort study from Quebec and Ontario, Canada, examining patients ≥ 65 years of age admitted to a hospital with a diagnosis of atrial fibrillation (AF) between 1998 and 2007. Patients were divided into dialysis patients and non-dialysis patients, as well as warfarin users and nonusers. The association between warfarin use and risk of stroke or bleeding was examined. There were 1626 dialysis patients and 204,210 nondialysis patients included. Among the dialysis patients, 46% were prescribed warfarin. Warfarin use was not associated with a lower risk of stroke in dialysis patients (hazard ratio [HR], 1.14; 95% CI, 0.78-1.67); however, it was associated with a lower stroke risk in nondialysis patients (HR, 0.87; 95% CI, 0.85-0.90). Warfarin use was associated with a significantly increased bleeding risk in dialysis (HR, 1.44; 95% CI, 1.13-1.85) and a slightly increased risk in nondialysis (HR, 1.19; 95% CI, 1.16-1.22) patients. The authors concluded that warfarin therapy in dialysis patients does not reduce stroke risk, but does increase the risk of bleeding.

■ COMMENTARY

Multiple prospective, randomized trials have proven that systemic anticoagulants significantly reduce the stroke risk in patients with AF and stroke risk factors. The oral Factor Xa and direct thrombin inhibitors, which have a fixed daily dose and no requirement for blood testing or dietary restriction, have been a welcome addition to our treatment armamentarium. However, since all these agents are predominantly metabolized in the kidneys, they cannot be used in patients with end-stage renal disease on hemodialysis (HD). Warfarin remains the main therapeutic option for HD patients, although it is well known that they have higher bleeding risk because of platelet dysfunction. In addition, repeated access to AV fistulae is needed, and anticoagulation can lead to persistent bleeding after HD catheter removal. However, HD patients also often have diabetes, congestive heart failure, peripheral vascular disease, and older age, which all increase stroke risk. Therefore, most believe that the benefit of systemic anticoagulation in dialysis patients with AF outweighs the risk. In this study, the authors question this wisdom. Interestingly, warfarin use was not associated with a lower stroke risk in HD patients and was associated with a 44% increased risk of bleeding. Were the included patients truly at high stroke risk? Since 73% of their HD patients had a CHADS2 score ≥ 2, this was in fact a high-risk group. Of note, 85% also had a HAS-BLED score ≥ 3, identifying that these patients also had a high risk of bleeding on anticoagulation.

Should we no longer recommend warfarin for HD

patients with AF? I think it is premature to change practice based on this retrospective, nonrandomized study. However, in an HD patient with relatively lower risk (CHADS2 = 1) where warfarin might be recommended, it is reasonable to reconsider its use. In addition, in patients with high HAS-BLED scores or those who have already experienced bleeding complications, ongoing use of warfarin should be carefully considered after weighing the risks and benefits. A prospective, multicenter study of HD patients with AF is certainly warranted based on these interesting data. ■

ABSTRACT & COMMENTARY

SYMPLICITY HTN-3 Tempers Enthusiasm for Renal Denervation in the United States

Jeffrey Zimmet, MD, PhD

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SOURCE: Bhatt DL, et al. A controlled trial of renal denervation for resistant hypertension. *N Engl J Med* 2014;370:1393-1401.

Resistant hypertension, defined as a systolic blood pressure (BP) that remains above goal despite treatment with at least three complementary antihypertensive agents of different classes at maximally tolerated doses, has become an increasingly common diagnosis in recent years. The prevalence of resistant hypertension is not precisely known, in part due to the use of slightly different definitions, but is widely considered to be at least 10% of the hypertensive population. Renal denervation, an invasive catheter-based procedure involving delivery of radiofrequency energy to the renal arteries, has recently emerged as potential treatment for this problem. Early studies showed great promise, such that the American Heart Association dubbed renal denervation one of the top advances in cardiology in 2012. The Symplicity system from Medtronic was one of the first devices to market, receiving CE mark approval in Europe in 2010, and has been the center of the most rigorous study. The first Symplicity trial (HTN-1), an open-label study of 153 patients undergoing the procedure, recently reported 3-year follow-up data showing reduction in BP of -33/-19 mmHg.[1] Symplicity HTN-2, a randomized, controlled trial of 106 patients, showed a similar magnitude of BP lowering in denervation patients at 6 months, with no significant change in controls.[2]

Bhatt et al now report the results of the Symplicity HTN-3 trial, which sought to overcome the well-recognized shortcomings of earlier studies. To this end, they enrolled 535 adult patients with resistant hypertension from 88 U.S. sites. These patients were randomized in a 2:1 fashion to undergo renal denervation or a sham procedure. Patients who had known secondary hypertension or who were hospitalized more than once in the prior year for hypertensive emergency were excluded, as were patients with anatomic exclusions such as renal artery stenosis. Inclusion criteria were strict, requiring a systolic BP ≥ 160 mmHg at two screening visits, with 2 weeks of ambulatory monitoring also confirming elevated BP. Patient lack of awareness of their treatment assignment was verified by blinding index. Changes to antihypertensive medications during the 6-month follow up were discouraged unless they were considered to be medically necessary. The primary efficacy endpoint was change in office BP at 6 months, with change in ambulatory BP included as a secondary endpoint.

At 6 months, office BPs decreased by a similar amount in the denervation and sham control groups: -14.13 ± 23.93 mmHg in the denervation group and -11.74 ± 25.94 mmHg in the sham group, resulting in a non-significant difference of -2.39 mmHg. Similarly, ambulatory BP decreases were also similar between the intervention and control groups. Further, analysis of diastolic BP, heart rate, renal function, and glycated hemoglobin levels showed no significant effect of renal denervation. The authors concluded that in a blinded, sham controlled study of resistant hypertension patients, renal denervation did not significantly reduce systolic BP after 6 months of follow-up.

■ COMMENTARY

This study contradicts the major findings of the majority of published investigations, and in so doing has already altered the fate of renal denervation therapy in the United States. How do we explain the discrepant data? The use of a sham control along with appropriate and measured

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blinding is certainly the most visible difference, suggesting that some of what was seen in prior investigations could be accounted for by the placebo effect. Sham control procedures are difficult to build into clinical studies, both from an operational and an ethical standpoint, and the authors are to be applauded for using them here. Prior nonrandomized trials did not include a concurrent control group, providing ample opportunities to inflate the observed treatment effect. Regression to the mean has been suggested as another element in this story, accounting for part of the observation that BP lowering in the denervation group was less than was seen in the randomized Symplicity HTN-2 trial,[2] while the decrease in the control group was substantially more.

What else was done well in this study? Prospective BPs were evaluated not only in an office setting, but also on an ambluatory basis. Inclusion criteria were overall more stringent than in prior investigations, and exclusions for anatomic criteria were strictly followed. Overall, medical therapy was excellent, including use of spironolactone in a significant proportion of patients. Significantly, the safety endpoint of the study was met, with a low rate of major adverse events.

The trial sponsor has pointed out that the adequacy of the procedure itself was not confirmed in the study. As Dr. Bhatt has said, "Unfortunately, it is not possible to determine definitively whether this trial demonstrated the failure of renal denervation to significantly reduce blood pressure or if there was a failure to achieve adequate renal denervation in these patients." Given that the system used and training procedures were similar to prior Symplicity studies, this observation does not explain the differing results.

The wide range of responses to renal denervation in the study, expressed as the standard deviations of the change in office systolic BP from baseline, suggests the possibility that renal denervation may be more effective in selected populations with increased sympathetic drive. The Medtronic Symplicity catheter, as well as five competing renal denervation systems, continues to be available for clinical use in more than 80 other countries around the world. For now, however, use in the United States awaits definitive evidence for efficacy. ■

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CME Questions

1. Which of the following supports a proximal LAD STEMI?
   a. ST depression in leads II, III, aVF
   b. ST depression in I and aVL
   c. ST elevation in V6
   d. ST elevation in aVR

2. Recent data on the preoperative use of beta-blockers in CAD patients undergoing non-cardiac surgery suggest benefit in:
   a. heart failure patients.
   b. recent MI patients.
   c. A and B
   d. none of the patients.

3. Warfarin therapy in renal dialysis patients increases the risk of:
   a. stroke.
   b. myocardial infarction.
   c. systemic embolism.
   d. bleeding.

4. Rate lowering calcium blockers as opposed to beta-blockers in permanent atrial fibrillation patients reduce:
   a. stroke risk.
   b. BNP levels.
   c. exercise capacity.
   d. diastolic filling of the left ventricle.

5. A sham controlled study of renal denervation for resistant hypertension showed:
   a. reduced office blood pressure.
   b. reduced average ambulatory blood pressure.
   c. reduced renal function.
   d. None of the above

6. Intravenous metoprolol prior to primary PCI for STEMI showed:
   a. reduced major adverse cardiac events.
   b. reduced LVEF.
   c. increased heart failure admissions.
   d. increased use of ICDs.

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Reader Survey 2014

In an effort to ensure *Clinical Cardiology Alert* is addressing the issues most important to you, we ask that you take a few minutes to complete and return this survey. The result will be used to ensure you are getting the information most important to you.

Instructions: Mark your answers by filling in the appropriate bubbles. Please write in your answers to the open-ended questions in the space provided. Either fax the completed questionnaire to 404-492-5933, or return it in the enclosed postage-paid envelope. The deadline is **July 1, 2014.**

In future issues of *Clinical Cardiology Alert*, would you like to see more or less coverage of the following topics?

	A. more coverage	B. less coverage	C. about the same amount
1. interventional techniques	O A	O B	O C
2. clinical trials	O A	O B	O C
3. prevention	O A	O B	O C
4. pacing	O A	O B	O C
5. ECG	O A	O B	O C
6. ischemic heart disease	O A	O B	O C
7. cardiomyopathy	O A	O B	O C
8. heart failure	O A	O B	O C
9. congenital heart disease	O A	O B	O C
10. cardiac surgery	O A	O B	O C

11. What other topics would you like to see discussed in *Clinical Cardiology Alert*?_____

12. Are the articles in *Clinical Cardiology Alert* written about issues of importance and concern to you?

O A. always O B. most of the time O C. some of the time O D. rarely O E. never

13. What type of information not currently provided in *Clinical Cardiology Alert* would you like to see added?

Please rate your level of satisfaction with the items listed.

	A. excellent	B. good	C. fair	D. poor
14. quality	O A	O B	O C	O D
15. article selections	O A	O B	O C	O D
16. timeliness	O A	O B	O C	O D
17. quality of commentary	O A	O B	O C	O D
18. clearness of abstracts	O A	O B	O C	O D
19. overall value	O A	O B	O C	O D
20. customer service	O A	O B	O C	O D

21. Are the articles in *Clinical Cardiology Alert*:

O A. too short O B. too long O C. about right

22. Please describe your work place.

O A. private practice O B. hospital O C. government institution O D. research

O E. Other (please specify) _____

23. To which other publications or information sources about cardiology do you subscribe?

_____

_____

24. Which publication or information source do you find most useful, and why? _____

_____

25. Please list the top three challenges you face in your job today.

_____

_____

_____

26. What do you like most about *Clinical Cardiology Alert*?

_____

_____

27. What do you like least about *Clinical Cardiology Alert* newsletter?

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_____

28. What issues would you like to see addressed in *Clinical Cardiology Alert*?

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29. Has reading *Clinical Cardiology Alert* changed your clinical practice? If yes, how? _____

_____

Contact information _____

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