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CLINICAL CARDIOLOGY ALERT

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INSIDE

Spinonolactone Post Myocardial Infarction

ABSTRACTS & COMMENTARY

Since aldosterone is extracted by the heart following acute myocardial infarction (MI), this group of investigators from Japan hypothesized that blocking its action may attenuate postinfarction remodeling. Thus, they studied 150 patients admitted for their first acute MI who were successfully treated by percutaneous coronary interventions. They were randomized to receive the mineralocorticoid receptor blocker canrenoate intravenously early after catheterization followed by spironolactone 25 mg/d or no aldosterone blocker. All patients were given enalapril 2.5 mg/d, which was up-titrated to a final mean dose of 9 mg/d, and aspirin. Beta blockers and other cardiovascular drugs were given as needed. Patients who developed creatinine > 2.0 mg/dL or potassium > 5.5 mEq/dL were excluded. At 1 month, all patients underwent repeat cardiac catheterization. Patients who developed significant culprit vessel restenosis were excluded. At the initial catheterization and the subsequent one, blood samples for aldosterone were taken from the aortic root and coronary sinus. Blood samples to measure a procollagen substance were taken from the coronary sinus as a marker of myocardial collagen formation. After the various exclusions, 134 of the initial 150 patients finished the protocol. Exclusions for heart failure, lethal arrhythmias, and restenosis were similar for both groups, but only the aldosterone antagonist group had 2 exclusions for renal failure and 2 for gynecomastia. Left ventricular ejection fraction increased in both groups after 1 month, but the increase was greater in the spironolactone group (7.2% vs 4.5%, $P < .05$). Left ventricular end-diastolic volume (LVEDVI) also increased at 1 month in both groups, but the increase was less in the spironolactone group (4 vs 19 mL/m^2; $P < .001$). After 1 month, aldosterone extraction by the myocardium was significantly reduced in both groups vs baseline but was suppressed more in the spironolactone group (7 vs 18 pg/mL; $P < .0001$). The procollagen marker was increased in both groups at 1 month but was significantly less in the spironolactone group. Also, the change in this marker was correlated with the change in LVEDVI, r = .685. Hayashi and colleagues concluded that spironolactone plus enalapril can prevent left ventricular remodeling better than angiotensin converting enzyme inhibitor

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alone (Hayashi M, et al. *Circulation* 2003;107:2559-1565; Pitt B. *Circulation*. 2003;107:2525-2527).

■ COMMENT BY MICHAEL H. CRAWFORD, MD

This study from Japan extends our knowledge regarding aldosterone antagonists following acute MI. The recent EPHESUS study[1] showed beneficial effects of eplerenone in post-MI heart failure patients, but due to fears of compromising hemodynamics early, it was not started until 3-14 days postinfarction. The modest gains in mortality (15% reduction) and a combined mortality/morbidity end point (13% reduction) in EPHESUS may have been better had eplerenone been started earlier. The Japanese study suggests that aldosterone blockade can be started acutely with an intravenous drug without adverse hemodynamic effects and with demonstrated improvement in left ventricular function at 1 month. The question now is whether we should start giving aldosterone blocking drugs early to all post-MI patients as we do with beta blockers and angiotensin converting enzyme inhibitors.

The first consideration in answering this question is what the patients who were selected by the Japanese study were like. Clearly, they were a sick group. Despite the fact that the average ejection fraction was 46%, 20% were on catecholamine infusions, and 10% had intraaortic balloon pumping. This raises the question of when percutaneous revascularization was done, which is not stated in the paper. What was the symptom onset or door to balloon time? Also, the patients were undertreated by our standards. Only 31% were on beta blockers, and the average dose of carvedilol was 6 mg/d. The average enalapril dose was 9 mg/d. In addition, 70% of the patients were on oral nitrates for unclear reasons: persistent pain, heart failure? Thus, the question becomes, if the patients were revascularized in < 6 hours from symptom onset and were treated with standard doses of beta blockers and ACE inhibitors, what would have been the additive effect of spironolactone? So, at this point, until a larger randomized trial is done with state-of-the-art care, I am reserving aldosterone antagonist usage to severe heart failure patients (classes III-IV).

This study does provide important information concerning the potential mechanism of any beneficial effect of aldosterone antagonists, in that biochemical markers of myocardial fibrosis are suppressed. This may explain the positive effects on remodeling observed. However, other treatments that reduced fibrosis formation in acute myocardial infarction, such as steroids, have led to increased cardiac rupture. So we must be cautious about applauding reduced collagen formation in the infarcted heart. Some is necessary to keep the myocardial wall intact. ■

Reference

1. Pitt B, et al. *N Engl J Med*. 2003;348:1309-1321.

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Restenosis in Drug-Eluting Stents

ABSTRACT & COMMENTARY

Synopsis: The pattern of restenosis in sirolimus-eluting stents is focal and mainly inside the stent.

Source: Colombo A, et al. *Circulation.* 2003;107:2178-2180.

Early trials with short sirolimus-eluting stents (RAVEL) showed no restenosis. A subsequent trial dealing with longer lesions (SIRIUS) showed restenosis in 9%, and most of the restenosis was at the edges or in the gap in the stent and was focal. This report details restenosis following the implantation of sirolimus-eluting stents in 735 lesions in 368 unselected consecutive patients. Mean lesion length was 17 mm, and mean stent length was 28 mm. Angiography was

performed in 24 patients who returned in an average of 4 months with symptoms suggestive of myocardial ischemia; 21 also had positive stress tests. Angiographic restenosis was seen in 11 of these 24 patients in 14 stented segments. The pattern in all 14 was focal and multifocal in 6, and inside the stent. One patient also had stent margin restenosis. Colombo and colleagues concluded that the pattern of restenosis in sirolimus-eluting stents is focal and mainly inside the stent.

■ COMMENT BY MICHAEL H. CRAWFORD, MD

There are several interesting points brought out by this experience by highly skilled operators in unselected patients. First, the incidence of symptom-driven angiographic restenosis is not zero. It was 3% of patients and 2% of lesions treated. However, it is also not 9%, probably because the operators fully covered the lesions. Second, restenosis is focal and largely inside the stent. Possible explanations include underexpansion of the stent, nonuniform coating or release of drug, and complex lesions, which may influence drug delivery. Finally, it is clear that the current drug-eluting stents do not completely eliminate in-stent restenosis as was once hoped. Better stent technology, better delivery systems, or other approaches need to be pursued before we can deliver on the promise to revolutionize revascularization as we know it. ■

Combined Cardiac Resynchronization and Implantable Cardioversion Defibrillator

ABSTRACT & COMMENTARY

Synopsis: Cardiac resynchronization therapy improves quality of life and New York Heart Association Functional class in patients with moderate-to-severe heart failure, wide QRS durations, and indications for an ICD.

Source: Young JB, et al. For The Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) Trial Investigators. *JAMA*. 2003;289:2685-2694.

Young and colleagues report a multicenter trial involving the use of cardiac resynchronization therapy (CRT) in patients with accepted indications for an implantable cardioverter defibrillator (ICD). In order to be eligible for the trial, patients had to have a standard indication for ICD placement. The trial enrolled patients with class II, III, and IV heart failure, but in this report only patients with class III and IV heart failure are discussed. The left ventricular ejection fraction had to be ≤ 0.35 and the QRS duration > 130 msec. Patients also had to have a left ventricular end diastolic diameter of ≥ 55 mm, and their medical therapy should have been stable for 1 month prior to enrollment.

In all patients who agreed to participate, an implant was attempted with a Medtronic biventricular ICD. Patients in whom the implant was unsuccessful, usually because of failure to place the coronary sinus lead, are not included in this study. After implant, patients underwent a cardiopulmonary exercise test to measure peak oxygen consumption and exercise duration. After completion of the exercise test, patients were randomized to receive active CRT or just optimal medical therapy and tachyarrhythmia therapy, but without CRT (control group). Most patients in the CRT group were programmed to track native atrial activity with biventricular pacing. Patients in the control group were programmed to a mode in which pacing was not required unless the native rate fell to less than 35 bpm. Follow-up evaluations were performed at 1, 3, and 6 months after enrollment. The 3 primary efficacy end points were changes in New York Heart Association functional class, quality-of-life score and 6-minute walk distance. Secondary end points included peak oxygen consumption, treadmill exercise duration, changes in left ventricular ejection fraction, end systolic and end diastolic volumes, and end diastolic dimensions.

All end points were analyzed according to an intention-to-treat principle. This paper primarily presents data at the 6-month time point.

A total of 369 patients were randomized in the trial. The mean age was about 67 years in both groups. Eighty-nine percent of the patients were New York Heart Association Functional class III, and 11% had New York Heart Association Functional class IV. The average QRS duration at baseline was 163 msec, with a mean ejection fraction of 24%. The indication for the ICD was cardiac arrest in 10%, sustained ventricular tachycardia in 40%, and induction of ventricular fibrillation or ventricular tachycardia at electrophysiologic study in the remainder. ACE inhibitors or an angiotensin blocking agent were taken by 90% of the patients. Sixty percent of the patients were on beta blockers. Ninety-four percent of the patients were on diuretics.

There was a slight imbalance in the form of heart disease in the 2 groups. In the control group, 76% of the

patients had ischemic heart disease, whereas in the CRT group only 64% had ischemic heart disease.

During the course of the study, 14 patients crossed over from the control group to CRT before 6 months. Ten patients in the CRT group crossed over to standard therapy because of either lead dislodgement, diaphragmatic stimulation, or programming errors.

Both groups showed some improvement in quality of life. However, the improvement was significantly higher in the CRT group. There was also a significantly greater median decrease in New York Heart Association functional class in the CRT group compared to the control group. However, there was no significant difference in the 6-minute walk test distance change between the 2 groups. The secondary end points also showed a trend toward favoring CRT. Treadmill exercise duration improved in patients on CRT, and CRT patients achieved a higher median increase in peak oxygen consumption. There were nonsignificant trends toward improvement in left ventricular volumes but no change in ejection fraction.

During the 6 months of randomization, 26% of patients in the control group and 22% of the patients in the CRT group experienced at least 1 spontaneous episode of ventricular tachycardia or fibrillation. There were 15 deaths in the control group and 14 deaths in the CRT group during the 6-month follow-up. Three of the deaths in each group were classified as sudden deaths. During the 6-month follow-up, there was no difference in the probability of hospitalization for worsening heart failure or death from any cause (25% control vs 25.7% CRT). The risk of death or all cause hospitalization was 48.3% in the control group vs 47.4% in the CRT group.

Young et al conclude that cardiac resynchronization therapy improves quality of life and New York Heart Association Functional class in patients with moderate-to-severe heart failure, wide QRS durations, and indications for an ICD.

■ COMMENT BY JOHN DiMARCO, MD, PhD

Cardiac resynchronization therapy using biventricular pacing has now become established as an effective therapy for patients with advanced heart failure, left ventricular dysfunction, and prolonged QRS durations. Within the last year, devices capable of providing both biventricular pacing and defibrillation have been released for general use. This paper confirms that combining ICD therapy with resynchronization therapy is feasible. However, the magnitude of changes in functional capacity are less than have been seen in earlier studies on biventricular pacing.

There are several possible reasons for the somewhat lesser degree of benefits seen with CRT in this paper. It must be remembered that the primary indication for device implantation in these patients was for treating their arrhythmias. In earlier CRT trials, the primary indication for device implant was heart failure, and CRT was an intervention used to reverse or slow a steady decline in functional status. Not all of the patients in this trial had recently unstable congestive heart failure. In such patients who were recently stable on optimal medical therapy, it will be harder to show any beneficial effects of device therapy. This will be increasingly true in the future as medical therapy for heart failure improves. Young et al were also careful to minimize any adverse effect of standard ICD implant. The probability of a patient being treated with pacing from the right ventricle only was minimized by careful programming. Therefore, any deleterious effects from RV pacing over and above those associated with the patient's intrinsic conduction defect were not encountered.

Based on data from this study and from preliminary data from the COMPANION Trial, it seems reasonable to use a cardiac resynchronization device in patients who will receive an ICD and either have a bundle branch block at baseline or will require ventricular pacing. Combined therapy to manage patients' arrhythmias with the ICD functions of the device and heart failure with CRT seems to be the strategy most likely to produce optimal results. ■

AMIOVIRT Trial

ABSTRACT & COMMENTARY

Synopsis: Data do not support early implantation of prophylactic ICDs in patients with nonischemic cardiomyopathy.

Source: Strickberger SA, et al. For the AMIOVIRT Investigators. *J Am Coll Cardiol*. 2003;41:1707-1712.

In this paper, strickberger and colleagues report the results of the Amiodarone Versus Implantable Cardioverter-Defibrillator: Randomized Trial in Patients With Nonischemic Dilated Cardiomyopathy and Asymptomatic Nonsustained Ventricular Tachycardia (AMIOVIRT). Patients could be included in this study if they had no evidence for, or only minor, coronary artery disease, an ejection fraction ≤ 0.35, asymptomatic nonsustained VT, and were older than 18. Study enrollment began in 1996. Optimal medical therapy according to current guidelines was encouraged in both groups.

Patients were randomized to receive either amiodarone or an ICD. The primary end point was total mortality. Secondary end points included sudden cardiac death, nonsudden cardiac death, syncope, arrhythmia-free survival, quality of life, and cost.

One hundred three patients were enrolled in the study, with 52 randomized to receive amiodarone and 51 randomized to receive an ICD. The mean age was 59 years. The mean left ventricular ejection fraction was 0.22. Symptoms related to their cardiomyopathy had been present for approximately 3 years. Although the study had a planned enrollment of 438 patients, the study was stopped after the first interim analysis. The event rates in the study were lower than expected, with no significant difference between the groups.

At the time the study was stopped, the mean follow-up was 2.0 ± 1.3 years and there were 52 patients randomized to amiodarone and 51 randomized to receive an ICD. The 1- and 3-year survival rates among the amiodarone-treated patients were 90% and 80%, respectively, compared with 96% and 88%, respectively, among the 51 patients treated with an ICD. There was no difference in the distribution of sudden vs nonsudden cardiac deaths between the 2 groups.

Arrhythmia-free survival was calculated using symptomatic arrhythmias in the amiodarone group and ICD-treated arrhythmias in the ICD group. The arrhythmia-free survival rates among the amiodarone-treated patients were 82% and 73% at 1 and 3 years vs 78% and 63% among the patients treated with an ICD.

There was no difference in 2 measures of quality of life between the 2 groups. Cost of medical therapy was significantly different in a subset of patients in whom these data were collected. The cost in the first year after entry into the study was $8,879 ± $27,614 in the amiodarone group compared with $22,079 ± $22,039 in the ICD group.

Amiodarone therapy was discontinued in 25 of 52 patients, a mean of 17.8 ± 13 months after initiation of therapy. The reasons that led to amiodarone discontinuation are not specified in the report. In the ICD group, 11 of 51 patients eventually received amiodarone for treatment of either frequent ventricular arrhythmias or atrial arrhythmias.

Strickberger et al conclude that their data do not support early implantation of prophylactic ICDs in patients with nonischemic cardiomyopathy. Amiodarone appears to have a modest effect on arrhythmia frequency. Empiric therapy with amiodarone, therefore, seems a reasonable first step in previously asymptomatic patients.

■ COMMENT BY JOHN DiMARCO, MD, PhD

A number of trials have now shown benefits with ICD therapy in patients with ischemic cardiomyopathy and left ventricular dysfunction. In the original Multicenter Automatic Defibrillator Implantation Trial (MADIT), patients with an ejection fraction < 0.35, nonsustained VT, and inducible VT showed benefit after ICD implant as compared to "conventional medical therapy." In MADIT II, electrophysiologic studies were not included, and a benefit from ICD therapy was shown in patients with ischemic cardiomyopathy and ejection fractions ≤ 0.30. Although benefit in patients with nonischemic dilated cardiomyopathy with a prior history of cardiac arrest was demonstrated in both the Antiarrhythmics vs Implantable Defibrillators Trial and the Canadian Implantable Defibrillator Study, the only previous trial, the Cardiomyopathy Trial, had reported no benefit in patients with nonischemic dilated cardiomyopathy.

When interpreting this trial, it is important to note the unexpectedly good outcome in both groups. Therapy for nonischemic dilated cardiomyopathy has changed significantly in the last decade. In this study, high proportions of patients received angiotensin converting enzyme inhibitors but relatively modest proportions of patients received beta blockers and spironolactone, 2 agents recently shown to improve survival significantly in patients with heart failure. As therapy has improved and the overall mortality has dropped, it has become more and more difficult to define a "high risk" group that is likely to benefit from an intervention directed at arrhythmias.

It must be recognized that this was a relatively small trial that was discontinued early because of futility. Two much larger studies, the DEFINITE Trial and the SCD-HeFT Trial hopefully allow us to better assess the role of ICD therapy for primary prevention in patients with primary cardiomyopathy. However, until the results of those trials become available, ICD implantation in these patients without prior symptomatic arrhythmias cannot be recommended. ■

Vasopressin for Vasodilatory Shock

ABSTRACT & COMMENTARY

Synopsis: The combined infusion of AVP and NE was superior to NE alone in catecholamine-resistant vasodilatory shock.

Source: Dunser MW, et al. *Circulation*. 2003;107: 2313-2319.

Vasodilatory shock frequently complicates sepsis and can occur after cardiopulmonary bypass

requiring surgery. The value of arginine vasopressin (AVP) vs norepinephrine (NE) alone or in combination is not fully understood. Thus, Dunser and colleagues randomized 48 patients with mean arterial pressure (MAP) < 70 mm Hg despite volume resuscitation and NE requirements > 0.5 mg/kg/min to continued NE or the addition of AVP at a constant infusion of 4 U/h. In the NE group, when the NE infusion to keep MAP > 70 mm Hg exceeded 2.26 mg/kg/h, NE was discontinued and AVP was infused. In both groups, if cardiac index remained < 2 L/min/m^2, then a milrinone infusion was added. The primary end point was the difference in hemodynamic parameters between the groups at 48 hours. Secondary end points focused on single organ function, such as gastric tonometry. The patient groups were well matched: about 60% had inflammatory or septic shock and 40% had postcardiotomy shock. AVP was associated with higher MAP and cardiac index and lower heart rate and NE requirements vs NE. New tachyarrhythmias were less with AVP vs NE (8% vs 54%; *P* < .001). Acid base status was improved more by AVP, but platelet counts were lower and bilirubin levels were higher on AVP. There was no difference in myocardial, skin, or intestinal ischemic events. In both groups, 75% of the patients also received a milrinone infusion. Almost all patients in both groups were on hemofiltration. Overall mortality was 70% for both groups. Dunser et al concluded that the combined infusion of AVP and NE was superior to NE alone in catecholamine-resistant vasodilatory shock.

■ COMMENT BY MICHAEL H. CRAWFORD, MD

Previous small studies have shown beneficial hemodynamic effects of AVP in vasodilatory shock. AVP is a potent constrictor of peripheral resistance vessels and raises MAP even in patients no longer responsive to catecholamines. The receptors for AVP seem to be preserved during hypoxia and acidosis, unlike the catecholamine receptors. Based upon this limited information, critical care specialists have been using AVP for shock patients, but little is known about specific organ perfusion and adverse effects in the shock patient.

This study showed that myocardial performance was enhanced perhaps because the use of AVP allowed NE to be down-titrated. Alternatively, the increase in MAP may have increased coronary blood flow. Also, there were less tachyarrhythmias in the AVP group. Whether AVP has a positive inotropic effect as has been shown in animals is difficult to determine in the clinical setting. Only 3 patients developed myocardial ischemia or infarction in this study, but all were in the NE group.

Ischemic skin injury occurred in about one-quarter of patients but was similar in both groups. Tonometric assessment of the gastric mucosa showed improved perfusion in the AVP group. One patient in the NE group died of intestinal ischemia. However, bilirubin was higher in the AVP group, which may indicate that hepatic blood flow was reduced. Finally, platelet counts were lower in the AVP group.

Clearly, this was a sick group of patients who were not doing well on NE infusions and 75% of whom required a continuous milrinone infusion. Although many parameters of organ perfusion appeared better on AVP and significant complications were less, the overall mortality was no different between the 2 groups and was high (70%). This trial was not powered for mortality and major morbidity differences, but the results are encouraging enough to support the use of AVP in selected patients until a larger trial is conducted. ■

New Hypertension Guidelines: JNC-7

ABSTRACT & COMMENTARY

Synopsis: A new classification of blood pressure in adults is suggested, with normal blood pressure (BP) as < 120 mm Hg and < 80 mm Hg.

Source: Chobanian AV, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA*. 2003;289:2560-2571.

The long-awaited jnc-7 report was recently published in summary form; a more comprehensive manuscript will be forthcoming. JNC-7 takes into account many of the randomized controlled trials dealing with hypertension (HBP) published over the past few years, and thus, is very much up to date. Some highlights of the report are as follows:

1. A new classification of blood pressure in adults is suggested, with normal blood pressure (BP) as < 120 mm Hg and < 80 mm Hg. A new category, prehypertension, is defined as systolic pressure (SBP) 120-139 or diastolic (DBP) 80-89. In this category, pharmacologic treatment is indicated only if there is a "compelling indication," such as diabetes, vascular disease, or kidney disease. Stage 1 hypertension is now defined as SBP 140-159 or DBP 90-99, and stage 2 hypertension is SBP > 160 or DBP > 100. Drug treatment is mandated for both stages, with combination therapy more likely to be nec-

essary in stage 2.

2. A thiazide-type diuretic is recommended as the first drug to be used except in patients with hyponaturemia or gout. Furthermore, a diuretic should be part of any multidrug combination.

3. The prevalence of hypertension is 50 million individuals in the United States. JNC-7 emphasizes the marked prevalence of HBP in the elderly; data from the Framingham Heart Study suggests that individuals with a normal BP at age 50-60 have a 90% lifetime risk of developing HBP. Hypertension is the most common primary diagnosis in the United States, with only modest gains in awareness, treatment, and control of BP over the past 25 years. Recent data suggest that only one-third of the hypertensive population is under adequate control (NHANES survey).

4. Recent clinical trials indicate that antihypertensive treatment can reduce stroke incidence by 35-40%, acute myocardial infarction by 20-25%, and more than a 50% reduction in new onset heart failure.

5. There was an emphasis on how to accurately determine BP measurements in the outpatient setting, (2 measurements in subjects seated quietly for at least 5 minutes).

6. JNC-7 recommends self-measurement of BP at home to determine response to therapy, confirm adherence, etc. The goals of antihypertensive therapy are stated as "the reduction of cardiovascular and renal morbidity and mortality." JNC-7 emphasizes that the "primary focus should be on achieving the systolic BP goal." A generic target for BP of < 140/90 mm Hg is associated with decreased cardiovascular complications. In high-risk patients, such as those with diabetes or renal disease, the goal is < 130-80 mm Hg, which Framingham considers to be the optimal blood pressure.

7. Healthy lifestyles are strongly emphasized throughout the report, including weight control; adoption of the DASH diet, with increased intake of potassium and calcium rich foods, fruits and vegetables; moderation of alcohol consumption to < 2 drinks a day; and regular physical activity.

8. Pharmacologic therapy is simplified, with the admonition that a thiazide-type diuretic should be the basis of therapy, followed by any of the major classes of antihypertensive drugs. These include angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), beta blockers, and calcium channel blockers. Virtually no mention is made of outlier drugs for BP control in JNC-7 (eg, alpha blockers or CNS active drugs, such as clonidine). Chobanian and associates strongly emphasize that the majority of patients with HBP will require 2 or more medications to achieve goals. Furthermore, they recommend that drugs from different classes be used in polypharmacy. Therapy may be initiated with 2 drugs, particularly if baseline blood pressure is high and/or the subject is at increased vascular risk. Follow-up should occur monthly after initiation, and more frequently in stage 2 patients. When BP is at goal and stable, follow-up visits are recommended at 3-6 month intervals. Co-morbidities or high-risk conditions are emphasized, requiring specific choices of drug classes. These are quite obvious and include beta blockers for individuals with co-existing ischemic heart disease and an ACE inhibitor for those with heart failure, acute coronary syndromes, or postmyocardial infarction. Aldosterone antagonists are also recommended in heart failure. Heart failure patients with hypertension should have "fastidious BP and cholesterol control," with the mainstay of hypertensive therapy being an ACE inhibitor and beta blocker. ARBs and aldosterone blockers, along with loop diuretics, are also appropriate for late-stage heart failure. Diabetics should be routinely treated with 2 or more drugs, with an optimal blood pressure target. Physicians need to keep in mind that ACE inhibitors and ARBs favorably affect progression of diabetic renal disease.

9. A newly recognized high-risk group is individuals with chronic kidney disease, as manifest by creatinine of > 1.3 in women and > 1.5 in men or a GFR of < 60 mLs/m^2. Such individuals should be targeted for a BP < 130/80 mm Hg. Again, drugs acting on the renin angiotensin system (RAS) are suggested. Chobanian et al accept a modest rise in serum creatinine of up to one-third over baseline if and when an ACE or an ARB is used.

10. Emphasis is given to obesity and the metabolic syndrome, stressing the high-risk aspects of these increasingly common conditions. Hypertensive control in the elderly is also stressed. JNC-7 recommends starting with smaller drug doses in the elderly, watching for postural hypotension, while stressing control of systolic BP.

The conclusion of the report deals with how to best motivate patients with hypertension, stressing individual engagement in the process with a "patient-centered strategy and an estimation of the time needed to achieve the goal" established by the patient and the physician. Chobanian et al stress physician-stimulated motivation and empathy as influencing adherence to therapy. A final comment highlights population increases in consumption of saturated fat and salt and decreases in physical activity as being partly responsible for the epidemic of overweight and obesity, contributing to hypertension and related conditions.

■ COMMENT BY JONATHAN ABRAMS, MD

In the heels of many recent well-performed trials in hypertension, including ALLHAT, LIFE, HOPE, RENAAL, PROGRESS, UKPDS, ANBP2, as well the recent guidelines for treatment of hypertension in African-Americans and numerous algorithms and guidelines, there are few to no surprises in the official JNC-7 report. There has been considerable noise and confusion in the hypertension world for many years, particularly relating to the controversy over the safety of thiazide diuretics and the concern raised by some that calcium channel blockers may actually induce adverse events. The premature discontinuation of the alpha blocker arm in ALLHAT raised concerns that there may be unproven adverse effects of some classes of drugs. JNC-7 does not favor any single class of drugs, and even its recommendations for initiating therapy with a thiazide is not revolutionary. These drugs have been the cornerstone of hypertension guidelines for years, although they have fallen out of favor, in part to the aggressive marketing of the newer classes of agents, such as drugs that interfere with the RAS system and the calcium channel blockers. I view the most important aspects of this report to be as follows:

1. The emphasis on the concept that lower is better. Blood pressure control should be analogous to our approach to LDL cholesterol, with more aggressive targets for patients at the highest risk. Similar to the level of < 100 mg/dL for LDL cholesterol, the goal of < 120/80 in high-risk hypertensives makes sense and should be followed by all physicians who treat patients with HBP.

2. The emphasis that systolic BP is the most important target, in spite of previous teaching that treatment of diastolic hypertension is the gold standard. Most of the morbidity and mortality from cardiovascular disease, including stroke, is related to systolic hypertension, with a wide pulse pressure with only normal or mild elevations of diastolic pressure. Health care personnel must understand that a systolic BP of 150-160 mm Hg is not benign, but actually is a hazardous level requiring therapy.

3. Polypharmacy or multiple drug combinations should be the rule rather than the exception. It is important for physicians to initiate therapy with low doses of 2 different classes of drugs or be prepared to add a second and even a third drug class to achieve optimal control, rather than pushing the doses of drugs to high and potentially toxic levels. A diuretic should always be included with ACE inhibitor or ARB therapy. The focus on risk stratification is useful and is comparable to the NCEP ATPIII guidelines for lipids. Highest-risk patients are those with established vascular disease, diabetes, metabolic syndrome, or mild renal disease (proteinuria, elevated creatinine). The target BP in all of these conditions should be the "optimal" blood pressure of < 120/80 mm Hg. Hypertension may not be the sexiest subject for cardiologists and primary care physicians, but it is truly an important condition requiring commitment and vigilance. Highly effective drugs are available, which decrease events and save lives. JNC-7 is an effective road map for those who are not yet on board. ■

CME Questions

Please review the text, answer the following questions, check your answers against the key, and then review the materials again regarding any questions answered incorrectly.

1. Which of the following is most correct concerning restenosis in sirolimus-eluting coronary stents?
   a. The incidence is almost zero.
   b. It is usually focal and inside the stent.
   c. It is almost always at the stent edge.
   d. It is diffuse but mild.

2. Spironolactone administered early post-MI:
   a. improves LV remodeling.
   b. decreases aldosterone uptake in the myocardium.
   c. decreases in-hospital mortality.
   d. a and b

3. The most important new recommendation in JNC-7 is:
   a. hypertension is a risk factor for CAD.
   b. hypertension needs to be better controlled.
   c. to lower target blood pressures.
   d. diuretics are important agents.

4. Biventricular pacing (cardiac resynchronization) should be considered in patients undergoing ICD placement if they have:
   a. moderate-to-severe heart failure.
   b. reduced systolic LV performance.
   c. a wide QRS.
   d. All of the above

5. In patients with nonischemic dilated cardiomyopathy, an ICD should be placed if they have:
   a. a wide QRS.
   b. an LVEF < .35.
   c. symptomatic ventricular arrhythmias.
   d. All of the above

6. Arginine vasopressin use in the catecholamine-resistant vasodilatory shock patient results in:
   a. improved hemodynamics.
   b. less tachyarrhythmias.
   c. reduced platelet levels.
   d. All of the above

Answers: 1(b); 2(d); 3(c); 4(d); 5(c); 6(d)