



Insight

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## Cardiology News



## Prevention of Cardiovascular Events in Hypertension and CAD & Management of Hypertension in HF of Ischemic origin

### 1. Prevention of Cardiovascular Events in Patients With Hypertension and CAD

#### 1.1. Antihypertensive Drugs for the Secondary Prevention of Cardiovascular Events in Patients With CAD

Meta-analyses of antihypertensive trials have demonstrated that BP lowering is more important than the particular drug class used in the primary prevention of the complications of hypertension, including IHD. Combination antihypertensive drug therapy is typically needed to achieve and to sustain effective long-term BP control. Thus, there is no evidence to support initiating therapy with any one antihypertensive drug class over another for the primary prevention of IHD. In contrast, for secondary protection in individuals with underlying comorbid illnesses such as IHD, CKD, or recurrent stroke, not all drug classes have been proven to confer optimal or even the same level of benefit.

Whether there are class effects for antihypertensive drugs and whether each drug should be considered individually on the basis of trial results are not clearly known. It is reasonable to assume that there are class effects for thiazide and thiazide type diuretics, ACE inhibitors, and ARBs, which have a high degree of homogeneity in both their mechanisms of action and side effects. There are major pharmacological differences between drugs within more heterogeneous classes of agents such as the  $\beta$ -blockers and CCBs. Finally, the most recent trials suggest that combining ACE inhibitors and ARBs is not

beneficial for the secondary prevention of cardiovascular events, whereas combinations of renin-angiotensin blocking agents with thiazide diuretics or with CCBs show important clinical benefits.

##### 1.1.1. Thiazide and Thiazide-Type Diuretics

Thiazide diuretics and the thiazide-type diuretics chlorthalidone and indapamide are highly effective in reducing BP and preventing cerebrovascular events. There have been concerns about whether thiazide-induced hyperglycemia and diabetes mellitus contribute to long-term IHD, but this does not seem to be the case.

##### 1.1.2. $\beta$ -Blockers

$\beta$ -Blockers make up a heterogeneous class of antihypertensive drugs with differing effects on resistance vessels and on cardiac conduction and contractility.  $\beta$ -Blocker administration remains the standard of care in patients with angina pectoris, those who have had an MI, and those who have LV dysfunction with or without symptoms of HF unless contraindicated. The  $\beta$ -blockers carvedilol, metoprolol, and bisoprolol have been shown to improve outcomes in patients with HF.

##### 1.1.3. ACE Inhibitors

The ACE inhibitors are effective in reducing initial IHD events and are recommended for consideration in all patients after MI. They are proven to prevent and improve both HF and the progression of CKD. When combined with thiazide diuretics, ACE inhibitors reduce the



incidence of recurrent stroke. Major trials have addressed the use of ACE inhibitors in patients with IHD but without HF or known significant LV systolic impairment.

Investigators concluded that ACE inhibitors might not be necessary as routine therapy in low-risk IHD patients with preserved LV function, especially those who have received intensive treatment with revascularization and lipid-lowering agents. Two large studies in high-cardiovascular-risk patients (HOPE and EUROPA) showed cardiovascular protective effects by ACE inhibitors, and 1 study in low-cardiovascular-risk patients (PEACE) did not. The Ongoing Telmisartan Alone and In Combination with Ramipril Global Endpoint Trial (ONTARGET) trial randomized 25,620 patients, of whom 74% had a history of CAD, to the ACE inhibitor ramipril (10 mg/d), the ARB telmisartan (80 mg/d), or the combination of these 2 drugs. After a median follow-up of 4.7 years, there was no difference in the primary outcome of cardiovascular death, nonfatal MI, nonfatal stroke, and hospitalization for HF among the 3 groups. In the combination treatment group, there was an increased risk of hypotensive symptoms, syncope and renal dysfunction compared with those in the ramipril group. The investigators concluded that ramipril and telmisartan had similar benefits but that the combination of the ACE inhibitor and ARB in this high-cardiovascular-risk group was associated with more side effects and no increase in benefit.

#### 1.1.4. Angiotensin Receptor Blockers

Several ARBs have been shown to reduce the incidence or severity of IHD events, the progression of renal disease in type 2 diabetes mellitus, and cerebrovascular events. ARBs are often considered to be an alternative therapy in individuals with cardiovascular disease who are intolerant of ACE inhibitors. In the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) study, protection against a composite of cardiovascular events that included MI and HF was similar to that observed for the CCB amlodipine. However, there were important differences in BP control in the early stages of the VALUE trial (a significant BP difference in favor of amlodipine) that may have confounded outcomes for MI and especially stroke.

Beneficial cardiovascular outcomes were not shown in the Optimal Trial in Myocardial Infarction With the Angiotensin II Antagonist Losartan (OPTIMAAL). The lack of benefit

may have been attributable to inadequate doses of losartan. In the Valsartan in Acute Myocardial Infarction Trial (VALIANT), the ARB valsartan had effects similar to those of the ACE inhibitor captopril in reducing cardiovascular event end points. The combination of the ARB with the ACE inhibitor yielded an increase in adverse events with no incremental benefit.

In the Telmisartan Randomised Assessment Study in ACE Intolerant Subjects With Cardiovascular Disease (TRANSCEND), 5,296 high-risk patients, of whom 75% had CAD, were randomized to telmisartan (80 mg daily) or placebo for a median duration of 4.7 years. The mean BP in the telmisartan group was 4.0/2.2 mm Hg lower than placebo. The primary outcome of cardiovascular death, nonfatal MI, nonfatal stroke, and hospitalization for HF occurred in 15.7% of the telmisartan group and 17.0% of the placebo group. The tolerability of telmisartan was similar to that of placebo. The investigators concluded that telmisartan had modest benefits on the composite outcome end point of cardiovascular death, MI, and stroke and was well tolerated.

#### 1.1.5. Aldosterone Antagonists

The aldosterone antagonists spironolactone and eplerenone lower BP alone or when added to other antihypertensive agents and have a protective effects in patients with chronic and advanced HF, in patients with LV dysfunction after MI, and in patients with chronic HF and mild symptoms.

#### 1.1.6. Calcium Channel Blockers

CCBs form a heterogeneous class of agents that lower BP but have differing effects on cardiac conduction and myocardial contractility. In Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), the primary prevention of cardiovascular events with the dihydropyridine CCB amlodipine was equivalent to that produced by the diuretic chlorthalidone or the ACE inhibitor lisinopril, and superiority over a  $\beta$ -blocker was claimed in Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT). Primary protection with verapamil-based therapy was shown to be similar to that of a diuretic (hydrochlorothiazide) or a  $\beta$ -blocker (atenolol) in the Controlled Onset Verapamil Investigation of Cardiovascular End Points (CONVINCE) and International Verapamil-Trandolapril Study (INVEST). In the Nordic



Diltiazem (NORDIL) study, overall cardiovascular event rates were similar for diltiazem and a combination of diuretic and  $\beta$ -blocker. Thus, CCBs are alternatives to  $\beta$ -blockers in the treatment of angina pectoris but are not recommended for secondary cardiac protection because of the relative lack of benefit of this class in preventing HF, particularly compared with ACE inhibitors or ARBs.

### 1.1.7. Direct Renin Inhibitors

The direct renin inhibitor aliskiren lowers BP alone or when added to other antihypertensive agents but has not been shown to have protective effects in patients with CVD, including HF. The general recommendation at present is to avoid the use of aliskiren in combination with another renin-angiotensin blocking agents in patients with hypertension for the primary prevention of CVD.

## 2. Management of Hypertension in HF of Ischemic Origin

Although guidelines from the ACC and the AHA exist for the treatment of chronic HF, evidence on which to base guidelines for the treatment of hypertension in patients with HF of ischemic origin is limited. On the basis of information from the Acute Decompensated Heart Failure National Registry (ADHERE),  $\approx 75\%$  of patients hospitalized with HF had hypertension, with most having SBPs  $>140$  mm Hg.

### 2.1. Hypertension and HF

Most patients with HF have arterial hypertension. Not only is hypertension an important concomitant disorder, but it also contributes to the pathogenesis of both HF with reduced ejection fraction and HF with preserved ejection fraction. Hypertension is a major risk factor for IHD and can lead to the development of HF by causing LV hypertrophy, impaired cardiac myocyte contractility, ventricular chamber remodeling, and eventually ventricular dysfunction.

### 2.2. Demographics

Elevated levels of DBP and especially SBP are major risk factors for the development of HF, and long-term treatment of both systolic and diastolic hypertension has been shown to reduce the risk of HF. Patients presenting with HF are more likely to be older and hypertensive, and more than half have a normal LV ejection fraction. However, recent randomized trials have probably underestimated the

contribution of hypertension to the development and progression of HF, possibly because elderly patients often are not included in clinical trials of HF. Of note, HF symptoms are rare in hypertensive individuals whose BP is well controlled at goal and who have not sustained an MI.

### 2.3. Hypertension and HF Pathophysiology

Initially, concentric hypertrophy of the LV compensates for pressure overload and normalizes systolic wall stress. The compensatory response may transition to HF with progressive contractile dysfunction. In the second stage, CAD causes myocardial ischemia or MI, which results in HF. BP falls as HF develops, so the contribution of hypertension to the HF syndrome may be underestimated. Traditionally, an MI has been viewed as an obligatory event in the transition to depressed systolic function. Because MI occurs in 16% of those who develop depressed LV ejection fraction compared with 3% of those who do not, it is an important risk factor. However, there must be other mechanisms because increased LV mass remains associated with the development of depressed LV ejection fraction even in patients free of clinically manifest CAD, including MI. With antihypertensive treatment, the incidence of LV hypertrophy is reduced by 35%, and the development of HF is reduced by 52%.

### 2.4. CAD and Acute HF

Ischemia may trigger acute pulmonary edema. The majority of patients with flash pulmonary edema have preserved systolic function. These patients are generally elderly and have severe CAD, typically with 1 occluded vessel and a severely stenosed coronary artery supplying collateral flow.

Patients with preserved systolic function and LV hypertrophy are particularly susceptible to this type of episode because of their reduced ventricular distensibility, in which small changes in ventricular volume status can lead to large changes in filling pressures. This abnormal diastolic pressure–volume relationship may also explain why these patients frequently improve quickly with diuresis and lowering of BP. In terms of management, the same principles apply when this occurs in the setting of ischemic cardiomyopathy as in ACS.

### 2.5. Therapeutic Strategies

The therapeutic goals in patients presenting with HF are to

reverse hemodynamic abnormalities, to relieve symptoms, and to initiate treatments that will decrease disease progression and improve survival.

## 2.6. Nonpharmacological Therapies

Sodium restriction is important in the management of both hypertension and LV dysfunction. Exercise training has been shown to reduce recurrent cardiac events in patients with LV dysfunction resulting from ischemic causes. Heart Failure exercise training was associated with modest reductions in both all-cause mortality or hospitalization and cardiovascular mortality or HF hospitalization. Exercise training also conferred significant improvements in self-reported health status compared with usual care. For patients with HF, close medical supervision and careful monitoring of the BP response to exercise and of the ECG for ventricular arrhythmias are appropriate. Other nonpharmacological therapies include management of dyslipidemia, diabetes mellitus, and obesity, as well as smoking cessation.

## 2.7. Pharmacological Therapies

When an antihypertensive regimen is devised, optimal control of BP should remain the primary goal, with the choice of drugs determined by the concomitant medical problems (eg, CAD, diabetes mellitus, or renal disease). Ultimately, an appropriate antihypertensive regimen frequently consists of several drugs used in combination.

### 2.7.1. Diuretics

Diuretic-based antihypertensive therapy has repeatedly been shown to prevent HF in a wide range of target populations. Thiazide or thiazide-type diuretics are effective in preventing HF in hypertensive patients. Thiazide or thiazide-type diuretics are the drugs of choice in patients with mild HF because of a more sustained natriuretic and diuretic action than loop diuretics, particularly in those individuals in whom BP control may be more important than correction of volume overload. In more severe HF, diuretics are used to reverse volume overload and associated symptoms. Loop diuretics such as furosemide and torsemide usually are used because they produce a greater diuresis for the same degree of natriuresis; they work even in the presence of renal impairment, a frequent accompaniment of severe HF; and their dose-response characteristics are linear and steep,

which allows escalation to high doses. By inducing sodium and water loss, diuretics also activate several adverse mechanisms. There may be a decrease in right ventricular filling pressure, with a decrease in stroke volume and activation of the RAAS and the sympathetic nervous system, effects that would be expected to be harmful. This problem is avoided by combining diuretic therapy with an ACE inhibitor or ARB, a  $\beta$ -blocker, and/or an aldosterone antagonist, all of which have been shown to provide effective therapy in HF. The Diuretic Optimization Strategies Evaluation (DOSE) trial in patients with acute HF demonstrated that a high-dose furosemide strategy was associated with a nonstatistically significant trend toward greater improvement in patients' global assessment of symptoms but no significant difference in creatinine levels. Although there were greater diuresis with the high-dose strategy and more favorable outcomes in a few secondary measures, there was also transient worsening of renal function.

### 2.7.2. ACE Inhibitors

ACE inhibitors are thought to reduce the remodeling that occurs after MI, to improve ischemic preconditioning, to reverse angiotensin II – induced vasoconstriction and inotropy, to prevent the depletion of high-energy phosphate stores, to enhance nitric oxide release through prevention of bradykinin breakdown, and to reduce blood coagulability through the endothelial release of tissue plasminogen activator. ACE inhibitors have been shown in many trials to be beneficial in patients with LV dysfunction of ischemic origin. In the Acute Infarction Ramipril Efficacy (AIRE) trial, ramipril administered 3 to 7 days after MI reduced the relative mortality risk by 27% in the total cohort, by 15% in normotensive subjects, and by 41% in hypertensive subjects, which supports the particular importance of ACE inhibition in hypertensive patients with LV dysfunction in the post-MI period. In the Assessment of Treatment With Lisinopril and Survival (ATLAS) trial, mortality was significantly lower in patients with HF who received a high dose of lisinopril (32.5–35 mg/d) than in those treated with a low dose of lisinopril (2.5–5 mg/d). Among patients with diabetes mellitus or other cardiovascular complications, ACE inhibitors have been most notable with respect to a reduction in the onset of HF and new-onset diabetes mellitus. However, the message has not impacted clinicians as well as it should.





### 2.7.3. Angiotensin Receptor Blockers

Compared with placebo, the ARBs losartan and irbesartan significantly reduced the incidence of HF in patients with type 2 diabetes mellitus and nephropathy. The VALIANT trial found valsartan to be noninferior to captopril. The Valsartan Heart Failure Trial (Val-HeFT) assessed the efficacy of valsartan at doses up to 320 mg/d added to standard therapy for reducing morbidity and mortality in patients with HF. Patients receiving valsartan demonstrated a 13.2% reduction in the combined end point of cardiovascular mortality and morbidity compared with patients receiving placebo. Additional insights into the value of ARBs are provided by the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. In patients not receiving ACE inhibitors because of previous intolerance, the use of candesartan was associated with a significant reduction in the primary composite end point of cardiovascular death and hospital readmission for HF compared with placebo. In the combination arm of VALIANT, valsartan and captopril together showed no increased effect over captopril alone and had a higher incidence of discontinuation because of adverse effects.

In stable HF patients undergoing an established ACE inhibitor therapy, the CHARM trial showed that the addition of an ARB was well tolerated and beneficial. This is a strategy that could be used to control BP if needed.

### 2.7.4. $\beta$ -Blockers

$\beta$ -Blockers lower BP and are negatively inotropic and chronotropic. They therefore alleviate ischemia and angina, in addition to lowering BP. The role of  $\beta$ -blockers in the management of patients with HF is well established. The Metoprolol CR/XL Randomized Intervention Trial in Heart Failure (MERIT-HF) randomized patients with NYHA class II to IV HF symptoms to receive metoprolol succinate versus placebo. This trial was stopped prematurely because of a 34% reduction in mortality in the metoprolol arm. Four clinical trials of carvedilol in HF were stopped prematurely because of a highly significant 65% reduction in mortality in patients treated with carvedilol compared with placebo.

Another longer-acting  $\beta$ -blocker, bisoprolol, showed similar long-term benefit on survival in patients with HF. The Cardiac Insufficiency Bisoprolol Study (CIBIS-II) showed a 32% reduction in all-cause mortality in bisoprolol-treated

patients with NYHA class III or IV HF caused by ischemic and nonischemic cardiomyopathy at a median follow-up of 1.3 years. In that trial, sudden deaths were reduced by 44% in the bisoprolol-treated group, whereas pump failure deaths were reduced by 26%.

Nebivolol is a  $\beta_1$ -selective  $\beta$ -blocker with vasodilating properties related to nitric oxide modulation. In 2,128 patients  $\geq 70$  years of age with a history of HF, nebivolol significantly decreased all-cause mortality or cardiovascular hospital admissions over a 21-month follow-up.

Although all 4 of these agents (metoprolol succinate, carvedilol, bisoprolol, and nebivolol) are beneficial in HF, the Carvedilol or Metoprolol European Trial (COMET) demonstrated a 17% greater mortality reduction in favor of carvedilol compared with metoprolol tartrate (not the formulation used in MERIT-HF, which was metoprolol succinate), with mean daily doses of 42 and 85 mg/d, respectively. Carvedilol may be particularly appealing because of its additional  $\alpha$ -blocking properties. There also may be a more favorable effect on glycemic control.

As a result of these studies,  $\beta$ -blockers are recommended for the long-term management of patients with hypertension related LV systolic dysfunction.

### 2.7.5. Nitrates and Hydralazine

Nitrate tolerance has limited the ability of long-term nitrates alone to be effective as antihypertensive agents. The addition of hydralazine to a nitrate reduces this tolerance. The African-American Heart Failure Trial (A-heFT) showed that a combination of a fixed dose of isosorbide dinitrate and hydralazine provides additional benefit in African American patients with advanced HF. The trial was stopped early because of a significantly higher mortality rate in the placebo group than in the group receiving isosorbide dinitrate plus hydralazine (10.2% versus 6.2%). Therefore, for African Americans who require further BP control and relief of symptoms of HF (NYHA class III or IV), the combination of hydralazine and isosorbide is recommended together with ACE inhibitors,  $\beta$ -blockers, and aldosterone antagonists. Given the lack of randomized trial evidence to support the prevention of cardiovascular events by the use of hydralazine in the treatment of primary hypertension and concerns that hydralazine may provoke angina, monotherapy with hydralazine in IHD is not recommended.



### 2.7.6. Aldosterone Receptor Antagonists

Aldosterone has been shown to promote myocardial fibrosis. RALES reported the effect of adding the competitive aldosterone antagonist spironolactone versus placebo to standard HF therapy in patients with stage 3 (NYHA class III or IV) HF. There was a 30% reduction in total mortality with spironolactone. Eplerenone, a selective aldosterone inhibitor, showed similar survival benefit in the EPHESUS trial. This class of drug is especially beneficial in patients with hypokalemia. Electrolytes and renal function should be monitored to prevent hyperkalemia.

### 2.8. Renal Denervation

The radiofrequency ablation of renal sympathetic nerves has recently gained attention for its ability to reduce BP in those with resistant hypertension. A small study has demonstrated the ability of renal denervation to induce LV hypertrophy regression and to improve LV systolic and diastolic function. However, in the first large-scale clinical trial of renal denervation in patients with resistant hypertension, with an appropriate control group, there was no significant difference between the 2 groups in the reduction of SBP, which leaves the future of renal denervation in the management of hypertension uncertain.

### 2.9. Goal BP

Healthcare providers should lower both SBP and DBP in accordance with the recommendations provided in published guidelines, including the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. BP targets in HF have not been firmly established, but in most successful trials, SBP was lowered to the range of 110 to 130 mm Hg. One trial COPERNICUS, demonstrated benefits of carvedilol in patients with entry criteria that included SBPs down to 85 mm Hg and who had a mean pretreatment BP of 123/76 mm Hg, which suggests that lower BPs (SBP <120 mm Hg) may be desirable in some patients. Therefore, we make the recommendation that the target BP in patients with HF should be <140/90 mm Hg, but we also suggest that consideration should be given to lowering the BP even further, to <130/80 mm Hg. Octogenarians should be checked for orthostatic changes with standing, and an SBP <130 mm Hg and a DBP <65 mm Hg should be avoided.

### 2.10. Drugs to Avoid

Several classes of drugs should be avoided in patients with ischemic systolic HF with hypertension. Because of their negative inotropic properties and the increased likelihood of worsening HF symptoms, nondihydropyridine CCBs such as diltiazem and verapamil should be avoided. The dihydropyridine CCB amlodipine appeared to be safe in patients with severe systolic HF in the Prospective Randomized Amlodipine Survival Evaluation (PRAISE) trial, as was felodipine. Although clonidine is an effective antihypertensive agent, another drug in the same class, moxonidine, was associated with increased mortality in patients with HF; therefore, clonidine also should probably be avoided. In the ALLHAT trial, the doxazosin arm of the trial was discontinued because of a 2.04-fold increase in relative risk of developing HF compared with chlorthalidone treatment. Although there are several caveats about extrapolating these data to the management of hypertension in patients with HF,  $\alpha$ -blockers should be used only if other agents used for the management of hypertension and HF are inadequate to achieve good BP control, and even then, they should be used with caution. Nonsteroidal anti-inflammatory drugs have been associated with increased BP accompanied by peripheral edema, weight gain, and worsening renal function, so they should be used with caution in HF patients. Studies of the direct renin inhibitor aliskiren added to ACE inhibitors or ARBs were stopped early because of concerns about increased adverse events, particularly in the setting of renal insufficiency or diabetes mellitus. Ongoing trials of aliskiren in HF with heightened safety monitoring should help define the role, if any, for this agent. Given the lack of randomized trial evidence to support the use of hydralazine without a nitrate in the treatment of primary hypertension and concerns that hydralazine may provoke angina, monotherapy with hydralazine in IHD is not recommended.

### 2.11. Recommendations

1. **The treatment of hypertension in patients with HF should include management of risk factors such as dyslipidemia, obesity, diabetes mellitus, smoking, and dietary sodium and a closely monitored exercise program (Class I; Level of Evidence C).**
2. **Drugs that have been shown to improve outcomes for patients with HF with reduced ejection fraction generally also lower BP. Patients should be treated**



- with ACE inhibitors (or ARBs),  $\beta$ -blockers (carvedilol, metoprolol succinate, bisoprolol, or nebivolol), and aldosterone receptor antagonists (Class I; Level of Evidence A).
3. Thiazide or thiazide-type diuretics should be used for BP control and to reverse volume overload and associated symptoms. In patients with severe HF (NYHA class III and IV) or those with severe renal impairment (estimated glomerular filtration rate <30 mL/min), loop diuretics should be used for volume control, but they are less effective than thiazide or thiazide-type diuretics in lowering BP. Diuretics should be used together with an ACE inhibitor or ARB and a  $\beta$ -blocker (Class I; Level of Evidence C).
  4. Studies have shown equivalence of benefit of ACE inhibitors and the ARBs candesartan or valsartan in HF with reduced ejection fraction. Either class of agents is effective in lowering BP (Class I; Level of Evidence A).
  5. The aldosterone receptor antagonists spironolactone and eplerenone have been shown to be beneficial in HF and should be included in the regimen if there is HF (NYHA class II–IV) with reduced ejection fraction (<40%). One or the other may be substituted for a thiazide diuretic in patients requiring a potassium-sparing agent. If an aldosterone receptor antagonist is administered with an ACE inhibitor or an ARB or in the presence of renal insufficiency, serum potassium should be monitored frequently. These drugs should not be used, however, if the serum creatinine level is  $\geq 2.5$  mg/dL in men or  $\geq 2.0$  mg/dL in women or if the serum potassium level is  $\geq 5.0$  mEq/L. Spironolactone or eplerenone may be used with a thiazide or thiazide-like diuretic, particularly in patients with resistant hypertension (Class I; Level of Evidence A).
  6. Hydralazine plus isosorbide dinitrate should be added to the regimen of diuretic, ACE inhibitor or ARB, and  $\beta$ -blocker in African American patients with NYHA class III or IV HF with reduced ejection fraction (Class I; Level of Evidence A). Others may benefit similarly, but this has not yet been tested.
  7. In patients who have hypertension and HF with preserved ejection fraction, the recommendations are to control systolic and diastolic hypertension (Class I; Level of Evidence A), ventricular rate in the presence of atrial fibrillation (Class I; Level of Evidence C), and pulmonary congestion and peripheral edema (Class I; Level of Evidence C).
  8. Use of  $\beta$ -adrenergic blocking agents, ACE inhibitors, ARBs, or CCBs in patients with HF with preserved ejection fraction and hypertension may be effective to minimize symptoms of HF (Class IIb; Level of Evidence C).
  9. In IHD, the principles of therapy for acute hypertension with pulmonary edema are similar to those for STEMI and NSTEMI, as described above (Class I; Level of Evidence A). If the patient is hemodynamically unstable, the initiation of these therapies should be delayed until stabilization of HF has been achieved.
  10. Drugs to avoid in patients with hypertension and HF with reduced ejection fraction are nondihydropyridine CCBs (such as verapamil and diltiazem), clonidine, moxonidine, and hydralazine without a nitrate (Class III Harm; Level of Evidence B).  $\alpha$ -Adrenergic blockers such as doxazosin should be used only if other drugs for the management of hypertension and HF are inadequate to achieve BP control at maximum tolerated doses. Nonsteroidal anti-inflammatory drugs should also be used with caution in this group, given their effects on BP, volume status, and renal function (Class IIa; Level of Evidence B).
  11. The target BP is <140/90 mm Hg, but consideration can be given to lowering the BP even further, to <130/80 mm Hg. In patients with an elevated DBP who have CAD and HF with evidence of myocardial ischemia, the BP should be lowered slowly. In older hypertensive individuals with wide pulse pressures, lowering SBP may cause very low DBP values (<60 mm Hg). This should alert the clinician to assess carefully any untoward signs or symptoms, especially those caused by myocardial ischemia and worsening HF (Class IIa; Level of Evidence B). Octogenarians should be checked for orthostatic changes with standing, and an SBP <130 mm Hg and a DBP <65 mm Hg should be avoided.

Reference: Selected sections are extracted from "Treatment of Hypertension in Patients With Coronary Artery Disease", A Scientific Statement From the American Heart Association, American College of Cardiology, and American Society of Hypertension. Circulation May 12, 2015.

## Cardiology News

### Stopping Hormone Therapy Linked to Cardiovascular Death

In the first year after a postmenopausal woman discontinues hormone therapy, her risk for cardiovascular mortality is higher than if she had continued the therapy. However, beyond 1 year, the risk was lower. Dr Mikkola and his colleagues identified 332,202 women who discontinued hormone therapy from 1992 to 2009 from two large Finnish registries. Hormone therapy guidelines for postmenopausal women recommend the lowest dose for the briefest period. But this study raises questions about that practice.

*Journal of Clinical Endocrinology and Metabolism, 2015.*

### Childhood Distress May Increase Cardiometabolic Risk in Adulthood

Persistent psychological distress that starts in childhood or anytime over a lifetime may increase cardiometabolic dysregulation in adulthood. Analysis of more than 6700 participants from the ongoing 1958 British Birth Cohort Study (BBCS) showed that, compared with those without persistent distress, those who experienced it primarily as children were significantly more likely by the age of 45 to be at risk for heart disease and diabetes — as were those who experienced distress only as adults or from childhood through adulthood. In addition, the estimated CVD risk from persistent distress through adulthood was higher than the risk from being overweight as a child.

*Journal of the American College of Cardiology, October 2015.*

### Taking BP Meds at Bedtime May Thwart Diabetes Onset

Blood pressure that does not drop as expected at night time (nondipping) seems to precede the development of diabetes. Moreover, popping a blood-pressure pill at bedtime instead of first thing in the morning appears to lower the risk of getting type 2 diabetes. Most hypertensive patients still take their prescribed medications in the morning, although no prospective, randomized study has ever reported any advantages of such a treatment regimen. On the contrary, there is growing evidence that ingesting hypertension medication at bedtime significantly reduces cardiovascular and cerebrovascular events.

*Diabetologia, September 2015.*

### BP Targets Far Below Guidelines Cut Mortality, CV Events: SPRINT Trial

A more intensive strategy of lowering blood pressure - one that aims to achieve a systolic blood-pressure target of 120 mm Hg - reduces the risk of death and cardiovascular events when compared with a strategy that lowers systolic blood pressure to conventional targets. Treating high-risk hypertensive adults 50 years of age and older to a target of 120 mm Hg significantly reduced cardiovascular events by 30% and reduced all-cause mortality by nearly 25% when compared with patients treated to a target of 140 mm Hg. The study, which included hypertensive patients with one additional cardiovascular risk factor or pre-existing kidney disease, was stopped earlier than the planned 2018 completion date, given the benefit of the intensive strategy, according to investigators.

<http://www.nih.gov/news/health/sep2015/nhlbi-11.htm>

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#### Editorial Note

Dear Doctor,

We are happy to present the 39<sup>th</sup> issue of "Insight Heart". It is a small endeavor to provide you compiled & updated information on cardiovascular diseases. We continue the "Treatment of Hypertension in Patients With Coronary Artery Disease" from the previous issue. We will appreciate your thoughtful comments. Thanks and regards.