

# Guidelines for management of HTN in CAD

By: Noha Khalil

Lecturer of internal medicine

# Case 1

MSA , male patient 62 ys old , came to ER with typical chest pain , increased by exertion patially releived with rest .

pain markedly improved by sublingual nitrates .

pulse was 85/mim

BP was 170/100

his resting ECG was normal

cardiac enzymes were normal

No Hx of DM , no previous coronay eveny

How can u manage ??

# Case 2

- SMA , 65 ys old , came to casualty with acute chest pain , occurred at rest , compressing , radiating to left shoulder and his back.
- ECG showed acute extensive MI.
- BP : 160/110
- Pulse :100/min
- He admitted to CCU and treatment for MI started immediately.
- Would u star antihypertensive medication??
- Which line of antihypertensive you should start with??

**A Scientific Statement From the American Heart Association, American College of Cardiology, and American Society of Hypertension.**

- Epidemiological studies have established a strong association between hypertension and CAD.
- Hypertension is a major independent risk factor for the development of CAD, stroke, and renal failure.

## Epidemiology of Hypertension and CAD

- Hypertension is a major independent risk factor for CAD for all age/race/sex groups.
- The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure uses the traditional definition of hypertension as an SBP of  $\geq 140$  mm Hg or a DBP of  $\geq 90$  mm Hg and/or the current use of antihypertensive medication.
- With this definition, an estimated 65 million adult Americans, or nearly one fourth of the adult population of the United States, have hypertension.
- Another quarter of the population have **prehypertension**, defined as an SBP of 120 to 139 mm Hg or a DBP of 80 to 89 mm Hg.

- a change with age is the relative importance of SBP and DBP as risk indicators.
- Before 50 years of age, DBP is the major predictor of IHD risk, whereas after 60 years of age, SBP is more important.
- It is important to note that, in this population  $\geq 60$  years of age, DBP becomes inversely related to CAD risk and pulse pressure becomes the strongest predictor for CAD.

# *Effects of Treatment*

- The risk of CVD in the patient with hypertension has been shown to be greatly reduced with effective antihypertensive therapy.
- Major reductions in CVD morbidity and mortality over the past 50 years have been attributed to the increased availability and use of drug treatment for hypertension.
- For example, a 10-mm Hg lower usual SBP (or a 5-mm Hg lower usual DBP) is associated with a 50% to 60% lower risk of stroke death and an  $\approx$ 40% to 50% lower risk of death resulting from CAD or other vascular causes at middle age, benefits that are only slightly smaller in older people.



Table 1. Applying Classification of Recommendations and Levels of Evidence.

SIZE OF TREATMENT EFFECT

PRECISION OF TREATMENT EFFECT

	CLASS I <i>Benefit &gt;&gt;&gt; Risk</i> Procedure/Treatment <b>SHOULD</b> be performed/administered	CLASS IIa <i>Benefit &gt;&gt; Risk</i> <i>Additional studies with focused objectives needed</i> <b>IT IS REASONABLE</b> to perform procedure/administer treatment	CLASS IIb <i>Benefit ≥ Risk</i> <i>Additional studies with broad objectives needed; additional registry data would be helpful</i> Procedure/Treatment <b>MAY BE CONSIDERED</b>	CLASS III <i>No Benefit</i> or CLASS III <i>Harm</i> <table border="1"> <thead> <tr> <th></th> <th>Procedure/Test</th> <th>Treatment</th> </tr> </thead> <tbody> <tr> <td>COR III: No benefit</td> <td>Not Helpful</td> <td>No Proven Benefit</td> </tr> <tr> <td>COR III: Harm</td> <td>Excess Cost w/o Benefit or Harmful</td> <td>Harmful to Patients</td> </tr> </tbody> </table>		Procedure/Test	Treatment	COR III: No benefit	Not Helpful	No Proven Benefit	COR III: Harm	Excess Cost w/o Benefit or Harmful	Harmful to Patients
	Procedure/Test	Treatment											
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LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is useful/effective</li> <li>■ Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation in favor of treatment or procedure being useful/effective</li> <li>■ Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation's usefulness/efficacy less well established</li> <li>■ Greater conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>■ Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>									
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is useful/effective</li> <li>■ Evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation in favor of treatment or procedure being useful/effective</li> <li>■ Some conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation's usefulness/efficacy less well established</li> <li>■ Greater conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>■ Evidence from single randomized trial or nonrandomized studies</li> </ul>									

<b>ESTIMATE OF CERTA</b>	<b>LEVEL C</b> Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is useful/effective</li> <li>■ Only expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation in favor of treatment or procedure being useful/effective</li> <li>■ Only diverging expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation's usefulness/efficacy less well established</li> <li>■ Only diverging expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>■ Only expert opinion, case studies, or standard of care</li> </ul>
	Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit <hr/> is not recommended is not indicated should not be performed/administered/other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		is not useful/beneficial/effective	

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

\*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

- Several studies (Heart Outcomes Prevention Evaluation [HOPE], Survival and Ventricular Enlargement [SAVE], and European Trial on Reduction of Cardiac Events With Perindopril in Stable Coronary Artery Disease [EUROPA])
- have shown a beneficial effect of angiotensin-converting enzyme (ACE) inhibitors on CVD outcomes in individuals, some hypertensive and some not, but all with established CVD or at high risk for its development.

- However, we do not yet have outcome studies of treatment of prehypertension in individuals with BPs in the range of 130 to 139/80 to 89 mm Hg.
- The only prospective clinical trial of BP reduction in individuals with normal BPs is the Trial of Preventing Hypertension (TROPHY) study, in which subjects with an SBP of 130 to 139 mm Hg or a DBP of 85 to 89 mm Hg were randomized to be treated for 2 years with either the angiotensin receptor blocker **(ARB)** candesartan or placebo and followed up for an additional 2 years.

- Hypertension developed in significantly ( $P < 0.007$ ) more participants in the placebo group (two thirds of this cohort at 4 years) than in the candesartan group, with a relative risk reduction of 66.3% at 2 years and 15.6% at 4 years.
- In addition, the treatment of prehypertension with candesartan appeared to be well tolerated, and serious adverse events occurred in 3.5% and 5.9% in patients treated with candesartan and placebo, respectively.
- However, the study was not designed or powered to assess CVD outcomes.

- In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, with a mean follow-up of 4.7 years, a target BP of <120 compared with <140 mm Hg was not associated with a reduced risk of a composite of CVD events (heart attack, a stroke, or a cardiovascular death).
- However, the incidence of stroke was significantly less in the intensively treated group.

## ***Risk Factor Interactions***

Data from the Framingham Heart Study have provided evidence of a predictive role of hypertension, dyslipidemia, glucose intolerance, cigarette smoking, and left ventricular (LV) hypertrophy in CVD.

These 5 primary risk factors are the most important modifiable determinants of CVD risk and appear to operate independently of one another.

this principle has been followed for patients with albuminuria and even modest chronic renal insufficiency, for which the BP threshold for the initiation of antihypertensive therapy is 130/80 mm Hg.

The American Diabetes Association has based its recommendation on age: People with diabetes mellitus should be treated to a BP of <140/80 mm Hg, except that “lower systolic targets, such as <130 mm Hg, may be appropriate for certain individuals, such as younger patients, if it can be achieved without undue treatment burden.



Furthermore, there is a correlation between hypertension and body mass index, with both strongly correlated with CAD. Hypertension and abdominal obesity are components of a larger risk factor constellation of cardiovascular risk.

# BP goal

- 1. The <140/90-mm Hg BP target is reasonable for the secondary prevention of cardiovascular events in patients with hypertension and CAD (*Class IIa; Level of Evidence B*).**
- 2. A lower target BP (<130/80 mm Hg) may be appropriate in some individuals with CAD, previous MI, stroke or transient ischemic attack, or CAD risk equivalents (carotid artery disease, PAD, abdominal aortic aneurysm)  
(*Class IIb; Level of Evidence B*).**
- 3. In patients with an elevated DBP and CAD with evidence of myocardial ischemia, the BP should be lowered slowly, and caution is advised in inducing decreases in DBP to <60 mm Hg in any patient with diabetes mellitus or who is >60 years of age.**

**Table 3. Summary of BP Goals**

BP Goal, mm Hg	Condition	Class/Level of Evidence
<150/90	Age >80 y	IIa/B
<140/90	CAD	I/A
	ACS	IIa/C
	HF	IIa/B
<130/80	CAD	IIb/C
	Post–myocardial infarction, stroke or TIA, carotid artery disease, PAD, AAA	IIb/C

AAA indicates abdominal aortic aneurysm; ACS, acute coronary syndrome; BP, blood pressure; CAD, coronary artery disease; HF, heart failure; PAD, peripheral arterial disease; and TIA, transient ischemic attack.

# Management of Hypertension in Patients With CAD and Stable Angina

The management of hypertension in patients **with chronic CAD and chronic stable angina** is directed toward the prevention of death, MI, and stroke; a reduction in the frequency and duration of myocardial ischemia; and the amelioration of symptoms.

Lifestyle changes with the usual attention to diet, sodium intake, moderation of alcohol intake, regular exercise, weight loss, smoking cessation, glycemic control, lipid management, and antiplatelet therapy.

Recognition and treatment of hypothyroidism and obstructive sleep apnea are important adjuncts in at-risk patients. Pharmacological management is inevitably required.

A reasonable BP target for hypertensive patients with demonstrated CAD is <140/90 mm Hg

- The management of symptomatic CAD, particularly angina pectoris, is directed to the relief of the angina and the prevention of both the progression of CAD and coronary events.
- The mainstays of angina treatment are  $\beta$ -blockers, CCBs, and nitrates.
- Pharmacological strategies for the prevention of cardiovascular events in these patients include ACE inhibitors, ARBs, thiazide and thiazide-like diuretics,  $\beta$ -blockers (particularly after MI), CCBs, antiplatelet drugs, and drugs for the treatment of dyslipidemia.
- **The recent ACC Foundation/AHA guidelines recommend ACE inhibitors and/or  $\beta$ -blockers, with the addition of drugs such as thiazide diuretics or CCBs for the management of high BP in patients with stable IHD.**

- There are no special contraindications in hypertensive patients for the use of nitrates, **antiplatelet or anticoagulant** drugs, or lipid-lowering agents for the management of angina and the prevention of coronary events, except that in patients with uncontrolled severe hypertension who are taking antiplatelet or anticoagulant drugs, BP should be lowered without delay to reduce the risk of hemorrhagic stroke.

**1. Patients with hypertension and chronic stable angina should be treated with a regimen that includes:**

**(a)  $\beta$ -blocker in patients with a history of prior MI**

**(b) An ACE inhibitor or ARB if there is prior MI, LV systolic dysfunction, diabetes mellitus, or CKD; and**

**(c) A thiazide or thiazide-like diuretic (*Class I; Level of Evidence A*).**

**2. The combination of a  $\beta$ -blocker, an ACE inhibitor or ARB, and a thiazide or thiazide-like diuretic should also be considered in the absence of a prior MI, LV systolic dysfunction, diabetes mellitus, or proteinuric CKD (*Class IIa; Level of Evidence B*).**

3. If  $\beta$ -blockers are contraindicated or produce intolerable side effects, a nondihydropyridine CCB (such as diltiazem or verapamil) may be substituted, but not if there is LV dysfunction (*Class IIa; Level of Evidence B*).
4. If either the angina or the hypertension remains uncontrolled, a long-acting dihydropyridine CCB can be added to the basic regimen of  $\beta$ -blocker, ACE inhibitor, and thiazide or thiazide-like diuretic.

The combination of a  $\beta$ -blocker and either of the nondihydropyridine CCBs (diltiazem or verapamil) should be used with caution in patients with symptomatic CAD and hypertension because of the increased risk of significant bradyarrhythmias and HF (*Class IIa; Level of Evidence B*).



5. For patients with stable angina, the BP target is <140/90 mm Hg. (*Class I; Level of Evidence A*). However, a lower target BP (<130/80 mm Hg) may be considered in some individuals with CAD, with previous stroke or transient ischemic attack, or with CAD risk equivalents (carotid artery disease, PAD, abdominal aortic aneurysm) (*Class IIb; Level of Evidence B*).

# Management of Hypertension in Patients With ACS

Because specific trials of BP lowering have not been performed in patients with ACS, the selection of antihypertensive agents for use in the patient with ACS should be focused on selecting drugs that have an established evidence-base for risk reduction for patients with ACS independently of BP lowering.

These drugs, which include  $\beta$ -blockers, ACE inhibitors (or ARBs), and, in selected patients, aldosterone antagonists, should typically be titrated to full doses before other agents that do not have an established evidence base are initiated.

- Therapeutic targets for BP have not been established specifically for patients with ACS.
- Current guidelines recommend a BP target of <140/90 mm Hg and <130/80 mm Hg for patients with diabetes mellitus or CKD, but this applies more to secondary prevention than the management of hypertension in the acute phase of MI.
- The BP may fluctuate early after ACS; thus, efforts should focus on pain control and clinical stabilization before BP is specifically targeted. Second, the BP should be lowered slowly, and caution is advised to avoid decreases in DBP to <60 mm Hg because this may reduce coronary perfusion and worsen ischemia.
- A BP target of <130/80 mm Hg at the time of hospital discharge is a reasonable option. In older hypertensive individuals with wide pulse pressures, lowering SBP may lead to very low DBP values, contributing to worsening myocardial ischemia

# Recommendations

1. If there is no contraindication to the use of  $\beta$ - blockers, in patients with ACS, the initial therapy of hypertension should include a short-acting  $\beta_1$ - selective  $\beta$ -blocker without intrinsic sympathomimetic activity (metoprolol tartrate or bisoprolol).

$\beta$ -Blocker therapy should typically be initiated orally within 24 hours of presentation (*Class I; Level of Evidence A*). For patients with severe hypertension or ongoing ischemia, an intravenous  $\beta$ -blocker (esmolol) can be considered (*Class IIa; Level of Evidence B*).

For hemodynamically unstable patients or when decompensated HF exists, the initiation of  $\beta$ -blocker therapy should be delayed until stabilization has been achieved (*Class I; Level of Evidence A*).

2. In patients with ACS and hypertension, nitrates should be considered to lower BP or to relieve ongoing ischemia or pulmonary congestion (*Class I; Level of Evidence C*). Nitrates should be avoided in patients with suspected right ventricular infarction and in those with hemodynamic instability.

Sublingual or intravenous nitroglycerin is preferred for initial therapy and can be transitioned later to a longer-acting preparation if indicated.

3. If there is a contraindication to the use of a  $\beta$ -blocker or intolerable side effects, then a nondihydropyridine CCB such as verapamil or diltiazem may be substituted for patients with ongoing ischemia, provided that LV dysfunction or HF is not present.

If the angina or hypertension is not controlled on a  $\beta$ -blocker alone, a longer-acting dihydropyridine CCB may be added after optimal use of an ACE inhibitor (*Class IIa; Level of Evidence B*).

4. An ACE inhibitor (*Class I; Level of Evidence A*) or an ARB (*Class I; Level of Evidence B*) should be added if the patient has an anterior MI, if hypertension persists, if the patient has evidence of LV dysfunction or HF, or if the patient has diabetes mellitus. For lower risk ACS patients with preserved LV ejection fraction and no diabetes mellitus, ACE inhibitors can be considered a first-line agent for BP control (*Class IIa; Level of Evidence A*).

5. Aldosterone antagonists are indicated for patients who are already receiving  $\beta$ -blockers and ACE inhibitors after MI and have LV dysfunction and either HF or diabetes mellitus.

Serum potassium levels must be monitored. These agents should be avoided in patients with elevated serum creatinine levels ( $\geq 2.5$  mg/dL in men,  $\geq 2.0$  mg/dL in women) or elevated potassium levels ( $\geq 5.0$  mEq/L) (*Class I; Level of Evidence A*).

6. Loop diuretics are preferred over thiazide and thiazide-type diuretics for patients with ACS who have HF (NYHA class III or IV) or for patients with CKD and an estimated glomerular filtration rate  $<30$  mL/min. For patients with persistent hypertension not controlled with a  $\beta$ -blocker, an ACE inhibitor, and an aldosterone antagonist, a thiazide or thiazide-type diuretic may be added in selected patients for BP control (*Class I; Level of Evidence B*).
  
7. The target BP is  $<140/90$  mm Hg in patients with ACS who are hemodynamically stable (*Class IIa; Level of Evidence C*). A BP target of  $<130/80$  mm Hg at the time of hospital discharge is a reasonable option (*Class IIb; Level of Evidence C*). The BP should be lowered slowly, and caution is advised to avoid decreases in DBP to  $<60$  mm Hg because this may reduce coronary perfusion and worsen ischemia.

# Management of Hypertension in HF of Ischemic Origin

## 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.



# Goal BP

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.

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.

checking for orthostatic changes with standing, and an SBP  $<130$  mm Hg and a DBP  $<65$  mm Hg should be avoided.

# 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*).

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*).

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*).

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.*

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*).

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*).

*If the patient is hemodynamically unstable, the initiation of these therapies should be delayed until stabilization of HF has been achieved.*

**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*).**

# Conclusion



**Table 2. Summary of Pharmacological Treatment of Hypertension in the Management of Ischemic Heart Disease.**

	ACEI or ARB	Diuretic	β-Blocker	Non-DHP CCB	DHP CCB	Nitrates	Aldosterone Antagonist	Hydralazine/ Isosorbide Dinitrate
Stable angina	1*	1†	1	2‡	2	1	2	
ACS	1*	1†	1§	2‡	2	2	2	
HF	1	1†	1¶			2	1	2

ACEI indicates angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DHP, dihydropyridine; HF, heart failure; 1, drug of choice; and 2, “add-on,” alternative drug, or special indications.

\*Especially if prior myocardial infarction, left ventricular systolic dysfunction, diabetes mellitus, or proteinuric chronic kidney disease is present.

†Chlorthalidone is preferred. Loop diuretic should be used in the presence of HF (New York Heart Association class III or IV) or chronic kidney disease with glomerular filtration rate <30 mL·min<sup>-1</sup>·m<sup>-2</sup>. Caution should be exercised in HF with preserved ejection fraction.

‡If β-blocker is contraindicated, a non-DHP CCB can be substituted, but not if left ventricular dysfunction or HF is present. Caution should be exercised if combining a non-DHP CCB with a β-blocker.

§Esmolol (intravenous) or metoprolol or bisoprolol (oral).

||Spironolactone or eplerenone if left ventricular dysfunction, HF, or diabetes mellitus is present.

¶Carvedilol, metoprolol succinate, or bisoprolol.

**Thank you**