Diagnosis and Treatment of Primary Hypertension

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Cover Illustration by Christie Grams
I. INTRODUCTION

Systemic arterial hypertension is currently the most common cardiovascular disorder in the United States, affecting 43 million people each year. More than 50% of people with hypertension are unaware that they have the condition, and even more go untreated. Moreover, the characteristics of hypertension change with race, age, gender, geography, and socio-economic status. A higher prevalence of hypertension is seen in African-Americans, elderly persons, men, and those living in the south-eastern United States.

From 1976 to 1991, the National Health and Nutrition Examination Survey (NHANES) showed a 73% increase in awareness of hypertension and a 55% increase in treatment, which may account for a dramatic reduction in coronary heart disease (CHD) and stroke (the first and third leading causes of death in the United States) during the study period. Health statistics during the past decade, however, have been less encouraging: age-adjusted rates of stroke incidence have risen, and age-adjusted incidence of CHD has reached a plateau. The incidence of end-stage renal disease and congestive heart failure (CHF), both attributable to longstanding hypertension, have been rising steadily. Hypertension remains a major modifiable risk factor for CHD. Yet despite our understanding of its pathophysiology and the availability of effective treatment strategies, nearly 75% of adults treated for hypertension do not achieve the target blood pressure (BP) of 140/90 mm Hg recommended in the Sixth Report of the Joint National Commission on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI).

This is the first of a 2-part article on hypertension, which describes the diagnosis and treatment of primary hypertension. The second part will describe clinical trials on hypertension as well as present several case patients to illustrate and highlight essential features about hypertension (see “Case Studies in Primary Hypertension” in Hospital Physician Cardiology Board Review Manual, Volume 9, Part 1).

II. DEFINITION

The definition of hypertension is arbitrary and based on normal BP variability. A deviation from the mean in the normal bell-shaped distribution curve of BP measurement, as determined from population studies, determines whether an individual has hypertension. Although no particular BP level triggers hypertension complications, definitions and guidelines are necessary for treatment and risk stratification.

Hypertension develops as either a primary or a secondary disorder. Primary hypertension, also referred to as idiopathic or essential hypertension, is systemic arterial hypertension of unknown cause. Comprising roughly 95% of all hypertension cases, primary hypertension is a heterogeneous disorder and (although no specific etiology has been identified) is associated with genetic factors as well as aging, alcohol consumption, sodium intake, sedentary lifestyle, obesity, insulin resistance, stress, inappropriate renin secretion, inadequate dietary intake of calcium and potassium, and tobacco use.

Secondary hypertension is defined as systemic arterial hypertension with a known cause and accounts for 5% of all hypertension cases. Unlike primary hypertension, the secondary disorder can potentially be reversed or cured. For example, patients with renal artery stenosis can undergo surgical revascularization or percutaneous angioplasty and stenting; thus, it is important to identify a cause of hypertension (Table 1). Because of the low prevalence of secondary hypertension, screening should be undertaken only when the clinical suspicion for a secondary cause is high. Secondary hypertension should be suspected when patients present at a young age, have poor response to drug therapy (usually requiring multiple medications), previously have been well controlled and then have increasing BP, have stage 3 hypertension, and have sudden onset or paroxysmal hypertension. Each of the secondary forms of hypertension has other distinctive characteristics that may suggest its presence, and heightened suspicion may come from the history and physical examination. Findings may include: the presence...
### Table 1. Differential Diagnoses in Hypertension

#### I. Systolic and diastolic hypertension

A. Primary, essential, or idiopathic

B. Secondary

   1. Renal
      a. Renal parenchymal disease
         1) Acute glomerulonephritis
         2) Chronic nephritis
         3) Polycystic disease
         4) Diabetic nephropathy
         5) Hydronephrosis
      b. Renovascular
         1) Renal artery stenosis
         2) Intrarenal vasculitis
      c. Renin-producing tumors
      d. Renoprival
      e. Primary sodium retention (e.g., Liddle’s syndrome, Gordon’s syndrome)

   2. Endocrine
      a. Acromegaly
      b. Hypothyroidism
      c. Hyperthyroidism
      d. Hypercalcemia (hyperparathyroidism)
      e. Adrenal
         1) Cortical
            a) Cushing’s syndrome
            b) Primary aldosteronism
            c) Congenital adrenal hyperplasia
            d) Apparent mineralocorticoid excess (licorice)
         2) Medullary: pheochromocytoma
      f. Extra-adrenal chromaffin tumors
      g. Carcinoid
      h. Exogenous hormones
         1) Estrogen
         2) Glucocorticoids
         3) Mineralocorticoids
         4) Sympathomimetics
         5) Tyramine-containing foods and monoamine oxidase inhibitors

   3. Coarctation of the aorta
   4. Pregnancy-induced hypertension
   5. Neurologic disorders
      a. Increased intracranial pressure
         1) Brain tumor
         2) Encephalitis
         3) Respiratory acidosis
      b. Sleep apnea
      c. Quadriplegia
      d. Acute porphyria
      e. Familial dysautonomia
      f. Lead poisoning
      g. Guillain-Barré syndrome
   6. Acute stress (including surgery)
      a. Psychogenic hyperventilation
      b. Hypoglycemia
      c. Burns
      d. Pancreatitis
      e. Alcohol withdrawal
      f. Sickle cell crisis
      g. Postresuscitation
      h. Postoperative
   7. Increased intravascular volume
   8. Alcohol and drug use

#### II. Systolic hypertension

A. Increased cardiac output
   1. Aortic valvular insufficiency
   2. Arteriovenous fistula, patent ductus
   3. Thyrotoxicosis
   4. Paget’s disease of bone
   5. Beriberi
   6. Hyperkinetic circulation

B. Rigidity of the aorta

of an abdominal bruit (renal artery stenosis); moon facies, buffalo hump, and abdominal striae (Cushing’s disease); discrepancy in BP between the upper and lower extremities (coarctation of the aorta); abdominal mass (polycystic kidney disease); and flushing, palpitations and pallor (pheochromocytoma). In this article, the remaining discussion will focus on primary hypertension.

III. GENETICS OF PRIMARY HYPERTENSION

Observing hypertension in clusters of families provided the first evidence that hypertension has a genetic basis. However, primary hypertension is a complex trait that does not follow classic Mendelian inheritance—rather, the condition is polygenic. Multiple genes may influence interindividual differences in BP because an individual’s BP is determined by multiple factors, including anatomic, physiologic, and biochemical components. Deciphering 3 billion base pairs (which is being done in The Human Genome Project) could potentially revolutionize clinical practice and understanding of primary hypertension on a molecular and genetic level.

Several means exist to investigate the genetics of hypertension. One approach is to identify families based on affected sibling pairs and to use linkage analysis to test whether particular versions of genetic markers correlate with hypertension and, therefore, are shared more often than by chance. A second approach is to compare people with and without hypertension and to examine the distribution of specific genetic markers, such as polymorphisms between the 2 groups. For example, specific genes under investigation for their association with hypertension include those encoding angiotensinogen, angiotensin II, endothelin, α1-adrenergic receptors, renin-binding protein, insulin receptor, dopamine receptor, and nitric oxide synthase. The ultimate goal of the genomic approach is to identify hypertensive patients who have a specific haplotype and to target those genes for a specific and effective treatment before adverse complications develop. From this approach, specific hypertensive syndromes may be discovered, each with its own genetic fingerprint and each requiring a unique “pharmacogenetic” treatment strategy.

IV. DIAGNOSIS

In adults, hypertension is diagnosed when the average of 2 or more systolic BP (SBP) measurements is greater than 140 mm Hg or when the average of 2 or more diastolic readings is greater than 90 mm Hg. These measurements are usually taken in successive clinic visits but may be obtained from self-measurements or with ambulatory BP devices. The latter 2 modalities have shown that some patients have elevated BP in the clinic but have normal BP in the home environment. This situation is termed white-coat hypertension or isolated office hypertension and occurs in more than 20% of patients with elevated BP readings measured in the office. Patients with white-coat hypertension do not have the increased morbidity and mortality as seen with fixed hypertension. Careful consideration must also be given to patients with consistently “high-normal” BP readings because these patients have a high risk of developing fixed hypertension over time, with associated sequelae.

Accurate and reproducible BP measurements are crucial in diagnosing hypertension. BP is measured indirectly by compressing the brachial artery from outside the arm in order to occlude the vessel. Pressure is decreased until the pulse is heard (Korotkoff’s sounds), which determines SBP. Auscultation continues while external pressure is decreased until the Korotkoff’s sounds disappear completely, which determines diastolic BP (DBP). Measurements should be taken after a few minutes of rest, half an hour after smoking or caffeine ingestion, and in comfortable seating with the patient’s arm at heart level. The average of at least 2 readings of both SBP and DBP should be evaluated, and measurements should be performed in both arms because certain conditions (aortic dissection, coarctation of the aorta, compressive lesions of the aorta, peripheral arterial disease) may cause a discrepancy in one extremity. Consideration should be given to several factors that may lead to inaccurate measurements. First, the BP cuff must be wide enough to occlude the artery in an even fashion; a cuff too small for the arm will cause an erroneously high reading. Heavily calcified arteries will lead to falsely elevated readings because higher pressures will be required to occlude the stiff vessel. A mercury sphygmomanometer is the most accurate device; however, the aneroid manometer and electronic devices are more commonly used today, and their validation is acceptable when calibrated to ensure accuracy.

Once a diagnosis has been made, the patient may be classified into 3 stages of hypertension as delineated by the JNCVI report (Table 2). When SBP and DBP fall into different categories, the higher category should be selected to classify the patient’s blood pressure status. For example, 160/92 mm Hg should be classified as stage 2 hypertension, and 174/120 mm Hg should be classified as stage 3 hypertension. Isolated systolic hypertension is
defined as SBP of 140 mm Hg or more and DBP less than 90 mm Hg; isolated systolic hypertension is staged appropriately (ie, 170/82 mm Hg is defined as stage 2 hypertension). In addition to classifying stages of hypertension based on average BP levels, clinicians should specify presence or absence of target organ disease (eg, hypertensive retinopathy and hypertensive heart disease) and should specify additional risk factors. This specificity is important for risk classification and treatment.

V. HYPERTENSION TREATMENT

LIFESTYLE MODIFICATION

Nonpharmacological intervention provides an effective means of lowering BP and has been increasingly used in treatment and prevention of high BP. Implementing lifestyle modification is important because drug therapy only reduces (rather than eliminates) risk, carries risks for adverse effects and events, causes undesirable biochemical changes, and confers expense. Furthermore, patients who engage in lifestyle modification will gain an improved sense of well-being and self-image, reduce their overall CHD risk, may decrease their medication requirements for BP control, and may benefit from an overall reduction in all-cause mortality. Specific modifications recommended for hypertensive patients include regular aerobic exercise, maintenance of ideal body mass index (weight in kilograms divided by the square height in meters), moderation of alcohol consumption, and dietary improvements.

Weight Reduction

Weight reduction is perhaps the most effective nonpharmacological means to reduce BP. In addition, weight loss can result in improved lipid profile, decreased insulin requirements in diabetic patients, decreased left ventricular mass, improved psychological state, and enhanced efficacy of antihypertensive drugs. The Trial of Nonpharmacological Interventions in the Elderly (TONE) showed a 30% decrease in need for antihypertensive medication when body weight was reduced by 3.5 kg. Estimates from the Framingham study suggest that SBP increases by 6.5 mm Hg for each 10% weight gain. Thus, even a 10-lb weight loss can result in significant BP reduction and should be encouraged for all patients with hypertension. Sustained weight loss can be difficult to achieve; patients often relapse into obesity or experience a “yo-yo” cycle of weight loss and gain, negating potential benefits of weight loss. With the cooperation of patient, physician, exercise counselor, and dietitian, a multidisciplinary approach involving an exercise program and caloric restriction will maximize success in achieving and maintaining weight reduction.

Alcohol Consumption

Alcohol use (≥2 drinks daily) may contribute to the development of primary hypertension by as much as 7% in women and 11% in men. Associations between alcohol use and high BP have been documented in more than 32 cross-sectional studies involving various ethnic groups, at least 7 prospective cohort studies, and in numerous clinical trials involving the administration or withdrawal of alcohol. The NHANES III study results provided the best epidemiologic evidence for a positive relationship between alcohol and hypertension. Alcohol affects BP both chronically and acutely, and BP continues to increase in a dose-dependent manner with increasing alcohol consumption. The exact mechanism by which alcohol increases BP is not clear. Conversely, moderate alcohol

Table 2. Stages of Hypertension as Classified by the JNC-VI*

<table>
<thead>
<tr>
<th>Category</th>
<th>SBP, mm Hg</th>
<th>DBP, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal†</td>
<td>&lt; 120</td>
<td>and</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt; 130</td>
<td>and</td>
</tr>
<tr>
<td>High-normal</td>
<td>130–139</td>
<td>or</td>
</tr>
<tr>
<td>Hypertension‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>140–159</td>
<td>or</td>
</tr>
<tr>
<td>Stage 2</td>
<td>160–179</td>
<td>or</td>
</tr>
<tr>
<td>Stage 3</td>
<td>≥ 180</td>
<td>or</td>
</tr>
</tbody>
</table>

DBP = diastolic blood pressure; JNC-VI = Sixth Report of the Joint National Commission on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; SBP = systolic blood pressure.

*For patients who are not taking antihypertensive drugs and are not acutely ill. When SBP and DBP fall into different categories, the higher category should be selected to classify the patient’s blood pressure status (see text).

†Optimal blood pressure with respect to cardiovascular risk is less than 120/80 mm Hg. However, unusually low readings should be evaluated for clinical significance.

‡Based on the average of 2 or more readings taken at each of 2 or more visits after an initial screening.

consumption has been shown to decrease overall CHD risk in the general population. Thus, health care providers must be careful when offering recommendations regarding alcohol consumption. The benefit of moderate consumption must be weighed against the risks, which include addiction and related social problems as well as hypertension. Patients who do not drink should not begin consuming alcohol for CHD benefits. In addition, no cardiovascular benefits accrue beyond 2 drinks per day.

Dietary Modification

One cannot underestimate the role of dietary modification in BP reduction. Several clinical trials have demonstrated a decrease in BP by dietary means alone comparable to or greater than that seen with mono-therapy for stage 1 hypertension. In The Dietary Approaches to Stop Hypertension (DASH) Trial, patients were randomly assigned to 3 groups of differing diets: a control group of “the usual American diet;” a diet rich in fruits and vegetables; and a “combination” diet rich in fruits and vegetables, low-fat dairy products, and with reduced saturated and total fat. All comers (ie, all subjects enrolled in the study) in the combination diet group had a reduction in SBP and DBP by 5.5 mm Hg and 3.0 mm Hg, respectively (Figure 1), whereas hypertensive patients in the combination diet group had an 11.4 mm Hg reduction in SBP and a 5.5 mm Hg reduction in DBP. African-American patients with hypertension on the DASH study diet had an even greater benefit (a 13.2/6.1 mm Hg reduction in SBP/DBP) when on the combination diet. Additional subgroup analysis indicated that the DASH diet is as effective as first-line drug therapy in patients with stage 1 isolated systolic hypertension.

PHARMACOLOGICAL TREATMENT

The benefits of reducing BP by pharmacological means include protection from stroke, coronary events, heart failure, progression of kidney disease, progression to more severe hypertension, and, most importantly, mortality from all causes. The success of pharmacologic treatment may be influenced by several factors, including adverse side effects, cost, low efficacy, changes in provider or insurance carrier, patients’ lack of knowledge, and absence of overt symptoms early in the disease. Physicians should be aware of these barriers in order to effectively achieve treatment goals. In addition, all pharmacologic regimens should be augmented with lifestyle modifications, as previously discussed (Figure 2).

The number of antihypertensive agents available in the United States grows considerably each year. These agents can be divided into 6 major classes: diuretics, antihypertensive agents, vasodilators, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin-receptor blockers. Selection of drug therapy is greatly affected by the presence of concomitant disease. Comorbid conditions are present in more than 50% of patients with primary hypertension; antihypertensive medications that improve or do not worsen these conditions (ie, diabetes mellitus, bronchial asthma, dyslipidemia, and renal insufficiency) should be prescribed as first-line treatment as outlined in Appendix 1. For example, ACE inhibitors—used in combination with diuretics—prevent congestive heart failure and reduce morbidity and mortality in patients with established failure and therefore are recommended as first-line agents for treating hypertensive patients with this condition.
Algorithm for the Treatment of Hypertension

Begin or continue lifestyle modifications

Not at goal blood pressure (< 140/90 mm Hg)
Lower goals for patient with diabetes or renal disease

Initial Drug Choice*

Uncomplicated hypertension†
- Diuretics
- β-Blockers

Specific indications for the following drugs
- ACE inhibitors
- Angiotensin II–receptor blockers
- α-Blockers
- α-β-Blockers
- β-Blockers
- Calcium antagonists
- Diuretics
  - Start with a low dose of a long-acting once-daily drug, and titrate dose
  - Low-dose combinations may be appropriate

Compelling indications†
- Diabetes mellitus (type 1) with proteinuria
  - ACE inhibitors
- Heart failure
  - ACE inhibitor
  - Diuretics
- Isolated systolic hypertension (older persons)
  - Diuretics preferred
  - Long-acting dihydropyridine calcium antagonists
- Myocardial infarction
  - β-Blockers (non-ISA)
  - ACE inhibitors (with systolic dysfunction)

Not at goal blood pressure

No response or troublesome side effects
- Substitute another drug from a different class

Inadequate response but well tolerated
- Add a second agent from a different class

Not at goal blood pressure

Continue adding agents from other classes
Consider referral to a hypertension specialist

Figure 2. Algorithm for the treatment of hypertension. ACE = angiotensin-converting enzyme; ISA = intrinsic sympathomimetic activity. *Unless contraindicated. †Based on randomized controlled trials. (Adapted with permission from Carretero OA, Oparil S. Essential hypertension. Part II: treatment. Circulation 2000;101:450.)
Medications that exacerbate existing conditions should not be chosen for first-line or second-line therapy (ie, β-blockers for patients with severe reactive airway disease) but may be ultimately needed if the hypertension is resistant to preferred therapy. For patients without serious comorbid conditions and without concomitant CHD risk factors, the JNC-VI guidelines recommend that initial hypertension therapy include a diuretic or a β-blocker. These agents have been studied the most in clinical trials and are less expensive than newer drugs.

Most patients with hypertension (uncomplicated stages 1 and 2) are started on a single drug because immediate BP reduction rarely requires more than one medication. Therapy should begin with the lowest dose of the drug and should be increased in 1 to 2 months if BP remains increased; at each step, the treatment goal is a reduction in BP of 5 to 10 mm Hg. In general, the patient’s baseline BP is not a reliable predictor of the amount of drug the patient will need. A slow deliberate strategy for treating hypertension will decrease the potential for adverse effects (eg, postural dizziness, weakness, fatigue) and for too abrupt a fall in BP. If the initial drug choice does not reduce BP after reaching the full dose, a second medication from another class should be added. If not chosen as first-line therapy, a diuretic should be added next because low doses of a diuretic can potentiate the effect of other agents without producing adverse metabolic effects and can decrease the volume overload that frequently develops after the use of vasodilators and adrenergic blocking drugs. Long-acting agents (especially once-daily dosing) are preferable because they improve adherence to therapy; provide more consistent BP control; and provide protection against sudden death, MI, and cerebrovascular accident related to abrupt increase in BP after waking from sleep.

Fixed drug combinations have greater efficacy with fewer adverse effects than either component alone and may be acceptable as first-line treatment. The effectiveness of fixed drug combinations relates to higher response rates in the low range of doses as a result of complementary mechanisms of antihypertensive effects as well as improved compliance from better tolerance and ease of dosing. Available fixed drug combinations include: diuretics with potassium-sparing agents; diuretics with β-blockers; diuretics with ACE inhibitors; diuretics with angiotensin-receptor blockers; and ACE inhibitors with calcium channel blockers.

Monotherapy is unlikely to provide adequate long-term BP control in patients with stage 2 or 3 hypertension. In fact, only 50% of patients with stage 2 and 3 hypertension treated in the large randomized clinical trials reached target BP with the first agent. For these patients and those at high risk for MI or cerebrovascular accident: (1) therapy should probably be initiated with more than one agent, (2) treatment should begin immediately, and (3) time to target BP should be shortened by decreasing the time interval between drug changes to weeks instead of months. After 1 year of successful hypertension control, attempts can be made to decrease the dose or number of antihypertensive drugs in a slow and closely monitored manner. Patients engaged in lifestyle modifications (eg, sodium restriction and weight loss) will have the most success with step-down therapy.

Pharmacological therapy for hypertension decreases the incidence of myocardial infarction and the occurrence of CHF in patients with pre-existing CHD. Analysis of previous data from clinical trials had raised concerns that lowering DBP too much, might increase the risk of coronary events by lowering diastolic perfusion pressure in the coronary circulation, the so-called J-curve hypothesis. All available and current data support the value of the reduction of DBP at all ages to the level achieved in clinical trials—usually to less than 90 mm Hg—and show a progressive reduction in both cerebrovascular and renal disease with even greater reductions in DBP. In the Hypertension Optimal Treatment (HOT) trial, patients were randomly assigned to 3 groups with different target DBP measurements (< 90, < 85, and < 80 mm Hg). Results showed a significantly lower rate of cardiovascular events in the less than 80 mm Hg target group indicating greatest benefit from a greater reduction in DBP, refuting the J-curve hypothesis in the pharmacological treatment of hypertension. A reasonable conclusion from most treatment studies (including HOT) is that lowering DBP is safe and beneficial in nonischemic hypertensives and in hypertensive patients with stable CHD.

All antihypertensive drugs lower BP by definition; however, differences in their effects on cardiovascular and extracardiovascular disorders (eg, malignancy, dementia) should be central to tailoring the choice of antihypertensive treatment to the patient’s unique profile of concomitant cardiovascular disease risk factors and/or comorbid conditions.

VI. SUMMARY POINTS

- Systemic arterial hypertension affects 43 million people each year in the United States.
- Of adults treated for hypertension, 75% do not achieve the target blood pressure of 140/90 mm Hg, which is recommended by the Sixth Report of the

- Secondary hypertension accounts for 5% of hypertensive patients, and screening for secondary causes should be pursued if clinical suspicion is high.
- Primary hypertension accounts for 95% of hypertensive patients and is a heterogeneous disorder with no precise etiology.
- Primary hypertension is associated with genetic factors, aging, alcohol consumption, sodium intake, sedentary lifestyle, obesity, insulin resistance, stress, inappropriate renin secretion, intake of calcium and potassium, and tobacco use.
- The diagnosis of hypertension is made when the average of 2 or more systolic blood pressure (SBP) measurements is greater than 140 mm Hg or when the average of 2 or more diastolic blood pressure (DBP) measurements is greater than 90 mm Hg.
- Isolated systolic hypertension is defined as a SBP greater than 140 mm Hg and a DBP less than 90 mm Hg.
- Hypertension is largely a result of adverse dietary habits, in both the quality and quantity of food intake.
- Lifestyle modification, including weight reduction, reduced alcohol consumption, and dietary modification have all shown to reduce BP.
- A diuretic or β-blocker is the first-line pharmacologic treatment unless comorbid conditions exist necessitating that treatment should be tailored to the specific condition.
- The effectiveness of fixed drug combinations relates to (1) higher response rates in the low range of doses because of complementary mechanisms of antihypertensive effects, (2) improved compliance from better tolerance, and (3) ease of dosing.
- When used in combination with diuretics, ACE inhibitors prevent congestive heart failure and reduce morbidity and mortality events in hypertensive patients with heart failure.
- The choice of antihypertensive treatment should be tailored to the patient’s unique profile of concomitant cardiovascular disease risk factors and/or comorbid conditions by selecting agents that have specific effects on cardiovascular and extracardiovascular disorders.

REFERENCES


## Appendix I. Recommended Antihypertensive Medications for Patients with Comorbid Conditions

<table>
<thead>
<tr>
<th>Indication</th>
<th>Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compelling indications unless contraindicated</strong></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus (type 1) with proteinuria</td>
<td>ACE inhibitors</td>
</tr>
<tr>
<td>Heart failure</td>
<td>ACE inhibitors, diuretics, β-blockers</td>
</tr>
<tr>
<td>Isolated systolic hypertension (older patients)</td>
<td>Diuretics (preferred), calcium channel blockers (long-acting dihydropyridine)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>β-Blockers (nonintrinsic sympathomimetic activity), ACE inhibitors (with systolic dysfunction)</td>
</tr>
<tr>
<td><strong>May have favorable effects on comorbid conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>β-Blockers, calcium channel blockers (long acting)</td>
</tr>
<tr>
<td>Atrial tachycardia and fibrillation</td>
<td>β-Blockers, calcium channel blockers (non-dihydropyridine)</td>
</tr>
<tr>
<td>Cyclosporine-induced hypertension</td>
<td>Calcium channel blockers</td>
</tr>
<tr>
<td>Diabetes mellitus (types 1 and 2) with proteinuria</td>
<td>ACE inhibitors (preferred), calcium channel blockers</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>α-Blockers</td>
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<tr>
<td>Essential tremor</td>
<td>β-Blockers (noncardioselective)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>β-Blockers, angiotensin II–receptor blockers, spironolactone</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>β-Blockers</td>
</tr>
<tr>
<td>Migraine</td>
<td>β-Blockers (noncardioselective), calcium channel blockers (nondihydropyridine)</td>
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<td>Myocardial infarction</td>
<td>Diltiazem, verapamil</td>
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<td>Osteoporosis</td>
<td>Thiazides</td>
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<td>Benign prostatic hyperplasia</td>
<td>α-Blockers</td>
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<td>Renal insufficiency (except in renovascular hypertension and creatinine ≥ 265.2 mmol/L [3 mg/dL])</td>
<td>ACE inhibitors</td>
</tr>
<tr>
<td><strong>Unfavorable effects on comorbid conditions</strong></td>
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<td>Bronchospastic disease</td>
<td>β-Blockers</td>
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<td>Depression</td>
<td>β-Blockers, central α-antagonists, reserpine</td>
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<td>Diabetes mellitus (types 1 and 2)</td>
<td>β-Blockers, high-dose diuretics</td>
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<tr>
<td>Dyslipidemia</td>
<td>β-Blockers (nonintrinsic sympathomimetic activity), diuretics (high dose)</td>
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<td>Gout</td>
<td>Diuretics</td>
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<td>Second-degree and third-degree heart blockers</td>
<td>β-Blockers, diltiazem, verapamil</td>
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<tr>
<td>Heart failure</td>
<td>Calcium channel blockers (except amlodipine, felodipine)</td>
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<td>Liver disease</td>
<td>Labetalol, methyldopa</td>
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<td>Peripheral vascular diseases</td>
<td>β-Blockers</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>ACE inhibitors, angiotensin II–receptor blockers</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>Potassium-sparing agents</td>
</tr>
<tr>
<td>Renovascular disease</td>
<td>ACE inhibitors, angiotensin II–receptor blockers</td>
</tr>
</tbody>
</table>

ACE = angiotensin-converting enzyme.