The use of modern technology in the diagnosis of hypertension, and the treatment of these patients. The systolic/diastolic BP levels at which treatment is initiated to ≥150/≥90 as a result, some of the key recommendations were on the basis of expert management of high blood pressure in adults: Report from the panel members appointed to the Eighth Joint National Committee (JNC 8). Hypertension is one of the most common conditions managed by generalists and is a major risk factor for multiple conditions. Surrounded by great debate, the committee appointed to the Eighth Joint National Committee published their suggestions for new hypertension treatment guidelines in early 2014. We suggest a new target blood pressure (BP) for the general population older than 60 years of less than 150/90 mm Hg, up from less than 140/90 mm Hg as recommended by the Seventh Joint National Committee, and in diabetic patients, a goal of less than 140/90 mm Hg, up from the Seventh Joint National Committee recommendation of less than 130/80 mm Hg. Regardless of the BP target, recommendations suggested by the Eighth Joint National Committee and other organizations, obtaining accurate BP readings and recognizing white-coat and masked hypertension is imperative. Home and ambulatory BP monitoring are useful tools in addition to proper in-office BP readings. The optimal care of the hypertensive patient involves accurate BP characterization, careful use of guidelines, and good clinical judgment.
WHY Treat Hypertension?

- Hypertension is the most common chronic condition treated by family physicians.
- Elevated blood pressure is associated with an increased risk of heart failure, myocardial infarction, cerebrovascular disease, renovascular disease, and death.
- Treatment of hypertension reduces the risk of these events.

Implications of Hypertension

- The public health goal of treating hypertension is the reduction of the atherothrombotic cardiovascular sequelae of heart disease, stroke, renovascular disease, and death.

Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies.

- Meta-analysis of 61 prospective, observational studies
- 1 million adults
- 12.7 million person-years

FINDINGS: With each decade of age at death, the proportional difference in the risk of vascular death associated with a given absolute difference in usual blood pressure (SBP and DBP) is about the same at usual blood pressures above 115/75 mm Hg and 75 mm Hg usual diastolic blood pressure (DBP), below which there is little evidence. At ages 40-49 years, each difference of 10 mm Hg usual SBP (or, approximately equivalently, 10 mm Hg usual DBP) is associated with more than a twofold difference in the risk of vascular death, and with twofold differences in the death rates from IHD and from other vascular causes. All of these proportional differences in vascular mortality are about half as extreme at ages 80-89 years as at ages 40-49 years, but the annual absolute differences in risk are greater in old age. The age-specific associations are similar for men and women, and for cerebral haemorrhage and cerebral ischaemia. For predicting vascular mortality from a single blood pressure measurement, the average of SBP and DBP is slightly more informative than either alone, and pulse pressure is much less informative.

INTERPRETATION: Throughout middle and old age, usual blood pressure is strongly and directly related to vascular (and overall) mortality, without any evidence of a threshold down to at least 115/75 mm Hg.

Benefits of BP Reduction in the Hypertension Optimal Treatment (HOT) Trial: Diabetic Cohort

- Target DBP (mm Hg) ≤ 90
- Achieved DBP (mm Hg) = 143.7
- Achieved DBP (mm Hg) = 85.2
- Achieved SBP (mm Hg) = 141.4
- Achieved SBP (mm Hg) = 83.2
- Achieved SBP (mm Hg) = 139.7
- Achieved SBP (mm Hg) = 81.1

Achieved = mean of all BPs from 6 months of follow-up to end of study

P = 0.05 for trend


Major CV Events (per 1000 patient yrs)

Achieved DBP (mm Hg)

0 25 50

85.2 83.2 81.1

Rates of Cardiovascular Events* When BP is Controlled

Adapted from JNC7 – Evidence from clinical trials

Cardiovascular Mortality Risk Doubles With Each 20/10 mm Hg BP Increment*

SBP = systolic blood pressure, DBP = diastolic blood pressure

Adapted from JNC7 – Evidence from clinical trials

*CV death, MI, stroke, heart failure; Adjusted for concomitant CV risk factors.

Midlife Hypertension and 20-Year Cognitive Change
The Atherosclerosis Risk in Communities Neurocognitive Study

- **Importance** Hypertension is a treatable potential cause of cognitive decline and dementia, but its greatest influence on cognition may occur in midlife.

- **Main Outcomes and Measures** Prespecified outcomes included the 20-year change in scores on the Delayed Word Recall Test, Digit Symbol Substitution Test, and Word Fluency Test and in global cognition.

- **Results** Having a JNC-8–specified indication for initiating antihypertensive treatment at baseline was associated with a greater 20-year decline in −0.044 (95% CI, −0.088 to −0.003) global z-score points than not having an indication. Each 20-mm Hg increment at baseline was associated with an additional decline of 0.048 (95% CI, −0.074 to −0.022) points in global cognitive z score in whites but not in African Americans. Individuals with hypertension who used antihypertensives had less decline during the 20 years than untreated individuals.

- **Conclusions and Relevance** Midlife hypertension and elevated midlife but not late-life systolic BP was associated with more cognitive decline during the 20 years of the study. Greater decline is found with higher midlife BP in whites than in African Americans.

**Effects of Blood Pressure Reduction in Mild Hypertension: A Systematic Review and Meta-analysis**
Ann Intern Med. 2015;162(3):184-191

- **Study Selection:** Patients without cardiovascular disease with blood pressures in the grade 1 hypertension range (140 to 159/90 to 99 mm Hg) who were randomly assigned to an active (antihypertensive drug or more intensive regimen) or control (placebo or less intensive regimen) blood pressure–lowering regimen.

- **Data Synthesis:** The average blood pressure reduction was about 3.6/2.4 mm Hg. Over 5 years, odds ratios were 0.86 (95% CI, 0.74 to 1.01) for total cardiovascular events, 0.72 (CI, 0.55 to 0.94) for strokes, 0.91 (CI, 0.74 to 1.12) for coronary events, 0.86 (CI, 0.57 to 1.12) for heart failure, 0.75 (CI, 0.57 to 0.98) for cardiovascular deaths, and 0.78 (CI, 0.67 to 0.92) for total deaths. Results were similar in secondary analyses. Withdrawal from treatment due to adverse effects was more common in the active groups.

- **Conclusion:** Blood pressure–lowering therapy is likely to prevent stroke and death in patients with uncomplicated grade 1 hypertension.

**JNC 8: Relaxing the Standards**
Editorial by ROBERT GAUER, MD, and JUSTIN LAROCQUE, PharmD, BCPS, Published in Am Fam Physician. 2014 Oct 1;90(7):449-452.

- **Evidence-based guidelines** are indispensable and assist clinicians in providing the most effective care for patients. The Eighth Joint National Committee (JNC 8) recently issued the most anticipated guideline in some time.

- **The JNC 8 committee** was initially appointed in 2008 by the National Heart, Lung, and Blood Institute. When the National Institutes of Health discontinued sponsorship of clinical recommendations, JNC 8 panel members published their guideline on the management of hypertension in the Journal of the American Medical Association the same week the American Society of Hypertension and the International Society of Hypertension released their guideline.

- **The JNC 8 guideline** was never endorsed by the American Heart Association or the American College of Cardiology.

**JNC 8: Relaxing the Standards**
Editorial by ROBERT GAUER, MD, and JUSTIN LAROCQUE, PharmD, BCPS, Published in Am Fam Physician. 2014 Oct 1;90(7):449-452.

- More than 25% of older adults who were receiving antihypertensive therapy under the more stringent JNC 7 targets will be reclassified as at goal under JNC 8, suggesting that millions of Americans are eligible for reduction or elimination of antihypertensive therapy.

- However, the panel recommended that therapy not be adjusted for these patients, which creates two distinct standards within the same age group.

- Do we know which group is receiving better care?

- Are we fostering a healthier population or merely tolerating higher blood pressure values?
JNC 8: Relaxing the Standards

As in JNC 7, physicians have been challenged to stay within the performance measures of blood pressure goals. With more relaxed blood pressure targets for older adults, it is conceivable that clinicians may become less vigilant and be satisfied with near-goal values. Will these slightly higher blood pressure targets improve care for patients or result in higher rates of cardiovascular and cerebrovascular events?

Patients who met the JNC 7 requirements for hypertension should be maintained on their current regimen. For others, achieving a systolic blood pressure closer to 140 mm Hg, compared with 150 mm Hg, is reasonable given the available evidence, assuming that the adverse effects of medication are minimal.

Current Hypertension Guidelines

- Journal of the American Medical Association (JAMA)
- American Diabetes Association (ADA)
- Hypertension Canada
- European Society of Hypertension (ESH)
- The International Society of Hypertension (ISH) and World Health Organization
- The International Society on Hypertension in Blacks (ISHIB)
- Journal of Clinical Hypertension (JCH)
- National Heart, Lung, and Blood Institute (NHLBI)
- National Institute for Health and Clinical Excellence (NICE)
- National Kidney Foundation (NKF)

Why Treat – When to Treat – HOW to Treat

- Assess lifestyle and identify other CV risk factors or concomitant disorders that may affect prognosis or guide treatment
- Reveal identifiable causes of high BP
- Assess the presence or absence of target-organ damage (TOD) and CVD
Identifiable Causes of Hypertension

- Sleep apnea
- Drug-induced or drug-related
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Chronic steroid therapy and Cushing syndrome
- Pheochromocytoma
- Coarctation of the aorta
- Thyroid or parathyroid disease

Physical Examination

- Appropriate measurement of BP
  - Verification in the contralateral arm
- Optic fundoscopy
- BMI calculation
- Auscultation for carotid, abdominal, and femoral bruits
- Palpation of the thyroid gland
- Thorough exam of the heart and lungs
- Abdominal exam for enlarged kidneys, masses, bruits, and abnormal aortic pulsation
- Lower extremities for edema and pulses
- Neurologic assessment

Initial Laboratory Evaluation of Hypertension

- 12-lead electrocardiography
- Blood glucose level
- Fasting cholesterol panel (including low-density lipoprotein and high-density lipoprotein cholesterol, triglycerides)
- Glomerular filtration rate
- Hematocrit level
- Serum calcium level
- Serum potassium level

- Optional
  - Urinary albumin excretion
  - Albumin/creatinine ratio

Components of the Dietary Approaches to Stop Hypertension (DASH) Diet

<table>
<thead>
<tr>
<th>Dietary component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fat</td>
<td>27% of calories</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>6% of calories</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>150 mg</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>55% of calories</td>
</tr>
<tr>
<td>Fiber</td>
<td>30 g</td>
</tr>
<tr>
<td>Protein</td>
<td>18% of calories</td>
</tr>
<tr>
<td>Sodium</td>
<td>1,500 mg</td>
</tr>
</tbody>
</table>

Lifestyle Recommendations for Lowering Blood Pressure

- Consume a diet that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils, and nuts; and limits intake of sweets, sugar-sweetened beverages, and red meat. Adapt this dietary pattern to appropriate caloric requirements, personal and cultural food preferences, and nutritional therapy for other medical conditions (including diabetes mellitus). Follow plans such as the DASH diet, the U.S. Department of Agriculture Food Patterns, or the American Heart Association diet.
- Consume no more than 2,400 mg of sodium per day. Further reduction of sodium intake to 1,500 mg per day is associated with even greater reduction in blood pressure. Reducing intake by at least 1,000 mg per day will lower blood pressure even if the desired daily intake is not achieved.
- Combine the DASH diet with lower sodium intake.

- Lifestyle Modifications for Hypertension
  - Lose weight if overweight (80% of type 2 diabetics)
  - Limit EtOH to 1 oz. (2 beers/wine/drinks) for men, 0.5 oz for women and lighter weight men
  - Increase aerobics to 30-45 min. most days
  - Reduce Na+ to 2.4 g; Reduce saturated fat
  - Adequate potassium, Ca++, and Mg++
  - Stop smoking; Control lipids
Anatomy of Health Effects of Mediterranean diet: Greek EPIC prospective cohort study


- High
  - Vegetables
  - Fruits
  - Nuts
  - Beans
  - Olive oil
  - Wine /alcohol (in moderation)
- Minimal
  - Fish
  - Whole grains
  - Low fat dairy
- Low
  - Meats


Mediterranean diet

- Two studies in coronary patients, the Lyon Diet Heart Study and the IndoMediterranean Diet study, have shown that, despite no difference in fasting lipid levels, a Mediterranean diet reduced myocardial infarction and death by 60% in four years and by 50% in two years compared with diets amounting to the American Heart Association diet that is usually prescribed to coronary patients.


Examples of Clinical Trials That Have Impacted Hypertension Treatment Management

1957 — VACBAA
HCTZ diuretics
Vasodilators
Sympathomimetics
CCBs
B-Blockers
ACEIs
ARBs/DRIs
Renin-Angiotensin System

FDR was rid of his phenobarbital

Roosevelt died two months after the Yalta Conference of a brain hemorrhage.

Evolution of Antihypertensive Therapy

1950s
Volume Diuretics
Vasoconstriction
Vasodilators
Sympathomimetics
CCBs
B-Blockers
ACEIs
ARBs/DRIs

Evolution of Treatment Recommendations

JNC I
1977
Stepped care: thiazides to methyldopa, reserpine, or propranolol

JNC II
1984
Stepped care: thiazides to enalapril-atenolol

JNC III
1993
Stepped care: thiazides to enalapril, ACE-I, or CCB

JNC IV
1997
Stepped care: thiazides or BB

JNC V
1999
Stepped care: thiazides or BB, for renin-activated patients: ACE-I or CCB

JNC VI
2003
Stepped care: thiazides, ACE-I, or CCB, for renin-activated patients: ACE-I or CCB

JNC 8 recommendations represent a paradigm shift in the pharmacologic management of hypertension

- Thiazide diuretics had previously been recommended as monotherapy for patients with stage 1 hypertension or in combination with other agents for patients with stage 2 hypertension.
- Now, thiazides, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and calcium channel blockers are indicated for monotherapy.
- There is insufficient evidence that beta blockers provide clinically significant benefits for cardiovascular and cerebrovascular outcomes.
- The availability of four first-line agents may seem more challenging, but it allows clinicians to incorporate their preferences—and those of their patients—into the accepted practice recommendations.
**Initial Antihypertensive Drug Selection by Patient Population**

<table>
<thead>
<tr>
<th>Patient population</th>
<th>American Society of Hypertension guideline</th>
<th>European Society of Hypertension/European Society of Cardiology guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black patients</td>
<td>CGB or thiazide diuretic ARB or ACE inhibitor</td>
<td>CCB, thiazide diuretic, ARB, ACE inhibitor, or beta blocker</td>
</tr>
<tr>
<td>Nonblack patients younger than 60 years</td>
<td>ARB or ACE inhibitor</td>
<td>CCB or thiazide diuretic</td>
</tr>
<tr>
<td>Nonblack patients 60 years and older</td>
<td>CCB, thiazide diuretic, ARB, or ACE inhibitor</td>
<td>CCB or thiazide diuretic</td>
</tr>
<tr>
<td>Patients with chronic kidney disease</td>
<td>ARB or ACE inhibitor</td>
<td>ARB or ACE inhibitor</td>
</tr>
</tbody>
</table>


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**Efficacy and Safety of Benazepril for Advanced Chronic Renal Insufficiency**

- Benefits did not appear to be attributable to blood-pressure control.
- Benazepril therapy was associated with a 55 percent reduction in the level of proteinuria and a reduction of 23 percent in the rate of decline in renal function.
- Group 1 had a serum creatinine level of 1.5 to 3.0 mg per deciliter, and group 2 had a serum creatinine level of 3.1 to 5.0 mg per deciliter at baseline.

**Kaplan–Meier Estimates of the Percentage of Patients Not Reaching the Primary Composite End Point of a Doubling of the Serum Creatinine Level, End-Stage Renal Disease, or Death**

- As compared with placebo, benazepril was associated with a 43 percent reduction in the risk of the primary end point in group 2 (P=0.005).
- Benazepril conferred substantial renal benefits in patients without diabetes who had advanced renal insufficiency.

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**Multiple Antihypertensive Agents Are Needed to Achieve Target BP**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Target BP (mm Hg)</th>
<th>No. of antihypertensive agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALLHAT</td>
<td>SBP &lt;140/DBP &lt;90</td>
<td>1</td>
</tr>
<tr>
<td>UKPOS</td>
<td>DBP &lt;85</td>
<td>2</td>
</tr>
<tr>
<td>ABCD</td>
<td>DBP &lt;75</td>
<td>3</td>
</tr>
<tr>
<td>MORD</td>
<td>MAP &lt;82</td>
<td>4</td>
</tr>
<tr>
<td>HOT</td>
<td>DBP &lt;80</td>
<td></td>
</tr>
<tr>
<td>AASK</td>
<td>MAP &lt;82</td>
<td></td>
</tr>
<tr>
<td>IDNT</td>
<td>SBP &lt;135/DBP &lt;95</td>
<td></td>
</tr>
</tbody>
</table>

**Concomitant Use of Antihypertensive Drugs**

- **Diuretics**
- **β-Blockers**
- **ACEIs, ARBs, and aliskiren**
- **Calcium Channel Blockers**
- **α1-Receptor Blockers**
Causes of Resistant Hypertension

- Improper BP measurement
- Volume overload and pseudotolerance
  - Excess sodium intake
  - Volume retention from kidney disease
  - Inadequate diuretic therapy
- Associated conditions
  - Obesity
  - Excess alcohol intake
- Identifiable causes of hypertension
  - Drug-induced/other causes
    - Nonadherence
    - Inadequate doses
    - Inappropriate combinations
    - NSAIDs/ Cox-2s
    - Cocaine, amphetamines…
    - Sympathomimetics
    - Oral contraceptives
    - Adrenal steroids
    - Cyclosporine/tacrolimus
    - Erythropoetin
    - Licorice (including some chewing tobacco)
    - Ephedra, ma huang, bitter orange
- Associated conditions
  - Obese
  - Excess alcohol intake

Identifiable causes of hypertension

Commonly Used Agents: Adverse Effects

<table>
<thead>
<tr>
<th>Diuretics</th>
<th>β-Blockers</th>
<th>CCBs</th>
<th>ACEIs</th>
<th>ARBs</th>
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</thead>
<tbody>
<tr>
<td>Muscle cramps</td>
<td>Impotence</td>
<td>Gout</td>
<td>Dyslipidemia</td>
<td>Glucose intolerance</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Hypertension</td>
<td>Impotence</td>
<td></td>
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<tr>
<td>Edema</td>
<td>Edema</td>
<td>Flushing</td>
<td>Edema</td>
<td>Hypertension</td>
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<td>Edema</td>
<td>Headache</td>
<td>MI</td>
<td>Edema</td>
<td>Hyperkalemia</td>
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<td>MI</td>
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Commonly Used Agents: Adverse Effects

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<tr>
<td>Glucose intolerance</td>
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<tr>
<td>Hypertension</td>
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</table>

Tolerability and Treatment Compliance

% of patients continuing prescribed drug regimen after 1 year


ALDOSTERONE CAUSES…

- Na+/K+/H+ exchange in distal nephron
  - Hypokalemia, salt/water retention, met.alk.
- ↑ catecholamine release
- ↓ NE uptake by myocardium
- ↑ oxidative stress
- ↓ fibrinolysis
- Endothelial dysfunction
- Vascular stiffening and injury
- Necrosis/fibrosis of myocardium
- Glomerulosclerosis /proteinuria
- Cardiac arrhythmias
- Heart failure
THINK ALDOSTERONE EFFECT WHEN....

• Serum K+ < 3.5 mmol/L
  - Na+ > 135 mmol/L
  - No thiazide or loop diuretic
  - Salt and water retention / edema
• BP uncontrolled w/ 3 drugs [not MRB]
• Resistant HT + sleep apnea
• Plasma aldosterone > 15 ng/dl
• Plasma aldosterone/renin activity ratio >25
• Salt-loading does not suppress aldosterone
• Adrenal enlargement / mass [incidental]

The kidney is a vital organ

• I call it the neglected target organ...

Glomerular Effects of CCBs vs ACEIs and ARBs

Dilation of afferent arteriole only

Dilation of both afferent and efferent arteriole

Emerging Science Indicates that Aldosterone Plays a Multi-Factorial Cardiovascular role
A family physician questions the conclusions from ALLHAT.

A key ALLHAT conclusion is that thiazide diuretics should be preferred for first-step antihypertensive therapy.

• ALLHAT was not a monotherapy trial, and rational drug combinations were discouraged by study design in the isonipril limb.
• ALLHAT was not a valid comparison trial because blood pressures were not equally controlled with the various study limbs.
• The ALLHAT conclusion that recommends chlorthalidone for initial hypertension therapy seems unjustified because ALLHAT was not a trial that initiated therapy for hypertension.
• ALLHAT was not of sufficient length to detect the poorer outcomes that are inevitable with increased rates of diabetes in the chlorthalidone limb.
• The heart failure subset analysis was not prospectively established.

ALLHAT was not designed to make the conclusions claimed by its authors.

Hypertension and Atherosclerosis:
Clinical Implications from the ALLHAT Trial.
Standridge JB.

• By failing to recognize the heterogeneity of hypertension, the authors of the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) study used a faulty premise to conduct a poorly designed clinical trial. By failing to control blood pressures equally across study drug groups, ALLHAT cannot be considered to be a definitive comparative trial. Being neither a monotherapy trial nor a trial that initiated therapy for blood pressure control, ALLHAT provided no data to recommend first-line therapy for hypertension, making the conclusions invalid.

• Thiazide-type diuretics increase angiotensin II and consequently promote atherosclerosis and arteriolarsclerosis.

• Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers retard atherosclerosis and are nephroprotective.

• Multiple randomized controlled trials show beneficial clinical outcomes, including cardioprotection and nephroprotection, with the use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. These agents, and not thiazide-type diuretics, should be used as first-line agents to retard the process of atherosclerosis and its clinical outcomes in the setting of arterial hypertension.

A Systematic Review of Randomized Controlled Trials Examining the Nephroprotective Properties of Antihypertensive Medications

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Instructor
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Current Hypertension Reviews. Volume 8, Number 3, August 2012, pp. 196-226(31)

• Abstract: Introduction: Despite improved control rates of hypertension in the United States during the last thirty years, the rate of chronic kidney disease and end-stage renal disease has not demonstrated a similar resultant improvement.

• Purpose: The purpose for this review is to determine interventions in the treatment of hypertension that improve outcomes in the promotion of nephroprotection.

• Method: A systematic comprehensive search of the National Library of Medicine utilizing Medline was conducted with search limits confined to randomized controlled trials.
A Systematic Review of Randomized Controlled Trials Examining the Nephroprotective Properties of Antihypertensive Medications

Current Hypertension Reviews, Volume 8, Number 3, August 2012, pp. 196-226(31)

• Results: Angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEIs) are nephroprotective alone and in combination with other classes of antihypertensive agents, but can result in renal dysfunction when used in combination with each other or with a direct renin inhibitor (DRI). Older L-type calcium channel blockers (CCBs) can be nephrotoxic when used as monotherapy. CCBs are additionally nephroprotective when combined with ACEIs or ARBs. Thiazide-type diuretics (TTDs) with the exception of indapamide are not nephroprotective and TTDs may have nephrotoxic properties.

Conclusion: ACEIs and ARBs are preferred first-line agents because they are effective in the prevention of renal as well as cardiovascular and cerebrovascular target organ damage associated with hypertension. CCBs are preferred when a second medication is needed for hypertension control. When diuretic therapy is indicated for hypertension control, indapamide is preferred over other TTDs for nephroprotection.

Effect of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers on all-cause mortality, cardiovascular deaths, and cardiovascular events in patients with diabetes mellitus: a meta-analysis.


• RESULTS: Twenty-three trials compared ACEIs with placebo or active drugs (32,827 patients) and 13 compared ARBs with no therapy (controls) (23,867 patients). When compared with controls, ACEIs significantly reduced the risk of all-cause mortality by 13%, CV deaths by 17%, and major CV events by 14%, including myocardial infarction by 21% and heart failure by 19%. Treatment with ARBs did not significantly affect all-cause mortality, CV death rate, and major CV events with the exception of heart failure. Both ACEIs and ARBs were not associated with a decrease in the risk for stroke in patients with DM. Meta-regression analysis showed that the ACEI treatment effect on all-cause mortality and CV death did not vary significantly with the starting baseline blood pressure and proteinuria of the trial participants and the type of ACEI and DM.

• CONCLUSIONS AND RELEVANCE: Angiotensin-converting enzyme inhibitors reduced all-cause mortality, CV mortality, and major CV events in patients with DM, whereas ARBs had no benefits on these outcomes. Thus, ACEIs should be considered as first-line therapy to limit excess mortality and morbidity in this population.