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Treatment of Hypertension

Updated September 2025

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WITHOUT CVD or CKD	CAD[b]	Stroke/ TIA[b]	CKD[b]	HF*r*EF[b]	HF*p*EF[b]	Other CVD
One, or low-dose combo[b] of two, of these: ACEI[h] or ARB,[h] thiazide,[a] long-acting DHP CCB[1,2,e]	Evidence-based ACEI,[h] ARB,[h] or BB[d] (BB especially for recent MI or ACS, or angina)[1,11] Add-ons: long-acting DHP CCB,[e] thiazide,[a] MRA[g,1,11]	Thiazide,[a] ACEI,[h] or ARB[1,h]	ACEI[h] or ARB.[1,h] Can add a long-acting DHP CCB[e] or thiazide (loop if eGFR <30 mL/min/1.73m^2).[1,4] Consider adding finerenone for diabetic kidney disease.[17]	Evidence-based BB;[d] MRA[g] (if symptomatic, eGFR >30 mL/min/1.73m^2, potassium <5 mEq/L); sacubitril/valsartan (NYHA Class II to III [preferred over ACEI[h] or ARB[h]]), and SGLT2 inhibitor (if symptomatic)[1] Loop diuretic as needed.[1] Can add hydralazine plus isosorbide dinitrate in Black patients, or other patients who can't take sacubitril/ valsartan, ACEI[h] or ARB.[1,h]	SGLT2 inhibitor.[1,5] Consider MRA[g] or sacubitril/ valsartan or ARB.[1,5,h] Loop diuretic as needed.[1] **HF*mr*EF[b]** SGLT2 inhibitor.[5] Consider MRA[g] or sacubitril/ valsartan or ARB.[5] Consider Evidence-based BB.[d,5]	**A-fib[b]** ACEI,[h] ARB,[h] or MRA[f,g,1,3] **Aortic disease[b]** BB[d] (largely extrapolated from acute management)[1] **Aortic VALVE regurgitation[b]** ACE,[h] ARB[h] (note: antihypertensives that reduce HR may increase SBP)

- Optimize dose, then add another appropriate first-line agent (e.g., thiazide,[a] ACEI,[h] ARB,[h] long-acting dihydropyridine CCB[e]).[2,4]
  - DO NOT combine an ACEI plus ARB and/or aliskiren.[1]
- Consider SGLT2 inhibitor (for diabetes, HF) or GLP-1 agonist (diabetes, obesity) for appropriate patients.[1,18]

Investigate resistant HTN (i.e., BP >goal despite optimal dosing of three antihypertensives from different classes,[6,7] or BP controlled with four antihypertensives.[6]) Consider pseudoresistance and secondary HTN. **See footnote c** for more information on resistant HTN.

Add a drug(s) from a class not currently in use.

Spironolactone (preferred[1,2,4]) or eplerenone[1,6,g] *OR* **Amiloride**[4,7,13]	If HR ≥70 bpm: **Beta-blocker** (consider carvedilol)[6,14,d] *OR* **Clonidine**[4,6] *OR* **Guanfacine**[6] *OR* **Long-acting diltiazem or verapamil**[6,e]	**Doxazosin** Consider for BPH[1,4] Risk of orthostatic hypotension, especially with first dose and in older patients.[1]	**Hydralazine** Max dose 50 mg TID to reduce lupus risk.[6] Use with BB and diuretic to counteract reflex tachycardia and fluid retention.[1] Add nitrate for HFrEF.[6] *OR* **Minoxidil**[6] Causes hirsutism.[6] Use with BB and diuretic to counteract reflex tachycardia and fluid retention.[1]	**Aprocitentan** (Tryvio [US]).[12] Risk of embryo-fetal toxicity. Lacks CV risk reduction data. Can cause fluid retention, hepatotoxicity, hemoglobin eGFR reduction, reduced sperm count.

Therapy Optimization (consider during all steps above)

- Optimize lifestyle interventions (e.g., healthy diet, exercise, weight loss, sodium restriction [e.g., 2,400 mg/day], increased dietary potassium [if appropriate], alcohol restriction, stress reduction).[1,6,7]
- Consider discontinuation or dose reduction of drugs or substances that may increase blood pressure.
- Consider use of once-daily antihypertensives (to improve adherence), giving at least one dose at bedtime; patients with resistant HTN often have BP that doesn't "dip" at night like it should.[6,10]
- Consider choosing indapamide or chlorthalidone (with azilsartan for resistant HTN) over hydrochlorothiazide.[6,7,a] See footnote a for details.
- Consider switching amlodipine to long-acting nifedipine.[6]

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Footnotes

a. **Thiazide considerations**. "Thiazide" includes thiazide-like diuretics. Chlorthalidone or indapamide have a longer duration of action than hydrochlorothiazide and may be preferable in patients with resistant HTN.[1,7] Chlorthalidone may provide better CV outcomes in patients with a history of stroke or MI, at the expense of higher risk of hypokalemia.[1,2] Thiazides are effective to eGFR 25 to 30 mL/min/1.73m^2.[6] Chlorthalidone is about twice as potent as hydrochlorothiazide.[9] Chlorthalidone is available alone or in combination with azilsartan (Edarbyclor).Azilsartan may provide more BP reduction than other ARBs or ACEIs.[6]

b. Combination Therapy vs. Stepped-Care
- Consider starting with a **combo** of two meds, especially if baseline BP ≥140/90 mm Hg, Black, or CV risk >7.5%.[1] Hypertension Canada recommends starting with a combo in all patients.[2]
  - Monitor older adults for orthostatic hypotension.[1]
  - Choose a single-pill combination with two meds to promote adherence.[1,2,4] Available single-pill combinations include ACEI/CCB, ARB/CCB, ACEI/diuretic, ARB/diuretic.
- Consider starting with a single agent, carefully uptitrating, then adding other agents if needed (**stepped care**) when starting antihypertensives in frail patients, patients with a history of adverse effects with antihypertensives (e.g., hypotension), and/or baseline BP 130 to 139/80 to 89 mm Hg.[1]

c. Resistant Hypertension
- Hypertension Canada recommends specialist referral for patients not at goal with three agents.[7]
- Consider pseudoresistance due to nonadherence, blood pressure measurement error, or white coat HTN.[6,7]
- Consider secondary HTN due to obstructive sleep apnea (very common),[8] primary hyperaldosteronism (AHA guidelines recommend screening all patients[6]), CKD, renal artery stenosis, chromaffin cell tumors (e.g., pheochromocytoma), coarctation of the aorta (even post-repair), Cushing's disease, rare endocrine disorders.[6]
- Adverse effects are an important consideration when choosing an add-on antihypertensive because evidence that BP reduction improves CV outcomes in resistant HTN is lacking.[7]

d. Beta-blocker considerations:
- BB are not recommended first-line for HTN unless the patient has CAD or HF.[1]
  - In **HTN**, BBs do not reduce stroke risk as much as ACEIs, ARBs, thiazides. or dihydropyridine CCBs.[2]
- For **CAD**, evidence-based BB choices include carvedilol, metoprolol succinate, nadolol, bisoprolol, propranolol, or timolol.[11]
- Avoid atenolol; it is inferior to other BBs for reducing CV events.[11]
- For **HF**, evidence-based BB choices include metoprolol succinate, bisoprolol, or carvedilol.[1]
- Avoid combining a BB with clonidine or a non-DHP CCB (diltiazem, verapamil).[12]
- For indications and dosing, see our chart, *Comparison of Oral Beta-Blockers*.

e. Calcium channel blocker considerations
- Do not use short-acting nifedipine.[1]
- Consider use of long-acting nifedipine over amlodipine for potentially better BP control; however, nifedipine may cause more edema than amlodipine.[6]
- Do not use a non-DHP CCB (diltiazem, verapamil) in patients with HF*r*EF.[1]
- A nondihydropyridine CCB (diltiazem, verapamil) can be used **instead of** a BB for angina unless the patient has significant left ventricular dysfunction.[11]
- DHP and non-DHP (diltiazem, verapamil) can be combined.[1]

f. Some evidence suggests that ACEIs or ARBs may reduce A-fib recurrence, and MRAs may reduce A-fib burden.[1,3]

g. Mineralocorticoid receptor antagonist considerations
- Do not combine MRAs (spironolactone, eplerenone, finerenone).[1]
- MRAs with evidence in HF*r*EF are spironolactone and eplerenone.[5]
- In HF*p*EF, consider MRAs (spironolactone or finerenone) for females, or males with ejection fraction <55% to 60%).[5,15,16]
- MRAs with evidence in HF*mr*EF are spironolactone and finerenone.[5,16]
- Spironolactone has been studied for BP control in resistant HTN, and is a first-line-add-on.[1]
- Eplerenone is dosed BID for HTN, but poses lower risk of gynecomastia and erectile dysfunction than spironolactone.[1]
- Like eplerenone, finerenone is less likely than spironolactone to cause gynecomastia.[17]

h. ACEIs and ARBs: for indications and dosing, see our chart, *Angiotensin Receptor Blockers and Angiotensin-Converting Enzyme Inhibitors*.

Abbreviations: ACEI = Angiotensin converting enzyme inhibitor; A-fib = atrial fibrillation; ARB = angiotensin receptor blocker; BB = beta-blocker; BID = twice daily; BNP = brain natriuretic peptide; BP = blood pressure; BPH = benign prostatic hypertrophy; bpm = beats per minute; CCB = calcium channel blocker; CKD = chronic kidney disease; CVD = cardiovascular disease; DBP = diastolic blood pressure; DHP = dihydropyridine; DM = diabetes mellitus; GLP-1 = glucagon-like peptide-1; HF = heart failure; HR = heart rate; HTN = hypertension; ISH = isolated systolic hypertension; LVH = left ventricular hypertrophy; MI = myocardial infarction; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; SGLT2 = sodium-glucose cotransporter-2

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