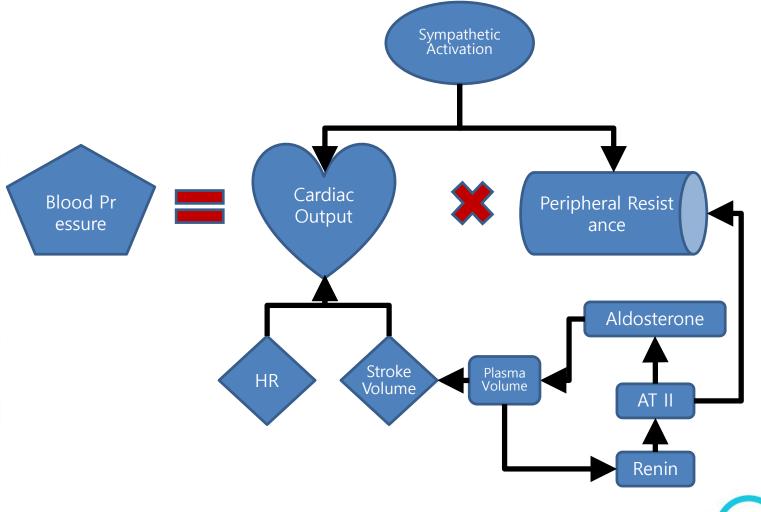
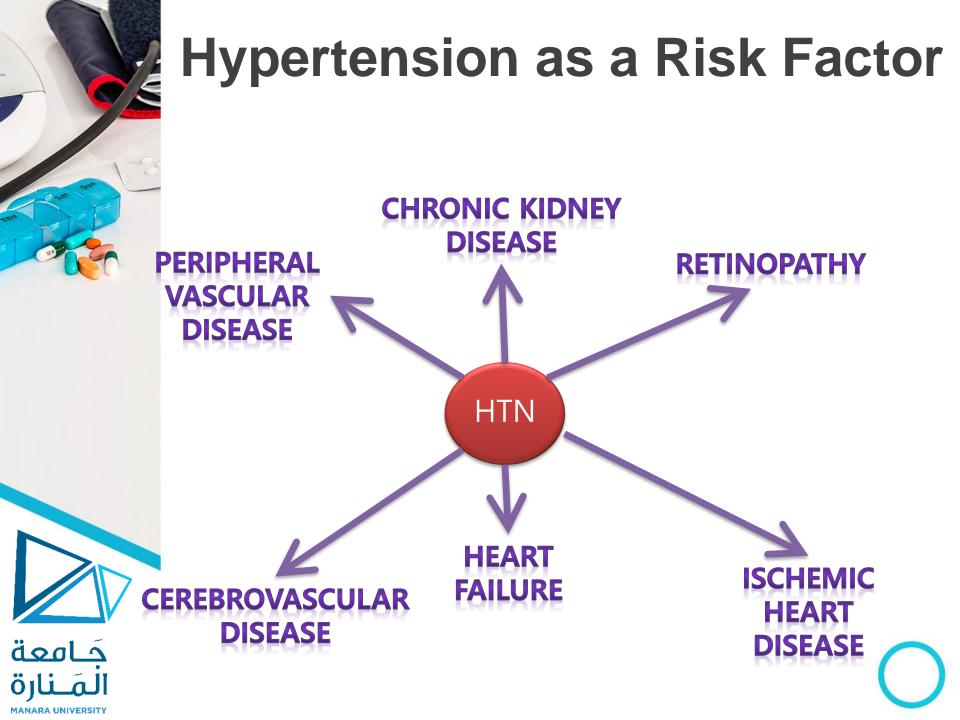


جامعة المنارة- كلية الصيدلة 6/1/2020



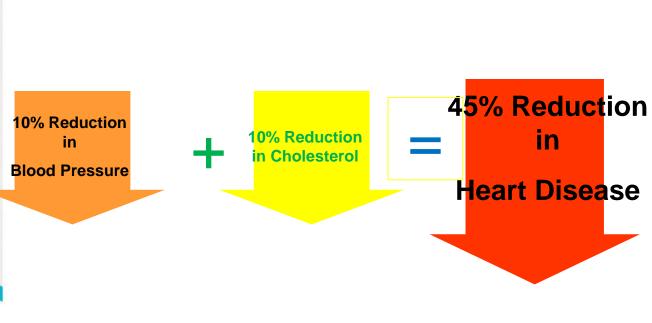
Pathophysiology of Hypertension







Effect of long-term modest reduction in heart disease risk factors



تصنيف ارتفاع الضفط الشرياني JNC8



Table 2. BP Classification (JNC 7 and the 2017 Hypertension Clinical Practice Guidelines)

SBP (mm Hg)	and/or	DBP (mm Hg)	JNC 7 ⁵	2017 GL⁴
<120	and	<80	Normal BP	Normal BP
120–129	and	<80	Prehypertension	Elevated BP
130–139	or	80–89	Prehypertension	Stage 1 hypertension
140–159	or	90–99	Stage 1 hypertension	Stage 2 hypertension
≥160	or	≥100	Stage 2 hypertension	Stage 2 hypertension

BP should be based on an average of ≥2 careful readings on ≥2 occasions. Adults with SBP or DBP in 2 categories should be designated to the higher BP category.

BP indicates blood pressure; DBP, diastolic blood pressure; GL, guideline; JNC, Joint National Committee; and SBP, systolic blood pressure.

عرب الضفط الشرياني- ESC/ESH الشرياني- ESC/ESH

Table 3 Classification of office blood pressure and definitions of hypertension grade b

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension ^b	≥140	and	<90

BP = blood pressure; SBP = systolic blood pressure.

The same classification is used for all ages from 16 years.



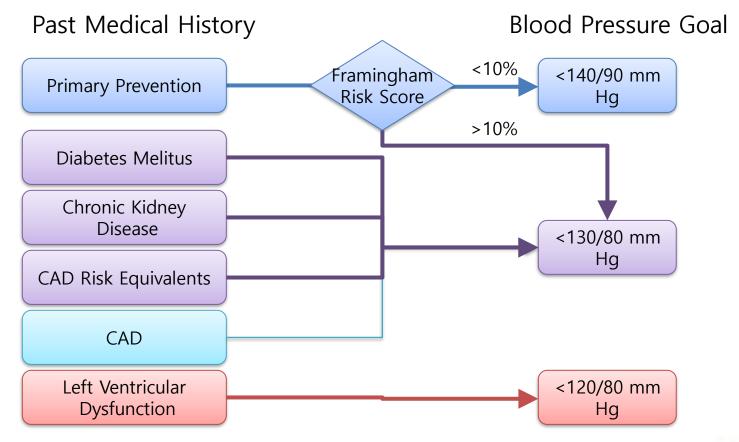
©ESC/ESH 20.

^aBP category is defined according to seated clinic BP and by the highest level of BP, whether systolic or diastolic.

blsolated systolic hypertension is graded 1, 2, or 3 according to SBP values in the ranges indicated.



From JNC-8 to 2014 AHA Guidelines





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Table 6 Risk modifiers increasing cardiovascular risk estimated by the Systemic COronary Risk Evaluation (SCORE) system³⁵

Social deprivation, the origin of many causes of CVD
Obesity (measured by BMI) and central obesity (measured by waist circumference)
Physical inactivity
Psychosocial stress, including vital exhaustion
Family history of premature CVD (occurring at age <55 years in men and <60 years in women)
Autoimmune and other inflammatory disorders
Major psychiatric disorders
Treatment for infection with human immunodeficiency virus
Atrial fibrillation
LV hypertrophy
CKD
Obstructive sleep apnoea syndrome

Hyportonoion			BP (mmHg) grading			
Hypertension disease staging	Other risk factors, HMOD, or disease	High normal SBP 130-139 DBP 85-89	Grade 1 SBP 140-159 DBP 90-99	Grade 2 SBP 160-179 DBP 100-109	Grade 3 SBP ≥180 or DBP ≥110	
	No other risk factors	Low risk	Low risk	Moderate risk	High risk	
Stage 1 (uncomplicated)	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk	
	≥3 risk factors	Low to Moderate risk	Moderate to high risk	High Risk	High risk	
Stage 2 (asymptomatic disease)	HMOD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to high risk	High risk	High risk	High to very high risk	
Stage 3 (established disease)	Established CVD, CKD grade ≥4, or diabetes mellitus with organ damage	Very high risk	Very high risk	Very high risk	Very high risk	

Figure I Classification of hypertension stages according to blood pressure levels, presence of cardiovascular risk factors, hypertension-mediated organ damage, or comorbidities. CV risk is illustrated for a middle-aged male. The CV risk does not necessarily correspond to the actual risk at different ages. The use of the SCORE system is recommended for formal estimation of CV risk for treatment decisions. BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; DBP = diastolic blood pressure; HMOD = hypertension-mediated organ damage; SBP = systolic blood pressure; SCORE = Systematic COronary Risk Evaluation.



Table 46.1 Classification of hypertension in children and adolescents [3]

	0-15-year	16-year and older
Category	SBP and/or DBP percentile	SBP and/or DBP values
Normal	<90th	<130/85 mmHg
High normal	≥90th to <95th percentile	130-139/85-89 mmHg
Hypertension	≥95th percentile	≥140/90 mmHg
Stage 1 hypertension	95th percentile to the 99th percentile plus 5 mmHg	140-159/90-99 mmHg
Stage 2 hypertension	>99th percentile plus 5 mmHg	160-179/100-109 mmHg
Isolated systolic	SBP ≥95th percentile and	≥140/<90 mmHg
hypertension	DBP<90th percentile	

Table 1. Comparison of BP Target Recommendations

		BP Categories ^a		
	BP Targets		SBP (mm Hg)	DBP (mm Hg)
JNC 7, 2003	< 140/90 mm Hg	Normal	< 120	< 80
	< 130/80 mm Hg for those with diabetes or chronic kidney disease	Prehypertension	120-139	80-89
	or emorne Runey disease	Stage 1 hypertension	140-159	90-99
		Stage 2 hypertension	≥ 160	≥ 100
JNC 8, 2014	< 150/90 mm Hg for patients ≥ 60 < 140/90 mm Hg for patients < 60, diabetes, and chronic kidney disease	Was not a comprehensive set of recommendations, and did not discuss hypertension diagnostic thresholds		
ACP/AAFP, 2017	< 150/90 mm Hg for patients ≥ 60 < 140/90 mm Hg for patients at higher CV risk, or with a history of stroke or TIA	Was not a comprehensive set of recommendations and did not discuss hypertension diagnostic thresholds Did not address recommendations in patients < 60		;
ACC/AHA, 2017	≤ 130/80 mm Hg	Normal	< 120	< 80
		Elevated	120-129	< 80
		Stage 1 hypertension ^b	130-139	80-89
		Stage 2 hypertension	≥ 140	≥ 90

^aPatients with SBP and DBP in two different categories should be classified in the higher category.

BP = blood pressure; TIA = transient ischemic attack.

^bAntihypertensive medication should be initiated in stage 1 hypertension only in patients with clinical CV disease, a 10-year risk of ASCVD of 10% or higher, diabetes mellitus, or chronic kidney disease.

Table 10 Comparison of ambulatory blood pressure monitoring and home blood pressure monitoring

ABPM	НВРМ
Advantages	Advantages
 Can identify white-coat and masked hypertension Stronger prognostic evidence Night-time readings Measurement in real-life settings Additional prognostic BP phenotypes Abundant information from a single measurement session, including 	 Can identify white-coat and masked hypertension Cheap and widely available Measurement in a home setting, which may be more relaxed than the doctor's office Patient engagement in BP measurement Easily repeated and used over longer periods to assess day-to-day BP
Disadvantages Expensive and sometimes limited availability Can be uncomfortable	Disadvantages Only static BP is available Potential for measurement error No nocturnal readings ^a

ABPM = ambulatory blood pressure monitoring; BP = blood pressure; HBPM = home blood pressure monitoring.

^aTechniques are being developed to enable nocturnal BP measurement with home BP devices.



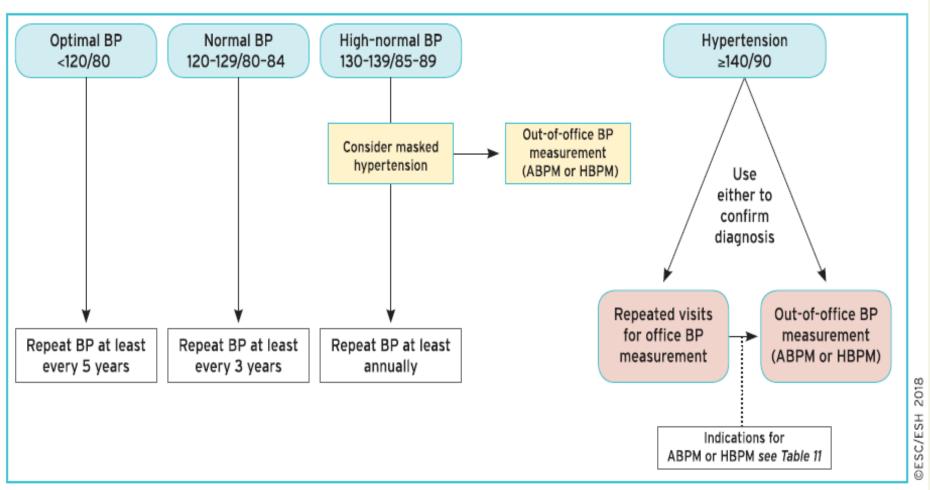


Figure 2 Screening and diagnosis of hypertension. ABPM = ambulatory blood pressure monitoring; BP = blood pressure; HBPM = home blood pressure monitoring.



Table 14 Routine workup for evaluation of hypertensive patients

Routine laboratory tests

Haemoglobin and/or haematocrit

Fasting blood glucose and glycated HbA_{1c}

Blood lipids: total cholesterol, LDL cholesterol, HDL cholesterol

Blood triglycerides

Blood potassium and sodium

Blood uric acid

Blood creatinine and eGFR

Blood liver function tests

Urine analysis: microscopic examination; urinary protein by dipstick test or, ideally, albumin:creatinine ratio

12-lead ECG

eGFR = estimated glomerular filtration rate; ECG = electrocardiogram; HbA_{1c} = haemoglobin A1c.



Renin- Angiotensin-ALDOSTERON



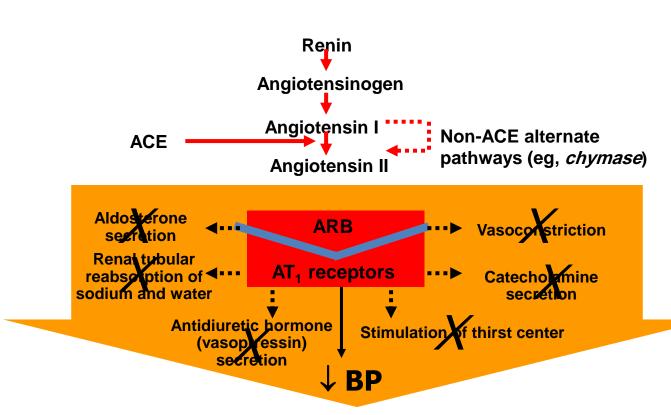




Table 15 Assessment of hypertension-mediated organ damage

Basic screening tests for HMOD	Indication and interpretation	
12-lead ECG	Screen for LVH and other possible cardiac abnormalities, and to document heart rate and cardiac rhythm	
Urine albumin:creatinine ratio	To detect elevations in albumin excretion indicative of possible renal disease	
Blood creatinine and eGFR	To detect possible renal disease	
Fundoscopy	To detect hypertensive retinopathy, especially in patients with grade 2 or 3 hypertension	
More detailed screening for HMOD		
Echocardiography	To evaluate cardiac structure and function, when this information will influence treatment decisions	
Carotid ultrasound	To determine the presence of carotid plaque or stenosis, particularly in patients with cerebrovas- cular disease or vascular disease elsewhere	
Abdominal ultrasound and Doppler studies	 To evaluate renal size and structure (e.g. scarring) and exclude renal tract obstruction as possible underlying causes of CKD and hypertension Evaluate abdominal aorta for evidence of aneurysmal dilatation and vascular disease Examine adrenal glands for evidence of adenoma or phaeochromocytoma (CT or MRI preferred for detailed examination); see section 8.2 regarding screening for secondary hypertension Renal artery Doppler studies to screen for the presence of renovascular disease, especially in the presence of asymmetric renal size 	



Therapeutic Treatment Options

- Diuretics
- ACE inhibitors
- Angiotensin II receptor blockers
- Calcium channel blockers
- Beta blockers
- Alpha blockers
- Centrally acting alpha agonists
- Direct vasodilators
- Peripheral adrenergic blockers
- RENIN agonists



Table 20 Compelling and possible contraindications to the use of specific antihypertensive drugs

Drug	Contraindications		
	Compelling	Possible	
Diuretics (thiazides/thiazide-like, e.g. chlortha- lidone and indapamide)	• Gout	 Metabolic syndrome Glucose intolerance Pregnancy Hypercalcaemia Hypokalaemia 	
Beta-blockers	 Asthma Any high-grade sinoatrial or atrioventricular block Bradycardia (heart rate <60 beats per min) 	 Metabolic syndrome Glucose intolerance Athletes and physically active patients 	
Calcium antagonists (dihydropyridines)		Tachyarrhythmia Heart failure (HFrEF, class III or IV) Pre-existing severe leg oedema	
Calcium antagonists (verapamil, diltiazem)	 Any high-grade sinoatrial or atrioventricular block Severe LV dysfunction (LV ejection fraction <40%) Bradycardia (heart rate <60 beats per min) 	Constipation	
ACE inhibitors	 Pregnancy Previous angioneurotic oedema Hyperkalaemia (potassium >5.5 mmol/L) Bilateral renal artery stenosis 	Women of child-bearing potential without reliable contraception	
ARBs	 Pregnancy Hyperkalaemia (potassium >5.5 mmol/L) Bilateral renal artery stenosis 	Women of child-bearing potential without reliable contraception	

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; HFrEF = heart failure with reduced ejection fraction; LV = left ventricular.

Hypertension



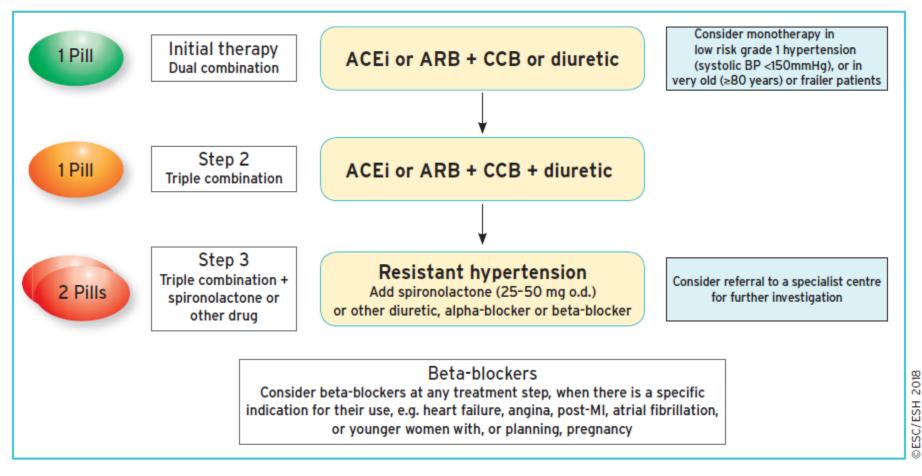


Figure 4 Core drug treatment strategy for uncomplicated hypertension. The core algorithm is also appropriate for most patients with HMOD, cerebrovascular disease, diabetes, or PAD. ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; HMOD = hypertension-mediated organ damage; MI = myocardial infarction; o.d. = omni die (every day); PAD = peripheral artery disease.

Hypertension and CAD



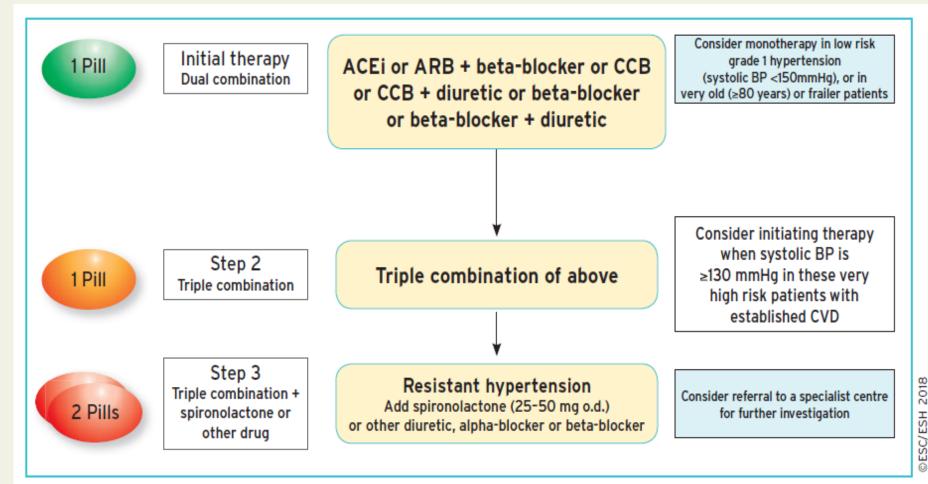
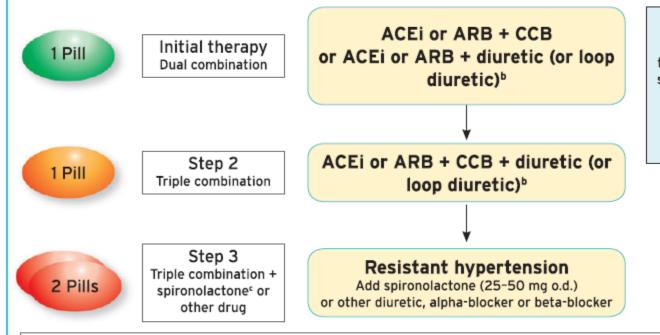


Figure 5 Drug treatment strategy for hypertension and coronary artery disease. ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium channel blocker; CVD = cardiovascular disease; o.d. = omni die (every day).

Hypertension and CKD





Beta-blockers

Consider beta-blockers at any treatment step, when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning, pregnancy

A reduction in eGFR and rise in serum creatinine is expected in patients with CKD who receive BP-lowering therapy, especially in those treated with an ACEi or ARB but a rise in serum creatinine of >30% should prompt evaluation of the patient for possible renovascular disease.

Figure 6 Drug treatment strategy for hypertension and chronic kidney disease. ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium channel blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; MI = myocardial infarction; o.d. = omni die (every day).

^aCKD is defined as an eGFR <60 mL/min/1.72 m² with or without proteinuria.

bUse loop diuretics when eGFR is <30 mL/min/1.72 m², because thiazide/thiazide-like diuretics are much less effective/ineffective when eGFR is reduced to this level.

^cCaution: risk of hyperkalaemia with spironolactone, especially when eGFR is <45 mL/min/1.72 m² or baseline K⁺ \ge 4.5 mmol/L.

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Hypertension and HF



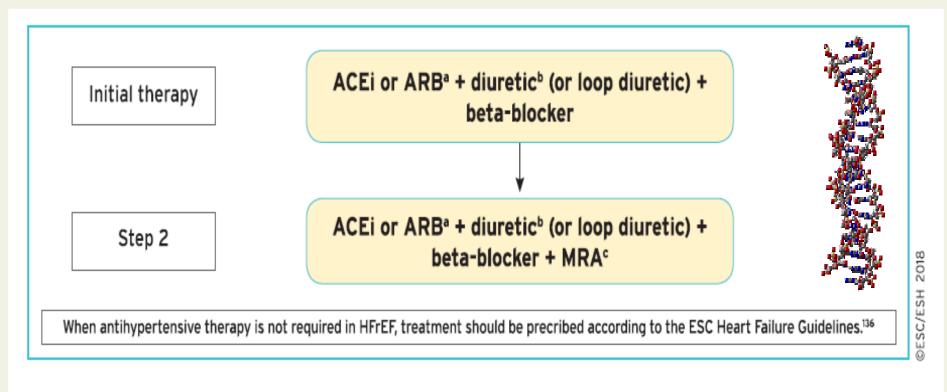


Figure 7 Drug treatment strategy for hypertension and hear failure with reduced ejection fraction. Do not use non-dihydropyridine CCBs (e.g. verapamil or diltiazem). ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; ESC = European Society of Cardiology; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist.

a Consider an angiotensin receptor/neprilysin inhibitor instead of ACEi or ARB per ESC Heart Failure Guidelines.

b Diuretic refers to thiazide/thiazide-like diuretic. Consider a loop diuretic as an alternative in patients with oedema.

^cMRA (spironolactone or eplerenone).

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Hypertension and AF



Initial therapy
Dual combination

or non-DHP CCB^a, or beta-blocker + CCB

Step 2
Triple combination

ACEi or ARB + beta-blocker
+ DHP CCB or diuretic
or beta-blocker + DHP CCB + diuretic

Add oral anticoagulation when indicated according to the CHA2DS2-VASc score, unless contraindicated.

^aRoutine combination of beta-blockers with non-dihydropyridine CCBs (e.g. verapamil or diltiazem) is not recommended due to a potential marked reduction in heart rate.

Figure 8 Drug treatment strategy for hypertension and atrial fibrillation. ACEi = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; CHA₂DS₂-VASc = CHA₂DS₂-VASc = Cardiac failure, Hypertension, Age ≥75 (Doubled), Diabetes, Stroke (Doubled) − Vascular disease, Age 65−74 and Sex category (Female); DHP = dihydropyridine.

aNon-DHP CCB (non-DHP CCB, e.g. verapamil or diltiazem).

HYPERTENSION RESISTANT



Table 24 Resistant hypertension characteristics, secondary causes, and contributing factors (adapted from reference³⁸⁵)

Characteristics of patients with resistant hypertension	Causes of secondary resistant hypertension	Drugs and substances that may cause raised BP	
 Demographics Older age (especially >75 years) Obesity More common in black people Excess dietary sodium intake High baseline BP and chronicity of uncontrolled hypertension 	 More common causes Primary hyperaldosteronism Atherosclerotic renovascular disease Sleep apnoea CKD 	Prescribed drugs Oral contraceptives Sympathomimetic agents (e.g. decongestants in proprietary cold remedies) Non-steroidal anti-inflammatory drugs Cyclosporin Erythropoietin Steroids (e.g. prednisolone and hydrocortisone) Some cancer therapies	
Concomitant disease HMOD: LVH and/or CKD Diabetes Atherosclerotic vascular disease Aortic stiffening and isolated systolic hypertension	 Uncommon causes Phaeochromocytoma Fibromuscular dysplasia Aortic coarctation Cushing's disease Hyperparathyroidism 	Non-prescription drugs Recreational drugs (e.g. cocaine, amphetamines, and anabolic steroids) Excessive liquorice ingestion Herbal remedies (e.g. ephedra and ma huang)	

HYPERTENSION RESISTANT



Table 2	 Fourth-line and 	l Beyond	Antihyperter	nsion Options
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Therapy	Potential Population	Precautions	Notes
MRA	Hypokalemia, HFrEF, proteinuria, edema	Advanced kidney disease, hyperkalemia, hormonal effects with spironolactone	Spironolactone is better studied in resistant hypertension; consider eplerenone for spironolactone intolerance because of antitestosterone effects
β-Blocker	HFrEF, MI, atrial fibrillation, tachycardia, migraine prophylaxis, tremor	Bradycardia, asthma	
α-Blocker	BPH, ED, PTSD/ nightmares	Orthostatic hypotension	
Hydralazine	HFrEF (in combination with nitrates)	Adherence problems with TID dosing, drug-induced lupus, increased BP variability, reflex tachycardia	
Minoxidil	Very resistant hypertension	Often profound salt and water retention. Reflex tachycardia, hirsutism, pericardial effusion	Give in conjunction with loop diuretic and rate control agent
Central α-agonist	Anxiety disorders, ADHD	Anticholinergic effects, sedation, and cognitive effects may be especially pronounced in older adult patients. Rebound hypertension and/ or bradycardia may be exacerbated in patients receiving β-blockers. Skin irritation and/or adhesion problems with clonidine patch	

ADHD = attention-deficit/hyperactivity disorder; BPH = benign prostatic hyperplasia; ED = erectile dysfunction; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; PTSD = posttraumatic stress disorder; TID = three times daily.

NICE guideline 2019

Hypertension in adults: diagnosis and management

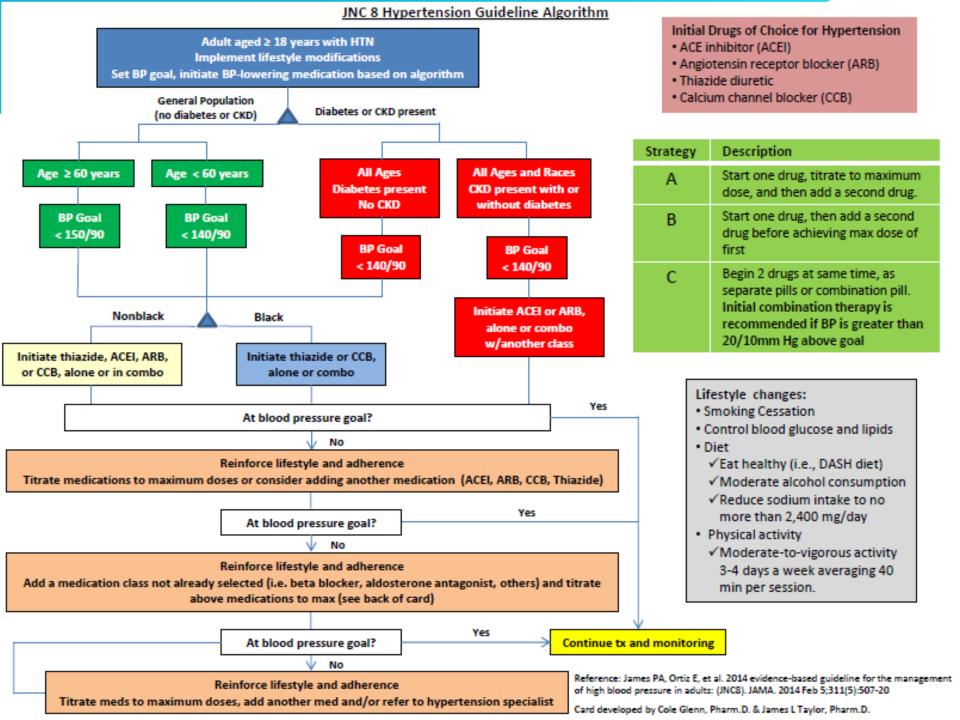
Step 4 treatment



- 2) Confirm elevated clinic blood pressure measurements using ambulatory or home blood pressure recordings.
- 3) Consider further diuretic therapy with low-dose spironolactone
- 4) [4] for adults with resistant hypertension starting step 4 treatm ent who have a blood **potassium of 4.5** mmol/l or less.
- 5) Consider an **alpha-blocker** or **beta-blocker** for adults with resistant hypertension starting step 4 treatment who have a blood potassium level of more than 4.5mmol/l







Compelling Indications				
Indication	Treatment Choice			
Heart Failure	ACEI/ARB + BB + diuretic + spironolactone			
Post –MI/Clinical CAD	ACEI/ARB AND BB			
CAD	ACEI, BB, diuretic, CCB			
Diabetes	ACEI/ARB, CCB, diuretic			
CKD	ACEI/ARB			
Recurrent stroke prevention	ACEI, diuretic			
Pregnancy	labetolol (first line), nifedipine, methyldopa			

Hypertension Treatment

Beta-1 Selective Beta-blockers – possibly safer in patients with COPD, asthma, diabetes, and peripheral vascular disease:

- metoprolol
- · bisoprolol
- betaxolol
- acebutolol

Drug Class	Agents of Choice	Comments	
Diuretics	HCTZ 12.5-50mg, chlorthalidone 12.5-25mg, indapamide 1.25-2.5mg triamterene 100mg K+ sparing — spironolactone 25-50mg, amiloride 5-10mg, triamterene 100mg furosemide 20-80mg twice daily, torsemide 10-40mg	Monitor for hypokalemia Most SE are metabolic in nature Most effective when combined w/ ACEI Stronger clinical evidence w/chlorthalidone Spironolactone - gynecomastia and hyperkalemia Loop diuretics may be needed when GFR <40mL/min	
ACEI/ARB	ACEI: lisinopril, benazapril, fosinopril and quinapril 10-40mg, ramipril 5- 10mg, trandolapril 2-8mg ARB: candesartan 8-32mg, valsartan 80-320mg, losartan 50-100mg, olmesartan 20-40mg, telmisartan 20-80mg	SE: Cough (ACEI only), angioedema (more with ACEI), hyperkalemia Losartan lowers uric acid levels; candesartan may prevent migraine headaches	
Beta-Blockers	metoprolol succinate 50-100mg and tartrate 50-100mg twice daily, nebivolol 5-10mg, propranolol 40-120mg twice daily, carvedilol 6.25-25mg twice daily, bisoprolol 5-10mg, labetalol 100-300mg twice daily,	Not first line agents – reserve for post-MI/CHF Cause fatigue and decreased heart rate Adversely affect glucose; mask hypoglycemic awareness	
Calcium channel blockers	Dihydropyridines: amlodipine 5-10mg, nifedipine ER 30-90mg, Non-dihydropyridines: diltiazem ER 180-360 mg, verapamil 80-120mg 3 times daily or ER 240-480mg	Cause edema; dihydropyridines may be safely combined w/ B-blocker Non-dihydropyridines reduce heart rate and proteinuria	
Vasodilators	hydralazine 25-100mg twice daily, minoxidil 5-10mg	Hydralazine and minoxidil may cause reflex tachycardia and fluid retention – usually require diuretic + B-blocker	
	terazosin 1-5mg, doxazosin 1-4mg given at bedtime	Alpha-blockers may cause orthostatic hypotension	
Centrally-acting Agents	clonidine 0.1-0.2mg twice daily, methyldopa 250-500mg twice daily	Clonidine available in weekly patch formulation for resistant hypertension	
	guanfacine 1-3mg		



متى نستخدم ABPM اوHBPM

- 1. إذا كان ضغط الدم في العيادة يتراوح بين 140/90 مم زئبق و 180/120 مم زئبق ، فقم بتقديم مراقبة ضغط الدم المتنقلة ((ABPMلتأكيد تشخيص ارتفاع ضغط الدم.
- 2. إذا كان ABPMغير مناسب أو كان الشخص غير قادر على تحمله ، فقم بتقديم مراقبة ضغط الدم في المنزل ((HBPM لتأكيد تشخيص ارتفاع ضغط الدم. [2019]
- 3. عند استخدام ABPMاتأكيد تشخيص ارتفاع ضغط الدم ، تأكد من إجراء قياسين على الأقل خلال ساعات استيقاظ الشخص المعتادة (على سبيل المثال ، من الساعة :8 00 إلى الساعة 02:00). استخدم متوسط القيمة لما لا يقل عن 14 قياسات تم إجراؤها خلال ساعات الاستيقاظ المعتادة للشخص لتأكيد تشخيص ارتفاع ضغط الدم.
- 4. عند استخدام HBPMاتأكيد تشخيص ارتفاع ضغط الدم ، تأكد من أنه: لكل تسجيل ل ضغط الدم ، يتم أخذ قياسين متتاليين ، على بعد دقيقة واحدة على الأقل ومع وجود ال شخص جالسًا ، ويتم تسجيل ضغط الدم مرتين يوميًا ، وبشكل مثالي في الصباح و ي ستمر تسجيل المساء وضغط الدم لمدة 4 أيام على الأقل ، من الناحية المثالية لمدة 7 أ يام.
 - 5. تأكيد تشخيص ارتفاع ضغط الدم لدى الأشخاص الذين يعانون من:
- 6. عيادة ضغط الدم من 140/90 مم زئبق أو أعلى ومتوسط النهار ABPM أو متوسط HBPM من 135/85 مم زئبق أو أعلى. [2019]



Therapy- Lifestyle Changes

Therapeutic Lifestyle Changes (TLC)

- Weight
- Exercise
- Diet
- Smoking
- Caffeine

Pharmacotherapy



Therapeutic Lifestyle Changes vs. Pharmacotherapy

Adapted From: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. 2004

Therapeutic Intervention	Approximate SBP Reduction
Weight Reduction (5-10% or 10kg)	5-20mmHg
DASH Diet (Low sodium, low fat)	8-14mmHg
Single Antihypertensive	10mmHg (10 over 5 rule)
30 minutes exercise most days	4-9mmHg
Dietary Sodium Reduction	2-8mmHg
Reduce alcohol to <=2 drinks/day	2-4mmHg





Hypertension Worldwide Statistics

Country	Diagnosed Hypertensive	Aware	Treated	Controlled
US	24%	42%	52%	24%
UK	19%	63%	50%	30%
France	41%	79%	59%	24%
Germany	53%	12%	32%	22%
Canada	22%	59%	40%	16%
Italy	58%	79%	51%	19%
China	14%	26%	12%	3%

Chockalingam, *Am J Hypertens*, 1998; Chamontin et al, *Am J Hypertens*, 1998; Marques-Vidal et al, *Q J M ed*, 1997; Trenkwalder et al, *J Hypertens*, 1994; Vincenzi et al, *G Ital Cardiol*, 2002; Colhoun et al, *J Hypertens*, 1998; Franklin et al, *Hypertension*, 2011; Tao et al, *Chin Med J*, 2008.





VALSARTAN AND AMLODIPIN VS TELMISARTAN AND AMLODIPIN IN TREATMINT OF HYPERTENTION IN DIABITIC PATENTS – META-ANALYSIS

