G.H.A Pocket Guidelines

Committee for Practice Guidelines
to improve the quality of clinical practice
and patient care in GCC countries

Management of Patients with Arterial Hypertension

2010

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TABLE OF CONTENTS

List of Abbreviations

ABPM	Ambulatory Blood Pressure Monitor
ACEI	ACE Inhibitors
ARB	Angiotensin Receptor Antagonists
BB	Beta-Blockers
BMI	Body Mass Index
BP	Blood Pressure
CA	Calcium Antagonists
CHD	Coronary Heart Hisease
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
DM	Diabetic Mellitus
ECG	Echocardiograph
ESC	European Society of Cardiology
ESH-ESC	European Society of Hypertension
ESRD	End Stage Renal Failure
HTN	Hypertension
ISH	Isolated Systolic Hypertension
LVH	left Ventricular Hypertrophy
MS	Metabolic Syndrome
OD	Organ Damage
SBP	Systolic Blood Pressure
TOD	Target Organ Damage

List of Tables

PREFACE

The purpose of the 2010 Gulf Hypertension Association (GHA) Guidelines for the Management of Arterial Hypertension is to provide an adequate review of the current clinical evidences in relation to classification, diagnoses, and management of hypertension and to make these evidences available for both primary care and specialist physicians in the Arabian Gulf Countries.

It is important to note that the contents of these guidelines, a significant amount of which are exerts from international guidelines, are meant to serve as general guideline and should therefore be used in conjunction with appropriate diagnoses and treatment approaches for hypertension.

The GHA task force for hypertension understands that the treating clinician's judgment in diagnosis, treatment, and follow up of the cases remains the single most important approach for an effective management of hypertension.

Gulf Heart Association

Classification of Hypertension:

Although there have been substantial studies in the field of hypertension, no universal agreement exists on the definition of hypertension. Historically, the term hypertension has been synonymous with an elevation of arm cuff blood pressure (BP) beyond an arbitrary cut off BP level. In 2005, the Hypertension Writing Group defines hypertension as:

- Progressive cardiovascular syndrome arising from complex and interrelated etiologies.
- Early markers of the syndrome are often present before blood-pressure elevation is sustained; therefore, hypertension cannot be classified solely by discreet blood-pressure thresholds.
- Progression is strongly associated with function and structural cardiac and vascular abnormalities that damage the heart, kidneys, brain, vasculature and other organs and lead to premature morbidity and death.

The 2007 European Society of Hypertension (ESH) / European Society of Cardiology (ESC) guidelines defined and classified hypertension in adults, as shown in Table 1.

Table 1: Classification of Hypertension According to BP Levels

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

Isolated systolic hypertension should be graded (1, 2, and 3) according to systolic BP values in the ranges indicated, provided that diastolic values are < 90mmHg.

High BP known as hypertension is highly prevalent in the Arabian Gulf countries. Hypertension is a powerful independent risk factor for the development of cardiovascular disease (CVD), and may have serious adverse prognostic effects. Hence, high priority should be given to the prevention, and treatment of hypertension.

White Coat Hypertension

It is defined as a persistently elevated clinic or office BP (>140/90 mm Hg) together with a normal daytime ambulatory pressure (<135/85 mm Hg).

Masked Hypertension

Some individuals with normal office BP (<140/90mmHg) may have elevated ambulatory or home BP values, a condition termed as a masked hypertension. These patients should be treated with antihypertensive drugs, particularly if end organ damage is evident.

Total Cardiovascular Risk Factors

All patients should be classified not only in relation to the grades of hypertension, but also in terms of the total cardiovascular risk resulting from the coexistence of different risk factors, organ damage and disease.

The Framingham Study indicated that hypertension is often associated with cluster of other risk factors. Less than 20% of the time, hypertension cases occur in isolation. Whereas, most of the time (50%) hypertension occurs with a cluster of two or three major risk factors., a rate twice that expected by chance.

The INTERHEART study reported that hypertensive patients with more than three risk factors had much higher (> 20-fold) increase of cardiovascular risk. Therefore, risk assessment is essential for making decisions on the type and intensity of therapy for hypertension.

Factors Influencing Prognosis

Presence of risk factors

- Age (Male>55 years; Female>65 years)
- Male gender
- Smoking
- Family history of premature cardiovascular disease (Male at age <55 years; Female at age<65 years)
- Dyslipidaemia
- Sedentary lifestyle
- Unhealthy eating
- Khat Chewing (Tree leaves chewed daily by a high proportion of the adult population in Yemen)
- Abdominal obesity
- Dysglycemia (diabetes, impaired glucose tolerance, impaired fasting glucose)

Presence of target organ damage

- Microalbuminuria or proteinuria
- Carotid wall thickening
- Left ventricular hypertrophy
- Chronic kidney disease (glomerular filtration rate < 60 ml/min/1.73 m2)

Presence of atherosclerotic vascular disease

- Previous stroke or TIA
- Coronary heart disease
- Peripheral arterial disease

Table 2: Stratification of cardiovascular risk in four categories.

	Blood Pressure (mm Hg)				
	Normal SBP 120-129 Or DBP 80-84	Normal SBP 120-129 Or DBP 80- 84	Grade 1 HT SBP 140-159 Or DBP 90-99	Grade 2 HT SBP 160-179 Or DBP 100-109	Grade 3 HT SBP ≥180 DBP≥110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	very high added risk
3 or more risk factors, MS, OD or DM	Moderate added risk	High added risk	High added risk	High added risk	very high added risk
Established CV or renal disease	very high added risk	very high added risk	very high added risk	very high added risk	very high added risk

In table 2 total CV Risk is stratified in four categories. Low, moderate, high and very high risks refer to 10 year risk of a CV fatal or non-fatal event. The term "added risk" is used to emphasize that in all categories relative risk is greater than average risk.

OD: subclinical organ damage; MS: metabolic syndrome.

Diagnosis and Evaluation of Hypertension

Objectives of initial evaluation

(1) Establish the diagnosis and grade of hypertension (Including office and none office BP reading)
(2) The likelihood of secondary hypertension
(3) The presence of target organ damage
(4) The level of global CVD risk

History

(a) Duration and previous levels of high BP.

(b) General symptomatology; Hypertensive individuals are commonly asymptomatic but can present with non specific symptoms.

(c) Symptoms of organ damage;

(1) Brain and eyes: headache, vertigo, impaired vision, transient ischemic attacks, sensory or motor deficit
(2) Heart: palpitation, chest pain, shortness of breath, swollen ankles
(3) Kidney: thirst, polyuria, nocturia, hematuria
(4) Peripheral arteries: cold extremities, intermittent claudication

(d) Symptoms suggestive of secondary causes

(e) Intake of drugs or substances that can raise BP; Such as nasal drops, cocaine, amphetamines(e.g Khat*), oral contraceptives, steroids, nonsteroidal anti- inflammatory drugs, erythropoietin, and cyclosporin;

(f) Lifestyle factors; Life style factors such as dietary intake of fat (animal fat in particular), salt and alcohol, quantification of smoking and physical activity, weight gain since early adult life;

(g) Sleep history; Is commonly associated with the development of hypertension. Sleep apnea should be suspected in obese individuals with disrupted sleep patterns. Snoring is a frequent finding but is oftentimes more reliably reported by the sleep partner.

(h) Past history; History or current symptoms of coronary disease, heart failure, cerebrovascular or peripheral vascular disease, renal disease, DM gout, dyslipidaemia, and asthma or any other significant illnesses, and drugs used to treat those conditions.

(i) Previous antihypertensive therapy; its results and adverse effects

(j) Personal, family and environmental factors that may influence BP, cardiovascular risk, as well as the course and outcome of therapy.

(k) A comprehensive family history should be obtained with particular attention to hypertension, DM, dyslipidaemia, premature coronary heart disease (CHD), stroke, peripheral artery or renal disease.

**Commonly used in Yemen*

Physical Examination

Cardiac examination

(a) Heart rate and rhythm should be noted. Ectopic beats and atrial fibrillation are common findings.
(b) An accentuated aortic second sound occurs frequent.
(c) A fourth heart sound suggests atrial enlargement and increased ventricular stiffness; a third heart sound suggests dilated cardiomyopathy and reduced left ventricular function.
(d) Certain murmurs are associated with hypertension such as pulmonic flow murmurs in conditions of high cardiac output.

Abdomen

(a) Periumbilical or flank bruits may suggest the presence of renal arterystenosis.
(b) Active, forceful pulsation along the aorta suggests an abdominal aorticaneurysm in older individuals.
(c) Polycystic kidney is usually palpable in the flanks and the related renalinsufficiency may be the etiology of the patient›s hypertension.

Neurologic Examination

A basic screening examination for motor and cranial nerve function, gait,stance, and coordination is important to establish a baseline for therapeutic follow-up.

Peripheral Pulses

The carotid arteries should be palpated and auscultated for the presence of bruits. Peripheral arteries: absence, reduction, or asymmetry of pulses, cold extremities, ischaemic skin lesions.

Blood Pressure Measurement

In general, the diagnosis of hypertension should be based on at least 2 BP measurements per visit and at least 2 to 3 visits, however, in some severe cases the diagnosis can be based on BP measurements taken at a single visit. Use ofstandardized measurement techniques is recommended when assessing BP (table 3).

Table 3: Recommended Technique for Measuring BP

1. The patient should be resting comfortably for 5 minutes in the seated position with back support. The arm should be bare or free of restrictive clothing or other materials and supported at heart level, as a lower position will result in an erroneously higher SBP and DBP. There should be no talking, and patients' legs should not be crossed. The patient should avoid exertion, temperature extremes, eating, caffeine, or smoking for 1 hour before BP measurement.
2. Choose a cuff with an appropriate bladder size matched to the size of the arm. For measurements taken by auscultation, bladder width should be close to 40% of arm circumference and bladder length should cover 80 – 100% of arm circumference. When using an automated device, select the cuff size as recommended by its manufacturer.
3. Place the cuff so that the lower edge is 3 cm above the elbow crease and the bladder is centered over the brachial artery. At least three measurements should be taken in the same arm with the patient in the same position. The first reading should be discarded and the latter two averaged. BP also should be assessed after 2 minutes standing (with arm supported) and at times when patients report symptoms suggestive of postural hypotension.
4. Supine BP measurements may also be helpful in the assessment of elderly and diabetic patients.
5. Increase the pressure rapidly to 30 mm Hg above the level at which the radial pulse is extinguished (to exclude the possibility of a systolic auscultatory gap).

6. Place the bell or diaphragm of the stethoscope gently and steadily over the brachial artery.
7. Open the control valve so that the rate of deflation of the cuff is approximately 2 mm Hg per heart beat. A cuff deflation rate of 2 mm Hg per beat is necessary for accurate systolic and diastolic estimation.
8. Read the systolic level — the first appearance of a clear tapping sound (phase I Korotkoff)– and the diastolic level (the point at which the sounds disappear (phase V Korotkoff)). Continue to auscultate at least 10 mm Hg below phase V to exclude a diastolic auscultatory gap. Record the BP to the closest 2 mm Hg on the manometer (or 1 mm Hg on electronic devices) as well as the arm used and whether the patient was supine, sitting or standing.
9. If Korotkoff sounds persist as the level approaches 0 mm Hg, then the point of muffling of the sound is used (phase IV) to indicate the diastolic pressure.
10. In the case of arrhythmia, additional readings may be required to estimate the average systolic and diastolic pressure. Isolated extra beats should be ignored. Note the rhythm and pulse rate.
11. Leaving the cuff partially inflated for too long will fill the venous system and make the sounds difficult to hear. To avoid venous congestion, it is recommended that at least one minute should elapse between readings.
12. BP should be taken in both arms on at least one visit and if one arm has a consistently higher pressure, that arm should be subsequently used for BP measurement and interpretation.

Table 4: Ambulatory Blood Pressure Monitor (ABPM)

Beyond the diagnosis of hypertension, ABPM measurement may also be considered for selected patients for the management ofhypertension (HTN).

Untreated patients

- Mild (Grade 1) to moderate (Grade 2) clinic BP elevation and without target organ damage.

Treated patients

- BP that is not below target values despite receiving appropriate antihypertensive therapy.
- Symptoms suggestive of hypotension.
- Fluctuating office BP readings.

How to interpret?

- Mean daytime ambulatory BP ≥ 135/85 mmHg is considered elevated.
- Mean 24 h ambulatory BP ≥130/80 mmHg is considered elevated.
- A drop in nocturnal BP of <10% is associated with increased risk of CV events.

Table 5: Home Blood Pressure

(1) Home BP readings can be used in the diagnosis of hypertension.

(2) The use of home BP monitoring on a regular basis should be considered for patients with hypertension, particularly those with:

a) Diabetes mellitus
b) Chronic kidney disease
c) Suspected nonadherence
d) Demonstrated white coat effect
e) BP controlled in the office but not at home (masked hypertension).

(3) When white coat hypertension is suggested by home monitoring, its presence should be confirmed with ABPM.

(4) Patients should be advised to purchase and use only home BP monitoring devices appropriate for the individual and meet international standards.

(5) Home SBP ≥ 135 mm Hg , or DBP ≥ 85 mm Hg should be considered to be elevated and associated with an increased overall mortality risk analogous to office SBP readings of 140 mm Hg or higher or DBP 90 mm Hg or higher.

(6) Health care professionals should ensure that patients who measure their BP at home have adequate training.
(7) The accuracy of all individual patients' validated devices (including electronic devices) must be regularly checked against a device of known calibration.
(8) Home BP values for assessing white coat hypertension or sustained hypertension should be based on duplicate measurements, morning and evening, for an initial seven-day period. First day home BP values should not be considered.

Table 6: BP thresholds (mmHg) for definition of hypertension with differenttypes of measurement

	SBP	DBP
Office or clinic	140	90
24-hour	130	80
Day	135	85
Night	120	70
Home	135	85

Table 7: Laboratory Investigations

Routine tests

- Fasting plasma glucose
- Fasting lipid profile
- Serum potassium
- Serum uric acid
- Serum creatinine
- Estimated creatinine clearance
- Hemoglobin and hematocrit
- Urinalysis (complemented by microalbuminuria via dipstick test and microscopic examination)
- Electrocardiogram

Other tests

- Echocardiogram
- Carotid ultrasound
- Quantitative proteinuria (if dipstick test positive)
- Ankle-brachial BP Index
- Fundoscopy
- Glucose tolerance test (if fasting plasma glucose >5.6 mmol/L (100 mg/dL)
- Home and 24 h ambulatory BP monitoring
- Pulse wave velocity measurement (where available)

Extended evaluation (domain of the specialist)

- Further search for cerebral, cardiac, renal and vascular damage. Mandatory in complicated hypertension
- Search for secondary hypertension when suggested by history, physical examination or routine tests.

Echocardiography in Hypertension

Echocardiography is more accurate than ECG in the assessment of cardiac TOD related to hypertension, thus leading to a more precise stratification of total CVD risk. However, routine echocardiographic evaluation of all hypertensive patients is not recommended.

Echocardiographic assessment of left ventricular mass, as well as of systolic and diastolic left ventricular function, is recommended for hypertensive patients suspected to have left ventricular dysfunction or coronary artery disease.

Fundoscopy

Examination of eye grounds is recommended in severe hypertensives only.

Mild retinal changes are largely non-specific except in young patients.

Hemorrhages, exudates and papilledema, only present in severe hypertension, are associated with increased CV risk.

Secondary Causes of Hypertension

A skillful physician may elicit clinical clues during history taking and physical examination which heightens suspicion to most secondary forms of HTN; presence of abdominal bruit (renal artery stenosis), reduced or delayed femoral pulses (coarctation of aorta), abdominal masses (polycystic kidney), abdominal striae (Cushing disease), paroxysmal headaches, pallor and palpitations (pheochromocytoma); and the use of contraceptive medications or illicit drug use (drug induced HTN).

Difficult to control HTN requiring multiple agents remains the most common reason for initiating secondary HTN workup.

Patients with hypertension secondary to obstructive sleep apnea often have the typical features of loud snoring, daytime sleepiness, and obesity. Weight loss, continuous positive airway pressure, and aldosterone antagonists are effective in lowering BP in hypertensive patients with sleep apnea, which (if left untreated) has a poor prognosis.

Table 8, summarizes the clinical clues suggesting secondary hypertension andthe recommended diagnostic procedures.

Table 8: Some Causes of Secondary Hypertension

Condition	Signs and Symptoms	Diagnostic Procedure	
		Initial	Additional
Hyperaldosteronism	Refractory HTN Hypokalemia, orthostatic BP drop	Plasma and urinary potassium; plasma renin and aldosterone	Plasma or urinary aldosterone after saline load; adrenal CT/ MRI scans
Renovascular	Sudden onset of severe HTN in young women (fibromuscular disease) Severe coronary, peripheral arterial or cerebrovascular disease; cigarette smoking history (atherosclerotic disease) Holosystolic bruit with or without diastolic component	Renal sonography Duplex Doppler sonography	Magnetic resonance or computed tomography (CT) angiography, aortography
Pheochromocytoma	Paroxysmal and/ or refractory HTN. Anxiety, tremor, headaches, sweating, rapid pulse, recent weight loss, orthostatic BP drop Multiple endocrine neoplasia: thyroid or parathyroid enlargement, neurofibromas, café au lait spots	Plasma metanephrine; urine metanephrine	Urinary catechols; plasma catechols (basal and after 0.3 mg clonidine); adrenal CT scans and scintiscans
Cushing's syndrome	Obesity, unusual truncal distribution of fat and abdominal striae, excessive body or facial hair (Cushing's syndrome)	*Morning plasmacortisol after 1mg dexamethasone at bedtime*	Urinary cortisol after variable doses of dexamethasone; adrenal CT scans and scintiscans
Aortic coarctation	Absent or diminished femoral pulses	*BP in legs*	Echocardiography, magnetic resonance imaging or contrast aortography

Management of Hypertension

Initially elevated BP above 140 mm Hg systolic or 90 mm Hg diastolic must always be re-measured at least three times over at least 4 weeks to ensure that hypertension is present. Only if the level is very high (>180/110 mm Hg) or if symptomatic target organ damage is present should therapy be begun before the diagnosis is carefully established.

Non Pharmacological Treatment

Table 9: Lifestyle therapy in Hypertension

Lifestyle Therapies in Hypertensive Adults		
Intervention	Target	
Reduce foods with added sodium	< 2300 mg/day	
Weight loss	BMI < 25 kg/m2	
Physical activity	30-60 minutes 4-7 days/week	
Dietary patterns	DASH diet	
Smoking cessation	Smoke free environment	
Waist Circumference Middle East (arbitrary)	**Men** < 94 cm	**Women** < 80 cm

Pharmacological Treatment

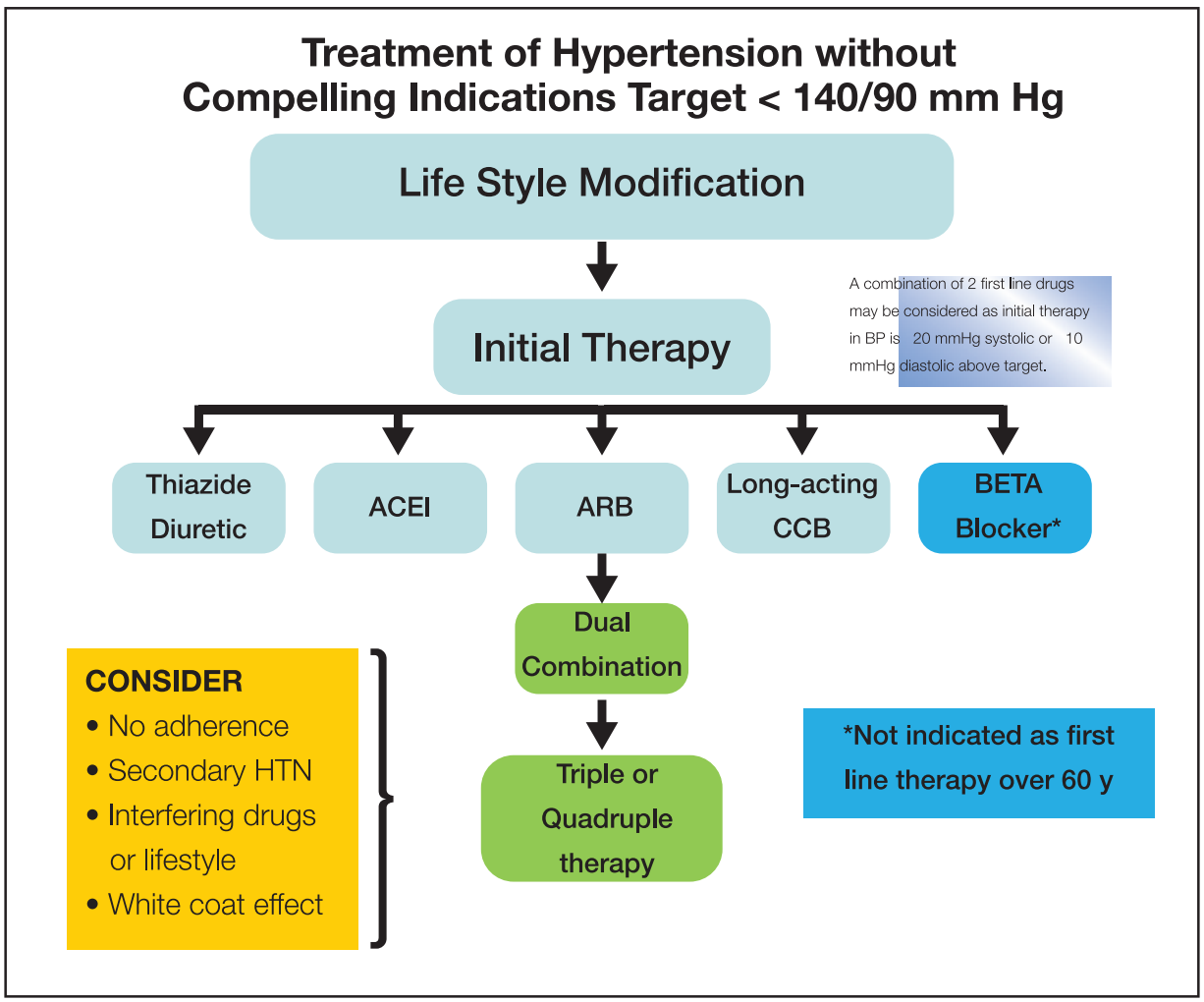
Initiation of drug therapy

Blood pressure (mmHg)		
Other risk factors OD or disease	NormalSBP 120-129 Or DBP 80-84	High normal SBP 130-139 Or DBP 85-89
No other risk factors	No BP intervention	No BP intervention
1-2 risk factors	Lifestyle changes	Lifestyle changes
≥3 risk factors, MS or OD	Lifestyle changes	Life style changes and consider drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + Drug treatment
Established CV or kidney disease	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment

2007 European guidelines for the managment of Arterial Hypertension

Grade 1 HT SBP 140-159 Or DBP 90-99	Grade 2 HT SBP 160-179 Or DBP 100-109	Grade 3 HT SBP ≥ 180 Or DBP ≥ 110
Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment
Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment

Hypertension Treatment without Compelling Indications



Monotherapy versus combined therapy

- Regardless of the drug employed, monotherapy allows achieving BP target in only a limited number of hypertensive patients.
- Use of more than one agent is necessary to achieve target

BP in the majority of patients. A vast array of effective and well tolerated combinations is available.

- Initial treatment can make use of monotherapy or combination of two drugs at low doses with a subsequent increase in drug doses or number, ifneeded.
- Monotherapy could be the initial treatment for a mild BP elevation with a low or moderate total cardiovascular risk. A combination of two drugs at lowdoses should be preferred as first step treatment when initial BP is in the grade 2 or 3 range or total cardiovascular risk is high or very high.
- Fixed combinations of two drugs can simplify treatment schedule and favour compliance.
- In several patients BP control is not achieved by two drugs, and a combination of three of more drugs is required.
- In uncomplicated hypertensives and in the elderly, antihypertensive therapy should normally be initiated gradually. In higher risk hypertensives, goal BP should be achieved more promptly, which favours initial combination therapy and quicker adjustment of doses.
- Based on the ONTARGET data we recommend not to regularly use a combination of ACEI and ARB, at least at the full doses employed in this trial, because of lack of additional cardiovascular benefit and increased risk of renal dysfunction (as well as of other adverse events).

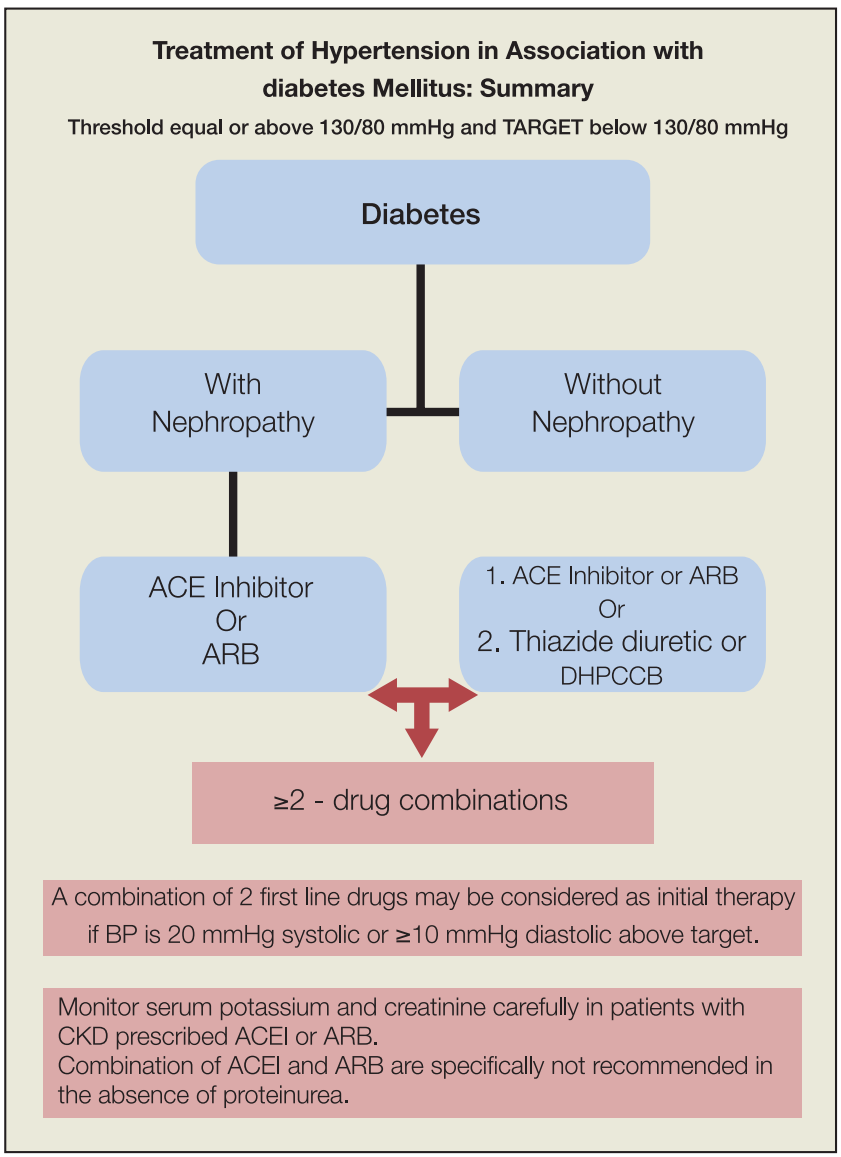
Table 10: Antihypertensive treatment: Preferred drugs

Subclinical Organ Damage	
LVH	ACEI, CA, ARB
Asymptomatic atherosclerosis	CA, ACEI
Microalbuminuria	ACEI, ARB
Renal dysfunction	ACEI, ARB
Clinical Event	
Previous stroke	ACEI, ARB, diuretics
Previous MI	BB, ACEI, ARB
Angina pectoris	BB, CA
Heart failure	diuretics, BB, ACEI, ARB, anti-aldosterone agents
Atrial fibrillation Recurrent Permanent	 ARB, ACEI BB, non-dihydropiridine CA
ESRD/proteinuria	ACEI, ARB, loop diuretics
Peripheral artery disease	CA
Condition	
ISH (elderly)	diuretics, CA
Metabolic syndrome	ACEI, ARB, CA
Diabetes mellitus	ACEI, ARB
Pregnancy	CA, methyldopa, BB
Blacks	diuretics, CA

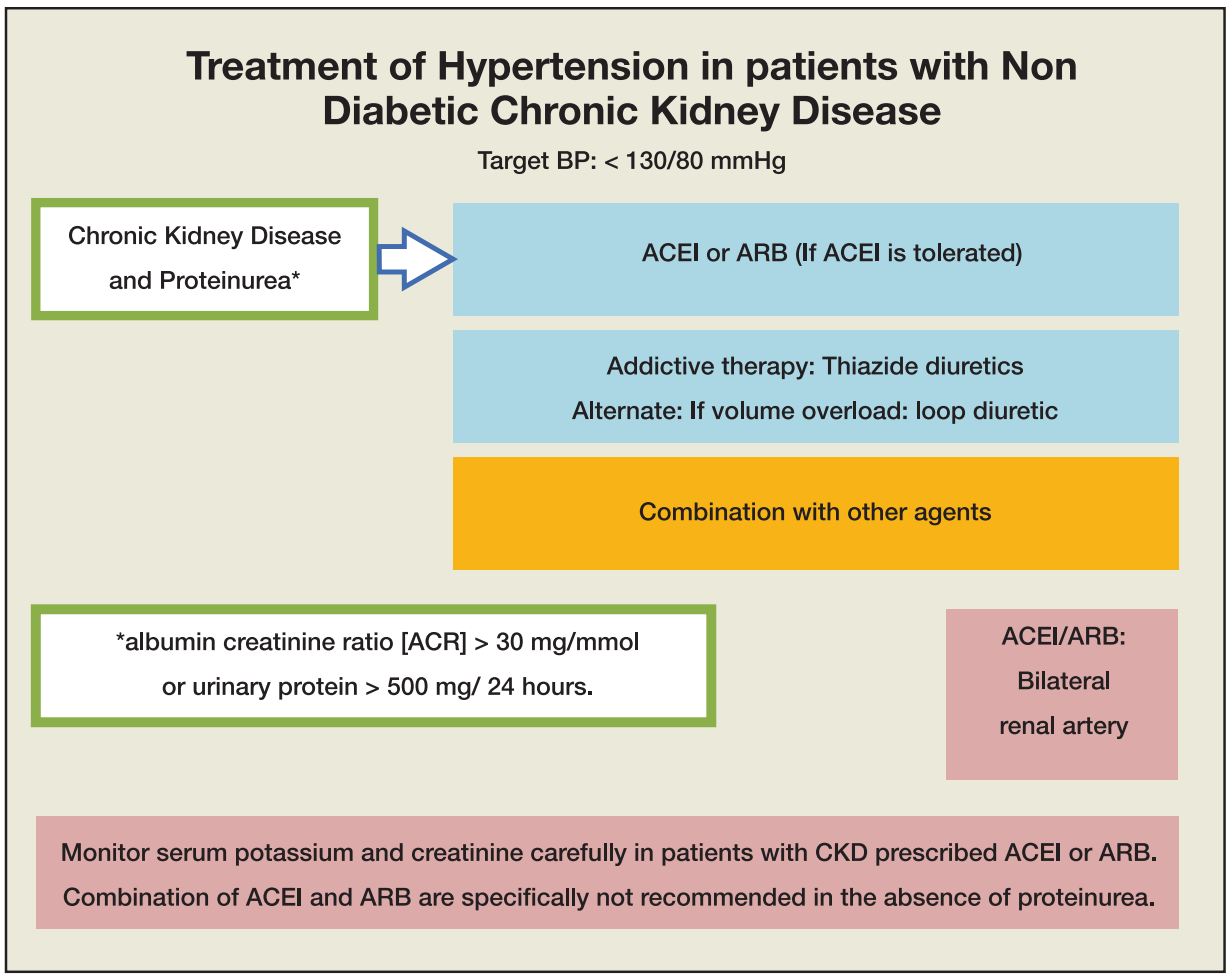
Abbreviations: LVH: left ventricular hypertrophy; ISH: isolated systolic hypertension; ESRD: renal failure; ACEI: ACE inhibitors; ARB: angiotensin receptor antagonists; CA: calcium antagonists; BB: b-blockers

Hypertension treatment with compelling evidences

Anti-hypertensive Treatment in Diabetes



Antihypertensive Treatment in Patients with Renal Dysfunction



Antihypertensive Treatment in Patients with Cerebrovascular Disease

Treatment of Hypertension in Patients with Cerebrovascular Disease

Strongly consider BP reduction in all patients after the acute phase of stroke or TIA.

Stroke
TIA

→ An ACEI/ARB/diuretic combination is preferred

Combinations of an ACEI with an ARB are not recommended

Antihypertensive Treatment in Patients with Heart Failure

Treatment of Hypertension with Left Ventricular Systolic Dysfunction

Systolic cardiac dysfunction	ACEI and Beta blocker If ACEI intolerant: ARB Titrate doses of ACEI or ARB to those used in clinical trails
	If additional therapy is needed: • Diuretic (Thiazide for hypertension; Loop for volume control) • For CHF class III-IV or post MI;Aldosterone Antagonist
	If ACEI and ARB are contraindicated: Hydralazine and Isosorbide dinitrate in combination
~~Non dihydropyridine CCB~~	If additional antihypertensive therapy is needed: • ACEI/ ARB Combination • Long-acting DHP-CCB (Amlodipine)

Treatment of Hypertension in Patients with coronary artery diseases:

A. Stable angina

Treatment of Hypertension in Patients with Ischemic Heart Disease

Stable angina →

- Beta-blocker
- Long-acting CCB

ACEI are recommended for most patients with established CAD*

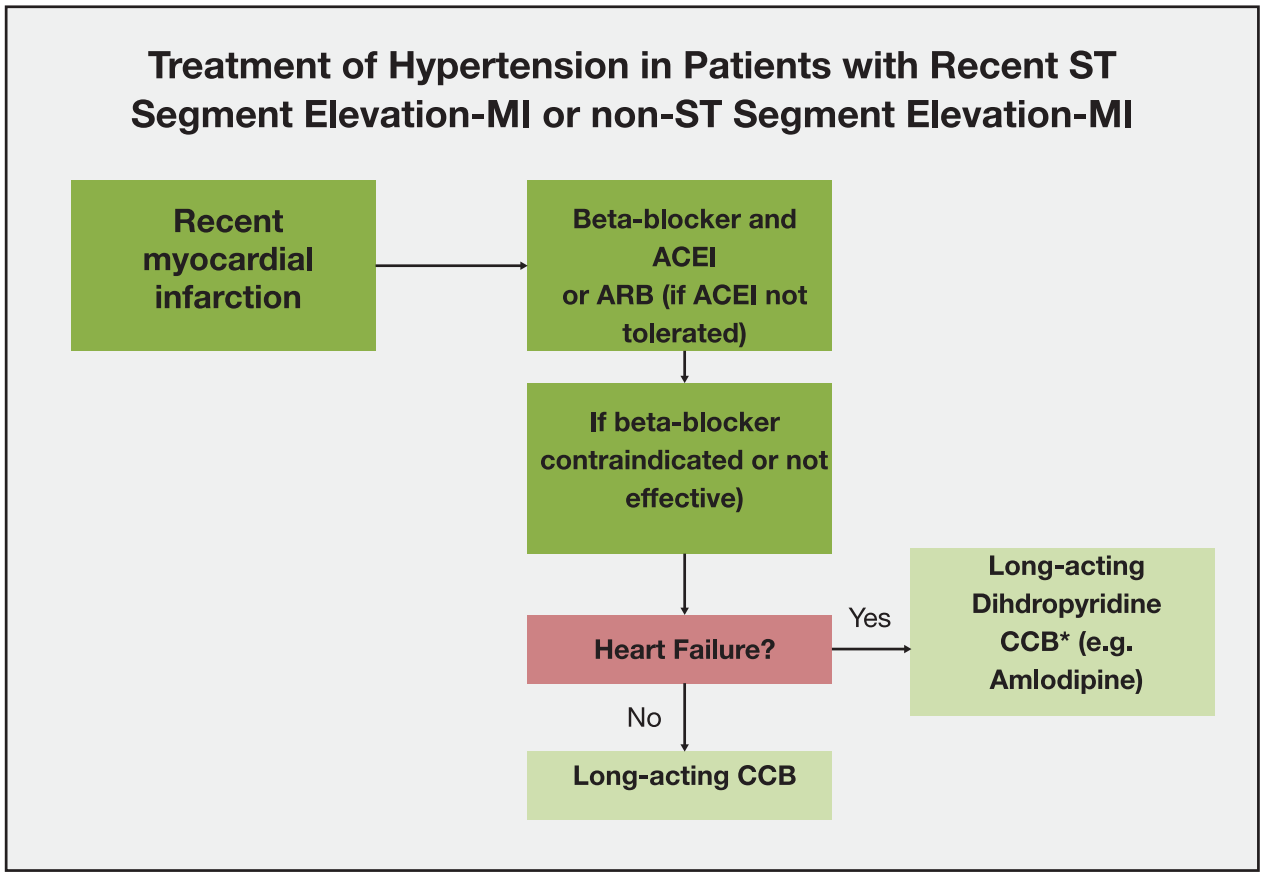
- Caution should be exercised when combing a non DHP-CCB and a betablocker
- If abnormal systolic left ventricular function: avoid non DHP-CCB (Verapamil or Diltiazem
- Combination of an ACEI with an ARB is not recommended in the absence of heart failure.

Those at low risk with well controlled risk factors may not benefit from ACEI therapy

~~Short-acting nifedipine~~

Not recommended and have deleterious effect.

B. Acute coronary syndrome



Hypertension in Pregnancy

Hypertensive disorders are one of the most common complications ofpregnancy and may be associated with significant maternal and fetalmorbidity and mortality. Although the etiology of these disorders is becomingincreasingly better understood, interventions to prevent hypertensivedisorders of pregnancy have had poor results.

The diagnosis of a hypertensive disorder in a pregnant woman depends, in part, upon the gestational age at presentation. ***Preeclampsia*** refers to the syndrome of new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman, or worsening hypertension with new onset proteinuria in a woman with preexisting hypertension (superimposed preeclampsia).

Preexisting hypertension is defined as systolic pressure ≥140 mmHg and/or diastolic pressure ≥90 mmHg that antedates pregnancy, is present before the 20th week of pregnancy, or persists longer than 12 weeks postpartum.

Gestational hypertension refers to elevated BP first detected after 20 weeks of gestation in the absence of proteinuria. Over time, some patients with gestational hypertension will develop proteinuria and be considered preeclamptic, while others will be diagnosed with preexisting hypertension because of persistent BP elevation postpartum.

Preeclampsia is associated with substantial risk to the mother and the fetus. Recognized risk factors include primiparity and preexisting chronic hypertension.

The “cure” for preeclampsia is delivery of the fetus, but delivery earlier than necessary poses major risks to the fetus; management involves close followup of the mother and the fetus to prolong the pregnancy as long as is safely possible.

Non-pharmacological management (including close supervision and

restriction of activities) should be considered for pregnant women with SBP 140–149mmHg or DBP 90–95mmHg.

In the presence of gestational hypertension (with or without proteinuria) drug treatment is indicated at BP levels ≥140/90mmHg. SBP levels ≥ 170 or DBP ≥110mmHg should be considered an emergency requiring hospitalization.

In non-severe hypertension, oral methyldopa, labetalol, calcium antagonists and (less frequently) b-blockers are drugs of choice.

In pre-eclampsia with pulmonary edema, nitroglycerine is the drug of choice. Diuretic therapy is inappropriate because plasma volume is reduced.

As emergency, intravenous labetalol, oral methyldopa and oral nifedipine are indicated.

Intravenous hydralazine is no longer the drug of choice because of an excessof perinatal adverse effects. Intravenous infusion of sodium nitroprusside is useful in hypertensive crises, but prolonged administration should be avoided.

Calcium supplementation, fish oil and low dose aspirin are not recommended.

However, low dose aspirin may be used prophylactically in women with a history of early onset pre-eclampsia.

Antihypertensive Treatment in the Elderly

Randomized trials in patients with systolic-diastolic or isolated systolic hypertension aged ≥ 60 years have shown that a marked reduction in cardiovascular morbidity and mortality can be achieved with antihypertensive treatment.

Drug treatment can be initiated with thiazide diuretics, calcium antagonists, angiotensin receptor antagonists, ACE inhibitors, and b-blockers, in line with general guidelines.

Trials specifically addressing treatment of isolated systolic hypertension have shown the benefit of thiazides and calcium antagonists but subanalysis of other trials also show efficacy of angiotensin receptor antagonists.

Initial doses and subsequent dose titration should be more gradual because of a greater chance of undesirable effects, especially in very old and frail subjects.

BP goal is the same as in younger patients, i.e. <140/90mmHg or below, if tolerated.

Because of the increased risk of postural hypotension, BP should always be measured also in the erect posture.

Resistant Hypertension

Resistant hypertension is defined as failure to achieve goal BP when a patient adheres to the maximum tolerated doses of 3 antihypertensive drugs including a diuretic.

Step 1: Confirm true resistant hypertension

A careful evaluation of the patient to confirm the diagnosis and exclude factors associated with "pseudo-resistance," (table 10).

Step 2: Education

Education and reinforcement of life-style issues that affect BP, such as sodium restriction, and weight loss if obese, are critical in treating resistant hypertension.

Step 3: Identify and reverse factors contributing to true resistance

(a) Specifically ask the patient about use of any pharmacological or herbal (Khat) agents that may increase BP; in case of identification of such a substance, discontinue or minimize its use.

(b) Evaluate the level of renal function with estimation of glomerular filtration rate and modify treatment accordingly.

(c) Perform a thorough search for secondary hypertension; if an identifiable cause is present, treat accordingly.

Step 4: Treat aggressively with optimal doses of appropriate antihypertensive medications (including drug combinations) according to patient characteristics.

Table 11: Causes of Pseudo-Resistant Hypertension

1. Improper BP measurement
2. Heavily calcified or arteriosclerotic arteries that is difficult to compress (in elderly persons)
3. White-coat effect
4. Poor patient adherence
   - Side effects of medication
   - Complicated dosing schedules
   - Poor relations between doctor and patient
   - Inadequate patient education
   - Memory or psychiatric problems
   - Costs of medication

(5) Related to antihypertensive medication

Inadequate doses

Inappropriate combinations

(6) Physician inertia (failure to change or increase dose regimens when not at goal).

Table 12: Factors Contributing to Resistant Hypertension

(1) Drug-induced

Nonsteroidal anti-inflammatory drugs (including cyclo-Oxygenase-2 inhibitors)

Sympathomimetics (decongestants, anorectics)

Cocaine, amphetamines, other illicit drugs

Oral contraceptive hormones

Adrenal steroid hormones

Erythropoietin

Cyclosporine and tacrolimus

Licorice (included in some chewing tobacco)

Over-the-counter dietary and herbal supplements (e.g.,ginseng, yohimbine, ma huang, bitter orange)

(2) Excess alcohol intake

(3) Volume overload

Excess sodium intake

Volume retention from kidney disease

Inadequate diuretic therapy

(4) Associated conditions

Obesity

Diabetes mellitus

Older age

(5) Identifiable causes of hypertension

Renal parenchymal disease

Renovascular disease

Primary aldosteronism

Obstructive sleep apnea

Pheochromocytoma

Cushing's syndrome

Thyroid diseases

Aortic coarctation

Intracranial tumors

Hypertension Emergencies and Urgencies Definitions

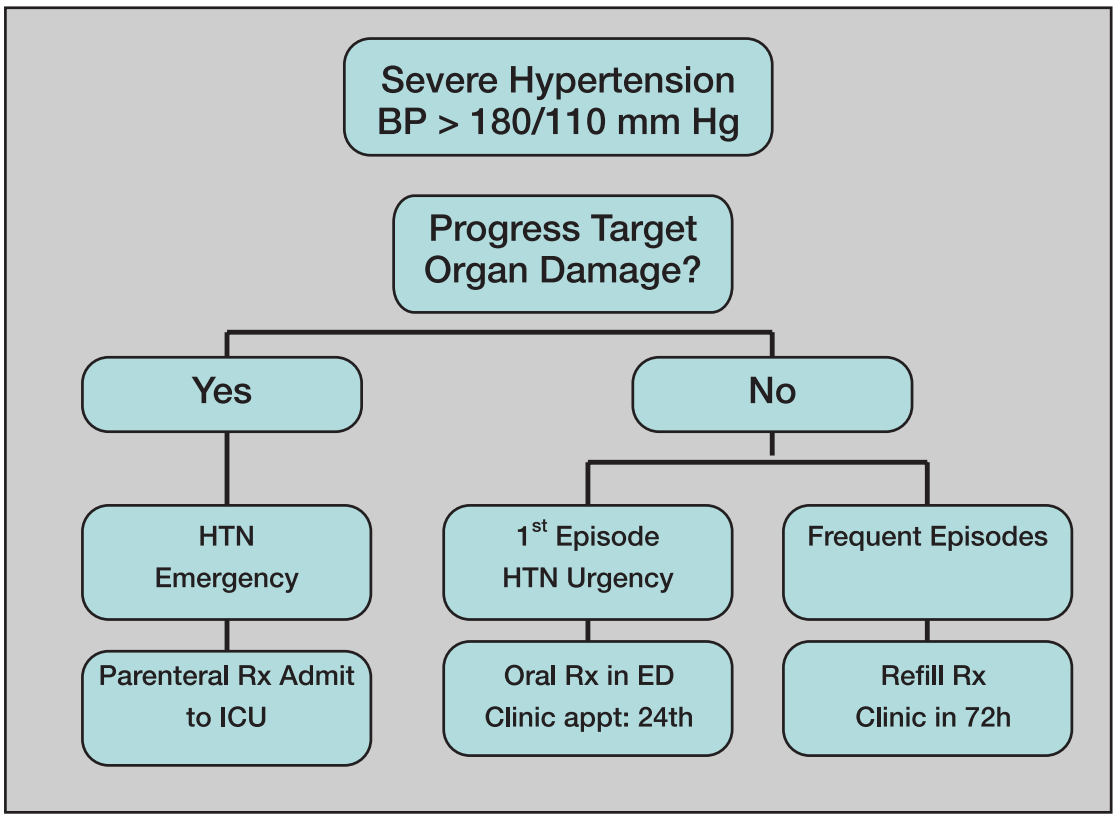


Table 13: Examples of hypertension emergencies

Accelerated/malignant hypertension
Hypertensive encephalopathy
Acute left ventricular failure
Acute aortic dissection
Intracranial hemorrhage
Pheochromocytoma crisis
Monoamine oxidase inhibitor + tyramine interaction
Eclampsia
Substance/drug-induced acute hypertension

Table 14: Examples of hypertension urgencies

Accelerated/malignant hypertension*
Severe hypertension associated with coronary artery disease
Severe hypertension in the organ transplant patient
Preoperative hypertension
Hypertension associated with burns
Severe, uncontrolled hypertension
*Can also be considered an emergency on the basis of acute target organ dysfunction.

Table 15: Initial Evaluation of Patients with Hypertensive Emergency

History

Prior diagnosis and treatment of hypertension

Intake of pressor agents: street drugs, sympathomimetics

Symptoms of cerebral, cardiac, and visual dysfunction

Physical examination

BP

Funduscopy

Neurologic status

Cardiopulmonary status

Body fluid volume assessment

Peripheral pulses

Laboratory evaluation

Hematocrit and blood smear

Urine analysis

Automated chemistry: creatinine, glucose, electrolytes

Plasma renin activity and aldosterone (if primary aldos- teronism is suspected)

Plasma renin activity before and 1 h after 25 mg captopril (if renovascular hypertension is suspected)

Spot urine or plasma for metanephrine (if pheochromocy- toma is suspected)

Chest radiograph (if heart failure or aortic dissection is suspected)

Electrocardiogram.

Goal of Therapy

The initial aim of treatment in hypertensive crises is to rapidly lower the diastolic pressure to about 100 to 105 mmHg; this goal should be achieved within two to six hours, with the maximum initial fall in BP not exceeding 25 percent of the presenting value. This level of BP control will allow gradual healing of the necrotizing vascular lesions. More aggressive hypotensive therapy is both unnecessary and may reduce the BP below the autoregulatory range, possibly leading to ischemic events (such as stroke or coronary disease).

Treatment

For many patients with urgent hypertension without symptoms of major target organ dysfunction, initiation of therapy with two oral agents is appropriate to lower BP to an intermediate target over 24 to 72 hours.

Agents that reliably cause an immediate fall in BP include central sympatholytics (clonidine 0.1–0.2 mg), labetalol (200–400 mg), and amlodipine (2.5–5 mg). Responses to angiotensin-converting enzyme (ACE) inhibitors are more variable. In keeping with the vasoconstrictive nature of hypertensive emergencies, the parenteral drugs that are safest and most effective are listed in Table 13.

Of the available choices, parenteral labetalol is particularly attractive because it does not require intra arterial BP monitoring, tends to protect the heart, and counteracts the marked sympathetic over activity and tachycardia that often accompany a hypertensive emergency. Sodium

nitroprusside is particularly attractive in hypertensive encephalopathy With the exception of pulmonary edema or marked fluid overload, diuretics are not indicated for initial therapy in hypertensive emergencies (owing to the volume contraction that usually accompanies the condition). Loop-diuretics in particular are not recommended for the routine treatment of hypertensive urgencies or emergencies in the absence of fluid overload because they can cause additional reflex vasoconstriction

Table 16: Parenteral Antihypertensive Drugs

Drug	Dose	Onset of Action	Duration of Action	Adverse Effects	Special Indications
VASODILATORS					
Nitroprusside	0.25- 10.00 µg/kg per min as i.v. infusion	immediate	1-2 min	Nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication	Most hypertensive emergencies; caution with high intracranial pressure or azotemia
Nitroglycerin	5-100 µg per min as i.v. infusion	2-5 min	5-10 min	Headache, vomiting, methemoglobinemia, tolerance with prolonged use	Coronary ischemia
Nicardipine	5-15 mg per h as i.v.	5-10 min	1-4 h	Headache, nausea, flushing, tachycardia, local phlebitis	Most hypertensive emergencies; caution with acute heart failure
Hydralazine	5-20 mg as i.v. 10-40 mg IM	10-20 min 20-30 min	1-4 h 4-6 h	Tachycardia, flushing, headache, vomiting, aggravation of angina	Eclampsia; caution with high intracranial pressure

ADRENERGIC INHIBITORS					
Phentolamine	5-15 mg as i.v	1-2 min	3-10 min	Tachycardia, flushing, headache	Catecholamine excess
Esmolol	200-500 µg/kg per min for 4 min, then 50-300 µg/kg per min as i.v.	10-20 min	10-20min	Hypotension, nausea	Aortic dissection, after operation
Labetalol	20-80 mg as i.v. bolus every 10 min or 2 mg per min as i.v. infusion	5-10 min	3-6 h	Vomiting, scalp tingling, burning in throat, dizziness, nausea, heart block, orthostatic hypotension	Most hypertensive emergencies except acute heart failure
Furosemide	20-40 mg in 1-2 min, repeated and higher doses with renal insufficiency	5-15 min	2-3 h	Volume depletion, hypokalemia	Usually needed to maintain efficacy of other drugs

Vascular Protection for Hypertension Patients

Lipid Lowering Agents

All hypertensive patients with established atherosclerotic vascular disease (previous stroke or TIA, or Coronary heart disease, or peripheral arterial disease) renal disease or with type 2 diabetes should be considered for statin therapy aiming at serum total and LDL cholesterol levels of, respectively, <4.5mmol/l (175 mg/dl) and <2.5 mmol/l (100 mg/dl), and lower, if possible.

Hypertensive patients without established atherosclerotic vascular disease, renal disease or type 2 diabetes but with 3 or more of the risk factors in table should also be considered for statin treatment even if their baseline total and LDL serum cholesterol levels are not elevated.

Table 17: Cardiovascular Risk Factors for Consideration of Statin Therapy in Non-dyslipidemic Patients with Hypertension

1- Male
2- Age ≥55 years
3- LVH
4- Other ECG abnormalities:
   - LBBB,
   - LV strain pattern,
   - abnormal Q-waves or ST-T changes compatible with IHD
5- Microalbuminuria or proteinuria
6- Smoking
7- Family history of premature CVD
8- Total cholesterol to HDL cholesterol ratio ≥ 6 mmol/l

Anti-platelet Therapy

Antiplatelet therapy, in particular low-dose aspirin, should be prescribed to hypertensive patients with previous cardiovascular events.

Low-dose aspirin should also be considered in hypertensive patients without a history of cardiovascular disease if older than 50 years, with a moderate increase in serum creatinine or with a high cardiovascular risk.

In all these conditions, the benefit-to-risk ratio of this intervention (reduction in myocardial infarction greater than the risk of bleeding) has been proven favourable.

To minimize the risk of haemorrhagic stroke, antiplatelet treatment should be started after achievement of BP control.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