HYPERTENSION & COVID-19

A)2020 INTERNATIONAL SOCIETY OF HYPERTENSION GLOBAL HYPERTENSION PRACTICE GUIDELINES (6 MAY 2020 ,PUBLISHED ON AHAJOURNALS)

B) COVID-19 AND HYPERTENSION--EVIDENCE AND PRACTICAL MANAGEMENT: GUIDANCE FROM THE HOPE ASIA NETWORK(9 JULY 2020, PUBLISHED ON "THE JHC" ,THE JOURNAL OF CLINICAL HYPERTENSION)

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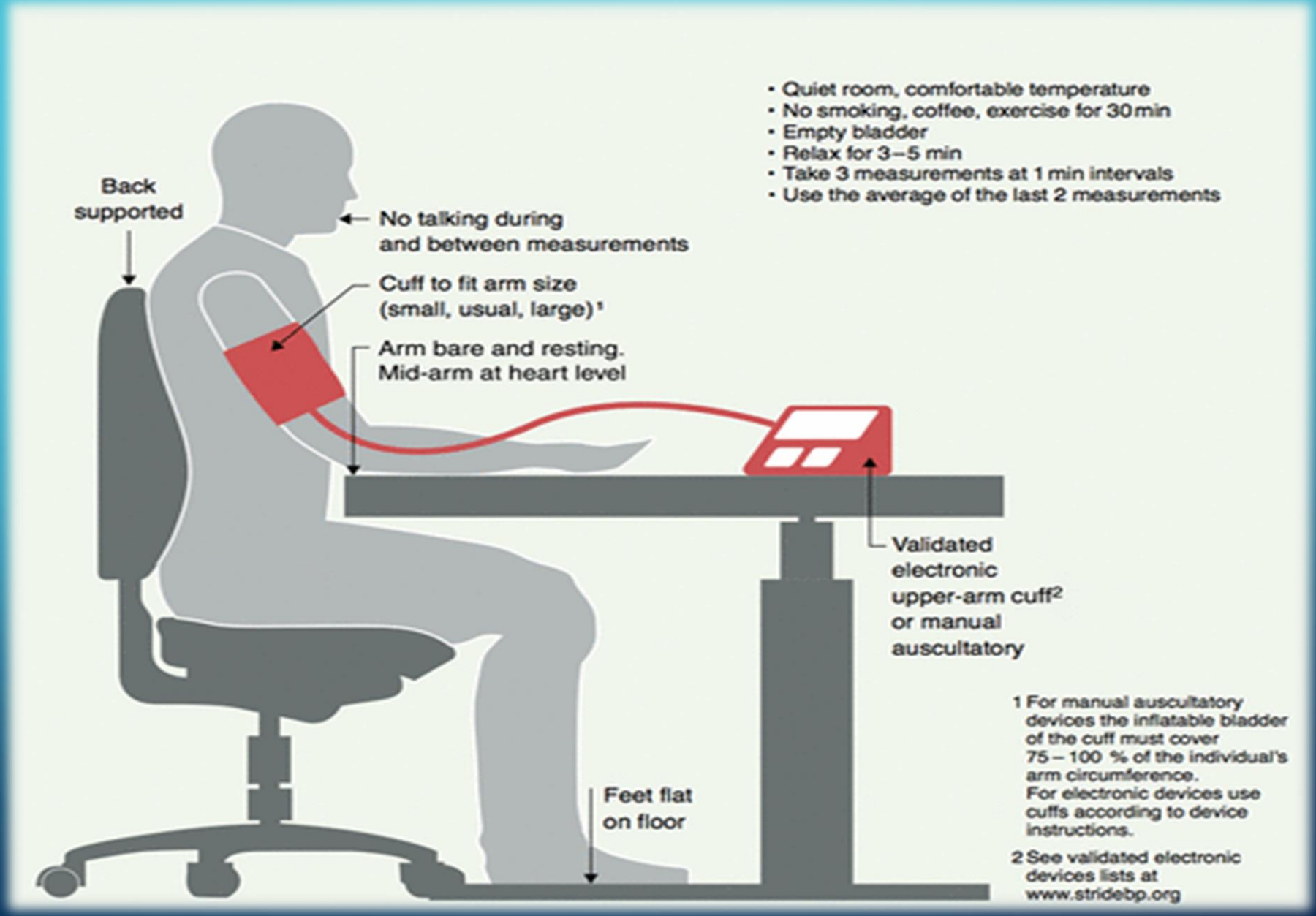
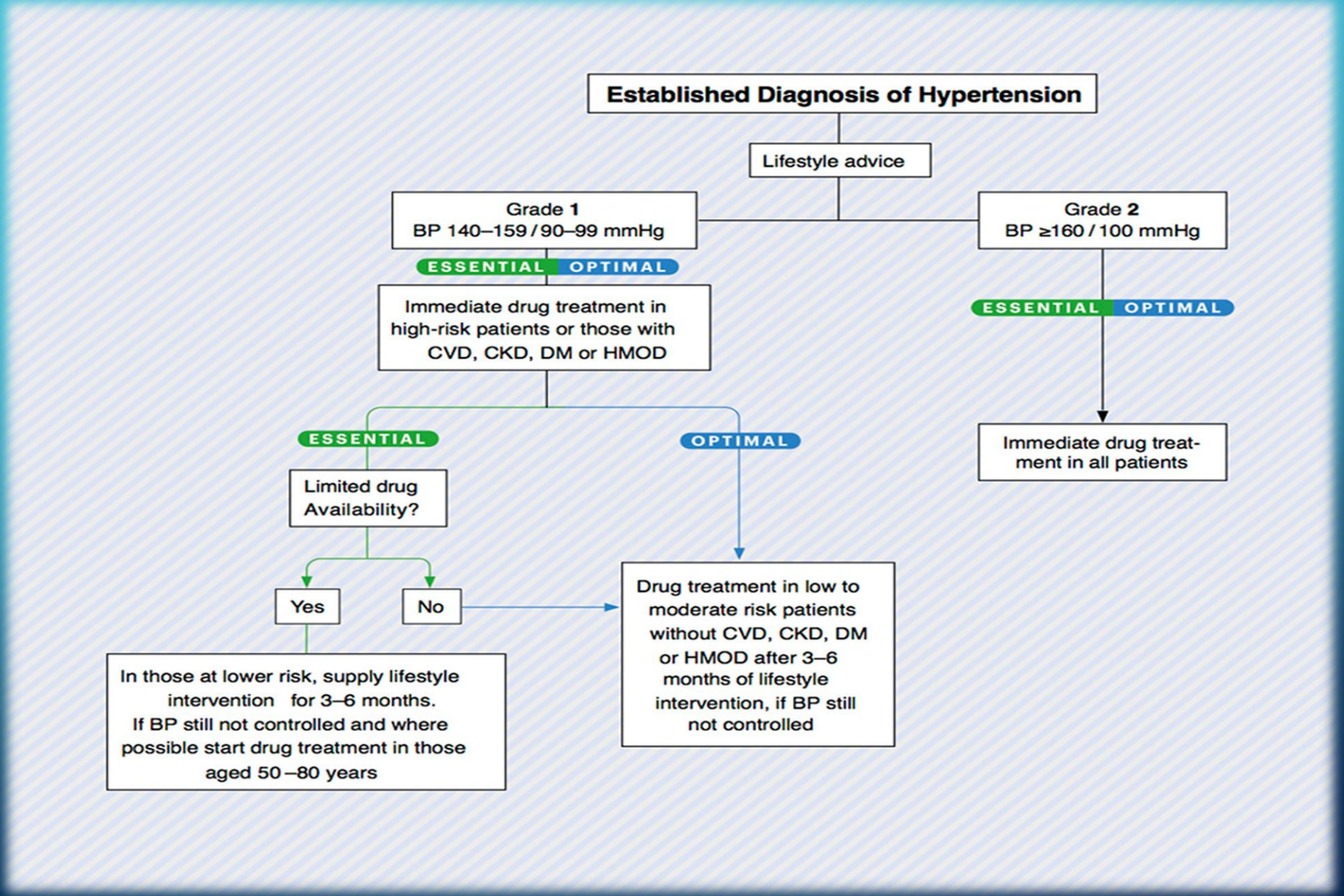
- ***Section 2: Definition of Hypertension***
- In accordance with most major guidelines it is recommended that hypertension be diagnosed when a person's systolic blood pressure (SBP) in the office or clinic is ≥140 mm Hg and/or their diastolic blood pressure (DBP) is ≥90 mm Hg following repeated examination (see below, Section 3). Table 1 provides a classification of BP based on office BP measurement, Table 2 provides ambulatory and home BP values used to define hypertension; these definitions apply to all adults (>18 year old). These BP categories are designed to align therapeutic approaches with BP levels.
- High-normal BP is intended to identify individuals who could benefit from lifestyle interventions and who would receive pharmacological treatment if compelling indications are present (see Section 9).
- Isolated systolic hypertension defined as elevated SBP (≥140 mm Hg) and low DBP (<90 mm Hg) is common in young and in elderly people. In young individuals, including children, adolescents and young adults, isolated systolic hypertension is the most common form of essential hypertension. However, it is also particularly common in the elderly, in whom it reflects stiffening of the large arteries with an increase in pulse pressure (difference between SBP and DBP).
- Individuals identified with confirmed hypertension (grade 1 and grade 2) should receive appropriate pharmacological treatment.
- Details of home-, office- and ambulatory BP measurement techniques are addressed in Section 3.

- ***Section 3: Blood Pressure Measurement and Diagnosis of Hypertension***
- ***Hypertension Diagnosis – Office BP Measurement***
- The measurement of BP in the office or clinic is most commonly the basis for hypertension diagnosis and follow-up. Office BP should be measured according to recommendations shown in Table 3 and Figure 1.
- Whenever possible, the diagnosis should not be made on a single office visit. Usually 2–3 office visits at 1–4-week intervals (depending on the BP level) are required to confirm the diagnosis of hypertension. The diagnosis might be made on a single visit, if BP is ≥180/110 mm Hg and there is evidence of cardiovascular disease (CVD).
- The recommended patient management according to office BP levels is presented in Table 4.
- If possible and available, the diagnosis of hypertension should be confirmed by out-of-office BP measurement (see below).
- ***Hypertension Diagnosis – Office Blood Pressure Measurement***
- **Initial evaluation:** Measure BP in both arms, preferably simultaneously. If there is a consistent difference between arms >10 mm Hg in repeated measurements, use the arm with the higher BP. If the difference is >20 mm Hg consider further investigation.
- **Standing blood pressure:** Measure in treated hypertensives after 1 min and again after 3 min when there are symptoms suggesting postural hypotension and at the first visit in the elderly and people with diabetes.
- **Unattended office blood pressure:** Multiple automated BP measurements taken while the patient remains alone in the office provide a more standardized evaluation but also lower BP levels than usual office measurements with uncertain threshold for hypertension diagnosis. Confirmation with out-of-office BP is again needed for most treatment decisions.
- ***Hypertension Diagnosis – Out-of-Office Blood Pressure Measurement***
- Out-of-office BP measurements (by patients at home or with 24-hour ambulatory blood pressure monitoring [ABPM]) are more reproducible than office measurements, more closely associated with hypertension-induced organ damage and the risk of cardiovascular events and identify the white coat and masked hypertension phenomena (see below).
- Out-of-office BP measurement is often necessary for the accurate diagnosis of hypertension and for treatment decisions. In untreated or treated subjects with office BP classified as high-normal BP or grade 1 hypertension (systolic 130–159 mm Hg and/or diastolic 85–99 mm Hg), the BP level needs to be confirmed using home or ambulatory BP monitoring (Table 5).
- Recommendations for performing home and ambulatory BP measurement are presented in Table 5.

How to measure blood pressure



Pharmacological treatment of hypertension: general scheme



Office blood pressure targets for treated hypertension

ESSENTIAL Target BP reduction by at least 20/10 mmHg, ideally to <140/90 mmHg

OPTIMAL <65 years : BP target <130 / 80 mmHg if tolerated (but >120 / 70 mmHg).
≥65 years : BP target <140 / 90 mmHg if tolerated but consider an individualised BP target in the context of frailty, independence and likely tolerability of treatment.

→ **Aim for BP control within 3 months**

ISH core drug-treatment strategy

ESSENTIAL

- Use whatever drugs are available with as many of the ideal characteristics (see ***Table 9***) as possible.
- Use free combinations if SPCs are not available or unaffordable
- Use thiazide diuretics if thiazide-like diuretics are not available
- Use alternative to DHP-CCBs if these are not available or not tolerated (i.e. Non-DHP-CCBs: diltiazem or verapamil).

OPTIMAL

Ideally Single Pill Combination Therapy (SPC)

Step 1 Dual low-dose# combination	A + C [a,b,c]
Step 2 Dual full-dose combination	A + C [a,b]
Step 3 Triple combination	A + C + D
Step 4 (Resistant Hypertension) Triple Combination + Spironolactone or other drug*	A + C +D Add Spironolactone (12.5 – 50 mg o.d.)[d]

ESSENTIAL **OPTIMAL**

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) Consider monotherapy in low risk grade 1 hypertension or in very old (≥80 yrs) or frailer patients.
b) Consider A + D in post-stroke, very elderly, incipient HF or CCB intolerance.
c) Consider A + C or C + D in black patients.
d) Caution with spironolactone or other potassium sparing diuretics when estimated GFR <45 ml/min/1.73m² or K⁺ >4.5 mmol/L.

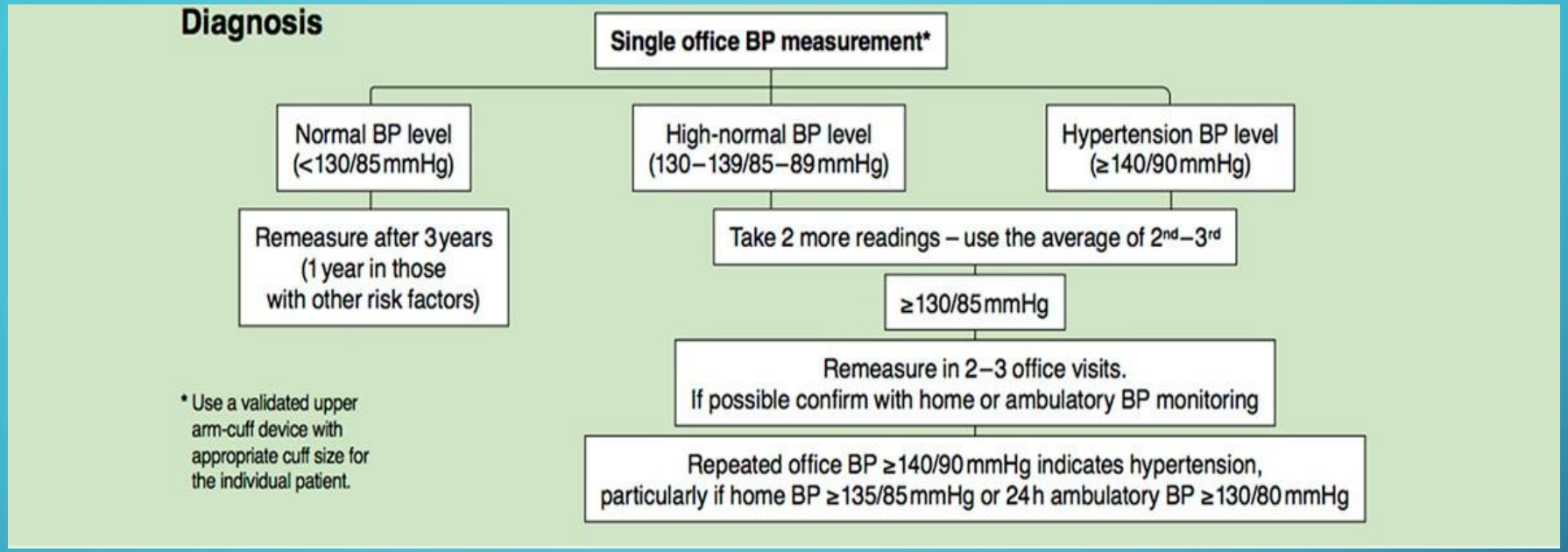
A = ACE-Inhibitor or ARB (Angiotensin Receptor Blocker)
C = DHP-CCB (Dihydropyridine -Calcium Channel Blocker)
D = Thiazide-like diuretic
Supportive references: A + C,[68,70] Spironolactone,[71] Alpha-blocker,[72] C + D[73].

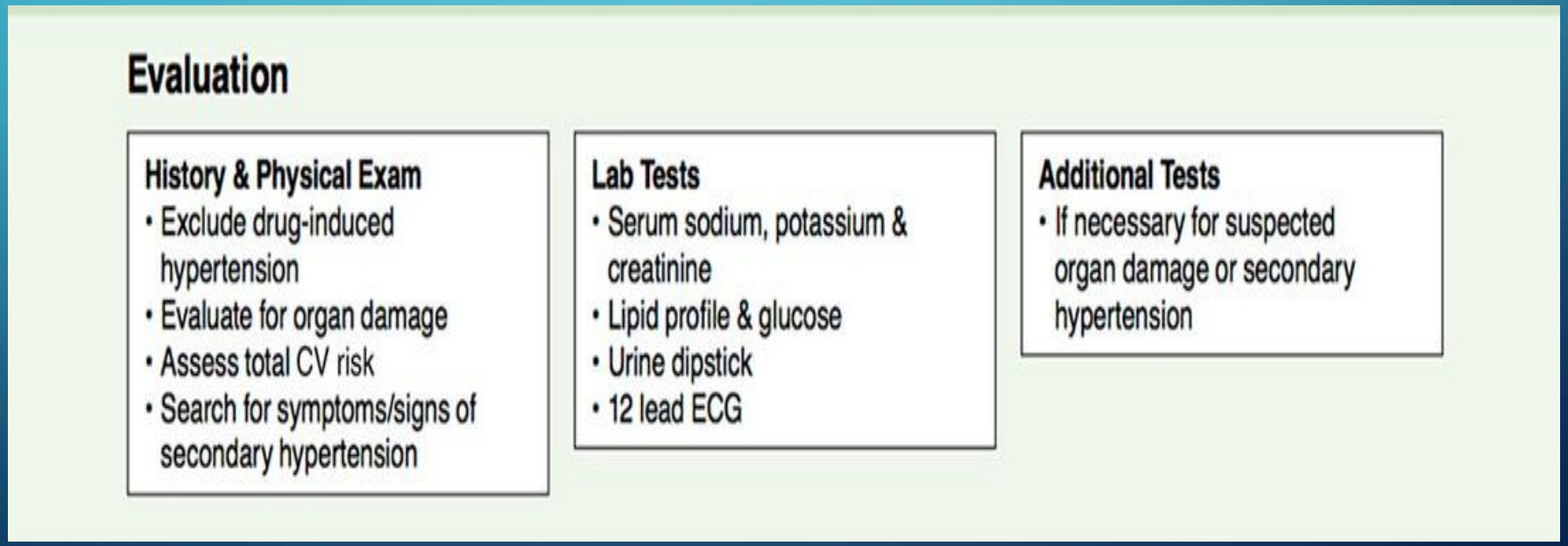
* Alternatives include: Amiloride, doxazosin, eplerenone, clonidine or beta-blocker.

low-dose generally refers to half of the maximum recommended dose

RCT-based benefits between ACE-I's and ARB's were not always identical in different patient populations. Choice between the two classes of RAS-Blockers will depend on patient characteristics, availability, costs and tolerability.

ISH 2020 recommendations (minimum standards of care):





ISH 2020 recommendations (minimum standards of care):

Treatment

Grade 1 Hypertension:
140–159/90–99 mmHg
1. Start lifestyle interventions
2. Start drug treatment in:
   – High-risk patients (CVD,CKD, diabetes, organ damage, or aged 50-80 years)
   – All others with persistent BP elevation after 3–6 months of lifestyle intervention

Grade 2 Hypertension:
≥160/100 mmHg
1. Start drug treatment immediately
2. Start lifestyle intervention

Lifestyle Interventions
- Stop smoking
- Regular exercise
- Lose weight
- Salt reduction
- Healthy diet and drinks
- Lower alcohol intake

Drug Therapy Steps
Use any drugs available and include as many of those below as possible. Consider monotherapy in low-risk grade 1 hypertension and in patients aged >80 years or frail. Simplify regimen with once daily dosing and single pill combinations.

Non-Black Patients
1. Low dose ACEI/ARB* + DHP-CCB
2. Increase to full dose
3. Add thiazide/thiazide-like diuretic
4. Add spironolactone or, if not tolerated or contraindicated, amiloride, doxazosin, eplerenone, clonidine or beta-blocker

Black Patients
1. Low dose ARB* + DHP-CCB or DHP-CCB + thiazide/thiazide-like diuretic
2. Increase to full dose
3. Add diuretic or ARB /ACEI
4. Add spironolactone or, if not tolerated or contraindicated, amiloride, doxazosin, eplerenone, clonidine or beta-blocker

* No ACEI/ARB in women with or planning pregnancy

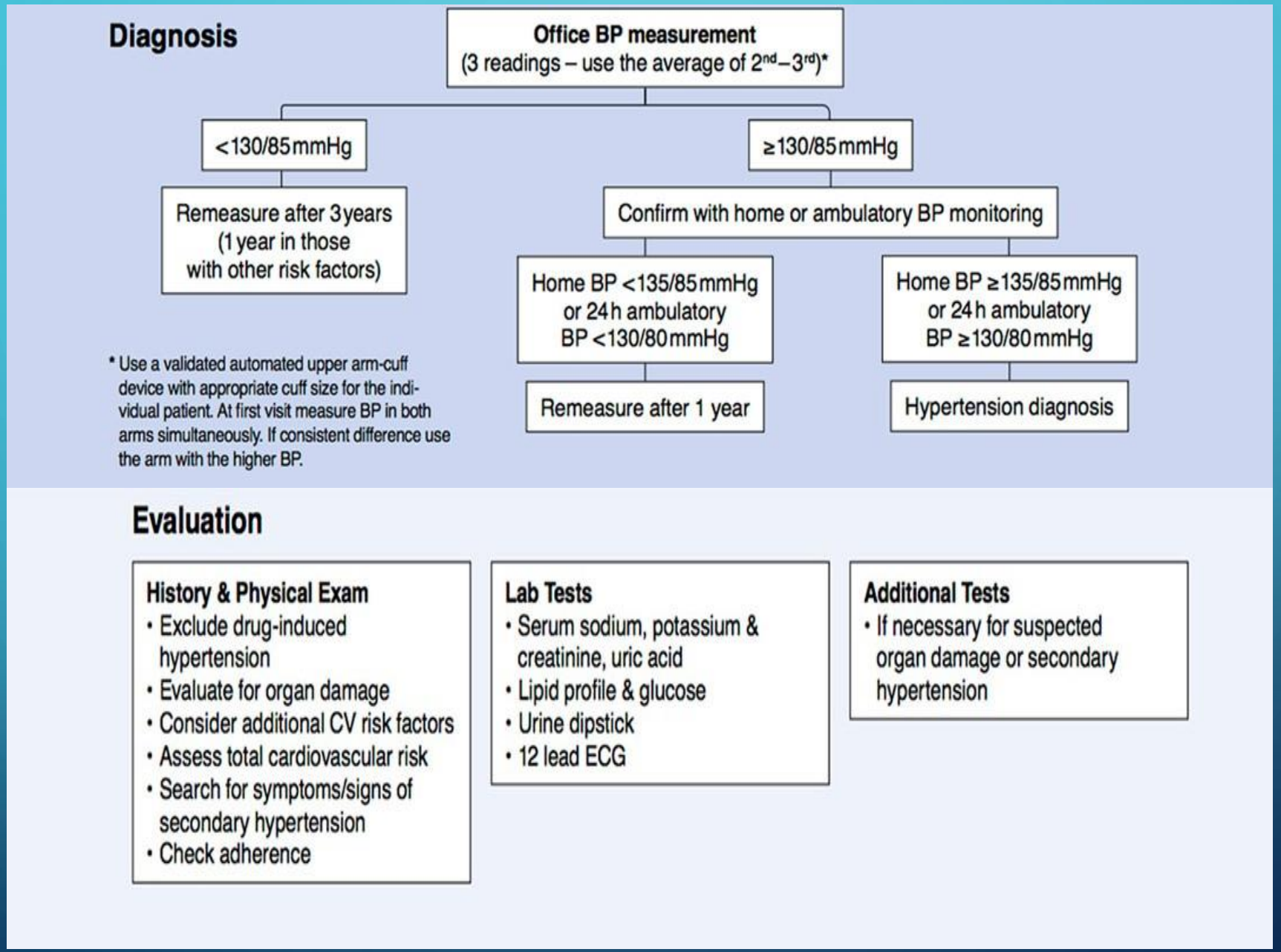
Monitoring

Target
- Reduce BP by at least 20/10 mmHg, ideally to < 140/90 mmHg
- Individualize for elderly based on frailty

Monitor
- BP control (achieve target within 3 months)
- Adverse effects
- Long-term adherence

Referral
- If BP still uncontrolled, or other issue, refer to care provider with hypertension expertise

ISH 2020 recommendations (evidence-based standards of care):



ISH 2020 recommendations (evidence-based standards of care):

Treatment

Grade 1 Hypertension:
140–159/90–99 mmHg
1. Start lifestyle interventions
2. Start drug treatment:
- ***Immediately:*** In high-risk patients (CVD, CKD, diabetes or organ damage)
- ***After 3–6 months of lifestyle intervention:*** In low-moderate risk patients with persistent BP elevation

Grade 2 Hypertension:
≥160/100 mmHg
1. Start drug treatment immediately
2. Start lifestyle intervention

Lifestyle Interventions
- Stop smoking
- Regular exercise
- Lose weight
- Salt reduction
- Healthy diet and drinks
- Lower alcohol intake
- Lower stress
- Reduce exposure to air pollution

Drug Therapy Steps
Simplify regimen with once daily dosing and single pill combinations.
Consider monotherapy in low-risk grade 1 hypertension and in patients aged >80 years or frail

Non-Black Patients
1. Low dose ACEI/ARB* + DHP-CCB
2. Increase to full dose
3. Add thiazide-like diuretic
4. Add spironolactone or, if not tolerated or contraindicated, amiloride, doxazosin, eplerenone, clonidine or beta-blocker

Black Patients
1. Low dose ARB* + DHP-CCB or DHP-CCB + thiazide-like diuretic
2. Increase to full dose
3. Add diuretic or ACEI/ARB
4. Add spironolactone or, if not tolerated or contraindicated, amiloride, doxazosin, eplerenone, clonidine or beta-blocker

* No ACEI/ARB in women with or planning pregnancy

Monitoring

Target
- BP <130/80 mmHg
- Individualise for elderly based on frailty

Monitor
- BP control (achieve target within 3 months)
- Adverse effects
- Long-term adherence

Referral
- If BP still uncontrolled, or other issue, refer to care provider with hypertension expertise

- ***White Coat and Masked Hypertension***
- The use of office and out-of-office (home or ambulatory) BP measurements identifies individuals with white coat hypertension, who have elevated BP only in the office (nonelevated ambulatory or home BP), and those with masked hypertension, who have nonelevated BP in the office but elevated BP out of the office (ambulatory or home). These conditions are common among both untreated subjects and those treated for hypertension. About 10%–30% of subjects attending clinics due to high BP have white coat hypertension and 10%–15% have masked hypertension.
- ***White coat hypertension:*** These subjects are at intermediate cardiovascular risk between normotensives and sustained hypertensives. The diagnosis needs confirmation with repeated office and out-of-office BP measurements. If their total cardiovascular risk is low and there is no hypertension-mediated organ damage (HMOD), drug treatment may not be prescribed. However, they should be followed with lifestyle modification, as they may develop sustained hypertension requiring drug treatment.
- ***Masked hypertension:*** These patients are at similar risk of cardiovascular events as sustained hypertensives. The diagnosis needs confirmation with repeated office and out-of-office measurements. Masked hypertension may require drug treatment aiming to normalize out-of-office BP.

- ***Section 4: Diagnostic / Clinical Tests***
- **Medical History**
- Patients with hypertension are often asymptomatic, however specific symptoms can suggest secondary hypertension or hypertensive complications that require further investigation. A complete medical and family history is recommended and should include:
- **Blood pressure:** New onset hypertension, duration, previous BP levels, current and previous antihypertensive medication, other medications/over-the counter medicines that can influence BP, history of intolerance (side-effects) of antihypertensive medications, adherence to antihypertensive treatment, previous hypertension with oral contraceptives or pregnancy.
- **Risk factors:** Personal history of CVD (myocardial infarction, heart failure [HF], stroke, transient ischemic attacks [TIA], diabetes, dyslipidemia, chronic kidney disease [CKD], smoking status, diet, alcohol intake, physical activity, psychosocial aspects, history of depression). Family history of hypertension, premature CVD, (familial) hypercholesterolemia, diabetes.
- **Assessment of overall cardiovascular risk:** In line with local guidelines/recommendations (see risk scores in Section 11 at the end of the document).
- **Symptoms/signs of hypertension/coexistent illnesses:** Chest pain, shortness of breath, palpitations, claudication, peripheral edema, headaches, blurred vision, nocturia, hematuria, dizziness.
- **Symptoms suggestive of secondary hypertension:** Muscle weakness/tetany, cramps, arrhythmias (hypokalemia/primary aldosteronism), flash pulmonary edema (renal artery stenosis), sweating, palpitations, frequent headaches (pheochromocytoma), snoring, daytime sleepiness (obstructive sleep apnea), symptoms suggestive of thyroid disease (see Section 10 for full list of symptoms).

- ***Physical Examination***
- A thorough physical examination can assist with confirming the diagnosis of hypertension and the identification of HMOD and/or secondary hypertension and should include:
- **Circulation and heart:** Pulse rate/rhythm/character, jugular venous pulse/pressure, apex beat, extra heart sounds, basal crackles, peripheral edema, bruits (carotid, abdominal, femoral), radio-femoral delay.
- **Other organs/systems:** Enlarged kidneys, neck circumference >40 cm (obstructive sleep apnea), enlarged thyroid, increased body mass index (BMI)/waist circumference, fatty deposits and coloured striae (Cushing disease/syndrome).
- ***Laboratory Investigations and ECG***
- **Blood tests:** Sodium, potassium, serum creatinine and estimated glomerular filtration rate (eGFR). If available, lipid profile and fasting glucose.
- **Urine test:** Dipstick urine test.
- **12-lead ECG:** Detection of atrial fibrillation, left ventricular hypertrophy (LVH), ischemic heart disease.

- ***Additional Diagnostic Tests***
- Additional investigations when indicated can be undertaken to assess and confirm suspicion of HMOD, coexistent diseases or/and secondary hypertension.
- ***Imaging Techniques***
- **Echocardiography:** LVH, systolic/diastolic dysfunction, atrial dilation, aortic coarctation.
- **Carotid ultrasound:** Plaques (atherosclerosis), stenosis.
- **Kidneys/renal artery and adrenal imaging:** Ultrasound/renal artery Duplex; CT-/MR-angiography: renal parenchymal disease, renal artery stenosis, adrenal lesions, other abdominal pathology.
- **Fundoscopy:** Retinal changes, hemorrhages, papilledema, tortuosity, nipping.
- **Brain CT/MRI:** Ischemic or hemorrhagic brain injury due to hypertension.
- **Functional Tests and Additional Laboratory Investigations**
- **Ankle-brachial index:** Peripheral (lower extremity) artery disease.
- **Further testing for secondary hypertension if suspected:** Aldosterone-renin ratio, plasma free metanephrines, late-night salivary cortisol or other screening tests for cortisol excess.
- Urinary albumin/creatinine ratio
- Serum uric acid (s-UA) levels
- Liver function tests

- ***Section 5: Cardiovascular Risk Factors***
- **Diagnostic Approach**
- More than 50% of hypertensive patients have additional cardiovascular risk factors.
- The most common additional risk factors are diabetes (15%–20%), lipid disorders (elevated low-density lipoprotein-cholesterol [LDL-C] and triglycerides [30%]), overweight-obesity (40%), hyperuricemia (25%) and metabolic syndrome (40%), as well as unhealthy lifestyle habits (eg, smoking, high alcohol intake, sedentary lifestyle).
- The presence of one or more additional cardiovascular risk factors proportionally increases the risk of coronary, cerebrovascular, and renal diseases in hypertensive patients.[1]
- An evaluation of additional risk factors should be part of the diagnostic workup in hypertensive patients particularly in the presence of a family history of CVD.
- Cardiovascular risk should be assessed in all hypertensive patients by easy-to-use scores based on BP levels and additional risk factors according to a simplified version of the approach proposed by ESC-ESH Guidelines (Table 6).[1]
- A reliable estimate of cardiovascular risk can be obtained in daily practice by including:
- **Other Risk Factors:** Age (>65 years), sex (male>female), heart rate (>80 beats/min), increased body weight, diabetes, high LDL-C/triglyceride, family history of CVD, family history of hypertension, early-onset menopause, smoking habits, psychosocial or socioeconomic factors. **HMOD:** LVH (LVH with ECG), moderate-severe CKD (CKD; eGFR <60 ml/min/1.73m^2), any other available measure of organ damage. **Disease:** previous coronary heart disease (CHD), HF, stroke, peripheral vascular disease, atrial fibrillation, CKD stage 3+.
- The therapeutic strategy must include lifestyle changes, BP control to target and the effective treatment of the other risk factors to reduce the residual cardiovascular risk.
- The combined treatment of hypertension and additional cardiovascular risk factors reduces the rate of CVD beyond BP control.

- ***Other Additional Risk Factors***
- Elevated serum uric acid (s-UA) is common in patients with hypertension and should be treated with diet, urate influencing drugs (losartan, fibrates, atorvastatin) or urate lowering drugs in symptomatic patients (gout with s-UA >6 mg/dl [0.357 mmol/L]).
- An increase in cardiovascular risk must be considered in patients with hypertension and chronic inflammatory diseases, chronic obstructive pulmonary disease (COPD), psychiatric disorders, psychosocial stressors where an effective BP control is warranted.[1]
- ***Section 6: Hypertension-Mediated Organ Damage (HMOD)***
- **Definition and Role of HMOD in Hypertension Management**
- Hypertension-mediated organ damage (HMOD) is defined as the structural or functional alteration of the arterial vasculature and/or the organs it supplies that is caused by elevated BP. End organs include the brain, the heart, the kidneys, central and peripheral arteries, and the eyes.
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- While assessment of overall cardiovascular risk is important for the management of hypertension, additional detection of HMOD is unlikely to change the management of those patients already identified as high risk (ie, those with established CVD, stroke, diabetes, CKD, or familial hypercholesterolemia). However, it can provide important therapeutic guidance on (1) management for hypertensive patients with low or moderate overall risk through reclassification due to presence of HMOD, and (2) preferential selection of drug treatment based on the specific impact on HMOD.[1]

- **Specific Aspects of HMOD and Assessment**

- **Brain:** TIA or strokes are common manifestations of elevated BP. Early subclinical changes can be detected most sensitively by magnetic resonance imaging (MRI) and include white matter lesions, silent microinfarcts, microbleeds, and brain atrophy. Due to costs and limited availability brain MRI is not recommended for routine practice but should be considered in patients with neurologic disturbances, cognitive decline and memory loss.

- **Heart:** A 12-lead ECG is recommended for routine workup of patients with hypertension and simple criteria (Sokolow-Lyon index: SV1+RV5 ≥35 mm, Cornell index: SV3+RaVL >28 mm for men or >20 mm for women and Cornell voltage duration product: >2440 mm•ms) are available to detect presence of LVH. Sensitivity of ECG-LVH is very limited and a two-dimensional transthoracic echocardiogram (TTE) is the method of choice to accurately assess LVH (left ventricular mass index [LVMI]: men >115 g/m^2; women >95 g/m^2) and relevant parameters including LV geometry, left atrial volume, LV systolic and diastolic function and others.

- **Kidneys:** Kidney damage can be a cause and consequence of hypertension and is best assessed routinely by simple renal function parameters (serum creatinine and eGFR) together with investigation for albuminuria (dipstick or urinary albumin creatinine ratio [UACR]) in early morning spot urine).

- **Arteries:** Three vascular beds are commonly assessed to detect arterial HMOD: (1) the carotid arteries through carotid ultrasound to detect atherosclerotic plaque burden/stenosis and intima media thickness (IMT); (2) the aorta by carotid-femoral pulse wave velocity (PWV) assessment to detect large artery stiffening; and (3) the lower extremity arteries by assessment of the ankle-brachial index (ABI). Although there is evidence to indicate that all three provide added value beyond traditional risk factors, their routine use is currently not recommended unless clinically indicated, that is, in patients with neurologic symptoms, isolated systolic hypertension, or suspected peripheral artery disease, respectively.

- **Eyes:** Fundoscopy is a simple clinical bedside test to screen for hypertensive retinopathy although interobserver and intraobserver reproducibility is limited. Fundoscopy is particularly important in hypertensive urgencies and emergencies to detect retinal hemorrhage, microaneurysms, and papilledema in patients with accelerated or malignant hypertension. Fundoscopy should be performed in patients with grade 2 hypertension, ideally by experienced examiners or alternative techniques to visualize the fundus (digital fundus cameras) where available.

- The following assessments to detect HMOD should be performed routinely in all patients with hypertension:
- Serum creatinine and eGFR
- Dipstick urine test
- 12-lead ECG
- All other techniques mentioned above can add value to optimize management of hypertension in affected individuals and should be considered where clinically indicated and available. Serial assessment of HMOD (LVH and albuminuria) to monitor regression with antihypertensive treatment may be helpful to determine the efficacy of treatment in individual patients but this has not been sufficiently validated for most measures of HMOD.
- ***Section 7: Exacerbators and Inducers of Hypertension***
- **Background**
- Several medications and substances may increase BP or antagonize the BP-lowering effects of antihypertensive therapy in individuals (Table 7). It is important to note that the individual effect of these substances on BP can be highly variable with greater increases noted in the elderly, those with higher baseline BP, using antihypertensive therapy or with kidney disease.

- Screen all patients (with hypertension and those at risk for hypertension) for substances that may increase BP or interfere with the BP-lowering effect of antihypertensive medications.
- Where appropriate, consider reducing or eliminating substances that raise BP. If these substances are required or preferred, then treat BP to target regardless. (See resource on possible antihypertensive therapies that target mechanisms underlying the raised BP induced by these substances).
- ***Section 8: Treatment of Hypertension***
- **8.1 Lifestyle Modifications**
- Healthy lifestyle choices can prevent or delay the onset of high BP and can reduce cardiovascular risk. Lifestyle modification is also the first line of antihypertensive treatment. Modifications in lifestyle can also enhance the effects of antihypertensive treatment. Lifestyle modifications should include the following (Table 8).
- **Seasonal BP Variation**
- BP exhibits seasonal variation with lower levels at higher temperatures and higher at lower temperatures. Similar changes occur in people traveling from places with cold to hot temperature, or the reverse. A meta-analysis showed average BP decline in summer of 5/3 mm Hg (systolic/diastolic). BP changes are larger in treated hypertensives and should be considered when symptoms suggesting over-treatment appear with temperature rise, or BP is increased during cold weather. BP below the recommended goal should be considered for possible downtitration, particularly if there are symptoms suggesting overtreatment.
- **8.2 Pharmacological Treatment**
- Contemporary data from over 100 countries suggest that on average, less than 50% of adults with hypertension receive BP-lowering medication, with few countries performing better than this and many worse. This is despite the fact that a difference in BP of 20/10 mm Hg is associated with a 50% difference in cardiovascular risk.
- The pharmacological treatment strategies recommended here (Figures 2–4) are largely compatible with those made in the most recent US and European guidelines.

- ***8.3 Adherence to Antihypertensive Treatment***
- **Background**
- Adherence is defined as to the extent to which a person's behaviors such as taking a medication, following a diet or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider. Nonadherence to antihypertensive treatment affects 10%–80% of hypertensive patients and is one of the key drivers of suboptimal BP control. Poor adherence to antihypertensive treatment correlates with the magnitude of BP elevation and is an indicator of poor prognosis in hypertensive patients. The etiology of nonadherence to antihypertensive treatment is multifactorial and includes causes associated with the healthcare system, pharmacological therapy, the disease, patients and their socioeconomic status.
- **Recommendations: Adherence to Antihypertensive Therapy**
- Evaluate adherence to antihypertensive treatment as appropriate at each visit and prior to escalation of antihypertensive treatment.
- Consider the following strategies to improve medication adherence
- a. reducing polypharmacy – use of single pill combinations
- b. once-daily dosing over multiple times per day dosing
- c. linking adherence behavior with daily habits
- d. providing adherence feedback to patients
- e. home BP monitoring
- f. reminder packaging of medications
- g. empowerment-based counseling for self-management
- h. electronic adherence aids such as mobile phones or short messages services
- i. multidisciplinary healthcare team approach (ie, pharmacists) to improve monitoring for adherence

- Objective indirect (ie, review of pharmacy records, pill counting, electronic monitoring devices) and direct (ie, witnessed intake of medications, biochemical detection of medications in urine or blood) are generally preferred over subjective methods to diagnose nonadherence to antihypertensive treatment.
- The most effective methods for management of nonadherence require complex interventions that combine counseling, self-monitoring, reinforcements and supervision.
- ***Section 9: Common and Other Comorbidities and Complications of Hypertension***
- **Background**
- Hypertensive patients have several common and other comorbidities that can affect cardiovascular risk and treatment strategies.
- The number of comorbidities increases with age, with the prevalence of hypertension and other diseases.
- Common comorbidities include coronary artery disease (CAD), stroke, CKD, HF, and COPD.
- Uncommon comorbidities include rheumatic diseases and psychiatric diseases.
- Uncommon comorbidities are largely underestimated by guidelines and frequently treated with drugs often self-prescribed and possibly interfering with BP control.
- Common and uncommon comorbidities should be identified and managed according to available evidence.

- **Common Comorbidities and Complications**
- **Hypertension and Coronary Artery Disease (CAD)**
- A strong epidemiological interaction exists between CAD and hypertension that accounts for 25%–30% of acute myocardial infarctions.
- Lifestyle changes are recommended (smoking cessation, diet and exercise).
- BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).
- RAS blockers, beta-blockers irrespective of BP levels with or without calcium channel blockers (CCBs) are first-line drugs in hypertensive patients.[1]
- Lipid-lowering treatment with an LDL-C target <55 mg/dL (1.4 mmol/L).
- Antiplatelet treatment with acetyl salicylic acid is routinely recommended.
- **Hypertension and Previous Stroke**
- Hypertension is the most important risk factor for ischemic or hemorrhagic stroke.
- Stroke can be largely prevented by BP control.
- BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).
- RAS blockers, CCBs, and diuretics are first-line drugs.
- Lipid-lowering treatment is mandatory with a LDL-C target <70 mg/dL (1.8 mmol/L) in ischemic stroke.
- Antiplatelet treatment is routinely recommended for ischemic stroke, but not hemorrhagic stroke, and should be carefully considered in patients with hemorrhagic stroke only in the presence of a strong indication.

- **Hypertension and Heart Failure (HF)**
- Hypertension is a risk factor for the development of HF with reduced ejection fraction (HFrEF), and with preserved ejection fraction (HFpEF). Clinical outcome is worse and mortality is increased in hypertensive patients with HF.
- Lifestyle changes are recommended (diet and exercise).
- Treating hypertension has a major impact on reducing the risk of incident HF and HF hospitalization. BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg but >120/70 mm Hg.
- RAS blockers, beta-blockers, and mineralocorticoid receptor antagonists are all effective in improving clinical outcome in patients with established HFrEF, whereas for diuretics, evidence is limited to symptomatic improvement.[1] CCBs are indicated on in case of poor BP control.
- Angiotensin receptor-neprilysin inhibitor (ARNI; sacubitril-valsartan) is indicated for the treatment of HFrEF as an alternative to ACE inhibitors or ARBs also in hypertensive populations. The same treatment strategy can be applied to patients with HFpEF even if the optimal treatment strategy is not known.
- **Hypertension and Chronic Kidney Disease (CKD)**
- Hypertension is a major risk factor for the development and progression of albuminuria and any form of CKD.
- A lower eGFR is associated with resistant hypertension, masked hypertension, and elevated nighttime BP values.
- The effects of BP lowering on renal function (and albuminuria) are dissociated from cardiovascular benefit.
- BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).
- RAS-inhibitors are first-line drugs because they reduce albuminuria in addition to BP control. CCBs and diuretics (loop-diuretics if eGFR <30 ml/min/1.73m^2) can be added.[1]
- eGFR, microalbuminuria and blood electrolytes should be monitored.[1]

- **Hypertension and Chronic Obstructive Pulmonary Disease (COPD)**
- Hypertension is the most frequent comorbidity in patients with COPD.
- BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).
- Lifestyle changes (smoking cessation) are mandatory.
- Environmental (air) pollution should be considered and avoided if possible.
- The treatment strategy should include an angiotensin AT_1-receptor blocker (ARB) and CCB and/or diuretic, while beta blockers ($ß_1$-receptor selective) may be used in selected patients (eg, CAD, HF).
- Additional cardiovascular risk factors should be managed according to cardiovascular risk profile.
- **HIV/AIDS**
- People living with HIV are at increased cardiovascular risk.
- There may be a drug interaction with CCB under most of the antiretroviral therapies.
- Hypertension management should be similar to the general hypertensive populations.
- **Management of Comorbidities**
- In addition to BP control, the therapeutic strategy should include lifestyle changes, body weight control and the effective treatment of the other risk factors to reduce the residual cardiovascular risk.[1]
- Lifestyle changes as in Table 8.
- LDL-cholesterol should be reduced according to risk profile: (1) >50% and <70 mg/dL (1.8 mmol/L) in hypertension and CVD, CKD, DM or no CVD and high risk; (2) >50% and <100 mg/dL (2.6 mmol/L) in high-risk patients; (3) <115 mg/dL (3 mmol/L) in moderate-risk patients.
- Fasting serum glucose levels should be reduced below 126 mg/dL (7 mmol/L) or HbA1c below 7% (53 mmol/mol).[1]
- s-UA should be maintained below 6.5 mg/dL (0.387 mmol/L), and <6 mg/dL (0.357 mmol/L) in patients with gout.
- Antiplatelet therapy should be considered in patients with CVD (secondary prevention only).

- **Diabetes**
- BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).
- The treatment strategy should include an RAS inhibitor (and a CCB and/or thiazide-like diuretic).
- The treatment should include a statin in primary prevention if LDL-C >70 mg/dL (1.8 mmol/L) (diabetes with target organ damage) or >100 mg/dL (2.6 mmol/L) (uncomplicated diabetes).
- The treatment should include glucose and lipid lowering as per current guidelines (see Section 11: Resources).
- **Lipid Disorders**
- BP should be lowered as done in the general population, preferentially with RAS-inhibitors (ARB, ACE-I) and CCBs.
- Statins are the lipid-lowering treatment of choice with or without ezetimibe and/or PCSK9 inhibitor (in the optimal setting). Serum triglyceride lowering should be considered if >200 mg/dL (2.3 mmol/L) particularly in patients with hypertension and DM. Possible additional benefits using fenofibrate in low HDL/high triglyceride subgroup.
- **Metabolic Syndrome (MS)**
- Patients with hypertension and MS have a high-risk profile.
- The diagnosis of MS should be made by separate evaluation of single components.
- The treatment of MS is based on changes in lifestyle (diet and exercise).
- The treatment of hypertension and MS should include BP control as in the general population and treatment of additional risk factors based on level and overall cardiovascular risk (SCORE and/or ASCVD calculator).

- **Other Comorbidities**
- **(Hypertension and Inflammatory Rheumatic Diseases (IRD)**
- IRD (rheumatoid arthritis, psoriasis-arthritis, etc) are associated with an increased prevalence of hypertension under diagnosed and poorly controlled.
- IRD show an increase in cardiovascular risk only partially related to cardiovascular risk factors.
- Rheumatoid arthritis is predominant among IRD.
- The presence of IRD should increase 1 step of cardiovascular risk.
- BP should be lowered as in the general population, preferentially with RAS-inhibitors (evidence of an overactive RAAS) and CCBs.
- Underlying diseases should be effectively treated by reducing inflammation and by avoiding high doses of NSAIDs.
- Lipid-lowering drugs should be used according to cardiovascular risk profile (SCORE/ASCVD calculator) also considering the effects of biologic drugs.[1]
- **Hypertension and Psychiatric Diseases**
- The prevalence of hypertension is increased in patients with psychiatric disorders and in particular depression.
- According to guidelines, psychosocial stress and major psychiatric disorders increase the cardiovascular risk.
- Depression has been associated with cardiovascular morbidity and mortality, suggesting the importance of BP control.
- BP should be lowered as in the general population, preferentially with RAS-inhibitors and diuretics with a lesser rate of pharmacological interactions under antidepressants. CCBs and alpha$_1$-blockers should be used with care in patients with orthostatic hypotension (eg, SRIs).
- The risk of pharmacologic interactions, ECG abnormalities and postural BP changes must be considered.
- Beta-blockers (not metoprolol) should be used in presence of drug-induced tachycardia (antidepressant, antipsychotic drugs).
- Additional risk factors should be managed according to cardiovascular risk profile (SCORE/ASCVD calculator, see Section 11: Resources).

- **Section 10: Specific Circumstances**
- ***10.1 Resistant Hypertension***
- **Background**
- Resistant hypertension is defined as seated office BP >140/90 mm Hg in a patient treated with three or more antihypertensive medications at optimal (or maximally tolerated) doses including a diuretic and after excluding pseudoresistance (poor BP measurement technique, white coat effect, nonadherence and suboptimal choices in antihypertensive therapy) as well as the substance/drug-induced hypertension and secondary hypertension. Resistant hypertension affects around 10% of hypertensive individuals, has a negative impact on well-being and increases the risk of coronary artery disease, chronic HF, stroke, end-stage renal disease, and all-cause mortality Approximately 50% of patients diagnosed with resistant hypertension have pseudoresistance rather than true resistant hypertension.[1]
- **Recommendations**
- If seated office BP >140/90 mm Hg in patients managed with three or more antihypertensive medications at optimal (or maximally tolerated) doses including a diuretic, first exclude causes of pseudoresistance (poor BP measurement technique, white coat effect, nonadherence and suboptimal choices in antihypertensive therapy), and substance-induced increases in BP.
- Consider screening patients for secondary causes as appropriate (refer to Section 10.2).
- Optimize the current treatment regimen including health behavior change and diuretic-based treatment (maximally tolerated doses of diuretics, and optimal choice of diuretic: use of thiazide-like rather than thiazide diuretics, and initiation of loop diuretics for eGFR <30 ml/min/1.73m^2 or clinical volume overload).
- Add a low dose of spironolactone as the 4th line agent in those whose serum potassium is <4.5 mmol/L and whose eGFR is >45 ml/min/1.73m^2 to achieve BP targets. If spironolactone is contraindicated or not tolerated, amiloride, doxazosin, eplerenone, clonidine, and beta-blockers are alternatives, or any available antihypertensive class not already in use.
- Resistant hypertension should be managed in specialist centers with sufficient expertize, and resources necessary to diagnose and treat this condition.

- ***10.2 Secondary Hypertension***
- **Background**
- A specific cause of secondary hypertension can be identified in 5%–10% of hypertensive patients (Table 11). Early diagnosis of secondary hypertension and the institution of appropriate targeted treatment have the potential to cure hypertension in some patients or improve BP control/reduce the number of prescribed antihypertensive medications in others. The most common types of secondary hypertension in adults are renal parenchymal disease, renovascular hypertension, primary aldosteronism, chronic sleep apnea, and substance/drug-induced.
- **Recommendations**
- Consider screening for secondary hypertension in (1) patients with early onset hypertension (<30 years of age) in particular in the absence of hypertension risk factors (obesity, metabolic syndrome, familial history etc.), (2) those with resistant hypertension, (3) individuals with sudden deterioration in BP control, (4) hypertensive urgency and emergency, (5) those presenting with high probability of secondary hypertension based on strong clinical clues.
- In patients with resistant hypertension, investigations for secondary hypertension should generally be preceded by exclusion of pseudoresistant hypertension and drug/substance-induced hypertension.
- Basic screening for secondary hypertension should include a thorough assessment of history, physical examination (see clinical clues), basic blood biochemistry (including serum sodium, potassium, eGFR, TSH), and dipstick urine analysis.
- Further investigations for secondary hypertension (additional biochemistry/imaging/others) should be carefully chosen based on information from history, physical examination and basic clinical investigations.
- Consider referring for further investigation and management of suspected secondary hypertension to a specialist center with access to appropriate expertize and resources.

- ***10.3 Hypertension in Pregnancy***
- Hypertension in pregnancy is a condition affecting 5%–10% of pregnancies worldwide. Maternal risks include placental abruption, stroke, multiple organ failure (liver, kidney), disseminated vascular coagulation. Fetal risks include intrauterine growth retardation, preterm birth, intrauterine death. Hypertension in pregnancy includes the following conditions:
- **Preexisting hypertension:** Starts before pregnancy or <20 weeks of gestation, and lasts >6 weeks postpartum with proteinuria.
- **Gestational hypertension:** Starts >20 weeks of gestation, and lasts <6 weeks postpartum.
- **Preexisting hypertension plus superimposed gestational hypertension** with proteinuria.
- **Preeclampsia:** Hypertension with proteinuria (>300 mg/24 h or ACR >30 mg/mmol [265 mg/g]). Predisposing factors are preexisting hypertension, hypertensive disease during previous pregnancy, diabetes, renal disease, first- or multiple pregnancy, autoimmune disease (SLE). Risks are fetal growth restriction, preterm birth.
- **Eclampsia:** Hypertension in pregnancy with seizures, severe headaches, visual disturbance, abdominal pain, nausea and vomiting, low urinary output: Immediate treatment and delivery required.
- **HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome:** Immediate treatment and delivery required.

- **Blood Pressure Measurement in Pregnancy**
- Office BP measurement following general guidelines. Take office BP measurement using a manual auscultatory device, or an automated upper-arm cuff device which has been validated specifically in pregnancy and preeclampsia (list of validated devices at www.stridebp.org).
- ABPM or home BP monitoring using devices validated specifically in pregnancy and preeclampsia to evaluate white coat hypertension, DM, nephropathy.
- **Investigation of Hypertension in Pregnancy**
- Urine analysis, full blood count, liver enzymes, hematocrit, serum creatinine and s-UA. Test for proteinuria in early pregnancy (preexisting renal disease) and second half of pregnancy (preeclampsia). A dipstick test >1+ should be followed up with UACR in a single spot urine; UACR <30 mg/mmol excludes proteinuria.
- Ultrasound of kidneys and adrenals, free plasma metanephrines (if clinical features of pheochromocytoma); Doppler ultrasound of uterine arteries (after 20 weeks of gestation is useful to detect those at higher risk of gestational hypertension, preeclampsia, and intrauterine growth retardation).
- **Prevention of Preeclampsia**
- Women at high risk (hypertension in previous pregnancy, CKD, autoimmune disease, diabetes, chronic hypertension), or moderate risk (first pregnancy in a woman >40 years, pregnancy interval >10 years, BMI >35 kg/m^2, family history of preeclampsia, multiple pregnancies): 75–162 mg aspirin at weeks 12–36. Oral calcium supplementation of 1.5–2 g/day is recommended in women with low dietary intake (<600 mg/day).

- **Management of Hypertension in Pregnancy**
- **Mild hypertension:** Drug treatment at persistent BP >150/95 mm Hg in all women. Drug treatment at persistent BP >140/90 mm Hg in gestational hypertension, preexisting hypertension with superimposed gestational hypertension; hypertension with subclinical HMOD at any time during pregnancy. First choices: methyldopa, beta-blockers (labetalol), and dihydropyridine-calcium channel blockers (DHP-CCBs) (nifedipine [not capsular], nicardipine). Contraindicated: RAS blockers (ACE-I, ARB, direct renin inhibitors [DRI]) due to adverse fetal and neonatal outcomes.
- **Severe hypertension:** At BP >170 mm Hg systolic and/or >110 mm Hg diastolic: immediate hospitalization is indicated (emergency). Treatment with intravenous labetalol (alternative intravenous nicardipine, esmolol, hydralazine, urapidil), oral methyldopa or DHP-CCBs (nifedipine [not capsular] nicardipine). Add magnesium (hypertensive crisis to prevent eclampsia). In pulmonary edema: nitroglycerin intravenous infusion. Sodium-nitroprusside should be avoided due to the danger of fetal cyanide poisoning with prolonged treatment.
- **Delivery in gestational hypertension or pre eclampsia:** At week 37 in asymptomatic women. Expedite delivery in women with visual disturbances, hemostatic disorders.
- **Blood pressure post partum:** If hypertension persists, any of recommended drugs except methyldopa (postpartum depression).
- **Breastfeeding:** All antihypertensives excreted into breast milk at low concentrations. Avoid atenolol, propranolol, nifedipine (high concentration in milk). Prefer long acting CCBs. Refer to prescribing information.
- **Long-term consequences of gestational hypertension:** Increased risk of hypertension and CVD (stroke, ischemic heart disease) in later life.
- Lifestyle adjustment
- Lifestyle adjustment and annual checkups (BP, metabolic factors)

- ***10.4 Hypertensive Emergencies***
- **Definition of Hypertensive Emergencies and Their Clinical Presentation**
- A hypertensive emergency is the association of substantially elevated BP with acute HMOD. Target organs include the retina, brain, heart, large arteries, and the kidneys. This situation requires rapid diagnostic workup and immediate BP reduction to avoid progressive organ failure. Intravenous therapy is usually required. The choice of antihypertensive treatment is predominantly determined by the type of organ damage. Specific clinical presentations of hypertensive emergencies include:
- **Malignant hypertension:** Severe BP elevation (commonly >200/120 mm Hg) associated with advanced bilateral retinopathy (hemorrhages, cotton wool spots, papilledema).
- **Hypertensive encephalopathy:** Severe BP elevation associated with lethargy, seizures, cortical blindness and coma in the absence of other explanations.
- **Hypertensive thrombotic microangiopathy:** Severe BP elevation associated with hemolysis and thrombocytopenia in the absence of other causes and improvement with BP-lowering therapy.
- Other presentations of hypertensive emergencies include severe BP elevation associated with cerebral hemorrhage, acute stroke, acute coronary syndrome, cardiogenic pulmonary edema, aortic aneurysm/dissection, and severe preeclampsia and eclampsia.
- Patients with substantially elevated BP who lack acute HMOD are not considered a hypertensive emergency and can typically be treated with oral antihypertensive therapy.
- **Clinical Presentation and Diagnostic Workup**
- The clinical presentation of a hypertensive emergency can vary and is mainly determined by the organ(s) acutely affected. There is no specific BP threshold to define a hypertensive emergency.
- Symptoms include headaches, visual disturbances, chest pain, dyspnea, neurologic symptoms, dizziness, and more unspecific presentations.
- Medical history: preexisting hypertension, onset and duration of symptoms, potential causes (nonadherence with prescribed antihypertensive drugs, lifestyle changes, concomitant use of BP elevating drugs [NSAIDS, steroids, immune-suppressants, sympathomimetics, cocaine, antiangiogenic therapy]).

- **Thorough physical examination:** Cardiovascular and neurologic assessment. Laboratory analysis: hemoglobin, platelets, creatinine, sodium, potassium, lactate dehydrogenase (LDH), haptoglobin, urinalysis for protein, urine sediment. **Examinations:** Fundoscopy, ECG.
- Additional investigations may be required and indicated depending on presentation and clinical findings and may be essential in the context: troponins (chest pain), chest x-ray (congestion/fluid overload), transthoracic echocardiogram (cardiac structure and function), CT/MRI brain (cerebral hemorrhage/stroke), CT-angiography thorax/abdomen (acute aortic disease). Secondary causes can be found in 20%–40% of patients presenting with malignant hypertension and appropriate diagnostic workup to confirm or exclude secondary forms is indicated.
- **Diagnostic Tests and Acute Therapeutic Management**
- The overall therapeutic goal in patients presenting with hypertensive emergencies is a controlled BP reduction to safer levels to prevent or limit further hypertensive damage while avoiding hypotension and related complications. There is a lack of randomized controlled trial data to provide clear cut guidance on BP targets and times within which these should be achieved. Most recommendations are based on expert consensus. The type of acute HMOD is the main determinant of the preferred treatment choice. The timeline and magnitude of BP reduction is strongly dependent on the clinical context. For example, acute pulmonary edema and aortic dissection require rapid BP reduction, whereas BP levels not exceeding 220/120 mm Hg are generally tolerated in acute ischemic stroke for certain periods. Table 12 provides a general overview of timelines and BP targets as well as preferred antihypertensive drug choices with most common clinical presentations. Availability of drugs and local experience with individual drugs are likely to influence the choice of drugs. Labetalol and nicardipine are generally safe to use in all hypertensive emergencies and should be available wherever hypertensive emergencies are being managed. Nitroglycerin and nitroprusside are specifically useful in hypertensive emergencies including the heart and the aorta.
- **Specific Situations**
- **Sympathetic hyperreactivity:** If intoxication with amphetamines, sympathomimetics or cocain is suspected as cause of presentation with a hypertensive emergency use of benzodiazepines should be considered prior to specific antihypertensive treatment. Phentolamine, a competitive alpha-receptor blocking agent and clonidine, a centrally sympatholytic agent with additional sedative properties are useful if additional BP-lowering therapy is required. Nicardipine and nitroprusside are suitable alternatives.
- **Pheochromocytoma:** The adrenergic drive associated with pheochromocytoma responds well to phentolamine. Beta-blockers should only be used once alpha-blockers have been introduced to avoid acceleration of hypertension. Urapidil and nitroprusside are additional suitable options.
- **Preeclampsia/eclampsia:** See Section 10.3: Hypertension in Pregnancy.
- **Follow-Up**
- Patients who experienced a hypertensive emergency are at increased risk of cardiovascular and renal disease. Thorough investigation of potential underlying causes and assessment of HMOD is mandatory to avoid recurrent presentations with hypertensive emergencies. Similarly, adjustment and simplification of antihypertensive therapy paired with advice for lifestyle modification will assist to improve adherence and long-term BP control. Regular and frequent follow-up (monthly) is recommended until target BP and ideally regression of HMOD has been achieved

- ***10.5 Ethnicity, Race and Hypertension***
- Hypertension prevalence, treatment and control rates vary significantly according to ethnicity. Such differences are mainly attributed to genetic differences, but lifestyle and socioeconomic status possibly filters through into health behaviors such as diet – which appear to be major contributors.
- **Populations From African Descent**
- Black populations, whether residing in Africa, the Caribbean, United States, or Europe, develop hypertension and associated organ damage at younger ages, have a higher frequency of resistant and nighttime hypertension, and a higher risk of kidney disease, stroke, HF, and mortality, than other ethnic groups.
- This increased cardiovascular risk may be due to physiological differences including a suppressed RAAS, altered renal sodium handling, increased cardiovascular reactivity, and early vascular aging (large artery stiffness).
- Management of hypertension:
  - – Wherever possible, annual screening for hypertension is advised for adults 18 years and older.
  - – Lifestyle modification should place additional focus on salt restriction, increased intake of vegetables and fruits (potassium intake), weight management, and reducing alcohol intake.
  - – First-line pharmacological therapy is recommended as a single pill combination including a thiazide-like diuretic plus CCB or CCB plus ARB (see Sections 8 and 12).– Among RAS-inhibitors, ARBs maybe preferred as angioedema is about 3 times more likely to occur with ACE inhibitors among black patients.
    Populations From Asia
- Ethnic-specific characteristics are recognized for East Asian populations. Hypertensive patients have a greater likelihood of salt-sensitivity accompanied with mild obesity. When compared to Western populations, East Asian people present a higher prevalence of stroke (particularly hemorrhagic stroke) and nonischemic HF.[1]
- Morning hypertension and nighttime hypertension are also more common in Asia, compared with European populations.
- South Asian populations originating from the Indian subcontinent have a particularly high risk for cardiovascular and metabolic diseases, including CAD and type 2 DM. With large hypertensive populations residing in India and China, clinical trials in these populations are required to advise whether current treatment approaches are ideal
- Management of hypertension:
  - – South East Asia: Standard treatment as indicated in these guidelines is advised, until more evidence becomes available.

- ***Section 12: Hypertension Management at a Glance***

Table 1. Classification of Hypertension Based on Office Blood Pressure (BP) Measurement			
Category	Systolic (mm Hg)		Diastolic (mm Hg)
Normal BP	<130	and	<85
High-normal BP	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	≥160	and/or	≥100

Table 2. Criteria for Hypertension Based on Office-, Ambulatory (ABPM)-, and Home Blood Pressure (HBPM) Measurement	
	SBP/DBP, mm Hg
Office BP	≥140 and/or ≥90
ABPM	
24-h average	≥130 and/or ≥80
Day time (or awake) average	≥135 and/or ≥85
Night time (or asleep) average	≥120 and/or ≥70
HBPM	≥135 and/or ≥85

Table 4. Blood Pressure Measurement Plan According to Office Blood Pressure Levels

Office Blood Pressure Levels (mm Hg)		
<130/85	130–159/85–99	>160/100
Remeasure within 3 years (1 year in those with other risk factors)	If possible confirm with out-of-office blood pressure measurement (high possibility of white coat or masked hypertension). Alternatively confirm with repeated office visits.	Confirm within a few days or weeks

- **Table 6. Simplified Classification of Hypertension Risk according to additional Risk Factors, Hypertension-Mediated Organ Damage (HMOD), and Previous Disease**

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 DBP ≥100	
No other risk factors	Low	Low	Moderate	High
1 or 2 risk factors	Low	Moderate	High	
≥3 risk factors	Low / Moderate	High	High	
HMOD, CKD grade 3, diabetes mellitus, CVD	High	High	High	

*Example based on a 60 year old male patient. Categories of risk will vary according to age and sex.

Other risk factors:
- Age(>65 years)
- Sex(male>female)
- Heart rate(>80)
- Increased body weight
- Diabetes
- High LDL-C/TG
- Family history of CVD
- Family history of HTN
- Early-onset of menopause
- Smoking habits
- Psychosocial or socioeconomic factors

*Average increase in blood pressure or risk of hypertension. However, the effect of these medications/ substances on blood pressure may highly vary between individuals.

Table 7. Drug/Substance Exacerbators and Inducers of Hypertension

Drug/Substance[32-43]	Comments on Specific Drugs and Substances*
Nonsteroidal anti-inflammatory drugs (NSAIDs)	No difference or an increase of up to 3/1 mm Hg with celecoxib 3/1 mm Hg increase with nonselective NSAIDs No increase in blood pressure with aspirin NSAIDs can antagonize the effects of RAAS-inhibitors and beta blockers
Combined oral contraceptive pill	6/3 mm Hg increase with high doses of estrogen (>50 mcg of estrogen and 1–4 mcg progestin)
Antidepressants	2/1 mm Hg increase with SNRI (selective norepinephrine and serotonin reuptake inhibitors) Increased odds ratio of 3.19 of hypertension with tricyclic antidepressant use No increases in blood pressure with SSRI (selective serotonin reuptake inhibitors)
Acetaminophen	Increased relative risk of 1.34 of hypertension with almost daily acetaminophen use
Other medications	Steroids Antiretroviral therapy: inconsistent study findings for increased blood pressure Sympathomimetics: pseudoephedrine, cocaine, amphetamines Antimigraine serotonergics Recombinant human erythropoeitin Calcineurin inhibitors Antiangiogenesis and kinase inhibitors 11 ß-hydroxysteroid dehydrogenase type 2 inhibitors
Herbal and other substances[44-45]	Alcohol, ma-huang, ginseng at high doses, liquorice, St. John's wort, yohimbine

Table 8. Lifestyle Modifications

Salt reduction	There is strong evidence for a relationship between high salt intake and increased blood pressure.[47] Reduce salt added when preparing foods, and at the table. Avoid or limit consumption of high salt foods such as soy sauce, fast foods and processed food including breads and cereals high in salt.
Healthy diet	Eating a diet that is rich in whole grains, fruits, vegetables, polyunsaturated fats and dairy products and reducing food high in sugar, saturated fat and trans fats, such as the DASH diet (http://www.dashforhealth.com).[48] Increase intake of vegetables high in nitrates known to reduce BP, such as leafy vegetables and beetroot. Other beneficial foods and nutrients include those high in magnesium, calcium and potassium such as avocados, nuts, seeds, legumes and tofu.[49]
Healthy drinks	Moderate consumption of coffee, green and black tea.[50] Other beverages that can be beneficial include karkadé (hibiscus) tea, pomegranate juice, beetroot juice and cocoa.[49]
Moderation of alcohol consumption	Positive linear association exists between alcohol consumption, blood pressure, the prevalence of hypertension, and CVD risk.[51] The recommended daily limit for alcohol consumptions is 2 standard drinks for men and 1.5 for women (10 g alcohol/standard drink). Avoid binge drinking.
Weight reduction	Body weight control is indicated to avoid obesity. Particularly abdominal obesity should be managed. Ethnic-specific cut-offs for BMI and waist circumference should be used.[52] Alternatively, a waist-to-height ratio <0.5 is recommended for all populations.[53,54]

Smoking cessation	Smoking is a major risk factor for CVD, COPD and cancer. Smoking cessation and referral to smoking cessation programs are advised.[55]
Regular physical activity	Studies suggest that regular aerobic and resistance exercise may be beneficial for both the prevention and treatment of hypertension.[56–58] Moderate intensity aerobic exercise (walking, jogging, cycling, yoga, or swimming) for 30 minutes on 5–7 days per week or HIIT (high intensity interval training) which involves alternating short bursts of intense activity with subsequent recovery periods of lighter activity. Strength training also can help reduce blood pressure. Performance of resistance/strength exercises on 2–3 days per week.
Reduce stress and induce mindfulness	Chronic stress has been associated to high blood pressure later in life.[59] Although more research is needed to determine the effects of chronic stress on blood pressure, randomized clinical trials examining the effects of transcendental meditation/mindfulness on blood pressure suggest that this practice lowers blood pressure.[60] Stress should be reduced and mindfulness or meditation introduced into the daily routine.
Complementary, alternative or traditional medicines	Large proportions of hypertensive patients use complementary, alternative or traditional medicines (in regions such as Africa and China)[61,62] yet large-scale and appropriate clinical trials are required to evaluate the efficacy and safety of these medicines. Thus, use of such treatment is not yet supported.
Reduce exposure to air pollution and cold temperature	Evidence from studies support a negative effect of air pollution on blood pressure in the long-term.[63,64]

Table 9. Ideal Characteristics of Drug Treatment	
1.	Treatments should be evidence-based in relation to morbidity/mortality prevention.
2.	Use a once-daily regimen which provides 24-hour blood pressure control.
3.	Treatment should be affordable and/or cost-effective relative to other agents.
4.	Treatments should be well-tolerated.
5.	Evidence of benefits of use of the medication in populations to which it is to be applied.

Table 10. Outline of Evidence-Based Management of Other Comorbidities and Hypertension		
Additional Comorbidity	Recommended Drugs	Warning
Rheumatic disorders	• RAS-inhibitors and CCBs±diuretics • Biologic drugs not affecting blood pressure should be preferred (where available)	High doses of NSAIDs
Psychiatric disorders	• RAS-inhibitors and diuretics • Beta-blockers (not metoprolol) if drug-induced tachycardia (antidepressant, antipsychotic drugs). • Lipid-lowering drugs/antidiabetic drugs according to risk profile	Avoid CCBs if orthostatic hypotension (SRIs)

Table 11. Features of Secondary Hypertension

Secondary Hypertension	Clinical History and Physical Examination	Basic Biochemistry and Urine Analysis	Further Diagnostic Tests
Renal parenchymal disease	• Personal/familial history of CKD	• Proteinuria, hematuria, leukocyturia on dipstick urine analysis • Decreased estimated GFR	• Kidney ultrasound
Primary aldosteronism	• Symptoms of hypokalemia (muscle weakness, muscle cramps, tetany)	• Spontaneous hypokalemia or diuretic-induced hypokalemia on blood biochemistry (50%–60% of patients are normokalemic). • Elevated plasma aldosterone-renin activity ratio	• Confirmatory testing (eg, intravenous saline suppression test) • Imaging of adrenals (adrenal computed tomography) • Adrenal vein sampling
Renal artery stenosis	• Abdominal bruit • Bruits over other arteries (ie, carotid and femoral arteries) • Drop in estimated GFR >30% after exposure to ACE-inhibitors/ARBs • For suspected atherosclerotic RAS, history of flash pulmonary edema or history of atherosclerotic disease or presence of cardiovascular risk factors • For suspected fibromuscular dysplasia, young women with onset of hypertension <30 years	• Decrease in estimated GFR	• Imaging of renal arteries (duplex ultrasound, abdominal computed tomography or magnetic resonance angiograms depending on availability and patient's level of renal function)
Pheochromocytoma	• Headaches • Palpitations • Perspiration • Pallor • History of labile hypertension	• Increased plasma levels of metanephrines • Increased 24-hour urinary fractional excretion of metanephrines and catecholamines	• Abdominal/pelvic computational tomography or MRI

Cushing's syndrome and disease	• Central obesity • Purple striae • Facial rubor • Signs of skin atrophy • Easy bruising • Dorsal and supraclavicular fat pad • Proximal muscle weakness	• Hypokalemia • Increased late-night salivary cortisol	• Dexamethasone suppression tests[118] • 24 hour urinary free cortisol • Abdominal/pituitary imaging
Coarctation of the aorta	• Higher blood pressure in upper than lower extremities • Delayed or absent femoral pulses		• Echocardiogram • Computational tomography angiogram • Magnetic resonance angiogram
Obstructive sleep apnea	• Increased BMI • Snoring • Daytime sleepiness • Gasping or choking at night • Witnessed apneas during sleep • Nocturia		• Home sleep apnea testing (eg, level 3 sleep study) • Overnight polysomnography testing
Thyroid disease	• Symptoms of hyperthyroidism: heat intolerance, weight loss, tremor, palpitations • Symptoms of hypothyroidism: cold intolerance, weight gain, dry brittle hair	• TSH, Free T4	

Table 12. Hypertensive Emergencies Requiring Immediate BP Lowering

Clinical Presentation	Timeline and Target BP	First Line Treatment	Alternative
Malignant hypertension with or without TMA or acute renal failure	Several hours, MAP −20% to −25%	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediate, MAP −20% to −25%	Labetalol Nicardipine	Nitroprusside
Acute ischaemic stroke and SBP >220 mm Hg or DBP >120 mm Hg	1 h, MAP −15%	Labetalol Nicardipine	Nitroprusside
Acute ischaemic stroke with indication for thrombolytic therapy and SBP >185 mm Hg or DBP >110 mm Hg	1 h, MAP −15%	Labetalol Nicardipine	Nitroprusside

Acute hemorrhagic stroke and SBP >180 mm Hg	Immediate, 130<SBP <180 mm Hg	Labetalol Nicardipine	Urapidil
Acute coronary event	Immediate, SBP <140 mm Hg	Nitroglycerine Labetalol	Urapidil
Acute cardiogenic pulmonary edema	Immediate, SBP <140 mm Hg	Nitroprusside or nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic disease	Immediate, SBP <120 mm Hg and heart rate <60 bpm	Esmolol and nitroprusside or nitroglycerine or nicardipine	Labetalol or metoprolol
Eclampsia and severe preeclampsia/HELLP	Immediate, SBP <160 mm Hg and DBP <105 mm Hg	Labetalol or nicardipine and magnesium sulphate	

Abbreviations

ABPM	**ambulatory blood pressure monitoring**
ACE	angiotensin converting enzyme
ARB	angiotensin AT-1 receptor blocker
ARNI	angiotensin receptor-neprilysin inhibitors
BMI	body mass index
BP	blood pressure
CAD	coronary artery disease
CCBs	calcium channel blockers
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
CVD	cardiovascular disease
DBP	diastolic blood pressure
DHP-CCB	dihydropyridine calcium channel blocker
DM	diabetes mellitus
DRI	direct renin inhibitor
ECG	electrocardiogram
eGFR	estimated glomerular filtration rate
ESC-ESH	European Society of Cardiology, European Society of Hypertension
HBPM	home blood pressure measurement
HDL	high density lipoprotein
HELLP	hemolysis, elevated liver enzymes and low platelets
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HIC	high-income countries
HIIT	high intensity interval training
HIV	human immunodeficiency virus
HMOD	hypertension-mediated organ damage

IRD	**inflammatory rheumatic disease**
ISH	International Society of Hypertension
LDH	IMT
LDL-C	low-density lipoprotein cholesterol
LMIC	low- and middle-income countries
LV	left ventricular
LVH	left ventricular hypertrophy
MAP	mean arterial pressure
MRI	magnetic resonance imaging
MS	metabolic syndrome
NSAIDs	nonsteroidal anti-inflammatory drugs
PWV	pulse wave velocity
RAAS	renin angiotensin aldosterone system
RAS	renin-angiotensin system
RCT	randomized control trials
SBP	systolic blood pressure
SNRI	selective norepinephrine and serotonin reuptake inhibitors
SPC	single pill combination therapy
SRI	serotonin reuptake inhibitors

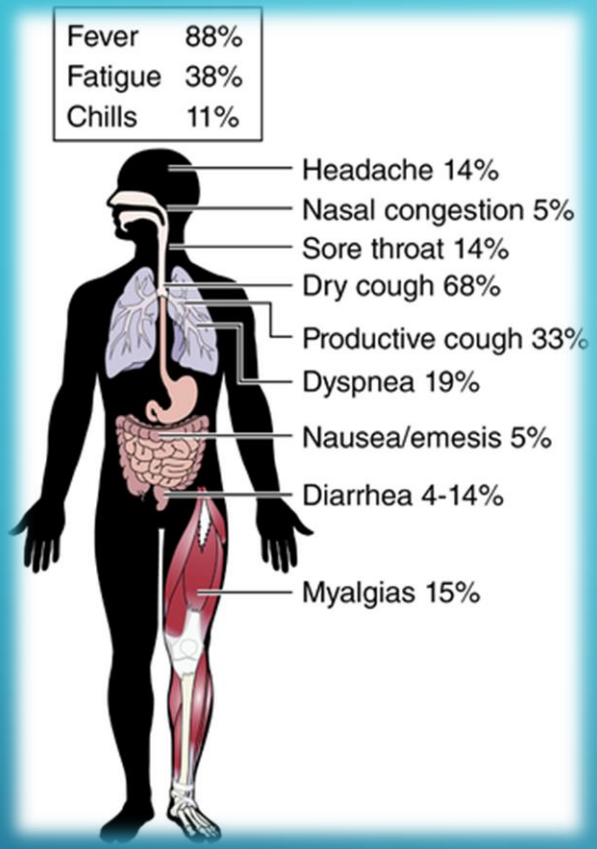
SSRI	**selective serotonin reuptake inhibitors**
s-UA	serum uric acid
T4	thyroxin 4
TIA	transient ischemic attack
TMA	thrombotic microangiopathy
TSH	thyroid stimulating hormone
TTE	two-dimensional transthoracic echocardiogram
UACR	urinary albumin creatinine ratio

PART B

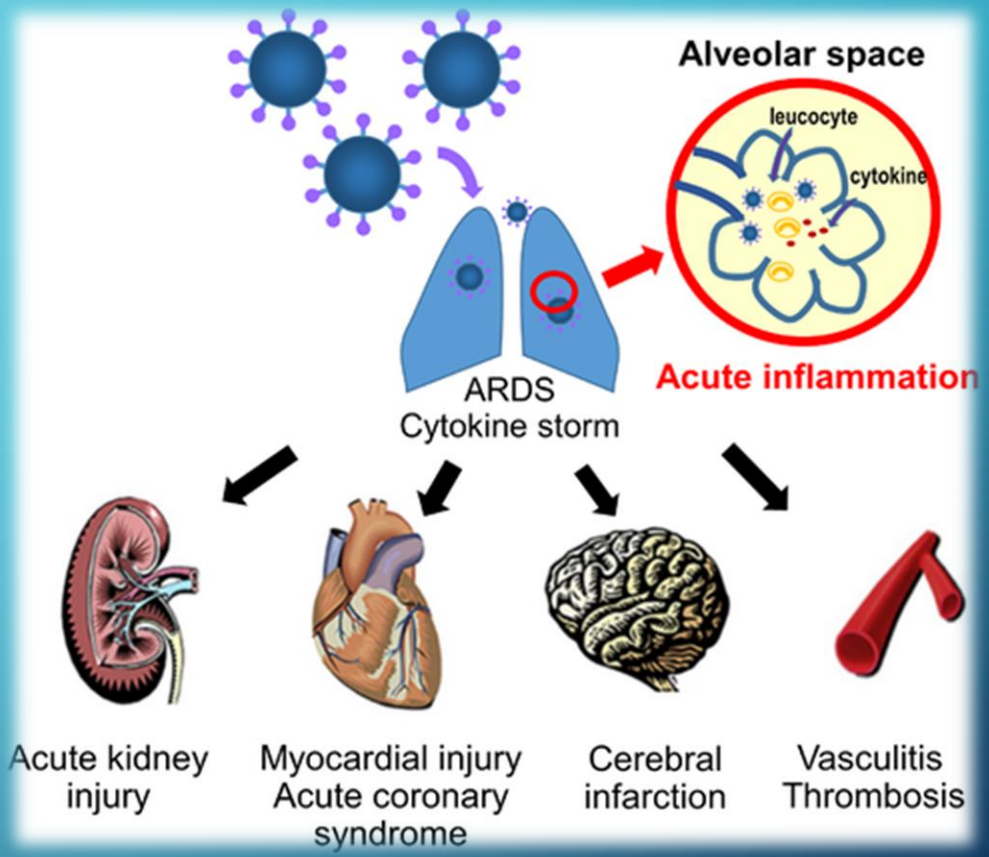
- **COVID-19 and hypertension--evidence and practical management: Guidance from the HOPE Asia Network**(9 JULY 2020, PUBLISHED ON "THE JHC" ,THE JOURNAL OF CLINICAL HYPERTENSION)

- **1 INTRODUCTION**

- The infectious disease caused by the new severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), COVID-19, broke out in Wuhan, China, and spread to almost every country in the world. Millions of people have been infected, many have died, and everyday life has changed completely. The disease is accompanied by range of different symptoms (Figure 1). Rapidly accumulating data show that prognosis for patients with COVID-19 is good in those with mild disease, but severe cases show relatively asymptomatic early progression followed by rapid worsening after symptom onset, culminating in acute respiratory distress syndrome (ARDS) and significant disease manifestations (Figure 2). The presence of SARS-CoV-2 has been detected in multiple organs on autopsy, including the pharynx, lungs, heart, liver, brain and kidneys, highlighting the multiorgan tropism of this virus.[1]



Wide range of symptoms in patients with COVID-19 (reproduced, with permission, from Clerkin KJ et al, 2020)[2]



Variety of organ damage seen in patients with COVID-19. ARDS, acute respiratory distress syndrome

- Early clinical experience suggested that older age and the presence of a number of comorbidities, including hypertension, cardiovascular disease, diabetes mellitus and chronic respiratory disease increased the risk of death in patients with COVID-19. In addition, the renin-angiotensin aldosterone (RAS) system (specifically the angiotensin-converting enzyme 2 [ACE2] protein) has been identified as playing an important role in facilitating entry of coronaviruses, including SARS-CoV-2, into target cells, especially in the lungs. Therefore, it has been suggested that angiotensin receptor blockers (ARBs) and ACE inhibitors, which affect ACE2 expression, may influence the susceptibility to and severity of infection with SARS-CoV-2.
- Hypertension is very common, affecting an estimated 1.39 billion individuals worldwide, and the prevalence of hypertension increases with age (affecting approximately 70% of older adults). In addition, RAS inhibitors such as ACE inhibitors and ARBs are recommended and widely used for the treatment of hypertension. However, hypertension is not a single clinical entity, but it instead manifests as a number of different phenotypes. In Asians, the disease is characterized by salt sensitivity, high rates of masked hypertension, exaggerated morning BP surge, and nocturnal hypertension. Nearly half of all patients with hypertension worldwide (44%) live in south or east Asia. The HOPE Asia Network was established in 2016 and is a member of the World Hypertension League.[1] The mission of the HOPE Asia Network is to improve the management of hypertension and organ protection toward achieving “zero” cardiovascular events in Asia.[1] This has become even more relevant in the current pandemic, with high rates of infection in several Asian countries.
- This guidance from the HOPE Asia Network summarizes the latest findings on COVID-19 and hypertension, including evidence-based recommendations for the management of hypertension during the current pandemic.

- **2 HYPERTENSION AS A RISK FACTOR IN PATIENTS WITH COVID-19**
- **Clinical Question 1.** Is hypertension a risk factor for COVID-19?
- Pre-existing hypertension appears to be common in patients with severe COVID-19. However, there is little direct evidence to indicate that hypertension itself is a risk factor for infection or aggravation of the disease independent of aging or other COVID-19 risk factors.
- On March 20, 2020, the Italian Institute of Health announced that there had been 3200 COVID-19 deaths in Italy. The patients who died had an average age of 78.5 years (median 80 years, range 31-103 years) and 98.7% had at least one comorbidity. Hypertension was a common comorbidity in Italian cases, affecting 73.8% of patients, 52% of whom were taking ARBs or ACE inhibitors. However, there are number of factors that could potentially confound a possible relationship between hypertension and severe COVID-19 (Table 1). The first is age: both severe COVID-19 and hypertension are common in the elderly. In addition, the identified risk factors (Table 1) are generally associated with aging and/or vascular disorders, both of which are common in patients with hypertension. Therefore, the risk of developing severe COVID-19 is more likely to be due to underlying vascular endothelial dysfunction and/or organ damage than high blood pressure (BP) per se. ACE2 receptors are expressed by endothelial cells, and post-mortem examinations have detected the presence of viral infection in endothelial cells.

- Risk factors for progression/severity of COVID-19

Aging
Hypertension
Diabetes mellitus
Smoking
Cardiovascular disease (heart failure, stroke, angina, myocardial infarction)
Chronic obstructive pulmonary disease
Chronic kidney disease
Malignancy (especially receiving current treatment with chemotherapy or radiotherapy)

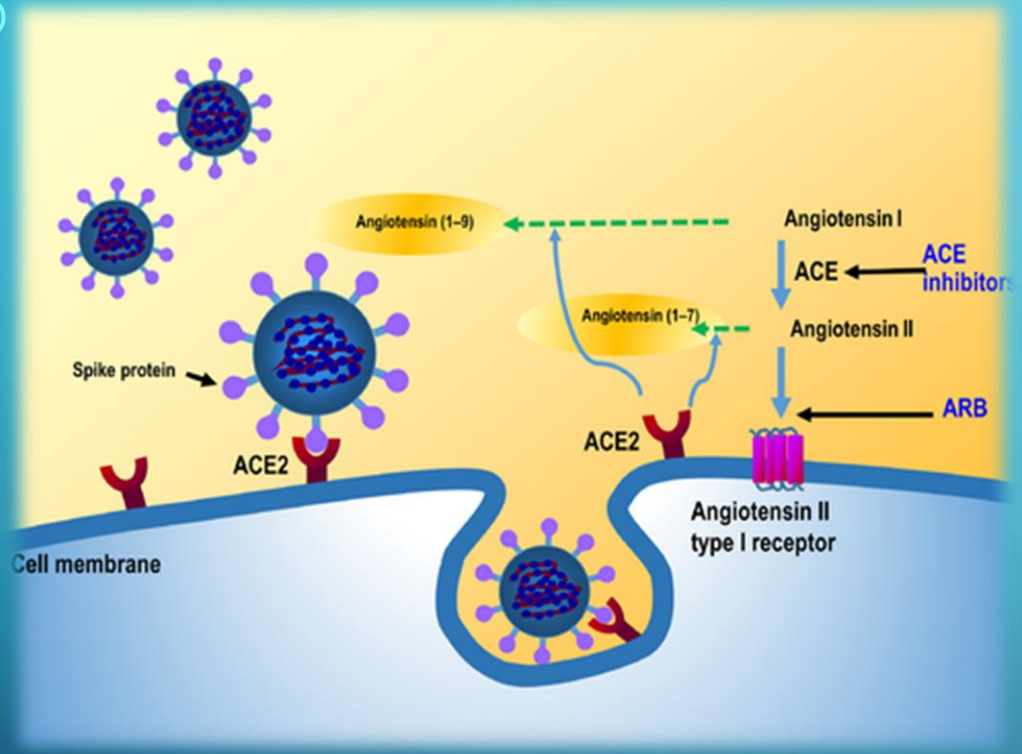
3 THERAPY WITH RENIN-ANGIOTENSIN SYSTEM INHIBITORS

Clinical Question 2. Is it safe to continue treatment with ACE inhibitors or ARBs?

As of early May 2020, there is no clinical data showing that use of ACE inhibitors or ARBs increases the risk of infection with the SARS-CoV-2 virus or worsens the course of COVID-19 disease. Scientific societies including the American Heart Association, European Society of Cardiology, Japanese Circulation Society, and Japanese Society of Hypertension recommend continuation of ACE inhibitor or ARB therapy in patients with hypertension.

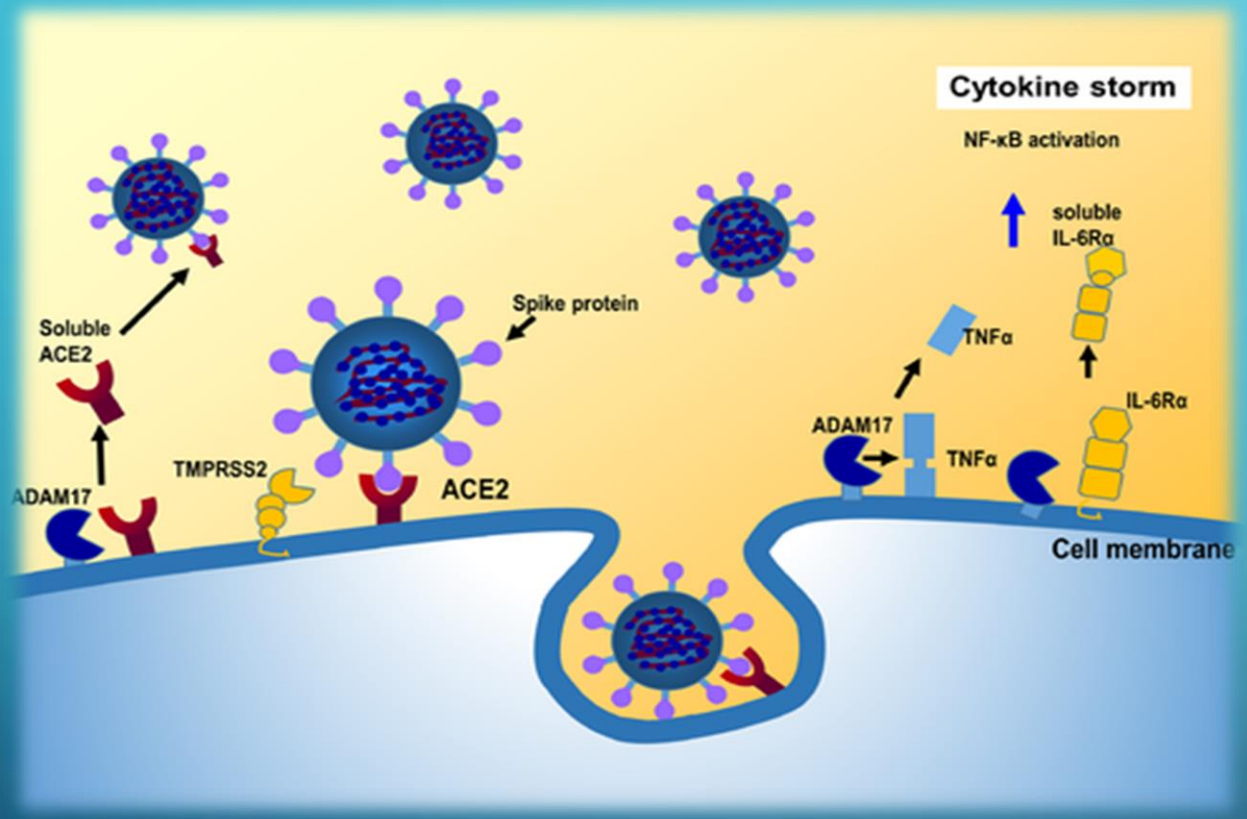
- 3.1 Mechanisms linking COVID-19 and ACE2
- The spike protein on the surface of SARS-CoV-2 binds to the extracellular domain of transmembrane ACE2, with S protein priming by transmembrane serine protease 2 (TMPRSS2), to gain entry to host cells (Figure 3). ACE2 plays a regulatory role in the RAS, converting angiotensin I (Ang I) into angiotensin 1-9 (Ang 1-9) or angiotensin II (Ang II) into angiotensin 1-7 (Ang 1-7). Currently, available data reflect a possible role for ACE2 in heart failure, myocardial infarction, hypertension, and the cardiovascular complications of diabetes mellitus, and preclinical investigations suggest that activation of ACE2 might have the potential to protect against hypertension and cardiovascular disease. In addition, angiotensin 1-7 appears to counteract the negative effects of Ang II, attenuating inflammation, suppressing vascular permeability and having vasorelaxant effects. Furthermore, ACE2 in the lungs and the renin-angiotensin system has been shown to play a role in the pulmonary manifestations of coronavirus infection.

- SARS-CoV-2 and the renin-angiotensin system. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker



Interaction of Ang II with angiotensin type 1 receptors (AT1R) activates A Disintegrin And Metalloproteinase 17 (ADAM17) on the cell membrane via phosphorylation. In turn, ADAM17 cleaves the precursors of tumor necrosis factor-α (TNFα) and interleukin (IL)-6 receptor-α (IL-6Rα) in the cell membrane to release TNFα and soluble IL-6Rα. TNFα activates the nuclear transcription factor system NF-κB to induce the production of various inflammatory cytokines, including IL-6 (Figure 4). This represents a potential mechanism for the cytokine storm seen in some patients with COVID-19 and highlights the potential for agents blocking cytokine pathways (especially the IL-6-STAT3 axis) in managing COVID-19-related cytokine storm.

- Cytokine storm associated with SARS-CoV-2 infection. ACE, angiotensin-converting enzyme; ADAM17, A Disintegrin And Metalloproteinase 17; IL-6Rα, interleukin-6 receptor-α; TMPRSS2, transmembrane serine protease 2; TNFα, tumor necrosis factor-α



The fact that the SARS-CoV-2 virus uses ACE2 as a mechanism to enter and infect cells meant that there was concern that cells with high ACE2 expression would be most susceptible to infection with SARS-CoV-2. Given that ARB and ACE inhibitors have been shown experimentally to increase expression of ACE2 on cell membranes, there was much discussion about the potential for higher infection rates and more severe disease in patients being treated with these agents.

- 3.2 Current clinical evidence
- Despite the theoretical possibility that use of RAS inhibitors increases the risk of infection with SARS-CoV-2 and the severity of COVID-19 illness, analyses including patients from the current pandemic indicate that this does not seem to be the case
- The effect of hypertension or therapy with ACE inhibitors or ARBs has been evaluated in at least three published studies to date (Table 2). Reynolds et al looked at history of antihypertensive usage in 12 594 patients undergoing COVID-19 testing in New York, USA. They did not find any association between the use of ACE inhibitors, ARBs, beta-blockers, calcium channel blockers or thiazide diuretics and the likelihood of a positive or negative result on COVID-19 testing. Also in the United States, Mehta and colleagues failed to find any significant association between the use of ACE inhibitors or ARBs and COVID-19 test positivity. Similar findings were reported in a population case-control study from Italy. Data from four studies published by early May 2020 also failed to find a significant association between RAS inhibitor use and worse outcomes in patients with COVID-19 (Table 2). In one retrospective case series, the proportion of patients using ACE inhibitors or ARBs did not differ significantly between those with severe vs non-severe COVID-19, or between survivors and non-survivors. However, the in-hospital COVID-19 mortality rate was higher in patients with vs without hypertension (21% vs 11%). In the other studies, death rates for patients taking ACE inhibitors and/or ARBs were actually lower than those in patients not receiving these antihypertensive therapies. One of the studies from China reported that levels of the inflammatory markers high sensitivity C-reactive protein and procalcitonin were significantly lower in patients with hypertension who were vs were not receiving ACE inhibitors or ARBs.

- **4 BIOMARKERS OF COVID-19-RELATED COMPLICATIONS**
- **Clinical Question 3.** What are the biomarkers of severe COVID-19?
- In addition to ARDS, patients with severe infection can develop myocardial injury and cytokine storm, resulting in heart failure, arteriovenous thrombosis (venous thromboembolism, acute coronary syndrome, cerebral infarction), and acute kidney injury. Biomarkers for these complications are troponin, N-terminal pro-B-type natriuretic peptide (NT-proBNP), D-dimer, and serum creatinine.
- High levels of a number of biomarkers are indicative of severe COVID-19 (Table 3). One of the most important biomarkers in patients with COVID-19 is troponin, which indicates the presence of myocardial injury. D-dimer and IL-6 are also important. D-dimer indicates the presence of arterial microthrombus and venous thrombosis (pulmonary embolism and deep vein thrombosis) and disseminated intravascular coagulation (DIC). IL-6 is an inflammatory marker, suggesting the presence of cytokine storm, while NT-proBNP and creatinine are biomarkers of heart failure and renal damage, respectively.

- **Table 3.** Biomarkers for progression of COVID-19-related complications

Biomarker	Clinical condition
Oxygen saturation <94%	Acute respiratory distress syndrome
Troponin	Myocardial injury
D-dimer	Thrombosis
Amino-terminal pro-B-type natriuretic peptide	Heart failure
Creatinine	Kidney injury
C-reactive protein	Cytokine storm
Interleukin-6	Cytokine storm

5 CLINICAL PATIENT MANAGEMENT IN THE COVID-19 ERA

Key points regarding the clinical management of COVID-19, particularly in patients with hypertension, based on evidence published before May 5, 2020, are shown in Table 4.

Table 4. Clinical practice guidance for patient management in the COVID-19 era (based on evidence available up to May 5, 2020)

COVID-19 and Comorbidities: Assessment and Management
•Patients with hypertension, especially older individuals and those with other known risk factors, are at increased risk of developing severe symptoms during COVID-19 infection
•High-risk patients, such as those with hypertension, are more likely to develop cardiac injury during COVID-19 infection
•Diabetes mellitus should be carefully managed and these patients need to be closely monitored for the development of myocardial injury and arteriovenous thrombosis
•Consider determining levels of key biomarkers, especially troponin and D-dimer, to get a complete clinical picture and information about prognosis in patients with COVID-19
•Oxygen saturation should be determined at presentation; if oxygen saturation is <94% then COVID-19 should be considered as severe
•COVID-19 progression and cardiovascular status can be monitored by measuring blood pressure and taking the patient's temperature
•Antihypertensive therapy with ACE inhibitors or ARBs in patients with COVID-19 should be carefully continued, with careful monitoring to detect hypotension and kidney injury
•Unmedicated older COVID-19 patients whose only comorbidity is hypertension can be treated with calcium channel blockers
•Physicians should be aware of physical manifestations of stress (eg, cardiovascular events), even in individuals not infected with COVID-19 (especially those with pre-existing hypertension)

- **6 TELEMEDICINE DURING COVID-19**

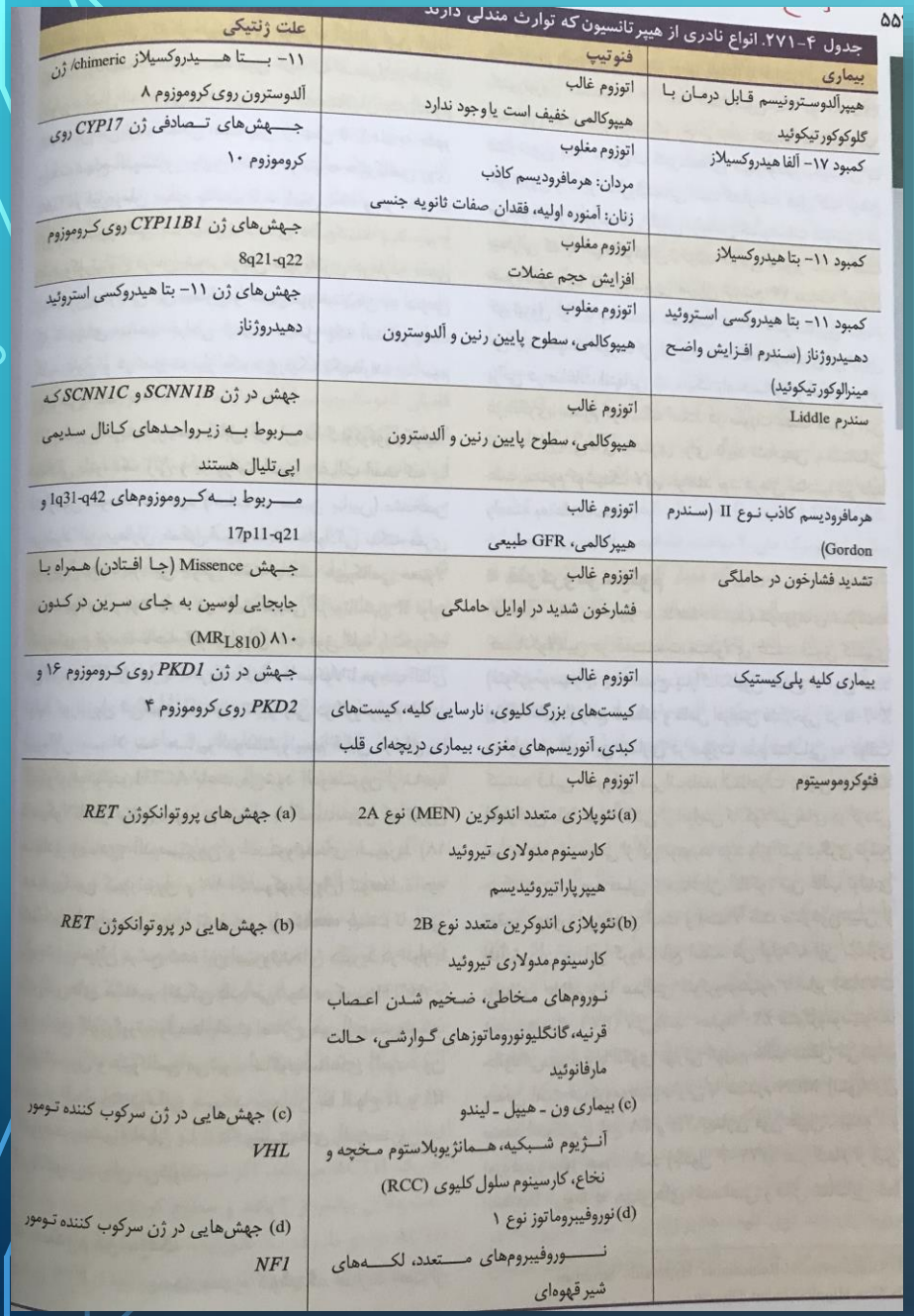
- Strict lockdown and social distancing rules are being enforced in many countries to slow the spread of the novel coronavirus. In addition, a large proportion of “elective” or “non-essential” procedures have been postponed or canceled to allow health care systems to cope with the influx of infectious disease cases. This has created a requirement for a large proportion of health consultations to be conducted remotely. Telemedicine strategies are ideally suited to facilitating patient management in the absence of face-to-face consultations, and the value of this approach (which has otherwise been slow to be widely used in clinical practice) has become clear. One of the hidden “blessings” of the COVID-19 pandemic may be the widespread adoption of telemedicine approaches to improve patient management.
- Out-of-office BP monitoring is a recommended approach for the diagnosis and management of hypertension. Therefore, this field of medicine is better placed than many to be able to continue to effectively manage patients during a global pandemic.
- New information and communication technology-based home BP monitoring devices that perform automatic, fixed-interval BP measurement during sleep and store or transmit the data could facilitate a novel approach to patient management. Validated wearable technologies for evaluation of home BP might also be useful for patient monitoring and management during the COVID-19 outbreak. Telemedicine-based strategies for managing BP were implemented and used effectively during the aftermath of the Great East Japan earthquake and tsunami in March 2011, highlighting their potential for use during the COVID-19 pandemic to ensure that patients with hypertension have well-controlled BP. This has the potential to help mitigate the negative effects of hypertension on prognosis in patients with COVID-19.

- **7 CONCLUSIONS**

- Patients with hypertension are at increased risk of morbidity and mortality if they become infected with SARS-CoV-2, although this is confounded by other factors such as age and vascular disorders. However, all usual antihypertensive therapy including RAS inhibitors should continue. Physicians need to take a holistic approach to patient management due the wide range of possible complications, and biomarkers can provide important prognostic information. Overall, multidisciplinary management of COVID-19 based on a rapidly growing body of evidence will help ensure the best possible outcomes for patients, including those with risk factors such as hypertension.

- ***اپیدمیولوژی***

- فشار خون باال یکی از علل اصلی ناتوانی و بیماری در جامعه میباشد که بیش از یک میلیارد نفر را گرفتار کرده و باعث مرگ حدود 4/9 میلیون نفر در هر سال میشود از سن 60 سالگی به بعد فشار خون سیستولیک زنان بیشتر از مردان میشود . فشار خون دیاستولیک نیزدر بزرگسالان تا حدود 55 افزایش میابد و پس از ان کاهش میابد و در نتیجه فشار نبض) اختالف بین فشار خون سیستولیک و دیاستولیک (بعد از 60 سالگی باال میرود . در ایاالت متحده در حدود 78 میلیون بزرگسال دچار فشار خون باال هستند که شیوع ان در سیاهپوستان غیر اسپانیایی تبار 5/33 % و در سفید پوستان غیر اسپانیایی تبار 9/28 %و در امریکایی مکزیکی 7/20 %است احتمال بیماری با افزایش سن باال رفته و در افرادی که حداقل 60 سال سن دارند شیوع ان 4/65 % است . شواهد اخیر حاکی از افزایش شیوع فشار خون باال در ایالت متحده که ناشی از باال رفتن شیوع چاقی است



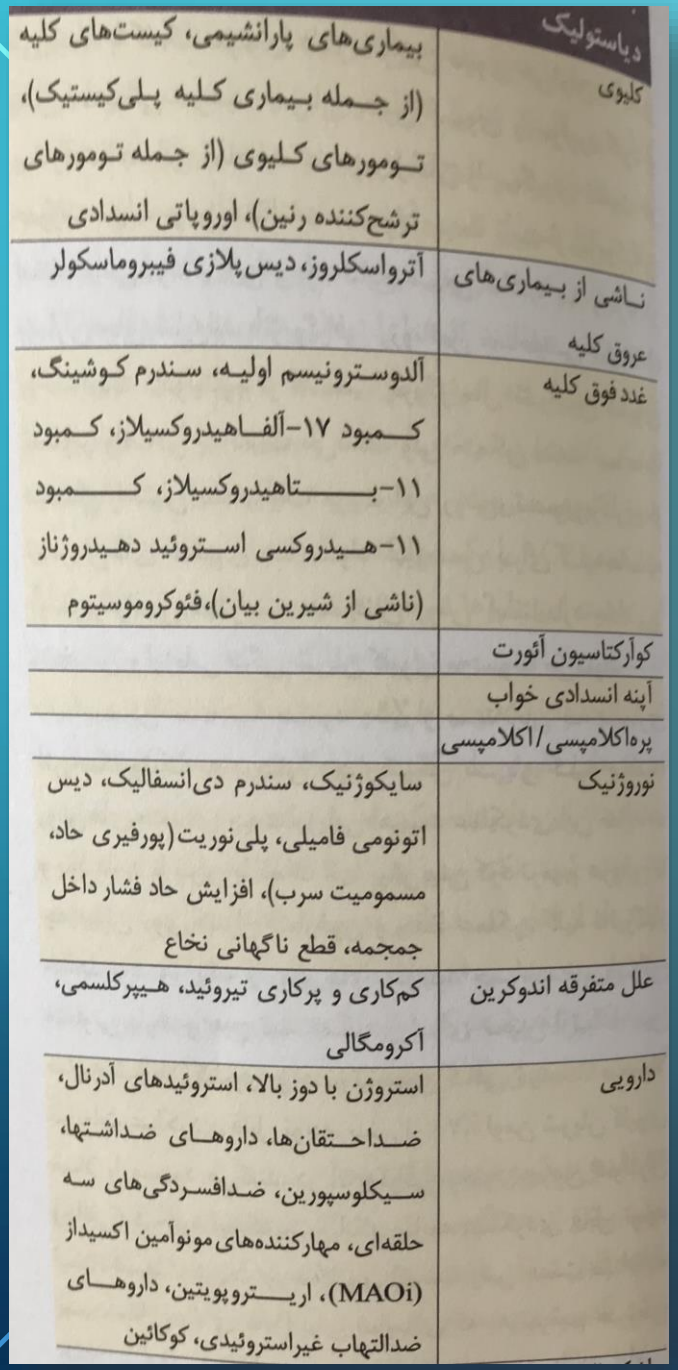
جدول ۴-۲۷۱. انواع نادری از هیپرتانسیون که توارث مندلی دارند

بیماری	فنوتیپ	علت ژنتیکی
هیپرآلدوسترونیسم قابل درمان با گلوکوکورتیکوئید	اتوزوم غالب هیپوکالمی خفیف است یا وجود ندارد	۱۱- بتا هیدروکسیلاز chimeric/ ژن آلدوسترون روی کروموزوم ۸
کمبود ۱۷- آلفا هیدروکسیلاز	اتوزوم مغلوب مردان: هرمافرودیسم کاذب زنان: آمنوره اولیه، فقدان صفات ثانویه جنسی	جهش‌های تصادفی ژن *CYP17* روی کروموزوم ۱۰
کمبود ۱۱- بتا هیدروکسیلاز	اتوزوم مغلوب افزایش حجم عضلات	جهش‌های ژن *CYP11B1* روی کروموزوم 8q21-q22
کمبود ۱۱- بتا هیدروکسی استروئید دهیدروژناز (سندرم افزایش واضح مینرالوکورتیکوئید)	اتوزوم مغلوب هیپوکالمی، سطوح پایین رنین و آلدوسترون	جهش‌های ژن ۱۱- بتا هیدروکسی استروئید دهیدروژناز
سندرم Liddle	اتوزوم غالب هیپوکالمی، سطوح پایین رنین و آلدسترون	جهش در ژن *SCNN1B* و *SCNN1C* که مربوط به زیرواحدهای کانال سدیمی اپی‌تلیال هستند
هرمافرودیسم کاذب نوع II (سندرم Gordon)	اتوزوم غالب هیپرکالمی، GFR طبیعی	مربوط به کروموزوم‌های 1q31-q42 و 17p11-q21
تشدید فشارخون در حاملگی	اتوزوم غالب فشارخون شدید در اوایل حاملگی	جهش Missence (جا افتادن) همراه با جابجایی لوسین به جای سرین در کدون ۸۱۰ (MR_{L810})
بیماری کلیه پلی‌کیستیک	اتوزوم غالب کیست‌های بزرگ کلیوی، نارسایی کلیه، کیست‌های کبدی، آنوریسم‌های مغزی، بیماری دریچه‌ای قلب	جهش در ژن *PKD1* روی کروموزوم ۱۶ و *PKD2* روی کروموزوم ۴
فئوکروموسیتوم	اتوزوم غالب (a) نئوپلازی متعدد اندوکرین (MEN) نوع 2A کارسینوم مدولاری تیروئید هیپرپاراتیروئیدیسم	(a) جهش‌های پروتوانکوژن *RET*
	(b) نئوپلازی اندوکرین متعدد نوع 2B کارسینوم مدولاری تیروئید نوروم‌های مخاطی، ضخیم شدن اعصاب قرنیه، گانگلیونوروماتوزهای گوارشی، حالت مارفانوئید	(b) جهش‌هایی در پروتوانکوژن *RET*
	(c) بیماری ون - هیپل - لیندو آنژیوم شبکیه، همانژیوبلاستوم مخچه و نخاع، کارسینوم سلول کلیوی (RCC)	(c) جهش‌هایی در ژن سرکوب کننده تومور *VHL*
	(d) نوروفیبروماتوز نوع ۱ نوروفیبروم‌های متعدد، لکه‌های شیر قهوه‌ای	(d) جهش‌هایی در ژن سرکوب کننده تومور *NF1*

- **ملاحظات ژنتیکی**
- بعضی از اشکال نادر فشار خون بالا با الگوی مندلی به ارث میرسند
- اما این واریانت ها در عمده افراد (بیش از% 98) نقش ایفا نمیکنند .
- در این افراد فشار خون بیان کننده یک اختلال که حاصل تعامل بین ژنها و محیط است.

- **تعریف فشار خون بالا**

جدول ۱-۲۷۱. طبقه‌بندی فشارخون		
طبقه‌بندی فشارخون بالا	سیستولیک (mmHg)	دیاستولیک (mmHg)
طبیعی	۱۲۰>	و ۸۰>
پیش فشارخون بالا	۱۳۹-۱۲۰	یا ۸۹-۸۰
مرحله ۱ فشارخون بالا	۱۵۹-۱۴۰	یا ۹۹-۹۰
مرحله ۲ فشارخون بالا	۱۶۰≤	یا ۱۰۰≤
فشارخون بالا سیستولیک مجزا	۱۴۰≤	و ۹۰>



دیاستولیک	
کلیوی	بیماری‌های پارانشیمی، کیست‌های کلیه (از جمله بیماری کلیه پلی‌کیستیک)، تومورهای کلیوی (از جمله تومورهای ترشح‌کننده رنین)، اوروپاتی انسدادی
ناشی از بیماری‌های عروق کلیه	آترواسکلروز، دیس‌پلازی فیبروماسکولر
غدد فوق کلیه	آلدوسترونیسم اولیه، سندرم کوشینگ، کمبود ۱۷-آلفاهیدروکسیلاز، کمبود ۱۱-بتاهیدروکسیلاز، کمبود ۱۱-هیدروکسی استروئید دهیدروژناز (ناشی از شیرین بیان)، فئوکروموسیتوم
کوآرکتاسیون آئورت	
آپنه انسدادی خواب	
پره‌اکلامپسی/اکلامپسی	
نوروژنیک	سایکوژنیک، سندرم دی‌انسفالیک، دیس اتونومی فامیلی، پلی‌نوریت (پورفیری حاد، مسمومیت سرب)، افزایش حاد فشار داخل جمجمه، قطع ناگهانی نخاع
علل متفرقه اندوکرین	کم‌کاری و پرکاری تیروئید، هیپرکلسمی، آکرومگالی
دارویی	استروژن با دوز بالا، استروئیدهای آدرنال، ضداحتقان‌ها، داروهای ضداشتها، سیکلوسپورین، ضدافسردگی‌های سه حلقه‌ای، مهارکننده‌های مونوآمین اکسیداز (MAOi)، اریتروپویتین، داروهای ضدالتهاب غیراستروئیدی، کوکائین

فشار خون بالا اولیه

فشار خون بالا اولیه معموال فامیلی میباشد و در نتیجه تعامل عوامل محیطی و ژنتیکی رخ میدهد . شیوع ان با افزایش سن بال میرود . در این افراد ارتباط ناهمگونی بین سطح الدسترون پالسما و میزان فشار خون توصیف شده است

چاقی و سندرم متابولیک

رابطه ثابت شده ای بین چاقی (شاخص توده بدنی بیشتر از 30) و فشار خون بالا وجود دارد که به صورت خطی میباشد . چاقی مرکزی نسبت به چاقی محیطی شاخص مهم تری از افزایش فشار خون میباشد .

• شرح حال و معاینه فیزیکی و ازمایشات پایه در ارزیابی اولیه

شرح حال
مدت زمان ابتلا به پرفشاری خون
درمان‌های قبلی: پاسخ‌ها و عوارض جانبی
شرح حال خانوادگی پرفشاری خون و بیماری قلبی ـ عروقی
رژیم غذایی شرح حال روانشناختی ـ اجتماعی
سایر عوامل خطر: تغییر وزن، دیس‌لیپیدمی، مصرف سیگار، دیابت، نداشتن فعالیت فیزیکی
شواهد پرفشاری خون ثانویه: شرح حال بیماری کلیوی، تغییر در ظاهر بیمار، ضعف عضلانی، تعریق زیاد، تپش قلب، لرزش، خواب آشفته، خرناس کشیده، خواب‌آلودگی در طول روز؛ علایم کم‌کالری یا پرکاری تیروئید؛ مصرف موادی که ممکن است فشارخون را بالا ببرند.
شواهدی از آسیب ارگان هدف: شرح حال TIA، سکته مغزی، کوری گذرا، آنژین، انفارکتوس میوکارد، نارسایی قلبی احتقانی؛ اختلال در عملکرد جنسی
سایر عوارض همراه
معاینه فیزیکی
سلامتی بدن
فشارخون در هر دو بازو
فشارخون در حالت خوابیده و ایستاده
معاینه فوندوسکوپیک شبکیه چشم
کیفیت نبض‌های فمورال و پدال
سمع برویی عروقی و شکمی
ضربان و ریتم قلب
علایم نارسایی قلبی احتقانی
علایم پرفشاری خون ثانویه

سیستم	تست
کلیوی	آنالیز میکروسکوپی ادرار، میزان ترشح آلبومین ادراری، BUN و/یا کراتی‌نین سرم
اندوکرین	سدیم، پتاسیم و کلسیم سرم، TSH
متابولیک	گلوکز ناشتا، کلسترول total، کلسترول HDL و LDL (که معمولاً محاسبه می‌شود)، تری‌گلیسریدها
متفرقه	هماتوکریت، الکتروکاردیوگرام

- قدم اول در درمان = اصلاح سبک زندگی

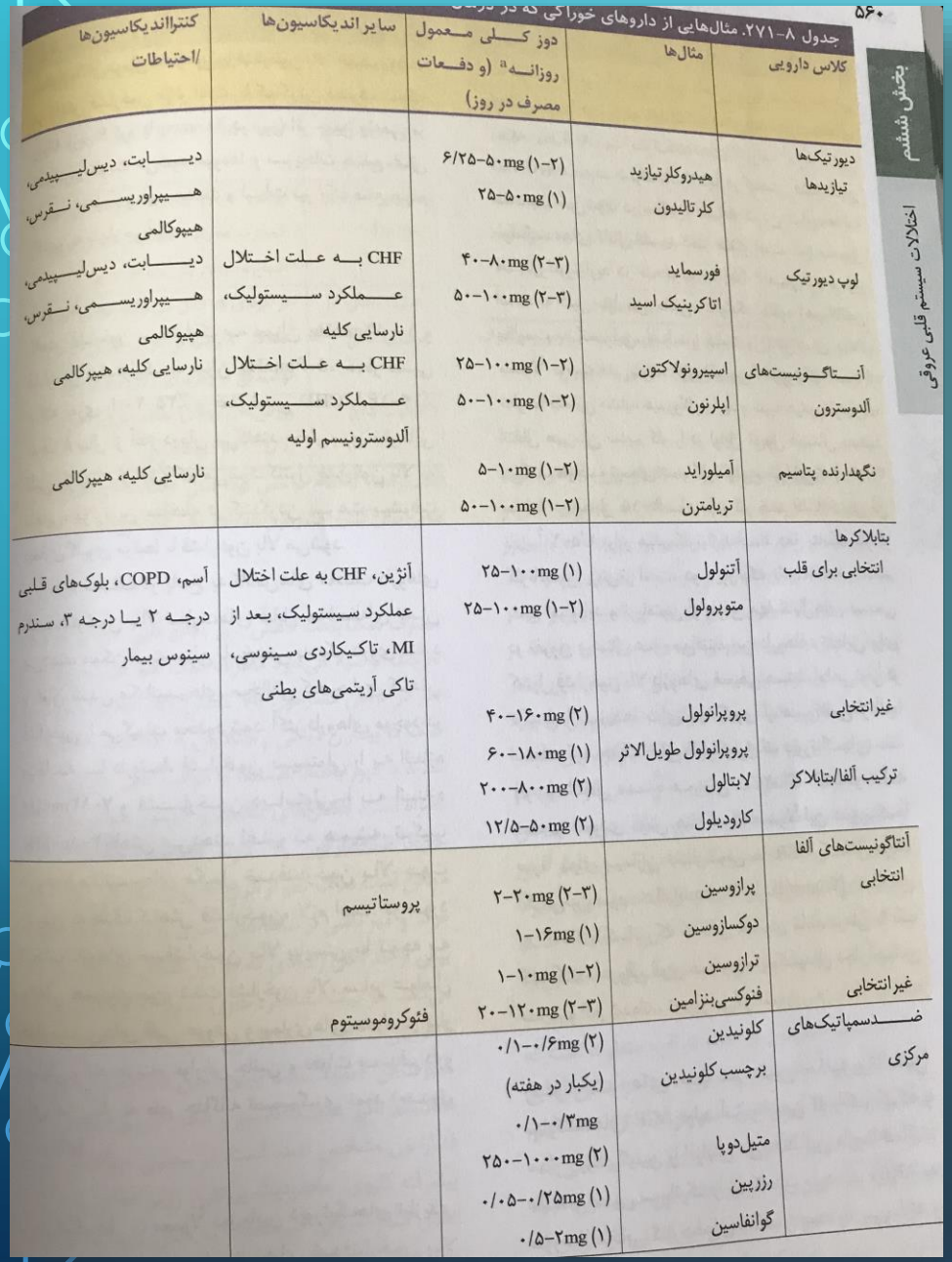
کاهش وزن	کم کردن وزن تا رسیدن به $<25 kg/m^2$ و حفظ آن
محدودکردن نمک مصرفی	مصرف روزانه کمتر از ۶ گرم نمک
الگوی تغذیه‌ای DASH	رژیمی سرشار از میوه، سبزیجات و لبنیات کم‌چرب همراه با کم کردن میزان چربی‌های اشباع و میزان کلی مصرف چربی
اعتدال در مصرف الکل	در افرادی که الکل می‌نوشند میزان مصرف به حداکثر ۲ نوشیدنی در روز برای مردان و ۱ نوشیدنی در روز برای زنان محدود شود
فعالیت بدنی	ورزش‌های هوازی منظم مثل پیاده‌روی سریع به مدت ۳۰ دقیقه در روز

درمان دارویی

جدول ۸-۲۷۱. مثال‌هایی از داروهای خوراکی که در درمان فشارخون بالا به کار می‌روند (ادامه)

کلاس دارویی	مثال‌ها	دوز کلی معمول روزانه[a] (و دفعات مصرف در روز)	سایر اندیکاسیون‌ها	کنتراندیکاسیون‌ها /احتیاطات
مهارکننده‌های ACE	کاپتوپریل	(۲) ۲۵–۲۰۰mg	بعد از MI، CHF با EF	نارسایی کلیه حاد، تنگی
	لیزینوپریل	(۱) ۱۰–۴۰mg	پایین، نفروپاتی، سندرم	دوطرفه شرایین کلیوی،
	رامی‌پریل	(۱–۲) ۲/۵–۲۰mg	کرونری	حاملگی، هیپرکالمی
آنتاگونیست‌های آنژیوتانسین II	لوزارتان	(۱–۲) ۲۵–۱۰۰mg	CHF با EF پایین،	نارسایی کلیه، تنگی دوطرفه
	والزارتان	(۱) ۸۰–۳۲۰mg	نفروپاتی، سرفه متعاقب	شرایین کلیوی، حاملگی،
	کاندزارتان	(۱–۲) ۲–۳۲mg	مصرف مهارکننده‌های ACE	هیپرکالمی
مهارکننده‌های رنین	آلیسکیرن	(۱) ۱۵۰–۳۰۰mg	نفروپاتی دیابتی	بارداری
آنتاگونیست‌های کلسیم دی‌هیدروپیریدینی غیردی‌هیدروپیریدینی	نفدیپین (طولانی‌اثر)	(۱) ۳۰–۶۰mg	بعد از MI، تاکیکاردی‌های فوق بطنی، آنژین	بلوک درجه ۲ یا ۳ قلبی
	وراپامیل (طولانی‌اثر)	(۱–۲) ۱۲۰–۳۶۰mg		
	دیلتیازم (طولانی‌اثر)	(۱) ۱۸۰–۴۲۰mg		
گشادکننده‌های مستقیم عروقی	هیدرالازین	(۲) ۲۵–۱۰۰mg		بیماری شدید شریان کرونر
	ماینوکسیدیل	(۱–۲) ۲/۵–۸۰mg		

ترجیح داده می‌شوند.



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بخش ششم اختلالات سیستم قلبی عروقی

جدول ۸-۲۷۱. مثال‌هایی از داروهای خوراکی که در درمان

کلاس دارویی	مثال‌ها	دوز کلی معمول روزانه[a] (و دفعات مصرف در روز)	سایر اندیکاسیون‌ها	کنتراندیکاسیون‌ها /احتیاطات
دیورتیک‌ها				
تیازیدها	هیدروکلرتیازید	(۱–۲) ۶/۲۵–۵۰mg		دیابت، دیس‌لیپیدمی، هیپراوریسمی، نقرس، هیپوکالمی
	کلرتالیدون	(۱) ۲۵–۵۰mg		
لوپ دیورتیک	فورسماید	(۲–۳) ۴۰–۸۰mg	CHF به علت اختلال عملکرد سیستولیک، نارسایی کلیه	دیابت، دیس‌لیپیدمی، هیپراوریسمی، نقرس، هیپوکالمی
	اتاکرینیک اسید	(۲–۳) ۵۰–۱۰۰mg		
آنتاگونیست‌های آلدوسترون	اسپیرونولاکتون	(۱–۲) ۲۵–۱۰۰mg	CHF به علت اختلال عملکرد سیستولیک، آلدوسترونیسم اولیه	نارسایی کلیه، هیپرکالمی
	اپلرنون	(۱–۲) ۵۰–۱۰۰mg		
نگهدارنده پتاسیم	آمیلوراید	(۱–۲) ۵–۱۰mg		نارسایی کلیه، هیپرکالمی
	تریامترن	(۱–۲) ۵۰–۱۰۰mg		
بتابلاکرها				
انتخابی برای قلب	آتنولول	(۱) ۲۵–۱۰۰mg	آنژین، CHF به علت اختلال عملکرد سیستولیک، بعد از MI، تاکیکاردی سینوسی، تاکی آریتمی‌های بطنی	آسم، COPD، بلوک‌های قلبی درجه ۲ یا درجه ۳، سندرم سینوس بیمار
	متوپرولول	(۱–۲) ۲۵–۱۰۰mg		
غیرانتخابی	پروپرانولول	(۲) ۴۰–۱۶۰mg		
	پروپرانولول طویل‌الاثر	(۱) ۶۰–۱۸۰mg		
ترکیب آلفا/بتابلاکر	لابتالول	(۲) ۲۰۰–۸۰۰mg		
	کارودیلول	(۲) ۱۲/۵–۵۰mg		
آنتاگونیست‌های آلفا				
انتخابی	پرازوسین	(۲–۳) ۲–۲۰mg	پروستاتیسم	
	دوکسازوسین	(۱) ۱–۱۶mg		
	ترازوسین	(۱–۲) ۱–۱۰mg		
غیرانتخابی	فنوکسی‌بنزامین	(۲–۳) ۲۰–۱۲۰mg	فئوکروموسیتوم	
ضددسمپاتیک‌های مرکزی	کلونیدین	(۲) ۰/۱–۰/۶mg		
	برچسب کلونیدین	(یکبار در هفته) ۰/۱–۰/۳mg		
	متیل‌دوپا	(۲) ۲۵۰–۱۰۰۰mg		
	رزرپین	(۱) ۰/۰۵–۰/۲۵mg		
	گوانفاسین	(۱) ۰/۵–۲mg		

اورژانس های فشار خون بالا

فشارخون بالا	دوز وریدی
نیتروپروساید	دوز آغازین ۰/۳μg/kg در دقیقه؛ دوز معمول ۲-۴μg/kg در دقیقه؛ حداکثر دوز مجاز ۱۰μg/kg در دقیقه تا ۱۰ دقیقه
نیکاردیپین	دوز شروع ۵mg/h؛ هر ۱۵-۵ دقیقه ۲/۵mg/h تغییر داده می‌شود تا پاسخ مطلوب حاصل گردد؛ حداکثر دوز ۱۵mg/h
لابتالول	۲mg/min تا حداکثر ۳۰۰mg یا ۲۰mg ظرف دو دقیقه و سپس ۸۰mg-۴۰ در فواصل ده دقیقه‌ای تا رسیدن به حداکثر دوز کلی ۳۰۰mg
انالاپریلات	دوز معمول ۱/۲۵mg-۰/۶۲۵ ظرف ۵ دقیقه هر ۸-۶ ساعت؛ حداکثر ۵mg در هر دوز
اسمولول	دوز اولیه ۵۰۰μg/kg-۸۰ ظرف یک دقیقه و سپس ۳۰۰μg/kg-۵۰ در دقیقه
فنتولامین	۱۵mg-۵ به صورت یکجا
نیتروگلیسیرین	ابتدا با سرعت ۵μg/min آغاز شده و سپس در فواصلی ۵-۳ دقیقه‌ای، ۵μg/min اضافه می‌شود تا پاسخ مطلوب حاصل شود؛ اگر تا دوز ۲۰μg/min هیچ پاسخی مشاهده نشود، می‌توان دوز دارو را هر بار ۲۰μg/min-۱۰ اضافه نمود
هیدرالازین	۵۰mg-۱۰ در فواصل ۳۰ دقیقه‌ای

انسفالوپاتی ناشی از فشارخون بالا	نیتروپروساید، نیکاردیپین، لابتالول
فشارخون بالای بدخیم (زمانی که درمان وریدی اندیکاسیون دارد)	لابتالول، نیکاردیپین، نیتروپروساید، انالاپریلات
سکته مغزی	نیکاردیپین، لابتالول، نیتروپروساید
انفارکتوس میوکارد/آنژین ناپایدار	نیتروگلیسرین، نیکاردیپین، لابتالول، اسمولول
نارسایی حاد بطن چپ	نیتروگلیسرین، انالاپریلات، دیورتیک‌های لوپ
دیسکسیون آئورت	نیتروپروساید، اسمولول، لابتالول
حملات آدرنرژیک	فنتولامین، نیتروپروساید
افزایش فشارخون پس از عمل جراحی	نیتروگلیسرین، نیتروپروساید، لابتالول، نیکاردیپین
پره‌اکلامپسی/اکلامپسی در حاملگی	هیدرالازین، لابتالول، نیکاردیپین

THANK YOU