Ipertensione arteriosa (ITA) 2023

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Conflitti di interesse

- Consulenze per ditta Bayer (2022)

Capitoli

1. Caso

2. ESH (ISH and ERA) Guidelines for the management of arterial hypertension 2023

3. Articoli interessanti del 2023

Paziente 67 enne

- 2012: Neuropatia isolata del VI nervo destro di origine microangiopatica
  Duplex carotideo: moderata ateromatosi carotidea bilaterale

  Pressione arteriosa **158/85 mmHg**, peso 120 kg, altezza 180 cm

  Laboratorio: creatinina 93 umol/l, eGFR-MDRD 66 ml/min/1.73 m,
LDL
  1.8 mmol/l, non albuminuria

  Terapia: enalapril 5 mg 1-0-0, atorvastatin 40 mg 0-0-1

  Remler: ipertensione arteriosa grado 1 media globale 146/77 mmHg, dipping pressorio normale

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A chi e come misuriamo la Pressione Arteriosa (OBPM)

Regular BP measurements are recommended in adults from the age of 40 years or earlier in patients at high-risk.	I	C

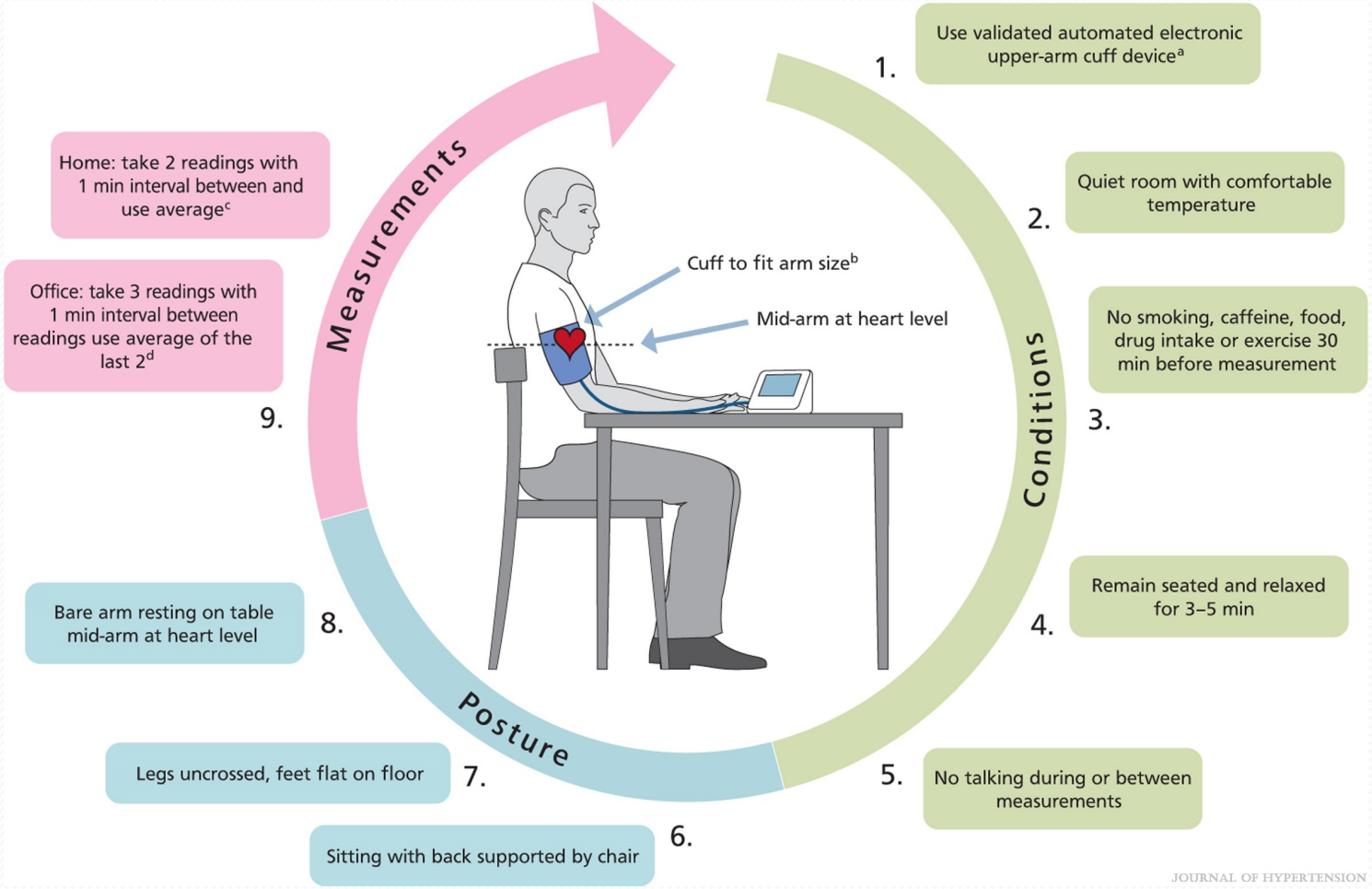
Recommendations and statements	CoR	LoE
Automatic electronic, upper-arm cuff devices are recommended for office and out-of-office BP measurement (home and ambulatory).	I	B

www.stridebp.org

Recommendations and statements	CoR	LoE
Office BP is recommended for diagnosis of hypertension, because it is the one method by which hypertension-related risk, benefits of antihypertensive treatment, and treatment-related BP thresholds and goals are based.	I	A
Office BP measurements should be performed in standardized conditions, using a standard measurement protocol. Triplicate measurements should be taken and the average of the last two should be referred to as the representative value.	I	C
It is recommended to diagnose hypertension during at least 2 separate office visits (within 4 weeks) unless office BP indicates grade 3 hypertension (≥180/110 mmHg) or patients presents with hypertension related symptoms or there is evidence of HMOD or CVD.	I	C
At the first office visit, BP should be measured in both arms. A consistent between-arm SBP difference >15-20 mmHg suggests atheromatous disease and is associated with increased CV risk. All subsequent measurements should be made on the arm with the highest BP readings.	I	C
Out-of-office BP is a source of multiple BP-related information before and during treatment. It is therefore recommended to obtain additional information on BP values by ABPM or HBPM or both if available.	I	C

Marcia G, Kreutz R et al. J Hypertension. 2023

Come misurare la pressione nello studio medico



Marcia G, Kreutz R et al. J Hypertension. 2023

OBPM: conseguenze di misurazioni imprecise

Best Practices for BP Measurement	Common Measurement Pitfalls	Impact of Improper Practice on SBP (mm Hg)
Use appropriate cuff size	Cuff too small	+ 5-20
	Cuff too large	- 1-6
Rest for 5 min before measurement	No rest period	+ 10-20
Sit quietly	Talking or texting during measurement	+ 10-15
Avoid caffeine for 30 min before measurement	Drinking coffee before measurement	+ 5-8
Have an empty bladder	Full bladder	+10-15
Avoid alcohol consumption	Excess alcohol consumption	+ 5-8
Sit with back supported	Sitting upright on examination table	+ 5-15
Keep both feet flat on floor	Crossing legs, legs dangling from examination table	+ 5-8
BP cuff should be placed on bare arm	Measurement over clothing	± 10-50

BP = blood pressure; SBP = systolic blood pressure.

www.stridebp.org

helton S, Ebinger J, Yang E.. 2023

Misurazione della pressione arteriosa a domicilio e ambulatoriale

Recommendations and statements	CoR	LoE
HBPM can be considered in addition to OBPM to improve CV risk prediction due to better reproducibility and prognostic value than OBPM	II	B

Recommendations and statements	CoR	LoE
ABPM can be considered in addition to OBPM to improve CV risk prediction due to better reproducibility and prognostic value than OBPM	II	B

TABLE 5 - Clinical indications for home and ambulatory BP monitoring

Conditions in which white-coat hypertension is more common, e.g.:

- Grade I hypertension on office BP measurement
- Marked office BP elevation without HMOD

Conditions in which masked hypertension is more common, e.g.:

- High-normal office BP
- Normal office BP in individuals with HMOD or at high total CV risk

In treated individuals:

- Confirmation of uncontrolled and true resistant hypertension
- Evaluation of 24 h BP control (especially in high-risk patients)
- Evaluating symptoms indicating hypotension (especially in older patients)

Suspected postural or postprandial hypotension in treated patients

Exaggerated BP response to exercise

Considerable variability in office BP measurements

Specific indications for ABPM rather than HBPM:

- Assessment of nocturnal BP and dipping status (e.g. sleep apnea, CKD, diabetes, endocrine hypertension, or autonomic dysfunction)
- Patients incapable or unwilling to perform reliable HBPM, or anxious with self-measurement
- Pregnancy

Specific indications for HBPM rather than ABPM:

- Long-term follow-up of treated individuals to improve adherence with treatment and hypertension control
- Patients unwilling to perform ABPM, or with considerable discomfort during the recording

Indications for repeat out-of-office BP evaluation (same or alternative method – HBPM/ABPM)

- Confirmation of white-coat hypertension or masked hypertension in untreated or treated individuals

BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; HMOD, Hypertension-mediated organ damage.

Marcia G, Kreutz R et al. J Hypertension. 2023

Grado e Stadio dell'ITA

Grado

TABLE 1 - Classification of office BP and definitions of hypertension grades

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

The BP category is defined by the highest level of BP, whether systolic or diastolic.

[a]Isolated systolic or diastolic hypertension is graded 1, 2 or 3 according to SBP and DBP values in the ranges indicated. The same classification is used for adolescents ≥16 years old (see Section 15.1).

Stadio

Recommendations and statements	CoR	LoE
It is recommended that BP is classified as optimal, normal, high normal, or grade 1, 2 or 3 hypertension, according to office BP.	I	C
In addition to grades of hypertension, which are based on BP values, it is recommended to distinguish stage 1, 2, and 3 hypertension. Stage 1: Uncomplicated hypertension without HMOD, diabetes, CVD and without CKD ≥ stage 3. Stage 2: Presence of HMOD, diabetes, or CKD stage 3. Stage 3: Presence of CVD or CKD stage 4 or 5.	I	C

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hypertension-mediated organ damage (HMOD)

Nelle nuove linee guida sono invariate:

- Storia medica, famigliare
- anamnesi
- Esami clinico e laboratorio

HOMD richieste

Marker of HMOD	Sensitivity to changes	Reproducibility and operator independence	Time to changes	Prognostic value of changes
LVH by ECG	Low	High	Moderate (> 6 months)	Yes
LVH by echocardiogram	Moderate	Moderate	Moderate (> 6 months)	Yes
LVH by MRI	High	High	Moderate (> 6 months)	No data
eGFR	Moderate	High	Moderate (> 6 months)	Yes
UACR	High	Moderate	Fast (weeks to months)	Yes
RRI	Low	High	Slow (>12 months)	Yes
Carotid IMT	Very low	Low	Slow (> 12 months)	Limited data
PWV	High	Low	Fast (weeks to months)	Limited data
ABI	Low	Moderate	Slow (> 12 months)	Limited data
Retina Microvasculature[a]	High	High	Moderate (> 6 months)	No data

Sospettare un'ITA secondaria

Younger patients (<40 years) with grade 2 or 3 hypertension or hypertension of any grade in childhood
Sudden onset of hypertension in individuals with previously documented normotension
Acute worsening of BP control in patients with previously well controlled by treatment
True resistant hypertension hypertension
Hypertensive emergency
Severe (grade 3) or malignant hypertension
Severe and/or extensive HMOD, particularly if disproportionate for the duration and severity of the BP elevation
Clinical or biochemical features suggestive of endocrine causes of hypertension
Clinical features suggestive of atherosclerotic renovascular disease or fibromuscular dysplasia
Clinical features suggestive of obstructive sleep apnea
Severe hypertension in pregnancy (>160/110 mmHg) or acute worsening of BP control in pregnant women with preexisting hypertension

Contattate uno specialista

Rischio cardiovascolare secondo grado e stadio dell'ITA

Hypertension disease staging	Other risk factors, HMOD, CVD or CKD	BP (mmHg) grading			
		High-normal SBP 130–139 DBP 85–89	Grade 1 SBP 140–159 DBP 90–99	Grade 2 SBP 160–179 DBP 100–109	Grade 3 SBP ≥ 180 DBP ≥ 110
Stage 1	No other risk factors[a]	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥3 risk factors	Low to moderate risk	Moderate to high risk	High risk	High risk
Stage 2	HMOD, CKD grade 3, or diabetes mellitus	Moderate to high risk	High risk	High risk	Very high risk
Stage 3	Established CVD or CKD grade ≥4	Very high risk	Very high risk	Very high risk	Very high risk

	<50 years	60–69 years	≥70 years
	<2.5%	<5%	<7.5%
	2.5 to <7.5%	5 to <10%	7.5 to <15%
	≥7.5%	≥10%	≥15%

Complementary risk estimation in Stage 1 with SCORE2/SCOR2-OP

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Marcia G, Kreutz R et al. J Hypertension. 2023

ITA: interventi sullo stile di vita

Recommendations and statements	CoR	LoE
In adults with elevated BP who are overweight or obese, weight reduction is recommended to reduce BP and improve CV outcomes.	I	A
Preferred dietary products include vegetables, fruits, beans, nuts, seeds, vegetable oils, and fish and poultry among meat products. Fatty meats, full-fat dairy, sugar, sweetened beverages, and sweets should be limited. Overall, a healthy dietary pattern including more plant-based and less animal-based food is recommended.	I	B
In adults with hypertension consuming a high sodium diet (most Europeans), salt substitutes replacing part of the NaCl with KCl is recommended to reduce BP and the risk for CVD.	I	A
Dietary salt (NaCl) restriction is recommended for adults with elevated BP to reduce BP. Salt (NaCl) restriction to < 5 g (~2g sodium) per day is recommended.	I	B
Increased potassium consumption, preferably via dietary modification, is recommended for adults with elevated BP, except for patients with advanced CKD.	I	B
Daily physical activity and structured exercise is recommended for adults with elevated BP to reduce BP and improve cardiovascular risk profile. It is recommended to strive for at least 150-300 minutes of aerobic exercise a week of moderate intensity, or 75-150 minutes a week of aerobic exercise of vigorous intensity or an equivalent combination. Sedentary time should also be reduced and supplemented with dynamic resistance exercise (2-3 times per week).	I	B
Adult men and women with elevated BP or hypertension who currently consume alcohol (≥3 drinks[a]/day) should be advised that reduction of alcohol intake close to abstinence will lower their BP.	I	B
Alcohol should not be recommended for CVD prevention, as previous studies linking moderate consumption to lower CV risk are likely confounded.	III	B
It is recommended to avoid excessive (binge) drinking to reduce BP, and the risks particularly for hemorrhagic stroke and premature death.	III	B
Smoking cessation, supportive care and referral to smoking cessation programs are recommended for all smokers to avoid ambulatory BP increases, reduce the risk of masked hypertension, and improve CV health outcome.	I	B
Reduced stress via controlled breathing exercises, mindfulness-based exercise and meditation may be considered.	II	C

[a]There are varying definitions for drinks used in the literature; a drink may relate to about 350 ml of regular beer containing 5% alcohol by volume or 150 ml of wine containing 12% alcohol by volume.

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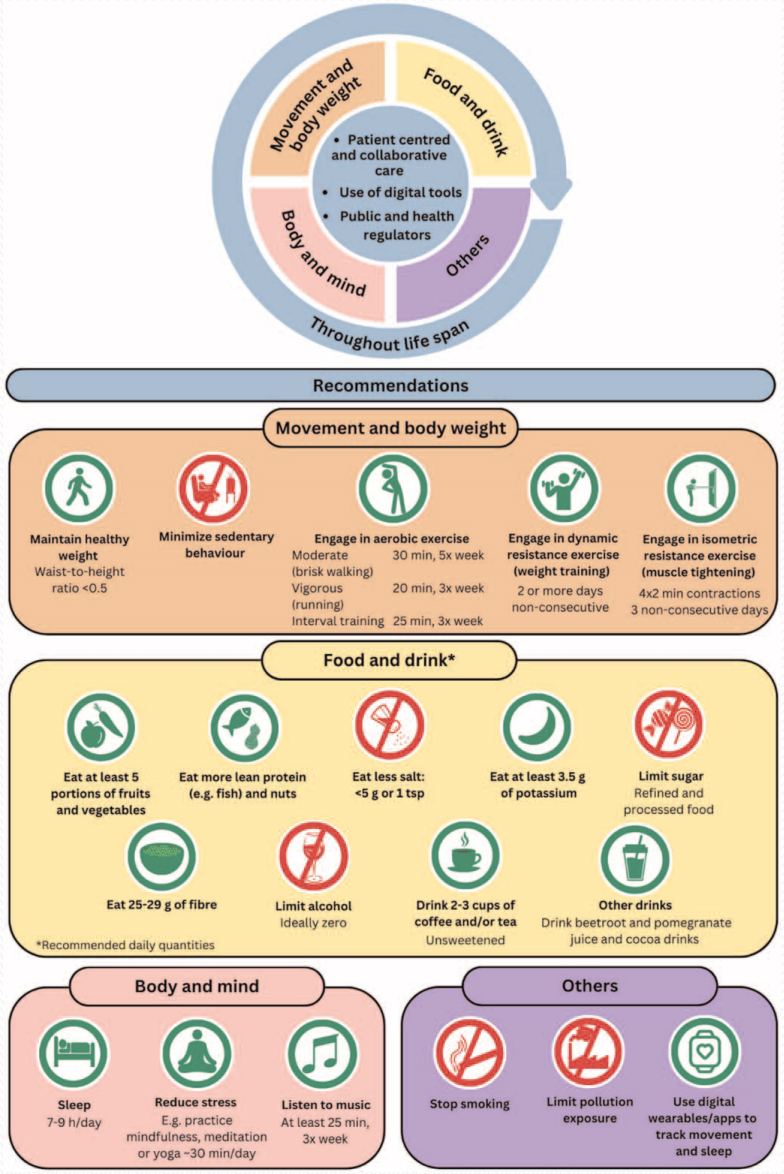

Charcar F J, Prestes P R et al. J Hypertension. 2023

Indipendemente dal grado di ITA!

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3. Articoli interessanti del 2023

Paziente 67 enne

- Dietista: tra 2012 e 2022 calo ponderale da 120 a 109 kg.

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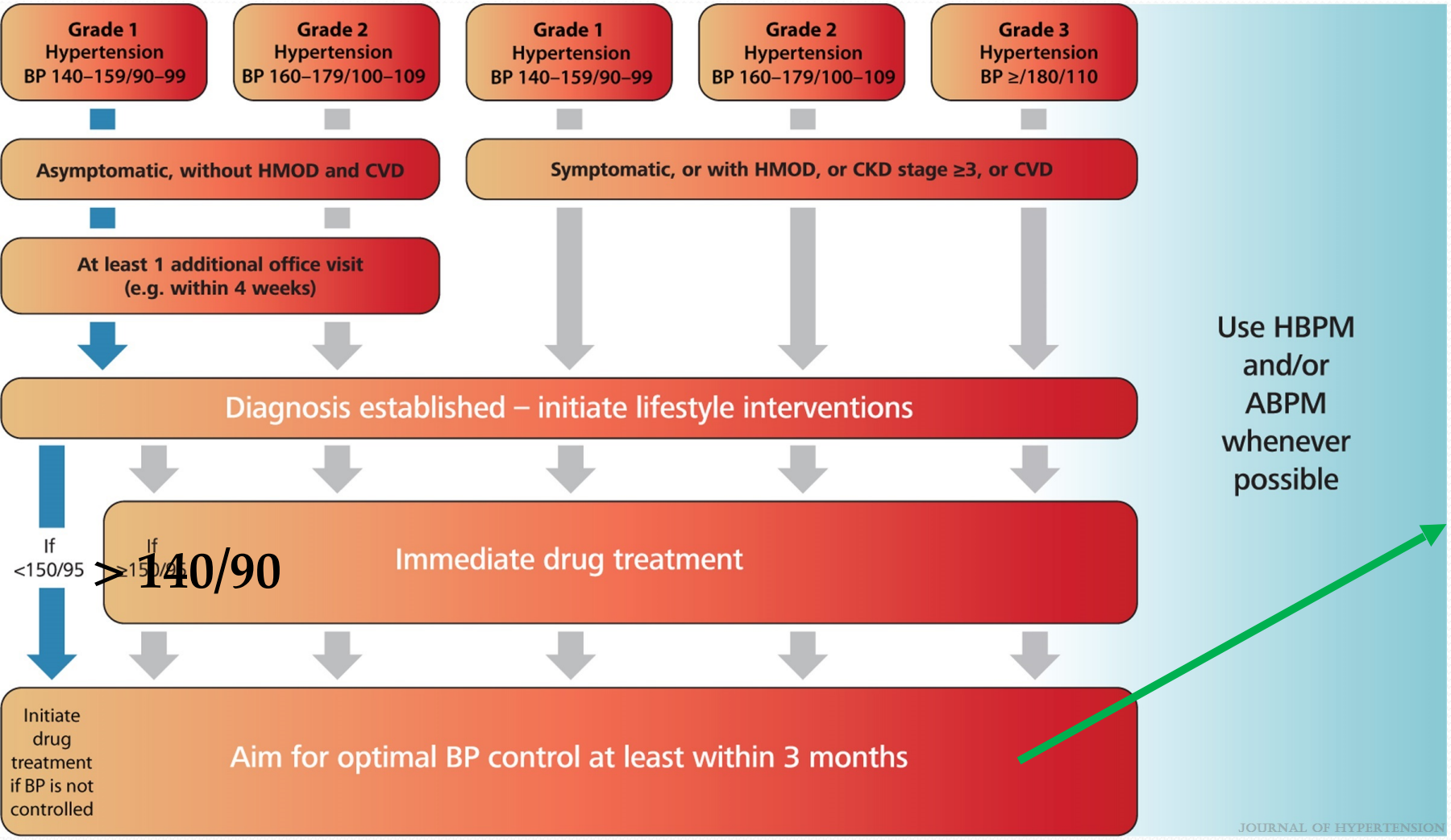
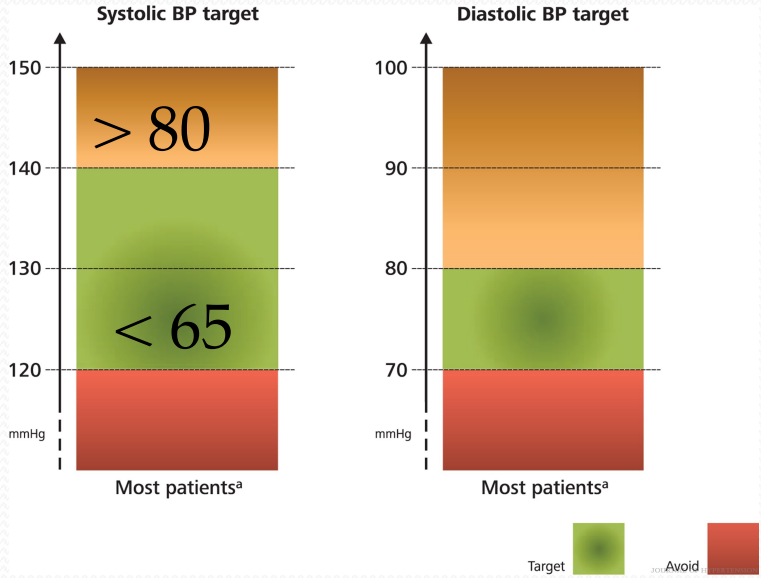
Trattamento iniziale dell'ITA (OBPM)





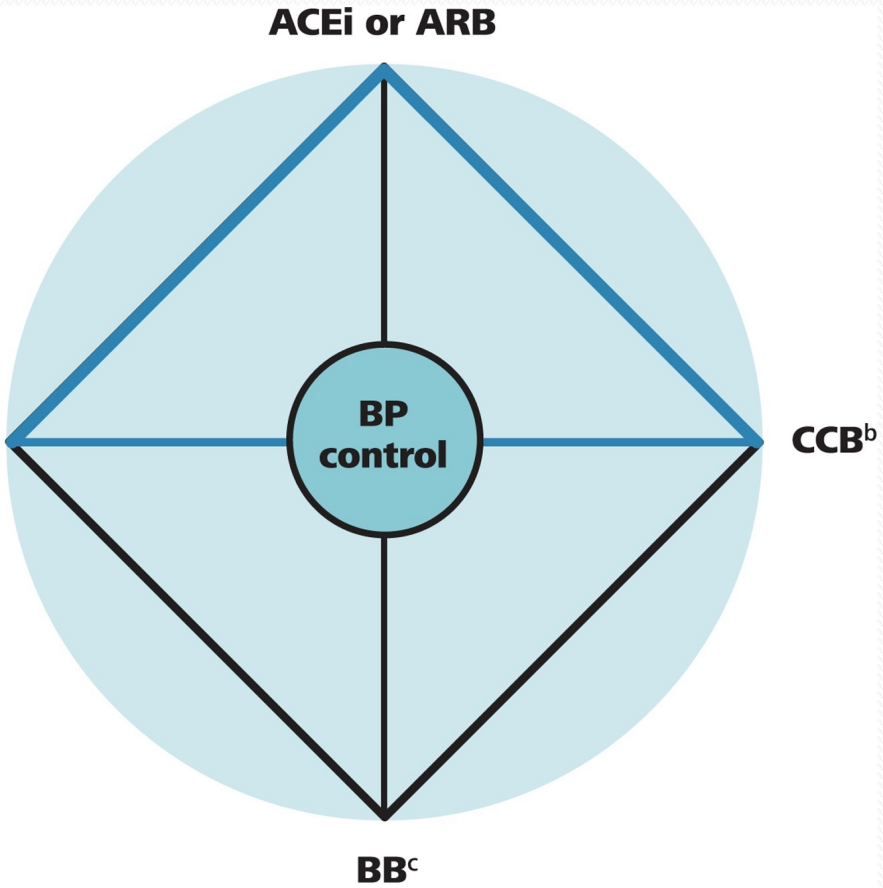
Evitare effetti collaterali

Marcia G, Kreutz R et al. J Hypertension. 2023

Principi della Terapia medicamentosa

Prescribing patterns:

- Start with dual combination therapy in most patients
- Uptitrate to maximum well tolerated doses and to triple therapy if needed
- **Once daily (preferred in the morning)**
- **Add further drugs if needed**
- **Preferred use of SPCs at any step**



Additional drug classes

General antihypertensive therapy:

- Steroidal MRA
- Loop Diuretic
- Alpha-1 Blocker
- Centrally acting agent
- Vasodilator

Special comorbidities:

- ARNi
- SGLT2i
- Non-Steroidal MRA

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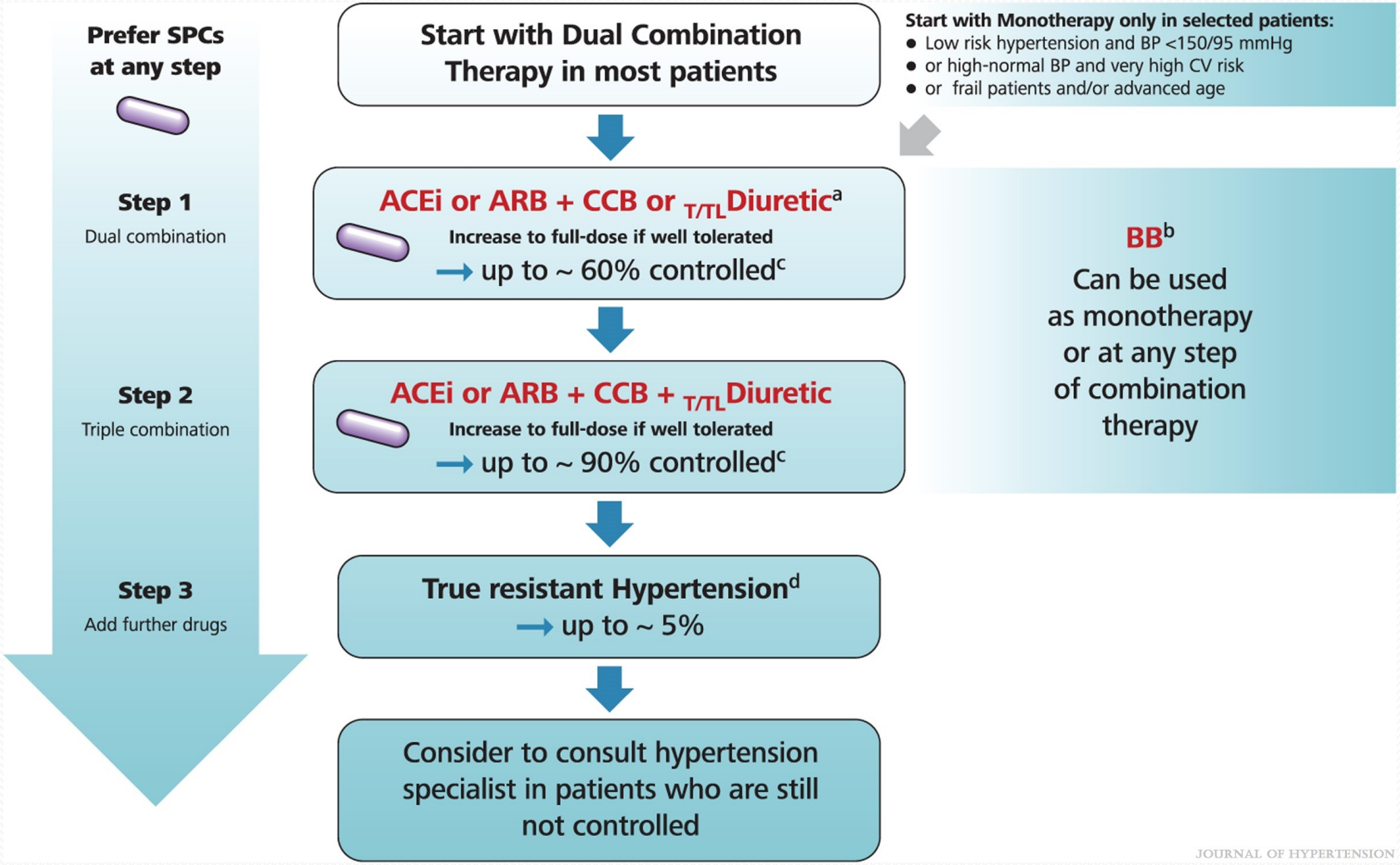
Marcia G, Kreutz R et al. J Hypertension. 2023

Terapia medicamentosa



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Paziente 67 enne

- 2012: Neuropatia isolata del VI nervo destro di origine microangiopatica
  Duplex carotideo: moderata ateromatosi carotidea bilaterale

  Pressione arteriosa **158/85 mmHg**, peso 120 kg, altezza 180 cm

  Terapia: enalapril 5 mg 1-0-0, atorvastatin 40 mg 0-0-1

  Remler: ipertensione arteriosa grado 1 media globale 146/77 mmHg, dipping pressorio normale

  Nuova terapia: enalapril 20 mg 1-0-0.5, lercanidipin 20 mg 1-0-0, atorvastatin 40 mg 0-0-1

  Pressione arteriosa in studio 138/80 mmHg dopo 1 mese ma a casa 120/80 mmHg

Paziente 77 enne

- 2015: paresi facciale periferica destra (di Bell)

- 2016: pressione arteriosa a domicilio 140-150/85 mmHg alta!
  pressione arteriosa in studio **188/100** mmHg

  Prende i medicamenti? Lui dice di si.

  terapia: peridopril 10 mg/amlodipina 10 mg/indapamid 2.5 mg 1-0-0

- Dopo 1 mese: pressione arteriosa in studio 138/74 mmHg e a domicilio 120/70 mmHg

- 2022: pressione arteriosa 129/73 mmHg
  Laboratorio: creatinina 101 umol/l, eGFR-EPI 60 ml/min/1.73 mq,
  non albuminuria

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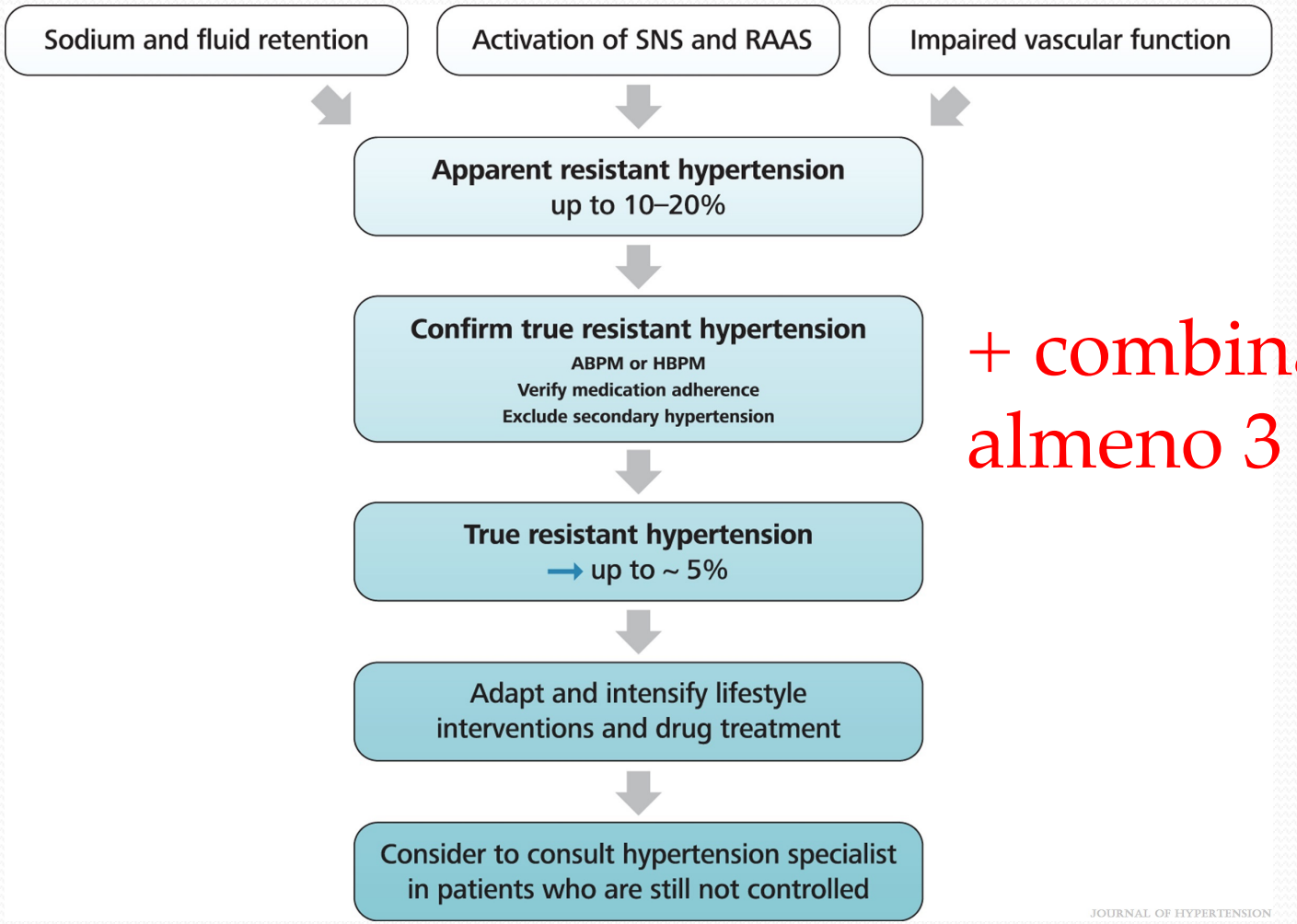
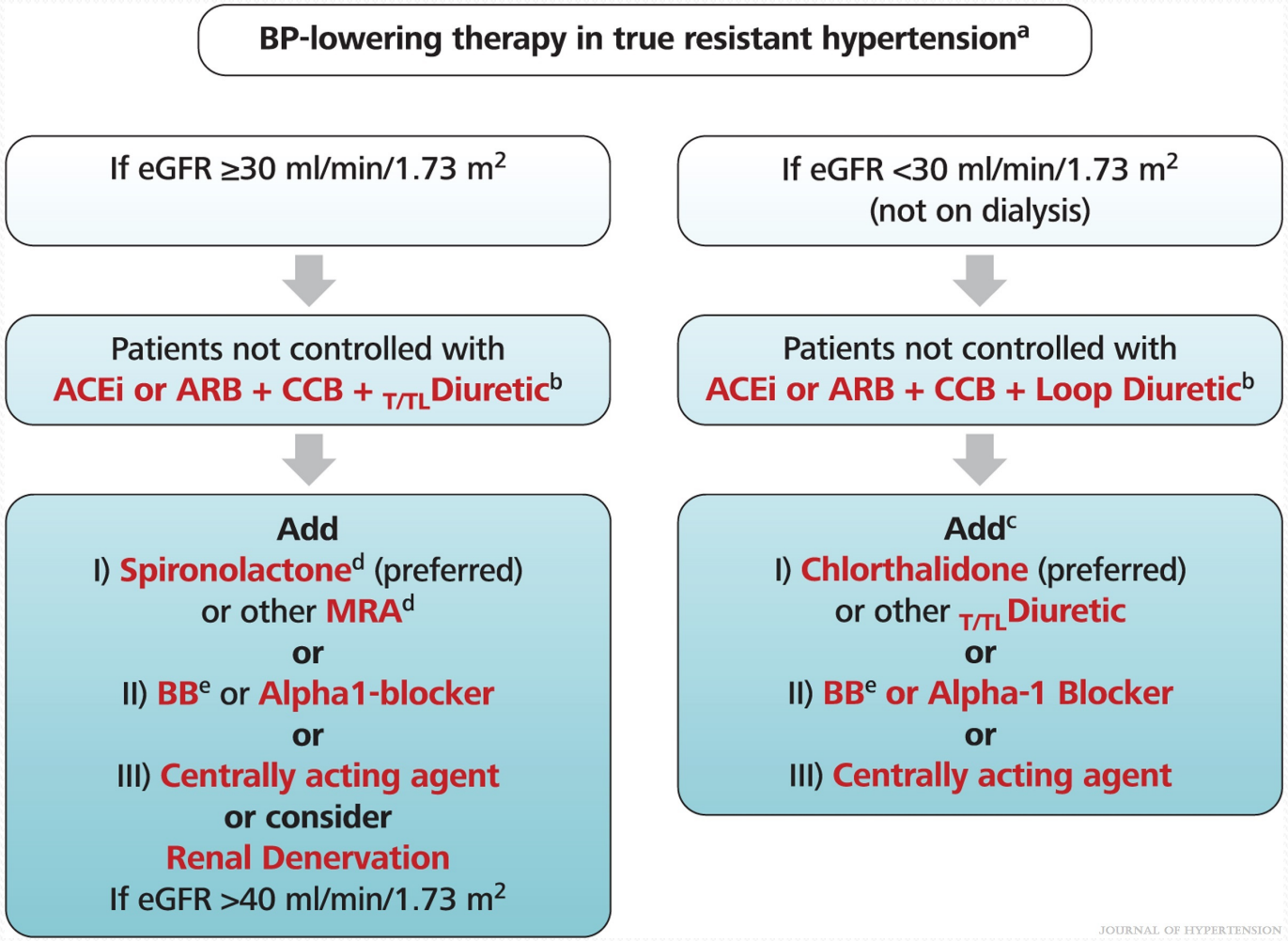
Vera ITA resistente alla terapia



+ combinazione di almeno 3 antipertensivi

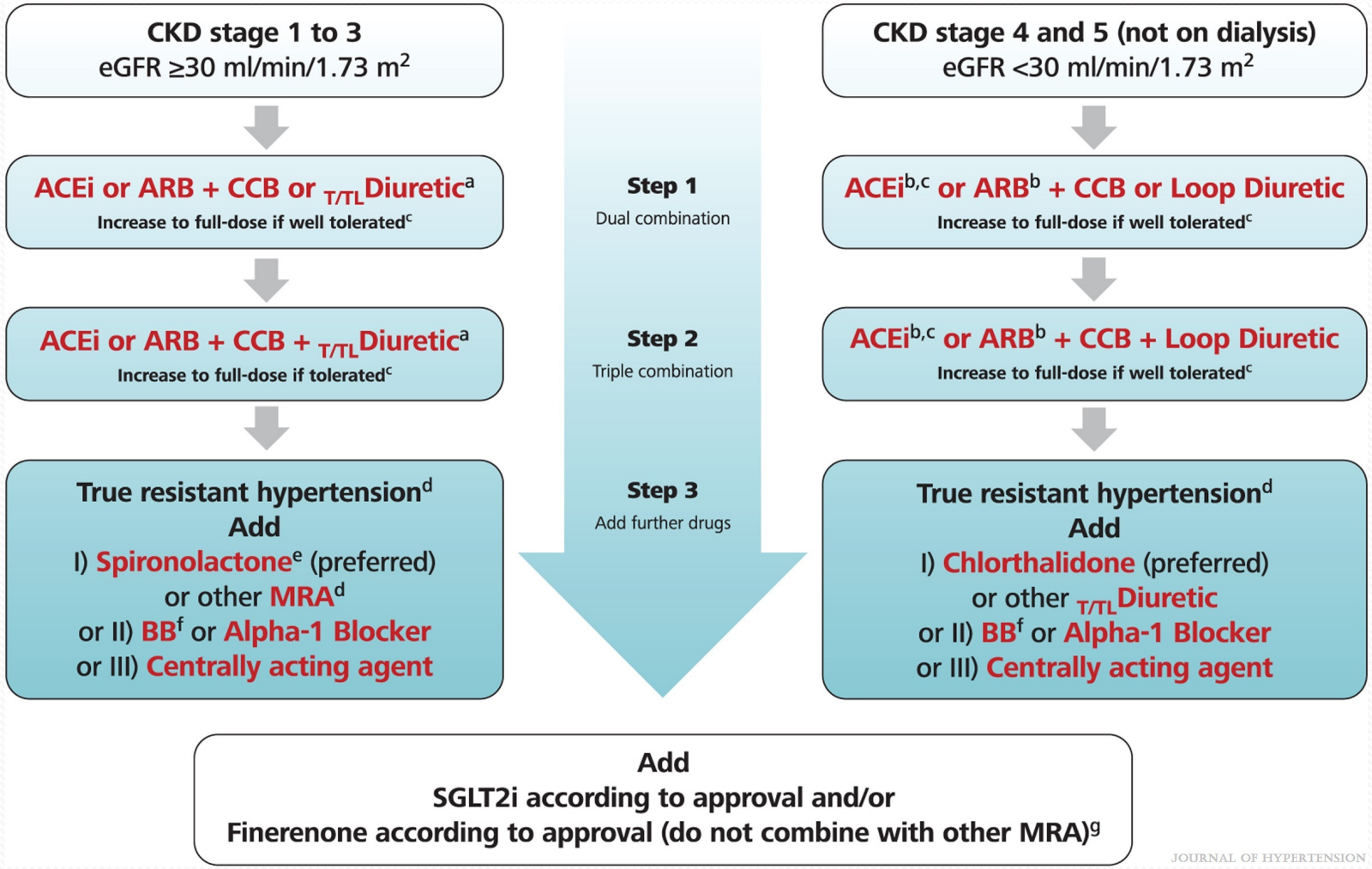
Marcia G, Kreutz R et al. J Hypertension. 2023

Vera ITA resistente alla terapia: trattamento



Marcia G, Kreutz R et al. J Hypertension. 2023

Terapia medicamentosa in presenza di malattia renale cronica



Marcia G, Kreutz R et al. J Hypertension. 2023

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ITA idroclortiazide vs clortalidone

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Chlorthalidone vs. Hydrochlorothiazide for Hypertension–Cardiovascular Events

Ishani A et al. DOI: 10.1056/NEJMoa2212270

CLINICAL PROBLEM

Thiazide diuretics are first-line treatments for hypertension. Guidelines have preferentially recommended chlorthalidone, although Medicare data suggest that prescriptions for hydrochlorothiazide far exceed those for chlorthalidone. Whether chlorthalidone is superior to hydrochlorothiazide for preventing major adverse cardiovascular events is unclear.

CLINICAL TRIAL

Design: A multicenter, pragmatic, open-label, randomized trial assessed the efficacy and safety of chlorthalidone as compared with hydrochlorothiazide in U.S. veterans with hypertension.

Intervention: 13,523 adults ≥65 years of age (97% men) with a most recent systolic blood pressure of ≥120 mm Hg and an active prescription for hydrochlorothiazide (25 or 50 mg per day) were assigned to continue that treatment or switch to chlorthalidone (12.5 or 25 mg per day). The primary outcome was a composite of nonfatal cardiovascular events (myocardial infarction, stroke, heart failure hospitalization, or urgent coronary revascularization for unstable angina) or non–cancer-related death.

RESULTS

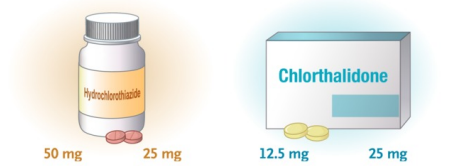
Efficacy: During a median follow-up of 2.4 years, the incidence of primary-outcome events did not differ significantly between the chlorthalidone and hydrochlorothiazide groups.

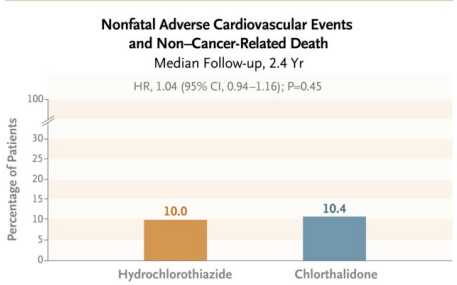
Safety: The incidence of hospitalization for any cause did not differ between the groups. Hypokalemia was more common in the chlorthalidone group than in the hydrochlorothiazide group.

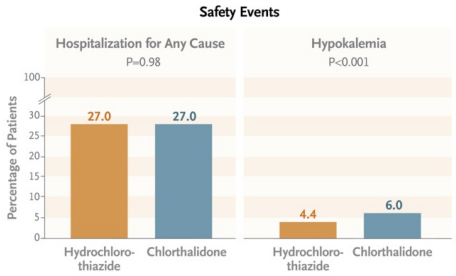
LIMITATIONS AND REMAINING QUESTIONS

- More patients assigned to receive chlorthalidone switched back to hydrochlorothiazide, as compared with patients assigned to continue treatment with hydrochlorothiazide switching over to chlorthalidone — possibly owing to the open-label nature of the trial.
- Only 5% of participants were receiving a daily 50-mg dose of hydrochlorothiazide at baseline; thus, the trial primarily compared hydrochlorothiazide at a daily dose of 25 mg with chlorthalidone at a daily dose of 12.5 mg, and the results should not be extrapolated to other dosages.

Links: Full Article | NEJM Quick Take | Editorial





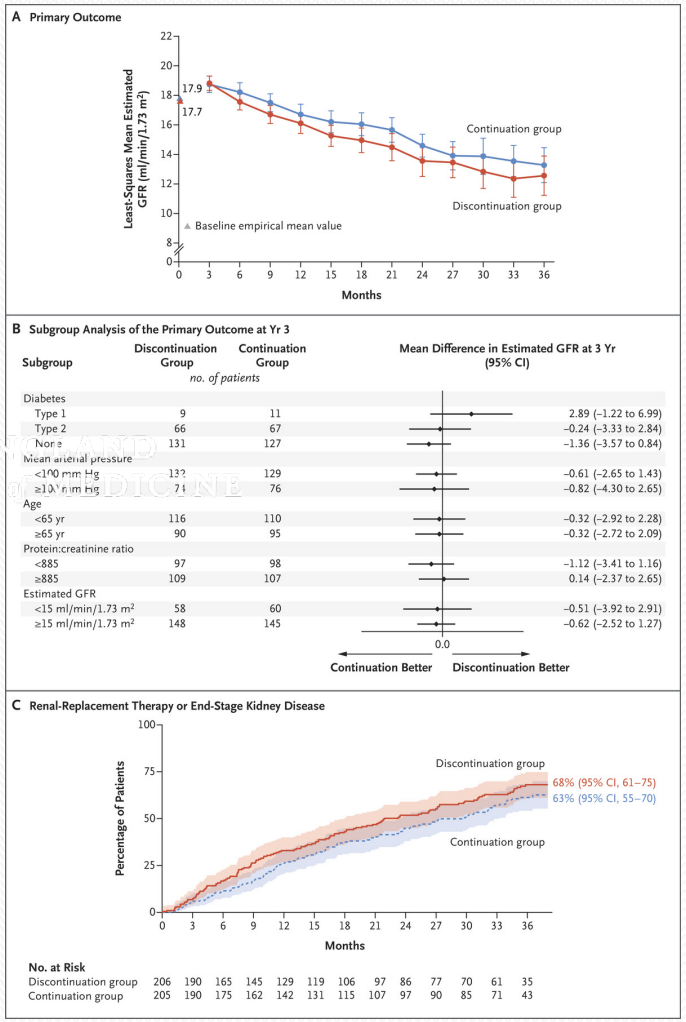


CONCLUSIONS

In a large pragmatic trial among U.S. veterans with hypertension, patients who received chorthalidone did not have a lower occurrence of nonfatal cardiovascular events or non–cancer-related death than those who received hydrochlorothiazide.

Renin–Angiotensin System Inhibition in Advanced Chronic Kidney Disease

- N= **411**
- **eGFR < 30 ml/min/1.73 mq**
- **RAS vs stop RAS**
- Multicentrico, aperto, randomizzato.
- Outcome primario e secondario nessuna differenza.



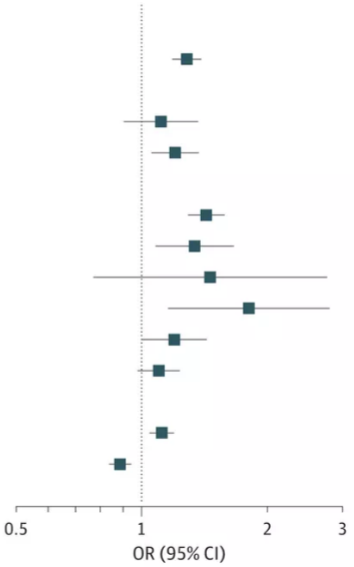
S Bhandari et al. N Engl J Med 2022;387:2021-2032.

Clinical Outcomes of Intensive Inpatient Blood Pressure Management in Hospitalized Older Adults

- N= **66140**
- **> 65 a, veterani, senza diagnosi CV e ITA nelle prime 48 h in ospedale**
- **Trattamento intensivo della PA (nuovi farmaci) dopo le prime 48 h in ospedale**
- Retrospettivo, coorte, aggiustato
- Outcome primario composito (Mortalità, ICU, AKI, BNP, troponina, ipotensione) favorisce NON trattamento

Figure 2. Clinical Outcomes of Intensive Inpatient Antihypertensive Treatment

	Intensively treated, No. (%) (n = 14 064)	Not intensively treated, No. (%) (n = 52 076)	OR (95% CI)
Primary outcome			
Composite	1220 (8.7)	3570 (6.9)	1.28 (1.18-1.39)
Clinical outcome			
Death	156 (1.1)	573 (1.1)	1.11 (0.91-1.37)
ICU transfer	408 (2.9)	1322 (2.5)	1.20 (1.05-1.37)
AKI			
Any stage	769 (5.5)	2031 (3.9)	1.43 (1.29-1.58)
Stage 2 or 3	165 (1.2)	440 (0.8)	1.34 (1.08-1.66)
Stroke	21 (0.2)	43 (0.1)	1.46 (0.77-2.78)
BNP elevation	38 (0.3)	95 (0.2)	1.81 (1.16-2.82)
Troponin elevation	227 (1.6)	710 (1.4)	1.20 (1.00-1.43)
Hypotension	2078 (14.5)	7283 (14.0)	1.22 (1.15-1.30)
Disposition			
SNF discharge	1714 (12.2)	5239 (10.1)	1.12 (1.04-1.20)
Home	11 936 (84.9)	45 372 (87.1)	0.89 (0.83-0.94)



Event rates presented for each treatment group are unadjusted, while odds ratios (ORs) are following overlap weighting. Composite outcome includes mortality, intensive care unit (ICU) transfer, any-stage acute kidney injury (AKI), stroke, troponin elevation, or B-natriuretic peptide (BNP) elevation. Hypotension defined as any systolic blood pressure less than 100 mm Hg in the post–48-hour hospitalization period. SNF indicates skilled nursing facility.

Anderson T S et al. JAMA Intern Med 2023 Jul 1; 183(7):715-723.

Alcohol Intake and Blood Pressure Levels: A Dose Response Meta-Analysis of Nonexperimental Cohort Studies

- N= **19548**
- **Adulti sani seguiti n media per 5.3 anni**
- Metanalisi di studi longitudinali
- Obiettivo: le differenze medie nel tempo delle pressioni sistolica e diastolica in base al consumo di alcol iniziale
- Risultato per 12 risp. 48 g OH vs NO OH:
  - **PAS + 1.25 e 4.9 mmHg**
  - **PAD + 1.14 e 3.1 mmHg**

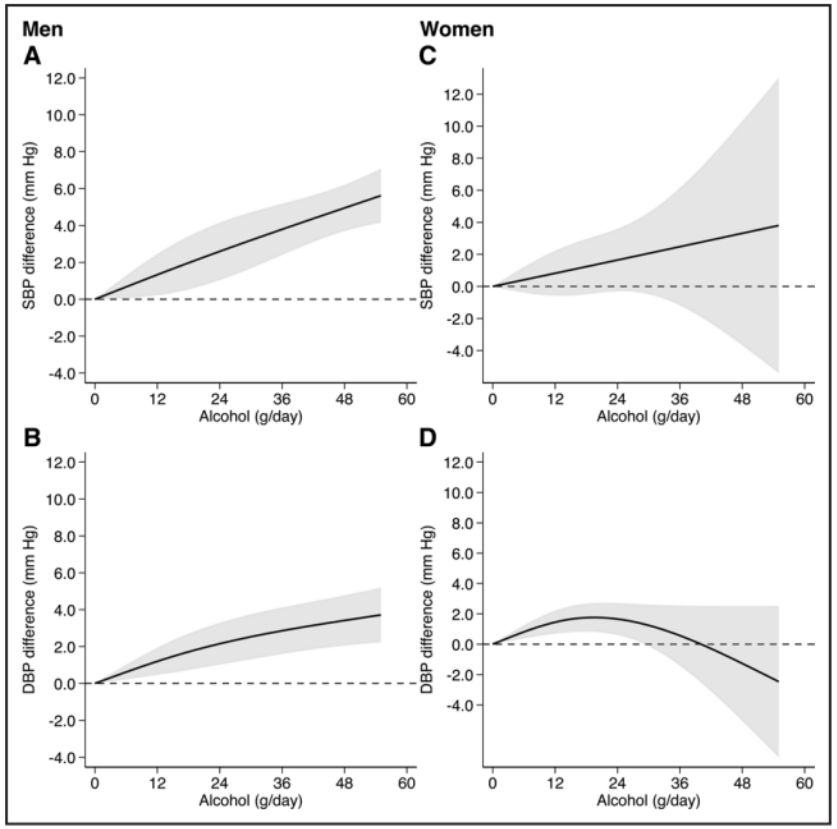


Figure 3. Dose-response relationship of baseline alcohol intake with systolic blood pressure (SBP) and diastolic blood pressure (DBP) divided by sex.
Studies conducted in men (**A** and **B**)[23–27] and women (**C** and **D**).[23,27] Spline curve (solid line) with 95% confidence limits (gray area).

Di Federico S et al. Hypertension. 2023;80:1961–1969.

Grazie per l'attenzione

Foglio extra

Mettere studio 1 misurazioni ospedale, 3 idroclorotiazide in CKD, 4 RAS in malattia renale avanzata, 5 antipertensivi notte e giorno nessuna differenza

TABLE 4 - Definitions of hypertension according to the correspondence of home and ambulatory BP values with office BP

Method	SBP (mmHg)		DBP (mmHg)
Office BP[a]	≥140	and/or	≥90
Ambulatory BP			
Awake mean	≥135	and/or	≥85
Asleep mean	≥120	and/or	≥70
24 h mean	≥130	and/or	≥80
Home BP mean	≥135	and/or	≥85

[a]Refers to standard office BP measurements (not unattended measurements). Data compare the averages from cohorts of untreated and treated individuals. Given the low correlation between office and out-of-office BP values, individuals can have considerable discrepancies from the averages.

Medical and family History

Personal history
• Time of thef irst diagnosis of hypertension, including records of any previous medical screening, hospitalization
• Stable or rapidly increasing BP
• Recordings of current and past BP values by self BP measurements
• Current/past antihypertensive medications including their effectiveness and intolerance
• Adherence to therapy
• Previous hypertension in pregnancy/preeclampsia
Risk factors [a]
• Family history of hypertension, CVD, stroke or kidney disease
• Smoking history
• Dietary history, alcohol consumption
• Lack of physical exercise/sedentary lifestyle
• Weight gain or loss in the past
• History of erectile dysfunction
• Sleep history, snoring, sleep apnea (information also from partner)
• Distress or eustress with job or at home (subjective stress level)
• Long-term cancer survivor
History and symptoms of HMOD, CVD, stroke and kidney disease
• Brain and eyes: headache, vertigo, syncope, impaired vision, TIA, sensory or motor deficit, stroke, carotid revascularization, cognitive impairment, memory loss, dementia (in older people)
• Heart: chest pain, shortness of breath, edema, myocardial infarction, coronary revascularization, syncope, history of palpitations, arrhythmias (especially AF), heart failure
• Kidney: thirst, polyuria, nocturia, hematuria, urinary tract infections
• Peripheral arteries: cold extremities, intermittent claudication, pain-free walking distance, pain at rest, ulcer or necrosis, peripheral revascularization
• Patient or family history of CKD (e.g. polycystic kidney disease)
History of possible secondary hypertension
• Young onset of grade 2 or 3 hypertension (<40 years), or sudden development of hypertension or rapidly worsening BP in older patients
• History of repetitive renal/urinary tract disease
• Repetitive episodes of sweating, headache, anxiety or palpitations, suggestive of pheochromocytoma
• History of spontaneous or diuretic-provoked hypokalemia, episodes of muscle weakness and tetany (hyperaldosteronism)
• Symptoms suggestive of thyroid disease or hyperparathyroidism

Comprehensive physical examination for hypertension

Body habitus
• Weight and height measured on a calibrated scale, with calculation of BMI
• Waist circumference
Signs of hypertension-mediated organ damage
• Neurological examination and cognitive status
• Fundoscopic examination for hypertensive retinopathy in emergencies
• Auscultation of heart and carotid arteries
• Palpation of carotid and peripheral arteries
• Ankle–brachial index
Signs of secondary hypertension (Section 6)
• Skin inspection: cafe-au-lait patches of neurofibromatosis (pheochromocytoma)
• Kidney palpation for signs of renal enlargement in polycystic kidney disease
• Auscultation of heart and renal arteries for murmurs or bruits indicative of aortic coarctation, or renovascular hypertension
• Signs of Cushing's disease or acromegaly
• Signs of thyroid disease

Assessment of hypertension-mediated organ damage (HMOD)

Basic screening tests for HMOD recommended for all hypertensive patients	Aim
12 lead ECG	Measure HR and AV conduction, detect cardiac arrhythmias, myocardial ischemia and infarction, screen for LVH
Urine albumin : creatinine ratio (UACR)	Detect and classify CKD
Serum creatinine and eGFR	Detect and classify CKD
Extended screening for HMOD	
Echocardiography	Evaluate structure and function of the ventricles and left atrium, detect valvular disease, aortic root diameter and ascending aortic aneurysm
cfPWV or baPWV	Evaluate aortic/large artery stiffness
Carotid artery ultrasound	Determine carotid intima-media thickness, plaque and stenosis
Coronary artery calcium scan	Determine the presence and extent of coronary calcium to predict CAD events
Abdominal aorta ultrasound	Screen for aortic aneurysm
Kidney ultrasound	Evaluate size and structure of kidney, detect renovascular disease, determine RRI (by spectral doppler ultrasonography)
Spectral doppler ultrasonography	Diagnosis of renovascular disease and determination of RRI
ABI	Screen for LEAD
Retina microvasculature	Detect microvascular changes
Cognitive function testing (MMSE, MoCA)	Screen for early stages of dementia
Brain imaging (CT, MRI)	Detect structural brain damage

Criteria to define HMOD

Measurement	Parameter	Abnormality threshold
ECG		
LVH	$S_{V1} + R_{V5}$ (Sokolow–Lyon)	>35 mm
	R wave aVL	≥11 mm
	$S_{V3} + R_{aVL}$ (Cornell voltage)	>28 mm (M), >20 mm (W)
LVH	Cornell voltage (+6 mm in W) × QRS duration (Cornell duration product)	>2440 mm s
ECHO		
LVH	LVM/BSA (g/m²)	>115 (M), >95 (W)
	LVM/height (g/m$^{2.7}$)	>50 (M), >47 (W)
RWT	LV conc. Remodeling	≥0.43
LV chamber size	LVDDiam/height	>3.4 (M), >3.3 (W) cm/m
LV diastolic dysfunction	*e'* velocity septal	<7 cm/s
	e' velocity lateral	<10 cm/s
LV filling pressure	*E*/*e'* average ratio	>14
	LAV/BSA	>34 ml/m²
	LAV/height²	>18.5 (M) or >16.5 (W) ml/m²
LV systolic dysfunction	GLS	<20%
Kidney		
Function	eGFR	<60 ml/min/1.73 m²
Albuminuria	UACR	>30 mg/g
Renal resistive index	RRI	>0.7
Large artery stiffness		
Pulse pressure	Brachial PP (>60 years)	≥60 mmHg
Pulse wave velocity	baPWV (in people 60–70 years)	>18 m/s
	cfPWV (in people 50–60 years)	>10 m/s
Carotid atherosclerosis		

TABLE 14 - Rare genetic causes of secondary hypertension [343]

Liddle syndrome	Hypokalemia, metabolic alkalosis, low PRA or PRC, low PAC	Increased renal tubular ENaC activity; responds to treatment with amiloride
Apparent mineralocorticoid excess	Hypokalemia, metabolic alkalosis, low PRA or PRC, low PAC	Decreased 11β-hydroxysteroid dehydrogenase isoenzyme 2; responds to spironolactone
Gordon syndrome	Hyperkaliemia, metabolic acidosis, low PRA or PRC, low/normal PAC	Overactivity of the sodium-chloride cotransporter; responds to thiazides
Geller syndrome	Pregnancy-exacerbated hypertension, low PRA or PRC, low PAC	Agonist effect of progesterone on the mineralocorticoid receptor (which is constitutively active); responds to amiloride, spironolactone activates instead of blocking the receptor
Glucocorticoid-remediable aldosteronism (familial hyperaldosteronism type 1)	Hypokalemia, metabolic alkalosis, low PRA or PRC, increased PAC	Chimeric *CYP11B1*/*CYP11B2* gene; responds to glucocorticoids
Familial hyperaldosteronism type 2	Hypokalemia, metabolic alkalosis, low PRA or PRC, increased PAC	Increased activity of CLCN2 chloride channel; responds to steroidal MRA
Familial hyperaldosteronism type 3	Hypokalemia, metabolic alkalosis, low PRA or PRC, increased PAC	Loss of selectivity of KCNJ5 potassium channel; patients who do not respond to steroidal MRA require bilateral adrenalectomy
Familial hyperaldosteronism type 4	Hypokalemia, metabolic alkalosis, low PRA or PRC, increased PAC	Increased activity of CACNA1H calcium channel; responds to steroidal MRA
PASNA syndrome (primary aldosteronism, seizures and neurological abnormalities)	Hypokalemia, metabolic alkalosis, low PRA or PRC, increased PAC; neurological defects coexists	Increased activity of CACNA1D calcium channel; responds to steroidal MRA and CCB
11beta-hydroxylase deficiency	Hypokalemia, metabolic alkalosis, low PRA or PRC, low PAC, virilization of female individuals	Reduced activity of 11β-hydroxylase with increase of DOC and androgens; responds to glucocorticoids
17alpha-hydroxylase deficiency	Hypokalemia, metabolic alkalosis, low PRA or PRC, low PAC, pseudohermaphroditism in male individuals	Reduced activity of 17α-hydroxylase with increase of DOC and reduction of androgens; responds to glucocorticoids
Autosomal dominant hypertension with	Brachydactyly type E (BDE), short stature, severe	PDE3A mutations upregulated the cAMP-hydrolytic activity