

HTA 2024

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GRACE-PENN
MEDICINE



European
Hypertension
Excellence
Center
Princess Grace
Hospital
Monaco

16 Chiffres clés

Hypertension

PRÉVALENCE



1 adulte sur **3**
est hypertendu^{1,16}

TRAITEMENT



1 hypertendu sur **2**
est traité
pharmacologiquement^{1,16}

CONTRÔLE



1 hypertendu sur **4**
a une pression artérielle
contrôlée^{1,16}

FARDEAU



17 millions

de personnes de plus de 18
ans atteintes d'HTA en
France²⁰

PRESSION ARTÉRIELLE MOYENNE

126/77 mm Hg

Pression artérielle moyenne de la
population française¹



SPÉCIALISTES

11%

des hypertendus
sont suivis par un
cardiologue³⁴



PRISE EN CHARGE

22% des hypertensions non traitées sont de grade 2 ou 3^{1,16}

TRAITEMENT

1,6 million de Français initient un traitement anti HTA chaque année¹⁸

DÉPISTAGE

84% De la population a eu une mesure de la pression artérielle dans l'année¹

CONNAISSANCE



1 hypertendu sur **2** ne sait pas qu'il est hypertendu^{1,16}

TRAITEMENT

60%



des hypertendus traités pharmacologiquement avaient une monothérapie^{1,16}

TRAITEMENT

93%



des patients émettent des réserves lors de la prescription d'un traitement antihypertenseur¹⁴

AUTOMESURE

59%



des hypertendus traités possèdent un appareil d'automesure tensionnelle¹

RECOURS AUX SOINS

10



consultations par an chez le généraliste pour les hypertendus³⁴

OBSERVANCE

40%

des hypertendus traités sont observants³⁴

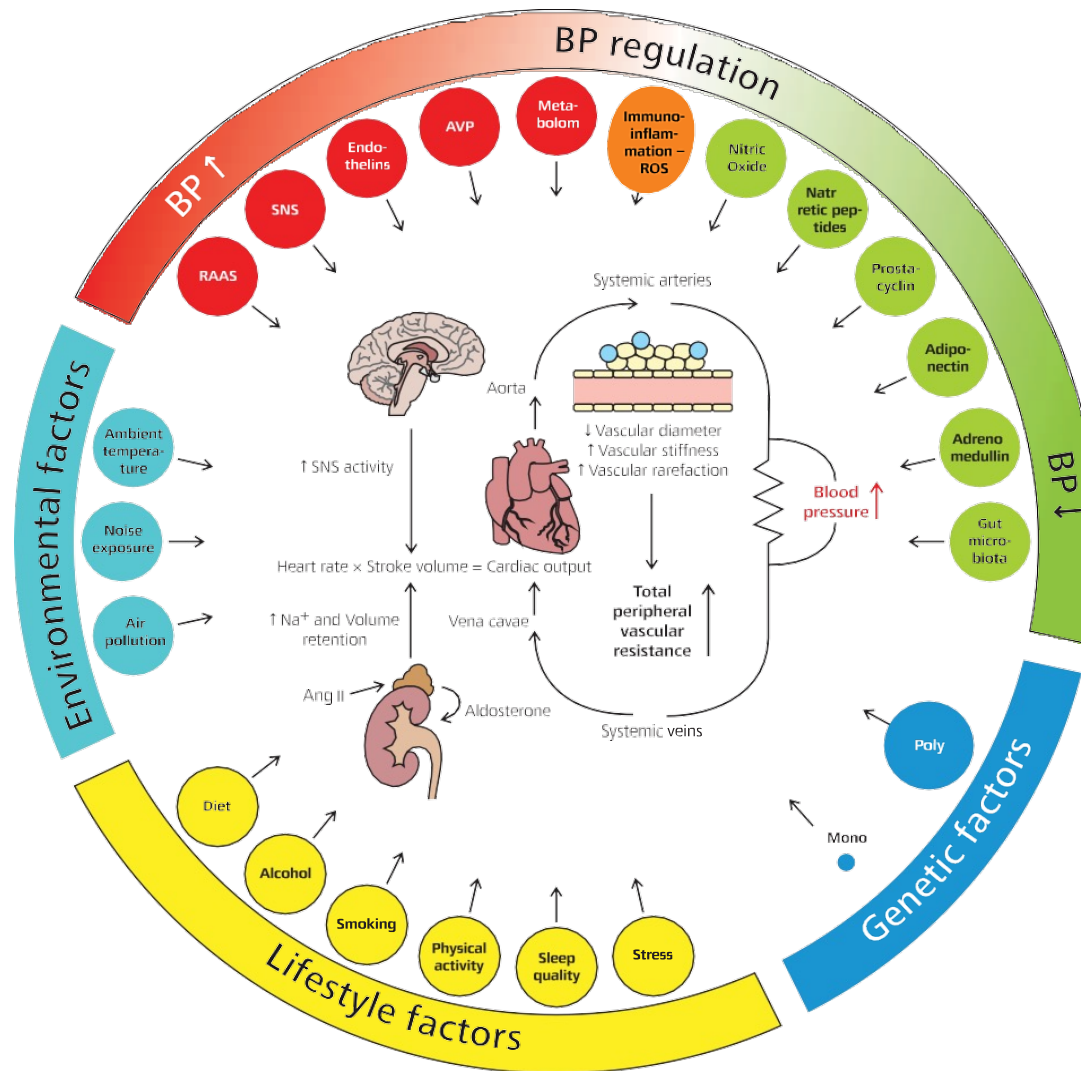
TRAITEMENT

57%

Des patients hypertendus déclarent ne pas avoir reçu de conseils hygiéno-diététiques dans l'année¹⁹



Mechanisms involved in BP regulation and the pathophysiology of hypertension






La classification de l'hypertension artérielle n'a pas changée

- à moins de 120/80 mm Hg, la pression est dite "optimale »
- à 120-129/80-85 la pression est "normale",
- à 130-140/85-90, la pression est dite "normale haute",
- au-delà, c'est "hypertension artérielle" grade 1, grade 2, grade 3.

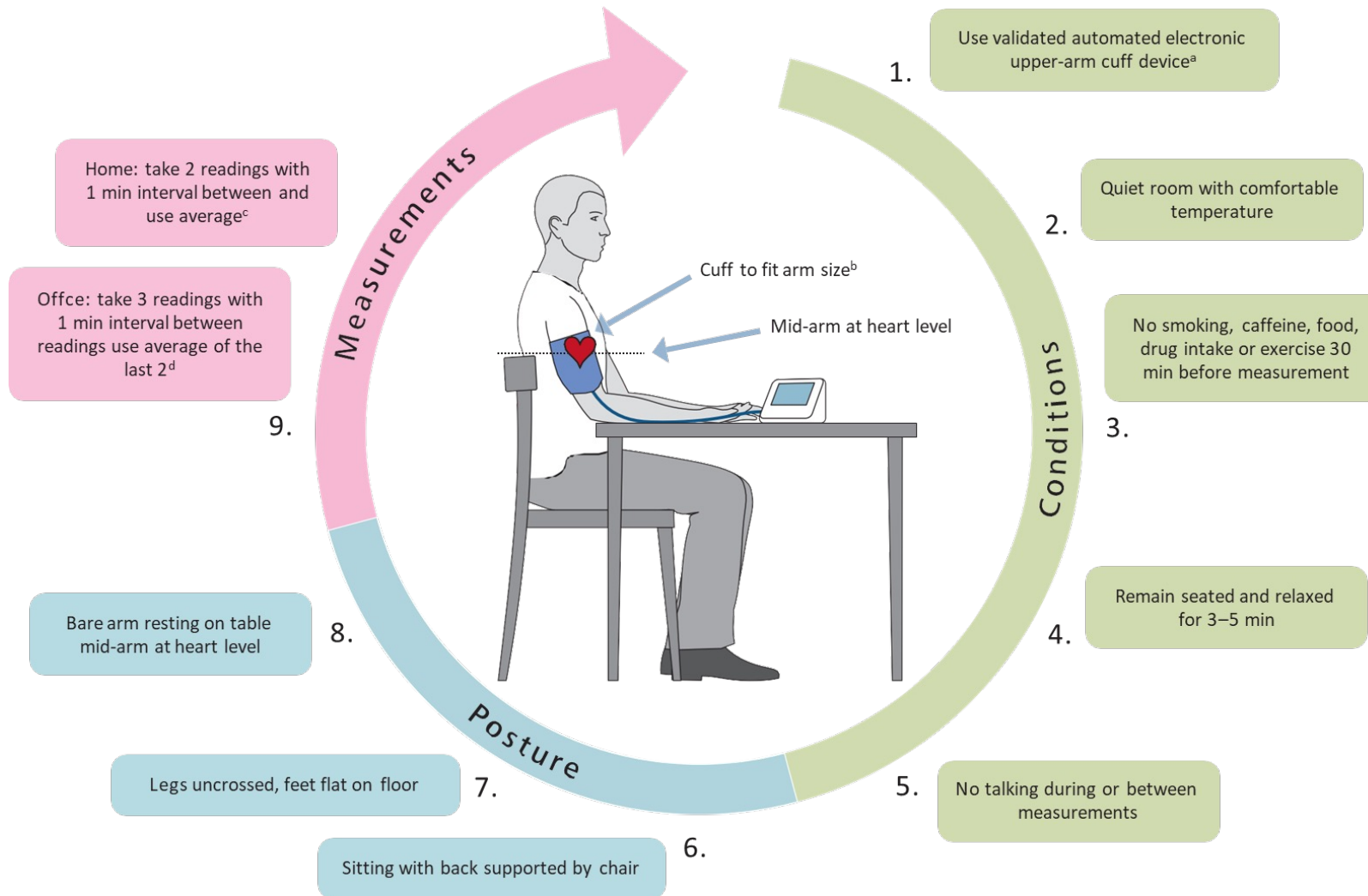
Grade , Stage et Risque CV

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	Complementary risk estimation in Stage 1 with SCORE2/SCOR2-OP
	<2.5%	<5%	<7.5%	
	2.5 to <7.5%	5 to <10%	7.5 to <15%	
	≥7.5%	≥10%	≥15%	

- *Stage 1*, le patient va bien à part son hypertension artérielle – pas d'atteinte d'organes, pas de risque cardiovasculaire.
- *Stage 2*, il a des atteintes d'organes cibles, un diabète ou une maladie rénale chronique jusqu'à stade 3.
- *Stage 3*, il a des complications cardiovasculaires, il est en prévention secondaire, ou il a une maladie rénale chronique avancée.

Recommendations for BP measurements in the office and at home



Les 4 clés pour contrôler tous vos patients



Sécuriser la mesure



Dépister d'emblée les causes secondaires



Titrer rapidement la thérapeutique



Adresser les patients sélectionnés

Ne pas rater les HTA secondaires

Après confirmation de l'HTA en ambulatoire



Le saviez-vous ?



10% des patients hypertendus chez le médecin généraliste sont porteurs d'une **forme secondaire** d'hypertension artérielle

*forme que l'on peut **guérir** ou nettement **améliorer** en **traitant la cause** de l'HTA*



Et vous, combien de patients hypertendus avez-vous vu cette semaine ?

Avez vous repéré les 10% présentant une HTA secondaire parmi eux ?

NON ?

Vous n'êtes pas les seuls !

L'HTA secondaire, un mythe ?

Journal of the American College of Cardiology
© 2006 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 48, No. 11, 2006
ISSN 0735-1097/06/\$32.00
doi:10.1016/j.jacc.2006.07.059

Hypertension

A Prospective Study of the Prevalence of Primary Aldosteronism in 1,125 Hypertensive Patients

Therefore, overall the prevalence of the disease was 11.2%, without gender differences (11.7% in men, 10.6% in women).

Rossi et al, JACC, 2006



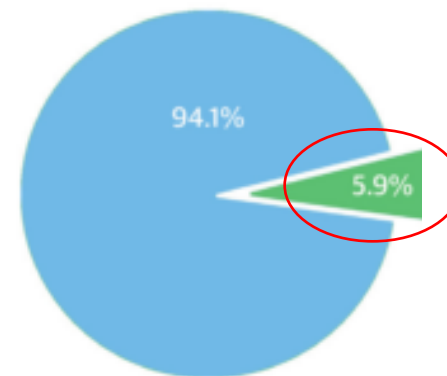
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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VOL. 69, NO. 14, 2017
ISSN 0735-1097/\$36.00
<http://dx.doi.org/10.1016/j.jacc.2017.01.052>

Prevalence and Clinical Manifestations of Primary Aldosteronism Encountered in Primary Care Practice



A. Prevalence of Primary Aldosteronism

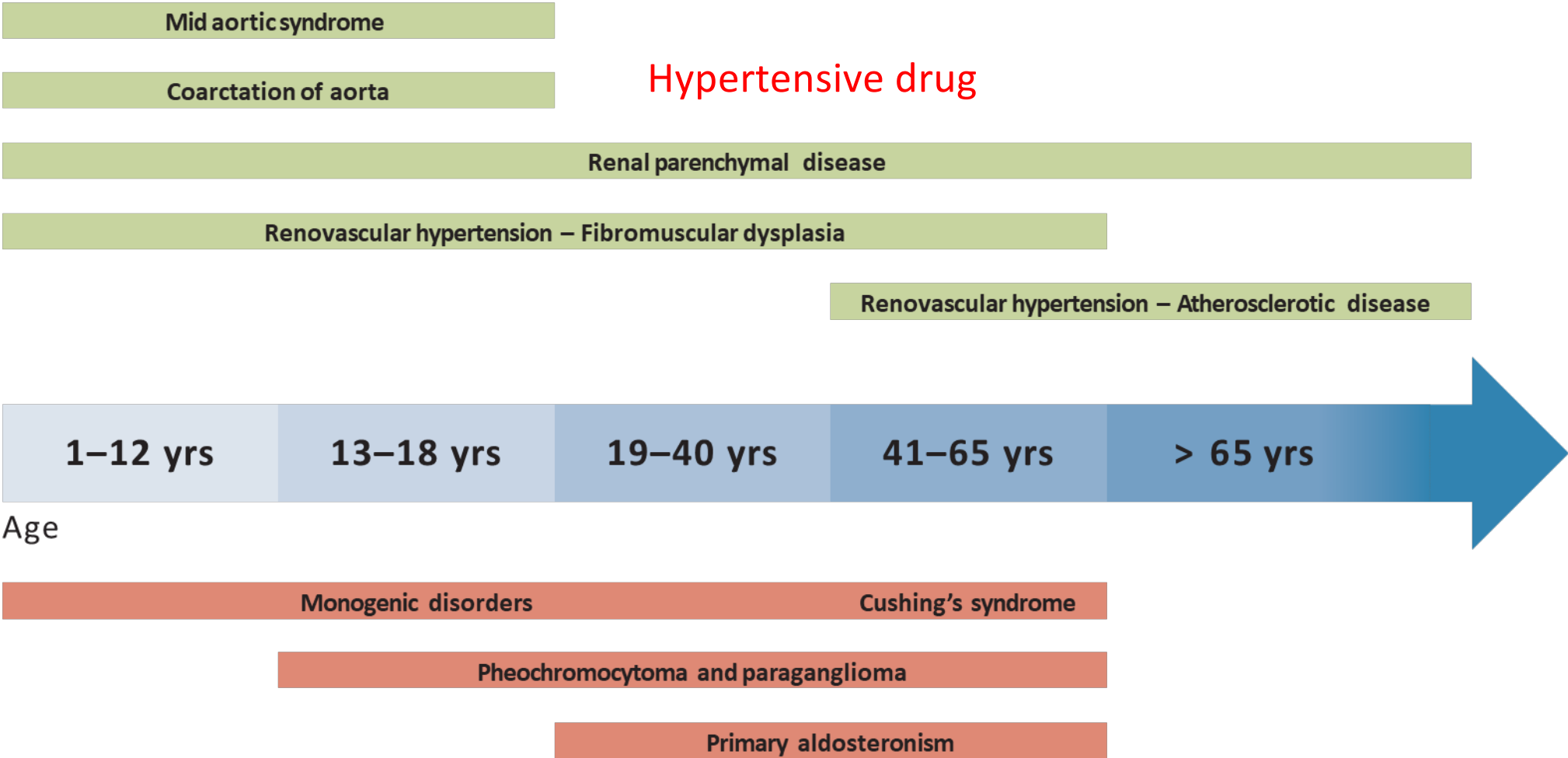


Monticone, S. et al. J Am Coll Cardiol. 2017;69(14):1811-20.

Les HTA secondaires, une **REALITE !!**

6 à 10 % de tous les patients hypertendus !

Incidence of selected forms of secondary hypertension according to age



Age

1-12 yrs

13-18 yrs

19-40 yrs

41-65 yrs

> 65 yrs

Monogenic disorders

Cushing's syndrome

Pheochromocytoma and paraganglioma

Primary aldosteronism

Atherosclerotic renovascular disease (ARVD)

Prevalence:
6–14%^a

Suggestive symptoms, signs and findings

Resistant hypertension
Flash pulmonary edema
Rapidly declining kidney function
Acute renal function degradation on ACEI or ARB
Generalized atherosclerosis^b

1st choice screening test

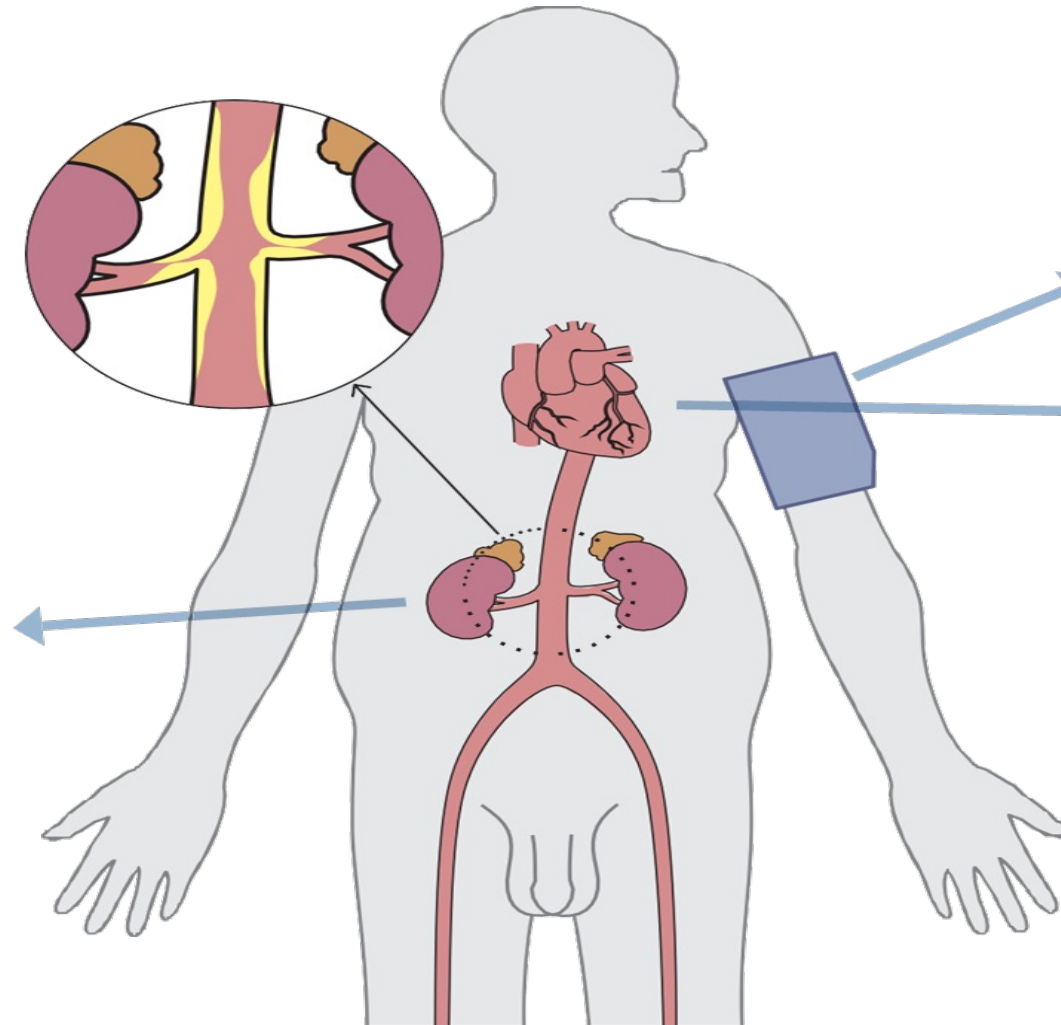
Renal artery duplex ultrasound;
otherwise CT or MR-angiography

Further work-up

Angio-CT or angio-MR
Invasive catheter angiography

Treatment^{c,d}

Antihypertensive treatment
Strict control of CV risk factors
Revascularization (selected cases)



Cardiovascular phenotype

24h ABPM – resistant hypertension,
frequent non-reverse dipping

- LVH
- Decreased diastolic function
- Decreased systolic function

Increased CV Risk and mortality

Fibromuscular Dysplasia (FMD)

Prevalence:
<1 to 6%^a

Suggestive symptoms, signs and findings

Early-onset/ severe hypertension
Migraine
Pulsatile tinnitus

1st choice screening test^b

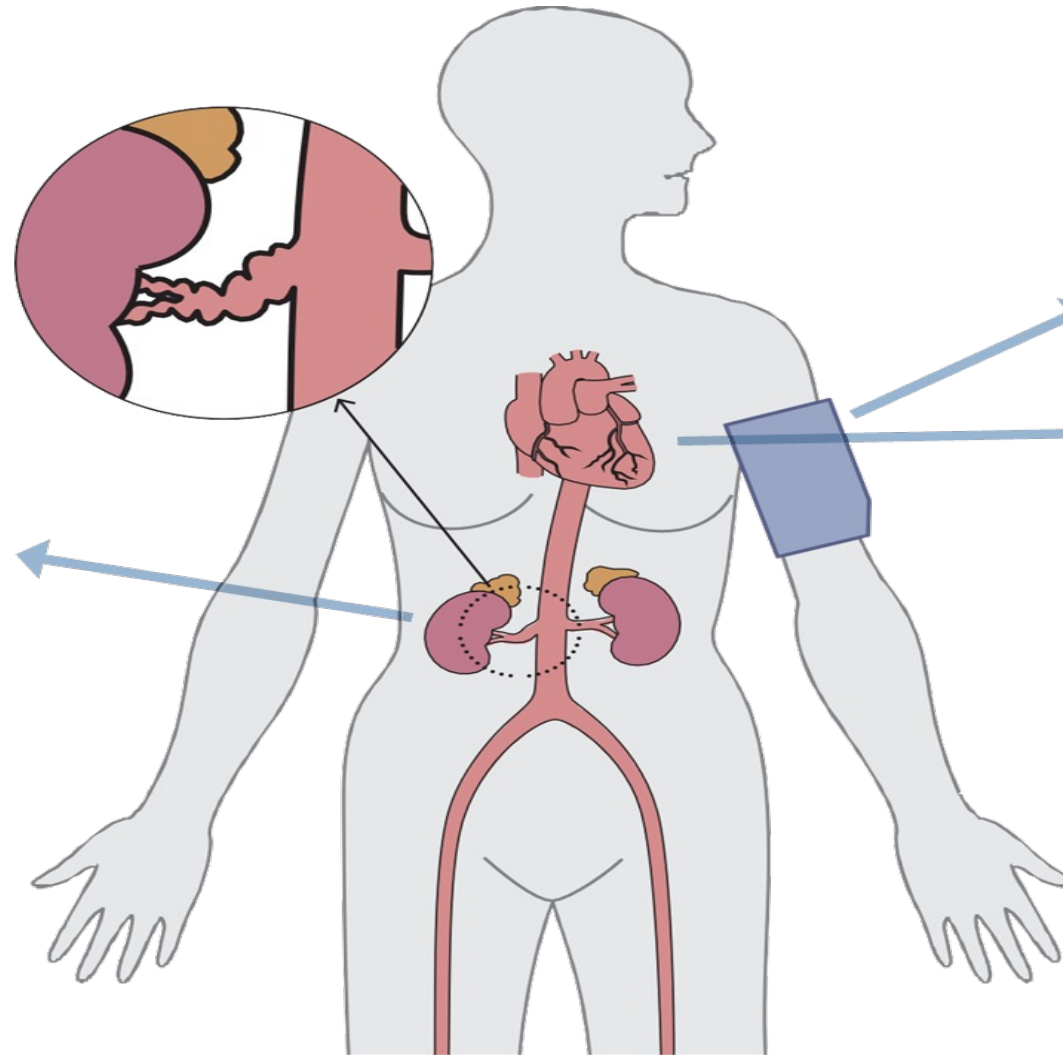
Renal artery duplex ultrasound;
otherwise CT or MR-angiography

Treatment

Antihypertensive treatment
Angioplasty without stenting^{c,d}

Follow-up

- Whole body CT- or MR-angiography at diagnosis^e
- Indefinite follow-up



Cardiovascular phenotype

24h ABPM – early onset or resistant hypertension

Frequent in patients with Spontaneous Coronary Artery Dissection (SCAD)

May affect all medium sized arteries (most frequent: renal and cervical arteries)

Often associated with arterial dissections and aneurysms

Cardiovascular phenotype:
From asymptomatic to resistant hypertension, stroke, renal, mesenteric or myocardial infarction

Primary aldosteronism (PA)

Prevalence:
6–20%^a

Suggestive symptoms, signs and findings

Resistant hypertension
Grade 2 or 3 hypertension
Hypokalemia/Potassium in the low-normal range
Atrial fibrillation
OSA
Adrenal incidentaloma^b
Family history of PA/early stroke

1st choice screening test^c

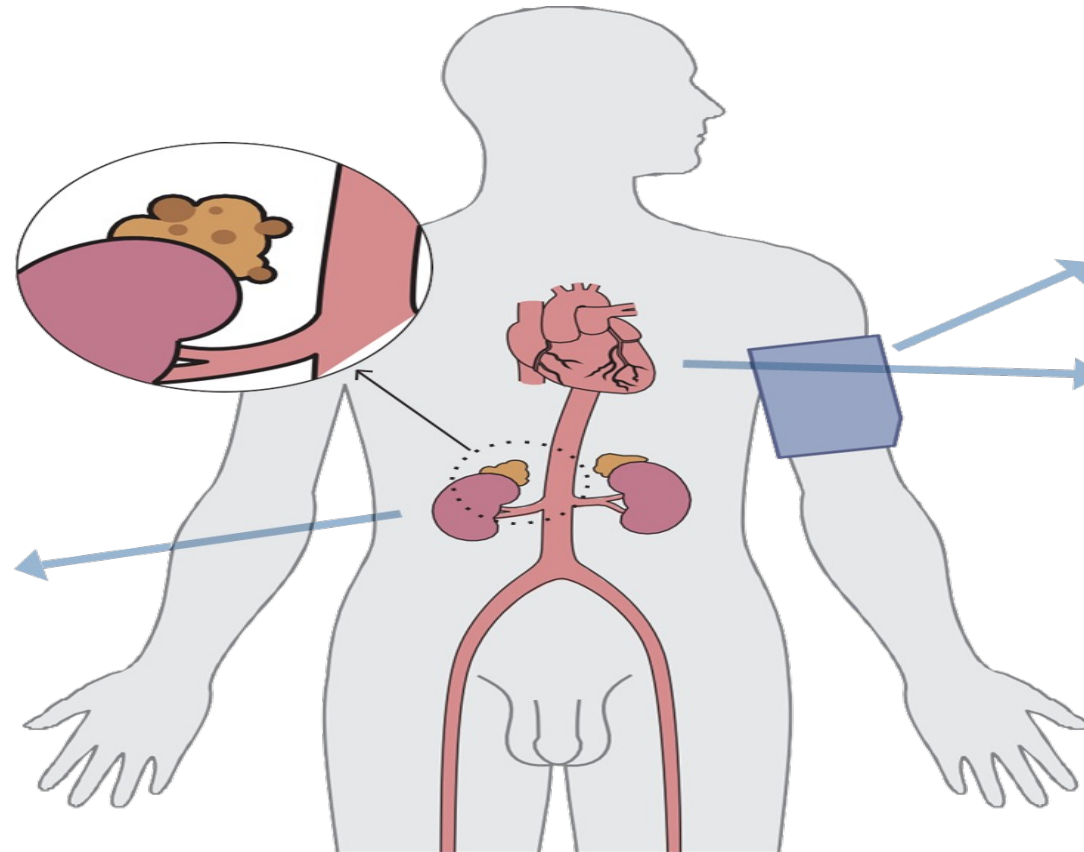
Plasma aldosterone to renin ratio (ARR)

Further work-up^d

CT scanning
IV saline infusion test (SIT)
Fludrocortisone suppression test (FST)
Oral sodium loading test (SLT)
Captopril challenge test (CCT)
Adrenal vein sampling
Genetic testing in selected cases^e

Treatment

Surgical treatment (laparoscopic adrenalectomy) – unilateral PA
Medical treatment – bilateral adrenal disease^f



Cardiovascular phenotype

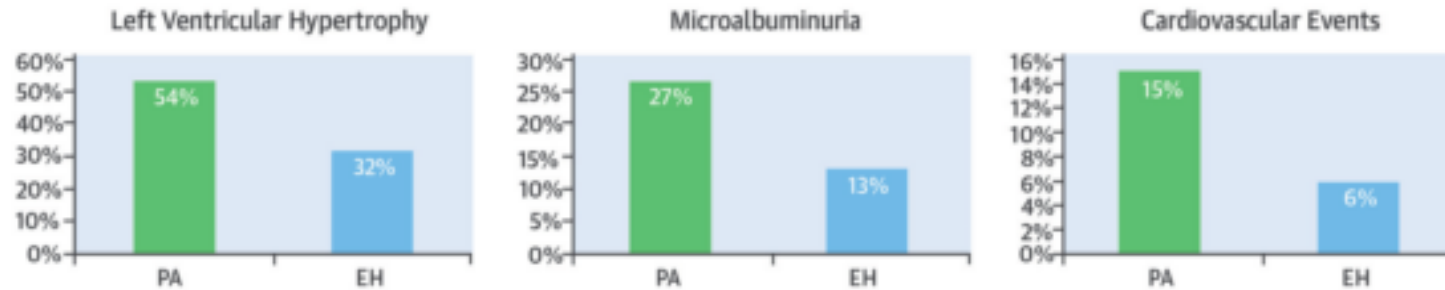
24 ABPM – true resistant hypertension, frequent non-reverse dipping

- LVH
- Decreased diastolic function
- Myocardial fibrosis (MRI)

Increased CV Risk and mortality

L'HTA secondaire, une opportunité !

B. Target Organ Damage and Cardiovascular Events



Monticone, S. et al. J Am Coll Cardiol. 2017;69(14):1811-20.

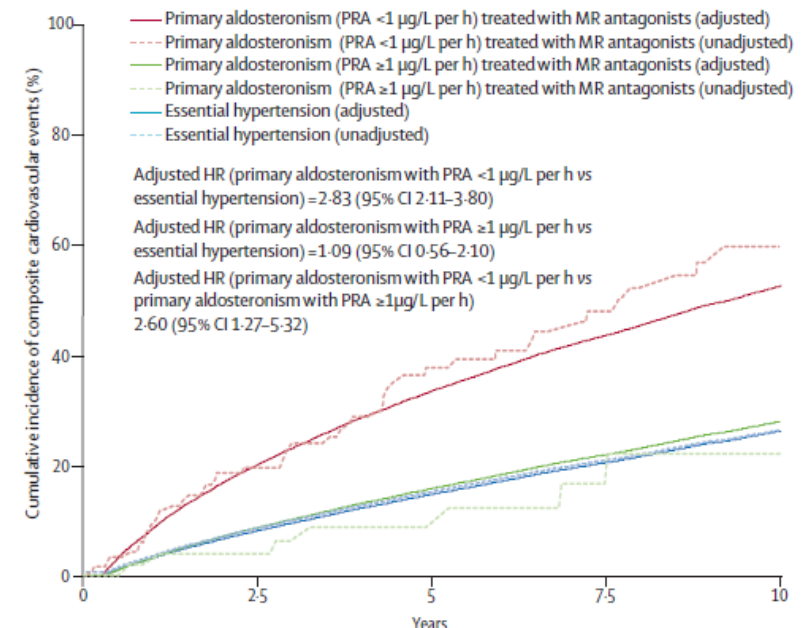
Cardiometabolic outcomes and mortality in medically treated primary aldosteronism: a retrospective cohort study

Gregory L Hundemer, Gary C Curhan, Nicholas Yozamp, Molin Wang, Anand Vaidya



Lancet Diabetes Endocrinol, 2018

**De guérison ou
D'avoir un traitement spécifique !**



L'HTA secondaire, une opportunité manquée !

Original Article

Diagnostic rate of primary aldosteronism in Emilia-Romagna, Northern Italy, during 16 years (2000–2015)

Ermanno Rossi^a, Franco Perazzoli^a, Aurelio Negro^a, and Antonia Magnani^b

Results: A total of 992 patients have been discharged with codes consistent with primary aldosteronism during 16 years in Emilia-Romagna, that is 1.9% of the expected cases of primary aldosteronism. A total of 160 of them underwent adrenalectomy in the same period, which corresponds to 1% of the expected cases of unilateral primary aldosteronism in Emilia-Romagna.

Conclusions: Our results clearly indicate that primary aldosteronism is dramatically underdiagnosed and undertreated.

What are the screening rates for primary aldosteronism among persons with resistant hypertension?

Hypertension

Retrospective cohort



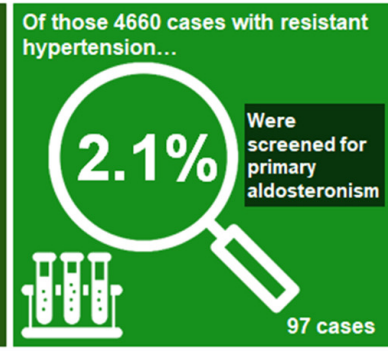
145,670 people with hypertension



Mean age 65 years



51.7% female



Conclusions: This study suggests substantial underscreening for primary aldosteronism, one of the most common causes of secondary hypertension.

Screening Rates for Primary Aldosteronism in Persons with Resistant Hypertension. G Jaffe, Z Gray, G Krishnan, M Stedman, Y Zheng, J Han, G Chertow, J Leppert, V Bhalla.

Hypertension 2021

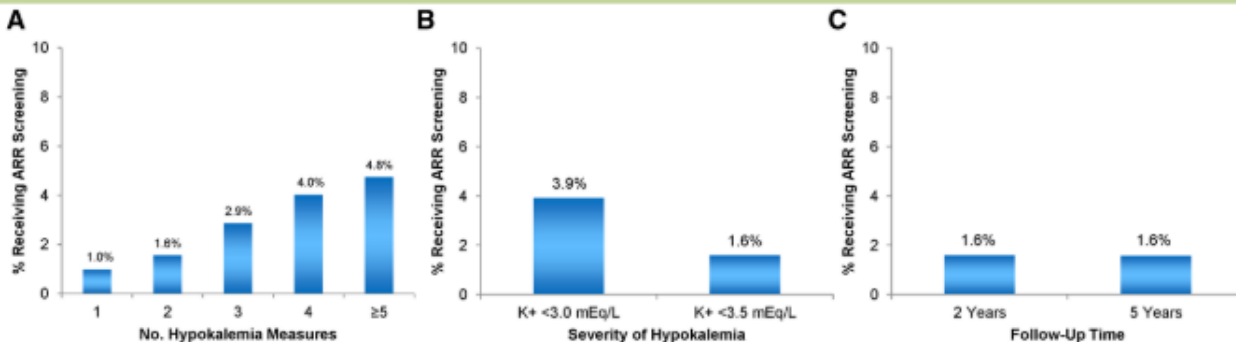
ORIGINAL ARTICLE

Screening Rates for Primary Aldosteronism Among Individuals With Hypertension Plus Hypokalemia

A Population-Based Retrospective Cohort Study

Gregory L. Hundemer^a, Haris Imsirovic^a, Anand Vaidya^a, Nicholas Yozamp, Rémi Goupil^a, François Madore, Mohsen Agharazii, Greg Knoll, Manish M. Sood

Overall Cohort



Que faut il faire ?
Que disent les recommandations

ESH 2023 ?

Mancia, Kreutz et al. Hypertens. 2023;41:1874-2071



Pheochromocytoma and paraganglioma (PPGL)

Prevalence:
<1%^a

Suggestive symptoms and signs^b

- paroxysmal symptoms (such as headache, sweating, palpitation, increased HR)
- large BP variation
- CV manifestations (e.g. MI, arrhythmias, Takotsubo cardiomyopathy)

1st choice screening test

Plasma or urinary free metanephrines

Further work-up

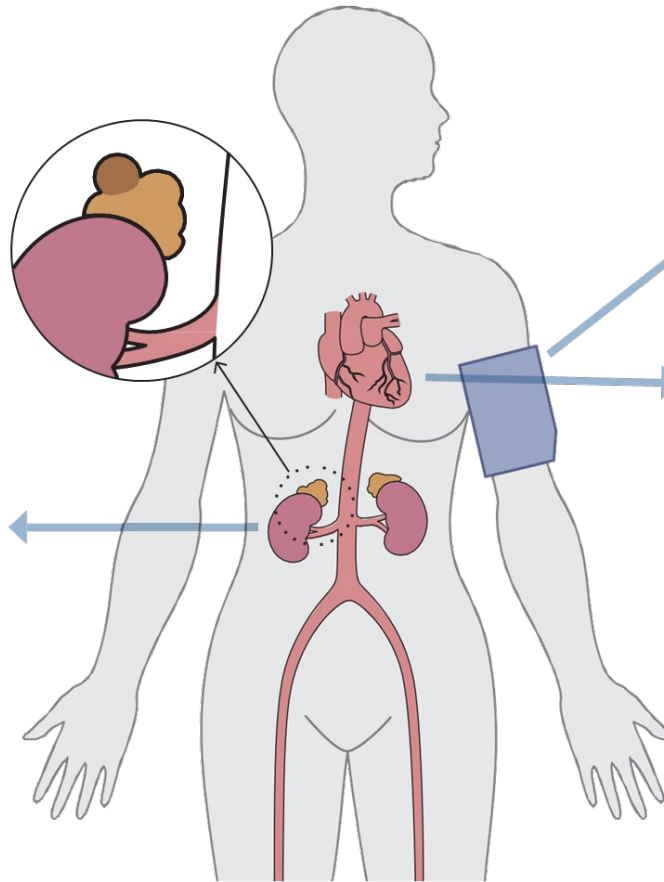
Contrast enhanced CT or MRI
Functional imaging
Genetic testing^c

Treatment^d

Surgical resection
(Pheochromocytoma: minimally invasive laparoscopic adrenalectomy)

Follow-up^e

In most cases > 10 yrs



Cardiovascular phenotype

24h ABPM – frequent non-reverse dipping

- LVH
- Decreased systolic function
- Myocardial fibrosis (MRI)

Increased CV Risk and mortality

Cushing's syndrome

Prevalence:
2–5%^a

Suggestive symptoms and signs

Resistant hypertension
Easy bruising, facial plethora,
'moon' face, skin thinning
Proximal myopathy
Weight gain with centripetal
distribution of body fat
Diabetes mellitus

1st choice screening test^b

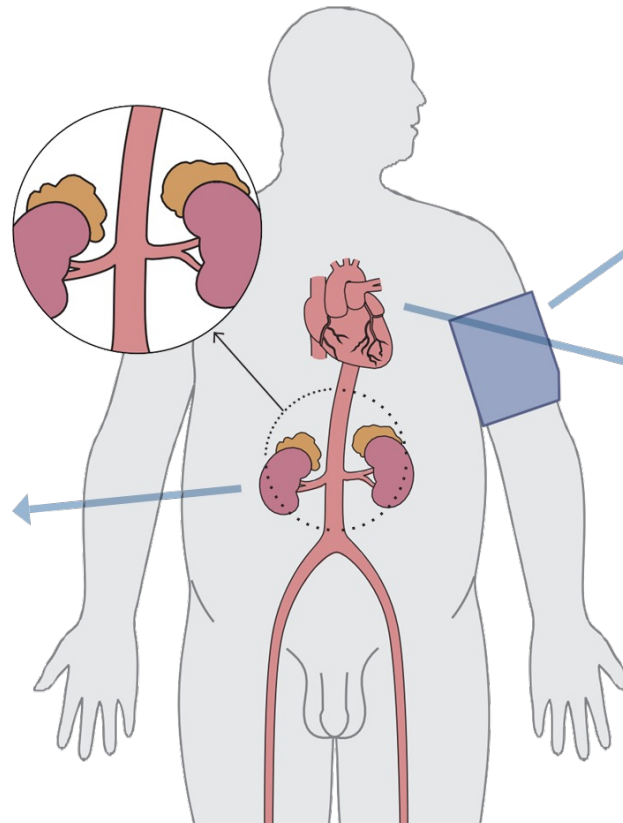
Overnight 1 mg dexamethasone
suppression test
24-h urinary free cortisol
Late-night salivary cortisol

Further work-up

Morning plasma ACTH
ACTH stimulation by CRH
or desmopressin
CT

Treatment

Medical – normalization of cortisol
levels
Surgical – first line treatment for
Cushing's disease, ectopic Cushing's
syndrome and ACTH-independent
hypercortisolism



Cardiovascular phenotype

24h ABPM – frequent non-reverse
dipping
Short-term BP variability

- LVH
- Decreased systolic function
- Decreased diastolic function

Increased CV Risk and mortality

HTA secondaire : que disent les recommandations ?

ESH Guidelines

2023 ESH Guidelines for the management of arterial hypertension *The Task Force for the management of arterial hypertension of the European Society of Hypertension*

Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA)

5. PATIENT WORK-UP

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
- History of or current pregnancy, postmenopausal status and oral contraceptive use or hormonal substitution

Signs of secondary hypertension (Section 6)

- Skin inspection: café-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

QUESTIONNAIRE DU SUJET HYPERTENDU



Ce document prépare la consultation que vous allez avoir au sujet de votre hypertension artérielle. Remplir ce questionnaire prend 20 à 30 minutes. Faites le attentivement à votre domicile pour préparer la consultation avec le médecin. Si besoin, faites vous aider par votre entourage. Cochez la bonne réponse (mettre une croix). Attention, si certaines questions sont difficiles à comprendre, il vaut mieux répondre « je ne sais pas » que de faire une réponse fausse. **N'oubliez pas d'apporter ce questionnaire lors**

BILAN HTA selon OMS : Examens paracliniques 1^{ère} intention

- ECG
- BU : Protéinurie / Hématurie
- Ionogramme sanguin (Kaliémie) → hypokaliémie : Hyperaldostérionisme ?
- Urée / Créatinémie avec clairance
- Glycémie à jeûn
- Bilan lipidique complet (Cholestérol total, HDLc, Triglycéridémie et calcul LDLc)

HTA secondaire : que disent les recommandations ?

“Diagnostic suspicion (Table 13) should prompt immediate referral to specialized hypertension centers where the appropriate diagnostic tests and subsequent treatments can be performed”

TABLE 13. Patient characteristics that should raise the suspicion of secondary hypertension

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
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

HTA secondaire : Quel bilan ?

BILAN HTA selon OMS : Examens paracliniques 1^{ère} intention

- ECG
- BU : Protéinurie / Hématurie
- Ionogramme sanguin (Kaliémie) → hypokaliémie : Hyperaldostéronisme ?
- Urée / Créatinémie avec clairance
- Glycémie à jeûn
- Bilan lipidique complet (Cholestérol total, HDLc, Triglycéridémie et calcul LDLc)

• Bilan biologique

- Aldostérone, rénine en condition standardisée :
 - Stop traitement interférant 2 à 6 semaines avant
 - Normokaliémie, consommation normosodée
 - Allongée ou assis depuis au moins 30 minutes
- Test dynamique (freination sodée)
- PTH, TSH, métanéphrines plasmatique

• Bilan urinaire des 24h

- Protéinurie, créatininurie
- Natriurèse
- Cortisol libre urinaire
- Sédiment urinaire
- ECBU

• Bilan morphologique

- Echodoppler des artères rénales
- TDM des surrénales +/- angioscanner des artères rénales

• (Polygraphie du sommeil)

• Test de freinage minute DXM

HTA secondaire : que disent les recommandations ?

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

Condition	Phenotype	Mechanism and Treatment
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 11 β -hydroxysteroid dehydrogenase isoenzyme 2; responds to spironolactone
Gordon syndrome	Hyperkalemia, 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 <i>CYP11B1/CYP11B2</i> 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 11 β -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 17 α -hydroxylase with increase of DOC and reduction of androgens; responds to glucocorticoids
Autosomal dominant hypertension with brachydactyly [342]	Brachydactyly type E (BDE), short stature, severe hypertension (salt-independent, age-dependent), high risk of death from stroke before age 50	PDE3A mutations upregulated the cAMP-hydrolytic activity that results in lower cAMP levels in vascular smooth muscle cells

Conclusion



Les HTA secondaires, c'est

- **Fréquent**
 - 6-10% de tous les hypertendus au moins
- **Grave**
 - Sur-risque cardiovasculaire et de mortalité net
- **Curable ou accessible à un traitement spécifique**

Mais largement sous diagnostiquée !

Il est temps de changer nos habitudes !

1/ Sécuriser la mesure

2/ Dépister d'emblée les causes secondaires

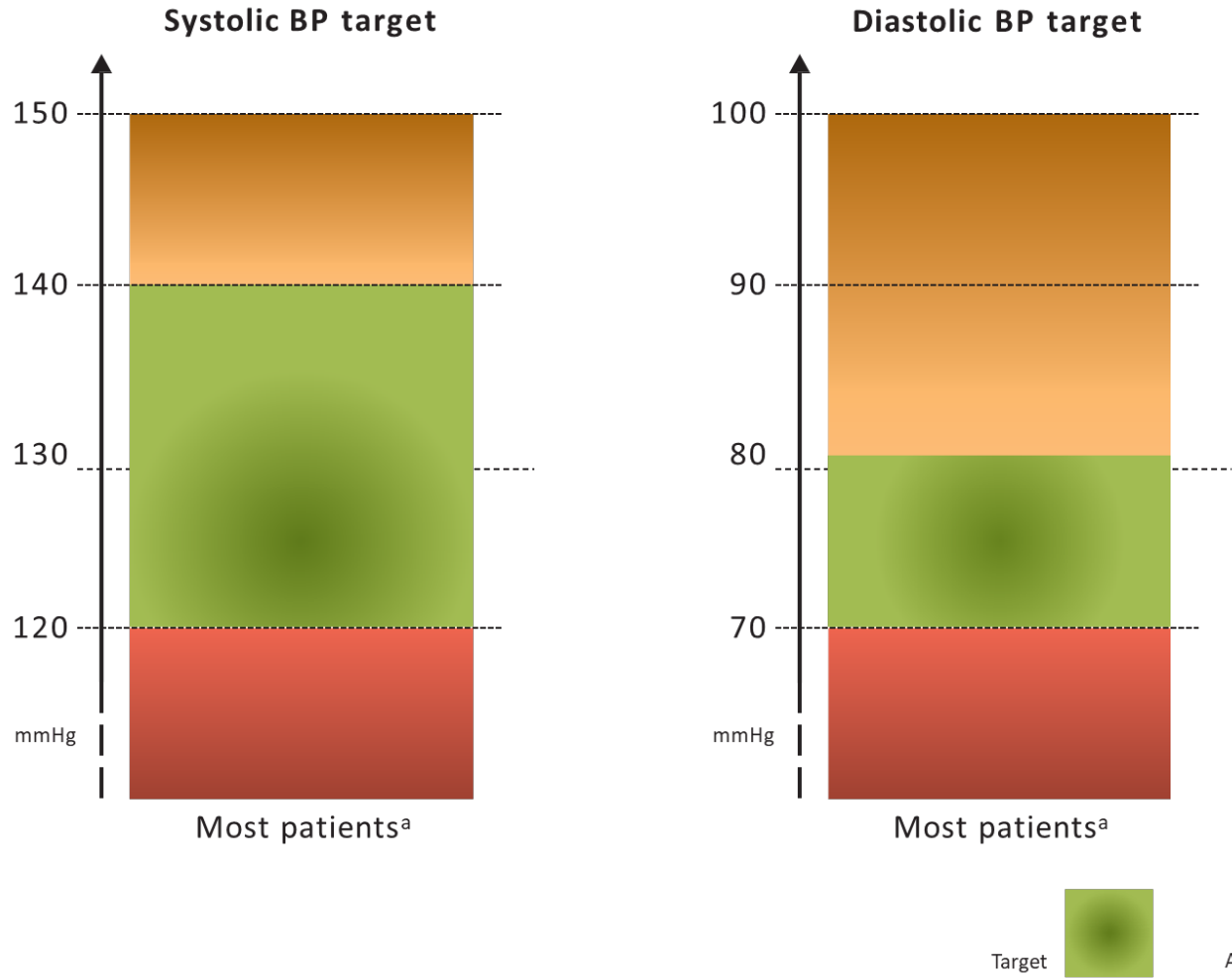
3/ Titrer rapidement la thérapeutique

4/ Adresser les patients sélectionnés

- atul.pathak@chpg.mc
- Bilan HTA
- Denervation
- Protocole
- Nouveaux traitements
- Gestion EI / adherence
- Avec retour aux correspondants !



Office BP targets in the general adult hypertensive population



Drug classes for BP-lowering therapy

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**



T/TL Diuretic^a

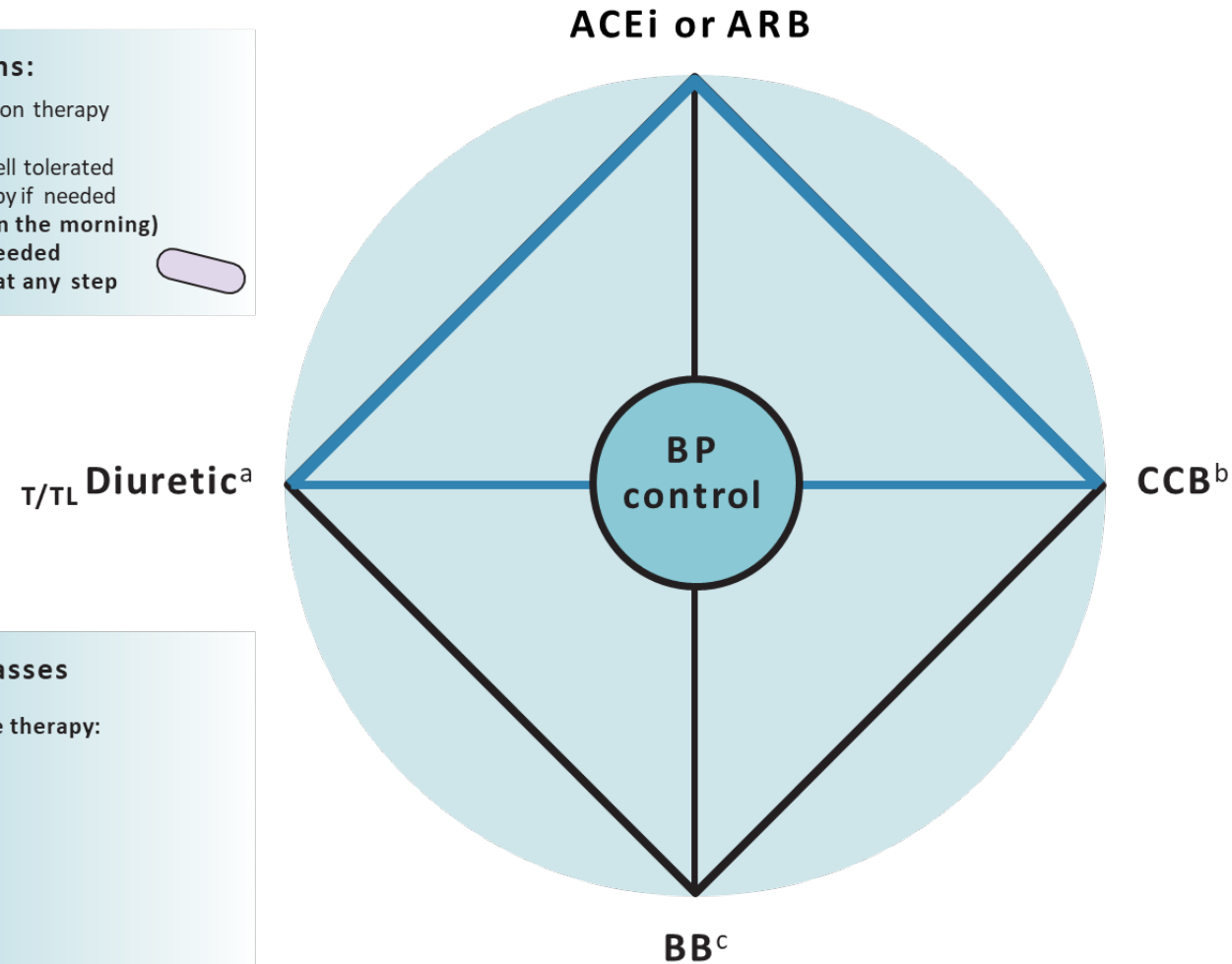
Additional drug classes

General antihypertensive therapy:

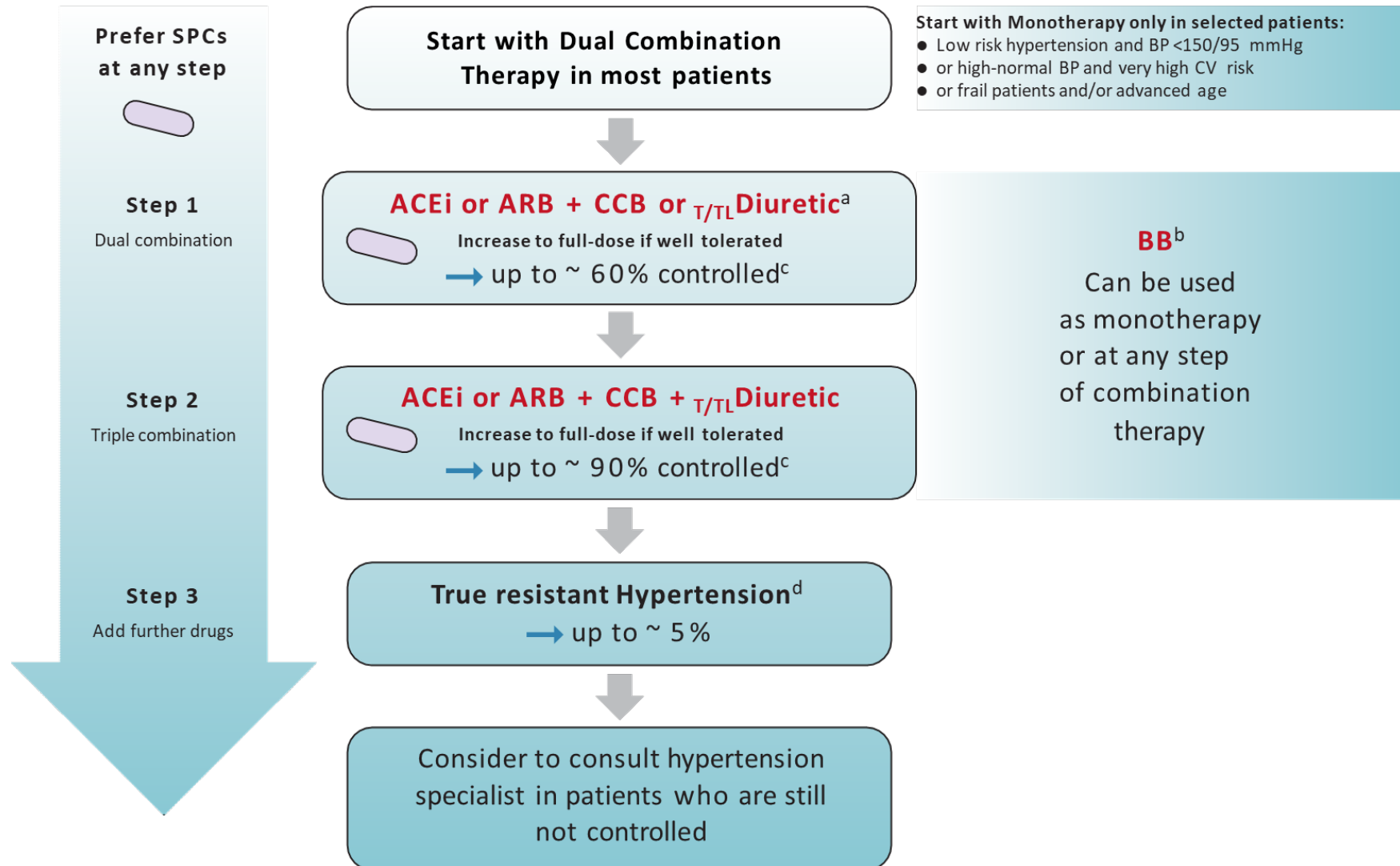
- Steroidal MRA
- Loop Diuretic
- Alpha-1 Blocker
- Centrally acting agent
- Vasodilator

Special comorbidities:

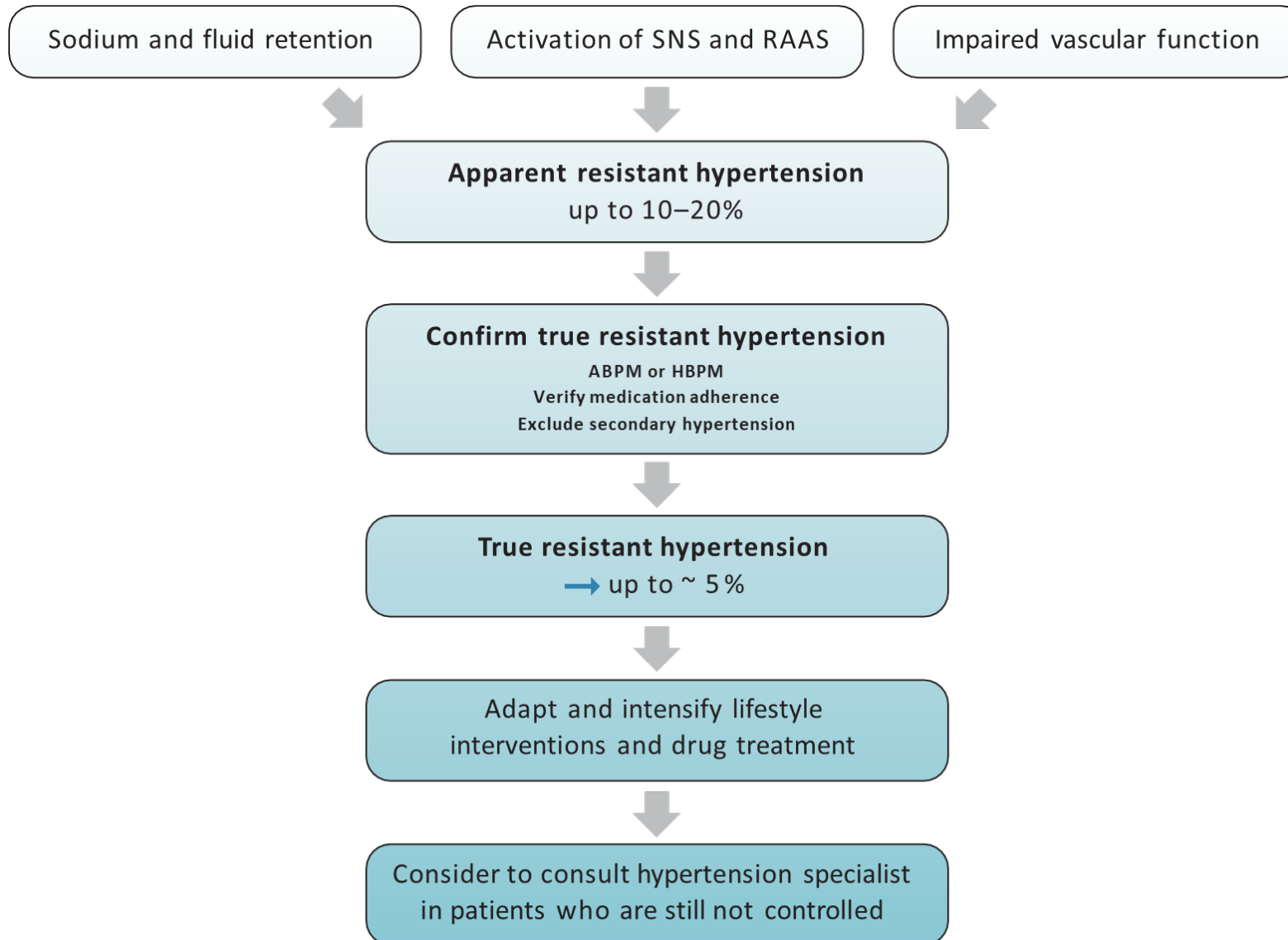
- ARNi
- SGLT2i
- Non-Steroidal MRA



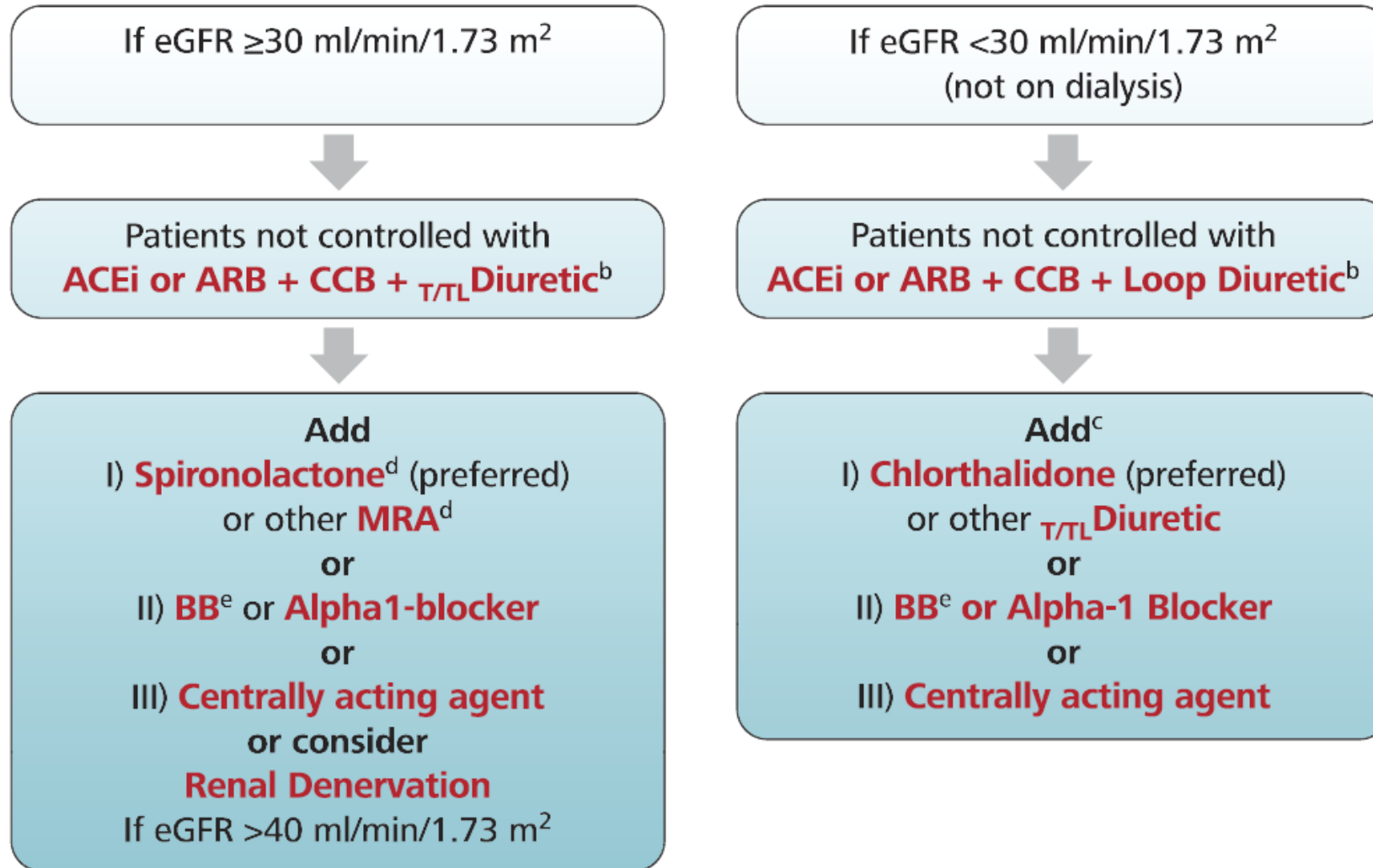
General BP-lowering strategy in patients with hypertension



Characteristics of true resistant hypertension



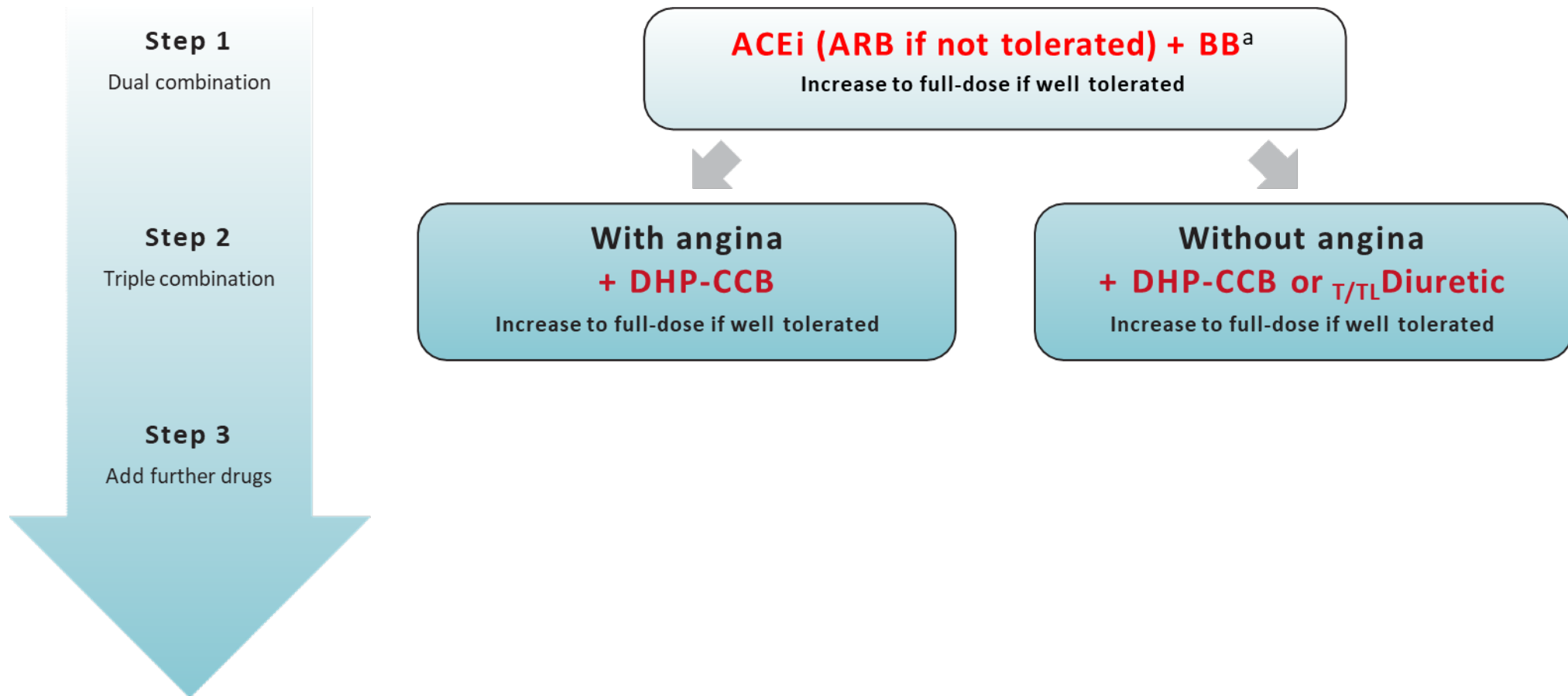
BP-lowering strategy in true resistant hypertension



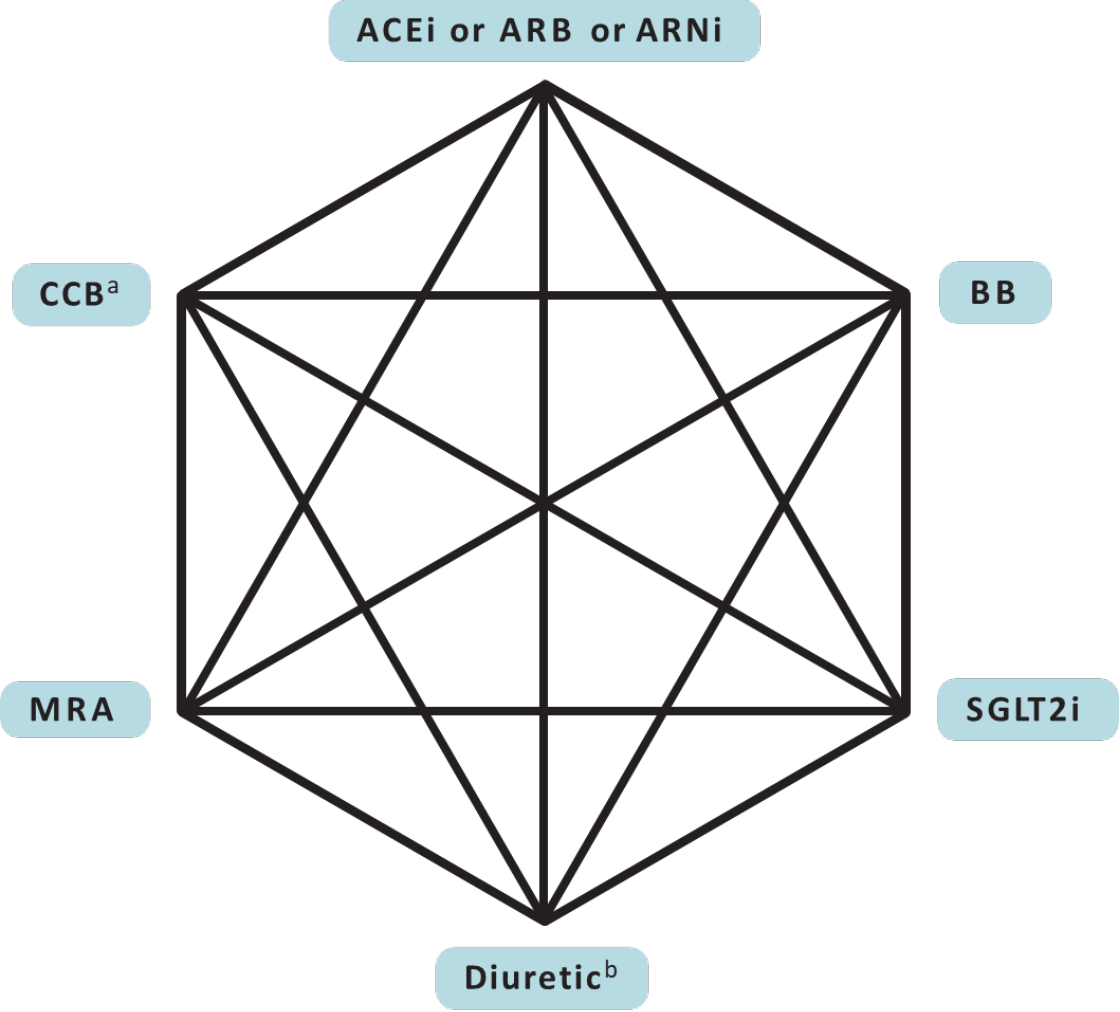
Use of renal denervation

Recommendations and statements	CoR	LoE
RDN can be considered as a treatment option in patients with an eGFR >40 ml/min/1.73m ² who have uncontrolled BP despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life.	II	B
RDN can be considered as an additional treatment option in patients with true resistant hypertension if eGFR is >40 ml/min/1.73m ² .	II	B
Selection of patients to whom RDN is offered should be done in a shared decision-making process after objective and complete patient's information.	I	C
RDN should only be performed in experienced specialized centers to guarantee appropriate selection of eligible patients and completeness of the denervation procedure.	I	C

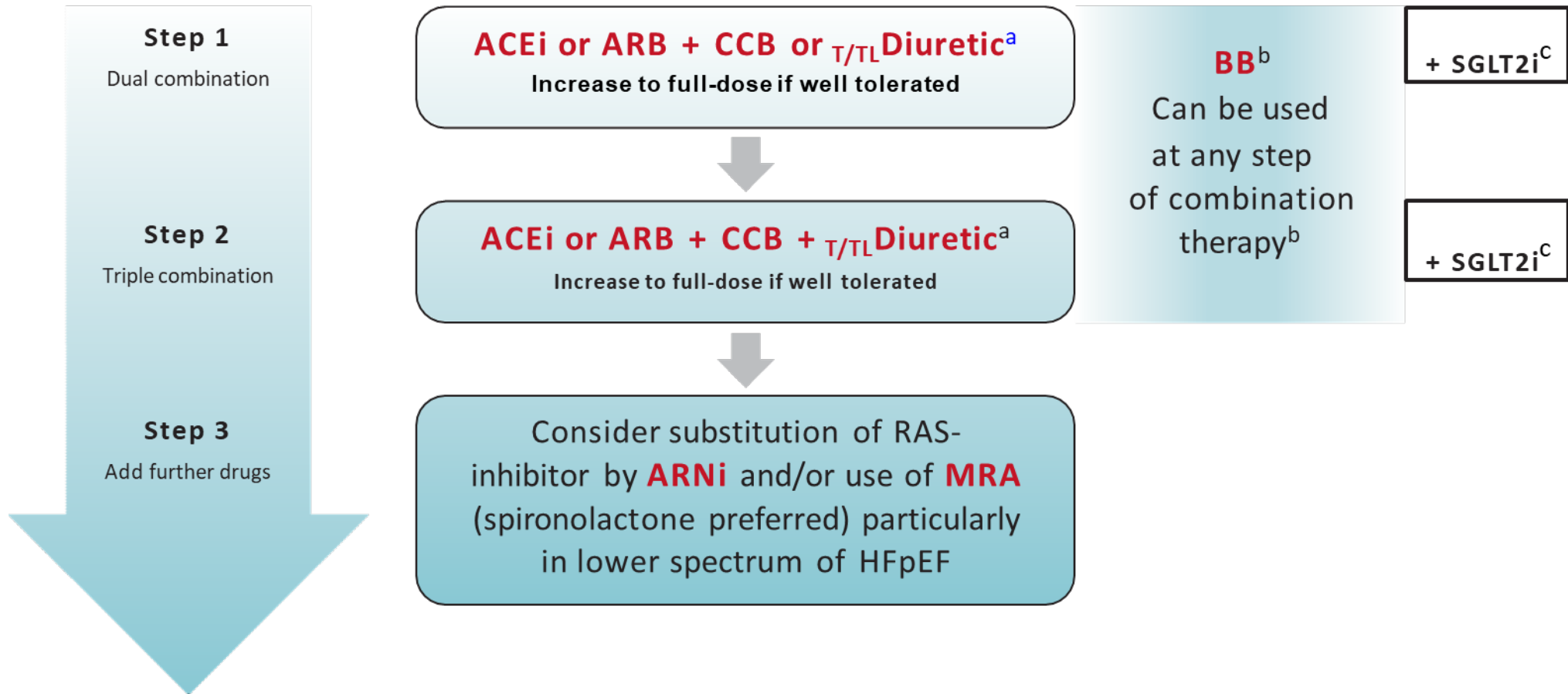
BP-lowering in hypertension and CAD



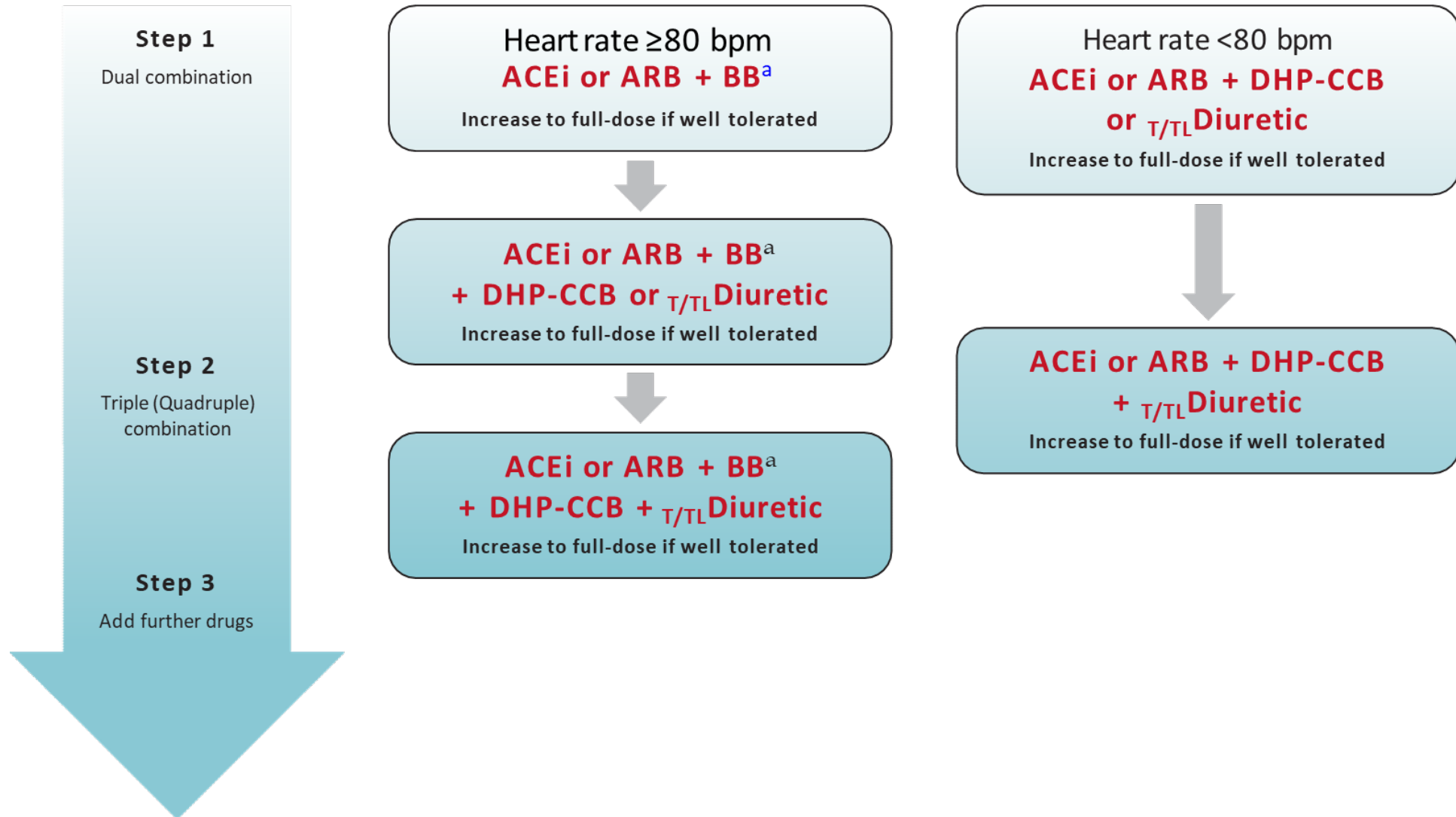
BP-lowering drugs in hypertension and heart failure



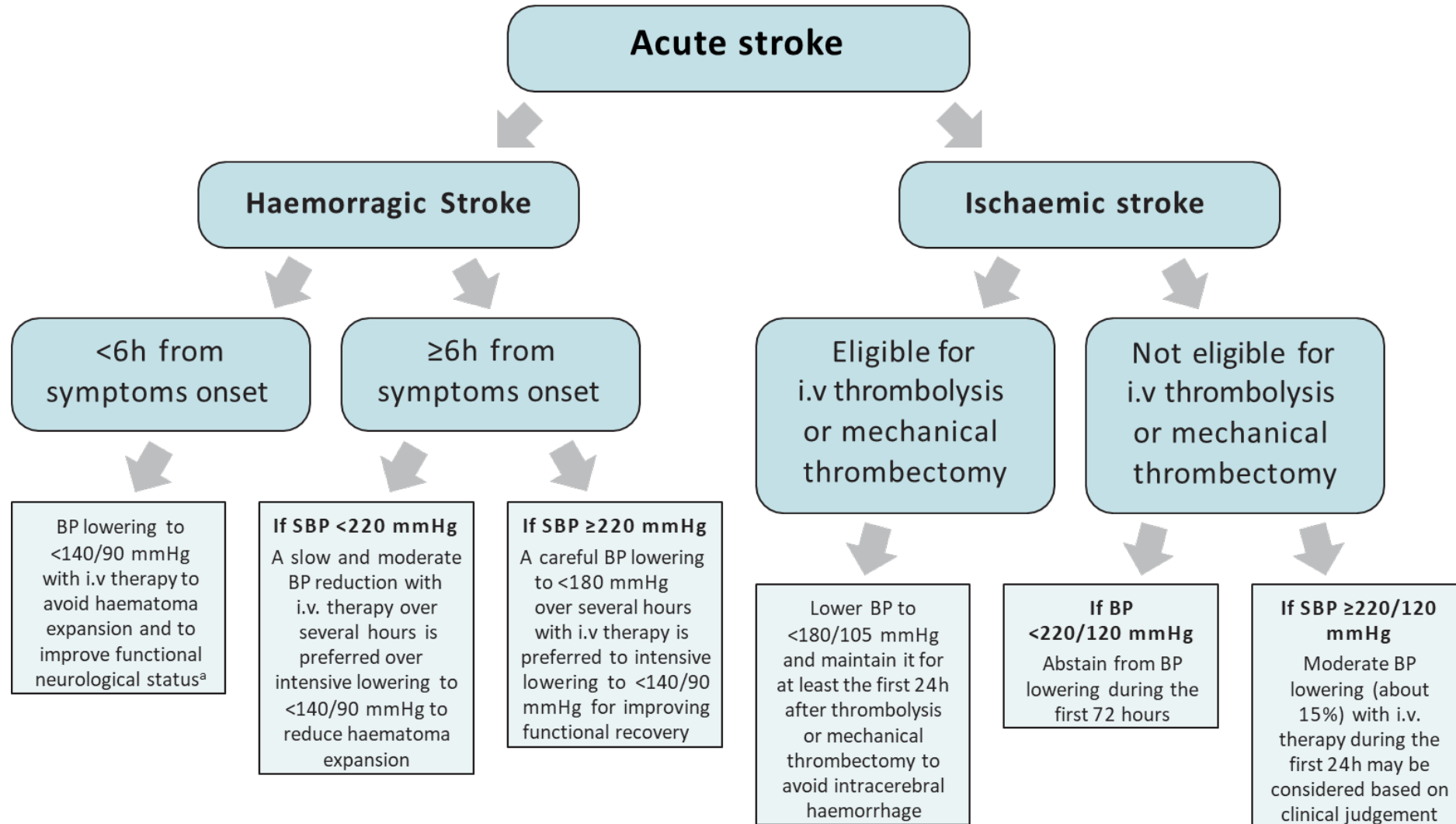
BP-lowering therapy in hypertension and HFpEF



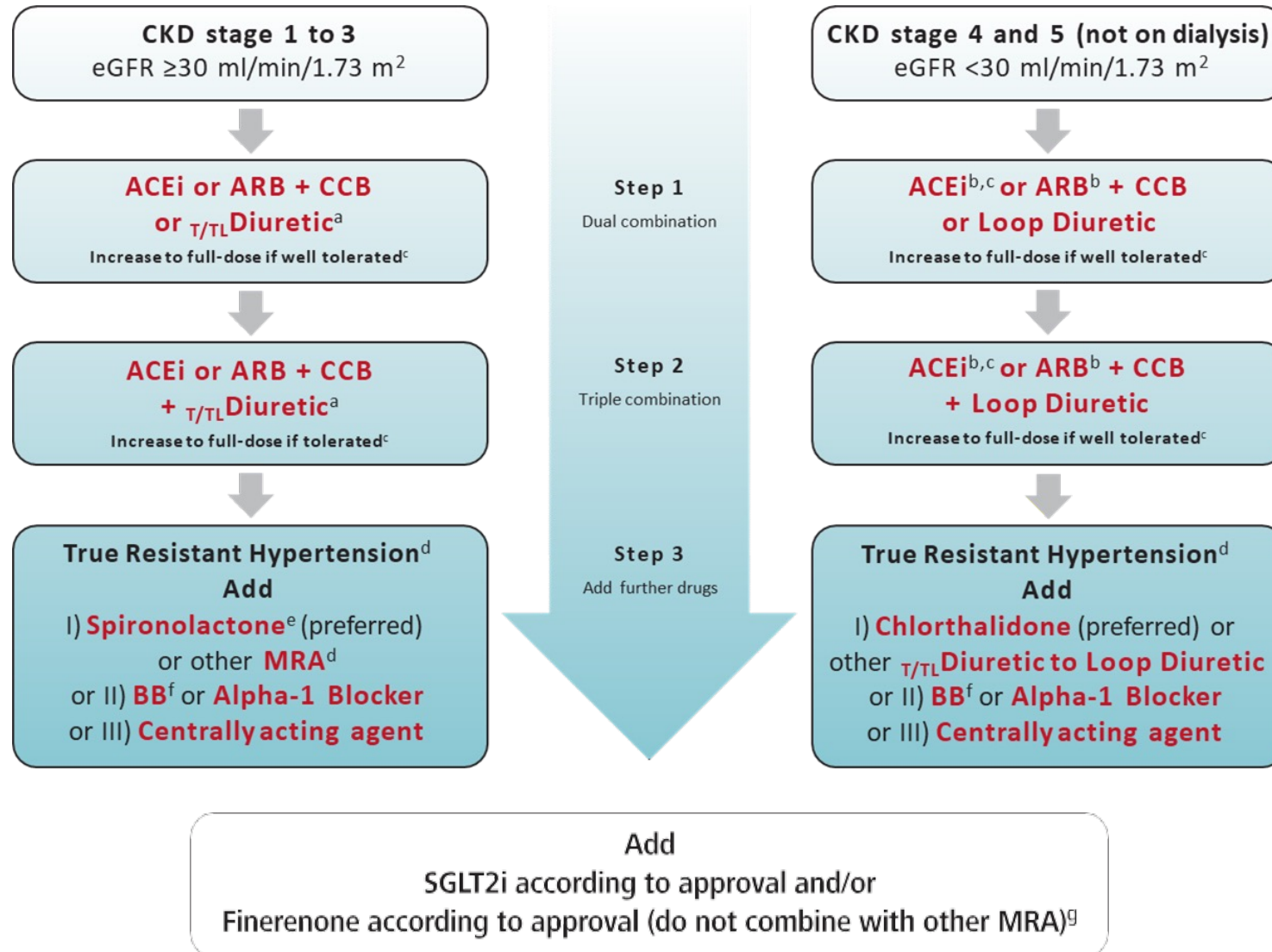
BP-lowering therapy in hypertension and atrial fibrillation



BP management in acute stroke



BP-lowering in patients with hypertension and chronic kidney disease



Dual endothelin antagonist



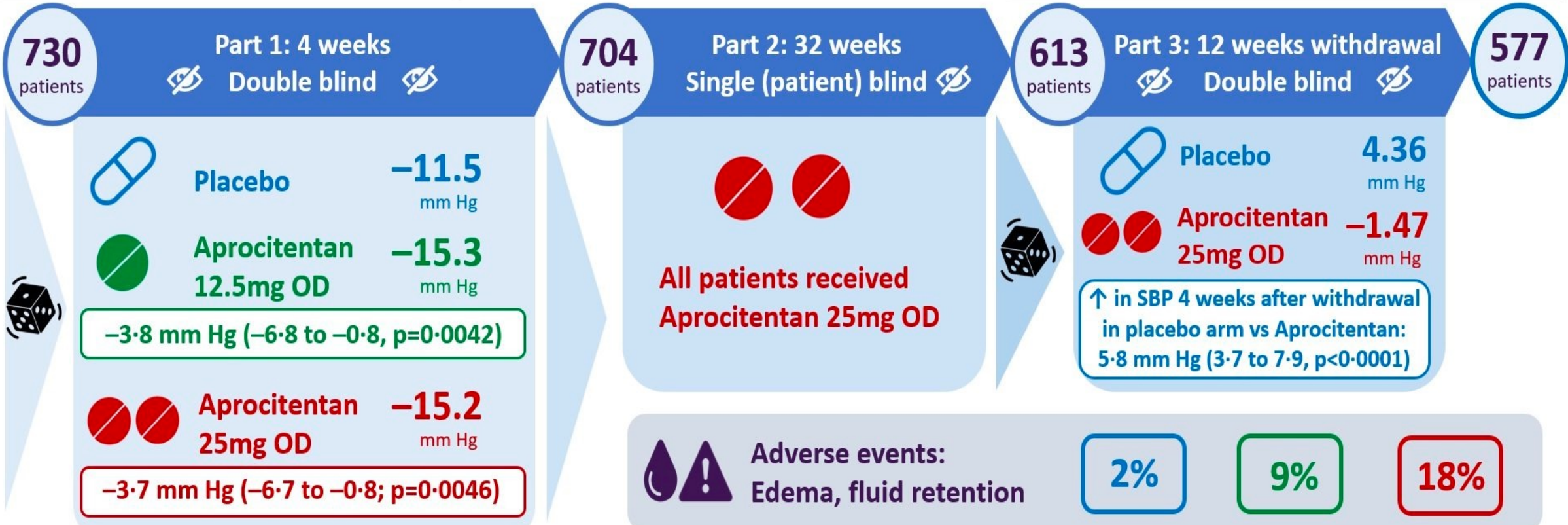
Multicenter – N. America, Europe, Asia, Australia



Systolic BP \geq 140/90 on 3 antihypertensives (including diuretic)

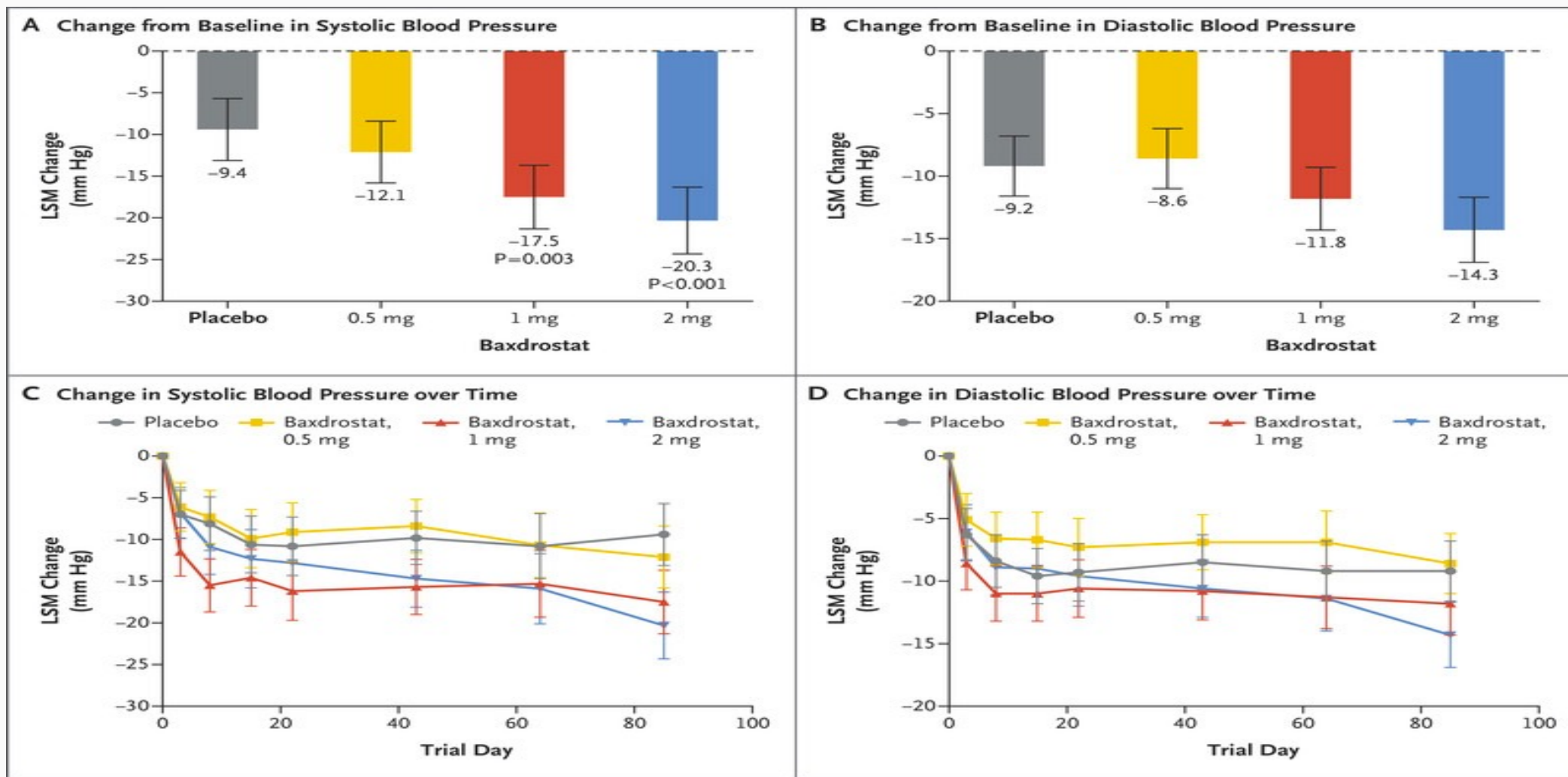


Primary end point: Least square mean change in office SBP from baseline to week 4 and from withdrawal to week 40

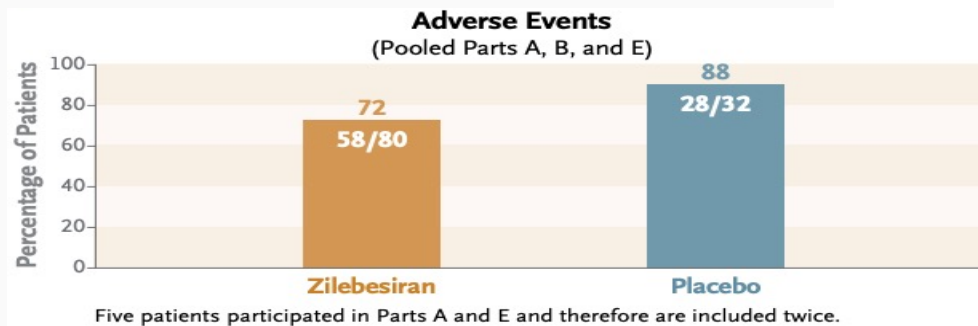
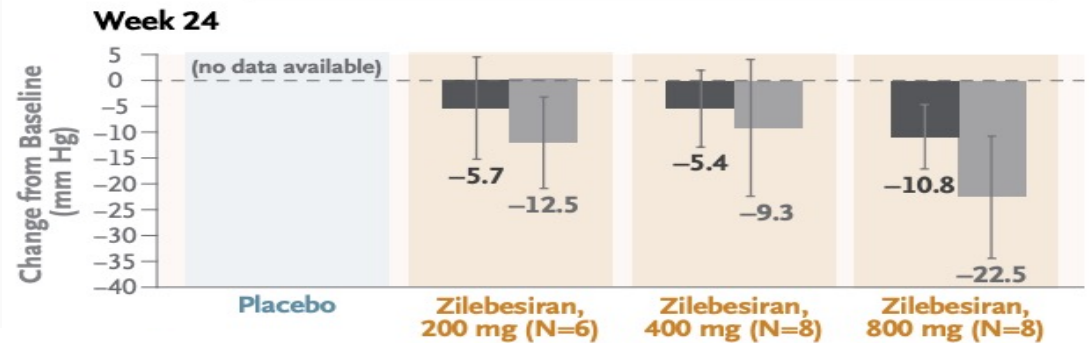
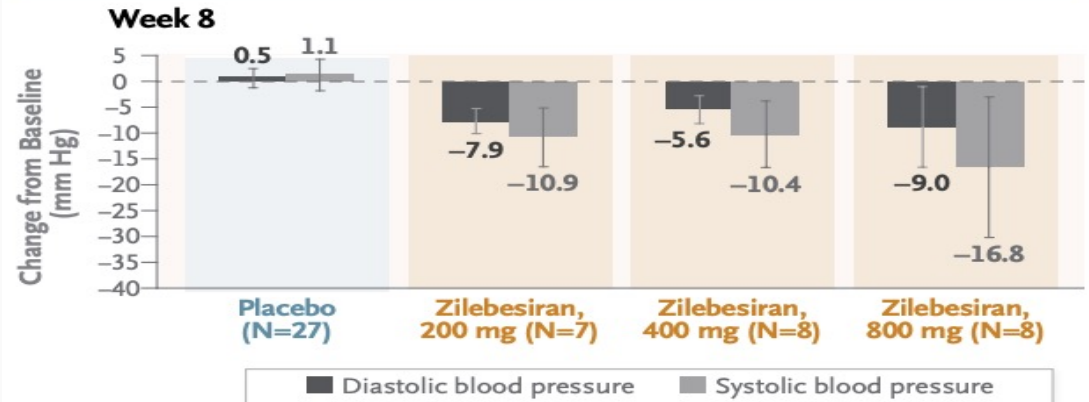
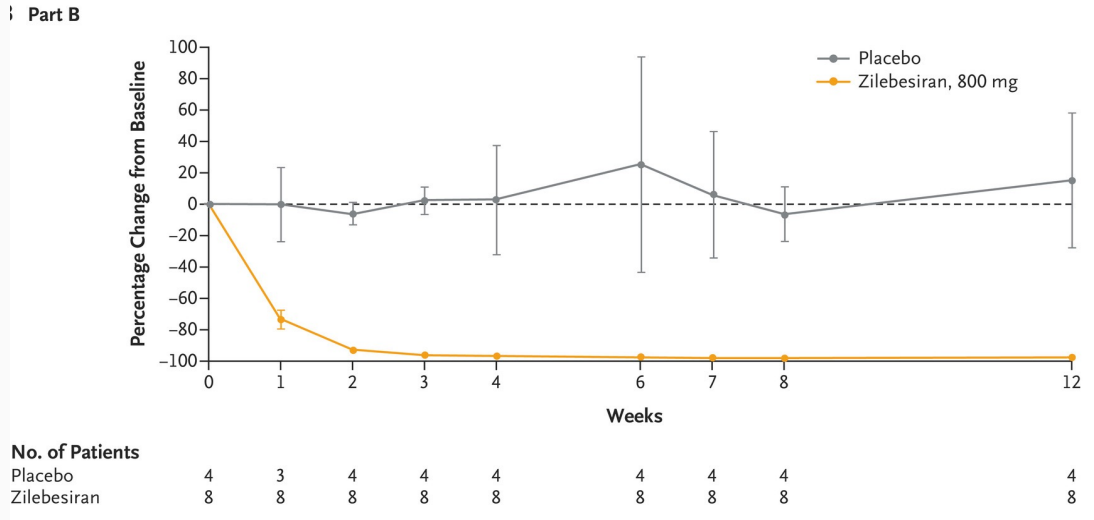


VA created by Sandhya Suresh @sandyrvsdav

Aldosterone synthase inhibitor



Zilebesiran, an RNA Interference Therapeutic Agent for Hypertension



Come back de l'HTA

- Evaluation
- Importance HTA secondaire
- Prise en charge therapeutique
- Innovations
- RDV en septembre : reco ESC 2024 !