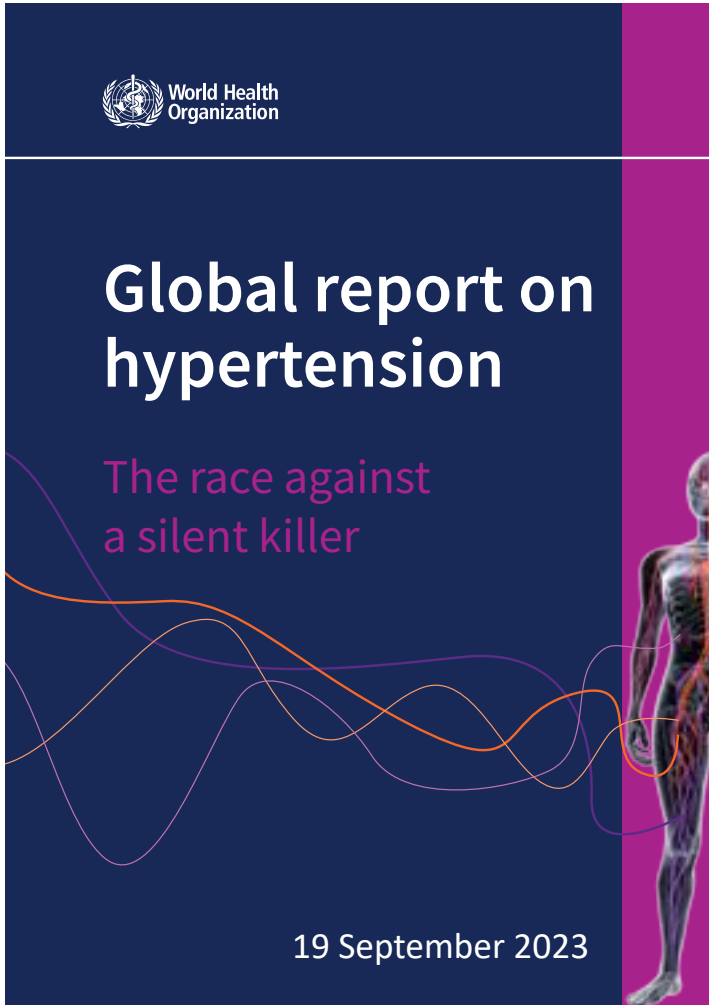
¿Qué hay de nuevo en Hipertensión Arterial?

15 de noviembre 2024

Junta de Castilla y León
Consejería de Sanidad

Sacyl

Complejo Asistencial Universitario de León



- La HTA afecta a uno de cada tres adultos en el mundo.

- "The number of people living with hypertension (blood pressure of ≥140 mmHg systolic or ≥90 mmHg diastolic or on medication) doubled between 1990 and 2019, from 650 million to 1.3 billion"

- Cuatro de cada cinco HTA no reciben un tto adecuado

Table 2. Age-standardized prevalence of hypertension among adults aged 30–79 years, and among those with hypertension, diagnosis, treatment and effective treatment coverage in 2019, by WHO region

Region	Hypertension (%)	Diagnosis coverage (%)	Treatment coverage (%)	Effective treatment coverage[a] (%)
African	36 (38, 33)	43 (46, 39)	27 (30, 24)	12 (14, 9)
The Americas	35 (38, 33)	70 (73, 67)	60 (64, 57)	36 (41, 32)
South-East Asia	32 (36, 29)	39 (44, 34)	30 (34, 25)	14 (18, 10)
European	37 (39, 35)	66 (69, 63)	53 (56, 50)	26 (29, 23)
Eastern Mediterranean	38 (41, 35)	49 (53, 45)	39 (43, 34)	15 (19, 13)
Western Pacific	28 (32, 25)	54 (59, 48)	41 (47, 35)	18 (23, 14)
Global	33 (35, 32)	54 (56, 51)	42 (45, 40)	21 (23, 19)

«Cada hora, más de 1000 personas mueren de accidentes CV e IAM. Muchas de estas muertes se deben a la HTA, y la mayoría podrían haberse evitado»

World Health Organization

PROGRAMA HEARTS: Technical package for cardiovascular disease management in primary health care: Risk-based CVD management

Tto con fármacos genéricos seguros, ampliamente disponibles y de bajo costo.

Si los países logran ampliar la cobertura, podrían evitarse 76 millones de muertes entre 2023 y 2050.

MODULES OF THE HEARTS TECHNICAL PACKAGE

Module	What does it include?	Who are the target users?		
		National	Subnational	Primary care
Healthy-lifestyle counselling	Information on the four behavioural risk factors for CVD is provided. Brief interventions are described as an approach to providing counselling on risk factors and encouraging people to have healthy lifestyles.		✓	✓
Evidence-based protocols	A collection of protocols to standardize a clinical approach to the management of hypertension and diabetes.	✓	✓	✓
Access to essential medicines and technology	Information on CVD medicine and technology procurement, quantification, distribution, management and handling of supplies at facility level.	✓	✓	✓
Risk-based CVD management	**Information on a total risk approach to the assessment and management of CVD, including country-specific risk charts.**	✓	✓	✓
Team-based care	Guidance and examples on team-based care and task shifting related to the care of CVD. Some training materials are also provided.		✓	✓
Systems for monitoring	Information on how to monitor and report on the prevention and management of CVD. Contains standardized indicators and data-collection tools.	✓	✓	✓

Spain

Hypertension profile

Total population (2019): 47 131 000

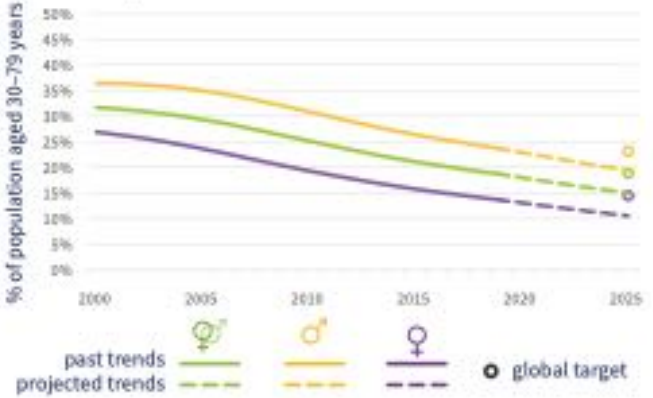
Total deaths (2019): 427 000

Age-standardized prevalence of hypertension among adults aged 30–79 years (2019)[a] ♂♀ 27% ♂ 34% ♀ 21%

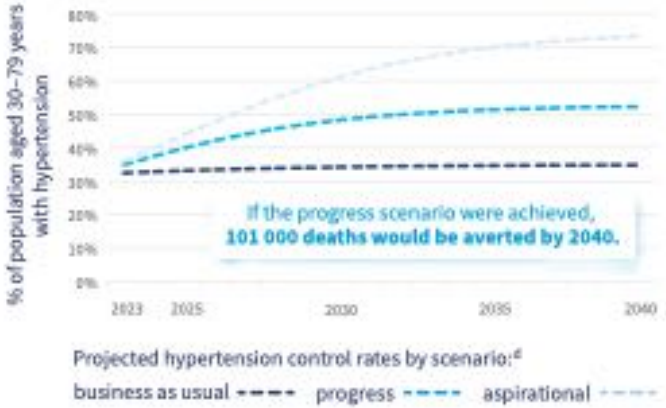
Prevalence of hypertension – global comparison (both sexes)[a]

Of the **9.9 million** adults aged 30–79 years with hypertension:

Trends in uncontrolled hypertension in adults aged 30–79 years[c]



Hypertension control rate scenarios



World Health Organization

Mortality	both sexes	males	females	year
Probability of premature mortality from NCDs (%)	10	13	6	2019
Cardiovascular disease deaths	118 000	55 100	62 800	2019
Cardiovascular disease deaths attributable to high systolic blood pressure (%)	47	49	46	2019

Risk factors[e]	both sexes	males	females	year
Mean population salt intake, adults aged 25+ years (g/day)	8	9	7	2019
Current tobacco use, adults aged 15+ years (%)[f]	28	29	27	2019
Obesity, adults aged 18+ years (%)	24	25	23	2016
Total alcohol per capita consumption, adults aged 15+ years (litres)	11	17	5	2019
Physical inactivity, adults aged 18+ years (%)	27	23	31	2016

National response

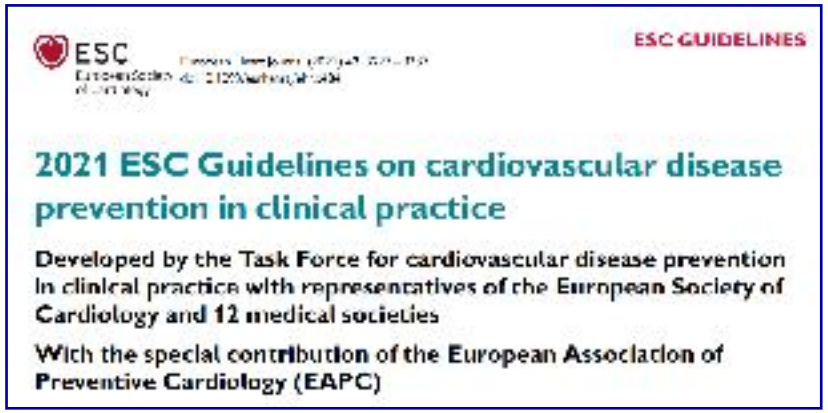
Targets		Treatment	
National target for blood pressure	✖	Guidelines for management of hypertension	✔
National target for salt consumption	✖		

Surveillance

Conducted recent, national survey measuring raised blood pressure/hypertension	✔
Conducted recent, national survey on salt/sodium intake	✖
Functioning system for generating reliable cause-specific mortality data on a routine basis	✔

Footnotes: a. SBP ≥140 mmHg or DBP ≥90 mmHg or taking medication for hypertension. b. Control rate: adults aged 30–79 years receiving treatment, with blood pressure SBP <140 mmHg and DBP <90 mmHg. c. SBP ≥140 mmHg or DBP ≥90 mmHg. d. Progress and aspirational scenarios reflect a theoretical scaling up of treatment and control. e. Age-standardized estimates are presented for all indicators except salt intake. f. Data refer to tobacco smoking only, in the absence of sufficient data on all tobacco use.

Guías…



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)

Practice Guidelines

2024 European Society of Hypertension clinical practice guidelines for the management of arterial hypertension

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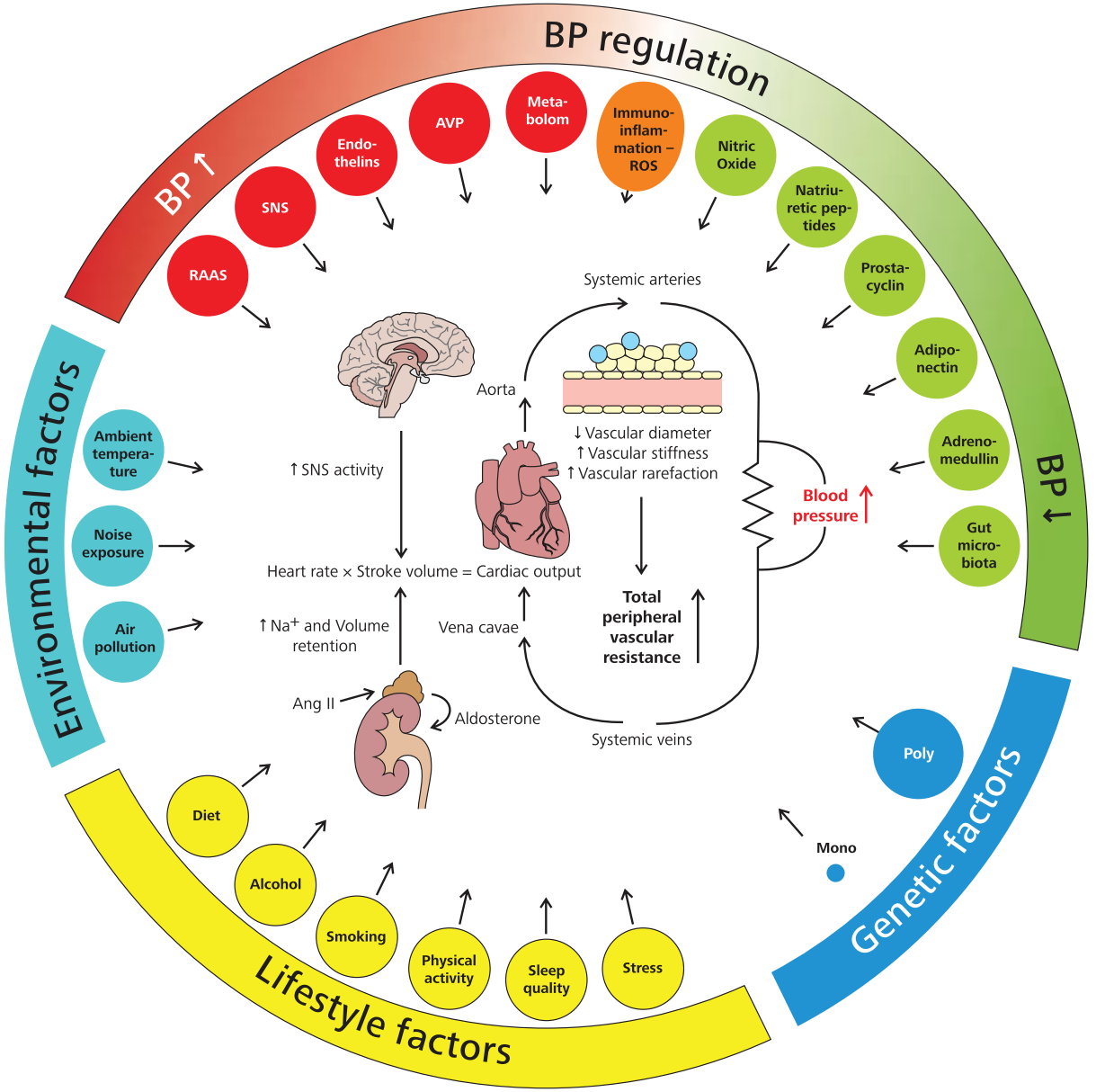
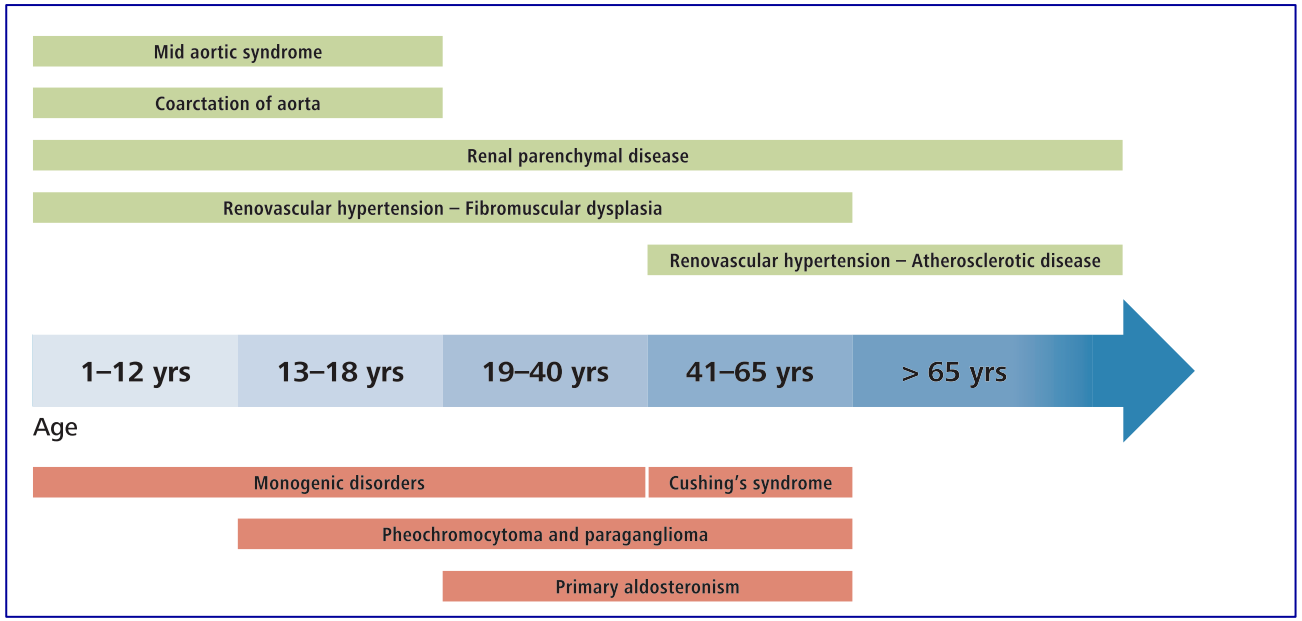
Hipertensión Primaria



HTA Secundaria

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 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



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MASTERplan

Measure Blood Pressure - Diagnose

In Office

Office BP measurement (OBPM)

*SBP ≥140
and/or
DBP ≥90

Conditions

1. Use validated automated electronic upper-arm cuff device[a] (www.stridebp.org).
2. Select appropriate cuff to fit arm size according to instructions by device manufacturer[b].
3. Quiet room with comfortable temperature.
4. No smoking, caffeine, food, or exercise 30 min before measurement.
5. Start measurement after patient remained seated and relaxed for 3-5 min[c].
6. No talking during and between measurements.

Posture

7. Sitting with back supported on chair.
8. Legs uncrossed, feet flat on floor.
9. Bare arm resting on table with mid-arm at heart level.

Measurement

10. Take 3 readings with 1 min intervals between them. Use the average of the last 2 readings for BP and also for pulse rate[d].

Relevance

- Was used in outcome trials and provides the basis for diagnosis and BP targets.

Out-of-office

Home BP monitoring (HBPM)

*SBP ≥135
and/or
DBP ≥85

Conditions and Posture

1.-9. From OBPM apply also to HBPM.

Measurement

10. Propose a standardized protocol to the patient:
    - Educate the patient on how to use a validated device and report the data.
    - Take 2 readings with 1 min intervals between them.
    - Measure in the morning and the evening (before drug intake if treated).
    - Measure for 3–7 days before office visits.
    -Use the average of all readings excluding the first day for both BP and pulse rate.
11. For long-term follow-up of treated hypertension, make duplicate measurements once or twice per week or month.

Relevance

- Recommended for long-term follow-up of treated hypertension, because it improves BP control, especially when combined with education and counseling.
- Confirmation of hypertension diagnosis and of true resistant hypertension, particularly if ABPM is not available.

Ambulatory BP monitoring (ABPM)

*24-h mean BP:
SBP ≥130
and/or
DBP ≥80

*Daytime (awake):
SBP ≥135 mmHg
and/or
DBP t≥85

*Nighttime (asleep):
SBP ≥120 mmHg
and/or
DBP ≥70

Conditions

1.-2. From OBPM applies also to ABPM.

3. Use fully automated devices programmed to record BP automatically at preselected intervals for 24 h.

Measurement

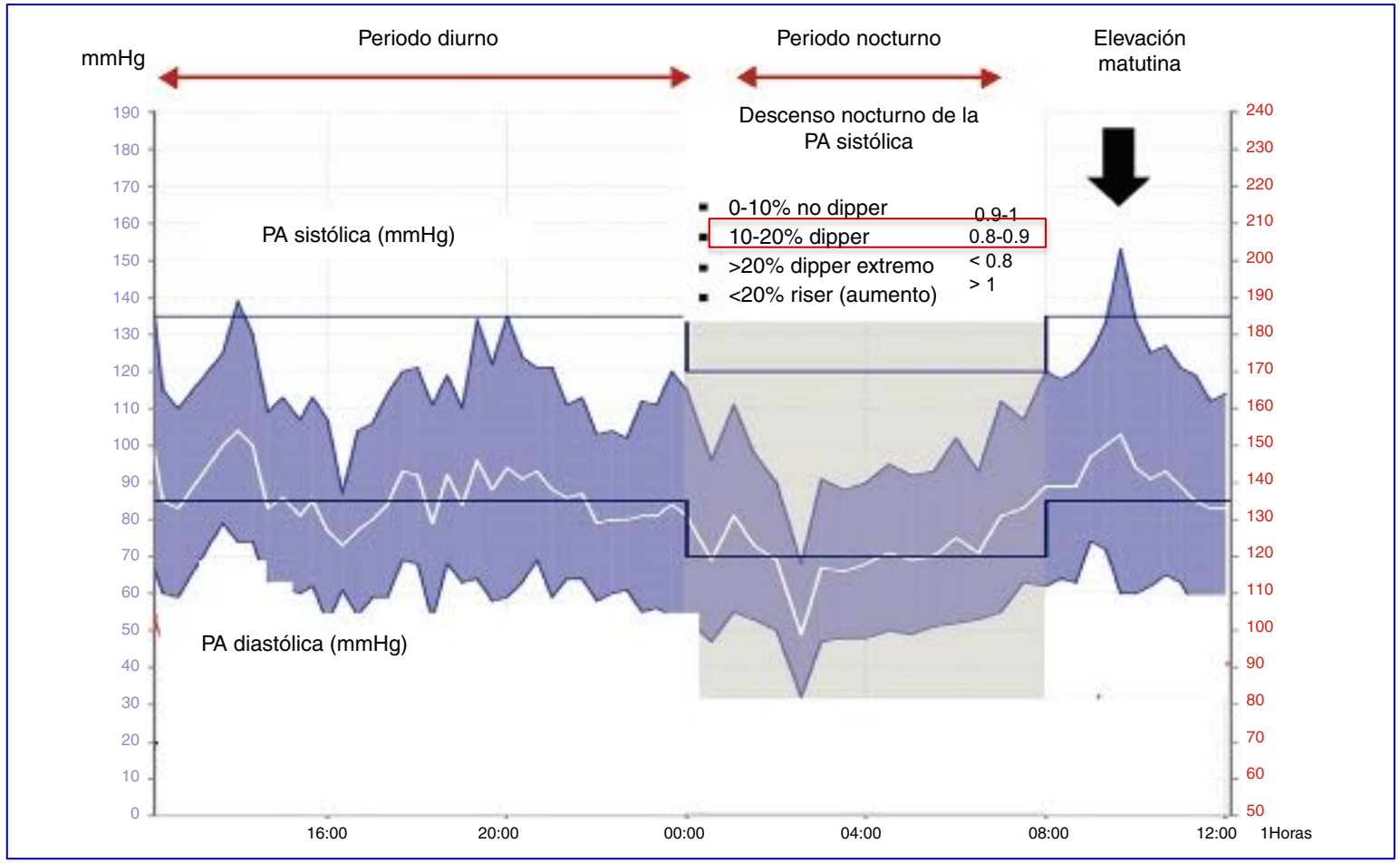
4. The recommended optimal time interval between measurements should be 20 minutes during day (awake) and night (sleep).
5. Measure during a routine workday for 24 h.
6. Instruct patients to keep a diary of their activities, symptoms, meals, drug intake times, sleep times or any unusual problems.

Relevance

- Obtaining 24-h BP profile and especially BP during night (sleep) not captured by OBPM or HBPM
- Confirmation of hypertension diagnosis and of true resistant hypertension.

*Definition of hypertension [a]A device that takes triplicate readings automatically is preferred. [b]The selection of an appropriate cuff size is crucial. A smaller than required cuff overestimates BP and a larger underestimates BP. [c]Use of electronic devices allowing automated storage and data transfer is encouraged. [d]At initial visit measure on both arms. An interarm SBP difference >10 mmHg must be confirmed with repeated measurements. If confirmed, the arm with the higher BP should be used for all subsequent measurements. If any two sequential BP readings in one arm differ by >10 mmHg, additional measurements are recommended. See also Table 1.

ABPM



PA en la MAPA			
Diurna	≥ 135	y/o	≥ 85
Nocturna	≥ 120	y/o	≥ 70
24 h	≥ 130	y/o	≥ 80

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

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

Grados

Estadios

TABLE 2. Factors that influence CV risk in patients with hypertension

Parameter for risk stratification, which are included in SCORE2 and SCORE2-OP
Sex (men >women)
Age
Level of SBP[a]
Smoking – current or past history
Non-HDL cholesterol
Established and suggested novel factors
Family or parental history of early onset hypertension
Personal history of malignant hypertension
Family history of premature CVD (men aged <55 years; women aged <65 years)
Heart rate (resting values >80 bpm)
Low birth weight
Sedentary lifestyle
Overweight or Obesity
Diabetes
Uric acid
Lp(a)
Adverse outcomes of pregnancy (recurrent pregnancy loss, preterm delivery, hypertensive disorders, gestational diabetes)
Early-onset menopause
Frailty
Psychosocial and socioeconomic factors
Migration
Environmental exposure to air pollution or noise
Additional clinical conditions or comorbidities
True resistant hypertension
Sleep disorders (including OSA)
COPD
Gout
Chronic inflammatory diseases
Nonalcoholic fatty liver disease (NASH)
Chronic infections (including long COVID-19)
Migraine
Depressive syndromes
Erectile dysfunction
Hypertension-mediated organ damage (HMOD)
Increased large artery stiffness:
Pulse pressure (in older people) ≥60 mmHg
Carotid–femoral PWV >10 m/s (if available)
Presence of non-hemodynamically significant atheromatous plaque (stenosis) on imaging
ECG LVH (Sokolow–Lyon index >35 mm, or R in aVL ≥11 mm; Cornell voltage-duration product (+6 mm in women) >2440 mm*ms, or Cornell voltage >28 mm in men or >20 mm in women)
Echocardiographic LVH (LV mass index: men >50 g/m$^{2.7}$; women >47 g/m$^{2.7}$ (m = height in meters); indexation for BSA may be used in normal-weight patients: >115 g/m^2 in men and >95/m^2 in women
Moderate increase of albuminuria 30–300 mg/24 h or elevated ACR (preferably in morning spot urine) 30–300 mg/g
CKD stage 3 with eGFR 30–59 ml/min/1.73 m^2
Ankle–brachial index <0.9
Advanced retinopathy: hemorrhages or exudates, papilledema
Established cardiovascular and kidney disease
Cerebrovascular disease: ischemic stroke, cerebral hemorrhage, TIA
Coronary artery disease: myocardial infarction, angina, myocardial revascularization
Presence of hemodynamically significant atheromatous plaque (stenosis) on imaging
Heart failure, including heart failure with preserved ejection fraction
Peripheral artery disease
Atrial fibrillation
Severe albuminuria > 300 mg/24 h or ACR (preferably in morning urine) >300 mg/g
CKD stage 4 and 5, eGFR < 30 mL/min/1.73m^2

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LV, left ventricle; OSA, obstructi sleep apnea.
[a]DBP is not included in the SCORE2/SCORE2-OP tool to estimate CV risk.

Sex (men >women)
Age
Level of SBP[a]
Smoking – current or past history
Non-HDL cholesterol

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

Risk assessment in hypertension with SCORE2 and SCORE2-OP

Recommendations and statements	CoR	LoE
CV risk assessment with the SCORE2 and SCOR2-OP system is recommended for hypertensive patients who are not already at high or very high risk due to established CVD or CKD, long-lasting or complicated diabetes, severe HMOD (e.g. LVH) or a markedly elevated single risk factor (e.g. cholesterol, albuminuria).	I	B

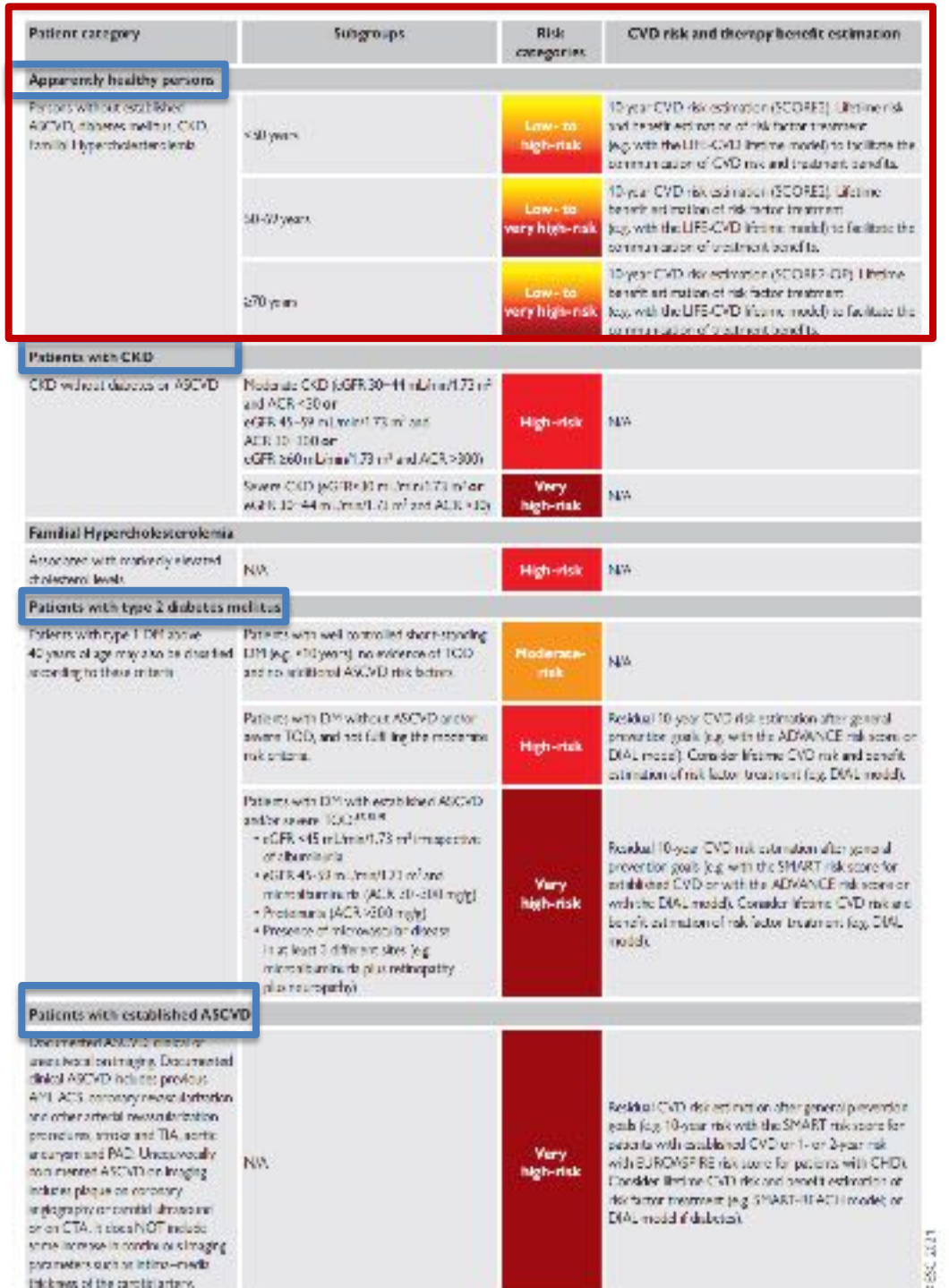
ESC

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)



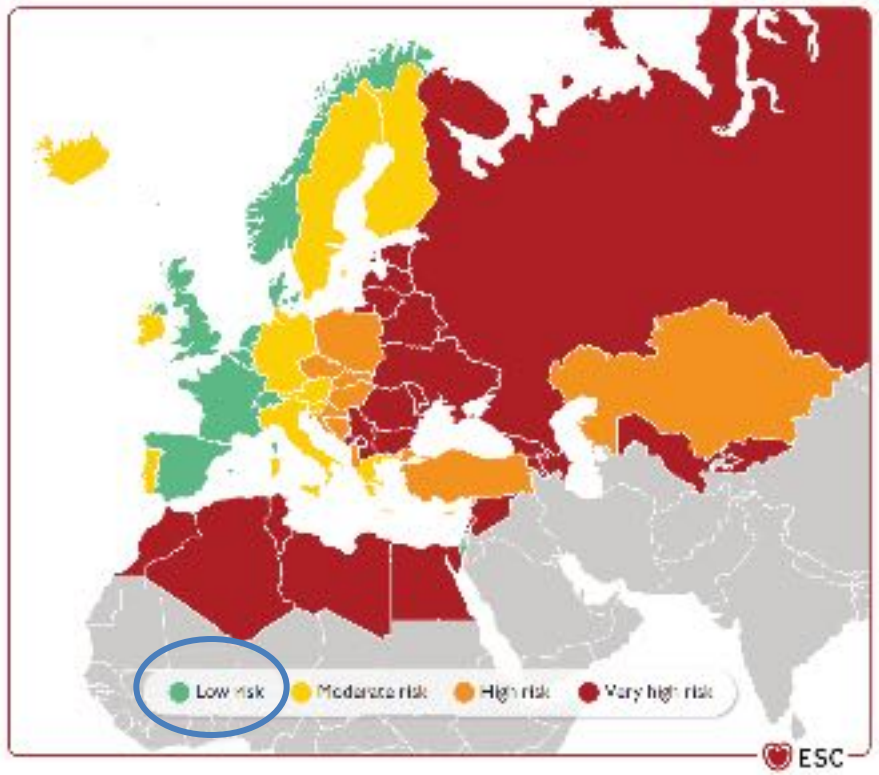
Patient category	Subgroups	Risk categories	CVD risk and therapy benefit estimation
Apparently healthy persons			
Persons without established ASCVD, diabetes mellitus, CKD, familial hypercholesterolaemia	<50 years	Low- to high-risk	10-year CVD risk estimation (SCORE2). Lifetime risk and benefit estimation of risk factor treatment (e.g. with the LIFE-CVD lifetime model) to facilitate the communication of CVD risk and treatment benefits
	50–69 years	Low- to very high-risk	10-year CVD risk estimation (SCORE2). Lifetime benefit estimation of risk factor treatment (e.g. with the LIFE-CVD lifetime model) to facilitate the communication of treatment benefits
	≥70 years	Low- to very high-risk	10-year CVD risk estimation (SCORE2-OP). Lifetime benefit estimation of risk factor treatment (e.g. with the LIFE-CVD lifetime model) to facilitate the communication of treatment benefits
Patients with CKD			
CKD without diabetes or ASCVD	Moderate CKD (eGFR 30–44 mL/min/1.73 m² and ACR <30 or eGFR 45–59 mL/min/1.73 m² and ACR 30–300 or eGFR ≥60 mL/min/1.73 m² and ACR >300)	High-risk	N/A
	Severe CKD (eGFR <30 mL/min/1.73 m² or eGFR 30–44 mL/min/1.73 m² and ACR >30)	Very high-risk	N/A
Familial Hypercholesterolemia			
Associated with markedly elevated cholesterol levels	N/A	High-risk	N/A
Patients with type 2 diabetes mellitus			
Patients with type 1 DM aged 40 years or age may also be classified according to these criteria	Patients with well controlled short-standing DM (e.g. <10 years), no evidence of TOD and no additional ASCVD risk factors	Moderate-risk	N/A
	Patients with DM without ASCVD and/or severe TOD, and not fulfilling the moderate risk criteria	High-risk	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the ADVANCE risk score or DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model)
	Patients with DM with established ASCVD and/or severe TOD (1 of the following): • eGFR <45 mL/min/1.73 m² irrespective of albuminuria • eGFR 45–59 mL/min/1.73 m² and microalbuminuria (ACR 30–300 mg/g) • Proteinuria (ACR >300 mg/g) • Presence of microvascular disease in at least 2 different sites (e.g. microalbuminuria plus retinopathy plus neuropathy)	Very high-risk	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the SMART risk score for established CVD or with the ADVANCE risk score or with the DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model)
Patients with established ASCVD			
Documented ASCVD (clinical or unambiguous local on imaging. Documented clinical ASCVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally non-stenotic ASCVD or lesions (plaque on coronary angiography or carotid ultrasound or on CTA; it does NOT include single increase in cardiac or imaging parameters such as intima-media thickness of the carotid arteries	N/A	Very high-risk	Residual CVD risk estimation after general prevention goals (e.g. 10-year risk with the SMART risk score for patients with established CVD or 1- or 3-year risk with EUROGPRE risk score for patients with CHD). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. SMART-REACH model or DIAL model if diabetes)

GRUPO “APARENTEMENTE SANOS” PERO CON FRCV

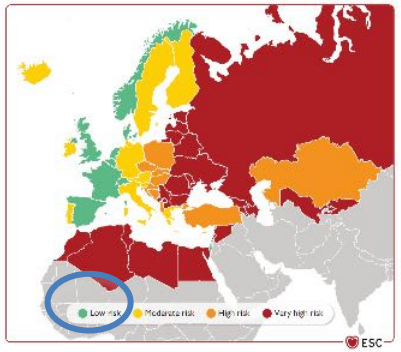
2 nuevas tablas (Riesgo de eventos cardio-vasculares fatales o no fatales a 10 años)

- **SCORE2** 40 - 69 años, que amplía el cálculo de riesgo a la morbilidad y no solo a la mortalidad

- **SCORE2-OP** 70 - 89 años, teniendo en cuenta consideraciones específicas de edades avanzadas y llevando a cabo una valoración a 5 y 10 años

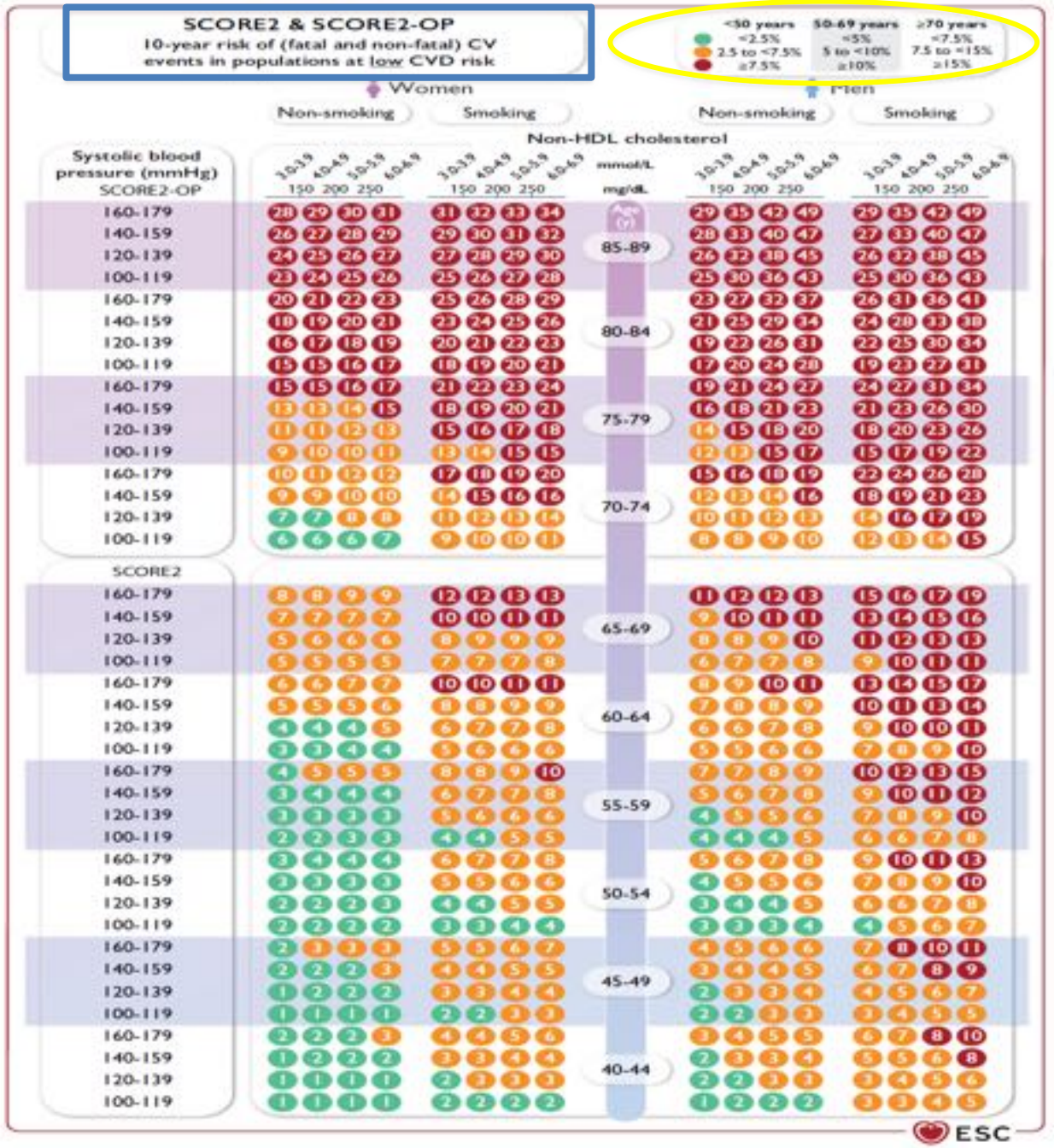


SCORE2 40 - 69 años



REGIÓN

SEXO
EDAD
TABACO
NO cHDL
PAS



U-prevent: SCORE2, SCORE2-OP

ESC CVD Risk

MASTERplan

Assess Patient

Assessment of patients should be adapted according to the severity of hypertension and clinical circumstances.

Basic

History

- Personal
  - -Hypertension related, including sex-specific aspects, e.g. HDP
  - -Co-morbidities
- Cardiovascular risk factors
- Symptoms of HMOD, CVD, stroke or CKD
- Possible secondary hypertension
- Other drug treatments or use including OTCs (See also Table 2 and Table 3)

Physical Examination

- Body habitus and BMI
- Signs of HMOD
- Signs of secondary hypertension
- Resting pulse rate (see BP measurement)
- Level of frailty/functionality in older persons (e.g. >80 years) (See also Table 4 and Table 5)

Lab Test

Blood (serum/plasma)

- Creatinine, eGFR
- Potassium and sodium
- (Fasting) glucose and HbAlc
- Total-, LDL, HDL-Cholesterol

Urine

- Urine analysis multicomponent dipstick test
- Urinary albumin-creatinine ratio (See also Table 6)

Other Investigations

- 12 lead ECG

Extended

HMOD
Select if deemed necessary and available

- Echocardiography
- MRI
- Coronary calcium score

- Ultrasound
- Doppler ultrasound

- Carotid ultrasound

- Pulse wave velocity
- Ankle-brachial index

- CT
- MRI
- Cognitive function tests

- Fundoscopy
- Retina microvasculature

(See also Table 3)

When to refer a patient

To a specialist

- Suspected secondary hypertension (depending on age, Figure 4)
- To exclude secondary hypertension in younger patients (<40 years) with grade 2 or 3 hypertension
- Sudden onset or aggravation of hypertension
- Patients with treatment resistant hypertension
- Need of more detailed assessment of HMOD, which might influence decision making (treatment and follow-up).
- Hypertension in pregnancy
- Requirement of more in-depth specialist evaluation from the referring physician

To a hospital

- Hypertensive emergencies, i.e. in severe hypertension (grade 3) associated with acute symptomatic HMOD
- Severe hypertension with conditions that need intensified BP management:
  - Acute stroke
  - Complicated aortic aneurysm
  - Acute heart failure
  - Acute coronary syndrome
  - Acute kidney failure
- Hypertension caused by phaeochromocytoma or exogenous sympathomimetic substances (e.g. substance abuse)
- Severe forms of HDP including preeclampsia/eclampsia

HMOD/LOD

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/m^2)	>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/m^2
	LAV/height^2	>18.5 (M) or >16.5 (W) ml/m^2
LV systolic dysfunction	GLS	<20%
Kidney		
Function	eGFR	<60 ml/min/1.73 m^2
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		
	Plaque	IMT ≥1.5 mm, or focal increase in thickness ≥0.5 mm, or 50% of surrounding IMT
	IMT	>0.9 mm
Coronary atherosclerosis		
	CAC	Age-specific and sex-specific reference value
LEAD		
	ABI	<0.9
Eye		
	KWB score	Grade III (hemorrhages, microaneurysms, hard exudates and cotton wool spots) and grade IV (papilledema and/or macula edema)
Microvascular changes	Wall-to-lumen ratio	no established reference value

When Does a Calcium Score Equate to Secondary Prevention?

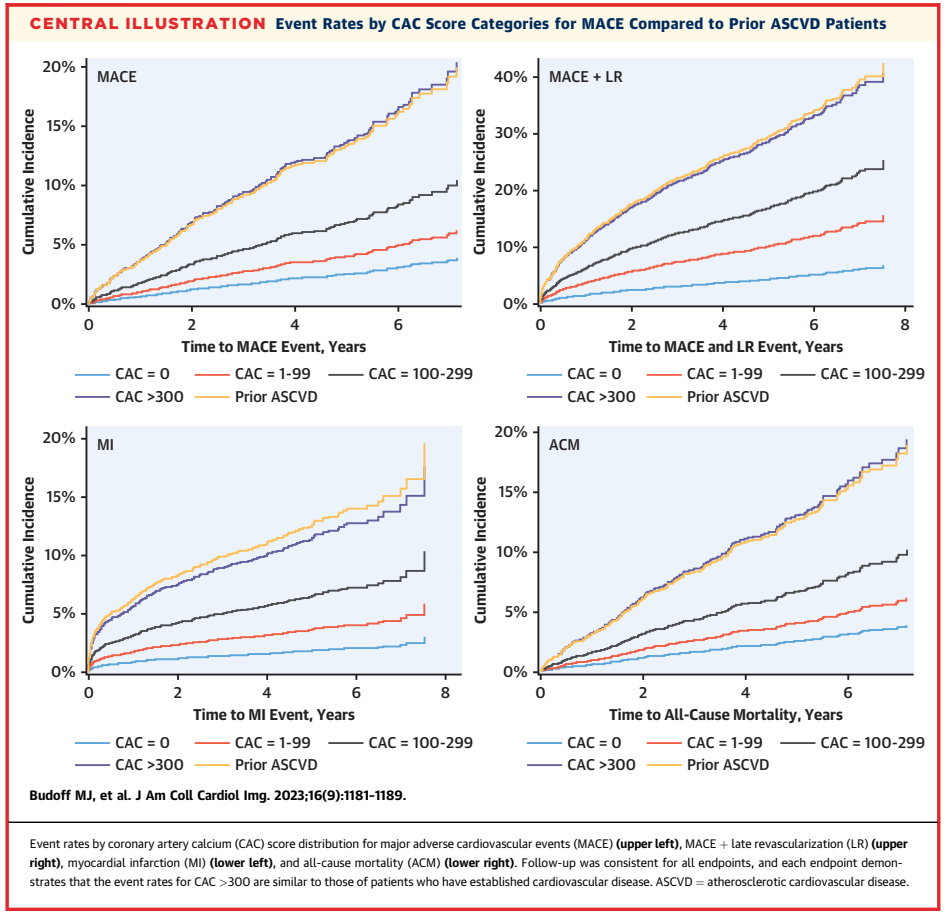
Insights From the Multinational CONFIRM Registry

La presencia de calcio en las arterias coronarias es un indicador de enfermedad coronaria aterosclerótica

- Papel calcio *score* en la reclasificación del riesgo de los pacientes (Riesgo moderado/intermedio)

- 4.511 personas sin enf coronaria Vs 438 con ECV establecida.

- Se clasificaron del calcio *score* en 4 grupos: 0, 1 - 100, 101-300 y > 300.



Los pacientes con CSC > 300 tienen un riesgo equivalente de eventos CV mayores que los pacientes con enfermedad establecida.

Coronary Artery Calcium Staging to Guide Preventive Interventions

A Proposal and Call to Action

David J. Maron, MD,[a] Matthew J. Budoff, MD,[b] Joseph C. Sky, MD,[c,] William J. Bommer, MD,[d] Sarah D. Epstein, PHD,[e] Dane A. Fisher, MD,[f] Eveline O. Stock, MD,[g] Allen J. Taylor, MD,[h] Nathan D. Wong, PHD,[i] Anthony N. DeMaria, MD[j]

JACC: ADVANCES, VOL. 3, NO. 11, 2024 NOVEMBER 2024:101287

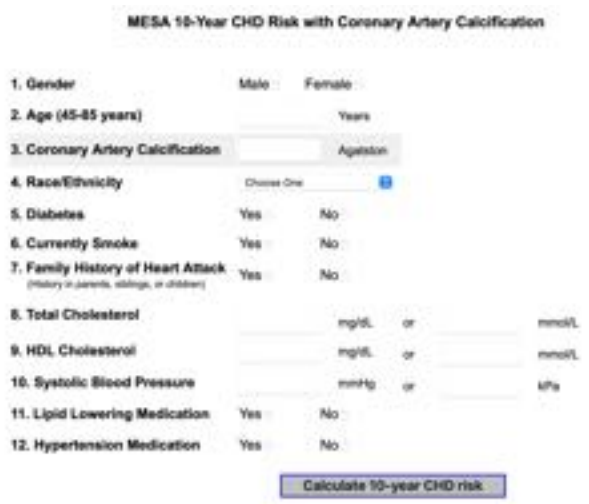
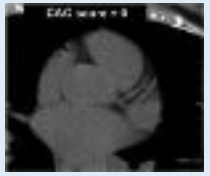
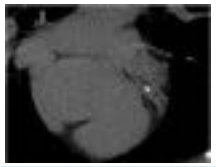
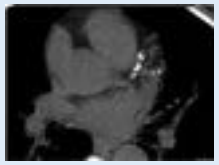
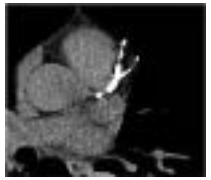
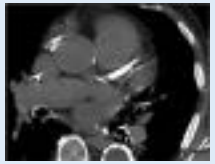
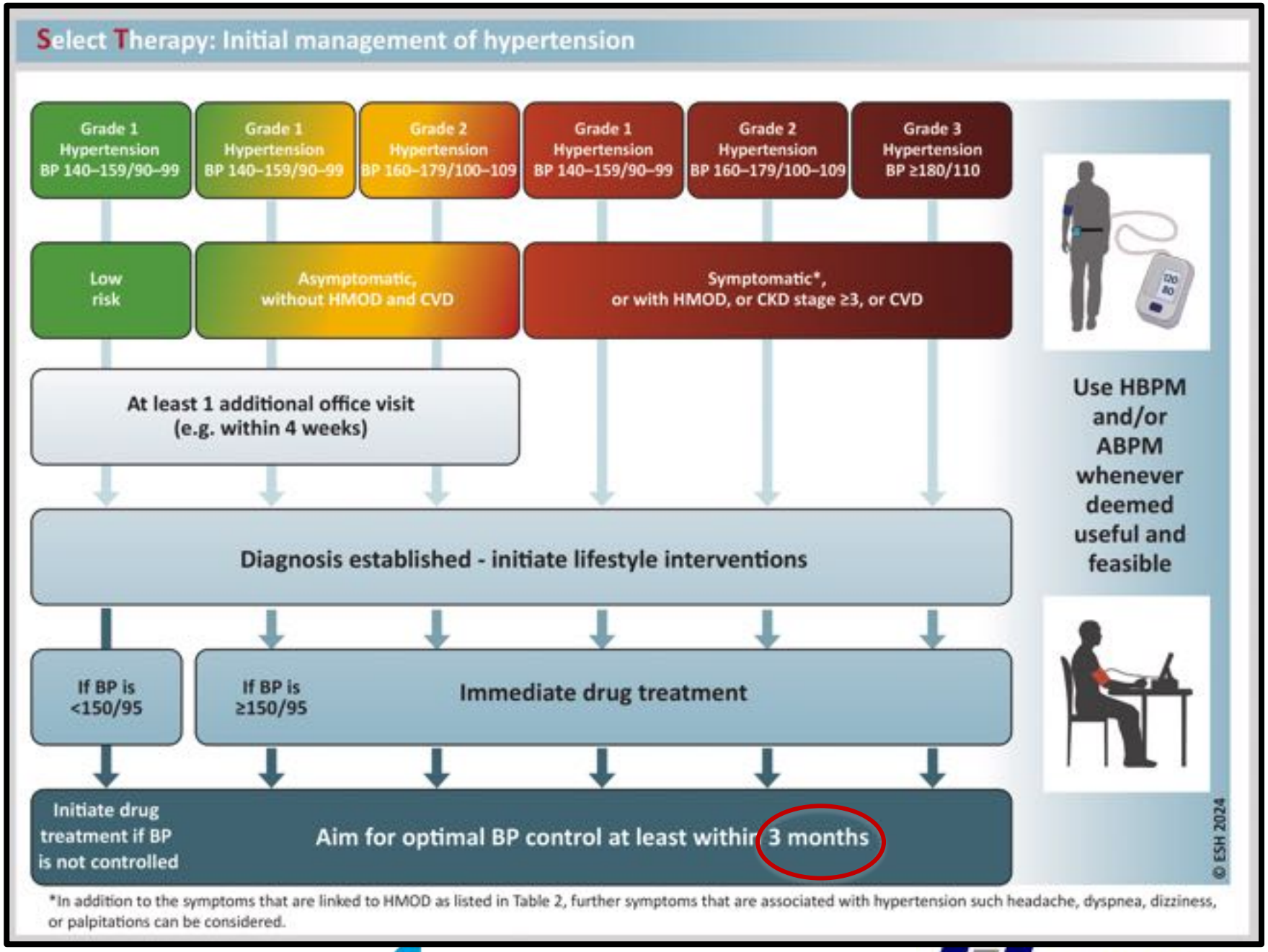


TABLE Proposed Coronary Artery Calcium Staging Guide to Therapy

Stage	CAC Score and Disease Level	Representative Scan Image (White = CAC)	Therapeutic Recommendations Based on ACC/AHA Expert Consensus and Guidelines[2,3]
0	• CAC Score: 0 • No calcified plaque • Visual score: CAC absent		• Promote American Heart Association Life's Essential 8 Optimal Risk Factor Goals[7] • Consider no statin *unless* diabetes, LDL-C ≥190 mg/dL, smoker, family history of premature ASCVD, 10-y ASCVD risk ≥20%, or high Lp(a) • Consider repeat CT for CAC or analysis of nongated chest CT at: ◦ 3 y for diabetes or high 10-y risk for ASCVD ◦ 3-5 y for intermediate 10-y risk for ASCVD ◦ 5-7 y for low 10-y risk for ASCVD
1	• CAC Score: 1-99 and <75th percentile for age and sex • Mild atherosclerotic burden		• Promote American Heart Association Life's Essential 8 Optimal Risk Factor Goals[7] • Statin (+nonstatin) therapy as needed to achieve LDL-C goal <100 mg/dL • Serial monitoring of all risk factors (eg, LDL-C, systolic blood pressure) to achieve critical biometric targets
2	• CAC Score: 100-299 or ≥75th percentile for age and sex • Moderate atherosclerotic burden		• All of the above plus: • Statin (+nonstatin) therapy as needed to achieve LDL-C goal <70 mg/dL • Consider low-dose aspirin therapy
3	• CAC Score: 300-999 • Severe atherosclerotic burden • Very high risk; risk associated with CAC ≥300 is similar to having had a myocardial infarction		• All of the above plus: • High-intensity statin (+nonstatin) therapy as needed to achieve LDL goal <55 mg/dL[3] • Low-dose aspirin
4	• CAC Score: ≥1,000 • Extensive atherosclerotic burden • Extreme risk; risk associated with CAC ≥1,000 similar to having had multiple ASCVD events		• All of the above plus: • Statin (+nonstatin) therapy as needed to achieve LDL-C goal <55 mg/dL[3] • Consider emerging therapies[a]

[a]For example, low-dose anticoagulant in combination with low-dose aspirin, anti-inflammatory therapy (eg, low-dose colchicine).

ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium; LDL-C = low-density lipoprotein cholesterol; Lp(a) = lipoprotein(a).


Select Therapy: Initial management of hypertension
Grade 1 Hypertension BP 140–159/90–99
Grade 1 Hypertension BP 140–159/90–99
Grade 2 Hypertension BP 160–179/100–109
Grade 1 Hypertension BP 140–159/90–99
Grade 2 Hypertension BP 160–179/100–109
Grade 3 Hypertension BP ≥180/110
Low risk
Asymptomatic, without HMOD and CVD
Symptomatic*, or with HMOD, or CKD stage ≥3, or CVD
At least 1 additional office visit (e.g. within 4 weeks)
Diagnosis established - initiate lifestyle interventions
If BP is <150/95
If BP is ≥150/95
Immediate drug treatment
Initiate drug treatment if BP is not controlled
Aim for optimal BP control at least within 3 months
Use HBPM and/or ABPM whenever deemed useful and feasible
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*In addition to the symptoms that are linked to HMOD as listed in Table 2, further symptoms that are associated with hypertension such headache, dyspnea, dizziness, or palpitations can be considered.

Select Therapy: Lifestyle Interventions

Relevance

- Prevent or delay onset of hypertension
- Improve overall/CV health and well-being
- Reduce BP
- Booster BP lowering effects of medications
- Reduce the number/dose of drugs needed for BP control

Prescribing

- To all patients with diagnosed hypertension
- To patients with white-coat or masked hypertension
- To patients with high-normal BP
- Individual patient counseling and support
- Prescribe with specific instructions, e.g. intensity and type of exercise
- Assess, adapt, and reinforce during follow-up

Supportive additional interventions

Smoking cessation

- Smoking cessation, supportive care and referral to smoking cessation programs are recommended for all smokers

Key interventions to reduce BP

Healthy diet

Prefer:

- DASH or Mediterranean type diets
- A healthy dietary pattern including more plant-based and less animal-based food
- Vegetables , fruits, beans, nuts, seeds, and vegetable oils
- Lean protein (e.g. fish, poultry)

Limit:

- Fatty meats, full-fat dairy
- Sugar, sweets and sweetened beverages

Daily physical activity and regular exercise

- Incorporate physical activity (e.g. walking, cycling) into everyday life and reduce sedentary behavior (e.g. sit less)
- Aim for:
  -150-300 min of aerobic exercise per week performed at a moderate intensity or
  -75-150 min of aerobic exercise per week performed at a vigorous intensity or
  -an equivalent combination of moderate and vigorous physical activities
- Add dynamic resistance (muscle strengthening) exercise 2-3 times per week
- Start slow and gradually to build up the amount/ intensity of activity

Weight reduction

- Combine a low-caloric diet with daily physical activity in patients with overweight or obesity
- Monitor waist circumference and weight

Restriction of sodium intake

- Sodium is mainly consumed as salt, which comes from processed foods or is added to the food during cooking or at the table
- Salt (NaCl) restriction to < 5 g (~2g sodium) or 1 teaspoon per day is recommended

Augmentation of potassium intake

- Increase potassium consumption, preferably via dietary modification, except for hypertensive patients with advanced CKD
- Foods high in potassium are for example white cannellini beans (1200 mg/cup), unsalted boiled spinach (840 mg/cup), avocado (708 mg/cup) and bananas (450 mg per medium fruit)
- Use salt substitutes replacing NaCl with KCl in patients consuming a high sodium diet

Limit alcohol intake

- Limit alcohol intake close to abstinence, particularly if intake is ≥3 drinks/day[a]
- Avoid excessive (binge) drinking

Improve stress management

- Reduce stress by use of
  -Regular physicial activity
  -Mindfulness-based exercise
  -Relaxation techniques, e.g. deep breathing, meditation, yoga or Tai Chi
- Get enough sleep (7-9 hours)
- Find individual ways to cope with stress, e.g. practicing mindfulness, engaging in hobbies or talking to a therapist
- Moderate alcohol and caffeine intake, avoid drugs

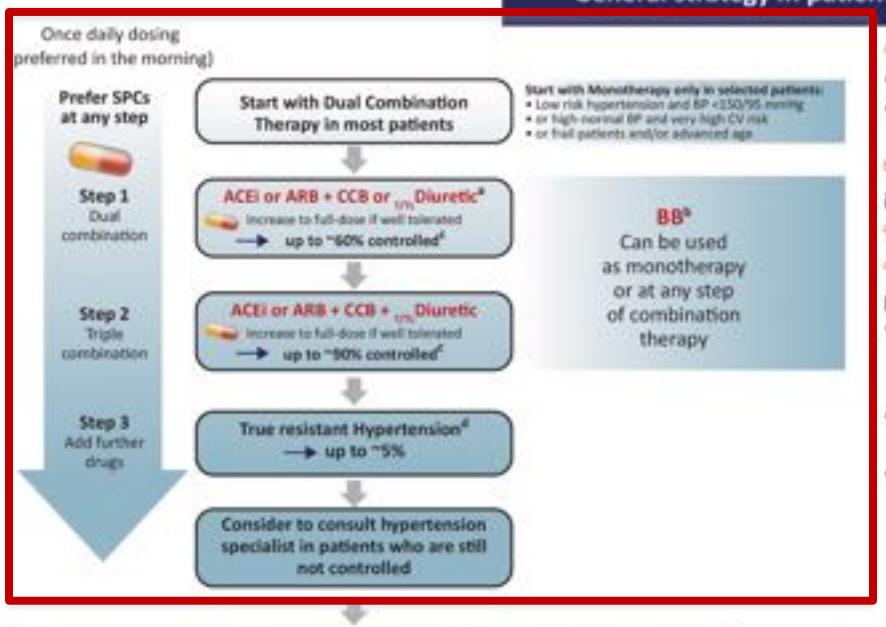
Minimize exposure to noise and air pollution

- Reduce indoor exposure to noise and air pollution.
- Consider to reduce exposure to air pollution by modifying the location, timing and type of outdoor activities

[a]About 350 ml of regular beer containing 5% alcohol by volume or 150 ml of wine containing 12% alcohol by volume per drink.

Select Therapy: Pharmacological Treatment

General strategy in patients with hypertension



[a]Use of Diuretics:
- Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m²
- If eGFR <30 ml/min/1.73m² use Loop Diuretic; consider combination with Chlorthalidone or other TL-Diuretic

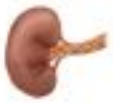
[b]Use of BB: should be used as guideline directed medical therapy in respective indications or considered in several other conditions (Table 8)

[c]Controlled BP: if <140/90mmHg

[d]True resistant Hypertension: when SBP is ≥140 mmHg or DBP is ≥90 mmHg provided that:
- maximum recommended and tolerated doses of a three-drug combination comprising a RAS blocker (either an ACEi or an ARB), a CCB and a Thiazide/ Thiazide-like diuretic were used
- inadequate BP control has been confirmed by ABPM or by HBPM if ABPM is not feasible
- various causes of pseudo-resistant hypertension (especially poor medication adherence) and secondary hypertension have been excluded.

Consider additional therapies: drugs or renal denervation

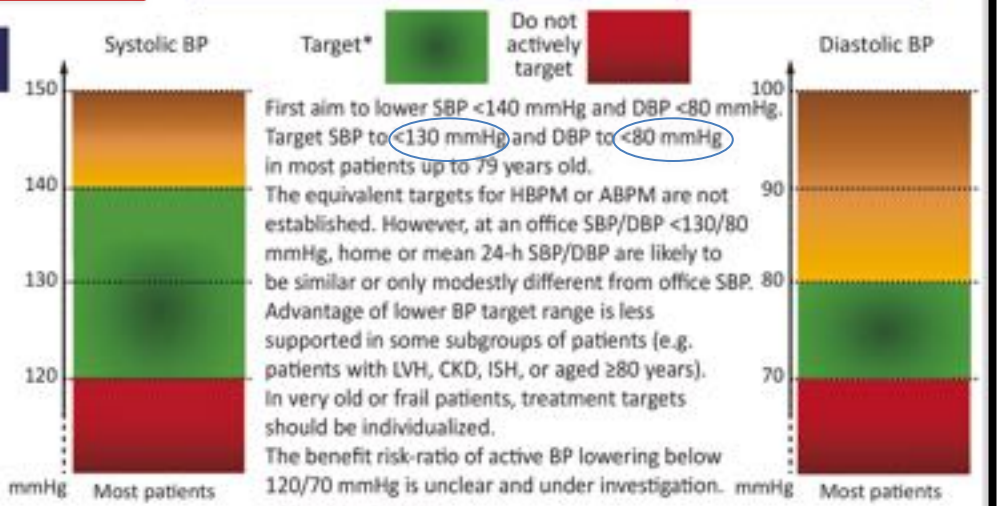
In true resistant hypertension:
- Spironolactone (preferred) or other MRA; with caution if eGFR <45 ml/min/1.73 m² or serum potassium >4.5 mmol/l.
- BB or alpha1-blocker or centrally acting agent
- Direct vasodilator (not preferred)
- Renal denervation, if eGFR >40 ml/min/1.73 m²



In Heart Failure
- ARNI
- SGLT2i

In CKD
- SGLT2i
- NsMRA Finerenone (not in combination with other MRA)

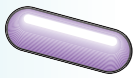
General office BP targets in patients with hypertension



First aim to lower SBP <140 mmHg and DBP <80 mmHg. Target SBP to <130 mmHg and DBP to <80 mmHg in most patients up to 79 years old.
The equivalent targets for HBPM or ABPM are not established. However, at an office SBP/DBP <130/80 mmHg, home or mean 24-h SBP/DBP are likely to be similar or only modestly different from office SBP.
Advantage of lower BP target range is less supported in some subgroups of patients (e.g. patients with LVH, CKD, ISH, or aged ≥80 years).
In very old or frail patients, treatment targets should be individualized.
The benefit risk-ratio of active BP lowering below 120/70 mmHg is unclear and under investigation.
*If well tolerated

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**



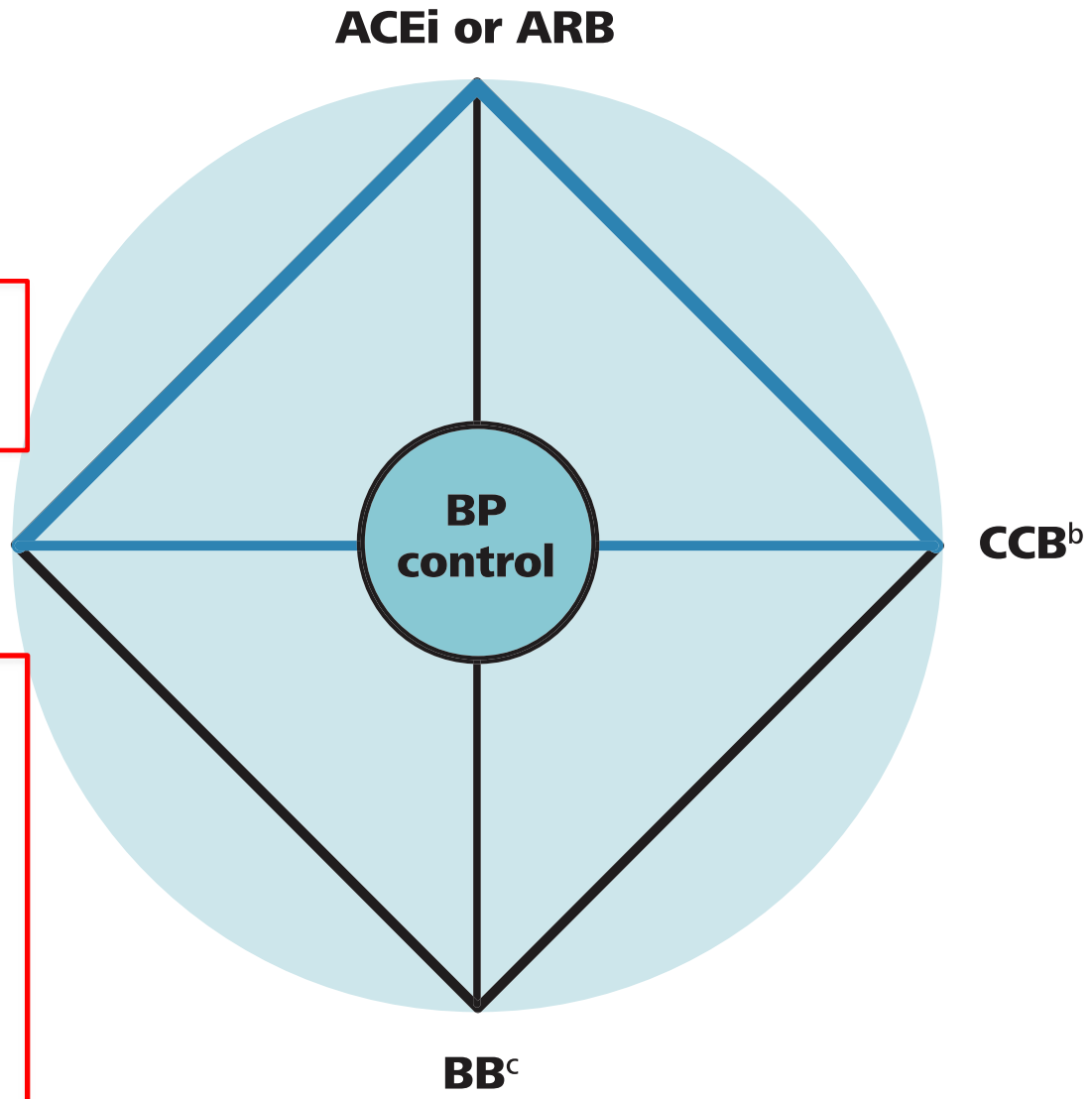
Additional drug classes

General antihypertensive therapy:

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

Special comorbidities:

- ARNi
- SGLT2i
- Non-Steroidal MRA



MASTERplan

Select Therapy: Older patients (>80 years)

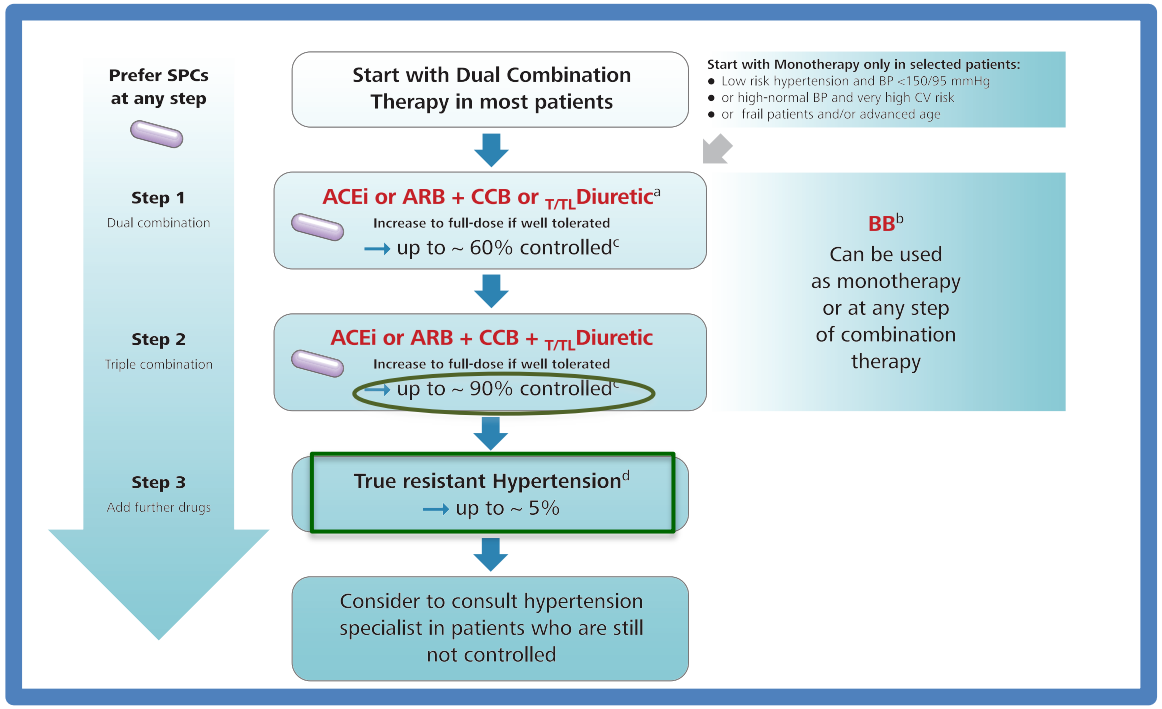
	Fit*	Slowed but autonomous for most activities*	Severely Dependent
Treatment initiation	1. If office SBP ≥160 mmHg. 2. Consider also in most cases if office SBP is between 140 and 159 mmHg.	1. If office SBP ≥160 mmHg. 2. Consider ialso in most cases if office SBP is between 140 and 159 mmHg.	1. According to comorbidities and polypharmacy. 2. Consider treatment if office SBP ≥160 mmHg.
Target BP	3. Office SBP in the range of 140 to 150 mmHg. 4. A range of 130-139 mmHg may be considered if well tolerated 5. Be cautious if DBP is already below 70 mmHg.	3-5 from Fit apply also.	3. Office SBP in the range of 140 to 150 mmHg.
Strategy	6. Consider starting with monotherapy. *See Table 5: How to Assess	6. Consider starting with monotherapy. 7. Uptitrate cautiously. 8. Reduce treatment if SBP is very low (<120 mmHg) or in patients with orthostatic hypotension. 9. Consider a detailed assessment of functional status with the tools below or equivalent:: • Mobility (Short Physical Performance Battery) • Muscular force (Handgrip) • Depression (Mini Geriatric Depression Scale) • Nutrition (Mini Nutritional Assessment Short Form)	4. Start treatment cautiously. 5. Reduce treatment if SBP is very low (<120 mmHg) or in patients with orthostatic hypotension. 6. Correct other factors and medications lowering BP.

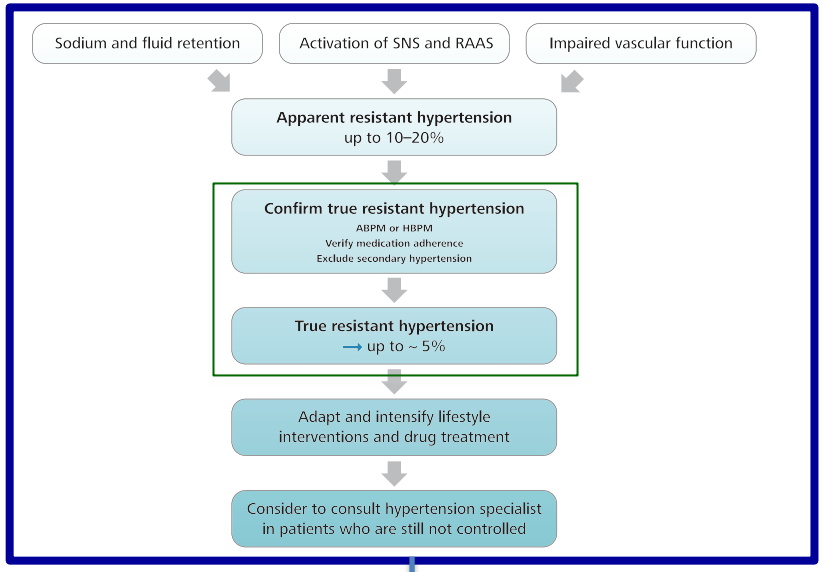
MASTERplan

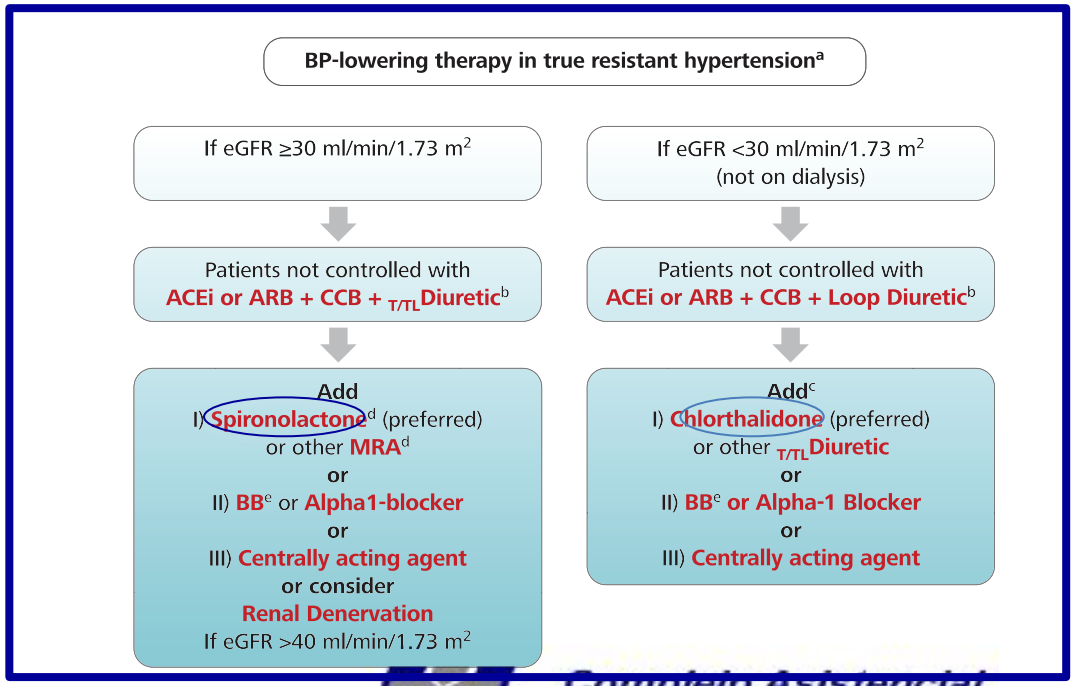
Evaluate Response

	Initiation (3 months)	Short-term FU (3 months - 1 year)	Long-term FU (>1 year)
Objective	Aim for BP control	Establish optimal BP control	Maintain optimal BP control
	1-2 visits (4-6 weeks)	1-2 visits depending on CV risk (4-6 weeks) More frequently in patients with high-risk and difficult to control BP	Low-risk:1 visit per year High risk and difficult to control BP: more frequent visits (2-3/year)
	Office BP and Home BP	Office BP and Home BP (before visits); verify consistency of BP control; consider seasonal variability ABPM in apparent treatment resistance hypertension; consider to refer to a specialist	
	Selected lab tests to address safety of drug therapy or risk factors	Depending on baseline profile and condition periodic re-assessment of parameters with impact on drug safety and selection, e.g. eGFR, potassium or important risk factors, e.g. glucose, HbA1c, LDL-cholesterol	
	Re-Assess modifiable risk factors and HMOD (Table 2 and Table 3)	In patients with pre-existing HMOD verify BP-induced changes (depending on sensitivity to change), e.g. eGFR, albuminuria, pulse wave velocity or left ventricular hypertrophy.	In patients without pre-existing HMOD re-assess in longer intervals, e.g. every 3 years In patients with pre-existing HMOD more frequent re-assessments of BP-induced changes
	Verify and adapt lifestyle interventions and recommended drug therapy prescribing patterns	Support implementation of lifestyle interventions. Consider adjustment of medications depending on BP control, tolerability and change in co-morbidities, avoid inertia. Consider deprescribing in symptomatic very old and frail patients with low BP	
	Verify initiation and discuss adherence	Monitor adherence/persistence to drug therapy: assess barriers, e.g. changes in co-morbidiies, side-effects, polypharmacy including OTC use	
	Support individual needs and shared decision making	Organize and implement patient support: consider use of team-based care, telehealth, virtual visits, self-monitoring and patient empowerment	Maintain patient support

HTA Resistente







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Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial

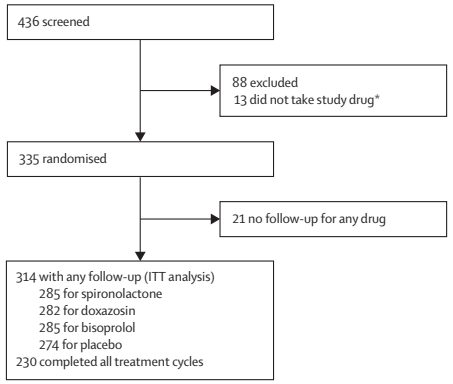
Lancet 2015; 386: 2059–68

*Bryan Williams, Thomas M MacDonald, Steve Morant, David J Webb, Peter Sever, Gordon McInnes, Ian Ford, J Kennedy Cruickshank, Mark J Caulfield, Jackie Salsbury, Isla Mackenzie, Sandosh Padmanabhan, Morris J Brown, for The British Hypertension Society's PATHWAY Studies Group**

- HTA < 80 años
- HTA refractaria(ISRAA+ACC+Diurético dosis plenas confirmado AMPA) y PA > 140/90 mmHg
- Asignados a uno de los 4 ttos, incluido placebo

Cada paciente recibía cada uno de los 4 ttos en dif orden sin período de lavado

- 12s con cada tto (48s en total)



	Mean (SD) or N (%)
Age (years)	61·4 (9·6)
Sex	
Male	230 (69%)
Female	105 (31%)
Weight (kg)	93·5 (18·1)
Smoker	26 (7·8%)
Home	
Systolic blood pressure (mm Hg)	147·6 (13·2)
Diastolic blood pressure (mm Hg)	84·2 (10·9)
Heart rate (beats per min)	73·3 (9·9)
Clinic	
Systolic blood pressure (mm Hg)	157·0 (14·3)
Diastolic blood pressure (mm Hg)	90·0 (1·5)
Heart rate (beats per min)	77·2 (12·2)
24 h urine (mmol/24 h)	
Sodium	137·1 (71·8)
Potassium	70·5 (29·5)
Blood electrolytes (mmol/L)	
Sodium	139·6 (3·0)
Potassium	4·1 (0·5)
eGFR (mL/min)	91·1 (26·8)
Diabetic	46 (14%)

eGFR=estimated glomerular filtration rate.

Table 1: **Baseline characteristics of the patients randomised into the PATHWAY-2 study (n=335)**

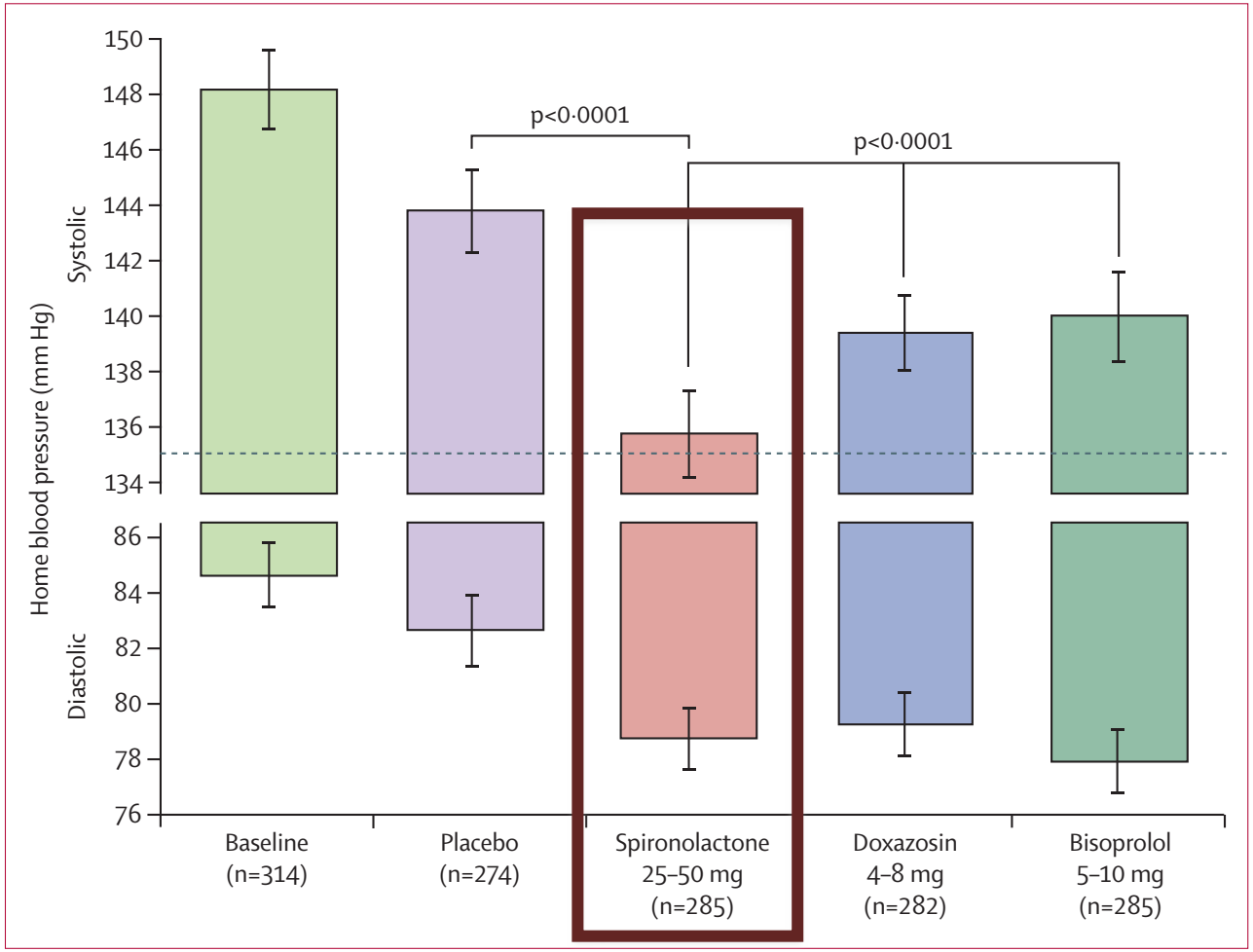


Figure 2: **Home systolic and diastolic blood pressures comparing spironolactone with each of the other cycles**

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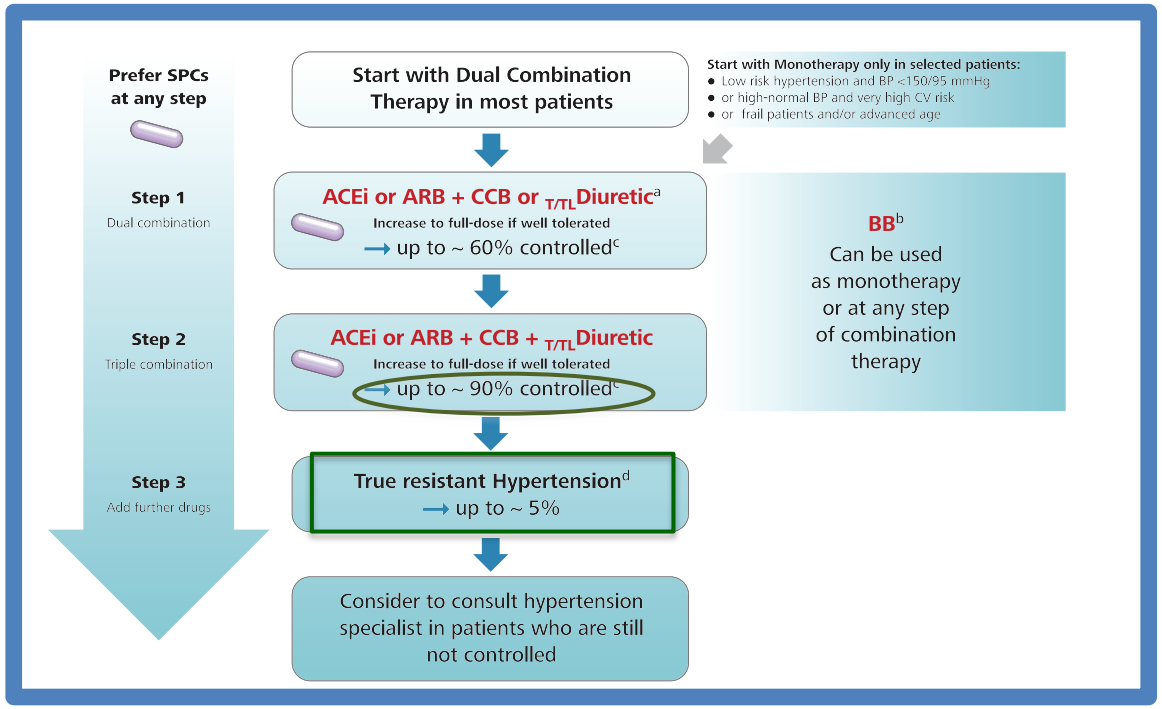
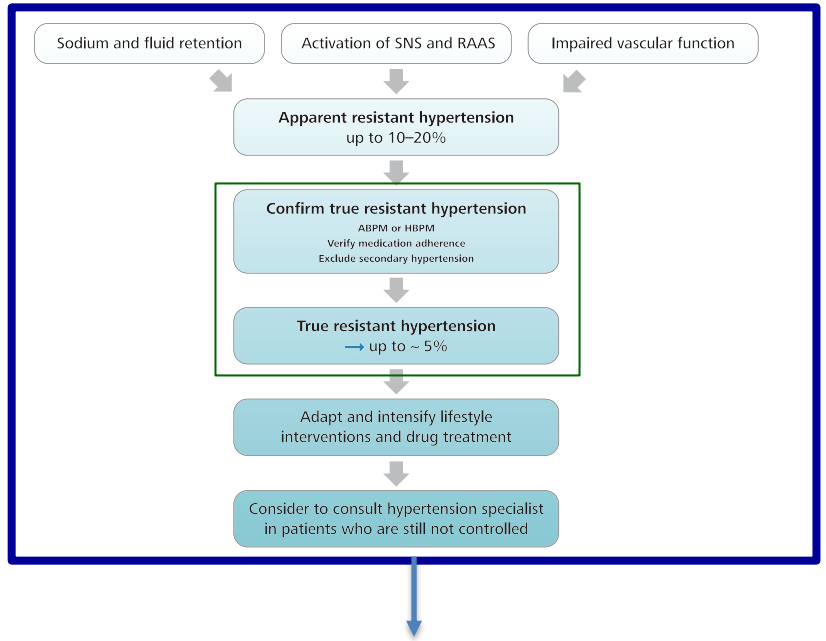
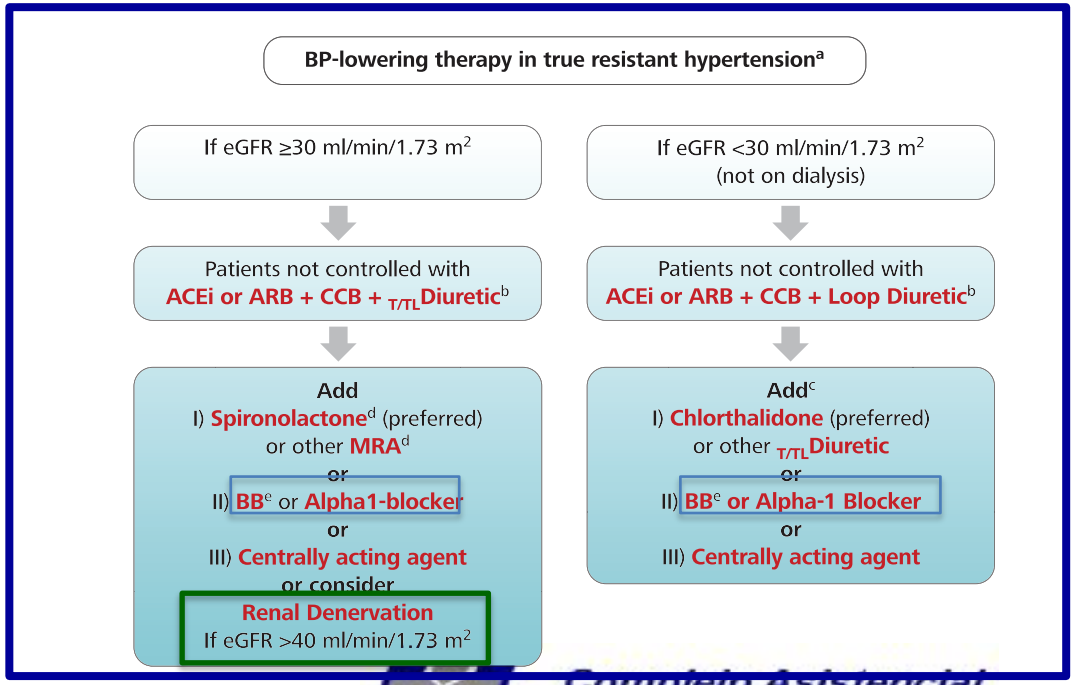
HTA Resistente







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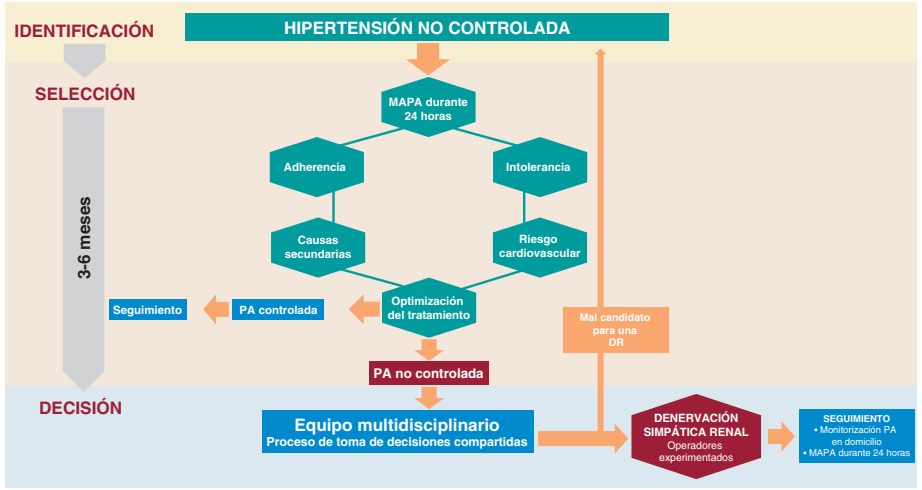
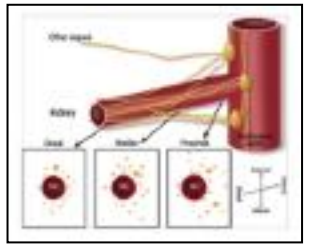
REC Interv Cardiol. 2022;4(1):39-46
https://doi.org/10.24875/RECIC.M21000231

Denervación renal en el tratamiento de la hipertensión arterial. Posicionamiento conjunto de la SEH-LELHA y la ACI-SEC





Tratamientos para la hipertensión basados en dispositivos

Recomendaciones	Clase[a]	Nivel[b]
No se recomiendan los tratamientos para la HTA basados en dispositivos en la práctica clínica habitual, excepto en el contexto de estudios clínicos, hasta que se disponga de evidencia sobre su seguridad y su eficacia[367,368]	III	B

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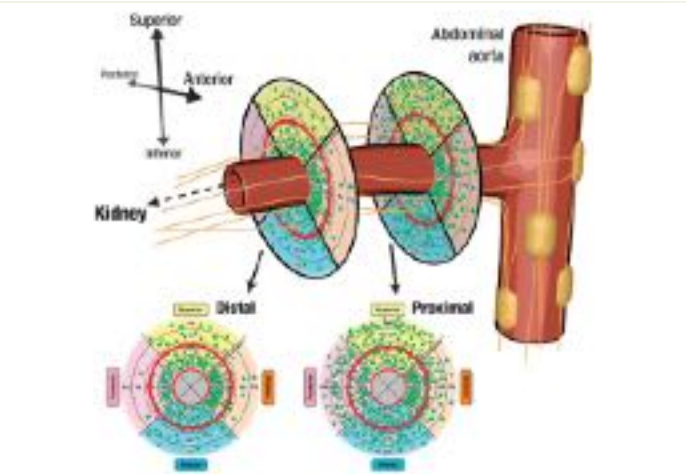
Use of renal denervation ESC/ESH 2023

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

ESC European Society of Cardiology
European Heart Journal (2023) **44**, 1313–1330
https://doi.org/10.1093/eurheartj/ehad054

Renal denervation in the management of hypertension in adults. A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI)



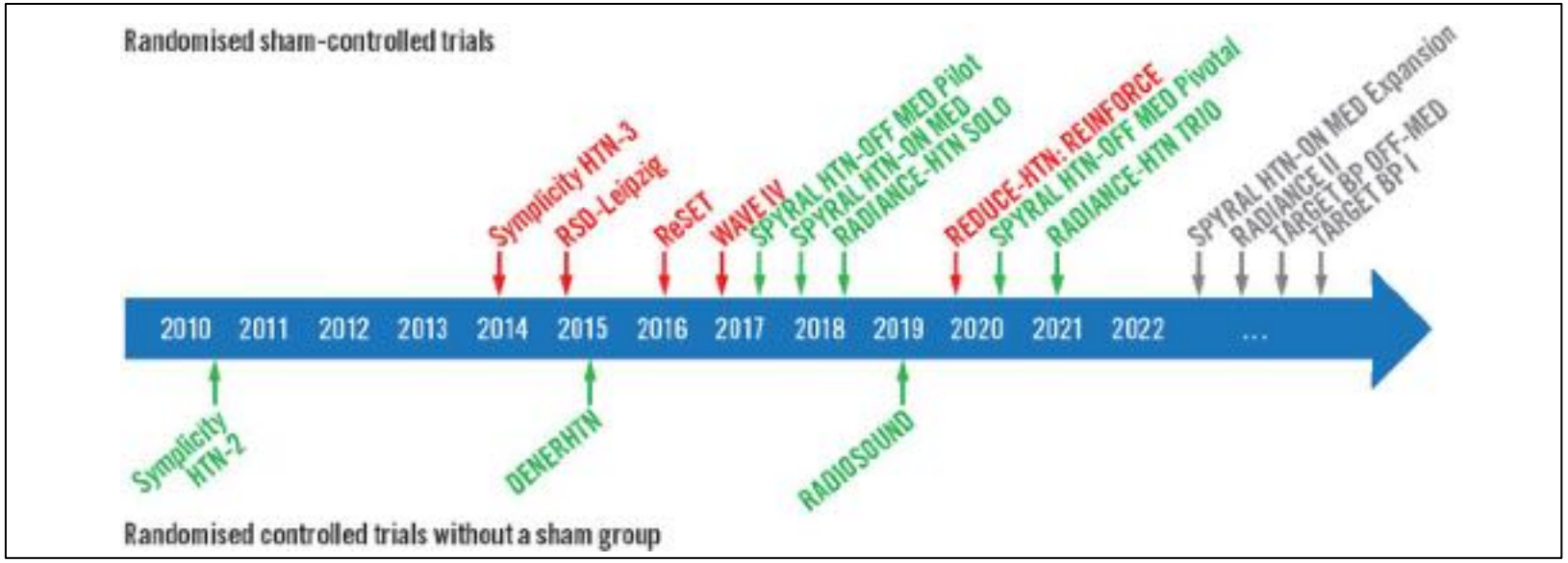


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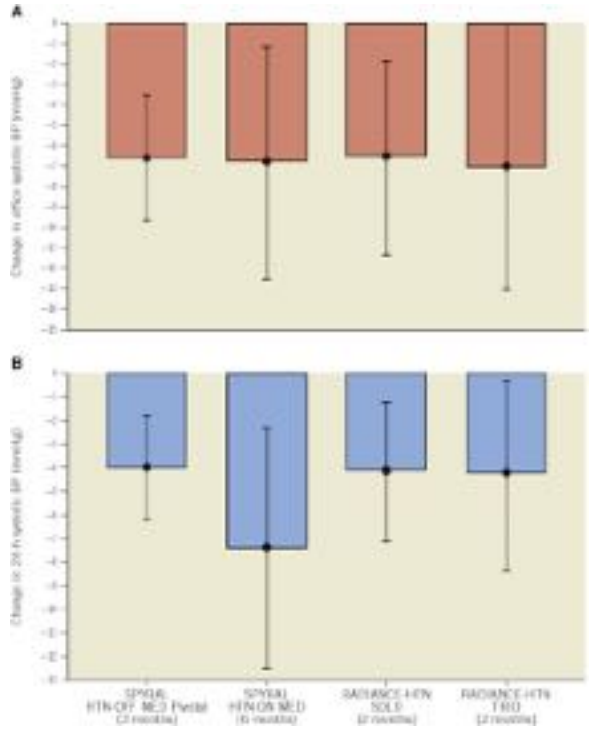
Table 1 Key characteristics of important randomised controlled RDN trials

Trial, year of publication	Investigational device	Design (randomisation ratio)	Sample size	Inclusion criteria	Primary efficacy outcome	BP reduction in RDN vs control group
Randomised controlled trials						
Symplicity HTN-2, 2010[92]	Symplicity Flex (mono-electrode RF)	Open-label, RDN vs control (1:1)	106	Uncontrolled office BP on ≥3 antihypertensive drugs	Change in office SBP at 6 months	−32 ± 23 vs −1 ± 21 mmHg; $p < 0.0001$
DENERHTN, 2015[93]	Symplicity Flex (mono-electrode RF)	Open-label, SSAHT + RDN vs SSAHT (1:1)	106	Uncontrolled office and 24-hr BP on ≥3 antihypertensive drugs	Change in daytime ambulatory SBP at 6 months	−9.9 (95% CI: −13.6 to −6.2) vs −5.9 mmHg (95% CI: −11.3 to −0.5); $p = 0.033$
RADIOSOUND-HTN, 2019[94]	Symplicity Spyral (multi-electrode RF) vs Paradise (US)	US-RDN vs RF-RDN of the main artery vs RF-RDN of main artery vs RF-RDN of the branches, and accessory arteries (1:1:1)	120	Uncontrolled office and 24-hr BP on ≥3 antihypertensive drugs	Change in daytime ambulatory SBP at 3 months	US: −13.2 ± 13.7 mmHg vs RF main artery: 6.5 ± 10.3 mmHg vs RF including branches: −8.3 ± 11.7 mmHg ($p = 0.043$ for US vs RF main artery; $p > 0.99$ for RF main artery vs RF branches)
First-generation randomised sham-controlled trials						
Symplicity HTN-3, 2014[16]	Symplicity Flex (mono-electrode RF)	RDN vs sham (2:1)	535	Uncontrolled office and 24-hr BP on ≥3 antihypertensive drugs	Change in office SBP at 6 months	−14.1 ± 23.9 vs −11.7 ± 25.9 mmHg; $p = 0.27$
RSD-Leipzig, 2015[95]	Symplicity Flex (mono-electrode RF)	RDN vs sham (1:1)	71	Uncontrolled 24-hr BP on ≥3 antihypertensive drugs	Change in 24-hr SBP at 6 months	−7.0 (95% CI: −10.8 to −3.2) vs −3.5 mmHg (95% CI: −6.7 to −0.2); $p = 0.15$
ReSET, 2016[96]	Symplicity Flex (mono-electrode RF)	RDN vs sham (1:1)	69	Uncontrolled daytime ambulatory BP on ≥3 antihypertensive drugs	Change in daytime ambulatory SBP at 6 months	−6.1 ± 18.9 vs −4.3 ± 15.1 mmHg; $p = 0.66$
WAVE IV, 2017[97]	Externally delivered therapeutic US energy (surround sound system)	RDN vs sham (1:1)	81	Uncontrolled office and 24-hr BP on ≥3 antihypertensive drugs	Change in office SBP	−13.2 ± 20 vs −18.9 ± 14 mmHg; $p = 0.181$
REDUCE-HTN: REINFORCE, 2020[98]	Vessix (multi-electrode RF)	RDN vs sham (2:1)	51	Uncontrolled office and 24-hr BP in absence of antihypertensive drugs	Change in 24-hr SBP at 2 months	−5.3 (95% CI: −8.8 to −1.8) vs −8.5 mmHg (95% CI: −13.3 to −3.8); $p = 0.30$
Second-generation randomised sham-controlled trials						
SPYRAL HTN-OFF MED Pilot, 2017[9]	Symplicity Spyral (multi-electrode RF)	RDN vs sham (1:1)	80	Uncontrolled office and 24-hr BP in the absence of antihypertensive drugs	Change in 24-hr SBP at 3 months	−5.5 (95% CI: −9.1 to −2.0) vs −0.5 mmHg (95% CI: −3.9 to 2.90); $p = 0.0414$
RADIANCE-HTN SOLO, 2018[12]	Paradise (US)	RDN vs sham (1:1)	146	Uncontrolled daytime ambulatory BP in the absence of antihypertensive drugs	Change in daytime ambulatory SBP at 2 months	−8.5 ± 9.3 vs −2.2 ± 10.0 mmHg; $p = 0.0001$
SPYRAL HTN-ON MED, 2018[10]	Symplicity Spyral (multi-electrode RF)	RDN vs sham (1:1)	80	Uncontrolled office and 24-hr BP on 1 to 3 antihypertensive drugs	Change in 24-hr SBP at 6 months	−9.0 (95% CI: −12.7 to −5.3) vs −1.6 mmHg (95% CI: −5.2 to 2.0); $p = 0.006$
SPYRAL HTN-OFF MED Pivotal, 2020[11]	Symplicity Spyral (multi-electrode RF)	Bayesian adaptive design, RDN vs sham (1:1)	331	Uncontrolled office and 24-hr BP, in the absence of antihypertensive drugs	Change in 24-hr SBP at 3 months	−4.7 (95% CI: −6.4 to −2.9) vs −0.6 mmHg (95% CI: −2.1 to 0.9); $p = 0.0005$
RADIANCE-HTN TRIO, 2021[13]	Paradise (US)	RDN vs sham (1:1)	136	Uncontrolled office and daytime ambulatory BP on 3 antihypertensive drugs	Change in daytime ambulatory SBP at 2 months	−8.0 (IQR −16.4, 0.0) vs −3.0 mmHg (IQR −10.3, 1.8); $p = 0.022$
REQUIRE, 2022[19]	Paradise (US)	RDN vs sham (1:1)	143	Uncontrolled office and 24-hr BP on ≥3 antihypertensive drugs	Change in daytime ambulatory SBP at 3 months	−6.6 (95% CI: −10.4 to −2.8) vs −6.5 mmHg (95% CI: −10.3 to −2.7); $p = 0.971$

BP: blood pressure; CI: confidence interval; IQR: interquartile ratio; RDN: renal denervation; RF: radiofrequency; SBP: systolic blood pressure; SSAHT: standardised stepped-care antihypertensive treatment; US: ultrasound



Trial, NCT*	Catheter system	Design, (randomisation ratio)	Sample size	Inclusion criteria	Primary efficacy outcome	Estimated trial completion
SPYRAL HTN-ON MED Expansion, NCT02439775	Symplicity Spyral (multi-electrode RF)	Bayesian adaptive design, RDN vs sham (1:1)	340	Uncontrolled office and 24-hour BP on 1-3 antihypertensive drugs	Change in 24-hour SBP at 6 months	2026
RADIANCE II, NCT03614260	Paradise (US)	RDN vs sham (1:1)	225	Uncontrolled stage II hypertension (office and daytime ambulatory BP) in absence of antihypertensive drugs	Change in daytime ambulatory SBP at 2 months	2022
TARGET BP OFF-MED, NCT03503773	Peregrine (ethanol injection via microneedles)	RDN vs sham (1:1)	90	Uncontrolled office and 24-hour BP in absence of antihypertensive drugs	Change in 24-hour ambulatory SBP at 2 months	2023
TARGET BP I, NCT02910414	Peregrine (ethanol injection via microneedles)	RDN vs sham (1:1)	300	Uncontrolled office and 24-hour BP on 2-5 antihypertensive drugs	Change in ambulatory 24-hour SBP at 3 months	2025

*NCTs found at ClinicalTrials.gov. BP: blood pressure; RDN: renal denervation; RF: radiofrequency; SBP: systolic blood pressure; US: ultrasound

No denervación renal si:

- Intervenciones previas en la arteria renal (angioplastia o stent)
- Estenosis arteria renal > 50%
- Presencia de múltiples arterias renales o art renales de menos de 20 mm de length
- FG < 40 ml/min/1,73 m²

Pacientes estables, **no es un tratamiento para las emergencias hipertensivas**

Al menos 3-6 meses después de un IAM, angina inestable o Ictus.

- **HTA resistente** (PA > 140/90 mmHg a pesar de cambios en el estilo de vida y tratamiento con ≥ 3 antihipertensivos en dosis óptimas, uno de los cuales es un diurético. **Mejor 4 fármacos tras añadir un antialdosterónico salvo contraindicación**

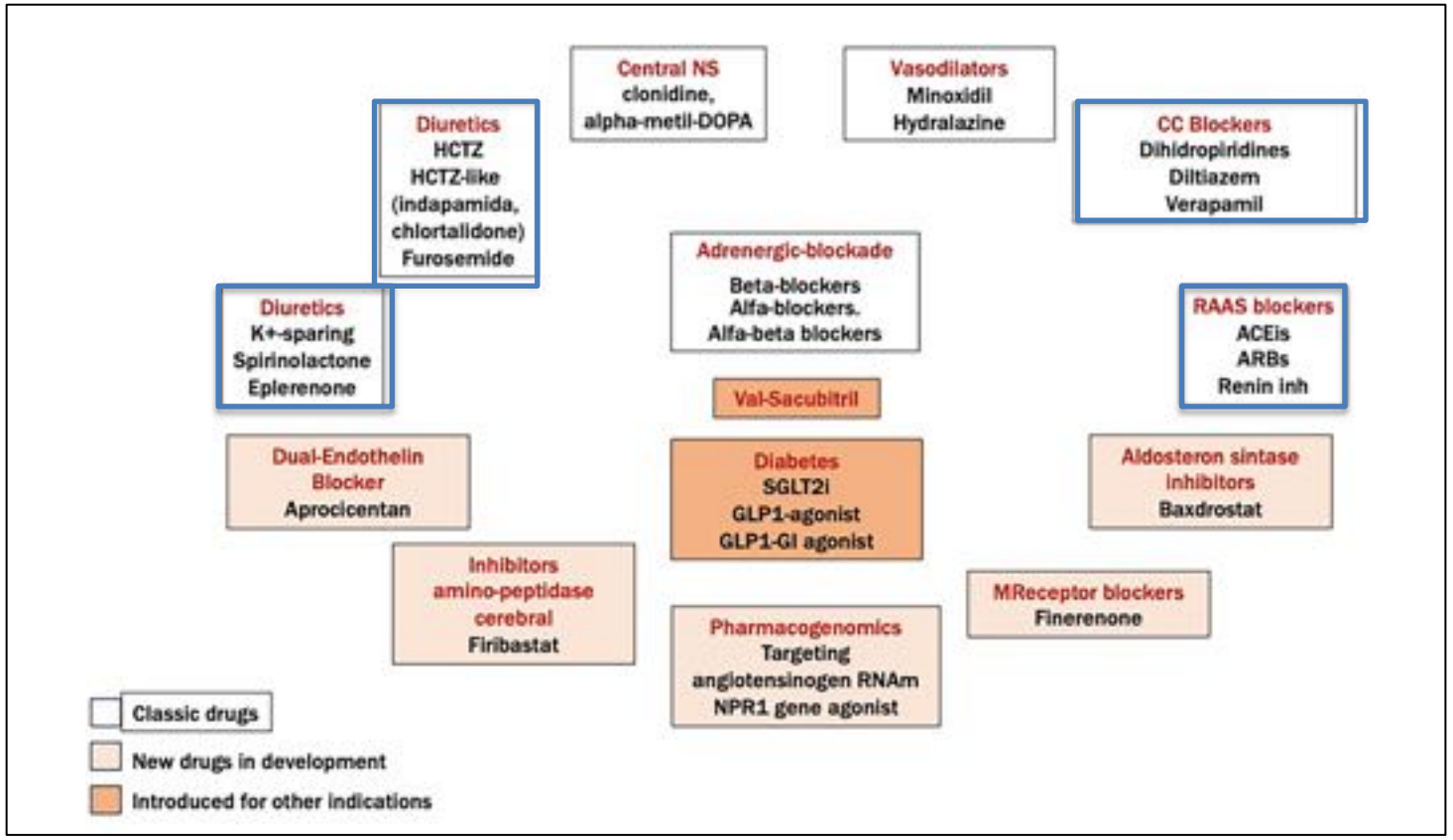
- Excluir HTA resistente falsa con **MAPA**, **HTA secundaria, SAHS**, **elevada ingesta de sal**, obesidad grave. **Fármacos que aumentan la PA**.

Considerar en pacientes con HTA no controlada (PA > 140/90 mmHg) y **alto riesgo cardiovascular** a pesar de tratamiento correcto o con mala adherencia muy difícil de mejorar y alto riesgo vascular.

Present and future of drug therapy in hypertension: an overview

Josep Redon & Rafael Carmena

BLOOD PRESSURE
2024, VOL. 33, NO. 1, 2320401
https://doi.org/10.1080/08037051.2024.2320401



ISGLT2

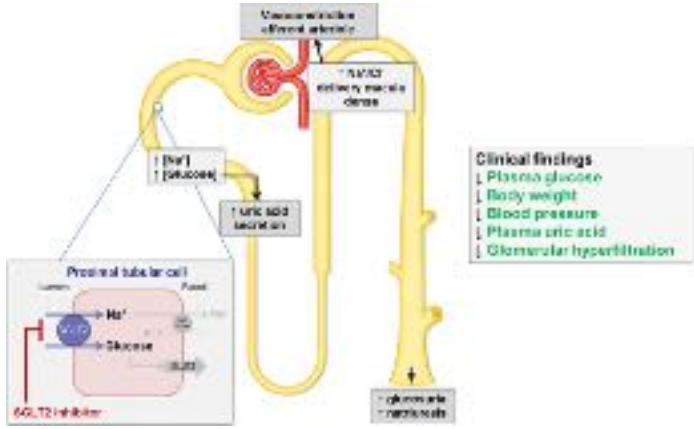
Current Hypertension Reports (2019) 21: 12
https://doi.org/10.1007/s11906-019-0920-4

ANTIHYPERTENSIVE AGENTS: MECHANISMS OF DRUG ACTION (MICHAEL E. ERNST, SECTION EDITOR)

Blood Pressure Lowering and Sodium-Glucose Co-transporter 2 Inhibitors (SGLT2is): More Than Osmotic Diuresis

Hillel Sternlicht [1] · George L. Bakris [1]

Published online: 12 February 2019



Diuresis osmótica inducida por glucosuria y natriuresis reduce la precarga y postcarga con descenso PA.

A dif de diuréticos no estimula el SRAA al no disminuir el vol intravascular

Hipertensión y riesgo vascular
www.elsevier.es/hipertension

ARTÍCULO ESPECIAL

Nuevos fármacos para la reducción del riesgo cardiovascular en pacientes con diabetes mellitus tipo 2

J.J. Gorgojo-Martínez

Unidad de Endocrinología y Nutrición, Hospital Universitario Fundación Alcorcón, Alcorcón, Madrid, E

	EMPA-REG OUTCOME	CANVAS Program	DECLARE	LEADER	SUSTAIN 6	HARMONY OUTCOMES
Fármaco	Empagliflozina	Canagliflozina	Dapagliflozina	Liraglutida	Semaglutida	Albiglutida
HbA1c (%)	−0,24 (10 mg)[a] −0,36 (25 mg)[a]	−0,58[a]	−0,42[a]	−0,4[a]	−0,66 (0,5 mg)[a] −1,05 (1 mg)[a]	−0,52[a]
Peso (kg)	−1,6 (10 mg)[a] −2,0 (20 mg)[a]	−1,6[a]	−1,8[a]	−2,3[a]	−2,87 (0,5 mg)[a] −4,35 (1 mg)[a]	−0,83[a]
PAS (mmHg)	−2,9 (10 mg)[b] −2,0 (25 mg)[b]	−3,9[a]	−2,7[a]	−1,2[a]	−1,27 (0,5 mg) −2,59 (1 mg)[a]	−0,67
PAD (mmHg)	−0,2 (10 mg)[b] 0,1 (25 mg)[b]	−1,4[a]	−0,7[a]	+0,6[a]	+0,04 (0,5 mg) +0,14 (1 mg)	NC
Colest. LDL (mg/dl)	+0,9 (10 mg)[b] +3,3 (25 mg)[b]	+4,7[a]	NC	NC	−4% (0,5 mg)[a] −1% (1 mg)	NC
Colest. HDL (mg/dl)	+1,2 (10 mg)[b] +2,0 (25 mg)[b]	+2,0[a]	NC	NC	0% (0,5 mg) +4% (1 mg)[a]	NC
F. cardíaca (lpm)	+0,4 (10 mg)[b] −0,3 (25 mg)[b]	NC	NC	+3[a]	+2,02 (0,5 mg)[a] +2,47 (1 mg)[a]	+1,4[a]
Hipoglucemias totales (%)	PBO: 28 EMPA 10: 27,6 EMPA 25: 27,9	PBO: 50 CANA: 46,4	NC	PBO: 45,6 LIRA: 43,7[a]	PBO:21,5 SEMA 0,5: 23,1 SEMA 1: 21,7	NC
Reducción significativa hipoglucemias graves	No	No	Sí	Sí	No	Sí

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Table 1. New antihypertensive drugs in development.

Drug and trial name	Phase trial	Inclusion criteria	Study design	Drug administration	Blood Pressure reduction mmHg	Comments
Dual endothelin A and B receptor blocker						
Aprocicentan [45] PRECISION	III	Resistant HTN	Placebo control over 3–4 drugs treatment[a]	Oral oid 12.5 and 25 mg	Sist/Diast Office −3.8/−3.7 24h −4.2/−5.9	The most frequent adverse event was mild-to-moderate oedema or fluid retention (18% with 25 mg)
Aminopeptidase A blocker						
Firibastat [50] FRESH	III	Dificult BP control	Placebo control over 2–3 drugs treatment[a]	Oral bid 500 mg	No superiority against placebo	No reported
Mineralocorticoid receptor blocker						
Eplerenone [56] ARTS-DN	IIb	Type 2 DM and CKD	Placebo control	Oral oid 10 and 15 mg	Sist 24h −8.3/−11.2	Serious AEs occurred in 3.3% of patients
Aldosterone synthase blocker						
Baxdrostat [59]	II	Resistant HTN	Placebo control over 3–4 drugs treatment[a]	Oral oid 1 and 2 mg	Sist Office −8.1/−11.0	Adverse events that occurred in 5% or more patients in any of the trial groups were urinary tract infections, hyperkalemia, headache, and fatigue
mRNA Angiotensinogen targeted						
IONIS-AGT-Lrx[b] [70]	II	Hypertensive	Placebo control over 2–3 drugs treatment[a]	Weekly subcutaneous 80 mg	Despite large Sist (Diast reduction no significant differences with placebo	
Zilebesiran[c] [71]	I	Hypertensive	Placebo control and over irbesartan	One subcutaneous 800 mg	Sist/Diast 24 h −9.1/−2.4 + low salt diet −18.8/−8.4 + irbesartan plus −6.3/−3.0	Attenuation of the effect on blood pressure by a high-salt diet and with an augmented effect through coadministration with irbesartan
Monoclonal antibody NPR1 gene activation						
XXB750 [69]	II	Resistant HTN	Placebo control over 3–4 drugs treatment[a]	Monthly subcutaneous Several dose 30 to 240 mg	24 h Sist/Diast	In development

[a]Multicentre, blinded, randomised, parallel-group
[b]Antisense oligonucleotide
[c]Small interfering molecule.

Nonsteroidal Dihydropyridine-Based Mineralocorticoid Receptor Antagonists

Espironolactona

Últimos años tratamiento clave HTA refractaria

Esaxerenona
Apararenona

Eplerenona a pesar de menos efectos secundarios no aprobado para tto HTA

Eplerenona

European Journal of Heart Failure (2016) **18**, 28–37
doi:10.1002/ejhf.444

REVIEW

Non-steroidal mineralocorticoid receptor antagonism for the treatment of cardiovascular and renal disease

Peter Bramlage[1,2]*, Stephanie L. Swift[1†], Martin Thoenes[3], Joan Minguet[1], Carmen Ferrero[2], and Roland E. Schmieder[4]

[1]Institute for Pharmacology and Preventive Medicine, Mahlow, Germany; [2]Department of Pharmacy and Pharmaceutical Technology, Faculty of Pharmacy, University of Sevilla, Spain; [3]Léman Research Institute, Oberägeri, Switzerland; and [4]Department of Nephrology and Hypertension, University Hospital of the University Erlangen-Nürnberg, Erlangen, Germany

Table 2 Finerenone in clinical trials

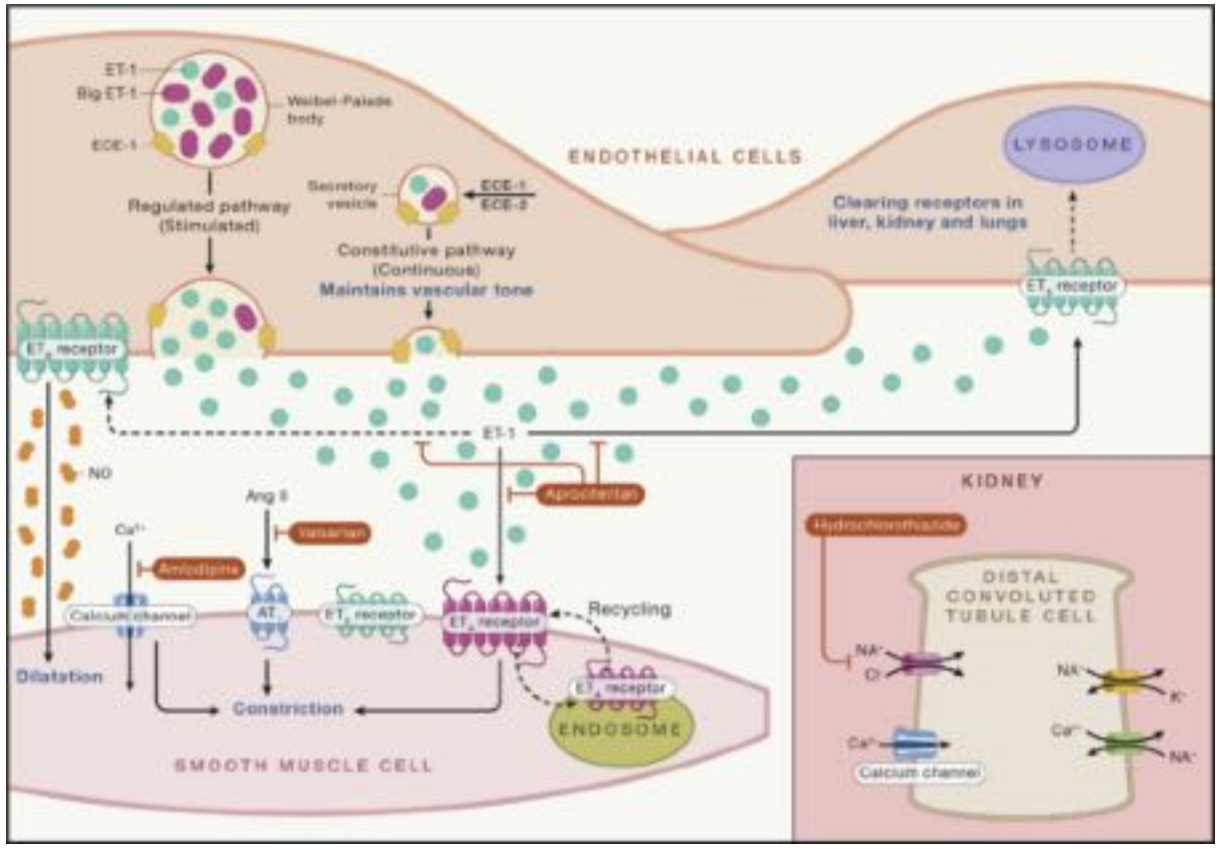
Clinical trial identifier	Phase	Study	Patient population	Estimated patient group size	Daily finerenone dose (mg)	Time frame	Comparator arm(s)	Primary (1°) and seconday (2°) outcome measures	Trial start date	Publications
NCT01473108	I	Safety, tolerability, pharmacokinetics, and pharmacodynamics after administration of 0.5 mg of fludrocortisone	Healthy male subjects	$n=67$	2.5, 5, 10, 15, or 20	Single dose, monitored up to 28 days	Placebo Eplerenone 50 mg/day	1° Pharmacodynamics (natriuresis) 2° Pharmacokinetics [maximum concentration (C_{max}) and area under curve (AUC)] and adverse events	March 2010	Lentini *et al.*[43]
NCT01687920	I	Dose proportion	Healthy male subjects	$n=25$	1.25, 2.5, 5, 7.5, or 10	Single dose, monitored up to 48 h	N/A	1° Pharmacokinetic dose proportionality 2° Adverse events	September 2012	
NCT01345656	II	Safety and tolerability (ARTS)	Part A: subjects with stable chronic HF with LV systolic dysfunction and mild CKD Part B: subjects with stable chronic HF with left ventricular systolic dysfunction and moderate CKD	$n=457$	2.5, 5, 10, or (5 × 2)	Daily dose for 4 weeks,monitored up to 4 weeks	Placebo Spironolactone 25–50 mg/day	1° Change in serum potassium 2° Change in serum magnesium, BP, and heart rate	May 2011	Pitt *et al.*[49,50]
NCT01874431	II	Safety and efficacy (ARTS-DN)	Subjects with type 2 diabetes mellitus and diabetic nephropathy	$n=821$	1.25, 2.5, 5, 7.5, 10, 15, or 20	Daily dose for 90 days, monitored up to 120 days	Placebo	1° Change in UACR 2° Change in serum potassium, renal function, quality of life, and adverse events	June 2013	Ruilope *et al.*,[52] Bakris *et al.*[53]
NCT01968668	II	Safety and efficacy (ARTS-DN Japan)	Japanese subjects with type 2 diabetes mellitus and diabetic nephropathy	$n=96$	1.25, 2.5, 5, 7.5, 10, 15, or 20	Daily dose for 90 days, monitored up to 90 days	Placebo	1° Change in UACR 2° Change in serum potassium	October 2013	
NCT01807221	IIb	Safety and efficacy (ARTS-HF)	Subjects with worsening chronic HF and LV systolic dysfunction and either type 2 diabetes mellitus with or without CKD or CKD alone	$n=1058$	2.5, 5, 7.5, 10, or 15	Daily dose for 90 days, monitored up to 120 days	Placebo Eplerenone 25–50 mg/day	1° Relative decrease in NT-proBNP 2° Change in serum potassium, BP, heart rate, and adverse events	June 2013	Pitt *et al.*,[54] Filippatos *et al.*[55]
NCT01955694	IIb	Safety and efficacy (ARTS-HF Japan)	Japanese subjects with worsening chronic HF and LV systolic dysfunction and either type 2 diabetes mellitus with or without CKD or moderate CKD alone	$n=96$	2.5, 5, 7.5, 10, or 15	Daily dose for 90 days, monitored up to 90 days	Placebo Eplerenone 25–50 mg/day	1° Percentage of patients with a relative decrease in NT-proBNP of >30% 2° Change in serum potassium	November 2013	

Data compiled from clinicaltrials.gov (1 May 2015).
BP, blood pressure; CKD, chronic kidney disease; HF, heart failure; N/A, not applicable; UACR, urinary albumin to creatinine ratio.

Finerenona

ARTS DN

Aprocitetan: Antagonista de receptores de endotelina



Aprobado USA en marzo-24, Tryvio®.

Europa proceso de pre-autorización por la EMA para HTA refractaria en combinación con otros fármacos.

Dosis recomendada: 12,5 mg v o una vez al día con o sin comida.

Teratogénico, precaución mujeres edad fértil

Ensayo clínico en fase 3 PRECISION

Efecto secundario más común: edemas, hepatotoxicidad

Cell *186*, January 19, 2023 a 2022 Elsevier Inc.

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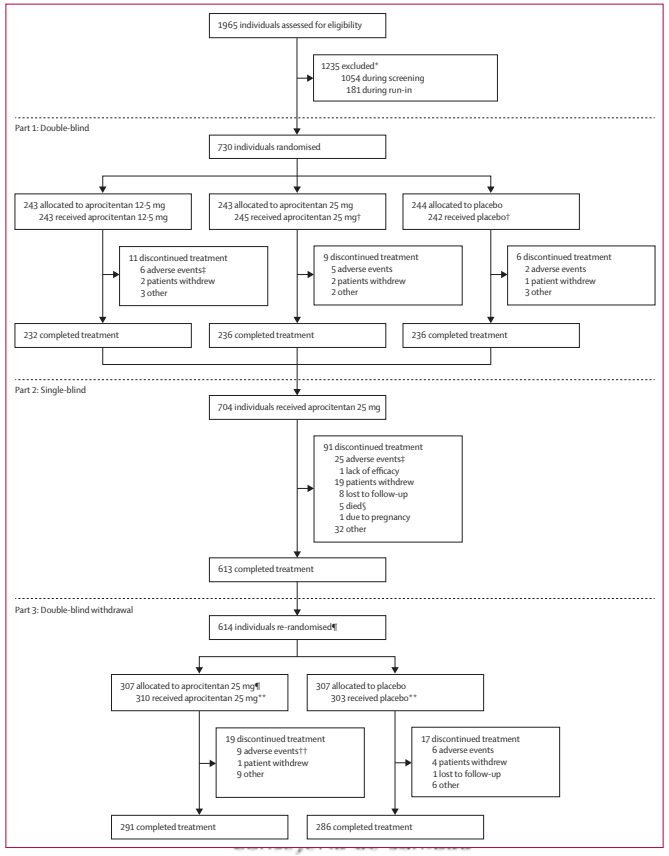
Dual endothelin antagonist aprocitentan for resistant hypertension (PRECISION): a multicentre, blinded, randomised, parallel-group, phase 3 trial

*Markus P Schlaich, Marc Bellet, Michael A Weber, Parisa Danaietash, George L Bakris, John M Flack, Roland F Dreier, Mouna Sassi-Sayadi, Lloyd P Haskell, Krzysztof Narkiewicz, Ji-Guang Wang, on behalf of the PRECISION investigators**

Lancet 2022; 400: 1927–37

HTA refractaria. 730 pacientes 48 semanas

4 fases:
1. Aleatorización: (4 a 12 semanas), todos (excepto betabloqueantes) polipíldora (amlodipino, valsartán e hidroclorotiazida 5/160/25 mg o 10/160/25 mg) exigiéndose la dosis máxima tolerada
2. Introducción del placebo (4 semanas) con diseño simple enmascarado
3. Tratamiento aleatorizado (48 semanas) se aleatorizaron a aprocitentan 12,5 mg, aprocitentan 25 mg o placebo (1:1:1), posteriormente aprocitentan 25 mg, diseño doble ciego controlado con placebo
4. De seguimiento (30 días) continuaron su terapia estándar.



	Aprocitentan 12·5 mg (n=243)	Aprocitentan 25 mg (n=243)	Placebo (n=244)
Age at screening, years			
Mean age at screening	61·2 (10·3)	61·7 (10·4)	62·2 (11·2)
18 to <65	143 (59%)	136 (56%)	130 (53%)
65 to <75	78 (32%)	85 (35%)	86 (35%)
≥75	22 (9%)	22 (9%)	28 (11%)
Gender			
Men	144 (59%)	145 (60%)	145 (59%)
Women	99 (41%)	98 (40%)	99 (41%)
Geographical area			
Europe	153 (63%)	143 (59%)	152 (62%)
North America	76 (31%)	81 (33%)	75 (31%)
Asia or Australia	14 (6%)	19 (8%)	17 (7%)
Race or ethnicity			
White	203 (84%)	200 (82%)	202 (83%)
Black or African American	28 (12%)	28 (12%)	26 (11%)
Asian	11 (5%)	14 (6%)	13 (5%)
Other†	1 (0)	1 (0)	3 (1%)
BMI at screening, kg/m²			
Mean BMI	33·6 (6·2)	34·3 (6·8)	33·3 (5·6)
Low to overweight (<30)	75 (31%)	70 (29%)	79 (32%)
Obese (30 to <40)	135 (56%)	132 (54%)	132 (54%)
Severely obese (≥40)	33 (14%)	41 (17%)	33 (14%)
Estimated glomerular filtration rate at baseline between 15 and <60 mL/min per 1·73 m²	55 (23%)	61 (25%)	46 (19%)
Urine albumin–creatinine ratio at baseline, mg/g‡			
<30	144 (60%)	155 (65%)	154 (65%)
30 to 300	63 (26%)	55 (23%)	56 (24%)
>300	34 (14%)	28 (12%)	28 (12%)
Medical history			
Diabetes	131 (54%)	137 (56%)	127 (52%)
Ischaemic heart disease	73 (30%)	79 (32%)	73 (30%)
Congestive heart failure	48 (20%)	51 (21%)	44 (18%)
Sleep apnoea syndrome	33 (14%)	39 (16%)	31 (13%)
Stroke§	20 (8%)	21 (9%)	16 (7%)
≥4 antihypertensive drugs at screening*	151 (62%)	158 (65%)	151 (62%)
Unattended automated office blood pressure at baseline, mm Hg			
Systolic blood pressure	153·2 (8·8)	153·3 (9·0)	153·3 (9·0)
Diastolic blood pressure	87·9 (9·4)	87·7 (9·7)	87·1 (9·9)
Ambulatory blood pressure monitoring at baseline, mm Hg¶			
24 h systolic blood pressure	137·7 (13·3)	137·6 (15·2)	137·1 (13·6)
24 h diastolic blood pressure	83·5 (8·7)	82·5 (10·0)	82·5 (9·1)

Data are mean (SD) or n (%). *The overall patient characteristics and antihypertensive drugs at screening have been previously published.[24] †Includes American Indian or Alaska Native; Native Hawaiian or other Pacific Islander; other; and not reported. ‡The number of patients used to calculate the urine albumin–creatinine ratio were: 241 (99%) patients for aprocitentan 12·5 mg; 238 (98%) patients for aprocitentan 25 mg; and 238 (98%) patients for placebo. §Includes ischaemic and haemorrhagic strokes and excludes other CNS disorders. ¶The number of patients used to calculate the ambulatory blood pressure monitoring at baseline were: 206 (85%) patients for aprocitentan 12·5 mg; 207 (85%) patients for aprocitentan 25 mg; and 220 (90%) patients for placebo.

Table 1: **Characteristics of the randomised patients***

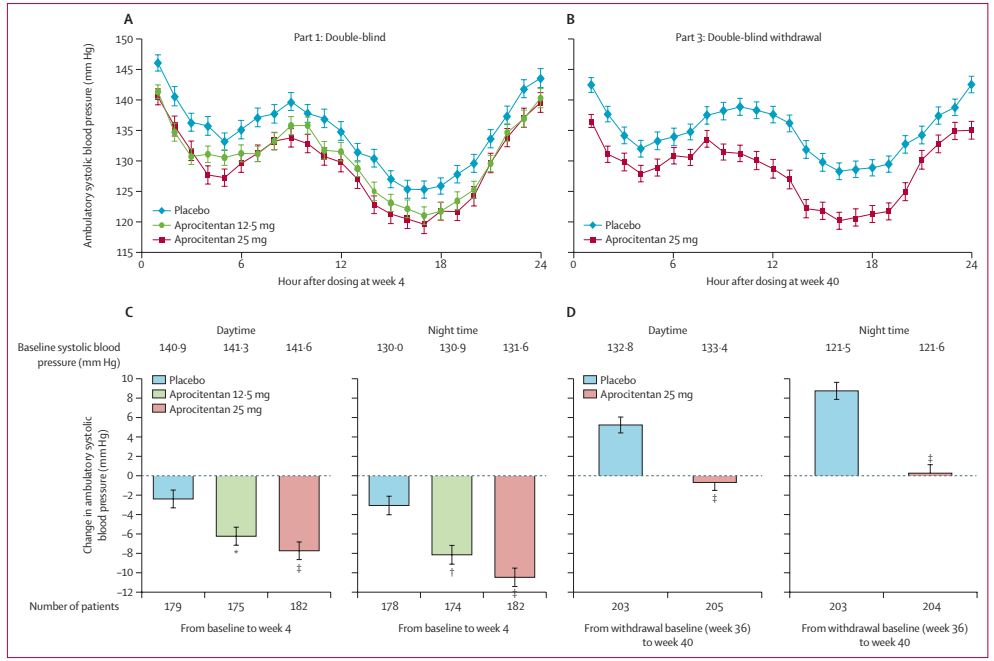


Figure 3: **Systolic blood pressure measured by 24-h ambulatory blood pressure monitoring after dosing (occurring after all visit assessments have been performed) at week 4 and week 40, and corresponding least square mean changes in daytime and night time ambulatory blood pressure from baseline to week 4 and week 40**
Bars are standard error of the mean. No correction for multiplicity was applied to the analysis of ambulatory blood pressure. *p=0·0033. †p=0·0002. ‡p<0·0001 (for comparison with placebo).

Descenso de PA frente a placebo fue de aprox 4 mmHg, lo cual obtuvo significación estadística.

El cambio medio PAS cta 15 mm Hg con aprocitentan y 11 mmHg con placebo.

	Aprocitentan 12·5 mg	Aprocitentan 25 mg	Placebo
Part 1: Double-blind	243	245	242
Patients with at least one event	30 (12·3%)	47 (19·2%)	7 (2·9%)
Oedema or fluid retention	22 (9·1%)	45 (18·4%)	5 (2·1%)
Anaemia or haemodilution	9 (3·7%)	3 (1·2%)	0
Hepatic disorder	0	1 (0·4%)	2 (0·8%)
Part 2: Single-blind	..	704	..
Patients with at least one event	..	185 (26·3%)	..
Oedema or fluid retention	..	128 (18·2%)	..
Anaemia or haemodilution	..	63 (8·9%)	..
Hepatic disorder	..	16 (2·3%)	..
Part 3: Double-blind withdrawal	..	310	303
Patients with at least one event	..	18 (5·8%)	15 (5·0%)
Oedema or fluid retention	..	8 (2·6%)	4 (1·3%)
Anaemia or haemodilution	..	6 (1·9%)	4 (1·3%)
Hepatic disorder	..	4 (1·3%)	7 (2·3%)

Data are n or n (%). Events are defined using the Medical Dictionary for Regulatory Activities (version 24.1). Safety analyses were done according to the received treatment group.

Table 2: **Treatment-emergent adverse events of special interest**

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Baxdrostat: Bloqueantes Aldosterona Sintasa

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 2, 2023 VOL. 388 NO. 5

Phase 2 Trial of Baxdrostat for Treatment-Resistant Hypertension

Mason W. Freeman, M.D., Yuan-Di Halvorsen, Ph.D., William Marshall, M.D., Mackenzie Pater, Ph.D., Jon Isaacsohn, M.D., Catherine Pearce, D.H.Sc., Brian Murphy, M.D., M.P.H., Nicholas Alp, M.D., Ajay Srivastava, M.D., Deepak L. Bhatt, M.D., M.P.H., and Morris J. Brown, M.D., for the BrigHTN Investigators*

La Aldosterona Sintasa controla la síntesis de Aldosterona, objetivo farmacológico desde hace décadas.

Selective inhibition of aldosterone synthase is essential but difficult to achieve because cortisol synthesis is catalyzed by another enzyme that shares 93% sequence similarity with aldosterone synthase.

In preclinical and phase 1 studies, baxdrostat had 100:1 selectivity for enzyme inhibition, and baxdrostat at several dose levels reduced plasma aldosterone levels but not cortisol levels.

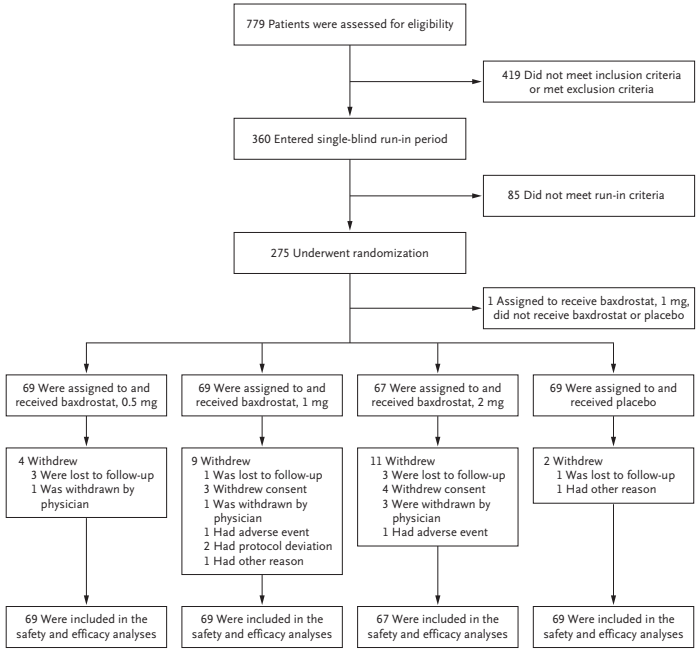
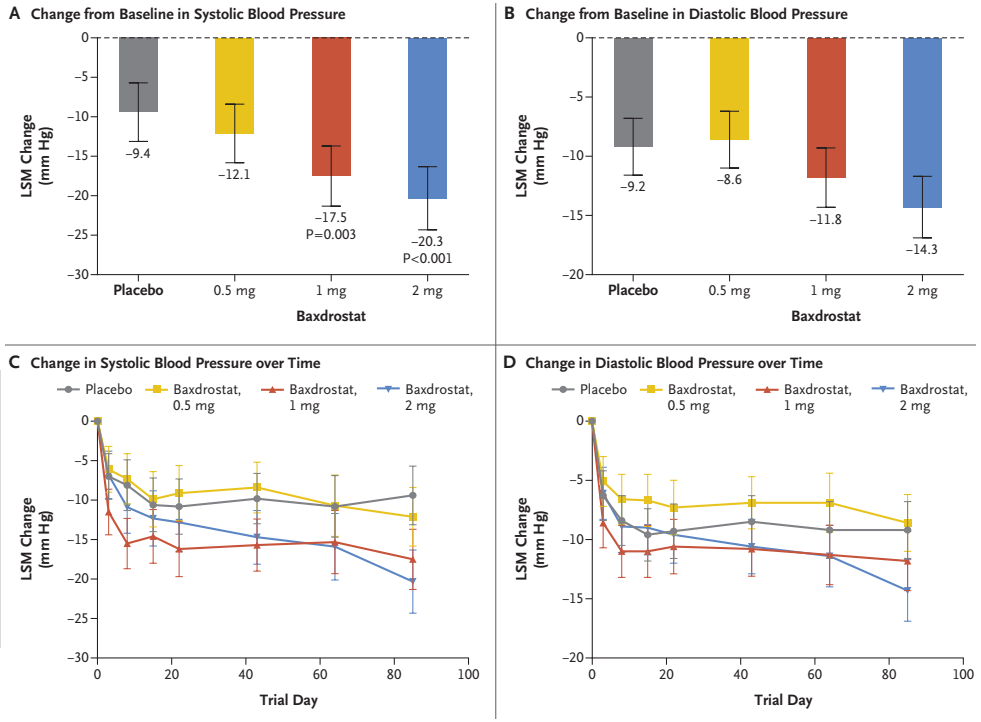


Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Placebo (N=69)	Baxdrostat, 0.5 mg (N=69)	Baxdrostat, 1 mg (N=70)	Baxdrostat, 2 mg (N=67)
Age				
Mean — yr	63.8±10.8	61.5±10.3	62.7±10.1	61.2±10.8
<65 yr — no. (%)	32 (46)	39 (56)	39 (56)	41 (61)
≥65 yr — no. (%)	37 (54)	30 (43)	31 (44)	26 (39)
Male sex — no. (%)	42 (61)	36 (52)	37 (53)	38 (57)
Race or ethnic group — no. (%)†				
White	51 (74)	45 (65)	48 (69)	47 (70)
Black	16 (23)	22 (32)	20 (29)	19 (28)
Asian	2 (3)	1 (1)	2 (3)	1 (1)
American Indian or Alaska Native	0	1 (1)	0	0
Hispanic or Latinx	30 (43)	33 (48)	23 (33)	32 (48)
Body-mass index‡	32.1±5.3	33.2±5.3	31.9±5.2	33.3±5.1
Seated blood pressure — mm Hg				
Systolic	148.9±12.4	147.6±12.5	147.7±13.1	147.3±11.8
Diastolic	88.2±6.1	87.6±7.7	87.7±6.0	88.2±7.1
Estimated glomerular filtration rate				
Mean — ml/min/1.73 m²	85.5±17.5	81.0±20.4	83.2±20.6	85.2±19.4
<60 ml/min/1.73 m² — no. (%)	6 (9)	14 (20)	11 (16)	8 (12)
≥60 ml/min/1.73 m² — no. (%)	63 (91)	55 (80)	59 (84)	59 (88)
Diabetes — no. (%)				
Yes	28 (41)	26 (38)	20 (29)	31 (46)
No	41 (59)	43 (62)	50 (71)	36 (54)
Sodium level — mmol/liter	139±3	139±2	138±3	140±2
Potassium level — mmol/liter	4.2±0.5	4.3±0.4	4.0±0.4	4.1±0.4
Creatinine level — mg/dl	0.9±0.2	1.0±0.3	0.9±0.3	0.9±0.3
Background antihypertensive drug — no. (%)				
Diuretic	69 (100)	69 (100)	70 (100)	67 (100)
Beta-blocker	47 (68)	44 (64)	41 (59)	35 (52)
Calcium-channel blocker	47 (68)	44 (64)	49 (70)	47 (70)
ACE inhibitor or ARB	63 (91)	64 (93)	65 (93)	64 (96)
General antihypertensive drug	9 (13)	8 (12)	11 (16)	8 (12)



248 pacientes

Dose-dependent changes in systolic blood pressure of −20.3 mm Hg, −17.5 mm Hg, −12.1 mm Hg, and −9.4 mm Hg were observed in the 2-mg, 1-mg, 0.5-mg, and placebo groups, respectively

Table 2. Adverse Events That Occurred during the Treatment Period.

Event	Placebo (N=69)		Baxdrostat, 0.5 mg (N=69)		Baxdrostat, 1 mg (N=69)		Baxdrostat, 2 mg (N=67)	
	No. of Patients with Event (%)	No. of Events	No. of Patients with Event (%)	No. of Events	No. of Patients with Event (%)	No. of Events	No. of Patients with Event (%)	No. of Events
Any serious adverse event*	2 (3)	3	0	0	2 (3)	3	6 (9)	12
Any adverse event	28 (41)	50	24 (35)	38	36 (52)	77	32 (48)	67
Adverse event of special interest†	0	0	1 (1)	1	5 (7)	6	2 (3)	3
Hyponatremia	0	0	0	0	2 (3)	2	1 (2)	1
Hypotension	0	0	0	0	1 (1)	1	0	0
Potassium level ≥6.0 mmol/liter	0	0	0	0	2 (3)	2	1 (2)	1
Potassium level between 5.5 and 5.9 mmol/liter on at least two consecutive occasions‡	0	0	1 (1)	1	2 (3)	2	1 (2)	1

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Table 1. New antihypertensive drugs in development.

Drug and trial name	Phase trial	Inclusion criteria	Study design	Drug administration	Blood Pressure reduction mmHg	Comments
Dual endothelin A and B receptor blocker						
Aprocicentan [45] PRECISION	III	Resistant HTN	Placebo control over 3–4 drugs treatment[a]	Oral oid 12.5 and 25 mg	Sist/Diast Office −3.8/−3.7 24h −4.2/−5.9	The most frequent adverse event was mild-to-moderate oedema or fluid retention (18% with 25 mg)
Aminopeptidase A blocker						
Firibastat [50] FRESH	III	Dificult BP control	Placebo control over 2–3 drugs treatment[a]	Oral bid 500 mg	No superiority against placebo	No reported
Mineralocorticoid receptor blocker						
Eplerenone [56] ARTS-DN	IIb	Type 2 DM and CKD	Placebo control	Oral oid 10 and 15 mg	Sist 24h −8.3/−11.2	Serious AEs occurred in 3.3% of patients
Aldosterone synthase blocker						
Baxdrostat [59]	II	Resistant HTN	Placebo control over 3–4 drugs treatment[a]	Oral oid 1 and 2 mg	Sist Office −8.1/−11.0	Adverse events that occurred in 5% or more patients in any of the trial groups were urinary tract infections, hyperkalemia, headache, and fatigue
mRNA Angiotensinogen targeted						
IONIS-AGT-Lrx[b] [70]	II	Hypertensive	Placebo control over 2–3 drugs treatment[a]	Weekly subcutaneous 80 mg	Despite large Sist (Diast reduction no significant differences with placebo	
Zilebesiran[c] [71]	I	Hypertensive	Placebo control and over irbesartan	One subcutaneous 800 mg	Sist/Diast 24 h −9.1/−2.4 + low salt diet −18.8/−8.4 + irbesartan plus −6.3/−3.0	Attenuation of the effect on blood pressure by a high-salt diet and with an augmented effect through coadministration with irbesartan
Monoclonal antibody NPR1 gene activation						
XXB750 [69]	II	Resistant HTN	Placebo control over 3–4 drugs treatment[a]	Monthly subcutaneous Several dose 30 to 240 mg	24 h Sist/Diast	In development

[a]Multicentre, blinded, randomised, parallel-group
[b]Antisense oligonucleotide
[c]Small interfering molecule.

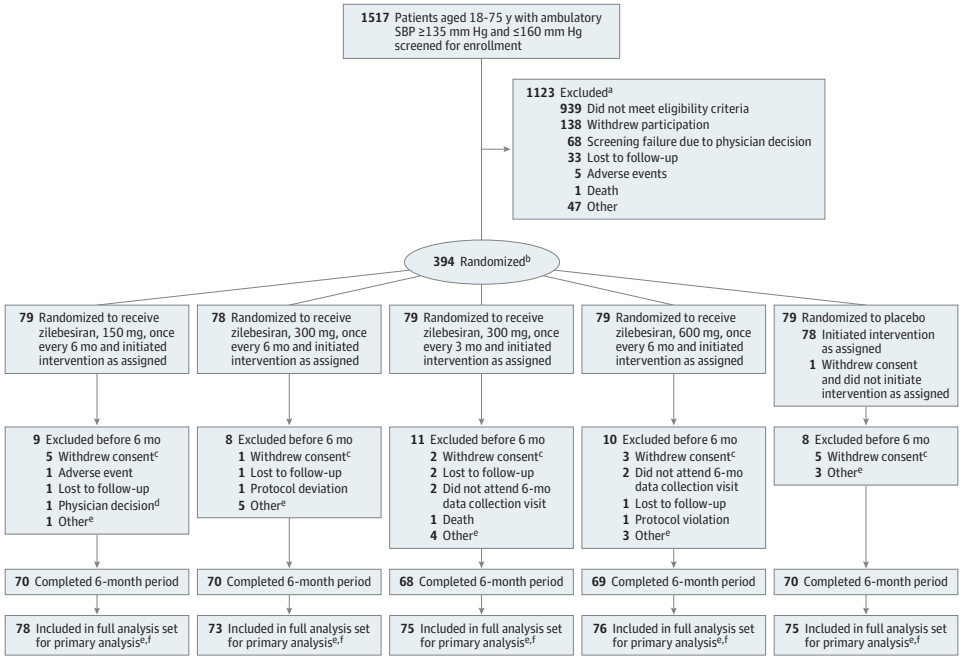
JAMA | Original Investigation

RNA Interference With Zilebesiran for Mild to Moderate Hypertension
The KARDIA-1 Randomized Clinical Trial

George L. Bakris, MD; Manish Saxena, MBBS; Anil Gupta, MD; Fadi Chalhoub, MD; Jongtae Lee, MD; Daniel Stiglitz, MSc; Nune Makarova, MD; Nitender Goyal, MD; Weinong Guo, MD; Dion Zappe, PhD; Akshay S. Desai, MD; for the KARDIA-1 Study Group

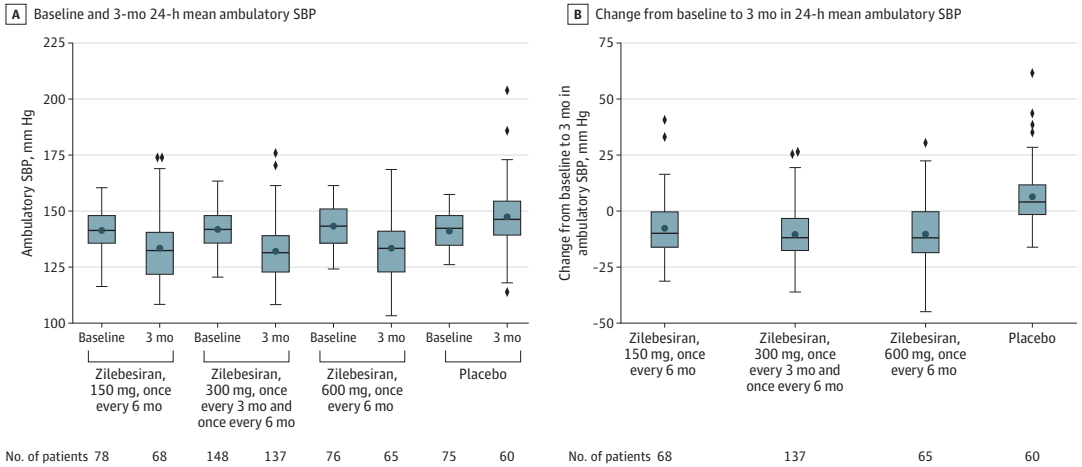
JAMA March 5, 2024 Volume 331, Number 9

El angiotensinógeno es el principal precursor del sistema renina-angiotensina-aldosterona, una vía clave en la regulación de la presión arterial.
Zilebesiran, una terapia de interferencia de ARN en fase de investigación, se dirige a la síntesis hepática de angiotensinógeno.



En adultos con hipertensión de leve a moderada, el tratamiento con zilebesiran en una gama de dosis a intervalos de 3 ó 6 meses redujo significativamente la PAS ambulatoria media en 24 horas al mes 3.

Estudio de fase 2, aleatorizado, doble ciego y de dosis variable de zilebesiran frente a placebo
78 centros de 4 países.
HTA Leve-moderada, PAS media diurna 135 -160 mm Hg tras un lavado antihipertensivo.
Se aleatorizaron a zilebesiran subcutáneo (150, 300 o 600 mg una vez cada 6 meses o 300 mg una vez cada 3 meses) o placebo (una vez cada 3 meses) durante 6 meses.



377 pacientes: 302 zilebesiran , 75 placebo

A los 3 meses, PAS 24 horas respecto basal
-7,3 mm Hg (IC del 95%: -10,3 a -4,4) zilebesiran, 150 mg, una vez cada 6 meses
-10,0 mm Hg (IC del 95%: -12,0 a -7 . 9) con zilebesirán, 300 mg, una vez cada 3 meses o cada 6 meses
-8,9 mm Hg (IC 95%, -11,9 a -6,0) con zilebesirán, 600 mg, una vez cada 6 meses
-6,8 mm Hg (IC 95%, 3,6-9,9) con placebo.

Reacciones adversas: reacciones en el punto de inyección e hiperpotasemia leve

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Crisis hipertensivas

- Urgencia hipertensiva
- Emergencia Hipertensiva

Urgencia hipertensiva

180/110

Crisis hipertensiva que no origina lesión orgánica ni complicaciones graves inmediatas.
SEC: **"hipertensión asintomática grave"**

- **La mayoría pacientes con HTA ya conocida mal controlada**
- 90% se resuelven espontáneamente o con modificaciones leves del tratamiento
- **Evitar descensos bruscos de la PA**

Fármaco	Inicio de acción	Duración de acción
Captopril 25 mg	15-30 minutos	4-6 horas
Enalapril 5-20 mg	1 hora	24 horas
Amlodipino 5 mg	1-2 horas	1-2 días
Furosemida 40 mg	30 minutos-1 hora	6-8 horas
Labetalol 100 mg	30 minutos-2 horas	6-12 horas

- Colocar en **condiciones óptimas** (lugar tranquilo y con poca luz).
- Adherencia al tratamiento
- Ansiolíticos si se considera que se encuentra bajo una situación de ansiedad.

Fármacos vía sublingual en general contraindicados

- **Hipertenso conocido abandono tto/mala adherencia**: reintroducción de su tto previo.
- **Hipertenso con buen cumplimiento**: subir la dosis o añadir otro fármaco.
- **No Dx previo HTA**: Iniciar tratamiento

Emergencia Hipertensiva

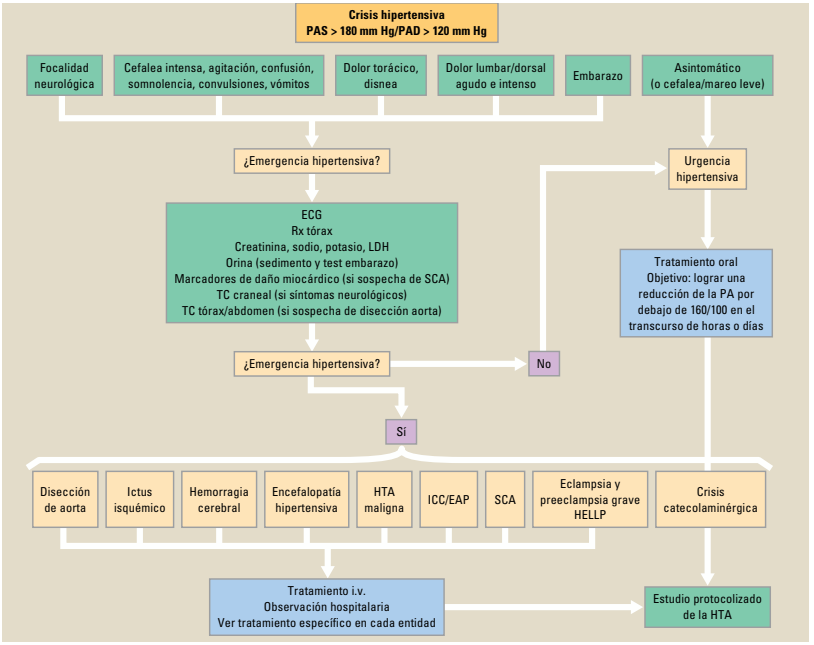
PAD > 120 mmHg y/o PAS > 210 mmHg

Elevación brusca PA complicada por la afectación aguda o progresiva de órganos diana

Reducción inmediata de la PA

Monitorización

Objetivo: reducción PA 10-20% en la primera hora, 5-15% siguientes 23 horas.
- PA < 180/120 la primera hora
- PA < 160/110 las siguientes 23 horas



Medicine. 2023;13(87):5164-8

SEC 2023

TABLE 24. Hypertensive emergencies requiring immediate BP-lowering with i.v. drug therapy

Clinical presentation	Timing and BP target	First-line treatment	Alternative
Malignant hypertension with or without acute renal failure	Several hours Reduce MAP by 20–25%	Labetalol[a] Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediately reduce MAP by 20–25%	Labetalol[a] Nicardipine	Nitroprusside
Acute coronary event	Immediately reduce SBP to <140 mmHg	Nitroglycerine Labetalol[a]	Urapidil
Acute cardiogenic pulmonary edema	Immediately reduce SBP to <140 mmHg	Nitroprusside or nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic dissection	Immediately reduce SBP to <120 mmHg and heart rate to <60 bpm	Esmolol AND nitroprusside or nitroglycerine or nicardipine	Labetalol[a] or metoprolol
Eclampsia and severe preeclampsia/HELLP	Immediately reduce SBP to <160 mmHg and DBP to <105 mmHg	Labetalol[a] or nicardipine and magnesium sulphate	Consider delivery

TABLE 25. Drug types, dose and characteristics for treatment of hypertension emergencies

Drug	Onset of action	Duration of action	Dose	Contraindications	Adverse effects
Esmolol	1 min	10–30 min	0.5–1 mg/kg i.v. bolus; 50–300 µg/kg/min i.v. infusion	Second-degree or third-degree AV block, systolic heart failure, asthma, bradycardia	Bradycardia
Metoprolol	1–2 min	5–8 h	2.5–5 mg i.v. bolus over 2 min; may repeat every 5 min to a maximum dose of 15 mg	Second-degree or third-degree AV block, systolic heart failure, asthma, bradycardia	Bradycardia
Labetalol[a]	5–10 min	3–6 h	10–20 mg i.v. bolus in 1 min; incremental doses ≥20 mg may be administered i.v. at 10 min intervals (max 80 mg) or 1–3 mg/min i.v. infusion until goal BP is reached	Second-degree or third-degree AV block; systolic heart failure, asthma, bradycardia	Bronchoconstriction, fetal bradycardia
Fenoldopam	5–15 min	30–60 min	0.1–0.3 µg/kg/min i.v. infusion, increase every 15 min with 0.1 µg/kg/min increments until goal BP is reached	Caution in glaucoma	
Clevidipine	2 min	10 min	1–2 mg/h i.v. infusion, increase every 2 min with 2 mg/h until goal BP, then titrate by smaller increments every 5–10 min		Headache, reflex tachycardia
Nicardipine	5–15 min	4–6 h	5–15 mg/h i.v. infusion, starting dose 5 mg/h, increase every 15–30 min with 2.5 mg until goal BP, maximum 15 mg/h	Liver failure	Headache, reflex tachycardia
Nitroglycerine	1–5 min	5–10 min	5–200 µg/min i.v. infusion, 5 µg/min increase every 5 min		Headache, reflex tachycardia
Nitroprusside	Immediate	1–3 min	0.3–0.5 µg/kg/min i.v. infusion, increase by 0.5 µg/kg/min every 5 min until goal BP (maximum dose 10 µg/kg/min)	Liver/kidney failure (relative)	Cyanide intoxication
Enalaprilat	5–15 min	4–6 h	0.62–1.25 mg i.v. bolus given over 5 min every 6 h	History of angioedema	
Urapidil	3–5 min	4–6 h	12.5–25 mg i.v. bolus; 5–40 mg/h as continuous infusion		
Clonidine	30 min	4–6 h	0.2–0.5 µg/kg/min i.v.		Sedation, rebound hypertension
Phentolamine	1–2 min	10–30 min	1–5 mg i.v. bolus or continuous i.v. infusion at a rate of 0.5–20 µg/kg/min		Tachyarrhythmia, chest pain

TRASTORNOS HIPERTENSIVOS DEL EMBARAZO

- **HIPERTENSIÓN CRÓNICA:** Presencia de HTA previa al embarazo o que aparece en gestantes de < 20 semanas.
- **HIPERTENSIÓN GESTACIONAL:** Presencia de HTA en gestantes de ≥ 20 semanas con TA previas normales, sin proteinuria ni afectación multisitémica materna ni afectación fetal.

Trascurridas 12 semanas después del parto se clasificará en HTA transitoria (cuando se normaliza la TA) o HTA crónica (cuando persiste elevada

- **HIPERTENSIÓN DE BATA BLANCA.** Se confirma con la demostración de tensiones normales tomadas en el domicilio, farmacia o centro de salud.
- **PREECLAMPSIA:** Presencia de hipertensión *de novo* que aparece después de la semana 20 de gestación y al menos una de las siguientes condiciones:

Proteinuria.

Evidencia de disfunción en algún órgano materno:

Trombocitopenia (< 100.000 plaquetas).

Insuficiencia renal de nueva aparición (Creatinina sérica > 1,2 mg/dl o una duplicación de la creatinina sérica en ausencia de enfermedad renal).

Alteraciones de función hepática (concentraciones de GPT (ALT) o GOT (AST) que duplican el límite superior del valor normal +/- dolor en epigastrio o hipocondrio derecho).

Edema pulmonar.

Síntomas neurológicos (hiperreflexia, cefalea severa, eclampsia, ACV) o visuales (escotomas).

Complicaciones hematológicas (CID, hemólisis). Restricción del crecimiento fetal (CIR). Disfunción útero-placentaria: restricción del crecimiento intrauterino (CIR) y/o aumento de resistencia en las arterias uterinas, disbalance angiogénico o muerte fetal intraútero.

- **SD HELLP:** Anemia hemolítica (LDH > 600, esquistocitos, bilirrubina indirecta…) + trombocitopenia < 100000 + elevación GOT > 2

- **ECLAMPSIA:** Preeclampsia asociada a convulsiones o coma no atribuibles a otra causa.

Se define como ***PE con criterios de gravedad*** la presencia de **uno o más** de los siguientes:

- HTA severa con PAS ≥ 160 y/o PAD ≥ 110 mmHg tomada en 2 ocasiones con al menos un intervalo corto de tiempo (15-30 minutos), ya que la HTA severa es criterio de inicio de tratamiento antihipertensivo y debe iniciarse cuanto antes.

  La aparición de cifras de PAS > 170-180 mmHg con/sin PAD > 110-120 mmHg se considera una emergencia por el alto riesgo de asociación con accidente vascular cerebral, por lo que requiere tratamiento inmediato.
- Alteraciones clínicas:
  - Síntomas prodrómicos de eclampsia: cefalea intensa, alteraciones visuales (escotomas, visión borrosa, diplopía o fotopsias), hiperreflexia con clonus, estupor.
  - Clínica de dolor hipocondrio derecho, epigastralgia, náuseas y/o vómitos persistentes.
  - Oliguria (< 500 ml/24 horas).
  - Edema de pulmón.
- Alteraciones analíticas:
  - Elevación de enzimas hepáticas GOT o GPT > 2DS
  - Elevación de LDH > 700 UI/l (hemólisis)
  - Creatinina sérica > 1,2 mg/dl
  - Trombocitopenia < 100.000/ml
  - Alteración de pruebas de coagulación.

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HTA CRÓNICA/PE

MANEJO: En consulta de Medicina Materno-fetal en conjunto con Medicina Interna (Unidad HTA y RV).

- Primer control:

- Analítica: Hemograma, ácido úrico, Cr, GOT, GPT, LDH, ACRO
- Ajustar medicación. Sustituir fármacos contraindicados (IECAs, atenolol, clortiazidas y ARA II), tener en cuenta que durante el primer trimestre puede ser necesario disminuir la dosis.
- AAS 100 mg/día al acostarse, inicio antes de semana 16 hasta 36 semanas.

- Seguimiento de la gestación: descartar preeclampsia añadida. MODELO FullPIERS

- Dieta normal.
- Control PA 2-3 veces/semana.
- Información sobre síntomas de preeclampsia.
- Seguimiento:
- Doppler uterinas en 2º Trimestre:
  - IP < p.75: Control en semana 28, 32 y 36.
  - IP > p.75: Control como alto riesgo PE, inicio semana 26.

- Fármacos antihipertensivos:

- Indicado con PA ≥ 140/90
- El objetivo es mantener PA entre 130-145/80-95
- Fármacos:
- **METILDOPA** (Aldomet ® 250 mg): 250-500 mg/8 horas. Dosis máxima 2-3 g/24 horas.
- **LABETALOL** (Trandate ®): 100-200 mg/6-8 horas. Dosis máxima 1200 mg/dl. De elección si no hay contraindicaciones. Desabastecimiento actualmente.
- NIFEDIPINO (Adalat ® 10 mg): 10 mg/6-8 horas. Puede ser retard (Adalat Oros ®) 30 mg/24 horas. Dosis máxima 60 mg/24 h.

- Finalización de la gestación: MODELO FullPIERS (si es > 5% considerar finalizar gestación)

  - Gestantes con EG < 37 semanas: manejo expectante, incluso en mujeres que requieren tratamiento antihipertensivo.
  - Gestantes con EG > 37 semanas: valoración individualizada, preferiblemente entre las 38 – 39+6 sem en función del Bishop y el pronóstico fetal.

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MANEJO HTA EN EL PUERPERIO

Mantener PA < 140/90.

- Seguimiento en Consultas Externas Unidad HTA-RV
- Ajustes de tratamiento.

FÁRMACOS ANTIHIPERTENSIVOS PUERPERIO

La clasificación de la asociación para la promoción e investigación científica y cultural de la lactancia materna de España (APILAM/e-lactancia) clasifica los fármacos en la lactancia en cuatro grupos:

- **Nivel 0**. Riesgo muy bajo. Compatible con lactancia, sin riesgo.
- **Nivel 1**. Riesgo bajo. Bastante seguro. Riesgo muy bajo.
- **Nivel 2**. Riesgo alto. Poco seguro. Valorar cuidadosamente, evitar o emplear una alternativa más segura.
- **Nivel 3**. Riesgo muy alto. Contraindicado. Alternativa o cesar lactancia.

Betabloqueantes

- ***Labetalol** 100-200/8-12 horas bloquea los receptores alfa y beta. Precaución en pacientes con insuficiencia cardíaca o asma. Como efectos secundarios puede causar hipotensión postural, dificultad para la micción, cefalea, fatiga… Nivel 0.
- **Metoprolol**, betabloqueante selectivo de los receptores beta 1. Indicación en tiroiditis postparto o pacientes con cardiopatías preexistentes. Precaución en asma y enfermedades pulmonares restrictivas. Efectos secundarios: hipotensión, BAV completo, bradicardia. Nivel 0.

Calcioantagonistas

- ***Nifedipino** Retard 30 mg cada 24 horas Nivel 0.
- Amlodipino: recomendado especialmente en hipertensas crónicas. Precaución en disfunción hepática (prolonga biodisponibilidad). Nivel 1

Inhibidores de la enzima convertidora de angiotensina (IECAs)

- ***Enalapril** De primera elección si betabloqueantes están contraindicados o en situación de desabastecimiento de Labetalol. Nivel 0 Inicio 5 mg/24 horas. 5-20 mg/12 horas

Antagonistas del receptor de angiotensina II (ARAII)

- **Losartán.** Nivel 1. Elevada fijación a proteínas plasmáticas y baja disponibilidad así que pasa poco a leche materna.

Diuréticos

- **Furosemida**. De elección si edema agudo de pulmón. Nivel 1.
- **Hidroclorotiacida**. Nivel 0, aunque su uso prolongado podría inhibir la lactancia.

Otros antihipertensivos

- **Hidralacina** De primera elección para las crisis hipertensivas en embarazo y postparto por su rápida acción. Efectos secundarios: Palpitaciones, taquicardia, náuseas y vómitos, diarrea, artralgias. Contraindicado en madres con lupus eritematoso sistémico y porfirias. Nivel 0.
- **Alfa-metildopa** es de los más usados y seguros. Actualmente no se recomienda en el postparto porque se asocia a depresión postparto. Nivel 0

*De elección

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DÍA MUNDIAL DE LA HIPERTENSIÓN 2024

¡Mida su presión arterial con precisión, contrólela y viva más tiempo!

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