Retos en hipertensión arterial secundaria

XIII Congreso Internacional de Cardiología
LII Jornada ACCI-SOLACI

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Conflicto de intereses

Conferencias (últimos 12 meses): Astra Zeneca, Boehringer Ingelheim, Novo Nordisk, Asofarma, Siegfried, Ferrer, Bayer, Merck, MDPharma

Advisory Board: Sanofi, Astra Zeneca, Novartis, Siegfried

Investigación clínica: MSD

Generalidades de HTA secundaria

- Conjunto de formas de HTA con una causa “orgánica” identificable y en consecuencia potencialmente curables
- La prevalencia es mayor a lo usualmente reportado
- En estudios de cohorte ronda entre un 10 y 35% (sesgo de selección?, Guías 2025: 5 a 25%); en pacientes con HTA resistente pueda alcanzar un 50%
- Claramente existe una **sobreposición etiopatogénica** (base fisiopatológica común)
- El hiperaldosteronismo primario y/o la apnea obstructiva del sueño son las causas mas frecuentes

Jones DW, Ferdinand KC, Taler SJ et al. Hypertension. 2025 Oct;82(10):e212-e316
McEvoy JW, McCarthy CP, Bruno RM et al. Eur Heart J. 2024 Oct 7;45(38):3912-4018

Hipertensión arterial secundaria
Causas según grupos etiológicos

Endocrine

- Primary aldosteronism (PA)
- Cushing's syndrome (CS)
- Pheochromocytoma / paraganglioma (PPGL)
- Primary hyperparathyroidism (PHPT)
- Hypothyroidism
- Thyrotoxicosis
- Acromegaly
- Apparent Mineralocorticoid Excess (congenital)

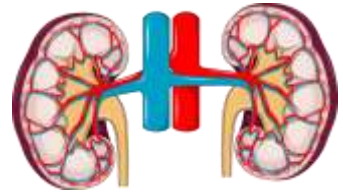
Renal

- Renal parenchymal disease
- Renin-producing tumor
- Primary sodium retention (Liddle's syndrome)
- Gordon' syndrome (hyperkalemia with metabolic acidosis, normal renal function, low or low-normal plasma renin activity, and normal or elevated plasma aldosterone concentration)

- Obstructive sleep apnea

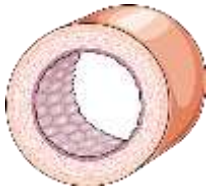
Reno-vascular hypertension (RVH)

- Atherosclerotic (ATS-RVH)
- Fibromuscular dysplasia (FMD-RVH)



Coarctation of the aorta

- Arteritis
- Intrarenal (i.e. microscopic polyangiitis, granulomatosis with polyangiitis)
- Schönlein-Henoch purpura
- Cryoglobulinemic vasculitis



Iatrogenic

- Drugs and exogenous hormones (i.e. contraceptive pills, immunosuppressive, non-steroidal anti-inflammatory drugs, etc.)
- Acquired Apparent Mineralocorticoid Excess (licorice, etc.)
- Cancer therapies (angiogenesis inhibitors as bevacizumab, and others)

Rossi GP, Bisogni V, Rossitto G et al. High Blood Press Cardiovasc Prev. 2020 Dec;27(6):547-560

HTA secundaria: prevalencia en pacientes hipertensos

Cause	Prevalence in hypertensive patients	Suggestive symptoms and signs	Screening Investigations
Obstructive sleep apnoea	5–10%	Snoring; obesity (can be present in non obese); morning headache; daytime somnolence	Epworth score and ambulatory polygraphy
Renal parenchymal disease	2–10%	Mostly asymptomatic; diabetes; haematuria, proteinuria, nocturia; anaemia, renal mass in adult polycystic CKD	Plasma creatinine and electrolytes, eGFR; urine dipstick for blood and protein, urinary albumin:creatinine ratio; renal ultrasound
Renovascular disease			
Atherosclerotic renovascular disease	1–10%	Older; widespread atherosclerosis (especially PAD); diabetes; smoking; recurrent flash pulmonary oedema; abdominal bruit	Duplex renal artery Doppler or CT angiography or MR angiography
Fibromuscular dysplasia		Younger; more common in women; abdominal bruit	
Endocrine causes			
Primary Aldosteronism	5–15%	Mostly asymptomatic; muscle weakness (rare)	Plasma aldosterone and renin, and aldosterone: renin ratio; hypokalaemia (in a minority): note hypokalaemia can depress aldosterone levels
Phaeochromocytoma	<1%	Episodic symptoms (the 5 'Ps'): paroxysmal hypertension, pounding headache, perspiration, palpitations, and pallor; labile BP; BP surges precipitated by drugs (e.g. beta-blockers, metoclopramide, sympathomimetics, opioids, and tricyclic antidepressants)	Plasma or 24 h urinary fractionated metanephrines
Cushing's syndrome	<1%	Moon face, central obesity, skin atrophy, striae and bruising; diabetes; chronic steroid use	24 h urinary-free cortisol
Thyroid disease (hyperthyroidism or hypothyroidism)	1–2%	Signs and symptoms of hyperthyroidism or hypothyroidism	Thyroid function tests
Hyperparathyroidism	<1%	Hypercalcaemia, hypophosphataemia	Parathyroid hormone, Ca^{2+}
Other causes			
Coarctation of the aorta	<1%	Usually detected in children or adolescence; different BP (≥20/10 mmHg) between upper–lower extremities and/or between right–left arm and delayed radial-femoral femoral pulsation; low ABI interscapular ejection murmur; rib notching on chest X-ray	Echocardiogram

Williams B, Mancia G, Spiering W et al. J Hypertens. 2018 Oct;36(10):1953-2041

Causas de hipertensión arterial secundaria (A)

	Prevalence	Indications for Additional Testing	Physical Examination Findings	Screening Tests	Confirmatory Tests
Common causes					
OSA[5–7]	25%-50%	Snoring, choking, gasping during sleep; daytime sleepiness; resistant hypertension	Obesity, large neck size (eg, >17 inches [men]; >16 inches [women], Mallampati class 3-4; loss of normal nocturnal BP fall	STOP-Bang Questionnaire[15]; Berlin Questionnaire[16]; overnight oximetry	Referral for polysomnography or home sleep apnea testing if no suspicion of nonrespiratory sleep disorders (eg, narcolepsy)
CKD[17,18]	14%	Diabetes, obstruction, hematuria; urinary frequency and nocturia; urinary incontinence, analgesic abuse; family history of polycystic kidney disease; elevated serum creatinine; abnormal urinalysis	Abdominal mass or large palpable kidneys (polycystic kidney disease); skin pallor	Electrolytes, including sodium, potassium, chloride, and bicarbonate, serum creatinine, urinalysis, urine microalbumin, serum cystatin C, renal ultrasound	Tests to evaluate cause of CKD
Primary aldosteronism[1–3,9,19]	5%-25%	Resistant hypertension; hypertension with hypokalemia (spontaneous or diuretic induced); hypertension and muscle cramps or weakness; hypertension and incidentally discovered adrenal mass; hypertension and obstructive sleep apnea; hypertension and family history of early-onset hypertension or stroke	Arrhythmias (with hypokalemia); especially AF	Electrolytes, including sodium and potassium, plasma aldosterone/renin activity ratio (correction of hypokalemia and withdrawal of MRA for 4-6 wks)	Oral sodium loading test (with 24-h urine aldosterone) or IV saline infusion test with plasma aldosterone at 4 h of infusion or captopril suppression test (in patients not on ACEi or ARB treatment), adrenal CT scan, adrenal vein sampling

OSA: apnea obstructiva del sueño
CKD: enfermedad renal crónica

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Causas de hipertensión arterial secundaria (B)

	Prevalence	Indications for Additional Testing	Physical Examination Findings	Screening Tests	Confirmatory Tests
Common causes					
Drug or alcohol induced[11]	2%-20%	Sodium-containing antacids; antidepressants; nicotine (smoking); alcohol; NSAIDs; oral contraceptives; cyclosporine or tacrolimus; sympathomimetics (decongestants, anorectics); cocaine, amphetamines and other illicit drugs; neuropsychiatric agents; erythropoiesis-stimulating agents; cancer treatment (VEGF inhibitors, Bruton tyrosine kinase inhibitors and others), clonidine withdrawal; herbal agents (Ma Huang, ephedra)	Fine tremor, tachycardia, sweating (cocaine, ephedrine, MAO inhibitors); acute abdominal pain (cocaine)	Urinary drug screen (illicit drugs)	Response to withdrawal of suspected agent
Renovascular hypertension[10]	0.1%-5%	Resistant hypertension; hypertension of abrupt onset or worsening or increasingly difficult to control; flash pulmonary edema (atherosclerotic); early-onset hypertension, especially in women (fibromuscular hyperplasia)	Abdominal systolic-diastolic bruit; bruits over other arteries (carotid, femoral)	Electrolytes, including sodium, potassium, chloride, and bicarbonate, renal duplex Doppler ultrasound; magnetic resonance arteriography; abdominal CT arteriography	Bilateral selective renal intra-arterial angiography

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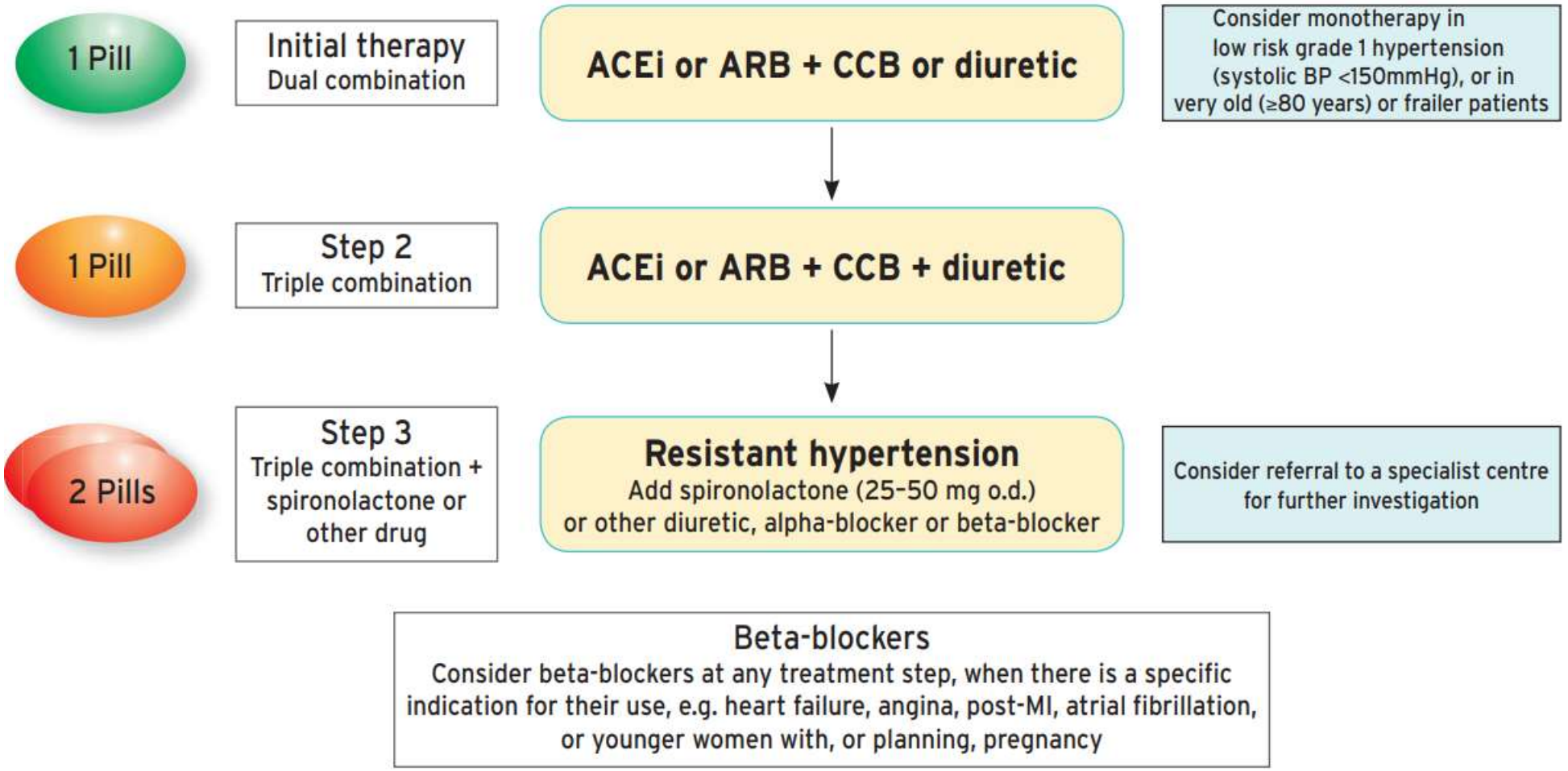
Abordaje de la Hipertensión Arterial



Williams B, Mancia G, Spiering W et al. Eur Heart J. 2018 Sep 1;39(33):3021-3104

Reto #1
Una sospecha meditada

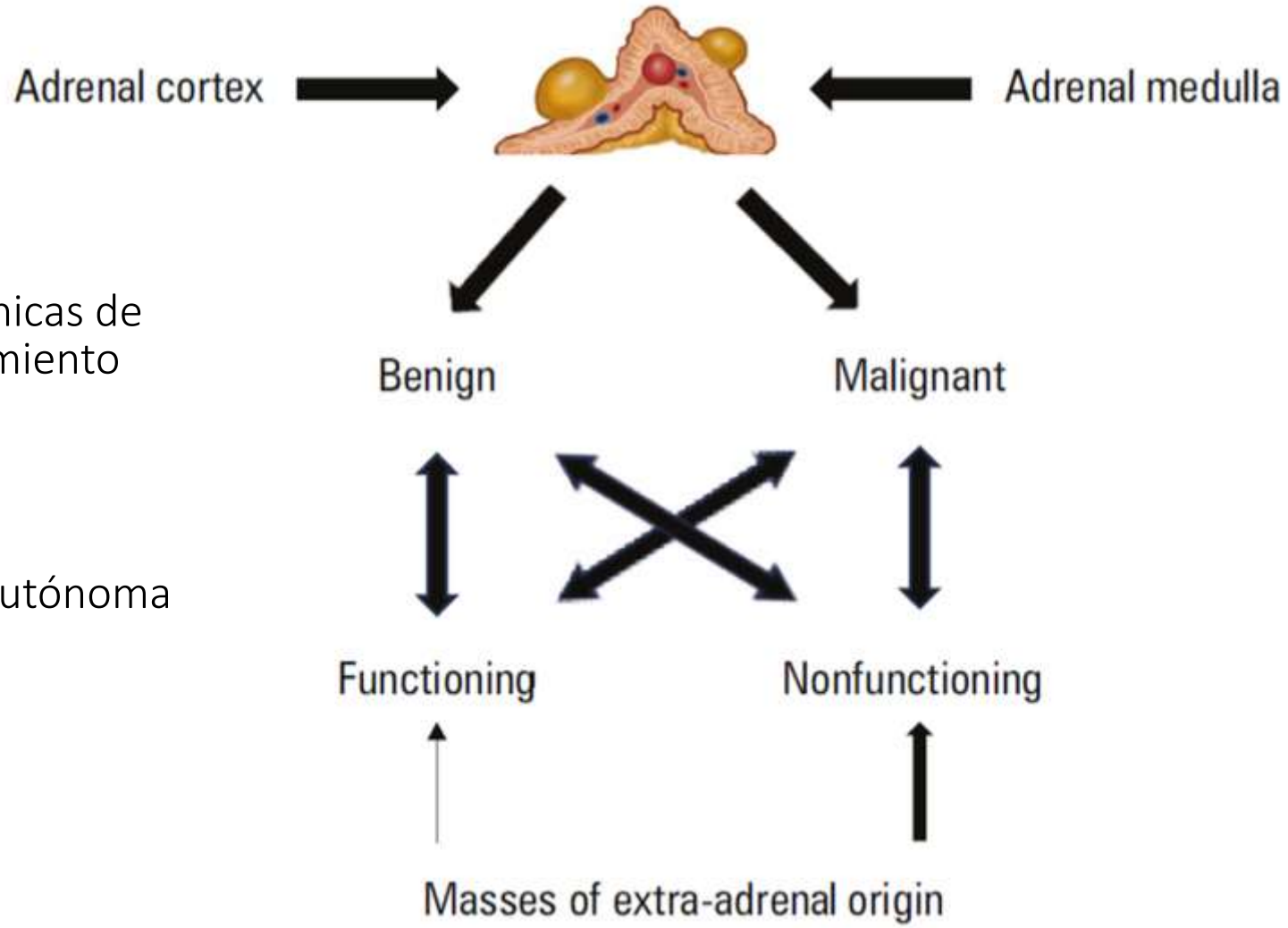
- Pacientes < 40 años, pero puede aparecer en cualquier rango etario
- Descompensación aguda en un hipertenso crónico previamente estable (un paciente dócil que se torna complejo)
- Hipertensión severa (grado 3)
- Hipertensión resistente
- Lesión extensa de órganos diana
- Un incidentaloma suprarrenal ? en un estudio diagnóstico justificado por otras razones en un paciente hipertenso

Rossi GP, Bisogni V, Rossitto G et al. High Blood Press Cardiovasc Prev. 2020 Dec;27(6):547-560

Etiología de los incidentalomas suprarrenales

↑ por mejores técnicas de imagen y envejecimiento poblacional

> frecuencia
MACS: secreción autónoma leve de cortisol



Araujo-Castro M, Calatayud Gutiérrez M et al. Endocrine. 2025 Sep 4. Online ahead of print
Łebek-Szatańska A, Januszewicz A, Kołodziejczyk-Kruk S et al. Pol Arch Intern Med. 2025 Feb 27;135(2):16949

Causas de hipertensión arterial secundaria según edad

Age group	Per cent with underlying cause	Typical causes
Young children (<12 years)	70–85	• Renal parenchymal disease • Coarctation of the aorta • Monogenic disorders
Adolescents (12–18 years)	10–15	• Renal parenchymal disease • Coarctation of the aorta • Monogenic disorders
Young adults (19–40 years)	5–10	• Renal parenchymal disease • Fibromuscular dysplasia (especially in women) • Undiagnosed monogenic disorders
Middle-aged adults (41–65 years)	5–15	• Primary aldosteronism • Obstructive sleep apnoea • Cushing's syndrome • Phaeochromocytoma • Renal parenchymal disease • Atherosclerotic renovascular disease
Older adults (>65 years)	5–10	• Atherosclerotic renovascular disease • Renal parenchymal disease • Thyroid disease

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Reto #2
Una investigación etiológica orientada

- Una historia clínica asertiva y un estetoscopio son las herramientas fundamentales
- En nuestro medio nunca ha sido fácil obtener muestras hormonales dirigidas a pesar de la gran colaboración de los cardiólogos intervencionistas
- No contamos con protocolos locales y el traslado de las muestras siempre ha sido complejo y burocrático
- Un diagnóstico bioquímico de un feocromocitoma sin masa suprarrenal, donde está el paraganglioma ?

Reto #3
Aceptación de un posible desliz clínico

- El incidentaloma suprarrenal era apático (no produce hormonas), maligno vs benigno ?
- Retirar el nódulo no resolvió el tenor hipertensivo (remodelado vascular negativo por exposición prolongada vs esencialidad)
- La disfunción tiroidea, el Cushing y la acromegalia elevan la presión arterial cuando el fenotipo es inequívoco y la reversibilidad clínica (para los últimos dos) es espúrea
- Una hipertensión de alerta (bata blanca) vició la ruta clínica. Siempre contamos con el automonitoreo de presión arterial (AMPA), el MAPA y el juicio clínico

Reto #4
¿Un tratamiento certero y definitivo?

- Los retos de la suprarrenalectomía (+ nefrectomía) son muy complejos (manejo prequirúrgico, expectativas). Status de monorrenal
- Los beta-bloqueadores y la espironolactona son las terapias puente y atienden ciertas comorbilidades
- En la hiperplasia suprarrenal hay que buscar consuelo eterno en el tratamiento farmacológico.
- La remisión de la apnea del sueño y la hipertensión esencial pueden lograrse en conjunto: manejo de la obesidad (quimérico?). Los aGLP-1 y agonistas duales aGLP-1 + aGIP ofrecen beneficios claros
- Aún cuando se resuelva el fenómeno anatómico vascular (aorta o riñón) el paciente debe continuar vigilancia permanente. Si el paciente se torna hipertenso a futuro debe evaluarse el motivo (oclusión vs debut esencial)

Anécdota