Hypertension Excellence Centre of the European Society of Hypertension

Università degli Studi Di Torino Scuola di Medicina

Dipartimento di Scienze Mediche

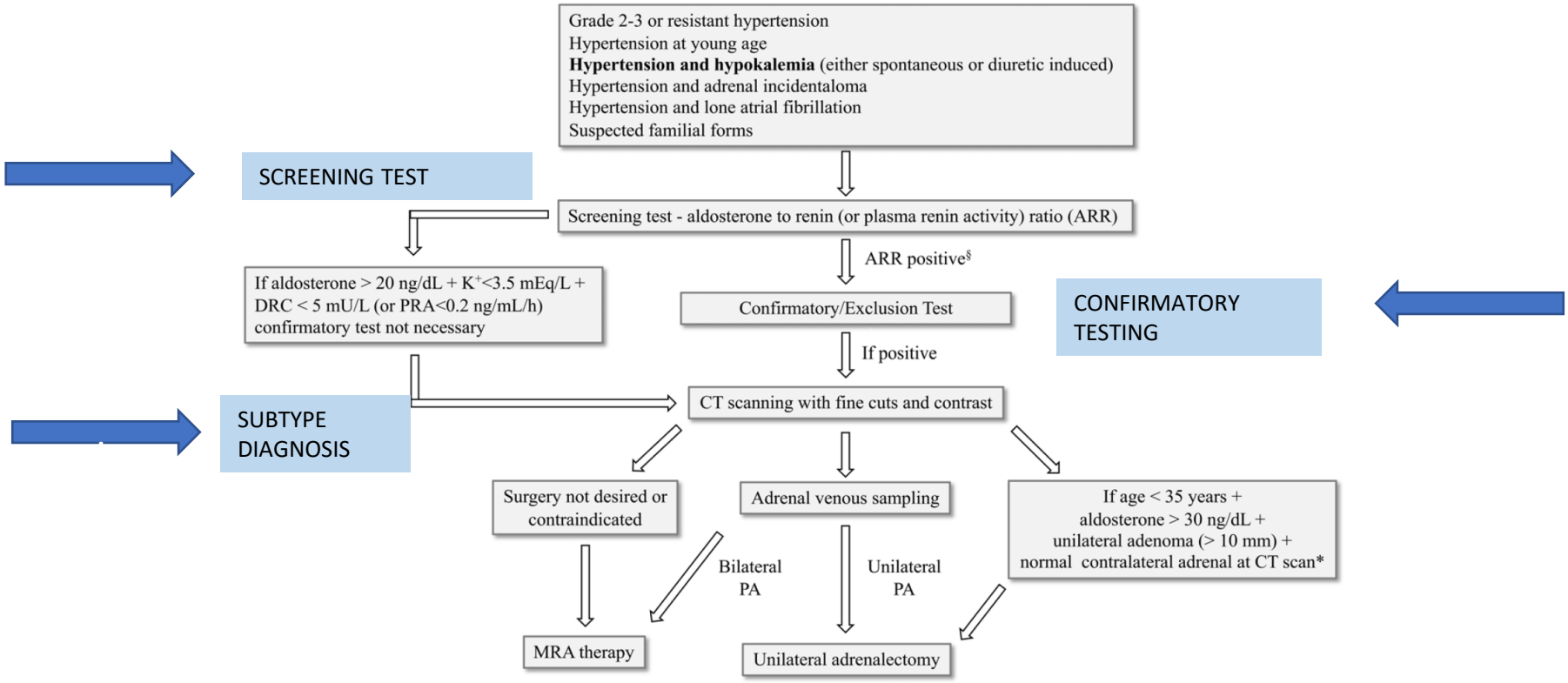
SIIA - Sezione Regionale Piemonte, Liguria e Valle d'Aosta

Le Nuove Linee Guida dell'Iperaldosteronismo Primario

Paolo MULATERO

Medicina Interna e Centro Ipertensione – Università di Torino

Consensus of the ESH Working Group on Endocrine Hypertension



Mulatero P et al. J Hypertens 2020

The Journal of Clinical Endocrinology & Metabolism, 2025, **00**, 1–43
https://doi.org/10.1210/clinem/dgaf284
Advance access publication 14 July 2025
Clinical Practice Guideline

Primary Aldosteronism: An Endocrine Society Clinical Practice Guideline

Gail K. Adler,[1] Michael Stowasser,[2] Ricardo R. Correa,[3] Nadia Khan,[4] Gregory Kline,[5] Michael J. McGowan,[6] Paolo Mulatero,[7] M. Hassan Murad,[8] Rhian M. Touyz,[9] Anand Vaidya,[1] Tracy A. Williams,[10] Jun Yang,[11,12] William F. Young,[8] Maria-Christina Zennaro,[13,14] and Juan P. Brito[8,15]

[1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA
[2]Endocrine Hypertension Research Centre, University of Queensland, Princess Alexandra Hospital, QLD 4102, Brisbane, Australia
[3]The Cleveland Clinic, Lerner College of Medicine, OH 44195, USA
[4]Department of Medicine, The University of British Columbia, Vancouver, T2T 5C7 Canada
[5]Department of Medicine, University of Calgary, Calgary, T2T 5C7 Canada
[6]Primary Aldosteronism Foundation, 3533 E Ahwatukee Ct, Phoenix, AZ 85044, USA
[7]Division of Internal Medicine and Hypertension, Department of Medical Sciences, University of Torino, Torino 10126, Italy
[8]Division of Endocrinology, Diabetes, Metabolism and Nutrition, Department of Medicine, Mayo Clinic, Rochester, MN 55905, USA
[9]Research Institute of McGill University Health Centre, McGill University, Montreal, H4A 3J1 Canada
[10]Department of Medicine IV, Ludwig Maximilian University of Munich, Munich 80336, Germany
[11]Centre for Endocrinology and Reproductive Health, Hudson Institute of Medical Research, Victoria 3168, Australia
[12]Department of Medicine, Monash University, Victoria 3168, Australia
[13]Université Paris Cité, Inserm, PARCC, Paris F-75015, France
[14]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service de Génétique, Paris F-75015, France
[15]Knowledge and Evaluation Research Unit, Division of Endocrinology, Diabetes, Metabolism and Nutrition, Department of Medicine, Mayo Clinic, Rochester, MN 55905, USA

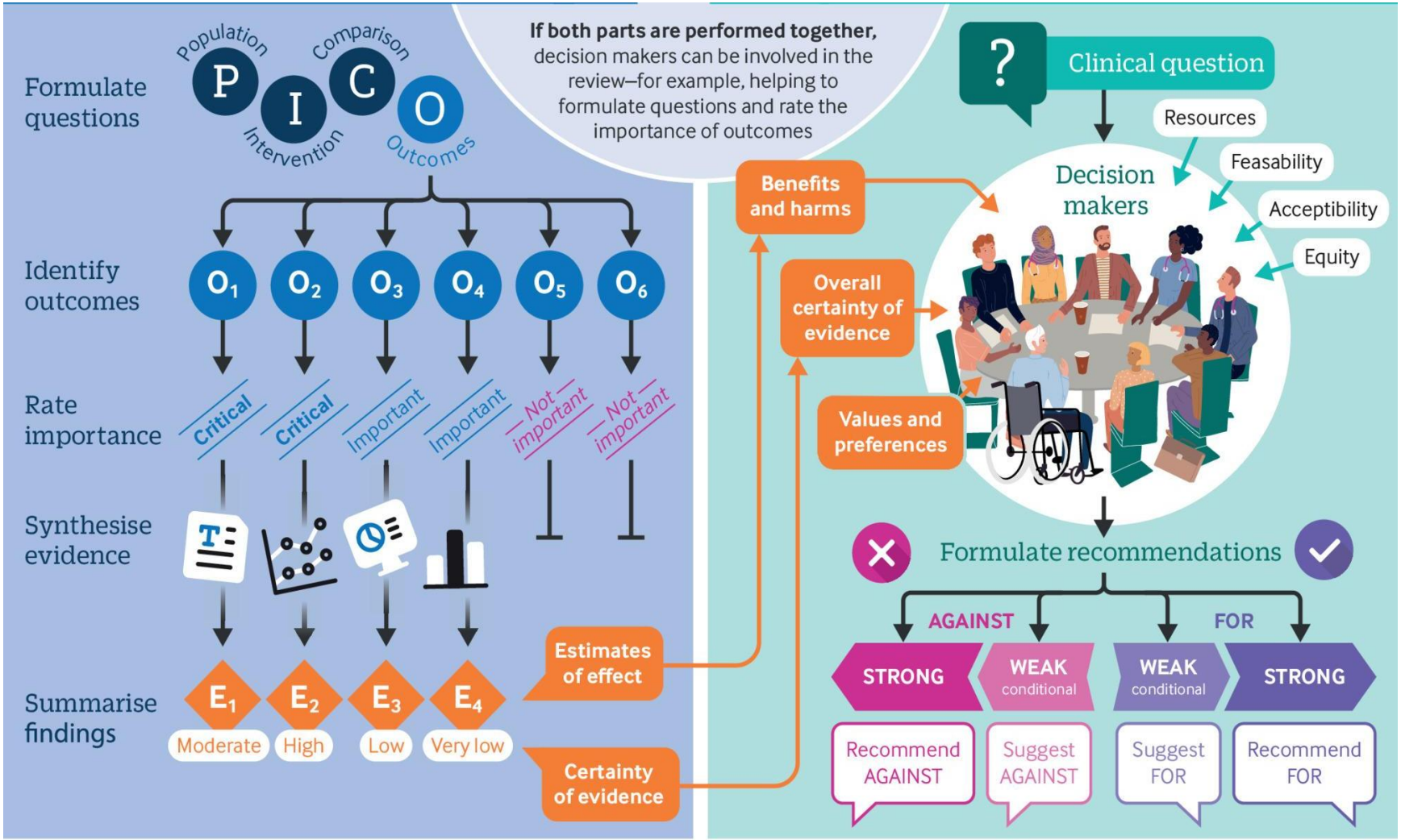
Primary Aldosteronism: An Endocrine Society Clinical Practice Guideline

Gail K. Adler,[1] Michael Stowasser,[2] Ricardo R. Correa,[3] Nadia Khan,[4] Gregory Kline,[5] Michael J. McGowan,[6] Paolo Mulatero,[7] M. Hassan Murad,[8] Rhian M. Touyz,[9] Anand Vaidya,[1] Tracy A. Williams,[10] Jun Yang,[11,12] William F. Young,[8] Maria-Christina Zennaro,[13,14] and Juan P. Brito[8,15]

The panel members were asked to prioritized 10 questions addressing the management of PA in adult individuals.

The 10 questions are presented using the PICO format

Population
Intervention
Comparator
Outcomes


Formulate questions
Population
Comparison
P
I
C
O
Intervention
Outcomes
Identify outcomes
O1
O2
O3
O4
O5
O6
Rate importance
Critical
Critical
Important
Important
Not important
Not important
Synthesise evidence
Summarise findings
E1
E2
E3
E4
Moderate
High
Low
Very low
Estimates of effect
Certainty of evidence
If both parts are performed together, decision makers can be involved in the review—for example, helping to formulate questions and rate the importance of outcomes
Clinical question
Resources
Feasability
Acceptibility
Equity
Decision makers
Benefits and harms
Overall certainty of evidence
Values and preferences
Formulate recommendations
AGAINST
FOR
STRONG
WEAK conditional
WEAK conditional
STRONG
Recommend AGAINST
Suggest AGAINST
Suggest FOR
Recommend FOR

Primary Aldosteronism: An Endocrine Society Clinical Practice Guideline

Gail K. Adler,[1] Michael Stowasser,[2] Ricardo R. Correa,[3] Nadia Khan,[4] Gregory Kline,[5] Michael J. McGowan,[6] Paolo Mulatero,[7] M. Hassan Murad,[8] Rhian M. Touyz,[9] Anand Vaidya,[1] Tracy A. Williams,[10] Jun Yang,[11,12] William F. Young,[8] Maria-Christina Zennaro,[13,14] and Juan P. Brito[8,15]

Question 1.

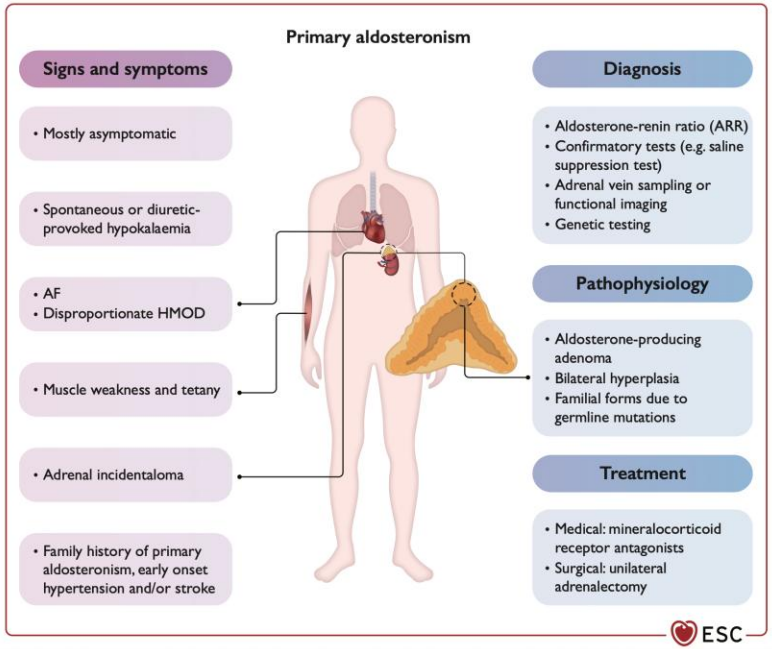
Should care that includes primary aldosteronism screening be applied to all individuals with hypertension, compared with care without screening?

Recommendation 1

In all individuals with hypertension, we suggest screening for primary aldosteronism (PA) (2 | ⊕⊕OO).

ESC European Society of Cardiology
European Heart Journal (2024) **45**, 3912–4018
https://doi.org/10.1093/eurheartj/ehae178

ESC GUIDELINES



AF, atrial fibrillation; HMOD, hypertension-mediated organ damage

Recommendation Table 13 — Recommendations for screening for secondary hypertension (see Evidence Tables 19 and 20)

Recommendations	Class[a]	Level[b]
It is recommended that patients with hypertension presenting with suggestive signs, symptoms or medical history of secondary hypertension are appropriately screened for secondary hypertension.[312,314,315,323,339]	I	B
Screening for primary aldosteronism by renin and aldosterone measurements should be considered in all adults with confirmed hypertension (BP ≥140/90 mmHg).[312,314,323,339]	IIa	B

© ESC 2024

ESC 2024

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2017 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER
VOL. 69, NO. 14, 2017
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2017.01.052

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

Silvia Monticone, MD, PhD,[a] Jacopo Burrello, MD,[a] Davide Tizzani, MD,[a] Chiara Bertello, MD,[a] Andrea Viola, MD,[a] Fabrizio Buffolo, MD,[a] Luisa Gabetti, MD,[b] Giulio Mengozzi, MD,[c] Tracy A. Williams, PhD,[a,d] Franco Rabbia, MD,[a] Franco Veglio, MD,[a] Paolo Mulatero, MD[a]

Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis

Silvia Monticone*, Fabrizio D'Ascenzo*, Claudio Moretti, Tracy Ann Williams, Franco Veglio, Fiorenzo Gaita, Paolo Mulatero

Summary
Background There is conflicting evidence, relying on heterogeneous studies, as to whether aldosterone excess is

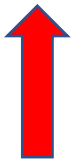
Lancet Diabetes Endocrinol 2017

ESC Hypertension Guideline McEvoy JW et al., Eur Heart J. 2024

American College of Cardiology/American Heart Association 2025 Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults

Recommendations for Primary Aldosteronism

COR	LOE	Recommendations
1	C-EO	1. In adults with hypertension, screening for primary aldosteronism is recommended in the presence of any of the following conditions to increase rates of detection, diagnosis, and specific targeted therapy: resistant hypertension (regardless of whether hypokalemia is present), hypokalemia (spontaneous or diuretic induced), OSA, incidentally discovered adrenal mass, family history of early-onset hypertension, or stroke at a young age (<40 years).
2b	C-EO	2. In adults with stage 2 hypertension, screening for primary aldosteronism may be considered to increase rates of detection, diagnosis, and specific targeted therapy.



Stage 2 BP >140/90

Circulation 2025

COR	LOE	Recommendations
1	C-LD	3. In adults with an indication for screening for primary aldosteronism, use of plasma aldosterone, renin activity, and the plasma aldosterone to renin activity ratio is recommended for initial screening to assess if there is biochemical evidence of primary aldosteronism.[1–3]
1	C-EO	4. In adults with an indication for screening for primary aldosteronism, it is recommended to continue most antihypertensive medications (other than mineralocorticoid receptor antagonists [MRAs]) prior to initial screening to minimize barriers to or delays in screening.

COR	LOE	Recommendations
1	C-EO	5. In adults with hypertension and a positive screening test for primary aldosteronism or continued suspicion for primary aldosteronism based on suppressed plasma renin or disproportionate target organ damage, referral to a hypertension specialist or endocrinologist is recommended for further evaluation and treatment.

Wilson JM & Jungner YG Principles and practice of mass screening for disease

Table 4. Evidence for the recommendation of primary aldosteronism screening

Importance *The condition should be an important health problem.*	PA is a frequent cause of secondary hypertension. PA, independent of blood pressure, is associated with increased mortality and morbidity if untreated.
Natural History *The condition being screened for should have a natural history that is understood and a recognized latent period.*	Individuals with PA develop organ damage and cardiovascular events if left untreated.
Difference in Management *Individuals with a positive screening test would receive different care than those with a negative test.*	Individuals with a positive screening test are candidates for PA-targeted therapy.
Available Treatment *Effective treatment should be available for the condition that improves outcomes if administered earlier than when the condition is clinically apparent.*	Specific medical therapies are available and effective. Also, adrenalectomy for lateralizing subtypes of PA is effective. PA-specific therapies reduce the rate of cardiovascular complications. Novel therapies are under investigation.
Difference in Outcomes *Improvement in outcomes based on management according to screening results outweighs harms of screening.*	Individuals with PA display a significant benefit from targeted treatment, with the possibility of cure in those with surgically resectable lateralizing adrenal disease. Individuals with potentially false-positive results are not exposed to harm if treated with aldosterone-blocking drugs since they also proved effective in individuals with primary hypertension. Careful selection for individuals undergoing AVS should be made to avoid unnecessary invasive procedures. Harms associated with screening are minimal as we provide pathways for screening that involve no or minimal withdrawal of current antihypertensive medications.
Accuracy *Certainty of evidence for a sufficient accuracy of the test is high or moderate.*	Screening tests are sufficiently accurate. False-negative results may be observed in mild forms or may be caused by variability in aldosterone concentration; aldosterone suppression testing can help to confirm PA.
Other Considerations *Screening should be cost-effective, acceptable to individuals, and feasible to implement.*	Screening for PA is cost-effective, convenient, and accepted by the individuals. Feasibility depends on collaboration between general practitioners, specialists, laboratories, and referral centers.

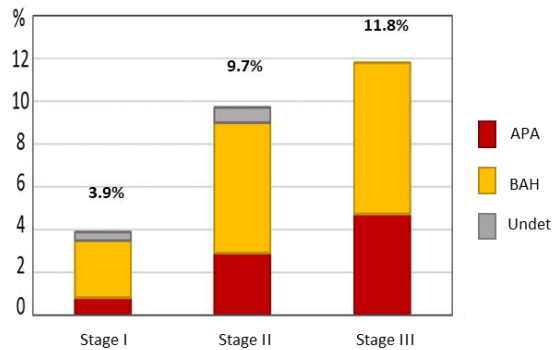
ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

PA Prevalence in the General Hypertensive Population and in Hypertensive Patients from Referral Centres

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

Silvia Monticone, MD, PhD,[a] Jacopo Burrello, MD,[a] Davide Tizzani, MD,[a] Chiara Bertello, MD,[a] Andrea Viola, MD,[a] Fabrizio Buffolo, MD,[a] Luisa Gabetti, MD,[b] Giulio Mengozzi, MD,[c] Tracy A. Williams, PhD,[a,d] Franco Rabbia, MD,[a] Franco Veglio, MD,[a] Paolo Mulatero, MD[a]

5.9%



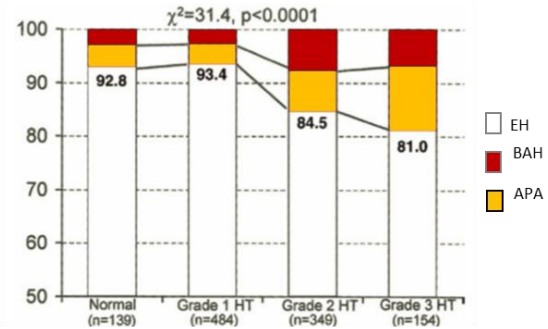
PATO Study
Monticone S, J Am Coll Cardiol 2017

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

Gian Paolo Rossi, MD, FACC, FAHA, Giampaolo Bernini, MD, Chiara Caliumi, MD, Giovambattista Desideri, MD, Bruno Fabris, MD, Claudio Ferri, MD, Chiara Ganzaroli, MD, Gilberta Giacchetti, MD, Claudio Letizia, MD, Mauro Maccario, MD, Francesca Mallamaci, MD, Massimo Mannelli, MD, Mee-Jung Mattarello, MD, Angelica Moretti, MD, Gaetana Palumbo, MD, Gabriele Parenti, MD, Enzo Porteri, MD, Andrea Semplicini, MD, FAHA, Damiano Rizzoni, MD, Ermanno Rossi, MD, Marco Boscaro, MD, Achille Cesare Pessina, MD, PhD, Franco Mantero, MD, for the PAPY Study Investigators

Padova, Ancona, Reggio Emilia, Pisa, L'Aquila, Palermo, Legnano, Roma, Firenze, Torino, and Reggio Calabria, Italy

11.2%

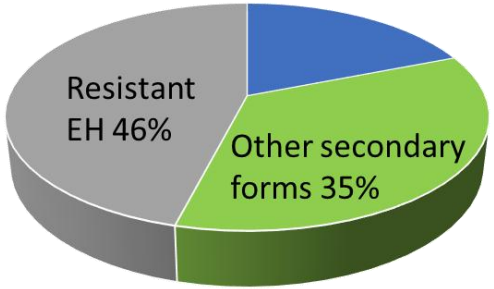


PAPY Study
Rossi GP, J Am Coll Cardiol 2006

Prevalence of primary aldosteronism and association with cardiovascular complications in patients with resistant and refractory hypertension

Mirko Parasiliti-Caprino[a], Chiara Lopez[a], Nunzia Prencipe[a], Barbara Lucatello[a], Fabio Settanni[b], Giuseppe Giraudo[c], Denis Rossato[d], Giulio Mengozzi[b], Ezio Ghigo[a], Andrea Benso[a], and Mauro Maccario[a]

PA 19%

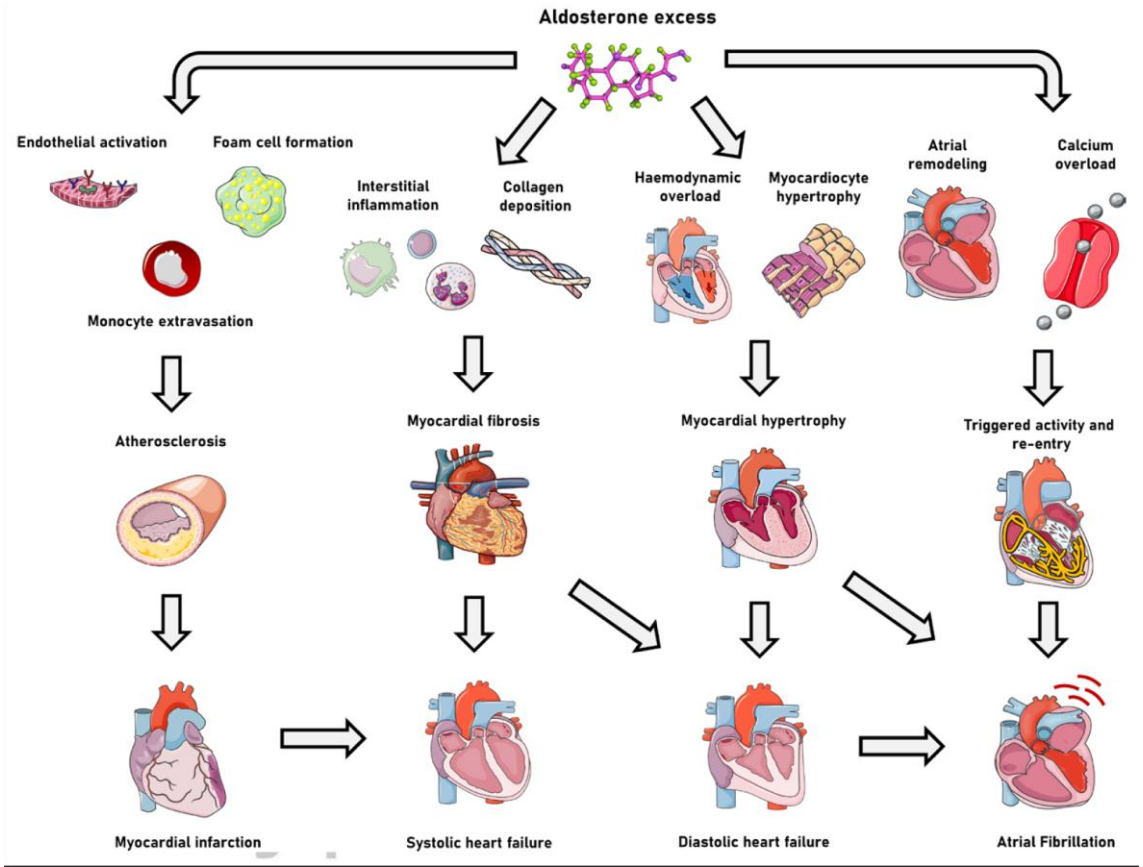


Parasiliti Caprino M,
J Hypertens 2020

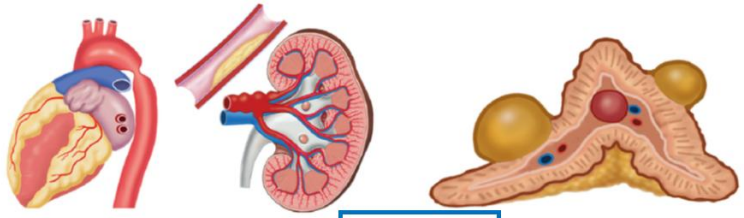
Aldosterone as a Mediator of Cardiovascular Damage

Hypertension 2022

Fabrizio Buffolo, Martina Tetti, Paolo Mulatero, Silvia Monticone



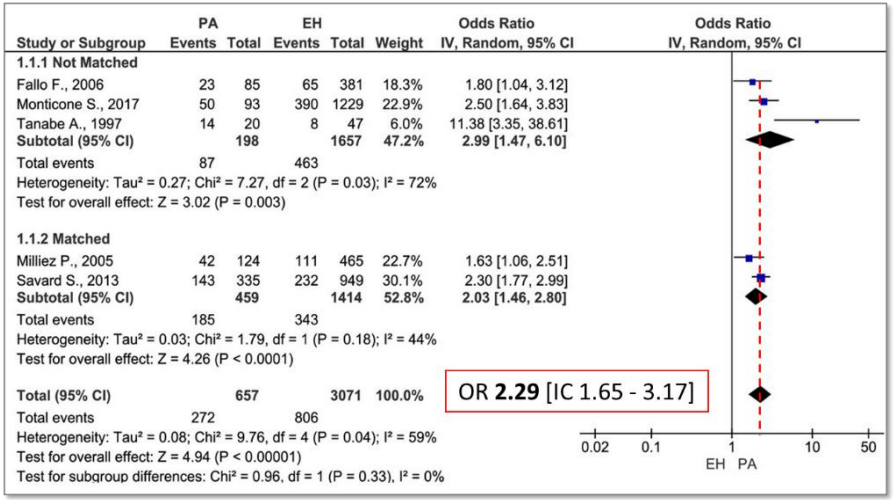
Organ Damage in PA: Heart



	Coartation of Aorta	Renovascular Hypertension	Primary Aldosteronism	Pheochromocytoma /Paraganglioma	Cushing Syndrome
	• Vasculopathy • Sympathetic activity	• Angiotensin II • Aldosterone • Sodium/volume retention	• Aldosterone • Sodium retention	• Catecholamines	• Cortisol
LVH	↑↑	↑ARAS ↔FMD	↑↑	↑	↑
Diastolic Function	↓	↑ARAS ↔FMD	↓↓	↔	↓
Systolic Function	↓(advanced)	-	↓↓strain	↓↓strain	↓
In CMR	LVH, aortic dilatation	-	LVH, fibrosis, edema	fibrosis, edema	↔fibrosis
Cardiac Events	CAD, HF	ARAS: CAD, AHF FMD: SCAD	CAD, HF, AF	TS, hypertrophic/dilated cardiomyopathy, arrhythmias, ACS, AHF	CAD

Januszewicz A & Mulatero P, J Am Coll Cardiol 2022

Left Ventricular Hypertrophy



Monticone S, Lancet DE 2018

Organ Damage in PA: Kidney

Study or Subgroup	Primary aldosteronism Mean	SD	Total	Non primary aldosteronism Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.10.1 SBP matched studies								
Freel M., 2012	110	131	27	43.9	71.4	53	8.9%	0.69 [0.21, 1.16]
Halimi J.M., 1995	66.2	165.94	23	16.55	80	46	8.8%	0.43 [-0.08, 0.93]
Iacobellis G., 2010	20.45	4	75	23.79	6.01	192	10.0%	-0.60 [-0.87, -0.33]
Liu G., 2014	25.9	7.7	50	9.7	5.9	51	8.7%	2.35 [1.84, 2.86]
Mulatero P., 2013	57	105	245	24	56	509	10.4%	0.44 [0.28, 0.59]
Ribstein J., 2005	72	110	25	33	45	25	8.4%	0.46 [-0.11, 1.02]
Sechi L.A., 2009	22	21.4	54	15	14.8	100	9.7%	0.40 [0.07, 0.73]
Somloova Z., 2010	23.33	25.15	44	11.2	16.29	10	7.6%	0.50 [-0.19, 1.19]
Subtotal (95% CI)			**543**			**986**	**72.5%**	**0.56 [0.06, 1.07]**
Heterogeneity: Tau² = 0.47; Chi² = 109.43, df = 7 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 2.20 (P = 0.03)								
1.10.2 SBP not matched studies								
Morillas P., 2008	172.9	270.1	11	52.9	179.2	172	8.1%	0.64 [0.03, 1.26]
Rosa J., 2012	14	20	49	6	4.44	49	9.3%	0.55 [0.14, 0.95]
Rossi G.P., 2006	28.14	33.9	64	18.3	22.7	426	10.0%	0.40 [0.14, 0.67]
Subtotal (95% CI)			**124**			**647**	**27.5%**	**0.47 [0.26, 0.68]**
Heterogeneity: Tau² = 0.00; Chi² = 0.71, df = 2 (P = 0.70); I² = 0%								
Test for overall effect: Z = 4.42 (P < 0.00001)								
Total (95% CI)			**667**			**1633**	**100.0%**	**0.55 [0.19, 0.91]**
Heterogeneity: Tau² = 0.32; Chi² = 110.87, df = 10 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 2.99 (P = 0.003)								
Test for subgroup differences: Chi² = 0.12, df = 1 (P = 0.73), I² = 0%								

Std. Mean Difference IV, Random, 95% CI

-2 -1 0 1 2

Higher in non-PA Higher in PA

Microalbuminuria

Study or Subgroup	Primary aldosteronism Mean	SD	Total	Non primary aldosteronism Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.9.1 SBP Matched studies								
Catena C., 2007	106	31	56	89	34	323	3.7%	17.00 [8.07, 25.93]
Freel M., 2012	110.1	26.8	27	116.1	33.9	53	2.4%	-6.00 [-19.62, 7.62]
Iwakura Y., 2016	78	19.39	94	83	20	100	5.1%	-5.00 [-10.54, 0.54]
Kobayashi H., 2017	79.4	18	73	80.5	19.3	24	3.8%	-1.10 [-9.86, 7.66]
Liu G., 2014	97.3	14.8	50	94.1	15.4	51	4.9%	3.20 [-2.69, 9.09]
Muiesan M.L., 2008	84	25	125	80	19	125	5.1%	4.00 [-1.50, 9.50]
Mulatero P., 2013	105.38	32.79	246	84.46	29.49	737	5.4%	20.92 [16.30, 25.54]
Murase K., 2013	65.26	17.47	14	61.6	27.69	110	3.2%	3.66 [-6.85, 14.17]
Murata M., 2017	74.84	23.38	292	70.8	15.5	498	0.0%	4.04 [1.03, 7.05]
Ohno Y., 2018	71.2	16.9	1263	70.1	4.7	1263	6.5%	1.10 [0.13, 2.07]
Ohno Y., 2018 (2)	71.1	18.6	236	71.9	17.1	236	6.0%	-0.80 [-4.02, 2.42]
Pimenta E., 2011	136.4	44.8	21	98.8	40.1	21	0.9%	37.60 [11.88, 63.32]
Ribstein J., 2005	102	15	25	95	15	25	4.0%	7.00 [-1.32, 15.32]
Savard S., 2013	85.1	24.1	459	86.7	20.7	1285	6.2%	-1.60 [-4.08, 0.88]
Wu V.C., 2011	83.5	27.3	330	72.42	26.8	246	5.5%	11.08 [6.62, 15.54]
Subtotal (95% CI)			**3019**			**4599**	**62.6%**	**4.82 [1.18, 8.46]**
Heterogeneity: Tau² = 34.74; Chi² = 122.73, df = 13 (P < 0.00001); I² = 89%								
Test for overall effect: Z = 2.60 (P = 0.009)								

Mean Difference IV, Random, 95% CI

eGFR

Study or Subgroup	After treatment Mean	SD	Total	Before treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.2.1 Adrenalectomy								
Catena C., 2007	87	30	25	105	30	25	1.9%	-18.00 [-34.63, -1.37]
Chiang W.F., 2013	78.98	33.27	55	93	30	55	3.2%	-14.02 [-25.86, -2.18]
Fourkiotis V., 2013	78.9	19.52	18	93	15.27	18	3.4%	-14.10 [-25.55, -2.65]
Iwakura Y., 2014	65	20.2	102	81	20.2	102	7.0%	-16.00 [-21.54, -10.46]
Kimura G., 1987	80	26.94	6	101	24.49	6	0.7%	-21.00 [-50.13, 8.13]
Kramers B.J., 2017	72.4	18.7	67	87.8	17.4	67	6.5%	-15.40 [-21.52, -9.28]
Mulatero P., 2013	86.24	26.64	20	104.57	37.46	32	1.8%	-18.33 [-35.79, -0.87]
Onohara T., 2018	64.9	19.9	90	72.9	19.4	90	6.8%	-8.00 [-13.74, -2.26]
Park K.S., 2017	70.5	21.3	206	81.3	22.9	206	8.1%	-10.80 [-15.07, -6.53]
Pimenta E., 2011(2)	124.4	47.6	24	138.9	51.3	24	0.8%	-14.50 [-42.50, 13.50]
Reincke M., 2009	64	18	51	73	22	51	5.3%	-9.00 [-16.80, -1.20]
Utsumi T., 2017	64.7	17.3	130	81.5	20.5	130	7.8%	-16.80 [-21.41, -12.19]
Wu V.C., 2011	82.6	26.7	185	85.2	26.6	185	7.1%	-2.60 [-8.03, 2.83]
Subtotal (95% CI)			**979**			**991**	**60.4%**	**-12.15 [-15.21, -9.08]**
Heterogeneity: Tau² = 12.69; Chi² = 23.23, df = 12 (P = 0.03); I² = 48%								
Test for overall effect: Z = 7.77 (P < 0.00001)								
3.2.2 Medical treatment								
Catena C., 2007	88	38.97	31	108	27.84	31	1.9%	-20.00 [-36.86, -3.14]
Fourkiotis V., 2013	86.6	21.89	11	95.5	12.93	11	2.2%	-8.90 [-23.92, 6.12]
Iwakura Y., 2014	69	21	111	79	21	111	7.0%	-10.00 [-15.52, -4.48]
Kramers B.J., 2017	78.6	17.9	56	89.8	17.9	56	6.1%	-11.20 [-17.83, -4.57]
Mulatero P., 2013	92.23	33.18	101	105.5	32.13	214	5.3%	-13.27 [-21.04, -5.50]
Park K.S., 2017	71.6	20.9	63	79.7	23.6	63	5.3%	-8.10 [-15.88, -0.32]
Reincke M., 2009	66	19	69	64	20	69	6.2%	2.00 [-4.51, 8.51]
Wu V.C., 2011	81	26.6	101	87.4	27.4	101	5.5%	-6.40 [-13.85, 1.05]
Subtotal (95% CI)			**543**			**656**	**39.6%**	**-8.40 [-12.47, -4.33]**
Heterogeneity: Tau² = 16.52; Chi² = 14.37, df = 7 (P = 0.05); I² = 51%								
Test for overall effect: Z = 4.04 (P < 0.0001)								
Total (95% CI)			**1522**			**1647**	**100.0%**	**-10.69 [-13.23, -8.16]**
Heterogeneity: Tau² = 15.90; Chi² = 42.79, df = 20 (P = 0.002); I² = 53%								
Test for overall effect: Z = 8.26 (P < 0.00001)								
Test for subgroup differences: Chi² = 2.08, df = 1 (P = 0.15), I² = 51.9%								

Mean Difference IV, Random, 95% CI

-50 -25 0 25 50

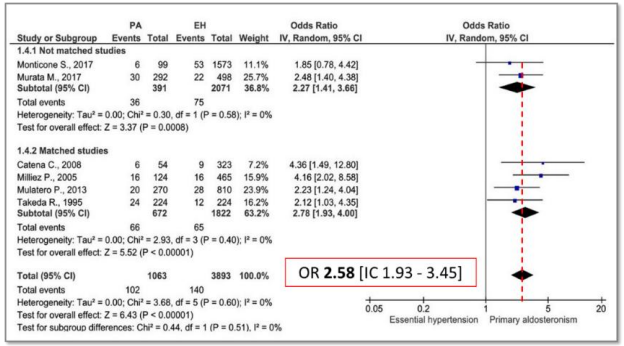
Lower after treatment Higher after treatment

Monticone S, J Hypertens 2020

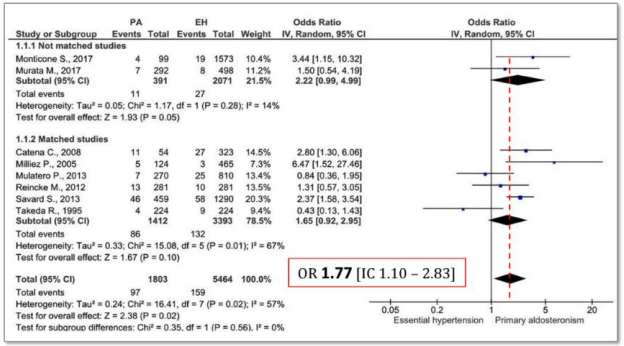
Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis

Silvia Monticone, Fabrizio D'Ascenzo*, Claudio Moretti, Tracy Ann Williams, Franco Veglio, Fiorenzo Gaita, Paolo Mulatero* **Lancet D&E 2018**

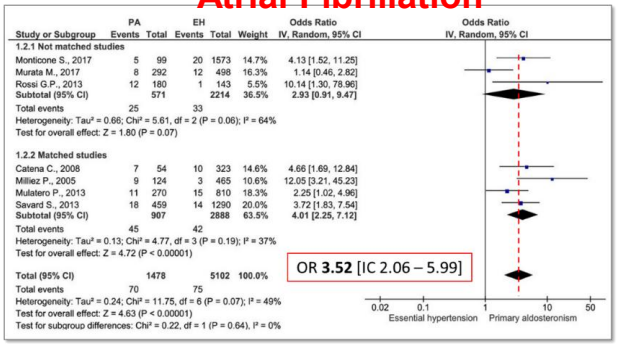
Stroke



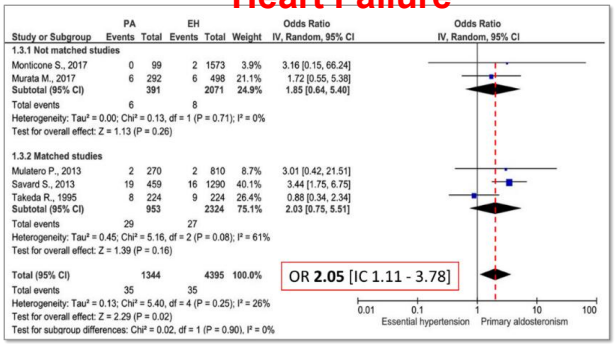
CAD



Atrial Fibrillation

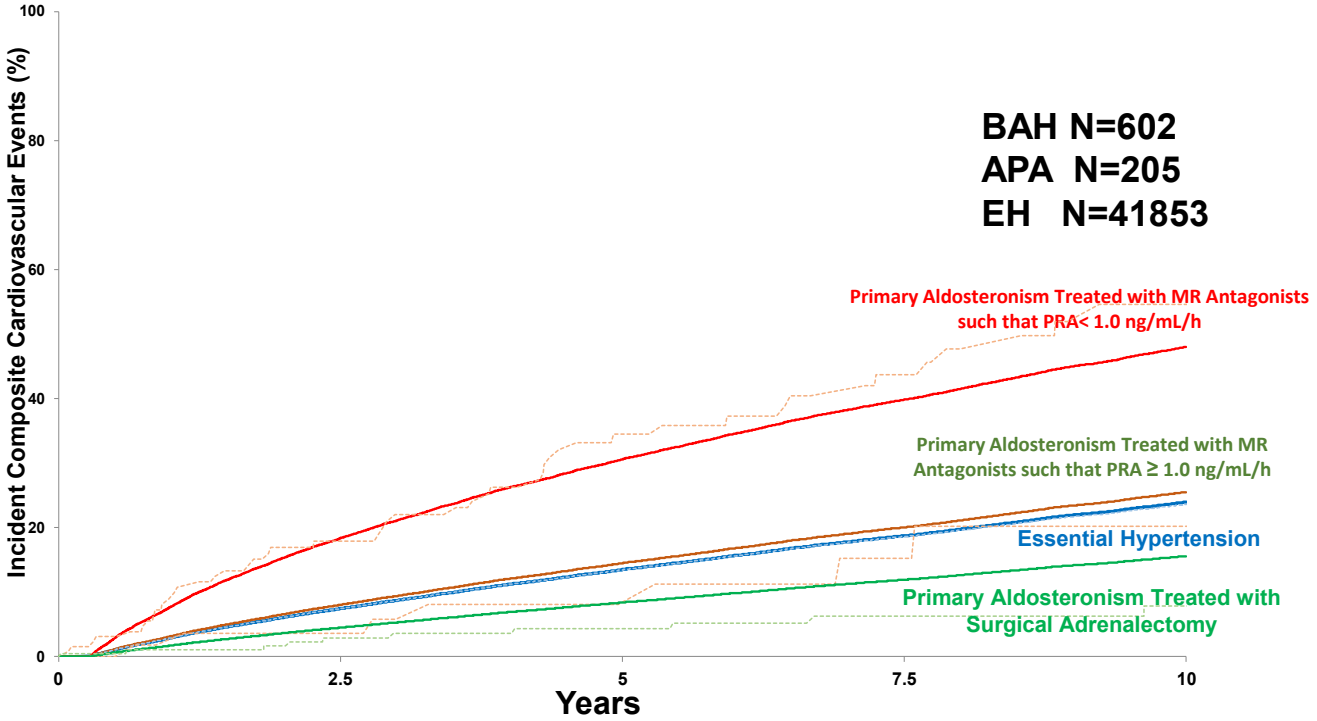


Heart Failure



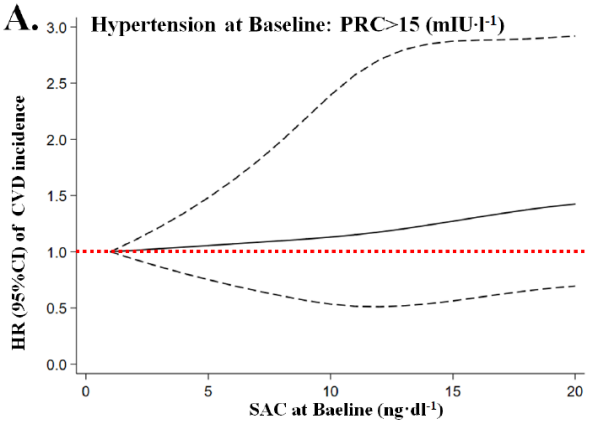
Incident Composite Cardiovascular Events in Medically and Surgically Treated Primary Aldosteronism compared with Essential Hypertension

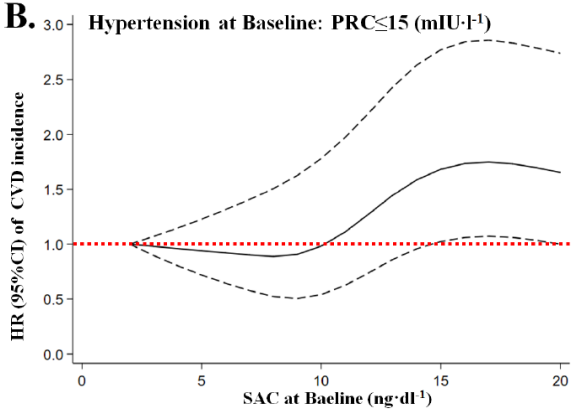
(primary outcome: myocardial infarction/coronary revascularisation, hospitalization for heart failure, or stroke)



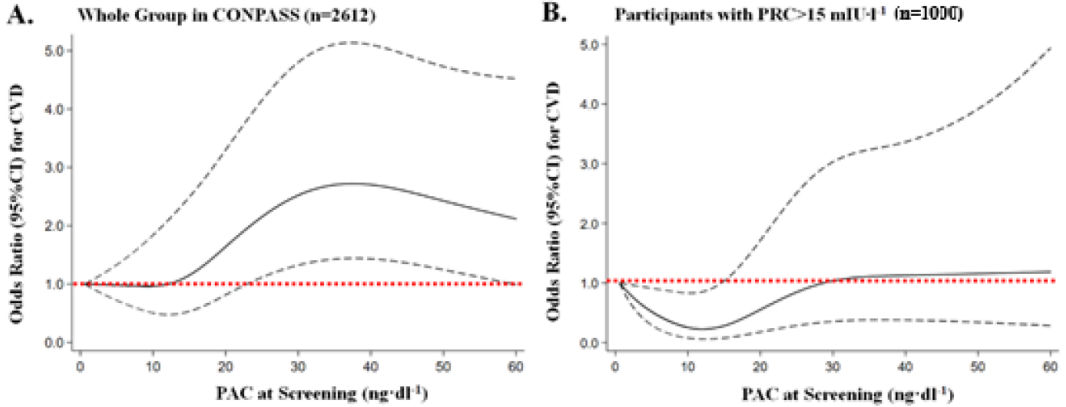
Vaidya A et al. Modified from Hundemer Lancet DE 2018

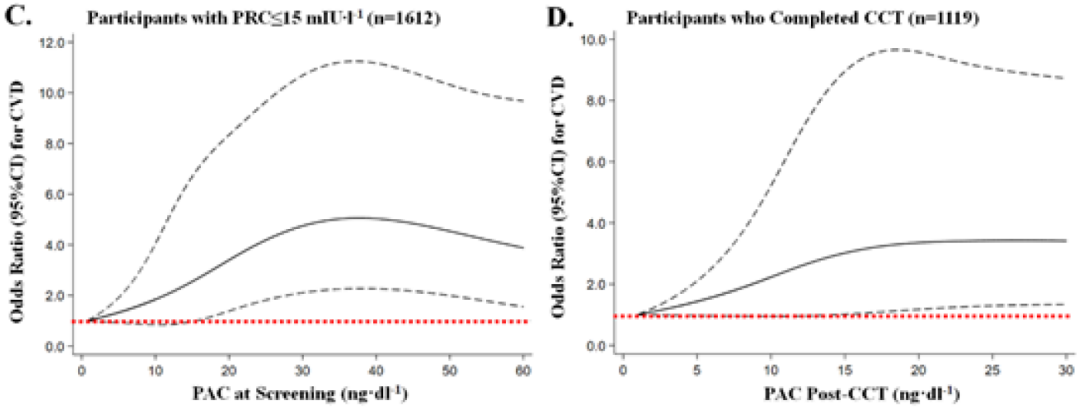
Framingham Offspring Study





COMPASS Study





Hu J, JAHA 2021

Subclinical Primary Aldosteronism and Major Adverse Cardiovascular Events: A Longitudinal Population-Based Cohort Study

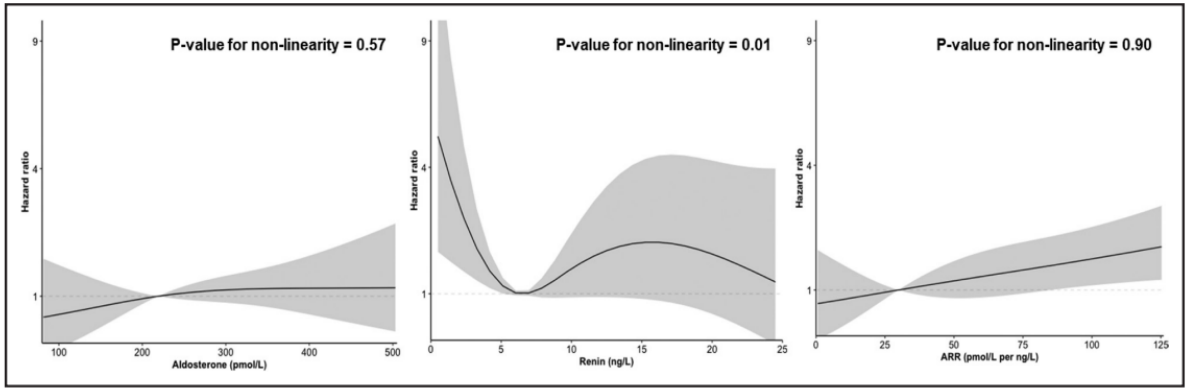


Figure 2. Assessment for nonlinear associations of aldosterone, renin, and aldosterone-to-renin ratio with major adverse cardiovascular events.

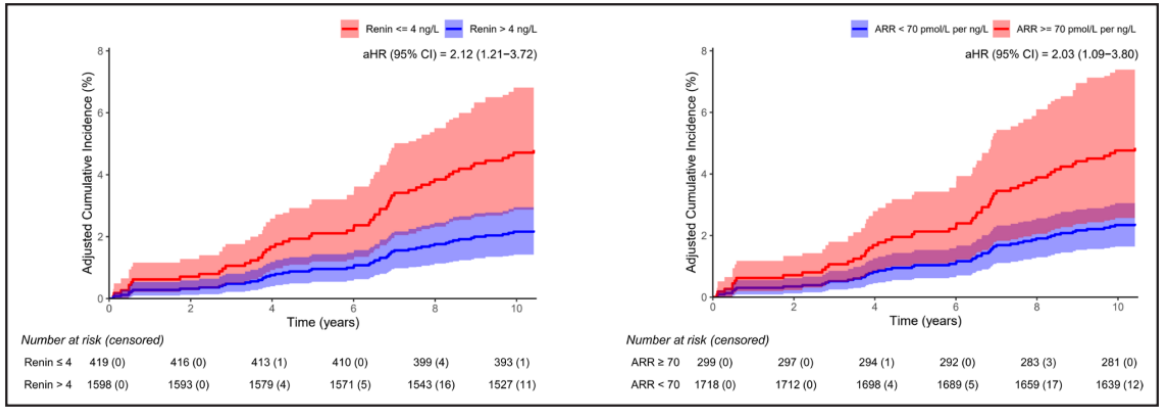
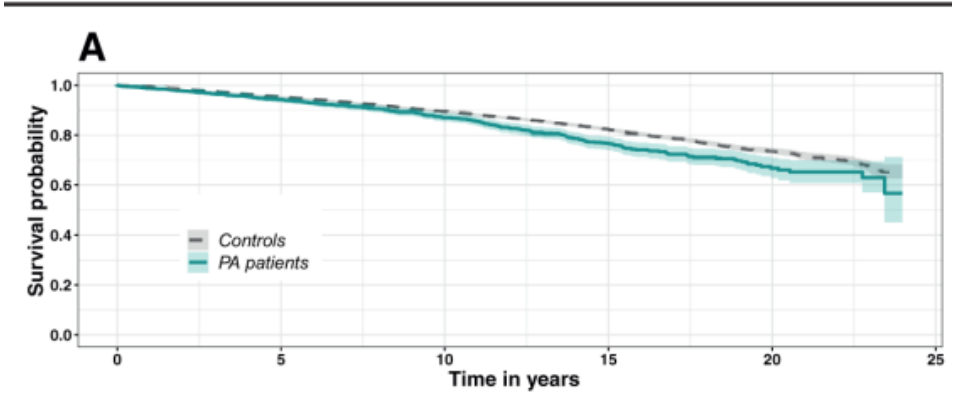


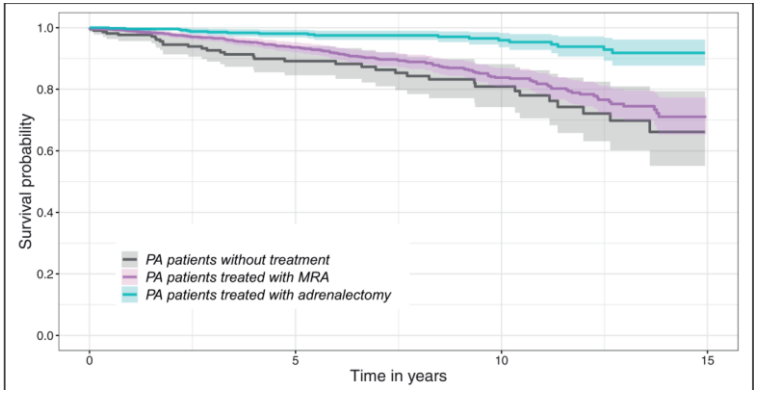
Figure 3. Adjusted cumulative incidence curves using outcome-derived thresholds for increased risk of major adverse cardiovascular events in subclinical primary aldosteronism.

Goupil R,
Circulation 2025

Mortality in Patients With Primary Aldosteronism: A Swedish Nationwide Study



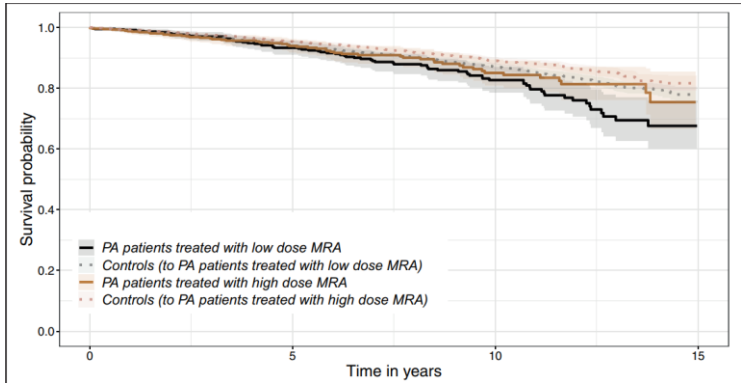
(HR 1.23 [95% CI 1.10–1.38]; P=0.0004)



patients with PA treated with adrenalectomy [HRs], 1.04 [95% CI, 0.77–1.42]; P=0.7850), mineralocorticoid receptor antagonists (MRA; HR, 1.23 [95% CI, 1.02–1.496]; P=0.0278), or neither adrenalectomy nor MRA (HR, 2.51 [95% CI, 1.72–3.67]; P<0.0001)

Table 2. All-Cause and Cause-Specific Mortality in Patients With PA and Controls Matched for Age, Gender, and County of Residence

Outcome	No. (%) of deaths in PA	No. (%) of deaths in controls	Model 1, HR (95% CI)*	P	Model 2, HR (95% CI)†	*P* value
All-cause mortality	346 (14.3)	2736 (11.3)	1.36 (1.21–1.52)	<0.0001	1.23 (1.10–1.38)	0.0004
Cause-specific mortality‡						
Cardiovascular death	134 (5.5)	851 (3.5)	1.71 (1.43–2.05)	<0.0001	1.57 (1.30–1.89)	<0.0001
Coronary heart disease	49 (2.0)	368 (1.5)	1.43 (1.06–1.92)	0.0199	1.27 (0.93–1.72)	0.1334
Stroke	23 (1.0)	118 (0.5)	2.14 (1.37–3.35)	0.0008	1.85 (1.16–2.93)	0.0094
Other	212 (8.8)	1885 (7.8)	1.20 (1.04–1.38)	0.0121	1.08 (0.94–1.25)	0.2858



high [HRs] 1.8 [95% CI, 0.88–1.58]; P=0.2661) or low (HR, 1.30 [95% CI, 1.02–1.66]; P=0.0365) doses of MRA and their matched controls.

Gkaniatsa E, Hypertension 2023

ARR Correlates with Vascular Stiffness

The Framingham Heart Study

Table 3. Association of the Entire Biomarker Panel and of Individual Biomarkers With Measures of Arterial Stiffness

Characteristics and Biomarkers†	Model R^2	Partial R^2	Global P*	β‡	P
Central pulse pressure, mm Hg	0.2683	0.0158	<0.0001	…	…
BNP	…	…	…	0.80±0.37	0.03
ARR	…	…	…	1.54±0.33	<0.0001
PAI-1	…	…	…	1.24±0.39	0.001
Fibrin	…	…	…	0.74±0.35	0.04
Carotid-femoral PWV, m/s	0.4665	0.006	0.0025	…	…
CRP	…	…	…	0.14±0.07	0.048
ARR	…	…	…	0.20±0.06	0.001
Mean arterial pressure, mm Hg	0.2075	0.0328	<0.0001	…	…
ARR	…	…	…	2.11±0.26	<0.0001
PAI-1	…	…	…	0.89±0.30	0.003
Forward pressure wave, mm Hg	0.2301	0.0103	0.0004	…	…
ARR	…	…	…	1.00±0.27	0.0002
PAI-1	…	…	…	0.80±0.31	0.01
Augmented pressure, mm Hg	0.2695	0.0119	<0.0001	…	…
CRP	…	…	…	0.62±0.17	0.0003
ARR	…	…	…	0.49±0.16	0.002

*A test of whether any of the biomarkers differed with respect to arterial stiffness–dependent measures. Covariates in the multivariable models included age, age squared, sex, heart rate, height, weight, ratio of total to high-density lipoprotein cholesterol, blood glucose, diabetes mellitus, smoking, prevalent cardiovascular disease, hormone replacement therapy, hypertension treatment, aspirin (≥3 d/wk), and lipid-lowering medication.

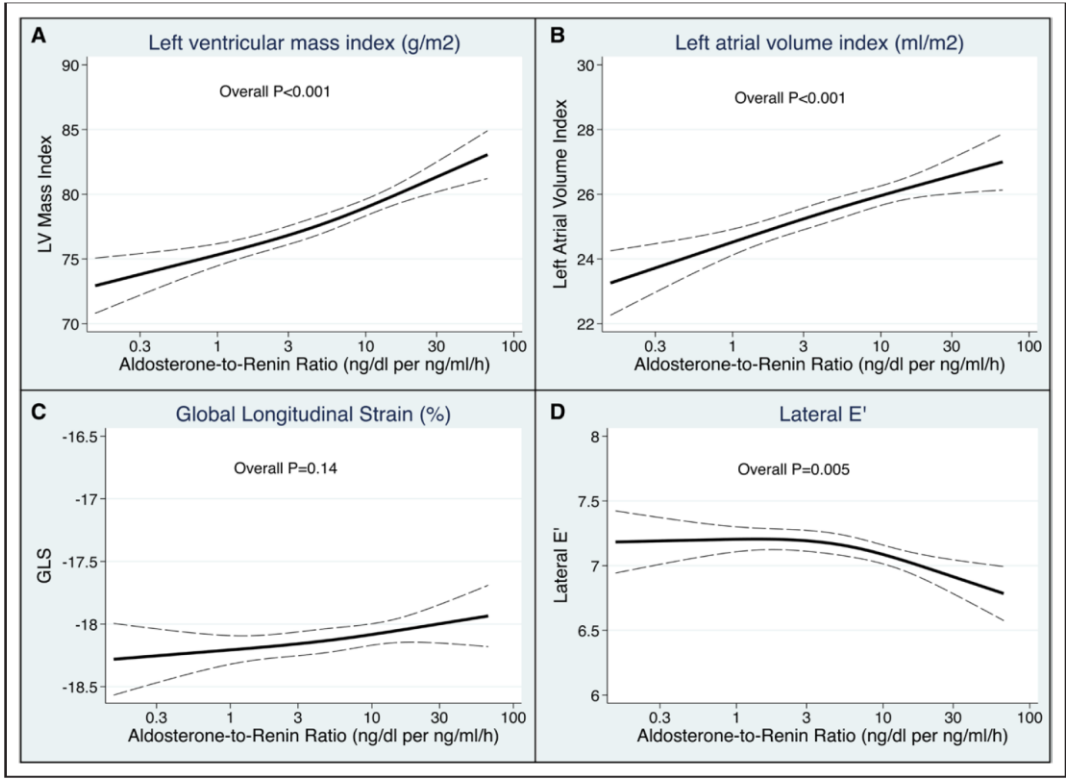
†For tonometry measures with a global $P<0.01$, individual biomarkers related ($P<0.05$) to vascular function measures after backward elimination are displayed.

‡β, the regression coefficient, shows a change in vascular function measure per 1-SD increment in log marker. Thus, an e^{SD}-fold increase in BNP (original units) results in an increase of 0.80 mm Hg in central pulse pressure.

Lieb W, Circulation 2009

Association between ARR and cardiac structure and function

The ARIC Study



Brown J, Hypertension 2022

Annals of Internal Medicine 2021

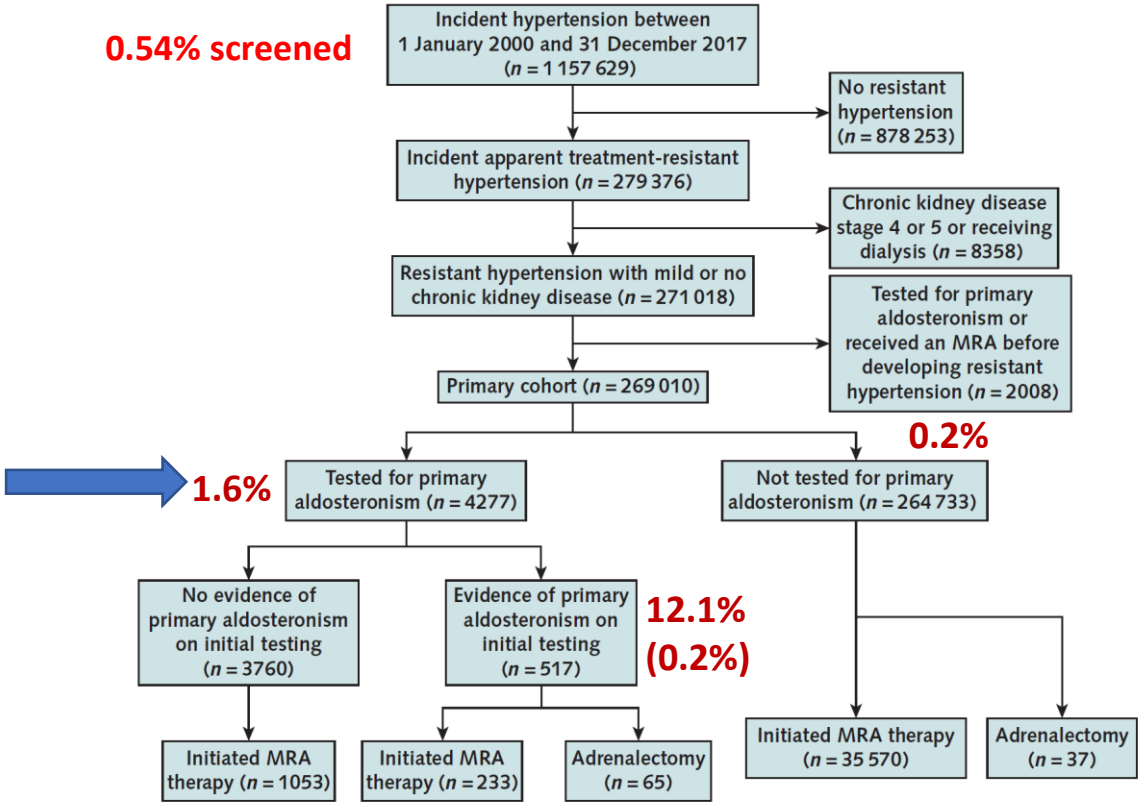
ORIGINAL RESEARCH

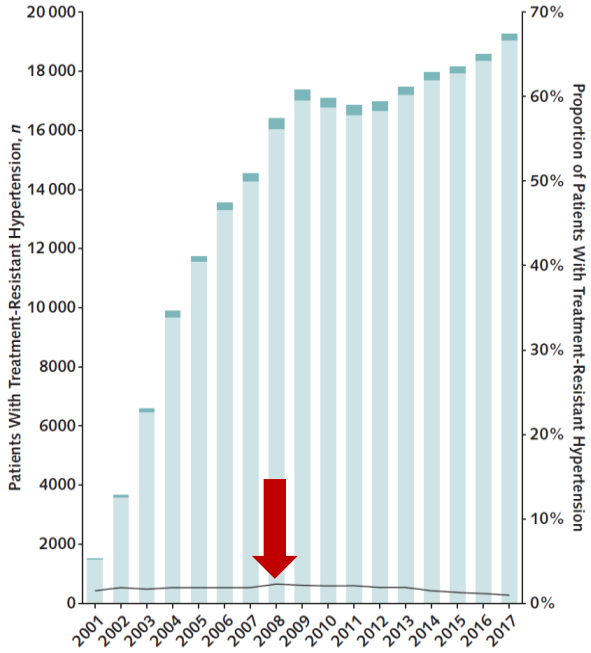
Testing for Primary Aldosteronism and Mineralocorticoid Receptor Antagonist Use Among U.S. Veterans

A Retrospective Cohort Study

Jordana B. Cohen, MD, MSCE; Debbie L. Cohen, MD; Daniel S. Herman, MD, PhD; John T. Leppert, MD, MS; James Brian Byrd, MD, MS*; and Vivek Bhalla, MD*

0.54% screened

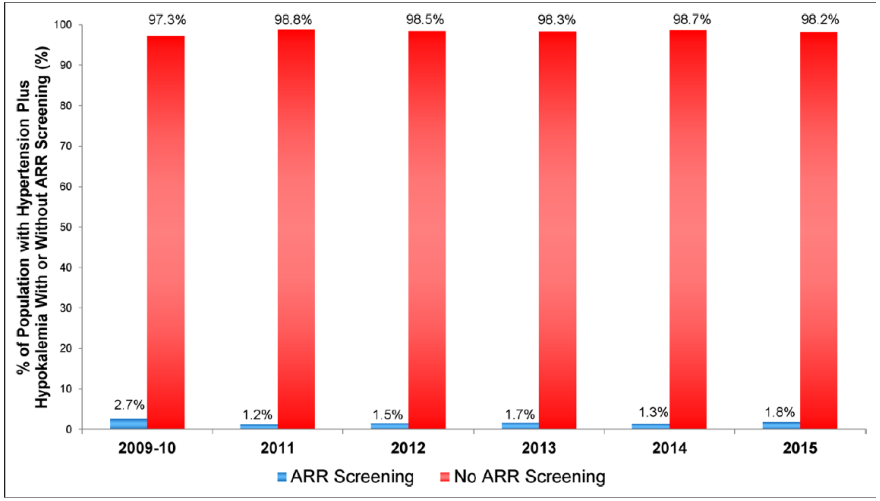


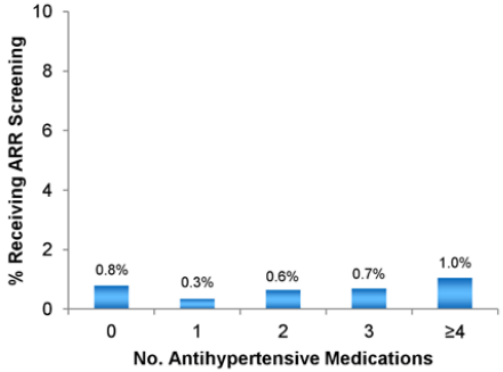


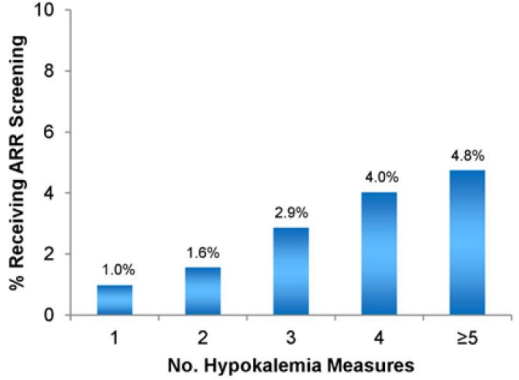
Testing for primary aldosteronism was associated with an average 1.47 mm Hg lower SBP over time, compared with no testing

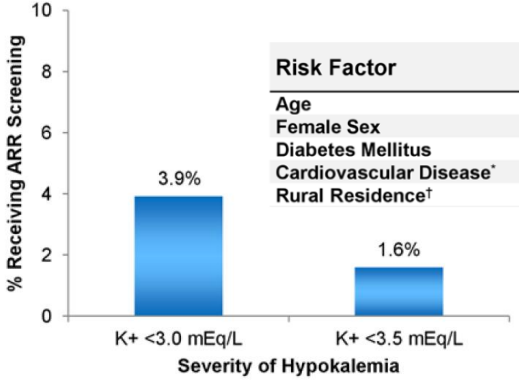
Primary Aldosteronism Screening Among Individuals with Hypertension + Hypokalemia

Ontario – Canada
hypertension + hypokalemia
(potassium <3.5 mEq/L)
from 2009 to 2015
cohort included **26 533** adults
of which only 422 (**1.6%**)
underwent PA screening







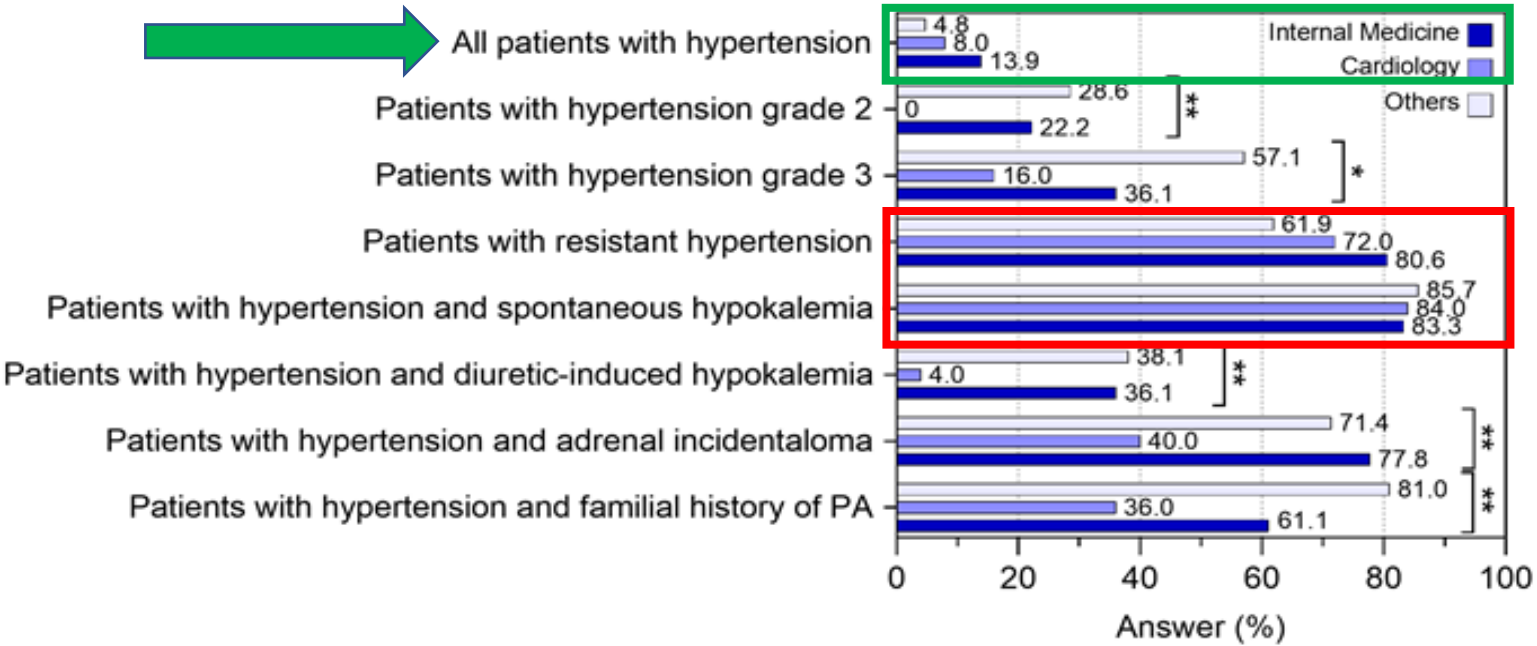


Risk Factor	Hazard Ratio (95% CI)	Forest Plot
Age	0.95 (0.94-0.96)	
Female Sex	0.94 (0.77–1.15)	
Diabetes Mellitus	0.66 (0.50–0.89)	
Cardiovascular Disease*	0.81 (0.60–1.09)	
Rural Residence†	1.08 (0.74–1.57)	

Hundemer GL, Hypertension 2022

SURVEY SIIA-ARCA: PA screening

[6] Which of the following patients, younger than 65, do you screen for PA with ARR?

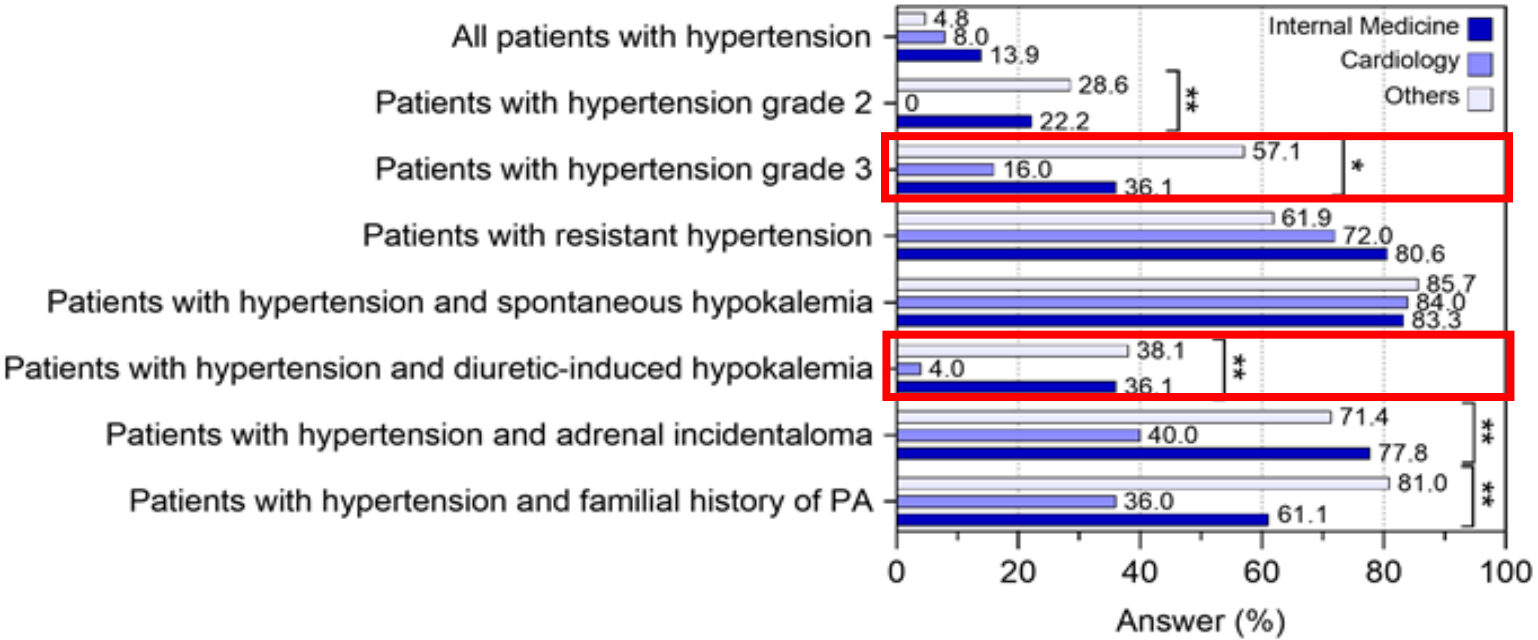


Monticone S, J Endocrinol Invest 2025

SURVEY SIIA-ARCA: PA screening

[6] Which of the following patients, younger than 65, do you screen for PA with ARR?

Specialty



Monticone S, J Endocrinol Invest 2025

Recommendation 3

In individuals with hypertension, we suggest primary aldosteronism (PA) screening with serum/plasma aldosterone concentration and plasma renin (concentration or activity) (2 | ⊕⊕OO).

How to Screen for PA

ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Individuals with Hypertension

↓

Measure Aldosterone, Renin, and Potassium*

↓

Meets Criteria for Primary Aldosteronism**

Renin concentration or activity is low or suppressed, while aldosterone concentration is inappropriately high relative to renin

- Plasma renin activity (PRA) ≤ 1 ng/mL/h
- Direct renin concentration (DRC) ≤ 8.2 mU/L
- Aldosterone (immunoassay) ≥ 10 ng/dL (≥ 277 pmol/L)
- Aldosterone (LC-MS/MS) ≥ 7.5 ng/dL (≥ 208 pmol/L)

AND

Aldosterone to renin ratio (ARR) is increased

- Aldosterone (immunoassay, ng/dL) / PRA (ng/mL/h) > 20
- Aldosterone (immunoassay, pmol/L) / DRC (mU/L) > 70
- Aldosterone (LC-MS/MS, ng/dL) / PRA (ng/mL/h) > 15
- Aldosterone (LC-MS/MS, pmol/L) / DRC (mU/L) > 52

Aldosterone (immunoassay, ng/dL) / DRC (mU/L) > 2.5

Renin		Aldosterone concentration measured by immunoassay		Aldosterone concentration measured by LC-MS/MS	
		≥10 ng/dL	≥277 pmol/L	≥7.5 ng/dL	≥208 pmol/L
Plasma renin activity	≤1 ng/mL/h	>20	>555	>15	>416
	≤12.9 pmol/L/min	>1.55	>43	>1.16	>32
	≤0.28 ng/L/s	>71	>2000	>53	>1500
DRC	≤5.2 ng/L	>4.0	>111	>2.8	>82
	≤8.2 mU/L	>2.5	>70	>1.8	>52

International Journal of *Molecular Sciences* 2024 MDPI

Article

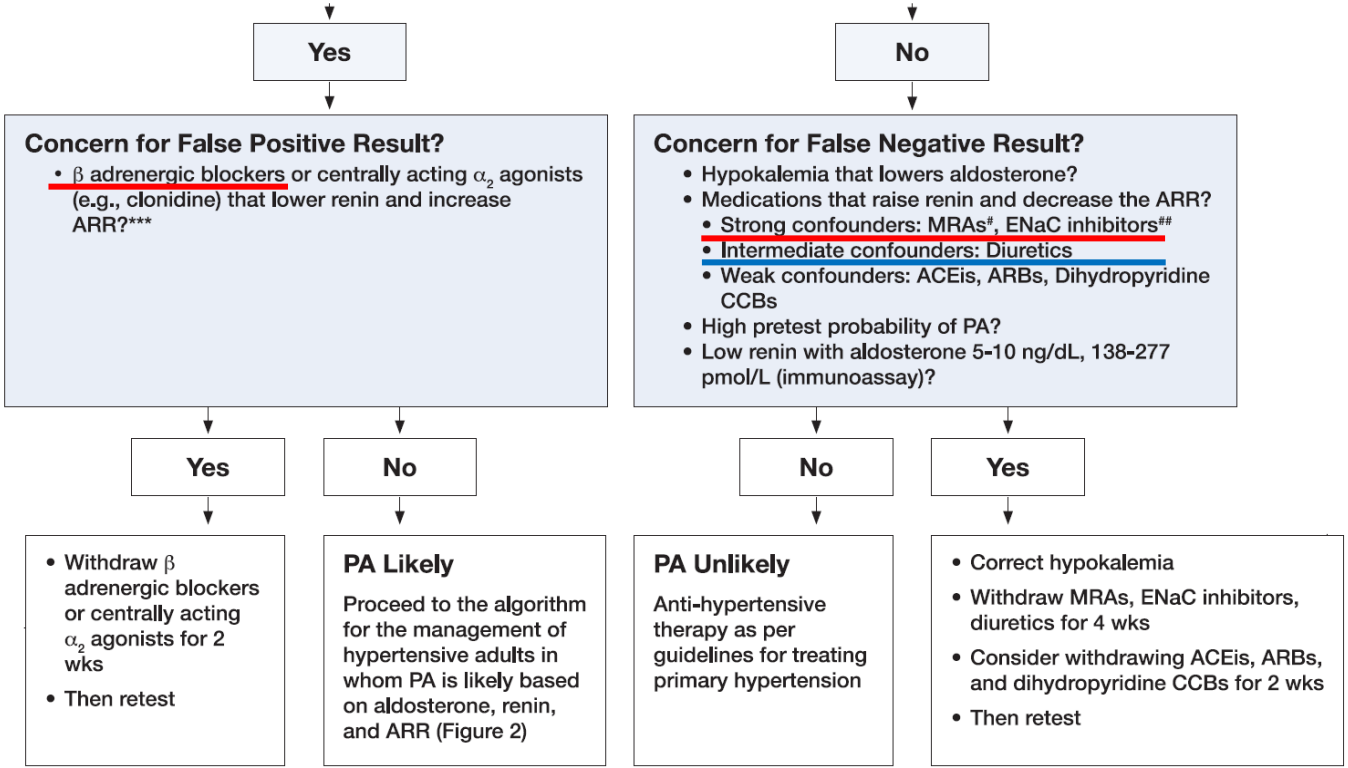
Diagnostic Accuracy of Aldosterone and Renin Measurement by Chemiluminescence for Screening of Patients with Primary Aldosteronism

Martina Tetti [1], Jacopo Burrello [1], Jessica Goi [1], Mirko Parasiliti-Caprino [2], Giulia Gioiello [3], Fabio Settanni [3], Silvia Monticone [1], Paolo Mulatero [1,*] and Giulio Mengozzi [3]

1100 patients

	Variable	N	AUC	95% CI	*P*-value	*Cut-off*	Sens (%)	Spec (%)
PA Patients	ADRR (DRC – CLIA) (AC ≥ 100 ng/L)	423 [87]	0.928	0.904-0.954	**<0.001**	9#	100.0	53.6
						20	93.3	81.1
						25*	91.1	85.3
						27	86.5	87.1
						436§	3.4	100.0
	ARR (PRA – RIA) (AC ≥ 100 ng/L)	359 [89]	0.943	0.920-0.966	**<0.001**	200#	100.0	66.5
						300	93.1	78.7
						436*	89.7	87.1
						2600§	13.8	100.0
UPA Patients	ADRR (DRC – CLIA) (AC ≥ 100 ng/L)	423 [23]	0.884	0.837-0.932	**<0.001**	11#	100	55.3
						20	95.7	69.3
						27	87.0	75.0
						37*	86.9	78.8
						483§	4.3	100.0
	ARR (PRA – RIA) (AC ≥ 100 ng/L)	359 [23]	0.885	0.835-0.934	**<0.001**	200#	100.0	53.9
						300	95.7	65.2
						460*	95.7	74.1
						8000§	8.7	100.0

Suggested cut-off for ARR 2-2.5 (aldo in ng/dL and DRC in mU/L)



ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Table 6. Managing interfering antihypertensive medications during PA screening and interpretation of aldosterone, renin, and ARR

Management strategy	Medication to withdraw	Timeline of withdrawal	Replacement antihypertensive agents	Interpretation of negative screen	Interpretation of positive screen
No medication withdrawal	None	–	–	Possible false negative if moderate to high pretest probability Repeat screen on different day with minimal- or full-medication withdrawal strategy	Possible false positive if individual taking β-adrenergic blockers or centrally acting α_2-agonists (clonidine, α-methyldopa) Repeat screen after withdrawing these medications
Minimal medication withdrawal	Stop MRAs and ENaC inhibitors (amiloride, triamterene) Stop β-adrenergic blockers and centrally acting α_2-agonists (clonidine, α-methyldopa)	4 weeks before testing 2 weeks before testing	Hydralazine[a] α_1-adrenergic blockers Non-dihydropyridine CCBs Moxonidine	Possible false negative if moderate to high pretest probability Repeat screen on different day with full withdrawal strategy If pretest probability is low, then likely true negative	Likely true positive Proceed to algorithm (Fig. 2)
Ideal full medication withdrawal	Stop MRAs, ENaC inhibitors (amiloride, triamterene), and other diuretics β-adrenergic blockers ACE inhibitors ARBs Dihydropyridine CCBs Centrally acting α_2-agonists (clonidine, α-methyldopa) SGLT2 inhibitors	4 weeks before testing 2 weeks before testing	Hydralazine[a] α_1-adrenergic blockers Non-dihydropyridine CCBs Moxonidine	Possible false negative if moderate to high pretest probability Repeat screen on different day. If repeat is negative, then likely true negative If pretest probability is low, then likely true negative	Likely true positive Proceed to algorithm (Fig. 2)

ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Table 6. Managing interfering antihypertensive medications during PA screening and interpretation of aldosterone, renin, and ARR

Management strategy	Medication to withdraw	Timeline of withdrawal	Replacement antihypertensive agents	Interpretation of negative screen	Interpretation of positive screen
No medication withdrawal	None	–	–	Possible false negative if moderate to high pretest probability Repeat screen on different day with minimal- or full-medication withdrawal strategy	Possible false positive if individual taking β-adrenergic blockers or centrally acting α_2-agonists (clonidine, α-methyldopa) Repeat screen after withdrawing these medications
Minimal medication withdrawal	Stop MRAs and ENaC inhibitors (amiloride, triamterene) Stop β-adrenergic blockers and centrally acting α_2-agonists (clonidine, α-methyldopa)	4 weeks before testing 2 weeks before testing	Hydralazine[a] α_1-adrenergic blockers Non-dihydropyridine CCBs Moxonidine	Possible false negative if moderate to high pretest probability Repeat screen on different day with full withdrawal strategy If pretest probability is low, then likely true negative	Likely true positive Proceed to algorithm (Fig. 2)
Ideal full medication withdrawal	Stop MRAs, ENaC inhibitors (amiloride, triamterene), and other diuretics β-adrenergic blockers ACE inhibitors ARBs Dihydropyridine CCBs Centrally acting α_2-agonists (clonidine, α-methyldopa) SGLT2 inhibitors	4 weeks before testing 2 weeks before testing	Hydralazine[a] α_1-adrenergic blockers Non-dihydropyridine CCBs Moxonidine	Possible false negative if moderate to high pretest probability Repeat screen on different day. If repeat is negative, then likely true negative If pretest probability is low, then likely true negative	Likely true positive Proceed to algorithm (Fig. 2)

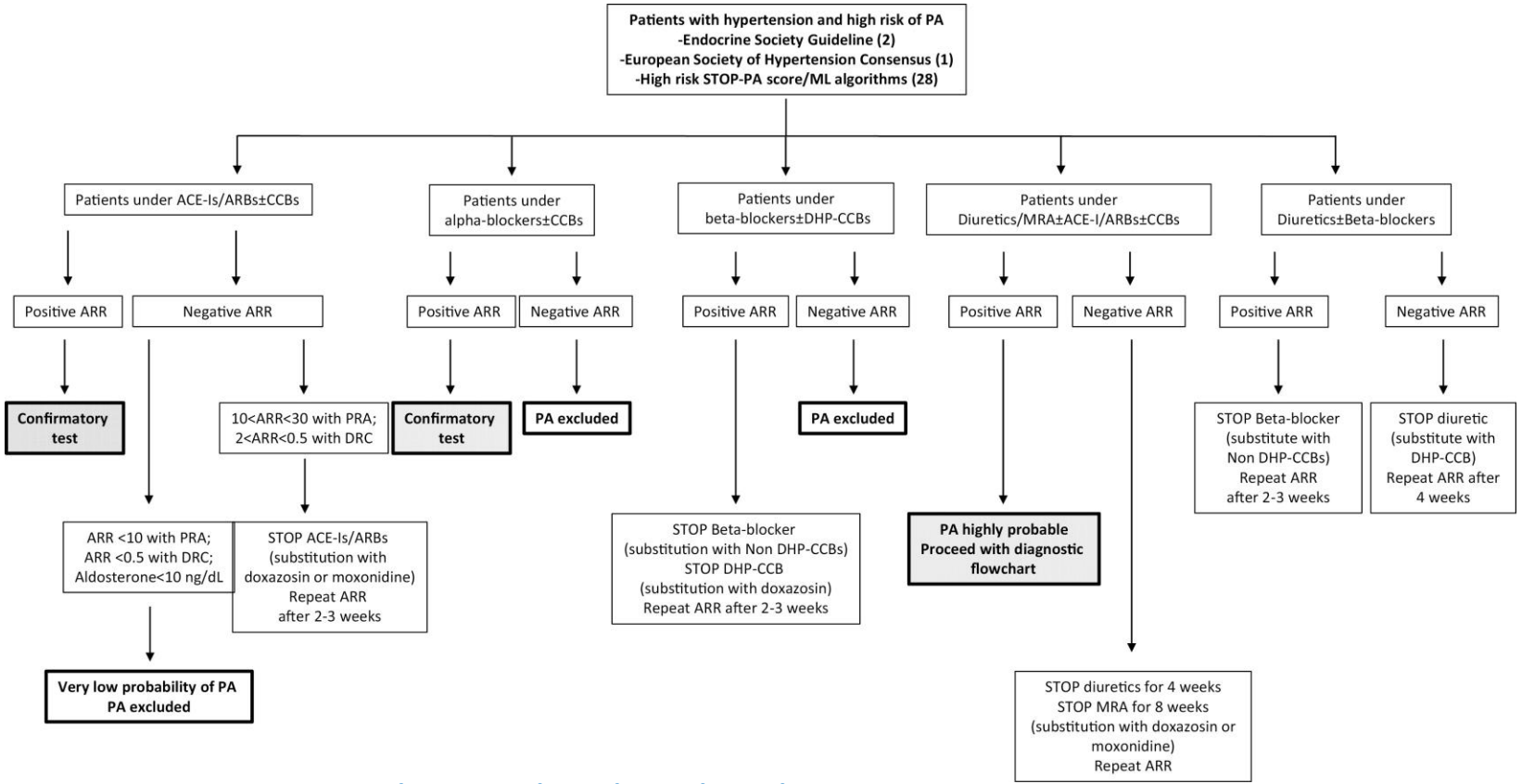
ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Table 6. Managing interfering antihypertensive medications during PA screening and interpretation of aldosterone, renin, and ARR

Management strategy	Medication to withdraw	Timeline of withdrawal	Replacement antihypertensive agents	Interpretation of negative screen	Interpretation of positive screen
No medication withdrawal	None	–	–	Possible false negative if moderate to high pretest probability Repeat screen on different day with minimal- or full-medication withdrawal strategy	Possible false positive if individual taking β-adrenergic blockers or centrally acting α_2-agonists (clonidine, α-methyldopa) Repeat screen after withdrawing these medications
Minimal medication withdrawal	Stop MRAs and ENaC inhibitors (amiloride, triamterene) Stop β-adrenergic blockers and centrally acting α_2-agonists (clonidine, α-methyldopa)	4 weeks before testing 2 weeks before testing	Hydralazine[a] α_1-adrenergic blockers Non-dihydropyridine CCBs Moxonidine	Possible false negative if moderate to high pretest probability Repeat screen on different day with full withdrawal strategy If pretest probability is low, then likely true negative	Likely true positive Proceed to algorithm (Fig. 2)
Ideal full medication withdrawal	Stop MRAs, ENaC inhibitors (amiloride, triamterene), and other diuretics β-adrenergic blockers ACE inhibitors ARBs Dihydropyridine CCBs Centrally acting α_2-agonists (clonidine, α-methyldopa) SGLT2 inhibitors	4 weeks before testing 2 weeks before testing	Hydralazine[a] α_1-adrenergic blockers Non-dihydropyridine CCBs Moxonidine	Possible false negative if moderate to high pretest probability Repeat screen on different day. If repeat is negative, then likely true negative If pretest probability is low, then likely true negative	Likely true positive Proceed to algorithm (Fig. 2)

ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

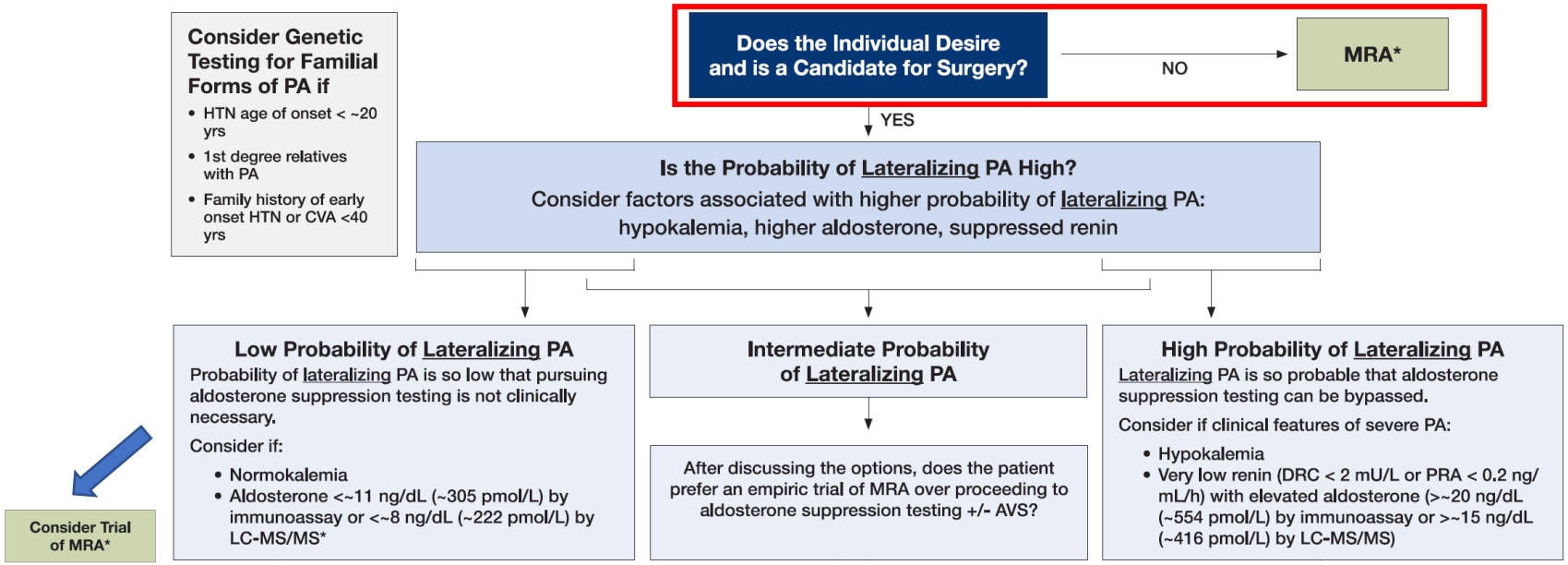
Screening Algorithm for Primary Aldosteronism in Hypertensive Individuals on Treatment



Mulatero P, J Clin Endocrinol Metab 2022

Recommendation 4

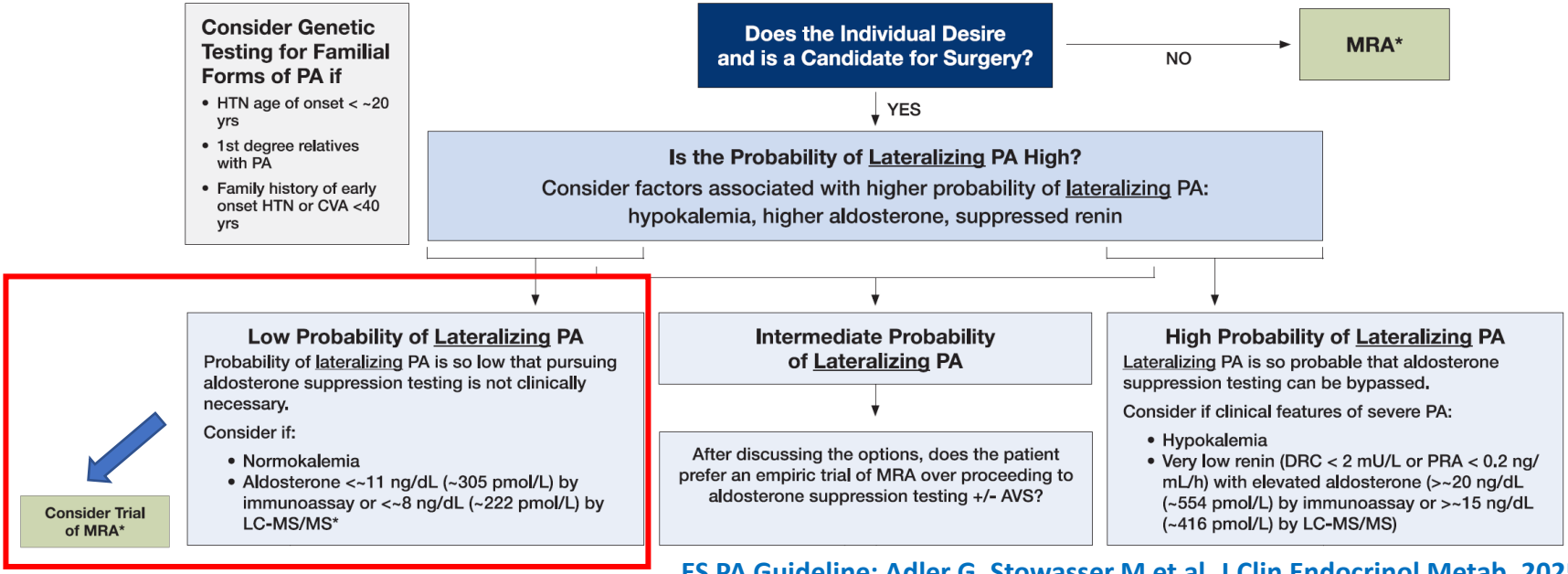
In individuals who screen positive for primary aldosteronism (PA), we suggest aldosterone suppression testing in situations when screening results suggest an intermediate probability for lateralizing PA and individualized decision making confirms a desire to pursue eligibility for surgical therapy (2 | ⊕OOO).



ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Recommendation 4

In individuals who screen positive for primary aldosteronism (PA), we suggest aldosterone suppression testing in situations when screening results suggest an intermediate probability for lateralizing PA and individualized decision making confirms a desire to pursue eligibility for surgical therapy (2 | ⊕OOO).



ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Mineralocorticoid Receptor Antagonists for the Treatment of Low-Renin Hypertension

MRAs vs Diuretics

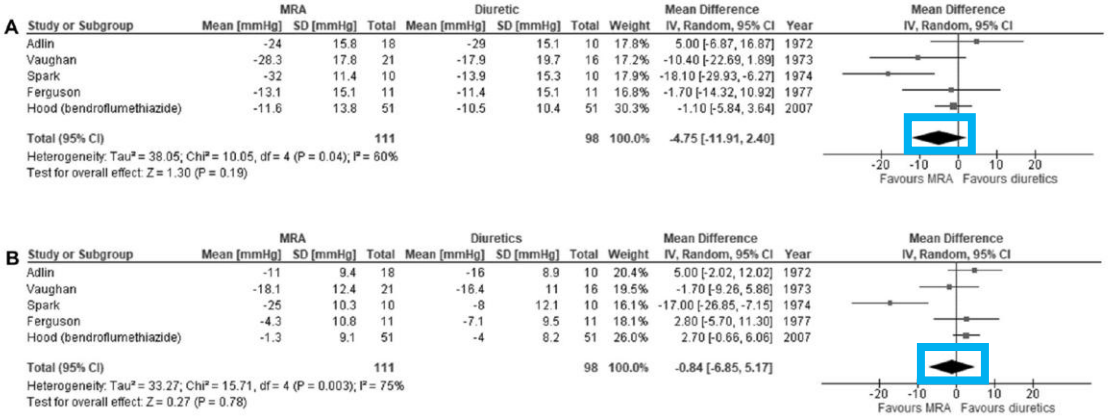


Fig. 2 Meta-analysis of blood pressure lowering effect with mineralocorticoid receptor antagonists (MRA) versus diuretics. A systolic blood pressure; **B** diastolic blood pressure.

MRAs vs ACE.Is/ARBs

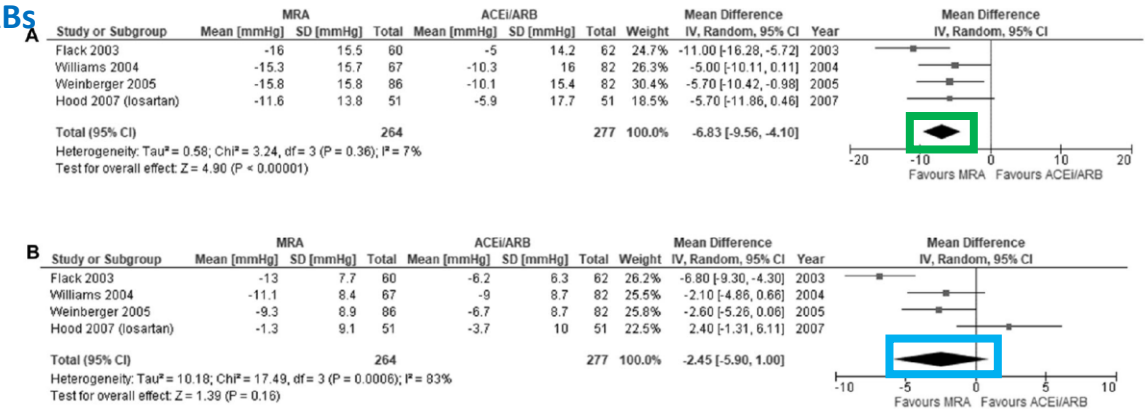
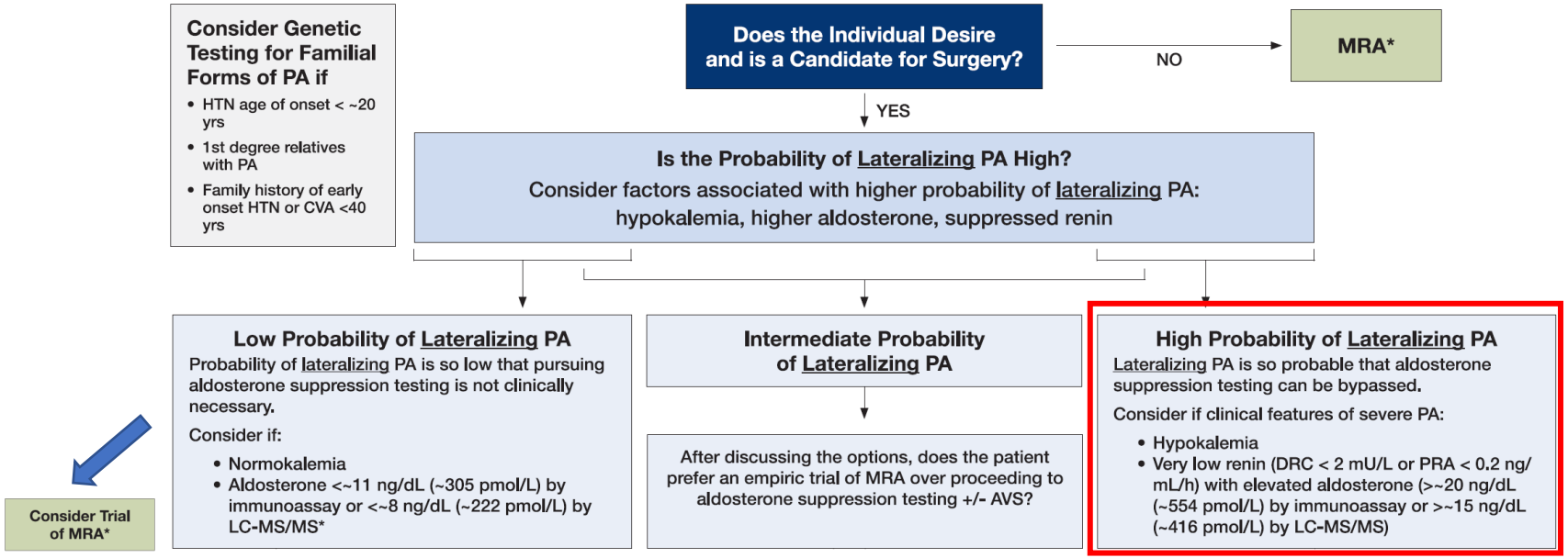


Fig. 3 Meta-analysis of blood pressure lowering effect with mineralocorticoid receptor antagonists (MRA) versus angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARB). A systolic blood pressure; **B** diastolic blood pressure.

Shah SS,
J Hum Hypertens 2024

Recommendation 4

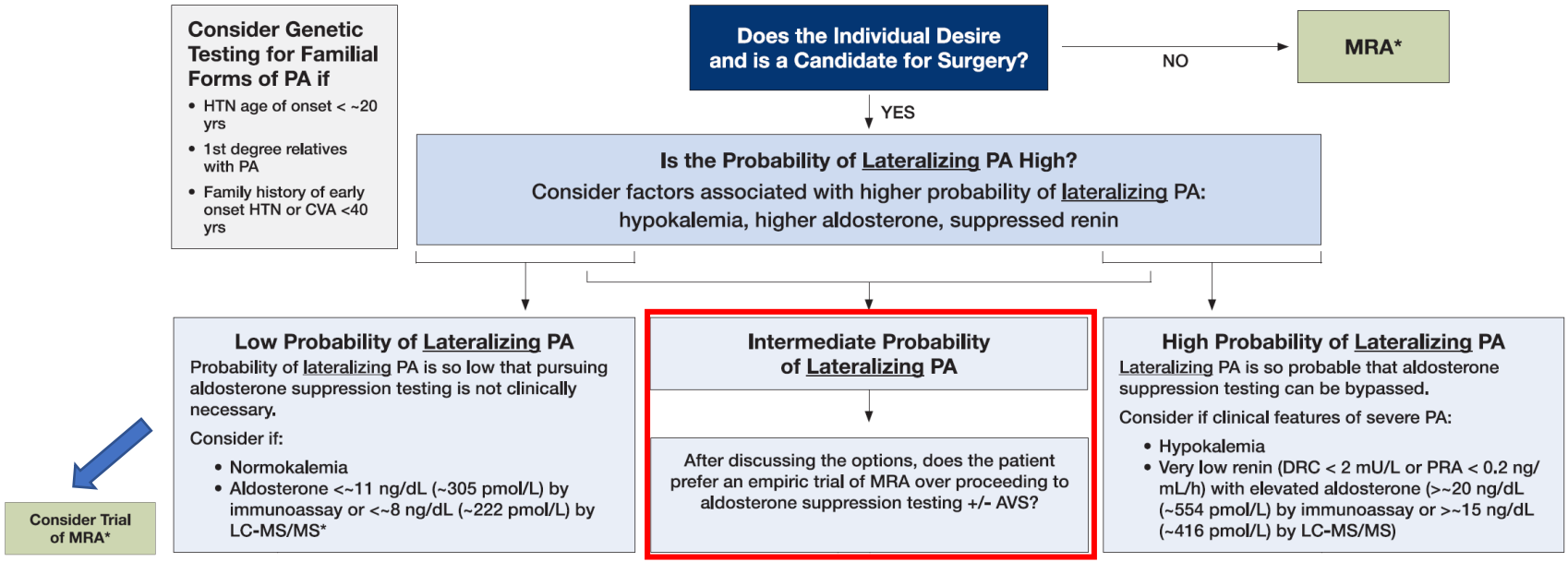
In individuals who screen positive for primary aldosteronism (PA), we suggest aldosterone suppression testing in situations when screening results suggest an intermediate probability for lateralizing PA and individualized decision making confirms a desire to pursue eligibility for surgical therapy (2 | ⊕OOO).



ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

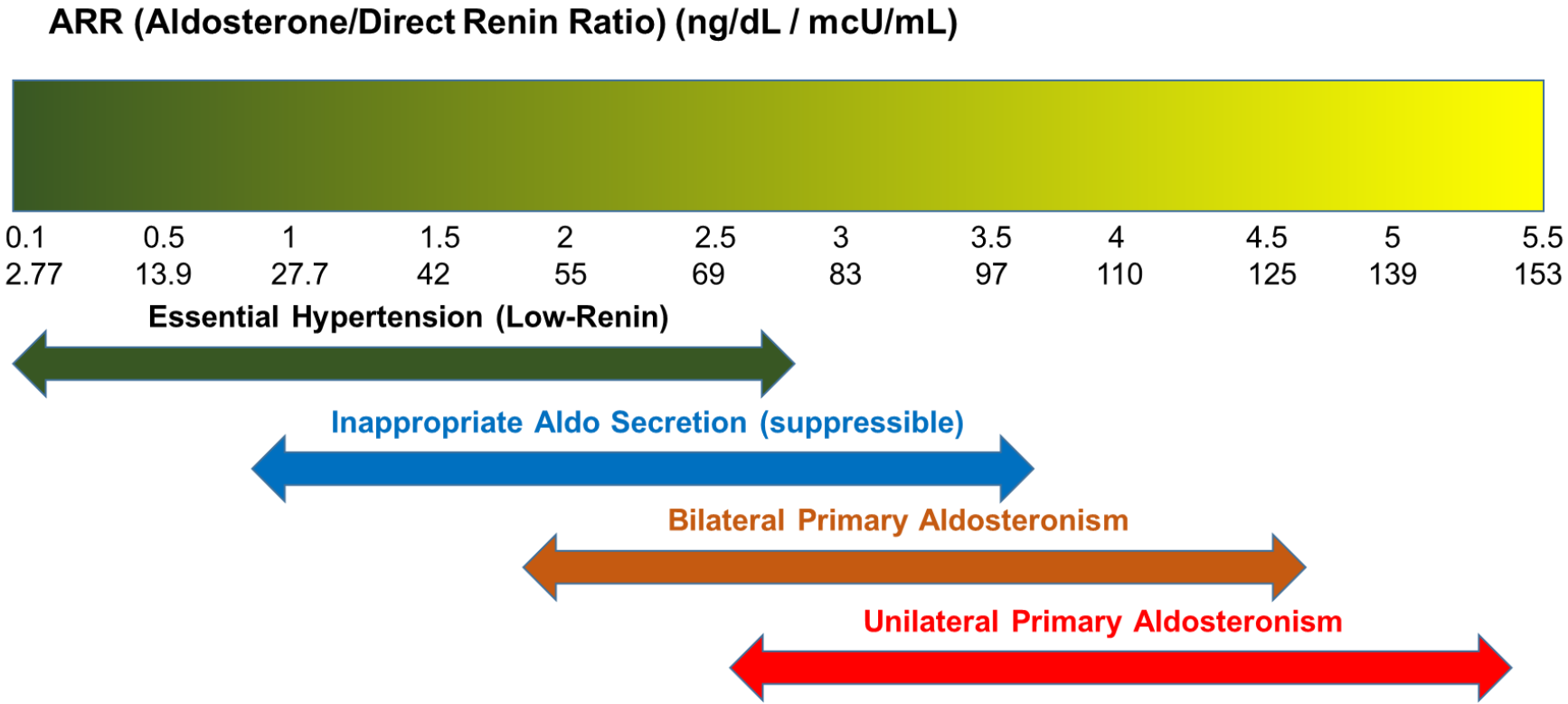
Recommendation 4

In individuals who screen positive for primary aldosteronism (PA), we suggest aldosterone suppression testing in situations when screening results suggest an intermediate probability for lateralizing PA and individualized decision making confirms a desire to pursue eligibility for surgical therapy (2 | ⊕OOO).



ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

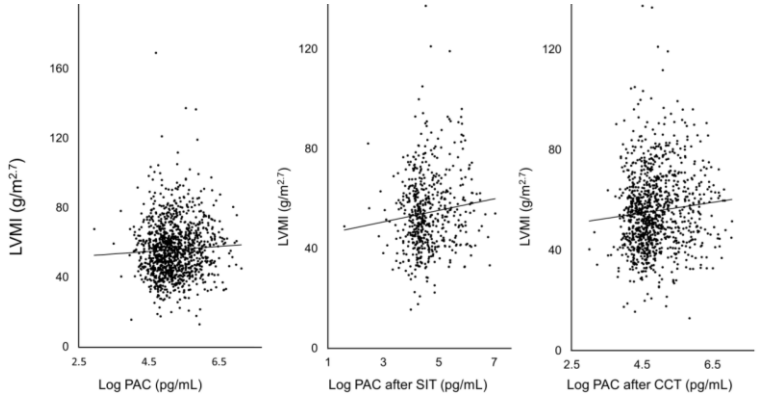
Confirmatory/Suppression tests



Aldosterone Levels After Confirmatory Tests Are Correlated With LV Mass in Primary Aldosteronism

Table 3. Correlation Between Left Ventricular Mass Index and Each Parameter in Single Regression Analyses

Parameter	Coefficient	SE	*P* Value	95% CI
Serum K^+, mEq/L	−4.067	0.874	<0.001*	−5.783 to −2.352
Hypokalemia, %	5.260	0.937	<0.001*	3.422 to 7.098
Log ARR, pg/mL per ng/(mL·h)	0.674	0.516	0.192	−0.339 to 1.687
Log plasma renin activity, ng/(mL·h)	−0.176	0.618	0.776	−1.390 to 1.037
Log PAC, pg/mL	1.446	0.812	0.075	−0.147 to 3.039
Log PAC after CCT, pg/mL	2.112	0.726	0.004*	0.688 to 3.536
Log PAC after SIT, pg/mL	2.319	0.892	0.010*	0.567 to 4.070
Unilateral subtype, %	3.280	1.115	0.003*	1.093 to 5.468



Ohno Y, Hypertension 2020

Table 8. Description of the most commonly used aldosterone suppression tests

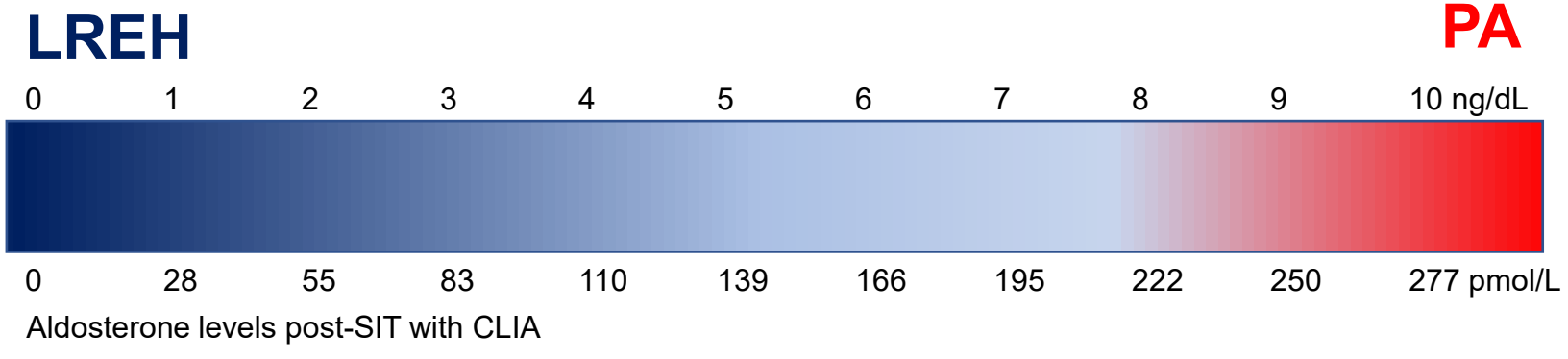
Aldosterone suppression test	Resource requirements	Protocol	Metrics	Interpretations	Comments
Oral sodium suppression test	Low	Individuals are instructed to consume 4-5 g of sodium per day for 3-4 days Collect 24-h urine collection on final day of high sodium intake	Measure urinary aldosterone, sodium, creatinine	24-h urine sodium should ideally be >200 mEq/24 hours 24-h urine creatinine is used to assess adequacy of urine collection 24-h urine aldosterone <10 mcg/nmol/24 hours makes PA unlikely (84)	Oral sodium can be consumed via sodium chloride tablets or sodium rich foods Because hypokalemia may cause false-negative interpretations, serum potassium should be normalized before the study protocol Interpretation of results is probabilistic and lacks evidence to recommend a precise diagnostic threshold (23) Protocol can be conducted in the ambulatory setting
Captopril challenge test	Moderate	After sitting for 1 hour, blood is drawn to mark t = 0 Individuals are then given 50 mg of captopril and remain seated for 2 hours following administration Blood should be drawn at t = 2 hours to complete the study	Measure plasma aldosterone and renin at t = 0 and t = 2h	In the context of a post-captopril suppressed renin (<1.0 ng/mL/h or <10 mU/L), a 2-h post-captopril plasma aldosterone level <277 pmol/L (10 ng/dL) by immunoassay or <203 pmol/L (7.5 ng/dL) by LC-MS/MS makes PA unlikely (84) (112)	Many individuals with hypertension are actively treated with ACE inhibitors or ARBs; plasma aldosterone and renin values measured after taking these routinely prescribed medications may serve as a proxy for the captopril challenge test Interpretation of results should be considered to be probabilistic as the evidence to support a singular diagnostic threshold is not firm (26) Protocol requires an in-person visit and space and staff to accommodate the procedures
Saline suppression test	Moderate	After sitting for 1 hour, blood should be drawn to mark t = 0 Two liters of normal saline are infused over 4 hours (500 mL/h for 4 hours), while maintaining a seated position, after which blood should be drawn	Measure plasma aldosterone and serum potassium at t = 0 and t = 4 hours	Plasma aldosterone <162 pmol/L (5.8 ng/dL) via LC-MS/MS assay makes PA unlikely Plasma aldosterone <217 pmol/L (7.8 ng/dL) via immunoassay assay makes PA unlikely (84, 100, 102, 113)	Because hypokalemia may cause false-negative interpretations, serum potassium should be normalized before the study protocol Interpretation of results should be considered to be probabilistic as the evidence to support a singular diagnostic threshold is not firm (25) Protocol requires an in-person visit, space and staff to accommodate the procedures, and IV infusion of saline Protocol should not be performed if baseline BP is uncontrolled, or in patients at high risk for pulmonary edema (such as in heart failure or advanced chronic kidney disease)

Captopril Challenge Test
post-CCT PAC level
<10 ng/dL makes PA unlikely

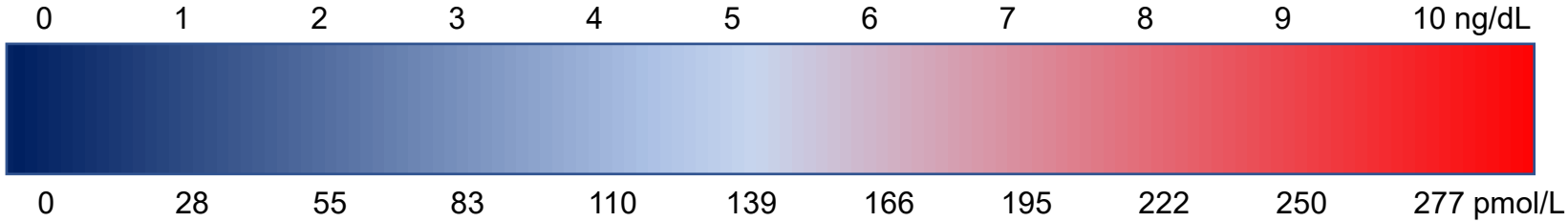
Seated Saline Suppression
post-SST PAC level
<7.8 ng/dL makes PA unlikely

ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Cut-off Levels for Confirmatory SIT



Aldosterone levels post-SIT with CLIA



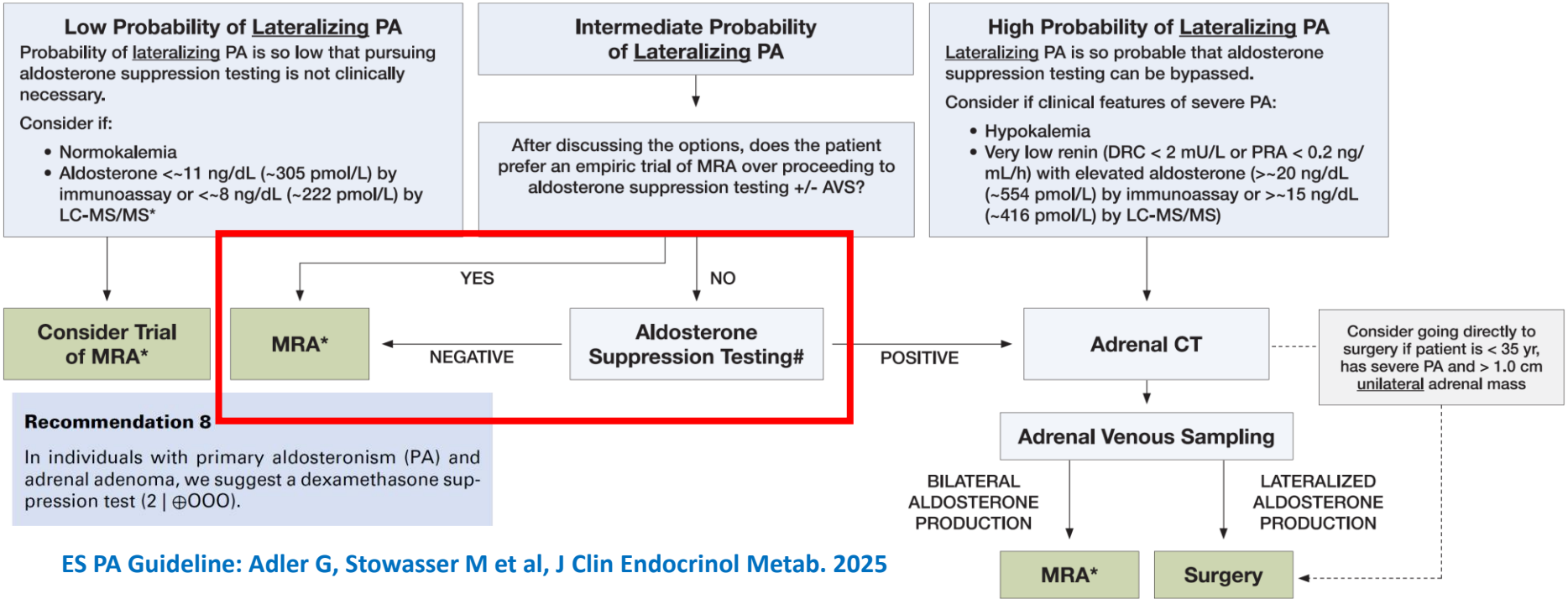
Aldosterone levels post-SIT with LC-MS/MS

Recommendation 5

In individuals with primary aldosteronism (PA), we suggest medical therapy or surgical therapy with the choice of therapy based on lateralization of aldosterone hypersecretion and candidacy for surgery (2 | ⊕OOO).

Recommendation 6

In individuals with primary aldosteronism (PA) considering surgery, we suggest adrenal lateralization with computed tomography (CT) scanning and adrenal venous sampling (AVS) prior to deciding the treatment approach (medical or surgical) (2 | ⊕⊕OO).



Recommendation 8

In individuals with primary aldosteronism (PA) and adrenal adenoma, we suggest a dexamethasone suppression test (2 | ⊕OOO).

ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Long-Term Follow-Up of Patients With Elevated ARR but Negative Confirmatory Test: The Progression of Primary Aldosteronism Phenotypes

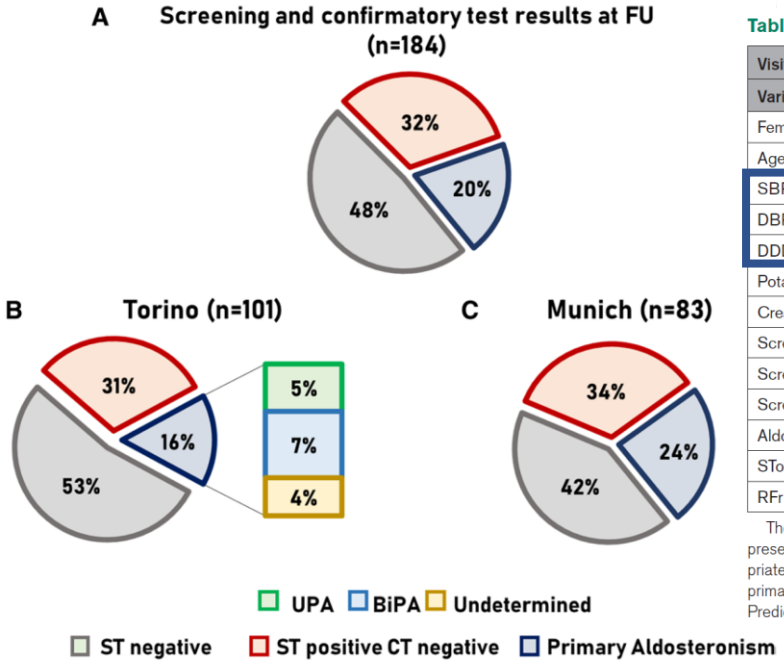


Table 2. Comparison of Patients With PA Diagnosis at Follow-Up and Patients Without PA

Visit	First visit			Second visit		
Variables	Non-PA (n=148)	PA (n=36)	*P* value	Non-PA (n=148)	PA (n=36)	*P* value
Female sex, n (%)	90 (60.8%)	23 (63.9%)	0.734	…	…	…
Age, y	47±10	46±8	0.645	52±10	51±8	0.483
SBP, mm Hg	146±15	147±18	0.343	133±12	142±17	0.005*
DBP, mm Hg	93±11	94±10	0.243	85±9	89±8	0.007*
DDD	1.00 (0.00–2.50)	1.58 (0.81–3.00)	0.122	2.00 (1.00–3.46)	2.13 (0.81–3.00)	0.941
Potassium, mmol L^{-1}	4.1±0.4	4.0±0.3	0.373	4.1±0.4	4.0±0.4	0.195
Creatinine, mg dL^{-1}	0.84±0.21	0.82±0.16	0.538	0.86±0.19	0.85±0.15	0.385
Screening test PRA, ng mL^{-1} h^{-1}†	0.30 (0.20–0.42)	0.25 (0.12–0.49)	0.405	0.72 (0.25–1.51)	0.30 (0.24–0.46)	0.023*
Screening test renin, μU mL^{-1}‡	3.7 (2.0–6.1)	3.2 (2.0–5.1)	0.422	7.0 (3.0–12.9)	4.8 (2.1–7.4)	0.013*
Screening test aldosterone, ng dL^{-1}	16.5 (9.4–24.4)	12.9 (8.4–26.6)	0.366	13.9 (6.7–19.7)	17.8 (12.6–26.7)	<0.001*
Aldosterone post-SSIT, ng dL^{-1}§	3.3 (2.5–4.6)	3.9 (3.1–5.0)	0.035*	4.6 (3.5–5.5)	8.1 (7.0–10.1)	<0.001*
SToP-PA score	8.5 (6.0–10.5)	9.5 (6.5–11.0)	0.229	8.5 (6.0–10.5)	10.0 (7.0–11.5)	0.046*
RFr coefficient	0.26 (0.00–0.45)	0.32 (0.25–0.44)	0.183	0.30 (0.25–0.44)	0.35 (0.26–0.56)	0.019*

The comparison of clinical and biochemical characteristics of patients without PA (n=148) and with confirmed PA (n=36). The first visit was performed before the present study while the second visit was part of the present study. Variables are reported as mean±SD, median (interquartile range), or absolute number (%), as appropriated. DDD: average maintenance dose per day for a drug used for its main indication in adults. DBP indicates diastolic blood pressure; DDD, defined daily dose; PA, primary aldosteronism; PRA, plasma renin activity; RFr, random forest regressor; SBP, systolic blood pressure; SSIT, seated saline infusion test; and SToP-PA, Score To Predict Primary Aldosteronism.

Buffolo F, Hypertension 2024

ORIGINAL RESEARCH

Annals of Internal Medicine

Confirmatory Testing for Primary Aldosteronism

A Study of Diagnostic Test Accuracy

Alexander A. Leung, MD, MPH; Raj S. Padwal, MD, MSc; Gregory L. Hundemer, MD, MPH; Erik Venos, MD, MSc; David J.T. Campbell, MD, PhD; Daniel T. Holmes, MD; Dennis J. Orton, PhD; C. Benny So, MBBS; Stefan J. Przybojewski, MD; Cori E. Caughlin, MD; Janice L. Pasieka, MD; Doreen M. Rabi, MD, MSc; and Gregory A. Kline, MD

Background: Confirmatory testing to verify the diagnosis of primary aldosteronism (PA) in patients who have an abnormal screening result is of uncertain benefit.

Objective: To perform a blinded assessment of the seated saline suppression test (SSST).

Design: Diagnostic test accuracy study. (ClinicalTrials.gov: NCT04422756)

Setting: The regional Endocrine Hypertension Clinic in Calgary, Alberta, Canada.

Participants: 156 adults with a positive screening result for PA.

Intervention: The SSST was done by administering 2 L of 0.9% sodium chloride intravenously over 4 hours with the patient seated.

Measurements: Treatment response was considered the reference standard for determining disease status and was based on blood pressure lowering, reduction of antihypertensive drug dose, and normalization of biochemistry. Measures of diagnostic test accuracy, including sensitivity, specificity, positive predictive value, and negative predictive value, were estimated.

Results: Post-SSST aldosterone concentrations measured using immunoassay overlapped between treatment responders (median, 329 pmol/L [IQR, 227 to 525 pmol/L]) and nonresponders (median, 255 pmol/L [IQR, 162 to 346 pmol/L]). The SSST could not discriminate between response statuses (area under the curve, 62.1% [95% CI, 45.1% to 79.1%]). The positive and negative likelihood ratios were equivocal for aldosterone cutoffs ranging from 140 to 300 pmol/L. These findings remained consistent after differences in treatment, occurrence of hypokalemia, and laboratory assay used were accounted for.

Limitation: The study population had many patients with high-risk features of PA and few nonresponders.

Conclusion: The SSST is associated with a high false-negative rate, and reliance on it may lead to missed opportunities for intervention.

Primary Funding Source: The Canadian Institutes of Health Research, Hypertension Canada, and the Heart and Stroke Foundation of Canada.

Ann Intern Med. 2025;178:948-956. doi:10.7326/ANNALS-24-03153
For author, article, and disclosure information, see end of text.
This article was published at Annals.org on 6 May 2025.

- Given the lack of a reliable reference standard for bilateral PA, the authors should have focussed on surgically treated patients alone.

-Conclusions invalid. BP reduction with MRA treatment should not be used as a reference standard for PA diagnosis

-Hypokalemia was not corrected prior to SSST (potential false negative results)

-Because circadian aldosterone secretion falls after midday, the SSST should commence by 8 a.m. and not “typically … between 8 to 10 a.m.”. 10 a.m. is too late: by 2 p.m. aldosterone would have dropped substantially

-Leung et al. claim poor specificity but, after excluding patients in whom cortisol rose during SSST or renin was unsuppressed, at the recommended LC/MS-MS cutoff there were only 3 false positives out of 134 studies, a minimal extra burden on AVS services

Stowasser M, Ann Int Med 2025

European Journal of Endocrinology, 2025, **193**, 348–358
https://doi.org/10.1093/ejendo/lvaf170
Advance access publication 12 August 2025
Original Research

Discordance and shortcomings of aldosterone suppression tests in primary aldosteronism

Cheng-Hsuan Tsai,[1,2,3,*] Stefanie Parisien-La Salle,[1,4] Jenifer M. Brown,[1,5] Andrew Newman,[1] Chin-Chen Chang,[3,6,7] Vin-Cent Wu,[3,8] Yen-Hung Lin,[2,3] and Anand Vaidya[1]

[1]Center for Adrenal Disorders, Division of Endocrinology, Diabetes, and Hypertension, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, United States
[2]Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei 100, Taiwan
[3]Primary Aldosteronism Center at National Taiwan University Hospital, Taipei 100, Taiwan
[4]Division of Endocrinology, Department of Medicine, Research Center, Centre Hospitalier de L'Université de Montréal (CHUM), Montreal 900, Canada
[5]Division of Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, United States
[6]Department of Medical Imaging, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei 100, Taiwan
[7]Department and Graduate Institute of Forensic Medicine, National Taiwan University College of Medicine, Taipei 100, Taiwan
[8]Division of Nephrology, Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei 100, Taiwan

*Corresponding author: Center for Adrenal Disorders, Division of Endocrinology, Diabetes, and Hypertension, Brigham and Women's Hospital, Harvard Medical School, 221 Longwood Ave, Boston, MA 02115, USA. Email: chenghsuan@ntuh.gov.tw

Abstract

Background: The saline suppression test (SST) and the captopril challenge test (CCT) have traditionally been used to confirm or exclude primary aldosteronism (PA). New guidelines recommend using these tests to predict the likelihood of unilateral PA. This study evaluated the diagnostic accuracy, consistency, and clinical implications of these tests.

Methods: We conducted a retrospective study of 531 patients with high-probability features of PA who underwent both SST and CCT to evaluate their accuracy and ability to predict unilateral PA. Adrenal lateralization and surgical treatment decisions were guided by individualized clinical judgment rather than strictly relying on SST/CCT results.

Results: The rate of PA diagnosis ranged from 47.8% to 97.2% based on SST and CCT criteria. Discordance rates between SST and CCT ranged from 10.9% to 51.6%. In analyses restricted to only patients with clinically overt PA, where suppression testing is not considered necessary, the positivity rates of the SST and CCT were still suboptimal and test discordance persisted. Among patients with lateralizing PA, 6.6% to 27.9% had either a negative SST or CCT interpretation, and among those who achieved Primary Aldosteronism Surgical Outcome-defined biochemical cure after unilateral adrenalectomy, 4.1% to 39.8% had either a negative SST or CCT, and up to 5.1% had false-negative results on both tests.

Conclusions: Well-established aldosterone suppression tests for PA demonstrated substantial inconsistency, false-negative interpretations, and the inability to reliably predict lateralization outcomes in PA. Aldosterone suppression testing, using SST and CCT, lack accuracy for the diagnosis and subtyping of PA in high-risk patients.

From a cohort of 2482 with high probability features 32 of PA, they selected 531 who had both SSST and CCT.

Using a sensitive cut-off of 6 ng/dL for SST:
-97% with high probability PA were positive
-In clinically overt PA, the sensitivity was 98%.
-The sensitivity for UPA was 98%
-For pts biochemically cured sensitivity was 99% and 100% for those clinically cured

Using a cut-off of 11 ng/dL for CCT:
-In clinically overt PA, the sensitivity was 95%.
-For pts biochemically cured sensitivity was 97% and 99% for those clinically cured

A negative SSST does not exclude mild bilateral PA. It certainly doesn't preclude the use of MRA which should be encouraged in all patients with low renin hypertension.
For these reasons, SSST does not lead to "missed opportunities" for targeted medical treatment.

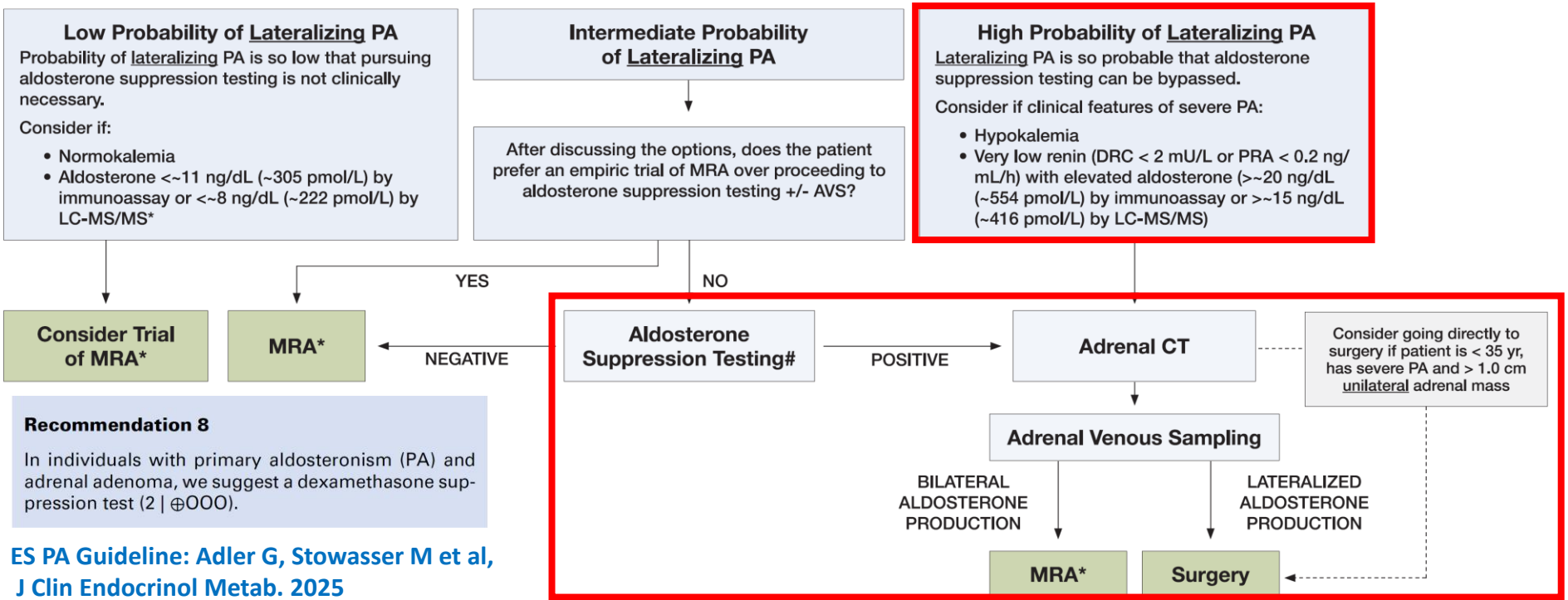
Stowasser M, Eur J Endocrinol 2025

Recommendation 5

In individuals with primary aldosteronism (PA), we suggest medical therapy or surgical therapy with the choice of therapy based on lateralization of aldosterone hypersecretion and candidacy for surgery (2 | ⊕OOO).

Recommendation 6

In individuals with primary aldosteronism (PA) considering surgery, we suggest adrenal lateralization with computed tomography (CT) scanning and adrenal venous sampling (AVS) prior to deciding the treatment approach (medical or surgical) (2 | ⊕⊕OO).



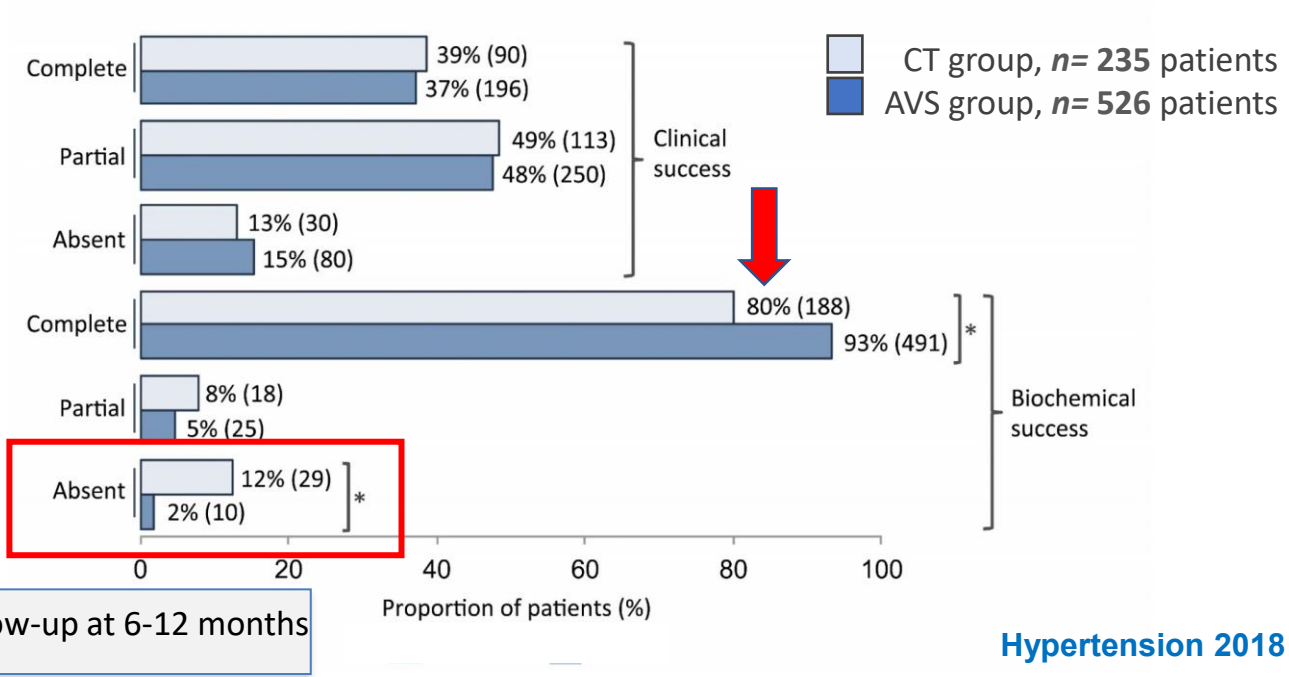
Recommendation 8

In individuals with primary aldosteronism (PA) and adrenal adenoma, we suggest a dexamethasone suppression test (2 | ⊕OOO).

ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Computed Tomography and Adrenal Venous Sampling in the Diagnosis of Unilateral Primary Aldosteronism

Tracy A. Williams, Jacopo Burrello, Leonardo A. Sechi, Carlos E. Fardella, Joanna Matrozova, Christian Adolf, René Baudrand, Stella Bernardi, Felix Beuschlein, Cristiana Catena, Michalis Doumas, Francesco Fallo, Gilberta Giacchetti, Daniel A. Heinrich, Gaëlle Saint-Hilary, Pieter M. Jansen, Andrzej Januszewicz, Tomaz Kocjan, Tetsuo Nishikawa, Marcus Quinkler, Fumitoshi Satoh, Hironobu Umakoshi, Jiří Widimský Jr, Stefanie Hahner, Stella Douma, Michael Stowasser, Paolo Mulatero,* Martin Reincke*



Follow-up at 6-12 months

Hypertension 2018

Table 9. Key indices and cutoffs for adrenal vein sampling interpretation

AVS index	Index formula	Cutoff values	Diagnostic significance
Selectivity index (SI)	$[\text{cortisol}]_{AV}/[\text{cortisol}]_{IVC}$	Unstimulated >1.4 to 3 Cosyntropin-stimulated >5	Indication of successful AV cannulation
Lateralization index (LI)	$([\text{aldosterone}]/[\text{cortisol}])_{highAV}/([\text{aldosterone}]/[\text{cortisol}])_{lowAV}$	Unstimulated or cosyntropin-stimulated ≥4	Distinguishes lateralizing from bilateral PA
Contralateral suppression index (CSI)	$([\text{aldosterone}]/[\text{cortisol}])_{lowAV}/([\text{aldosterone}]/[\text{cortisol}])_{IVC}$	Unstimulated or cosyntropin-stimulated <1	Consistent with suppressed aldosterone production by the contralateral adrenal gland

Abbreviations: AV, adrenal vein; highAV, adrenal vein measurement from the dominant adrenal; IVC, inferior vena cava; lowAV, adrenal vein measurement from the nondominant adrenal gland.

ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

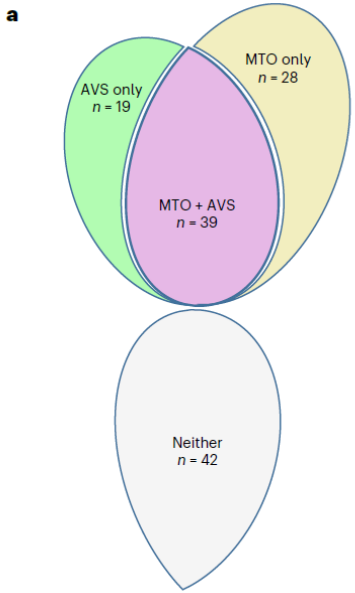
nature medicine

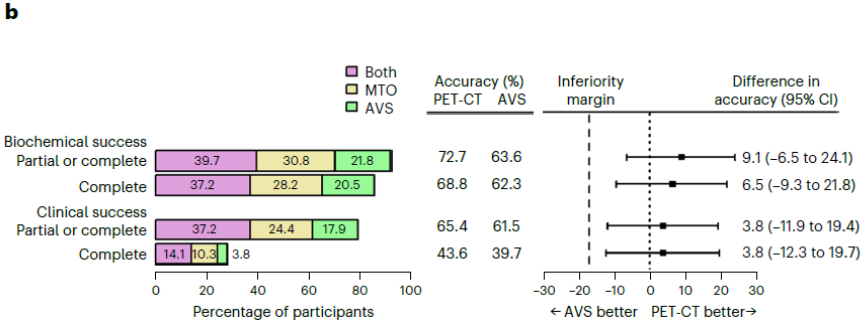
Article

https://doi.org/10.1038/s41591-022-02114-5

[^{11}C]metomidate PET-CT versus adrenal vein sampling for diagnosing surgically curable primary aldosteronism: a prospective, within-patient trial

Xilin Wu[1,2,3], Russell Senanayake[4,5,6,25], Emily Goodchild[1,2,3,25], Waiel A. Bashari[4,5,6], Jackie Salsbury[1,2], Claudia P. Cabrera[7], Giulia Argentesi[1,2,3], Samuel M. O'Toole[1,2,3,8], Matthew Matson[9], Brendan Koo[10], Laila Parvanta[3], Nick Hilliard[10], Vasilis Kosmoliaptsis[11], Alison Marker[12], Daniel M. Berney[13], Wilson Tan[14], Roger Foo[14], Charles A. Mein[15], Eva Wozniak[15], Emmanuel Savage[15], Anju Sahdev[9], Nicholas Bird[10], Kate Laycock[1,2,3], Istvan Boros[16], Stefan Hader[16], Victoria Warnes[17], Daniel Gillett[17], Anne Dawnay[18], Elizabeth Adeyeye[19], Alessandro Prete[20], Angela E. Taylor[20], Wiebke Arlt[20,21], Anish N. Bhuva[22], Franklin Aigbirhio[16], Charlotte Manisty[22], Alasdair McIntosh[23], Alexander McConnachie[23], J. Kennedy Cruickshank[19,24], Heok Cheow[10], Mark Gurnell[4,5,6,26], William M. Drake[2,3,26] & Morris J. Brown[1,2,3,26]





Original Investigation | Diabetes and Endocrinology

Accuracy of Gallium-68 Pentixafor Positron Emission Tomography–Computed Tomography for Subtyping Diagnosis of Primary Aldosteronism

JAMA Network 2023

Jinbo Hu, MD, PhD; Tingting Xu, MD; Hang Shen, MD; Ying Song, MD, PhD; Jun Yang, PhD; Aipin Zhang, PhD; Haoyuan Ding, MD; Naiguo Xing, MD, PhD; Zhuoyuan Li, MD; Lin Qiu, MD, PhD; Linqiang Ma, MD, PhD; Yi Yang, MD, PhD; Zhengping Feng, MD, PhD; Zhipeng Du, MD; Wenwen He, MD; Yue Sun, MD, PhD; Jun Cai, MD, PhD; Qifu Li, PhD; Yue Chen, MD; Shumin Yang, PhD; for the Chongqing Primary Aldosteronism Study (CONPASS) Group

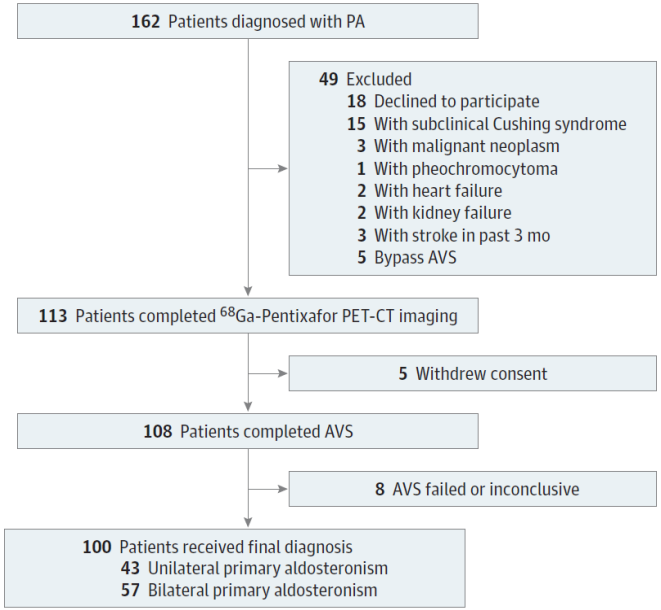
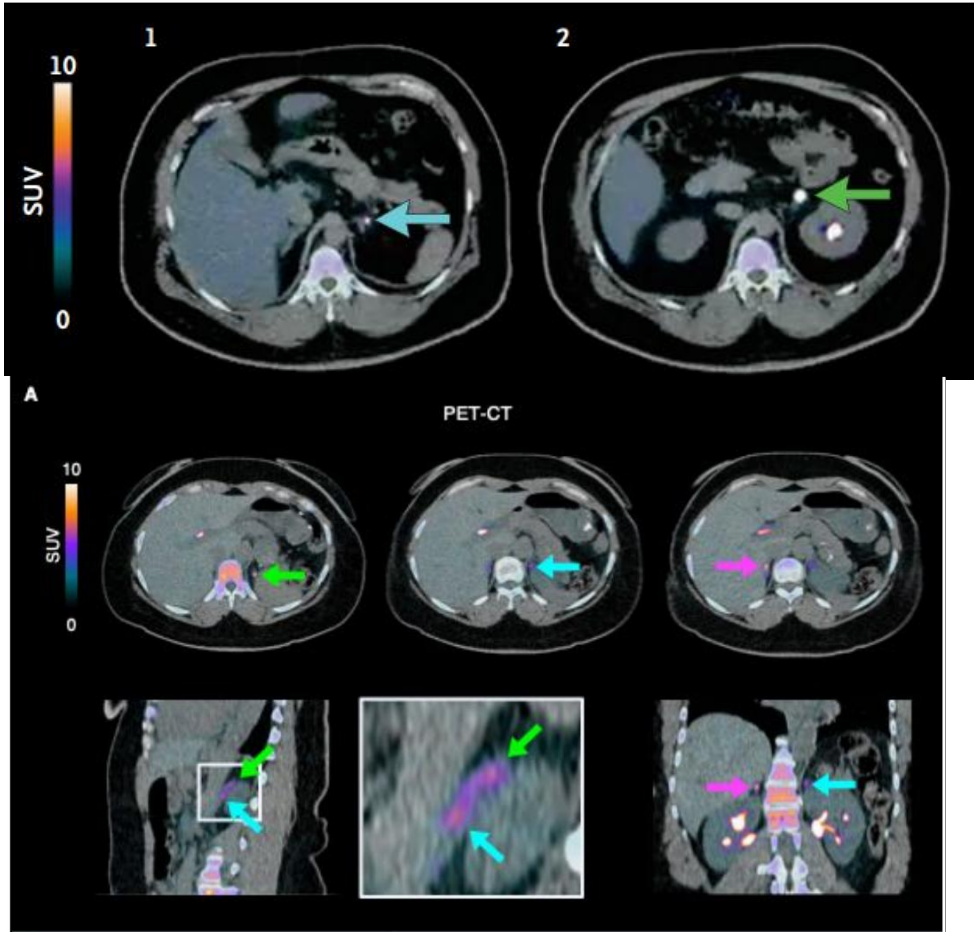


Table 3. Diagnostic Accuracy for Primary Aldosteronism Subtyping Using LI Based on SUVmax

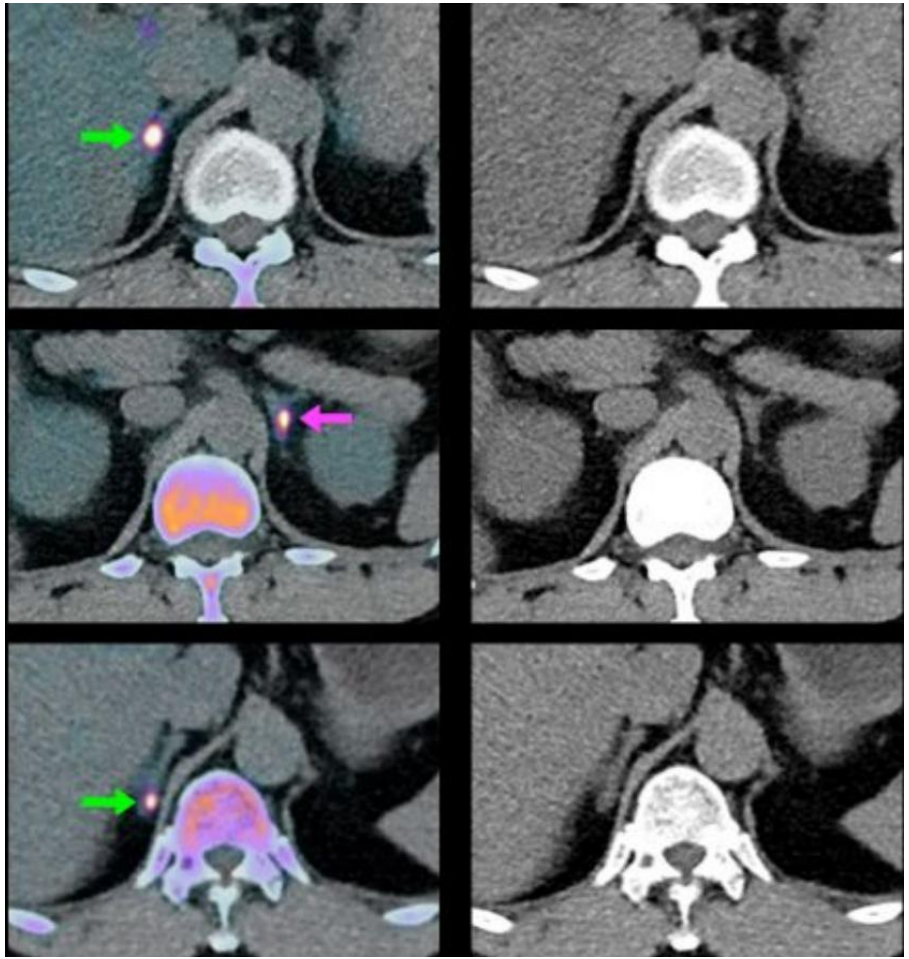
Cutoff	No. TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
LI based on SUVmax at 10 min						
1.10	42	42	1	15	0.98 (0.88-1.00)	0.26 (0.16-0.40)
1.56	33	4	10	53	0.77 (0.61-0.88)	0.93 (0.83-0.98)
1.65	33	0	10	57	0.77 (0.61-0.88)	1.00 (0.94-1.00)
LI based on SUVmax at 40 min						
1.12	40	40	3	17	0.93 (0.81-0.99)	0.30 (0.18-0.43)
1.57	37	5	6	52	0.86 (0.72-0.95)	0.91 (0.81-0.97)
3.15	19	0	24	57	0.44 (0.29-0.60)	1.00 (0.94-1.00)

A cutoff value for lateralization index based on SUVmax at 10 minutes set at 1.65 displayed a specificity of 1.00 and sensitivity of 0.77.
The diagnostic concordance rate of PET-CT and AVS was 90 patients (90.0%) compared with 54 patients (54.0%) between traditional CT and AVS

Adrenal Aldosterone Synthase Expression Imaging in Primary Aldosteronism



Årstad E, New Engl J Med

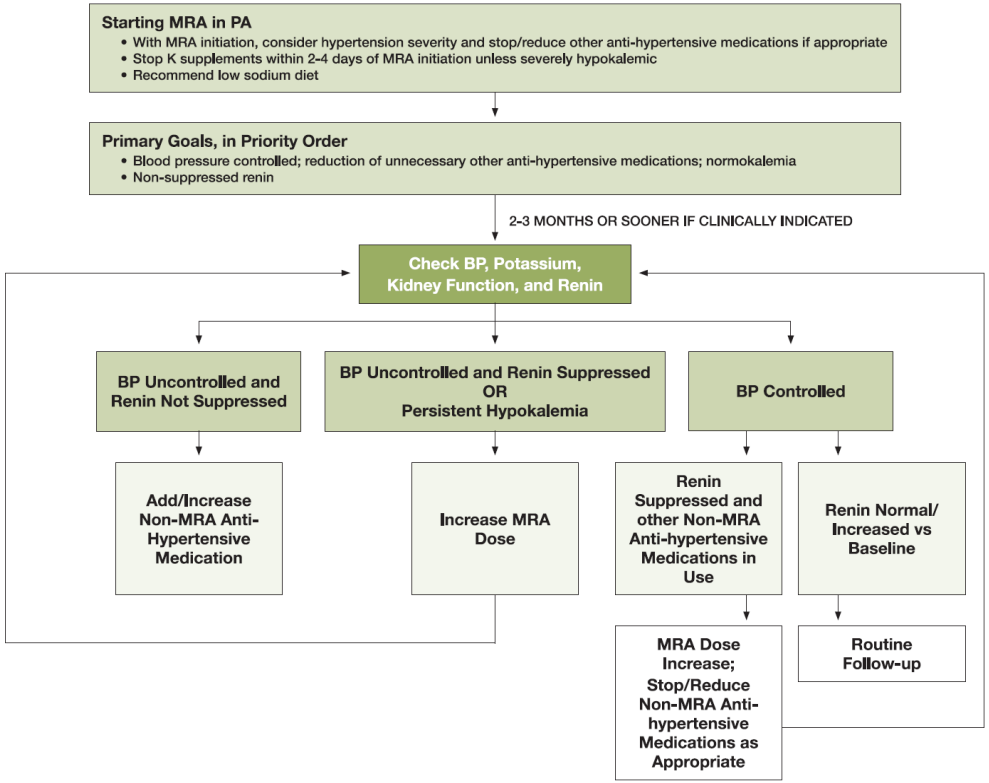


Recommendation 7

In individuals with primary aldosteronism (PA) receiving PA-specific medical therapy whose hypertension is not controlled and renin is suppressed, we suggest increasing PA-specific medical therapy to raise renin (2 | ⊕OOO).

Recommendation 9

In individuals with primary aldosteronism (PA) receiving PA-specific medical therapy, we suggest spironolactone over other mineralocorticoid receptor antagonists (MRAs) due to its low cost and widespread availability (2 | ⊕OOO).



Recommendation 10

For individuals with primary aldosteronism (PA) receiving PA-specific medical therapy, we suggest using mineralocorticoid receptor antagonists (MRAs) rather than epithelial sodium-channel (ENaC) inhibitors (amiloride, triamterene) (2 | ⊕OOO).

ES PA Guideline: Adler G, Stowasser M et al, J Clin Endocrinol Metab. 2025

Patients were randomized in a 1:1 ratio to receive 12.5 mg/d of spironolactone or 5 mg/d of amiloride. If home SBP remained >130 mmHg and serum K+< 5.0 mmol/L after 4 weeks, dosages were increased to 25 mg/d and 10 mg/d, respectively.

Amiloride: the long forgotten drug

JAMA | Original Investigation 2025

Spironolactone vs Amiloride for Resistant Hypertension
A Randomized Clinical Trial

Chan Joo Lee, MD; Sang-Hyun Ihm, MD; Dong-Ho Shin, MD; Jin-Ok Jeong, MD; Ju Han Kim, MD; Kyeong-Hyeon Chun, MD; JiWung Ryu, MD; Hae-Young Lee, MD; Seonghoon Choi, MD; Eun Mi Lee, MD; Jung Hyun Choi, MD; Kwang-Il Kim, MD; Jinho Shin, MD; Wook Bum Pyun, MD; Dae-Hee Kim, MD; Sungha Park, MD; Bryan Williams, MD

Table 2. Home Blood Pressure Change From Baseline to Week 12

	Amiloride (n = 56)			Spironolactone (n = 58)			Difference in change, spironolactone – amiloride[a]	
End points	Baseline	Week 12	Change	Baseline	Week 12	Change	With 90% CI	With 95% CI
Primary end point								
Total home systolic blood pressure, mean (SD), mm Hg[b]	141.5 (7.9)	128.0 (8.9)[c]	−13.6 (8.6)[c]	142.3 (8.5)	127.6 (10.8)[d]	−14.7 (11.0)[d]	−0.68 (−3.50 to 2.14)	−0.68 (−4.05 to 2.69)
Secondary end points								
Systolic blood pressure, mean (SD), mm Hg								
Morning[e]	142.9 (9.8)	129.1 (11.2)[c]	−13.8 (9.6)[c]	142.0 (9.3)	127.7 (10.8)[d]	−14.3 (12.0)[d]	−0.95 (−4.03 to 2.13)	−0.95 (−4.63 to 2.73)
Evening[f]	140.2 (8.1)	126.7 (8.0)[c]	−13.5 (9.1)[c]	142.6 (9.3)	127.6 (11.7)[d]	−15.0 (11.2)[d]	−0.29 (−3.18 to 2.60)	−0.29 (−3.74 to 3.16)
Diastolic blood pressure, mean (SD), mm Hg								
Total home[b]	86.1 (9.1)	79.2 (7.6)[c]	−6.8 (6.1)[c]	87.0 (8.6)	80.4 (8.1)[d]	−6.7 (7.3)[d]	0.52 (−1.30 to 2.33)	0.52 (−1.65 to 2.68)
Morning[e]	87.8 (9.7)	81.1 (8.7)[c]	−6.7 (6.5)[c]	87.3 (8.6)	81.1 (8.1)[d]	−6.2 (7.4)[d]	0.33 (−1.57 to 2.24)	0.33 (−1.94 to 2.61)
Evening[f]	84.3 (9.4)	77.4 (7.6)[c]	−6.9 (6.9)[c]	86.7 (9.2)	79.5 (8.6)[d]	−7.1 (7.9)[d]	0.82 (−1.14 to 2.78)	0.82 (−1.62 to 3.16)

[a] Analysis-of-covariance model, adjusted for corresponding baseline blood pressure, 2-sided.

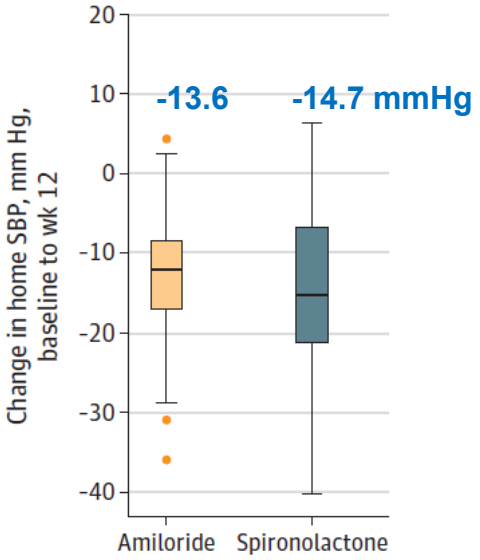
[b] Mean of morning and evening measurements.

[c] Four missing values were imputed by the last-observation-carried-forward method.

[d] Two missing values were imputed by the last-observation-carried-forward method.

[e] Mean of 2 measurements between 7 AM and 9 AM or within 2 hours of waking.

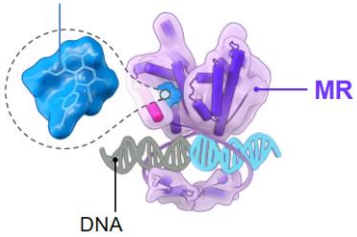
[f] Mean of 2 measurements between 9 PM and 11 PM or within 1 hour before sleep.



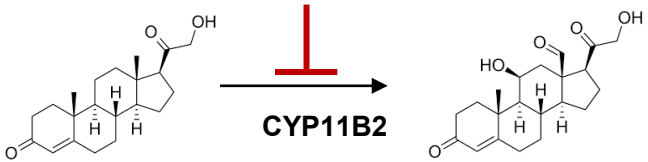
New Treatment Options for Primary Aldosteronism

MEDICAL TREATMENT
Bilateral PA, not desired / failed surgery

Non steroidal MRAs



Aldosterone Synthase Inhibitors



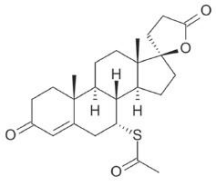
SURGICAL TREATMENT
Unilateral PA; difficult to control BiPA

- Endoscopic, ultrasound-guided, radiofrequency ablation
- Percutaneous CT radiofrequency ablation
- Transvenous radiofrequency catheter ablation
- Super-selective adrenal arterial embolization

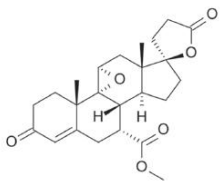
Steroidal and non-Steroidal MRAs

Steroidal MRAs
(aldosterone antagonists)

1960

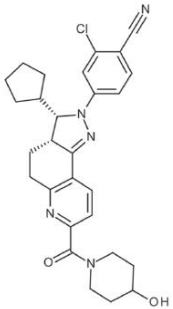


Spironolactone



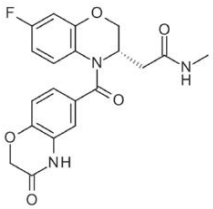
Eplerenone

Non-steroidal MRAs



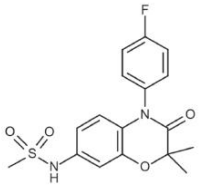
KBP-5074
(Phase II)

Ocedurenone



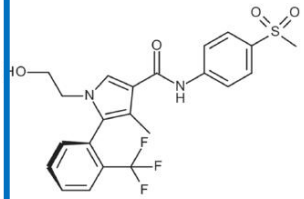
AZD9977
(Phase II)

Balcinrenone



Apararenone
MT-3995
(Phase II)

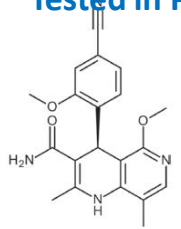
Tested in PA



Esaxerenone
CS-3150
(launched in Japan)

Available in Italy

Tested in PA



Finerenone
BAY 94-8862
(launched in the United States)

Kintscher U, Bakris GL, Kolkhof P. Br J Pharmacol. 2022

Effects of Esaxerenone on blood pressure, urinary albumin excretion, serum levels of NT-proBNP, and quality of life in patients with primary aldosteronism

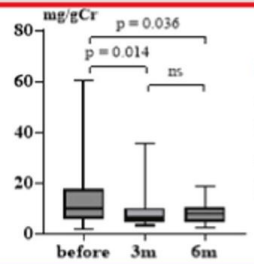
Esaxerenone A nonsteroidal skeletal MRA with a strong affinity for MR and an extended blood half-life.

PA patients

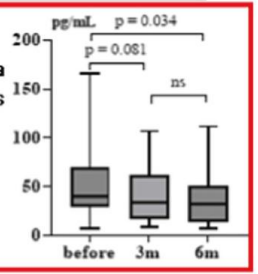
	Pre-treatment	3 months	6 months
SBP	136 mmHg	123 mmHg ↓	125 mmHg ↓
DBP	87 mmHg	79 mmHg ↓	80 mmHg ↓
ARC	1.9 pg/mL	3.6 pg/mL ↑	4.3 pg/mL ↑
QOL	→	→	↑

-13/8 mmHg **-11/7 mmHg**

UACR showed a decrease at both 3 and 6 months after treatment compared to pretreatment levels.



NT-proBNP showed a decrease at 6 months after treatment compared to pretreatment levels.



Reductions in SBP, DBP, UACR, and NT-proBNP were independent of the effects of salt restriction.

Yoshida Y,
Hypert Res 2023

Circulation **2025**

RESEARCH LETTER

Efficacy and Safety of Finerenone in Patients With Primary Aldosteronism: A Pilot Randomized Controlled Trial

Jinbo Hu, MD, PhD*; Qixin Zhou, MD*; Yue Sun, MD, PhD*; Zhengping Feng, MD, PhD; Jun Yang, MD, PhD; Wenwen He, MD; Ying Song, MD, PhD; Yue Wang, MD, PhD; Xiangjun Chen, MD, PhD; Hang Shen, MD; Ying Jing, MD, PhD; Shumin Yang, MD, PhD†; Qifu Li, MD, PhD†; on behalf of the CONPASS Group‡

Spironolactone 20 mg (29 pts, 10 APA) vs Finerenone 20 mg (30 pts 5 APA)

	Finerenone (n=30)			Spironolactone (n=29)			
	Baseline	Final visit	Change from baseline	Baseline	Final visit	Change from baseline	Mean difference (95% CI)
Daytime SBP, mm Hg	143.2±12.8	133.3±16.2	−9.9±13.0	142.5±12.4	134.7±13.6	−7.8±10.2	−2.1 (−8.2 to 4.0)
Daytime DBP, mm Hg	90.2±9.9	85.3±12.2	−4.9±7.9	89.2±8.3	84.2±10.8	−5.0±8.4	0.1 (−4.1 to 4.3)
24-h SBP, mm Hg	141.8±12.5	130.9±15.7	−10.9±12.5	141.8±12.1	134.1±13.5	−7.8±9.5	−3.1 (−8.9 to 2.7)
24-h DBP, mm Hg	88.6±9.8	82.7±11.7	−5.9±7.4	87.8±8.1	83.2±9.5	−4.7±6.7	−1.2 (−4.9 to 2.4)
Office SBP, mm Hg	151.5±16.7	133.8±13.6	−17.7±19.7	154.2±24.2	137.1±18.9	−17.1±19.0	−0.6 (−10.7 to 9.5)
Office DBP, mm Hg	95.0±10.0	85.9±11.0	−9.1±8.3	94.0±12.9	87.2±11.7	−6.8±11.9	−2.3 (−7.6 to 3.1)
Serum potassium, mmol/L	3.9±0.4	4.1±0.4	0.2±0.4	3.7±0.4	4.2±0.4	0.5±0.4	−0.3 (−0.5 to −0.1)*

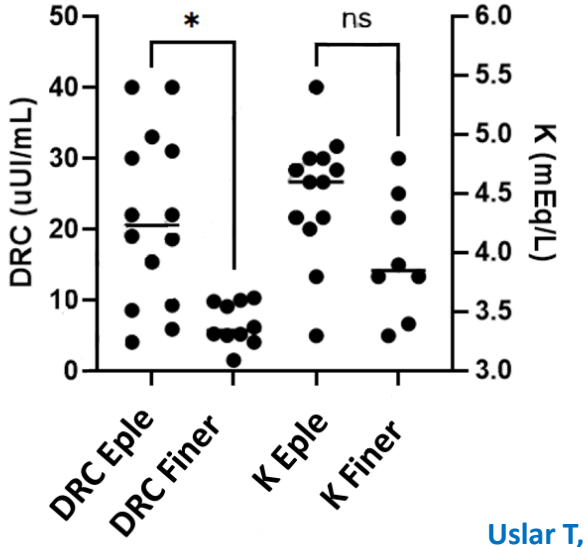
"Hypokalemia was not corrected in 2 pts treated with finerenone. Because most patients recruited had mild PA, the lack of protection by finerenone may be more evident in individuals with florid PA"

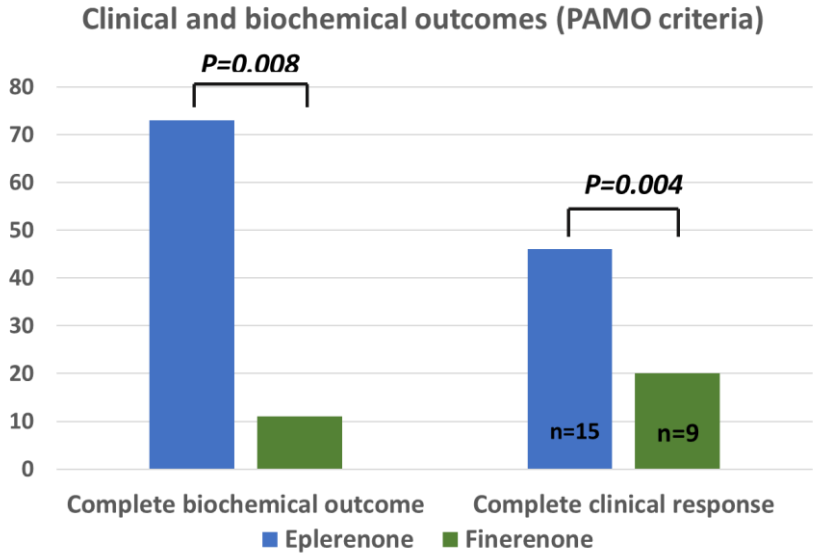
Finerenone – Real World data In Patients with PA

15 PA patients
switched from eplerenone to finerenone
93% males; mean age 52.3±17.5 yrs
mean finerone dose 20 mg

Systolic and diastolic BP and non MRA DDD did not change

DRC and K in Eplerenone vs Finerenone

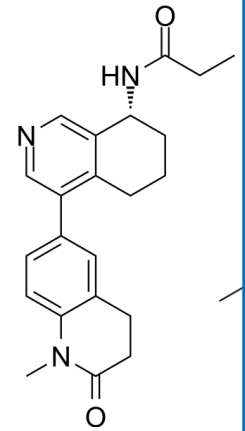




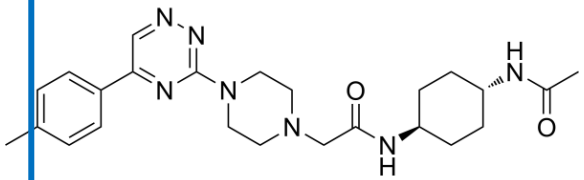
Uslar T, Eur J Endocrinol 2025

Novel Aldosterone Synthase Inhibitors

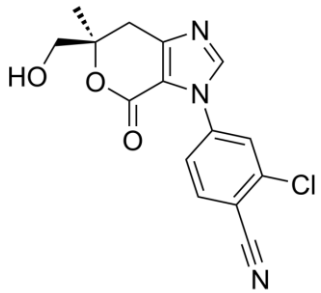
Tested in PA



Baxdrostat
Astra-Zeneca

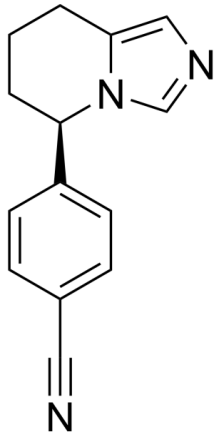


Lorundrostat
Mineralys



Vicadrostat
Boehringer

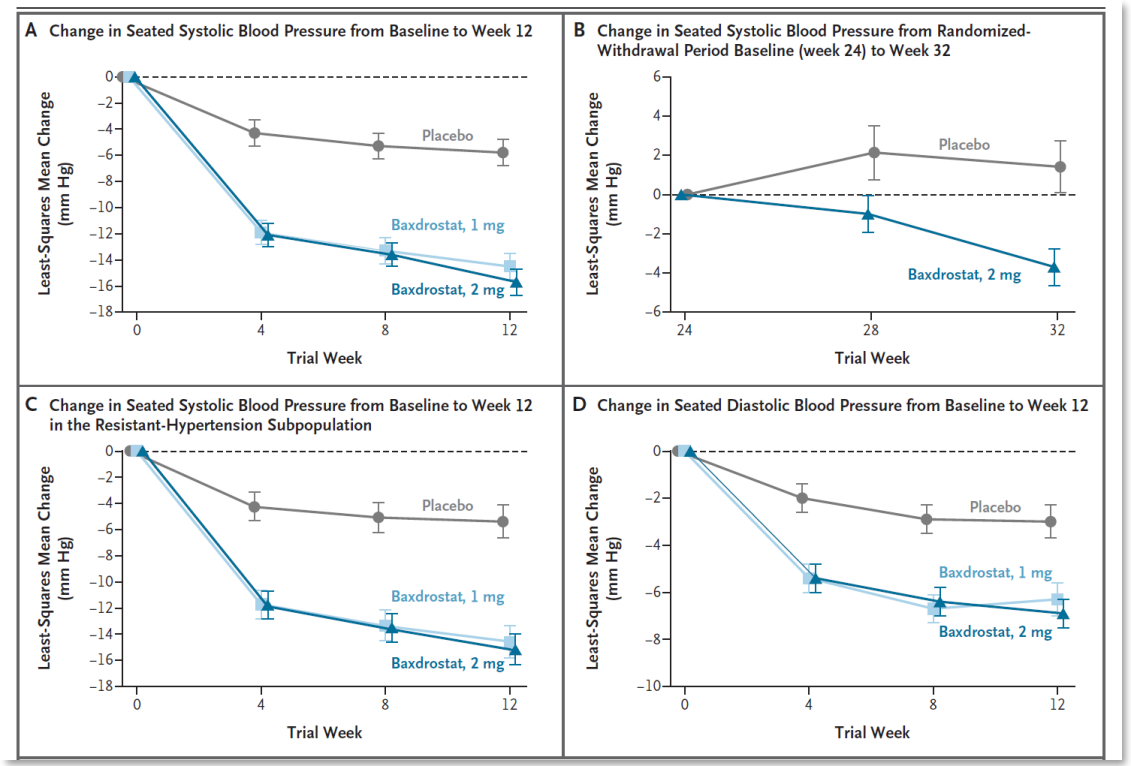
Tested in PA



Dexfadrostat
Damian Pharma

Phase 3 Trial of Baxdrostat in Uncontrolled or Resistant Hypertension (BaxHTN)

-9.8 mmHg
2mg SBP placebo-corrected

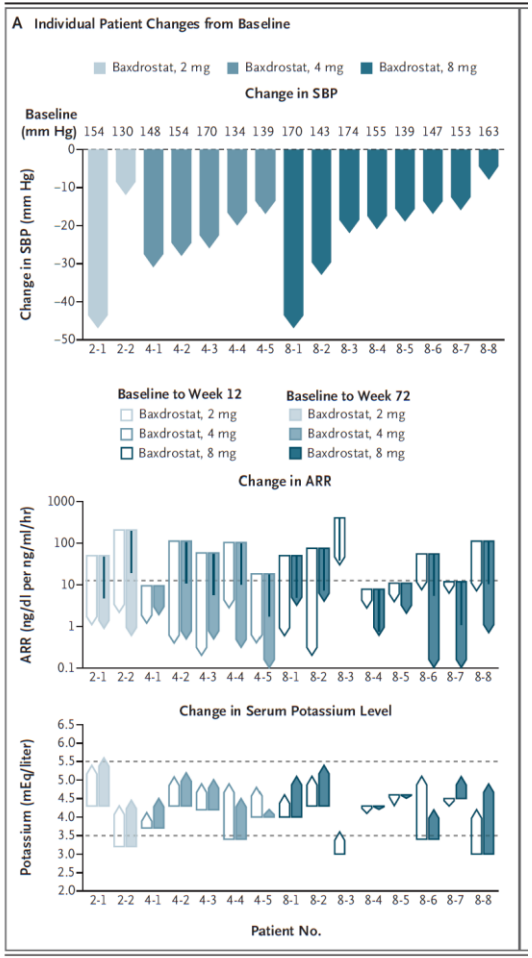


-5.1 mmHg
2mg SBP placebo-corrected

-3.9 mmHg
2mg DBP placebo-corrected

Flack JM, N Engl J Med 2025

Phase 2a study of Baxdrostat in Primary Aldosteronism (SPARK)

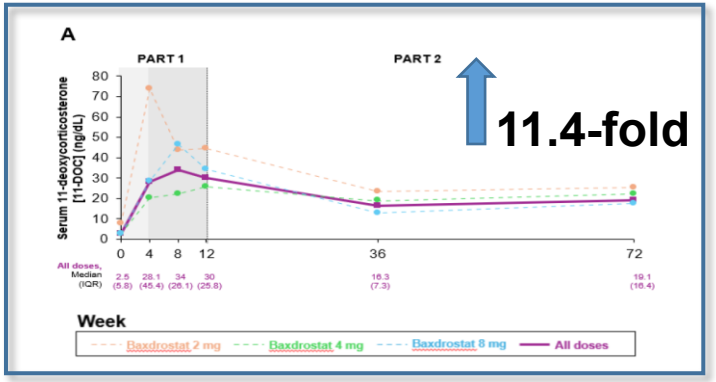


- 24.9 mmHg

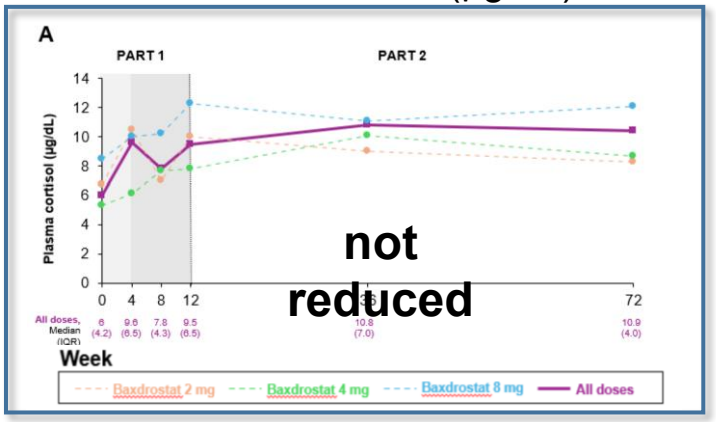
ARR reduced by 97.3%

Hypokalemia corrected in 5/5 pts

Serum [11-DOC] (ng/dL)



Plasma cortisol (µg/dL)



Turcu A, N Engl J Med 2025

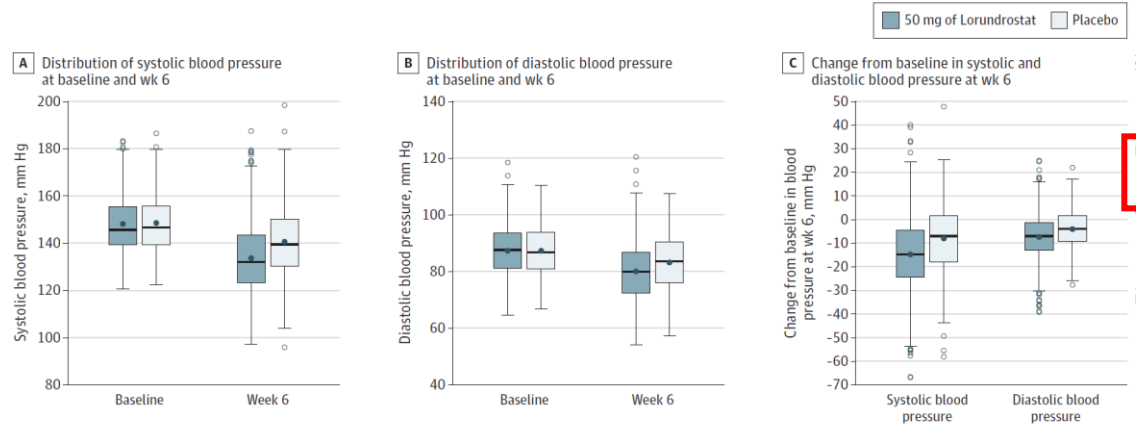
Launch-HTN of Lorundrostat for the Treatment of Uncontrolled or Resistant Hypertension

The Launch-HTN trial was a randomized, double-blinded, placebo-controlled Phase 3 trial, which enrolled eligible adult participants who failed to achieve their blood pressure goal despite being on two to five antihypertensive medications

Launch-HTN Phase 3 Trial
(automated office systolic blood pressure measure, n=1,083)

	Week 6 (50 mg pooled)		**Week 12**	
	Absolute Reduction	Placebo-Adjusted Reduction	Absolute Reduction	Placebo-Adjusted Reduction
50 mg	-16.9 mmHg	-9.1 mmHg (p<0.0001)*	-19.0 mmHg	-11.7 mmHg (p<0.0001)
50 to100 mg			-15.7 mmHg	-8.4 mmHg (p=0.0016)

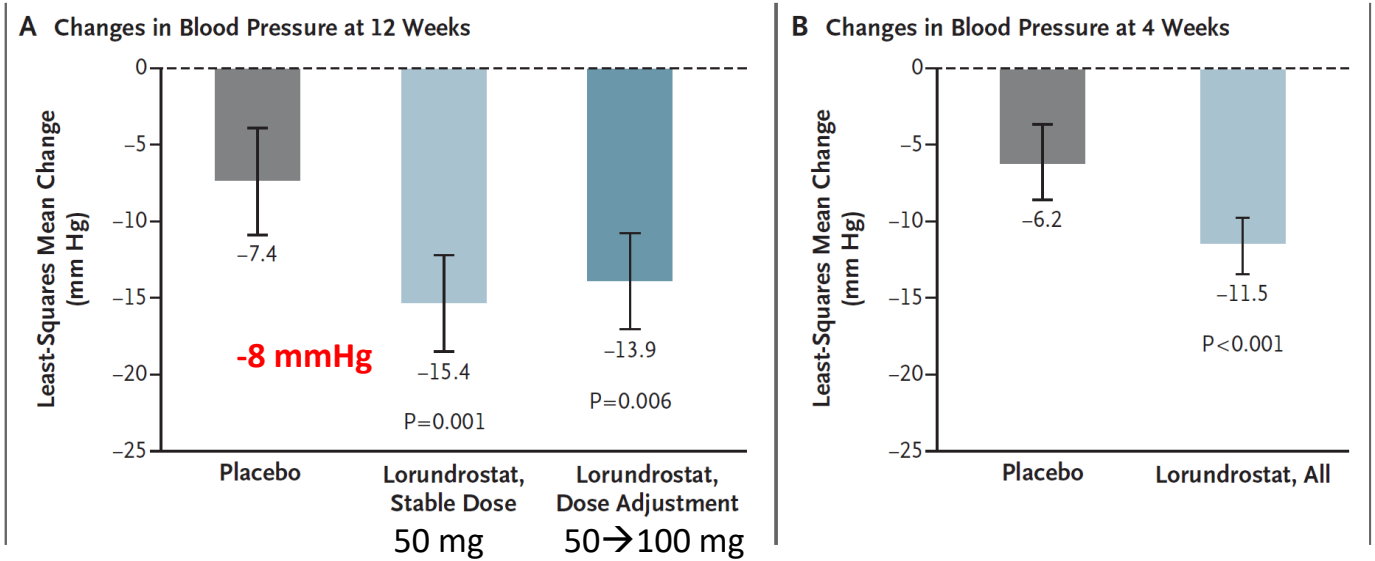
** Primary endpoint*



Baseline characteristics	No. of participants: 50 mg of Lorundrostat[a]	Placebo
No. of antihypertensive therapies		
2	318	112
≥3	490	158
Age group, y		
<65	471	161
65-74	265	80
≥75	72	29
Sex		
Female	374	132
Male	434	138
Race		
Black or African American	223	87
White	554	175
Other[b]	31	8
Systolic blood pressure, mm Hg		
<140	218	73
140-159	445	144
≥160	145	53
Body mass index[c]		
<30	293	103
≥30	515	167
Waist-to-hip ratio		
Healthy	97	42
Obese	473	149
High risk	238	79
Estimated glomerular filtration rate, mL/min/1.73 m^2		
<60	173	49
60-89	401	150
≥90	234	71

Saxena M, JAMA 2025

Lorundrostat Efficacy and Safety in Patients with Uncontrolled Hypertension (Advance-HTN trial)



The Advance-HTN trial was a randomized, double-blind, placebo-controlled Phase 2 pivotal trial that evaluated the efficacy and safety of lorundrostat for the treatment of confirmed uHTN or rHTN, when used as add-on therapy to an optimized background treatment of two or three antihypertensive medications in adult subjects (ARB: olmesartan 40 mg + diuretic: HCTZ 25 mg or indapamide 2.5 mg ± CCB: amlodipine 10 mg).

Laffin LJ, N Engl J Med 2025

Safety and efficacy of once-daily dexfadrostat phosphate in patients with primary aldosteronism: a randomised, parallel group, multicentre, phase 2 trial

Paolo Mulatero,[a,*] Gregoire Wuerzner,[b] Michael Groessl,[c] Elisa Sconfienza,[a] Aikaterini Damianaki,[b] Vittorio Forestiero,[a] Bruno Vogt,[c] Hans Brunner,[d] Teresa Gerlock,[e] Ronald Steele,[e] and Christoph Schumacher[e]

[a]Division of Internal Medicine and Hypertension, Department of Medical Sciences, University of Turin, Turin, Italy
[b]Service of Nephrology and Hypertension, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland
[c]Department of Nephrology and Hypertension, Bern University Hospital, Bern, Switzerland
[d]Faculty of Biology and Medicine, Lausanne University, Lausanne, Switzerland
[e]DAMIAN Pharma AG, Walchwil, Switzerland

Summary

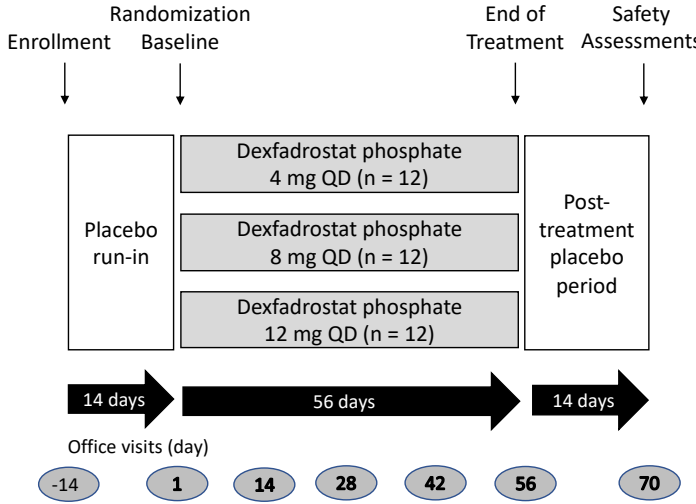
Background Primary aldosteronism (PA) is caused by autonomous aldosterone overproduction and characterised by uncontrolled hypertension. There are currently no treatments that target aldosterone synthesis. We evaluated the safety and efficacy of a novel aldosterone synthase inhibitor, dexfadrostat phosphate, in patients with PA.

Methods This multi-centre, randomised, phase 2 trial was conducted between November 2019 and May 2022 (NCT04007406; EudraCT code 2019-000919-85). Adults with PA and an office systolic blood pressure of 145–190 mmHg were included. After a 2-week single-blind placebo run-in period, participants were randomised 1:1:1 to receive oral dexfadrostat phosphate 4, 8, or 12 mg once daily for an 8-week double-blind treatment period, followed by a 2-week single-blind placebo withdrawal period. Randomisation was conducted centrally and stratified by centre and sex. At the beginning and end of the treatment period, 24 h ambulatory systolic blood pressure (aSBP) was recorded. Blood samples were taken every 2 weeks. Primary endpoints were the change in aldosterone-to-renin ratio (ARR) and mean 24 h aSBP from baseline to the end of the treatment period in the combined dose group of all participants receiving any dose of dexfadrostat phosphate. Safety endpoints were the occurrence of treatment-emergent adverse events (TEAEs) and serious adverse events over the entire study in all randomised participants who received at least one dose of dexfadrostat phosphate.

Findings In total, 35 participants received dexfadrostat phosphate and all participants completed the study. Twenty-six participants (74.3%) were male, the mean age was 51.9 years (SD 8.7), and most were White (n = 32, 91.4%). The median ARR and the mean 24 h aSBP significantly decreased from the beginning to the end of the treatment period in the combined dose group (ARR: 15.3 vs 0.6, least-squares mean [LSM] change in log-normal values −2.5, p < 0.0001; aSBP: 142.6 vs 131.9 mmHg, LSM change −10.7 mmHg, p < 0.0001). There were no safety concerns; all TEAEs were mild or moderate and there were no serious TEAEs.

Interpretation Dexfadrostat phosphate corrected the ARR and aSBP and was well tolerated in patients with PA, demonstrating the benefit of pharmacologically targeting the source of hyperaldosteronism.

eClinicalMedicine
2024;71: 102576
Published Online xxx
https://doi.org/10.1016/j.eclinm.2024.102576



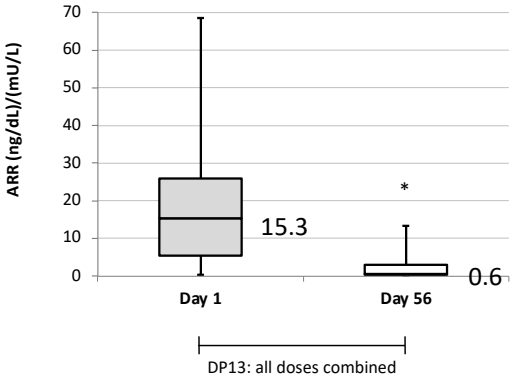
PA diagnosis
1. ARR
2. Suppression Test
3. < 1 year of enrolment
4. No interfering medications
5. No hyperkalemia

Clinical management
1. oSBP > 145 mmHg < 190 mmHg
2. Hypertension control therapy
3. eGFR ≥ 45
4. Contraception

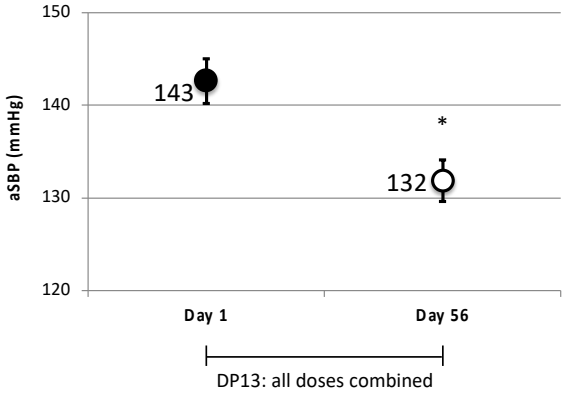
Primary Objectives (Hierarchical)
1. Change in ARR
2. Change in 24-hour ambulatory SBP

Secondary & Exploratory Objectives
1. Safety & Tolerability
2. Change in office SBP
3. Change in 24-hour aSBP by dose
4. Change in oSBP by dose
5. Change in potassium by dose
6. Change in urinary THA by dose

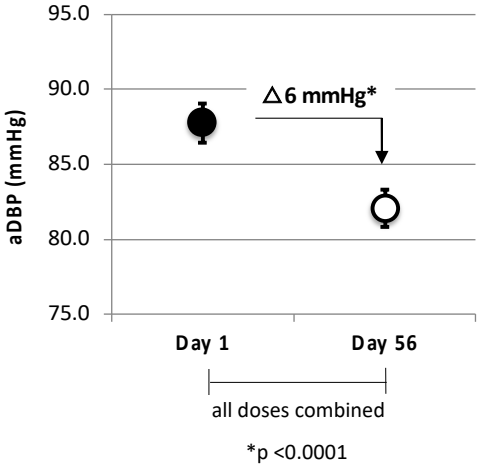
Dexfadrostat DP13C201: Primary Endpoints ARR and aSBP



*** Change: 92% reduction**
Significance: p < 0.0001



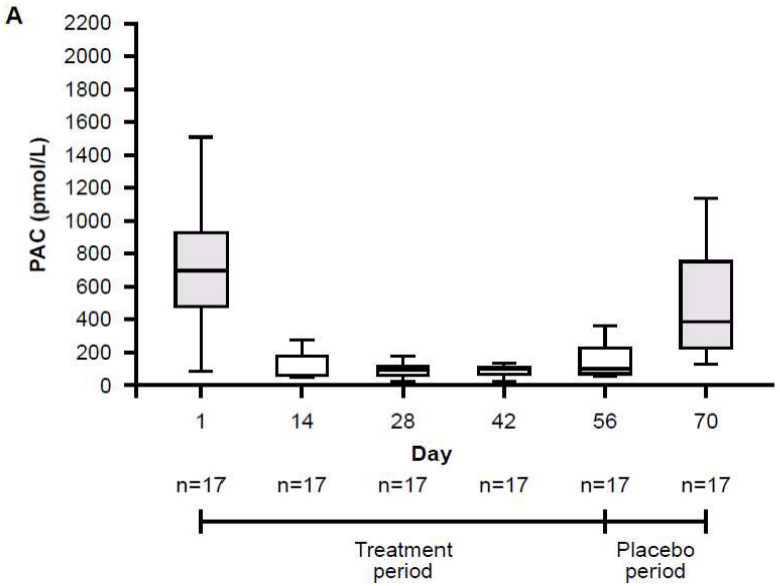
*** Change: 11 mmHg reduction**
Significance: p < 0.0001



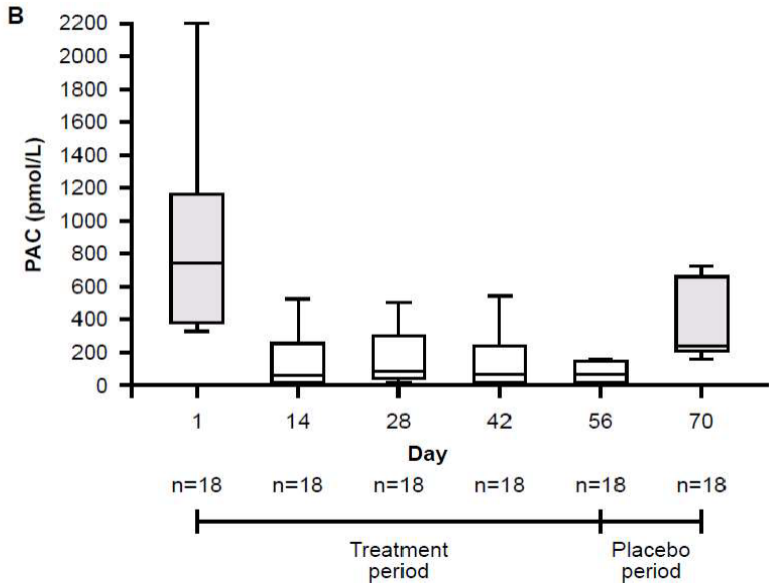
*p <0.0001

Mulatero P. et al. eClinicalMedicine 2024

Change in PAC in patients with unilateral or bilateral and undetermined disease



Patients with APA



Patients with BiPA or Und

Mulatero P. et al. eClinicalMedicine 2024

Adrenal surgery for bilateral Primary Aldosteronism

	Unilateral surgery (n=43)	Bilateral surgery (n=13)	Total (n=56)	95% CI	p value
Outcomes at 6–12 months of follow-up					
Clinical					
Complete	7/37 (19%)	6/13 (46%)	13/50 (26%)	0·32–16·23	0·197
Partial	23/37 (62%)	6/13 (46%)	29/50 (58%)	..	..
Absent	7/37 (19%)	1/13 (8%)	8/50 (16%)	..	..
Biochemical					
Complete	24/37 (65%)	11/13 (85%)	35/50 (70%)	0·29–9·27	0·264
Partial	10/37 (27%)	1/13 (8%)	11/50 (22%)	..	..
Absent	3/37 (8%)	1/13 (8%)	4/50 (8%)	..	..
Outcomes at >12 months of follow-up					
Clinical					
Complete	5/28 (18%)	5/12 (42%)	10/40 (25%)	0·27–14·55	0·217
Partial	17/28 (61%)	4/12 (33%)	21/40 (53%)	..	..
Absent	6/28 (21%)	3/12 (25%)	9/40 (23%)	..	..
Biochemical					
Complete	13/27 (48%)	10/12 (83%)	23/39 (59%)	1·91–12·99	0·098
Partial	7/27 (26%)	2/12 (17%)	9/39 (23%)	..	..
Absent	7/27 (26%)	0	7/39 (18%)	..	..

Data are n/N (%). A subset of 34 (68%) of 50 patients with follow-up at 6–12 months also had a follow-up evaluation at more than 12 months. All analyses were performed using a 10 000 bootstrapping algorithm, with stratification for recruitment centre. The 95% CI for χ^2 and p values are reported for each comparison. The algorithm used to generate statistics and bootstrapping analyses is available online.

***Table*: Clinical and biochemical outcomes of patients with bilateral primary aldosteronism treated with adrenal surgery**

CLINICAL BENEFIT at 6-12 months follow-up

- 81% following unilateral surgery
- 92% following bilateral surgery

Despite the persistence of aldosteronism, patients with **absent biochemical success** showed a marked reduction in systolic and diastolic blood pressure, and in antihypertensive medication dosage.

Williams TA, Lancet Diabetes Endocrinology 2022

Endoscopic, ultrasound-guided, radiofrequency ablation of aldosterone-producing adenomas (FABULAS): a UK, multicentre, prospective, proof-of-concept trial

Lancet 2025

Giulia Argentesi, Xilin Wu*, Alexander Ney, Emily Goodchild, Kate Laycock, Yun-Ni Lee, Russell Senanayake, James MacFarlane, Elisabeth Ng, Jessica Kearney, Sam O'Toole, Jackie Salsbury, Nick Carroll, Daniel Gillett, John A Tadross, Alison Marker, Edmund M Godfrey, George Goodchild, Jonathan P Bestwick, Mark Gurnell, Heok Cheow, Stephen P Pereira*, William M Drake*, Morris J Brown*, on behalf of the FABULAS study group†*

	Number of events
Radiological	
Perforation	0
Haemorrhage	0
Infarction of major organs	0
Biochemical or haematological	
Rise in amylase	1
Fall in haemoglobin	0

Pre-specified major hazards are grouped into radiological findings on the abdomen CT performed at 24 h or 48 h post-ablation and abnormalities on blood tests performed for safety at 24 h post-ablation. The only pre-specified adverse event was a rise in amlyase in one individual, from 87 IU/L at baseline to 195 IU/L at 24 h. Study-related SAEs and given SAEs not related to the study are shown in the appendix (p 16). IU=international unit. SAE=serious adverse event.

Table 2: **Primary outcomes of safety data for pre-specified major hazards**

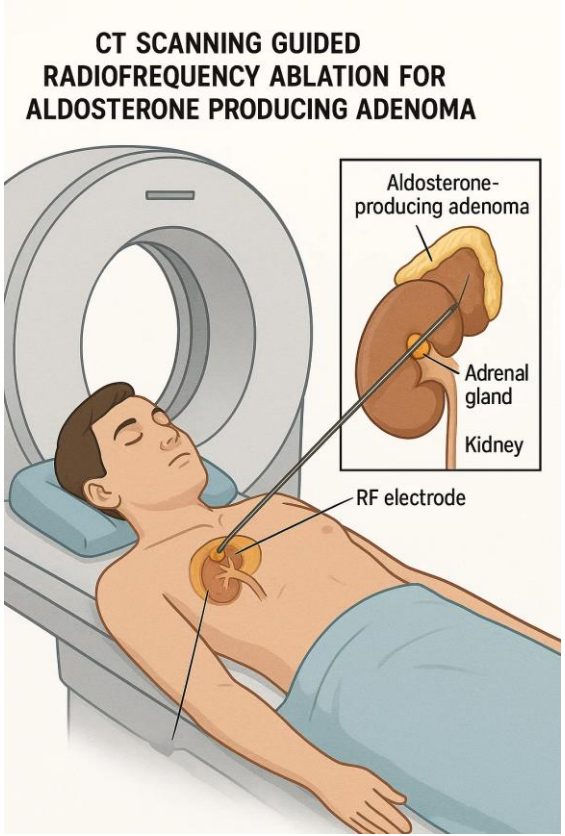
28 participants with **left-sided APAs**

Supplementary Table S5. PASO Outcomes

	Clinical			Biochemical		
	Complete	Partial	Absent	Complete	Partial	Absent
Post 1st ablation	4 (14.2%)	4 (14.2%)	20 (71.6%)	14 (50.0%)	3 (10.7%)	11 (39.3%)
Post 1st / 2nd ablation*	4 (14.2%)	8 (28.6)	16 (57.2%)	16**(57.2%)	5 (17.8%)	7 (25%)

Table showing PASO outcomes at six months' post-ablation. *Seven participants underwent two ablations. In these seven participants PASO outcomes were assessed at three months' post-ablation due to time constraints. **Please see Supplementary Table S3 for details of medications at the time of assessment.

- 57.2% complete biochemical success
- 25% absent biochemical success
- 25% had to repeat the procedure



Recruiting

Randomised Trial Comparing Thermal Ablation With Adrenalectomy in the Treatment of Unilateral Asymmetric PA (WAVE)

ClinicalTrials.gov ID NCT05405101

Sponsor Queen Mary University of London

Information provided by Queen Mary University of London (Responsible Party)

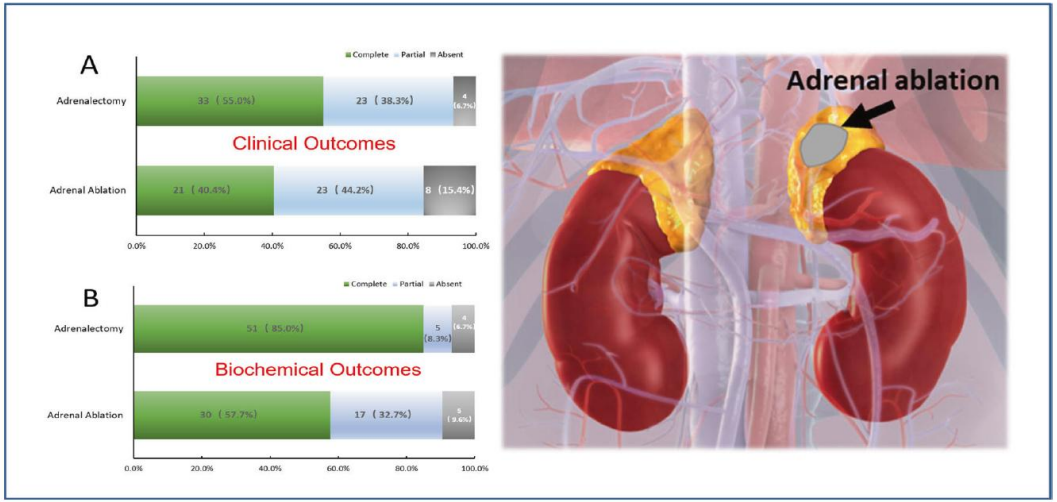
Last Update Posted 2025-02-26

Study of efficacy of thermal ablation vs adrenalectomy is currently recruiting.

In the WAVE study, surgery is being compared to thermal ablation of left-sided and right-sided APAs by internal (endoscopic) and external (percutaneous) routes, respectively, and **follow-up extends to 2 years** after each intervention.

Super-selective adrenal arterial embolization

- Attempted in both UPA and BiPA
- No difference in overall clinical success was observed between the embolization and adrenalectomy groups
- **Complete biochemical success was more frequent in the adrenalectomy group**



Sun F, Hypertension Research 2023

UNIVERSITÀ DI TORINO

Hypertension Excellence Centre of the European Society of Hypertension

Medicina Interna 4 1988-2023

Medicina Interna 3 2024-2025