The Burden, Outcomes, and Management of Patients with Aldosterone Dysregulation: A Targeted Literature Review

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Table S1: Key research questions for the TLR (parts 1 and 2)

Part 1	**Research question:** What factors describe the disease which manifests as "aldosterone dysregulation" and who are the patients who have this disease? **Objective (s):** Gain a comprehensive understanding of disease prevalence, disease burden, and current knowledge on the process through which aldosterone levels influence disease including pathophysiology and mechanisms of action. **Topics to be covered (*not specific search terms)*:** • Epidemiology • Clinical (including mortality), economic, and humanistic (e.g., health-related quality of life) burden across spectrum of disease • Disease state definition and endpoints important to capture impact of disease • Different phenotypes of patients and/or factors used to describe patients • Factors supporting a need to treat (e.g., impact of treating blood pressure but not underlying aldosterone dysregulation) • Biomarkers that are important to define the disease and/or identify specific patients • Continuum of aldosterone dysregulation across the spectrum/stages of hypertension − how patients align with hypertension spectrum (by phenotype) • Role of aldosterone as the first manifestation of disease which leads to cardiovascular/cardiorenal outcomes (i.e., in patients where hypertension has not yet been diagnosed) • How do aldosterone levels influence disease pathway? • What are the relevant clinical outcomes for these patients (i.e., not only cardiovascular disease but also cardiorenal disease and outcomes as well as comorbidities)?

Part 2	**Research question:** What is the clinical management pathway for patients with this disease and how do different factors influence that clinical journey? **Objective (s):** Gain a comprehensive understanding of treatment patterns Develop deep understanding of the role of aldosterone on influencing clinical outcomes **Topics to be covered (*not specific search terms)*:** • Expectations of treatment outcomes for existing treatments (overall and by phenotype/biomarker) • How do outcomes/risk get impacted by other interventions (e.g., how does blood pressure control link to outcomes in these patients)? • Understanding the mineralocorticoid receptor antagonist (drug) treatment journey • Use of non-drug interventions (e.g., salt intake, dietary management, renal denervation) • Patient journey through detection (including delay in treatment) testing, treatment initiation, interventions, events, outcomes (per phenotype) • Adherence to therapy/interventions • How does aldosterone dysregulation influence treatment pathway and outcomes (compared with non-aldosterone dysregulation)? • Equity issues regarding patient access to treatments

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Table S2: TLR Part 1 search strategy: Embase

	Query (search cut-off date: February 16, 2024)	
1	'aldosterone dysregulation':ti,ab OR 'hyperaldosteronism'/exp OR 'hyperaldosteronism' OR hyperaldosteronism:ti,ab OR 'hyper aldosteronism':ti,ab OR raas:ti,ab OR 'renin angiotensin*':ti,ab	62,791
2	aldosterone:ti,ab AND (dysregulation:ti,ab OR dysregulated:ti,ab OR regulation:ti,ab OR regulated:ti,ab OR low:ti,ab OR lower*:ti,ab OR decrease*:ti,ab OR deficien*:ti,ab OR insufficient:ti,ab OR underproduced:ti,ab OR underproduction:ti,ab OR excess:ti,ab OR high*:ti,ab OR increase*:ti,ab OR elevated:ti,ab OR overproduced:ti,ab OR overproduction:ti,ab OR 'plasma renin activity':ti,ab OR mediat*:ti,ab OR concentration*:ti,ab OR level*:ti,ab)	43,820
3	#1 OR #2	87,989
4	'epidemiology' OR 'epidemiology'/exp OR 'epidemiology':ti,ab OR 'incidence':ti,ab OR 'prevalence':ti,ab OR 'risk-factor':ti,ab OR 'risk-factors':ti,ab OR 'natural history':ti,ab OR 'demograph':ti,ab OR 'outcome':ti,ab OR 'prognosis':ti,ab OR 'risk':ti,ab OR 'predict':ti,ab OR 'prediction':ti,ab OR 'mechanism':ti,ab OR 'pathology':ti,ab OR 'physiology':ti,ab OR 'pathophysiology':ti,ab OR 'quality of life':ti,ab OR 'hrqol':ti,ab OR 'burden of illness':ti,ab OR 'burden of disease':ti,ab	13,202,767
5	'chronic kidney failure'/exp OR 'heart infarction'/exp OR 'cardiovascular disease' OR 'chronic kidney disease':ti,ab OR 'chronic renal disease':ti,ab OR 'nephropathy':ti,ab OR 'cardiovascular disease':ti,ab OR 'cvd':ti,ab OR 'congestive heart failure':ti,ab OR 'ami':ti,ab OR 'left ventricular hypertrophy':ti,ab OR 'ejection fraction':ti,ab OR 'cardiorenal':ti,ab OR 'cardio-renal':ti,ab OR 'hypertension'/exp OR 'hypertension':ti,ab OR 'metabolic syndrome':ti,ab OR atherosclerosis:ti,ab OR stroke:ti,ab OR 'cardiometabolic dis*':ti,ab OR adiposity*:ti,ab OR obesity*:ti,ab	3,190,648
6	#3 AND #4	59,972
7	#3 AND #5	48,791
8	#6 OR #7	35,158

9	'in vitro study'/exp OR 'case report' OR 'case study' OR editorial OR 'in vitro' OR 'editorial'/de OR 'letter'/de OR 'case report'/de	12,559,903
10	[conference abstract]/lim	5,047,676
11	#9 OR #10	16,129,643
13	**#8 NOT #11 AND [english]/lim AND [2013-2024]/py**	**12,269**

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Table S3: TLR Part 1 search strategy: MEDLINE

	Query (search cut-off date: February 16, 2024)	**Hits**
1	"aldosterone dysregulation"[Title/Abstract] OR hyperaldosteronism[Mesh] OR hyperaldosteronism[Title/Abstract] OR hyper-aldosteronism[Title/Abstract] OR RAAS[Title/Abstract] OR renin-angiotensin*[Title/Abstract]	45,284
2	aldosterone[Title/Abstract] AND (dysregulation[Title/Abstract] OR dysregulated[Title/Abstract] OR regulation[Title/Abstract] OR regulated[Title/Abstract] OR low[Title/Abstract] OR lower*[Title/Abstract] OR decrease*[Title/Abstract] OR deficien*[Title/Abstract] OR insufficient[Title/Abstract] OR underproduced[Title/Abstract] OR underproduction[Title/Abstract] OR excess[Title/Abstract] OR high*[Title/Abstract] OR increase*[Title/Abstract] OR elevated[Title/Abstract] OR overproduced[Title/Abstract] OR overproduction[Title/Abstract] OR "plasma renin activity"[Title/Abstract] OR "plasma renin activity"[Title/Abstract] OR mediat*[Title/Abstract] OR concentration*[Title/Abstract] OR level*[Title/Abstract])	32,335
3	#1 OR #2	64,520
4	"Epidemiology"[All Fields] OR "Epidemiology"[MeSH Terms] OR "Epidemiology"[Title/Abstract] OR "Incidence"[Title/Abstract] OR "Prevalence"[Title/Abstract] OR "risk-factor"[Title/Abstract] OR "risk-factors"[Title/Abstract] OR "natural history"[Title/Abstract] OR "demograph"[Title/Abstract] OR "outcome"[Title/Abstract] OR "prognosis"[Title/Abstract] OR "risk"[Title/Abstract] OR "predict"[Title/Abstract] OR "prediction"[Title/Abstract] OR "mechanism"[Title/Abstract] OR "pathology"[Title/Abstract] OR "physiology"[Title/Abstract] OR "pathophysiology"[Title/Abstract] OR "quality of life"[Title/Abstract] OR "HRQoL"[Title/Abstract] OR "burden of illness"[Title/Abstract] OR "burden of disease"[Title/Abstract]	9,073,693
5	"renal insufficiency, chronic"[MeSH Terms] OR "kidney failure, chronic"[MeSH Terms] OR "myocardial infarction"[MeSH Terms] OR "cardiovascular diseases"[MeSH Terms] OR "Chronic kidney disease"[Title/Abstract] OR "Chronic renal disease"[Title/Abstract] OR	3,614,033

	"nephropathy"[Title/Abstract] OR "Cardiovascular disease"[Title/Abstract] OR "CVD"[Title/Abstract] OR "Congestive heart failure"[Title/Abstract] OR "AMI"[Title/Abstract] OR "Left ventricular hypertrophy"[Title/Abstract] OR "ejection fraction"[Title/Abstract] OR "cardiorenal"[Title/Abstract] OR "cardio-renal"[Title/Abstract] OR "hypertension"[MeSH Terms] OR "hypertension"[Title/Abstract] OR "metabolic syndrome"[Title/Abstract] OR Atherosclerosis[Title/Abstract] OR Stroke[Title/Abstract] OR "cardiometabolic dis*"[Title/Abstract] OR adiposity*[Title/Abstract] OR obesity*[Title/Abstract]	
6	#3 AND #4	22,374
7	#3 AND #5	36,290
8	#6 OR #7	42,698
9	**#8 Filters: from 2013 – 2024, humans, English**	**11,330**

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Table S4: TLR Part 2 search strategy: Embase

	Query (search cut-off date: February 5, 2024)	**Hits**
1	'aldosterone dysregulation':ti,ab OR 'hyperaldosteronism'/exp OR hyperaldosteronism:ti,ab OR 'hyper aldosteronism':ti,ab OR raas:ti,ab OR 'renin angiotensin*':ti,ab	62,585
2	aldosterone:ti,ab AND (dysregulation:ti,ab OR dysregulated:ti,ab OR regulation:ti,ab)	5553
3	#1 OR #2	65,928
4	'treatment-resistant hypertension':ti,ab OR 'drug-resistant hypertension':ti,ab OR 'drug-refractory hypertension':ti,ab OR 'therapy-resistant hypertension':ti,ab OR 'therapy-refractory hypertension':ti,ab OR 'resistant hypertension':ti,ab OR 'refractory hypertension':ti,ab OR 'uncontrolled hypertension':ti,ab	13,592
5	#3 OR #4	78,137
6	'electrocortin':ti,ab OR 'reichstein':ti,ab OR 'ace inhibitor':ti,ab OR 'angiotensin-converting enzyme':ti,ab OR 'pril':ti,ab OR 'angiotensin receptor blocker':ti,ab OR 'sartan':ti,ab OR 'calcium channel blocker':ti,ab OR 'amlodipine':ti,ab OR 'diuretic*':ti,ab OR 'mineralocorticoid receptor antagonist*':ti,ab OR 'spironolactone':ti,ab OR 'eplerenone':ti,ab OR 'aldosterone synthase inhibitors':ti,ab OR 'osilodrostat':ti,ab OR 'baxdrostat':ti,ab OR 'endothelin receptor antagonists':ti,ab OR 'aprocitentan':ti,ab OR 'aminopeptidase a inhibitor':ti,ab OR 'apa inhibitor':ti,ab	158,591
7	'treatment pattern*':ti,ab OR 'treatment option*':ti,ab OR 'treatment trend*':ti,ab OR 'prescribing practice*':ti,ab OR 'prescription practice':ti,ab OR 'treatment strateg*':ti,ab OR 'treatment switch*':ti,ab OR 'time on treatment':ti,ab OR 'discontinuation':ti,ab OR 'time to discontinuation':ti,ab OR 'line of treatment':ti,ab OR 'standard of care':ti,ab OR 'standard therapy':ti,ab OR 'recent advances':ti,ab OR 'recent advancement':ti,ab OR 'position statement' OR 'policy statement':ti,ab OR 'best practice':ti,ab OR 'novel treatment':ti,ab OR 'real world treatment':ti,ab OR 'guideline adherence':ti,ab OR 'treatment adherence':ti,ab	823,305

8	‘treatment':ti,ab AND ('guideline':ti,ab OR 'guidelines':ti,ab OR 'recommendations':ti,ab OR 'consensus':ti,ab OR 'pathway':ti,ab OR 'landscape':ti,ab)	742,515
9	#7 OR #8	1,478,880
10	'efficacy':ti,ab OR 'effectiveness':ti,ab OR 'response':ti,ab OR 'recovery':ti,ab OR 'improve' OR 'improved' OR 'improvement' OR 'improvements' OR 'improves' OR 'improving' OR 'improvment' OR 'efficiency':ti,ab OR 'mortality':ti,ab OR 'survival':ti,ab OR 'outcome':ti,ab OR 'safety':ti,ab OR 'toxicity':ti,ab	12,990,042
11	'adverse':ti,ab AND ('events':ti,ab OR 'effects':ti,ab OR 'reaction':ti,ab)	790,274
12	#10 OR #11	13,195,203
13	#5 AND #6 AND #9	9765
14	#5 AND #12	6177
15	#13 OR #14	14,457
16	'in vitro study'/exp OR 'case report' OR 'case study' OR editorial OR 'in vitro' OR 'editorial'/de OR 'letter'/de OR 'case report'/de	12,544,684
17	[conference abstract]/lim	5,031,890
18	#16 OR #17	17,576,574
19	**#15 NOT #18 AND [english]/lim AND [2013-2024]/py**	**3936**

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Table S5: TLR Part 2 search strategy: MEDLINE

	Query (search cut-off date: February 5, 2024)	**Hits**
1	"aldosterone dysregulation"[Title/Abstract] OR aldosterone[Title/Abstract] AND (dysregulation[Title/Abstract] OR dysregulated[Title/Abstract] OR regulation[Title/Abstract]) OR hyperaldosteronism[Mesh] OR hyperaldosteronism[Title/Abstract] OR hyper-aldosteronism[Title/Abstract] OR RAAS[Title/Abstract] OR renin-angiotensin*[Title/Abstract]	28,132
2	aldosterone[Title/Abstract] AND (dysregulation[Title/Abstract] OR dysregulated[Title/Abstract] OR regulation[Title/Abstract])	4330
3	"treatment-resistant hypertension"[Title/Abstract] OR "treatment-resistant hypertension"[Title/Abstract] OR "drug-resistant hypertension"[Title/Abstract] OR "drug-resistant hypertension"[Title/Abstract] OR "drug-refractory hypertension"[Title/Abstract] OR "drug-refractory hypertension"[Title/Abstract] OR "therapy-resistant hypertension"[Title/Abstract] OR "therapy-resistant hypertension"[Title/Abstract] OR "therapy-refractory hypertension"[Title/Abstract] OR "therapy-refractory hypertension"[Title/Abstract] OR "resistant hypertension"[Title/Abstract] OR "refractory hypertension"[Title/Abstract] OR "uncontrolled hypertension"[Title/Abstract]	5791
4	#1 OR #2 OR #3	38,253
5	"Electrocortin"[Title/Abstract] OR "Reichstein"[Title/Abstract] OR "ACE inhibitor"[Title/Abstract] OR "angiotensin-converting enzyme"[Title/Abstract] OR "pril"[Title/Abstract] OR "angiotensin receptor blocker"[Title/Abstract] OR "sartan"[Title/Abstract] OR "calcium channel blocker"[Title/Abstract] OR "amlodipine"[Title/Abstract] OR "diuretic*"[Title/Abstract] OR "mineralocorticoid receptor antagonist*"[Title/Abstract] OR "spironolactone"[Title/Abstract] OR "eplerenone"[Title/Abstract] OR "aldosterone synthase inhibitors"[Title/Abstract] OR "osilodrostat"[Title/Abstract] OR "baxdrostat"[Title/Abstract] OR "endothelin receptor antagonists"[Title/Abstract] OR "aprocitentan"[Title/Abstract] OR "aminopeptidase A inhibitor"[Title/Abstract] OR "APA inhibitor"[Title/Abstract]	66,161

6	"treatment pattern*"[Title/Abstract] OR "treatment option*"[Title/Abstract] OR "treatment trend*"[Title/Abstract] OR "prescribing practice*"[Title/Abstract] OR "prescription practice"[Title/Abstract] OR "treatment strateg*"[Title/Abstract] OR "treatment switch*"[Title/Abstract] OR "time on treatment"[Title/Abstract] OR "discontinuation"[Title/Abstract] OR "time to discontinuation"[Title/Abstract] OR "line of treatment"[Title/Abstract] OR "standard of care"[Title/Abstract] OR "standard therapy"[Title/Abstract] OR "recent advances"[Title/Abstract] OR "recent advancement"[Title/Abstract] OR "position statement"[All Fields] OR "policy statement"[Title/Abstract] OR "best practice"[Title/Abstract] OR "novel treatment"[Title/Abstract] OR "real world treatment"[Title/Abstract] OR "guideline adherence"[Title/Abstract] OR "treatment adherence"[Title/Abstract]	640,623
7	"Treatment"[Title/Abstract] AND ("guideline"[Title/Abstract] OR "guidelines"[Title/Abstract] OR "recommendations"[Title/Abstract] OR "consensus"[Title/Abstract] OR "pathway"[Title/Abstract] OR "landscape"[Title/Abstract])	311,025
8	#6 OR #7	951,648
9	"Efficacy"[Title/Abstract] OR "efficiency"[Title/Abstract] OR "effectiveness"[Title/Abstract] OR "response"[Title/Abstract] OR "recovery"[Title/Abstract] OR "improve"[All Fields] OR "improved"[All Fields] OR "improvement"[All Fields] OR "improvements"[All Fields] OR "improves"[All Fields] OR "improving"[All Fields] OR "improvment"[All Fields] OR "efficiency"[Title/Abstract] OR "mortality"[Title/Abstract] OR "survival"[Title/Abstract] OR "outcome"[Title/Abstract] OR "safety"[Title/Abstract] OR "toxicity"[Title/Abstract]	5,673,261
10	"adverse"[Title/Abstract] AND ("events"[Title/Abstract] OR "effects"[Title/Abstract] OR "reaction"[Title/Abstract])	372,394
11	#9 OR #10	6,045,655
12	#4 AND #8	2682
13	#4 AND #5 AND #11	4762
14	**#12 OR #13 Filters: from 2013 – 2024; humans, English (applied from #1 onwards)**	**3678**

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Table S6: Thresholds/ measures used to characterize patients with aldosterone dysregulation

Aldosteronism terms	**Threshold**	
	Aldosterone (PAC [ng/dL])	**Renin (PRA [ng/dL/hr][a], PRC [ng/dL])**
Primary aldosteronism [1]	20 ng/dL	40 ng/dL
Primary aldosteronism [2]	>15 ng/dL	<100 ng/dL/hr
Primary aldosteronism [3]	≥15 ng/dL	≤1 ng/dL
Primary aldosteronism [4]	≥15 ng/dL	–
Primary aldosteronism (fludrocortisone suppression) [4]	>6 ng/dL	<100 ng/dL/hr
Primary aldosteronism (captopril challenge) [4]	>11 ng/dL	–
Primary aldosteronism (oral sodium loading) [4]	>12,000 ng/day	–
Primary aldosteronism (saline infusion) [4]	>6 ng/dL; >10 ng/dL (recumbent)	–
Primary aldosteronism (fludrocortisone suppression) [5]	≥6 ng/dL	–
Primary aldosteronism (captopril challenge) [5]	≥11 ng/dL	–
Primary aldosteronism (saline infusion) [5]	≥8 ng/dL	–
Primary aldosteronism [6]	≥15 ng/dL; ≥10 ng/dL (after SIT)	–
Primary aldosteronism [7]	≥15 ng/dL	–
Primary aldosteronism [8]	≥9–16 ng/dL	–
Primary aldosteronism [9]	>42.7 ng/dL	–
Primary aldosteronism [10]	≥21.8 ng/dL	–
Primary aldosteronism [11]	≥21.8 ng/dL	–
Primary aldosteronism [12]	>15 ng/dL	–

Primary aldosteronism [13]	>12,000 ng/24 hr	–
Primary aldosteronism [14]	≥15 ng/dL	–
Primary aldosteronism [15]	≥12 ng/dL	–
Suspicious primary aldosteronism [16]	≥12 ng/dL	–
Primary hyperaldosteronism [17]	>10 ng/dL	–
Aldosterone terms/phenotypes[b]	**Threshold[a]**	
Low aldosterone [18]	<120 ng/dL/24 hr[c]	
High aldosterone [18]	>120 ng/dL/24 hr[c]	
Elevated aldosterone [19]	>30 ng/dL[d]	
Above upper limit of normal [20]	>47 ng/dL	
Above upper limit of normal [21]	>23.2 ng/dL	
Primary aldosteronism [22]	30 ng/dL	
Overt hyperaldosteronism [23]	≥12,000 ng[e]	
Hyperaldosteronism [24]	>15,000 ng[e]	
Renin terms/phenotypes[b]	**Threshold (ng/mL/hr)[a]**	
Suppressed renin level [25]	≤0.50[c]	
Suppressed renin level [26]	≤0.50[c]	
Very low or suppressed renin levels [2, 4]	<1.00[f]	
Indeterminate renin level [25]	0.51–0.99[c]	
Unsuppressed renin level [25]	≥1.00[c]	
Unsuppressed renin level [26]	>0.50[c]	
Aldosterone + renin terms/phenotypes[b]	**Threshold[a]**	
	Aldosterone	**Renin**
Pseudoaldosteronism [10]	<7.77 ng/dL[g]	<100 fmol/l/s
Renin-independent aldosteronism [27]	≥10 ng/dL	≤70.5 ng/dL[h]
Renin-dependent aldosteronism [27]	≥10 ng/dL	>70.5 ng/dL[f]

Indications	Aldosterone thresholds associated with positive diagnosis per indication
Hypertensive patients [27]	≥10 ng/dL
Patients hospitalized for acute heart failure [21]	≥23.2 ng/dL
Non-alcoholic fatty liver disease [28]	≥13 ng/dL
Preserved ejection fraction [29]	0.5−107.2 ng/dL
Increase cardiovascular disease risk [16]	≥12.5 ng/dL
Higher risk of aortic dissection and aneurysm [30]	>13.9 ng/dL

[a]Certain values were measured as a rate and could not be converted to a concentration

[b]Related terms/phenotypes have been grouped and then ordered by year of publication

[c]Units converted from μg/L to ng/dL or ng/mL

[d]Units converted from pg/mL to ng/dL

[e]Units converted from μg to ng

[f]Units converted from ng/mL to ng/dL or ng/mL

[g]Units converted from pmol/L to ng/dL

[h]Units converted from mIU/L to ng/dL

PAC, plasma aldosterone concentration; PRA, plasma renin activity; PRC, plasma renin concentration; SIT, Saline Infusion Test

Table S7: Conversion factors for patients with aldosterone dysregulation

Aldosterone or renin	**Conversions**	
	US (United States) Units	**SI (Standard International) Units**
Serum or plasma aldosterone concentration [31]	1 ng/dL	27.7 pmol/L
Serum or plasma aldosterone concentration [31]	0.036 ng/dL	1 pmol/L
Plasma renin activity [31]	1 ng/mL/h	12.8 pmol/L/min
Plasma renin activity [31]	0.08 ng/ml/h	1 pmol/l/min
Plasma renin concentration to plasma renin activity [32]	0.122 ng/mL per hour	1 mU/L
Plasma renin activity to plasma renin concentration [32]	1 ng/mL per hour	8.2 mU/L

Please note that a serum aldosterone concentration value is roughly equivalent to 50% of a plasma aldosterone concentration value (Median difference of 50% was reported in published literature) [33].

References

1. Maiolino G, Rossitto G, Bisogni V, et al. Quantitative value of aldosterone-renin ratio for detection of aldosterone-producing adenoma: The Aldosterone-Renin Ratio for Primary Aldosteronism (AQUARR) Study. J Am Heart Assoc. 2017; 6.
2. Suntornlohanakul O, Sakarin S, Kietsiriroje N, Sriplung H. Geographical inequality in service utilization for primary aldosteronism screening: spatial epidemiological study in Southern Thailand. BMC Health Serv Res. 2022; 22:458.
3. Yuan YE, Haas AV, Williams GH, Taylor H, Seely EW, Adler GK. Association between life's simple 7 and biomarkers of cardiovascular disease: Aldosterone, interleukin-6, c-reactive protein. J Am Heart Assoc. 2023; 12:e028718.
4. Ha J, Park JH, Kim KJ, et al. 2023 Korean Endocrine Society consensus guidelines for the diagnosis and management of primary aldosteronism. Endocrinol Metab (Seoul). 2023; 38:597-618.
5. He C, Li R, Yang J, et al. Optimizing the aldosterone-to-renin ratio cut-off for screening primary aldosteronism based on cardiovascular risk: a collaborative study. Clin Exp Hypertens. 2024; 46:2301571.
6. Bioletto F, Lopez C, Bollati M, et al. Predictive performance of aldosterone-to-renin ratio in the diagnosis of primary aldosteronism in patients with resistant hypertension. Front Endocrinol (Lausanne). 2023; 14:1145186.
7. Rizer ND, X; Cohen, DL; Herman, DS. Effect of hypokalemia on screening for primary aldosteronism. medRxiv. 2022; 06.16.22276370.
8. Hung A, Ahmed S, Gupta A, et al. Performance of the aldosterone to renin ratio as a screening test for primary aldosteronism. J Clin Endocrinol Metab. 2021; 106:2423-35.
9. Kokko E, Nevalainen PI, Choudhary MK, et al. Aldosterone-to-renin ratio is related to arterial stiffness when the screening criteria of primary aldosteronism are not met. Sci Rep. 2020; 10:19804.
10. Van Der Sande NGC, Blankestijn PJ, Visseren FLJ, et al. Prevalence of potential modifiable factors of hypertension in patients with difficult-to-control hypertension. J Hypertens. 2019; 37:398-405.
11. Vorselaars W, Valk GD, Vriens MR, Westerink J, Spiering W. Case detection in primary aldosteronism: high-diagnostic value of the aldosterone-to-renin ratio when performed under standardized conditions. J Hypertens. 2018; 36:1585-91.

12. Florczak E, Prejbisz A, Szwench-Pietrasz E, et al. Clinical characteristics of patients with resistant hypertension: The RESIST-POL study. J Hum Hypertens. 2013; 27:678-85.
13. Baudrand R, Guarda FJ, Fardella C, et al. Continuum of Renin-Independent Aldosteronism in Normotension. Hypertension. 2017; 69:950-6.
14. Gkaliagkousi E, Anyfanti P, Triantafyllou A, et al. Aldosterone as a mediator of microvascular and macrovascular damage in a population of normotensive to early-stage hypertensive individuals. J Am Soc Hypertens. 2018; 12:50-7.
15. Lin M, Heizhati M, Gan L, et al. Higher aldosterone is associated with increased renal impairment risk in patients with hypertension and abnormal glucose metabolism: a longitudinal study. J Hypertens. 2022; 40:561-9.
16. Gan L, Li N, Heizhati M, et al. Higher plasma aldosterone is associated with increased risk of cardiovascular events in hypertensive patients with suspected OSA: UROSAH data. Front Endocrinol (Lausanne). 2022; 13:1017177.
17. Imiela AM, Mikołajczyk TP, Siedliński M, et al. Th17/Treg imbalance in patients with primary hyperaldosteronism and resistant hypertension. Pol Arch Intern Med. 2022; 132.
18. Tzamou V, Vyssoulis G, Karpanou E, Kyvelou SM, Gialernios T, Stefanadis C. Aldosterone levels and inflammatory stimulation in essential hypertensive patients. J Hum Hypertens. 2013; 27:535-8.
19. Gregori M, Giammarioli B, Tocci G, et al. Synergic effects of renin and aldosterone on right ventricular function in hypertension: A tissue Doppler study. J Cardiovasc Med (Hagerstown). 2015; 16:831-8.
20. Markou A, Sertedaki A, Kaltsas G, et al. Stress-induced aldosterone hyper-secretion in a substantial subset of patients with essential hypertension. J Clin Endocrinol Metab. 2015; 100:2857-64.
21. Biegus J, Nawrocka-Millward S, Zymliński R, et al. Distinct renin/aldosterone activity profiles correlate with renal function, natriuretic response, decongestive ability and prognosis in acute heart failure. Int J Cardiol. 2021; 345:54-60.
22. Brown JM, Siddiqui M, Calhoun DA, et al. The unrecognized prevalence of primary aldosteronism: A cross-sectional study. Ann Intern Med. 2020; 173:10-20.
23. Siddiqui M, Judd EK, Zhang B, et al. Masked uncontrolled hypertension is accompanied by increased out-of-clinic aldosterone secretion. Hypertension. 2021; 77:435-44.

24. Kim V, Shi J, An J, et al. Hyperaldosteronism screening and findings from a large diverse population with resistant hypertension within an integrated health system. Perm J. 2024; 28:3-13.
25. Brown JM, Robinson-Cohen C, Luque-Fernandez MA, et al. The spectrum of subclinical primary aldosteronism and incident hypertension: A cohort study. Ann Intern Med. 2017; 167:630-41.
26. Inoue K, Goldwater D, Allison M, Seeman T, Kestenbaum BR, Watson KE. Serum aldosterone concentration, blood pressure, and coronary artery calcium: The multi-ethnic study of atherosclerosis. Hypertension. 2020; 76:113-20.
27. Hu J, Shen H, Huo P, et al. Heightened cardiovascular risk in hypertension associated with renin-independent aldosteronism versus renin-dependent aldosteronism: A collaborative study. J Am Heart Assoc. 2021; 10:e023082.
28. Hu J, Cai X, Zhu Q, et al. Relationship between plasma aldosterone concentrations and non-alcoholic fatty liver disease diagnosis in patients with hypertension: A retrospective cohort study. Diabetes Metab Syndr Obes. 2023; 16:1625-36.
29. Ke B, Tan X, Ren L, et al. Aldosterone dysregulation predicts the risk of mortality and rehospitalization in heart failure with a preserved ejection fraction. Sci China Life Sci. 2022; 65:631-42.
30. Zhu Q, Heizhati M, Lin M, et al. Higher plasma aldosterone concentrations are associated with elevated risk of aortic dissection and aneurysm: A case-control study. Hypertension. 2022; 79:736-46.
31. Lin B, Robinson L, Soliman B, Gulizia J, Usala S. Autoimmune Implications in a Patient with Graves' Hyperthyroidism, Pre-eclampsia with Severe Features, and Primary Aldosteronism. Medicina (Kaunas). 2024; 60.
32. Chee MR, Hoo J, Libianto R, et al. Prospective Screening for Primary Aldosteronism in Patients With Suspected Obstructive Sleep Apnea. Hypertension. 2021; 77:2094-103.
33. Glinicki P, Jeske W, Kapuścińska R, Zgliczyński W. Comparison of aldosterone levels and aldosterone /direct renin concentration ratio (ADRR) in serum and in plasma ($EDTA_2K$) in healthy males. 2014; 35:P176.