THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

67 F with Hypertension

Caroline Abe, MD, MPH
Adult Endocrinology Fellow
Date 6/5/25

To earn credit for today's activity text code:

CATGEQ to 773-245-0068

Dr. Abe does not have any relevant financial relationships with any commercial interests.

Objectives

- Discuss primary aldosteronism as cause of secondary hypertension
- Review screening guidelines for primary aldosteronism
- Discuss diagnostic testing for primary aldosteronism
- Review treatment recommendations of primary aldosteronism

HPI

- 67 F with history of hypokalemia referred for progressive hypertension
  - 2016: BP 110/64, no meds
  - 2023: BP 134/79, amlodipine 5 qD
  - 2/2024: BP 130-140/80-90 (home readings), no meds
  - 4/2024: BP 132/74, losartan 25 daily
  - 6/2024: BP 151/84, losartan 25 BID
  - 12/2024: BP 136/80, losartan 25 BID, amlodipine 5 qD
  - 2/2025: BP 130-140/80, losartan 50 BID, amlodipine 5 qD, carvedilol 6.25 mg qD
- K+ is noted to be low since 2015
  - 2017-2023, K 3.6-3.7
  - 12/2023: K 3.1
  - 12/2024: K 2.6
  - Now taking K 20 mEq x4 d/week, 40 mEq x 3 d/week

History and Physical Exam

Medical:

- HTN
- GERD

Surgical:

- Breast implants
- Abdominoplasty
- C-section x2

Family:

- No hx HTN
- Dementia in mother and father

Social:

- Healthy
- Daily exercise
- Vegetarian
- Eats high K foods
- No licorice

Medications:

- Losartan 50 BID
- Amlodipine 5
- Carvedilol 6.25 mg qD
- Potassium supplement

Exam

Vitals
BP 136/69 | Pulse 58 | Temp 36.4 °C
Ht 157.5 cm (5' 2.01") | Wt 54.2 kg
| SpO2 99% | BMI 21.83 kg/m²

Exam
General: NAD
HEENT: PERRL, no thyromegaly
CV: RRR
Pulm: CTAB
Abd: Soft, NT, ND
MSK: No peripheral edema
Neuro: A&O x4

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Endocrine ddx for secondary causes of hypertension?

Endocrine Ddx for HTN

Table 1. Endocrine Causes of Hypertension

Etiology
Adrenal-dependent causes
1. Pheochromocytoma and sympathetic paraganglioma
2. Primary aldosteronism
3. Hyperdeoxycorticosteronism
a. Congenital adrenal hyperplasia
i. 11β-Hydroxylase deficiency
ii. 17α-Hydroxylase deficiency
b. Deoxycorticosterone-producing tumor
c. Primary cortisol resistance
4. Cushing syndrome
Apparent mineralocorticoid excess/11β-hydroxysteroid dehydrogenase deficiency
1. Genetic
2. Acquired
a. Licorice or carbenoxolone ingestion
b. Cushing syndrome
Parathyroid-dependent causes
1. Hyperparathyroidism
Pituitary-dependent causes
1. Acromegaly
2. Cushing syndrome
Secondary hyperaldosteronism
1. Renovascular hypertension
Thyroid-dependent causes
1. Hypothyroidism
2. Hyperthyroidism
Complex effects
1. Obstructive sleep apnea

(Vukusich, 2002)

Labs

- Na 143 / K 3.3 / Cl 104 / Co2 30 / BUN 8 / Cr 0.7 / Ca 9.1
- TSH 2.33 / FT4 0.99
- Aldosterone 26 ng/dL (ULN 21)
- Renin <0.6 ng/dL/h
- Plasma metanephrines:
  - Normetanephrine 0.31 nmol/L
  - Metanephrines < 0.2 nmol/L

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Notable findings?

Labs

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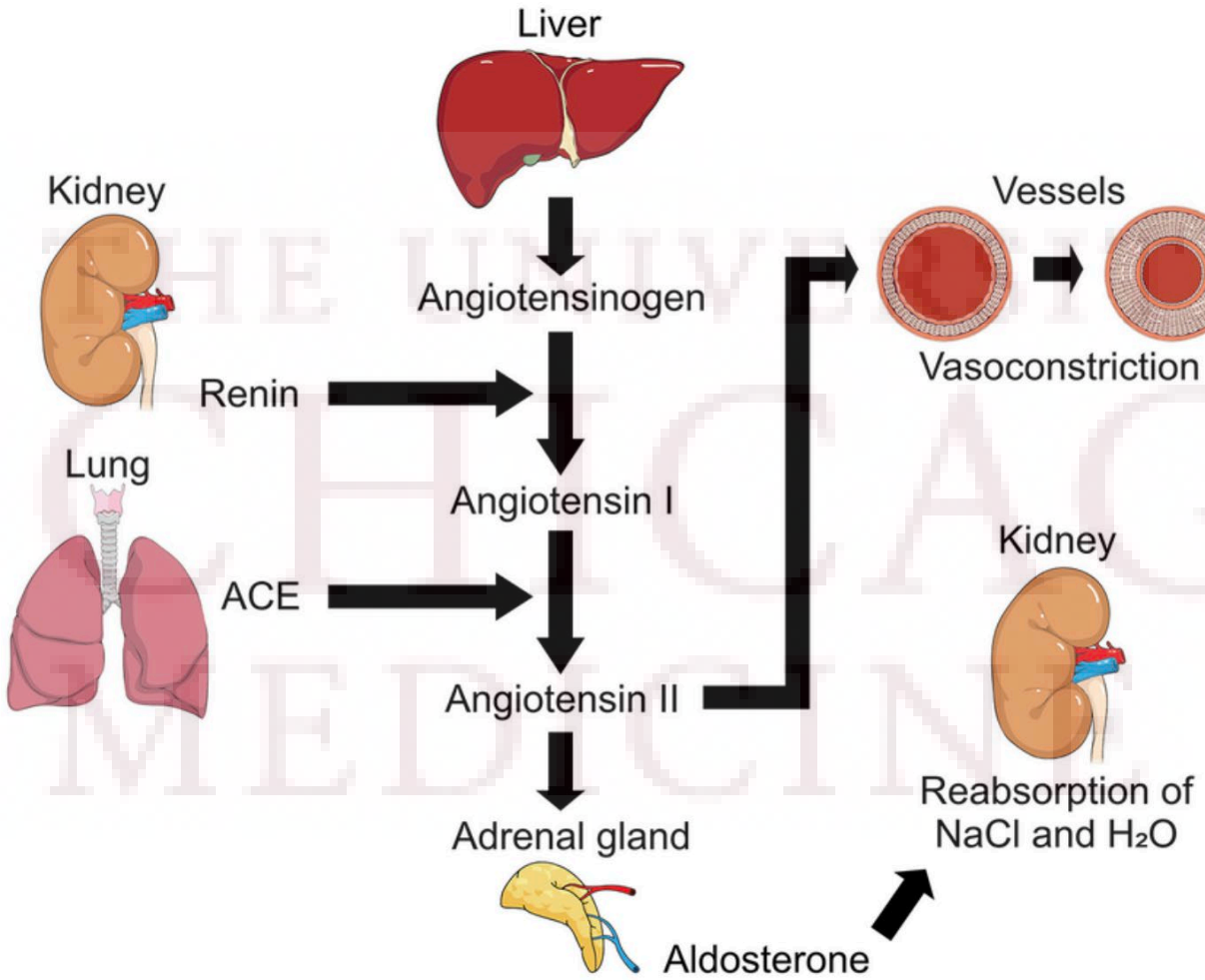
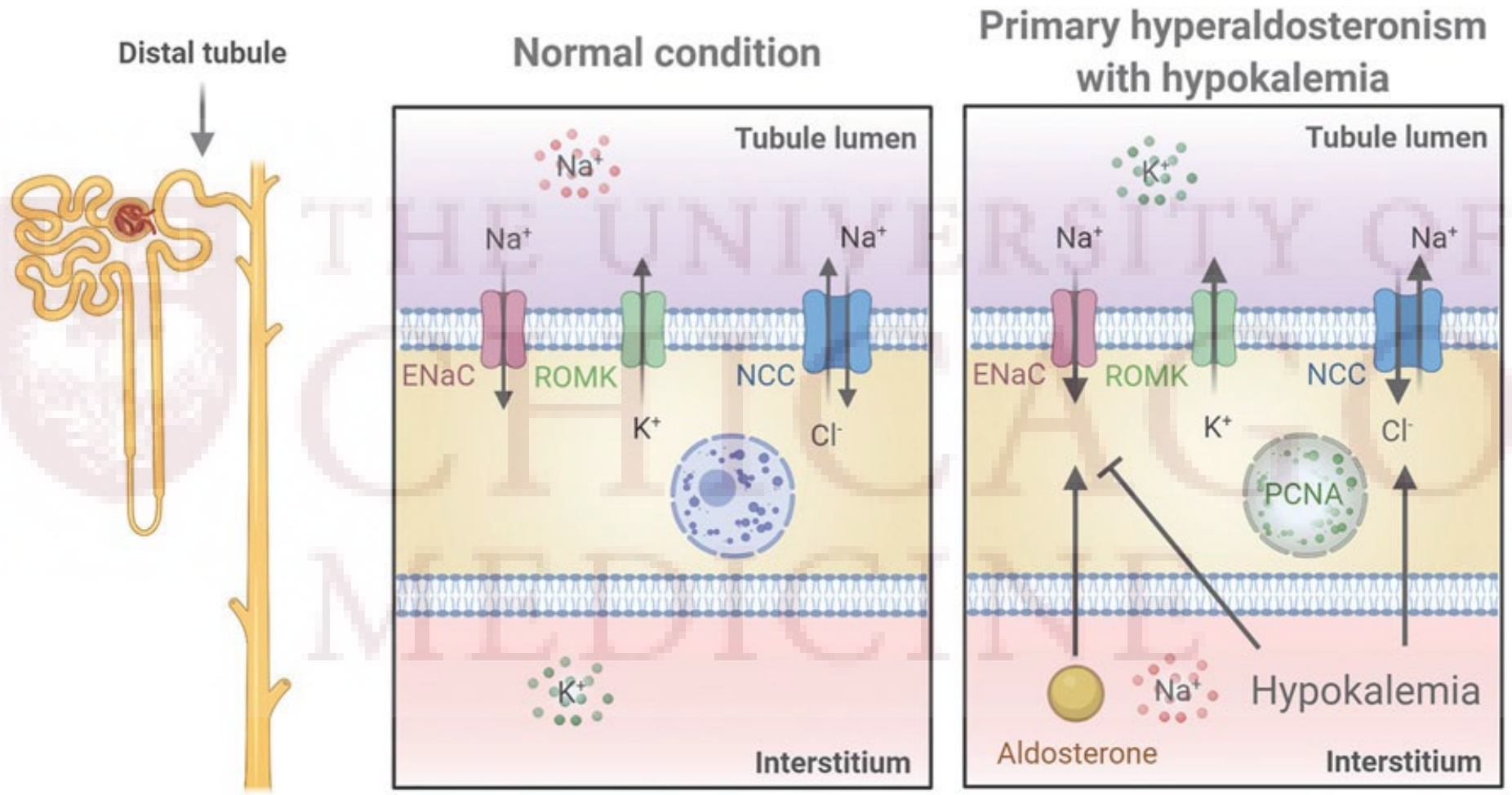
Notable findings?

Renin Angiotensin Aldosterone System



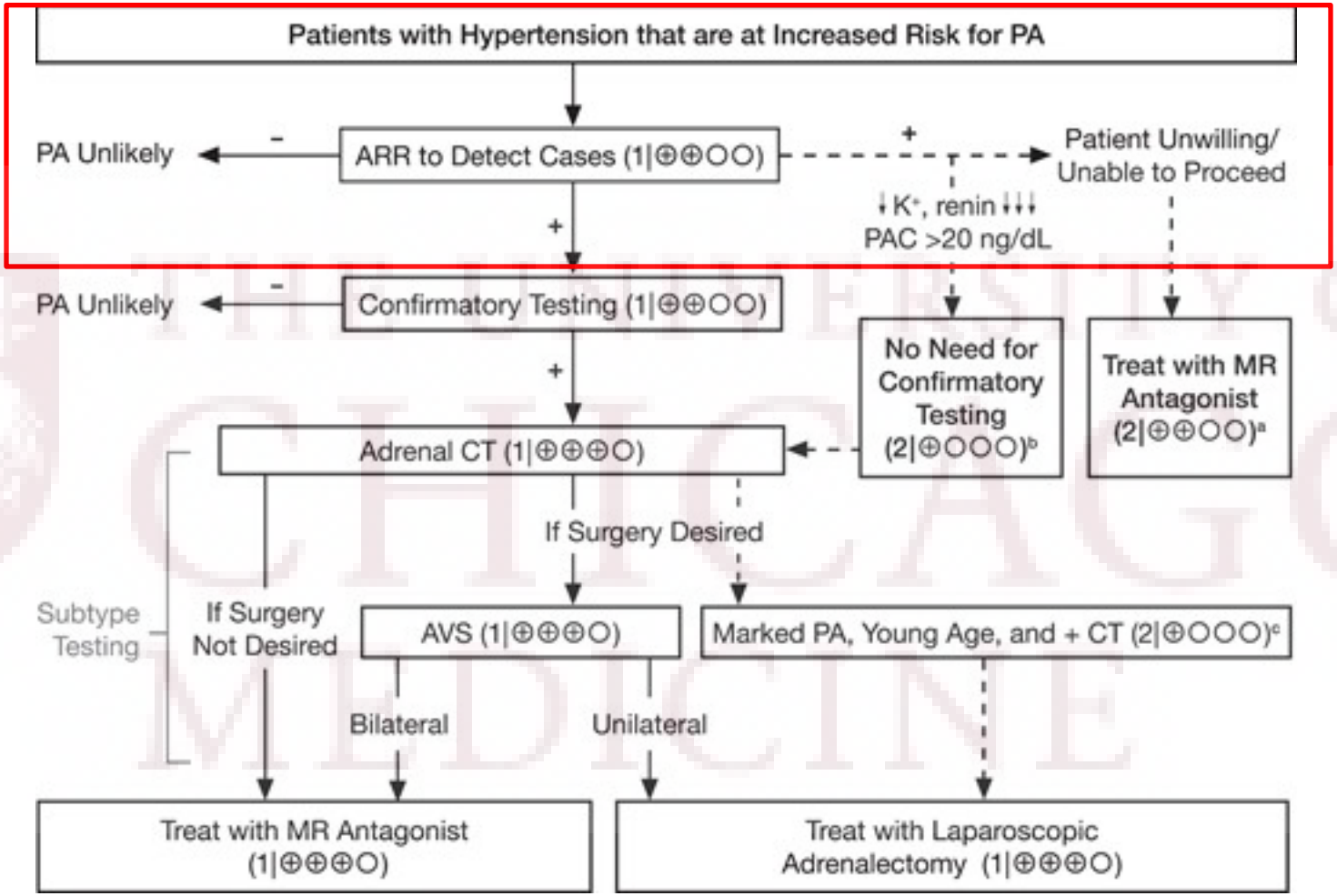
(Vargas, 2021)

Renin Angiotensin Aldosterone System – Why Hypo K?



(Kristensen, 2022)

Screening Algorithm (Endo Society, 2016)



(Funder, 2016)

Primary Aldosteronism Screening

- Screening recommendations:
  - Sustained BP >150/100 x3 measurements
  - BP >140/90 on 3 anti-HTN drugs including diuretic
  - BP >140/90 on 4+ anti-HTN drugs
  - HTN + spontaneous hypoK
  - HTN + adrenal incidentaloma
  - HTN + OSA
  - HTN + family hx early onset HTN or CVA <40 yo
  - 1st degree relative with PA

(Funder, 2016)

Primary Aldosteronism Screening

Population	Estimated Prevalence of Primary Aldosteronism	Guideline-Recommended Testing	Actual Eligible Population Testing Rates
General hypertension	10–20%	In some patients	<2%
Resistant hypertension	20–30%	In all patients	<3%
Hypertension with hypokalemia	Approximately 30%	In all patients	<3%
Hypertension with severe hypokalemia (<3.0 mmol/liter)	>50%	In all patients	<5%

(Vaidya, 2025)

Aldosterone Renin Ratio

Ideal Testing Conditions

- Most sensitive with morning samples, out of bed for 2+ hours, seated 5-15 minutes
- Unrestricted salt
- K+ replete
- Withdraw ARR effecting agents 4 weeks before testing
  - MR specifically: Spironolactone, eplerenone, amiloride, triamterene
  - K wasting diuretics: thiazide and loop diuretics
  - Licorice

Most times, can interpret even if not ideal testing conditions

- Often not feasible to withdraw all antihypertensive medications
- If non-diagnostic, then can retest after discontinuing other medications x2 weeks
  - May start verapamil SR +/- hydralazine, prazosin, doxazosin, terazosin

Aldosterone Renin Ratio Cutoffs

ARR Cutoff Values, Depending on Assay and Based on Whether PAC, PRA, and DRC Are Measured in Conventional or Système International (SI) Units

	PRA, ng/mL/h	PRA, pmol/L/min	DRC, mU/L[a]	DRC, ng/L[a]
PAC (as ng/dL)	20	1.6	2.4	3.8
	30[b]	2.5	3.7	5.7
	40	3.1	4.9	7.7
PAC (as pmol/L)	750[b]	60	91	144
	1000	80	122	192

ARR False Positives or Negatives

D = Down arrow
U = Up arrow
R = Right arrow
FP = False positive
FN = False negative

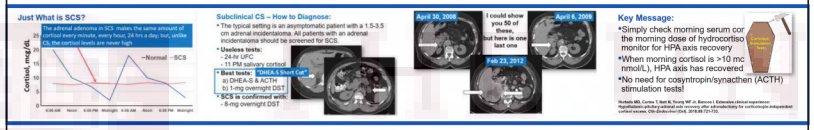
Table 3.

Factors That May Lead to False-Positive or False-Negative ARR Results

Factor	Effect on Aldosterone Plasma Levels	Effect on Renin Levels	Effect on ARR
Medications[a]			
β-Adrenergic blockers	D	D D	U (FP)
Central agonists (eg, clonidine, α-methyldopa)	D	D D	U (FP)
NSAIDs	D	D D	U (FP)
K^+-wasting diuretics	R U	U U	D (FN)
K^+-sparing diuretics	U	U U	D (FN)
ACE inhibitors	D	U U	D (FN)
ARBs	D	U U	D (FN)
Ca^{2+} blockers (DHPs)	R D	U	D (FN)
Renin inhibitors	D	D U	U (FP)
			D (FN)

ILACE Meeting – Talk from Dr. Bill Young

Clinical Perspectives on Adrenal Disorders: Answers to Common Questions



William F. Young, Jr., MD, MSc
Tyson Family Endocrinology Clinical Professor
Mayo Clinic, Rochester, MN USA

ILACE Annual Meeting 2024 - October 5, 2024
Tobin Hall – Loyola University Campus – Maywood

#5 What medications should be stopped before testing for primary aldosteronism (eg, mineralocorticoid receptor antagonists, ACE-I, ARBs, diuretics, renin inhibitors, beta-adrenergic blockers, etc)?

NONE!

Unfortunately, I see Bill's scenario every week

- Bill, with his 7-drug hypertension, had hypokalemia dating back 13 yrs. It is likely that he was never tested for PA because clinicians thought that they couldn't—due to his potentially interfering meds. Now he had stage 3 CKD.
- Although all of Bill's meds can affect the RAA system in people without PA, THEY RARELY CAUSE A PROBLEM IN PATIENTS WITH TRUE PA
- If renin is suppressed (PRA <1 ng/mL/hr or PRC <8 mU/L), then meds are not interfering and you can do any test you want—case detection testing, confirmatory testing, and AVS on ANY DRUG!!!

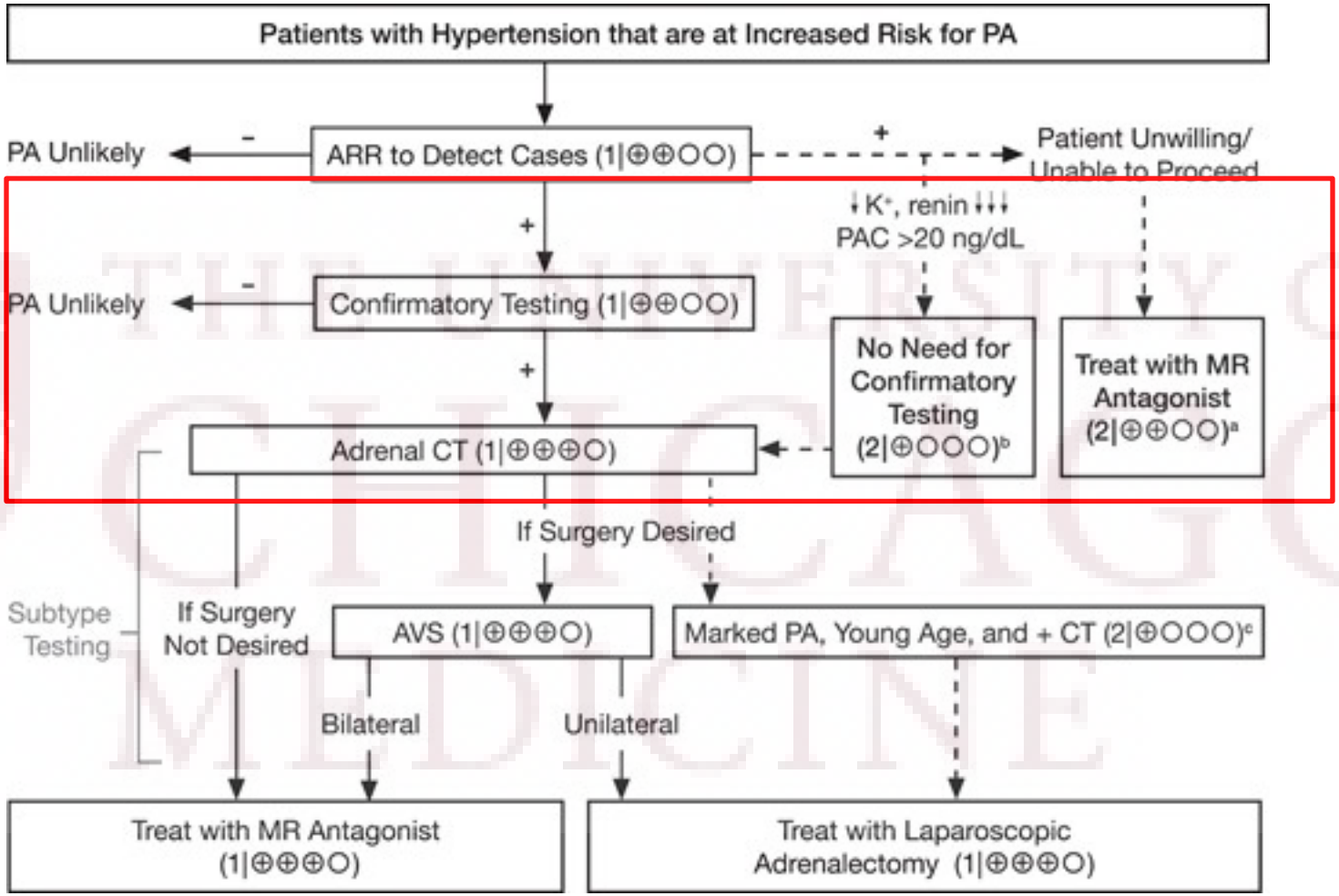
*Caveat on Mineralocorticoid Receptor Antagonists

- Spironolactone (SPL) and eplerenone (EPL) do not directly affect the laboratory measurement of aldosterone
- SPL and EPL can only affect the evaluation of PA if the dosage is high enough to completely block the mineralocorticoid

Clinical Pearl: Most patients with PA who are treated with SPL or EPL are on subtherapeutic doses and renin will be suppressed—never stop SPL or EPL to screen for PA

*WF Young. Diagnosis of primary aldosteronism. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed Sep-30-2024.

Screening Algorithm (Endo Society, 2016)



(Funder, 2016)

Confirmatory Testing

- If positive ARR, use 1 or more confirmatory tests
- If spontaneous hypokalemia, undetectable renin, and plasma aldosterone >20, then may not need to confirm

(Funder, 2016)

Confirmatory Testing

- No “gold standard” confirmatory test
  - Oral sodium loading test
    - NA intake 6 g /d for 3 days, verify 24-h urine Na, PA unlikely if 24-hr urine aldo <10 ug
    - KCl SR for normal K, on day 3 collect 24 hr urine; PA likely if urine aldo >12 ug/24 hr
  - SIT – saline infusion test / seated saline suppression test
    - Recumbent patient, NS 2 L over 4 hrs, draw renin, aldo, cortisol, and K at time 0 and 4 hr; PA unlikely if aldo <5, likely if >10
  - FST – fludrocortisone
    - 0.1 mg fludro q6 hr x4 days + KCl + NaCl; day 4 measure plasma aldo, renin 10 AM, cortisol 7 and 10 AM; Aldo > 6 confirms PA if renin <1
  - Captopril challenge test
    - Captopril 25-50 mg oral; renin, aldo, cortisol at time 0 and 1-2 hr; Aldo normally suppressed >30%; if PA remains elevated

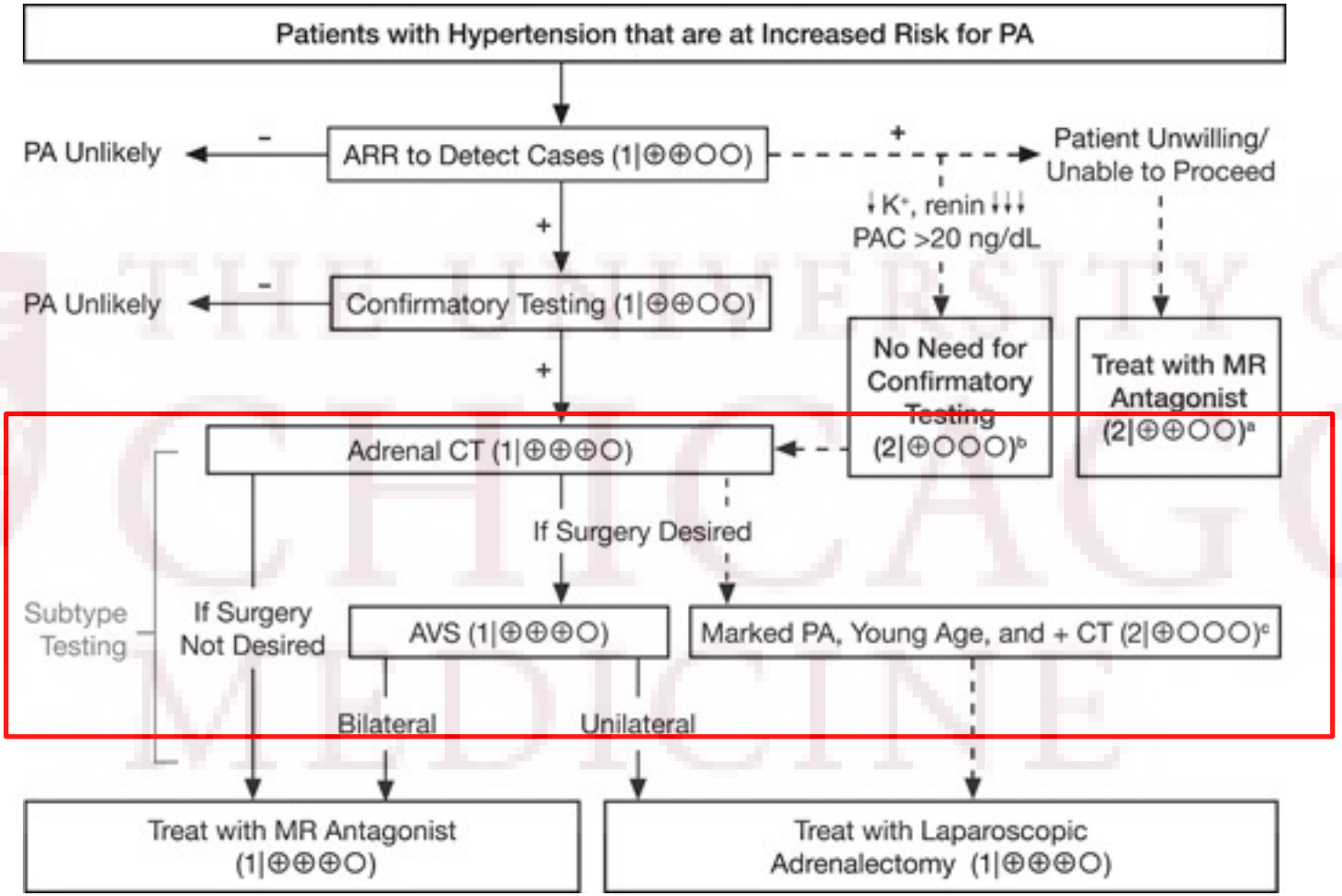
(Funder, 2016)

Notes on Confirmatory Testing

- The prevalence of primary aldosteronism is high and largely unrecognized (estimates of 11-22%)
- In hypertension, there is a spectrum of renin-independent aldosteronism which may contribute to “essential hypertension”
- Saline suppression test is associated with a high false-negative rate, and reliance on it may lead to missed opportunities for intervention
- My takeaway: maybe just move on to the CT scan

(Pilz, 2020; Leung, 2025)

Screening Algorithm (Endo Society, 2016)



(Funder, 2016)

Adrenal CT / AVS

- Adrenal CT (sensitivity 78%, specificity 75%)
  - Normal adrenals
  - Unilateral macroadenoma >1 cm
  - Unilateral adrenal limb thickening
  - Unilateral microadenoma
  - Bilateral macro- or microadenoma
  - Aldo-producing adrenal carcinomas typically >4 cm

Adrenal CT / AVS

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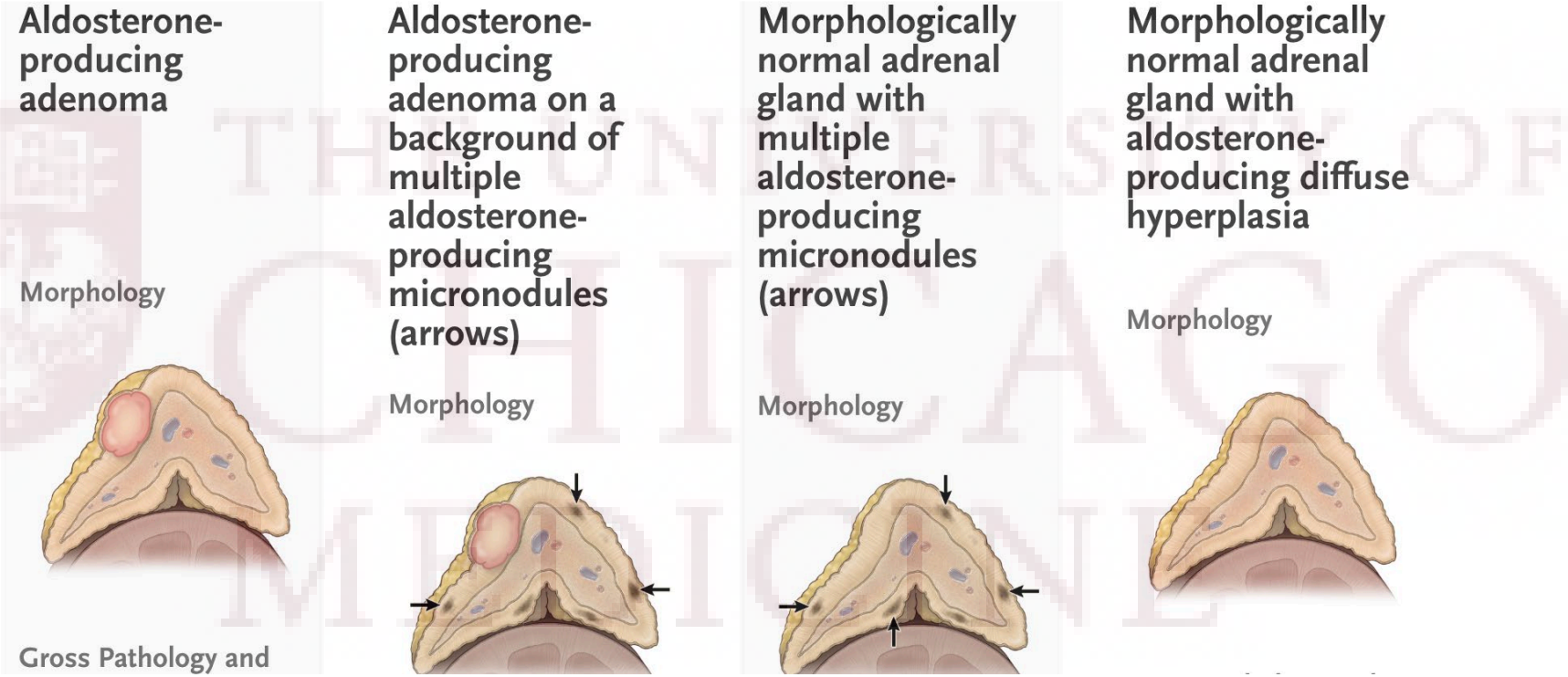


(Vaidya, 2025)

CT A/P 7/2023

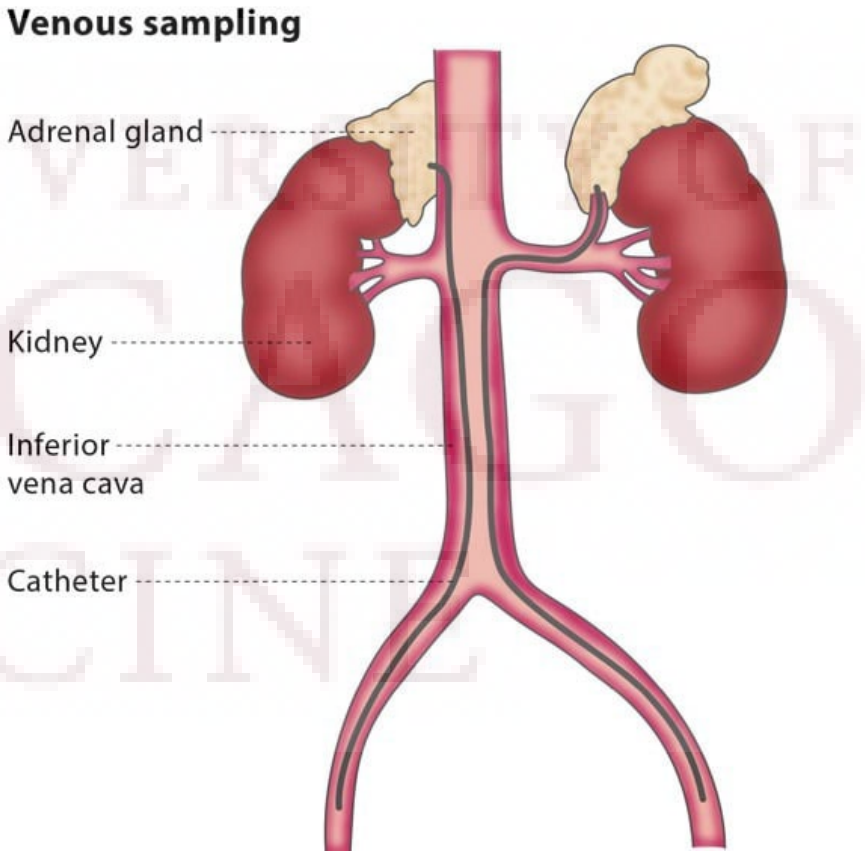
Select Findings:

ADRENAL GLANDS: No significant abnormality noted

KIDNEYS, URETERS: No hydronephrosis. Symmetric nephrograms.

Adrenal Vein Sampling

- Adrenal vein sampling essential (sensitivity 95%, specificity 100%)
  - Gold standard in distinguishing unilateral vs bilateral disease
  - Difficult procedure, cannulating R adrenal vein (smaller and empties directly into IVC)
  - Better with experienced angiographer
  - Most common protocol with continuous cosyntropin infusion with sequential bilateral AVS



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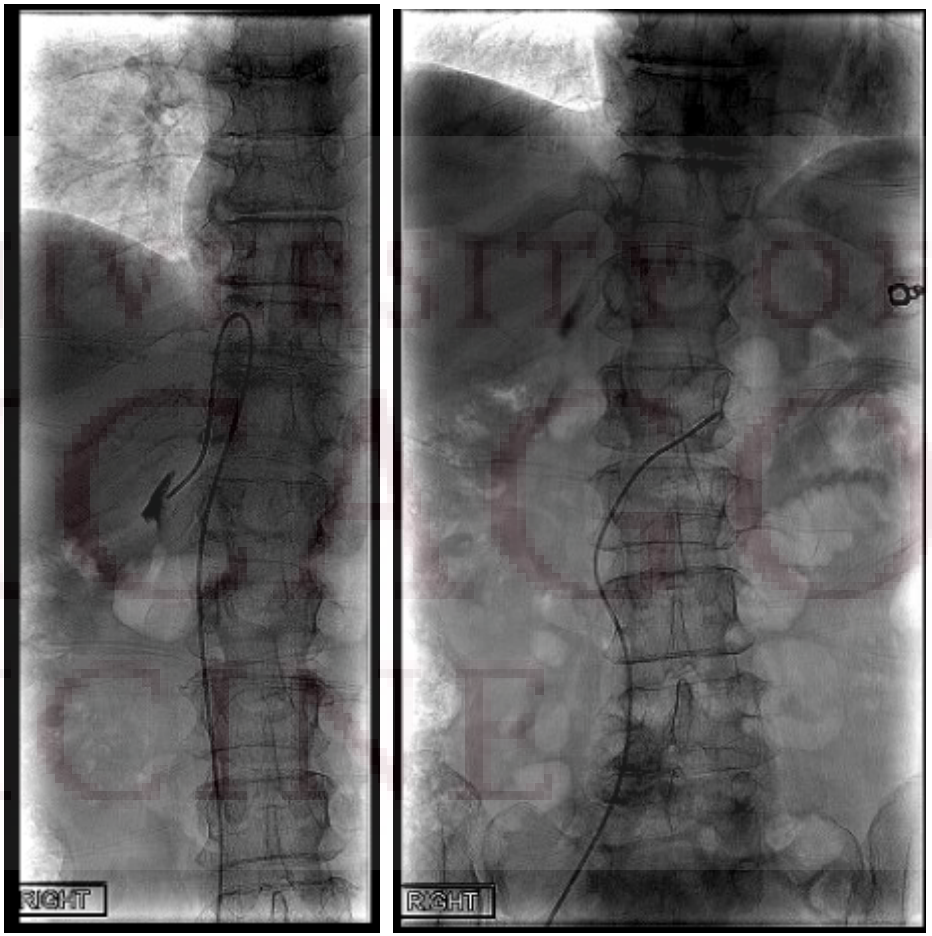

Adrenal Vein Sampling

	MEASURED VALUES		CALCULATED VALUES				
Location	Aldosterone (ng/dL)	Cortisol (ug/dL)	Aldosterone (pmol/L)	Cortisol (nmol/L)	Adrnl/IVC Cortisol Ratio	Aldo/Cortisol Ratio	A
Right Adrenal Vein	344	1030	9529	28428	32.2	0.34	
Left Adrenal Vein	1030	141	28531	3892	4.4	7.33	21
Femoral Vein	84	32	2327	883		2.63	
Right Adrenal Vein	427	1040	11828	28704	33.5	0.41	
Left Adrenal Vein	1350	183	37395	5051	5.9	7.40	
Femoral Vein	76	31	2105	856		2.46	

How do I interpret?

Adrenal Vein Sampling

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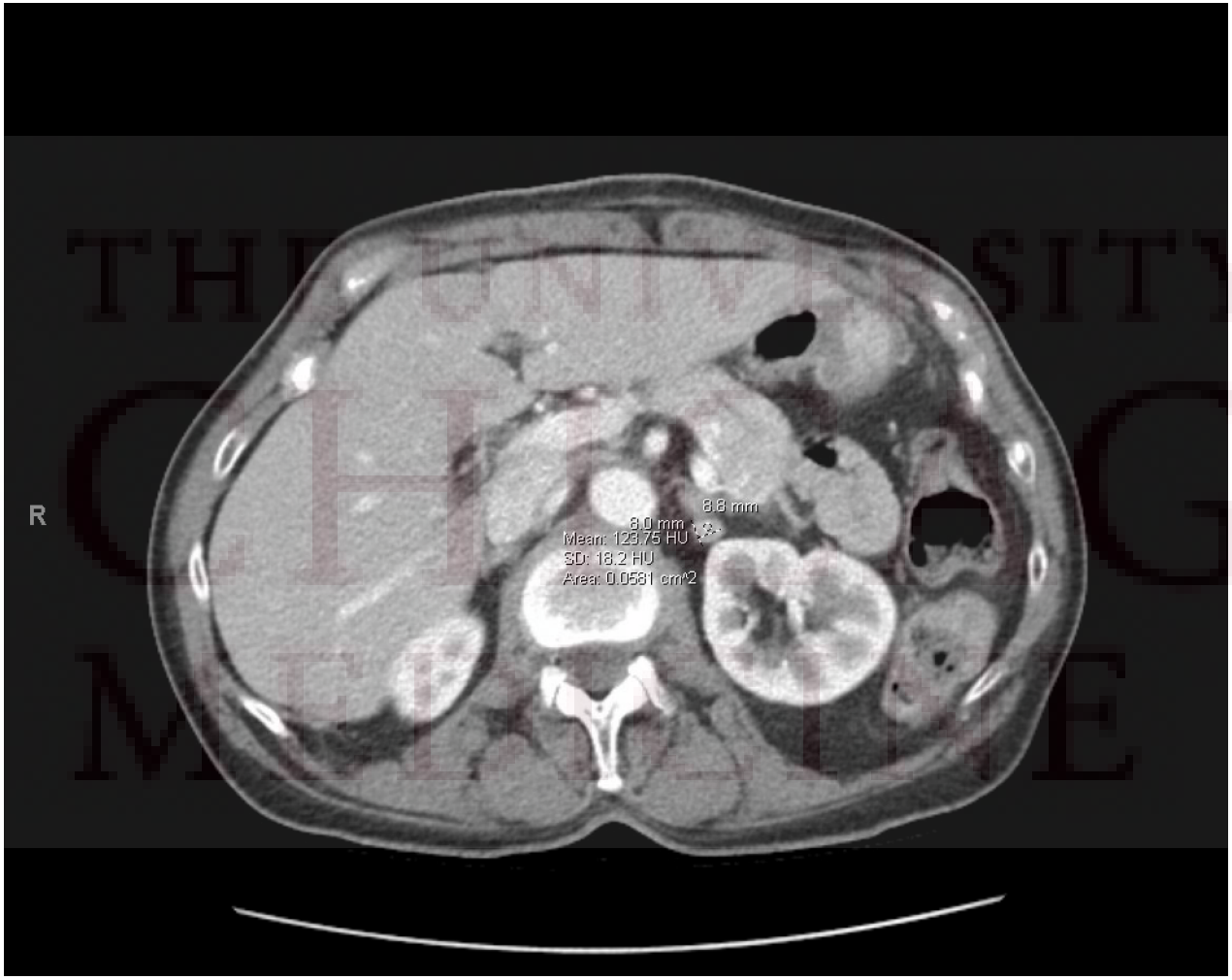
Correct aldosterone for cortisol = aldo / cortisol
Ratio 4:1 indicates unilateral excess
Ratio < 3:1 indicates bilateral aldosterone hypersecretion

CT A/P 7/2023



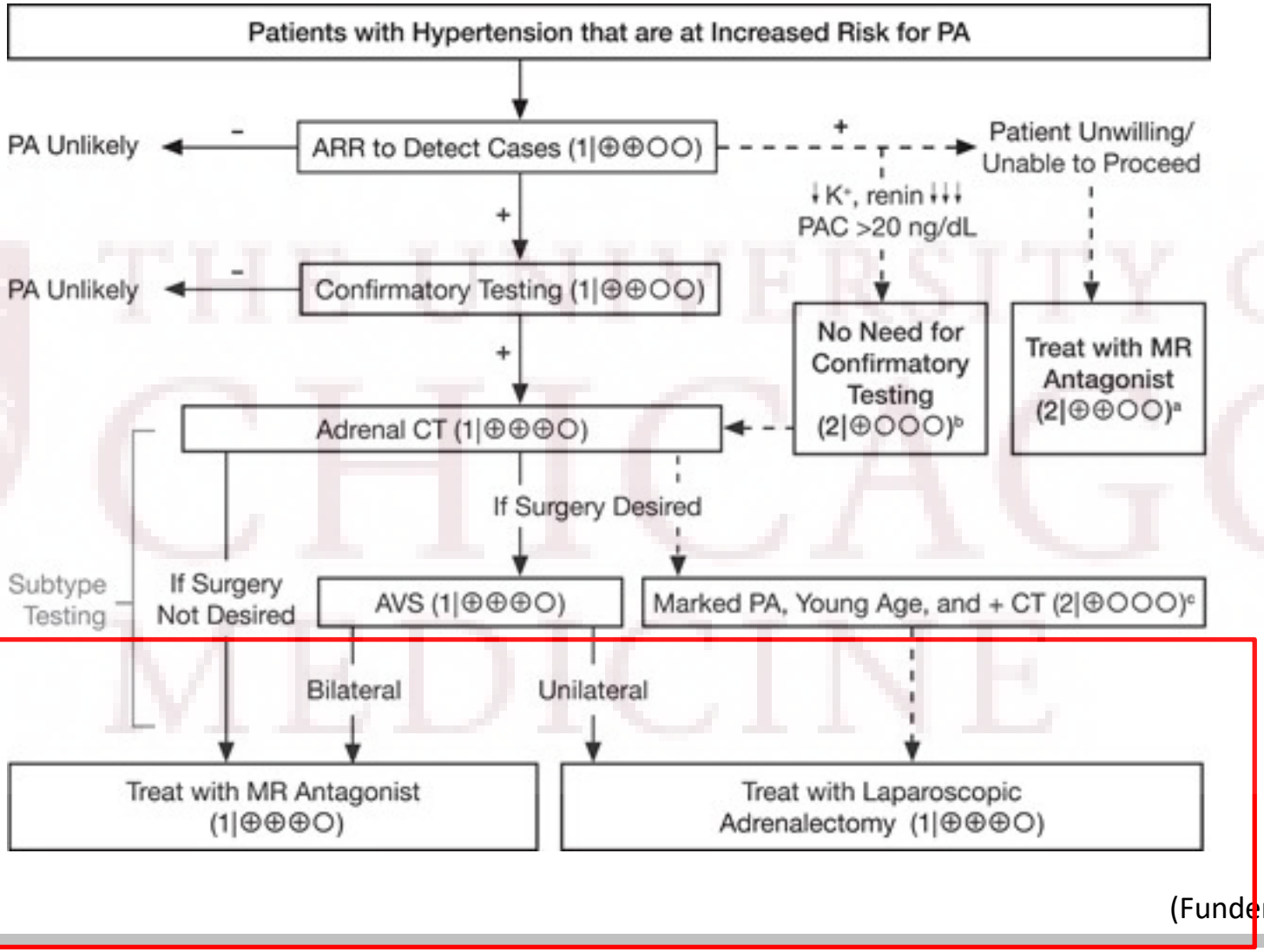
CT A/P 7/2023

Select Findings:

ADRENAL GLANDS: **Left adrenal nodule** best seen on image 29, series 7 again noted measuring **0.9 x 0.8 cm**. This lesion measures 124 Hounsfield units on portal venous phase and demonstrates rapid washout on delayed imaging.

IMPRESSION: Left adrenal nodule again noted. This nodule demonstrates relatively high attenuation on portal venous phase and rapid washout. While these kinetic characteristics support the diagnosis of adrenal adenoma, the high attenuation on portal venous phase indicates that pheochromocytoma cannot be excluded. Would recommend correlation with blood/urine biomarkers.

Screening Algorithm (Endo Society, 2016)



(Funder, 2016)

Treatment

- Unilateral laparoscopic adrenalectomy recommended for cure/improvement of hypertension in patients with unilateral disease
  - Nearly 100% of post-op improvements in BP and K
  - HTN cured in about 50%
  - PA patients have increased risk of CV/renal complications including arrhythmias, MI, stroke, CKD, death, which is why surgical intervention recommended
  - More reduction in LV mass index, reversal of carotid intima-media thickness and arterial stiffness compared to medical management
- HTN improved by MR antagonists in remaining patients
  - Can also help improve CV mortality
- This patient is meeting with endocrine surgery to plan for unilateral laparoscopic adrenalectomy

Take Home Points

- Encourage screening for broad range of patient with resistant hypertension or additional risk factors for primary hyperaldosteronism
- Screening starts with aldosterone to renin ratio, typically > 30
- For those without spontaneous hyperkalemia, suppressed renin, and ARR >20, confirmatory testing can be considered
- Adrenal CT is preferred imaging modality, which is correlated with adrenal vein sampling for lateralization
- Recommended treatment is unilateral laparoscopic adrenalectomy or if unable, MR antagonist

Special thank you to Dr. Jain!

References

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ENDORAMA

June 5, 2025

Presented by:

Caroline Abe, M.D.

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