THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

45-Year-Old Female Referred for Adrenal Mass

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Adult Endocrinology Fellow

Endorama 1/9/2025

Patient Presentation

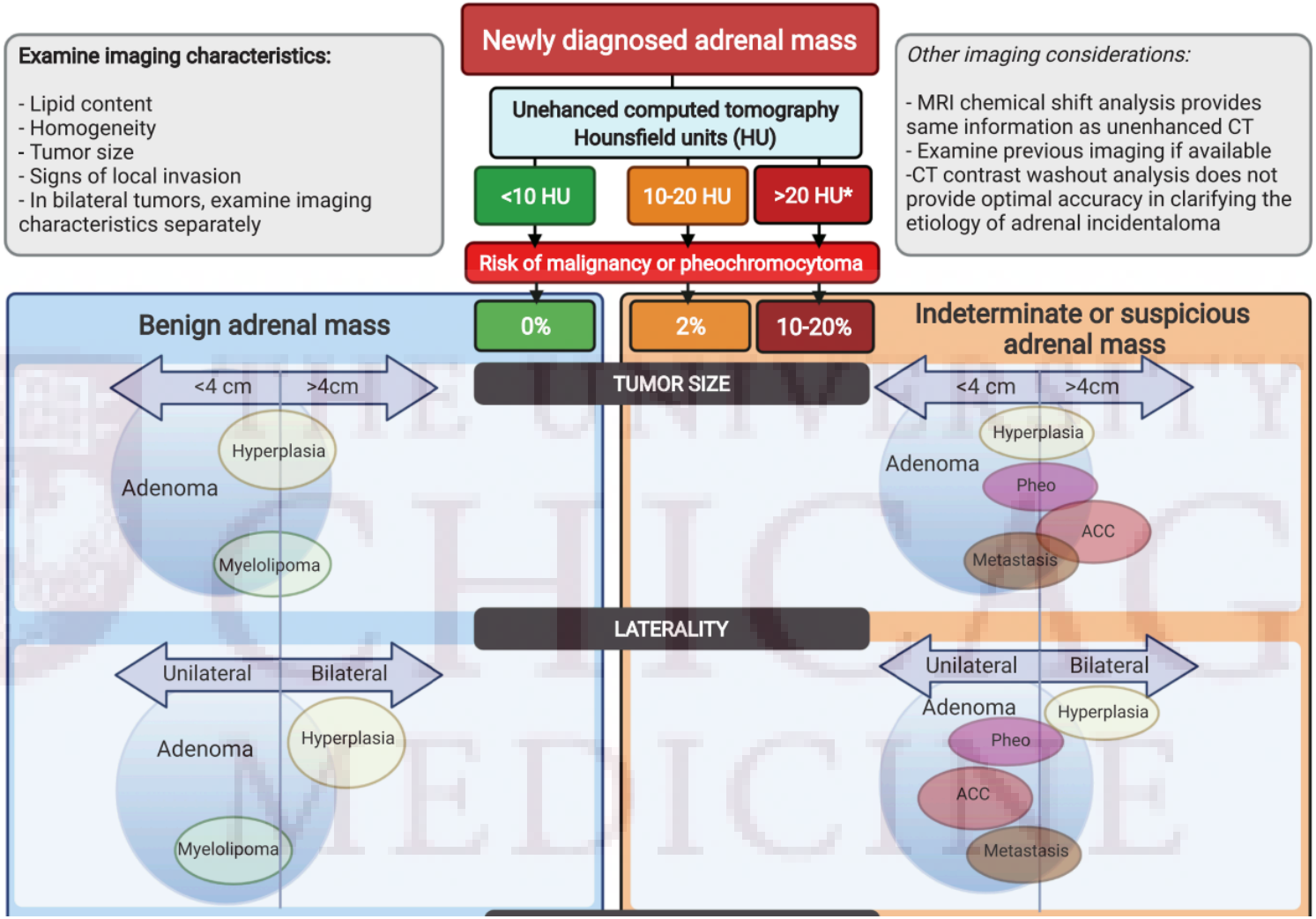
45-year female physician with PMH of HTN and headaches is seen for evaluation of an adrenal mass.

What are key questions would like to know about this patient?

Past Medical History

- History of HTN
  - Long-standing hypertension.
  - Trialed lisinopril and metoprolol (ineffective; metoprolol caused bradycardia).
  - Currently on nifedipine XL 30 mg TID (BP spikes with missed doses).
- **Hypertensive Emergency (August 2024)**
  - Severe headaches, stroke-like symptoms, and BP of 200/114.
- **Workup:**
- CT abdomen revealed a **left adrenal nodule** (1.5 cm, previously 1.4 cm).No Hounsfield units reported.
- Patient denies any symptoms including weight gain or changes in appearance, easy bruising, acne, purple striae, proximal muscle weakness, osteoporosis, diabetes mellitus, hyperlipidemia, or cognitive changes

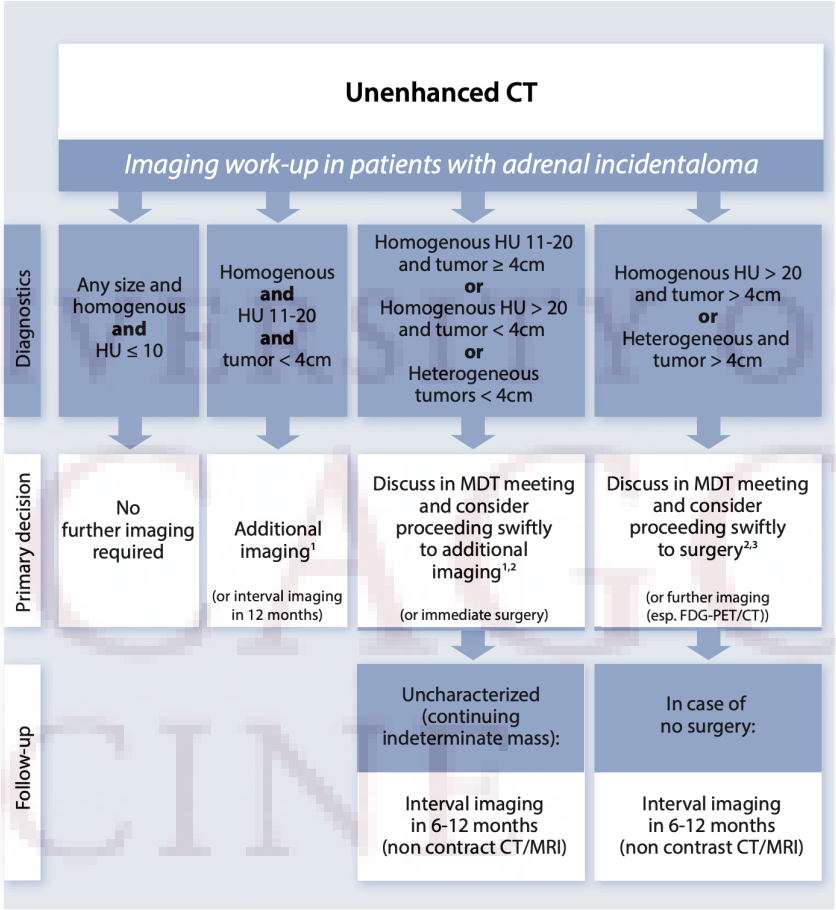
Work up for adrenal adenoma?



Irina Bancos, Alessandro Prete, Approach to the Patient With Adrenal Incidentaloma, The Journal of Clinical Endocrinology & Metabolism, Volume 106, Issue 11, November 2021, Pages 3331–3353, https://doi.org/10.1210/clinem/dgab512

Use of Unenhanced Attenuation vs CT With Adrenal-Washout Protocol Is

- CT with adrenal-washout protocol (adrenal-protocol CT) has been used as the recommended test to differentiate an adrenal adenoma from other adrenal lesions by the American College of Radiology
- Recent clinical practice guidelines from the European Society of Endocrinology highlight the value of unenhanced attenuation as the best method for initial assessment



Fassnacht, M. et al. European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors. Eur. J. Endocrinol. 189, G1–G42 (2023)

Performance of CT With Adrenal-Washout Protocol in Heterogeneous Adrenal Nodules: A Multi institutional Study

- Retrospective study included 164 patients (mean age, 59.1 years; 61men, 103 women) with a total of 164 heterogeneous adrenal nodules evaluated using adrenal-protocol CT at seven institutions.
- All nodules had an available pathologic reference standard

TABLE 1: Pathologic Diagnosis of Heterogeneous Adrenal Nodules

Pathologic Diagnosis	No. of Nodules (n = 164)
Adenoma	82
Pheochromocytoma	36
Metastasis[a]	20
Adrenocortical carcinoma	12
Ganglioneuroma	3
Hemangioma	2
Myxoid neoplasm	2
Oncocytoma	1
Sarcoma	1
Schwannoma	1
Adrenal gland with organizing hematoma	1
Chronic granulomatous inflammatory process	1
Hemorrhagic cyst	1
Adrenal hyperplasia	1

[a]Primary malignancy: lung cancer (n = 6); renal cell carcinoma (n = 6); unknown primary malignancy (n = 2); and breast cancer, colon cancer, gallbladder cancer, leiomyosarcoma, melanoma, and thyroid cancer (all n = 1).

Corwin MT, et al. Performance of CT With Adrenal-Washout Protocol in Heterogeneous Adrenal Nodules: A Multiinstitutional Study. AJR Am J Roentgenol. 2024 May;222(5):e2330769. doi: 10.2214/AJR.23.30769. Epub 2024 May 29. PMID: 38415578.

Performance of CT With Adrenal-Washout Protocol in Heterogeneous Adrenal Nodules: A Multi-institutional Study

TABLE 2: Sensitivity and Specificity of Unenhanced CT Attenuation of 10 HU or Less for Differentiating Adenoma From Non adenoma Among Heterogeneous Adrenal Nodules for Each ROI Method

ROI Method	Sensitivity	Specificity
Standard	22.0 (13.6–32.5) [18/82]	96.3 (89.7–99.2) [79/82]
High	11.0 (5.1–19.8) [9/82]	98.8 (93.4–100.0) [81/82]
Low	58.5 (47.1–69.3) [48/82]	84.1 (74.4–91.3) [69/82]
Average	30.5 (20.8–41.6) [25/82]	97.6 (91.5–99.7) [80/82]

TABLE 4: Sensitivity and Specificity of Adrenal-Protocol CT Overall a for Differentiating Adenoma From Non adenoma Among Heterogeneous Adrenal Nodules for Each ROI Method in All Nodules, Nodules Measuring Less Than 4 cm, and Nodules Measuring 4 cm or Greater

ROI Method	All Nodules		Nodules < 4 cm		Nodules ≥ 4 cm	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Standard	57.3 (45.9–68.2) [47/82]	84.1 (74.4–91.3) [69/82]	70.6 (56.2–82.5) [36/51]	76.7 (57.7–90.1) [23/30]	35.5 (19.2–54.6) [11/31]	88.5 (76.6–95.7) [46/52]
High	63.4 (52.1–73.8) [52/82]	51.2 (39.9–62.4) [42/82]	72.5 (58.3–84.1) [37/51]	43.3 (25.5–62.6) [13/30]	48.4 (30.2–66.9) [15/31]	55.8 (41.3–69.5) [29/52]
Low	68.3 (57.1–78.1) [56/82]	62.2 (50.8–72.7) [51/82]	82.4 (69.1–91.6) [42/51]	66.7 (47.2–82.7) [20/30]	45.2 (27.3–64.0) [14/31]	59.6 (45.1–73.0) [31/52]
Average	59.8 (48.3–70.4) [49/82]	85.4 (75.8–92.2) [70/82]	72.5 (58.3–84.1) [37/51]	76.7 (57.7–90.1) [23/30]	38.7 (21.9–57.8) [12/31]	90.4 (79.0–96.8) [47/52]

Corwin MT, et al. Performance of CT With Adrenal-Washout Protocol in Heterogeneous Adrenal Nodules: A Multiinstitutional Study. AJR Am J Roentgenol. 2024 May;222(5):e2330769. doi: 10.2214/AJR.23.30769. Epub 2024 May 29. PMID: 38415578.

Hormonal Evaluation of Adrenal Mass

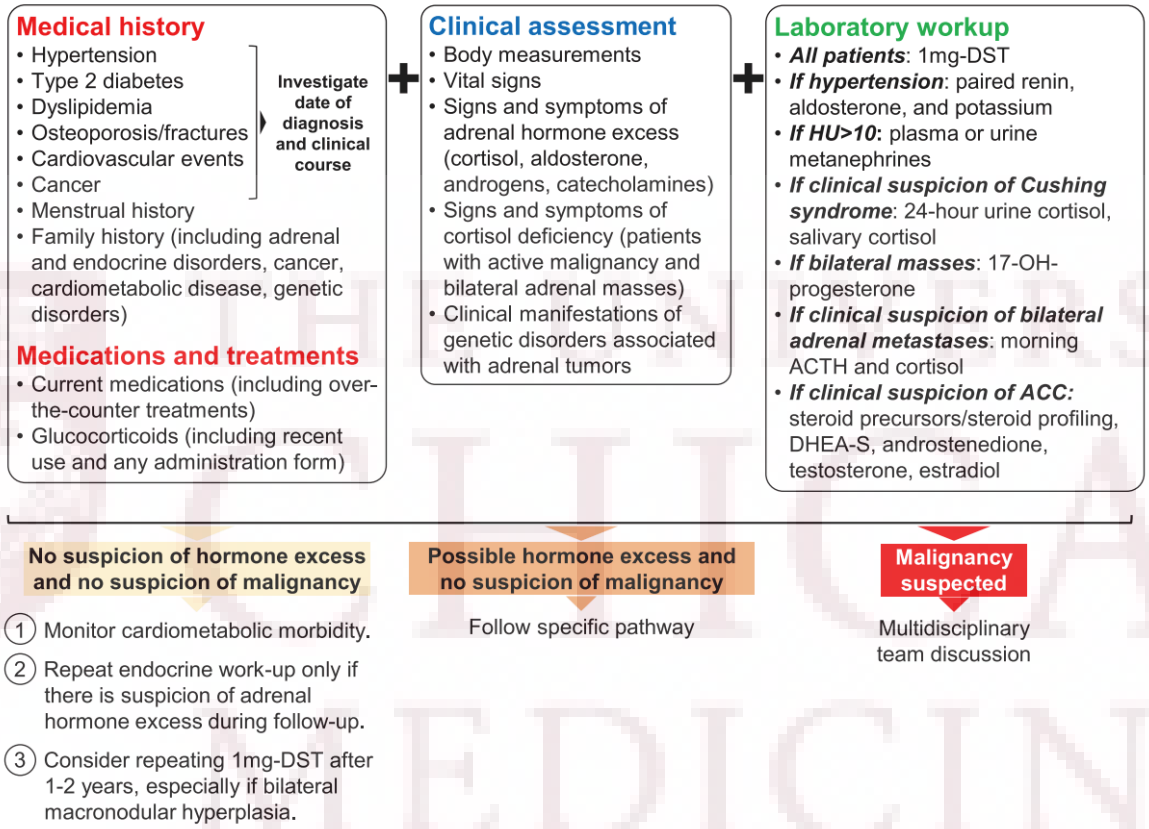


Figure 3. Adrenal incidentaloma evaluation: clinical and hormonal assessment. Abbreviations: 1-mg DST, 1-mg overnight dexamethasone suppression test; ACC, adrenocortical cancer; DHEA-S, dehydroepiandrosterone sulfate.

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Evaluation

Labs	Result
Sodium 135 - 145 mmol/L	**139**
Potassium 3.4 - 5.1 mmol/L	**3.9**
Chloride 97 - 110 mmol/L	**110**
Carbon Dioxide 21 - 32 mmol/L	**25**
Anion Gap 7 - 19 mmol/L	**7**
Glucose 70 - 99 mg/dL	**92**
BUN 6 - 20 mg/dL	**7**
Creatinine 0.51 - 0.95 mg/dL	**0.51**
Glomerular Filtration Rate >=60	**>90**

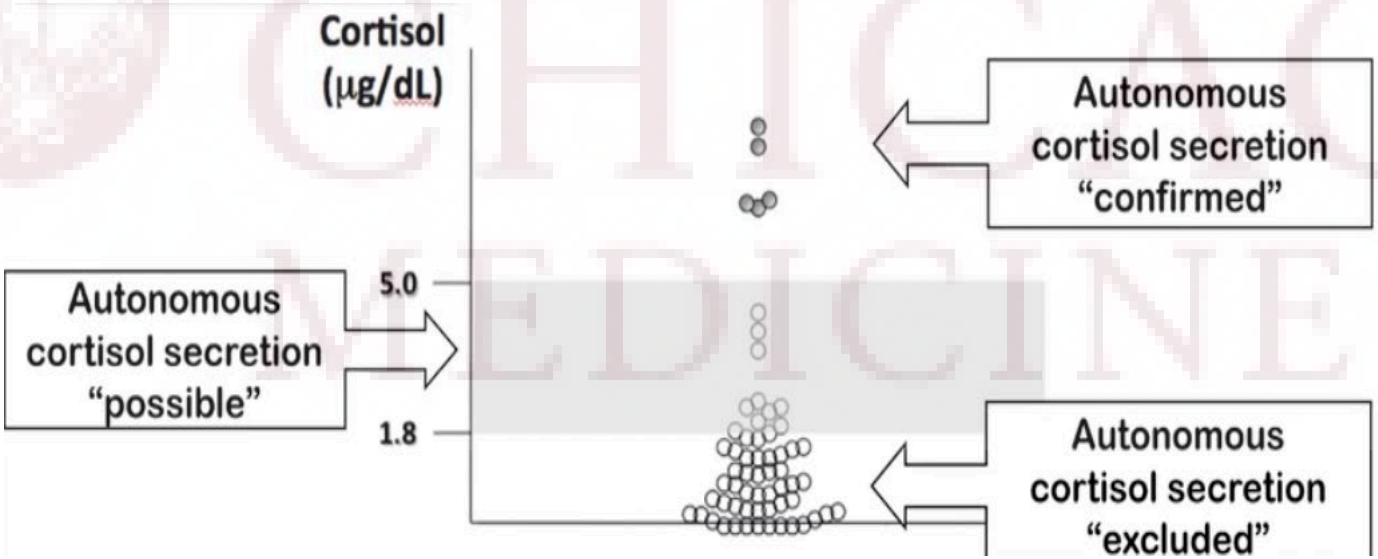
Biochemical evaluation	Result	Reference Range
ACTH, pg/L	4.9	7.2-63pg/mL
DHEA-S, mcg/dL	14	8-391.0mcg/dL
Aldosterone, ng/dL	16.6	
Plasma renin activity, ng/mL/h	1.1	0.2-1.6 ng/mlhr
Plasma metanephrines	30	<57 pg/nL
Urine metanephrines, mcg/24 h	136	<400
Urine normetanephrines, mcg/24h	184	<900
Urine free cortisol, mcg/24h	34	3.5-45

Further Evaluation

Biochemical evaluation	Result	Reference Range
1 mg DST, mcg/dL	3.4	<1.8 mcg/dL
8 mg DST, mcg/dL	5.4	<1.8 mcg/dL

Mild Autonomous Cortisol Secretion (MACS)

- Cortisol >1.8 mcg/dL following 1 mg Dexamethasone suppression test
- Patient without overt features of Cushing syndrome
- “Subclinical Cushing syndrome” – no longer to be used.



Diagnostic Accuracy of Dehydroepiandrosterone Sulfate and Corticotropin in Autonomous Cortisol Secretion

Fig A. Comparison of serum DHEA-S concentrations to 1-mg overnight dexamethasone suppression test (DST) results for post-DST serum cortisol concentrations of ≤1.8 versus >1.8 mcg/dL

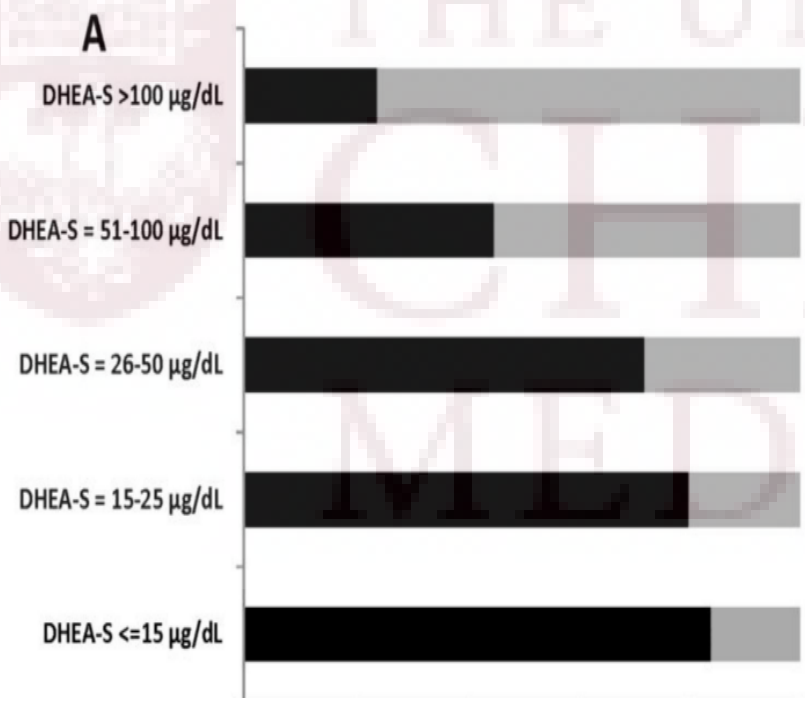
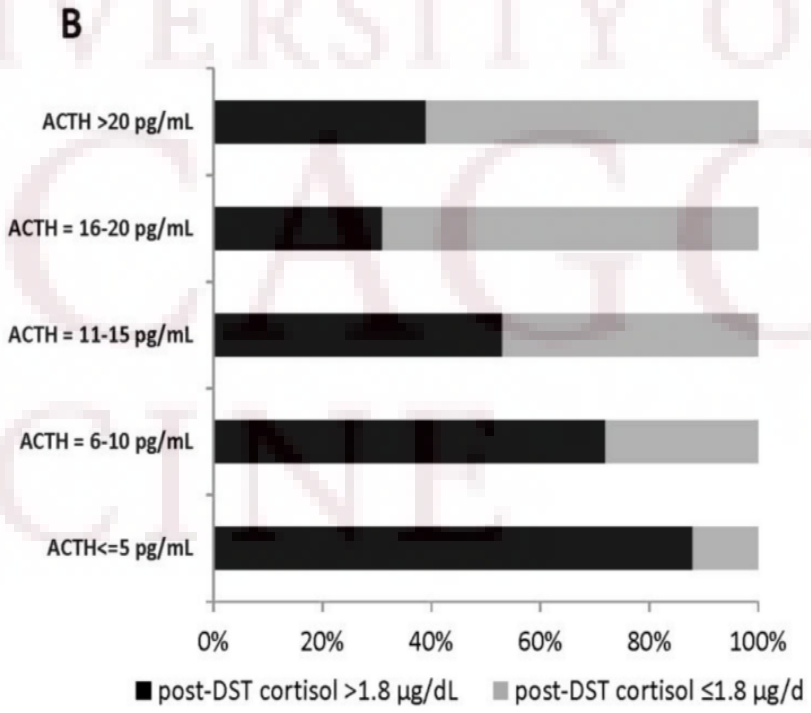


Fig B. Comparison of serum ACTH concentrations to 1-mg overnight dexamethasone suppression test (DST) results for post-DST serum cortisol concentrations of ≤1.8 versus >1.8 mcg/dL



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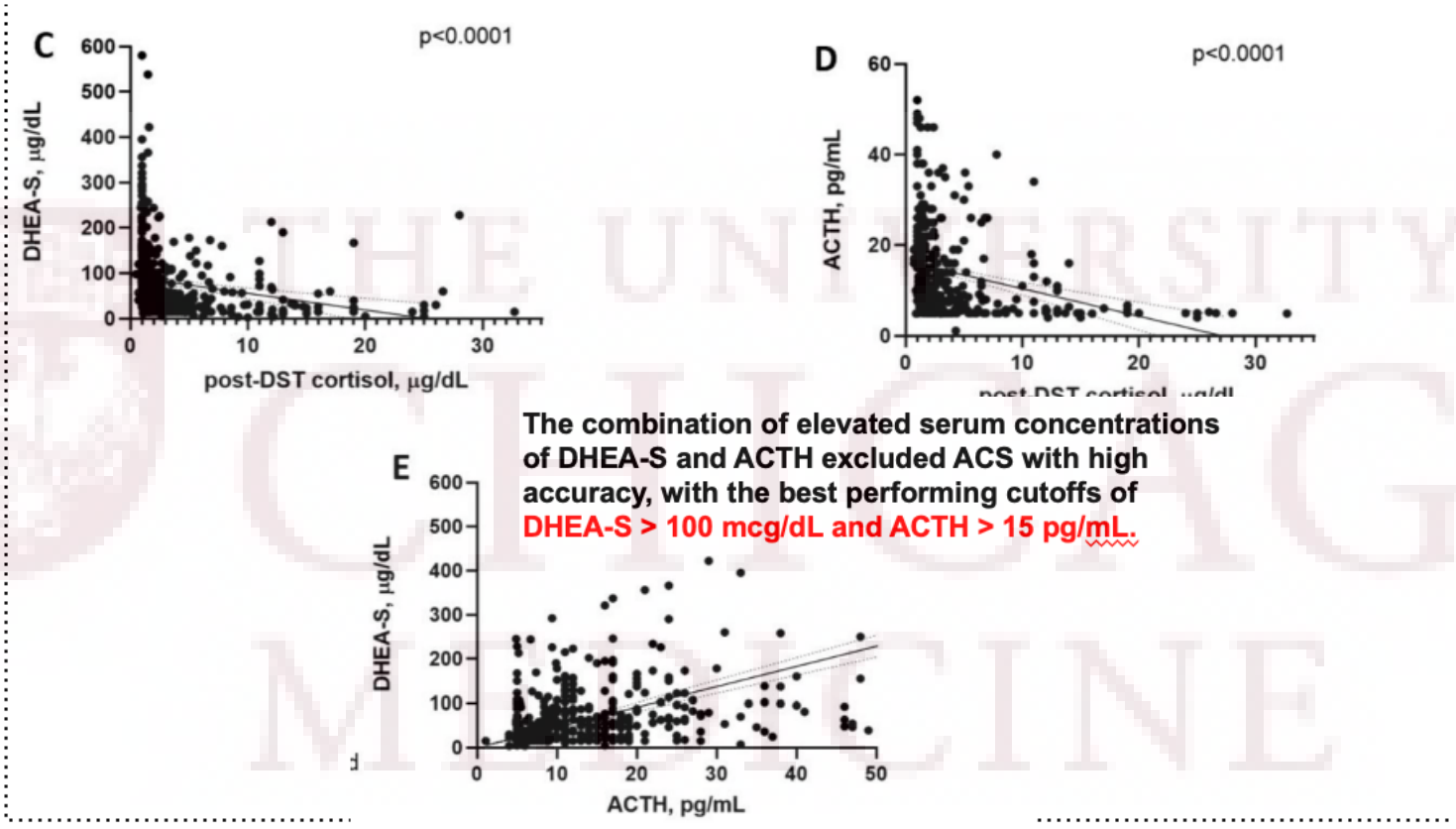
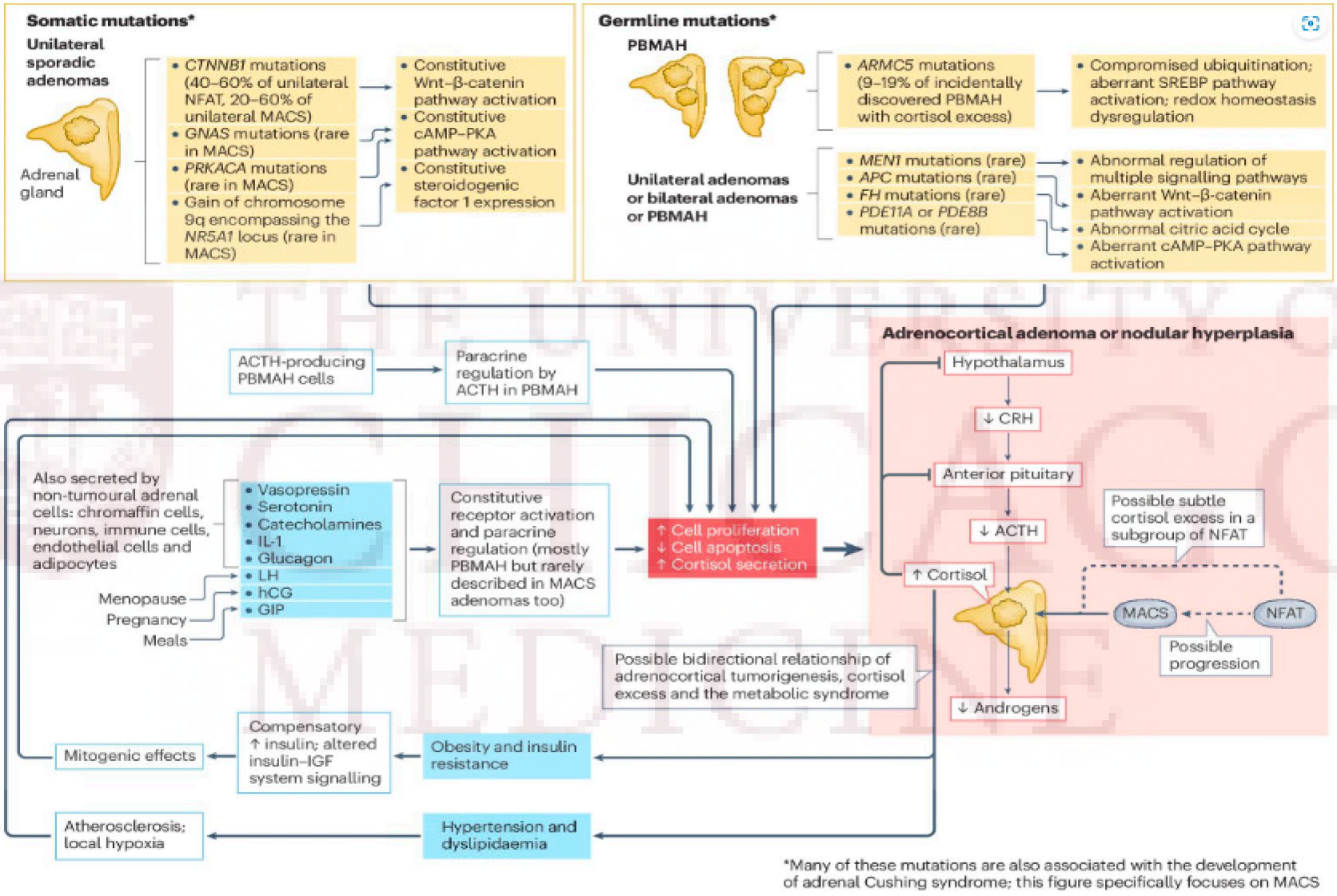


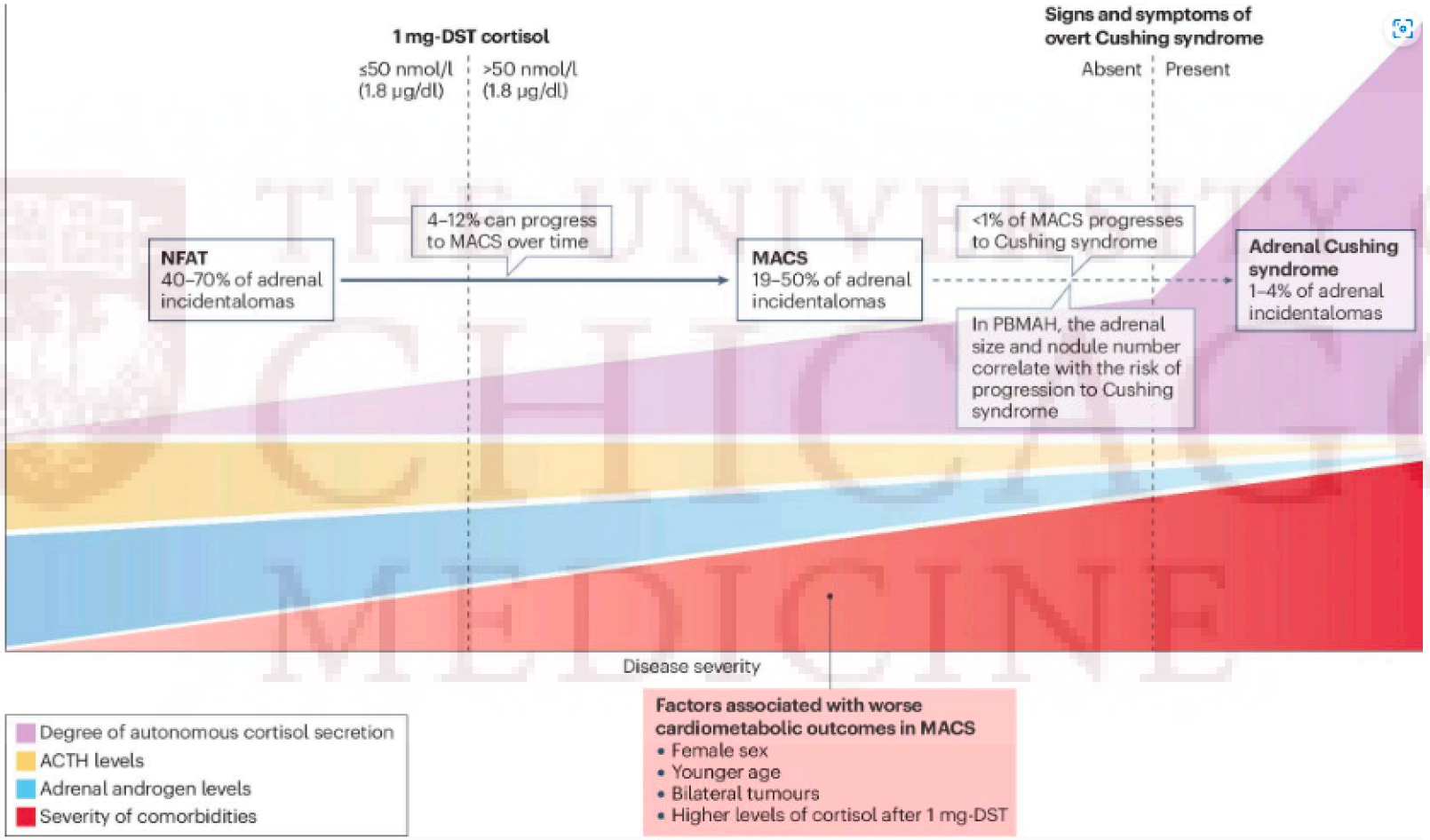
The combination of elevated serum concentrations of DHEA-S and ACTH excluded ACS with high accuracy, with the best performing cutoffs of DHEA-S > 100 mcg/dL and ACTH > 15 pg/mL.

Carafone LE, Zhang CD, Li D, Lazik N, Hamidi O, Hurtado MD, Young WF Jr, Thomas MA, Dy BM, Lyden ML, Foster TR, McKenzie TJ Bancos I. Diagnostic Accuracy of Dehydroepiandrosterone Sulfate and Corticotropin in Autonomous Cortisol Secretion. Biomedicines. 2021 Jun 28;9(7):741. doi: 10.3390/biomedicines9070741. PMID: 34203283; PMCID: PMC8301396.

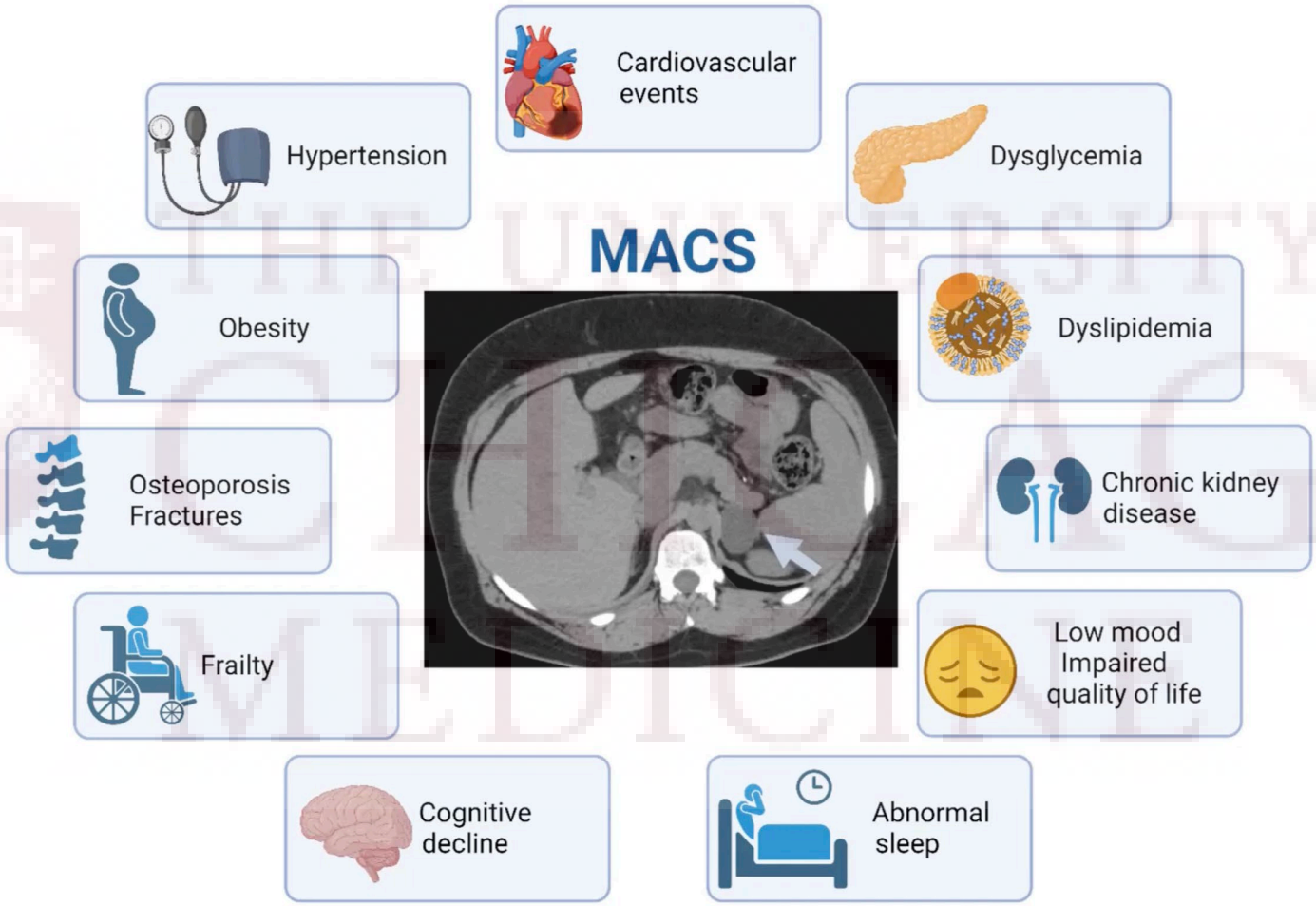
MACS: Pathophysiology



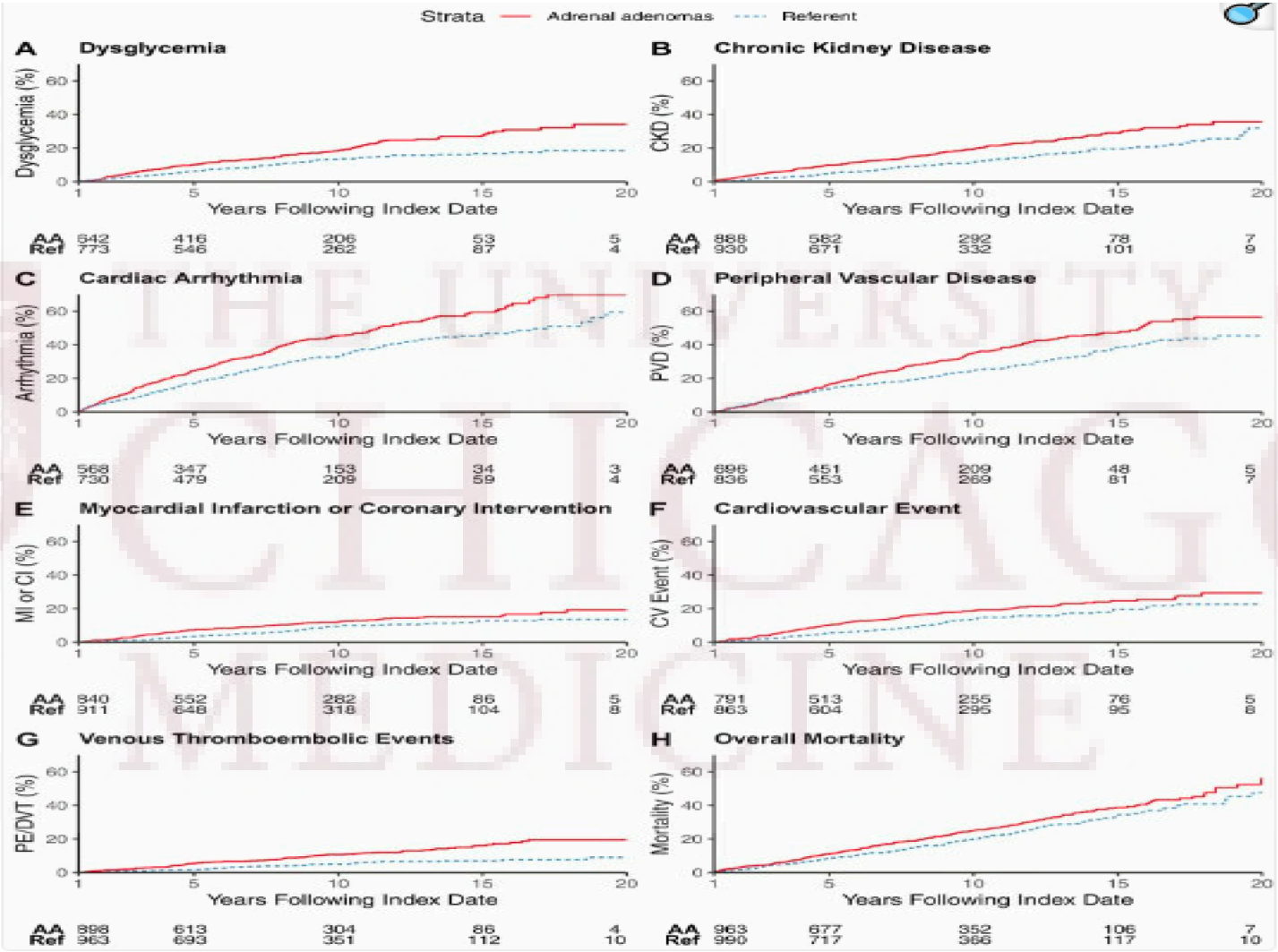
Natural History of Mild Autonomous Cortisol Secretion



Comorbidities and Complications of MACS



Incidence of Cardiometabolic Disease



Zhang CD et all. Cardiometabolic Outcomes and Mortality in Patients with Adrenal Adenomas in a Population-based Setting. J Clin Endocrinol Metab. 2021 Oct 21;106(11):3320-3330. doi: 10.1210/clinem/dgab468. PMID: 34185830; PMCID: PMC8530703.

MACS: Treatment

- No standardized treatment
- **Conservative**: Monitoring and treatment of MACS-associated comorbidities.
- **Surgical**: Adrenalectomy
- **Medical Therapy**: Targeting cortisol production, metabolism, or sensitivity/clinical trials.
- **Other:** Genetic testing if PBMAH (Primary bilateral macronodular adrenal hyperplasia) is suspected

Surgical Management

- Improvement in HTN, DM, Obesity and Hyperlipidemia in patient with MACa after adrenalectomy

Table 3 Effect of adrenalectomy on outcomes in patients with subclinical Cushing's syndrome.

Outcome	Number of studies	% improved	Difference in means	CI 95% lower limit	CI 95% upper limit	I^2 (%)
Hypertension ($n=265$)	21	60.5%		50%	71%	72
Diabetes mellitus type 2 ($n=120$)	20	51.5%		39%	64%	59
Dyslipidemia ($n=102$)	13	24%		13%	35.5%	58
Obesity ($n=128$)	16	45%		32%	57%	64
Systolic blood pressure (mmHg)	8		−12.72	−18.33	−7.1	61
Diastolic blood pressure (mmHg)	7		−9.34	−14.83	−3.85	76
BMI (kg/m^2)	7		−1.96	−3.32	−0.59	68
Fasting glucose (mmol/L)	4		−7.99	−13.9	−2.09	27
HbA1c (SMD)*	3		−0.96	−1.43	−0.49	53
LDL cholesterol (mg/dL)	2		−0.12	−37.7	37.5	53
HDL cholesterol (mg/dL)	3		2.9	−3.4	9.2	53
Triglycerides (mg/dL)	3		−23	−36.7	−9.2	0

BMI, body mass index; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SDM, standardized mean difference, I^2, study heterogeneity.

- Post-operative adrenal insufficiency is seen in around 50% of patients with MACS who undergo unilateral adrenalectomy

Irina Bancos, et all. , THERAPY OF ENDOCRINE DISEASE: Improvement of cardiovascular risk factors after adrenalectomy in patients with adrenal tumors and subclinical Cushing's syndrome: a systematic review and meta-analysis, European Journal of Endocrinology, Volume 175, Issue 6, Dec 2016, Pages R283–R295, https://doi.org/10.1530/EJE-16-0465

Back to our patient

- Diagnosed with MACS
- Evaluated by Endocrine Surgery: Underwent left adrenalectomy in December 2024
- Postoperative Course: Developed glucocorticoid withdrawal syndrome with concern for adrenal insufficiency
- Discharged on hydrocortisone (HC) taper
- Post-hospital follow-up visit :
- On Hydrocortisone (Total daily dose 20 mg daily)
- Re-evaluation of HPA axis
  - AM cortisol 11.3
  - ACTH 23
- Hydrocortisone stopped

Summary

- **Epidemiology of MACS:**
  30% of all adrenal adenomas
- **Diagnosis of MACS:**
- **Dexamethasone suppression test**
  - Low or low normal ACTH and DHEAS
  - Cortisol >1.8 mcg/dL
- **Consequence of MACS:**
  - Hypertension, diabetes, weight gain, muscle mass loss, osteoporosis, fractures
  - Insomnia, mood changes, brain fog, low quality of life
- **Management of MACS:**
  - Individualized
- **Options:**
    - Adrenalectomy
    - Medical therapy targeting cortisol
    - Management of consequences of MACS with medications (antihypertensive medications, etc)

Learning Objectives

1) Review the general approach to evaluating adrenal dysfunction, with a focus on Mild Autonomous Cortisol Secretion (MACS) and its diagnostic criteria

2) Discuss the clinical spectrum of MACS, including associated comorbidities, potential complications, and differential diagnoses

3) Explore treatment strategies and management options for MACS, including considerations for surgical and nonsurgical approaches

References

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Departments of Medicine and Pediatrics
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ENDORAMA

"45-Year-Old Female Referred for Adrenal Mass"
Presented by:
Fawsia Osman, M.D.

And

"An approach to MASLD in the endocrine clinic"
Presented by:
Kerim Kaylan, M.D., Ph.D.

January 9, 2025 - 4:30 p.m. - via ZOOM

Attendance earns 1 *AMA PRA Category 1 credit™*

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