Ipertensioni resistenti endocrine

10.000 bambini

4%

400

10.000 adulti

40%

4000

Neonati		Età scolare		Adolescenti		Adulti	
Primitiva	**0**	**Primitiva**	**50**	**Primitiva**	**350**	**Primitiva**	**3600**
Secondaria	**400**	**Secondaria**	**350**	**Secondaria**	**50**	**Secondaria**	**400**
Coartazione aortica	120	**Nefropatie**	220	**Nefropatie**	30	**OSAS**	120
Renovascolare	100	**Coartazione aorta**	70	**Coartazione aorta**	10	**Iperaldosteronismo primario**	90
Nefropatie	80	**Renovascolare**	35	**Renovascolare**	5	**Renovascolare**	80
Neoplastica	10	**Endocrina**	15	**Endocrina**	1	Nefropatie	40
Endocrina	4	Neoplastica	15	Neoplastica	1	**Endocrina**	20
Altre	…	Altre		Altre		Altre	

ESH/ESC guidelines

In che caso valutare se presente una ipertensione secondaria?

Cause endocrine di ipertensione (resistente)

Patologie surrenaliche	**Iperaldosteronismo primario (20%)**	Sporadico, familiare (tipo1-4)
	Feocromocitoma	Sporadico (80%), genetico (20%)
	Ipercortisolismo endogeno ACTH-indipendente	Adenomi, carcinomi, iperplasia (PPNAH, AIMAH)
	Eccesso deossicorticosterone	Deficit 11β-idrossilasi 17α-idrossilasi Neoplasia DOC secernente Resistenza cortisolo
Patologia extrasurrenalica	Distiroidismo	Tireotossicosi/Ipotiroidismo
	IperPTH	
	Ipercortisolismo endogeno ACTH-dipendente	Malattia Cushing o ACTH ectopico
	Acromegalia	
	Pseudoiperaldosteronismo	Difetto 11βHSD2 AME acquisita (liquerizia) Sindrome di Liddle

William, Endocrine Reviews, 2017

Cause endocrine di ipertensione (resistente)

		SCREENING
Patologie surrenaliche	**Iperaldosteronismo primario (20%)**	ARR
	Feocromocitoma	Metanefrine
	Ipercortisolismo endogeno ACTH-indipendente	1mg-DEX, 24h UFC, LNSC
	Eccesso deossicorticosterone	steroidi
Patologia extrasurrenalica	Distiroidismo	TSH, FT4
	IperPTH	Calcio fosforo, PTH, 25OHvitD
	Ipercortisolismo endogeno ACTH-dipendente	1mg-DEX, 24h UFC, LNSC
	Acromegalia	IGF-1
	Pseudoiperaldosteronismo	steroidi

William, Endocrine Reviews, 2017

Quali alterazioni di laboratorio nell’iperaldosteronismo primario?

(perché no ipernatriemia)

Quale differenza tra iperaldosteronismo primario e apparente eccesso mineralocorticoidi non mediato da aldosterone (pseudoiperladosteronismo)?

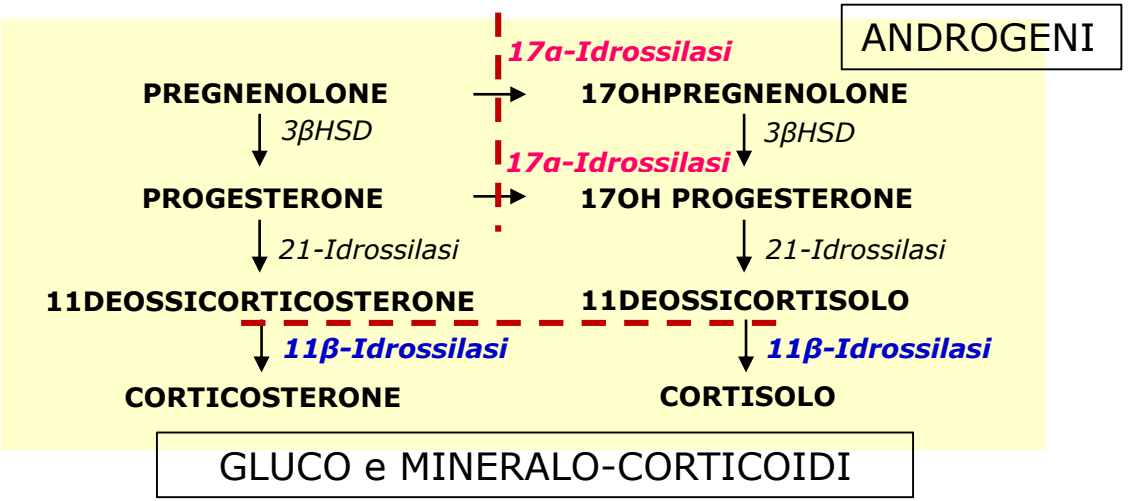
Quali alterazioni di laboratoirio nella renovascolare?

Eccesso mineralocorticoidi non mediato da aldosterone

Ipertensione arteriosa, ipokaliemia (± alcalosi metabolica), soppressione RAAS

SURRENE (DOC) Deficit 17α-idrossilasi, 11β-idrossilasi
Neoplasia DOC secernente
Resistenza cortisolo

EXTRA SURRENE Difetto genetico 11βHSD2 o liquerizia
Sindrome di Liddle (difetto canale Na^+)



Patologia	24h UFC	Urinary cortisol: cortisone ratio	DOC	11deossicortisolo	Androstenedione	DHEAS
17α-idrossilasi	↓	-	↑↑	-	↓	↓
11β-idrossilasi	↓	-	↑↑↑	↑↑↑	↑↑↑	↑↑↑
Neoplasia DOC secernente	-	-	↑↑↑	-	-	-
Difetto 11βHSD2	↑↑↑	↑↑↑		-	-	-

William, Endocrine Reviews, 2017

Caso clinico

SINDROME CONN

La sindrome di Conn è una malattia causata da un eccesso di mineralocorticoidi (aldosterone) o **iperladosteronismo primitivo**.

Essa è stata descritta per la prima volta nel **1955** da **Jerome W Conn**, in una giovane donna di 34 anni che si presentava per astenia, spasmi muscolari, ipertensione arteriosa e ipokaliemia e che veniva riscontrata affetta da un aldosteronoma, adenoma zona glomerulosa del surrene.

L'iperladosteronismo primitivo ha una prevalenza che varia dal 5.9 al 6.8% nella popolazione generale, arrivando fino al **12% nei pazienti con ipertensione e 20% nei pazienti con ipertensione resistente**.

L'iperladosteronismo primitivo può avere diverse cause tra cui: **adenoma** unilaterale o bilaterale, iperplasia surrenalica, carcinoma corticosurrene (pazienti giovani con masse voluminose). Tra le forme rare ricordiamo il GRA *glucocorticoid-remediable aldosteronism* (rara) legata alla fusione di CYP11B1 e CYP11B2.

L'iperaldosteronismo porta a eliminazione renale di potassio e aumentato riassorbimento di sodio con conseguenti **ipokaliemia**, espansione del volume extracellulare e **ipertensione**. Alcalosi (per aumentata eliminazione di idrogenioni a livellorenale). Astenia e spasmi muscolari (muscolo non si riesce a depolarizzare e contrarre). Stipsi.

Harrison

Gianluca, M, 48 anni

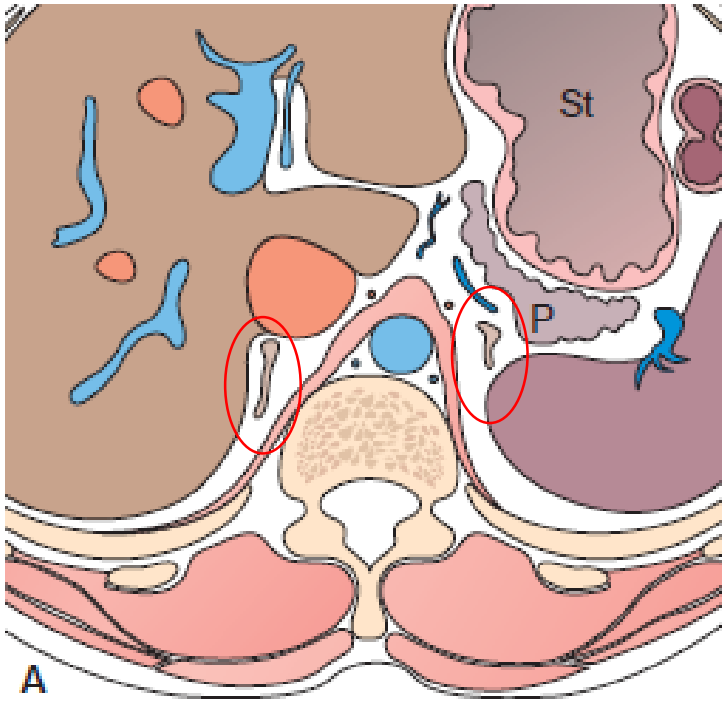
giunge in ambulatorio per **incidentaloma con ipertensione arteriosa resistente**.

PA 145/90 mmHg in terapia con nebivololo/idroclortiazide 5/25 mg, ramipril 10 mg, amlodipina 10 mg.
TC addome (controllo post nefrectomia per ca cellule chiare 3 anni prima) nodulo surrene destra di 1 cm densità <10HU.
LADA
Fratture vertebrali (D4,D5,D10) traumatiche.

Table 1
Categories of patients where the screening for primary aldosteronism is recommended.

Condition	Description
Severe hypertension	Hypertension stage 3, i.e. systolic blood pressure ≥180 mmHg and/or diastolic blood pressure ≥110 mmHg
* Resistant hypertension	Blood pressure values that remain above goal in spite of concurrent use of three antihypertensive agents of different classes. If tolerated, one of the three agents should be a diuretic, and all agents should be prescribed at maximum recommended (or maximally tolerated) antihypertensive doses.
Patients with hypertension associated with (permanent or intermittent) spontaneous or diuretic-induced hypokalemia	Serum potassium (K^+) < 3.5 mmoL/l in absence of other potential causes of hypokalemia (i.e. gastrointestinal disorders, abuse of licorice, etc.).
* Hypertension or hypokalemia associated with adrenal incidentaloma	Hypertensive patients with an adrenal mass detected on imaging.
Normal potassium levels (≥3.5 to ≤ 5.0 mmoL/l) associated with another of the above-mentioned indications for PA screening	
When hypertension-mediated organ damage and cardiovascular or renal morbidity are more severe than expected from the level and duration of hypertension	Hypertension-mediated organ damage such as microalbuminuria, renal disease, hypertensive retinopathy, left ventricular hypertrophy and diastolic dysfunction, etc.
Hypertension and sleep apnea	See 'Comorbidities' section for further explanations.
Hypertension and atrial fibrillation	See 'Comorbidities' section for further explanations.
Hypertension and a family history of early onset hypertension and/or cerebrovascular accident at a young age (<40 years) and of first-degree relatives with primary aldosteronism	See 'Testing for familial forms of primary aldosteronism and detection of genetic mutations' for further explanations.
Newly-presenting patients with hypertension and a high chance of cure with adrenalectomy, as, for example, young, women, with a short duration of hypertension	

Rossi GP, International Journal of Cardiology Hypertension, 2020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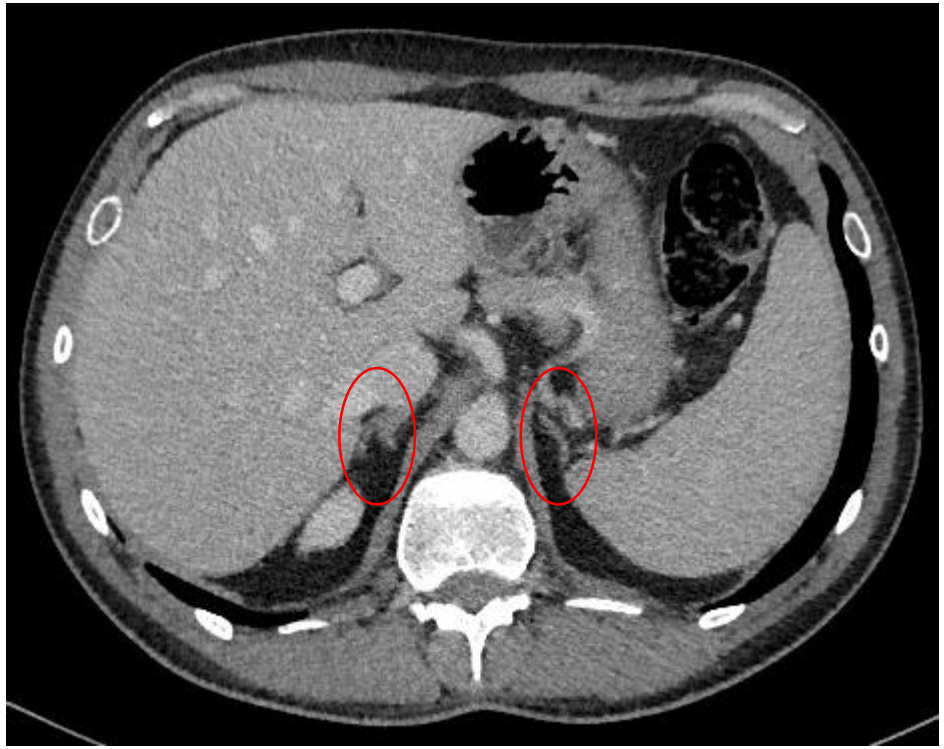
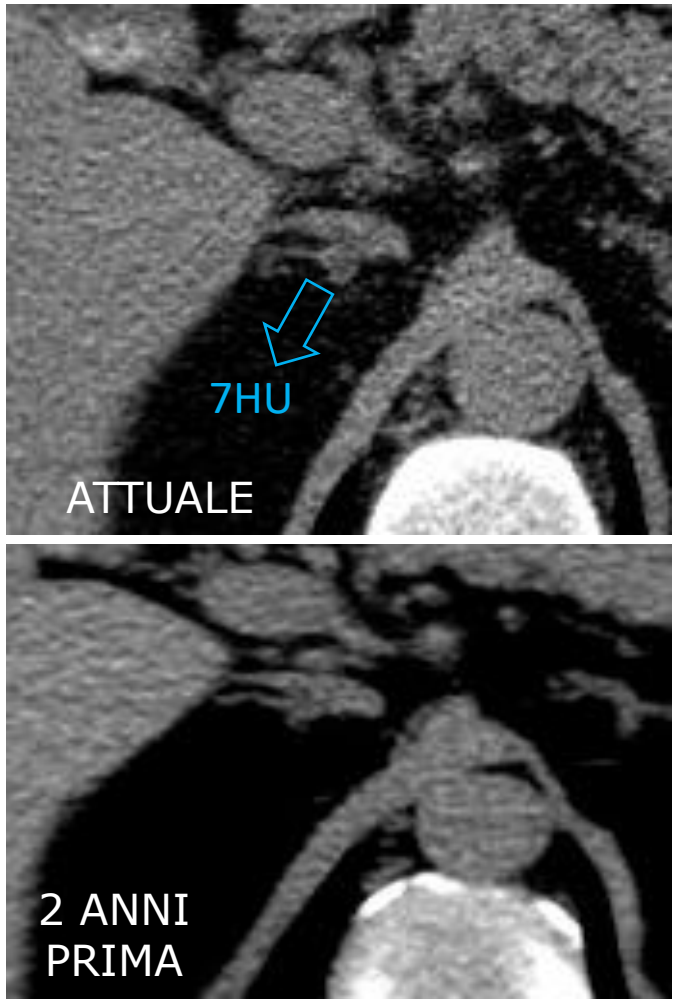


1. Definizione natura incidentaloma



TC SENZA MDC
per valutare densità (HU)

<10HU; < 4 cm → **STOP**

>10HU; > 4 cm →
- TC con mdc (tempi per studio surreni)
- RM (Chemical Shift)
- TC senza mdc a 6-12 mesi (follow-up)
- FDG-PET/TC
- Chirurgia

Extra-adrenal malignancy. Younger patients with a history of malignancy are more likely to have a metastasis. (…) Neverheless, adrenal lesions characterized as benign by noncontrast CT require no further imaging FU.

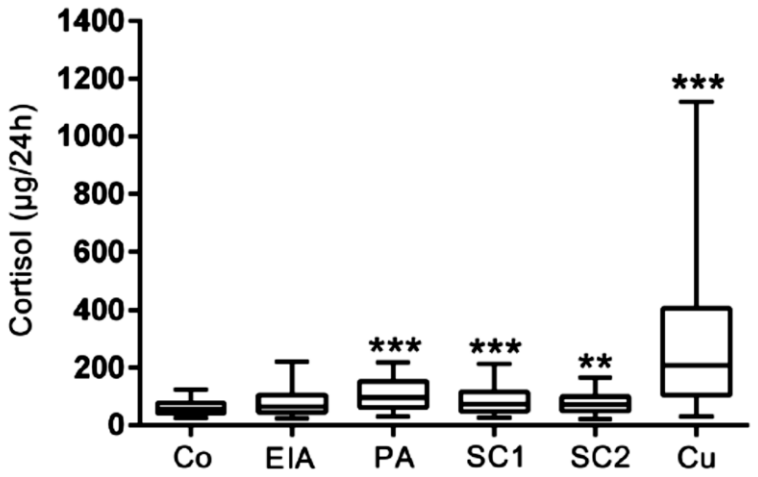
Fassnacht M, EJE 2016

2. Test di screening: ARR (e non solo)

Esame	Esito	Valori di riferimento
Aldosterone	26.4 ng/dL	1.5-15
Renina	0.5 uU/mL	2.8-40
ARR	559	< 2.06 (**ARR-App**)
Potassio	3.53 mEq/L	3.5-5.10
Cortisolo 1 mg DEX	0.74 ug/dL	<1.8

PRIMA di misurare ARR:

- Correggere ipokaliemia
- Normale intake sodico
  [considerare sodiuria e potassiuria 24h]
- Sospendere bloccanti RAAS, diuretici, βbloccanti NSAIDs EP per 4 settimane

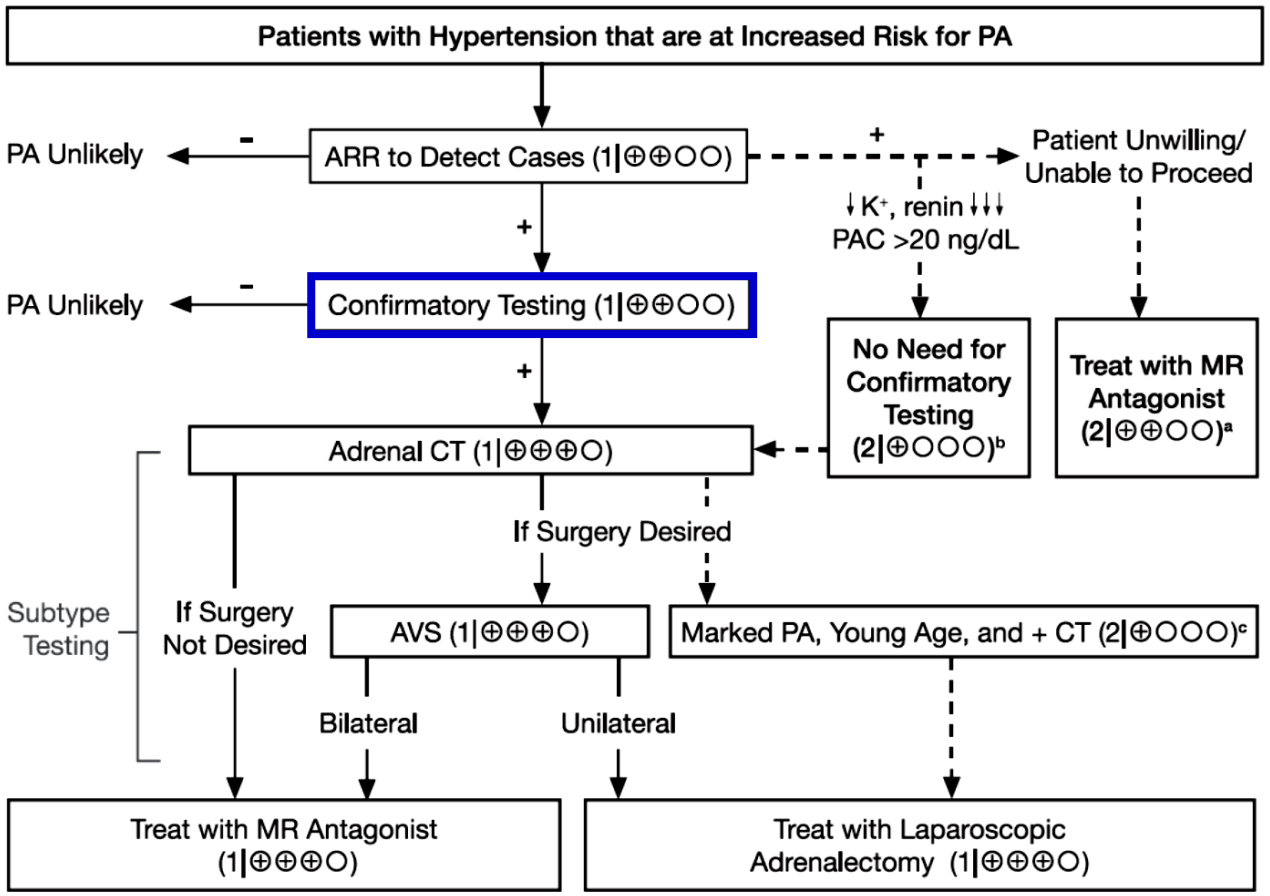


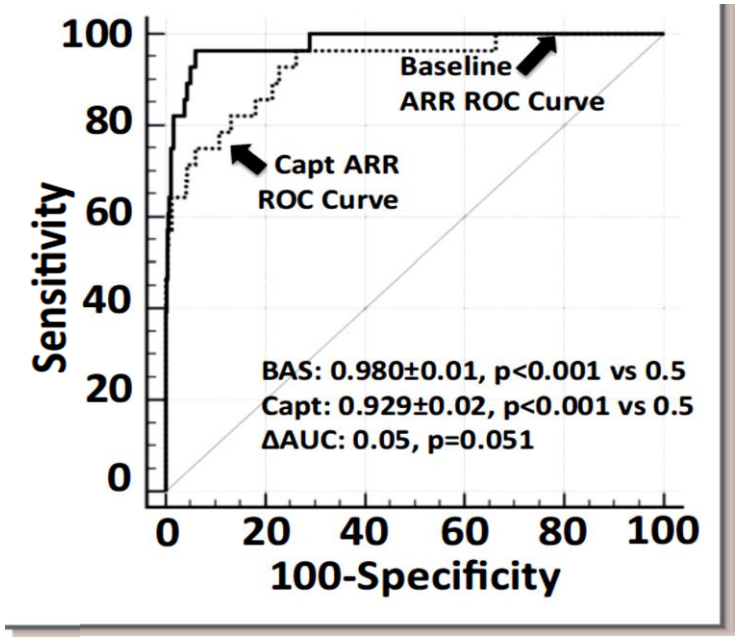
Arlt W, JCI Insight 2017

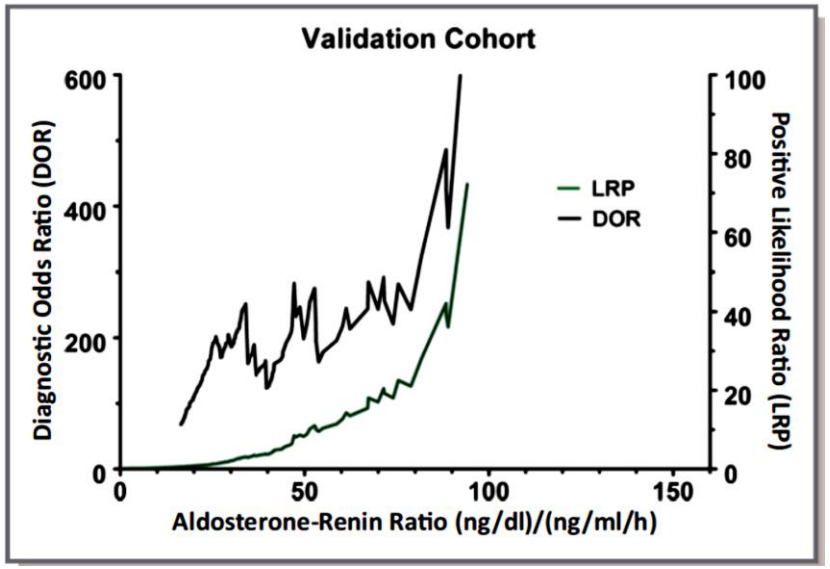
In patients with adrenal incidentalomas, a 1mg DEX <1.2 µg/dl rules out postsurgical hypocortisolism
Eller-Vainicher C, J Endocr Soc 2020

3. Test di conferma iperaldosteronismo primario

Aldosterone dopo salina	18	< 5 ng/dL assente







3. Adrenal vein sampling

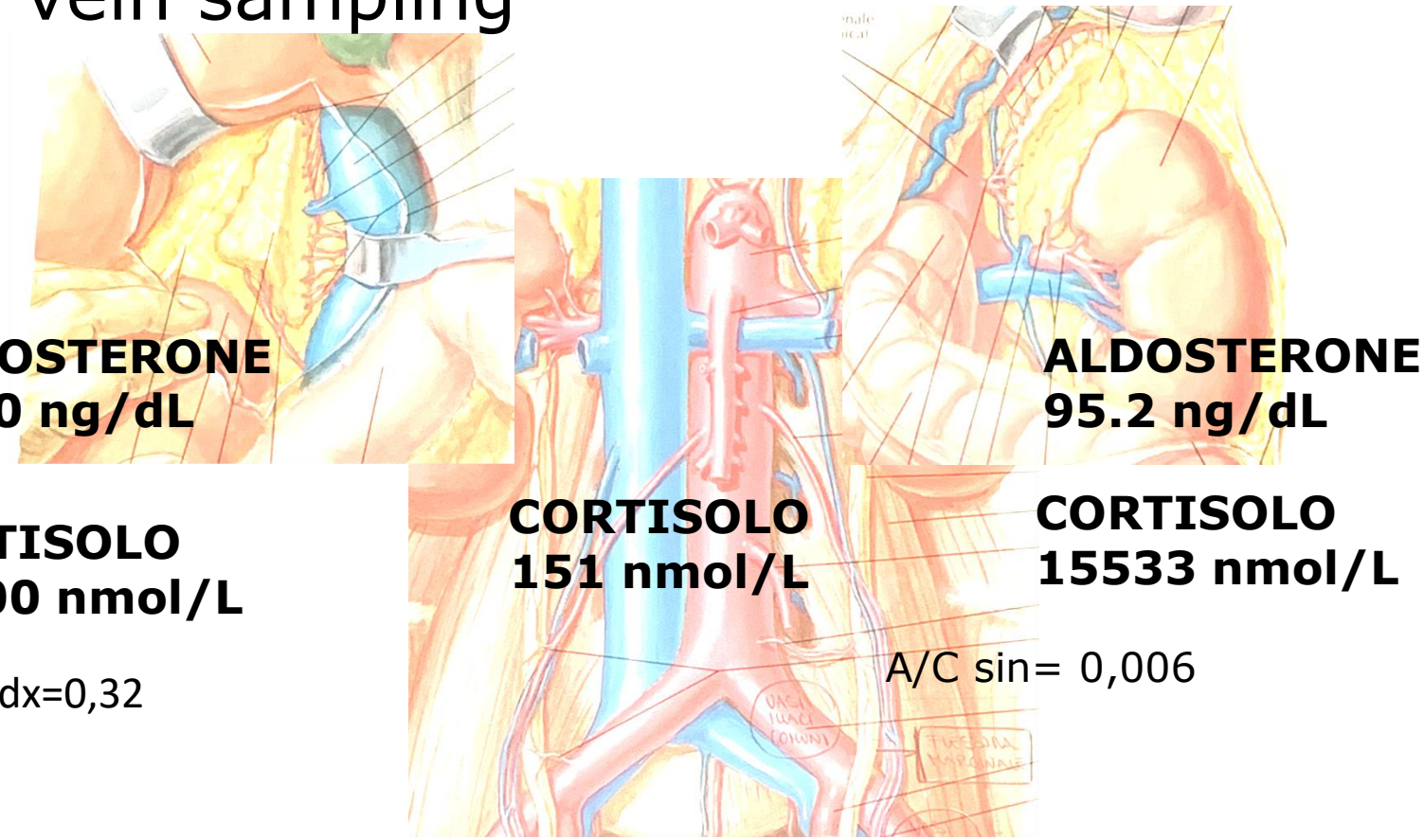
10 good reasons why adrenal vein sampling is the preferred method for referring primary aldosteronism patients for adrenalectomy

Gian Paolo Rossi[a,b], Paolo Mulatero[c], and Fumitoshi Satoh[d]

1. **Size of the disorder** – even when an adrenal lump is visible on imaging in many cases the primary aldosteronism is sustained by one, or more, smaller, and CT-invisible nodules not even reaching 5 mm in maximal diameter
2. **Lack of specificity of the adrenal masses**
3. **Safety** AVS is safe, the rate of complications being in the range of 0.5-0.6% (hematomas and adrenal vein rupture)

Rossi GP, J Hypertens 2019

3. Adrenal vein sampling



ALDOSTERONE
9780 ng/dL

CORTISOLO
29700 nmol/L

A/C dx=0,32

CORTISOLO
151 nmol/L

ALDOSTERONE
95.2 ng/dL

CORTISOLO
15533 nmol/L

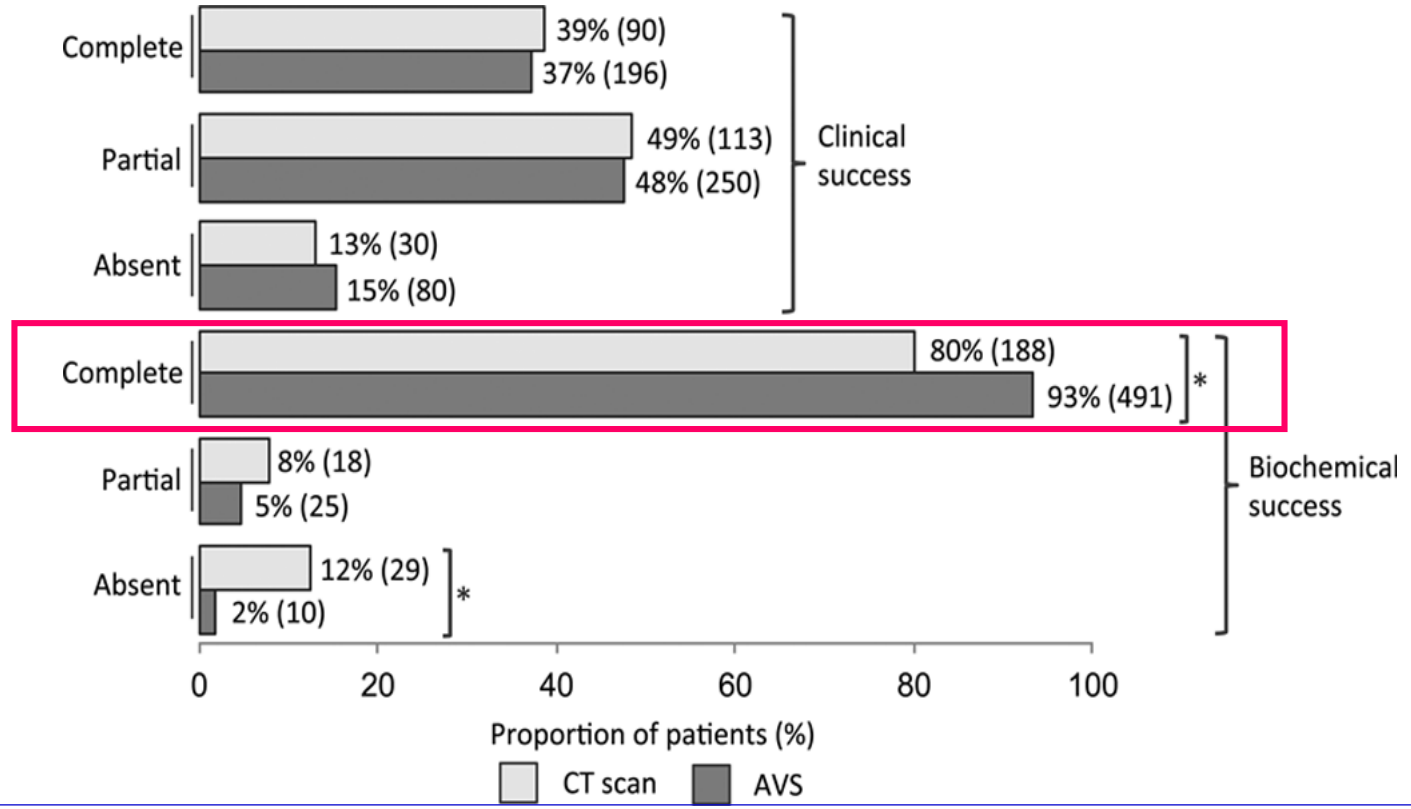
A/C sin= 0,006

1. **SELECTIVITY INDEX**. ADRENAL VEIN TO PERIPHERAL VEIN CORTISOL RATIO. SI ≥ 2 unstimulated ≥3 during cosyntropin stimulation
2. ALDOSTERONE LEVELS are NORMALIZED TO CORTISOL (A/C)
3. **LATERAZLIZATION INDEX** (LI). Each side A/C ratio is divided by the other. LI between 2-4 under unstimulated conditions, and 2.6-4 during cosyntropin stimulation

England RW, J Clin Med 2018

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*



Williams TA, Hypertension 2018

SURRENECTOMIA LAPAROSCOPICA

Descrizione microscopica/Diagnosi. Il quadro morfoistopatologico può essere coerente con quello di una iperplasia adenomatoide della corticale del surrene in sindrome di Conn.

Sodio 139 mEq/L, Potassio 3.9 mEq/L,
Cortisolo 335 nmol/L con ACTH 43 pg/mL,
Aldosterone 4.1 ng/dL; Renina 2.5 µUI/mL

PA 120/75 mmHg, ridotto la terapia antipertensiva (triatec 5 mg x 1 e nebivololo 5 mg x 1)