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PROF. DOUTOR FERNANDO FONSECA EPE HOSPITAL

Incidentalomas da Supra-renal

Avaliação Funcional

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9 de Maio 2013

Clínica sugestiva de hiperfunção ou malignidade

Diagnóstico	Clínica	Rastreio laboratorial
FEOCROMOCITOMA	HTA Crises paroxísticas (cefaleias, palpitações, palidez, tremor, hipersudorese)	**Metanefrinas fraccionadas urinárias e Plasmáticas**
S. CUSHING **Clínico / sub-clínico**	Obesidade central, Plétora facial, pele fina, estrias purpuricas >1cm Fragilidade vascular, Fraqueza muscular prox.	**Cortisol livre ur** **P. Dexametasona 1mg**
Hiperaldosteronismo 1º	**HTA** Hipokaliémia (< 3.8)	**Aldosterona pl e ARP**
Carcinoma S-R	Sintomas efeito de massa, sintomas do excesso de CE, mineralocorticoides, androgenios ou estrógénios.	**SDHEA** **Doseamento de acordo com clínica**

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Avaliação Laboratorial do Incidentaloma

Table 2. Laboratory Evaluation of the Patient with Adrenal Incidentaloma.

Possible Diagnosis	Screening Test	Causes of False Positive Results	Confirmatory Tests
Subclinical Cushing's syndrome	Overnight dexamethasone (1 mg) suppression test; abnormal result: serum cortisol, >5 μg per deciliter (138 nmol per liter); some clinicians use a higher dose of dexamethasone (e.g., 3 mg instead of the standard 1 mg) to reduce the possibility of a false positive result without a change in sensitivity	Medications that accelerate hepatic metabolism of dexamethasone (e.g., anticonvulsants); noncompliance with dexamethasone regimen	Consider the following tests: serum corticotropin, cortisol in a blood specimen and 24-hr urine specimen, midnight salivary measurement of cortisol, and a formal 2-day high-dose dexamethasone suppression test (the result is considered abnormal when the cortisol level in the 24-hr urine specimen is greater than the lower limit of the normal range for the local laboratory)
Pheochromocytoma	Measurement of fractionated metanephrines and catecholamines in a 24-hr urinary specimen; imaging phenotype may also suggest pheochromocytoma	Any situation (e.g., illness requiring hospitalization) or medication (e.g., tricyclic antidepressant) that increases endogenous production of catecholamines[7]	Consider iodine-123 metaiodobenzylguanidine scintigraphy, MRI, subspecialty consultation, and surgery
Primary aldosteronism	Morning measurement of the plasma aldosterone concentration and plasma renin activity,* which can be performed while the patient is receiving any antihypertensive drug except spironolactone (Aldactone, Searle), eplerenone (Inspra, Pfizer), or high-dose amiloride (Midamor, Merck); the plasma aldosterone concentration and plasma renin activity ratio of ≥20 and a plasma aldosterone concentration of ≥15 ng per deciliter are positive results (but the cutoff for a positive result is laboratory-dependent)	Assay and biologic variability	To confirm the diagnosis of primary aldosteronism: aldosterone suppression testing with either a saline infusion test or 24-hour urinary aldosterone excretion test while the patient maintains a high-sodium diet[8] To confirm that the adrenal mass (and not bilateral adrenal hyperplasia) is the source of aldosterone excess in patients with documented primary aldosteronism, adrenal venous sampling should be considered[8]

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Young We. NEJM 2007

Feocromocitoma

European Journal of Endocrinology (2009) 161 355–361 ISSN 0804-4643

CLINICAL STUDY

Frequent incidental discovery of phaeochromocytoma: data from a German cohort of 201 phaeochromocytoma

Robert Kopetschke, Mario Slisko[1], Aylin Kilisli, Ulrich Tuschy[2], Henri Wallaschofski[3], Martin Fassnacht[4], Manfred Ventz, Felix Beuschlein[1], Martin Reincke[1], Nicole Reisch[1] and Marcus Quinkler

Conclusions: Owing to better availability and accessibility of imaging procedures, the number of incidentally discovered phaeochromocytoma is increasing and reaches nearly 30% in our study population. Every adrenal incidentaloma should be investigated for the presence of phaeochromocytoma.

Excluir sempre o feocromocitoma num Incidentalmoma

Kopetschke R et al. EJE 2009

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Feocromocitoma

Table 3. Sensitivities and Specificities of Biochemical Tests for Diagnosis of Hereditary and Sporadic Pheochromocytoma*

	Sensitivity, %†		Specificity, %‡	
	Hereditary	Sporadic	Hereditary	Sporadic
Plasma				
Free metanephrines	97 (74/76)	99 (137/138)	96 (326/339)	82 (249/305)
Catecholamines	69 (52/75)	92 (126/137)	89 (303/339)	72 (220/304)
Urine				
Fractionated metanephrines	96 (26/27)	97 (76/78)	82 (237/288)	45 (73/164)
Catecholamines	79 (54/68)	91 (97/107)	96 (312/324)	75 (159/211)
Total metanephrines	60 (27/45)	88 (61/69)	97 (91/94)	89 (79/89)
Vanillylmandelic acid	46 (30/65)	77 (66/86)	99 (310/312)	86 (132/153)

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Lenders et al, Jama 2002

Feocromocitoma

- Se valores normais em indiv. assintomático: exclui o dx
- Se 3-4 x o limite superior do normal estabelece o dx
- Se valores intermédios: repetir doseamentos/outros exames

- Factores de interferência:

  - Antidepressivos tricíclicos
  - Situações de stress (internamentos)

- Não é recomendado suspender antihipertensores pelo risco clínico

  - *Não há um teste Gold standard*.

Síndrome de Cushing subclínico

- Termo correcto SC “moderado”

- Desafio dx: largo espectro de apresentações

  Heterogeneidade fenotípica traduz a variabilidade da secreção de cortisol

- Não há um teste Standard (tal como no SC)

Síndrome de Cushing subclínico

- P. DEXA 1mg: TESTE UNIVERSAL

Cortisol plasmático 8-9h: Cut-off não é consensual:

> 5 µg/dl / > 1,8 µg/dl (↑ F +)

< 1,8 µg/dl excluí dx

- Cortisol plasmático 24h/Cortisol salivar 24h
- ACTH
- UFC

27% dos doseamentos UFC são incorrectos

Perry LA and Grossman AB. Ann Clin Biochem 1997

- P. DEXA 2mg, P. CRH, SDHEA

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Hiperaldosteronismo Primário (HAP)

- Rastreio do HAP em doentes com incidentaloma e HTA

- Doseamento:

1. Aldosterona plasmática (>15ng/dL)
2. Renina directa / Actividade da renina plasmática

  - Manhã, 2h após levantar
  - Dieta sem restrição de sal (3 dias)
  - Após correcção da hipokaliémia
  - Suspender Espironolactona 4 sem.
  - Suspender outros antihipertensores ??

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Hiperaldosteronismo Primário (HAP)

TABLE 5. ARR cut-off values, depending on assay and based on whether PAC, PRA, and DRC are measured in conventional or SI units

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

ARR, Aldosterone-renin ratio; PAC, plasma aldosterone concentration; PRA, plasma renin activity; DRC, direct renin concentration; SI, Système International.

Primary Aldosteronism: The Endocrine Society's Clinical Aldosteronism 2008

Testes Confirmatórios de HAP
DD do HAP

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Carcinoma Adrenocortical (ACC)

- Não há um teste (Bq ou citológico) pré-operatório definitivo
- RISCO de ACC: Imagiológico
- IMPORTÂNCIA da avaliação Hormonal Prévia:
    - ACC secretor de cortisol: risco de Insuficiência adrenal pós cirurgia
    - QQ marcador hormonal identificado previamente é útil no follow-up pós-operatório
    - Clínica orienta a avaliação: androstenediona, test, SDHEA, 17β estradiol (pós-menopausa, homens)

Follow-up do Incidentaloma

Table 6 Long-term follow-up of adrenal incidentalomas.

Study (reference)	Follow-up (years (range))	Mass size enlargement	Mass size reduction	Malignancy	Hyperfunction
Reincke *et al.* 1989 (103)	1.2 (0.5–4)	0/11 (0%)	0/11 (0%)	0/11 (0%)	0/11 (0%)
Vitkkala *et al.* 1989 (73)	2 (0.8–4.1)	0/12 (0%)	1/12 (8.3%)	0/12 (0%)	0/12 (0%)
Herrera *et al.* 1991 (20)	2 (0.1–5.6)	5/159 (3.1%)	4/159 (2.5%)	0/159 (0%)	0/287 (0%)
Jockenhovel *et al.* 1992 (104)	2.7 (1–8.4)	1/18 (5.5%)	2/18 (11.1%)	0/18 (0%)	2/18 (11.1%)
Osella *et al.* 1994 (64)	1.0	2/9 (22.2%)	0/9 (0%)	0/9 (0%)	1/9 (11.1%)
Benesik *et al.* 1995 (55)	1.5 (0.3–3.4)	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/27 (0%)
Courtade *et al.* 1997 (105)	3.6 (0.3–6.3)	0/25 (0%)	10/25 (40%)	0/25 (0%)	0/32 (0%)
Bastounis *et al.* 1997 (54)	3.6 (1–5.3)	2/60 (3.3%)	0/60 (0%)	0/60 (0%)	0/60 (0%)
Bondanelli *et al.* 1997 (56)	(0.5–1.5)	1/14 (7.1%)	0/14 (0%)	0/14 (0%)	0/14 (0%)
Terzolo *et al.* 1998 (71)	1	1/41 (2.4%)	NA	0/41 (0%)	0/41 (0%)
Barry *et al.* 1998 (106)	7 (0.1–11.7)	4/91 (4.4%)	0/91 (0%)	0/224 (0%)	0/224 (0%)
Terzolo *et al.* 1998 (87)	>1	0/53 (0%)	0/53 (0%)	0/53 (0%)	0/53 (0%)
Rossi *et al.* 2000 (67)	3.2 (0.7–6.1)	1/32 (3.1%)	0/32 (0%)	0/32 (0%)	1/32 (3.1%)
Siren *et al.* 2000 (107)	7 (2–16.3)	4/21 (19.0%)	7/21 (33.3%)	0/21 (0%)	0/27 (0%)
Mantero *et al.* 2000 (62)	>1	14/53 (26.4%)	NA	0/53 (0%)	2/53 (3.8%)
Grossrubatscher *et al.* 2001 (90)	2 (0.5–6.5)	10/53 (18.9%)	1/53 (1.9%)	0/53 (0%)	0/53 (0%)
Barzon *et al.* 2002 (53)	4.6 (2–12)	19/130 (14.4%)	3/130 (2.3%)	0/130 (0%)	10/130 (7.7%)
Libè *et al.* 2002 (108)	2.1 (1–10)	13/64 (20.3%)	0/64 (0%)	1/64 (1.6%)	4/64 (6.2%)
Total		78/873 (9.0%)	28/779 (3.6%)	1/1081 (0.09%)	20/1147 (1.7%)

Hiperactividade endócrina na evolução

Barzon L et al. EJE 2003

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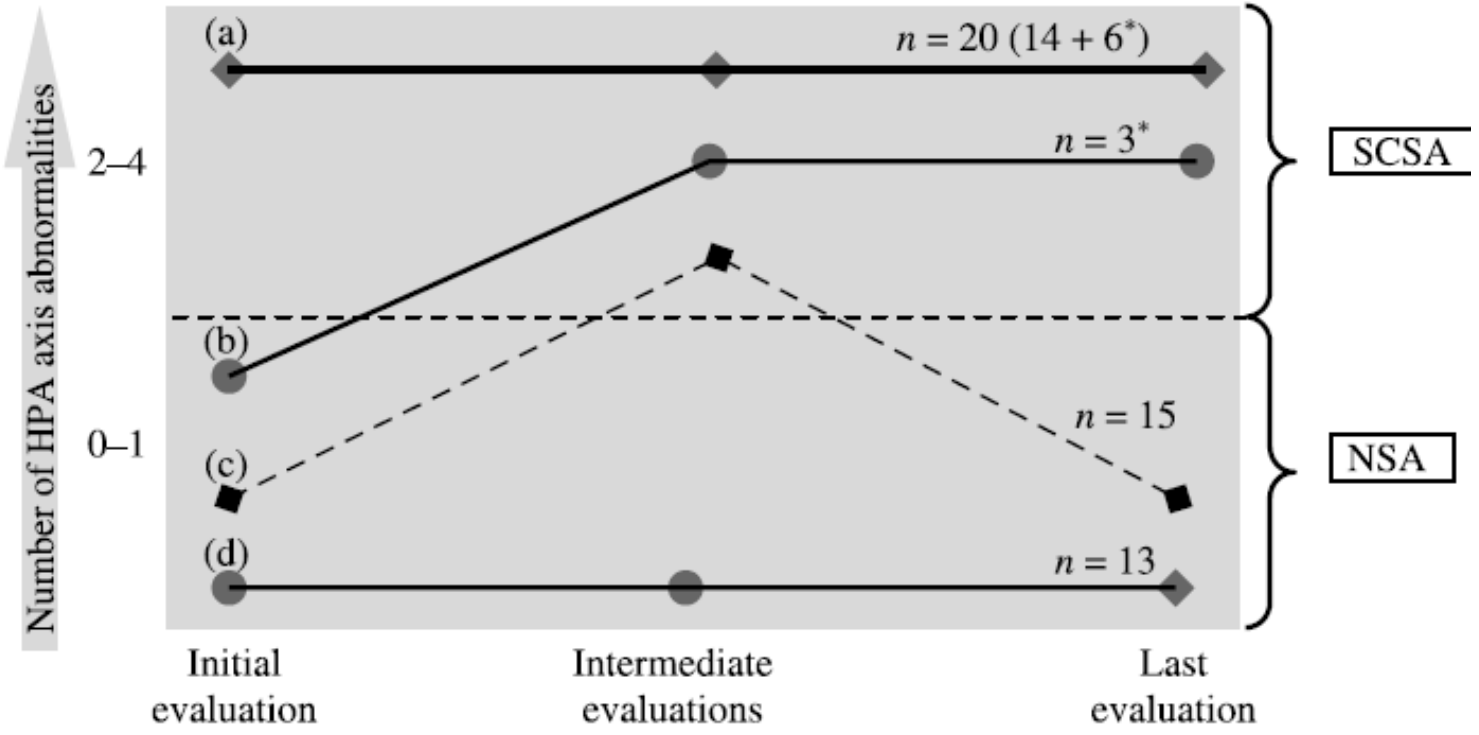
Follow-up do Incidentaloma

Avaliação hormonal anualmente durante 5 anos.



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Fagour et al, EJE 2009