

Adrenal Incidentalomas

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Adrenal Incidentalomas - Basics

- ✓ **Definition : Incidental Discovery**
- ✓ **Rate of discovery # 4 % over 50 yo**
Bilateral AI : 10-15 % of cases
- ✓ **Exclusion :**
 - **Find on purpose (ex: Workup of Hypertension)**
 - **Investigation/Staging of patients with cancer**
 - **Families with genetic disease**

Etiologies of adrenal incidentalomas.

Tumors of the cortex

Adenomas

Macronodular hyperplasia (including CYP21 enzymatic deficiency)

Carcinoma

Tumors of the medulla

Pheochromocytoma

Ganglioneuroma, ganglioneuroblastoma

Malignancy

Other tumors

Myelolipoma

Lipoma

Lymphoma, hemangioma

Liposarcoma, myoma, fibroma, neurofibroma, teratoma

Hormonal Hyperactivity

Cysts and pseudocysts

Hematoma and hemorrhage

Infections, granulomatosis (including tuberculosis)

Metastase, lymphoma, leukemia

Extra-adrenal masses (diverticula of the digestive tract, tail of pancreas, kidney cysts and tumors, accessory spleen, vascular lesions)

Adrenal Incidentalomas Basics

Etiologies

- ✓ The prevalence of etiologies depends on the inclusion criteria and referral pattern of the studies

Etio	Clinical Studies(%)	Surgical Series (%)
Aldosterone secreting Adenoma	1	6
Pheochromocytoma	5	14
Carcinoma	5	11
Metastasis	2	9

Etiologies of Incidentalomas in an endocrinology setting

Number of patients	Age Mean (years)	Size of mass Mean or median (cm)	Malignant		Benign				
			Primary adrenal carcinoma (%)	Metastases (%)	Total (%)	Non-functional (%)	Subclinical Cushing's (%)	Phaeo (%)	Aldosteronoma (%)
342	61	NG	1.2	0.3	98.6	95.9	1.2	2.9	0.0
66	58	3.1	0.0	0.0	100.0	85.3	11.8	1.5	1.5
46	NG	NG	4.3	2.2	93.5	NG	6.5	4.3	0.0
85	54	3.6	2.0	NG	NG	NG	6.0	1.0	NG
38	58	2.6	2.6	0.0	97.4	86.8	7.9	5.3	0.0
86	61	4.1	1.2	2.3	96.5	92.5	4.5	3.0	0.0
1004	56	3.6	4.7	0.7	94.6	85.1	9.2	4.2	1.6
70	54	2.9	1.4	0.0	98.6	94.3	5.7	0.0	0.0
67	59	2.5	0.0	0.0	100.0	88.1	4.5	5.3	1.8
200	58	3.2	1.9	0.7	97.4	89.7	6.4	3.1	0.6
			0.8–3.0	0.0–1.4	95.7–99.0	86.4–93.0	4.4–8.3	1.8–4.3	0.0–1.2
70	58	3.1	1.4	0.2	98.0	88.1	6.0	3.0	0.0

✓ The vast majority of AI are non functional benign tumors

Work-Up of Adrenal Incidentalomas

a step wise approach

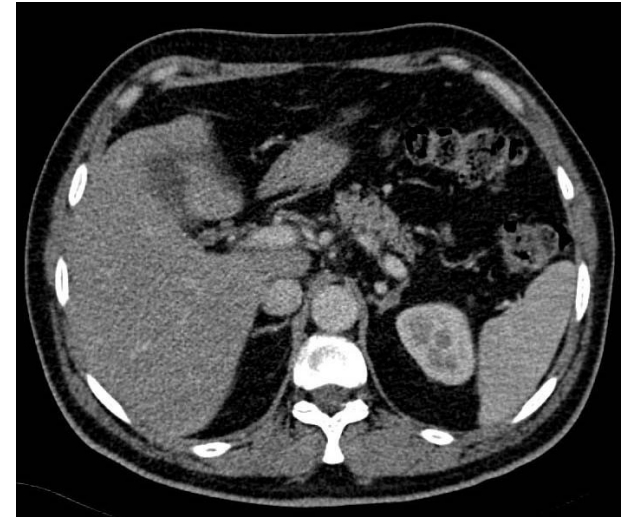


Case 1

68 yo woman : A 7 mm left adrenal nodule is found incidentally on CT for abdominal pain.

History : obesity associated to T2D treated with metformin. No history of malignancy.

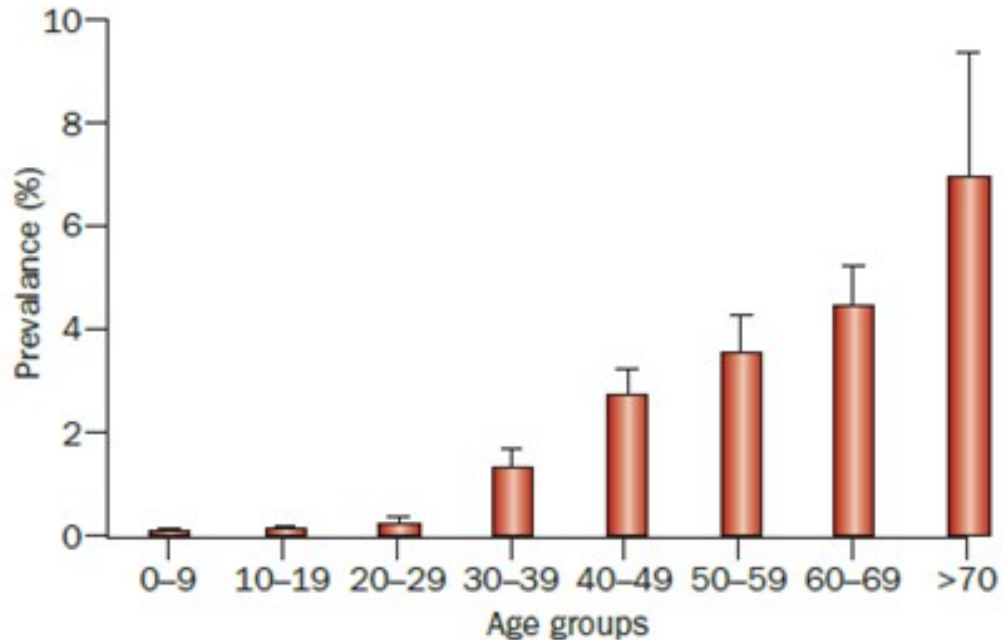
The nodule is homogeneous, density = 25 UI after contrast injection (no image in basal condition).



Which investigations do you recommend ?

E - Do nothing

Adrenal Incidentalomas - Definitions

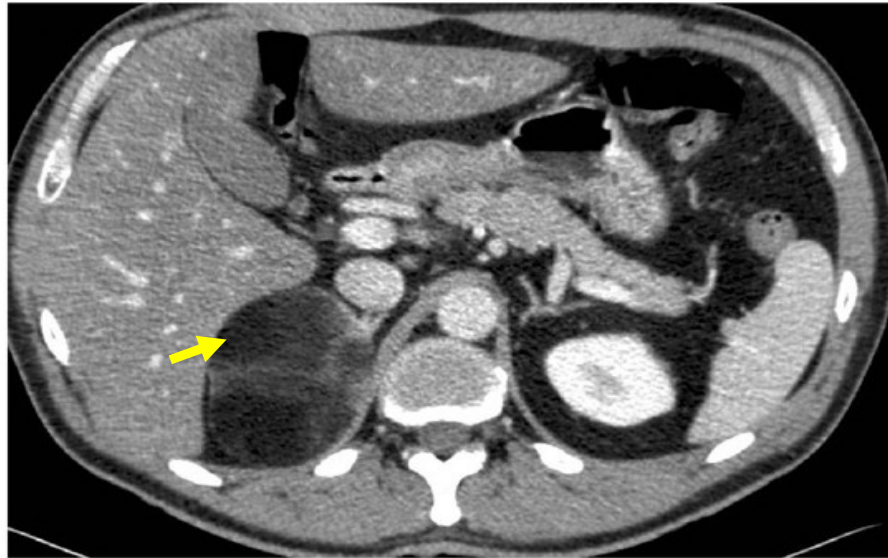


Vassiliadi D et al. Nat Endocrinol 2011

No indication to perform work up or follow up for AI < 10 mm

CT Scanning is the primary imaging test

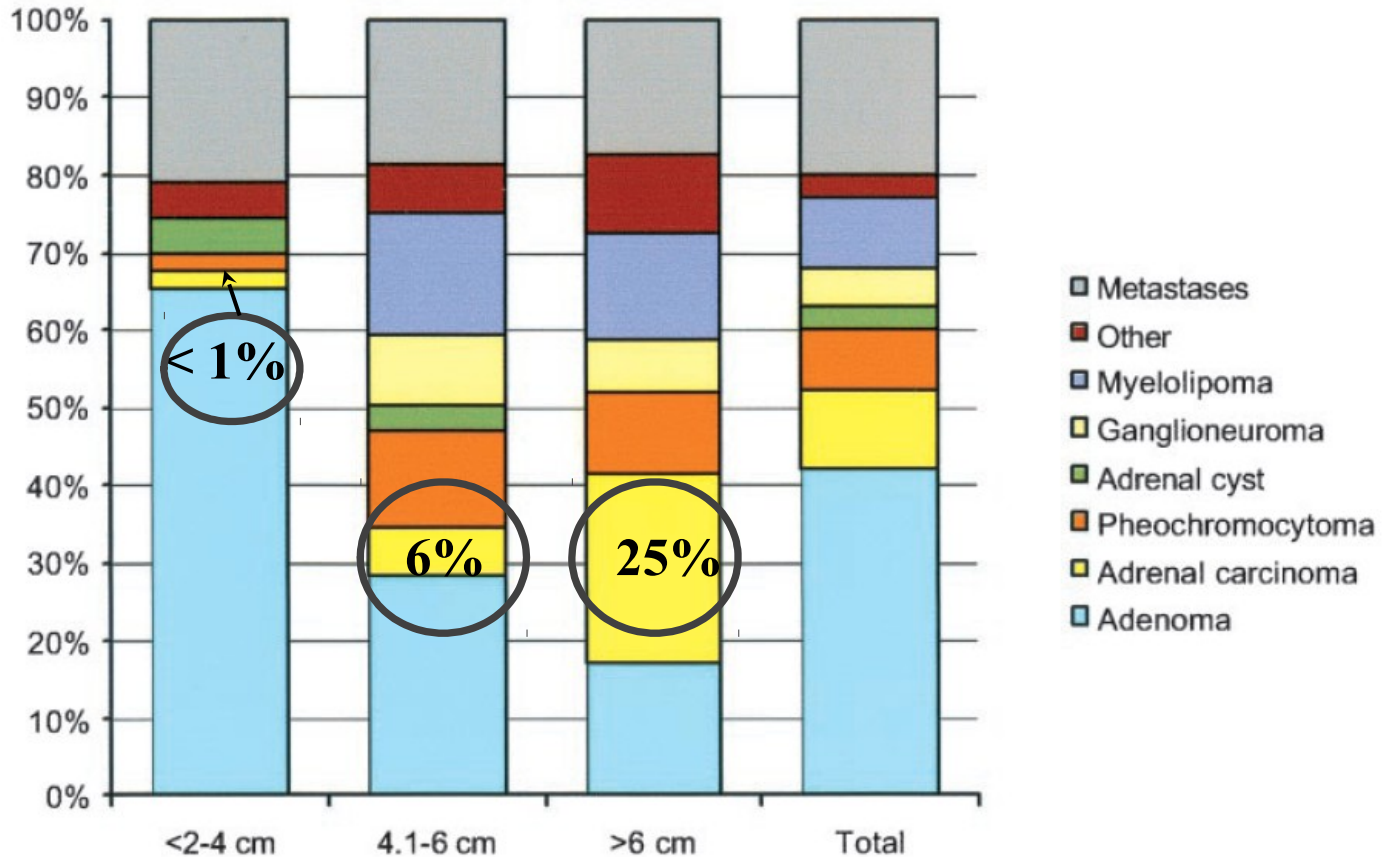
- ✓ Definitive differential diagnosis in rare cases



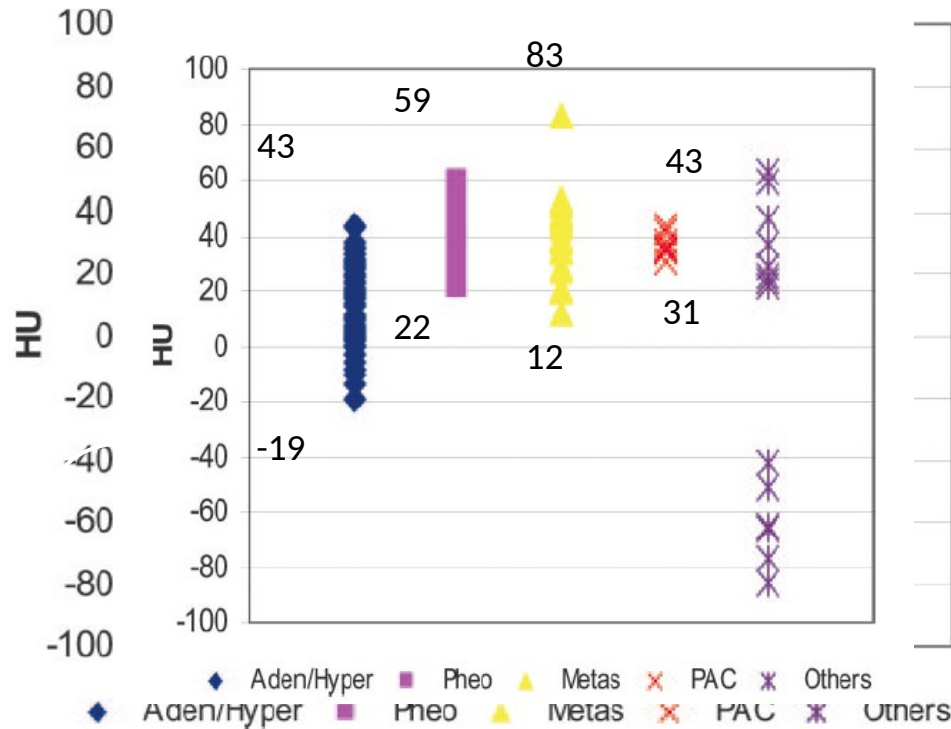
Myelolipoma

- ✓ Probabilistic approach of differential diagnosis in most cases : i) Size ii) Density iii) Wash Out

Etiologies of Incidentalomas according to size



Etiologies of Incidentalomas according to spontaneous attenuation



	PPV (%)	NPV (%)
HU ≤ 10	100 (32/32)	57.7 (64/111)
HU ≤ 20	95.8 (46/48)	65.3 (62/95)
Tumor size ≤ 2 cm	89.3 (50/56)	59.7 (108/181)
Tumor size ≤ 4 cm	69.4 (100/144)	75.3 (70/93)
HU ≤ 20 and tumor size ≤ 4 cm	100 (37/37)	65.1 (95/146)

Indeterminate Incidentalomas : additional tools

$$= \frac{\text{Enhanced attenuation value} - \text{Delayed enhanced value}}{\text{Enhanced attenuation value} - \text{Unenhanced attenuation value}}$$



Lipid poor adenoma

UA : 17 UH; EA = 107 UH; DEA = 44 UH *Absolute WO* : $107-44/107-17 = 70\%$



Metastasis of colorectal cancer

UA : 38 UH; EA = 60 UH; DEA = 55 UH *Absolute WO* : $60-55/60-38 = 22\%$

Limitations of CT Scanning Studies

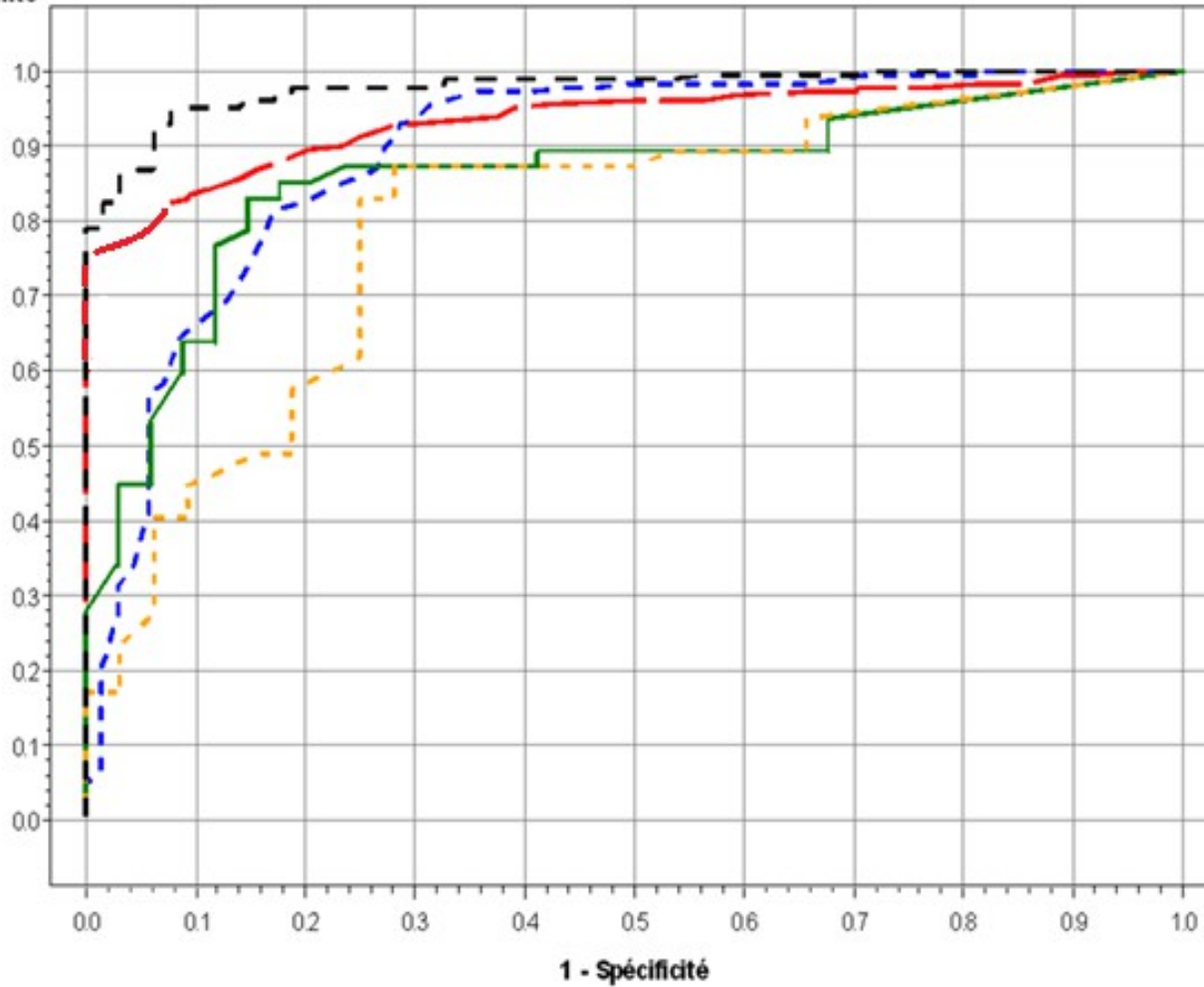
- ✓ Heterogeneity between series
- ✓ Lack of histological confirmation in a number of cases
- ✓ *Rare series of «true » AI in an endocrinology setting (malignancy is often Mets)*
- ✓ *Variability of Wash-Out protocols*

Performance of CT scanning in an « Endocrinology » Setting

Diagnosis	N	% of Total	Histo Confirmation
Benign AI	192	76	59
Pheos	33	13	31
ACC	28	11	28

Marty M et al. unpublished

Sensibilité



-- Size + UA

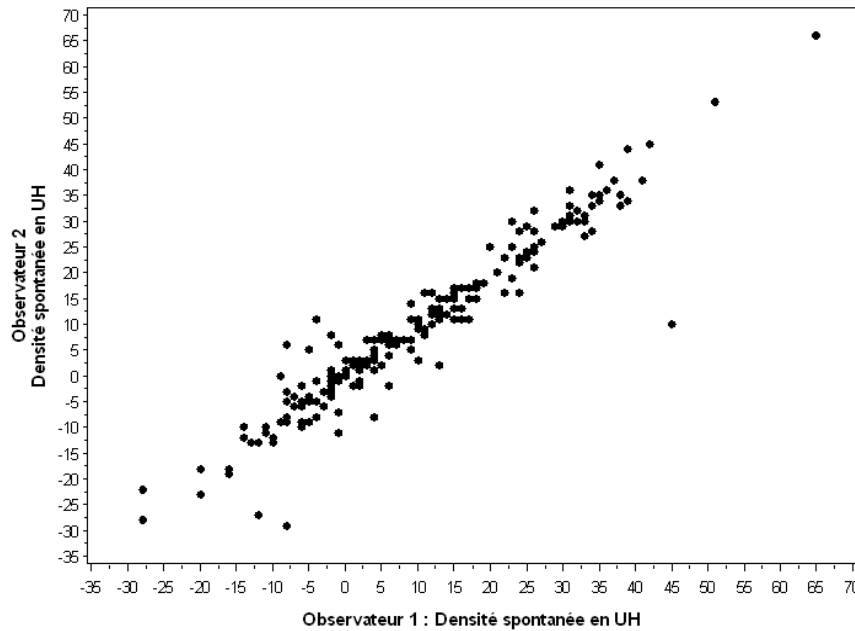
- UA

-R WO

-- Size

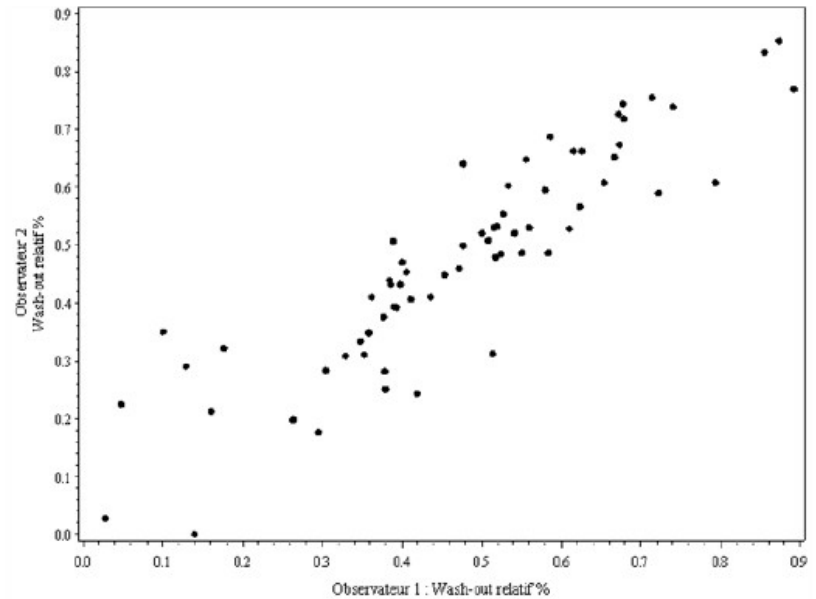
-- A WO

Marty M et al. unpublished



Unhanced Attenuation
ICC = 0.96

Absolute WO
ICC = 0.90



Marty M et al. unpublished

Case 2

82 yo man: 42 mm right adrenal nodule found during the workup of nephrolithiasis.

Unenhanced density is 23 UH and absolute WO < 50%.

The patient suffers from severe coronary heart disease and hypertension.

1 mg DST, plasma androgens and potassium are normal

Surgical excision of the tumor has been proposed but refused by the patient.

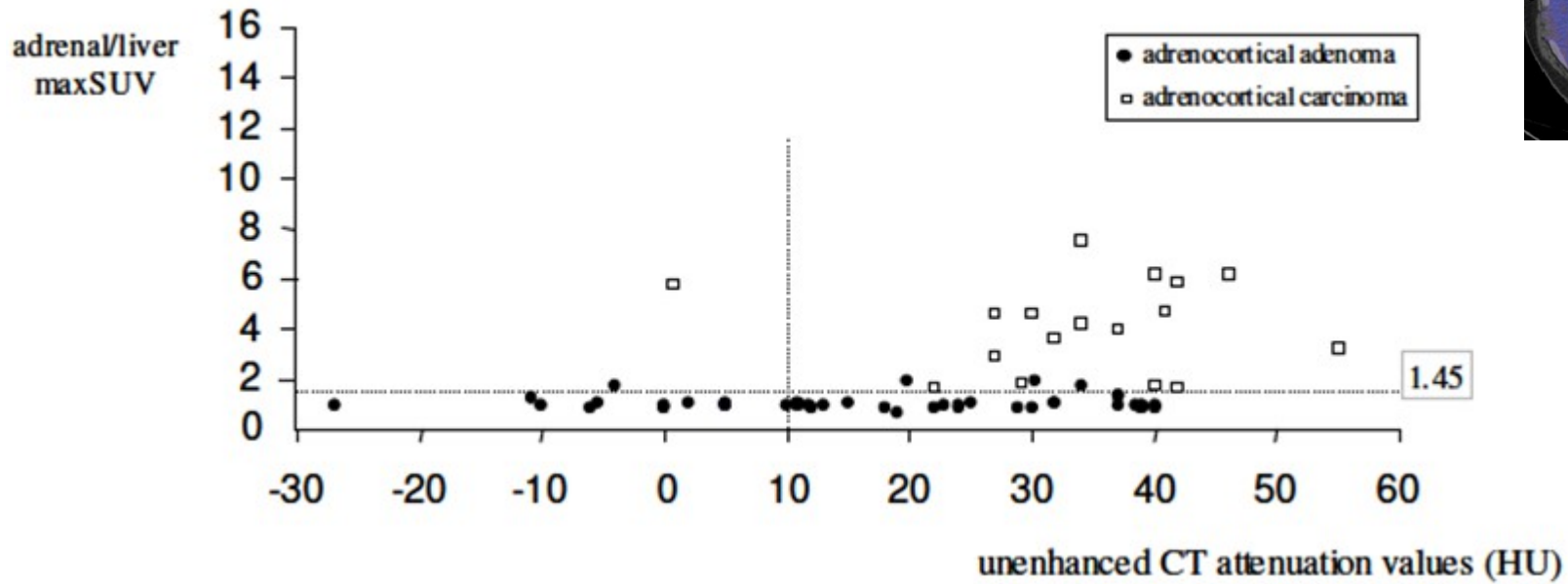
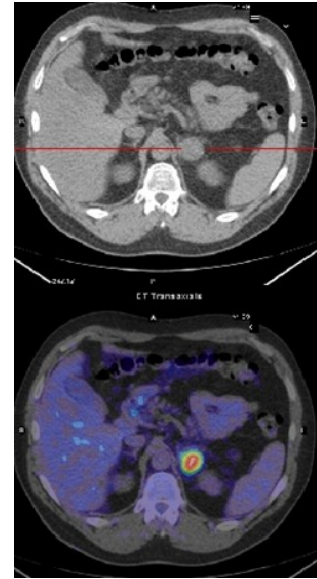


What is the most appropriate management in your opinion ?

D - Perform ^{18}F FDG-PET

E - Repeat CT scan 6 Mo later

¹⁸F FDG PET



¹⁸F FGD-PET

Table 2

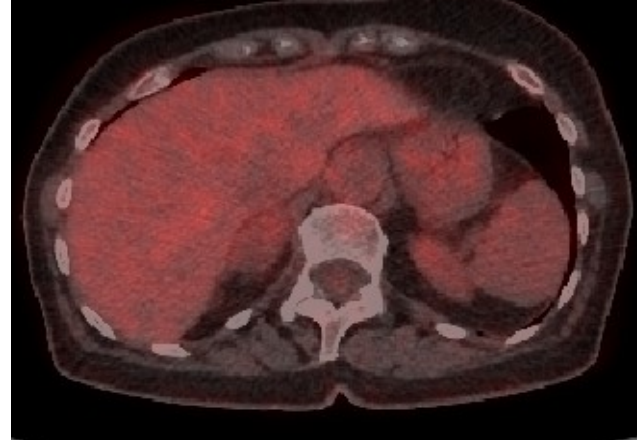
Subgroup and Overall Performance Values for PET in Differentiating between Malignant and Benign Adrenal Disease

- ✓ Excellent Negative Predictive Value for Cancer
- ✓ « False positives » :
 - Some Adenomas
 - Pheochromocytomas
 - Other rare lesions

Case 2



UA : 26 UH ; absolute WO < 50%.

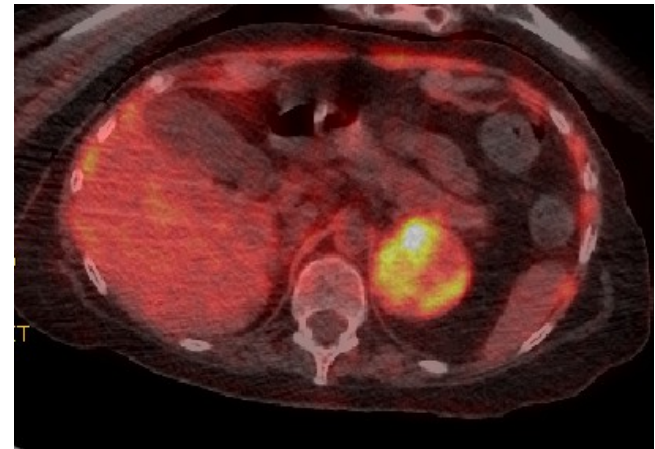


SUV max < SUV liver

occult ACC



51 mm; UA : 37 UH;
Absolute WO : 20 %



SUV max : 13,5

Case 2

82 yo man: 42 mm right adrenal nodule found during the workup of nephrolithiasis.

Unenhanced density is 23 UH and absolute WO < 50%.

The patient suffers from severe coronary heart disease and hypertension.

1 mg DST, plasma androgens and potassium are normal

Surgical excision of the tumor has been proposed but refused by the patient.



F Up : patient has a second CT scan 12

Months later that is unchanged.

Conclusion : definitive diagnosis is

unknown but AI is benign !

Case 3

62 yo man. A 40 mm left AI is found during the workup of abdominal pain. No other lesion on CT.

He is in remission for 5 years of a stage 1 colorectal cancer

Physical examination is unremarkable; BP : 135/80 mm Hg.
The mass is heterogeneous, display a density of 37 UH, with a low wash-out.

A ^{18}F FDG-TEP has been performed and exhibit a significant uptake with no extradrenal uptake

What is your attitude ?

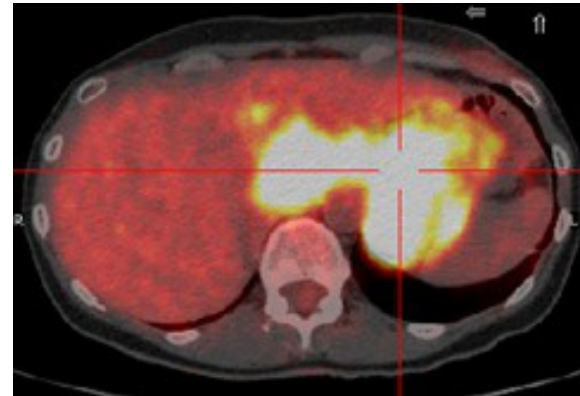
- A - The AI is a metastasis of the CRC. Biopsy
- B - The AI is a metastasis of the CRC. Operate
- C - Measure plasma or urinary metanephrines
- D - Perform an MRI
- E - Measure plasma CEA



Adrenal Incidentalomas Basics

Etiologies in Cancer patients

- ✓ Prevalence of adrenal Mets in cancer patients : 10 – 25 %
- ✓ Mets are bilateral in 50% of cases
- ✓ Mets are contemporary of primary cancer in 2/3rd of cases
- ✓ **Mets are rarely unilateral and isolated**
*Lee JE et al. (Surgery 1998) Cancer Center
1693 patients
Isolated unilateral adrenal Met : 0.2%*



18 FGD-PET

- ✓ Excellent Negative Predictive Value for Cancer
- ✓ « False positives » :
 - Some Adenomas
 - **Pheochromocytomas**
 - Other rare lesions

Case 3

Plasma Methyl-Noradrenaline level is 1.5 x ULN
and Plasma Methyl-Adrenaline level is normal.

Which further investigation do you suggest ?

Changing spectrum of pheos

Changes in Clinical Features and Long-Term Prognosis in Patients With Pheochromocytoma

Takao Noshi
Wakako Miu

0021-972X/06/15:000
Printed in U.S.A.

Watanabe, Hiroyoshi Akama, Satoru Shibukawa,

The Journal of Clinical Endocrinology & Metabolism 90(4):2110-2116
Copyright © 2005 by The Endocrine Society
doi: 10.1210/jc.2004-1395

Year of Diagnosis, Features at Presentation, and Risk of Recurrence in Patients with Pheochromocytoma or Secreting Paraganglioma

ISSN 0804-4643

Laurence Amar, Ann...
Pier...
European Journal of Endocrinology (2009) 161 355-361

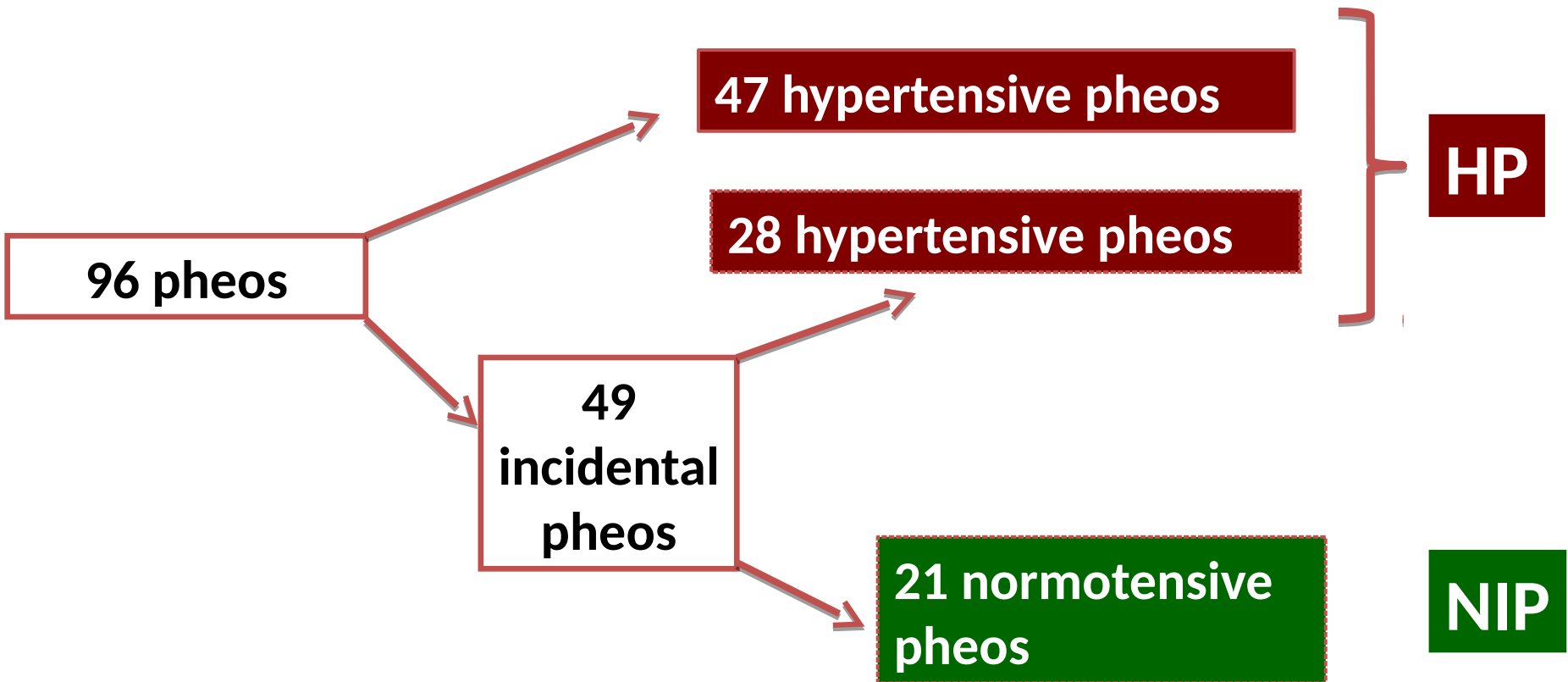
CLINICAL STUDY

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

Robert Kopetschke, Mario Slisko¹, Aylin Kilisli, Ulrich Tuschy², Henri Wallaschofski³, Martin Fassnacht⁴,
Manfred Ventz, Felix Beuschlein¹, Martin Reincke¹, Nicole Reisch¹ and Marcus Quinkler

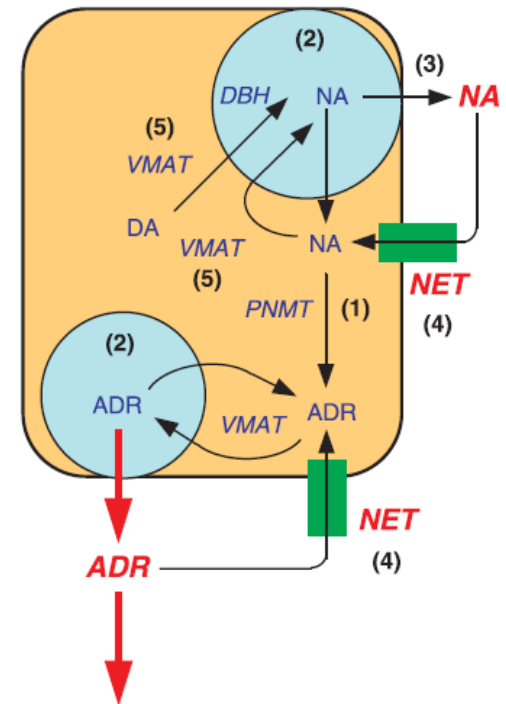
Incidental Pheochromocytoma

96 sporadic pheochromocytomas



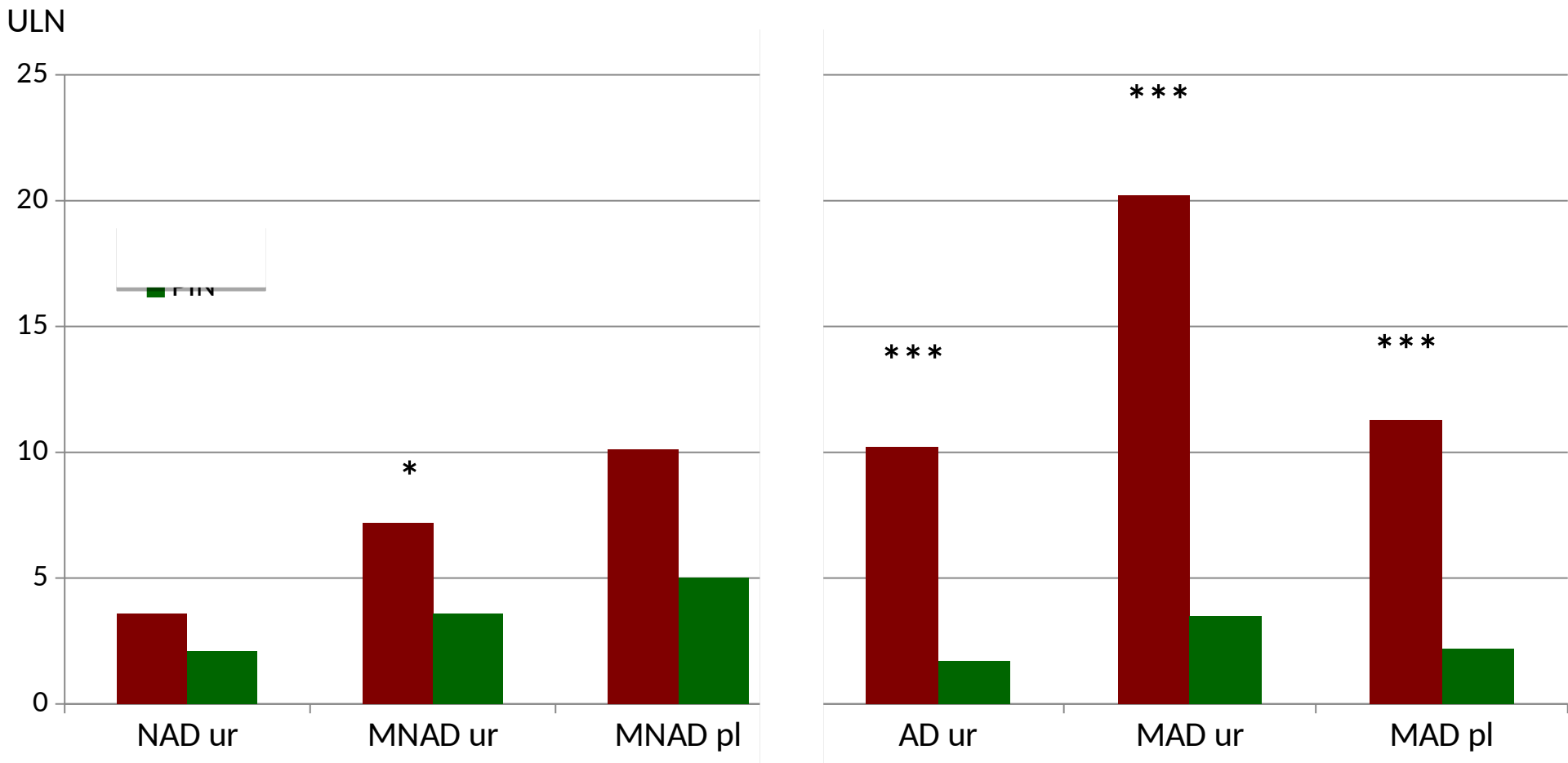
Normotensive Incidental Pheos

	HP	NIP	p
Synthesis			
DBH	22,9	22,2	p=0,32
PNMT	87,3	11,5	p=0,03
TH	10,2	6,3	p=0,08
Granines			
CGA	13,0	8,1	p=0,51
CGB	11,2	5,4	p=0,64
SGII	15,6	9,2	p=0,01
Catabolism			
COMT	21,3	18,9	p=0,26
MAO	6,8	8,9	p=1,00
Transport			
VMAT1	28,2	14,7	p=0,04
VMAT2	85,2	78	p=0,21
NET	20,6	8,9	p=0,04
Maturation/Secretion			
NPY	87,7	33,1	p=0,02
PAM	18,6	15,0	p=0,35
PC1	115,6	90,0	p=0,34
PC2	12,4	6,0	p=0,09
SNAP25	15,9	15,6	p=0,63

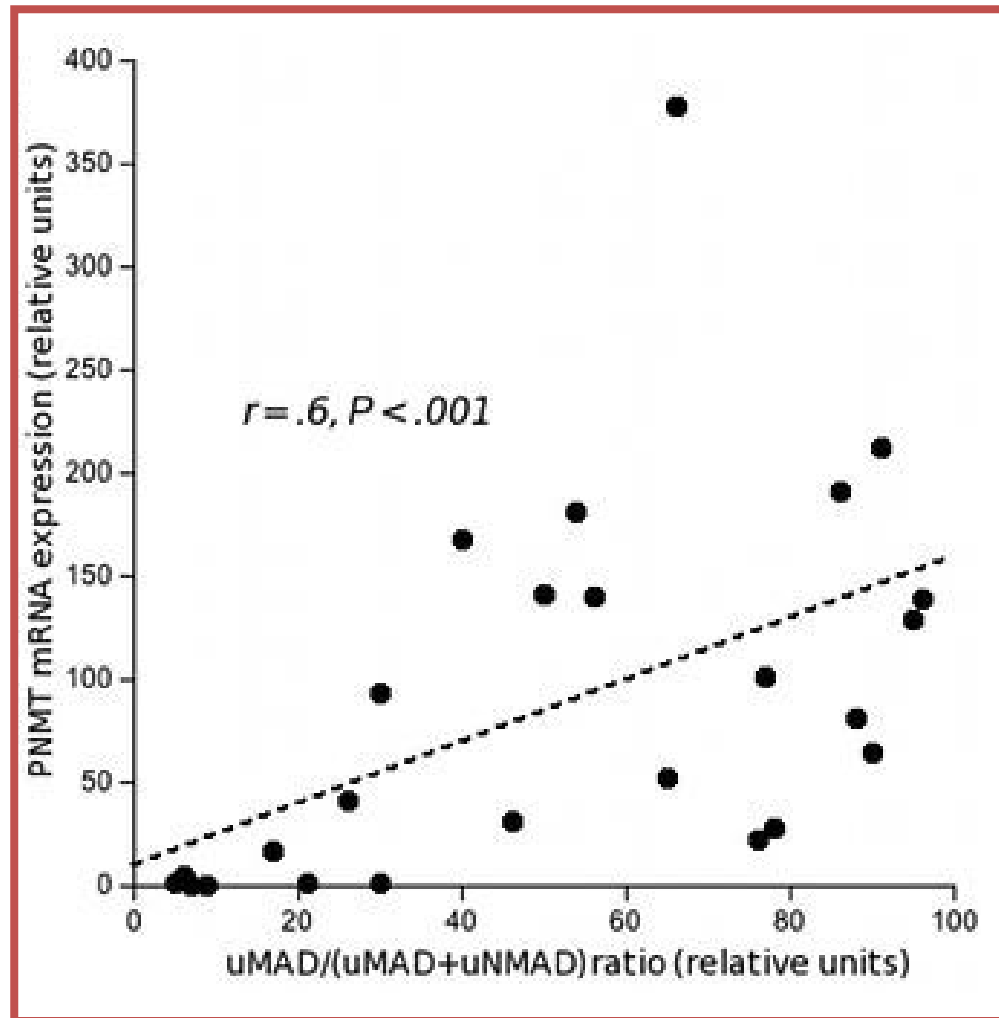


Haissaguerre M et al, JCEM 2012

Normotensive Incidental Pheos



Normotensive Incidental Pheos



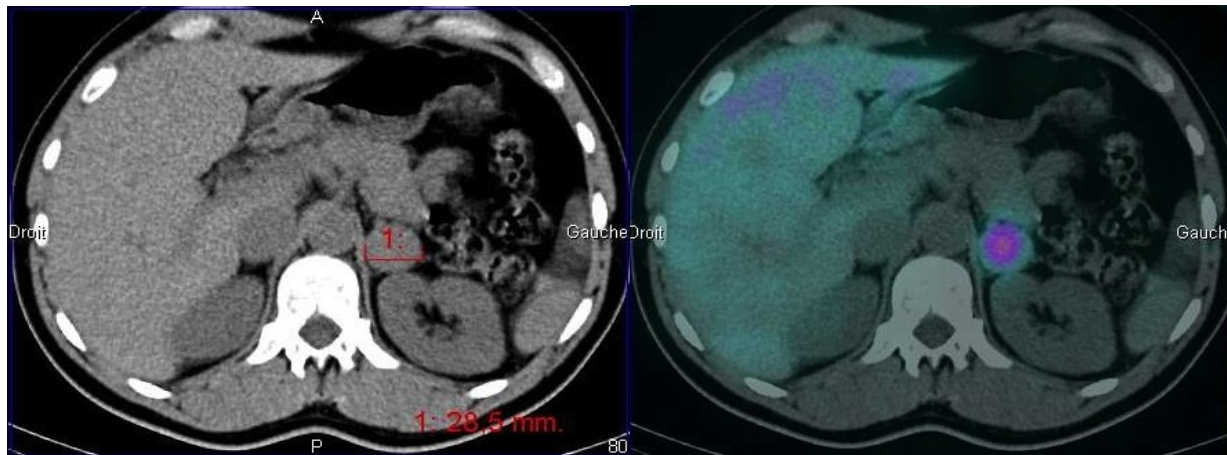
Normotensive Incidental Pheos

Sensitivity	HP
24h Urinary MN	98 %
Plasma MN	100 %
24h Urinary Catecholamines	88 %

Case 3

Plasma Methyl-Noradrenaline is 1.5 x ULN
and Plasma Methyl-Adrenaline is normal.

Any further investigation ?



¹³¹I MIBG scintigraphy

✓ Question ?

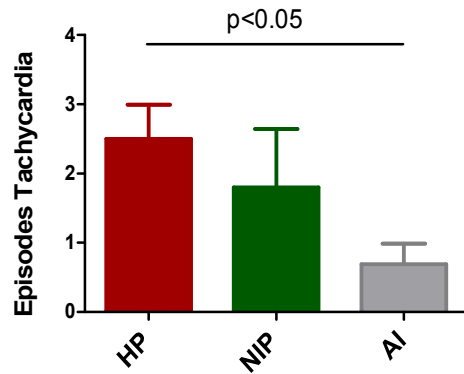
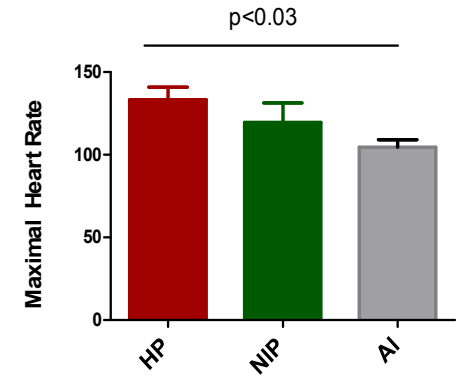
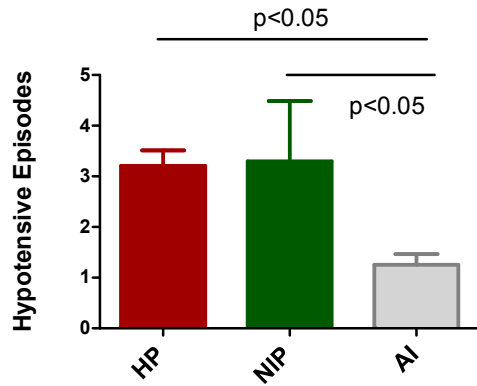
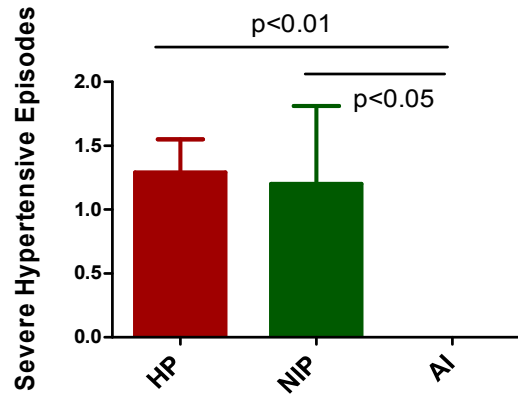
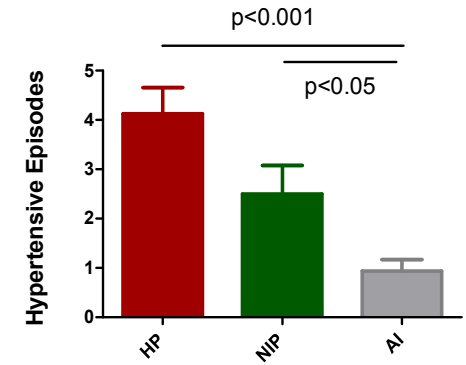
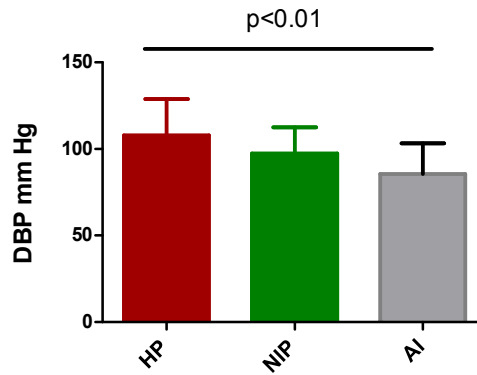
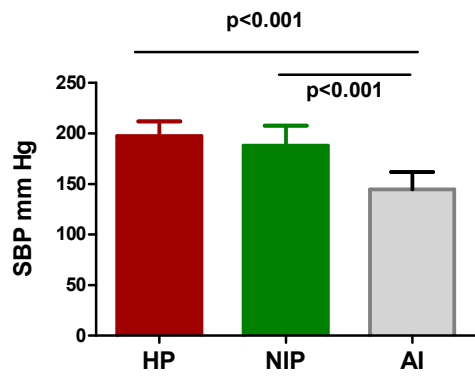
What is the per-operative hemodynamic behavior of NIP compared to hypertensive pheochromocytomas (HP) ?

✓ Retrospective study

- 10 NIP, 24 HP and 16 normotensive adrenal incidentalomas (AI)
- Operated by the same team (2004 – 2012) and using a *similar per-operative hemodynamic monitoring*

✓ Surgery

- 78% operated using coelioscopy
- Pre-operative antihypertensive treatment
23/24 HP patients , 6/10 NIP patients



Drugs (%)

Antihypertensive

HP

NIP

AI

- ✓ Despite the lack of spontaneous hemodynamic features, **NIP are roughly comparable to HP in terms of hemodynamic instability during surgical resection and differ markedly from non-pheochromocytoma AI**
- ✓ **It is crucial to identify NIP amongst adrenal incidentalomas that are scheduled for surgery and the standard of care for anesthesia must be used during surgical excision of NIP.**

Case 4

53 yo man: 25 mm left adrenal nodule is found during the workup of abdominal pain. Unenhanced attenuation: 3UH

Physical examination: BMI : 28, Hypertension not controlled despite ACE inhibitors and diuretics.

There is a family history of hypertension.

Aldo/renin ratio is normal

Cortisol after 1 mg DST : 100 nmol/L (3.7 μ g/dL)

and 8 am plasma ACTH is 10 pg/mL



Which option do you suggest ?

A - FDG-PET

B - Measurement of Plasma Metanephrines

C - SubClinical Cortisol Secreting Incident : operate

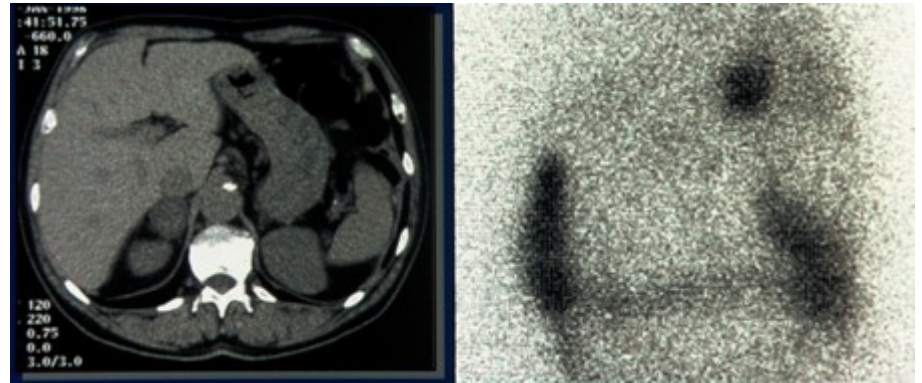
D - Perform 8 mg DST

E - Follow-Up and repeat investigations of the HPA axis

6 Mo Later

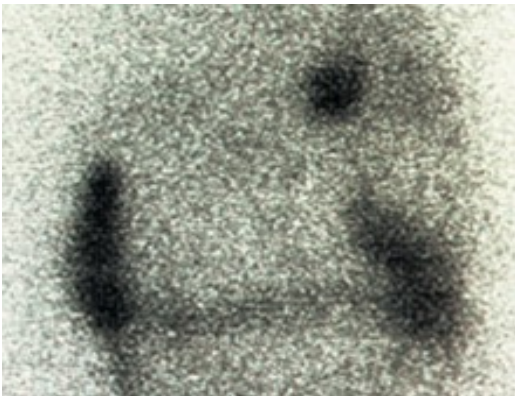
«SubClinical» Cortisol Secreting Incidentaloma (SCSI)

- Benign tumor arising from the adrenal cortex
- Secretion of cortisol
 - autonomous
 - \pm intensity
- Does not lead to overt clinical Cushing's syndrome



SCSI

Main issues



- Diagnostic Criteria
- Evolution towards overt Cushing's syndrome
- Long-term consequences

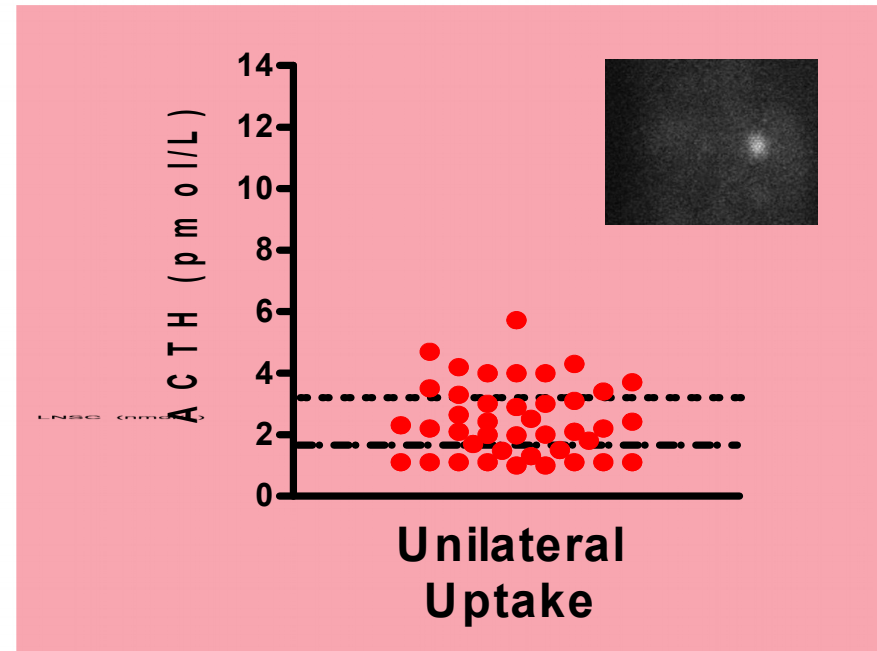
Diagnostic Criteria

First author, year (Ref.)	DEX dose, DST cutoff	SH criteria
Reincke, 1992 (34)	1 mg, 3 $\mu\text{g}/\text{dl}$	DST
Osella, 1994 (35)	1 mg, 5 $\mu\text{g}/\text{dl}$	DST
Flecchia, 1995 (36)	1 mg, 5 $\mu\text{g}/\text{dl}$	DST
Ambrosi, 1995 (37)	1 mg, 5 $\mu\text{g}/\text{dl}$	DST plus ≥ 1 out of CRH, CCR, ACTH, UFC
Bardet, 1996 (38)	1 mg, 3.5 $\mu\text{g}/\text{dl}$	DST
Bondanelli, 1997 (39)	1 mg, 3.5 $\mu\text{g}/\text{dl}$	DST plus ACTH
Kasperlik-Zeluska, 1997 (40)	LDDST, 2 mg/24 h ^a	DST plus HDDST
Tsagarakis, 1998 (41)	LDDST, 2.5 $\mu\text{g}/\text{dl}$	DST
Terzolo, 1998 (42)	1 mg, 5 $\mu\text{g}/\text{dl}$	DST plus UFC
Torlontano, 1999 (43)	1 mg, 5 $\mu\text{g}/\text{dl}$	UFC
Rossi, 2000 (18)	LDDST, 3.0 $\mu\text{g}/\text{dl}$	DST plus ≥ 1 out of CRH, CCR, ACTH, UFC
Mantero, 2000 (9)	1 mg, 5 $\mu\text{g}/\text{dl}$	≥ 2 out of CRH, CCR, ACTH, UFC, DST
Favia, 2000 (45)	1 mg, 5 $\mu\text{g}/\text{dl}$	DST ^c
Tanabe, 2001 (44)	1 mg, 3 $\mu\text{g}/\text{dl}$	DST
Midorikawa, 2001 (46)	1 mg, 3 $\mu\text{g}/\text{dl}$	DST or HDDST
Grossrubatscher, 2001 (47)	1 mg, 5 $\mu\text{g}/\text{dl}$	DST plus ≥ 1 out of CRH, CCR, ACTH, UFC
Valli, 2001 (48)	1 mg, 5 $\mu\text{g}/\text{dl}$	Unilateral uptake ^d
Chiodini, 2001 (49)	1 mg, 3 $\mu\text{g}/\text{dl}$	≥ 2 out of ACTH, UFC, DST
Libè, 2002 (52)	1 mg, 5 $\mu\text{g}/\text{dl}$	≥ 2 out of CRH, CCR, ACTH, UFC, DST
Chiodini, 2002 (53)	1 mg, 3 $\mu\text{g}/\text{dl}$	≥ 2 out of ACTH, UFC, DST
Emral, 2003 (54)	3 mg, 3 $\mu\text{g}/\text{dl}$	DST and HDDST
Hadjidakis, 2003 (55)	LDDST, 2.5 $\mu\text{g}/\text{dl}$	LDDST
Chiodini, 2004 (19) ^b	1 mg, 3 $\mu\text{g}/\text{dl}$	≥ 2 out of ACTH, UFC, DST
Katabami, 2005 (56)	1 mg, 3 $\mu\text{g}/\text{dl}$	DST and HDDST
Terzolo, 2005 (22)	1 mg, 5 $\mu\text{g}/\text{dl}$	n.a.
Chiodini, 2009 (21) ^b	1 mg, 3 $\mu\text{g}/\text{dl}$	≥ 2 out of ACTH, UFC, DST
Masserini, 2009 (32) ^b	1 mg, 3 $\mu\text{g}/\text{dl}$	≥ 2 out of ACTH, UFC, DST
Eller-Vainicher, 2010 (60) ^b	1 mg, 3 $\mu\text{g}/\text{dl}$	≥ 3 out of CCR, ACTH, UFC, DST
Chiodini, 2010 (61) ^b	1 mg, 3 $\mu\text{g}/\text{dl}$	≥ 2 out of ACTH, UFC, DST

Pitfalls in the diagnosis of SCSl

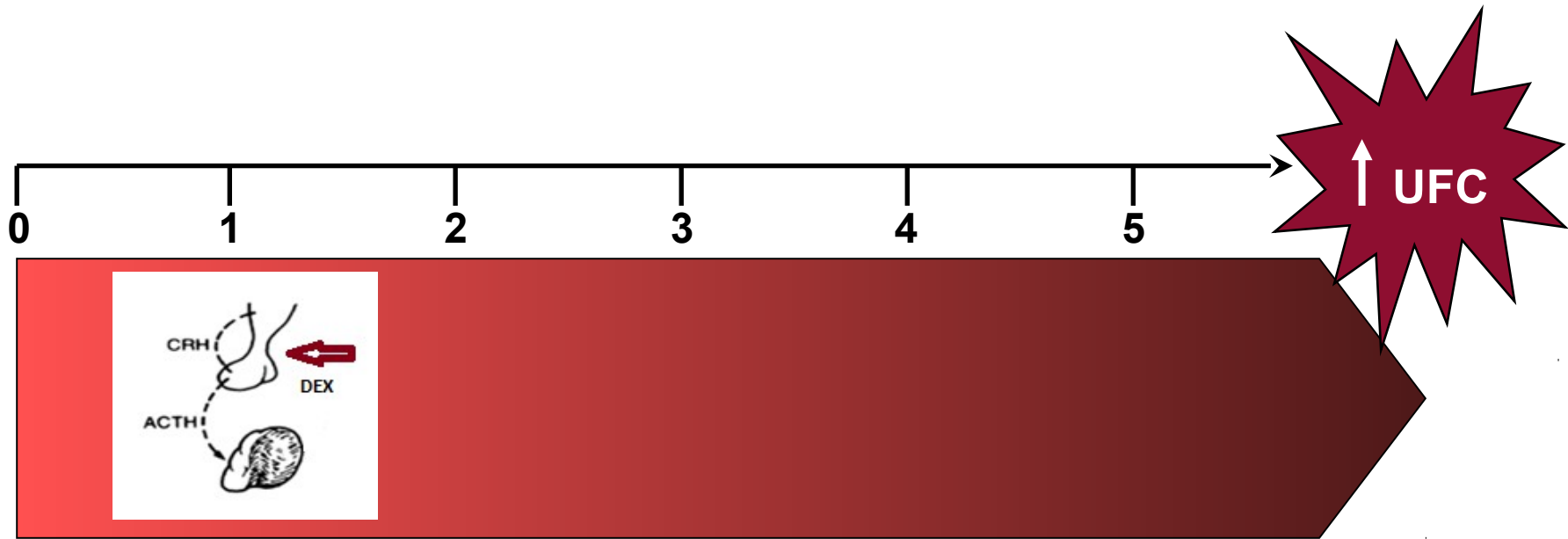
Atypical Biological signature of SCSl

- Increased UFC
in < 30% of cases
- Suppression of Plasma ACTH
- Performance of LNSC ?
- **Lack of agreement between tests**



Nunès ML et al. JCEM 2009

Spectrum of cortisol secretion in adrenal incidentalomas



Non secreting
adenoma

Cortisol
Secreting Adenoma

Cardiovascular Consequences of SCS

- **Correlative Studies (Cross-sectional)**
- **Long-term observational studies**
- **Interventional surgical studies**



Evidence

Cardiovascular Risk

Cross-sectional studies

DST
(nmol/L)



Secreting pattern

	NSA (n=203)	ImP (n=71)	IMP (n=55)	SCS (n=19)	P value ^a
Clinical outcomes					
Hypertension (n; %)	149 (73.4)	58 (81.7)	43 (78.2)	18 (94.7)	0.173
T2D (n; %)	31 (15.2)	13 (18.3)	18 (32.7) ^b	8 (42.1) ^{b,c}	0.004
CHD (n; %)	6 (2.9)	9 (12.6) ^b	6 (10.9) ^d	5 (26.3) ^b	0.002
Stroke (n; %)	1 (0.5)	2 (2.8)	3 (5.4) ^d	1 (5.2)	0.194
Osteoporosis (n; %)	30 (14.8)	7 (9.8)	8 (14.5)	9 (47.3) ^{b,e,f}	0.003
Osteoporotic fractures (n; %)	5 (2.5)	3 (4.2)	1 (1.8)	3 (15.8) ^d	0.056

Cardiovascular Risk

Long-term follow-up studies

- 206 patients with ≥ 5 y FUp
- 11.6 % had SCSl at baseline and 8.2 % developed SCSl during FUp

	SH- Group	SH+ Group	P
n	167	39	
Duration of follow-up, mo	83.2 \pm 33.6 (60–186)	79.4 \pm 25.2 (60–178)	.826
New CVE	14 (8.4)	8 (20.5)	.040
New CVE in CVE- patients at baseline	11 (6.6)	4 (10.0)	.343
Increased body weight ^a	40 (24.0)	13 (33.3)	.229
Worsened blood pressure control ^b	52 (31.1)	18 (46.2)	.070
Worsened glycemc control ^f	39 (23.4)	12 (30.8)	.334
Worsened LDL ^e	20 (12.0)	7 (17.9)	.303

Cardiovascular Risk

Long-term follow-up studies

- 114 patients with stable NFA
- 61 with IP or SCS
- 21 with worsening pattern during FUp

Median Follow Up : 7.5 y

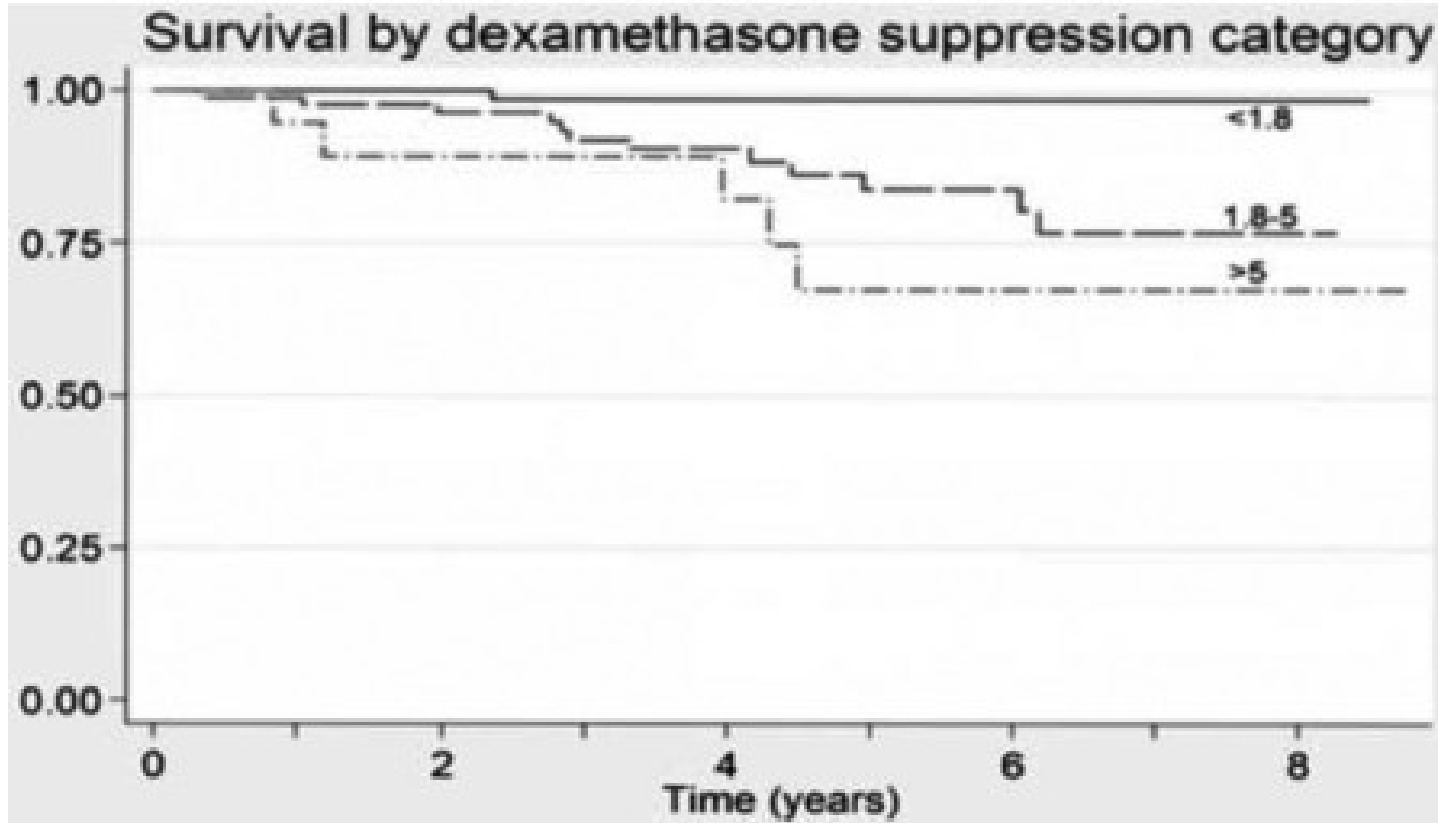
Follow-up (years)

Follow-up (years)

45

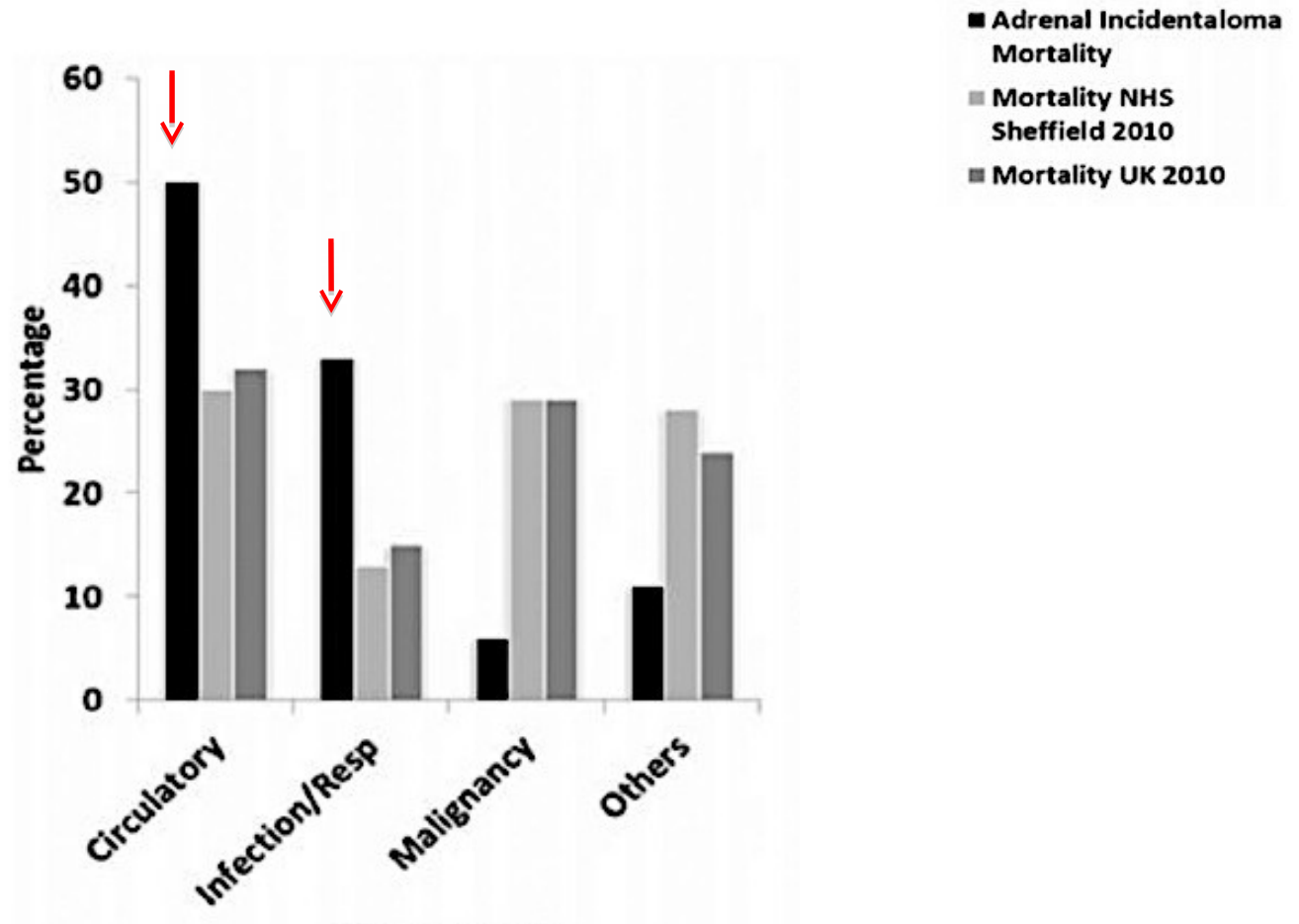
Cardiovascular Risk

Long-term follow-up studies



Cardiovascular Risk

Long-term follow-up studies



Lessons from 2014 cohort studies

- ✓ SCSl defined by a cortisol post-dex > 50 nmol/L are associated with increased CVE prevalence during follow-up and increased CV mortality
- ✓ Mild hypercortisolism is an independent CV risk factor in multivariate analysis
- ✓ CV consequences of SCSl are potentiated by the presence of Hypertension, previous stroke and MI
- ✓ *Switch from NFA to SCSl during FUp is associated with worse CV outcome*

Cardiovascular Risk

Surgical Intervention studies

	N Patients	HYPERTENSION		CARDIOVASC RISK FACTORS	
		Cure	Improve	Obesity	Diabetes
Reincke 1992	8	25%	75%	100%	100%
<ul style="list-style-type: none"> • Small number of patients • Heterogeneous definition of SCSi • All but one Retrospective - Selection ? • Inaccurate evaluation of end points • Few series with medical treatment control group • Non controlled medical intervention 					
Guerrieri 2010	19	?	66%	?	47%
Chiodini 2010	25	?	56%	32%	48%

Investigator Meeting

25th September 2014

« CHIRACIC »

Sponsor's code: CHUBX 2012/34

Surgery of Subclinical Cortisol-Secreting
Adrenal Incidentaloma

Biomedical research

Follow-up of Adrenal Incidentalomas

Hormonal Overt Hypersecretion

First author	Year	Number of patients (n> 20)	Mean age (years)	Size of masses (mean or median)	Follow-up duration (years)	Became functional (%)
Song (35)	2007	71	NG	NG	2.7	NG
Song (35)	2007	209	NG	NG	NG	NG
Song (35)	2007	41	NG	NG	3.3	NG
Favia (23)	2000	90	NG	NG	1.8	0
Barzon (43)	1999	75	56	2.5	4.0	8
Bulow (44)	2006	229	64	2.5	2.1	2.6
Tsvetov (19)	2007	88	NG	2.6	2.0	0
Barry (33)	1998	231	64	2.0	7.0	0
Libe (45)	2002	64	61	2.5	2.1	0
Siren (46)	2000	27	59	2.5	7.1	0
Rossi (36)	2000	32	NG	NG	2.8	0
Bastounis (41)	1997	60	NG	3.2	3.6	NG
Grossrubatscher (47)	2001	53	NG	2.5	2.0	0
Emral (39)	2003	60	NG	NG	2.0	0
Mantero (49)	2000	53	NG	NG	>1	0
Bencsik (48)	1995	27	NG	<3	1.8	0
Mean		83.8	60.8	2.5	3.2	0.9

*Cawood TJ et al.
EJE 2009*

Further analysis of 8 FUp series, including 807 patients
*Anagnositis 2010, Cho 2013, Comlecki 2010, Fagour 2009, Giordano 2010,
 Kim 2005, Morelli 2014, Vassilatou 2009*

The risk of developing overt hypersecretion is < 1% (range 0-2.6%)

Follow-up of Adrenal Incidentalomas *“Subclinical” Hypercortisolism*

✓ *SCSI and switch from NFA to SCSI during FUp is associated with worse CV outcome*

✓ *7.2 to 14% of patients change of « phenotype »*

Morelli V et al JCEM 2014, Di Dalmazi G et al 2014 Lancet Endocr.

- ***Predictive Factors ?***

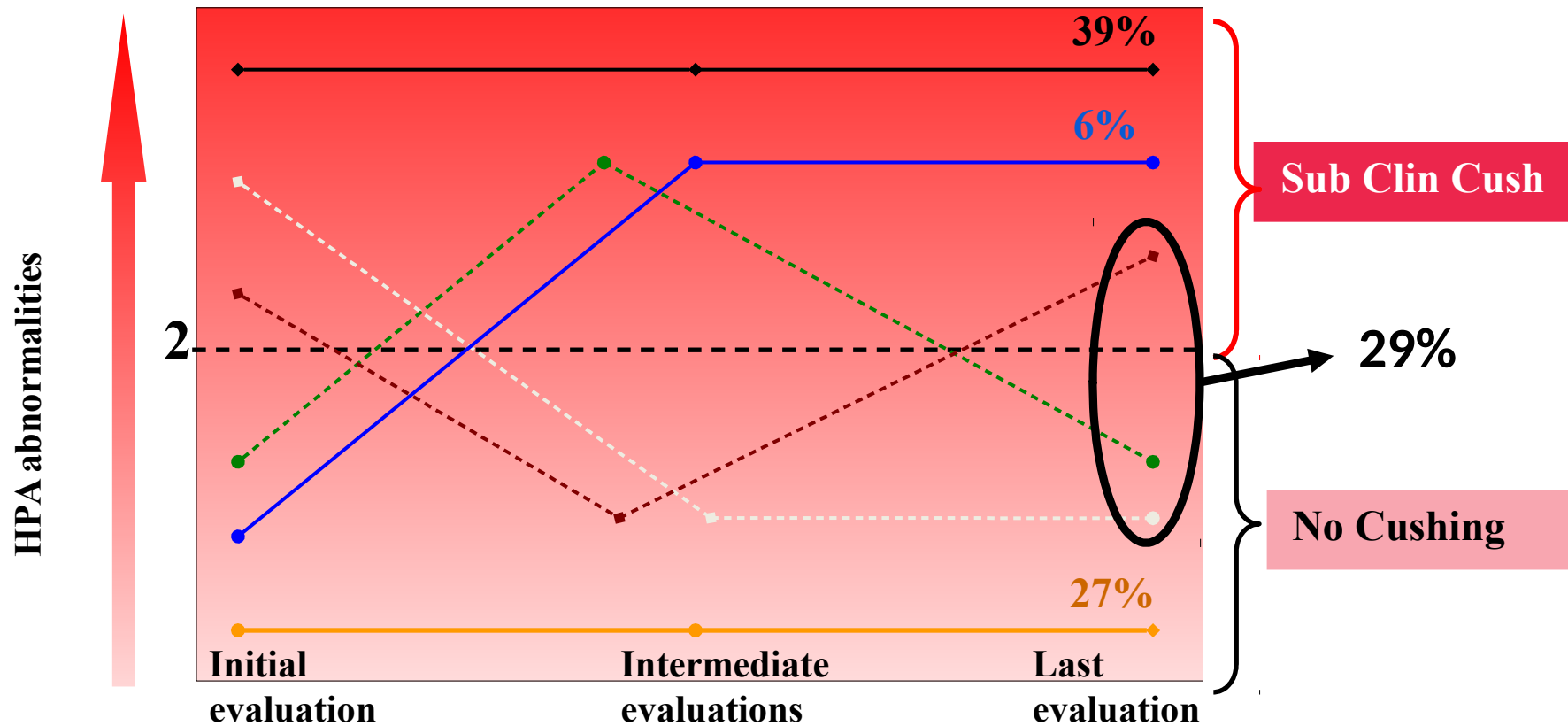
- ***Bilateral AI ?***

- ***Size > 2.4 cm : PPV : 14%; NPV 96%***

Morelli V et al JCEM 2014

Variable Hormonogenesis in SCSl

51 AI followed at yearly intervals for 4.1 y



Follow-up of Adrenal Incidentalomas

	NIH 2003	French Endocr 2008	AACE/AAES 2009	Italian Endocr 2011
CT	6 Mo - 1 y	6 Mo - 2 y - 5 y	3~6 Mo - 1y - 2y	3~6 Mo if > 2 cm
Biology	DST + UMN 1y-2y-3y-4y	DST + UMN 6 Mo 1mg DST 2y-5y	1y-2y-3y-4y-5 y	Mostly clinical Discuss DST

- *Importance of clinical FUp and treatment of CV Risk Factors*
- *Individualized FUp according to phys exam, size AI and 1 mg DST*

Case 5

39 yo man: 25 mm left adrenal nodule is found during the workup of abdominal pain. Unenhanced attenuation is 34 UH and absolute WO < 50%.

Past history : Grave's disease, hypertension treated by calcium channels inhibitors

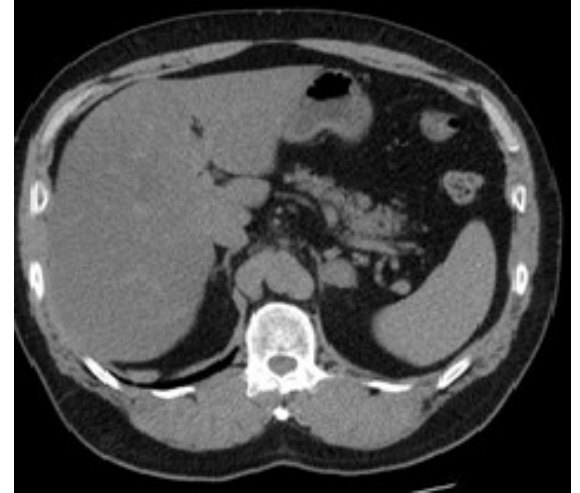
Physical examination : BMI : 30, no sign of Cushing

Plasma potassium is 3.1 mmol/L

Supine Aldo 574 pmol/l (N: 150-500), PRA: 0.3 (N: 0.2-2.5)

Cortisol after 1 mg DST : 356 nmol/L. UFC is normal

Plasma Metanephrines are normal



What is your opinion ?

A - Conn adenoma : operate

B - Conn adenoma ? Perform AVS

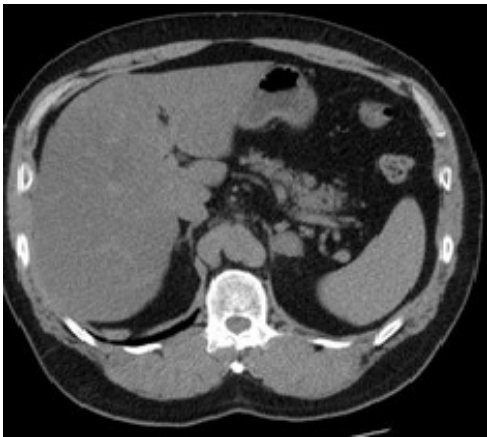
B - SCSl : operate

C - Suspicion of adrenal carcinoma : operate

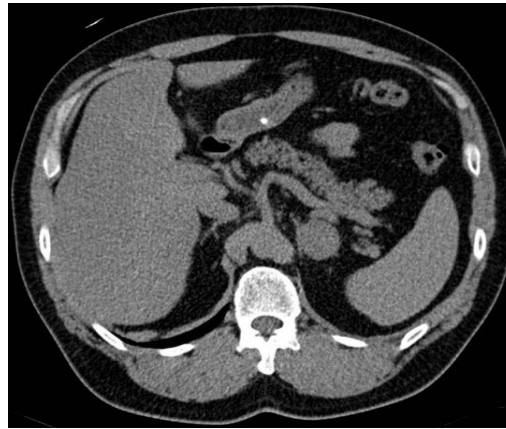
D - Repeat CT scan 6 Mo later

Case 5

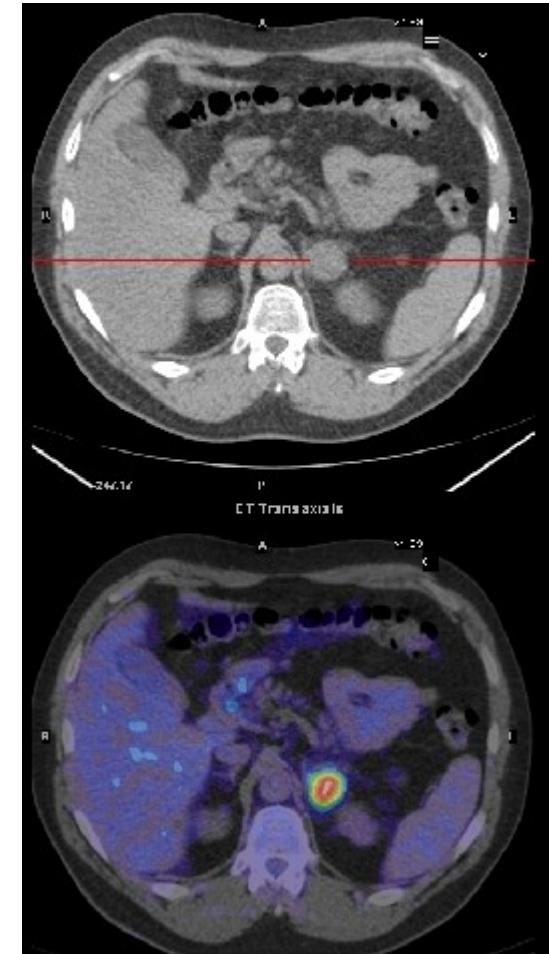
Patient decline surgery
Follow-Up



Feb 2008
25 mm; UA : 34 UH



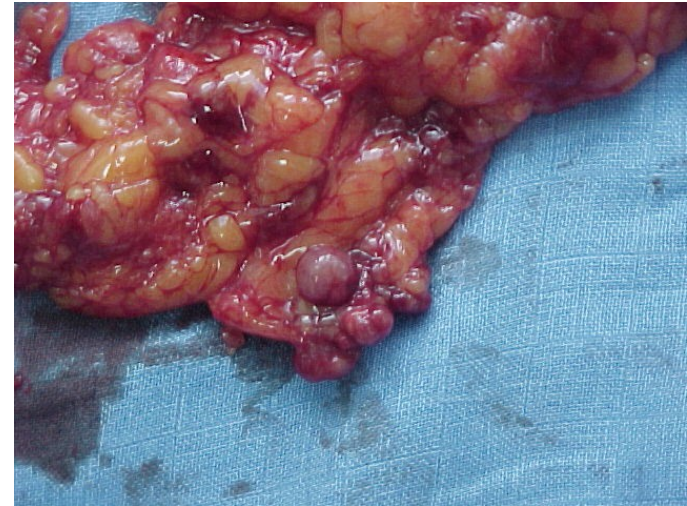
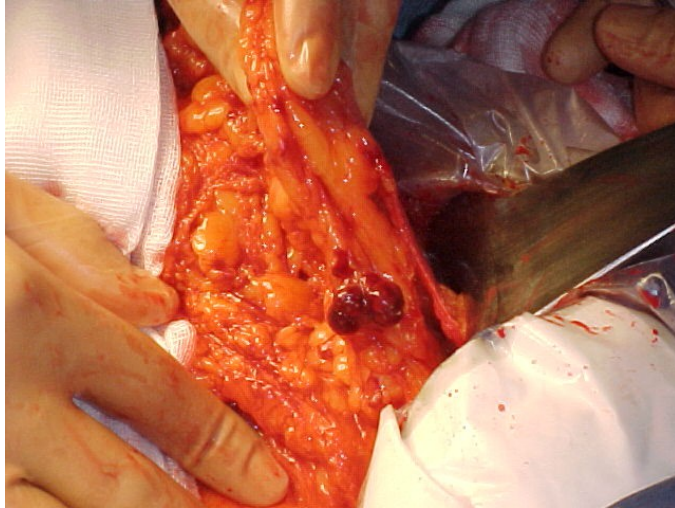
Aug 2008
32 mm; UA 36 UH



Sept 2008. Laparoscopic Surgery
ACC; Weiss = 5, Ki67 : 30%

Case 5

April 2009



Follow-up of Adrenal Incidentalomas

- ✓ Screen for malignant transformation of an adrenal incidentaloma / Growth



Imaging

- ✓ Screen for evolution towards endocrine hypersecretion



Biology

Follow-up of Adrenal Incidentalomas

Malignant transformation

First author	Year	Number of patients (n> 20)	Mean age (years)	Size of masses (mean or median)	Follow-up duration (years)	Increased in size (%)	Unchanged in size (%)	Decreased in size (%)
Song (35)	2007	71	NG	NG	2.7	0.0	NG	NG
Song (35)	2007	209	NG	NG	NG	NG	NG	NG
Song (35)	2007	41	NG	NG	3.3	NG	NG	NG
Favia (23)	2000	90	NG	NG	1.8	NG	NG	NG
Barzon (43)	1999	75	56	2.5	4.0	16.0	81.0	2.7
Bulow (44)	2006	229	64	2.5	2.1	7.4	87.4	5.2
Tsvetov (19)	2007	88	NG	2.6	2.0	12.5	87.5	0.0
Barry (33)	1998	231	64	2.0	7.0	4.0	96.0	0.0
Libe (45)	2002	64	61	2.5	2.1	20.0	0.0	0.0
Siren (46)	2000	27	59	2.5	7.1	25.0	31.0	44.0
Rossi (36)	2000	32	NG	NG	2.8	15.6	84.6	0.0
Bastounis (41)	1997	60	NG	3.2	3.6	3.7	97.3	0.0
Grossrubatscher (47)	2001	53	NG	2.5	2.0	41.5	47.2	11.3
Emral (39)	2003	60	NG	NG	2.0	0.0	NG	NG
Mantero (49)	2000	53	NG	NG	>1	26.4	NG	NG
Bencsik (48)	1995	27	NG	<3	1.8	3.7	NG	NG
Mean		83.8	60.8	2.5	3.2	14.7	68.0	7.0

Follow-up of Adrenal Incidentalomas

Screen for malignant transformation

Further analysis of 8 FUp series (766 patients)

Anagnositis 2010, Cho 2013, Comleki 2010, Fagour 2009, Giordano 2010, Kim 2005, Muth 2011, Vassilatou 2009

No case of malignancy in AI (< 5 cms) when initial imaging studies (and biology) exclude malignancy

Back Up Slides

Unilateral Adrenal Incidentalomas

✓ Mandatory Complementary Endocrine Investigations

- **1 mg DST**
- **Plasma or urinary fractionated metanephrines regardless of Blood Pressure**
- **PA/DRC or PA/PRA ratio in hypertensive or hypokalemia**

Biological Evaluation

✓ *Purpose*

- Determine the etiology of the AI
- Identify hypersecreting lesions (pheos, cortisol hypersecreting tumors, Conn's adenoma)
- Identify adrenal insufficiency in bilateral AI

Bilateral Adrenal Incidentalomas

✓ Complementary Biological Investigations

- 8 am plasma Cortisol / ACTH or SST
- plasma 17 hydroxyprogesterone



✓ Increased prevalence of Mild Hypercort ?

Vassiliadi DA et al. 2011, Olsen H et al. Endocrine 2012

Surgery of Adrenal Incidentalomas : When ?

Always :

- ✓ **Suspected ACC**
- ✓ **Suspected Pheochromocytoma**
- ✓ **Overt Hypercortisolism**

Discuss

- **Size > 4 - 6 cms ?**
- **Increase in size during follow-Up ?**
- **SCSI ?**
- **Primary Aldosteronism ?**
- **Metastasis ?**

Cardiovascular Risk

Medical Intervention studies

GR antagonism during 4 weeks

