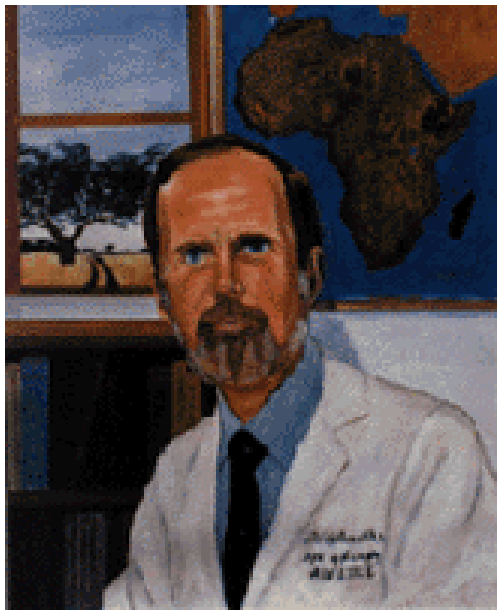
What is new in Adrenal Incidentaloma?

Dimitrios Linos, M.D., Ph.D.
Professor of Surgery
National & Kapodistrian University of Athens

What is an adrenal incidentaloma?

An adrenal incidentaloma is defined as an adrenal tumor initially diagnosed by imaging studies (CT, Ultrasound, MRI) for a clinical condition unrelated to adrenal disease.

The term **incidentaloma** was first coined by Dr. Glenn Geelhoed in 1982 at the meeting of the American Association of Endocrine Surgeons.



Adrenaloma: a better term than incidentaloma

Linos DA: Surgery, 1989:105(3):456

Clinically Inapparent Adrenal Mass

National Institute of Health, Vol 3, Bethesda, 2002

How frequent?

The overall frequency of adrenal adenomas in 87,065 autopsies in 25 studies was **5.9%**.

Young WF, Endocrinol Metab Clin North Am, 2000;29(1)159-185

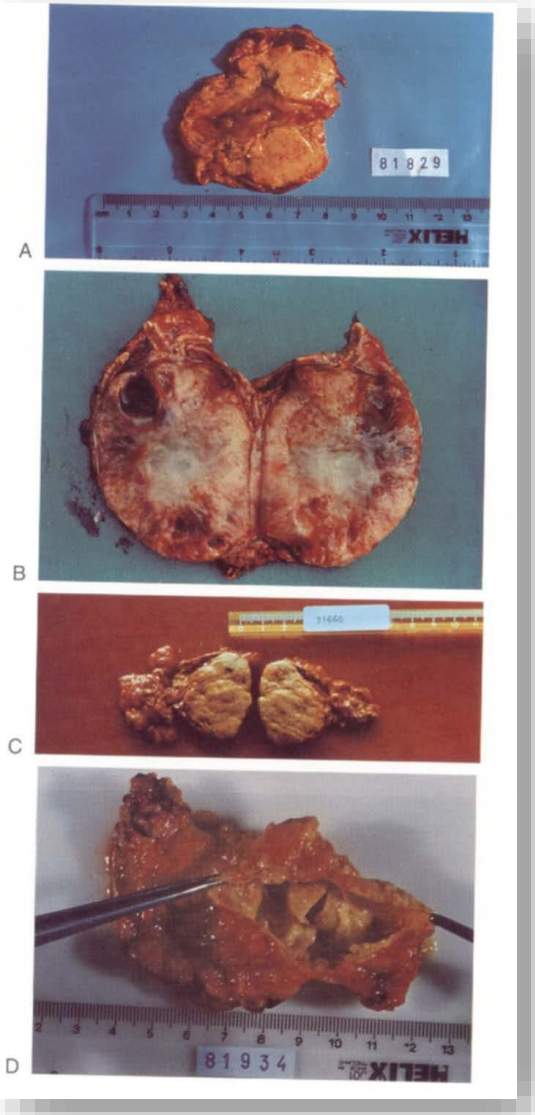
At Mayo Clinic, in a 5-year period **61,054** patients underwent **CT scanning**.

In **2.066 (3.4%)** patients, an adrenal abnormality was found.

Among these, 259 patients **(12.5%) had an incidentaloma.**

In the era of widespread use of high-resolution ultrasonography, new generation CT scans and MRI, we can anticipate **a 5% incidence of incidentalomas**.

What is the Pathology?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380 patients (Single Institution)

Non functioning adenoma	63%
Subclinical cushing adenoma	15%
Pheochromocytoma	7%
Myelolipoma	6%
Aldosteronoma	2%
Carcinoma primary	4%
Carcinoma metastatic	3%

Arnaldi G, Best Pract & Res Clin Endocr Metabol, 2012: 26(4), 405-419

3088 compiled patients with Incidentaloma

Non Functioning adenoma	74%
Subclinical Cushing	7%
Pheochromocytoma	4.7%
Aldosteronoma	1.2%
Primary Adrenocortical Carcinoma	4.8%
Metastatic adrenal carcinoma	2.3%

Androulakis II, Eur J Clin Invest 2011:41(5):552-560

European Society of Endocrinology Clinical Practice Guidelines:

- Management of patients with adrenal incidentalomas should involve a multidisciplinary team including endocrinologists, radiologists, surgeons and pathologists.
- Imaging characteristics (specifically density on a non-contrast CT scan) is more important than the size of adrenal incidentalomas in determining risk of malignancy and indication for surgery.
- Autonomous cortisol secretion is a disease on a continuum that is best assessed by a 1 mg dexamethasone suppression test. Surgical indication depends on the presence of comorbidities and severity of autonomous cortisol secretion.
- Laparoscopic adrenalectomy is the usual recommended approach when surgery is indicated. Open adrenalectomy is indicated for large or locally invasive tumours.
- Small, non-secreting, benign-appearing adrenal tumours require no long-term follow-up.

QY Duh, Nature Reviews, Endocrinol, 148, Aug. 2016

The Goal of Evaluation

Rule out:

- **Function**
- **Malignancy**

Although by definition incidentalomas are not "obviously" functioning tumors clinically apparent as Cushing's disease, Primary Aldosteronism, Pheochromocytoma, or sex steroid producing tumors, **they should be evaluated for potential "subclinical" function**.

1.096 patients with adrenal incidentaloma:

- **9.2% had subclinical Cushing's syndrome**
- **4.2% had pheochromocytoma**
- **1.6% had clinically unsuspected aldosteronomas**

Mantero F, Horm Res, 1997;47:284-289

Subclinical Cushing's Syndrome

An ill defined condition of altered phypothalamic-pituitary-adrenal axis secretion in patients who do not have the classical signs and symptoms of clinically apparent Cushing's syndrome.

Chiodini et al, J Clin Endocrinol Metab, 2010;95:2736-45

Subclinical hypercortisolism: a state, a syndrome, or a disease?

Di Dalmazi G et al, Eur J Endocrinol, 2015;173(4):M61-71

Adrenal Mild Hypercortisolism

Goddard GM, Endocrinol Metab Clin North Am. 2015;44(2):371-9

2016 ESE-ENSAT Guidelines

Mild hypercortisolism as a disease continuum

Autonomous cortisol secretion (>138nmol/Lt)

Possible autonomous cortisol secretion (>50nmol/Lt)

30% of patients with AI have mild increase in cortisol secretion.

Di Dalmazi G et al, Lancet, 2014;(2):396-405.

Patients with SCS comprise between **0.2% to 2% in the general population**.

Chiodini I et al, J Clin Endocrinol Metab, 2010;95(6):2736-2745.

Screening for SCS

1mg dexamethasone suppression test with the traditional threshold of 5µg/dl or 138nmol/L to define adequate suppression.

National Intuition of Health ed, Vol 3, Bethesda, 2002
American Association of Clinical Endocrinologists
American Association of Endocrine Surgeons

JAMA, Aug 30, 1965 • Vol 193, No 9

A Rapid Screening Test for Cushing's Syndrome

Fotios Ch. Pavlatos, MD, Renata P. Smilo, MD, and Peter H. Forsham, MD

The suppressibility of morning plasma 17-hydroxycorticosteroid (17-OHCS) levels by 1 mg dexamethasone given by mouth at 11 PM the preceding night was used as a screening test for Cushing's syndrome. Plasma 17-OHCS in 16 normal subjects, 20 with simple obesity and 10 with diseases other than Cushing's syndrome were suppressed to levels below 5μg/100 ml. In contrast, in 17 patients with Cushing's syndrome, the lowest observed value was 13μg/100 ml and no false-negative results were obtained. Two obese, hirsute women proved to be partial responders only, as their plasma levels were not suppressed below 10.5μg/100 ml. Mild abnormalities of adrenal cortical secretory activity may be present in such cases. Therefore, a single morning 17-OHCS value of less than 5μg/100 ml plasma should exclude Cushing's syndrome.

carefully timed 24-hour urine collections and the cooperation of the patient in taking dexamethasone four times a day for two to four days.

We investigated a very simple and rapid screening method, first suggested by Nugent et al,[14] which obviates some of the difficulties mentioned above. Normal and obese subjects, patients with Cushing's syndrome, and patients with other disorders were studied. The test requires only a single measurement of 17-OHCS in a morning specimen of plasma after the subject has been given 1 mg dexamethasone by mouth at 11 PM the preceding night.

Method

Plasma 17-OHCS.—Blood was drawn into hepar-

- A 2- or 3-mg dose is better than the usual 1-mg dose to **reduce false-positive results**.

- A suppressed serum cortisol **(<3µg/dL or 80 nmol/L) excludes Cushing's syndrome**.

Adrenal scintigraphy with ^{131}I-6β-iodomethylnorcholesterol (NP 59) can reveal a "functioning" but not "hypersecretory" tumor when there is an uptake of the nucleotide in the tumor site and no-uptake in the contralateral suppressed gland.

Barzon L, J Clin Endocrinol Metab, 1998;83(1):55-62

Patients with AI and SCS have:

- **Increased Mortality**
- **Associated Comorbidities**

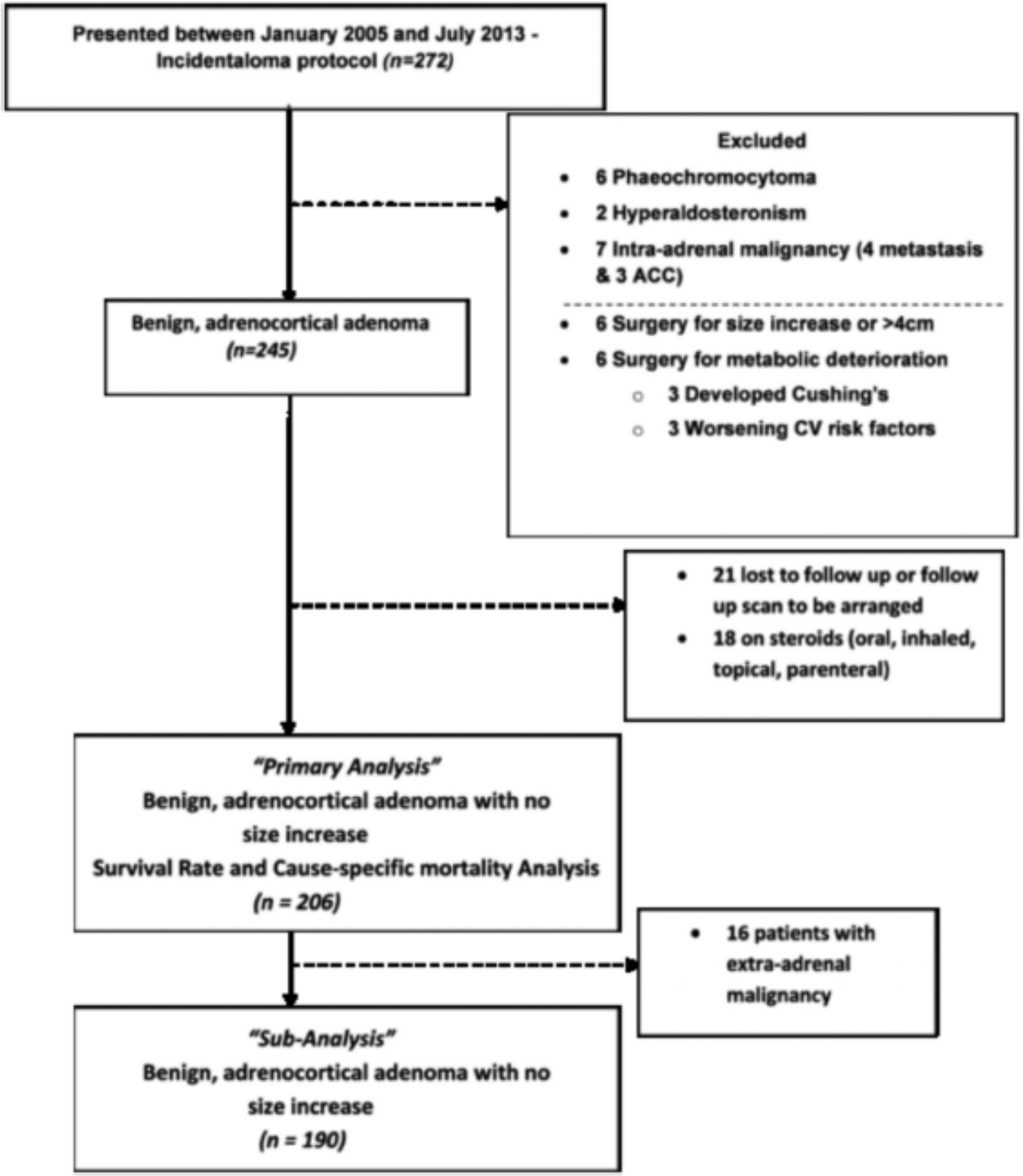
ORIGINAL ARTICLE

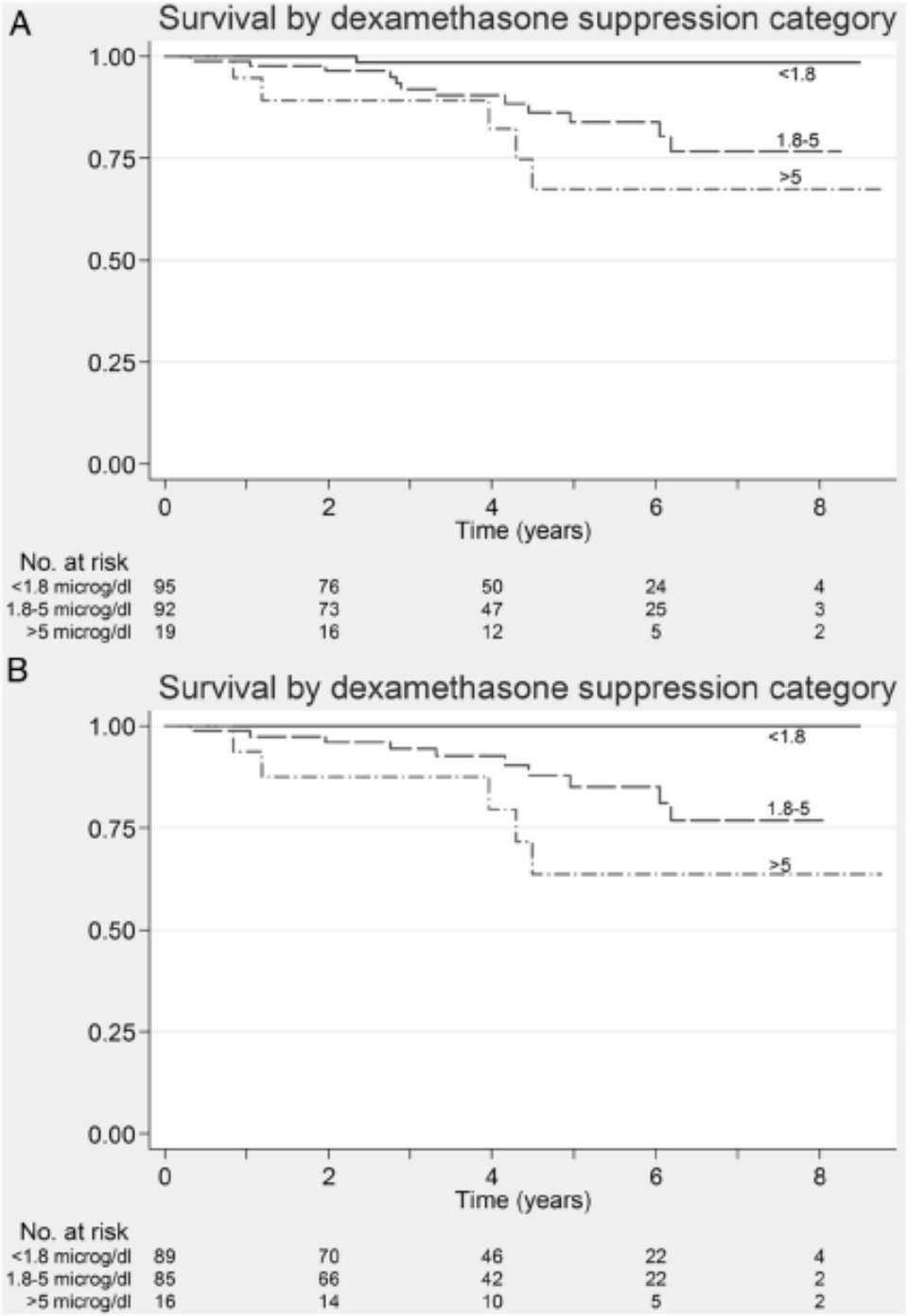
Endocrine Care

Cortisol as a Marker for Increased Mortality in Patients with Incidental Adrenocortical Adenomas

Miguel Debono, Mike Bradburn, Matthew Bull, Barney Harrison, Richard J. Ross, and John Newell-Price

J Clin Endocrinol Metab, December 2014, 99(12):4462–4470


Presented between January 2005 and July 2013 - Incidentaloma protocol (n=272)
Excluded
6 Phaeochromocytoma
2 Hyperaldosteronism
7 Intra-adrenal malignancy (4 metastasis & 3 ACC)
6 Surgery for size increase or >4cm
6 Surgery for metabolic deterioration
3 Developed Cushing's
3 Worsening CV risk factors
Benign, adrenocortical adenoma (n=245)
21 lost to follow up or follow up scan to be arranged
18 on steroids (oral, inhaled, topical, parenteral)
"Primary Analysis"
Benign, adrenocortical adenoma with no size increase
Survival Rate and Cause-specific mortality Analysis
(n = 206)
16 patients with extra-adrenal malignancy
"Sub-Analysis"
Benign, adrenocortical adenoma with no size increase
(n = 190)


A
Survival by dexamethasone suppression category
1.00
0.75
0.50
0.25
0.00
<1.8
1.8-5
>5
0
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4
6
8
Time (years)
No. at risk
<1.8 microg/dl 95 76 50 24 4
1.8-5 microg/dl 92 73 47 25 3
>5 microg/dl 19 16 12 5 2
B
Survival by dexamethasone suppression category
1.00
0.75
0.50
0.25
0.00
<1.8
1.8-5
>5
0
2
4
6
8
Time (years)
No. at risk
<1.8 microg/dl 89 70 46 22 4
1.8-5 microg/dl 85 66 42 22 2
>5 microg/dl 16 14 10 5 2

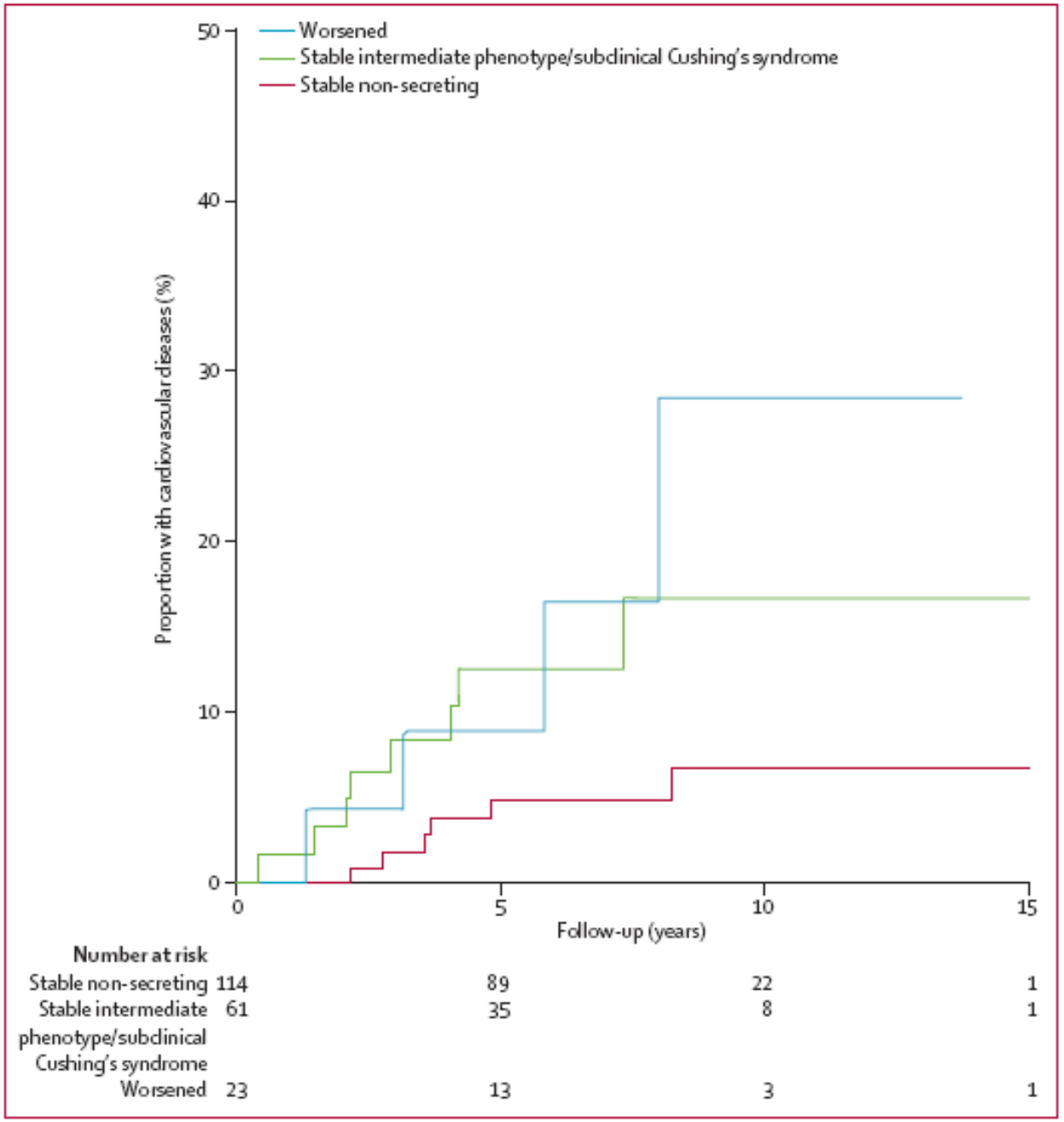
Patients with AI and post dexamethasone serum cortisol >1.8µg/dl have **increased mortality**, mainly related to cardiovascular disease and infection.

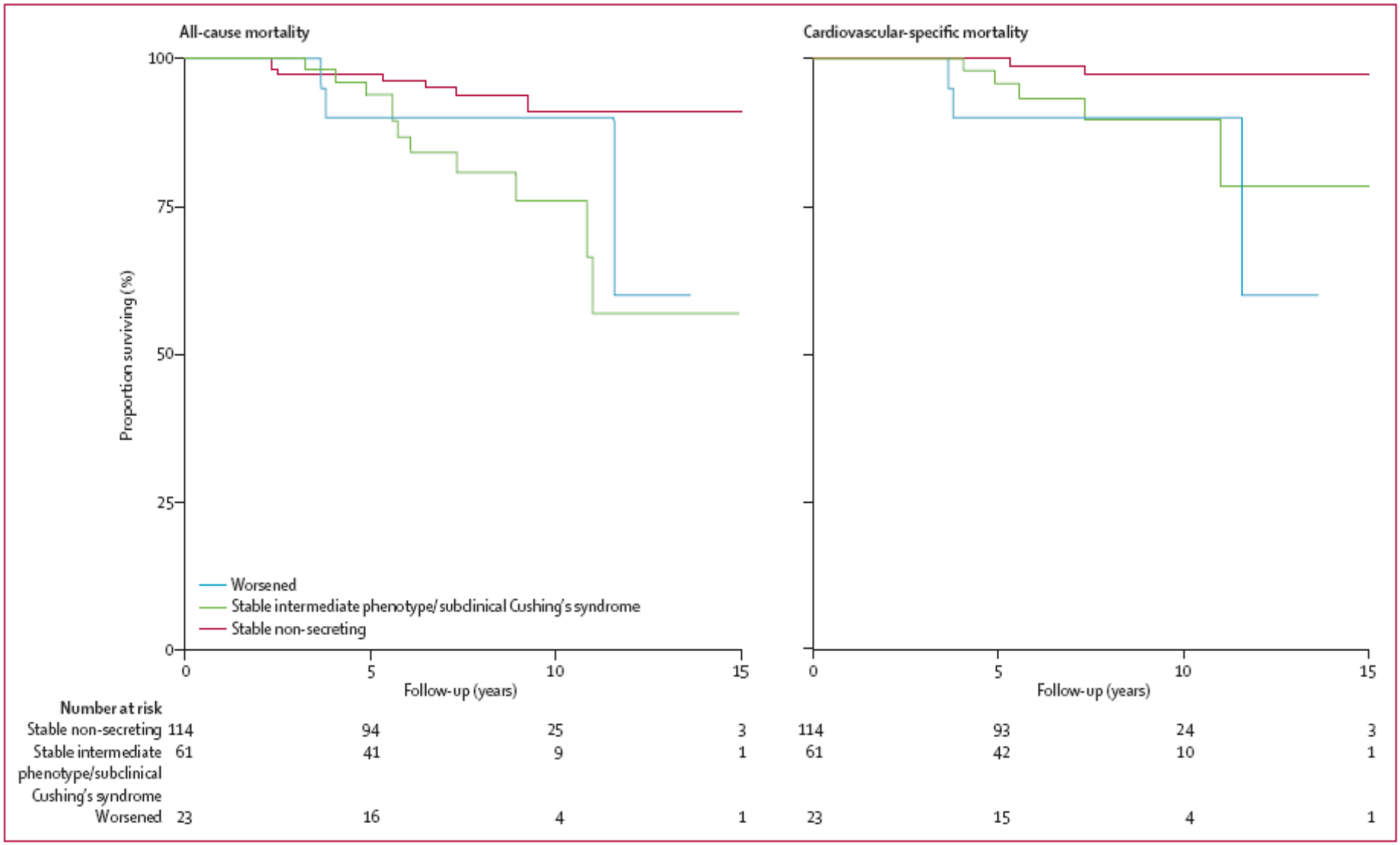
Articles

Cardiovascular events and mortality in patients with adrenal incidentalomas that are either non-secreting or associated with intermediate phenotype or subclinical Cushing's syndrome: a 15-year retrospective study

Guido Di Dalmazi, Valentina Vicennati, Silvia Garelli, Elena Casadio, Eleonora Rinaldi, Emanuela Giampalma, Cristina Mosconi, Rita Golfieri, Alexandro Paccapelo, Uberto Pagotto, Renato Pasquali

www.thelancet.com/diabetes-endocrinology Vol 2 May 2014


Worsened
Stable intermediate phenotype/subclinical Cushing's syndrome
Stable non-secreting
Proportion with cardiovascular diseases (%)
50
40
30
20
10
0
0
5
10
15
Follow-up (years)
Number at risk
Stable non-secreting 114 89 22 1
Stable intermediate phenotype/subclinical Cushing's syndrome 61 35 8 1
Worsened 23 13 3 1


All-cause mortality
Cardiovascular-specific mortality
Proportion surviving (%)
100
75
50
25
0
Worsened
Stable intermediate phenotype/subclinical Cushing's syndrome
Stable non-secreting
0
5
10
15
Follow-up (years)
Number at risk
Stable non-secreting 114 94 25 3 114 93 24 3
Stable intermediate phenotype/subclinical Cushing's syndrome 61 41 9 1 61 42 10 1
Worsened 23 16 4 1 23 15 4 1

Patients with adrenal incidentaloma and mild hypercortisolism have an **increased risk of cardiovascular events and mortality**.

ASSOCIATED COMORBIDITIES

- Metabolic Syndrome
- Cardiovascular Disease
- Osteoporosis

0021-972X/00/$03.00/0
The Journal of Clinical Endocrinology & Metabolism

Vol. 85, No. 4
Printed in U.S.A.

Subclinical Cushing's Syndrome in Patients with Adrenal Incidentaloma: Clinical and Biochemical Features

R. ROSSI, L. TAUCHMANOVA, A. LUCIANO, M. DI MARTINO, C. BATTISTA, L. DEL VISCOVO, V. NUZZO, AND G. LOMBARDI

JCE & M • 2000
Vol 85 • No 4

50 pts with AI (12/50 had SCS):

- **92%** **hypertension**
- **50%** **obesity**
- **42%** **type 2 diabetes mellitus**
- **50%** **abnormal serum lipid concentrations**

- The **clinical and hormonal features improved in all patients treated by adrenalectomy** but were **unchanged** in all those who did not undergo surgery (follow up 9-73 months).

- Interestingly, **all 13 patients who had resection of truly nonfunctioning adenomas because of large size had improved clinically** to such an extent that antihypertensive and antidiabetic therapy was reduced or discontinued.

41 pts with AI (12 SCS) and compared them with 41 controls.

Patients with these tumors (subclinically functioning or nonfunctioning) display some features of the **metabolic syndrome** such as impaired glucose tolerance, increased blood pressure and high triglyceride levels.

Terzolo M et al, Clin Endocrinol (Oxf), 1998;48:89-97.

ORIGINAL ARTICLE

Endocrine Care

Beneficial Metabolic Effects of Prompt Surgical Treatment in Patients with an Adrenal Incidentaloma Causing Biochemical Hypercortisolism

Iacopo Chiodini, Valentina Morelli, Antonio Stefano Salcuni, Cristina Eller-Vainicher, Massimo Torlontano, Francesca Coletti, Laura Iorio, Antonello Cuttitta, Angelo Ambrosio, Leonardo Vicentini, Fabio Pellegrini, Massimiliano Copetti, Paolo Beck-Peccoz, Maura Arosio, Bruno Ambrosi, Vincenzo Trischitta, and Alfredo Scillitani*

J Clin Endocrinol Metab, June 2010, 95(6):2736–2645

180 patients with AI:

Surgery in: 25pts with SH
30pts without SH

No surgery in: 16pts with SH
37pts without SH

Patients with **SH treated** with surgery had **improvement in weight (32%), blood pressure (56%)** and **glucoses levels (48%)**.

Patients with **SH non-treated BP**, Glucose and LDL levels **worsened** more frequently than the ones treated surgically.

Surgery
Volume 152, Number 6
December 2012

Adrenalectomy may improve cardiovascular and metabolic impairment and ameliorate quality of life in patients with adrenal incidentalomas and subclinical Cushing's syndrome

Maurizio Iacobone, MD, Marilisa Citton, MD, Giovanni Viel, MD, Riccardo Boetto, MD, Italo Bonadio, MD, Isabella Mondi, MD, Saveria Tropea, MD, Donato Nitti, MD, *and* **Gennaro Favia, MD,** *Padua, Italy*

20 pts operated **15 pts non operated**

The operated pts had:

- Normalization of laboratory corticosteroid parameter
- Decrease in BP(53%)
- Glymetabolic control improved (50%)
- BMI decreased
- Improvement of SF-36 evaluation

The Non-operated pts had:

- No improvement
- Worsening

ORIGINAL ARTICLE

Endocrine Care

Patients With Apparently Nonfunctioning Adrenal Incidentalomas May Be at Increased Cardiovascular Risk Due to Excessive Cortisol Secretion

Ioannis I. Androulakis,* Gregory A. Kaltsas,* Georgios E. Kollias, Athina C. Markou, Aggeliki K. Gouli, Dimitrios A. Thomas, Krystallenia I. Alexandraki, Christos M. Papamichael, Dimitrios J. Hadjidakis, and George P. Piaditis

J Clin Endocrinol Metab, August 2014, 99(8):2754–2762

60 pts with AI but no Diabetes, Hypertension, Hyperlipidemia

32 healthy controls with normal adrenal imaging

- Ultrasonographic measurement of **carotid intima-media thickness** (IMT) and **flow-mediated dilatation** (FMD)

26 pts had Cortisol Secreting AI

34 pts had Non Functioning AI

Patients with cortisol secreting adrenal incidentaloma **without** hypertension, diabetes, dyslipidemia **exhibit adverse** metabolic and CVR factors

World J Surg (2009) 33:2099–2105
DOI 10.1007/s00268-009-0178-0

World Journal of Surgery

Cardiovascular Risk in Patients with Nonfunctional Adrenal Incidentaloma: Myth or Reality?

Yesim Erbil · Nese Ozbey · Umut Barbaros · Haluk Recai Unalp · Artur Salmashoglu · Selçuk Özarmagan

35 pts NFA **35 controls**

Even patients with nonfunctioning AI also had less **flow-mediated vasodilation** compared with controls.

0013-7227/01/$03.00/0
Printed in U.S.A.

The Journal of Clinical Endocrinology & Metabolism 86(11):5337–5341

Bone Loss Rate in Adrenal Incidentalomas: A Longitudinal Study

IACOPO CHIODINI*, MASSIMO TORLONTANO*, VINCENZO CARNEVALE, GIUSEPPE GUGLIELMI, MARIO CAMMISA, VINCENZO TRISCHITTA, AND A. SCILLITANI

J Clin Endocrinol Metab, November 2001, 86(11):5337–5341

- 24 women with AI divided into two groups on the basis of the median value of urinary cortisol excretion.

- The group with higher cortisol values (subclinical Cushing levels) **had more lumbar trabecular bone loss** than those with low cortisol secretion (not hypersecreting tumors).

ORIGINAL ARTICLE

Endocrine Care

Bone Mineral Density, Prevalence of Vertebral Fractures, and Bone Quality in Patients with Adrenal Incidentalomas with and without Subclinical Hypercortisolism: An Italian Multicenter Study

Iacopo Chiodini, Valentina Morelli, Benedetta Masserini, Antonio Stefano Salcuni, Cristina Eller-Vainicher, Raffaella Viti, Francesca Coletti, Giuseppe Guglielmi, Claudia Battista, Vincenzo Carnevale, Laura Iorio, Paolo Beck-Peccoz, Maura Arosio, Bruno Ambrosi, and Alfredo Scillitani

J Clin Endocrinol Metab, September 2009, 94(9):3207–3214

Multicenter, **retrospective** study 287 patients with AI (85 had SCS)

Patients with SCS had lower bone mineral density, increased spinal deformity index compared with both AI nonfunctioning and controls.

Bilateral Adrenal Incidentalomas

Endocrine (2012) 42:164–173
DOI 10.1007/s12020-012-9622-2

ORIGINAL ARTICLE

Subclinical hypercortisolism and CT appearance in adrenal incidentalomas: a multicenter study from Southern Sweden

Henrik Olsen · Erik Nordenström · Anders Bergenfelz · Ulf Nyman · Stig Valdemarsson · Erik Palmqvist

Nine hospitals in S. Sweden

223 pts with AI

- Unilateral 180 76 (42%) had SH
- Bilateral 43 30 (70%) had SH

Subclinical hypercortisolism is more common in bilateral AIs

Bilateral adrenal incidentalomas differ from unilateral adrenal incidentalomas in subclinical cortisol hypersecretion but not in potential clinical implications

Evangeline Vassilatou, Andromachi Vryonidou[1], Dimitrios Ioannidis[2], Stavroula A Paschou[1], Maria Panagou[2] and Ioanna Tzavara[2]

BAI patients present **more often** with SCS when compared with UAI patients.

However **comorbidities were of similar frequency** in both groups.

Clinical Endocrinology (2009) 70, 674–679 doi: 10.1111/j.1365-2265.2008.03492.x

ORIGINAL ARTICLE

Hormonal activity of adrenal incidentalomas: results from a long-term follow-up study

E. Vassilatou*, A. Vryonidou‡, S. Michalopoulou*, J. Manolist, J. Caratzast, C. Phenekos‡ and I. Tzavara*

- Non Functioning AI are not necessarily evolving to functional , but
- An increased prevalence of CV and Metabolic Risk Factors has been described in pts with NFAI

Due to:

- A mild cortisol excess that cannot be detected with the available diagnostic test
- Periodic secretion

0021-972X/99/$03.00/0
Journal of Clinical Endocrinology and Metabolism

Vol. 84, No. 2
Printed in U.S.A.

Risk Factors and Long-Term Follow-Up of Adrenal Incidentalomas*

LUISA BARZON, CARLA SCARONI, NICOLETTA SONINO, FRANCESCO FALLO, AGOSTINO PAOLETTA, AND MARCO BOSCARO

75 patients (median follow up 4 years)

The estimated cumulative risks for **mass enlargement and hyperfunction** were **18%** and **9.5%** respectively after 5 years, and **22.8%** and **9.5%** after 10 years**.**

J. Endocrinol. Invest. *24:* 846-855, 2001

The natural history of incidentally discovered adrenocortical adenomas: A retrospective evaluation

E. Grossrubatscher*, F. Vignati*, M. Possa**, and P. Loli*

53 patients with incidentalomas followed for 6-78 months.

22 lesions (41.5%) increased in size and 6 lesions (11.3%) decreased in size or disappeared.

Clinical Endocrinology (2009) 70, 674–679 doi: 10.1111/j.1365-2265.2008.03492.x

ORIGINAL ARTICLE

Hormonal activity of adrenal incidentalomas: results from a long-term follow-up study

E. Vassilatou*, A. Vryonidou‡, S. Michalopoulou*, J. Manolis†, J. Caratzas†, C. Phenekos‡ and I. Tzavara*

77 patients with adrenal incidentaloma followed for a medium follow-up of **60 months** using annual hormonal and CT evaluation.

A proportion of the non functioning incidentalomas developed overt hyperfunction.

Increase in size was not uncommon.

“Subclinical pheochromocytoma”

The totally asymptomatic incidentaloma that histologically proves to be a pheochromocytoma.

Measurement of catecholamines and their metabolites (metanephrines) in plasma and/or urine.

There is **no indication for routine use of ^{131}I-meta-iodobenzylguanidine (I-MIBG) scintigraphy** in the evaluation of an incidentaloma unless catecholamine and urinary metabolites are elevated.

Prophylactic measures should always be taken (e.g., arterial line, immediate access to intravenous nipride) during surgery.

“Subclinical primary aldosteronism”

- **More than 40% of patients with primary aldosteronism are normokalemic.**

- The previously recommended measurement of potassium as the only test to rule out primary aldosteronism in the case of incidentaloma should be abandoned.

In a normotensive patient with **a serum potassium level greater than 3.9 nmol/L, no further hormonal evaluation** is necessary.

A detailed time-consuming evaluation is necessary, especially **in all hypertensive patients**, to rule out primary aldosteronism which may be the **cause of hypertension in up to 15%** of these patients.

The screening for subclinical primary aldosteronism should include, in addition to serum potassium, **the upright aldosterone level to plasma renin activity (PRA) ratio.**

- Patients with two or more samples positive aldosterone/PRA ratio (>40) should undergo the **fluorocortisone suppression test** (0.4 mg every day for 4 days).

- The **acute saline suppression test** (2L of 0.9% NaCl solution infused intravenously in 4 hours) to confirm the diagnosis.

Bilateral adrenal venous sampling with measurements of aldosterone and cortisol levels is the necessary next step to lateralize, determine the subtype of primary aldosteronism in order to identify the patient who will be cured through surgery.

Risk for Cancer

Adrenal Incindentaloma:

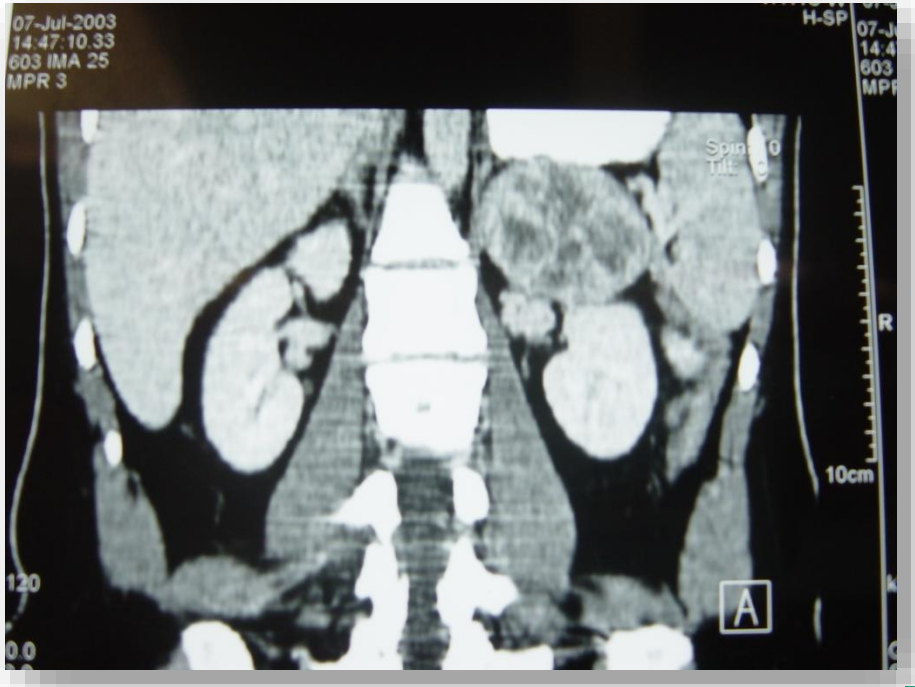
- Primary carcinoma 5%
- Metastatic carcinoma 3%

Imaging

In addition to assessing distant metastasis and tumor size, imaging studies may suggest malignancy.

CT

A poorly delineated ragged tumor with stippled calcifications and with areas of necrosis.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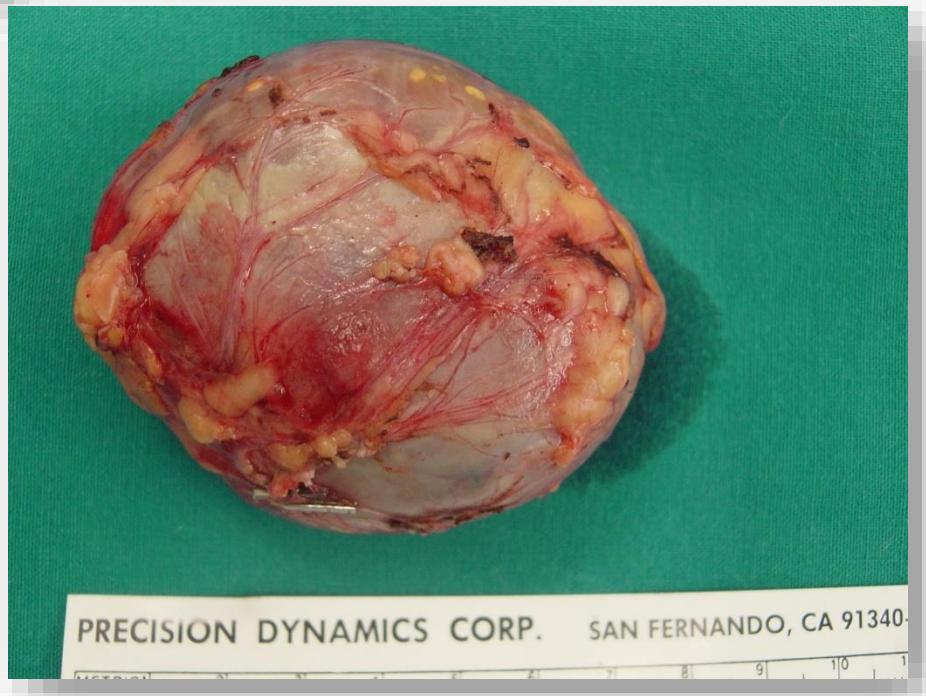

PRECISION DYNAMICS CORP.
SAN FERNANDO, CA 91340

CT

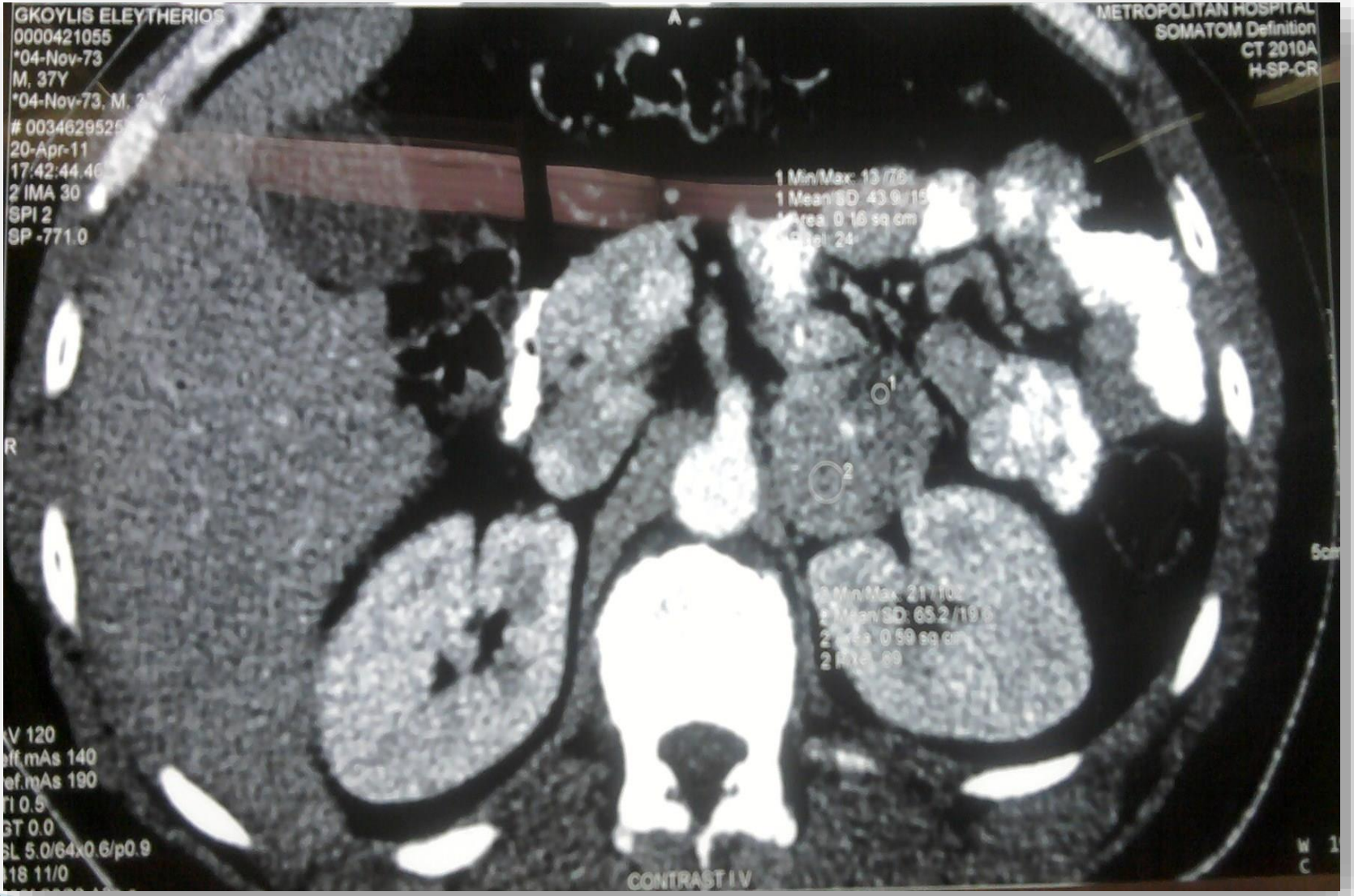
Attention value

≤10 Hounsfield units probably a benign tumor

>10 Hounsfield units …… suspicious

MRI

Heterogeneously increased, early T2-weighted signal, weak and late enhancement after gadolinium injection or an intravascular signal identical to the tumor signal.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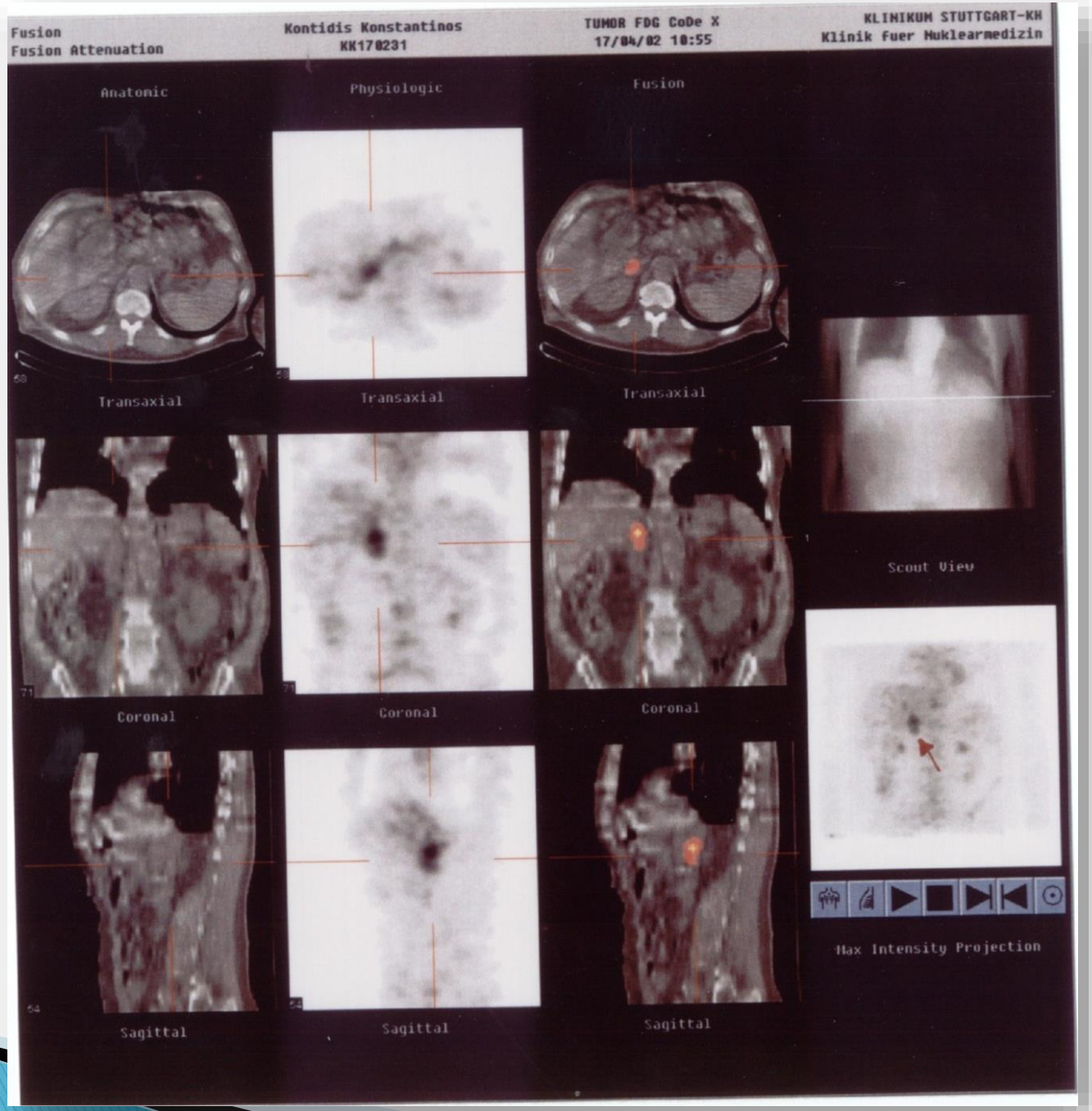
CONTRAST I.V

The **18 F-FDG-PET-scan** is a useful tool confirming isolated metastases and selecting patients for adrenalectomy.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Klinik Fuer Nuklearmedizin
Anatomic
Physiologic
Fusion
Transaxial
Transaxial
Transaxial
Coronal
Coronal
Coronal
Sagittal
Sagittal
Sagittal
Scout View
Max Intensity Projection

Fine-Needle Aspiration

- Fine-needle aspiration (FNA) biopsy of an incidentaloma has a **limited role**.

- FNA cannot differentiate cortical adenoma from carcinoma because it cannot detect invasion of the tumor into the capsule.

Size of tumor

Although most clinically treated adrenal malignancies are discovered when they are **larger than 6 cm** in diameter, several reports have described very large tumors that never metastasized and small adrenal tumors that proved malignant.

> 6cm

> 4cm Indication for surgery

> 3cm

The size of an incidentaloma as reported on a CT scan is usually less than the size reported on the histology report.

ORIGINAL ARTICLE

How Accurate Is Computed Tomography in Predicting the Real Size of Adrenal Tumors?

A Retrospective Study

Dimitrios A. Linos, MD; Nicholas Stylopoulos

The regression line (y=0.85 + 1.09x) relating CT-estimated and histological tumor size was linear (r=0.90, P<.001).

Background: The ability to accurately assess tumor s
is an important consideration during the preoperative eva
ation of adrenal tumors, particularly solid nonfunctio
ing masses (incidentalomas or adrenalomas). Does the h
tological size of the adrenal tumor correspond to the p
operative computed tomography (CT)–estimated size

Objective: To evaluate the accuracy of CT in predicting the real size of adrenal tumors.

Design: Retrospective review of all clinical records of patients who underwent adrenalectomy from 1984 through 1995. The mean tumor size reported from CT examinations was compared with the corresponding size obtained from the pathology reports and the statistical difference was evaluated.

Setting: University and private hospitals in Athens, Greece.

Patients: Seventy-six patients who underwent adrenalectomy for various adrenal diseases and who met strict entry criteria.

Results: For the entire population, the mean diameter

tumors measuring from 2.6 to 2. addition, 4 pheochromocytomas were y and laboratory "silent" at the time of thei discovery. The regression line ($y=0.85+1.09x$) relating CT-estimated and histological tumor size was linear ($r=0.90$, $P<.001$).

Conclusions: Computed tomography underestimates the real size of adrenal tumors. The CT-estimated value should be corrected accordingly to obtain the real size. The size of an adrenal tumor, even when corrected, cannot predict the tumor's clinical behavior in many cases. Surgeons should always cautiously interpret the proposed diagnostic cutoffs, especially when considering surgical or conservative management of small nonfunctioning adrenal tumors.

Arch Surg. 1997;132:740-743

World J. Surg. 28, 494–497, 2004
DOI: 10.1007/s00268-004-7292-9

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Correlation between Radiologic and Pathologic Dimensions of Adrenal Masses

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Abstract. The size of adrenal tumors has been shown to be a good predictor of malignancy. There is still some controversy about the concordance between radiologic and real pathologic measurements. The aim of this study is to determine the correlation between direct and corrected radiologic computed tomography scan dimensions and the measurements of the resected specimen. A total of 41 adrenal tumors were included. Direct and corrected measurements of the largest diam
pathologic dimensions. The Linos formula v
surements. Proper statistics were used co
cance level of 0.05. The intraclass correlati
measurements were 0.89 [95% confidence i
0.00001) and 0.90 (95%CI 0.82–0.95, $p = 0.0$
ate analysis using Pearson´s correlation b
variables showed $r = 0.82$ ($p < 0.0001$) wh
surements were compared and $r = 0.83$ (p
values were compared with the real dimen
strate good correlation between radiolog
of adrenal tumors. The Linos formula
accurate than direct radiologic measur
were compared, whereas when individual c
two were similar. The Linos formula and ra
used to determine the proper management
individual patients.

The Linos formula turned out to be significantly more accurate than direct radiologic measurements when means of the groups were compared, whereas when individual correlations were determined the two were similar. The Linos formula and radiologic measurements can be used to determine the proper management of adrenal incidentalomas in individual patients.

Genetic and Molecular Biology Studies

- Currently, the only accepted criteria to determine whether an incidentaloma is benign or malignant are **metastasis** (synchronous or metachronous) **and local invasion** into adjacent structures.

- The mapping and identification of genes responsible for hereditary syndromes (e.g. multiple endocrine neoplasia type 1, Li-Fraumeni) have increased our understanding of adrenocortical tumorigenesis.

What is the best surgical approach in the management of adrenal incidentalomas?

- Laparoscopic adrenalectomy
- Posterior retroperitoneoscopic adrenalectomy

Open adrenalectomy should be reserved for very large adrenal carcinomas invading the surrounding tissue.

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journal homepage: www.europeanurology.com

European Association of Urology

Adrenals

Retrospective Evaluation of the Outcome of Open Versus Laparoscopic Adrenalectomy for Stage I and II Adrenocortical Cancer

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Suspicious AI for malignancy

43 patients with Stage I and II ACC (25 patients open adrenalectomy and 18 laparoscopic).

Recurrence rate, median recurrence free survival, overall survival did not differ between the two groups.

The German ACC Registry published their results on 152 patients with Stage I and II tumors less than 10cm in diameter. 35 had undergone laparoscopic and 117 open adrenalectomy.

Disease-specified survival as well as recurrence free survival, frequency of tumor capsule violation and postoperative peritoneal carcinomatosis were not different between the two groups.

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Open versus endoscopic adrenalectomy in the treatment of localized (stage I/II) adrenocortical carcinoma: Results of a multiinstitutional Italian survey

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156 patients with stage I and II adrenocortical carcinoma. (30 laparoscopic and 126 open adrenalectomy).

No significant differences were found between the two groups in terms of 5 year disease free survival and 5 year overall survival rates.

The most important factor for the success of any adrenalectomy, especially for tumors suspicious for carcinoma is **the experience of the surgeon on how to approach the adrenal tumors**. This is true for either open or laparoscopic adrenalectomy.

Surg Endosc (2011) 25:3584–3589
DOI 10.1007/s00464-011-1762-6

Impact of posterior retroperitoneoscopic adrenalectomy in a tertiary care center: a paradigm shift

Andreas Kiriakopoulos · Konstantinos P. Economopoulos · Efthimios Poulios · Dimitrios Linos

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Abstract

Background Posterior retroperitoneoscopic adrenalectomy has substituted its anterior laparoscopic counterpart as the treatment of choice in the management of adrenal tumors at the authors' institution. The authors present their comparative results between these operative techniques, demonstrating the reasons for this change.

Methods From May 2008 to September 2010, 30 patients underwent posterior retroperitoneoscopic adrenalectomy. Operative time, complications, hospital stay, postoperative pain, and cost were compared with those of 30 selected laparoscopic control subjects treated from 2005 to 2010. Statistical analysis was based on Chi-square, the Mann–Whitney *U* test, the independent-samples *t*-test, and the Wilcoxon matched pairs test, as appropriate.

Results The median tumor size was 3.8 cm (range, 1.5–8.0 cm) in the retroperitoneoscopic group and 4.9 cm (range, 2.4–8.0 cm) in the laparoscopic group. The median operative time was similar between the two groups (90.0 min; range, 60–165 min vs. 77.5 min; range, 55–120 min; $P = 0.138$). It was, however, significantly reduced after the 20th case (97.5 min; range, 80–165 min vs. 70 min; range, 60–110 min; $P < 0.001$) in the retroperitoneoscopic group. The median visual analog pain scores were significantly lower in the retroperitoneoscopic group on both the first and the third postoperative days, respectively (1; range, 0–1 vs. 4; range, 3–6; $P < 0.001$ and 0; range, 0–1 vs. 3;
median postoperative hos
retroperitoneoscopic gro
4 days; range, 3–6 days;
terior approach was signi
aroscopic technique ($P <$
Conclusions Posterior
tomy compared with lapa
fast, and vastly superior
hospital stay in thi
reproduce such ex
patient recover
cost, the authors sugges
approach should become the
mally invasive adrenal surgery.

Keywords Adrenal tumors · Laparoscopic adrenalectomy · Retroperitoneoscopic adrenalectomy · Retroperitoneum

The authors suggest that the retroperitoneoscopic approach should become the method of choice in minimally invasive adrenal surgery.

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DOI 10.1007/s00268-010-0453-0

World Journal of Surgery

Posterior Retroperitoneoscopic Adrenalectomy for Clinical and Subclinical Cushing's Syndrome

Pier F. Alesina · Silvia Hommeltenberg · Beate Meier · Stephan Petersenn · Harald Lahner · Kurt W. Schmid · Klaus Mann · Martin K. Walz

170 pts with clinical (n=99) and subclinical (n=71) Cushing's syndrome.

There were no mortalities or major complications reported.

World J Surg (2008) 32:847–853
DOI 10.1007/s00268-008-9513-0

World Journal of Surgery

Retroperitoneoscopic Adrenalectomy in Conn's Syndrome Caused by Adrenal Adenomas or Nodular Hyperplasia

Martin K. Walz · Roland Gwosdz · Stephanie L. Levin · Piero F. Alesina · Anna-Carinna Suttorp · Klaus A. Metz · Frank A. Wenger · Stephan Petersenn · Klaus Mann · Kurt W. Schmid

183 pts with Conn's syndrome

The retroperitoneoscopic approach provided a time efficient and safe surgical approach.

Posterior Retroperitoneoscopic Adrenalectomy: A Contemporary American Experience

Paxton V Dickson, MD, Camilo Jimenez, MD, Gary B Chisholm, MS, Debra L Kennamer, MD, Chaan Ng, MD, Elizabeth G Grubbs, MD, FACS, Douglas B Evans, MD, FACS, Jeffrey E Lee, MD, FACS, Nancy D Perrier, MD, FACS

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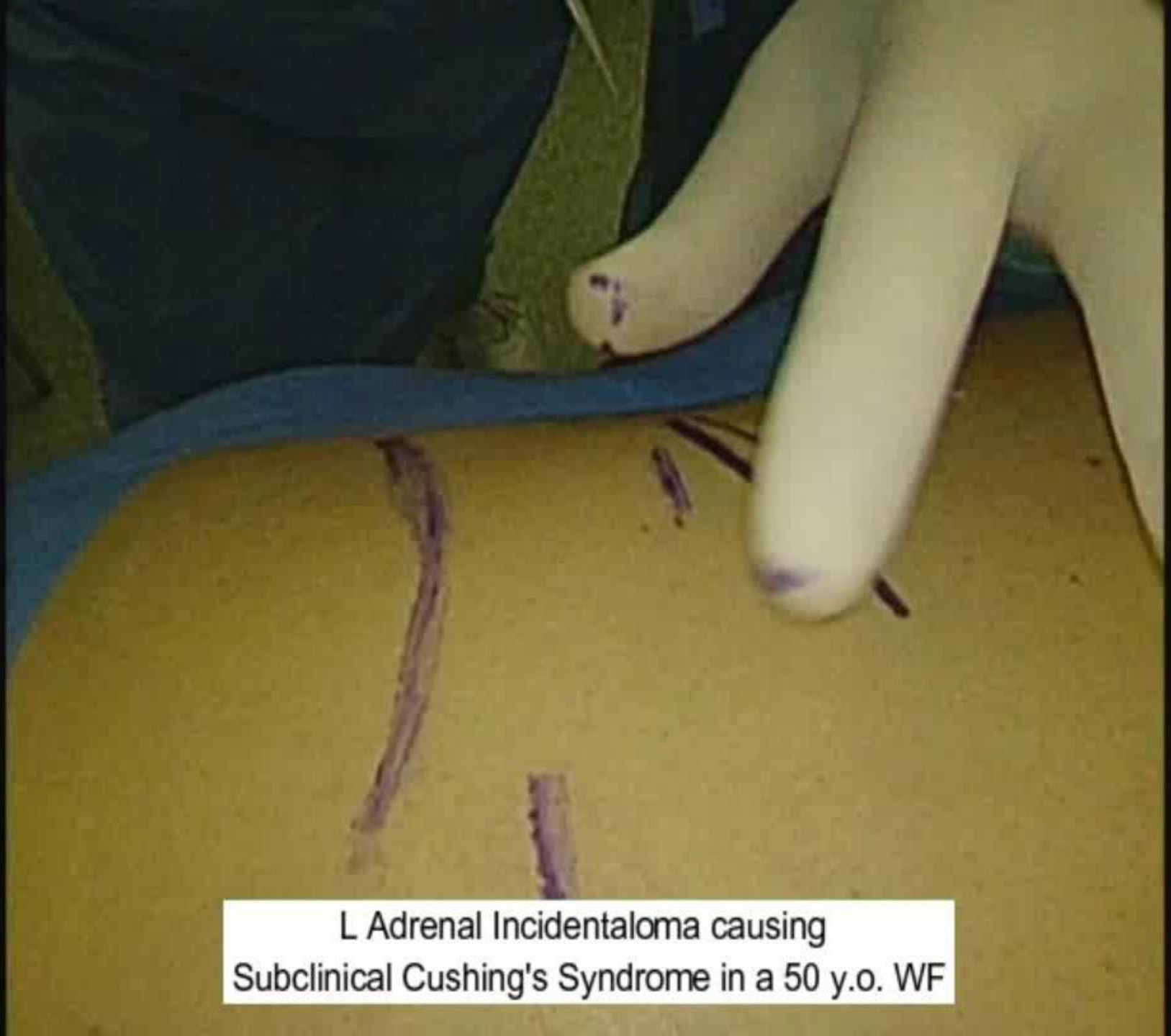
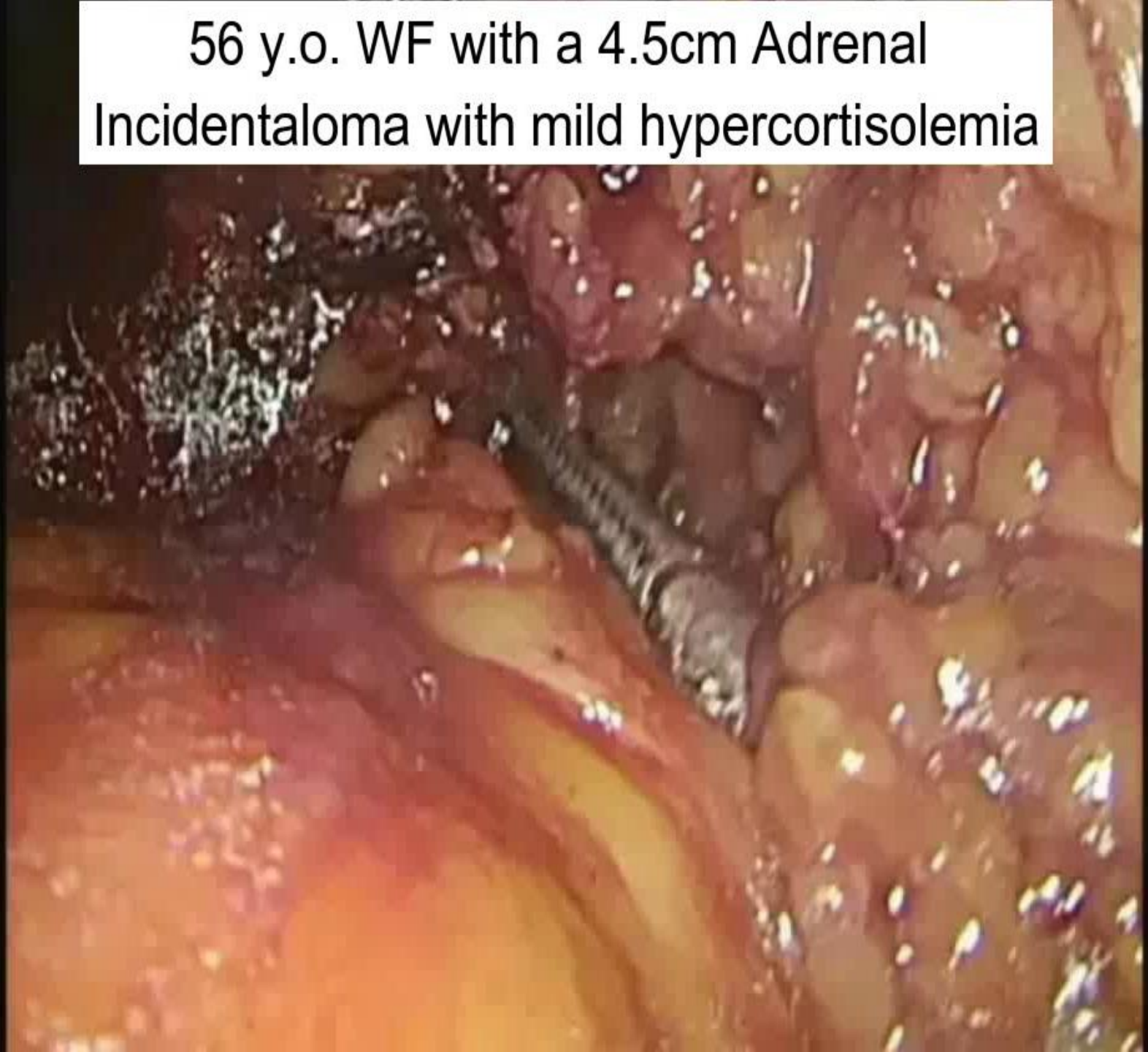
doi:10.1016/j.jamcollsurg.2010.12.023

PRA resulted in decreased operative times, blood loss and postoperative length of stay compared with LA.



L Adrenal Incidentaloma causing
Subclinical Cushing's Syndrome in a 50 y.o. WF

56 y.o. WF with a 4.5cm Adrenal Incidentaloma with mild hypercortisolemia



Most endocrinologists treat this

***A**drenal **I**ncidentaloma **D**iscovered **S**erendipitously*

Conservatively…….

But .....

- The Increased Mortality of pts with AI
- The Associated Comorbidities (Metabolic Sx, CVR Factor, Osteoporosis) frequently followed by significant improvement after surgery
- The safety of endoscopic adrenalectomy

Should we change our current management?

Surgical management:

- Evidence for a subclinically functioning tumor (mild hypercortisolism)
- Associated comorbidities (hypertension, obesity, diabetes, osteoporosis, etc)
- Size >4cm
- Age
- Radiological suspicion (CT>10HU)

Conservative management:

- No clinical or laboratory evidence for subclinical function of the tumor.
- No associated comorbidities potentially related to the incidentaloma.
- No suspicion of adrenal carcinoma.

World J. Surg. 20, 788–793, 1996

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Adrenaloma: A Call for More Aggressive Management

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Abstract. We review our experience from the surgical management of 57 patients (24 males, 33 females) with a mean age of 48.5 years who underwent adrenalectomy because of the computed tomography (CT) finding of a "nonfunctioning" adrenal tumor (adrenaloma). We found that CT consistently underestimated the real histologic size of the adrenal tumor ($p = 0.001$). Of the 57 resected tumors, 23 were cortical adenomas, 7 myelolipomas, 8 adrenal cysts, 11 nodular hyperplasias, 2 primary adenocarcinomas, 2 metastatic carcinomas, and 4 pheochromocytomas. The mean diameter was 5.89 cm and the mean weight 114.07 g. The mean diameter of the resected primary adenocarcinomas was 3.0 cm and 1 respectively. The operative mortality was zero and the morbidity minimal. The mean operating time was 137 min (range 60–240 minutes). The posterior approach had the shortest and the laparoscopic approach the shortest hospital stay and postoperative need for narcotics. During the 6.2 years mean period, five patients with preoperative hypertension remained hypertensive, and both patients with the resected primary adenocarcinomas are alive without recurrence. We suggest a more liberal surgical approach in patients with adrenalomas because: (1) even small adrenal tumors may be malignant or potentially lethal (e.g., pheochromocytoma), (2) tumors that appear to be nonfunctioning may in reality be functioning, and (3) other nonfunctioning tumors may, with time (and without our notice), function. The low risk of adrenalectomy especially via the laparoscopic approach can provide an early definitive diagnosis and treatment, avoiding the cost of repeated CT scans and other studies as suggested by the currently prevailing conservative management of these tumors.

The low risk of adrenalectomy especially via the laparoscopic approach can provide an early definitive diagnosis and treatment

Thank you!