

Adrenal Sparing Surgery for Pheochromocytoma: Indications, Techniques and Outcomes

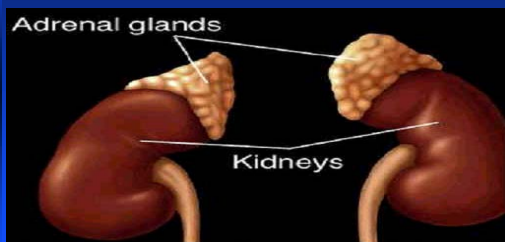
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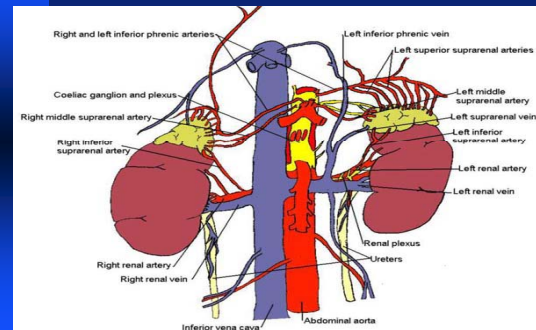
Disclosures

- No financial disclosures
- I believe in adrenal preservation
- I believe that adrenal insufficiency is dangerous

Adrenals



Adrenals



Surgery: Routine adrenalectomy in renal cancer—an antiquated practice

Gennady Bratslavsky & W. Marston Linehan

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PHEOCHROMOCYTOMA



Why not remove the entire adrenal gland?

Adrenal gland is not safe

- New Tumors
 - ◆ Carcinoma - 1 case per 1.7 million people
 - ◆ Pheochromocytoma - 0.8 per 100,000 person-years
 - ◆ Aldosteronoma - 10 per 100,000 people
 - ◆ Adenoma -
 - 1-5% of all cross-sectional imaging
 - Autopsy, 2-10% of cases involve a benign cortical adrenal adenoma
 - A fraction of these will need to be removed
 - ◆ Metastatic
 - 50% of melanomas
 - 30-40% of breast and lung cancers
 - 10-20% of renal and gastrointestinal tumors
- Trauma - 0.22% of all trauma admissions
- Primary adrenal insufficiency (Addison's disease) 5/100,000
 - ◆ Idiopathic adrenal atrophy
 - ◆ Granulomatous disease
 - ◆ Infarction and hemorrhage
 - ◆ Metastatic tumor
 - ◆ Infiltration lesions (i.e., amyloidosis)

Idiopathic		Amyloidosis
Autoimmune		Iron Deposition
Polyglandular autoimmune syndrome type 1		
Polyarteritis nodosa		Neoplastic
True idiopathic		Primary adrenal neoplasm
Infectious		Secondary adrenal neoplasm
Bacterial		Loss of adrenal during treatment of
Meningococcemia, acute fulminating		Renal Cell Carcinoma
Granulomatous		Hemorrhage
Tuberculosis		Waterhouse-Friderichsen syndrome
Protozoal & Fungal		Heparin-induced thrombocytopenia
Histoplasmosis		Antiphospholipid syndrome
Blastomycosis		Trauma
Coccidioidomycosis		Drug related
Candidiasis		Activation of cortisol metabolism
Cryptococcosis		Inhibition of enzymes responsible for
Viral		cortisol synthesis
Cytomegalovirus		Endocrine disorders
Herpes simplex virus		Hashimoto's disease
HIV/AIDS		Pernicious anemia
Infiltrative		Diabetes Mellitus
Sarcoidosis		Other
Metastatic disease		POEMS syndrome
Lymphoma/Leukemia		Irradiation
Hemochromatosis		Anorexia-Nervosa
		Adrenoleukodystrophy

The old rule of 10% for pheochromocytoma is old and not correct



The NEW ENGLAND
JOURNAL of MEDICINE

GERM-LINE MUTATIONS IN NONSYNDROMIC PHEOCHROMOCYTOMA

GERM-LINE MUTATIONS IN NONSYNDROMIC PHEOCHROMOCYTOMA

HARTMUT P.H. NEUMANN, M.D., BIKE BAUSCH, SARAH R. McWHIRNEY, B.A., BERNHARD U. BENDER, M.D.,
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FOR THE FREIBURG-WARSZAW-COLUMBUS PHEOCHROMOCYTOMA STUDY GROUP*

N Engl J Med 2002;346:1459-66

Hereditary Pheochromocytoma

- von Hippel-Lindau
- Multiple-Endocrine-Neoplasia-2 (MEN-2)
- Von-Recklinghausen's Disease (VRD)
- Familial Pheochromocytoma (FP)
- SDH (B or D)
- More is coming

Hereditary Pheochromocytoma

Von-Hippel-Lindau (VHL)

- 47-58% will present with tumors bilaterally
- Not always synchronous - 50% are metachronous
- Risk of bilateral pheochromocytomas is related to mutation type (0-57%)
- 14-22% of patients will recur locally after complete adrenalectomy

Pros and cons of partial adrenalectomy

- Partial adrenalectomy can preserve adrenal cortical function
- Avoidance of adrenal insufficiency/ Addisonian crisis/ excess exogenous steroids
- Must estimate risk of new/recurrent disease

Morbidity of adrenal insufficiency

- Steroid replacement is not physiological
- Patients will either have too much or too little exogenous steroid at given times
- “DO NOT GET STRESSED”

Morbidity of Adrenal Insufficiency: Steroids

■ Adverse effects

- **Common:** mood changes, diarrhea, abdominal distention, nausea, dyspepsia, increased appetite, peptic ulcer, adrenal suppression, candidiasis, weight gain, hirsutism, increased intraocular pressure, immunosuppression, hypertension, edema, hypokalemia (fludrocortisone, hydrocortisone)
- **Rare:** psychic derangements, suicidality, depression, seizures, thromboembolism, pancreatitis, leukocytosis, menstrual irregularities, glucose intolerance, poor wound healing, euphoria, Kaposi's sarcoma, osteoporosis, corneal perforation, growth suppression (pediatric patients)

Morbidity of Adrenal Insufficiency: Steroids

■ Monitor

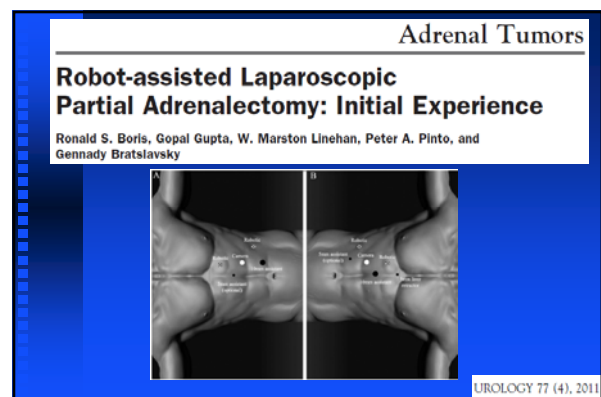
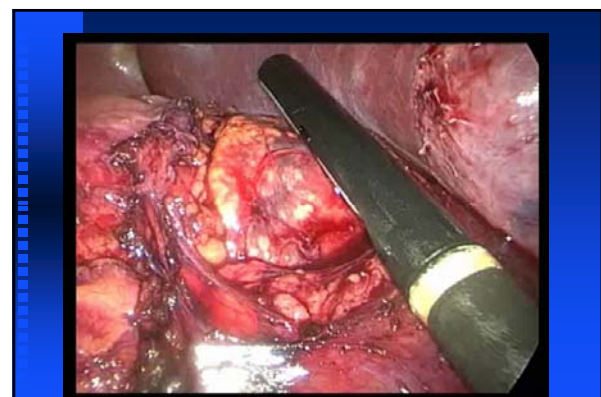
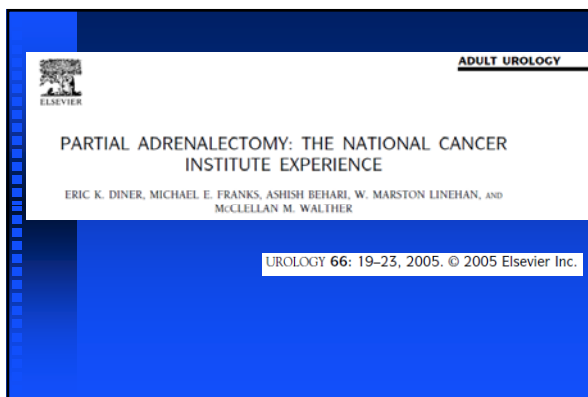
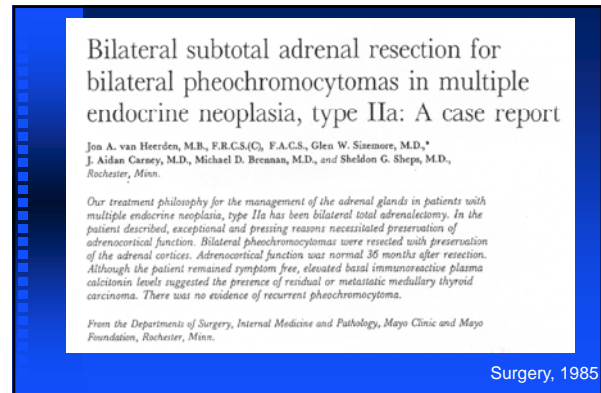
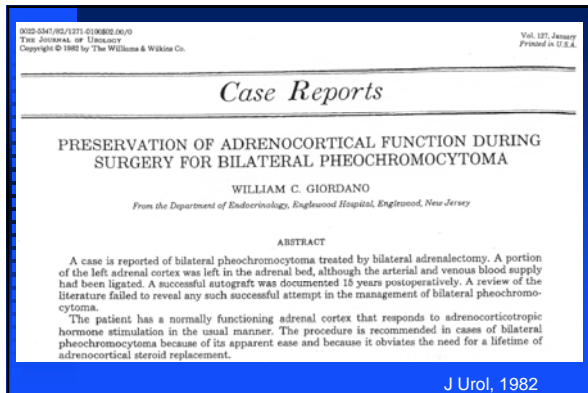
- ◆ Blood pressure
- ◆ Weight
- ◆ Serum electrolyte levels
- ◆ Blood glucose level
- ◆ Growth (pediatric patients)
- ◆ Bone density
- ◆ Ophthalmological examinations

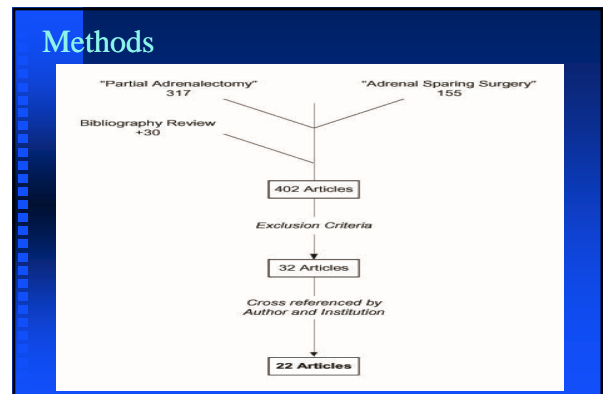
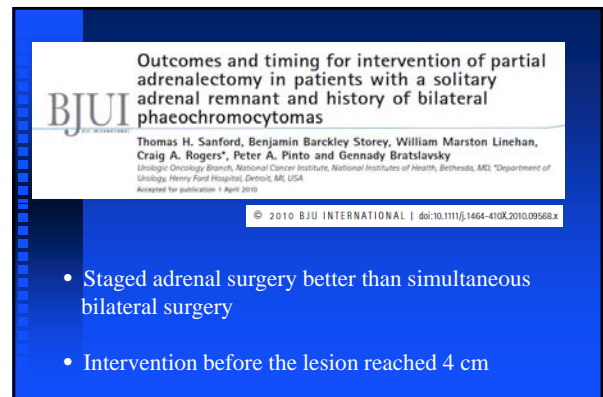
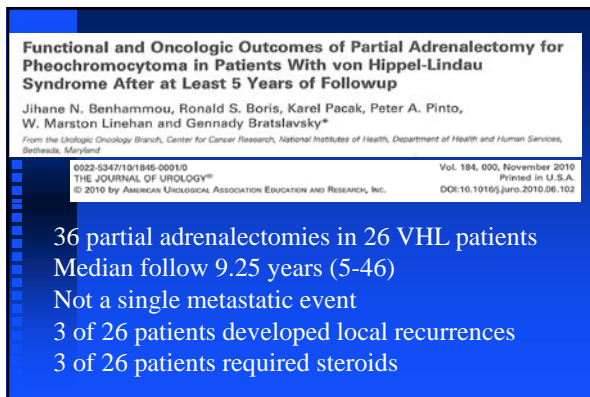
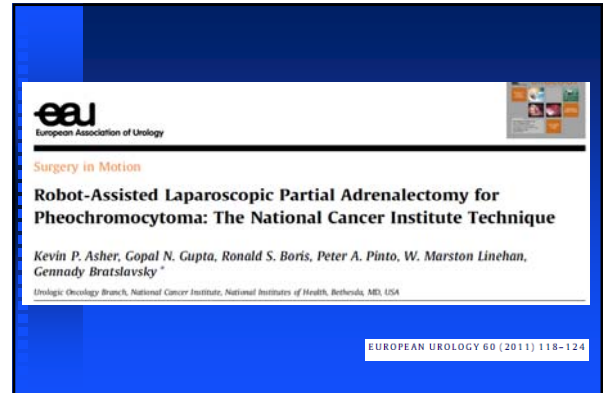
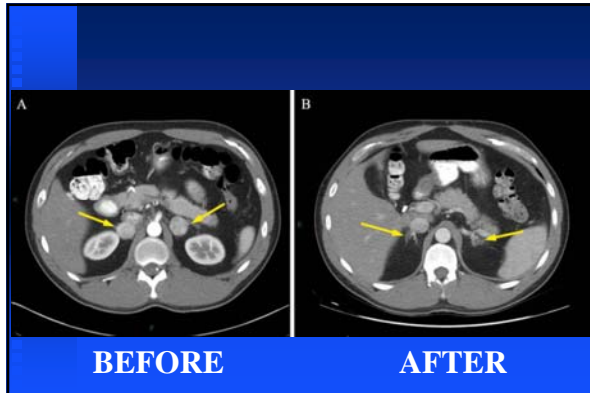
Morbidity of Adrenal Insufficiency: Steroids Interactions

- Antidiabetics (decreased hypoglycemic effect)
- Antihypertensives (decreased antihypertensive effect)
- Barbiturates (increased serum prednisone level)
- Cholestyramine (reduced absorption of corticosteroid)
- Colestipol (reduced absorption of corticosteroid)
- Cyclosporine (increased serum levels of both medications; increased risk of seizures)
- Digoxin (increased risk of digoxin toxicity)
- Diuretics (decreased diuretic effect)
- Estrogens (increased serum corticosteroid level)
- Isoniazid (decreased serum isoniazid level)
- Ketoconazole (increased serum corticosteroid level)
- Macrolides (increased serum corticosteroid level)
- Noncorticosteroidal anti-inflammatory drugs (increased risk of gastrointestinal ulceration/bleeding)
- Salicylates (increased serum salicylate level)
- Vaccinations (avoid concomitant use; decreased acquired-immunity effect)
- Warfarin (increased risk of altered clotting time)

Morbidity of adrenal insufficiency after bilateral adrenalectomy

- ◆ 29% had to stop work or decrease workload
- ◆ 60% reported chronic fatigue
- ◆ 44% categorize themselves as “handicapped”
- ◆ 33% hospitalized with Addisonian crisis
- ◆ 4% death from Addisonian crisis





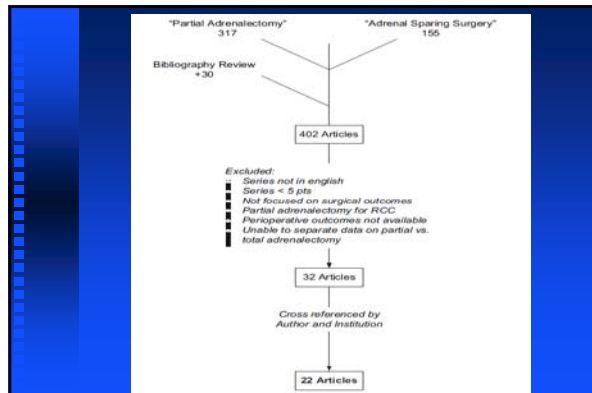
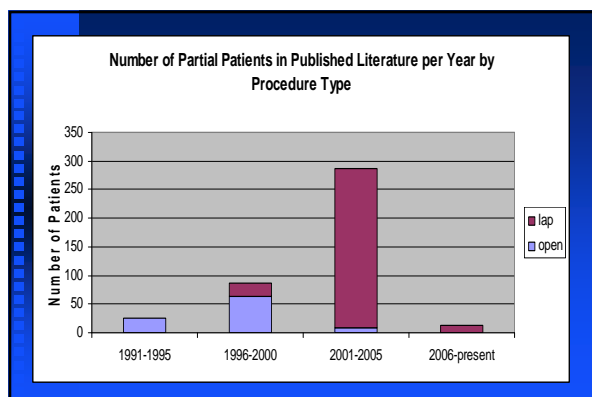
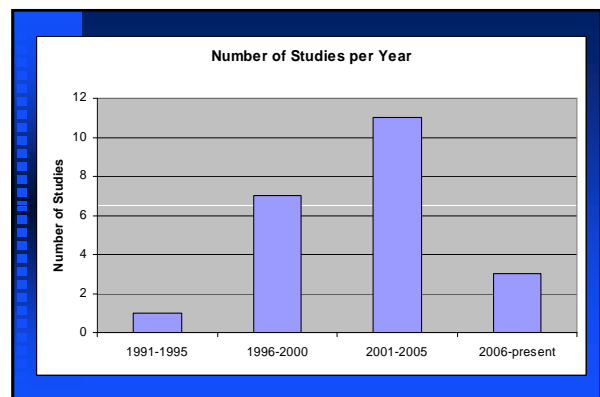


Table 1. Studies

References	No. Pts/No. Partial Adrenalectomy
Al-Sobhi et al ¹¹	7/7
Brauckhoff et al ¹⁰	14/14
Castillo et al ⁷	22/7
Diner et al ⁸	33/23
Edstrom et al ⁵	5/5
Iihara et al ¹³	9/5
Iweda et al ¹⁴	10/10
Imai et al ¹⁷	5/5
Inabnet et al ²⁰	32/5
Ishidoya et al ¹²	92/29
Ishikawa et al ¹⁵	55/11
Jeschke et al ⁶	13/13
Kok and Yapp ¹⁶	8/8
Lee et al ¹	15/15
Liao et al ¹⁹	8/8
Meria et al ²⁴	212/20
Nakada et al ²³	48/26
Nambirajan et al ⁹	7/7
Neumann et al ²⁵	39/29
Roukounakis et al ¹²	7/7
Sasagawa et al ¹¹	47/47
Walz et al ¹⁸	318/96
Totals	1,006/417

Author	Institution	Year	No of Patients	No of Partial Adrenalectomies
Nakada	Yamagata, Japan	1995	48	26
Lee	Houston, USA	1995	15	15
Edstrom	Stockholm, Sweden	1999	5	5
Neumann	Freiburg, Germany	1999	39	39
Imai	Nagoya, Japan	1999	5	5
Ishikawa	Osaka, Japan	2000	55	11
Al-Sobhi	Innsbruck, Austria	2000	7	7
Inabnet	New York, USA	2000	32	5
Iweda	Tokyo, Japan	2002	10	10
Kok	Bandar Seri Begawan BA	2002	8	8
Iihara	Tokyo, Japan	2003	9	5
Meria	Paris, France	2003	212	20
Jeschke	Klagenfurt, Austria	2003	13	13
Sasagawa	Yamagata, Japan	2003	47	47
Brauckhoff	Halle/Saale, Germany	2003	14	14
Walz	Essen, Germany	2004	318	96
Diner	Bethesda, USA	2005	33	33
Ishidoya	Sendai, Japan	2005	92	29
Nambirajan	Linz, Austria	2005	7	7
Liao	Taipei, Taiwan	2006	8	8
Castillo	Santiago de Chile, Chile	2007	22	7
Roukounakis	Athens, Greece	2007	7	7



Partial Adrenalectomy Review

	# of Patients	# of Studies
Total patients	417	22
Clinical Diagnosis	422 (100)	22
Conn's Syndrome/APA (%)	174 (42)	14
Pheochromocytoma (%)	157 (37)	12
Non-functional tumors (%)	51 (12)	6
Cushing's Syndrome/CPA (%)	40 (9)	5

Table 3. Surgical characteristics

	No. Pts/Total No.	No. Studies
Surgical approach description	417	22
Laparoscopy	319 (76)	17
Open approach	98 (24)	6
Laparoscopy–open conversion	2/308 (0.7)	16
Partial–total adrenalectomy	7/281 (2.5)	12
Periop transfusion	2/231 (0.9)	7
Periop complication	27/319 (8.5)	16
Improved or normalized hypertension	74/79 (94)	7
Recurrence	9/303 (3.0)	15
Long-term daily steroid requirement	6/133 (4.5)	10

Conclusions

- Partial adrenalectomy is feasible and being increasingly reported
- Partial adrenalectomy in VHL patients provides excellent functional and oncologic outcomes
- Low long-term exogenous steroid use
- Low recurrence rate
- Partial adrenalectomy in VHL patients should be a standard of care

NIH Clinical Center

