INCIDENTAL ADRENAL MASSES

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DISCLOSURES

- Bayer HealthCare - Grant
- Co-Investigator, with no salary support
Incidental Adrenal Masses

Outline

- Definition of incidentaloma
- Malignancy determinants
- Common adrenal masses
- Techniques for distinguishing adenoma vs. malignancy incl. pitfalls and mimics
- Guidelines for management of incidentalomas- Europe and US
- Summary
Incidental Adrenal Masses

- Definition of “incidentaloma”
- An incidentally discovered mass or lesion, detected by CT, MRI or another imaging modality performed for an unrelated reason
Incidental Adrenal Masses

• “Incidentalomas”
• Incidentally discovered > 1 cm adrenal mass
• Two important issues to be addressed
  • 1. Is the lesion malignant?
    - Is it a primary adrenal neoplasm or metastases?
  • 2. Is the lesion functional?
Incidental Adrenal Masses

- **Malignancy Determinants**
- Density - >10 HU on unenhanced CT or loss of signal intensity on CS MRI
- Washout - <60% Absolute washout or <40% relative washout
- Size - > 4 cms increases risk of malignancy
- All masses > 4 cms that lack benign imaging features should be resected
Incidental Adrenal Masses

- **Risk of ACC**
- Threshold of 4 cms. best trade-off between missing an ACC and limiting unnecessary surgery
- This is derived from retrospective data sets and in empirical fashion (Seer Database)
- Other size cut-off also studied: but less evidence for support of adrenalectomy for lesions of other sizes

* Young WF Endoc & Metab Cl of NA 2000
* Mantero F J Clin Endocr and Metabol 2000
* Sturgeon C J Am Coll Surg 2006
* Kaseperlik-Zaluska AA Hor & Metab Res 2008
ADRENAL MASS
Normal Adrenal Function

- Adenoma-non-functioning or subclinical Cushing’s
- Metastasis
- Rare:
  - Carcinoma
  - Pheochromocytoma
ADENOMAS vs. NON ADENOMAS
UNENHANCED CT DENSITY

<table>
<thead>
<tr>
<th>Threshold Value (H)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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<tbody>
<tr>
<td>0</td>
<td>41</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
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<td>3</td>
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<td>20</td>
<td>88</td>
<td>84</td>
</tr>
</tbody>
</table>

*Boland et al, AJR 1998;171:201-204*
Unenhanced (U), enhanced (E) [60 sec] and delayed images (D) [15 min]

Percentage enhancement washout

\[
\frac{(E-D)}{(E-U)} \times 100
\]

Threshold = or >60% - Adenoma

Relative percentage enhancement washout

\[
\frac{(E-D)}{E} \times 100
\]

Threshold = or >40% - Adenoma

SPECIFICITY FOR ADENOMA DIAGNOSIS >93%
Adenoma: Intracellular Lipid on MRI

Signal loss on OP
• Qualitative
• Quantitative
  – Dual-echo sequence
  – Signal Intensity Index (SII)

\[ SII = \frac{\text{IP} - \text{OP}}{\text{IP}} \times 100 \]

Adenoma >16.5% (or 20%)

Schindera ST Radiology 2008; 248:140
Adenoma: Mimicking Malignancy

Central Hemorrhage in adenoma
Adrenal adenoma with hemorrhage and lipomatous metaplasia
Adenoma: Mimics

- Lipid-Containing Adrenal Cortical Carcinoma (ACC)
Adenoma: Mimics

- Lipid containing metastasis from clear cell renal cell carcinoma (RCC)

SII = 35%

Left adrenal gland, resection:
Metastatic renal cell carcinoma, clear cell

Subtraction
Incidental Adrenal Masses

Prevalence of functioning tumors in “incidentalomas”

- Approx. 5% incidence of subclinical Cushing’s adenoma
- Approx. 3% prevalence of pheochromocytomas
- Approx. 1% of aldosteronomas

Zeiger MA et al J Clin Endocrin and Metab 2011
FOLLOW UP OF SILENT OF ADRENAL MASSES > 3 CM

- **Hormonal evaluation:**
  - overnight dexamethasone suppression test, urinary/plasma metanephrines
  - Serum K⁺, plasma aldosterone concn.-plasma renin activity

- **Imaging evaluation:** CT or MRI
  Homogeneous masses with smooth border and attenuation of < 10 HU or homogenous loss of SI on MRI

- **Follow up:**
  - Two imaging studies- 6 months apart
  - Annual hormonal evaluation over 4 year period
  - If the mass shows no interval growth in this 1 yr. period and is not hormonally activity at end of 4 yr. surveillance- no further follow up is needed

* NIH Consensus and State-of-the- Science Statements Vol 19, Number 2: Feb 4-6, 2002*
FOLLOW UP OF NON-FUNCTIONING ADRENAL INCIDENTALOMAS

Guidelines for management: recommendations of the AACE and AAES

- For lesions < 4 cms and radiologic features of benign adenoma
  - CT/ MR follow up at 3 and 6 months and then annually for 1-2 years
  - Hormonal evaluation at diagnosis and then annually for 5 years

* Zeiger MA et al Endoc Practice 2009
Nature of incidental adrenal mass in the non-oncological patient

- 1049 masses studied
- 788 adenomas (75%)
- 68 myelolipomas, 47 hematomas, 13 cysts
- 3 pheochromocytomas and 1 cortisol-producing adenoma

In 973 pts. with incidental adrenal mass and no history of cancer, there were no malignant lesions

In the non-oncological pt. most small incidental adrenal masses are benign

96.4% of masses under 4 cms

* Song JH AJR 2008
Incidental Adrenal Masses

Prevalence of functioning and malignant transformation of “incidentalomas”

- Frequency of functional and malignant lesions has been overestimated (Cawood et al.)
- ACC <2%, metastases < 1%, and 3% for pheochromocytomas
- Risk of malignant transformation of incidentaloma is low: approx. < 1 per 1000
- Risk of silent incidentaloma becoming a hyperfunctioning tumor is also very low < 1%

Cawood TJ  J Clin Endocrin and Metab 2009
Zeiger  MA J Clin Endocrin and Metab 2011
Incidental Adrenal Masses

Prevalence of functioning and malignant transformation of “incidentalomas”

- False positives of recommended tests are 50 times greater than true positives
- Follow up CT exams- added radiation- increases risk of fatal cancer-
- Risk is similar to the risk of developing malignancy during the follow up period
- Current guidelines for clinical and imaging follow up of all incidentalomas needs to be reviewed

*Cawood TJ*  *J Clin Endocrin and Metab 2009*
Incidental Adrenal Masses

Prevalence of functioning and malignant transformation of “incidentalomas”

- Aim is to avoid missing functional or malignant lesions
- Low prevalence of such conditions results in very high sensitivity and low specificity leads to a high false-positive rate
- This leads to significant financial and emotional cost, with the potential for further tests and/or unnecessary adrenalectomy
- Furthermore little attention paid to the possible harm from exposure to ionizing radiation from repeated CT

Cawood TJ, J Clin Endocrin and Metab 2009
### Table 8: Implications of current clinical recommendations, applying the data described in the current paper.

<table>
<thead>
<tr>
<th>Approximate risk of event during 2-year radiological follow-up and 4-year biochemical follow-up of an adrenal incidentaloma initially thought to be benign and non-functional</th>
<th></th>
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<tbody>
<tr>
<td>Approximate financial cost of tests</td>
<td>1630 USS (based on average 2.3 scans)</td>
</tr>
<tr>
<td>Radiation exposure from CT imaging during follow-up</td>
<td>23 mSv</td>
</tr>
<tr>
<td>Risk of inducing fatal cancer from radiation exposure during follow-up CT imaging</td>
<td>1 in 430 to 1 in 2170&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Risk of detecting cancer during follow-up</td>
<td>0–1 in 500&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Risk of detecting non-metastatic cancer during follow-up</td>
<td>0–1 in 1000</td>
</tr>
<tr>
<td>Risk of false-positive diagnosis/suspicion of malignancy during CT imaging</td>
<td>1 in 20&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Risk of false-positive diagnosis of subclinical Cushing’s syndrome</td>
<td>Between 1 in 10 and 1 in 4&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Risk of true-positive diagnosis of subclinical Cushing’s syndrome</td>
<td>1 in 250&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Based on risk of causing fatal cancer of between 1 in 1000 and 1 in 5000 CT scans, and 2.3 CT scans occurring during follow-up.

<sup>b</sup>Approximately, half of tumours detected will be metastases, and so diagnosis unlikely to affect outcome.

<sup>c</sup>Based on specificity of CT of 95% for malignancy, see Table 6.

<sup>d</sup>Based on specificity of 1 mg DXT of 90% and four annual follow-up tests.

<sup>e</sup>Based on 2 cases per 1000 developing over 2 years of follow-up, see Table 6.
WORK UP ALGORITHM

White Paper - ACR Incidental Findings Committee

- Diagnostic imaging features- of myelolipoma or cyst-
  stop
- Small (1-4 cm) mass and no underlying cancer
  - < 10 HU or loss of SI on CS-MRI - stop
  - If mass is stable for > 1 yr.- stop
  - In suspicious lesions, may consider washout CT (CS-
    MRI ) or PET
  - In pts. with history of underlying cancer, with
    atypical findings and no prior imaging, consider
    washout CT (CS-MRI ) or PET
- Masses > 4 cm
  - Prior h/ o cancer,- PET or biopsy
  - No prior h/ o cancer- Resection

* Berland et al J ACR 2010
1. Recommend surgery for any adrenal mass with radiological aspects compatible with malignancy

2. Recommend surgery in all patients with functional adrenal tumors causing overt steroid hormone or catecholamine excess

3. Data are insufficient to make firm recommendations on endocrine and radiologic follow-up

4. Suggest to repeat imaging (CT or MRI) 3-6 months after discovery of an adrenal incidentaloma to recognize early a rapidly growing mass, except when the adrenal mass is small (≤ 2cm) with clear benign features (density ≤ 10 HU). If an adrenal mass has clear features of myelolipoma or cysts, no additional follow-up is needed

5. Suggest considering adrenalectomy if the mass enlarges by 1 cm or more and/ or changes its appearance during observation

Terzolo M et al Eur J Clin Endocrin 2011
Incidental Adrenal Masses

Reporting

• When an incidental adrenal nodule with CT or MR features of adenoma is discovered
• One suitable way to report is:
  • “Findings consistent with a benign adenoma. If there are clinical signs or symptoms of adrenal hyperfunction, biochemical evaluation may be appropriate.”
• Avoids excessive expensive workup with biochemistry of numerous non-functioning small adrenal adenomas
SUMMARY

• Silent “functioning” adrenal masses- rare

• In the non-oncological pt. most incidental adrenal masses are benign

• NIH Consensus Conference Recommendations for follow-up- biochemical evaluation + imaging- too stringent and expensive

• Should be reserved for masses > 3 cms?

• Smaller incidental lesions probably could be reported as benign adenomas