CT findings in adrenal adenoma: a new sign, the vessel sign

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Aims and objectives

Introduction

Adrenal adenomas (AA) are benign tumors of glandular type that arise from the cortex of the adrenal gland. They commonly occur in adults, but they can be found at any age. Non-functioning AA are asymptomatic and are not considered to have the potential for malignant transformation. They are usually found incidentally when CT scans or MRI are performed for other reasons, thereby included in what is called "adrenal incidentalomas" [1]. The differential diagnosis of adrenal incidentalomas includes myelolipoma, adrenocortical carcinoma, metastases and pheochromocytoma among others.

Adrenal incidentalomas are seen in approximately 4% to 6% of the imaged population [2, 3] and most of them are benign lesions in patients without a history of cancer [4, 5]. Adenomatous lesions are detected in less than 1% of patients younger than 30 years, around 7% in patients aged 70 years or older and approximately 94% of these lesions correspond to non-functioning AA [1, 4, 6, 7]. 2% to 3% of adrenal incidentalomas are malignant, percentage that increases with age and the frequency is around 2% for adrenocortical carcinoma and less than 1% for adrenal metastases [8, 9]. In patients studied for a known malignancy the rate of metastatic disease is as high as 25% to 36% of the visualized adrenal lesions [10]. Other adrenal malignancies include angiosarcoma, lymphoma and pheochromocytoma, which are even more rare in the general population.

Normal adrenal gland anatomy and vascularization [11]

The adrenal glands are a pair of triangular-shaped organs that sit on the top of the kidneys. They weight around 6 grams and their size ranges from 40 to 50 mm in length, 20 to 40 mm wide and 8 to 10 mm thick. Each suprarenal gland is composed of two different tissues: The suprarenal cortex and the suprarenal medulla. The cortex serves as an outer layer and the medulla as an inner layer, both of which are encapsulated by connective tissue.

Arteries

Each gland is irrigated by three different arterial sources, called the adrenal arteries. The medium adrenal artery, which is inconstant, originates from the aorta to reach the medial border of the gland where it divides to irrigate both sides of its body. The superior adrenal artery, that ranges in number from 1 to 3, derives from the upper phrenic artery
and provides thin vascularization to the superior and medial part of the gland. Finally, the inferior suprarenal artery comes from the renal artery or one of its terminal branches to irrigate the lower adrenal pole.

**Veins (Figure 1) [11, 12]**

The adrenal venous drainage bears no analogy to the arterial vascular system and is very constant. There is a central adrenal vein that collects almost all of the venous blood. It merges from the major groove of the gland to end at the mid-posterior wall of the inferior vena cava on the right side and at the superior margin of the left renal vein on the left side. In normal conditions the adrenal vein can be seen during contrast-enhanced computed tomography (CE-CT) studies, especially the extra-glandular portion of it.

The central vein on the right side may be duplicated and even triplicated, but although some of these supernumerary veins may drain to the inferior phrenic or right renal vein, there will always be a central vein entering the inferior vena cava.

The central vein on the left side is also very constant, taking a downward path into the superior margin of the left renal vein and taking most of the times a tributary, the inferior phrenic vein.

Both adrenal glands also have a number of superficial or capsular veins that extend from the surface of the gland into the perirenal fat or sometimes penetrate the renal capsule.

**State of the art of imaging characteristics for AA**

The adrenal glands are abdominal organs difficult to access, thus, imaging examinations such as CT, MRI or PET are required for their correct assessment. Next we describe the main CT features of AA.

**Computed Tomography**

CT not only detects adrenal incidentalomas but also offers one of the best means for achieving the right diagnosis and differentiating a benign from a malignant mass. Key features of AA include: Homogeneous density; smooth contour and sharp margins; low attenuation values; negative pixels on CT histogram analysis; rapid contrast medium washout; small size and time stability. Because these findings are not always present or equivocal, multiple CE-CT protocols have been described for their assessment. Also,
other tests such as MRI or PET examinations could be performed when the clinical context needs it or further information is required.

Homogeneous density

AA are usually homogeneous in attenuation either in non CE-CT images, as well as in CE-CT images. Haemorrhage, calcifications, necrosis and macroscopic fat are infrequent findings [7, 13, 14].

Morphology

AA tend to have a smooth contour and sharp margins, whereas malignant lesions tend to have an irregular border [8, 10]. These characteristics alone are not specific, because when found most of the adrenal lesions are small in size, smooth and uniform in shape regardless of their histologic characteristics.

Attenuation

Adrenal adenomas contain lipid in varying degrees and this lowers their attenuation coefficient on non CE-CT. A threshold value of 10 HU is generally accepted as a cut-off value for diagnosing a lipid-rich AA, as the 10 HU threshold has a 71% sensitivity and specificity of 98% for AA [7, 8, 10, 15]. Unfortunately, nowadays most examinations are performed with the use of contrast medium agents, thus, not being possible to assess attenuation in many cases.

CT histogram analysis

The technique involves analysis of a region of interest of the adrenal lesion, which is processed with a histogram analysis tool. The amount of lipid in the lesion is proportional to the number of negative pixels within it [10, 16]. AA contain negative pixels whereas metastases don't. However, results of histogram analysis studies are varied and negative pixels have been described in AA and non AA, including metastases, pheochromocytoma and adrenocortical carcinoma. Then, it seems that the most practical clinical application of the histogram analysis it to serve as an adjunct tool for non CE-CT, where it can improve the sensitivity while maintaining the specificity. Nevertheless, most departments do not routinely use this tool as an analysis method.

Washout
Non CE-CT is a relatively inexpensive highly specific test for differentiating AA from malignant lesions. Several researchers have shown that the use of washout formulas are able to distinguish AA from malignant lesions in a better way than non CE-CT alone. Both lipid-rich and lipid-poor AA tend to wash out faster after the administration of intravenous contrast mediums than malignant lesions do and this may result from the increased leakiness of malignant vessels compared with benign lesions. Most investigators use a 40% relative percentage washout (RPW) and a 60% absolute percentage washout (APW) as cut-off values on a 15 minutes delayed scan. Therefore, any lesion that demonstrates more than 40% of RPW or more than 60% of APW is considered an AA, with a sensitivity and specificity close to a 100%. This technique is the main tool used for distinguishing AA from non AA at many institutions and is superior to non CE-CT alone. Lesions that demonstrate less than 40% of RPW or less than 60% of APW on a 15 minutes delayed scan are almost always malignant [7, 8, 10].

Size

Size is an important variable for predicting malignancy on an incidentally discovered adrenal mass. Smaller lesions are usually benign and conversely larger lesions are often malignant, however, it is important to distinguish between populations with or without a history of malignancy. In general, the cutting point is located around 6 cms, because the chance of malignancy increases to approximately 85% if the lesion is larger than that measure [7, 8, 17, 18].

Time stability

As a general rule, any adrenal lesion that increases in size on serial images can be considered malignant and in clinical practice, any increase in size is generally considered malignant until proven otherwise. On the contrary, stability of a lesion suggests benignity, because it’s highly unusual for an untreated malignant lesion to remain stable after a follow-up of 6 months [4, 10, 14]. The threshold for qualifying an increase in size as significant is unknown, but it should be argued that most adrenal masses that exhibit a pattern of slow growth are not malignant. On the contrary, it’s been described that adrenocortical carcinomas typically have a rapid growth rate of more than 2 cms per year [1, 19].

The American College of Radiology appropriateness criteria for the incidentally discovered adrenal masses recommends, that because in patients with no history of malignancy, most small (<4 cm) incidentally discovered adrenal masses are benign an extensive and costly workup is usually not justified. If a mass of any size has typical features of a benign lesion such as a lipid-rich AA or myelolipoma, no additional workup or follow-up imaging is needed. In those with non diagnostic imaging features, if prior
imaging is available and the lesion is stable for at least 1 year, it can be considered benign with no additional imaging follow-up. While a specific size change threshold is unknown, if the lesion is enlarging, then it may be prudent to proceed to an adrenal biopsy or resection [20].

**Aim:** To describe a new helpful CT sign for the diagnosis of AA.

**Abbreviations:** AA = Adrenal adenoma; CE-CT = Contrast-enhanced computed tomography; CT = Computed tomography; MRI = Magnetic resonance imaging; PET = Positron emission tomography.

**Images for this section:**

![Fig. 1](image_url)
Methods and materials

We designed a descriptive study based on the review of the clinical history and follow-up of 50 patients who undergone the diagnosis of AA by means of CE-CT and who presented with The Vessel Sign (Figures 2, 3 and 4 [video] ). Patients were followed up by CE-CT, being possible to evaluate the measures of the AA, the best phase for depiction of The Vessel Sign and time interval between examinations.

Confident diagnosis was made on the basis of CT findings according to the state of the art of imaging characteristics for AA and time stability. MRI and PET examinations were also performed to some patients demonstrating consistent results and some underwent surgery, being histological diagnosis possible. Because most of our studies were performed on patients with neoplasms of other organs, therefore carried out directly on a CE-CT venous phase, is that we did not assess attenuation as a CT finding. Also, these were not washout-directed examinations and we do not routinely use histogram tools as an analysis method.

As a control group we assessed CT scans of patients with histologically confirmed differential diagnoses for AA, such as adrenal cortical carcinoma (2 cases), metastases (15 cases), lymphoma (2 cases), pheochromocytoma (6 cases), hemangioma (1 case) and myelolipoma (2 cases).

Images for this section:
Fig. 2: The Vessel Sign.
Fig. 3: The Vessel Sign.

Fig. 4: Video: The Vessel Sign.
Results

All AA presented with a smooth contour and sharp margins, involving a portion or all of the body of the adrenal gland. The mean size at basal CE-CT for right AA was 21.8 mm (long axis) and 22.3 mm (long axis) for left AA. At control CE-CT, mean sizes were 22.5 mm and 22.4 mm respectively. We found an average time stability of 1080 days (35.5 months) and an increase in size of 0.71 mm for right AA and 0.13 mm for left AA, all findings consistent with the state of the art of imaging characteristics for AA (Table 1).

None histologically confirmed control pathologies, such as adrenal cortical carcinoma (all cases), metastases (all cases), lymphoma (all cases), pheochromocytoma (all cases), hemangioma (all cases) or myelolipoma (all cases) presented The Vessel Sign (Table 2, figures 5 and 6 [video]).

MRI (1 case) and PET (2 cases) examinations were performed to some patients demonstrating consistent results, no changes in diagnoses and could be used as controls to assess our study variables. Also, some patients underwent surgery (2 cases), being AA the histological diagnosis. Then, all lesions with The Vessel Sign behaved as adenomas (Table 3).

The Vessel Sign was best depicted at a venous phase (96%) and the larger the adenoma and the higher the lipid load was, the better The Vessel Sign was seen.

Images for this section:
### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Right AA Average size (long axis in mm)</th>
<th>Left AA Average size (long axis in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal CE-CT</td>
<td>21.8</td>
<td>22.3</td>
</tr>
<tr>
<td>Control CE-CT</td>
<td>22.5</td>
<td>22.4</td>
</tr>
<tr>
<td>Size increase</td>
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<td>0.1</td>
</tr>
<tr>
<td>Time Stability (days)</td>
<td>1080</td>
<td></td>
</tr>
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\[ n = 50 \]

### Table 2

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases</th>
<th>Vessel Sign</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Adrenal cortical carcinoma</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Metastases</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>1</td>
<td>0</td>
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</tr>
<tr>
<td>Myelolipoma</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

\[ n = 27 \]
Fig. 5: None histologically confirmed control pathology presented The Vessel Sign.

Fig. 6: Video: Adrenal lymphoma, no Vessel Sign.
<table>
<thead>
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<th>Lesions presenting with The Vessel Sign ( (n = 50) )</th>
<th>( \text{Presenting with the state of the art of imaging characteristics for adrenal adenomas} )</th>
<th>( \text{Time stability (1080 days)} )</th>
<th>( \text{Changes in diagnosis after MRI or PET} )</th>
<th>( \text{Changes in diagnosis after surgery} )</th>
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</thead>
<tbody>
<tr>
<td>All</td>
<td>All</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

Table 3
Conclusion

The sum of these findings represent a high degree of correlation between The Vessel Sign and the diagnosis of AA, what we believe is close to a 100%. Thus, when present, The Vessel Sign is a helpful and reliable sign for the diagnosis of AA.

Personal information

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