Original research

Nonfunctional adrenal lesions without loss of signal intensity on MRI: Whose problem is it? The patient’s? The surgeon’s?

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**Abstract**

**Background:** Current indications for adrenalectomy include functional adrenal tumors and potentially malignant tumors based on imaging studies. We evaluated the effectiveness of magnetic resonance imaging (MRI) in obtaining a correct preoperative diagnosis.

**Method:** Fifty-three patients with nonfunctional adrenal lesions were analyzed. Indications for adrenalectomy of nonfunctional adrenal lesions included $>6$ cm in size and $\leq 6$ cm in size with atypical characteristics on MRI. Lesions with a size of $>6$ cm, local invasion, irregular margins, and chemical-shift imaging that demonstrated no loss of signal intensity on out-of-phase images were considered suspected of malignancy.

**Results:** Adrenal lesions of $>6$ cm in size exhibited an 80-fold increased prediction of malignancy (OR: 80; 95% CI $7.8 \times 813$), whereas irregular margins and local invasion exhibited a 45-fold (OR: 45; 95% CI $6.4 \times 312.5$) and a 12-fold (OR: 12; 95% CI $4.6 \times 30.6$) increased occurrence of malignancy, respectively. The loss of signal intensity did not affect the prediction of malignancy.

**Conclusion:** The rate of unnecessary tumor resections that are $<6$ cm in size can be decreased by performing adrenal biopsies in selected cases or by short-term follow-up to prevent the insufficiency of imaging techniques.

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1. Introduction

Non-functioning adrenal lesions have become a common clinical problem as a result of the more widespread use of high-resolution anatomical imaging procedures.\textsuperscript{1–3} Incidental adrenal masses are present in 4% of imaging studies in the general population, and the risk of finding an adrenal incidentaloma increases with age.\textsuperscript{4–7} Most of these lesions are benign in nature. Typically, the goals of an initial workup are to distinguish benign from malignant processes and to distinguish nonfunctioning from hyperfunctioning tumors.\textsuperscript{8–11}

Chemical-shift imaging is most commonly used to distinguish between benign and malignant adrenal lesions.\textsuperscript{12–15} Benign adrenal masses typically demonstrate a loss of signal intensity on chemical-shift magnetic resonance (MR) imaging using opposed-phase images with a 95% sensitivity.\textsuperscript{12–15} Although chemical-shift MR imaging is a well-known predictor of malignancy, the indication for surgery in surgical series is common in nonfunctioning adenosmas.\textsuperscript{10,15–18}

Current indications for adrenalectomy include functional adrenal tumors and potentially malignant tumors based on the results of imaging studies.\textsuperscript{2,5,17,18} Because MR finding are often inconsistent with a diagnosis of adenoma, the majority of surgically removed adrenal lesions are classified as benign nonfunctioning adenosmas. The aim of this work was to evaluate the effectiveness of combined CT parameters for distinguishing benign from malignant adrenal masses.

2. Material and methods

2.1. Patients

We reviewed the data for 132 consecutive adrenalectomy patients from 2005 to 2012 at the Department of Surgery at the Istanbul Faculty of Medicine. After excluding 58 patients with functional adenomas (27 patients with adrenal and pituitary Cushing’s syndrome, 23 pheochromocytomas and 8 patients with Conn syndrome), 13 patients with metastatic carcinoma, 3 patients with cortical carcinoma and 6 patients with incomplete records, 53 consecutive patients with...
nonfunctional adrenal masses were analyzed. The study population included 39 women and 14 men with a mean age of 44.1 years (range 23–76 years). The study plan was reviewed and approved by the hospital’s institutional ethics committee.

2.2. Operation

Indications for adrenalectomy of nonfunctional adrenal masses were masses that were ≥6 cm in size (29 patients, 15%) and <6 cm in size showing atypical characteristics on MRI (28 patients, 15%). Adrenalectomy was performed by endocrine surgeons either laparoscopically or through open surgery. The patients who manifested preoperative radiologic features of gross local invasion or systemic metastases underwent open adrenalectomy.

2.3. Magnetic resonance imaging

Routine magnetic resonance imaging was used to predict benign or malignant status and size of all adrenal masses. Chemical-shift imaging was performed using a T1-weighted gradient-recalled echo sequence. Masses that appeared hypo-or isointense relative to the liver on T1-weighted images and hyper-or isointense to the liver on T2-weighted images, as well as those that lost signal intensity on opposed-phase images compared with in-phase images, were diagnosed as adenomas. High signal intensity of homogenous adrenal masses on T2-weighted images and no signal loss on opposed-phase images compared with in-phase images were considered inconsistent with a diagnosis of benign adenoma. The following MRI parameters were assessed in all adrenal masses: (i) size; (ii) local invasion; (iii) irregular margins; and (iv) chemical-shift imaging demonstrating loss of signal intensity on out-of-phase images.

2.4. Evaluation of the diagnostic value

Lesions with a size ≥6 cm, local invasion, irregular margins, and chemical-shift imaging demonstrating no loss of signal intensity on out-of-phase images were suspected of malignancy. Suspicious imaging results and malignant pathology were considered true positive (TP) for cases in which histological examination revealed a malignancy, and the results were considered false positive (FP) when no malignancy was found (including myelolipoma, ganglioneuroma, or Schwannoma). The benign imaging results and benign pathology were considered true negative (TN) if no malignancy was found (including myelolipoma, ganglioneuroma, or Schwannoma). The sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV) and negative predictive value (NPV) of imaging and histopathologic results were calculated. Sensitivity, specificity and accuracy were determined according to the following formulas:

- \( \text{PPV} (%) = \frac{TP}{TP + FP} \times 100 \)
- \( \text{NPV} (%) = \frac{TN}{TN + FN} \times 100 \)
- \( \text{Sensitivity} (%) = \frac{TP}{TP + FN} \times 100 \)
- \( \text{Specificity} (%) = \frac{TN}{TN + FP} \times 100 \)
- \( \text{Accuracy} (%) = \frac{TP + TN}{TP + TN + FP + FN} \times 100 \)

2.5. Statistical analysis

The results were reported as the mean ± SD and median. Statistical analyses were performed with SPSS software (SPSS Inc., Chicago, IL). Differences between the parameters were compared with the Mann Whitney U and the chi-square test. Correlation analyses were performed using the non-parametric Spearman’s correlation test. Chi-square analysis was used to evaluate the accuracy of MRI characteristics with histopathologic correlations.

3. Results

The mean adrenal lesion size was 6.6 ± 5.2 cm (range 3–30 cm). Open adrenalectomy was required in 5 patients due to the large size of the lesion or invasion of the adjacent organs on preoperative imaging. Laparoscopic adrenalectomies were performed in 48 patients; all procedures were performed using a lateral transabdominal approach. None of the laparoscopic adrenalectomies were converted to an open approach.

Histopathological evaluation revealed a benign pathology in 44 (83%) adrenal lesion (38 adenoma, 2 infiltrated necrosis, 3 Schwannoma, and 1 myelolipoma) and a malignant pathology in 9 (17%) adrenal lesions (6 adenocortex carcinoma and 1 liposarcoma).

3.1. MRI results

Of the 53 adrenal lesions, 9 (16.9%) lesions were more than 6 cm in size, 8 (15.1%) lesions exhibited irregular margins, and 5 (9.4%) lesions exhibited local invasion. All of these lesions exhibited a malignant pathology. Forty-three lesions (81.1%) exhibited no loss of signal intensity. Of the 43 adrenal lesions with no loss of signal intensity, 8 (18.6%) lesions exhibited a malignant pathology, but 35 (81.4%) lesions exhibited a benign pathology.

3.2. MR imaging findings vs. final pathology

Based on the MR imaging findings, size correctly diagnosed (true positive and true negative) 53 adrenal lesions and failed to diagnose 0 lesions. Irregular margins correctly diagnosed 52 adrenal lesions and failed to diagnose 1 lesion. Local invasion correctly diagnosed 49 adrenal lesions and failed to diagnose 4 lesions. Loss of signal intensity on out-of-phase images correctly diagnosed 17 adrenal lesions and failed to diagnose 36 lesions.

The sensitivity of size, irregular margins, local invasion, and no loss of signal intensity in predicting malignancy was 100%, 88%, 55% and 88%, respectively. The specificity of size, irregular margins, local invasion, and no loss of signal intensity in predicting malignancy was 100%, 100%, 100% and 20%, respectively. The diagnostic accuracy of size, irregular margins, local invasion, and loss of signal intensity in predicting malignancy was 100%, 98%, 92% and 32%, respectively (Table 1).

3.3. The evaluation of the adrenal lesions according to the final pathology

The adrenal lesions were divided into 2 groups according to the final pathology. Group 1 (n = 9) consisted of malignant pathologies; group 2 (n = 44) consisted of benign pathologies. The mean size (16.4 ± 6.5 cm), the ratio of irregular margins (88.9%), and the ratio of local invasion (55.6%) in group 1 was significantly higher than that of group 2 (4.6 ± 1 cm, 0%, and 0%) (p < 0.001). The ratio of no loss of signal intensity did not significantly differ between groups 1 and 2 (88.9% and 79.5%) (Table 2).

3.4. Correlations

There was a positive correlation between the malignant pathology and size (r = 0.653, p = 0.0001), irregular margins (r = 0.932, p = 0.0001) and local invasion (r = 0.714, p = 0.0001). The malignant pathology did not correlate with the loss of signal intensity (r = −0.090, p = 0.523) (Table 3).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>MR imaging findings vs. final pathology.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size &gt;6 cm</td>
<td>Irregular margin</td>
</tr>
<tr>
<td>TP (n)</td>
<td>9</td>
</tr>
<tr>
<td>TN (n)</td>
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</tr>
<tr>
<td>FP (n)</td>
<td>0</td>
</tr>
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<tr>
<td>Specificity (%)</td>
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<tr>
<td>Diagnostic accuracy (%)</td>
<td>100</td>
</tr>
</tbody>
</table>

TP, true positive; FP, false positive; TN, true negative; FN, false negative; PPV, positive predictive value; NPV, negative predictive value.
3.5. The detection of malignant adrenal lesions by MR imaging

An adrenal lesion size greater than 6 cm had an 80-fold (OR: 80; 95% CI 7.8–813) increased prediction of malignancy, whereas irregular margins and local invasion exhibited a 45-fold (OR: 45; 95% CI 6.4–312.5) and a 12-fold (OR: 12; 95% CI 4.6–30.6) increased prediction of malignancy, respectively. The loss of signal intensity did not affect the prediction of malignancy.

4. Discussion

We investigated the accuracy of MR imaging features for distinguishing malignant from benign adrenal lesions. We found that the most helpful diagnostic MR imaging features included tumor size, irregular margins, and local invasion. Adrenal lesion size was found to be a better diagnostic parameter than other features. Chemical-shift imaging was not useful in distinguishing malignant from benign adrenal lesions.

With improving quality and wider availability of imaging techniques, incidental detection of adrenal masses is an increasing trend. Incidental discoveries of adrenal masses are observed in 4%–10% of patients undergoing imaging. Most of these lesions are found to be benign and nonfunctioning adenomas.1–4

In the management of adrenal incidentalomas, two issues must be discussed thoroughly: the lesion’s malignancy and its functionality. The two major predictors of malignancy are the tumor’s size and the features observed during imaging.5,6 The larger the mass, the more likely it is to be malignant. Adrenocortical carcinomas represent 2% of all tumors that are 4 cm or less in diameter, 6% of tumors ranging from 4.1 to 6 cm, and 25% of tumors that are larger than 6 cm.7,8,16,19

Although tumor size is a well-known predictor of malignancy, it is not the best indicator of malignancy. The NIH consensus statement emphasized removing an adrenal tumor if there is a suspicion of malignancy based on imaging findings, regardless of tumor size.19

CT and MR imaging have been the principal imaging techniques for observing adrenal glands for many years. More recently, chemical-shift MR imaging has been widely used to distinguish between benign and malignant tumors. Several studies revealed that chemical-shift imaging MR exhibits a diagnostic accuracy of 96%–100%.7,12–15 However, the diagnostic accuracy of chemical-shift MR was only 32% in our study. Thirty-five benign adenomas (79.5%) could not be differentiated from adenomatous lesions using this technique due to their failure to exhibit signal loss on out-of-phase images.

We observed a difference in the chemical-shift MR results between our study and the radiology series in the literature. In surgical series such as our study, approximately 50% of the lesions removed for surgical indications were nonfunctional adenomas,10,15–18 whereas nonfunctional adenomas account for 10% of lesions removed in radiology studies.12–15 Due to the uncertain results of imaging studies, most of the lesions smaller than 6 cm are resected, resulting in benign pathologies after histological examination. The operative indications for these lesions are the result of imaging studies.

Conzo et al.10 reported that out of 114 nonfunctional adenomas smaller than 6 cm that were resected due to the imaging results, only one malignant pathology was observed. In another study of 196 adrenalectomies, a total of 61 (31%) adenomas were identified, all with benign pathologies.15 We believe that if imaging studies were able to correctly diagnose lesions during the preoperative evaluation, surgeons would be able to prevent needless surgical resections in these studies.

Although the indications for adrenalectomy have not changed, a large number of small incidentalomas have been removed in the past few years.3,11,18 In our opinion, the large number of incidentalomas is the result of indecisive identification based on imaging results.

In our study, 35 nonfunctional adenomas with suspicious MR imaging results exhibited benign pathologies. Discordance between imaging modalities occurred in 35 adrenal lesions. Adrenal lesions with imaging characteristics that were inconsistent with adenoma were commonly benign and lipid-poor adenomas, resulting in the needless resection of approximately 66% of benign nonfunctional adrenal lesions.

Although chemical-shift imaging has been the most popular technique for predicting the malignancy of adrenal lesions, it may exhibit limitations in particular situations, especially in cases of lipid-poor adenomas. CT or MR imaging, adrenal biopsy, surgical resection and clinical follow-up have been widely used to distinguish between benign and malignant tumors.3–5 The adrenal biopsy of the adrenal glands is recommended in patients with a known history of malignancy who are suspected to have adrenal metastases.4,8

In conclusion, we believe that the rate of unnecessary resections for tumors that are less than 6 cm in size can be decreased by performing adrenal biopsies in selected cases or by short-term follow-up to prevent the inconclusiveness of imaging techniques.

Ethical approval

1568/2012.

Funding

No.

Authors contributions

Nihat Aksakal: study design.
Alper Şahbaz: study design.
Beyza Özçınar: writing.
Ali Özemir1: data collection.
Kasım Çağlayan1: data collection.
Orhan Ağaçoğlu1: data collection.
Umut Barbaros: data analysis.
Artür Salmaslıoğlu: data collection.
Yeşim Erbil: writing, critical revision.

Conflict of interest

No.

Acknowledgments

None.

Table 2

| The evaluation of the adrenal lesions according to the final pathology. |
|-------------------------|--------------------------|--------------------------|
|                         | Group 1 (n = 9)           | Group 2 (n = 44)          |
|                         | Size (cm)                | 16.4 ± 6.5               | 4.6 ± 1                   |
|                         | Irregular margin (n; %)   | 8; 88.9                  | 0; 0                     |
|                         | Local invasion (n; %)     | 5; 55.6                  | 0; 0                     |
|                         | No loss of signal intensity (n; %) | 8; 88.9                  | 35; 79.5                 |
| p                       |                         | 0.001                    | 0.001                    |

Table 3

<table>
<thead>
<tr>
<th>Correlations.</th>
<th>r</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Malignant</td>
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References


