

## Prevalence of malignancy in adrenal incidentaloma on CT studies in patients with unknown primary malignancy

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**Kunchai W, Chaopathomkul B. Prevalence of malignancy in adrenal incidentaloma on CT studies in patients with unknown primary malignancy. Chula Med J 2014 Mar – Apr;58(2): 101 - 12**

**Background** : *Cross-sectional imaging has been increasingly used. The adrenal incidentaloma was detected and caused problem to diagnose benign or malignant especially unknown primary cases.*

**Objective** : *To determine the prevalence of malignancy in adrenal incidentaloma in patients with unknown primary malignancy.*

**Setting** : *Department of Radiology, Faculty of Medicine, Chulalongkorn University/ King Chulalongkorn Memorial Hospital, Thai Red Cross Society*

**Research design** : *Retrospective study*

**Methods** : *The CT study was retrospectively reviewed from January 2004 to April 2010 to identify adrenal incidentaloma in patients without clinical history of malignancy. The diagnosis of benign adrenal lesion was based on specific imaging criteria. Imaging diagnosis of benign had to be confirmed by its attenuation, washout rate study, 1-year stability in diameter on follow-up CT or MRI or at least 2-years stability on clinical follow-up.*

- Results** : *Forty-eight adrenal incidentalomas were included. Histopathology was confirmed for 1 lesion, MRI with at least 1-year stability for 3 lesions, more than 1-year follow-up CT studies for 18 lesions and at least 2-year clinical stability for 26 lesions. One lesion showed slightly increased in diameter but had well-defined margin and low attenuation value on unenhanced CT. Most of the incidentalomas were adenomas, followed by myelolipomas, hematomas, adrenal cortical hyperplasia and disseminated histoplasmosis. No malignant adrenal lesion was identified.*
- Conclusions** : *No malignancy was confirmed in patients with adrenal incidentaloma with unknown primary malignancy.*
- Keywords** : *Adrenal gland, adrenal incidentaloma, cross-sectional imaging, computed tomography, incidental adrenal lesion, unknown primary malignancy.*

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Received for publication. August 16, 2013.

วิษุพันธ์ กัญชัย, บัณฑิต เจ้าปฐมกุล. ความชุกของการเกิดมะเร็งในผู้ป่วยที่ไม่มีประวัติ  
มะเร็งทางคลินิกที่ตรวจพบก้อนที่ต่อมหมวกไตโดยบังเอิญจากการตรวจด้วยเครื่อง  
เอกซเรย์คอมพิวเตอร์. จุฬาลงกรณ์เวชสาร 2557 มี.ค - เม.ย; 58(2): 101 - 12

- เหตุผลของการทำวิจัย** : การตรวจทางรังสีวิทยาวินิจฉัยแบบภาพตัดขวางเป็นที่นิยมในปัจจุบัน  
ทำให้การตรวจพบก้อนที่ต่อมหมวกไตโดยบังเอิญโดยที่ผู้ป่วยไม่มี  
อาการมีมากขึ้นเป็นสาเหตุให้รังสีแพทย์มีปัญหาในการวินิจฉัยว่าเป็น  
ก้อนเนื้อออกธรรมดาหรือเป็นก้อนมะเร็ง โดยเฉพาะในผู้ป่วยที่ไม่มี  
ประวัติของโรคมะเร็งมาก่อน
- วัตถุประสงค์** : เพื่อหาความชุกของการเกิดมะเร็งของต่อมหมวกไตในผู้ป่วยที่ไม่มี  
ประวัติของโรคมะเร็งมาก่อน ในผู้ป่วยที่ตรวจพบก้อนที่ต่อมหมวกไต  
โดยบังเอิญจากการตรวจทางรังสีวิทยาวินิจฉัยแบบภาพตัดขวาง
- สถานที่ทำการศึกษา** : ภาควิชา/ฝ่ายรังสีวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย  
โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย
- รูปแบบการวิจัย** : การศึกษาแบบย้อนหลัง
- วิธีการศึกษา** : ได้ทำการศึกษาย้อนหลังในช่วงเดือนมกราคม พ.ศ. 2547 ถึงเดือน  
เมษายน พ.ศ. 2553 โดยอาศัยเกณฑ์จากภาพทางรังสีวิทยาวินิจฉัย  
ทั้งการวัด attenuation การศึกษา wash out rate ของ adrenal nodule  
การติดตามผู้ป่วยในช่วงระยะเวลา 1 - 2 ปี
- ผลการศึกษา** : จำนวนก้อนทั้งหมดมี 48 ก้อนในจำนวนนี้มีเพียงหนึ่งก้อนที่มีผลยืนยัน  
จากพยาธิวิทยา มี 3 ก้อนได้จากการติดตามด้วย MRI ที่มีระยะ  
การติดตามอย่างน้อยหนึ่งปี มี 18 ก้อนได้จากการติดตามด้วยการตรวจ  
ทางเอกซเรย์คอมพิวเตอร์ที่มีระยะการติดตามที่มากกว่าหนึ่งปี ที่เหลือ  
อีก 26 ก้อนใช้วิธีการติดตามด้วยอาการทางคลินิกที่มีระยะการติดตาม  
ผู้ป่วยอย่างน้อยสองปี ซึ่งมีอยู่หนึ่งก้อนที่มีขนาดโตขึ้นเล็กน้อยจาก  
การติดตามก้อนที่ต่อมหมวกไตที่พบโดยบังเอิญ โดยส่วนใหญ่ถูก  
วินิจฉัยว่าเป็น adenomas การวินิจฉัยอื่น ๆ ได้แก่ myelolipomas,  
hematomas, adrenal cortical hyperplasia และ disseminated  
histoplasmosis

- สรุป** : จากการศึกษานี้เราไม่พบมะเร็งในผู้ป่วยที่ถูกตรวจพบว่ามีก้อนที่ต่อมหมวกไตจากการตรวจด้วยเครื่องเอกซเรย์คอมพิวเตอร์โดยที่ผู้ป่วยไม่มีประวัติมะเร็งทางคลินิกมาก่อน
- คำสำคัญ** : ต่อมหมวกไต, *adrenal incidentaloma*, การวินิจฉัยทางรังสีวิทยา วินิจฉัยด้วยภาพตัดขวาง, เครื่องเอกซเรย์คอมพิวเตอร์, *incidental adrenal lesion, unknown primary malignancy*.

Adrenal incidentaloma is an adrenal lesion that incidentally increasingly found by an abdominal imaging, especially cross-sectional imaging which is widely available now. It is approximately 4% - 6% of the imaging to detect adrenal lesion incidentally. <sup>(1)</sup>

Adrenal incidentaloma has its diversity in its pathology. It may be benign or malignant diseases such as benign non-hyperfunctioning adrenocortical adenoma, pheochromocytoma, myelolipoma, ganglioneuroma, adrenal cyst, hematoma, adrenal cortical carcinoma, metastases and other rare adrenal malignancies such as primary lymphoma, hemangiosarcoma and neuroblastoma. However most cases of adrenal incidentaloma are benign. Nevertheless it may be primary or metastatic malignancies, which shows subclinical hyperfunction.

It is important to discriminate between benign and malignant conditions when radiologists detect adrenal incidentaloma. Imaging is non-invasive method to identify the nature of the adrenal incidentaloma. It includes computed tomography (CT) without contrast administration <sup>(1-4)</sup>, percentage wash out study by CT <sup>(1-4)</sup>, and magnetic resonance imaging (MRI) with chemical shift imaging. <sup>(1, 2)</sup>

The issue that makes radiologists concern about adrenal incidentaloma is the prevalence of malignancy. While one study revealed the prevalence of malignancy as 2% – 3% <sup>(1)</sup>, some studies showed no malignancy on CT with adrenal incidentaloma in patients with unknown primary malignancy. <sup>(5, 6)</sup>

Thus, the objective of this research study is to determine the prevalence of malignancy in adrenal incidentaloma on CT scan in patients with unknown malignancy.

## Methods

### Subjects

After receiving approval from the Ethics Committee of the Faculty of Medicine, we retrospectively reviewed abdominal CT reports from January 2004 to April 2010 by searching with the keywords as shown below from the hospital electronic database: adrenal incidentaloma, adrenal mass, adrenal lesion, adrenal nodule, adrenal tumor, and enlarged adrenal gland.

A total of 93 patients with adrenal lesions were available from the electronic database of the hospital. We excluded 31 patients with previous clinical history of malignancy; 2 patients with clinical suspicion of functioning adrenal lesion; 8 patients who were loss to follow-up and 7 patients who died before having adequate follow-up even though the cause of death was not related to cancer.

The remaining 45 patients with 48 adrenal incidentalomas met the inclusion criteria: available image in the picture archiving and communication system (PACS), available protocols for CT imaging analysis, available MRI study with chemical shift imaging, having histopathology result, for at least 1-year of stability in size on imaging or at least 2-year stability on clinical follow-up.

### Imaging techniques

#### Adrenal CT

All studies were done by 4- or 16-detector-row computed tomography (Somatom sensation 4 and 16, Siemens AG, Germany).

The CT protocol began with pre contrast study and followed by an intravenous injection of 100 mL of nonionic contrast material at the rate of 3 mL per

seconds. Post contrast study was done by using bolus-tracking technique with region of interest (ROI) placed at the aorta at the mid-hepatic level; the arterial phase was obtained at 8 seconds after reaching the attenuation value about 100 Hounsfield unit (HU). The portovenous phase was obtained about 90 seconds after the contrast material administration and then repeated delayed imaging at 10 -15 minutes. The routine slice thickness was 5 - 8 mm. and some cases had additional thin slice thickness ranging from 2 - 3 mm. The electronic ROIs were placed in the adrenal mass to measure attenuation value in HU and then absolute percentage washout was calculated by using formula of enhanced CT (HU)-delayed CT (HU)/enhanced CT (HU)-pre contrast CT (HU) × 100%.

### Adrenal MRI

MRI was performed on 1.5 Tesla systems (Signa Excite, GE Healthcare). With body coil, Gradient T1-weighted images of in-phase and opposed-phase study on axial plane with breath-hold technique were obtained with a 2D gradient-refocused echo sequence. The parameters included TR ranged of 102 -165 milliseconds, TE of in-phase study ranged of 4.4 - 4.91 milliseconds, TE of opposed-phase ranged of 1.9 - 2.62 milliseconds, flip angle ranged of 60 - 80 degree, field of view was about 320 - 480 mm, matrix was about 128 - 192 × 256, the slice thickness ranged 2 - 7 mm.

### Definite diagnosis and follow-up

We recorded the number, diameter, side, signal intensity (SI) on MRI study and attenuation value in HU of each adrenal lesion on pre and post-contrast CT study. Final diagnosis of each adrenal

incidentaloma was established by used histopathology results, imaging criteria and stability in size on imaging or clinical follow-up.

As for imaging criteria, the benign lesions were diagnosed by signal drop on oppose phase MRI with 1-year stability in size after follow-up by imaging study either on MRI or on CT study. <sup>(1, 2, 7)</sup>

The diagnostic criteria for benign lesions on CT study were an attenuation value less than or equal to 10 HU or absolute washout rate was greater than 60% <sup>(1, 3, 7)</sup> with 1-year stability in diameter after follow-up by imaging study either with MRI or on CT scan or 2-year stability after clinical follow-up.

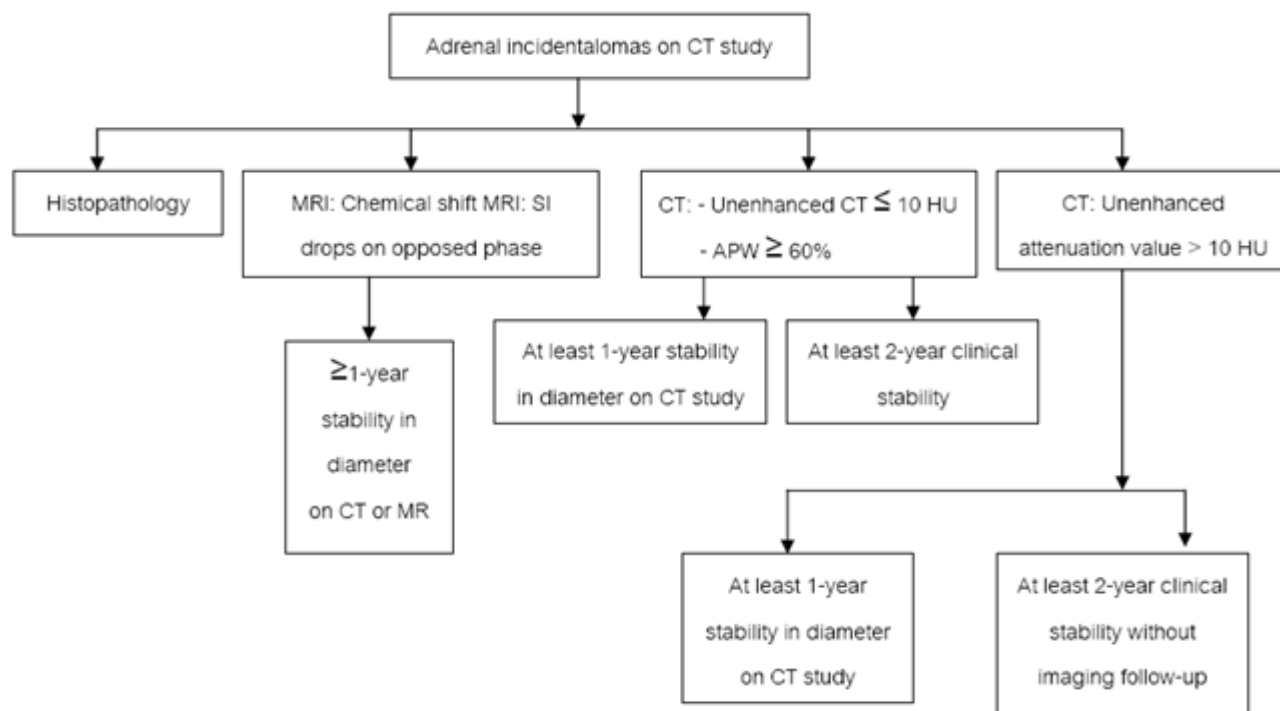
In case of initial CT study of adrenal lesions had attenuation on unenhanced CT study greater than 10 HU, the patients were followed-up by imaging or clinical. At least 1-year imaging follow-up for diameter stability or 2-year stability on clinical follow-up was considered benign. <sup>(8)</sup>

Clinical information was obtained from the medical record or calls to the patients to confirm that no clinical diagnosis of malignancy or adrenal disease after the initial imaging study. Figure 1 and 2 show summarized diagram about how to reach the diagnosis and follow-up.

### Results

Forty-five patients with 48 adrenal lesions were included in this study. The lesion was on the left side in 29 cases and, 19 cases on the right side. The mean diameter of the adrenal lesion was 1.6 cm (range, 0.6 - 3.5 cm).

The pathological diagnosis was obtained from the left adrenal mass in the patient with bilateral adrenal lesions. The pathological report was cortical



**Figure 1.** Shows summarized diagram about how to diagnose and follow-up. SI = signal intensity; APW = absolute percentage washout.

hyperplasia. The diagnosis of the right adrenal lesion in this patient was confirmed by chemical shift MRI and the result showed signal drop on opposed phase study and showed stable in size on follow-up CT study at 4 years later: adenoma (Figure 3).

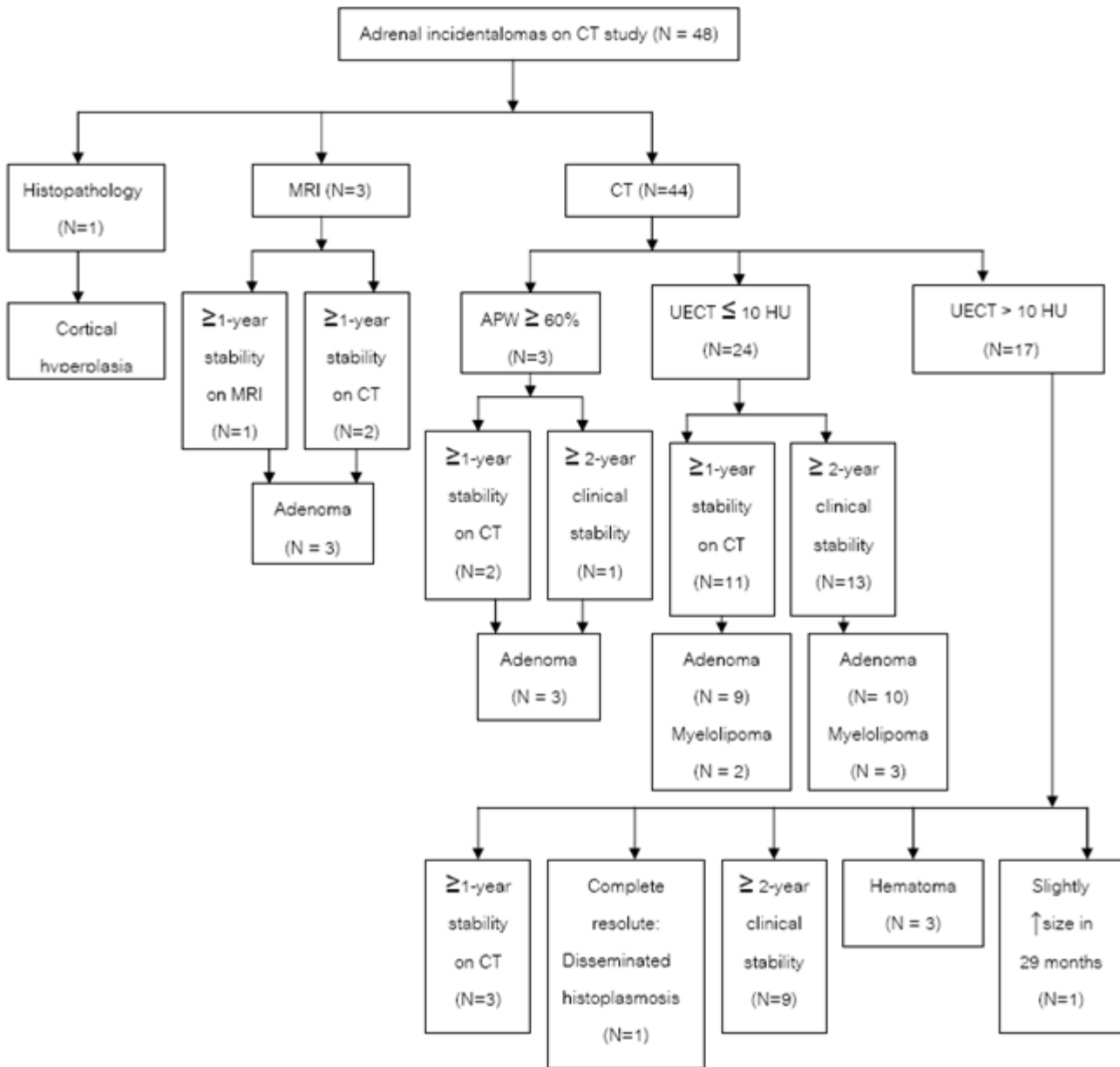
Thirty lesions were diagnosed as benign based on CT and MRI criteria. All of these lesions were stable in diameter with 1-year follow-up by imaging study either on MRI or on CT study or 2 years of clinical follow-up. The diagnosis of adenoma was established in 25 cases (Figure 4) and myelolipoma in 5 cases. Myelolipoma was diagnosed by gross fat in the adrenal lesions on CT study.

Seventeen lesions were diagnosed as benign by based on follow-up with CT study or clinical follow-up. Three lesions were stable with more than 1-year follow-up by CT study. One lesion with a diagnosis of

disseminated histoplasmosis was completely resolute on CT follow-up study (Figure 5). Twelve lesions were diagnosed as benign by using criteria of at least two-year clinical stability, including three lesions with adrenal hematoma. An adrenal hematoma was diagnosed by a high-density mass with attenuation of 40 - 50 HU without contrast enhancement on CT study.

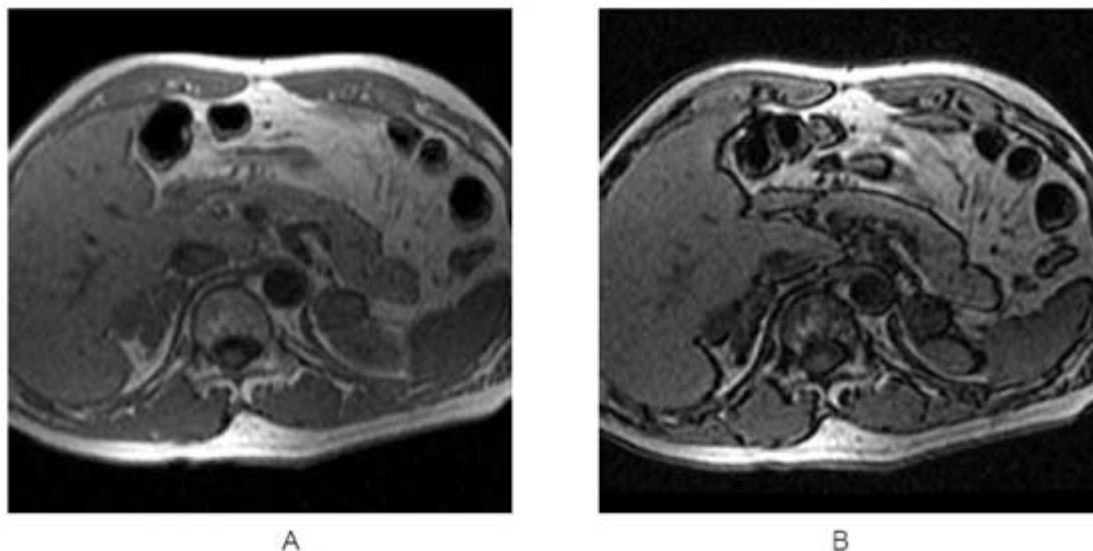
One adrenal lesion showed slowly increase in diameter on serial CT examinations from 2.0 cm to 2.7 cm in 29 months with well-defined margin and the attenuation value was about 3-15 HU on unenhanced CT without absolute wash out percentage study. The patient had no clinical symptom and abnormal biochemical results (Figure 6).

No malignant adrenal lesion was found in this study.



**Figure 2.** Diagram illustrates how to diagnose and follow-up patients with adrenal incidentaloma. APW = absolute percentage washout; UECT = unenhanced CT study.





**Figure 3.** A 49-year-old male patient with bilateral adrenal incidentalomas; A) GR T1 WI in-phase MRI and B) GR T1 WI opposed-phase. Images demonstrate signal drop on opposed phase of bilateral adrenal lesions. The pathology result for the left adrenal mass is cortical hyperplasia. The right adrenal lesion is stable in size with 4-year follow-up by CT study: adenoma.

### Discussion

Our study showed no malignant adrenal lesions in all 48 incidentaloma cases. Similar finding was reported by Song<sup>(6)</sup> that no malignant lesions in adrenal incidentaloma on CT in patients with unknown malignancy. Although the adrenal gland is the common site of metastasis in oncologic patients but it is extremely rare for an incidental adrenal lesion to be metastatic lesion of unrecognized primary malignancy.<sup>(7)</sup>

Terzolo<sup>(9)</sup> reported that the prevalence of adrenocortical carcinoma is not rare, about 13% of studied population. However, the average size of the adrenal lesion in their study was 9.4 cm with imaging features of malignancy including heterogeneous density and irregular margin. The mean diameter of adrenal lesions in our study was 1.6 cm with well-defined margin and homogeneous density.

One adrenal lesion in our study had slightly increased in diameter on follow-up imaging. We

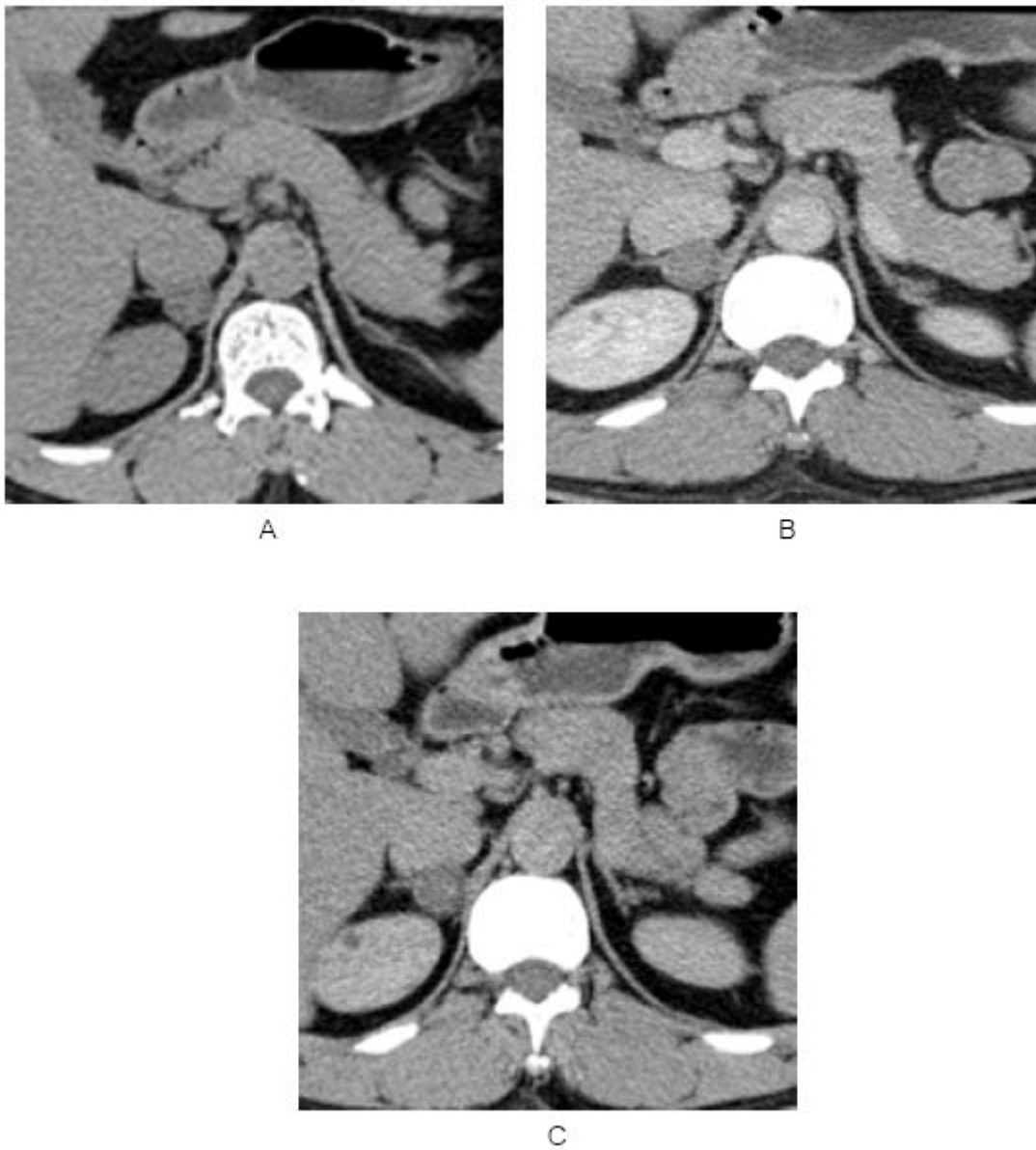
concluded that this lesion was benign because there was no clinical symptom during the follow-up period of two years. Barzon reported that mass with increased size about 1 - 2 cm over 1 - 2 years could be found in approximately 9% of benign adenoma.<sup>(10)</sup>

In our study, the most common benign adrenal lesion was adenoma and followed by myelolipoma, hematoma, adrenal cortical hyperplasia and disseminated histoplasmosis.

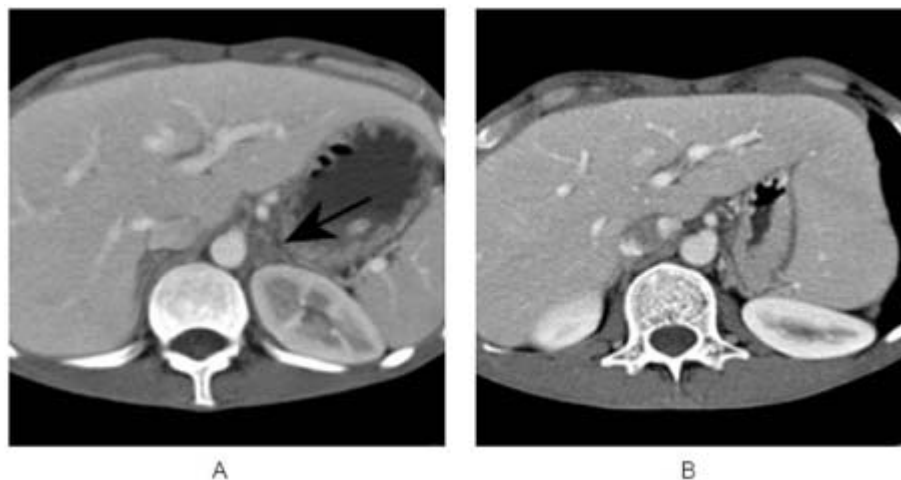
Limitations of our study were its retrospective approach and the small number of cases, which may not reflect to true malignant prevalence of adrenal incidentaloma.

### Conclusion

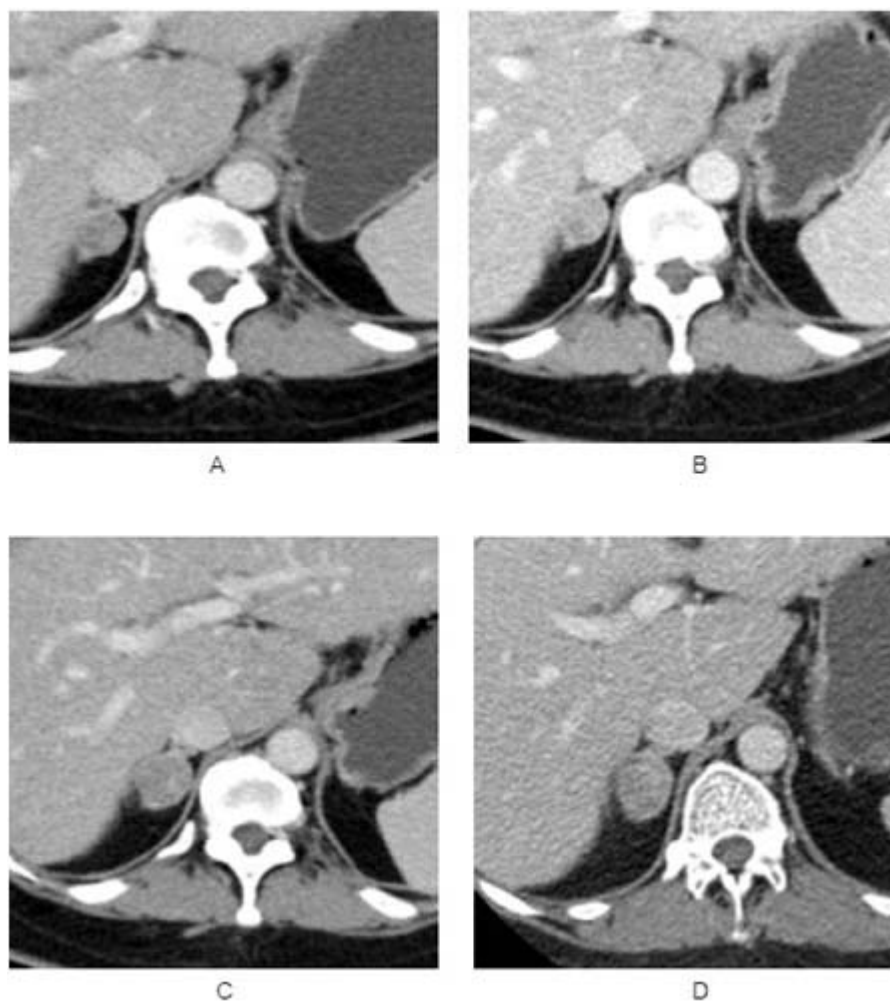
Cross-sectional imaging has been increasingly used while adrenal incidentaloma has been increasingly detected. However, the prevalence of the malignancy in this lesion is rare in patients who have no underlying malignancy.



**Figure 4.** A 47-year-old male patient with right adrenal incidentaloma; A) Axial unenhanced CT scan shows 1.9-cm right adrenal mass with attenuation of 16 HU. B) Portovenous phase CT study shows attenuation of the right adrenal mass about 63 HU. C) On 15-minute delayed CT scan, attenuation of the right adrenal mass is 28 HU. Absolute percentage washout in this case is about 74%, representing adenoma.



**Figure 5.** A 40-year-old male patient with disseminated histoplasmosis; A) Axial contrast-enhanced CT scan shows 1.6-cm left adrenal lesion (black arrow). B) Follow-up axial contrast-enhanced CT study about 3 years later reveals complete resolution of the adrenal lesion.



**Figure 6.** A 41-year-old female patient with right adrenal incidentaloma. Images from A) to D) show progression of the size of the right incidentaloma from 2.0 to 2.7-cm in diameter with serial follow-up CT study at beginning, 6, 15 and 29 months, respectively. The patient has no clinical symptom and abnormal biochemical results.

### Acknowledgements

The author would like to thank Mano Mettanando Laohavanich MD, PhD, Lecturer of Chulabhorn International College of Medicine, Thammasat University for editing the manuscript.

Conflict of interest: None

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