

Radiographic Factors Predictive of Malignant Adrenal Masses in Pathological Proven Setting

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Objective: Adrenal masses are one of important clinical radiographic issues particularly whether causes are malignant in origin or not. As there were several radiographic findings such as size, enhancement, or contour, a previous study found that size may be a factor to differentiate adenoma from non adenoma adrenal mass. The present study aimed to determine if which radiographic findings are highly suggestive for malignant adrenal mass.

Materials and Methods: This was a retrospective, analytical study. We enrolled adult patients who had adrenal mass by computed tomography (CT) with pathological findings of adrenal masses. Factors associated with adrenal malignancy were evaluated by logistic regression analysis.

Results: There were 32 patients met the study criteria. Of those, 13 patients (40.63%) were in malignant group. The malignant group had older age (52.23 vs. 29.32 years; $p=0.018$). By multivariate logistic regression analysis, only irregular contour was independently associated with malignant adrenal mass with adjusted odds ratio of 40.500 ($p=0.034$).

Conclusion: Irregular adrenal contour was suggestive for malignant adrenal mass with pathological proven setting.

Keywords: Age; Contour; Margin; Predictors

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Adrenal masses are one of important clinical radiographic issues. The approach of adrenal masses include functioning or incidentaloma and benign or malignant. The prevalence of adrenal incidentaloma is reported to be approximately 5% from 65,231 patients but can be high as 10% in elderly patients^(1,2). Even though an incidence of adrenal carcinoma may not be high, these adrenal mass may lead to patient's anxiety and concerns on causes of the adrenal mass⁽³⁾.

Radiologists may be crucial to identify cancer in origin of the adrenal mass prior to surgical resection. Radiographic findings may be suggestive for malignant tumor and facilitate prompt management. Computed tomography

(CT) is a standard evaluation for adrenal mass and widely available particularly in resource-limited setting⁽⁴⁾. A previous study found that size may be a factor to differentiate adenoma from non adenoma adrenal mass⁽⁵⁾. Radiographic score or findings such as enhancement may be related to carcinoma in origin⁽⁶⁾. As there were several radiographic findings such as size, enhancement, or contour, we determined in the present study if which radiographic findings are highly suggestive for malignant adrenal mass.

Materials and Methods

This was a retrospective, analytical study conducted at Srinagarind Hospital, a university hospital of Khon Kaen University, Thailand. The inclusion criteria were adult patients who had adrenal mass by computed tomography (CT) with pathological findings of adrenal masses. Those patients who were pregnant were excluded. The CT scan of adrenal glands were performed by four-detector rows CT scanner (SomatomPlus 4, Seimens, Erlangen, Germany) with 8 mm slice thickness. The images were obtained before and after non-ionic iodinated contrast material administration. The adrenal characteristics were reported in terms of size, consistency, margin, density, contrast enhancing pattern. The radiographic findings of the adrenal gland were reported by experienced genitourinary radiologist (JK) with more than 20 years of experiences.

Eligible patients were divided into two groups:

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benign or malignant by pathological diagnosis. The pathological diagnosis was blind to the radiologist. Clinical factors (age, sex) and radiographic findings were compared by descriptive statistics. Factors associated with adrenal malignancy were evaluated by logistic regression analysis. A univariate logistic regression analysis was firstly computed for each factor. Those factors with the p-value of less than 0.20 were put in subsequent multivariate logistic regression analysis. Factors with collinearity were excluded. Results were reported as mean (SD), number (percentage), and unadjusted/adjusted odds ratio with 95% confidence interval. The goodness of fit of the final predictive model was tested by Hosmer-Lemeshow method. Statistical analyses were performed by STATA software, version 10.1 (College Station, Texas, USA).

The study protocol was reviewed and approved by the institutional review board of Khon Kaen University (approval number HE521262).

Results

There were 32 patients met the study criteria. Of those, 13 patients (40.63%) were in malignant group. The pathological findings of the benign group comprised of adrenal adenoma (13 patients), myelolipoma (4 patients), pheochromocytoma (1 patient), and leiomyoma (1 patient). For the malignant group, pathological findings were adrenal carcinoma (3 patients), adrenal leiomyosarcoma (1 patient), adjacent/metastatic cancer (9 patients: metastatic cancer 5 patients, renal cell carcinoma 1 patient, seminoma 1 patient, round cell carcinoma 1 patient, and diffuse large B cell lymphoma 1 patient).

There were four significant factors between the benign and malignant groups (Table 1) including age, irregular contour, ill-defined margin, and size of 6 cm or more. The malignant group had older age (52.23 vs. 29.32 years; $p=0.018$) and higher proportions of the three radiologic

findings than the benign group. By multivariate logistic regression analysis, only irregular contour was independently associated with malignant adrenal mass with adjusted odds ratio of 40.500 ($p=0.034$). The Hosmer-Lemeshow Chi-square of the final model was 2.85 ($p=0.943$).

Discussion

A previous report found that a prevalence of primary adrenal carcinoma was 0.06% in general population and 1.2% in adrenal incidentalomas^(6,7). Malignant in origin may be not common in general or those with undetermined adrenal mass. However, prevalence of adrenal cancer may be high as 57% for those with abnormal clinical signs⁽⁸⁾. This study also found the high prevalence of malignant adrenal tumor as we studied in those who had pathological diagnosis (40.63%).

Previous studies showed that some radiographic findings are suggestive for malignant adrenal mass including size of 5 cm or over, non-lipid lesion, or contrast media enhancement^(6,7,9). Among these factors, the present study found that irregular contour was independently associated with malignant in origin (Table 2). Among score S for predicting metastatic adrenal tumor from adrenal adenoma, irregular contour had the highest score⁽⁸⁾. There were nine patients (69%) with adjacent/metastatic cancer. A previous report found that most adrenal adenoma masses have hypodensity, homogenous, and well defined margin⁽¹⁰⁾. Even though ill-defined margin was a quite strong predictor by univariate analysis (p -value=0.015 in Table 1), it was no longer significant after adjusted with age and irregular contour, a more independent factor for malignancy.

There were some limitations in the present study. First, we enrolled patients with evidence of pathological diagnosis. The diagnosis of malignancy in origin is definite, but this may cause high rate of cancer group in the present study. Second, most factors in the model or in the study were

Table 1. Clinical and computed tomographic features of patients with malignant and benign adrenal mass with pathologically proven

Variables	Benign n=19	Malignant n=13	p-value
Mean (SD) age, years	29.32 (16.27)	52.23 (15.55)	0.018
Male gender, n (%)	9 (47.37)	7 (53.85)	0.999
Irregular contour, n (%)	1 (5.26)	9 (69.23)	<0.001
Ill-defined margin, n (%)	2 (10.53)	7 (53.85)	0.015
Size ≥ 6 cm, n (%)	6 (31.58)	10 (76.92)	0.029
Low density lesion, n (%)	11 (57.89)	3 (23.08)	0.075
Calcified lesion, n (%)	2 (10.53)	1 (7.69)	1.000
Fatty lesion, n (%)	5 (26.32)	2 (15.38)	0.671
Cystic lesion, n (%)	1 (5.26)	0	0.999
Non enhancing lesion, n (%)	9 (47.37)	9 (69.23)	0.289
Rim enhancing lesion, n (%)	1 (5.26)	7 (53.85)	0.552

Table 2. Factors associated with malignant adrenal mass by logistic regression analysis

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Age	1.055 (1.001 to 1.111)	1.043 (0.975 to 1.117)
Irregular contour	40.500 (3.929 to 417.432)	17.409 (1.233 to 245.794)
Ill-defined margin	9.916 (1.596 to 61.596)	3.478 (0.175 to 1.117)

radiographic findings. There is limited data on other clinical factors such as symptoms, signs, or laboratory methods^(8,11). For those with hypertension, associated clinical factors also were not evaluated⁽¹²⁻¹⁶⁾. Diagnostic methods for adrenal cancer may be different from previous studies^(17,18). Finally, there was small study population. However, there is still independent factor for malignancy prediction.

In conclusion, irregular adrenal contour was suggestive for malignant adrenal mass with pathological proven setting.

What is already known on this topic?

Size may be a factor to differentiate adenoma from non adenoma adrenal mass.

What this study adds?

This study showed that irregular adrenal contour was suggestive for malignant adrenal mass with pathological proven setting.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

- Song JH, Chaudhry FS, Mayo-Smith WW. The incidental adrenal mass on CT: prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy. *AJR Am J Roentgenol* 2008;190:1163-8.
- Terzolo M, Stigliano A, Chiodini I, Loli P, Furlani L, Arnaldi G, et al. AME position statement on adrenal incidentaloma. *Eur J Endocrinol* 2011;164:851-70.
- Cawood TJ, Hunt PJ, O'Shea D, Cole D, Soule S. Recommended evaluation of adrenal incidentalomas is costly, has high false-positive rates and confers a risk of fatal cancer that is similar to the risk of the adrenal lesion becoming malignant; time for a rethink? *Eur J Endocrinol* 2009;161:513-27.
- Koo HJ, Choi HJ, Kim HJ, Kim SO, Cho KS. The value of 15-minute delayed contrast-enhanced CT to differentiate hyperattenuating adrenal masses compared with chemical shift MR imaging. *Eur Radiol* 2014;24:1410-20.
- Park SH, Kim MJ, Kim JH, Lim JS, Kim KW. Differentiation of adrenal adenoma and nonadenoma in unenhanced CT: new optimal threshold value and the usefulness of size criteria for differentiation. *Korean J Radiol* 2007;8:328-35.
- Herrera MF, Grant CS, van Heerden JA, Sheedy PF, Ilstrup DM. Incidentally discovered adrenal tumors: an institutional perspective. *Surgery* 1991;110:1014-21.
- Willatt JM, Francis IR. Radiologic evaluation of incidentally discovered adrenal masses. *Am Fam Physician* 2010;81:1361-6.
- Gufler H, Eichner G, Grossmann A, Krentz H, Schulze CG, Sauer S, et al. Differentiation of adrenal adenomas from metastases with unenhanced computed tomography. *J Comput Assist Tomogr* 2004;28:818-22.
- Hamrahian AH, Ioachimescu AG, Remer EM, Motta-Ramirez G, Bogabathina H, Levin HS, et al. Clinical utility of noncontrast computed tomography attenuation value (hounsfield units) to differentiate adrenal adenomas/hyperplasias from nonadenomas: Cleveland Clinic experience. *J Clin Endocrinol Metab* 2005;90:871-7.
- Terzolo M, Osella G, Ali A, Borretta G, Magro GP, Termine A, et al. Different patterns of steroid secretion in patients with adrenal incidentaloma. *J Clin Endocrinol Metab* 1996;81:740-4.
- Techatrasak K, Dangrat C, Waeteeul S. PCR for rapid detection of nine loci of Y-chromosomal DNA including SRY sequences in Turner syndrome patients. *Asia Pac J Sci Technol* 2020;25:APST-25-03-02.
- Jingmark S, Kuhirunyaratn P, Theeranut A, Nonjui P. Subjective well-being and related factors among community-dwelling elderly in Udon Thani Province, Thailand. *Asia Pac J Sci Technol* 2020;25:APST-25-01-09.
- Wangsan K, Chaiear N, Sawanyawisuth K, Klainin P, Simajareuk K. Pattern of shiftwork and health status among nurses in a university hospital in northeastern Thailand. *Asia Pac J Sci Technol* 2019;24:APST-24-02-08.
- Buttichak A, Leelayuwat N, Bumerraj S, Boonprakob Y. The effects of a yoga training program with fit ball on the physical fitness and body composition of overweight

- or obese women. *Asia Pac J Sci Technol* 2019;24:APST-24-02-07.
15. Perera A, Mudannayake SD, Azamathulla HM, Rathnayake U. Recent climatic trends in Trinidad and Tobago, West Indies. *Asia Pac J Sci Technol* 2020;25: APST-25-02-05.
 16. Wongsurawat N, Somboonporn C, Raruenrom Y, Thinkhamrop B. Prevalence and determinants of misclassification of the risk of recurrence of differentiated thyroid cancer after the first ¹³¹I post-therapeutic scintigraphy. *Asia Pac J Sci Technol* 2021;26:APST-26-02-05.
 17. Saiyut P, Suriya P. An economic assessment of the information system for the surveillance of liver fluke and cholangiocarcinoma of the Fluke Free Thailand Project (Isan cohort). *Asia Pac J Sci Technol* 2021;26: APST-26-01-02.