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Correlation between Radiologic and Pathologic Dimensions of Adrenal Masses

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Abstract. The size of adrenal tumors has been shown to be a good predictor of malignancy. There is still some controversy about the concordance between radiologic and real pathologic measurements. The aim of this study is to determine the correlation between direct and corrected radiologic computed tomography scan dimensions and the measurements of the resected specimen. A total of 41 adrenal tumors were included. Direct and corrected measurements of the largest diameter were contrasted with the pathologic dimensions. The Linos formula was used for the corrected measurements. Proper statistics were used considering a two-tailed significance level of 0.05. The intraclass correlations using direct and corrected measurements were 0.89 [95% confidence interval (95%CI) 0.81–0.94, $p = 0.00001$) and 0.90 (95%CI 0.82–0.95, $p = 0.00001$), respectively. The bivariate analysis using Pearson´s correlation between two-dimensional group variables showed $r = 0.82$ ($p < 0.0001$) when direct and pathologic measurements were compared and $r = 0.83$ ($p < 0.0001$) when the corrected values were compared with the real dimensions. In this study, we demonstrate good correlation between radiologic and pathologic measurements of adrenal tumors. The Linos formula turned out to be significantly more accurate than direct radiologic measurements when means of the groups were compared, whereas when individual correlations were determined the two were similar. The Linos formula and radiologic measurements can be used to determine the proper management of adrenal incidentalomas in individual patients.

Adrenal incidentalomas are adrenal tumors discovered serendipitously by noninvasive abdominal imaging techniques performed in the absence of symptoms or clinical findings suggestive of adrenal disease [1–3]. They are most commonly found by computed tomography (CT), and adrenal lesions as small as 0.5 cm can be detected using this technique [2–4].

The evaluation of adrenal incidentalomas includes laboratory tests to evaluate hormone activity and imaging studies to rule out malignancy [2–4]. All functioning tumors and tumors suggestive of malignancy are candidates for surgical exploration; but considering that adrenocortical carcinomas are generally large at diagnosis and present with invasion to the surrounding structures, a cutoff size of 4 to 6 cm has been suggested to remove nonsuspicious incidentalomas, with 4 cm the size most commonly used. This cutoff value has been selected based on the size of benign and malignant tumors in large series, the fact that nonfunctioning malignant tumors < 4 cm have been rarely described, and the result of receiver operating characteristic (ROC) curves [5–7]. Moreover, incidentally found adrenal masses are usually small, nonfunctioning, and benign. The most common lesion is adrenocortical adenoma [1, 8, 9]. Lesions between 4 and 6 cm that are hormonally inactive and exhibit a benign imaging appearance can be monitored according to the recent consensus for the management of these lesions [10]. Size, on the other hand, has not been considered of any value when adrenal metastases are suspected [11].

Because surgical indications in many patients are based on tumor size, the correlation between the radiologic and real measurements is of paramount importance. It has been recognized that CT scanning underestimates the size of adrenal tumors by 20% to 47% [8, 11–14]. Linos [8], in a study comparing CT and histology reports, proposed a mathematical calculation to correct the tumor size determined by radiology.

The aim of this study was to assess the correlation between radiologic and pathologic measurements of adrenal tumors using direct CT scan measurements and the corrected values obtained by the Linos formula.

Methods

A series of 41 consecutive patients with adrenal tumors who underwent adrenalectomy at our institution were included in the study. Preoperative CT scanning was performed using a Somatom Plus helicoidal scanner (Siemens, fourth generation). The anteroposterior, lateral, and cephalocaudal measurements were reported in the official reading of the scans for each patient. All tumors were resected and measured by a pathologist who was blind to the CT measurements. Corrected CT values were obtained using the Linos formula (Histologic size (cm) = 0.85 + [(1.09)(CT major size in cm)] [8].

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Table 1. Differential diagnosis for adrenal incidentalomas (adrenalomas).

Histopathologic diagnosis	No.	Frequency (%)
Adrenal cyst	1	2.44
Cortical adenomas		
Simple cortical adenomas	18	43.90
Adenoma with myelolipoma	1	2.44
Pheochromocytoma		
Simple pheochromocytoma	18	43.90
Pheochromocytoma with ganglioneuroma	1	2.44
Adrenocortical carcinoma		
Simple carcinoma	1	2.44
With extensive necrosis and vascular permeation	1	2.44
Total	41	100

Table 2. Level of estimation of adrenal tumor size by direct radiologic measurements and the Linos formula.

	1 cm Difference		0.5 cm Difference	
Estimation level	Direct (no.)	Linos (no.)	Direct (no.)	Linos (no.)
Overestimated	1 (2%)	10 (24%)	4 (9.8%)	18 (43.9%)
Correct	22 (54%)	23 (56%)	14 (34.1%)	12 (29.3%)
Underestimated	18 (44%)	8 (20%)	23 (56.1%)	11 (26.8%)
Total	41 (100%)	41 (100%)	41 (100%)	41 (100%)

Comparisons were made using the CT scan measurements, the corrected values (by the Linos formula), and the pathology measurements. All comparisons were performed using the largest tumor diameter. Student's *t*-test, single-measure intraclass correlation for absolute agreement, and the kappa test were used for bivariate parametric statistics; and for the bivariate nonparametric analysis, Pearson's, Kendall's, and Spearman´s correlations for linearity were used. The single-measure intraclass correlation index was used because it can compare two tied dimensions (between two measurement methods or times) by individual item but not consider sample parameters such as the mean and standard deviation; therefore it could be more precise among individual differences. A pretest two-tailed significance level of 0.05 and 95% confidence intervals were established.

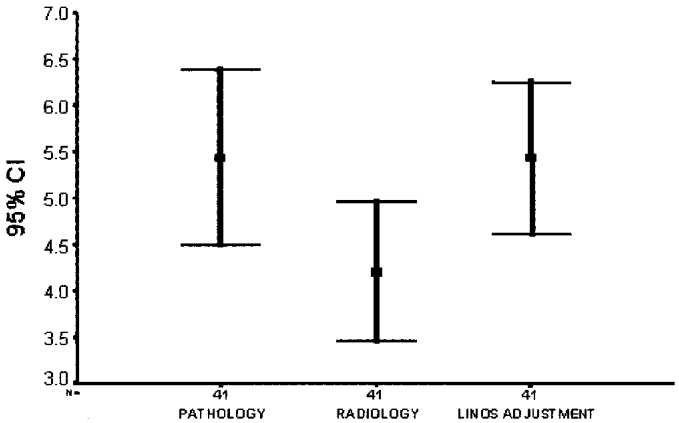

Fig. 1. Mean diameters and 95% confidence interval (95%CI) comparisons for three measurements between groups.

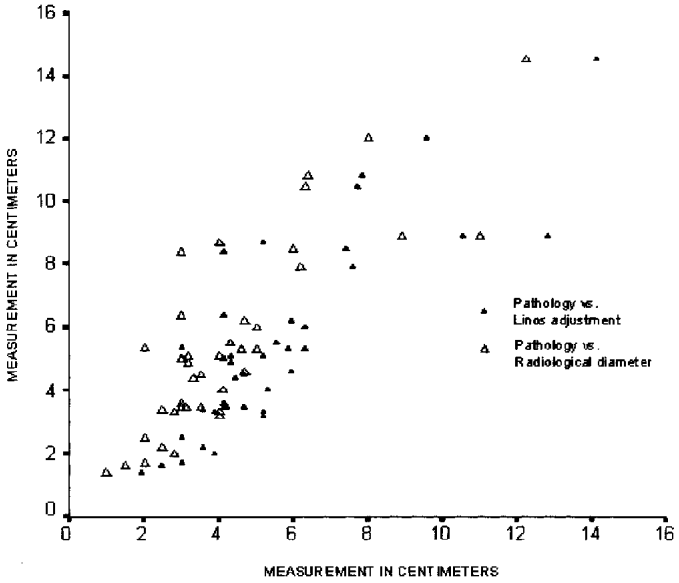

Fig. 2. Correlation between two distributions of measurements (pathology versus radiology) and (pathology versus Linos formula). Note that both correlations are similar when the linear adjustment is fitted.

Results

Of the 41 patients, 34 were women and 7 were men with a mean age at surgery of 38 ± 14 years (range 18–71 years). In 21 cases the tumor was localized on the right adrenal (51.2%) and in 20 on the left (48.8%). The final diagnoses of the tumors are shown in Table 1.

On pathologic examination the mean largest diameter for the total group was found to be 5.4 ± 3.0 cm (range 1.4–14.5 cm); the same dimension found by radiology was 4.2 ± 2.4 cm (range 1.0–12.2 cm). The mean Linos corrected value of the largest diameter was 5.4 ± 2.6 cm (range 1.94–14.15 cm). Considering 1.0 cm and 0.5 cm differences in size as significant, direct radiologic measurements and the Linos formula arrived at different estimations of tumor size when compared with the real diameters. These results are shown in Table 2. The Linos adjustment had a tendency to overestimate tumor size.

Simple bivariate analysis comparing arithmetic means with their 95% confidence intervals demonstrated a more accurate appreciation of the size using the Linos formula (Fig. 1). When the pathology size was compared with the radiologic direct measurement using the paired *t*-test, differences in size were statistically significant ($p < 0.0001$). In contrast, when the pathologic size was compared with the Linos adjustment, there were no statistically significant differences ($t = 0.029, p = 0.97$).

Using the bivariate Pearson's correlation and Spearman's rho (Fig. 2), both direct and corrected (Linos) measurements showed similar degrees of linear correlation ($r = 0.8$ and 0.7, respectively) with statistical significant differences with the pathologic size ($p < 0.0001$). Kendall's analysis showed similar results.

Using the single measure intraclass correlation coefficient to compare the pathologic size with the direct radiographic diameter in each patient (tied measurements), the correlation index was 0.89 (95%CI 0.8–0.94; $p = 0.00001$). A comparison between the pathologic size and the Linos formula result revealed the index to be 0.90 (95%CI 0.82–0.95; $p = 0.00001$).

Table 3. Prevalence of adrenal incidentalomas on image and autopsy studies.

Study	Year	Total patients	Frequency (%)
Glazer [15]	1982	2,200	0.7
Abecassis [11]	1985	1,459	1.3
Belldegrun [16]	1986	12,000	0.7
Ross [17]	1990	13,593	2.0
Herrera [6]	1991	61,054	0.5
Caplan [18]	1994	1,779	1.5
Xiao [19]	1998	14,621	1.5
Young [20]	2000	79,915	0.9
Mantero [5]	2000	> 1,000	1–5
Grumbach [10]	2003	NIH consensus	0.1–4.3

NIH: National Institutes of Health.

The prevalences are general, although it is well known that this prevalence is directly related to age.

Table 4. Differential diagnosis of imaging phenotypes by CT scanning: benign versus malignant masses.[a]

Radiologic morphology	Benign	Malignant
Size	Small (< 4 cm)	Large (> 5 cm)
Shape	Round to oval	Irregular
Margins	Smooth	Unclear or blurred
Texture	Homogeneous	Heterogeneous
Density (without contrast)	< 10 Hounsfield units	> 10 Hounsfield units
MR imaging (compared with liver)	Isointense	Hyperintense
Necrosis/hemorrhage	Rare	Common
Growth	Very slow	Usually rapid

CT: computed tomography; MRI: magnetic resonance imaging.

[a]Data are from Mantero and Arnaldi [5], Grumbach et al. [10], Caoili et al. [22], Young [20], Ng and Libertino [23], and Thompson and Young [24].

Discussion

Based on the results of various clinical series, adrenal tumors are discovered incidentally on 0.35% to 5.00% of abdominal CT scans obtained for different reasons (Table 3). Once an adrenal tumor is found and hormone hypersecretion is ruled out, we must decide between surgical excision and close observation [10].

Imaging phenotype and mass size are the two major predictors of malignancy [8, 10, 17, 21, 22]. Some radiologic characteristics may help in the differential diagnosis between benign and malignant adrenal tumors (Table 4). However, considering that most adrenal incidentalomas have a nonspecific appearance using imaging techniques, decisions are based mainly on the diagnostic likelihood of each specific tumor. Moreover, the imaging phenotype is not accurate in many cases, often varying with the visual interpretation [1, 5, 8, 15, 20].

In the absence of imaging characteristics suggestive of malignancy, tumor size has shown the closest correlation to malignancy [1, 7, 22, 25]. The number of asymptomatic nonfunctioning tumors < 3 cm that are malignant is low compared to the high prevalence of malignancy in tumors > 6 cm [3, 7, 8, 15, 21, 26].

Computed tomography scanning is the method most commonly used to evaluate adrenal incidentalomas. However, some investigators have highlighted problems in the exactitude of this method that may affect clinical judgment [5, 12, 25–28]. Discrepancies in the measurement may arise from two aspects: the accuracy of the procedure itself and the way measurements are performed. For most CT scans the anteroposterior and lateral axes are measured, and the cephalocaudal axis is taken into account less frequently. To improve these discrepancies, measurements must be taken considering all three axes [11, 12, 29].

Mantero and Arnaldi [5] found good correlation between radiologic size [CT or magnetic resonance imaging (MRI)] and the size measured at pathologic examination ($r = 0.92$, $p < 0.0001$), with higher accuracy of MRI for lesions < 3 cm [5, 11, 28–30]. In contrast, Linos and Jossart found that the adrenal mass size determined by radiology using CT scans was usually inferior to the size reported by pathology. The underestimation in their study ranged from 20% to 47% and was consistent in all groups [8, 23, 25, 30].

The present study was conducted to evaluate the accuracy of CT measurement of adrenal tumors. It is true that the ideal population for the study would include only adrenal incidentalomas. However, considering that not all adrenal incidentalomas are conducive to surgical excision and that adrenal incidentaloma is a clinical presentation rather than a pathologic entity (and that all tumors analyzed in the study could present as adrenal incidentalomas), we decided to include a representative group of cortical and medullar adrenal masses. One of the included tumors clinically presented as an incidentaloma.

To avoid underestimating any of the axes, all three axes were routinely measured on all CT scans; moreover, considering that decisions are usually based on the largest diameter, the largest diameter was chosen for our evaluations. On the bivariate analysis, the direct measurement and the corrected value using the Linos formula were similar. However, when the overestimation and underestimation of real dimensions were taken into account, the Linos correction resulted in fewer underestimated values. Overestimation would lead to an increase in the number of patients selected for surgical treatment; and underestimation would deprive patients with adrenal cortical carcinomas proper medical attention. Therefore for the purpose of this particular pathology and considering that the risk of laparoscopic adrenalectomy is negligible in most patients, we favor overestimation of tumor size.

Based on the analysis of this small series, we can see that CT scanning tends to underestimate the real dimension of adrenal tumors. However, for predicting the real pathologic size of the tumor the two methods—direct and corrected measurements using the Linos formula—provided similar results in 83.1% of the patients.

Conclusions

Based on our data, we concluded that when we compare the mean tumor size of a population the Linos adjustment is better than direct radiologic measurements for estimating the real size of an adrenal mass. Further analysis showed that the use of the single-measure intraclass correlation coefficient (r_1) which is the most reliable test for determining differences between tied measures in an individual patient, showed similar results. We believe that a direct measurement or the Linos adjustment can be used when an individual patient is being evaluated. We also recognize that the general overestimation of the Linos formula can be advantageous, as it can minimize the number of false-negative results when evaluating adrenal tumors.

Résumé. Il est démontré que la taille des tumeurs de la surrénale est un facteur prédicteur de la malignité. Il existe cependant des controverses en

ce qui concerne la concordance entre la taille estimée par la radiologie et celle obtenue à l'examen anatomopathologique. Le but de cette étude a été de déterminer la corrélation entre les dimensions obtenues par l'examen radiologique (tomodensitométrie) et celles mesurées sur la pièce réséquée. Au total, 41 tumeurs de la surrénale ont été inclues. On a tenu compte des mesures directes et corrigées du plus grand diamètre, comparées aux données de l'examen de la pièce. La formule de Linos a été utilisée pour la mesure corrigée. Les tests statistiques étaient bilatéraux : la limite de la signification a été de 0.05. La corrélation intraclasse en utilisant les mesures directes et corrigées ont été, respectivement, de 0.89 (CI_{95}0.81–0.94, $p = 0.00001$) et de 0.90 (CI_{95}0.82–0.95, $p = 0.00001$). L'analyse bivariée utilisant la corrélation de Pearson entre les groupes de variables à deux dimensions a montré un r = 0.82 ($p < 0.0001$) lorsqu'on a comparé les dimensions directes et pathologiques et un $r = 0.83$ ($p < 0.0001$) lorsque les valeurs corrigées ont été comparées aux dimensions réelles. Dans cette étude, nous avons mis en évidence une corrélation entre les dimensions radiologiques et anatomopathologiques des tumeurs de la glande surrénale. On a trouvé que la formule de Linos a été significativement plus précise que les mesures radiologiques lorsqu'un on a comparé les valeurs moyennes des groupes, mais lorsqu'on a déterminé les valeurs individuelles, les deux étaient similaires. La formule de Linos et les mesures individuelles peuvent être utilisées pour décider de la meilleure prise en charge des incidentalomes de la surrénale chez un patient donné.

Resumen. El tamaño de los tumores de las cápsulas suprarrenales constituye un factor pronóstico por lo que a la malignidad de los mismos se refiere. Se discute si existe una concordancia entre el tamaño radiológico y el real, detectado en el especimen anatomopatológico. El objetivo de este estudio es determinar si existe correlación entre las dimensiones reales del especimen resecado y las medicaciones radiológicas (CT) realizadas tanto directamente como con la corrección adecuada. Se estudiaron 41 tumores de cápsula suprarrenal. El diámetro mayor medido tanto directamente como con la adecuada corrección en la imagen obtenida mediante tomografía axial computerizada (CT) se comparó con el obtenido en el especimen anatomopatológico. La fórmula de Linos fue utilizada para la corrección de las medidas obtenidas. Se empleó un método estadístico apropiado para que la significación estadística entre los dos brazos del estudio fuera 0.05. La correlación entre las mediciones directas fue de 0.89 (CI_{95}0.81–0.94, $p = 0.00001$) y entre las corregidas de 0.90 (CI_{95}0.85–0.95, $p = 0.00001$). En un análisis bivariante utilizando la correlación de Pearson entre dos grupos de dimensiones variables se obtuvo una r = 0.82 ($p < 0.0001$) cuando se compararon el tamaño medido directamente en la imagen del CT (TAC) y el registrado en la pieza anatomopatológica; cuando, se compararon los valores corregidos y las dimensiones reales, obtuvimos una $r = 0.83$ ($p < 0.0001$). Este estudio demuestra que existe en los tumores de las cápsulas suprarrenales una exacta correlación entre las medidas radiológicas y las de la pieza anatomopatológica. La utilización de la fórmula correctora de Linos proporciona una significación más exacta, que la medición radiológica directa cuando se comparan los valores medios entre los grupos, pero cuando se efectúa una medición individual la correlación fue similar. Las mediciones radiográficas, corregidas o no, mediante la fórmula de Linos, pueden utilizarse para decidir el tratamiento más adecuado en pacientes con incidentalomas de las cápsulas suprarrenales.

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