Use of Volume Measurement in Adrenal Mass Follow Up

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Abstract

Purpose:

The purpose of our study was to assess the use of volume measurement in addition to or together with linear measurement in adrenal mass follow up. Since the morphologies of the adrenal gland may differ (such as Y,Z, andV), adrenal masses may also be visualized in different geometrical forms.If adrenal masses are hormonally inactive and do not exhibit significant changes in dimension they can be follow up for years, and measurements can therefore exhibitinterobserver differences.

Method:

Linear measurements and manual and automatic volume values obtained from first abdominal computerized tomography (CT) images from 49 patients under monitoring for adrenal adenoma were compared with final control abdominal CT measurements. No significant difference was observed in any measurements.We observed 99.7% correlation between 'first linear measurement' and' first volume,' and a similar level between 'final linear measurement' and 'final volume.'

Conclusion:

Volume measurement can be performed separately or together with three-dimensionallinear measurements in adrenal mass follow up.

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INTRODUCTION

The adrenal gland may exhibit different morphological variants. Similarly, adrenal masses may exhibit different geometrical patterns([1]).The risk of malignancy in adrenal adenomas in quite low,([2]) and follow-up may continue for up to 5 years. If adrenal adenomas are hormonally inactive and do not exhibit significant changes in dimension(≥ 5 mm) they can be monitored for a number of years, and measurements can therefore exhibit interobserver differences([2].The ability of computerized tomography (CT) to show glandular extension is diagnostically significant, and the high accuracy of adrenal volume measurement at CT means that volume measurement with CT is highly practicable([3,4,5]). In our study, axial and reconstructed coronal plane images, on which the adrenal mass is best visualized, were obtained from first and final control abdominal CT images from 49 patients with hormonally inactive adrenal adenomas[6]. Data were analyzed with three-dimensional linear measurements and volume measurements taken from these sections. The guidelines recommend surgical resection in the event of 20% or higher growth of the adrenal mass (in addition to an increase of at least 5 mm in maximum diameter)[7]. An increase of ≥ 5 mm

in three-dimensional linear measurement and a volume increase exceeding 20% were observed in11 patients (22.5%) in our study, but resection was not recommended since these were hormonally inactive at follow-up.
Volume measurement is employed in incidentaloma follow-up, monitoring at extended intervals will facilitate comparative assessment. Similarly to prostate monitoring, we think that three-dimensional linear measurement (mm) and volume (mm^3) can be used together with volume measurement (mm^3) to monitor adrenal masses. The addition of volume to these measurements will contribute to the effectiveness of follow-up.

Materials and Methods

Ethical Approval

Approval for the study was granted by our university ethical committee (No. 40465587-62 dated 06.04.2017) and the training research hospital administration.

Patients

Abdominal CT images from 49 patients followed-up due to adrenal mass between 2014 and 2017 were evaluated retrospectively. Theseconsisted of patients referred to the radiology unit for abdominal CT under the adrenal mass follow-up protocol. Patients with preliminary diagnosis ofadrenal adenoma and undergoing at least two consecutive abdominal CT sessions were included in the study. Patients with endocrine disease, septic shock, trauma, depression, adrenalectomy, and long-term therapy with glucocorticoids were excluded. Medical information recorded on the hospital system was investigated. Biochemical and endocrine analyses(metanephrine, cortisol, dexamethasone suppression test, aldosterone, renin, HbA1c, DHEA-sulfate, ACTH, 25OH Vitamin D, and insulin values),endoscopy results if available (for investigating the presence of accompanying gastritis), type of operation and pathology data were examined. Levels of metanephrine, normetanephrine, and vanillylmandelic acid in 24-h urine were examined at pre-operative endocrinological examination of all patients recommended for surgical resection. In hypertensive cases, plasma aldosterone concentration, plasma renin activity and the aldosterone/renin ratio were also analyzed following adjustment of antihypertensive therapy such as not to affect the renin-angiotensin-aldosterone system in order to investigate primary hyperaldosteronism.The analysis results were evaluated, and patients with a preliminary diagnosis of hormonally inactive adrenal adenoma were included in the study.

CT scan protocol

All abdominal CT imaging was performed with a 256slice-6 mm CT scanner (Somatom Sensation 256, Siemens Medical Solutions, Germany). Rotation time was 0.33 sec, reference tube current 220 mA and tube voltage120 kVp. The thickness and reconstruction range in the images obtained were standardized at0.625 mm. Window width and level for volume and linear measurements were at standard abdominal settings.
For contrast increase, 1 ml/kg contrast materialwas injected into an antecubital vein with a3 mL / sec flow rate using an18-21 catheter. Automatic determination of the peak increase in theabdominal aorta was used for bolus timing. Three-phase (arterial-venous–late (15 min)) abdominal CT scanning was performed.

Measurements

Axial and coronal sections on which the adrenal mass was best visualized were obtained from initial and final control abdominal CT images from 49 patients under follow-up for hormonally inactive adrenal adenoma as outlined below:
First, linear measurements of the mass were performed in mm in three planes -inferosuperior (height), ventrodorsal (depth) and mediolateral (width from reconstructed coronal images).
Second, manual volume estimations of the masses were performed from three-dimensional linear measurements using the formula height (mm) x depth (mm) x width (mm) x0.523/0.5 (cm3).
Third, estimated 20% growth amounts were calculated for each mass using manual volume values with the formula(initial volume x 20)/ 100+(initial volume).
Fourth, automatic volumes were calculated using commercially available software (AW-server, GE, andsyngo Volume, Siemens) in 25 patients capable of being transported to the workstation from adrenal masses subjected to manual volume measurement in order to assess any potential difference between automatic or manual calculation in mass volume measurements (Figure 1).

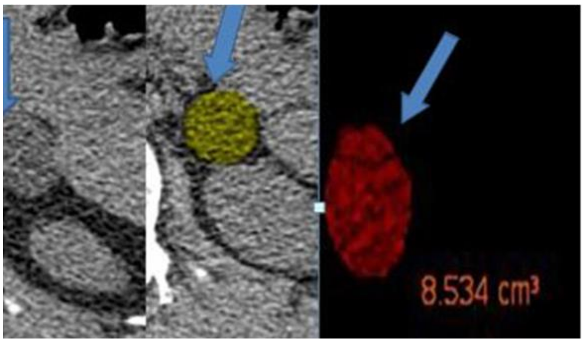

Figure 1. Automatic calculation in mass volume measurements

Fifth, linear measurement and three-dimensional volume values obtained from first and final control abdominal CTs were subjected to statistical analysis.

Statistical analysis

Descriptive statistics for continuous (numerical) variables in this study of volume measurement for use in adrenal adenoma were expressed as mean, standard deviation, minimum andmaximum values, while categorical variables were expressed as number (N) and percentage (%).

The Shapiro-Wilk test was applied to determine whether the volume values obtained were compatible with normal distribution (N<50) (Table 1). All volume measurements were determined not to be normally distributed according to both tests (p<0.05). Non-parametric tests were therefore applied. All calculations were performed onSPSS (IBM SPSS for Windows, Ver.24) software.

Results

The patients consisted of 23 men (46.9%) and 26 women (53.1%) with a mean age of59±9 years. Follow-up durations were one year in two patients(4.1%), two years in 15 (30.6%), three years in 17 (34.7%), four years in six(12.2%), and five years in nine(18.4%). Endoscopy was performed on 12 of these patients, and various stages of gastritis (active, chronic, or superficial) were determined in all (Table2).

General descriptive statistics for volume and three-dimensional linear measurements are shown in Table 3. Mean values were determined, and the distribution of all measurements was shown in graph form. Volume measurements and three-dimensional linear measurements were then compared (Table 4). 'Automatic volume' produced values close to those of 'manual volume obtained from three-dimensional linear measurement.'Finally, the statistical significance of differences between the volume measurements was analyzed (Table5). Accordingly, a significant difference was determined between first and final volumes (p=0.011). Similarly, a significant difference was determined between first volume and three-dimensional linear measurement (p<0.001).

In summary, all two-way comparisons yielded statistically significant differences (p<0.05), and results for three-dimensional linear measurements were more effective than those elicited from first and final volume. Correlation analysis of manual and automatic volume measurements revealed a high level of correlation between all measurements, with 99.7% correlation between first three-dimensional linear measurement and first volume. The correlation between these measurements is also shown as a scatter plot.

Table 1. All volume measurements were normally distributed at volume and linear measurement analysis using the Shapiro-Wilk (N<50) test (p<0.05)

	Kolmogorov-Smirnov			Shapiro-Wilk		
	Statistic	**df**	**p.**	**Statistic**	**df**	**p.**
First volume	,212	23	,009	,799	23	<,001
Final control volume	,271	23	<,001	,770	23	<,001
First linear measurement	,209	23	,010	,807	23	<,001
Final linear measurement	,241	23	,001	,799	23	<,001
Auto-volume	,239	23	,001	,803	23	<,001

df: Degree of freedom

Table 2. Patients' demographic and laboratory data

Male	23 (46,9%)
Female	26 (53,1%)
Age (mean)	59±9
	Range
metanephrin (mcg/day)	50-250
Dexamethasonesuppression test	1<
cortisol (ug/dL)	3,7-19,4
Aldosteron (ng/ml/hour)	
Renin (ng/ml/hour)	
HbA1c (mmol/ml)	20-42
DHEA- sulfate (µg/dL)	35 – 430
ACTH (pg/mL)	0–46
25-OH Vitamin D (ng/ml)	9,5-55,5
İnsülin (µU/mL)	5-10
Endoscopyresults	active, chronicgastritis (n: 12)
surgicaloperation	
Pathology	

Table 3. General descriptive statistics for volume and linear measurements; first volume and final control volumes were low, and three plane linear measurement values were higher than other measurements. However, automatic volume produced a result close to the three plane linear measurement values

	N	**Median**	**Mean**	**Std. Dev.**	**Min.**	**Max.**
First volume	49	3,91	6,0302	5,92642	,36	26,20
Final controlvolume	47	4,14	7,8006	9,22048	,30	44,29
First linearmeasurement	49	7,750	11,72612	11,642752	,580	52,320
Final linearmeasurement	48	8,140	15,46479	17,796315	,590	84,500
Auto-volume	24	7,56	10,5720	11,85912	,26	45,70

Table 4. Statistical comparisons of differences between volume and linear measurements; a significant difference was determined between first volume and final volume (pair 1) (p=0.011). Similarly, a significant difference was determined between first volume and three-dimensional linear measurement (pair 2) (p<0.001). In other words, three-dimensional linear measurement was more effective. A significant change was also determined between first volume and final linear measurement (p<0.05). We concluded that final linear measurements are more effective than first volume (p<0.05).

		N	**Mean**	**Difference**	**Std. Dev.**	***p.**
Pair 1	First volume	47	5,8580	-1,9426	5,95328	,011
	Final control volume	47	7,8006		9,22048	
Pair 2	First volume	49	6,0302	-5,69596	5,92642	<,001
	First linear measurement	49	11,73		11,643	
Pair 3	First volume	48	5,8777	-9,58713	5,89118	<,001
	Final linear measurement	48	15,46		17,796	
Pair 4	First volume	24	6,5095	-4,06246	6,70455	,005
	Auto-volume	24	10,5720		11,85912	
Pair 5	Final control volume	47	7,8006	-3,59149	9,22048	<,001
	First linear measurement	47	11,39		11,709	
Pair 6	Final control volume	47	7,8006	-7,64851	9,22048	<,001
	Final linear measurement	47	15,45		17,988	
Pair 7	Final controlvolume	23	7,9904	-2,68465	9,22087	,100
	Auto-volume	23	10,6751		12,11464	
Pair 8	First linear measurement	48	11,44	-4,026	11,588	,003
	Final linear measurement	48	15,46		17,796	
Pair 9	First linear measurement	24	12,88	2,30638	13,344	,014
	Auto-volume	24	10,5720		11,85912	
Pair 10	Final linear measurement	24	16,49	5,91304	17,649	,002
	Auto-volume	24	10,5720		11,85912	

*. *Wilcoxon Test*

Table 5. Correlation coefficients between measurements; all measurements were compared wıth one another. Statistically significant correlations are indicated by asterisks (*) (p<0.01). High correlation was determined between all measurements. For example, 99.7% correlation was determined between first linear measurement and first volume.

		First volume	**Final control volume**	**First linear measurement**	**Final linear measurement**
Final control volume	R	,918**			
First linear measurement	R	,997**	,916**		
Final linear measurement	R	,922**	,950**	,925**	
Auto-volume	R	,746**	,838**	,750**	,769**

R: Spearman's correlation coefficients
*** P<0.01*

Discussion
This study evaluated the use of volume measurement in the monitoring of adrenal masses. Abdominal CT is the most widely employed sectional imaging method for evaluating the adrenal glands([1,8]), particularly due to its ability to show glandular extension. A high level of accuracy in volume determination with CT makes adrenal volume measurement with CT particularly practicable([3,4]).
The recommendations for the management of adrenal incidentaloma in clinical guidelines may be listed as follows: ([7])When an adrenal mass is first detected, the clinician should aim to determine whether it is benign or malignant. The application of an imaging procedure, non-contrast CT scanning, is recommended in alladrenal incidentalomas to determine whether the mass is homogeneous and rich in lipids([7,2]). These guidelines seek to answer four important questions during the monitoring of adrenal masses; how the risk of malignancy will be assessed with imaging, how Cushing's syndrome will be identified and managed,which patients should receive surgical treatment, and what are the monitoring indications if the adrenal mass cannot be excised surgically?([2]).The recommendations include patients with adrenal masses not considered for surgical resection following initial evaluation but undergoing growth re-assessment with non-contrast CT or MRI after 6-12 months([7]). In addition, the guidelines recommend surgical resection of the adrenal mass in case of growth of 20% or more (in addition to an increase in diameter of at least 5 mm) during follow-up([2]), while long-term monitoring is restricted to lesions of4 cm and less (6-12 months) and an increase in volume less than 20% ([7]). This will result in a safe approach being maintained in the management of adrenal masses. While there have been other studies of adrenal gland volume measurement, we encountered no previous studies of the use of volume in adrenal adenoma follow-up.
Our hospital's endocrinology polyclinic adrenal mass monitoring protocol recommends biochemical and radiological follow-up if the mass is 4 cm in size or less, monitoring at a range of 4-6 cm if the mass is hormonally inactive and radiological imaging suggests that it is benign, and surgical resection if it is larger than 6 cm or hormonally active([9]). In our study we observed an increase of 5 mm or more at linear measurement and a volume increase exceeding 20% in 11 of the 49 cases (22.5%), but resection was not advised since these were hormonally inactive.
One critical question not addressed in the guideline concerns biochemical analysis when an adrenal incidentaloma is first detected and the radiologist's subsequent monitoring protocol. The literature recommends that all adrenal incidentalomas be subjected to endocrinological and biochemical evaluation([7]). Interobserver observation was present in those of our cases with increases of 5 mm or more at three-dimensional linear measurements ([10]). We think that when volume measurement is employed in incidentaloma follow-up, monitoring at extended intervals will facilitate comparative assessment. Similarly to prostate monitoring, we think that three-dimensional linear measurement (height (mm) x depth (mm) x width (mm) and volume (mm^3)) can be used together with volume measurement (mm^3) to monitor adrenal masses. Further prospective controlled studies involving real postoperative volume correlation with larger sample groups are now needed.

Limitations

1. The fact that this is the first study of volume measurement in adenoma follow-up,
2. The volume values obtained could not be confirmed with true volumes,
3. The effects of sex, weight and BMI on volume measurements were not evaluated, and
4. The retrospective nature of the study.

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