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Adrenal Adenomas and Nonadenomas: Assessment of Washout at Delayed Contrast-enhanced CT¹

PURPOSE: To measure the changes in wash-in and washout of contrast material on contrast material-enhanced computed tomographic (CT) scans in patients with adrenal adenomas and nonadenomas.

MATERIALS AND METHODS: One hundred twenty-two patients with 135 adrenal masses (74 adenomas, 61 nonadenomas) underwent helical CT. Unenhanced CT was followed by enhanced CT at 30, 60, and 90 seconds and 3, 10, and 30 minutes.

RESULTS: The adenomas enhanced significantly more than the nonadenomas at 60 seconds ($P < .001$), but the percentage enhancement of the adenomas was significantly greater than that of the nonadenomas at 30, 60, and 90 seconds ($P < .001$). At 3, 10, and 30 minutes, the absolute percentage loss of enhancement and the relative percentage loss of enhancement were significantly greater for the adenomas than for the nonadenomas ($P < .001$). Delayed enhanced CT at 10 minutes (sensitivity, 92%; specificity, 95%) and 30 minutes (sensitivity, 97%; specificity, 100%) was more accurate for differentiation of adenomas and nonadenomas than unenhanced CT (sensitivity, 82%; specificity, 95%).

CONCLUSION: Adrenal adenomas exhibit greater washout of contrast material than do adrenal nonadenomas. The percentage change in washout of contrast material is a useful adjunct to absolute CT attenuation values in differentiation of adrenal adenomas and nonadenomas.

Recently, much interest has been focused on use of delayed contrast material-enhanced computed tomography (CT) to accurately distinguish adrenal adenomas and nonadenomas (1-3). Previous reports demonstrated that adrenal nonadenomas have significantly higher attenuation than adenomas on delayed enhanced CT scans obtained at arbitrarily chosen times (3-60 minutes) after initiation of contrast material administration (1-3). For example, in our previous study (2), the mean attenuation 30 minutes after injection of 120 mL of nonionic contrast material was $59 \text{ HU} \pm 16$ for nonadenomas versus $20 \text{ HU} \pm 10$ for adenomas.

These findings may substantially affect the daily routine work of CT radiologists and may be accurate enough to use in most cases of adrenal masses. However, absolute attenuation values must be used carefully, in part because of the possibility of erroneous misinterpretation in cases of borderline enhancement. In three recent studies (1-3), different types of CT scanners, different types (ionic and nonionic) and amounts of contrast material, and different delivery rates were used.

To our knowledge, no CT data are available on both the absolute and relative changes in attenuation of adrenal masses. Therefore, the purpose of this study was to evaluate the wash-in and washout of contrast material in patients with adrenal adenomas or nonadenomas. To corroborate our previous findings on absolute attenuation values, several time windows were again used to measure (a) the absolute and percentage increase in attenuation and (b) the absolute and relative percentage loss of enhancement in a representative study population with adrenal masses.

MATERIALS AND METHODS

Study Population

The study protocol was approved by and in accordance with the recommendations of the human research committee at our institution. All patients gave written informed consent.

One hundred seventy-three patients with 192 adrenal masses were consecutively examined with helical CT and considered for entry into the protocol. The study group comprised 104 male and 69 female patients aged 12–87 years (mean, 66 years). The presence of individual masses was proved with biopsy ($n = 36$), surgery ($n = 15$), or imaging (repeated CT examinations) and clinical follow-up ($n = 71$). Stable lesion size or an attenuation less than 10 HU at unenhanced follow-up CT for at least 12 months (mean, 13 months; range, 12–25 months) was accepted as proof of a diagnosis of benign adenoma. Patients in whom neither follow-up CT nor cytologic or histologic analysis was possible ($n = 48$) and patients with adrenal cysts ($n = 2$) or adrenal hematomas ($n = 1$) were excluded from the study.

The remaining 122 patients (71 male and 51 female patients aged 12–87 years; mean, 64 years) fulfilled the criteria for inclusion in the protocol. At diagnostic investigation, 67 patients (77 masses) had known malignant disease: small cell lung carcinoma ($n = 7$), non-small cell lung carcinoma ($n = 25$), breast carcinoma ($n = 6$), renal cell carcinoma ($n = 6$), colorectal carcinoma ($n = 5$), non-Hodgkin lymphoma ($n = 3$), pancreatic carcinoma ($n = 3$), prostate carcinoma ($n = 2$), hepatocellular carcinoma ($n = 2$), undifferentiated carcinoma ($n = 2$), malignant melanoma ($n = 1$), esophageal carcinoma ($n = 1$), transitional cell carcinoma ($n = 1$), endometrial carcinoma ($n = 1$), uterine sarcoma ($n = 1$), or cervical carcinoma ($n = 1$). Fifty masses in 47 patients were found incidentally (during CT performed for other reasons). Only eight patients (eight masses) were examined because of abnormal results at chemical analysis of blood and urine (three patients with pheochromocytoma, three with Cushing syndrome, and two with primary aldosteronism). In all, there were 135 masses in 122 patients: 74 adenomas (69 nonhyperfunctioning adenomas, three cortisol-secreting adenomas, two aldosterone-secreting adenomas) and 61 nonadenomas (47 metastases, six pheochromocytomas, six adrenocortical carcinomas, one neuroblastoma, and one ganglioneuroma).

Imaging Protocol

Studies were performed on a Somatom Plus 4 helical CT scanner (Siemens, Erlangen, Germany). Helical scans were obtained at 292 mA and 120 kV. The protocol consisted of a volumetric data acquisition through the adrenal glands (upper abdomen) with 5-mm collimation, 7.5 mm/sec table feed, and 4-mm increments before and after intravenous bolus injection of contrast material. The scanning time for one revolution of the x-ray tube was 0.75 seconds. Each scan (acquisition time, 18–24 seconds) was obtained with the patient in full inspiration to optimize the reproducibility of starting measurements.

Initially, an unenhanced scan was obtained through the adrenal glands. An 18- or 20-gauge intravenous catheter (Angiocath; Becton Dickinson, Franklin Lakes, NJ) was then placed in an antecubital vein and tested by rapidly infusing 10 mL of saline by hand. Subsequently, 120 mL of nonionic contrast material (iopromide 300; Ultravist, Schering Pharmaceuticals, Berlin, Germany) was administered at 2.5 mL/sec with a power injector (MCT Plus; Medrad, Pittsburgh, Pa). For the second and third scans (which were preprogrammed for the same collimation, table feed, and duration as the first scan), patients were separated into two groups according to the following scan delays: (a) 30 seconds and 90 seconds ($n = 48$); 29 adenomas, 21 nonadenomas) and (b) 60 seconds and 180 seconds ($n = 74$); 45 adenomas, 40 nonadenomas) after the start of contrast material injection.

In addition, a fourth scan was obtained in 39 patients with adenomas ($n = 24$) or nonadenomas ($n = 21$) at 10 minutes (range, 8–13 minutes) and in 69 patients with adenomas ($n = 37$) or nonadenomas ($n = 34$) at 30 minutes (range, 24–36 minutes) after the start of contrast material injection. Images were obtained with standard soft-tissue settings (window width, 400 HU; window level, 40 HU).

Image and Data Analysis

Image interpretation and attenuation measurement were performed retrospectively with a commercially available Sparc 10 CT/MR workstation (Sienet MagicView 1100; Siemens) by two radiologists experienced in CT (D.H.S., F.H.K.) who had no knowledge of clinical, histologic, or follow-up findings and who worked independently (without consultation). For all adrenal masses detected in the original CT examination, the attenuation was mea-

sured by means of circular region-of-interest cursors placed over the area of disease. The region-of-interest circle was made as large as possible; lesion edges were avoided to preclude partial volume effects. Cystic, necrotic, and hemorrhagic components of the adrenal mass were excluded whenever possible. The measurements obtained by the two radiologists were averaged.

For all masses, the absolute and percentage increase in attenuation (wash-in) and the absolute and relative percentage loss of enhancement (washout) were determined. The absolute increase in attenuation was calculated as follows: $A_E - A_U$, where A_E is the attenuation at enhanced CT and A_U is the attenuation at unenhanced CT. The percentage increase in attenuation was calculated as follows: $(A_E - A_U)/A_U \times 100$. The absolute percentage loss of enhancement was calculated as follows: $[1 - (A_{DE} - A_U)/(A_E - A_U)] \times 100$, where A_{DE} is the attenuation at delayed enhanced CT. The percentage loss of enhancement relative to the amount of initial enhancement was calculated as follows: $(A_E - A_{DE})/A_E \times 100$.

Statistical analyses were performed with commercially available software (StatView; Abacus Concepts, Berkeley, Calif). Primary statistical analysis of the pooled data was performed with the paired Student *t* test to determine mean differences in objective region-of-interest measurements of attenuation between the different helical scans. A confirmatory analysis was performed by using repeated measures of analysis of variance (4). With this method, means for more than one group can be compared when measurements are obtained at more than one point in time; the method allows control of differences among patients, differences among lesions within individual patients, and interactions between patients and helical scan sequences. The mean attenuations at unenhanced CT and enhanced CT were calculated for the groups and analyzed with the unpaired Student *t* test. A *P* value less than .01 was considered to indicate a statistically significant difference. The Bonferroni correction was applied to the results to correct for the multiple comparisons made.

RESULTS

Unenhanced CT

The 74 adenomas had a mean attenuation of 7 HU \pm 15 versus 37 HU \pm 12 for the 61 nonadenomas ($P < .001$). Table 1 gives the sensitivity and specificity at sev-

TABLE 1
Sensitivity and Specificity at Several Thresholds for Diagnosis of Adenoma with Unenhanced and Delayed Enhanced CT

Type of CT Study	Threshold (HU)	Sensitivity (%)	Specificity (%)	PPV* (%)	NPV† (%)
Unenhanced	11	55	100	100	65
	18	82	95	95	82
	35	100	54	73	100
3-min scan	48	47	100	100	63
	64	91	80	84	89
	71	100	70	79	100
10-min scan	44	80	100	100	81
	52	92	95	96	91
	60	100	71	80	100
30-min scan	37	97	100	100	97
	42	100	97	97	100

Note.—At unenhanced CT, 74 adenomas and 61 nonadenomas were evaluated. At delayed enhanced CT, 45 adenomas and 40 nonadenomas were evaluated at 3 minutes, 24 adenomas and 21 nonadenomas were evaluated at 10 minutes, and 37 adenomas and 34 nonadenomas were evaluated at 30 minutes.

* PPV = positive predictive value.
† NPV = negative predictive value.

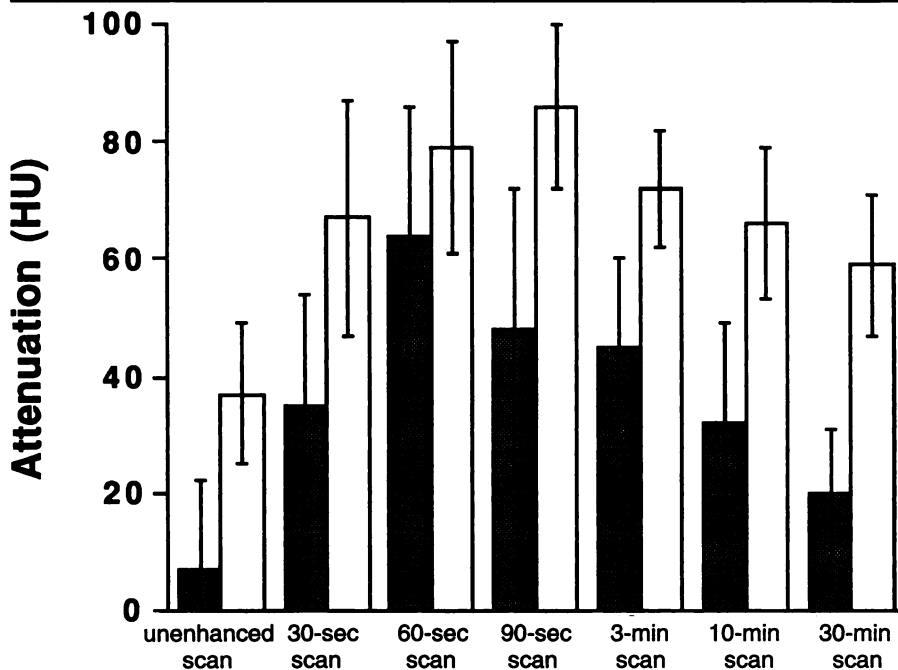


Figure 1. Graph shows mean attenuations of adrenal adenomas (gray bars) and nonadenomas (white bars) on unenhanced and enhanced CT scans. Note the substantial difference in the attenuations of adenomas and nonadenomas on all images except the 60-second scan. Error bars indicate standard deviations.

eral thresholds for diagnosis of adenoma with unenhanced and delayed enhanced CT. None of the 61 nonadenomas had an attenuation below 11 HU, whereas 41 of the 74 adenomas (55%) did. Therefore, the sensitivity and specificity were 55% and 100%, respectively, at a threshold of 11 HU (Table 1). The positive predictive value was 100%, and the negative predictive value was 65%.

Three of the 61 nonadenomas (5%)

(two metastases of small cell carcinoma, one metastasis of colorectal carcinoma) had an attenuation above 10 HU but below 18 HU, whereas 61 of the 74 adenomas (82%) had an attenuation below 18 HU. However, all three low-attenuating metastases followed the enhancement pattern of nonadenomas. Thirteen adenomas (11 nonhyperfunctioning adenomas, one cortisol-secreting adenoma, one aldosterone-secreting adenoma) had

an attenuation above 18 HU but clearly showed the enhancement characteristics of adenomas. Thus, the sensitivity and specificity for diagnosis of adenoma were 82% and 95%, respectively, at a threshold of 18 HU. The positive predictive value was 95%, and the negative predictive value was 82% (Table 1).

Early Enhanced CT and Wash-in of Contrast Material

Thirty seconds after the start of contrast material injection, the mean attenuation of the 29 adenomas (35 HU ± 19) was significantly different from that of the 21 nonadenomas (67 HU ± 20) ($P < .001$). Peak attenuation occurred at 60 seconds for the adenomas and at 90 seconds for the nonadenomas (Fig 1). At 60 seconds, the mean attenuation was 64 HU ± 22 for the 45 adenomas and 79 HU ± 18 for the 40 nonadenomas ($P = .021$). At 90 seconds, the mean attenuation of the nonadenomas (86 HU ± 14) was significantly greater than that of the adenomas (48 HU ± 24) ($P < .001$). Although the mean attenuation of the nonadenomas was significantly greater than that of the adenomas at 30 and 90 seconds ($P < .001$), there was much greater overlap in the attenuation values of the adenomas and nonadenomas than on the unenhanced images.

The mean enhancement of the adenomas, however, was substantially greater than that of the nonadenomas. Thirty seconds after the start of contrast material injection, the absolute enhancement of the adenomas (34 HU ± 20) was slightly but not significantly greater than that of the nonadenomas (25 HU ± 16) ($P = .091$) (Fig 2a). The relative enhancement, however, was significantly greater for the adenomas (460% ± 512) than for the nonadenomas (62% ± 39) ($P < .001$) (Fig 2b). At 60 seconds, the absolute enhancement and relative enhancement of the adenomas (57 HU ± 21 and 1,296% ± 2,021, respectively) were significantly greater than those of the nonadenomas (41 HU ± 19 and 119% ± 70, respectively) ($P < .001$). At 90 seconds, the absolute enhancement of the adenomas (47 HU ± 24) and nonadenomas (44 HU ± 13) was similar ($P = .54$) but the relative enhancement again differed significantly (adenomas, 642% ± 616; nonadenomas, 111% ± 51) ($P = .0007$).

Delayed Enhanced CT and Washout of Contrast Material

Three minutes after the start of contrast material injection, the attenuation of the

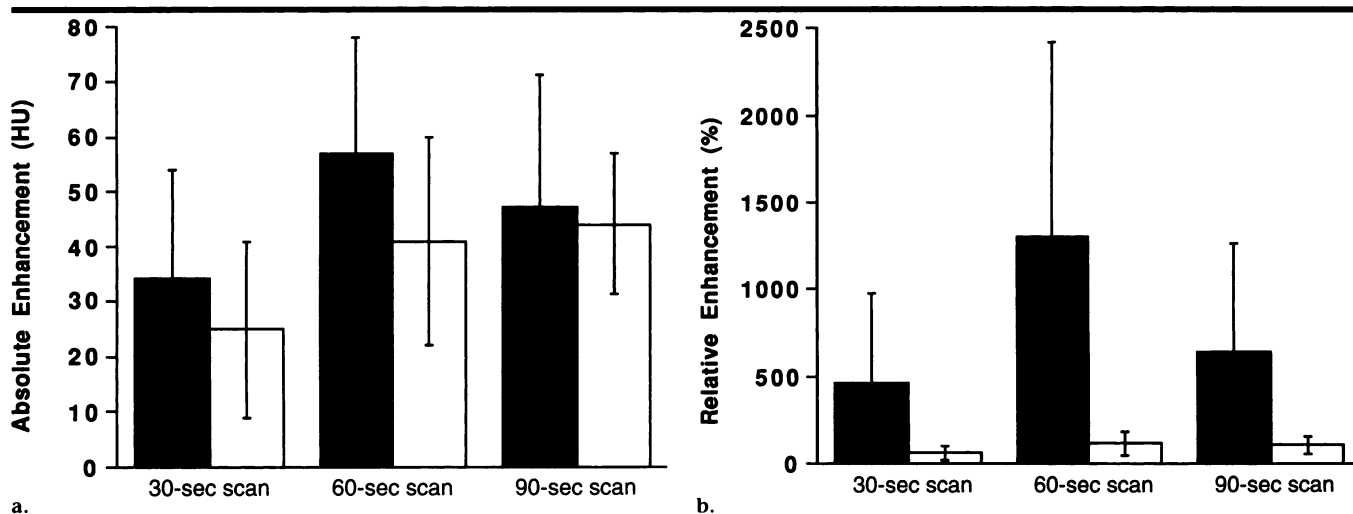


Figure 2. (a) Graph shows absolute enhancement of adenomas (gray bars) and nonadenomas (white bars). On the 60-second scan, adenomas exhibited significantly greater enhancement than nonadenomas ($P < .001$). Error bars indicate standard deviations. (b) Graph shows relative enhancement of adenomas (gray bars) and nonadenomas (white bars). The relative enhancement was significantly greater for adenomas than for nonadenomas ($P < .001$). Error bars indicate standard deviations.

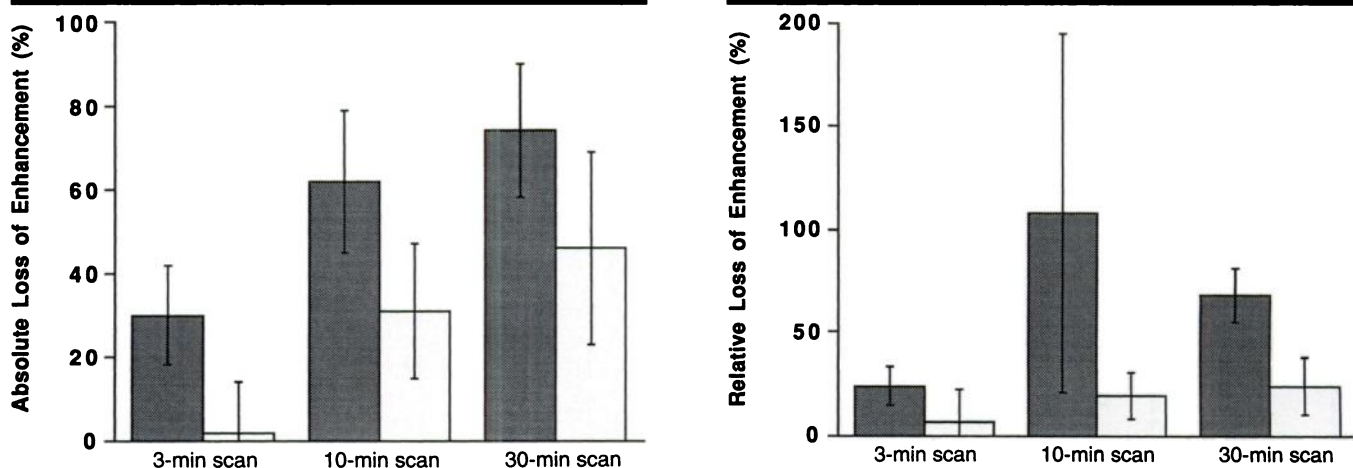


Figure 3. Graph shows the absolute percentage loss of enhancement of adenomas (gray bars) and nonadenomas (white bars). Loss of enhancement was significantly greater for adenomas than for nonadenomas ($P < .001$). Error bars indicate standard deviations.

Figure 4. Graph shows the relative percentage loss of enhancement of adenomas (gray bars) and nonadenomas (white bars). Relative to the amount of initial enhancement, washout of contrast material was significantly greater for adenomas than for nonadenomas ($P < .001$). Error bars indicate standard deviations.

45 adenomas ($45 \text{ HU} \pm 15$) was significantly lower than that of the 40 nonadenomas ($72 \text{ HU} \pm 10$) ($P < .001$). Forty-one of the 45 adenomas (91%) had an attenuation below 64 HU, whereas 32 of the 40 nonadenomas (80%) had an attenuation above 64 HU. Therefore, the sensitivity and specificity for diagnosis of adenoma were 91% and 80%, respectively, at this threshold (Table 1). The positive predictive value was 84%, and the negative predictive value was 89%. The absolute percentage loss of enhancement was $30\% \pm 12$ for the adenomas versus $2\% \pm 12$ for the nonadenomas ($P < .001$) (Fig 3). The percentage loss of enhancement relative to the amount of

initial enhancement was $24\% \pm 9$ for the adenomas versus $7\% \pm 15$ for the nonadenomas ($P < .001$) (Fig 4).

On the 10-minute scan, the mean attenuation of the 24 adenomas ($32 \text{ HU} \pm 17$) was significantly less than that of the 21 nonadenomas ($66 \text{ HU} \pm 13$) ($P < .001$). At a threshold of 52 HU, the sensitivity and specificity for diagnosis of adenoma were 92% and 95%, respectively (Table 1). The positive predictive value was 96%, and the negative predictive value was 91%. The absolute percentage loss of enhancement was $62\% \pm 17$ for the adenomas versus $31\% \pm 16$ for the nonadenomas ($P < .001$) (Fig 3). The percentage loss of enhancement relative to the

amount of initial enhancement was $108\% \pm 87$ for the adenomas versus $19\% \pm 11$ for the nonadenomas ($P < .001$) (Fig 4).

On the 30-minute scan, all of the adenomas ($n = 37$) except one (attenuation, 41 HU) had an attenuation below 37 HU (mean, $20 \text{ HU} \pm 11$), whereas all 34 nonadenomas had an attenuation above 41 HU (mean, $59 \text{ HU} \pm 12$). At a threshold of 37 HU, the sensitivity and specificity for diagnosis of adenoma were 97% and 100%, respectively (Table 1). The positive predictive value was 100%, and the negative predictive value was 97%. The absolute percentage loss of enhancement was $74\% \pm 16$ for the adenomas versus $46\% \pm 23$ for the nonadenomas

TABLE 2
Attenuation of the Pheochromocytomas and Ganglioneuroma at Unenhanced, Enhanced, and Delayed Enhanced CT

Final Diagnosis	Attenuation by Type of CT Scan (HU)						
	Unenhanced	30-second	60-second	90-second	3-minute	10-minute	30-minute
Pheochromocytoma	35	58	...	83	...	72 (23, 13)	...
Pheochromocytoma	42	61	...	104	...	82 (35, 21)	...
Pheochromocytoma	37	...	82	...	78 (9, 5)	69 (29, 16)	60 (49, 27)
Pheochromocytoma	39	...	108	...	105 (4, 3)	...	77 (45, 29)
Pheochromocytoma	34	...	85	...	86 (-2, -1)	...	63 (43, 26)
Pheochromocytoma	46	...	99	...	94 (9, 5)	...	69 (57, 30)
Ganglioneuroma	43	49	...	54	46 (73, 15)

Note.—Numbers in parentheses are the absolute and relative percentage loss of enhancement, respectively.

($P < .001$) (Fig 3). The percentage loss of enhancement relative to the amount of initial enhancement was $68\% \pm 13$ for the adenomas versus $24\% \pm 14$ for the nonadenomas ($P < .001$) (Fig 4).

The relative percentage loss of enhancement for the adenomas at 10 minutes ($108\% \pm 87$) was substantially higher than that at 30 minutes ($68\% \pm 13$). This difference must be attributed to three adenomas that demonstrated a relative percentage loss of enhancement of 264%–361% (mean, 319%) at 10 minutes. Unfortunately, 30-minute scans were not obtained in these cases.

Two nonadenomas (one ganglioneuroma, one metastasis of transitional cell carcinoma) demonstrated an absolute percentage loss of enhancement of more than 70% (73% and 85%, respectively) at 30 minutes. The relative percentage loss of enhancement for these two masses was 15% and 49%, respectively. Both masses, however, exhibited inhomogeneous enhancement and had an attenuation above 37 HU (43 HU and 38 HU, respectively) on the unenhanced scan. Table 2 gives the attenuation values and percentage changes in enhancement on the unenhanced, enhanced, and delayed enhanced scans for the six pheochromocytomas and one ganglioneuroma in our study.

The adenoma that had an attenuation of 41 HU at 30 minutes demonstrated an absolute percentage loss of enhancement of 66% at 10 minutes and 74% at 30 minutes. The percentage loss of enhancement relative to the amount of initial enhancement was 50% at 10 minutes and 119% at 30 minutes for this adenoma.

We compared the percentage loss of enhancement for adenomas ($n = 12$) and nonadenomas ($n = 13$) that were evaluated at both 10 and 30 minutes. The absolute percentage loss of enhancement

was $49\% \pm 12$ at 10 minutes and $79\% \pm 9$ at 30 minutes for the adenomas versus $34\% \pm 20$ and $51\% \pm 21$, respectively, for the nonadenomas. The percentage loss of enhancement relative to the amount of initial enhancement was $66\% \pm 17$ at 10 minutes and $75\% \pm 13$ at 30 minutes for the adenomas versus $21\% \pm 13$ and $26\% \pm 14$, respectively, for the nonadenomas.

DISCUSSION

Incidental detection of an adrenal mass in a patient with a history of malignant disease raises concern because the adrenal gland is one of the more common sites for metastatic spread and as many as 36% of such masses may harbor metastases (5–7). Therefore, accurate characterization of adrenal masses has major clinical implications; resection of the primary lesion in patients with adrenal metastases offers no hope of cure and is associated with surgical mortality. More important, however, is the risk of denying potentially curative surgery on the basis of false-positive imaging findings.

A variety of imaging techniques including unenhanced CT, magnetic resonance (MR) imaging, and nuclear medicine have been used in an attempt to distinguish metastases from benign nonhyperfunctioning adenomas. Studies have confirmed the value of unenhanced CT densitometry (8–10), chemical shift and T2-weighted MR imaging (11–13), and iodomethylnorcholesterol (NP-59) imaging (14,15) in the characterization of many adrenal masses as benign, with relatively high specificity and acceptable sensitivity. Practical use of these imaging techniques, however, is limited by several factors. Many, if not most, abdominal CT studies are routinely performed

with intravenously administered contrast material. The high cost and limited availability of both MR imaging and nuclear medicine techniques, particularly positron emission tomography, will continue to limit their use to specialized centers or certain circumstances (ie, an adverse reaction to contrast material).

Thus, many oncology patients with an incidentally detected adrenal mass will still undergo percutaneous biopsy. The accuracy of percutaneous biopsy can approach 100% when performed by skilled operators and experienced cytopathologists, but in practice the accuracy is only 80%–90% due to sampling error or inadequate specimens (16). Negative results necessitate performance of repeated aspiration to rule out malignancy.

Recently, quantitative evaluation of adrenal masses on delayed enhanced CT scans has been shown to be highly accurate in distinguishing adrenal adenomas from nonadenomas. Recent investigations demonstrated that adrenal adenomas have statistically significantly lower attenuation than nonadenomas on delayed enhanced CT scans; this finding presumably indicates greater washout of contrast material in adenomas than in nonadenomas (1–3). In our preliminary experience, use of delayed enhanced CT substantially reduced the need for adrenal biopsy and, in particular, obviated repetition of unenhanced CT on a subsequent day.

The attenuation values of adrenal adenomas on unenhanced scans, however, are often widely variable and less reliable than those measured 10 or 30 minutes after the start of contrast material injection. In our study population, for example, the sensitivity and specificity for diagnosis of adenoma on unenhanced scans were 55% and 100% at a threshold of 11 HU and 100% and 54% at a thresh-

old of 35 HU. On the 30-minute scan, however, the sensitivity and specificity were 97% and 100% at a threshold of 37 HU and 100% and 97% at a threshold of 42 HU.

However, absolute attenuation values must be used carefully, in part because of the possibility of erroneous misinterpretation in cases of borderline enhancement. In three recent studies (1-3), different types of CT scanners, different types (ionic and nonionic) and amounts of contrast material, and different delivery rates were used. In addition, use of internal standards (ie, aortic or splenic enhancement) for characterization of adrenal masses is not effective.

To circumvent potential sources of error in use of absolute attenuation values from delayed enhanced scans, we also assessed both the absolute and relative change in enhancement at several arbitrarily chosen times. The absolute percentage loss of enhancement at 3, 10, and 30 minutes was significantly greater for the adenomas ($30\% \pm 12$, $62\% \pm 17$, and $74\% \pm 16$, respectively) than for the nonadenomas ($2\% \pm 12$, $31\% \pm 16$, and $42\% \pm 23$, respectively) ($P < .001$). Similarly, the percentage loss of enhancement relative to the amount of initial enhancement was significantly greater for the adenomas than for the nonadenomas ($P < .001$) on all three delayed enhanced scans. The discrepancy between the relative and absolute percentage change in enhancement can be attributed to the different attenuation values of the masses on the unenhanced scan. Because most CT examinations are performed after intravenous administration of contrast material, knowledge of the relative degree of contrast enhancement might be of much greater practical use than knowledge of absolute attenuation values. Moreover, calculations of the washout of contrast material can be done on a calculator, and data can be obtained easily and quickly (within 1 minute) without use of a sophisticated program.

Our findings are in concordance with those obtained from contrast-enhanced MR imaging studies that demonstrated that imaging the adrenal gland within 1 hour after initial imaging can aid in the characterization of adrenal masses (17-19). These MR imaging studies demonstrated a statistically significant greater washout of gadolinium from adenomas than from nonadenomas. The finding in our study that other benign adrenal masses (ie, ganglioneuroma, benign variant of pheochromocytoma) did not show the washout pattern of adrenal adenomas

is of particular interest. Therefore, our results suggest that the rapid and greater washout of contrast material is a unique characteristic of adrenal adenomas. There are no pathophysiologic data on this subject in the literature, to our knowledge; possible histopathologic explanations of the different angioarchitecture of adenomas and nonadenomas might be relative preservation of cellular membrane integrity and less expansion of the effective extracellular space due to tumor infiltration in adrenal adenomas.

Contrary to the findings of Krestin et al (17,18), we found that adenomas also demonstrate greater wash-in of contrast material than do nonadenomas. In a study of 38 adrenal masses with gadolinium-enhanced fast gradient-echo MR imaging, Krestin et al (17) found that adenomas had moderate initial enhancement whereas malignant lesions had more pronounced early enhancement. However, the difference between the results of Krestin et al (17) and our results is not surprising: Our finding of an adenoma with an attenuation of 4 HU on the unenhanced scan that enhanced to 32 HU on the 60-second scan reflects a relative increase of 700% above baseline. In comparison, the relative enhancement of a nonadenoma with the same absolute enhancement of 28 HU (ie, from 34 HU to 62 HU) represents an increase of only 82% above baseline. The findings obtained during the early phase of contrast enhancement, however, are unreliable for distinguishing adenomas from nonadenomas because of the substantial overlap in attenuation.

On the basis of our experience and studies, we use the following algorithm to assess an adrenal mass detected on unenhanced or enhanced CT scans (obtained with bolus injection of the type and amount of contrast material described herein and the imaging protocol described herein): If the attenuation is below 11 HU on the unenhanced scan, a presumptive diagnosis of a benign lesion (usually an adenoma) is made and no further evaluation is advised. If the attenuation is above 11 HU, an enhanced scan (to assess other parenchymal abdominal organs) and a 10-minute delayed enhanced scan are obtained. If the attenuation is below 45 HU on this delayed enhanced scan, generation of a time-attenuation curve is not necessary and a diagnosis of adenoma is made. If the attenuation is above 45 HU, the absolute washout of contrast material is below 40%, or the relative washout of contrast material is below 50%, a second delayed

enhanced scan is obtained 30 minutes after the start of contrast material injection. If the attenuation is below 35 HU on the 30-minute scan, generation of a time-attenuation curve is not necessary and a diagnosis of adenoma is made. If the attenuation is above 35 HU, a time-attenuation curve is generated. If the absolute washout of contrast material is below 50% or the relative washout of contrast material is below 60%, we recommend percutaneous biopsy (in oncology patients if the adrenal gland is the only site of possible metastatic disease) or surgery (in nononcology patients with an adrenal mass more than 4 cm in diameter). In a nononcology patient with an adrenal mass less than 4 cm in diameter, we recommend a follow-up study in 6 months. If a patient inadvertently undergoes a contrast-enhanced study first, we use the relative washout of contrast material to make the diagnosis. The patient is not brought back to the CT department on a subsequent day for an unenhanced CT scan.

In conclusion, delayed enhanced CT scans obtained 10 minutes and 30 minutes after the start of contrast material injection have higher sensitivity and specificity for differentiation of adenomas and nonadenomas than do unenhanced CT scans. With the techniques described herein, an adrenal mass can be diagnosed as an adenoma with a specificity of 100% and sensitivity of 97%. The important role of absolute attenuation values at delayed enhanced CT in discriminating adenomas from nonadenomas is corroborated by the differential washout of contrast material in adenomas and nonadenomas. Adrenal adenomas exhibit greater washout of contrast material than do adrenal nonadenomas. Therefore, the percentage change in washout of contrast material is a useful adjunct to absolute attenuation values in differentiation of adrenal adenomas and nonadenomas. Most diagnostic issues in the work-up of adrenal masses are accordingly clarified. Use of delayed enhanced CT may obviate an additional unenhanced CT examination, as well as the expense and invasiveness of percutaneous biopsy in some cases.

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