Radiology

Adrenocortical Carcinomas and Adrenal Pheochromocytomas: Mass and Enhancement Loss Evaluation at Delayed Contrast-enhanced CT[1]

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Abbreviation:
ROI = region of interest

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PURPOSE: To retrospectively measure the adrenal gland attenuation and the percentage loss of adrenal gland enhancement at delayed contrast medium–enhanced computed tomography (CT) in patients with adrenocortical carcinomas and pheochromocytomas and to compare these data with those in patients with adenomas and metastases.

MATERIALS AND METHODS: The study protocol was approved by the ethics committee, which waived informed consent. Eleven patients with proved adrenocortical carcinoma, 17 with proved pheochromocytoma, 23 with adrenal adenoma, and 16 with metastasis to the adrenal gland underwent helical CT. Nonenhanced CT was followed by contrast-enhanced CT 1 minute and 10 minutes later. Attenuation and enhancement loss values were calculated.

RESULTS: The mean attenuation of adenomas (8 HU ± 18 [standard deviation]) was significantly lower than those of adrenocortical carcinomas (39 HU ± 14), pheochromocytomas (44 HU ± 11), and metastases (34 HU ± 11) on nonenhanced CT scans ($P < .001$). Although the mean attenuation values for nonadenomas (ie, adrenocortical carcinomas, pheochromocytomas, and metastases) were significantly higher than the value for adenomas on the 1-minute contrast-enhanced CT scans ($P < .001$), there was more overlap in attenuation between adenomas and nonadenomas on contrast-enhanced scans than on nonenhanced scans. On the 10-minute delayed contrast-enhanced scans, the mean attenuation of adenomas (32 HU ± 17) was significantly lower than the mean attenuations of carcinomas (72 HU ± 15), pheochromocytomas (83 HU ± 14), and metastases (66 HU ± 13) ($P < .001$). At optimal threshold values of 50% for absolute percentage of enhancement loss and 40% for relative percentage of enhancement loss at 10 minutes, both the sensitivity and the specificity for the diagnosis of adenoma were 100% when adenomas were compared with carcinomas, pheochromocytomas, and metastases.

CONCLUSION: The enhancement loss in adrenocortical carcinomas and pheochromocytomas is similar to that in adrenal metastases but significantly less than that in adrenal adenomas. The percentage change in contrast material washout is a useful adjunct to absolute CT attenuation values in differentiating adrenal adenomas from adrenocortical carcinomas and pheochromocytomas.

Extensive research has been focused on strategies to differentiate benign from malignant adrenal lesions by using noninvasive imaging methods (1–23). Several studies have addressed the value of delayed contrast medium–enhanced computed tomography (CT) in distinguishing adrenal adenomas from adrenal nonadenomas (9–14). The results of several studies have demonstrated that adrenal adenomas have significantly lower attenuation

and significantly greater loss of enhancement than nonadenomas on delayed contrast-enhanced CT scans (9–14). However, detailed information on attenuation and percentage change in contrast material washout in nonadenomas has been based primarily on data regarding metastases to the adrenal glands (hereafter referred to as adrenal metastases).

To our knowledge, very few data on either the attenuation or the percentage change in contrast material washout in adrenocortical carcinomas and pheochromocytomas are available. Therefore, the purpose of this study was to measure retrospectively the adrenal attenuation and the percentage loss of adrenal gland enhancement (ie, percentage change in washout) in patients with adrenocortical carcinomas and pheochromocytomas and to compare these data with those in patients with adenomas and metastases.

MATERIALS AND METHODS

Study Population

The study protocol was approved by and conducted in accordance with the recommendations of the ethics committee at Karl Franzens University. The ethics committee waived informed consent. Between 1996 and 2002, 211 patients with 248 adrenal masses were consecutively examined with helical CT and considered for entry into our study. There were a total of 126 male and 85 female patients ranging in age from 12 to 84 years (mean age, 64 years). The presence of 173 masses in 136 patients was proved at biopsy (40 masses), surgery (29 masses), or imaging (repeated CT) and clinical follow-up (104 masses). The diagnosis of adenoma was proved on the basis of a stable lesion size or an attenuation value of less than 10 HU at nonenhanced follow-up CT for at least 12 months (mean, 13 months; range, 12–26 months).

Excluded from the study were 70 patients in whom neither follow-up CT nor cytologic or histologic analysis was possible, two patients with adrenal cysts, and one patient each with adrenal hematoma, neuroblastoma, and ganglioneuroma. Also excluded were 69 patients who underwent imaging protocols other than those described herein (eg, contrast-enhanced CT 30 and 90 seconds and delayed contrast-enhanced CT 3 and 30 minutes after the start of the contrast material administration).

The remaining 67 patients (31 men and 36 women aged 22–83 years; mean age, 60 years) fulfilled the criteria for inclusion. Eleven patients (seven men and four women aged 22–58 years; mean age, 42 years) had adrenocortical carcinomas, and 17 (five men and 12 women aged 38–64 years; mean age, 49 years) had pheochromocytomas. Ten of the 17 patients with pheochromocytoma were examined because of abnormal plasma catecholamine levels and abnormal 24-hour urine vanillylmandelic acid and metanephrine levels. In the remaining seven patients, who had no endocrine dysfunction, the masses were found incidentally during CT performed for other reasons. In four of the 11 patients with adrenocortical carcinoma, metastatic spread to the liver, lungs, and bone was evident. Thirty-nine patients—23 (nine men and 14 women aged 28–74 years; mean age, 55 years) with 24 adrenal adenomas and 16 (10 men and six women aged 36–83 years; mean age, 64 years) with 21 adrenal metastases—provided reference data (11). The primary cancers from which the adrenal metastases stemmed were small lung cell carcinoma in two patients, non–small lung cell carcinoma in 10 patients, breast carcinoma in one patient, renal cell carcinoma in two patients, and colorectal carcinoma in one patient.

A total of 73 masses—11 adrenocortical carcinomas, 17 pheochromocytomas, 24 adenomas, and 21 metastases—in 67 patients were investigated with an identical imaging protocol. Diagnoses for the final study group of 73 masses were established when histologic proof was obtained at surgery or percutaneous biopsy ($n = 28$), when stability or change in the size of the mass was observed at a subsequent CT examination after at least 6 months ($n = 28$), or when an attenuation value of 10 HU or less was measured on nonenhanced CT scans ($n = 17$).

Imaging Protocol

Imaging examinations were performed with a Somatom Plus 4 Volume Zoom (Siemens, Erlangen, Germany) or LightSpeed QX/i (GE Medical Systems, Milwaukee, Wis) CT scanner. All patients gave written informed consent to undergo CT. The protocol for the single-section helical CT examinations performed in 51 patients included volumetric data acquisition through the upper part of the abdomen with 5-mm collimation, a 7.5 mm/sec table feed, and 4-mm increments before and after the intravenous bolus injection of contrast material (iopromide 300, Ultravist, Schering Pharmaceuticals, Berlin, Germany; or iohexol 300, Omnipaque, Nycomed-Amersham, London, England). The scanning time for one revolution of the x-ray tube was 0.75 second.

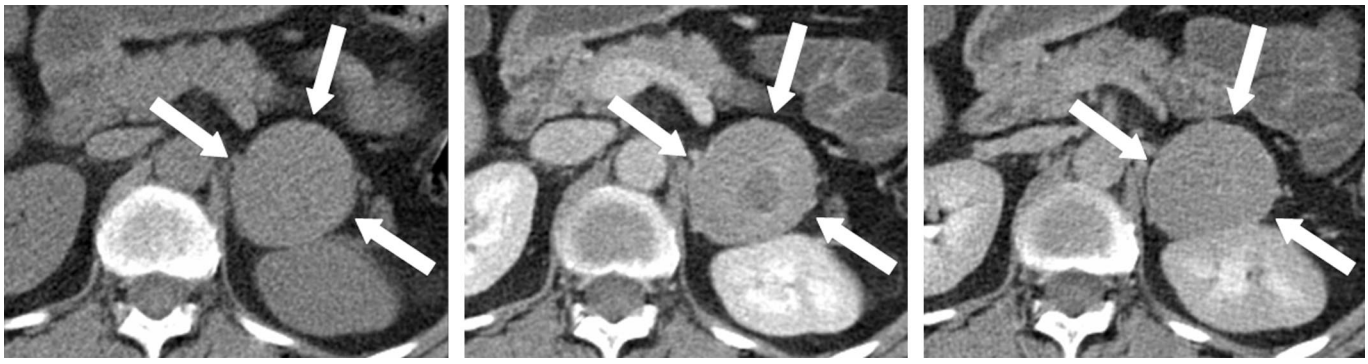
For the multisection helical CT examinations, the parameters varied because of the different detector array systems used. With use of the Volume Zoom scanner, which was used to examine nine patients, the protocol consisted of 2.5-mm collimated sections acquired with four detectors (4 × 2.5-mm collimation), a 12.5-mm section thickness with a pitch of 1.25, and 3.0-mm reconstruction intervals. With use of the LightSpeed QX/i scanner, which was used to examine seven patients, the parameters were 120 kVp, 200–240 mA, 4 × 2.5-mm collimation, a 0.8-second rotation time, a pitch of 3 (in thin-section mode), and 3.0-mm reconstruction intervals. To optimize the reproducibility of the starting measurements, each scan was obtained while the patient was in full inspiration.

First, a nonenhanced 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 or iohexol 300) was administered at 2.5 mL/sec by using a power injector (MCT Plus; Medrad, Pittsburgh, Pa). In all patients, the second and third scans were obtained, respectively, 1 minute after and 10 minutes after the start of the contrast material injection. The imaging protocol was preprogrammed so that these scans were obtained by using the same parameters that were used to obtain the first nonenhanced scan. The scans (Figs 1, 2) were obtained with standard soft-tissue settings (window width, 400 HU; window level, 40 HU).

Image and Data Analyses

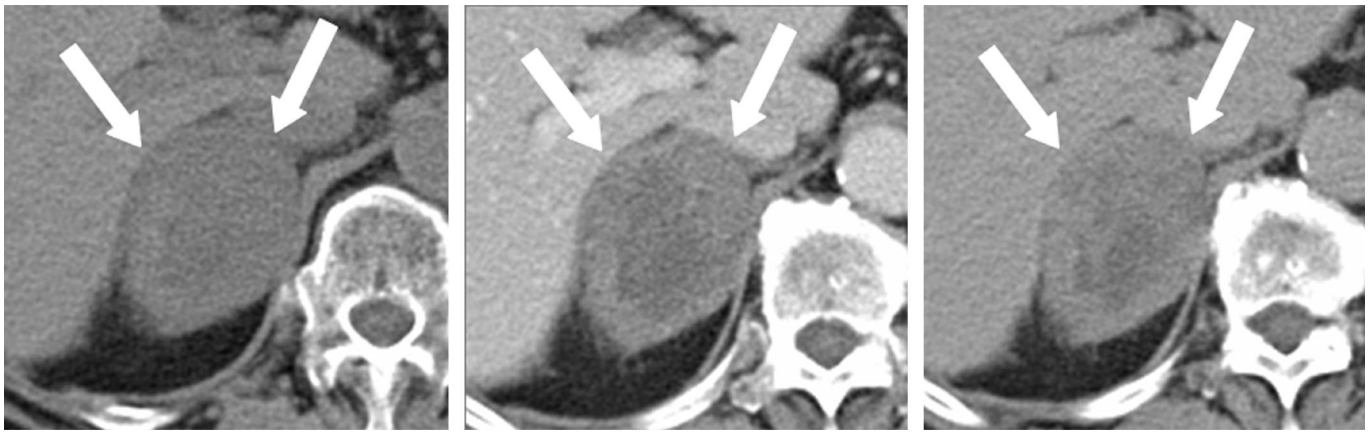
CT scans were interpreted and attenuation values were measured retrospectively by using a commercially available CT–magnetic resonance (MR) imaging workstation (Sienet Magic View 1100; Siemens). These tasks were performed by two radiologists who were experienced in performing CT of the adrenal glands (D.H.S. with 11 years experience; P.R. with 7 years experience). These radiologists had no knowledge of the clinical, histologic, or follow-up findings, and they worked independently without consultation with one another.

For all adrenal masses detected at CT (regardless of the type of scan [nonen-



a. b. c.

Figure 1. Transverse CT scans obtained in 49-year-old woman with adrenal pheochromocytoma. **(a)** Nonenhanced scan obtained at level of middle portion of left adrenal gland shows well-defined mass (arrows) with isoattenuation relative to liver parenchyma. **(b, c)** Contrast-enhanced scans obtained at same level as in **a**. The tumor (arrows) has heterogeneous enhancement on **(b)** the 1-minute scan and homogeneous enhancement on **(c)** the 10-minute scan. Tumor attenuation is 56 HU in **a**, 107 HU in **b**, and 94 HU in **c**. Thus, the absolute percentage of enhancement loss in this tumor is 25%, and the relative percentage of enhancement loss is 12%.



a. b. c.

Figure 2. Transverse CT scans obtained in 63-year-old woman with adrenocortical carcinoma. **(a)** Nonenhanced scan obtained at level of middle portion of right adrenal gland shows well-defined mass (arrows) with isoattenuation relative to kidney parenchyma. **(b, c)** Contrast-enhanced scans obtained at same level as in **a**. The tumor (arrows) has heterogeneous enhancement on both **(b)** the 1-minute scan and **(c)** the 10-minute scan. Tumor attenuation is 41 HU in **a**, 88 HU in **b**, and 75 HU in **c**. Thus, the absolute percentage of enhancement loss in this tumor is 28%, and the relative percentage of enhancement loss is 15%.

hanced, contrast-enhanced, or delayed contrast-enhanced] obtained), the attenuation was measured by using circular region-of-interest (ROI) cursors placed over the area of disease. The ROI circle was made as large as possible, and lesion edges were avoided to preclude partial volume effects. Cystic, necrotic, and hemorrhagic components, as well as calcifications of the adrenal masses, were excluded if they were present. Necrosis was defined as a region (within the mass) with an attenuation value similar to that of water (<20 HU) at 1-minute contrast-enhanced CT. Calcification was defined as a region with an attenuation value greater than 120 HU at nonenhanced CT.

Attenuation values were recorded and averaged for final data analysis. To determine the sizes of the masses, a distance cursor was used to measure the diameter in the transverse plane. The section that encompassed the largest square area of the adrenal mass was used for analysis. The measurements obtained by the two radiologists were averaged.

For all masses, the absolute and relative percentage losses of enhancement (ie, washout) were determined. The absolute percentage loss of enhancement was calculated as follows: $[1 - (A_D - A_N)/(A_E - A_N)] \cdot 100$, where A_D is the attenuation at delayed (10-minute) contrast-enhanced CT; A_E; the attenuation at contrast-enhanced (1-minute) CT; and A_N; the attenuation at nonenhanced CT. The percentage loss of enhancement relative to the amount of initial enhancement (ie, relative loss of enhancement) was calculated as follows: $[(A_E - A_D)/A_E] \cdot 100$.

Statistical Analyses

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 ROI measurements of attenuation between the different helical CT scans (nonenhanced, delayed contrast-enhanced, and contrast-enhanced scans). Repeated measures

TABLE 1
Mean Diameters of Adrenal Masses

Adrenal Mass	Diameter (cm)
Adenoma (n = 24)	2.2 ± 0.8 (1.3–3.5)
Adrenocortical carcinoma (n = 11)	9.8 ± 2.5 (4.5–16.2)
Pheochromocytoma (n = 17)	5.1 ± 1.9 (4.7–10.8)
Metastasis (n = 21)	4.5 ± 2.2 (1.6–10.4)

Note.—Diameters are given as means ± standard deviations, with ranges in parentheses. The mean diameter of adrenocortical carcinomas was significantly larger than the mean diameters of adenomas, pheochromocytomas, and metastases ($P < .001$).

TABLE 2
Mean Attenuation of Adrenal Masses at Nonenhanced, Contrast-enhanced, and Delayed Contrast-enhanced CT

Adrenal mass	Nonenhanced CT	Contrast-enhanced CT (at 1 min)	Delayed Contrast-enhanced CT (at 10 min)
Adenoma (n = 24)	8 ± 18 (−21 to 27)	60 ± 27 (30–84)	32 ± 17 (15–52)
Adrenocortical carcinoma (n = 11)	39 ± 14 (23–52)	83 ± 29 (51–108)	72 ± 15 (40–93)
Pheochromocytoma (n = 17)	44 ± 11 (28–60)	94 ± 20 (72–131)	83 ± 14 (60–123)
Metastasis (n = 21)	34 ± 11 (17–55)	81 ± 30 (49–110)	66 ± 13 (50–84)

Note.—Data are mean attenuation values (in Hounsfield units) ± standard deviations, with ranges in parentheses. Adenomas were significantly lower in attenuation than adrenocortical carcinomas, pheochromocytomas, and metastases at nonenhanced, contrast-enhanced, and delayed contrast-enhanced CT ($P < .001$). There were no significant differences in attenuation between adrenocortical carcinomas, pheochromocytomas, and metastases.

analysis of variance also was used. With this method, the mean values for more than one tumor group can be compared when measurements are obtained at more than one point in time. The method also allows one to control differences among patients, differences among lesions within individual patients, and associations between patient characteristics and helical CT sequences. The mean size and mean attenuation for the tumor groups at nonenhanced and contrast-enhanced CT were calculated and analyzed with analysis of variance. $P < .01$ was considered to indicate statistical significance. For the post hoc tests, Bonferroni correction was applied to the results to correct for the multiple comparisons made.

RESULTS

Mass Size

The mean diameters and the ranges of diameters of the different adrenal masses are listed in Table 1. Adrenocortical carcinomas were significantly larger than adrenal adenomas, pheochromocytomas, and metastases ($P < .001$). Of the 11 adrenocortical carcinomas, only three (27%) were smaller than 6.0 cm in diameter. The mean diameter of the pheochromocytomas (5.1 cm ± 1.9 [standard deviation]) was significantly greater than that of the adenomas (2.2 cm ± 0.8, $P < .001$) but similar to that of the metastases (4.5 cm ± 2.2). At a threshold diameter of 2.5 cm, the sensitivity and specificity for the diagnosis of adrenal adenoma were 75% (18 of 24 masses) and 88% (21 of 24 masses), respectively.

Nonenhanced CT

At nonenhanced CT, the 11 adrenocortical carcinomas had a mean attenuation of 39 HU ± 14, as compared with a mean attenuation of 44 HU ± 11 for the 17 pheochromocytomas. The 24 adenomas had a mean attenuation of 8 HU ± 18, as compared with a mean attenuation of 34 HU ± 11 for the 21 adrenal metastases (Table 2). The mean attenuation of the adenomas was significantly lower than the mean attenuations of the adrenocortical carcinomas, pheochromocytomas, and metastases ($P < .001$) (Fig 3). There were no significant differences in attenuation between the adrenocortical carcinomas, pheochromocytomas, and metastases ($P = .24$). None of the 17 pheochromocytomas, as compared with one (9%) of the 11 adrenocortical carcinomas and two (10%) of the 21 metastases, had an attenuation value lower than 28 HU. On the other hand, none of the 24 adenomas had an attenuation value greater than 27 HU at nonenhanced CT. The sensitivity and specificity for the diagnosis of adenoma at a threshold attenuation value of 11 HU were 79% (19 of 24 masses) and 100% (24 of 24 masses), respectively. The positive predictive value was 100%, and the negative predictive value was 65%.

Contrast-enhanced CT

One minute after the start of the contrast material injection, the mean attenuation was 83 HU ± 29 for the adrenocortical carcinomas and 94 HU ± 20 for the pheochromocytomas ($P = .29$). The mean attenuation was 60 HU ± 27 for the adenomas and 81 HU ± 30 for the metastases (Table 2). There were no significant differences in attenuation between the adrenocortical carcinomas, pheochromocytomas, and metastases ($P = .31$) (Fig 3). Although the mean attenuation values for all of the nonadenomas (ie, adrenocortical carcinomas, pheochromocytomas, and metastases) were significantly greater than that for the adenomas at 1 minute ($P < .001$), there was much more overlap in attenuation between the adenomas and nonadenomas on the contrast-enhanced CT scans than on the nonenhanced images.

Contrast Material Washout at Delayed Contrast-enhanced CT

Ten minutes after the start of the contrast material injection, the adrenocortical carcinomas had a mean attenuation of 72 HU ± 15 (range, 40–93 HU), as compared with a mean attenuation of 83 HU ± 14 (range, 60–123 HU) for the pheochromocytomas. The adenomas had a mean attenuation of 32 HU ± 17 (range, 15–52 HU), as compared with a mean attenuation of 66 HU ± 13 (range, 50–84 HU) for the adrenal metastases (Table 2, Fig 4). The mean attenuation of the adenomas was significantly lower than those of the adrenocortical carcinomas, pheochromocytomas, and metastases ($P < .001$). There were no significant differences in attenuation between the adrenocortical carcinomas, pheochromocytomas, and metastases ($P = .25$) at delayed contrast-enhanced CT. At a threshold attenuation value of 52 HU, the sensitivity and specificity for the diagnosis of adenoma were 92% (22 of 24 masses) and 96% (23 of 24 masses), respectively. The positive predictive value was 96%, and the negative predictive value was 91%.

On the 10-minute scans, the mean absolute percentage loss of enhancement was 34% ± 9 for the adrenocortical car-

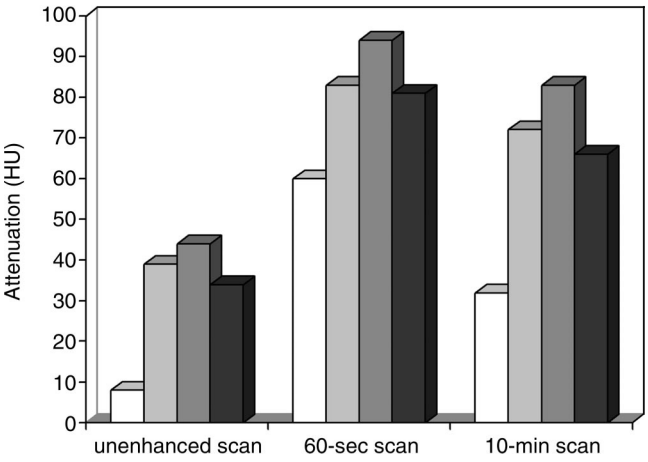


Figure 3. Graph shows mean attenuation values for adrenal adenomas (white bars), adrenocortical carcinomas (light gray bars), pheochromocytomas (dark gray bars), and metastases (black bars) on nonenhanced, contrast-enhanced (1-minute), and delayed contrast-enhanced (10-minute) CT scans. Note the substantial difference in attenuation values between the adenomas and the nonadenomas on all scans.

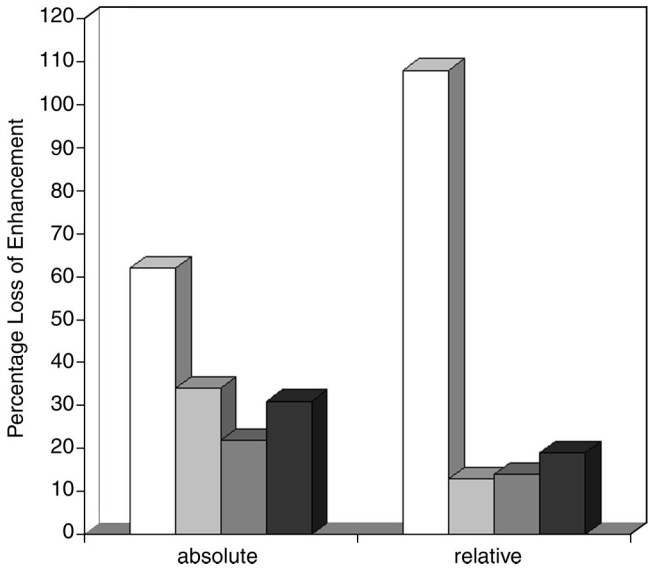


Figure 4. Graph shows mean absolute and relative percentage losses of enhancement for adrenal adenomas (white bars), adrenocortical carcinomas (light gray bars), pheochromocytomas (dark gray bars), and metastases (black bars). Adenomas had significantly greater enhancement loss than nonadenomas ($P < .001$).

cinomas and 22% ± 12 for the pheochromocytomas, as compared with 62% ± 17 for the adenomas ($P < .001$) and 31% ± 16 for the metastases (Table 3). The percentage loss of enhancement relative to the amount of initial enhancement was 13% ± 12 for the adrenocortical carcinomas and 14% ± 7 for the pheochromocytomas, as compared with 108% ± 87 for the adenomas ($P < .001$) and 19% ± 11 for the metastases ($P = .35$). Both the absolute loss of enhancement and the relative loss of enhancement were significantly greater for adenomas than for adrenocortical carcinomas, pheochromocytomas, and metastases ($P < .001$). At threshold values of 50% for absolute enhancement loss and 40% for relative enhancement loss, both the sensitivity and the specificity for the diagnosis of adenoma were 100% (24 of 24 adenomas), as compared with the sensitivity and specificity for the diagnosis of the 11 adrenocortical carcinomas and the 17 pheochromocytomas ($P < .001$).

There were no calcifications in the pheochromocytomas or adrenocortical carcinomas. Unlike most of the adenomas, seven of the 11 adrenocortical carcinomas, three of the 21 adrenal metastases, and 10 of the 17 adrenal pheochromocytomas had regions of necrosis. As mentioned earlier (see Materials and Methods), care was taken to exclude these regions from the attenuation measurements. In any case, there were no obvious differences in attenuation characteristics among the adrenal metastases.

DISCUSSION

Adrenal masses are common: They are found at an estimated 9% of postmortem examinations (1,20). Even in oncologic settings, approximately 70% of adrenal masses are benign (24–26). However, the precise characterization of adrenal masses is important for therapeutic guidance. Adrenocortical carcinomas and pheochromocytomas of the adrenal glands are rare, and both occur with equal frequency in women and men (15,16). Adrenocortical carcinomas account for only 0.02% of malignant tumors, and the true incidence of pheochromocytomas is unknown (15,16). More than 50% of adrenocortical carcinomas are endocrine related and caused by extensive cortisol production; Cushing syndrome is the most frequently seen condition at clinical presentation (15,16). Occasionally, patients present with symptoms of virilization or Conn syndrome.

The use of CT and MR imaging has resulted in more frequent and incidental detections of adrenal masses. More recent research has been focused on different approaches to characterizing adrenal masses on cross-sectional images, including assessing lesion size, describing morphologic criteria, measuring attenuation or signal intensity, calculating the percentage loss of enhancement, and determining the lipid content (1–23). However, to our knowledge, there are no literature reports of comparisons between the attenuation and percentage loss of enhancement values for adrenocortical carcinomas and pheochromocytomas and those for the more frequently encountered adrenal adenomas and adrenal metastases.

Two main CT features used to distinguish adenomas from nonadenomas have been identified: the intracellular lipid content and the enhancement loss in adrenal masses. Adenomas often contain abundant intracytoplasmatic fat and thus have low attenuation on nonenhanced CT scans and signal loss on opposed phase MR images. Conversely, nonadenomas contain little or no intracytoplasmatic fat and thus have higher attenuation at nonenhanced CT and no signal loss at opposed phase MR imaging (4,5,8,18,23). Korobkin et al (23) observed that the intratumoral lipid content of resected adrenal adenomas correlated with lower attenuation at nonenhanced CT. Although an attenuation value of less than 10 HU at nonenhanced CT is considered sufficient for characterizing an adrenal mass as an adenoma, it has been estimated that up to 30% of adenomas do not contain large amounts of lipid and may remain indeterminate and indistinguishable from nonadenomas on nonenhanced CT scans or chemical shift MR images.

Quantitative evaluation of adrenal mass enhancement on delayed contrast-

enhanced CT scans has been shown to be highly accurate for differentiating adenomas from nonadenomas (9–14). Adenomas exhibit rapid enhancement and contrast medium washout; nonadenomas also enhance vigorously but have prolonged contrast material washout. Korobkin et al (9) reported that adrenal adenomas have a much earlier and more rapid contrast material washout than do nonadenomas. In their study, the mean percentage loss of enhancement for adrenal adenomas was 51% at 5 minutes and 70% at 15 minutes after the start of the contrast material administration, as compared with 8% and 20%, respectively, for nonadenomas. Caoili et al (13,14) reported a sensitivity of 98% and a specificity of 92% for the diagnosis of adenoma with use of 15-minute delayed contrast-enhanced CT scans obtained in 166 patients with adrenal masses.

Although a few adrenocortical carcinomas and pheochromocytomas have been described in previously published related series, to our knowledge, little detailed information on the behavior of these masses as compared with the behavior of adenomas has been provided. For instance, Szolar and Kammerhuber (11) included six pheochromocytomas and six adrenocortical carcinomas in their nonadenoma group. All of the pheochromocytomas had delayed enhancement and percentage of enhancement loss values in the range of nonadenoma values, but data on the individual carcinomas were not reported.

The results of the present study indicate that at nonenhanced CT, both adrenocortical carcinomas and pheochromocytomas have mean attenuation values similar to those of metastases but significantly higher than those of adenomas. On the 1-minute contrast-enhanced CT scans, however, there was considerable overlap in attenuation between the adenomas and all three types of nonadenomas, and, hence, it was not possible to identify a threshold attenuation value that could be used to reliably differentiate the different masses. On the 10-minute delayed contrast-enhanced scans, both the mean attenuation and the mean percentage loss of enhancement for adenomas differed significantly from those observed for pheochromocytomas, adrenocortical carcinomas, and metastases.

In a study of 52 adenomas and 24 nonadenomas (mainly metastases), Korobkin et al (9) reported that 10 minutes after contrast material administration, the optimal thresholds for absolute and relative enhancement loss were 50% and 40%, respectively. Applying these same threshold values to the data in our series yielded a sensitivity of 100% and a specificity of 100% for the diagnosis of adenoma when we compared the 24 adenomas with the 11 cortical carcinomas and the 17 pheochromocytomas. Caoili et al (14) reported that one patient with adrenocortical carcinoma and one patient with pheochromocytoma had a percentage of enhancement loss greater than the optimal threshold value of 60% with a 15-minute enhancement delay, so the high accuracy observed in our series certainly may not apply to all of these uncommon neoplasms. Our findings do suggest, however, that enhancement loss calculations at 10-minute delayed CT can be helpful in differentiating adrenal adenomas from adrenal carcinomas, pheochromocytomas, and metastases.

TABLE 3
Absolute and Relative Losses of Enhancement of Adrenal Masses

Adrenal Mass	Absolute Loss of Enhancement (%)	Relative Loss of Enhancement (%)
Adenoma ($n = 24$)	62 ± 17	108 ± 87
Adrenocortical carcinoma ($n = 11$)	34 ± 9	13 ± 12
Pheochromocytoma ($n = 17$)	22 ± 12	14 ± 7
Metastasis ($n = 21$)	31 ± 16	19 ± 11

Note.—Values are given as means ± standard deviations. Absolute and relative losses of enhancement were significantly greater for adenomas than for adrenocortical carcinomas, pheochromocytomas, and metastases ($P < .001$). There were no significant differences in contrast material washout between adrenocortical carcinomas, pheochromocytomas, and metastases.

In patients with a solitary adrenal mass and no evidence of either a hyperfunctioning endocrine disorder or an extraadrenal primary neoplasm, the differential diagnosis usually includes adenoma and adrenocortical carcinoma. Most solid adrenal masses larger than 6 cm in diameter are resected because a substantial proportion of them are found to be malignant and most adrenocortical carcinomas are larger than 6 cm when they are first detected clinically. Although only a small fraction of adrenocortical carcinomas are smaller than 6 cm and only a small fraction of adenomas are larger than 4 cm at presentation, it is the group of adrenal masses that have diameters between 4 and 6 cm that is so challenging to characterize at imaging. In our study, three of 11 adrenocortical carcinomas were smaller than 6 cm. The nonenhanced CT attenuation, delayed contrast-enhanced CT attenuation, and percentage of delayed enhancement loss values for these three masses were all in the range of nonadenoma values; thus, these lesions would not have been incorrectly categorized as adenomas.

The present study may have had several limitations. First, the diagnosis of adrenal adenomas was not histologically verified in most cases. However, the findings of multiple studies (6–14) have confirmed that the presence of adrenal adenoma can be proved on the basis of an attenuation value of less than 10 HU at nonenhanced CT and a stable mass size during a follow-up period of at least 6 months. Second, although our series included a substantial number of adrenal masses, the numbers of adrenocortical carcinomas and pheochromocytomas still may have been too small for an adequate statistical work-up. Third, we did not standardize the rate of administration or the injected volume of contrast material with consideration of the cardiac output and weight of each patient. Had we done so, we might have obtained different results, but these approaches are not used in clinical practice. Therefore, we believe that the results we obtained are more likely to reflect actual daily clinical routine.

In summary, adrenocortical carcinomas and pheochromocytomas have enhancement loss that is similar to that of adrenal metastases and significantly less than that of adrenal adenomas. The percentage change in contrast material washout is a useful adjunct to absolute CT attenuation values in differentiating adrenal adenomas from adrenocortical carcinomas and pheochromocytomas.

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