Adrenal Adenoma and Pheochromocytoma: Comparison of Multidetector CT Venous Enhancement Levels and Washout Characteristics

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Purpose: The aim of the study was to compare multidetector CT venous enhancement level and washout characteristics of adrenal adenoma and pheochromocytoma, with the goal of defining a venous enhancement level predictive of pheochromocytoma.

Methods: Retrospective review of medical records between 2002 and 2012 was performed to identify adrenal masses measuring less than 4 cm. Inclusion criteria for adrenal adenomas was venous phase contrast-enhanced computed tomography (CT), confirmatory adrenal CT (precontrast ± washout), 1 to 2 years stability, and absence of clinical indicators of pheochromocytoma. All pathologically proven pheochromocytomas with venous phase CT imaging were evaluated. Nodule size and attenuation (venous ± precontrast, delayed) were recorded. Student *t* test analysis compared venous enhancement levels.

Results: One hundred eighty-three subjects with 200 adenomas were compared with 22 subjects with 26 pheochromocytomas. The mean (SD) venous enhancement level for all adenomas (58 [26] Hounsfield units [HU]) and lipid-poor adenomas (76 [25]) was lower than that of pheochromocytomas (111 [38] HU, $P < 0.01$). No adenomas enhanced greater than 130 HU, compared with 38% (10/26) of the pheochromocytomas. A threshold of 130 HU to identify pheochromocytoma was 38% sensitive and 100% specific for pheochromocytoma. Of the 17 pheochromocytomas with washout imaging, rapid washout was identified in all (10/10, 100%) that enhanced greater than 130 HU on the venous phase, compared with 43% (3/7) that enhanced less than 130 HU.

Conclusions: An indeterminate adrenal lesion that enhances greater than 130 HU on multidetector CT cannot be assumed to be an adenoma. Hypervascular pheochromocytoma (>130 HU) mimics adenoma washout pattern; absolute venous phase enhancement level must be considered.

Key Words: adenoma, pheochromocytoma, incidental adrenal nodule, computed tomography

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Management of incidental findings on body computed tomography (CT) scans has become an active area of research, with evolving consensus statements from the American College of Radiology (ACR) providing valuable guidance.[1–5] Among the most common incidental findings are small adrenal nodules. Large series have shown that in noncancer patients, adrenal adenoma (75%–80%), myelolipoma (6%), or pheochromocytoma (0.3%–5.1%) account for most incidental adrenal nodules.[1,6–8] In fact, a recent investigation of the 57 pheochromocytomas diagnosed for a 7-year period in 1 institution reported that 70% (40/57) were unsuspected and that 40% (16/40) of these were classified as truly incidental findings with no correlative clinical symptomatology.[9] Most abdominal CT examinations are performed with intravenous (IV) contrast in the venous phase, such that the definitive diagnosis of a lipid-rich adenoma, which requires documentation of noncontrast density less than 10 Hounsfield units (HU),[10] cannot be made. Accordingly, management recommendations for indeterminate nodules include a 1-year follow-up for benign-appearing lesions that measure less than 4 cm or additional work-up if the lesion contains any suspicious features (heterogeneity, necrosis, irregular margins).[1,11] Investigations confirm an association of heterogeneity with both pheochromocytoma[11–13] and metastatic disease.[14]

For lesions that warrant additional characterization, adrenal imaging can be performed with adrenal protocol CT or magnetic resonance imaging (MRI). With respect to adrenal CT, using precontrast, venous, and delayed acquisitions to determine washout characteristics, it is important to recognize that the research defining absolute percentage washout (APW) and relative percentage washout (RPW) values was primarily designed to distinguish adenoma from metastasis.[15–18] Several studies have revealed that these washout characteristics can be misleading in cases of hypervascular tumors, such as pheochromocytoma, renal cell carcinoma and hepatocellular carcinoma metastasis, which can also display rapid washout.[11,19,20]

Two recent studies have compared adenomas and pheochromocytomas using IV contrast-enhanced CT protocols.[11,12] One series that included 41 adenomas suggested that venous phase attenuation greater than 110 HU was highly specific for pheochromocytoma; however, this study was limited by the small sample size.[11] The second study did not define a venous phase threshold for distinction but did report that 33% of 47 pheochromocytomas washed out like adenomas, confirming the limited ability of adrenal CT to distinguish these 2 entities.[12] Accordingly, defining a reliable venous phase threshold value to identify pheochromocytoma would help avoid improper diagnosis of adenoma in the setting of a pheochromocytoma that displays rapid washout.

The purpose of this study was to test the venous phase threshold of 110 HU[11] by comparing the CT enhancement of adrenal adenoma and pheochromocytomas with a larger sample size, to determine whether a reliable venous phase enhancement level could be defined to distinguish pheochromocytoma from adenoma.

MATERIAL AND METHODS

Subjects

This institutional review board–approved retrospective study included subjects with CT-proven adenomas and pathologically proven pheochromocytomas that had venous phase CT performed between December 2002 and December 2012. The requirement for informed consent to review records was waived.

Pheochromocytoma

A retrospective search of pathology performed at our institution revealed 111 patients with pathologically proven

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pheochromocytomas. The inclusion criteria for the pathologically proven pheochromocytoma subjects were an existing abdominal CT with portal venous phase imaging (adrenal protocol CT, dual-phase CT, single portal venous phase CT). Patients were excluded if they had no presurgical venous phase CT imaging (60 patients), if the lesion was greater than 4 cm (26 patients), if the lesion did not arise from the adrenal gland, or if there were other lesions besides pheochromocytoma in the adrenal glands (3 patients). The pheochromocytoma study sample, therefore, consisted of 22 patients (10 patients previously published[11]) with 26 pheochromocytomas, because 1 patient had 3 lesions and 2 patients had 2 lesions. The previous study reported arterial and venous phase enhancement levels but focused on differences in arterial enhancement and patterns of enhancement across arterial and venous phases.[11] The current study aims to define a reliable venous threshold to distinguish the 2 entities on a single venous phase CT and evaluates how pheochromocytoma venous enhancement level correlates with washout pattern on venous and delayed acquisitions.

Adrenal Adenoma

Adrenal adenomas were identified by a retrospective search of the radiology information system, which was performed using the key words "adrenal" and "adenoma" or "adrenal adenoma." Patients had to have an abdominal CT that included a portal venous phase (single portal venous phase CT, dual-phase CT, adrenal protocol CT). Additional confirmatory inclusion criteria were the following:

(1) Existing noncontrast CT displaying a lipid-rich adenoma less than 10 HU or
(2) For lipid-poor adenomas, venous and delayed-phase CT washout calculations had to show APW of more than 60% and/or RPW of more than 40%.
(3) All lipid-rich and remaining lipid-poor adenomas as defined by (1) and (2) had to have at least 1-year follow-up imaging to confirm stability.
(4) Lesions that were stable for at least 2 years were considered lipid-poor adenomas, even if they measured greater than 10 HU on precontrast, did not display rapid washout, or did not have washout imaging available.

The retrospective search for the key words adrenal and adenoma or adrenal adenoma yielded 1351 patients. Subjects were excluded if their CT scan had no noncontrast or venous phase imaging (512 patients), if the adrenal mass was greater than 4 cm (16 patients), or the adrenal mass was not proven to be an adenoma on the basis of the criteria listed previously (616 patients).

Owing to the absence of pathologic proof, additional exclusion criteria for these subjects were applied. Accordingly, any patient with a lipid-poor lesion was then evaluated via medical records for symptoms or laboratory data suggesting pheochromocytoma including recurrent headaches, palpitations or arrhythmias, or severe hypertension and were excluded if present (3 patients). All patients' records were reviewed for history of cancer during the time that the CT examinations were performed and excluded if they had a lipid-poor lesion that did not display rapid washout (21 patients).

There were a total of 133 patients with 145 lipid-rich adenomas and 50 patients with 55 lipid-poor adenomas (39 patients previously published,[11] see previous details).

Imaging Technique

A total of 275 examinations were performed for the 205 patients. Because of the large time evaluated, scanners and techniques varied. Most of the studies (195 examinations, 71%) were conducted at our institution on either 128- or 64-multidetector CT scanners: 57 examinations, Somatom Definition Flash; 29 examinations, Definition; 92 examinations, Sensation 64; 17 examinations, Sensation Cardiac (all Siemens Healthcare). Earlier generation scanners included Sensation 16 (Siemens Healthcare) for 57 examinations. Some examinations were performed as part of a positron emission tomography-CT: 8 examinations, Discovery RX; 3 patients, Discovery LS; 1 patient Discovery STE; 2 patients, Discovery QX (all GE Healthcare). Five subjects' with a total of 9 studies were performed at other institutions and submitted for second opinion: 2 examinations, Emotion 16 (Siemens Healthcare); 3 examinations, Lightspeed (GE Healthcare); 1 examination, Brightspeed (GE Healthcare), 2 examinations, Volume Zoom (Siemens Healthcare); and 1 examination, Aquillon (Toshiba Medical).

Most patients (136/205) had both their noncontrast and venous acquisition performed on the same examination. In total, 68 patients with 71 adrenal adenomas and 1 patient with 3 pheochromocytomas had noncontrast and venous phase imaging performed on different examinations.

Our single venous phase abdominal CT includes portal venous phase (60 seconds) after infusion of IV contrast at 3 to 4 mL/s. Our dual-phase abdominal CT includes arterial phase (25–35 seconds), followed by venous phase imaging (60 seconds) with contrast infused at 5 mL/s. Our adrenal protocol consists of a precontrast CT, followed by venous phase (60 seconds) and delayed phase (15 minutes) after infusion contrast at 3 to 4 mL/s. For all protocol, 100 to 120 mL of either 320 mgI/mL isosmolar contrast (iodixanol; GE Healthcare) or 350 mgI/mL low-osmolar contrast (iohexol, GE Healthcare) is administered intravenously.

Image and Data Analysis

All studies were reviewed by a fellowship-trained body CT attending (8 years in practice) blinded to diagnosis. Computed tomography images were evaluated retrospectively as axial sections on a picture archive and communication system (Utravisual, Emageon, run on a Dell computer). Noncontrast density measurements were performed for all lesions, if available. Postcontrast density measurements were performed on venous phase acquisitions. If adrenal protocol imaging was performed with precontrast and postcontrast acquisitions, the noncontrast, venous, and 15-minute delayed-phase density were recorded. For cases where the delayed timing for a lipid-poor adenoma or pheochromocytoma was less than 15 minutes, the washout data were determined inadequate unless the lesion met the criteria of APW of ≥60% or RPW of ≥40%, because 15 minutes is our standard delay. However, lesions that displayed APW of ≥60% or RPW of ≥40% on a study with delayed imaging less than 15 minutes were included as adequate studies because these lesions would also show APW of ≥60% and RPW of ≥40% on a 15-minute delay image. Absolute percentage washout was defined as (venous phase HU − delayed-phase HU) / (venous phase HU − noncontrast HU) × 100. Relative percentage washout was defined as (venous phase HU − delayed-phase HU) / (venous phase HU) × 100.

The largest axial diameter was recorded for every lesion. An ovoid or circular region of interest was placed in the center of each lesion, with a region of interest that encompassed slightly more than one half of the area of the lesion at this level, avoiding calcification, necrosis, and lesion borders to reduce partial-volume averaging effects.

Statistical Analysis

A Student *t* test of independent samples assuming unequal variances was performed using MedCalc statistical software

TABLE 1. Subject Age, Sex, and Lesion Size

	Adenoma	Pheochromocytoma	*P*
No. subjects	183	22	—
No. nodules	200	26	—
Age, y	65 (37–92)	53 (27–74)	<0.01
Sex	81 males, 102 females	8 male, 14 female	—
Lesion size, cm	2.1 (0.69)	2.4 (0.98)	<0.05

Lesions ≥ 4 cm in size excluded from analysis per ACR guidelines.

version 12.7.7. This was performed for patient age, aortic enhancement level, lesion size, and adenoma and pheochromocytoma venous attenuation levels. A *P* value of 0.05 or less was considered significant. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated for differentiating pheochromocytomas from adenomas on the basis of venous phase attenuation of ≥110 HU and ≥130 HU. Adenomas and pheochomocytomas were then directly compared for the presence of APW of ≥60% or RPW of ≥40% and the concomitant presence of venous phase attenuation of ≥110 HU or ≥130 HU expressed as a percentage.

RESULTS

One hundred eighty-three patients with 200 adenomas were compared with 22 patients with 26 pheochromocytomas. The pheochromocytoma subjects were younger, and the pheochromocytomas were slightly larger than adenomas; however, all lesions were less than 4 cm (Table 1).

There was a significant difference in the enhancement levels of adenomas and pheochromocytomas on venous phase imaging (Table 2). As shown in Figure 1, the enhancement levels of the lesions overlap considerably; however, no adenoma enhanced greater than 130 HU, compared with 10 (38%) of 26 pheochromocytomas. Thirteen (50%) of 26 pheochromocytomas exceeded 110 HU on the venous phase, compared with 6 (3%) of 200 adenomas. Four of the 6 venous phase adenomas that enhanced greater than 110 HU were lipid poor (Table 2). With respect to a venous phase threshold for distinction of adenoma from pheochromocytoma, relative sensitivity, specificity, positive predictive value, and negative predictive value for 110 and 130 HU are shown in Table 3.

Of 32 lipid-poor adenomas with 15-minute washout adrenal protocol imaging, 30 (94%) displayed rapid washout with APW ≥60% or RPW ≥40%. One of the 30 met washout criteria by APW, but the RPW was 35%; this was stable for 2 years. The remaining two were included on the basis of at least 2-year stability

TABLE 2. Mean (Range) Venous Phase Enhancement Levels of Adenomas and Pheochromocytomas

	Venous Phase, Mean (SD)	Venous Phase, Range
Pheochromocytoma (n = 26), HU	111 (38)	46–179
All adenomas (n = 200), HU	58 (26)	6–124
Lipid-poor adenomas (n = 55), HU	76 (25)	24–124
Lipid-rich adenomas (n = 145), HU	51 (22)	6–118

Differences in venous phase enhancement between pheochromocytoma and lipid-poor adenoma, pheochromocytoma and lipid-rich adenoma, pheochromocytoma and all adenoma, as well as lipid-rich and lipid-poor adenoma were all significant ($P < 0.01$).

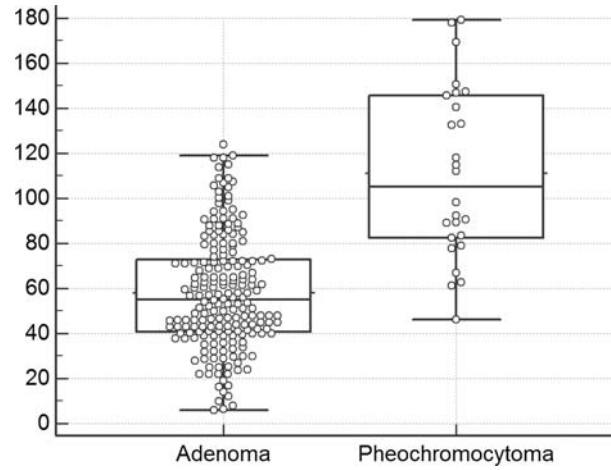

FIGURE 1. Box and whisker plot of venous phase enhancement for 200 adenomas and 26 pheochromocytomas. Despite considerable overlap at levels greater than 130 HU, 38% (10/26) of the pheochromocytomas exceeded 130 HU compare with 0% of adenomas. Figure 1 can be viewed online in color at www.jcat.org.

by serial imaging. Two adenomas had adrenal protocol imaging with delay of less than 15 minutes. One of these adenomas displayed APW ≥60% at 10-minute delay and was therefore classified as adenoma with rapid washout. The other case that displayed APW less than 60% at 5-minute delay was regarded as an inadequate adrenal protocol study was stable for 2 years. A total of 21 lipid-poor adenomas did not have washout imaging but were stable for 2 years.

Thirteen of 17 pheochromocytomas with washout studies met APW or RPW criteria (Table 4). Almost all of the pheochromocytomas that met washout criteria displayed venous phase attenuation greater than 110 HU (12/13, 92%) or greater than 130 HU (10/13, 77%), with 4 of these showing rapid washout at 5- to 6-minute delay (Table 5). Rapid washout was identified in all (10/10, 100%) pheochromocytomas that enhanced greater than 130 HU on the venous phase, compared with 43% (3/7) that enhanced less than 130 HU. Average venous phase attenuation of pheochromocytomas that met washout criteria was 141 HU, compared with 72 HU for those that did not display rapid washout.

Given the increased specificity of 130 HU on venous phase imaging for pheochromocytoma compared with 110 HU, 130 HU was further evaluated as a possible threshold for distinguishing adenoma from pheochromocytoma. Combining absolute venous enhancement and washout criteria, a pattern of venous phase attenuation 130 HU or greater and adenoma-like washout was seen in 10 (59%) of 17 pheochromocytomas compared with 0 (0%) of 32 lipid-poor adenomas (Fig. 2). A pattern of venous phase attenuation less than 130 HU and adenoma-like washout pattern was seen in 3 (18%) of 17 pheochromocytomas and

TABLE 3. Sensitivity, Specificity, PPV and NPV of 110 and 130 HU Venous Phase Threshold for Identifying Pheochromocytoma

	110 HU	130 HU
Sensitivity, %	50	38
Specificity, %	97	100
PPV, %	68	100
NPV, %	98	93

PPV indicates positive predictive value; NPV, negative predictive value.

TABLE 4. Comparison of Venous Phase Enhancement of 17 Pheochromocytoma and 32 Lipid-Poor Adenoma With Washout Characteristics on Adequate Adrenal Protocol CT (Noncontrast, 60-Second Venous Phase, 15-Minute Delay Phase, or Earlier Delay Phase If Washout Criteria Met [n = 4 Pheochromocytomas])

Venous Phase HU	Met Washout Criteria	Did Not Meet Washout Criteria
Pheochromocytoma >130	10	0
Pheochromocytoma <130	3	4
Lipid-poor adenoma >130	0	0
Lipid-poor adenoma <130	30	2

A total of 3 pheochromocytomas that did not fulfill washout criteria on adrenal protocol imaging with delay phase acquisition at <15 minutes were excluded because 15-minute delay enhancement could not be determined. Washout criteria defined as APW >60% or RPW >40%.

30 (94%) of 32 lipid-poor adenomas (Fig. 3). A pattern of venous phase attenuation less than 130 HU and nonadenoma-like washout pattern was seen in 4 (24%) of 17 pheochromocytomas and 2 (6%) of 32 lipid-poor adenomas (Fig. 4). A management algorithm has been proposed for incidental adrenal lesions that enhance greater than 130 HU on a venous phase MDCT (Fig. 5).

DISCUSSION

The ACR white paper on managing incidentalomas provides an excellent framework to guide management of indeterminate adrenal nodules.[1] If an incidental adrenal nodule is indeterminate (absence of documentation of long-term stability, no precontrast CT showing attenuation < 10 HU and no identifiable macroscopic fat), the primary features that are considered are size and morphology. Although benign-appearing indeterminate lesions less than 4 cm can be followed with repeat imaging in 1 year, the presence of suspicious features such as heterogeneity, necrosis, or irregular margins warrants further characterization.[1,11] Several studies have shown that heterogeneity is a feature associated with pheochromocytoma (58%) and not common in adenomas (22%).[11–13] More recently, a large comparative study of 211 subjects with and without primary malignancy revealed that peripheral enhancement should be considered suspicious for metastatic disease.[14]

Any additional information that can be gleaned from the original CT examination where an adrenal lesion is disclosed could potentially improve the radiologist's discriminatory ability. If the original CT examination was performed with arterial and venous acquisitions, certain patterns of enhancement and absolute enhancement levels have been shown to be associated with pheochromocytoma.[11] These include arterial enhancement greater than venous enhancement and arterial enhancement greater than 110 HU, both highly specific findings for pheochromocytoma.[11] Most CT examinations, however, are conducted with a single venous phase acquisition. In this recent series of 41 adenomas and 12 pheochromocytomas, only 7% (3/41) of the adenomas enhanced greater than 110 HU on the venous phase acquisition compared with 58% (7/12) of the pheochromocytomas, suggesting a potential venous phase threshold predictive of pheochromocytoma.[11] The purpose of our study was to sample a larger patient population and compare the venous enhancement levels of these 2 lesions, as well as the contrast kinetics during adrenal washout imaging with 60-second and 15-minute acquisitions.

The early studies revealing the utility of washout imaging for diagnosis of adrenal adenoma primarily compared adenomas with metastasis.[15–18] Several subsequent studies have since shown that these washout characteristics can be mimicked by pheochromocytoma, renal cell carcinoma, and hepatocellular carcinoma metastasis.[12,19,20] Important to recognize, to avoid these diagnostic pitfalls, is the fairly predictable enhancement pattern and enhancement level of adenomas. The early work on CT of adrenal adenomas provides valuable information in this regard. In 1998, Szolar and Kammerhuber[15] evaluated the pattern of adrenal adenoma enhancement on a 4-slice MDCT scanner, using 120 mL of 300 mgI/mL contrast infused at 2.5 mL/s. Patients were imaged at either 30 and 90 seconds or 60 and 180 seconds, and additional subjects had 10- or 30-minute delayed acquisitions. A total of 74 adenomas were included, including lipid rich and lipid poor. The highest enhancement level for adenomas occurred at 60 seconds, and the mean (SD) enhancement at 60 seconds was 64 (22) HU. In 2005, Szolar et al[21] reported similar enhancement characteristics with 24 adenomas, which enhanced to a mean (range) of 60 (30–84) HU at 60 seconds. The purpose of reanalyzing adenoma enhancement in this study was to determine whether currently performed contrast infusion protocols, using higher infusion rates and a higher contrast concentration, resulted in substantially higher venous phase enhancement levels. The contrast concentrations used in our department range from 320 to 350 mgI/mL and target

FIGURE 2. Patient with pathologically proven pheochromocytoma. Noncontrast (A), venous (B), and delayed-phase axial IV contrast-enhanced CT show a 1.3-cm right adrenal mass (arrow) that measures 42 HU on noncontrast phase, 178 HU on venous phase, and 64 HU on 15-minute delay phase. These venous enhancement level and pattern were seen with 59% (10/17) of pheochromocytomas and 0% (0/32) adenoma.

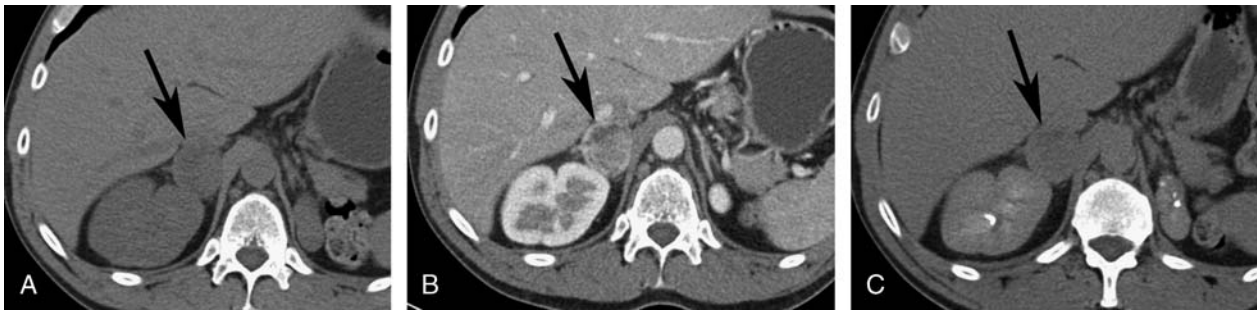

FIGURE 3. Patient with pathologically proven pheochromocytoma. Noncontrast (A), venous (B), and delayed-phase axial IV contrast-enhanced CT show a 3.5-cm right adrenal mass (arrow) that measures 30 HU on noncontrast phase, 83 HU on venous phase, and 46 HU on a 15-minute delay phase. These venous enhancement level and pattern were seen with 18% (3/17) of pheochromocytomas and 94% (30/32) adenoma.

infusion rates are 3 to 5 mL/s. Nonetheless, our results were very similar to the earlier work, with the 60-second mean (SD, range) enhancement of 200 adenomas measuring 58 (26, 6–124) HU.

Similarly, previous investigations have demonstrated relatively higher enhancement levels of pheochromocytomas. The study by Szolar et al[21] from 2005 reported the mean (SD, range) venous enhancement of 17 pheochromocytomas to be 94 (20, 72–131) HU, which was significantly higher than that of adenomas (60 [27] HU). In 2009, Ctvrtlík et al[13] demonstrated that 9 pheochromocytomas had higher postcontrast enhancement (mean [range], 79 [50–111] HU) compared with 37 lipid-rich and lipid-poor adenomas (mean [range], 37 [3–95] HU). In our series, the mean (SD) contrast enhancement level of pheochromocytoma was 111 (38) HU, significantly higher than that of adenoma and greater than that reported in these earlier investigations, presumably attributed to higher concentration contrast infused at a higher rate.

With the use of the infusion parameters defined in our study, a venous phase threshold of 130 HU can be used to create a new management algorithm, which takes into consideration that a lesion measuring greater than 130 HU should not be assumed to be an adenoma. In this situation, clinical assessment should be performed and additional tests such as plasma and urine metanephrines and follow-up CT or MRI in 1 year to assess for growth considered, because rapid washout on adrenal protocol imaging becomes less specific for adenoma. Of note, recent research has shown that pheochromocytomas are often clinically unsuspected at the time of diagnosis, with as many as 29% to 70% of pheochromocytomas identified incidentally on imaging, likely secondary to increased CT utilization and improvement in CT imaging technique.[9,22,23] Metanephrine testing should be considered in these patients, at considerably less cost than additional CT or MRI, and without the risks associated with radiation and iodinated IV contrast infusion. The cost for plasma or urine metanephrines at our institution is US $59, compared with US $762 for adrenal protocol CT and US $1213 for adrenal MRI.

A recent paper by Patel et al[12] compared venous phase enhancement levels and washout characteristics of adenomas and pheochromocytomas. With respect to a venous threshold for pheochromocytomas, the authors were unable to delineate a reliable attenuation value. The biggest discrepancy between their study and ours is the venous phase enhancement level of the adenomas. They included 20 lipid-rich and 78 lipid-poor adenomas and reported mean (range) attenuation values (95, 43–202 HU) for all adenomas, which were similar to the mean (range) 96 (22–221) HU for their pheochromocytoma subjects. In their study, 24 (31%) of 78 lipid-poor adenomas enhanced greater than 110 HU; no lipid-rich adenomas reached this venous phase enhancement level. The results do not indicate how many adenomas exceeded 130 HU. The explanation for this discrepancy is unclear. The inclusion and exclusion criteria seem similar. Our contrast infusion protocol delivers more iodine at a higher infusion rate (320–350 mgI/mL at 3–5 mL/s) compared with their infusion protocol (300 mgI/mL infused at 2–3 mL/s). The 60-second venous timing was comparable. Perhaps the difference in measurement technique affected the enhancement levels recorded. We attempted to measure the central 60% to 70% of each mass, whereas their measurement technique was "Regions of interest were placed to encompass as much of the mass as possible on a singe axial 2D image while avoiding partial-volume effects."

FIGURE 4. Patient with pathologically proven pheochromocytoma. Noncontrast (A), venous (B), and delayed-phase axial IV contrast-enhanced CT show a 1.2-cm left adrenal mass (arrow) that measures 56 HU on noncontrast phase, 84 HU on venous phase, and 70 HU on a 15-minute delay phase. These enhancement level and pattern were seen with 24% (4/17) of pheochromocytomas and 6% (2/32) adenoma.

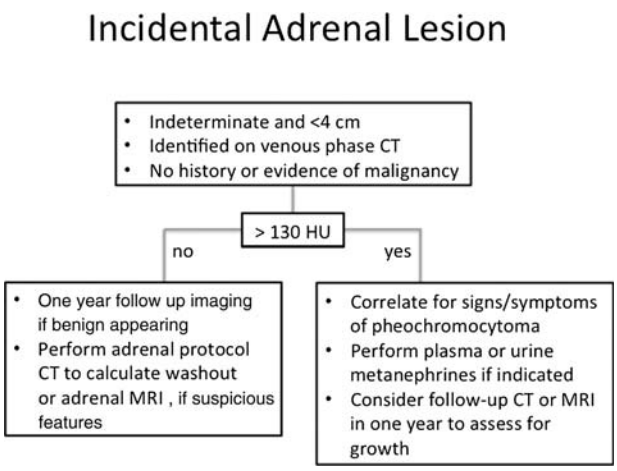

FIGURE 5. Proposed management algorithm for incidental adrenal lesions that enhance greater than 130 HU on venous phase MDCT.

Regardless, our results are very similar to previously performed studies of adrenal adenoma enhancement,[15,21] supporting the cut-offs we have defined in our comparative analysis.

Adrenal washout CT is excellent for distinguishing most types of metastatic disease from adenoma, with the exception of hypervascular metastases such as renal cell carcinoma and hepatocellular carcinoma.[20] In 2005, Park et al[19] reported the potential for misdiagnosis of pheochromocytoma as an adenoma on the basis of washout characteristics. With the use of single and multidetector CT scanners, 120 mL of 300 mgI/mL contrast was infused at 3 mL/s. Similar results were shown in our investigation. Patel et al[12] noted in their recent study that 33% (12/47) of pheochromocytomas displayed adenoma washout pattern, and 67% (8/12) had high venous enhancement level (>110 HU). Of note, the pheochromocytomas in that study were not limited to those less than 4 cm in size (size range, 0.6-14 cm), and larger masses tend to be heterogenous with areas of necrosis, which may have affected the washout characteristics.[12]

Our study has a number of limitations. The inclusion and exclusion criteria were different for the 2 lesion types, resulting in heterogenous comparison groups. There was a large discrepancy between the sample size for the 2 groups, but this is reflective of the relative incidence of the 2 lesion types. The pheochromocytoma sample size is relatively small, a result of both the low incidence of this tumor and the fact that patients referred from other facilities with known diagnosis of pheochromocytoma have no presurgical imaging performed at our institution. Metastases were not evaluated in our study restricted to adenoma and pheochromocytoma; however, the primary extra-adrenal tumor will often be disclosed on CT imaging or the patient will have a known history of malignancy. Adrenal cortical carcinomas were not evaluated in our study because these rarely present less than 4 cm, which was the size threshold for biopsy or resection per ACR criteria. Adenomas were not pathologically proven; however, it met accepted diagnostic criteria for inclusion.[1] The retrospective nature of this investigation results in a number of limitations, in particular, the diversity of imaging protocols and scanners. There was no prospective control over the CT protocol and infusion parameters, which likely resulted in diversity of enhancement levels. Some subjects' noncontrast and venous phase attenuation values were recorded on different studies, because they did not have noncontrast and venous phase acquisitions on the same CT examination. Target injection rate varied from 3 to 5 mL/s across our 205 subjects. Whether a higher infusion rate (5 vs 3 mL/s) results in significantly higher contrast enhancement level cannot be determined from these data. Contrast agent and volume varied, which may also affect absolute enhancement values. Infusion protocols will vary depending on indication and institution. Higher concentration contrast and even higher infusion rates in excess of 5 mL/s, which are currently used for vascular imaging, may result in higher enhancement levels for incidentally identified adrenal lesions. The contrast infusion parameters used should be taken into consideration when applying these results. Finally, the results have not defined criteria that are 100% reliable in distinguishing the 2 lesions; the small percentage of pheochromocytomas that mimic an adenoma (enhance < 110 HU and meet washout criteria) may still be misdiagnosed as an adenoma. This is in keeping with the wide variability of imaging appearances for pheochromocytoma.[24]

CONCLUSIONS

In summary, the results from this study identify a venous phase enhancement level that may aid in distinguishing adrenal adenoma and pheochromocytoma on IV contrast-enhanced MDCT. First, using the infusion parameters defined in this study, no adenoma in this series exceeded 130 HU. Indeterminate incidental lesions that enhance greater than 130 HU using similar infusion protocols cannot be assumed to be an adrenal adenoma. Patient history should be reviewed to determine whether metanephrine testing is warranted. Secondly, pheochromocytomas with venous attenuation greater than 130 HU in this study mimicked adrenal adenoma washout pattern; accordingly, the absolute venous phase enhancement level must be taken into consideration when interpreting adrenal washout studies. Given the limitations defined in this retrospective investigation, additional prospective studies will be valuable in determining protocol-specific venous phase thresholds for identifying pheochromocytoma.

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