The Journal of Chulabhorn Royal Academy
eISSN : 2697-5203 (Online)

Research article

Distinguishing Lipid-Poor Adrenal Adenoma from Non-Adenomatous Lesions: Accuracy of Identification and the Most Appropriate Contrast Washout Index Using the Contrast-Enhanced Washout Multidetector CT 10-Minute Delayed Imaging Protocol

Parames Seevaleephan, MD*, Nithida Na Songkhla, MD

Department of Radiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

*Corresponding Author, e-mail: pseevaleephan@gmail.com

Received: 8 October 2021 ; Revised: 19 April 2022 ; Accepted: 25 May 2022

Abstract

Background: Because of the contrast washout characteristic of adrenal adenoma, Siriraj Hospital uses the 10-minute delayed imaging computed tomography (CT) protocol to evaluate adrenal masses. No reports in Thailand have described the performance of this protocol to date.

Objective: This study was performed to identify the accuracy of identification and the most appropriate contrast washout index to distinguish lipid-poor adrenal adenoma from non-adenomatous lesions using the 10-minute delayed imaging CT protocol.

Materials and Methods: This retrospective review involved patients who underwent the CT adrenal protocol with 10-minute delayed imaging at Siriraj Hospital from January 2005 to December 2017. In total, 285 adrenal masses that were smaller than 4 cm and had a poor lipid component (density of >10 HU) were assessed in 261 patients who were given a pathologic diagnosis or underwent follow-up imaging. Non-contrast images were obtained before intravenous contrast administration with an 80-second and 10-minute scan delay. The absolute percentage washout (APW) and relative percentage washout (RPW) of the adrenal masses were calculated. Receiver operating characteristic analysis was performed to evaluate the protocol performance and the most appropriate contrast washout value with which to identify lipid-poor adrenal adenoma.

Results: The test appeared to be the most accurate when using an APW of 47% and RPW of 34%. The APW of 47% showed a sensitivity of 96.5%, specificity of 89.3%, and accuracy of 95.8% ($p < 0.001$), while the RPW of 34% showed a sensitivity of 89.5%, specificity of 96.4%, and accuracy of 90.2% ($p < 0.001$).

Conclusion: An APW of 47% and RPW of 34% were the most appropriate washout indexes, offering high accuracy to distinguish lipid-poor adrenal adenoma from non-adenomatous lesions.

Keywords: 10-minute contrast washout CT, Adrenal adenoma, Absolute percentage washout, Lipid poor adenoma, Relative percentage washout

Introduction

Adrenal adenoma is a benign tumor of the adrenal cortex and is incidentally found in most patients. However, it can cause endocrinological symptoms in some patients. The incidence of adrenal adenoma was 9% in one autopsy series[1]. Adrenal adenoma can be divided into lipid-rich adenoma (≤10 Hounsfield units [HU])

© Chulabhorn Royal Academy. Terms and conditions of Creative Commons Attribution 4.0 International (CC BY NC ND 4.0) apply

and lipid-poor adenoma (>10 HU). It is important to distinguish adrenal adenoma from other malignant masses because of the differences in the prognosis and further management. For example, adrenocortical carcinoma should be detected early and staged for surgical planning, whereas adrenal adenoma can be observed and followed up[2]. However, it is not easy to distinguish lipid-poor adrenal adenoma from other non-adenomatous lesions (including infection) and malignancies (such as adrenocortical carcinoma, metastases, and pheochromocytoma) based on the general character of the mass on computed tomography (CT) images. Because of the rapid contrast washout characteristic of adrenal adenoma, radiologists currently use the 10- or 15-minute delayed imaging CT protocol to evaluate adrenal masses and to diagnose lipid-poor adrenal adenoma. Radiologists measure adrenal masses in HU and then calculate both the absolute percentage washout (APW) and relative percentage washout (RPW).

In a study by Blake et al.[2], the proper washout values for the 10-minute delayed protocol were an APW of 52%, which showed a sensitivity of 100% and specificity of 98%, and an RPW of 37.5%, which showed a sensitivity of 100% and specificity of 95%. A study by Patel et al.[3] suggested that the proper washout values for the 15-minute delayed protocol were an APW of 60%, which showed a sensitivity of 97.8%, specificity of 94.7%, and accuracy of 98.4%, and an RPW of 40%, which showed a sensitivity of 100%, specificity of 100%, and accuracy of 98.9%. Adenomas typically have an APW and RPW above the threshold values. Adrenal metastases, adrenocortical carcinomas, and some pheochromocytomas usually washout to a lesser degree[4].

Siriraj Hospital has been using the 10-minute delayed imaging CT protocol to evaluate adrenal masses since 2005. This protocol is very useful and time-saving for busy CT departments. However, no reports in Thailand have yet described the performance of this protocol or the most appropriate contrast washout index to distinguish lipid-poor adrenal adenoma from non-adenomatous lesions.

Thus, the objective of the current study was to identify the accuracy of identification and the most appropriate contrast washout index to distinguish lipid-poor adrenal adenoma from non-adenomatous lesions by using the 10-minute delayed imaging CT protocol.

Materials and Methods

This retrospective study was approved by the Siriraj Institutional Review Board (Si 874/2019 and SIRB protocol number 782/2562(IRB1)). The data of all patients were reviewed by approval and confidentially. All CT cases in the picture archiving and communication system in which the 10-minute delayed imaging protocol was used at Siriraj Hospital in Bangkok, Thailand from January 2005 to December 2017 were reviewed. In total, 286 adrenal masses that were smaller than 4 cm and had a poor lipid component (>10 HU) were assessed in 262 patients who were given a pathologic diagnosis or had at least 2-year CT images and clinical follow-up data.

Multidetector CT images were obtained with a non-contrast scan comprising an 80-second portal phase and a 10-minute delayed phase. A genitourinary radiologist with 17 years' experience and a third-year radiologic resident assessed all the adrenal masses and measured them in HU. The region of interest encompassed at least two-thirds of the mass and avoided cystic areas or calcification. Measurements of the masses in the non-contrast phase, 80-second portal phase, and 10-minute delayed phase were

$$\text{APW (\%)} = \frac{(\text{HU of mass in portal phase} - \text{HU of mass in delayed phase}) \times 100}{(\text{HU of mass in portal phase} - \text{HU of mass in non-contrast phase})}$$

$$\text{RPW (\%)} = \frac{(\text{HU of mass in portal phase} - \text{HU of mass in delayed phase}) \times 100}{(\text{HU of mass in portal phase})}$$

confirmed by consensus. The APW and RPW of the adrenal masses were then calculated as follows.

The results of the pathologic diagnosis and follow-up CT images of all the included adrenal masses were reviewed. Pathologic findings that suggested adrenal adenoma or follow-up CT images that were obtained within at least 2 years and exhibited size stability were used as the gold standard for diagnosis of adrenal adenoma.

The APW, RPW, gold standard results of adrenal lesions, and other descriptive information were statistically analyzed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Receiver operating characteristic (ROC) analysis was carried out to evaluate the test performance and determine the most appropriate contrast washout value to distinguish lipid-poor adrenal adenoma from non-adenomatous lesions. The chi-square test was also performed to obtain the sensitivity, specificity, and accuracy of the APW and RPW in the identification of adrenal adenomas by using the most appropriate contrast washout value.

Results

This study involved 261 patients (92 men and 169 women) with an adrenal lesion; 11 men and 13 women had 2 adrenal lesions (Table 1). The chi-square test showed that sex did not have a significant impact on the incidence of lipid-poor adrenal adenoma ($p > 0.05$) (Table 2). The 261 patients had 285 adrenal lesions, which were divided into 257 lipid-poor adenomas, 1 adrenocortical carcinoma, 7 pheochromocytomas, and 20 other lesions (16 tuberculosis and granulomatous infections, 1 adrenal cortical tumor, 1 ganglioneuroma, 1 lymphoma, and 1 fibrous tissue with lymphocytes) (Table 1).

Table 1. Characteristics of patients and types of adrenal masses

Characteristics	n	Percentage (%)
Sex		
Male	92	35.25
Female	169	64.75
Total	261	100
Age (years)		
Mean	56.252	
Minimum	19	-
Maximum	88	
Types of adrenal masses		
Lipid-poor adenoma	257	90.18
Adrenocortical carcinoma	1	0.35
Pheochromocytoma	7	2.46
Others	20	7.02
Total	285	100

Table 2. Sex and types of adrenal masses

			Type of adrenal mass		Total
			Other	Adenoma	
Sex	Female	n	14	168	182
		% within adenomas	50.0%	65.4%	63.9%
	Male	n	14	89	103
		% within adenomas	50.0%	34.6%	36.1%
Total		n	28	257	285
		% within adenomas	100.0%	100.0%	100.0%
Exact Sig. (two-sided)				0.102	
Exact Sig. (one-sided)				0.055	

Sig., significance

The ROC analysis of APW and RPW showed that the area under the ROC curve was 0.948 and 0.957 for APW and RPW, respectively, with statistical significance (Figures 1, 2; Tables 3, 4).

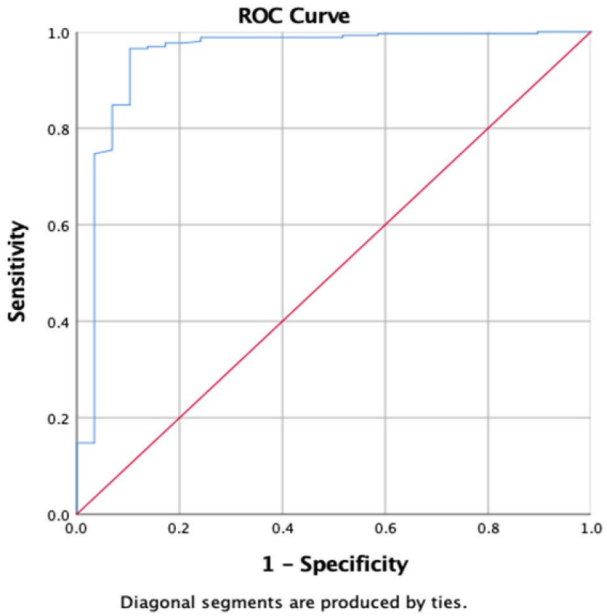


Figure 1. ROC curve of APW. ROC, receiver operating characteristic; APW, absolute percentage washout.

Table 3. Area under the curve of APW

Test result variable: APW

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% CI	
			Lower bound	Upper bound
0.948	0.030	0.000	0.889	1.000

[a]Under the nonparametric assumption.

[b]Null hypothesis: true area = 0.5.

CI, confidence interval; APW, absolute percentage washout; Std., standard; Sig., significance

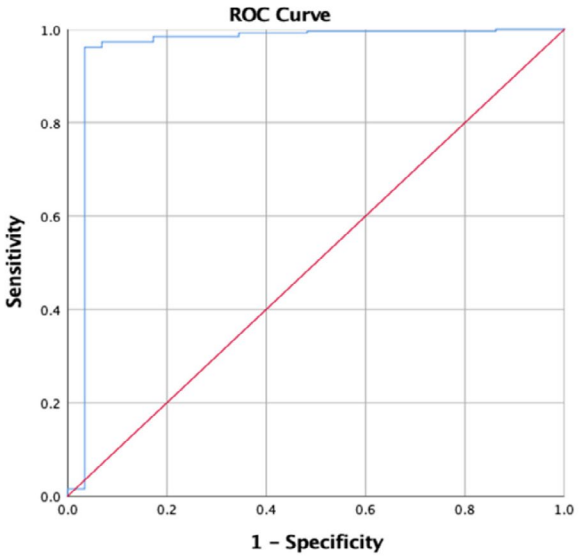


Figure 2. ROC curve of RPW. ROC, receiver operating characteristic; RPW, relative percentage washout.

Table 4. Area under the curve of RPW

Test result variable: RPW

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% CI	
			Lower bound	Upper bound
0.957	0.033	0.000	0.891	1.000

[a]Under the nonparametric assumption.

[b]Null hypothesis: true area = 0.5.

CI, confidence interval; RPW, relative percentage washout; Std., standard; Sig., significance

The test appeared to be the most accurate when using an APW of 47% and RPW of 34%, whereby non-adenomatous lesions, including malignancy, were detected with significant accuracy ($p < 0.001$).

The APW of 47% could distinguish lipid-poor adrenal adenoma from non-adenomatous lesions, including malignancy, with a sensitivity of 96.5% (248 of 257 lesions), specificity of 89.3% (25 of 28 lesions), and accuracy of 95.8% (Table 5).

The RPW of 34% could distinguish lipid-poor adrenal adenomas from non-adenomatous lesions, including malignancy, with a sensitivity of 89.5% (230 of 257 lesions), specificity of 96.4% (27 of 28 lesions), and accuracy of 90.2% (Table 6).

Table 5. Sensitivity and specificity of APW of 47%

			Type of adrenal mass		Total
			Other	Adenoma	
APW	<47%	n	25	9	35
		% within adenoma	89.3%	3.5%	12.3%
	≥47%	n	3	248	251
		% within adenoma	10.7%	96.5%	88.1%
Total		n	28	257	285
		% within adenoma	100.0%	100.0%	100.0%

APW, absolute percentage washout

Table 6. Sensitivity and specificity of RPW of 34%

			Type of adrenal mass		Total
			Other	Adenoma	
RPW	<34%	n	27	27	54
		% within adenoma	96.4%	10.5%	18.9%
	≥34%	n	1	230	231
		% within adenoma	3.6%	89.5%	81.1%
Total		n	28	257	285
		% within adenoma	100.0%	100.0%	100.0%

RPW, relative percentage washout

Discussion

In this study, lipid-poor adrenal adenoma showed rapid and significant contrast washout in the 10-minute scan delayed CT images, corresponding to the nature of the disease, whereas other non-adenomatous lesions showed relatively less contrast washout in the delayed phase.

The ROC analysis showed that the most appropriate contrast washout values to distinguish lipid-poor adrenal adenomas from non-adenomatous lesions were an APW of 47% and RPW of 34%, with statistical significance. According to the chi-square test, the APW of 47% showed a sensitivity of 96.5%, specificity of 89.3%, and accuracy of 95.8% (Table 5), and the RPW of 34% showed a sensitivity of 89.5%, specificity of 96.4%, and accuracy of 90.2% (Table 6).

In comparison, Blake et al.[2] reported that the proper washout values for the 10-minute delayed protocol were an APW of 52%, which showed a sensitivity of 100% and specificity of 98%, and an RPW of 37.5%, which showed a sensitivity of 100% and specificity of 95%. This previous work showed higher sensitivity and specificity than those reported in the present work. This might be explained by the fact that our study included more than twice as many adrenal masses as that in the previous study.

The RPW threshold of our study was lower than that in a study by Peña et al.[5], who evaluated indeterminate (lipid-poor) adrenal masses using a mean 9-minute delayed scanning protocol and an RPW threshold of 50% to characterize benign or malignant lesions correctly in 99 of 101 lesions. The RPW in their study was much higher than that in our study. According to the nature of the rapid washout of an adenoma, waiting less time on the delayed images should provide a lower threshold value. For example, in the study of the 15-minute delayed protocol by Patel et al.[3], a 40% RPW was recommended as a cut-off threshold.

Furthermore, compared with the results obtained by Szolar et al. [6], who reported a 50% APW and 40% RPW with a 10-minute delayed protocol, both the sensitivity and specificity for the diagnosis of adenomas were 100%. However, the number of adenomas in that study was only 23.

Finally, we can compare our results with those from the study by Sangwaiya et al.[7], who used a 10-minute delayed protocol to distinguish adrenal adenomas from other non-adenomatous conditions. Their study concluded that the 10-minute delayed protocol reduced the sensitivity for the detection of adenomas. The sensitivity for the detection of adenomas was 71.3% for an APW threshold of 50% and 81.4% for an RPW threshold of 35% in their study, which were lower than the values obtained in our study.

Thus, in our opinion, it is acceptable to use the 10-minute delayed imaging protocol in abdominal CT scans to distinguish lipid-poor adrenal adenomas from non-adenomatous lesions, including malignancy, by using an APW of 47% and RPW of 34%.

Our study had two main limitations. First, for patients with no pathological diagnosis, we used CT and clinical follow-up data obtained within at least 2 years to confirm the benignity of the masses. Second, instead of calculating the interobserver agreement, we used the consensus between two readers.

Conclusion

An APW of 47% and RPW of 34% were the most appropriate washout indexes and demonstrated high accuracy to distinguish lipid-poor adrenal adenomas from non-adenomatous lesions, including malignancy, with statistical significance ($p < 0.001$). The APW of 47% showed a sensitivity of 96.5%, specificity of 89.3%, and accuracy of 95.8%, and the RPW of 34% showed a sensitivity of 89.5%, specificity of 96.4%, and accuracy of 90.2%. Thus, this study demonstrated that it is acceptable to use a 10-minute delayed imaging CT protocol to distinguish lipid-poor adrenal adenoma from non-adenomatous lesions, including malignancy. This protocol is highly convenient for institutions with busy CT schedules, such as Siriraj Hospital, and can also be more comfortable for patients than the 15-minute delayed protocol because of the shorter CT scanning time.

Acknowledgment

We thank Angela Morben, DVM, ELS, from Edanz (www.edanz.com/ac), for editing a draft of this manuscript.

References

1. Song JH, Chaudhry FS, Mayo-Smith WW. The incidental adrenal mass on CT: prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy. *AJR Am J Roentgenol*. 2008; 190(5):1163-1168. doi:10.2214/AJR.07.2799
2. Blake MA, Kalra MK, Sweeney AT, et al. Distinguishing benign from malignant adrenal masses: multi-detector row CT protocol with 10-minute delay. *Radiology*. 2006;238(2): 578-585. doi:10.1148/radiol.2382041514
3. Patel MN, Rajpura HKK, Solanki RN, Patel H. Distinguishing benign lesion from malignant adrenal masses by CT scan with 15 minutes delayed protocol. *J Evid Based Med Healthc*. 2018;5(38):2747-2751. doi:10.18410/jebmh/2018/563
4. Johnson PT, Horton KM, Fishman EK. Adrenal Imaging with multidetector CT: evidence-based protocol optimization and interpretative practice. *Radiographics*. 2009;29(5):1319-1331. doi:10.1148/rg.295095026
5. Peña CS, Boland GW, Hahn PF, Lee MJ, Mueller PR. Characterization of indeterminate (lipid-poor) adrenal masses: use of washout characteristics at contrast-enhanced CT. *Radiology*. 2000;217(3):798-802. doi:10.1148/radiology.217.3.r00dc29798
6. Szolar DH, Korobkin M, Reittner P, et al. Adrenocortical carcinomas and adrenal pheochromocytomas: mass and enhancement loss evaluation at delayed contrast-enhanced CT. *Radiology*. 2005;234(2):479-485. doi:10.1148/radiol.2342031876
7. Sangwaiya MJ, Boland GW, Cronin CG, Blake MA, Halpern EF, Hahn PF. Incidental adrenal lesions: accuracy of characterization with

contrast-enhanced washout multidetector CT--10-minute delayed imaging protocol revisited in a large patient cohort. *Radiology*. 2010;256(2):504-510. doi:10.1148/radiol.10091386

License, Supplymentary Material and Copyright

This is an open-access article distribute under the terms of the Creative Commons Attribution (CC by NC ND 4.0) License. You may share the material, but must give appropriate credit to the source, provide a link to the license and indicate if changes were mades. You may not use the material for commercial purpose. If you remix, tranform, or build upon the material, you may not distribute the modified material

Any supplymentary material reference in the article can be found in the online version.

This article is copyright of the Chulabhorn Royal Academy, 2022

Citation

Seevaleephan P., Na Songkhla N. Distinguishing Lipid-Poor Adrenal Adenoma from Non-Adenomatous Lesions: Accuracy of Identification and the Most Approapriate Contrast Washout Index Using the Contrast-Enhanced Washout Multidetector CT 10-Minute Delayed Imaging Protocol. *J Chulabhorn Royal Acad.* 2022; 4(3): 95-102 https:// he02.tci-thaijo.org/index.php/jcra/article/view/ 253958

Online Access

https://he02.tci-thaijo.org/index.php/jcra/article/view/ 253958