

Dual energy spectral CT imaging of pulmonary embolism with *Mycoplasma pneumoniae* pneumonia in children

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Research article

Keywords: gemstone spectral CT, pulmonary embolism, *Mycoplasma pneumoniae* pneumonia

Posted Date: November 17th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-105767/v1>

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Version of Record: A version of this preprint was published at *La radiologia medica* on January 16th, 2022. See the published version at <https://doi.org/10.1007/s11547-021-01442-9>.

Abstract

Background: Pulmonary embolism (PE) associated with *Mycoplasma pneumoniae pneumonia* (MPP) in children has already attracted more attention. We aimed to evaluate the application of dual-energy spectral CT in diagnosing PE in children with MPP.

Methods: Eight-three children with MPP and highly suspected PE, underwent CT pulmonary angiography (CTPA) with spectral imaging mode. Noise, clot-to-artery contrast-to-noise ratio, image quality and diagnosis confidence were calculated and assessed on nine monochromatic image sets (40 to 80keV). CTPA images were observed for the presence, localization, and embolic degrees of PE. Emboli were divided between intra and extra-consolidation. For extra-consolidation clots, iodine concentration (IC) of perfusion defects and normal lung, perfusion defects of 4 children before and after the treatment were measured and compared. For intra-consolidation clots, IC of consolidation areas with clots and consolidation areas without clot were measured and compared.

Results: The optimal energy level for detecting PE in children was 55 keV. 116 clots (29 extra consolidations) were found in 25 children, IC of defect regions associated with PE was $0.69\pm 0.28\text{mg/mL}$ (extra-consolidations) and $0.90\pm 0.23\text{mg/mL}$ (intra-consolidations), both significantly lower than the $2.76\pm 0.45\text{mg/mL}$ in normal lungs and $10.25\pm 1.76\text{mg/mL}$ in consolidations without clots ($P<0.001$). Significant difference was found in the presence or absence of perfusion defects between occlusive clots and nonocclusive clots ($P<0.001$). IC of the perfusion defects significantly increased after treatment ($P<0.001$).

Conclusions: In spectral CTPA 55 keV images optimize PE detection for children. and MD images quantify pulmonary blood flow of PE, and may help to detect small clots and quantify embolic degrees.

Introduction

The incidence of Pulmonary embolism (PE) in children is increasing over the years[1], and it is associated with many risk factors[2]. *Mycoplasma pneumoniae pneumonia* (MPP) is generally believed a self-limiting illness, but in recent years, severe MPP, which causes various pulmonary and extrapulmonary complications, including PE, has already attracted more attention[3, 4].

CT pulmonary angiography (CTPA) has been the preferred method for diagnosing PE[5, 6], and pediatric studies reported a high diagnostic performance of CTPA for diagnosing PE in children using multidetector CT (MDCT) technology[7]. But the ability to detect tinnier and peripheral embolus is limited[8], especially in children with tinnier pulmonary artery diameter, and it cannot provide information for pulmonary perfusion. With the technological advances in MDCT in recent years, dual-energy spectral CT imaging is also used for the diagnosis of PE, it can generate both monochromatic CTPA images for morphologic analysis of PE and material decomposition images for quantitative depiction of pulmonary blood flow and perfusion defects. We reviewed imaging data of children with PE associated with MPP, who

underwent CT scan with dual-energy spectral CT imaging mode, to evaluate the application of dual-energy spectral CT imaging in diagnosing PE in children with MPP.

Materials And Methods

This study was approved by the Ethics Committees of our institution (No.2020-K-005), and the requirement of informed consent was waived.

Case inclusion

83 children with MPP and highly suspected PE, underwent CTPA with spectral imaging mode from December 2017 to November 2019 in our hospital. We diagnosed children with MPP based on the signs and symptoms of pneumonia, and positive laboratory results. Children were highly suspected of PE, when they developed extra symptoms, including chest pain, hemoptysis etc, with increased D-dimer level.

CT protocol

All children underwent examination on a Revolution CT scanner (GE Healthcare, WI, USA), infants or younger children (≤ 5 years) with poor compliance were scanned under sedation. The contrast-enhanced CT was performed using the dual-energy spectral imaging mode with fast tube voltage switching between 80 kVp and 140 kVp on adjacent views during a single rotation, fixed tube current was 200 mA. Children were injected with nonionic iodinated contrast material (Iodixanol 320, 320 mg/mL, Visipaque™; GE Healthcare, Cork, Ireland) at a dose of 1.2–1.8 ml/kg of body weight, with 75 ml as the maximum dose, using a high-pressure injector at a rate of 0.8–2.5 ml/sec. The automatic triggering technique was used for the contrast-enhanced scans with the region of interest (ROI) placed in the main pulmonary artery aorta to monitor the contrast rushing in, and data acquisition started 7 s after the signal attenuation in ROI reached the predefined threshold of 100 Hounsfield units (HU). Images were reconstructed at 0.625 mm slice thickness using the second-generation adaptive statistical iterative reconstruction (ASIR-V) algorithm with 50% strength (50%ASIR-V).

Image and data analysis

The original image data was transmitted to an AW4.7 workstation, and image processing and data measurement were performed using a dedicated Gemstone Spectral Imaging (GSI) Viewer software (GE Healthcare). The image data included 101 sets of virtual monochromatic images with photon energies from 40 keV to 140 keV and iodine-based material decomposition images. Two experienced radiologists (with 14 and 5 years of relevant experience) were aware that the studies were performed for clinically suspected PE, jointly performed objective measurement and subjective assessment on all image data, in case of any inconsistency, the final score was given after consultation. The 65 keV monochromatic images were initially used to identify clots and place region of interest (ROI), based on related literature[9]. ROI was placed on each endoluminal clot and pulmonary artery (PA) in the same slice. The ROI size changed based on the clot size and was drawn to include at least two thirds of the object on each image series. Clot contrast-to-noise ratio (CNR) was calculated using the following formula: $CNR = (CT$

number(PA) - CT number(clot)) / SD(PA). Background noise of the images was determined as the standard deviation of air measured presternally in front of the child. The CNR values of nine sets of monochromatic images at the following energy levels: 40, 45, 50, 55, 60, 65, 70, 75 and 80 keV were analyzed and compared. Other monochromatic image sets were discarded due to low CNR values for clots. Subjective assessment included overall CTPA image quality and diagnostic confidence were also performed on these 9 sets of monochromatic CTPA images. Image quality was evaluated with a 5-point scale (5, excellent; 4, good; 3, adequate; 2, suboptimal; 1, unacceptable or poor), diagnostic confidence for PE was evaluated with a 5-point scale (5, excellent confidence; 4, good confidence; 3, moderate confidence not affecting diagnosis; 2, insufficient confidence for diagnosis; and 1, without confidence).

The number of clots, their anatomical locations, degree of the embolic occlusions and other imaging manifestations were observed by the 2 reviewers on the optimal monochromatic energy level images and recorded. PE was grouped in occlusive (complete arterial occlusion with a stop of contrast medium enhancement) and non-occlusive (partial filling defect surrounded by contrast medium). The iodine-based material decomposition images with "rainbow" color-coded scheme were then presented to the same reviewers to visualize the iodine distribution and to further identify clots based on perfusion defects in lung parenchyma. In cases of different interpretations by the 2 reviewers, an additional consensus reading was performed.

Pulmonary consolidations were found in all children, and clots were found intra-consolidations and extra-consolidations. For clots that located extra-consolidations, perfusion defects were found on the iodine-based material decomposition images by using iodine distribution in the lung parenchyma, ROIs were placed on the perfusion defects and adjacent normal lung or normal lung on the other side in the same slice. For clots that located-intra consolidations, ROIs were placed on the consolidation areas with clots in proximal arteries which showed lower iodine enhancement and adjacent consolidation areas without clots with obvious enhancement. Necrotic areas, emphysematous areas, large vessels, and prominent artifacts were carefully avoided.

Statistical Analysis

All statistical analyses were performed using SPSS software (version 25.0). A value of $P < 0.05$ was considered statistically significant. background noise, CNR, and iodine concentration were presented as mean \pm standard deviation. The repeated measures analysis of variance with Bonferroni correction was performed on background noise, CNR from the different monochromatic image sets and paired t-test was performed on iodine concentrations between perfusion defect and normal area (consolidation area without clot). Subjective image quality and diagnostic confidence was tested using Friedman's test. Fisher's exact test was used to compare the correlation between embolic clots in CTPA images and perfusion defects in iodine-based material decomposition images.

Results

25 children(13 boys and 12 girls, median age 7 years, ranging from 3 years to 14 years) were diagnosed with PE on CTPA images.

Optimal Monochromatic Levels

Background noise and CNR

The noise on different monochromatic image sets differed based on x-ray energy, and the minimum value was observed at 80 keV, the mean noise on the 80 keV VMS images was statistically lower than the noise on 40 keV, 45 keV and 50 keV. CNR for clots differed on different monochromatic image sets, the maximum CNR value was observed at 40 keV, but there was no significant difference among the mean value on different energy levels. Background noise and CNR decreased as the monochromatic level increased (Table 1).

Table 1

Quantitative noise, CNR measurements and subjective assessment scores as function of energy level.

Energy level	40	45	50	55	60	65	70	75	80
Noise	19.64 ± 2.75	17.49 ± 2.17	15.66 ± 1.88	14.16 ± 1.84	12.97 ± 1.87	11.79 ± 1.85	11.05 ± 1.86	10.30 ± 1.87	9.93 ± 1.84
CNR	13.11 ± 3.04	12.65 ± 2.98	12.19 ± 2.96	11.71 ± 2.90	11.12 ± 2.93	10.60 ± 2.90	10.10 ± 2.98	9.58 ± 3.06	9.09 ± 3.15
Quality score	3.95 ± 0.21	4.17 ± 0.39	4.44 ± 0.51	4.78 ± 0.42	4.67 ± 0.57	4.00 ± 0.52	3.91 ± 0.42	3.52 ± 0.51	3.22 ± 0.42
Diagnosis confidence	3.91 ± 0.28	4.13 ± 0,34	4.47 ± 0.51	4.83 ± 0.38	4.70 ± 0.47	4.26 ± 0.54	4.00 ± 0.52	3.48 ± 0.51	3.17 ± 0.38

Subjective assessment

Subjective image quality score for PE for 55 keV monochromatic image set were statistically higher than all other image sets ($P < 0.05$), with the exception of 60 keV where no difference was observed ($P = 1.000$). And diagnosis confidence for PE for 55 keV monochromatic image set were statistically higher than all other image sets ($P < 0.05$), with the exception of 50, 60 and 65 keV ($P = 1.000$, $P = 1.000$ and $P = 0.104$, respectively) (Table 1).

PE detection and corresponding perfusion defect

113 clots in 25 children were found using the CTPA images: 88 clots in subsegmental pulmonary arteries, 23 clots in segmental pulmonary arteries and 2 clots in lobar pulmonary arteries. The use of combined monochromatic images and iodine-based material decomposition images, found additional 3 clots located in the subsegmental pulmonary arteries that were missed at first readings on CTPA images, with

positive perfusion defects on the iodine-based material decomposition images, and increased the PE detection to a total of 116. Among the 116 clots, 29 clots (21 occlusive and 8 nonocclusive) were found extra consolidations in 6 children, all occlusive clots and 2 nonocclusive clots (with 75% diameter reduction) showed clear evidence of wedge-shaped perfusion defects (Fig. 1). With Fisher's exact test, there was a significant difference ($P < 0.001$) in the presence or absence of perfusion defects between occlusive clots and nonocclusive clots (Table 2).

Table 2
Correlation between embolic clots in CTPA images and perfusion defects in iodine-based material decomposition images

Degree of embolic occlusions	Perfusion defect present	Without perfusion defect
Occlusive PE	21 (100%)	0 (0%)
Nonocclusive PE	2 (25%)	6 (75%)

Quantification of iodine concentration on iodine-based material decomposition images

Iodine concentration were measured in the perfusion defect areas associated with PE, and adjacent normal lung or normal lung on the other side in the same slice for the extra consolidation clots, and consolidation area with clots in proximal arteries and adjacent consolidations without clots were measured with same size ROI for the intra consolidation clots. For clots located extra consolidations, the mean iodine concentration of the perfusion defect areas associated with PE was 0.69 ± 0.28 mg/mL, ranging from 0.32 mg/mL to 1.20 mg/mL, the mean iodine concentration of the normal lung was 2.76 ± 0.45 mg/mL, ranging from 2.12 mg/mL to 3.64 mg/mL, and there was a significant difference between them ($P < 0.001$). 4 children with 20 occlusive clots that located extra consolidations underwent a follow-up spectral CT after anticoagulant and antibiotic treatment (ranging from 2 weeks days to 2 months), for observing the recovery of thrombus and pulmonary blood flow. Other children underwent follow-up non-enhanced CT, for evaluating therapeutic efficacy of MPP. 7 clots shrink, and 13 clots disappeared. Their perfusion defects disappeared on the iodine-based material decomposition images after treatment, the iodine concentration for the corresponding areas on the iodine-based material decomposition images before and after treatment were 0.43 ± 0.18 mg/mL and 3.10 ± 0.64 mg/mL, respectively, there was a statistical difference between them ($P < 0.001$) (Fig. 2). For clots that located intra consolidations, the mean iodine concentration of consolidations with clots and consolidations without clots were 0.90 ± 0.23 mg/mL (0.34–1.30 mg/mL) and 10.25 ± 1.76 mg/mL (7.13–13.48 mg/mL), respectively, with a statistically significant difference between them ($P < 0.001$). In addition, the iodine concentration of consolidations without clots was statistical higher than the iodine concentration of the normal lungs ($P < 0.001$) (Table 3).

Table 3
Iodine concentration of different areas in Iodine-based material decomposition images

ROI location	Clots located extra consolidations		Clots located intra consolidations	
	Perfusion defect with clots	Normal lung	Consolidations with clots	Consolidations without clots
Iodine concentration (mg/mL)	0.69 ± 0.28	2.76 ± 0.45	0.90 ± 0.23	10.25 ± 1.76

Radiation dose

The volumetric CT dose index (CTDIvol) for the dual-energy spectral CT acquisition was a fixed value at 3.06 mGy because a fixed scan protocol was used for the spectral CT imaging, and the dose-length product (DLP) value was 114.57 ± 26.25 mGy-cm(60.07-159.46 mGy-cm)

Discussion

The dual-energy scan mode used in our study is based on the single-tube, dual-tube voltage, fast-switching technique provides a set of virtual monochromatic images at energy levels ranging from 40 to 140 keV. The monochromatic images can reduce the averaging attenuation effect and increases contrast resolution[10]. Recent studies on the first-generation dual-energy spectral CT scanner (HDCT, GE Healthcare) have indicated that the optimal monochromatic energy level for PE detection is 65 keV in adult, with the lowest noise, highest subjective scores, and the second highest CNR[9]. However, our results indicated that the optimal monochromatic energy level had shifted towards lower values. The highest CNR for PE happened at 40 keV and the highest subjective assessment scores including image quality and diagnosis confidence happened at 55 keV, followed by 60 keV, and there was no statistical difference in subjective assessment scores between the 55 and 60 keV ($P > 0.05$). Considering the fact that 55 keV images had excellent CNR and the highest subjective assessment scores for the diagnosis of PE, 55 keV was considered the optimal energy level for detecting pulmonary embolism in children using dual-energy spectral CTPA. There are at least two reasons why the optimal energy level was lower than the previously reported values of 65 keV. First, the study population in our study were pediatric patients with smaller body sizes that are more dose efficiency and provide higher CNR at lower photon energy than adults, resulted in the highest CNR values at the lowest photon energy level, even though the image noise was still higher than the images with higher energy levels. Second, the CT scans were carried out on a second-generation dual-energy spectral CT scanner (Revolution CT) with more advanced iterative reconstruction algorithm (ASIR-V) that further suppresses image noise and favors the lower energy images in terms of balancing contrast and image noise.

In our study, 25 children with MPP were finally diagnosed with PE. Unlike PE associated with other risk factors in children, clots were mainly distributed in lobar and segmental arteries[7, 11], most of

clots(78,4%) in children with MPP in our study were found in subsegmental arteries. Timely diagnosis of PE and early anticoagulant therapy, are critical[4, 12]. Detecting the clot in pulmonary arteries is the diagnostic criteria for PE in conventional CTPA, but it can only provide morphologic evaluation, and the ability to detect tinnier and peripheral embolus is limited. Except the morphologic changes, the assessment of lung perfusion defect is an important part of diagnosis for PE,and it can improve the diagnosis rate of peripheral PE. Dual-energy (DECT) has been used in children for the diagnosis of PE, which can provide functional information for PE and identify pulmonary perfusion defects[13]. In addition, the dual-energy spectral CT imaging can reflect the true iodine concentration accurately and objectively[14], which was introduced for the diagnosis of PE in adult by quantitative depicting pulmonary blood flow and perfusion defects on Iodine-based material decomposition images[15], but there is not report on the application of dual-energy spectral in children for diagnosis of pulmonary embolism. In our study, clots were found intra consolidations and extra consolidations. For extra-consolidation clots, changes of iodine concentration distribution could be used to easily identify perfusion defects in the lung parenchyma, with typical territorial triangular shape with lobar, segmental, or subsegmental distribution[16]. which are more prominent in iodine-based material decomposition images than the emboli themselves, especially those small and peripheral emboli. In our study, we found 3 clots in subsegmental arteries that missed on CTPA images, which had positive perfusion defects on the iodine-based material images. This finding may suggest that iodine-based material decomposition images might be able to increase the sensitivity of CTPA for tiny peripheral clots, by detecting perfusion defects. Changes of iodine concentration can also provide quantitative measurement for pulmonary perfusion. And the iodine concentration of lung area with PE was statistically lower than normal lung, as earlier reports, and may be used to differentiate lesions with PE from normal lungs, and the presence or absence of perfusion defects may also be used to further differentiate the occlusive PE from nonocclusive PE. Owing to completely occluded or almost completely occluded vessels have a far greater influence than nonocclusive vessels, that can affect the therapeutic strategy[17].

The iodine concentration measurement could also be used to evaluate the treatment for PE. Our results indicated that besides the findings of emboli either decreased or disappeared on CTPA images, perfusion defect disappeared and iodine concentration increased in corresponding areas on material decomposition images also indicated the recovery of regional blood flow in the PE area. For clots that located intra consolidations, there was a significant difference between consolidations with clots and consolidations without clots, and the quantitative changes in iodine concentration could be suggestive for identification of PE intra consolidations. The iodine concentration of consolidations without clots was significantly higher than the iodine concentration of normal lungs ($P = 0.000$), which is conformed with the pathological mechanism. As is well known that inflammatory lesions usually have high blood supplies and are homogeneously enhanced because of the rich and dilatate capillaries stimulated by inflammation gradually[18].

Our study had some limitations: First, this study was based on a small sample size, further studies with large sample size are needed to confirm our results. Second, iodine concentration may be influenced by injection parameters, scan time and so on, that need to be normalized. Third, for clots intra

consolidations, necrosis and cavitation, atelectasis and emphysema were found in corresponding areas on follow-up CT, so we did not compare the iodine concentration of consolidations before and after the treatment.

Conclusion

The optimal energy level for detecting PE in children using dual-energy spectral CT pulmonary angiography was 55keV. The iodine-based material decomposition images can be used to quantitatively depict pulmonary blood flow of PE that occurred intra or extra-consolidations, and the perfusion defects may help to detect small clots and distinguish the degree of embolisms.

Abbreviations

MPP Mycoplasma pneumoniae pneumonia

CTPA Computed tomography pulmonary angiography

PE Pulmonary embolism

MD Material decomposition

ROI Region of interest

GSI Gemstone Spectral Imaging

Declarations

Ethics approval and consent to participate:

This retrospective study was approved by the Ethics Committees of Beijing Children's Hospital for using the data.

Consent for publication:

Not applicable.

Competing interests:

The author of this manuscript declares relationship with the following companies: GE Healthcare (JL). Authors with no financial ties to GE Healthcare (LY, JS, BW, TY and YP)

Funding:

The Special Fund of The Pediatric Medical Coordinated Development Center of Beijing Municipal Administration (XTCX201814 and XTZD20180104), and Advanced Innovation Center of Beijing (BHME-

201908). The funding bodies played no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Authors' contributions:

LY, JS, BW and TY carried out the studies, participated in collecting data, and drafted the manuscript. JL and YP helped to draft the manuscript. All authors read and approved the final manuscript.

Acknowledgements

None.

Availability of data and materials:

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

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Figures

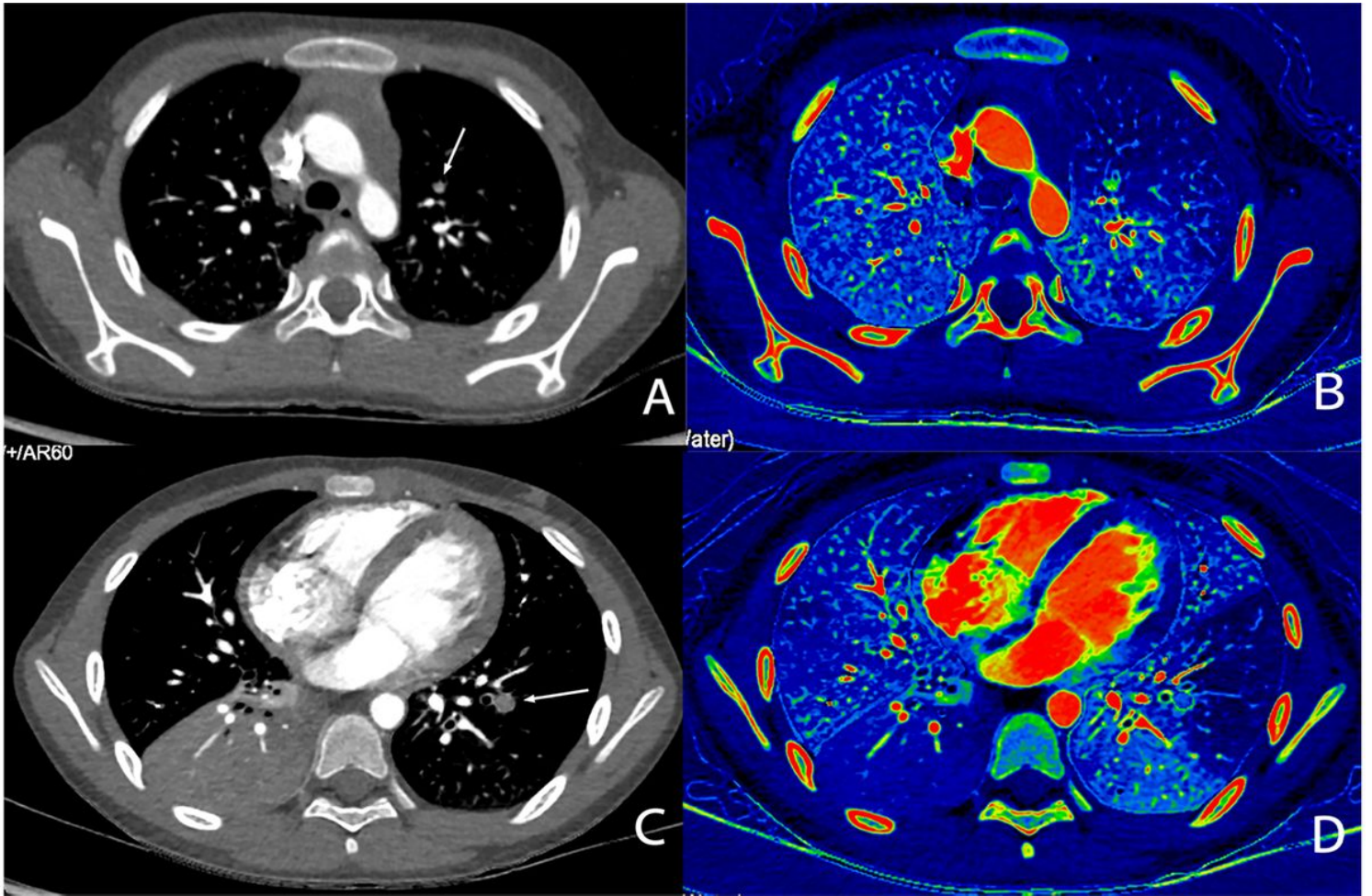


Figure 1

a school-age girl with fever and cough, D-dimer 11.326mg/L A, C Contrast-enhanced axial CT images showed filling defects(arrows) in segmental and subsegmental pulmonary arteries in the left upper lobe and left lower lobe, which located extra consolidation. B, D Transverse iodine-based material decomposition image showed wedge-shaped perfusion defects in the corresponding lobe.

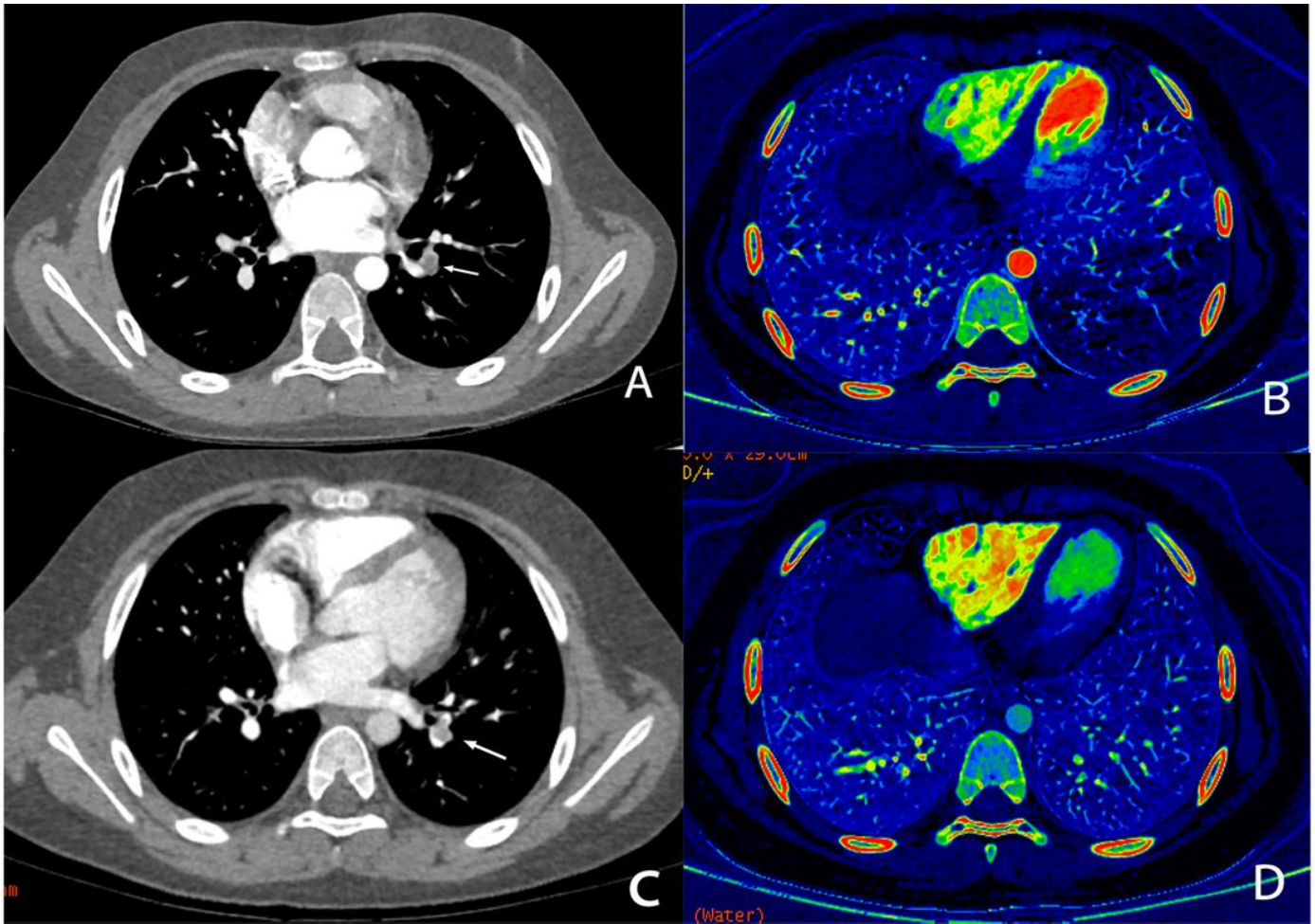


Figure 2

a school-age boy with fever and cough, D-dimer 4mg/L A, Contrast-enhanced axial showed filling defect(arrow) in segmental pulmonary artery in the left lower lobe. B, Transverse iodine-based material decomposition image showed a wedge-shaped perfusion defect in the corresponding lobe. C, D After 1 month of anticoagulant and antibiotic treatment, the contrast-enhanced axial showed the filling defect shrank(arrow), and perfusion defect on iodine-based material decomposition image of corresponding lobe disappeared.