The Lancet Infectious Diseases

Findings of acute pulmonary embolism in COVID-19 patients

--Manuscript Draft--

Manuscript Number:	THELANCETID-D-20-00678
Article Type:	Article (Original Research)
Keywords:	SAR-CoV-2, COVID-19, Pneumonia,Acute pulmonary embolism
Corresponding Author:	Yuanliang Xie, M.D. Central Hospital of Wuhan, Tongji Medical College, HUST Wuhan, Hubei CHINA
First Author:	Jianpu Chen, MD
Order of Authors:	Jianpu Chen, MD
	Xiang Wang, MD
	Shutong Zhang, MD
	Bin Liu, MD
	Xiaoqing Wu, MD
	Yanfang Wang, MD
	Xiaoqi Wang, PHD
	Ming Yang, MD
	Jianqing Sun, PHD
	Yuanliang Xie, MD
Manuscript Region of Origin:	CHINA
Abstract:	Summary Background Elevated level of D-dimer was reported in some patients with COVID-19 pneumonia on admission, especially in severe COVID-19 patients. However, it was still unknown this abnormality was associated with acute pulmonary embolism (APE). This study aimed to uncover the findings of APE diagnosed by computed tomography pulmonary angiography (CTPA) in COVID-19 patients. Methods This study retrospectively analyzed the results of COVID-19 patients who were admitted to out hospital and had undergone CTPA scans due to suspected APE and other clinical concerns. Relevant laboratory data and radiology images were collected for each patient. All diagnostic findings in laboratory data and CTPA features were confirmed according to clinical diagnostic criteria. Findings 1008 patients with COVID-19 pneumonia were hospitalized in our institution between January 2020 and February 2020. And 25 patients confirmed COVID-19 pneumonia who also underwent CTPA scans were enrolled. The median of D-dimer for the 25 patients was 6•06ug/ml (IQR, 1•90-14•31ug/ml). 10 patients were APE positive as presented on CTPA and the median D-dimer level was 11•07ug/ml (IQR, 7•12-21•66); 15 patients were APE negative and median D-dimer levels was 2•44ug/ml (IQR, 1•68-8•34). There is a significant difference (P < 0 . 05) between the two groups. Lymphopenia (lymphocyte count, median 0•81×10 9 /L, IQR, 0•55-1•05×10 9 /L) mostly occurred in 19 patients (76%). Serum CRP and B-type BNP frequently increased with a decline of Albumin and PaO 2 among 25 patients, however no significant differences in laboratory data but D-dimer were found between these two

	groups. APE in the 10 patients was found dominantly located in small branches of the pulmonary artery. Thrombus was partly or completely absorbed after anticoagulant therapy in 3 patients who underwent a follow-up CTPA. Interpretation Patients with COVID-19 pneumonia are at risk of APE. When D-dimer remarkable increases, CTPA facilitates the diagnosis of APE and assesses its change during the course. Special attention needs to be paid to the danger of APE associated with COVID-19 infection.

Summary

Background Elevated level of D-dimer was reported in some patients with COVID-19 pneumonia on admission, especially in severe COVID-19 patients. However, it was still unknown this abnormality was associated with acute pulmonary embolism (APE). This study aimed to uncover the findings of APE diagnosed by computed tomography pulmonary angiography (CTPA) in COVID-19 patients.

Methods This study retrospectively analyzed the results of COVID-19 patients who were admitted to out hospital and had undergone CTPA scans due to suspected APE and other clinical concerns. Relevant laboratory data and radiology images were collected for each patient. All diagnostic findings in laboratory data and CTPA features were confirmed according to clinical diagnostic criteria.

Findings 1008 patients with COVID-19 pneumonia were hospitalized in our institution between January 2020 and February 2020. And 25 patients confirmed COVID-19 pneumonia who also underwent CTPA scans were enrolled. The median of D-dimer for the 25 patients was 6·06ug/ml (IQR, 1·90-14·31ug/ml). 10 patients were APE positive as presented on CTPA and the median D-dimer level was 11·07ug/ml (IQR, 7·12-21·66); 15 patients were APE negative and median D-dimer levels was 2·44ug/ml (IQR, 1·68-8·34). There is a significant difference ($P < 0·05$) between the two groups. Lymphopenia (lymphocyte count, median $0·81\times10^9$/L, IQR, $0·55\text{-}1·05\times10^9$/L) mostly occurred in 19 patients (76%). Serum CRP and B-type BNP frequently increased with a decline of Albumin and PaO_2 among 25 patients, however no significant differences in laboratory data but D-dimer were found between these two groups. APE in the 10 patients was found dominantly located in small branches of the pulmonary artery. Thrombus was partly or completely absorbed after anticoagulant therapy in 3 patients who underwent a follow-up CTPA.

Interpretation Patients with COVID-19 pneumonia are at risk of APE. When D-dimer remarkable increases, CTPA facilitates the diagnosis of APE and assesses its change during the course. Special attention needs to be paid to the danger of APE associated with COVID-19 infection.

Introduction

In December 2019, the novel coronavirus, now known as SARS-CoV-2, rapidly outbroke in Wuhan City, and caused the COVID-19 epidemics which is not fully under control in early 2020 yet.[1,2] In the course of COVID-19 disease, most patients presented mild symptoms, such as fever, cough and sputum. However, a small portion (15~18%) of patients rapidly developed acute respiratory distress syndrome (ARDS), acute respiratory failure, and other serious complications.[3] By 29 February 2020, there have been 79394 patients diagnosed positive with COVID-19 in china, and 2838 patients died of this disease.[4] Our hospital, first reported the novel coronavirus-infected pneumonia, has been designated to admit only COVID-19 patients, and have hospitalized more than one thousand patients.

From the experience treating this disease, we found that D-dimer levels of serum increased in some COVID-19 patients. Elevated D-dimer is related to venous thromboembolism (VTE) and acute pulmonary embolism (APE), and APE can be fatal. However, APE cannot be diagnosed by the elevated D-dimer solely, because D-dimer can also be elevated in a series of other conditions such as cancer, peripheral vascular disease, pregnancy, and inflammatory diseases.[5] For patients suspected with APE, the timely and accurate diagnosis of APE, along with prompt treatment, significantly influence the patient management and clinical outcomes.[6,7] With the wide availability of multidetector CT scan, computed tomography pulmonary angiography (CTPA) has been an effective imaging technology to

detect APE and assess its severity.[8,9]

Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), two other coronavirus causing epidemic situation previously, can also lead to ARDS (1). However, no articles were found reporting pulmonary embolism occurred in patients with MERS coronavirus pneumonia, while only one case report mentioned APE detected by CTPA in SARS patients.[10] Several previous studies reported elevated D-dimer in patients with COVID-19,[1,3] but did not conclude whether these patients had APE.

Therefore, the aim of this retrospective study was to uncover the findings of APE diagnosed by CTPA in COVID-19 patients.

Methods

Study design and patients

This was a retrospective study done at a single center in Wuhan. Our institution hospitalized 1008 patients with COVID-19 pneumonia between January 2020 and February 2020. In this study, we retrospectively identified 25 COVID-19 patients in total, who had CTPA examinations during the COVID-19 course, by searching in the electronic medical records database in the Central Hospital of Wuhan between January 2020 and February 2020. Diagnosis of COVID-19 pneumonia was based on Guidelines for the Diagnosis and Treatment of Novel Coronavirus（2019-nCoV）Infection published by the National Health Commission of China (Trial Version 5).[11,12] All patients enrolled in our study were COVID-19 positive according to this clinical diagnostic criterion. They had undergone CTPA scans due to suspected APE and other clinical concerns, and also underwent D-dimer tests. Twenty patients received one or more follow-ups of D-dimer test, and 3 patients underwent a follow-up CTPA examination to assess remission of APE after anticoagulant therapy. The interval between CTPA examination and D-dimer test was less than 2 days.

This study was approved by the Ethics of Committees of The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology The need for patient informed consent was waived because of its retrospective nature.

CTPA image acquisition

CTPA examinations were performed in multi-detector CT scanners (Philips Ingenuity Core128, Philips Medical Systems, Best, the Netherlands; Somatom Definition FLASH; Siemens, Erlangen, Germany) by using a standard CTPA protocol. The whole chest was craniocaudally scanned from lung apex to the lowest hemidiaphragm for each patient in the supine position. All patients were instructed to hold breath to minimize motion artifacts, and CTPA images were acquired during a single breath-hold. Scan parameters were as follows: tube voltage of 120 kV, tube current of 100–300 mAs, collimation of 0·6-0·625mm, pitch of 0·937-1·0, table speed of 39·37 mm/s, gantry rotation time of 0·5s. Soft tissue reconstruction kernel (iDose4 for iCT, B30f for Definition FLASH) was used. 50–70 mL (volume calculated based on the patient's body weight) nonionic iodinated contrast media (iopamidol, Iopamiron 370; Bracco, Milan, Italy) was injected into an antecubital vein at a flow rate of 5·0 mL/s followed by a 25mL saline flush using a mechanical power injector. For optimal intraluminal contrast enhancement, the automatic bolus-tracking technique had the region of interest positioned at the level of the main pulmonary artery with a trigger threshold of 100 HU, and a fixed delay of 5s was employed for data acquisition. Images were reconstructed with a thickness of 1mm and an increment of 1mm or1·25 mm. The image data were transmitted to both post-processing workstations for multiplanar reconstructions

and picture archiving and communication systems (PACS).

Clinical data collection

Relevant clinical and laboratory data were obtained from electronic medical records. 4 clinical classifications were defined as: Mild, Moderate, Server, and Critical, according to previously published criterial.[11,13]

Image interpretation

All CT and CTPA image analysis were performed by two radiologists experienced in thoracic radiology (Yuanliang Xie, with 20 years of experience; Xiang Wang, with 22 years of experience) blinded to clinical information. After separate evaluation, disagreements were resolved through discussion until consensus was reached. Based on previously published articles,[14] four stages of lung involvement were defined based on CTPA images at lung widow: (1) Early stage, (2) Progressive stage, (3) Peak stage. (4) Absorption stage. The lung window was set as below: width, 1500 HU; level, -700 HU. And CTPA images were analyzed on mediastinal window setting (width, 250 HU; level, 50 HU). Sites of APE detected by CTPA were recorded.

Statistical analysis

Continuous variables were expressed as median with its interquartile range (IQR), and compared with the Mann-Whitney U test. Categorical variables were described as number (%), and proportions for categorical variables were compared using the Fisher exact test. A two-sided α of less than 0·05 was considered statistically significant. Statistical analyses were done using the SPSS version 21·0 software (IBM, New York, USA).

Role of the funding source

There was no funding source for this study.

Results

A total of 25 patients (15 males and 10 females) were retrieved from medical record. The median age was 65 years old (IQR, 56-70, range, 36-78 years). Fifteen patients were diagnosed positive for SARS-CoV-2 infection by real time reverse-transcription–polymerase chain-reaction (RT-PCR); 10 patients negative in RT-PCR test were diagnosed COVID-19 positive according to clinical diagnostic criteria. 11 cases (44%) were moderate, 14 cases (56%) were severe according to diagnostic criterial of COVID-19 classification. Based on the COVID-19 staging in CTPA images at lung window, three (12%) patients were at progressive stage, 16 (64%) were at peak stage, and 6 (24%) were at absorption stage. Several chronic medical diseases, including hypertension (ten [40%]), diabetes (five [20%]), and cardiovascular disease (four [16%]) were recorded in some patients. By Feb 29, 2020, nine patients remained in hospital under close observation with improvement in symptoms, 10 patients were discharged and 6 patients (2 with APE and 4 without APE on CTPA) died. Relevant clinical and radiological records of patients involved in this study are presented in Table 1.

Abnormalities in laboratory tests were shown at the time when CTPA were performed. An increase of D-dimer level (median 6·06ug/ml, IQR, 1·90-14·31ug/ml) was detected in all 25 patients. 10 patients were APE positive according to CPTA images, and have D-dimer levels with median value at 11·07ug/ml [IQR, 7·12-21·66]; 15 patients were APE negative, and have D-dimer levels with median

value at 2·44ug/ml [IQR, 1·68-8·34]. There is a significant difference in D-dimer levels between the two groups with $P < 0·05$. CRP (median, 3·12 mg/dL; IQR, 2·16-6·16) increased in 21 patients (84%). White blood cell count (median, $6·90\times10^9$/L; IQR, 5·44-9·48) increased in 5 patients (20%) and decreased in 2 patients (8%). Lymphocyte count (median, $0·81\times10^9$/L; IQR, 0·55-1·05) decreased in 19 patients (76%) and normal in 6 patients (28%). B-type BNP (median, 142·00 pg/ml; IQR, 81·70-301·30) increased in 16 cases. Albumin (median, 33·70g/L; IQR, 30·10-35·55) was decreased with a decline of the ratio of Albumin to Globulin in almost all cases. Arterial blood gas analysis demonstrated PaO_2 declined (median, 69·00mmHg; IQR, 58·50-94·00) in 16 out of 25 patients. Other test results including ALT, AST, GGT, BUN, $PaCO_2$ and SO_2 were mostly normal. No significant difference was found between APE positive and APE negative groups for all laboratory data except for D-dimer. The median time from onset of COVID-19 symptoms to CTPA examination was 10 days (IQR, 7·00-10·75) in patients with APE positive, and 10 days (IQR, 7·00-19·00) in patients with negative APE. And there is no significant difference between two groups with $P > 0·05$. Relevant laboratory results of the 25 patients are presented in Table 2. Figure 1 indicates D-dimer values for patients (n=25) tested over multiple days. Color-coded squares correspond to D-dimer values for different dates. Red arrows indicate patients deceased during treatment.

In addition, twenty patients were treated with anticoagulant therapy (low molecular weight heparin, 0·6mg/kg per 12hours) regardless to the findings of APE in CTPA, and underwent a follow-up D-dimer test afterwards. The D-dimer levels decreased in all patients.

According to chest CT image staging criterial of COVID-19, 3 patients were in progressive stage, 16 were in peak stage and 6 were in absorption stage. Ten (40%) patients (1 progressive stage, 7 peak stage and 2 absorption stage), presented APE positive on CTPA imaging, fifteen (60%) patients (2 progressive stage, 9 peak stage and 4 absorption stage) presented APE negative. Of note, deep vein thrombosis (DVT) was detected by ultrasonography in one patient with negative APE finding in CTPA. For the 3 patients who have undergone a follow-up CTPA examination after anticoagulant therapy, all APE lesions were smaller compared with the first CTPA examination, and the corresponding D-dimer levels also decreased. In all these patients, filling defects occurred in the small branches of each lobe or segmental artery, while not revealed in pulmonary trunk on CTPA images. Among 10 patients with APE, six patients (60%) had bilateral pulmonary artery branches with thrombosis, and 4 patients (40%) had unilateral pulmonary artery branches with thrombosis. The thrombus-prone sites are the right lower lobe (70%), left upper lobe (60%), bilateral upper lobe (40%) and right middle lobe (20%). Relevant characteristics of the 10 patients with APE involved in this study are presented in Table 3. Figure 2-3 shows typical images of APE in patients with COVID-19.

Discussion

Similar to SARS-CoV-2, two previous known epidemic coronavirus infecting human beings, SARS and MERS, also caused severe lung damage and acute respiratory distress syndrome (1). It was estimated that more than 10000 cumulative people have been infected by MERS and SARS in the past two decades, with mortality rates of 37% for MERS-CoV and 10% for SARS-CoV.[15,16] Global concerns and efforts have been made to diagnose and treat these diseases. However, no articles have previously reported that APE occurred in patients with MERS pneumonia, only one case report mentioned PE in SARS patients.[10] Our study reports the finding of APE in COVID-19 patients, especially among patients at severe or worse stages. Therefore, we should be alert to the APE events, which can be fatal, in patients with COVID-19 pneumonia.

In this study, we demonstrate the clinical and imaging characteristics of 25 patients with COVID-19 pneumonia suspected of pulmonary embolism. Results suggest that elevated D-dimer is possibly common in patients with COVID-19, especially those at severe stage. When D-dimer levels elevated, CTPA shall be applied to detect APE and monitor the changes of APE in patients with COVID-19.

It is well known that elevated D-dimer is associated with APE, and also is associated with a series of other conditions such as DVT, cancer, peripheral vascular disease, pregnancy, and inflammatory diseases.[5] Therefore, CTPA examinations and ultrasonography are very important for COVID-19 patients with rising D-dimer level to correctly diagnose APE and DVT. Unfortunately, only one COVID-19 patient in our study underwent lower-extremity ultrasonography for with suspected DVT. Our study demonstrates that severe stage COVID-19 patients with elevated D-dimer level are with high occurrence rate of APE. Future prospective studies with a large sample may better illustrate whether the COVID-19 patients have risks of DVT. No significant difference between APE positive patients and APE negative ones was found for blood gas test results, such as $PaCO_2$, PaO_2 and SO_2, which might suggest severe hypoxemia in COVID-19 patients does not directly relate to APE but relates to the severity of lung inflammation or both.

In our study, APE lesions only occurred in the small branches of each lobe artery. Six patients (60%) presented with thrombus in bilateral pulmonary artery branches, and 4 (40%) in unilateral pulmonary artery branches, which indicates the thrombus might derive from other sites, such as deep vein of lower extremity.[10,17] One patient in our study underwent ultrasonography of deep vein of lower extremity, and result found thrombus in the deep vein of lower extremity. In addition, three patients in our study underwent a follow-up CTPA examination after anticoagulant therapy, as the D-dimer levels decreased, the size of APE lesions became smaller compared with the first CTPA examination, suggesting the importance role of CTPA in monitoring the changes of APE after anticoagulant therapy.

The reason for APE's occurrence in COVID-19 patients is unclear. There is no relevant animal research about this yet. Only a few reports stated APE in SARS patients in previous studies. Autopsy results of multiple series of SARS patients showed that vascular thromboses were common in lung specimens, suggesting the underlying thrombophilia in the lungs. However, another autopsy study of 8 SARS patients showed that PE was found in the pulmonary arteries in 4 patients, in which 3 patients had deep vein thrombosis (DVT), which suggests that pulmonary artery thrombus derive from the deep vein of lower limb.[10] Due to the COVID-19 quarantine requirement, the reduced physical movements results in higher risk of DVT in patients' lower limbs. Previous study[18] also demonstrated that epithelial damage, platelets and endothelial cells dysfunction may contributed to thrombosis associated influenza viral pneumonia. However, there is no sufficient autopsy study for COVID-19 fatalities, hence the pathogenesis of APE in patients with COVID-19 could not be confirmed yet.

Not all patients in this study were positive in RT-PCR test, but all patients were diagnosed positive for SARS-CoV-2 infection. The sensitivity of RT-PCR is low (estimated at 70·6%) on initial positive RT-PCR,[19] resulting in false negative RT-PCR tests for many patients. Besides, due to the severe shortage of the 2019-nCoV nucleic acid detection kits in Wuhan at that time,[20] multiple tests for patients with previous negative results could not be afforded. Therefore, we relied on clinical diagnostic criteria other than RT-PCR in this study.

This study has several limitations: First, the sample size of this study is relatively small. However, the 10 incidences of acute pulmonary embolism in the 25 patients suggests a frequent occurrence. Hereby we call for more attention to be paid regarding to APE in the course of COVID-19 treatment. Second, the nature of this study is retrospective, which could not shed the light on the statistics of APE in all

COVID-19 patients, so a possible prospective study might be needed to investigate the true occurrence rate and the fatality rate with APE complication in patients with COVID-19 pneumonia. In addition, ultrasonography for screening lower extremity deep vein thrombosis was not performed for these patients for various reasons, thus whether inflammation or secondary lower extremity deep vein thrombosis was the primary cause of acute pulmonary embolism could not be verified.

In conclusion, special attends need to be paid to the risk of APE due to COVID-19 infection. When D-dimer abnormally increases, CTPA examination can identify APE. Hereby we urgently call for special considerations to other medical professionals involved in this epidemic situation.

Contributors

Yuanliang Xie, Xiang Wang, Shutong Zhang and Jianpu Chen conceived and designed the study. Jianpu Chen, Yanfang Wang, and Xiaoqing Wu contributed to the literature search. Yuanliang Xie, Jianpu Chen, and Bin Liu contributed to data collection. Yuanliang Xie, Jianqing Sun, Xiaoqi Wang, and Ming Yang contributed to data analysis and data interpretation. Yanfang Wang, Xiaoqing Wu, and Bin Liu contributed to the tables and figures. Jianqing Sun,_Yuanliang Xie and Jianpu Chen contributed to writing of the report.

Declaration of interests

We declare no competing interests.

Acknowledgments

The authors would like to thank all of the emergency services, nurses, doctors, and other medical workers from many provinces of China for their efforts to combat the COVID-19 outbreak.

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Table 1: Clinical characteristics of COVID-19 patients with suspected APE

	Total (n=25)	APE (n=10)	Non-APE (n=15)	P value
Characteristics				
Age (years)	65 (56·5-70)	66·5 (57-71.5)	65 (54-70)	0·605
Gender (n)				0·691
Male	15 (60%)	6 (60%)	9 (60%)	..
Female	10 (40%)	4 (40%)	6 (40%)	..
Time to CTPA (days)	10 (7-16.5)	10 (7-10·75)	11 (7-19)	0·397
Any comorbidity (n)				
Hypertension	10 (40%)	6 (60%)	4 (27%)	0·034
Diabetes	5 (20%)	3 (30%)	2 (13%)	0·699
CVDs	4 (16%)	2 (20%)	2 (13%)	0·532
Smoking	6 (24%)	2 (20%)	4 (27%)	0·023
Surgery	6 (24%)	2 (20%)	4 (27%)	0·545
DVT	1 (4%)	0	1 (7%)	..
Cancer	0	0	0	..
Clinical classification (n)				0·653
Mild	0	0	0	..
Moderate	17 (68%)	6 (60%)	11 (73%)	..
Severe	8 (32%)	4 (40%)	4 (27%)	..
Critical	0	0	0	..
Stage of imaging (n)				0·545
Early	0	0	0	..
Progressive	3 (12%)	1 (10%)	2 (13%)	..
Peak	16 (64%)	7 (70%)	9 (60%)	..
Absorption	6 (24%)	2 (20%)	4 (27%)	..
Outcome (n)				
Hospitalization	9 (36%))	3 (30%)	6 (40%)	..
Discharged	10 (40%)	5 (50%)	5 (33%)	..
Died	6 (24%)	2 (20%)	4 (27%)	..

Data are median (IQR) or n (%). The rate of moderate and severe type compared with Fisher's exact test between group APE and group Non-APE. The rate of progressive and peak stages compared with Fisher's exact test between group APE and group Non-APE. CTPA=computed tomography pulmonary artery; APE=acute pulmonary embolism; CVDs=cardiovascular diseases; DVT=deep vein thrombosis.

Table 2: Laboratory data of COVID-19 patients with suspected APE

	Normal range	Median (IQR)			P value
		Total (n=25)	APE (n=10)	Non-APE (n=15)	
D-dimer (ug/ml)	0-1	6·06 (1·90-14·31)	11·07 (7·12-21·66)	2·44 (1·68-8·34)	0·003
CRP (mg/dL)	0-0·6	3·12 (2·16-6·16)	3·09 (2·21-7·03)	3·41 (2·16-6·19)	0·978
WBCC (*10^9/L)	3·5-9·5	6·90 (5·44-9·48)	7·03 (6·17-10·02)	6·25 (3·70-9·18)	0·428
LC (*10^9/L)	1·1-3·2	0·81 (0·55-1·05)	0·88 (0·64-1·14)	0·78 (0·54-0·86)	0·285
BNP (pg/mL)	0-100	142·00 (81·70-301·30)	213·50 (131·75-500·03)	95·90 (55·00-245·30)	0·091
ALT (U/L)	9-50	32·00 (19·65-56·75)	40·85 (24·50-78·48)	21·90 (13·30-54·30)	0·160
AST (U/L)	15-40	37·90 (23·70-48·50)	43·70 (22·16-58·50)	35·70 (24·50-40·00)	0·338
GGT (U/L)	10-60	35·00 (20·65-82·50)	49·00 (25·16-125·73)	29·50 (15·70-61·60)	0·177
Alb (g/L)	40-55	33·70 (30·10-35·55)	33·90 (30·18-35·90)	33·50 (29·70-35·40)	0·683
Alb/Glb	10-60	1·00 (0·80-1·20)	1·10 (0·86-1·33)	1·00 (0·79-1·17)	0·285
Cr (μmol/L)	57-111	65·70 (55·45-81·40)	65·30 (54·05-75·95)	66·70 (63·50-81·90)	0·683
BUN (mmol/L)	2·9-8·2	5·66 (4·05-6·96)	5·78 (4·62-8·10)	5·66 (3·84-6·58)	0·338
$PaCO_2$ (mmHg)	35-45	38·00 (34·50-43·50)	39·00 (33·00-47·00)	38·00 (36·00-42·00)	0·531
PaO_2 (mmHg)	80-100	69·00 (58·50-94·00)	76·50 (58·25-102·75)	69·00 (57·00-88·00)	0·723
SO_2 (%)	91·9-99	95·00 (90·00-97·50)	96·00 (90·75-98·25)	95·00 (90·00-97·00)	0·807

Continuous variables were expressed as median (IQR) and compared with the Mann-Whitney *U* test between group APE and group Non-APE. IQR=interquartile range; CRP=c-reacted protein; WBCC=white blood cell count; LC=lymphocyte count; ALT=alanine aminotransferase; AST=aspartate transaminase; GGT=glutamyl transferase; Alb=albumin; Glb=globulin; Cr=Creatinine; BUN=blood urea nitrogen; BNP=brain natriuretic peptide; CVDs=cardiovascular diseases; DVT=deep vein thrombosis; $PaCO_2$=arterial partial pressure of carbon dioxide; PaO_2=arterial oxygen partial pressure; SO_2=oxygen saturation.

Table 3: Characteristics of COVID-19 patients with APE

	Age (y)	Sex	RT-PCR	D-dimer (ug/ml)		Sites of the APE	Outcome
				First	Second		
Patient 1	65	M	P	20·41	4·57	L2、R1、R3	Hospitalization
Patient 2	70	M	P	13·72	12·97	L1、R3	Hospitalization
Patient 3	57	M	P	21·44	3·65	L1、L2、R1、R2、R3	Hospitalization
Patient 4	76	F	N	121·8	19·94	L2、R3	Died
Patient 5	36	F	N	8·42	7·28	L1、L2、R2、R3	Discharge
Patient 6	64	M	P	3·87	0·81	R3	Discharge
Patient 7	68	M	P	8·02	1·33	L2	Discharge
Patient 8	57	F	P	8·32	1·23	R3	Discharge
Patient 9	70	M	N	22·32	..	L1、L2、R1	Died
Patient 10	77	F	N	4·40	4·08	R1	Discharge

APE=acute pulmonary embolism; y=year; M=male; F=female; RT-PCR=real-time reverse transcription polymerase chain reaction; P=positive; N=negative; NA=not applicable; L1=left upper lobe; L2=left lower lobe; R1=right upper lobe; R2=right middle lobe; R3=right lower lobe.

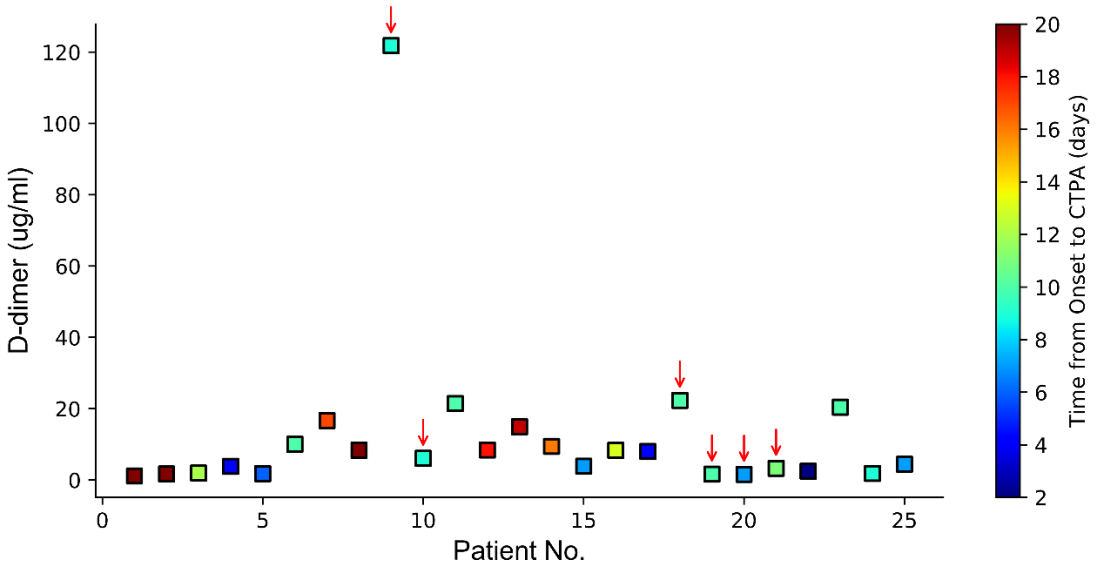

Figure 1: **25 Serum (D-dimer) levels in patients with COVID-19**

D-dimer values for patients (n=25) tested over multiple days. Color-coded squares correspond to D-dimer values for different dates. Red arrows indicate patients deceased during treatment.

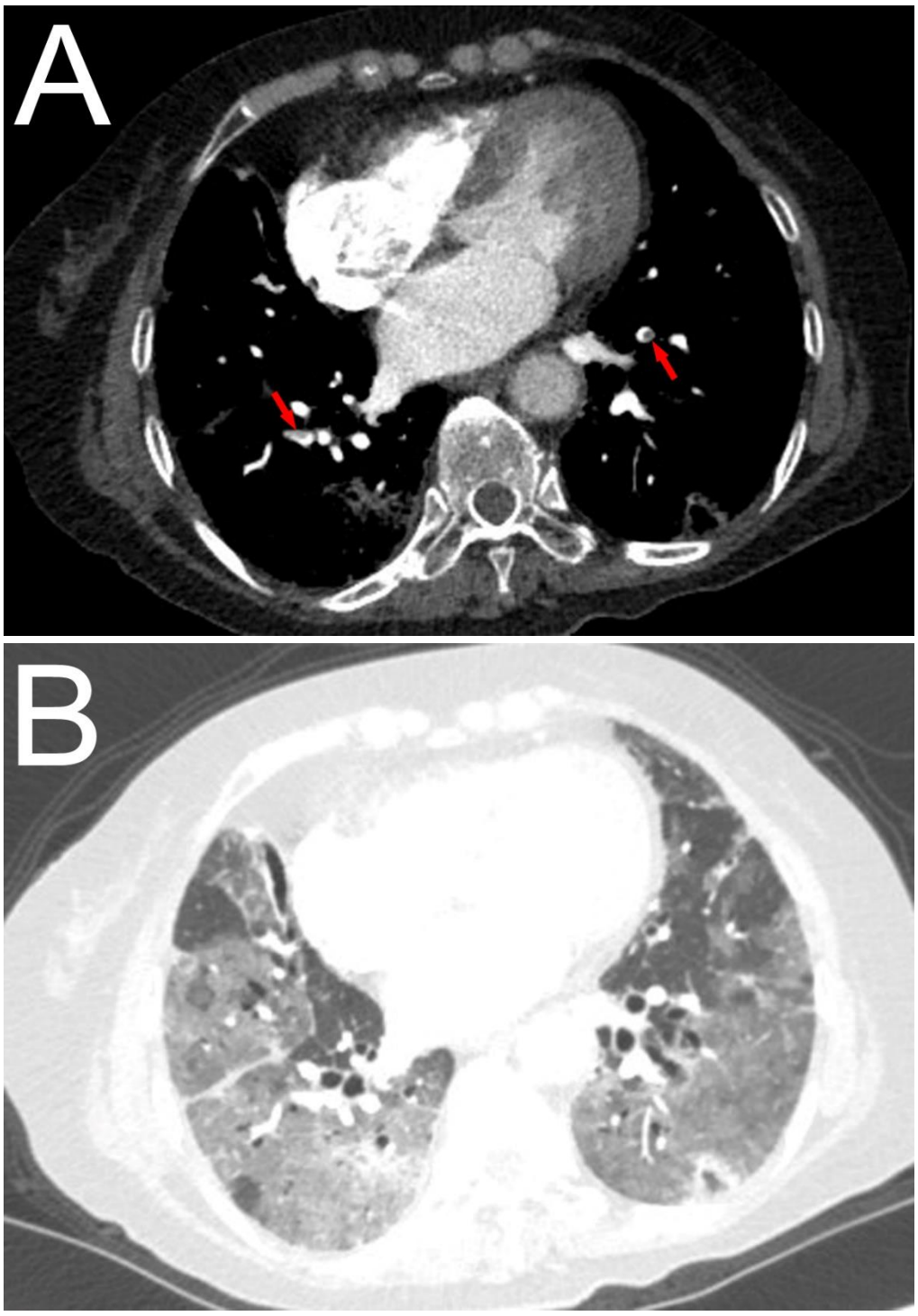

Figure 2: **CTPA findings in a 76-year-old female patient with severe COVID-2019 pneumonia.** (A): thrombus (arrow) occurred in bilateral lower lobe pulmonary artery on axial CTPA image. (B): axial CT image showed that density of both lungs increased widely, showing a "white lung" appearance, indicating the patient was at peak stage.

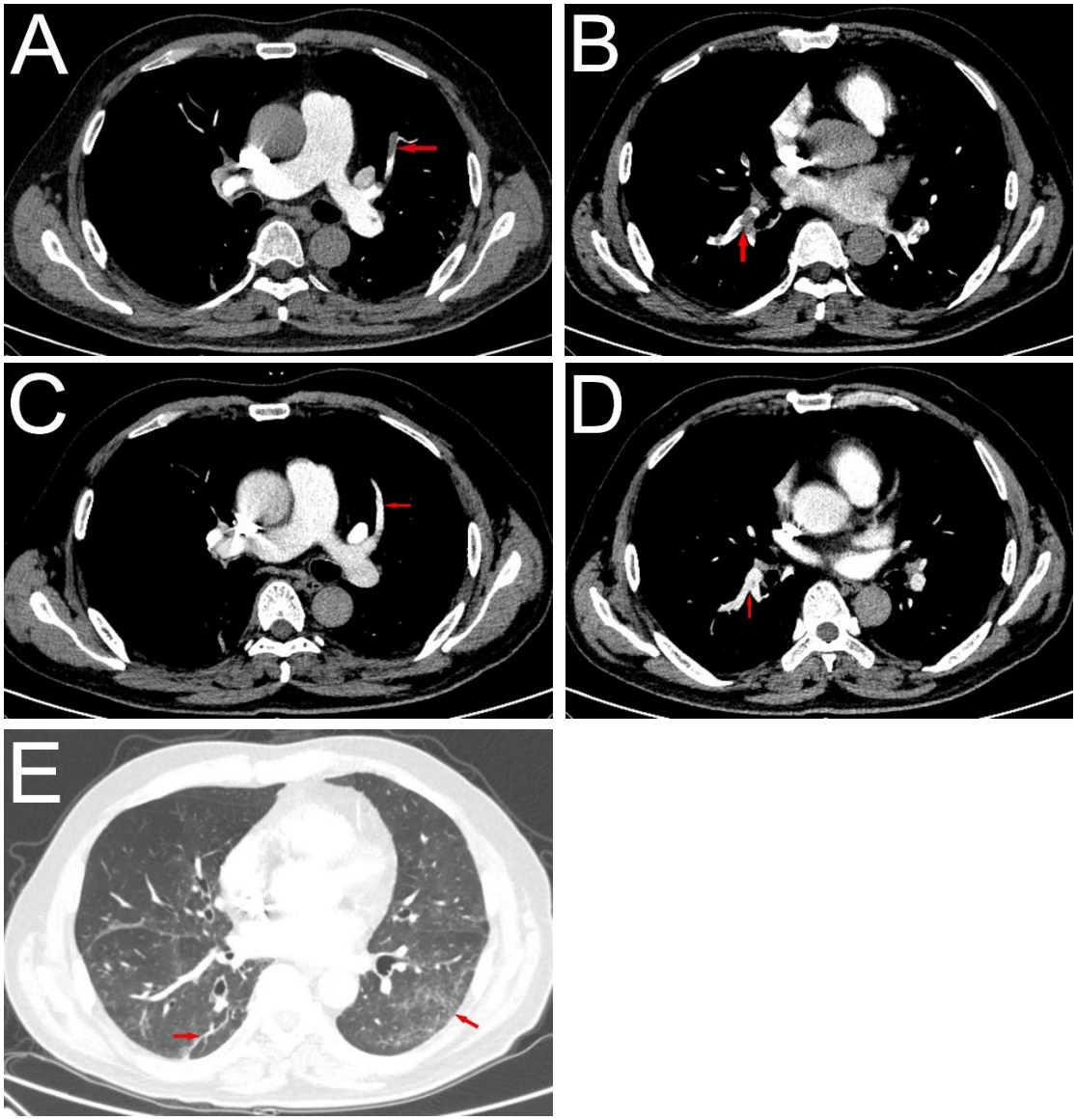

Figure 3: **CTPA findings in a 57-year-old male patient with moderate COVID-19 pneumonia.** (A, B) The first CTPA examination: thrombus (thick arrow) occurred in left upper lobe pulmonary artery and right lower lobe pulmonary artery. (C, D) Follow-up CTPA examination: corresponding APE lesions (thin arrow) at the same location were absorbed after anticoagulant therapy. (E) The first CTPA images at lung window: axial CT image showed a little fibrous stripe (arrow), indicating the patient was at absorption stage.

Figure 1

Click here to download Figure Fig.1.tif

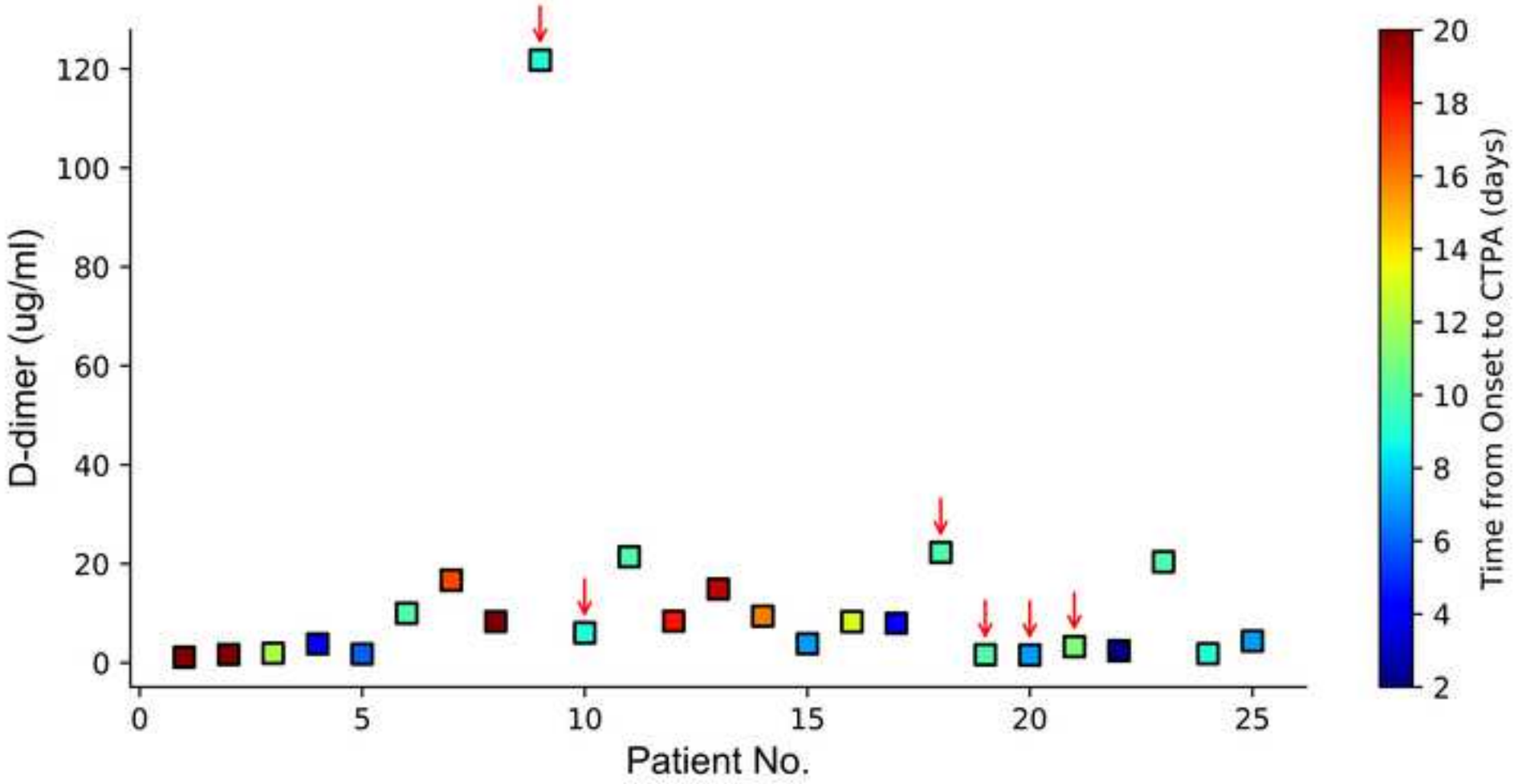

Figure 2A

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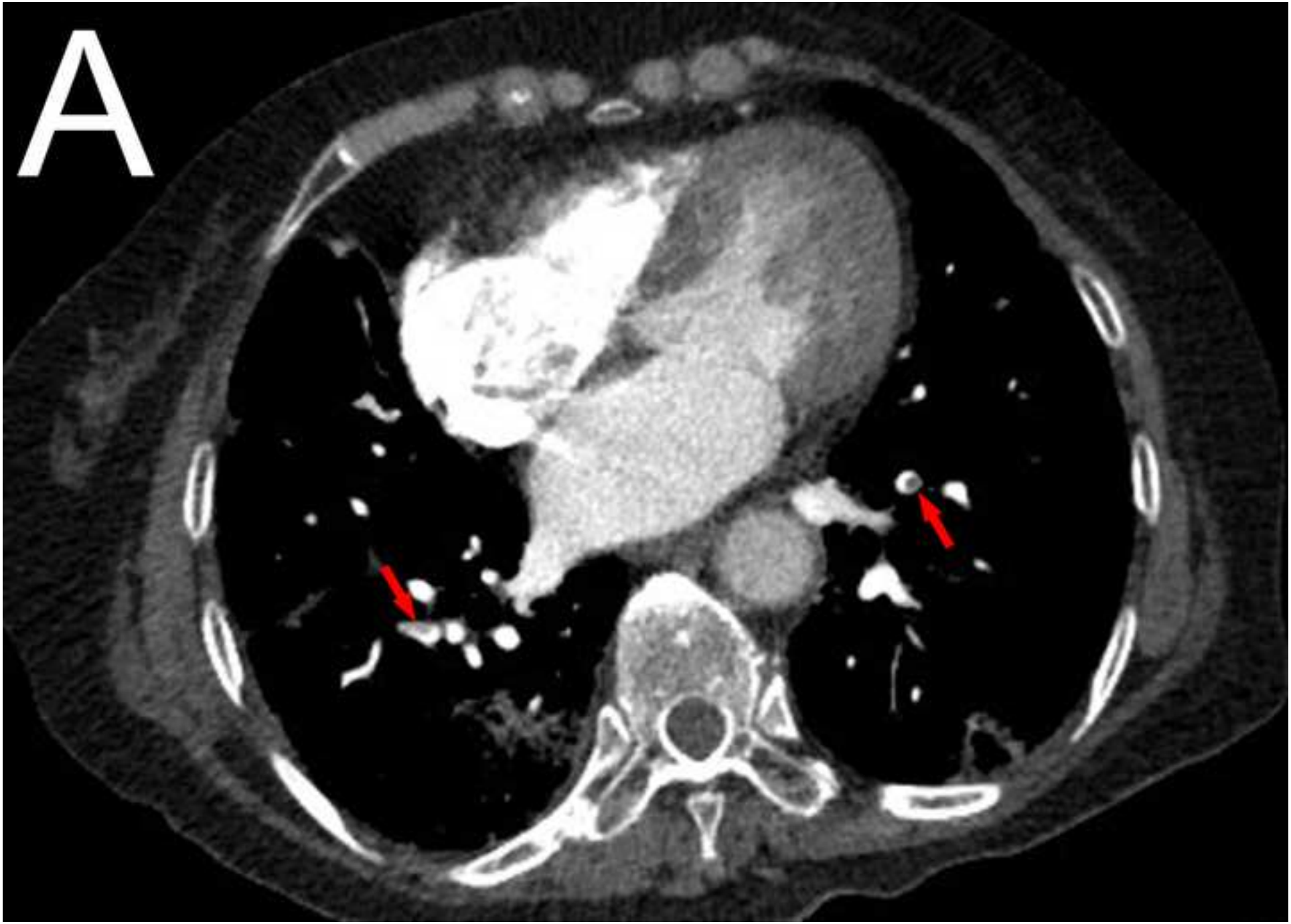

Figure 2B

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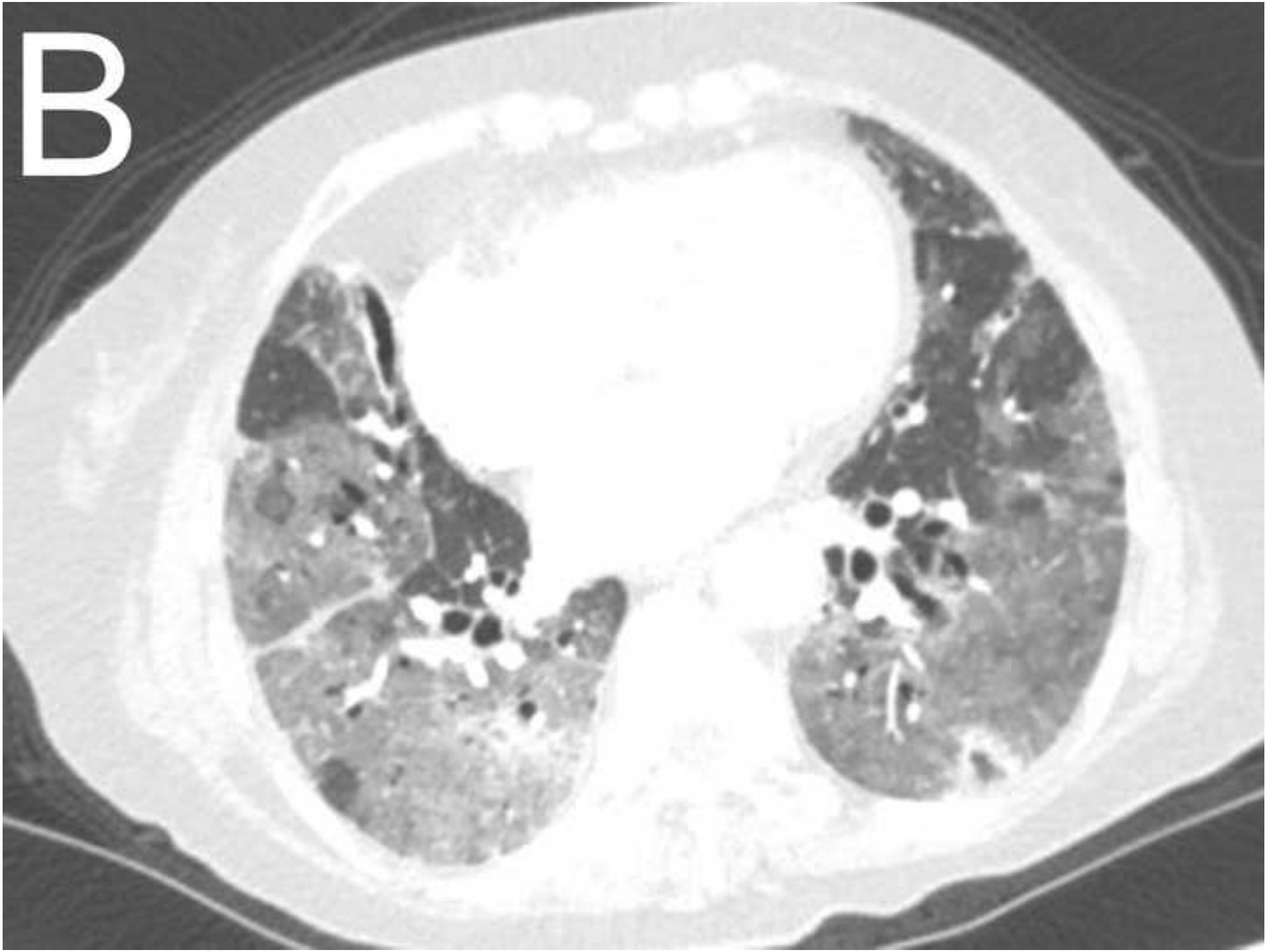

Figure 3A

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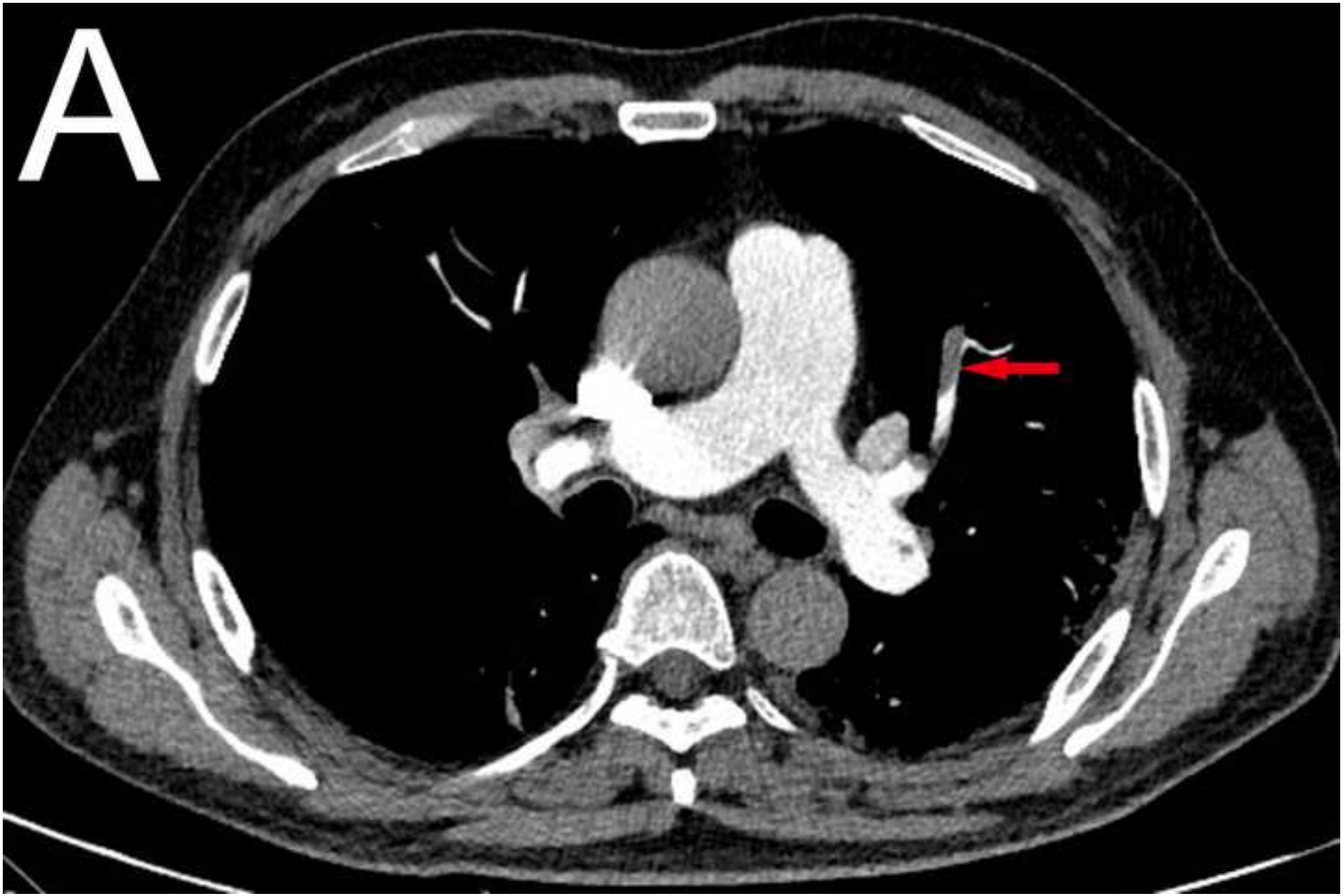

Figure 3B

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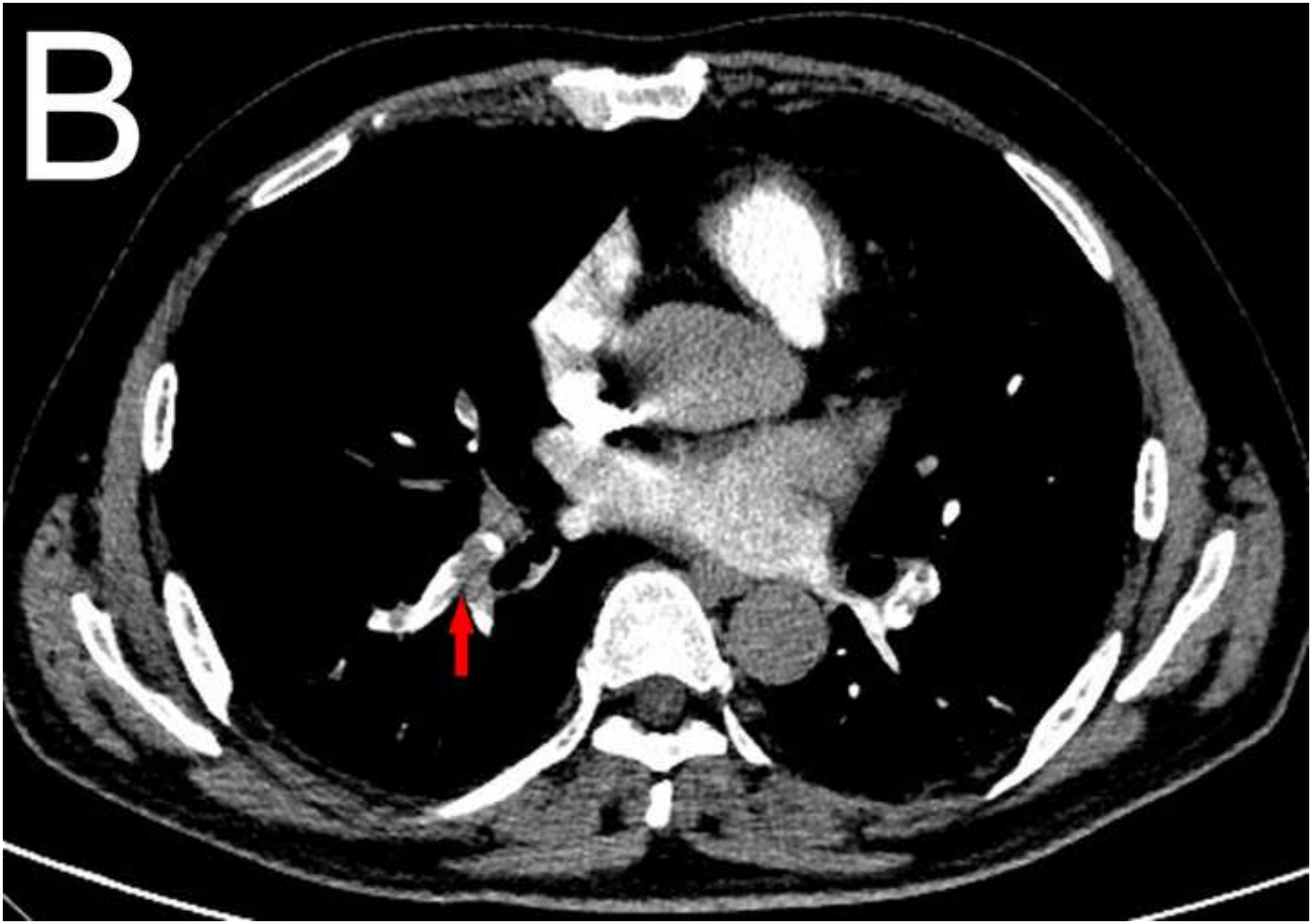

Figure 3C

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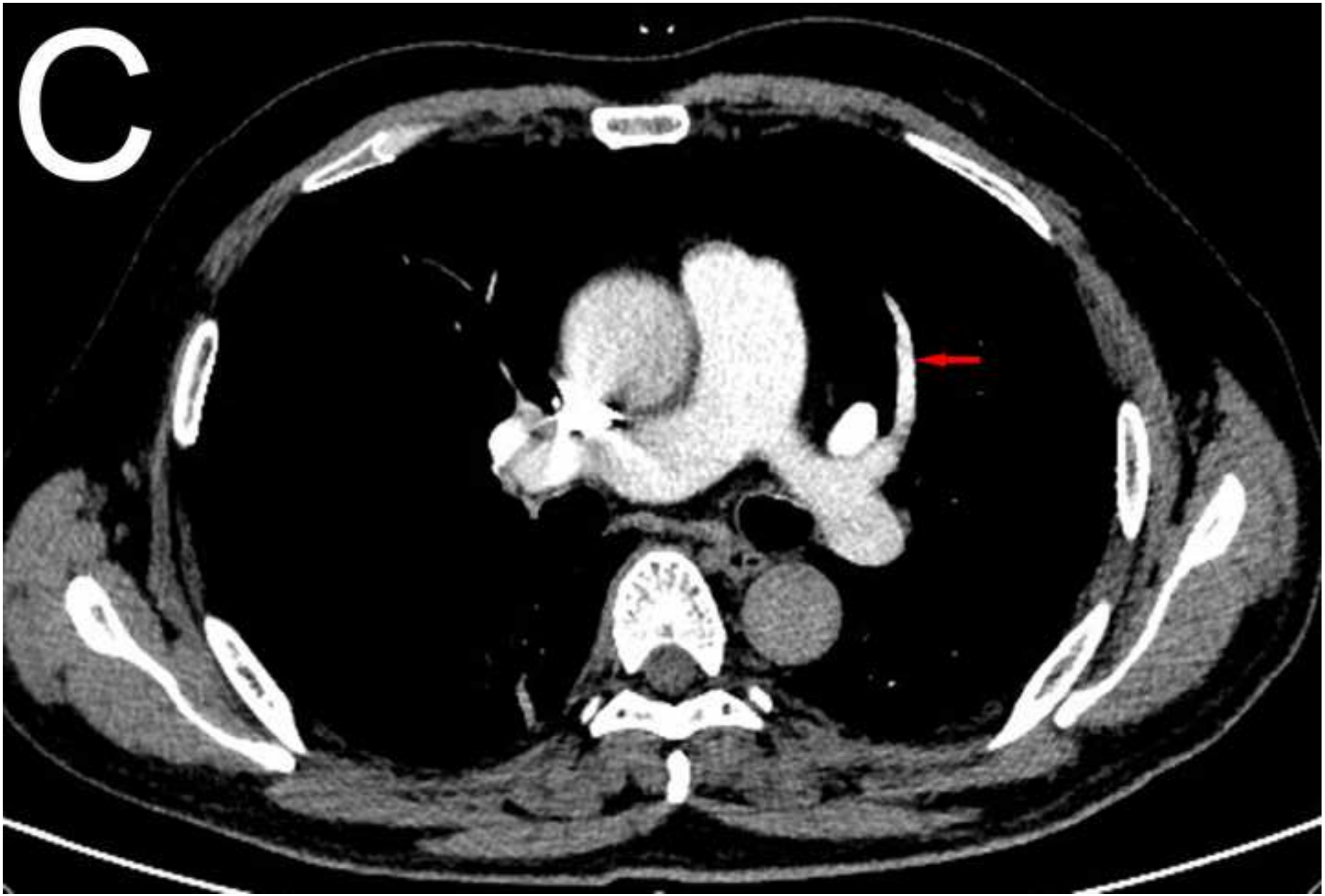

Figure 3D

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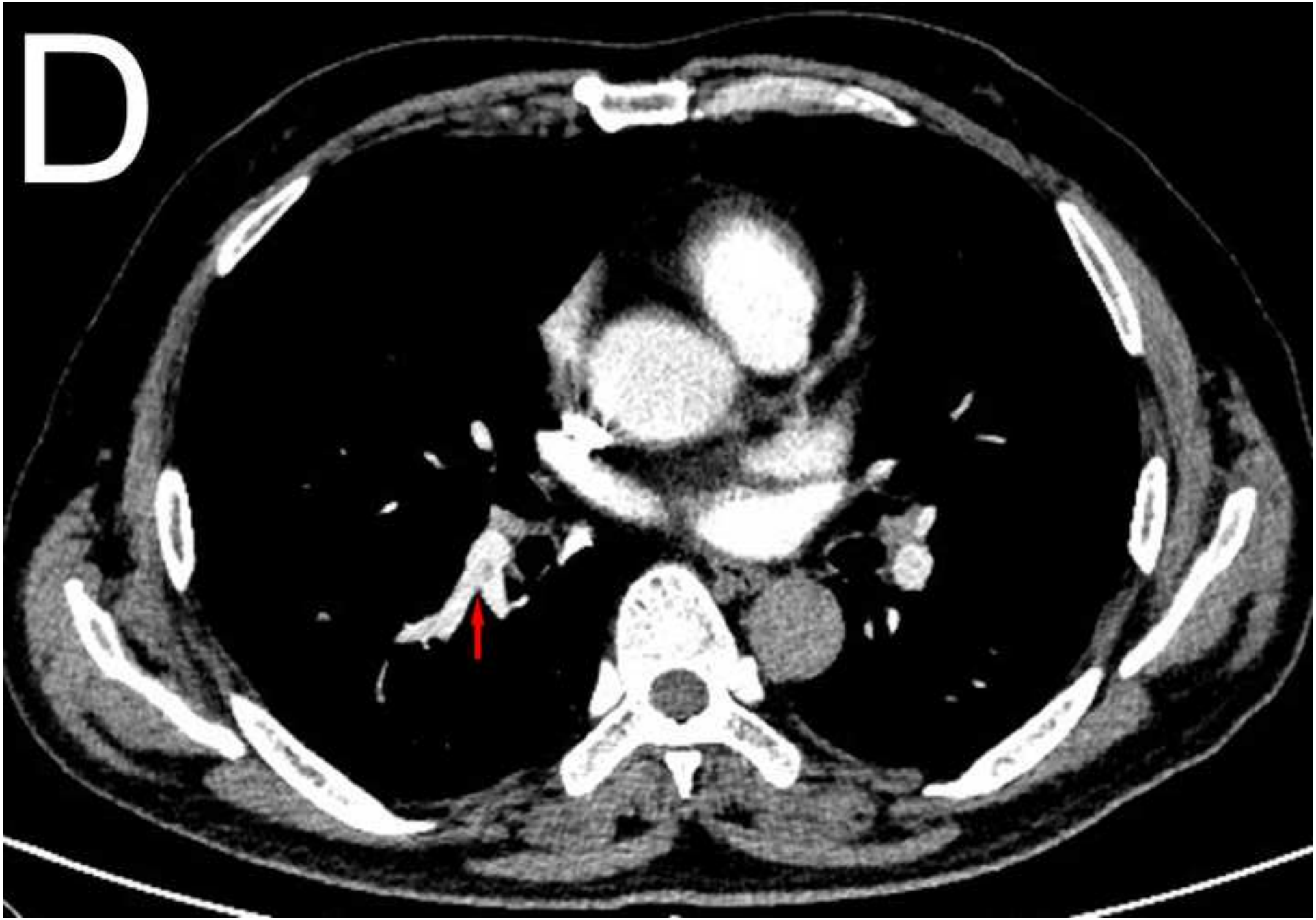

Figure 3E

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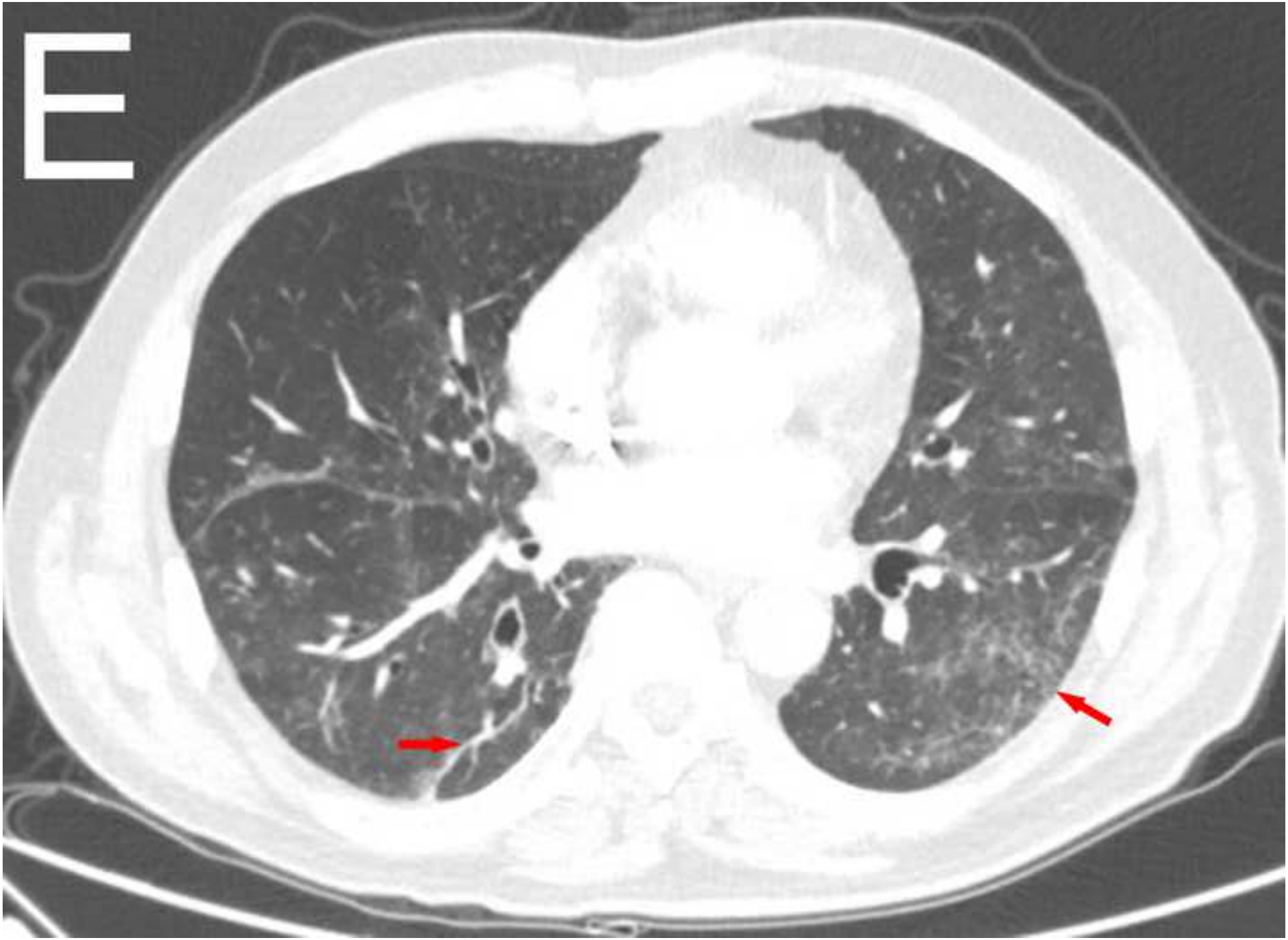

Table 1: Clinical characteristics of COVID-19 patients with suspected APE

	Total (n=25)	APE (n=10)	Non-APE (n=15)	P value
Characteristics				
Age (years)	65 (56.5-70)	66.5 (57-71.5)	65 (54-70)	0.605
Gender (n)				0.691
Male	15 (60%)	6 (60%)	9 (60%)	..
Female	10 (40%)	4 (40%)	6 (40%)	..
Time to CTPA (days)	10 (7-16.5)	10 (7-10.75)	11 (7-19)	0.397
Any comorbidity (n)				
Hypertension	10 (40%)	6 (60%)	4 (27%)	0.034
Diabetes	5 (20%)	3 (30%)	2 (13%)	0.699
CVDs	4 (16%)	2 (20%)	2 (13%)	0.532
Smoking	6 (24%)	2 (20%)	4 (27%)	0.023
Surgery	6 (24%)	2 (20%)	4 (27%)	0.545
DVT	1 (4%)	0	1 (7%)	..
Cancer	0	0	0	..
Clinical classification (n)				0.653
Mild	0	0	0	..
Moderate	17 (68%)	6 (60%)	11 (73%)	..
Severe	8 (32%)	4 (40%)	4 (27%)	..
Critical	0	0	0	..
Stage of imaging (n)				0.545
Early	0	0	0	..
Progressive	3 (12%)	1 (10%)	2 (13%)	..
Peak	16 (64%)	7 (70%)	9 (60%)	..
Absorption	6 (24%)	2 (20%)	4 (27%)	..
Outcome (n)				
Hospitalization	9 (36%))	3 (30%)	6 (40%)	..
Discharged	10 (40%)	5 (50%)	5 (33%)	..
Died	6 (24%)	2 (20%)	4 (27%)	..

Data are median (IQR) or n (%). The rate of moderate and severe type compared with Fisher's exact test between group APE and group Non-APE. The rate of progressive and peak stages compared with Fisher's exact test between group APE and group Non-APE. CTPA=computed tomography pulmonary artery; APE=acute pulmonary embolism; CVDs=cardiovascular diseases; DVT=deep vein thrombosis.

Table 2: Laboratory data of COVID-19 patients with suspected APE

	Normal range	Median (IQR)			P value
		Total (n=25)	APE (n=10)	Non-APE (n=15)	
D-dimer (ug/ml)	0-1	6.06 (1.90-14.31)	11.07 (7.12-21.66)	2.44 (1.68-8.34)	0.003
CRP (mg/dL)	0-0.6	3.12 (2.16-6.16)	3.09 (2.21-7.03)	3.41 (2.16-6.19)	0.978
WBCC (*10^9/L)	3.5-9.5	6.90 (5.44-9.48)	7.03 (6.17-10.02)	6.25 (3.70-9.18)	0.428
LC (*10^9/L)	1.1-3.2	0.81 (0.55-1.05)	0.88 (0.64-1.14)	0.78 (0.54-0.86)	0.285
BNP (pg/mL)	0-100	142.00 (81.70-301.30)	213.50 (131.75-500.03)	95.90 (55.00-245.30)	0.091
ALT (U/L)	9-50	32.00 (19.65-56.75)	40.85 (24.50-78.48)	21.90 (13.30-54.30)	0.160
AST (U/L)	15-40	37.90 (23.70-48.50)	43.70 (22.16-58.50)	35.70 (24.50-40.00)	0.338
GGT (U/L)	10-60	35.00 (20.65-82.50)	49.00 (25.16-125.73)	29.50 (15.70-61.60)	0.177
Alb (g/L)	40-55	33.70 (30.10-35.55)	33.90 (30.18-35.90)	33.50 (29.70-35.40)	0.683
Alb/Glb	10-60	1.00 (0.80-1.20)	1.10 (0.86-1.33)	1.00 (0.79-1.17)	0.285
Cr (μmol/L)	57-111	65.70 (55.45-81.40)	65.30 (54.05-75.95)	66.70 (63.50-81.90)	0.683
BUN (mmol/L)	2.9-8.2	5.66 (4.05-6.96)	5.78 (4.62-8.10)	5.66 (3.84-6.58)	0.338
$PaCO_2$ (mmHg)	35-45	38.00 (34.50-43.50)	39.00 (33.00-47.00)	38.00 (36.00-42.00)	0.531
PaO_2 (mmHg)	80-100	69.00 (58.50-94.00)	76.50 (58.25-102.75)	69.00 (57.00-88.00)	0.723
SO_2 (%)	91.9-99	95.00 (90.00-97.50)	96.00 (90.75-98.25)	95.00 (90.00-97.00)	0.807

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