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Could Bronchial Artery Embolization Be a Modality for Treating Severe Acute Respiratory Syndrome Coronavirus 2?

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Editor:

Bronchial artery circulation has not been carefully studied in human severe acute respiratory syndrome (SARS). However, bronchial artery circulation has been studied in detail in animal models of smoke inhalation–induced lung injury (1,2). These models recapitulate the classic features of SARS, which is characterized histologically by diffuse alveolar damage and by new vessel growth: biologically by an intense inflammatory reaction with a cytokine storm (1), by coagulation disorders, and by increased angiotensin-converting enzyme and angiotensin-converting enzyme 2 expression in the lungs and radiologically by bilateral diffuse ground-glass opacity on computed tomography (CT) scan (2,3). All of these findings have been described in patients with 2019 novel coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

In a smoke inhalation ovine model, bronchial artery flow (normally 1% of cardiac output) was increased 15-fold in the left main bronchus, 20-fold in the right main bronchus, and approximately 4- and 6-fold in the right and left lungs, respectively (2). Sclerosis of the bronchial artery after smoke inhalation has been reported to greatly improve lung function and to drastically reduce animal mortality (2,4). Thus, bronchial artery sclerosis resulted in a statistically significant improvement of the arterial partial pressure of oxygen/fraction of inspired oxygen ratio and led to attenuation of the increase of pulmonary pressure and elevation of pulmonary artery vascular resistance, suppression of formation of bronchial casts; and reduction of myeloperoxidase activity compared with an animal smoke inhalation control group (4).

The mechanism by which the bronchial circulation contributes to the pathogenesis in lung parenchyma has not been fully elucidated. Cellular and humoral mediators of inflammation produced in response to local pulmonary injury may enter into the bronchial circulation and could be delivered to the whole pulmonary parenchyma, as the bronchial arterial circulation mainly drains into the pulmonary arterial circulation by precapillary anastomoses. Thus, the increase in bronchial circulation could spread inflammatory mediators and cells throughout the whole pulmonary parenchyma and accelerate lung damage (2,4). In 2012, Hamahata et al (4) concluded that with the advances in interventional radiology, it would be possible to suppress the bronchial artery flow in situations of pulmonary hyperemia in humans.

To verify the hypothesis that the flow of the bronchial arteries can be increased in cases of COVID-19 pneumonia, the diameters of bronchial arteries at their origin and in the hilum were measured in patients who underwent CT angiography. The institutional review board approved this retrospective study. Chest CT angiography was performed on a 256-slice multidetector CT scanner (Revolution; GE Healthcare, Milwaukee, Wisconsin, USA) after intravenous injection of 60 mL of iodinated contrast agent at a flow rate of 4 mL/s, triggered on the main pulmonary artery. Chest CT scans were studied on a workstation (Advantage Windows Workstation 4.6; GE Healthcare). Two radiologists (L.M. and V.F. with 15 years and 4 years of experience, respectively) analyzed lung parenchyma abnormalities. The diameters of the bronchial arteries were measured by 2 interventional radiologists (Y.C. and J.S. with 15 years and 20 years of experience, respectively) in mediastinal window without visualization of the CT angiography in parenchymal window. Readers were blinded to patient status as well as clinical and biologic features. In cases of disagreement, a simultaneous reading was achieved to reach a consensus. The study included consecutive adult patients ($\geq$ 18 years old) who underwent chest CT angiography performed for suspected pulmonary embolism from March 13, 2020, to May 5, 2020, at a single center. Patients with conditions associated with bronchial artery dilatation (proximal interruption of the pulmonary artery, chronic thromboembolic disease, lung cancer, and bronchiectasis) and non–aortic or non–intercostal artery opacification were excluded. If several bronchial arteries were identified, only the vessel with the largest diameter was used for analysis. In 90 patients, 93 CT angiography scans were performed for suspected pulmonary embolism (3 patients underwent 2 scans). There were 23 CT angiography scans excluded because of lack of aortic or intercostal artery opacification. After blinded CT) angiography analysis, patients were divided into 2 groups: patients with reverse transcriptase polymerase chain reaction (PCR)–confirmed COVID-19 and CT signs of COVID-19–associated

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Table. Patient Characteristics

	CT^+PCR^+ (n = 37)	CT^-PCR^- (n = 30)	*P* Value*
Age, y, median (IQR)	65 (57–76)	68 (53–80)	.64
Female sex	9 (25)	15 (50)	.03†
Current or past tobacco use	6 (16)	8 (27)	.30
Diabetes mellitus	8 (22)	3 (10)	.32
Hypertension	17 (46)	15 (50)	.74
Pulmonary history	3 (8)‡	5 (17)§	.45
Mechanical ventilation	8 (22)	1 (3)	.03†
Deaths	3 (8)	3 (10)	.80
CT angiography scans	40	30	
Pulmonary embolism	6 (15)	6 (20)	.69
Right bronchial artery	33 (82)	23 (77)	.56
Involvement < 10%	1 (2.5)	NA	
10% < Involvement < 25%	16 (40)	NA	
25% < Involvement < 50%	8 (20)	NA	
50% < Involvement < 75%	9 (22.5)	NA	
Involvement > 75%	6 (15)	NA	

Note–Values are reported as number or number (%) except for age.
CT = computed tomography; IQR = interquartile range; NA = not available; PCR = polymerase chain reaction.
*Fisher exact test was used for diabetes mellitus, pulmonary history, mechanical ventilation, and death status, whereas for all other categorical variables, χ^2 test of independence was used.
†Statistically significant.
‡2 chronic obstructive pulmonary disease, 1 pulmonary tuberculosis without lung sequelae.
§1 cancer lung, 2 chronic obstructive pulmonary disease, 1 asthma.

pneumonia (CT^+PCR^+ group) and patients with reverse transcriptase PCR–negative COVID-19 and absence of lung damage on CT (CT^-PCR^- group).

Characteristics of the study groups are presented in the Table. There were 37 patients (40 CT angiography scans) in the CT^+PCR^+ group and 30 patients (30 CT angiography scans) in the CT^-PCR^- group. The median age was 65 years (interquartile range [IQR] 57–76 years) in the CT^+PCR^+ group versus 68 years (IQR 53–80 years) in the CT^-PCR^- group ($P = .64$). The median diameter of the bronchial artery at the origin was drastically increased in the CT^+PCR^+ group (Figs 1, 2) compared with the CT^-PCR^- group (Figs 3, 4): 2.00 mm (IQR 1.50–3.00 mm) versus 0.40 mm (IQR 0.00–1.50 mm) ($P < .01$). Similarly, a much larger median diameter of the bronchial artery in the hilum was observed in the CT^+PCR^+ group compared with the CT^-PCR^- groups: 1.50 mm (IQR 1.00–2.05 mm) versus 0.35 mm (IQR 0.00–1.00 mm) ($P < .01$). Patients in the CT^+PCR^+ group displayed different levels of damage: > 10% damage (n = 1), 10%–25% (n = 16), 25%–50% (n = 8), 50%–75% (n = 9), and > 75% (n = 6). The median diameter of the bronchial artery at the origin was found to increase in parallel with the percentage of damage, from 0.70 mm (IQR 0.70–0.70 mm) in the 10% class to 3.60 mm (IQR 2.55–3.75 mm) in the > 75% class ($P < .01$).

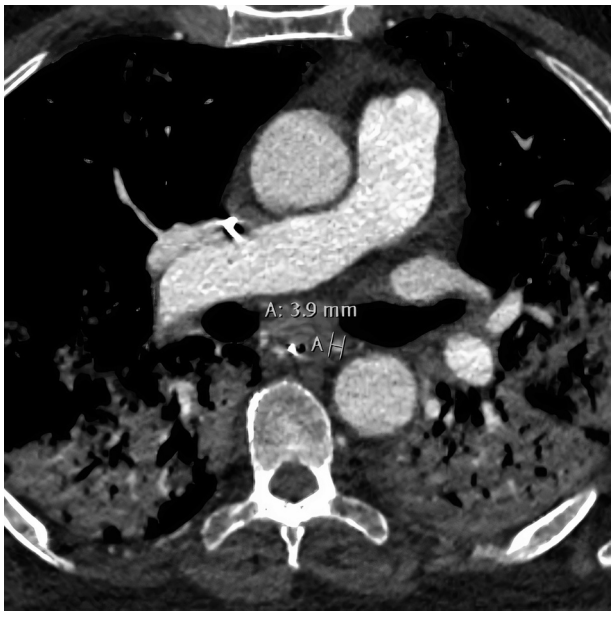

Figure 1. A 73-year-old man in CT^+PCR^+ group without medical history. CT angiography in the axial plane shows 3.9-mm right bronchial artery diameter.

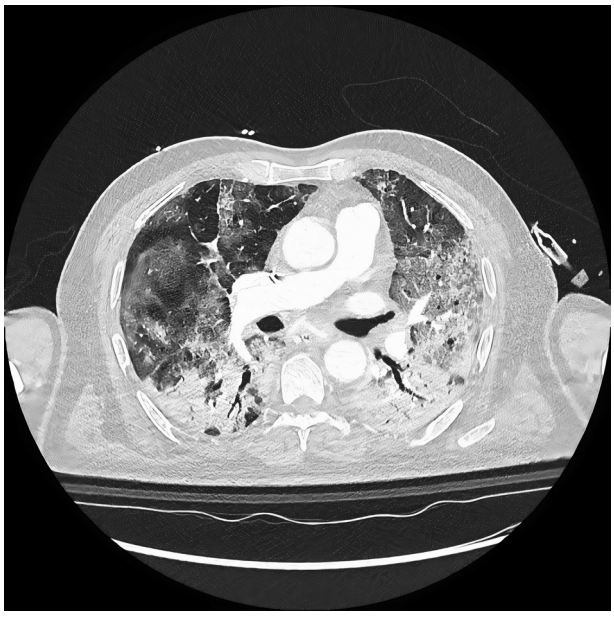

Figure 2. Same patient as in Fig 1. CT of the chest (lung window: width 1600 HU/length −500 HU) in the axial plane shows critical lung involvement.

These observations seem to show that bronchial artery dilatation could be either a pre-existing factor spreading the disease to the whole lung parenchyma or a consequence of SARS-CoV-2 infection. Bronchial artery occlusion, before or after smoke inhalation, significantly improves clinical parameters and animal survival. Bronchial artery embolization studies are required to evaluate the efficacy, safety, and

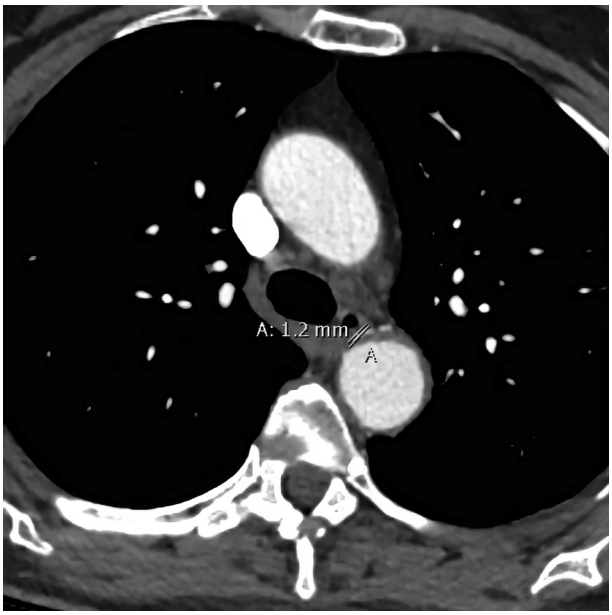

Figure 3. A 61-year-old woman in CT⁻PCR⁻ group with tobacco use. CT angiography in the axial plane shows 1.2-mm left bronchial artery diameter.

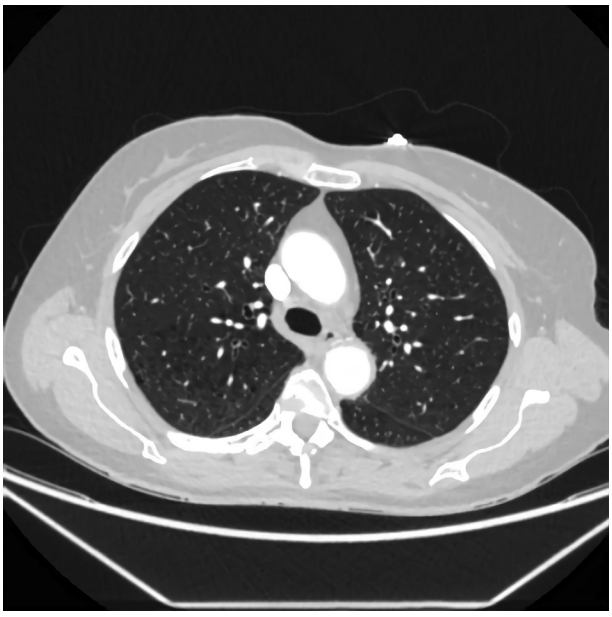

Figure 4. Same patient as in Fig 3. CT of the chest (lung window: width 1600 HU/length −500 HU) in the axial plane shows no lung involvement.

role of bronchial artery embolization among the different therapeutic options for COVID-19 treatment.

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Acute Limb Ischemia in Minimally Symptomatic SARS-CoV-2 Infection

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Editor:

Patients with coronavirus disease 2019 (COVID-19) present with a wide spectrum of symptoms, but mounting experience is noted with an apparent prothrombotic state. In addition to microvascular thromboses, there are reports of macrovascular thrombotic events in critically ill patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1,2). However, acute limb ischemia was also seen in a patient only minimally symptomatic with SARS-CoV-2 infection and no other risk factors for embolus or thrombosis. The present case report was approved by the institutional review board.

The patient is a 60-year-old obese nonsmoker with hypertension presenting with a 10-day history of fever, sinus congestion, anosmia, ageusia, and 3 days of new-onset left-foot aching pain and coolness, digital numbness, and inability to bear weight. Cardiovascular examination demonstrated a normal sinus rhythm. Physical examination was consistent with acute limb ischemia (Rutherford class IIa). An emergent arteriogram demonstrated thrombus in the distal left profunda femoris artery (Fig 1), occlusion of the

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