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REVIEW ARTICLE

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The role of imaging in detecting and monitoring COVID-19 complications in the Intensive Care Unit (ICU) setting

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Abstract

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Most people infected with the virus experience mild to moderate respiratory illness. However, some might become seriously ill and may develop acute respiratory distress syndrome (ARDS), thus requiring non-invasive or invasive mechanical ventilation. Furthermore, COVID-19 disease can involve also other organs and systems, causing several extra-pulmonary manifestations and, thus, negatively influencing the patient's outcome. Imaging studies play a pivotal role in the monitoring of severely ill patients, especially those admitted to the intensive care unit (ICU), who can develop several potentially life-threatening complications, both from the infection itself and the mechanical supporting system. This widespread utility of imaging modalities calls for a deeper understanding of potential radiologic findings in this disease and the need for multidisciplinary collaboration between radiologists and anesthesiologists to provide actionable guidance to appropriate interventions under such conditions.

Keywords COVID-19, Intensive Care Unit, Barotrauma, Complications, Imaging

1 Introduction

Since its onset in December 2019, the coronavirus disease 2019 (COVID-19) pandemic has become a global challenge for healthcare systems, particularly due to limited resources of intensive care units (ICU), and the shortage of trained medical personnel. Most people infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) experience mild to moderate respiratory illness. However, some might become seriously ill and may develop acute respiratory distress syndrome (ARDS), thus requiring non-invasive or invasive mechanical ventilation. COVID-19 has a wide range of clinical presentations, varying from asymptomatic or mildly symptomatic infection to severe bilateral pneumonia, with a high risk of developing acute ARDS (20–67%) and thus the need for non-invasive or invasive mechanical ventilation [1–3]. Furthermore, it has now been proven that COVID-19 disease involvement is not limited to the respiratory system, but it can also affect other organs and systems, causing several extra-pulmonary manifestations and, thus, negatively influencing the clinical outcomes of these patients, especially those who are severely ill [4–7]. Since the number of infected subjects requiring critical care support is still significant, critical care and anesthesiology teams must be prepared for their sustained care and advocate for a multidisciplinary approach.

In the early phase of the COVID-19 outbreak, when reverse transcription polymerase chain reaction (RT-PCR) tests had limited availability and the number of infected people was higher, initial efforts focused on the use of imaging examinations at the forefront of diagnosis. Since the lungs are the main organ involved, chest X-rays were usually performed as the first-line imaging test because they are widely available and economical

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and might help support the diagnosis. However, due to its higher sensitivity, chest computed tomography (CT) represented the most accurate technique for screening patients who have epidemiological and clinical features of COVID-19 [8]. In addition, CT studies make it possible to identify complications as well as suggest extra-pulmonary involvement diagnoses [9]. Nonetheless, this technique has low specificity for distinguishing lung lesions of COVID-19 pneumonia from findings of other viral pneumonia [10]; furthermore, it poses an increased risk of infection transmission to other patients or healthcare workers [11]. Therefore, with the progressively increased availability of RT-PCR during the pandemic, the role of imaging techniques progressively changed from primarily diagnostic to prognostic and, at present, are predominantly performed to evaluate the severity of COVID-19 disease and stratify patients. In particular, imaging studies still yield a pivotal role in the monitoring of severely ill patients, especially those admitted to the ICU, who can develop several potentially life-threatening complications, both from the infection itself and the mechanical supporting system [7, 12].

Interpretation of imaging studies is not usually in the domain of anesthesiologists and most of them have only rudimentary skills in the radiological evaluation. However, imaging studies can provide a wealth of information regarding the pathophysiological course of COVID-19 and the potential development of critical complications, helping to formulate a proper management plan [13].

The aim of the present pictorial review is to illustrate the imaging findings of the main complications that can arise in COVID-19 critical patients admitted to the ICU. Providing a comprehensive insight into the imaging hallmarks of such complex but common scenarios, anesthesiologists can appropriately approach these conditions, achieve an early diagnosis, correctly stratify the disease severity and provide effective treatment.

2 Barotraumas

Pneumothorax occurs when alveoli rupture and the air subsequently spreads in the pleural space causing partial or complete lung collapse; in some cases, the air can further leak into other extra-alveolar spaces, resulting in pneumomediastinum, pneumopericardium, pneumoperitoneum and/or subcutaneous emphysema [14–16].

Patients requiring invasive mechanical ventilation due to significant respiratory insufficiency are at greater risk of developing barotraumas since the high positive end-expiratory pressure can cause an elevation of the trans-alveolar pressure, overdistention in the alveoli units and eventually their rupture. Furthermore, air leakage can be secondary to several medical interventions frequently performed in the ICU setting, including central venous catheter placement and extracorporeal membrane oxygenation (ECMO) [17–19].

Every underlying pulmonary disease that causes the breakdown of the alveolar membrane integrity, including pulmonary infection due to SARS-CoV-2, has the potential to increase the risk of pulmonary barotraumas [6]; furthermore, the increase of intra-alveolar pressure caused by coughing might further contribute to its development [14]. This could explain why 30–40% of air leaks occurred in infected subjects without breathing support [20, 21]. However, the incidence of both pneumothorax and pneumomediastinum is reported to be higher in ICU patients with COVID-19 compared to ICU patients with ARDS from other causes, regardless of the mechanical ventilation strategies, raising the question of whether COVID-19 patients are more susceptible to air leaks [22–26]. Some experts have speculated that the increased risk of barotrauma in COVID-19 patients might be due to the common involvement of peripheral or subpleural regions typical of this disease, along with the concomitant pulmonary embolism with infarction and the strong inspiratory efforts in these patients, that might represent additional risk factors [24].

Since pulmonary barotrauma is linked with a worse outcome [27, 28], its prompt and accurate detection is pivotal to guarantee an early treatment and thus reduce both morbidity and mortality.

Chest X-ray is a simple imaging test used to evaluate patients on respiratory support, but it has a low sensitivity (38%) for diagnosing pneumothorax despite its high specificity (99%) [29]. At radiography, the separation of the visceral from parietal pleural layers caused by an air-filled space in between produces a visible visceral pleural line and hyperlucency of the area beyond this line, containing neither lung tissues nor vascular structures. The absence of distal lung markings is also another notable signs [30]. In general, the intrapleural air begins to gather in the nondependent portion of the pleural space, i.e., apical and lateral regions rather than medial ones. Nevertheless, patients admitted to the ICU are usually bedridden and present several motor problems, thus radiographs are acquired supine, which makes it hard to detect pneumothorax [31]. Because the highest portion of the pleural space lies in the anterior and anteromedial aspect at the base near the diaphragm in a supine patient, pneumothorax rises to that region, where it can outline the structures of the mediastinum and/or enlarge the costophrenic angle (deep sulcus sign) [29]. The radiographic signs of pneumomediastinum rely on the presence and amount of radiolucent air outlining the normal mediastinal structures, clearly demarcating the great vessel and the heart, especially along its left border. When air dissects inferiorly into the infracardiac

region, the diaphragm counter can be seen to its entire extent [30]. The air can also extend upwards into the soft tissue of the neck and shoulders and lead to subcutaneous emphysema, which appears as striated lucencies outlining muscle fibers or simply beneath the skin surface, usually covering a large area of the body [32]. Pneumopericardium is rare and refers to substernal air anterior to the heart. It requires a lateral view chest radiograph for detection and it may be the only radiographic finding in patients with pneumomediastinum. It appears as a single band of gas around the pericardium, especially along the contours of the left ventricle and right atrium [29]. Finally, the presence of subdiaphragmatic free gas and/or air outlining both sides of the bowel wall (Rigler sign) is highly suggestive of pneumoperitoneum.

Chest CT with lung windows is performed to confirm the presence of pulmonary barotraumas in radiographic equivocal cases, to assess the severity of the pneumomediastinum, and to evaluate the presence of pneumopericardium, which is more difficult to confirm on plain radiographs and has a poor prognosis [33, 34]. The typical findings on CT scan suggestive of pneumothorax include the presence of rims of gas around the edges of the lung which may track up the fissures, eventually associated with collapse of the lung in moderate-severe cases. Air collection in the extra-pleural space may mimic pneumothorax but the presence of thin connective tissue webs outside of the pleural line is typical of pneumomediastinum and can help achieve a correct differential diagnosis [29]. Despite its primary diagnostic role, increasing evidence support that the Macklin effect could be an excellent predictor of disease severity and risk for clinically relevant barotrauma; therefore, its early detection in CT scans could aid in choosing the most adequate ventilatory support system [35]. Therefore, chest CT imaging could play a crucial role in predicting outcomes and guiding appropriate patient treatment (Fig. 1).

3 Thromboembolic complications

ICU patients are known to have a higher risk for thromboembolic complications due to prolonged immobilization, administration of sedatives and neuromuscular blockers, and mechanical ventilation. Additionally, the placement of vascular devices such as central venous catheters may cause vessel injury, which further increases the risk of blood clots; similarly, long-term vascular access may develop catheter-related thrombosis, especially when devices are in peripheral veins and in the context of hemodialysis [36, 37]. Finally, even the use of ECMO can disrupt the normal balance of hemostasis, leading to activation of coagulation, complement, and inflammatory cascades, as well as increased platelet activation [38].

Nonetheless, several studies have demonstrated that COVID-19 patients in ICU patients have a higher risk of developing pulmonary embolism compared to non-COVID-19 patients, despite similar severity of ARDS (23–47% vs. 7.5%) [39–43]. Moreover, thromboembolic complications have been described even in patients treated with anticoagulation therapy from admission, highlighting the intrinsic thrombogenicity of this novel coronavirus [40]. Following COVID-19 infection, in fact, the exaggerated systemic immune response caused by the virus stimulates the production and release of high levels

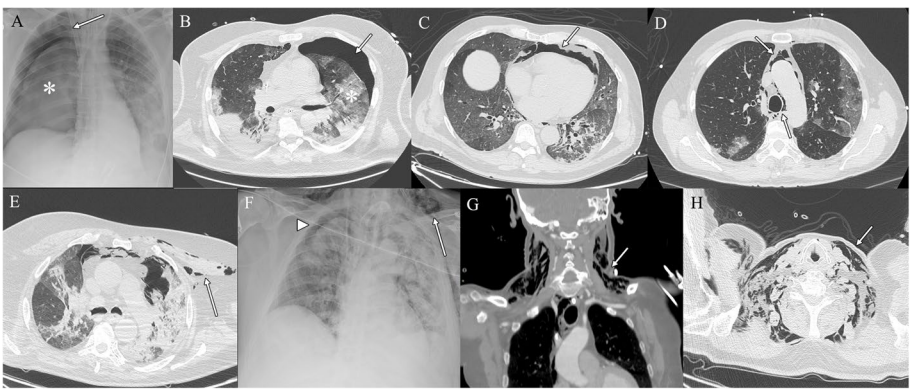

Fig. 1 Plain X-ray chest of a critically ill COVID-19 patient admitted to the ICU demonstrating the presence of radiolucent air in the pleural space (arrow in **A**) and the partial collapse of the right lung (asterisk in **A**), causing a mediastinal shift. Axial HRCT images of severely ill patients infected with the SARS-CoV-2 virus showing imaging features suggestive of barotrauma: a large pneumothorax (arrow in **B**) with collapsed left lung (asterisk in B), a large pneumopericardium (arrow in **C**), a pneumomediastinum with air collecting around the trachea and the main mediastinal vessels (arrows in **D**), pneumothorax and pneumomediastinum associated with extensive left subcutaneous emphysema (arrow in **E**). Plain X-ray chest of a critically ill COVID-19 patient demonstrating the presence of both a right pneumothorax (arrowhead in **F**) and free air entering the neck (arrow in **F**); coronal and axial CT images of the same patients, showing the presence of free air dissecting within the fascia spaces of the neck (arrows in **G** and **H**)

of numerous hyperinflammatory cytokines, with the subsequent activation of endothelial cells, promotion of leukocyte recruitment, trigger of the coagulation cascade and increase of vascular permeability; additionally, due to the high levels of angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 expressed by the endothelium, there is also evidence of direct viral infection of endothelial cells [44].

The imaging features of venous thrombosis in COVID-19 patients are analogous to those associated with other diseases and include the presence of a filling defect within a vessel with hypodense thrombus, venous distension, rim enhancement of the vein, and perivenous edema or fat stranding [45].

In subjects infected with SARS-CoV-2 virus, the majority of pulmonary embolisms are in the segmental arteries rather in the central pulmonary arteries and their distribution might be very extensive, supporting the hypothesis of a diffuse vascular process [46]. In this context, postprocessing vascular mapping using maximum intensity projection (MIP) has been reported to be diagnostically useful since it can clearly delineate vessels up to subsegmental levels and thus help identify even the smallest filling defects. Interestingly, the vascular enlargement frequently described in COVID-19 pneumonia could explain why many of the patients with pulmonary embolism have only mild symptoms or are even asymptomatic, since it might not dramatically increase the resistance of the pulmonary circulation and thus lower the hemodynamic impact of this complication [47].

Among the abdominal vessels, thrombosis of mesenteric vessels is one of the most frequent complications described in COVID-19 disease and it mostly involves the large bowel alone (about 50%) [48]. It appears as a filling defect within the lumen of the abdominal aorta, the celiac axis, the superior mesenteric artery and/or the inferior mesenteric artery at contrast-enhanced CT; sometimes, especially using MIP reconstruction, low contrast opacification of the mesenteric vascular brances can be documented, with or without absent or decreased contrast enhancement of the corresponding small bowel segments. The early phase of bowel ischemia may only show contracted and thicked gasless loops due to mural edema. When the ischemic process persists, intestinal loops progressively dilate, air-fluid levels appear, and walls become paper-thin. Finally, in the late phase, transmural infarction may lead to intestinal wall pneumatosis, mesenteric venous gas and, potentially, pneumoperitoneum due to perforation [49–51].

Imaging features of acute ischemic stroke in COVID-19 patients are similar to those described in non-COVID-19 patients, including abnormal hypoattenuation of the brain parenchyma, loss of gray-white differentiation, and sulcal effacement on unenhanced CT. After contrast media administration, an extensive vascular occlusive disease may be revealed, typically involving the large vessel [52].

The renal arteries have been reported as another common site of thromboembolic complications caused by COVID-19. In most cases, the presence of solitary or multiple triangular-shaped areas of renal parenchyma with decreased enhancement and apex pointing toward the medulla arouses suspicion of renal infarctions, suggesting checking for the presence of a filling defect in the aorta or the renal arteries [49, 53–55] (Fig. 2).

4 Hemorrhagic complications

Bleeding is a less frequent possibility in COVID-19 patients, but it can be more frequent in ICU patients (8% vs. 2%), causing significant morbidity and representing a potential cause of death [56]. Due to the intrinsic high risk of thromboembolic events, in fact, COVID-19 patients are often on some form of anticoagulation therapy that, if unbalanced, might predispose them to the development of hemorrhagic complications [12, 57, 58]. In addition, the development of disseminated intravascular coagulation as well as the binding of SARS-CoV-2 to ACE2 receptors with the subsequent activation of the renin-angiotensin-aldosterone axis and the increase in blood pressure can further favor endothelial dysfunction and bleeding.

Contrast-enhanced CT is pivotal to confirming active bleeding and identifying its location, presenting as a blush in the arterial and/or venous phase. The gastrointestinal system is the most common site of spontaneous bleeding but iatrogenic hemorrhages following medical and surgical procedures can represent an important burden, being described in about 30% of cases [59].

Some critically ill COVID-19 patients may experience intracerebral hemorrhages, which can happen spontaneously due to circulation instability or as a result of the transformation of acute ischemic stroke, resembling those secondary to anticoagulant therapy. They typically appear as strongly hyperdense areas with surrounding hypodense edema on unenhanced CT scans. In severe cases, hemorrhages can affect large parts of the brain, occurring in both supra and infra-tentorial locations and extending into the ventricles, and cause a midline shift [60, 61].

Hematomas are localized collections of blood outside the vessels and appear as hyperdense masses that might vary in size and even cause displacement and/or compression of surrounding structures. They may be hyperacute to chronic in duration and therefore their internal contents will vary from fresh hemorrhage to chronic hemoglobin degradation products (i.e., hemosiderin and

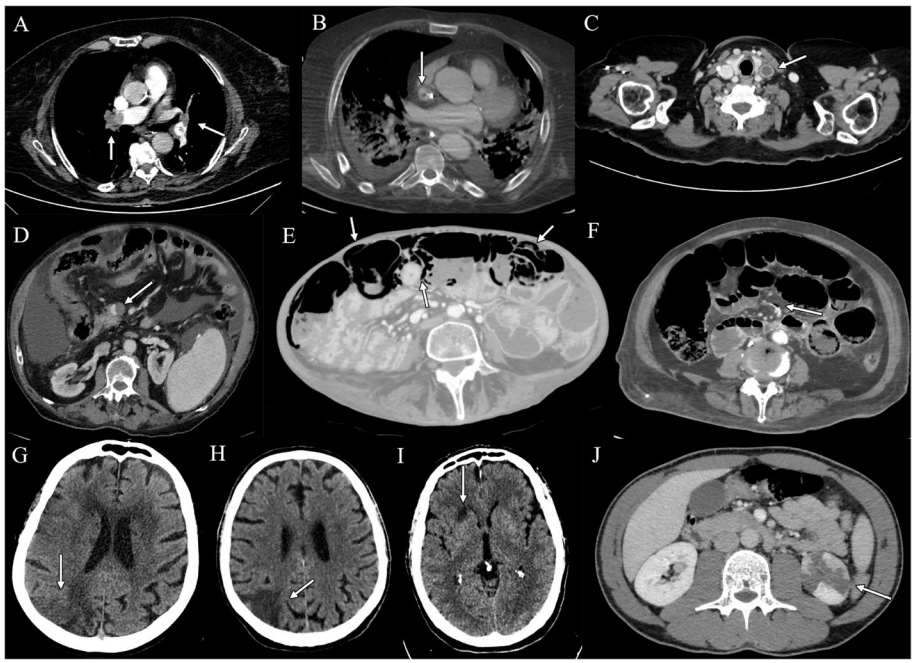

Fig. 2 Axial contrast-enhanced CT images patients infected with SARS-CoV-2 virus admitted to ICU demonstrating filling defects indicative of thromboembolic complications: a massive and multiple lung embolism in the right and the left pulmonary arteries (arrows in **A**), partial thrombosis of the superior vena cava caused by the placement of a peripherally inserted central venous catheter (arrow in **B**) and complete thrombosis of the left jugular vein (arrow in **C**). Axial contrast-enhanced CT scan of a severely ill COVID-19 patient demonstrating a partial filling defect in the superior mesenteric vein (arrow in **D**); axial contrast-enhanced CT scan of the same patients performed after 4 days showing the appearance of gas in intramural space of the dilatated small bowel walls referable to pneumatosis intestinalis (arrows in **E**) and mesenteric intra-venous gas (arrow in **F**). Axial contrast-enhanced CT images of several patients admitted to ICU due to severe COVID-19 infection demonstrating an acute ischemic stroke in the right parietal lobe (arrows in **G** and **H**) and at the level of basal ganglia (arrow in **I**). Axial contrast-enhanced images of a COVID-19 patient with multiple triangle-shaped hypointense areas at the inferior pole of the left kidney, referable to renal infarctions (arrow in **J**)

ferritin), thus presenting with blood-fluid levels due to the mixture of differently aged components. Soft tissue hematoma can occur anywhere but mostly in the rectus sheath and the iliopsoas muscle [56, 62–64] (Fig. 3).

5 Bacterial and fungal pulmonary co-infections and superinfections

Bacterial and fungal superimposed infections play an important role in COVID-19 disease and occur more frequently during hospitalization (superinfections, > 48–72 h after admission) rather than presenting at the time of admission or right after (co-infections, ≤ 48–72 h after admission). In particular, ICU patients are highly susceptible to these complications (45% of cases), which, as it is easy to imagine, are associated with significant morbidity and mortality [3, 65–69].

In particular, ventilator-associated pneumonia (VAP) is the commonest ICU-acquired infection and is defined as an infection of lung parenchyma developed in patients who have been on mechanical ventilation for more than 48 h [70]. Previous reports indicated that COVID-19 patients have an increased risk of VAP compared to other ARDS (30–80% vs. 13%) and present even higher mortality rates [71, 72].

These patients, in fact, are extremely vulnerable and more susceptible to infection because of the more severe form of illness, the immunosuppressed state induced by the virus and the greater number of comorbidities; moreover, they undergo several invasive procedures (such as endotracheal tube and vascular devices placement) and are more prone to receive corticosteroids and monoclonal antibodies compared to other patients, further amplifying the COVID-19-induced immunosuppression [67, 73].

In the vast majority of cases (50–70%), a simultaneous bacterial and fungal infection is detected but a multibacterial infection is also very common (25%) [74, 75].

Gram-negative bacteria cause most infections and *Klebsiella pneumoniae, Pseudomonas aeruginosa, Haemophilus influenzae, Escherichia Coli,* and *Acinetobacter baumannii* are typically the most commonly isolated pathogens, although *Mycoplasma pneumoniae* and *Staphylococcus aureus* have also been frequently reported [65, 67, 76, 77]. Among the fungal pathogens, *Aspergillus*

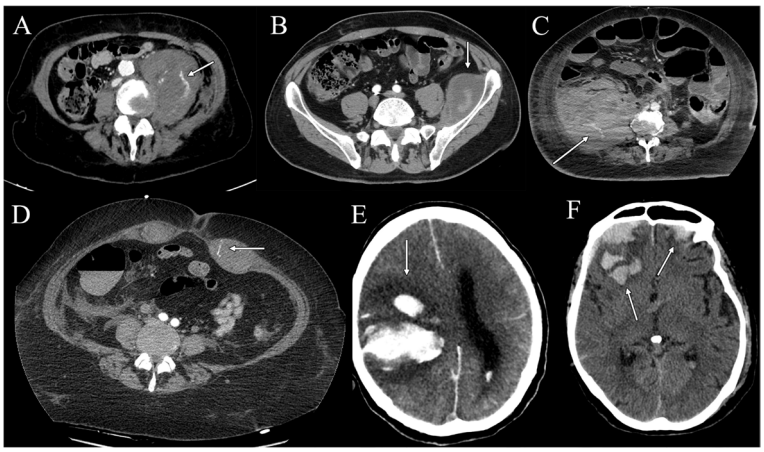

Fig. 3 Axial contrast-enhanced CT images of different patients with COVID-19 admitted to ICU with extensive bleeding in the ilio-psoas muscle (arrows in **A**, **B** and **C**); note the presence of arterial blush referable to active bleeding in A and C. Axial contrast-enhanced CT image of another COVID-19 patient with active bleeding of the left rectus abdominis muscle (arrow in **D**). Axial contrast-enhanced CT showing a spontaneous massive intracerebral hemorrhage with surrounding edema and significant midline shift (arrow in **E**). Axial contrast-enhanced CT of another COVID-19 patients admitted to ICU demonstrating an intracerebral hemorrhage located in both frontal lobes (arrows in **F**)

spp. and *Candida spp*. are the most frequently detected species [78]. In particular, COVID-19-associated pulmonary aspergillosis has emerged as an important complication among patients in the ICU, with a higher mortality rate (up to 50%) and increased incidence (18–39% vs. 7% of patients) compared to patients with other causes of ARDS [79, 80].

Diagnosis of a concomitant bacterial and/or fungal infection is challenging in COVID-19 patients, due to the overlap of their imaging features with those of worsening COVID-19 pneumonia, and laboratory results provide essential support to both clinicians and radiologists [81]. Generally, the appearance of lobar consolidations, pleural effusion, cavitations and/or mediastinal lymphadenopathy should raise suspicion for bacterial and/or fungal infection, particularly when they are unilateral. Serial chest radiographs are helpful in the detection of new imaging findings [82]. Chest high-resolution computed tomography (HRCT) can help clinicians to achieve a prompt and correct diagnosis demonstrating the presence of a unilateral lobar consolidation with an air bronchogram, large bilateral areas of consolidations or atypical imaging features such as cavitations and bronchiectasis, especially when newly appeared. Despite these findings can be suggestive of bacterial and/or fungal superimposed infections, they are not pathognomonic. Nevertheless, prompt suspicion can direct the execution of downstream cultural and/or laboratory test to confirm or exclude the diagnosis. Sometimes, invasive aspergillosis can be suspected in the presence of nodular infiltrates, large centrilobular nodules, nodules with halo sign/reversed halo sign, cavitation with a fungus ball within the cavity (air crescent sign); moreover, the irregular thickening of the tracheobronchial walls, presence of extraluminal air pockets communicating with the airway lumen representing ulcerations or multifocal nodular mucosal thickening may be also identified [83, 84]. However, it is important to remember that lung cavitations have also been described as an imaging finding of the late stages of COVID-19 pneumonia (necrotic evolution) and they can also result from barotraumas or pulmonary embolism with infarction [85].

Finally, mechanically ventilated patients are also at increased risk of aspiration pneumonia, which can mimic a bacterial or fungal superinfection. The presence of airway thickening with ground-glass opacities showing a centrilobular and peribronchovascular distribution is highly suspicious for aspiration pneumonia, especially when in the gravity-depending parts of the lungs (the lower lobes in supine patients and the upper lobes and the right middle lobe in prone patients). The presence of centrilobular nodules, dependent tree-in-bud nodularity, and, when present, complications such as lung abscess, empyema, or visible aspirated material are other helpful differentiating features [29] (Fig. 4).

6 Direct involvement of abdominal parenchymal organs

During pulmonary infection, the virus can enter the bloodstream and thus infects extrapulmonary organs, causing direct viral injury as well as indirect damage through the development of a hyperinflammatory and hypercoagulable state [86].

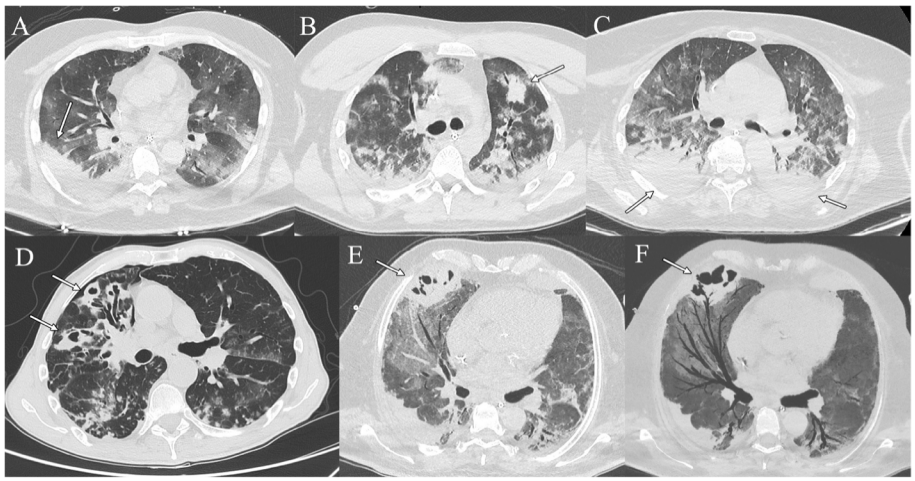

Fig. 4 Axial HRCT images of ICU patients infected with SARS-CoV-2 virus demonstrating the appearance of extensive consolidations associated with worsening of COVID-19 pneumonia (arrows in **A**, **B** and **C**). Superimposed secondary bacterial infections sustained by *Acinetobacter* (**A**), *Pseudomonas Aeruginosa* (**B**) and *Klebsiella pneumoniae* (**C**) were later confirmed. A different COVID-19 patient admitted to ICU showing lung consolidations complicated by small cavitations in the medium and right inferior lobes (arrows in **D** and **E**) caused by a superinfection by *Aspergillus fumigatus*; minimum Intensity Projection reconstruction demonstrating a direct communication between the cavitation and the bronchial tree (arrow in **E**); superinfection of was detected

Gastrointestinal symptoms and complications are frequently described in COVID-19 patients and the involvement of this system by the COVID-19 virus is higher in ICU patients compared to both those with mild disease (16.6% vs. 11.7%, respectively) [50, 87–89] and patients admitted to ICU for other reasons [90].

Besides the above-mentioned thrombotic and hemorrhagic complications, imaging has a limited role in the diagnosis of other gastrointestinal complications. A few cases of large bowel infection with SARS-CoV-2 have been reported, which on imaging, manifest with diffuse, circumferential, homogeneously enhancing bowel wall thickening in a variable distribution with fluid-filled mildly distended intestinal lumen and pericolic fat stranding, in the absence of filling defects suggestive of thrombi in the abdominal arteries; the wall thickening may involve one or more segments of the colon [87].

In confirmed COVID-19 cases, several studies have demonstrated a considerably greater frequency of hepatic steatosis by CT as compared to controls, suggesting a possible association between these two conditions. Unenhanced CT alone is highly specific for moderate to severe hepatic steatosis, which can be documented whenever liver attenuation drops below 40 hounsfield unit (HU) or is at least 10 HU less than that of the spleen [91]. However, this hepatic alteration is highly non-specific and could also possibly result from the extensive multidrug treatment offered to these patients rather than representing a direct sign of SARS-CoV-2 invasion [92].

COVID-19-associated pancreatic injury has been observed in 1–2% of mild cases and 17% of severe cases, including patients in ICU, [93] and is thought to be mediated by the expression of ACE2 receptors expressed on pancreatic islet cells, which is the viral receptor for the entry of SARS-CoV-2 [94]. COVID-19-attributed acute pancreatitis should be diagnosed by sufficient exclusion of other etiologies of pancreatic damage [95]. At the CT scan, most patients have diffuse enlargement of the pancreas with ill-defined borders, due to inflammatory edema. On contrast-enhanced CT, the pancreatic parenchyma shows relatively homogeneous enhancement, but unenhanced (necrotic) areas might be present. The peripancreatic fat usually shows some inflammatory changes of haziness or mild stranding and peripancreatic fluid is common [49].

Due to highly expressed ACE2 receptors in proximal tubular epithelial cells and podocytes, which serves as an entrance door for the SARS-CoV-2 virus, COVID-19 patients could experience high rates of acute kidney injury, especially those in the ICU (20–40%) [54, 96, 97]. Contrast-enhanced CT can easily detect acute renal damage, demonstrating an enlarged kidney with loss of corticomedullary differentiation. Since impaired renal function increases patients' susceptibility to contrast-induced nephropathy, contrast-enhanced imaging studies should be employed with caution and Ultrasound, despite its lower sensitivity, could represent a valid alternative [91] (Fig. 5).

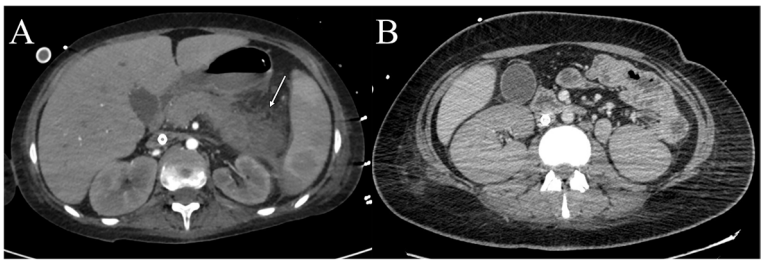

Fig. 5 Axial abdominal contrast-enhanced CT image of a severely ill patient infected with SARS-CoV-2 virus and admitted to ICU undergoing ECMO treatment with a sudden worsening of symptoms revealing a diffusely enlarged and edematous pancreatic tail, with ill-defined borders, stranding of the peri-pancreatic fat and presence of free peri-pancreatic fluid, highly suggestive of acute pancreatitis (arrow in **A**). Axial contrast-enhanced CT image of an ICU patient with COVID-19 ARDS in ECMO treatment revealing an enlargement of both kidneys and the loss of corticomedullary differentiation, compatible with an acute kidney injury (**B**)

7 Sarcopenia

During ICU hospitalization, patients infected with SARS-CoV-2 virus can experience an important decrease in skeletal muscle mass and strength [98, 99], with subsequent increased morbidity and mortality; moreover, in about 30% of cases, this decline persists even after discharge [100]. The inflammatory and procoagulant state associated with severe COVID-19 may contribute to the development of sarcopenia due to the increased glucocorticoid and catecholamine production which leads to increased catabolism and a progressive withdrawal of anabolism [101, 102]. This process progressively reduces muscle regeneration capacity, affecting both muscle quality and quantity. In this context, sarcopenia may impair the respiratory musculature and cause diaphragmatic dysfunction, increasing the difficulty to generate appropriate tidal volumes and perform high-force expulsive airway clearance maneuvers [103]. CT is the preferred method for examining quantitative and qualitative changes in muscle and fat, particularly in the thoracic region. In addition to measuring muscle mass, CT can indeed assess muscle quality by identifying the fat content within the muscle through the evaluation of its attenuation [104]. Recent research has shown that skeletal muscle mass at the level of the fifth and twelfth thoracic vertebra may predict the risk of ICU admission and death in COVID-19 patients [99, 105]. Similarly, perturbations in muscle quality were also found to be predictive of the length of hospitalization, in-hospital mortality, and the need for reintubation after discontinuation of mechanical ventilation [106] (Fig. 6) (Table 1).

8 Monitoring COVID-19 complications in the ICU populations throughout the pandemic

During the initial outbreak, there was limited information about the novel COVID-19 virus. However, as subsequent waves of the pandemic occurred, the scientific understanding of the disease improved, and clinicians gained expertise in providing better medical care. For instance, corticosteroids were used more frequently, while there was a general decrease in the use of lopinavir/ritonavir, tocilizumab, hydroxychloroquine, and interferon. Additionally, non-invasive mechanical ventilation with a high-flow nasal cannula and the prone position were increasingly adopted [107]. Despite these improvements, the need for invasive mechanical ventilation

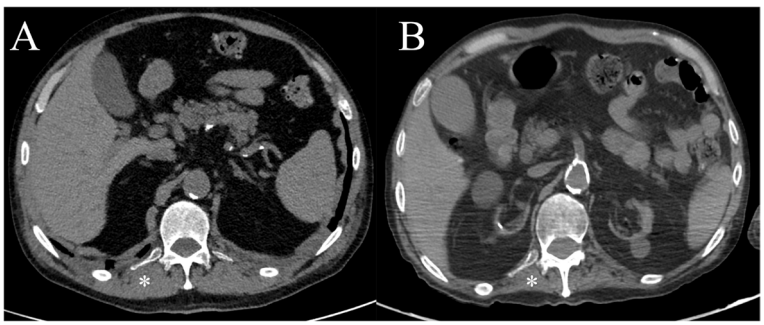

Fig. 6 Axial unenhanced CT images of the same patient after 2 months from the ICU admission for severe COVID-19. Note how the muscle mass in the left para-vertebral muscle at the level of T12 was drastically reduced between the admission (asterisk in **A**) and the follow-up imaging study (asterisk in **B**)

Table 1 Main CT imaging findings of COVID-19-related complications that can arise in ICU patients

Barotraumas	Thromboembolic complications	Hemorrhagic complications	Bacterial and fungal pulmonary co-infections and superinfections	Direct involvement of abdominal parenchymal organs	Sarcopenia
Invasive mechanical ventilation, central venous catheter placement and ECMO increased the risk Chest X-ray has a low sensitivity for the diagnosis Chest CT can confirm the presence of barotraumas, demonstrating the presence of rims of gas around the edges of the lung, with or without a collapsed lung (pneumothorax), or in extra-alveolar spaces (pneumomediastinum, pneumopericardium, pneumoperitoneum and/or subcutaneous emphysema)	Thromboembolic complications are frequently described CT demonstrates the presence of a filling defect within a vessel with hypodense thrombus, venous distension, rim enhancement of the vein, and perivenous edema or fat stranding Thromboembolic events might involve: • *pulmonary arteries*: CT shows often the involvement of the segmental arteries with a very extensive distribution • *mesenteric arteries*: it involves more often the large bowel alone (50%); at the early phase only contracted and thicked gasless loops can be seen; over time, intestinal loops progressively dilate, air-fluid levels appear, and walls become paper-thin; finally, intestinal wall pneumatosis and mesenteric venous gas may appear • *renal arteries*: CT documents solitary or multiple triangular-shaped areas of renal parenchyma with decreased enhancement and apex pointing toward the medulla • *intracranial arteries*: acute ischemic stroke appears at CT as an abnormal hypoattenuated area, with loss of gray-white differentiation and sulcal effacement	Bleeding complications are generally rare but life-threatening CT can identify the site of active bleeding (blush) and its origin (arterial or venous) based on the contrast-enhanced phase The most common site of spontaneous bleeding include: the gastrointestinal system and the brain (both supra and infra-tentorial locations) Hematomas appear as hyperdense masses, varying in size and content, with blood-fluid levels due to the mixture of differently aged components The most common site of spontaneous hematomas include: the rectus sheath and the iliopsoas muscle	In 50–70% of cases, a simultaneous bacterial and fungal infection can be detected The most common bacteria include: Klebsiella pneumoniae, Pseudomonas aeruginosa, Haemophilus influenzae, Escherichia Coli, Acinetobacter baumannii, Mycoplasma pneumoniae and Staphylococcus aureus The most common fungal pathogens include: Aspergillus spp. and Candida spp. Chest X-ray has a low sensitivity for the diagnosis Diagnosis at CT is challenging due to the overlap of imaging features. The appearance of atypical findings (lobar consolidations, pleural effusion, cavitations and/or mediastinal lymphadenopathy) at CT should raise suspicion Pulmonary aspergillosis has a higher mortality rate (up to 50%) and presents as nodular infiltrates, large centrilobular nodules, nodules with halo sign/reversed halo sign, cavitation with a fungus ball within the cavity (air crescent sign) Cultural and/or laboratory tests to confirm or exclude the diagnosis are always needed	The direct involvement of the abdominal organs is rare and the most common findings include: • *large bowel infection*: CT shows diffuse, circumferential, homogeneously enhancing bowel wall thickening with fluid-filled distended intestinal lumen and pericolic fat stranding; absence of filling defects suggestive of thrombi in the abdominal arteries • *hepatic steatosis*: CT documents hypoattenuation (< 40 HU or at least 10 HU < than the attenuation of the spleen) • *pancreatic injury*: CT shows diffuse enlargement of the pancreas with ill-defined borders, mild fat stranding and peripancreatic fluid; exclusion of other etiologies is required • *acute kidney injury*: CT demonstrates an enlarged kidney with loss of corticomedullary differentiation	Sarcopenia is common in long-hospitalized patients and can persist even after discharge (30%) CT is the modality of choice for evaluating the fat content within the muscle (at the level of T5 and T12) Can be used to predict the risk of ICU admission, the length of hospitalization, the in-hospital mortality and the need for reintubation

remained high, as well as the mortality among critical COVID-19 patients [107–112]. Furthermore, the patients who were admitted during the second, third, fourth, and fifth waves of COVID-19 were comparatively younger than those who were hospitalized during the first wave [107, 110, 112–115]. Additionally, these patients had a longer stay in the ICU, which can be attributed to the changes in management protocols of the treatment centers, which shifted from initially recommended "early intubation and ventilation" to the use of non-invasive ventilation to avoid intubation as long as possible [107, 111, 116]. Due to the ongoing impact of COVID-19, it is not unexpected that there are still a high number of complications related to ICU care. Even with the emergence of new variants of the virus, lung CT patterns have remained relatively consistent across different waves of the pandemic. These patterns typically involve multiple areas of consolidation and ground glass opacities, located mainly in the subpleural space, and tend to be most severe within the first week of hospitalization [117]. More recent studies have found that pneumonia severity was highest for the Delta variant of SARS-CoV-2 [66] compared to wild-type and Alpha variants, although with more rapid repair capabilities [118]. Conversely, the most recent variant, Omicron, despite being the most highly mutated and presenting increased contagiousness and infectivity, tends to involve the lungs to a lesser extent and predominantly infects the upper respiratory tract. Patients with the Omicron variant presented a lower pneumonia prevalence than in the previous waves and a peribronchial distribution (rather than peripheral), as compared to patients infected with the Delta variant. However, lung involvement in the Omicron variant has been more frequently characterized by atypical chest CT findings such as cluster-like or randomly distributed ground-glass opacities, or the absence of pneumonia [119].

Following the first wave, the incidence of pneumothorax and pneumomediastinum increased. Some have speculated that this increase may be due to the use of noninvasive respiratory support and dexamethasone, which could lead to pulmonary frailty, although a worse presentation of the disease cannot be ruled out. This hypothesis is indeed supported by the significantly higher rate of barotraumas in non-intubated COVID-19 during the second pandemic wave as compared with the first pandemic wave reported in two recent Italian studies [120, 121]. Nonetheless, studies from the UK and Australia did not find significant differences in the incidence of primary spontaneous barotrauma among different waves [115, 119], although healthcare disparities across the world must be considered. Whether these complications have become more frequent or simply remain stable, the risk of barotrauma in severely ill COVID-19 patients is still high despite the wide implementation of the most recent ICU recommendations. Therefore, healthcare providers must remain vigilant in detecting and promptly treating these potentially life-threatening events.

Contrary to barotraumas, the rate of thromboembolic complications following COVID-19 infection showed a global decrease during the subsequent waves of the pandemic compared to the first wave [109, 114, 119, 122]. This lower rate of thrombotic events is likely inherent to the increased intensity of routine thromboprophylaxis, the reduced length of hospitalization, the introduction of vaccination and the reduced virulence of new SARS-CoV-2 variants, although the lower rate of CT pulmonary angiographies performed during the second/third waves might have impacted these results [123]. Nonetheless, a recent study reported a 41% and 60% increased risk of pulmonary embolism with ancestral variants compared to Delta and Omicron periods respectively, regardless of CT pulmonary angiography performing rate [124]. Intriguingly, unvaccinated patients demonstrated a 2.75-fold increased risk of COVID-associated pulmonary embolism during the Delta and Omicron periods compared to vaccinated or recovered patients, thus awareness must still be high among this specific population. Similarly, the overall incidence and severity of ischemic stroke also declined over time during the pandemic, although the COVID-19 patients affected were younger and with higher in-hospital mortality compared to pre-COVID controls [115, 125, 126]. Spontaneous bleeding remains a rare complication of COVID-19 disease and was more frequently reported during the first two pandemic waves possibly as a consequence of anticoagulant treatment and consumption of coagulation factors [119, 127, 128].

After the first wave of the pandemic, there has been a noticeable increase in bacterial and fungal superimposed infections, probably due to the prolonged use of mechanical ventilation and the widespread use of corticosteroids [108, 115, 129]. In addition, the prevalence of fungal species noticeably varied during the pandemic, with a significant increase in the isolation of *Aspergillus spp.* during the second/third waves. This could be due to changes in environmental conditions, host factors, healthcare practices or even to differences between the main circulating strains of the SARS-CoV-2 virus which may predispose certain fungal species to co-infect or superinfect patients with COVID-19 [130]. Furthermore, during the second and third waves, patients were more susceptible to developing antimicrobial resistance, sometimes even to two or more drugs, leading to an increase in both severity and mortality [108]. Therefore, more stringent antimicrobial stewardship and innovative therapeutic approaches are

still urgently needed in future waves as newer and more severe co-infections may arise.

During the first wave of the pandemic, COVID-19 infection was mainly considered a pulmonary infection and clinicians focused on its most life-threatening manifestations (such as thromboembolic events), thus data regarding the involvement of abdominal organs are scarce. As time passed, different clinical and radiological manifestations were observed, including direct damage to the liver and the kidney. Data regarding COVID-19-related gastrointestinal symptoms are conflicting, with some studies reporting an increased frequency in the last waves of the pandemic [114, 131] and others observing no difference or an even lower prevalence compared to the outbreak [116–128]. Therefore, future studies are needed to demonstrate whether the newer variants of the SARS-CoV-2 virus are more prone to hepatic, pancreatic and intestinal involvement. Despite some discrepancies in the current literature [132], the majority of analyses suggest that acute kidney injury rates have decreased through subsequent waves of the pandemic. Although the reasons for this are unclear, it has been speculated that the lower incidence of renal complications is related to changes in patient demographics as well as adjustments in COVID-19 treatment protocols [133–137].

Only one Italian study analyzed the rate of sarcopenia among different waves, reporting a much higher prevalence of this complication during the first wave compared to the second wave (57.9% vs. 21.6%) [138]. This findigns could be partially explained by the different health policies in Italy, where healthcare authorities recommended home quarantine for individuals with mild to moderate symptoms during the first wave, possibly leading to a more compromised general condition at the moment of hospital admission due to the progression of the disease; conversely, in the second wave, the total number of ICU beds increased, primary care doctors were directly involved in the initial management of COVID-19 patients and an earlier hospitalization was promoted. These results are also consistent with the evidence of a younger population hospitalized for COVID-19 disease following the first wave.

9 Conclusions

Despite RT-PCR is now regarded as the gold standard for COVID-19 diagnosis, imaging studies are still essential for detecting and monitoring the unpredictable evolution of this disease, especially in severely ill patients like those admitted to ICU. Difficulty weaning, lack of progress, and clinical deterioration should prompt a thorough evaluation for persistent or untreated manifestations of COVID-19, as well as complications from COVID-19 itself, including superimposed barotrauma-related damage, bacterial/fungal infections and thromboembolic manifestations. Since many of these potential complications may be difficult to disentangle from the underlying condition, imaging modalities play an essential role in the monitoring and management of these patients. In particular, clinicians need to maintain a high level of suspicion and promptly pursue imaging tests, especially in patients who either fail to improve or worsen despite optimal management. Moreover, they should be conscious of the potential involvement of other extra-pulmonary organs and systems in order to guide appropriate therapeutic decisions and thus improve the patient's prognosis. This widespread utility of imaging modalities calls for a deeper understanding of potential radiologic findings in this disease and the need for multidisciplinary collaboration between radiologists and anesthesiologists to provide actionable guidance to appropriate interventions under such conditions.

Abbreviations

ACE2	Angiotensin-converting enzyme 2
ARDS	Acute respiratory distress syndrome
CT	Computed tomography
COVID-19	Coronavirus disease 2019
ECMO	Extracorporeal membrane oxygenation
HRCT	High-resolution computed tomography
HU	Hounsfield unit
ICU	Intensive care unit
MIP	Maximum intensity projection
PEEP	Positive end-expiratory pressure
RT-PCR	Reverse transcription polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
VAP	Ventilator-associated pneumonia

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