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The evolution of lung CT findings in COVID-19 from 2020-2023: more signs of co-infection!

Sabrina Romagny, MD, PhD², Thibault Sixt, MD², Florian Moretto, MD², Patrick Ray, MD, PhD¹, Frederic Ricolfi, MD, PhD³, Lionel Piroth, MD, PhD²,³, Mathieu Blot, MD, PhD²,³,⁴,⁵

¹ Emergency Department, Dijon-Bourgogne University Hospital, Dijon, France
² Department of Infectious Diseases, Dijon-Bourgogne University Hospital, Dijon, France
³ Department of Radiology, Dijon-Bourgogne University Hospital, Dijon, France
⁴ CHU Dijon-Bourgogne, INSERM, Université de Bourgogne, CIC 1432, Module Épidémiologie Clinique, F21000 Dijon, France and LabEx LipSTIC, University of Burgundy, Dijon, France
⁵ Lipness Team, INSERM Research Centre LNC-UMR1231 and LabEx LipSTIC, University of Burgundy, Dijon, France

Correspondence address.
Mathieu Blot, MD, PhD
Infectious Diseases Department; Dijon Bourgogne University Hospital
14 rue Paul Gaffarel 21079 Dijon France
Tel +33 3 80 29 33 05 Fax +33 3 80 29 36 38
E-mail: mathieu.blot@chu-dijon.fr

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Abbreviations.

COVID-19: coronavirus disease 2019

CT: computed tomography

IQR: interquartile range
Abstract

Introduction: Bacterial co-infection was infrequent in first waves of COVID-19. Our study aimed to describe how radiological findings have evolved among patients hospitalized with COVID-19.

Methods: We retrospectively included all COVID-19 patients hospitalized in the department of infectious diseases of the Dijon University Hospital (France) between February 27, 2020, and May 15, 2023. We recorded patient characteristics and standardized chest CT findings, in particular typical COVID-19 patterns and superimposed signs of co-infection. We analyzed data according to chronological periods in 6-month increments.

Results: 878 patients were included (median age 72 (interquartile range 58-83), 745 (85%) required oxygen. 743 (85%) patients had at least one chest CT scan. Radiologists reported typical signs of COVID-19 in 624 (84%) patients and signs of co-infection in 118 (16%) patients. Between the first semester of 2020 and July 2022-May 2023, there was a significant decrease in the proportion of typical signs of COVID-19 (82% vs. 11%, p<0.001), but a significant increase of atypical signs suggestive of bacterial co-infection (4% vs. 57%, p<0.001).

Conclusion: We observed significant changes in the lung imaging of hospitalized COVID-19 patients, with the emergence of more features of co-infection. This may suggest a transition toward the model of influenza and bacterial co-infection.
To the Editor,

Bacterial co-infection is commonly identified in viral respiratory infections such as influenza (1). Therefore, antibiotic therapies were frequently prescribed at the onset of COVID-19 pandemic, but were then largely reduced since bacterial co-infection was infrequent [1]. The current guidelines recommend that antibiotics not be routinely prescribed in patients with COVID-19 unless bacterial co-infection is suspected or confirmed [2,3]. Computed tomography (CT) has been widely used to help identify typical COVID-19 findings and distinguish them from co-infection [2,4]. COVID-19 has progressively changed, yet most guidelines are still based on data from the 1st wave. Our study aimed to describe how radiological findings have evolved among patients hospitalized with COVID-19.

We retrospectively included all COVID-19 patients (confirmed by RT-PCR assay) older than 18 years and hospitalized in the department of infectious diseases of the Dijon University Hospital (France) between February 27, 2020, and May 15, 2023.

From the onset of the pandemic, in our hospital, a chest CT scan was almost systematically performed to help identify typical COVID-19 findings and to distinguish it from bacterial causes, to detect pulmonary embolism, and to evaluate the severity of lung involvement. A standardized assessment of chest CT was implemented to detect and characterize typical COVID-19 patterns, including ground glass opacities, crazy paving pattern and/or predominantly peripheral bilateral consolidations. The presence of a pulmonary embolism and other signs suggestive of bacterial co-infection (isolated lobar or segmental consolidations, mucoid impactions and/or centrolobular micro-nodules), were also assessed [2,4].

We also examined clinical data. Immunosuppression was defined as human immunodeficiency virus seropositivity with CD4 < 400/mm³, immunosuppressive treatments including corticosteroids (> 0.15mg/kg/d of prednisone), anti-cancer chemotherapy for less than 6 months, hypogammaglobulinemia, asplenia or primary immunodeficiency.
Study protocol and data collection were registered with the French national data protection authority and are in accordance with French (Loi Informatique et Liberté n°78-17 du 6 janvier 1978) and European regulations (GRPD EU 2016/679) on data protection and patient information (Commitment of compliance MR004 n°2210228). Informed consent was waived given the non-interventional study design.

Quantitative values were expressed as medians and interquartile ranges (IQR), and qualitative variables as numbers and percentages. We analyzed data according to chronological periods in 6-month increments. Analyses were performed using GraphPad Prism (v.9.1.1) software.

Over the study period, 878 patients were hospitalized in our department for COVID-19. The median age was 72 (IQR 58-83) years and the male/female sex ratio was 1.3. The median Charlson comorbidity score was 4 (2-6), 86 (10%) patients were immunocompromised, 221 (25%) had diabetes, and 382 (44%) had chronic cardiovascular disease. The median NEWS2 severity score was 5 (3-6) at admission, and 745 (85%) patients required oxygen. Admission to intensive care was required for 158 (18%) patients, and 122 (14%) in-hospital deaths were reported. Over time, we observed a significant increase in the proportion of immunocompromised patients (p<0.001) (Figure 1A).

Among included patients, 743 (85%) had at least one chest CT scan, which was done in the 24 hours following admission in 682 (92%) cases. Radiologists reported typical signs of COVID-19 in 559 (75%) patients, atypical suggestive signs of bacterial co-infection in 52 (7%) patients, signs of both COVID-19 and bacterial coinfection in 66 (9%) and no signs in 66 (9%). Among the 118 patients with atypical signs suggestive of bacterial co-infection, isolated segmental lobar consolidations were reported in 113 (96%), mucoid impactions in 60 (51%) and centrolobular micronodules in 25 (21%). Only 16 (14%) had a respiratory sample analysis, and 6 (5%) patients had a microbiologically proven bacterial co-infection (Streptococcus pneumoniae, Haemophilus influenzae, b, Staphylococcus aureus/Pseudomonas aeruginosa, Serratia marsescens/Proteus mirabilis, Klebsiella oxytoca/Citrobacter koseri).
Between the first semester of 2020 and July 2022-May 2023, there was a significant decrease in the proportion of typical signs of COVID-19 (82% vs. 11%, p<0.001), but a significant increase of atypical signs of COVID-19 suggestive of bacterial co-infection (4% vs. 57%, p<0.001). These two curves intersected in the last year of the study (Figure 1B). To illustrate our findings, we describe the lung imaging of 2 patients hospitalized either during the early or the late pandemic period (Figures 1C-D).

Our study shows that, over time, there have been significant changes in the lung imaging of patients hospitalized for COVID-19. In the more recent period, signs of co-infection were considerably more common, while classical pathological COVID-19 lung patterns were less frequent.

Existing data indicate that rates of bacterial co-infection were relatively low, but COVID-19 has evolved considerably and little is known about the new facets of the disease. Lung imaging has been widely used, and the data collected can provide a dynamic snapshot of the disease. Several studies have reported a trend shifting CT pneumonia patterns toward an atypical predominance over time during the transition from the Delta to the Omicron variant [5–7]. Indeed, Omicron was found to be associated with less frequent typical peripheral bilateral ground-glass opacities, more frequent peribronchovascular predilection, and lower visual pneumonia extent compared to Delta [5]. In addition, atypical CT pneumonia patterns increased during the Omicron BA.5 subvariants (61%) compared with the Omicron BA.1 and BA.2 subvariants (43%). The most common finding was bronchopneumonia (88%) which may correspond to coinfection pneumonia and aspiration pneumonia [8].

Among the crucial questions when a patient is admitted for pneumonia is whether the infection is bacterial or not. To date, there is no reliable test to rule out a bacterial origin, but only a set of arguments based on clinical, (micro-)biological and radiological characteristics. In this setting, and even if it is not a stand-alone evaluation, chest CT can provide strong arguments in favor of a bacterial origin, such as the presence of isolated segmental lobar consolidation, mucoid impactions and/or
centrolobular micronodules [4,9]. Here, we observed a significant reduction in the classical pathological COVID-19 lung pattern along with increased radiological features of bacterial co-infection. This change could be explained by the increase in natural immunization and vaccination of the population and the gradual reduction in the severity of variants.

Although it is not possible to certify bacterial origin, these changes demonstrate the evolving nature of lung imaging in COVID-19. This may suggest a transition toward the model of influenza and bacterial co-infection [10], where the most affected populations are aged and immunocompromised patients, as we observed in our study.

The limitations of this study are related to its retrospective and monocentric nature. Not all, but a majority of patients admitted to our hospital with Covid-19 were included in this study, since the Infectious Diseases Department is the first to receive such patients. Eight radiologists interpreted CT-scan but with a standardized assessment, limiting inter-operator variability. Finally, as mentioned above, radiological data do not confirm co-infection, but only suggest it.

In conclusion, we observed significant changes in the lung imaging of hospitalized COVID-19 patients, with the emergence of more features of co-infection. Clinicians need to keep in mind that SARS-Cov-2 continues to evolve, and possibly toward the model of influenza and bacterial co-infection. This calls for recommendations to be updated in the light of current data, and clinicians should start probabilistic antibiotics in cases of severe COVID-19 pneumonia with radiological features of co-infection.
Conflict of interest: All authors have read the journal’s policy on disclosure of potential conflicts of interest. The authors have no conflict of interest to declare.

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Ethical approval statement: The study protocol and data collection are in accordance with French (Information Technology and Freedom Law n°78-17 of January 6, 1978) and European (GRPD EU 2016/679) good practice recommendations on data protection and patient information (Commitment of compliance MR004 n°2210228 of December 3, 2018), with written patient consent not being required for this non-interventional study.

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Figure 1. Evolution of radiological findings of patients hospitalized with COVID-19 from 2020 to 2023. Changes in the proportion of immunocompromised patients hospitalized with COVID-19 (n=878) over time since the start of the pandemic (A); changes in chest CT-scan interpretation by radiologist (proportion of patients with typical signs of COVID-19, and with signs of bacterial co-infection) (B); Chest CT-scan finding of a 66-year-old female patient with overweight and hypertension who presented in April 2020 with severe COVID-19 requiring mechanical ventilation. Chest CT-scan showed bilateral ground glass opacities characteristic of COVID-19 with no signs of co-infection (C); 46-year-old female patient with kidney transplant under anti-rejection immunosuppressive therapy who presented in December 2022 with fever, respiratory signs and hypoxemia. A COVID-19 infection was diagnosed but chest CT-scan showed no signs of COVID-19 pneumonia but a left inferior lobar consolidation evocative of co-infection (D)
References


A. Immunocompromised patients

- % of patients over time from 01-06/20 to 07/22-05/23

B. Radiological lung interpretation (CT-scan)

- Graph showing different categories of lung interpretation:
  - No signs of COVID-19 and coinfection
  - Signs of COVID-19 without signs of coinfection
  - Signs of coinfection without signs of COVID-19
  - Signs of COVID-19 and coinfection

C. CT scans showing lung patterns

D. CT scans showing lung patterns