The evolution of lung computed tomography findings in COVID-19 from 2020 to 2023: more signs of co-infection

Received: 1 Oct 2023
Accepted: 28 Nov 2023

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 the coronavirus disease 2019 (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 used widely 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 first wave. Our study aimed to describe how radiological findings have evolved among patients hospitalised with COVID-19.

We retrospectively included all COVID-19 patients (confirmed by reverse transcriptase PCR assay) aged >18 years and hospitalised in the department of infectious diseases of the Dijon University Hospital (Dijon, France) between 27 February 2020 and 15 May 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 standardised assessment of chest CT was implemented to detect and characterise 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 micronodules) were also assessed [2, 4].

In addition, we examined clinical data. Immunosuppression was defined as HIV seropositivity with CD4 <400 cells·mm^{-3}, immunosuppressive treatments including corticosteroids (>0.15 mg·kg^{-1} per day of prednisone), anticancer chemotherapy for <6 months, hypogammaglobulinaemia, 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 78–17 du 6 janvier 1978) and European regulations (European Union General Data Protection Regulation 2016/679) on data protection and patient information (commitment of compliance MR004 2210228). Informed consent was waived given the noninterventional study design.

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

Over the study period, 878 patients were hospitalised 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 National Early Warning Score 2 severity score was 5 (3–6) at admission; and 745 (85%) patients required oxygen. Admission to intensive care was required for

Shareable abstract (@ERSpublications)
Significant changes were observed in the lung imaging of hospitalised COVID-19 patients from 2020 to 2023, with the emergence of more signs of co-infection https://bit.ly/3TaQlJ2

Cite this article as: Romagny S, Sixt T, Moretto F, *et al*. The evolution of lung computed tomography findings in COVID-19 from 2020 to 2023: more signs of co-infection. *ERJ Open Res* 2024; 10: 00727-2023 [DOI: 10.1183/23120541.00727-2023].

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 h 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 co-infection in 66 (9%) patients and no signs in 66 (9%) patients. 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 six (5%) patients had a microbiologically proven bacterial co-infection (*Streptococcus pneumoniae*, *Haemophilus influenzae* b, *Staphylococcus aureus*/*Pseudomonas aeruginosa*, *Serratia marscescens*/*Proteus mirabilis*, *Klebsiella oxytoca*/*Citrobacter koseri*).

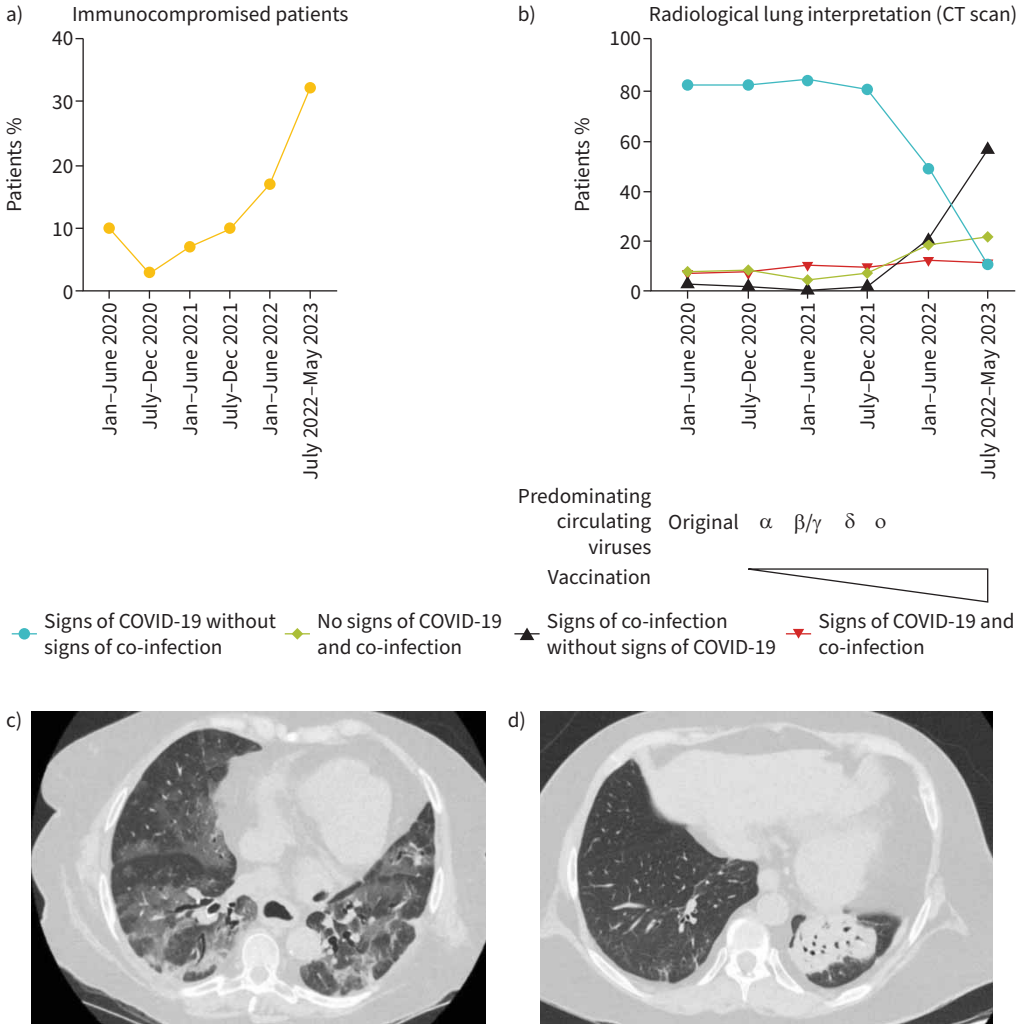

FIGURE 1 Evolution of radiological findings of patients hospitalised with coronavirus disease 2019 (COVID-19) from 2020 to 2023. a) Changes in the proportion of immunocompromised patients hospitalised with COVID-19 (n=878) over time since the start of the pandemic; b) changes in chest computed tomography (CT) scan interpretation by radiologist (proportion of patients with typical signs of COVID-19, and with signs of bacterial co-infection); c) 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; d) 46-year-old female patient with kidney transplant under antirejection immunosuppressive therapy who presented in December 2022 with fever, respiratory signs and hypoxaemia. A COVID-19 infection was diagnosed; chest CT scan showed no signs of COVID-19 pneumonia, but a left inferior lobar consolidation evocative of co-infection. Jan: January; Dec: December.

Between the first semester of 2020 and July 2022 to May 2023, there was a significant decrease in the proportion of typical signs of COVID-19 (82% *versus* 11%, p<0.001), but a significant increase of atypical signs of COVID-19 suggestive of bacterial co-infection (4% *versus* 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 two patients hospitalised during the early and late pandemic period (figure 1c,d).

Our study shows that, over time, there have been significant changes in the lung imaging of patients hospitalised 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 co-infection 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 standalone evaluation, chest CT can provide strong arguments in favour 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 immunisation 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 scans, but with a standardised assessment, limiting interoperator variability. Finally, as mentioned earlier, radiological data do not confirm co-infection, only suggest it.

In conclusion, we observed significant changes in the lung imaging of hospitalised 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, 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.

Sabrina Romagny[1], Thibault Sixt[2], Florian Moretto[2], Patrick Ray[1], Frederic Ricolfi[3], Lionel Piroth[2,4,5] and Mathieu Blot[2,4,5,6]

[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, Dijon, France. [5]LabEx LipSTIC, University of Burgundy, Dijon, France. [6]Lipness Team, INSERM Research Centre LNC-UMR1231 and LabEx LipSTIC, University of Burgundy, Dijon, France.

Corresponding author: Mathieu Blot (mathieu.blot@chu-dijon.fr)

Provenance: Submitted article, peer reviewed.

Acknowledgements: The authors thank the patients, Nadia Buthiot (Dijon-Bourgogne University Hospital, Dijon, France) for collecting the data, Maud Carpentier (Direction de la Recherche Clinique et de l'Innovation, Dijon-Bourgogne University Hospital), and Suzanne Rankin (Dijon-Bourgogne University Hospital) for proofreading and editing the manuscript.

Conflict of interest: None declared.

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

References

1 Langford BJ, So M, Raybardhan S, *et al.* Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. *Clin Microbiol Infect* 2020; 26: 162–129.
2 Rubin GD, Ryerson CJ, Haramati LB, *et al.* The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. *Chest* 2020; 158: 106–116.
3 Moretto F, Sixt T, Devilliers H, *et al.* Is there a need to widely prescribe antibiotics in patients hospitalized with COVID-19? *Int J Infect Dis* 2021; 105: 256–260.
4 Revel MP, Parkar AP, Prosch H, *et al.* COVID-19 patients and the radiology department – advice from the European Society of Radiology (ESR) and the European Society of Thoracic Imaging (ESTI). *Eur Radiol* 2020; 30: 4903–4909.
5 Yoon SH, Lee JH, Kim BN. Chest CT findings in hospitalized patients with SARS-CoV-2: Delta *versus* Omicron variants. *Radiology* 2023; 306: 252–260.
6 Crombé A, Bensid L, Seux M, *et al.* Impact of vaccination and the Omicron variant on COVID-19-related chest CT findings: a multicenter study. *Radiology* 2023; 307: e222730.
7 Tsakok MT, Watson RA, Saujani SJ, *et al.* Reduction in chest CT severity and improved hospital outcomes in SARS-CoV-2 Omicron compared with Delta variant infection. *Radiology* 2023; 306: 261–269.
8 Lee JE, Hwang M, Kim YH, *et al.* SARS-CoV-2 variants infection in relationship to imaging-based pneumonia and clinical outcomes. *Radiology* 2023; 306: e221795.
9 Debray MP, Carette MF, Loubet P, *et al.* CT features of community-acquired pneumonia at the emergency department. *Respir Med Res* 2022; 81: 100892.
10 McCullers JA. The co-pathogenesis of influenza viruses with bacteria in the lung. *Nat Rev Microbiol* 2014; 12: 252–262.