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Short communication

Evolution of lung function and chest CT 6 months after COVID-19 pneumonia: Real-life data from a Belgian University Hospital

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1. Introduction

Long-term pulmonary consequences after COVID-19 pneumonia have yet to be elucidated. In our 10-week follow-up study of 220 patients with COVID-19 pneumonia, pulmonary restriction was found to be the most prevalent pulmonary function impairment [1]. Probably in patients with COVID-19 pneumonia, pulmonary restriction was found to have yet to be elucidated. In our 10-week follow-up study of 220 patients, assessed at a median follow up of 10 weeks (visit FU1), a subgroup of patients was invited for a second follow-up visit 6 months after diagnosis of COVID-19 pneumonia (visit FU2), based on clinical judgment of the treating chest

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ABSTRACT

Introduction: Most post COVID-19 follow-up studies are limited to a follow-up of 3 months. Whether a favorable evolution in lung function and/or radiological abnormalities is to be expected beyond 3 months is uncertain.

Methods: We conducted a real-life follow-up study assessing the evolution in lung function, chest CT and ventilation distribution between 10 weeks and 6 months after diagnosis of COVID-19 pneumonia.

Results: Seventy-nine patients were assessed at 6 months of whom 63 had chest CT at both follow-up visits and 46 had multiple breath washout testing to obtain lung clearance index (LCI). The study group was divided into a restrictive (n = 39) and a non-restrictive subgroup (n = 40) based on TLC z-score. Restriction was associated with a history of intubation, neuromuscular blockade use and critical illness polyneuropathy. Restriction significantly improved over time, but was not resolved by 6 months (median TLC z-score of −2.2 [IQR: −2.7; −1.5] at 6 months versus −2.7 [IQR: −3.1; −2.1] at 10 weeks). LCI did not evolve between both follow-up visits. Symptoms and chest CT score improved irrespective of restriction.

Conclusion: We observed a disconnect between the improvement of COVID-19 related symptoms, chest CT lesions, and corresponding lung function. While CT imaging is almost normalized at 6 months, a further reduction of pulmonary restriction may be hoped for beyond 6 months in those patients showing restriction at their first follow-up visit.

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physician, who took into account lung function and visual inspection of CT images at FU1. At both FU1 and FU2, patients underwent complete pulmonary function testing (MasterScreen PFT, SentrySuite2.19, Mettawa, IL, USA). Where feasible, N2 multiple breath washouts (EasyPro; Wbreath3.55, NDDMedizintechnik, Switzerland) were performed to obtain lung clearance index (LCI). Chest CT was scored 0–25 based as described [1,7] and was also examined for predominant CT patterns (ground glass opacity, crazy paving, consolidation) using a deep learning algorithm specifically designed to quantify COVID-19 related lung lesions (https://icometrix.com/services/icolung).

3. Results

Of the initial cohort assessed at 10 weeks post-COVID-19 pneumonia, 92 patients were invited for a second follow-up at 6 months. Of these 92 patients, 79 (86%) presented at FU2 for lung function testing. Of the 79 patients, 63 (80%) had a CT at both follow-up visits (FU1 and FU2) which could be compared to their CT at diagnosis. Based on staff and equipment availability within the constraints of a COVID-19 safe environment, 46 (58%) of these patients also had LCI measurement. Both symptoms and radiological abnormalities improved between FU1 and FU2 (Table 1), irrespective of restriction. In addition, the CT score, which had markedly improved from a median of 15 (IQR: 12–16) at diagnosis to 7 (IQR: 4–10) at FU1 for the group as a whole, continued to significantly decrease to 2 (IQR: 0–5) at FU2 (Friedman; p < 0.001). In the 22 patients with a CT score ≥ 5 at FU2 (Restr: 12; Non-Restr: 10), ground glass was the most prevalent pattern (in 22 out of 22).

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4. Discussion

This study in 79 patients documents the evolution of symptoms, chest CT and lung function including ventilation distribution between 10 weeks and 6 months after COVID-19 pneumonia. We extend previous reports of short-term improvements in chest CT abnormalities [1,10] by showing that the majority of CT score improvement occurs in the first 10 weeks, but that a further decrease is obtained when patients are reassessed at 6 months. Importantly, we observed a disconnect between the improvement of COVID-19-related CT lesions, and corresponding lung function abnormalities, in particular restriction.

Having ruled out ethnicity and BMI as determinants of those COVID-19 patients with persistent residual restriction, our data are suggestive of

| Table 1 | Clinical characteristics, symptoms scores, CT scores and lung function represented per subgroup (restrictive and non-restrictive patients). |
|---------|-------------------------------------------------------------------------------------------------------------------------------------|
| Total n = 79 | Restrictive (\( ^{\dagger} \)) n = 39 | Non-Restrictive n = 40 | p-value |
| **Anthropometrics** | | | |
| Caucasian | 28 (72%) | 39 (98%) | 0.002 |
| Age (years) | 56 [50; 64] | 57 [50; 64] | NS |
| BMI (kg/m\(^2\)) | 28.1 [25.3; 31.7] | 27.1 [24.4; 30.5] | NS |
| Male | 29 (74%) | 29 (73%) | NS |
| **Clinical History** | | | |
| DM | 7 (18%) | 5 (13%) | NS |
| AHT | 17 (44%) | 11 (28%) | NS |
| Intubation | 6 (15%) | 1 (3%) | 0.045 |
| Neuromuscular blockade | 4 (10%) | 0 (0%) | 0.039 |
| Critical illness | 4 (10%) | 0 (0%) | 0.039 |
| **PNP** | | | |
| Hospitalization days | 11 [6; 15] | 8 [5; 10] | 0.09 |

Continuous data are expressed as median [interquartile range]. P-values (between both subgroups at FU1): Chi-squared and Mann-Whitney test. NS: non-significant (p > 0.1).

\( ^{\dagger} \): significant difference (p < 0.05) in Wilcoxon test between FU1 and FU2 within each subgroup.

BMI: body mass index, DM: diabetes mellitus, AHT: arterial hypertension, smoking: actively or history of smoking (> 5 pack years), ICU: intensive care unit, PNP: polyneuropathy, FU: follow up, FEV\(_1\): forced expiratory volume in 1 second, FVC: forced vital capacity, TLC: total lung capacity, TLC\(_\text{CO}\): diffusing capacity for carbon monoxide, K\(_\text{CO}\) = TLC\(_\text{CO}$$/V_{\text{A}}$$; transfer coefficient for carbon monoxide, MIP: maximum inspiratory pressure; LCI: lung clearance index. (\( ^{\dagger} \)) on n = 21 and 25 in respectively, restrictive and non-restrictive group.

In restrictive groups are patients with z-score for TLC below -2.7 [8,9], to TLC. As a result, ethnicity-adjusted median TLC was 77% instead of 74% predicted for the Restr group. Significant improvements in TLC\(_\text{CO}\) were observed between FU1 and FU2, but not in transfer coefficient (K\(_\text{CO}\)), which remained normal throughout. At FU1, LCI was above the upper limit of normal in 6 (Restr) and 8 (Non-Restr) patients, who were all smokers. No significant changes in LCI were observed between FU1 and FU2 (p > 0.1).

\( ^{\ddagger} \): included in restrictive groups are patients with z-score for TLC below – 1.64.

Based on COVID-19 specific CT scoring system [7]; on n = 30 and 33 in respectively, restrictive and non-restrictive group.

Reference values based on GJL 2012 (http://gilgastransfer.org.au/calcs/spiro.html); Caucasians, African Americans and North and South East Asians.

Reference values for Caucasians based on GJL 2017: Caucasians only, taking into account GLI correction on September 25, 2020 (http://gilgastransfer.org.au/calcs/tlco.html).

Local reference values based on [13–15]: Caucasians only.
two mechanisms that could be further examined in these patients. The first one is expiratory muscle strength since MEP values were significantly lower in the Restr group, which could in turn be associated with history of intubation or neuromuscular blockade in this subgroup. To tease out whether this represents isolated respiratory as opposed to generalized muscle weakness requires a measurement of quadriceps and bicipal muscle strength. Second, we cannot exclude that some COVID-19 patients may have developed microthromboses and associated parenchymal damage [11], resulting in loss of alveolar volume. To explore this possibility, COVID-19 patients with long-term restriction could benefit from dual energy CT and lung compliance or impulse oscillometry measurements.

We also investigated whether ventilation distribution could be affected by the pulmonary restriction, and this was not the case. The slightly higher LCI values were related to smoking history, and did not show any change at all between 10 weeks and 6 months follow-up. This indicates that restriction inflicted by COVID-19 is homogeneously distributed over the lungs in contrast to for instance radiotherapy-induced localized restriction affecting both TLC and LCI [12].

Strengths of our study are the addition of a 6-month post-infection follow-up point, full lung function testing including plethysmography to obtain a direct measurement of restriction rather than surrogate measures such as FVC, verification of ventilation maldistribution where possible, and availability of chest CT at the different follow-up points. An inherent limitation to this kind of real-life study is that we cannot exclude that prior to contracting COVID-19, some patients might have had undiagnosed lung restriction.

In conclusion, this study reveals that both symptoms, lung function and chest CT scan continue to improve until 6 months after COVID-19 pneumonia. The potential mechanisms of persistent restriction at 6 months in those patients showing restriction at their first follow-up visit, could be interrogated with dedicated measurements of muscle weakness and lung compliance.

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None.

CRediT authorship contribution statement

Dimitri Stylemans: Conceptualization, Methodology, Investigation, Formal analysis, Writing – original draft. Jelle Smet: Conceptualization, Methodology, Investigation, Formal analysis, Writing – original draft. Shane Hanon: Conceptualization, Methodology, Investigation, Formal analysis, Writing – review & editing. Daniel Schuermans: Methodology, Investigation. Bart Ilsen: Methodology, Investigation. Jef Vanmeulebroucke: Methodology, Investigation. Eef Vanderhelst: Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision. Sylvia Verbanck: Validation, Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2021.106421.

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