Post-COVID-19 Condition: Respiratory Manifestations

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Outline

- **Incidence of respiratory symptoms**
- **Breathlessness as a complex, multifactorial symptom**
- **Post-COVID-19 Pulmonary Evaluation**
- **Summary and future directions**

Post-acute COVID-19 syndrome

David Montani [1], Laurent Savale [1], Nicolas Noel [2], Olivier Meyrignac[3], Romain Colle[4], Matthieu Gasnier[4], Emmanuelle Corruble[4], Antoine Beurnier[1], Etienne-Marie Jutant [1,5], Tài Pham [6], Anne-Lise Lecoq [7], Jean-François Papon[8], Samy Figueiredo[9], Anatole Harrois[9], Marc Humbert [1] and Xavier Monnet [6] for the COMEBAC Study Group

JOHNS HOPKINS MEDICINE

- **Breathlessness** is most common respiratory symptom
  - At 12 months: 5-80% post-hospital; 14% non-hospitalized
  - Not closely associated with initial COVID-19 severity of illness
- **Cough** occurs in 2-42% of patients post-COVID
  - No clinical or hospitalization factors associated with persistent cough
- Both associated with **worse quality of life**

Eur Respir Rev 2022; 31: 210185

6-month consequences of COVID-19 in patients discharged from hospital: a cohort study

Chaolin Huang, MD * • Lixue Huang, MD * • Yeming Wang, MD * • Xia Li, MD * • Lili Ren, PhD * • Xiaoying Gu, PhD *

THE LANCET

- **N=1733 – 6 month f/u**
  - **10 patients required IMV/ECMO**
- **1265 (76%) ≥1 symptom**
- **Pulmonary:** **Dyspnea - mMRC ≥1 419/1615 (26%)**
  PFTs - DLCO < 80% (56% HFNC/NIV/MV)
- **Physical function:** **6MWT 88% (76-101%)**
- **N=390 with ultrasound → no LE DVT**

Greater proportion in the HFNC/NIV/MV group w/ dyspnea, decreased mobility (EQ5D), anxiety/depression

1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study

Lancet 2021; 398: 747–58

JOHNS HOPKINS MEDICINE

Lixue Huang*, Qun Yao*, Xiaoying Gu*, Qiongya Wang*, Lili Ren*, Yeming Wang*, Ping Hu*, Li Guo*, Min Liu, Jiuyang Xu, Xueyang Zhang, Yali Qu, Yanqing Fan, Xia Li, Caihong Li, Ting Yu, Jiaan Xia, Ming Wei, Li Chen, Yanping Li, Fan Xiao, Dan Liu, Jianwei Wang†, Xiangguang Wang†, Bin Cao†

- **N=1276 (54 admitted to ICU)**
- **1265 (49%) ≥1 symptom**
- **Pulmonary: Dyspnea - mMRC ≥1 30% (vs 26%, p<.02, at 6m)**

PFTs – HFNC/NIV/MV - 29% TLC<80% (vs 39%, p=.02, at 6m)

No improvement in DLCO from 6 to 12 months

- **Physical function: 6MWT – no change from 6 months**

Compared with matched controls, greater proportion of COVID-19 survivors had dyspnea

3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study

Xiaojun Wu*, Xiaofan Liu*, Yilu Zhou*, Hongying Yu*, Ruiyun Li*, Qingyuan Zhan*, Fang Ni, Si Fang, Yang Lu, Xuhong Ding, Hailing Liu, Rob M Ewing, Mark G Jones†, Yi Hu†, Hanxiang Nie†, Yihua Wang†

JOHNS HOPKINS MEDICINE

- **83 patients w/ severe COVID-19 (not MV) Feb – March 2020**
  - **Excluded: baseline HTN, DM, CV disease, chronic lung disease**
  - **No steroids**

Parameter	3 mos	6 mos	12 mos
DLCO (% predicted) (median [IQR])	77 (67-87)	76 (68-90)	88 (78-101)
6-min walk distance (median [IQR])	535 (490-565)	585 (552-626)	615 (583-633)
Ground glass opacity on CT (N (%))	65 (78%)	38 (46%)	19 (23%)

- **24% with abnormal CT at 12 months**
  - **HFNC/NIV and longer hospital LOS associated with worse DLCO**
- **33% with impaired DLCO (<80% predicted) at 12 months**
  - **Female gender associated with worse DLCO**

Lancet Respir Med 2021; 9:747–54

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  - Post-COVID-19 ILD
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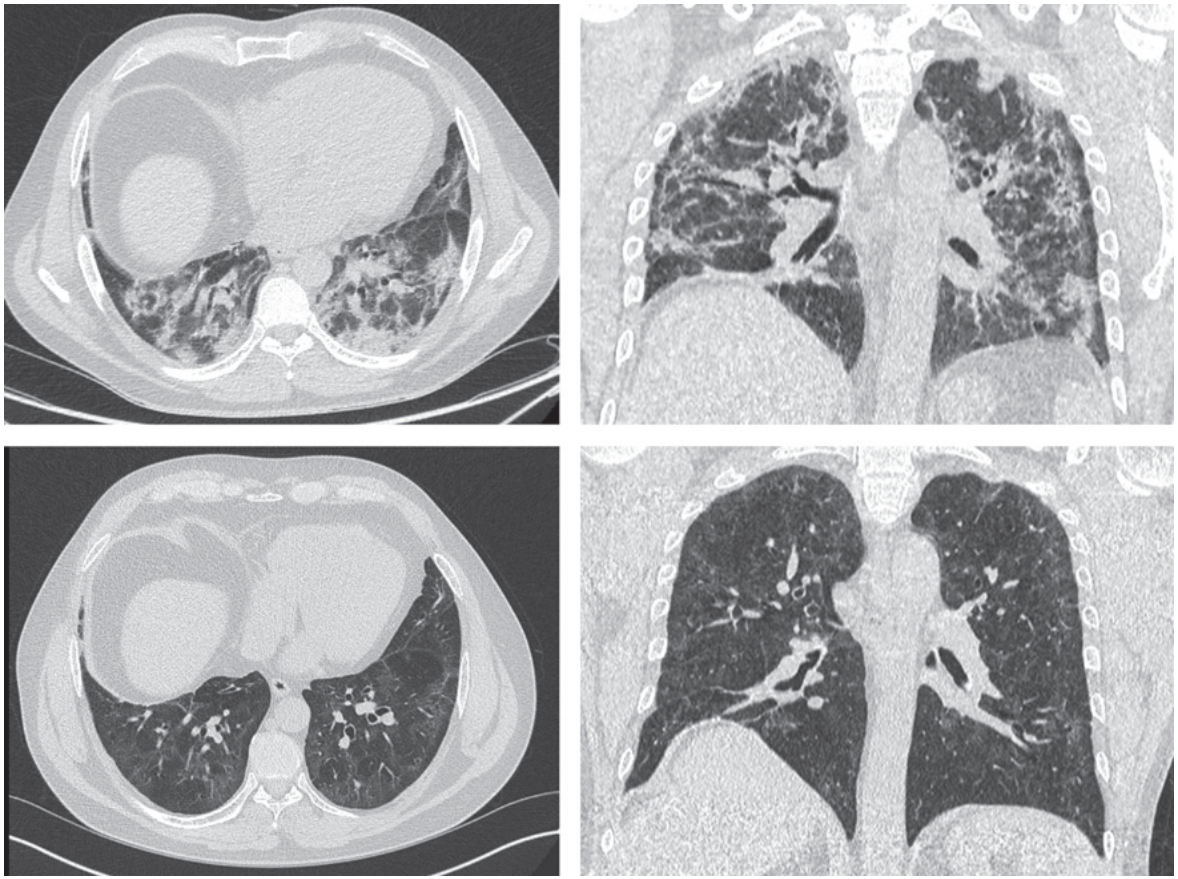
Post-COVID-19 Pulmonary Radiographic Findings



Myall et al. *Annals of the American Thoracic Society*. 2021;18(5):799-806. doi:10.1513/AnnalsATS.202008-1002OC

Outline

- Incidence of respiratory symptoms
- Breathlessness as a complex, multifactorial symptom
  - Post-COVID-19: Asthma
- Summary and future directions

Asthma and COVID-19

- Asthma not a consistent risk factor for severe COVID-19
- However, inverse relationship between asthma control in the year prior to infection and COVID-19 severity
- Hypotheses:
  - Differences in TH2 inflammation
  - Decreased expression of ACE2
  - Inhaled corticosteroid use
  - Airway hyperresponsiveness following other viral infections

Palmon et al. J Allergy & Clin Immunol 10:3, March 2022; 658-663

Impact of COVID-19 on people with asthma: a mixed methods analysis from a UK wide survey

BMJ Open Respiratory Research

Keir Elmslie James Philip [1,2,3] Sara Buttery,[1,2,3] Parris Williams,[1,2,3] Bavithra Vijayakumar,[1,2,3] James Tonkin,[1,2,3] Andrew Cumella,[4] Lottie Renwick,[5] Lizzie Ogden,[4] Jennifer K Quint,[1,3,6] Sebastian L Johnston,[1,2] Michael I Polkey,[1,2,3] Nicholas S Hopkinson [1,2,3]

- N=4900 with asthma (N=471 with self-reported COVID-19)
  - Asthma UK and British Lung Foundation Survey
- Self-reported "Long COVID" N=261 (56%)
  - Greater % of those with Long COVID reported:
    - Breathing worse/much worse (74% vs 35%, p<0.001)
    - Increase in rescue inhaler use (68% vs 35%, p<0.001)
    - Asthma management worse/much worse (60% vs 26%, p<0.001)

Philip KEJ, *et al. BMJ Open Resp Res* 2022;9:e001056. doi:10.1136/bmjresp-2021-001056

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- Incidence of respiratory symptoms
- Breathlessness as a complex, multifactorial symptom
  - Post-COVID-19: Hyperventilation and Deconditioning
- Post-COVID-19 Pulmonary Evaluation
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Hyperventilation as one of the mechanisms of persistent dyspnea in SARS-CoV-2 survivors

EUROPEAN RESPIRATORY *journal*

- **N=114 patients at 3-months after diagnosis**
  - **91% hospitalized; 18% MV**
- **40% with dyspnea and 32% with fatigue**
- **40% with DLCO < 80%**
- **CPET → exercise limited by:**
  - **Peripheral deconditioning 43%**
  - **Hyperventilation 16%**

Hypothesis: Abnormal central ventilatory control → hyperventilation → alkalosis→ activation of autonomic nervous system

Motiejunaite J et al. Eur Respir J 2021; in press. https://doi.org/10.1183/13993003.01578-2021

Outline

- Incidence of respiratory symptoms
- Breathlessness as a complex, multifactorial symptom
  - Diaphragmatic weakness
  - POTS
  - ME/CFS
  - Pre-existing ILD/Chronic lung disease
  - Pulmonary embolism
  - Cardiovascular
- Post-COVID-19 Pulmonary Evaluation
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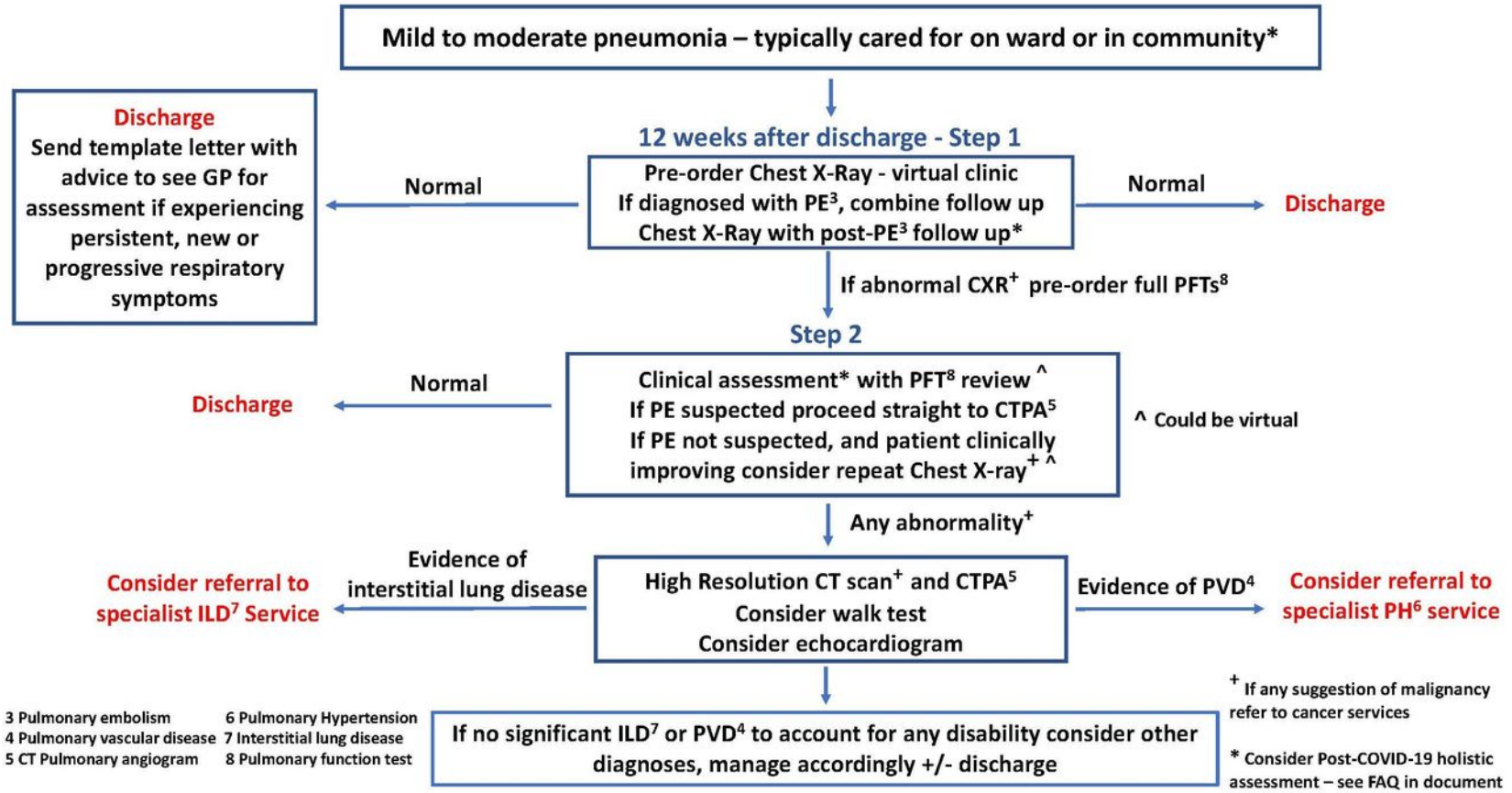
Respiratory follow-up algorithm for patients with mild to moderate COVID-19 pneumonia– typically cared for on the ward or in the community.



Peter M George et al. Thorax 2020;75:1009-1016

Summary

- **Breathlessness and cough are common post-COVID-19**
  - **Complex, multifactorial symptoms**
  - **Evidence-based treatment**
    - **Co-morbid conditions**
    - **Limited COVID-specific therapeutic options**

- **Key research priorities**
  - **Natural history**
  - **Risk factors**
    - **Patient-specific**
    - **Acute phase/hospitalization**
    - **Recovery**
  - **Therapeutic interventions (steroids, anti-fibrotics, etc)**
  - **Long-term association with patient-centered outcomes**