中日友好医院
CHINA-JAPAN FRIENDSHIP HOSPITAL

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

Bin Cao, MD

National Center for Respiratory Medicine

Institute of Respiratory Medicine, Chinese Academy of Medical Science

National Clinical Research Center for Respiratory Diseases

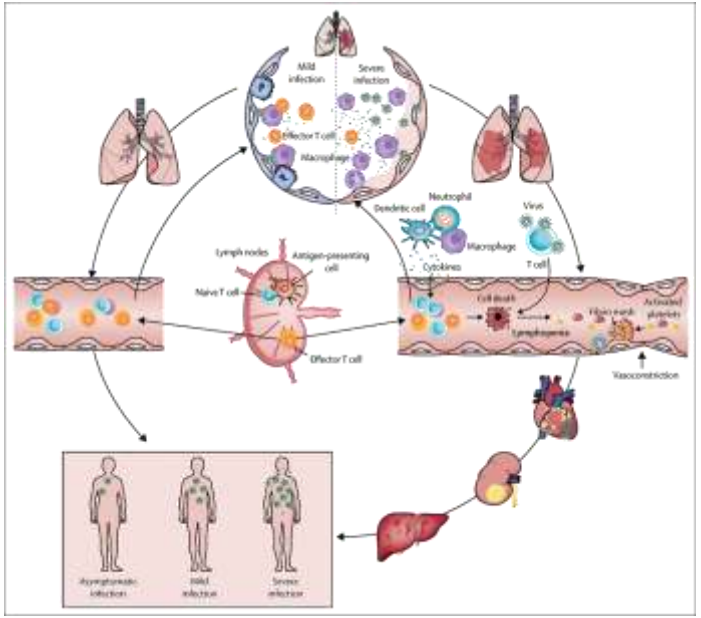
China-Japan Friendship Hospital

caobin_ben@163.com

SARS-CoV-2 Viral sepsis—Observations and Hypotheses

Multi-organ dysfunction

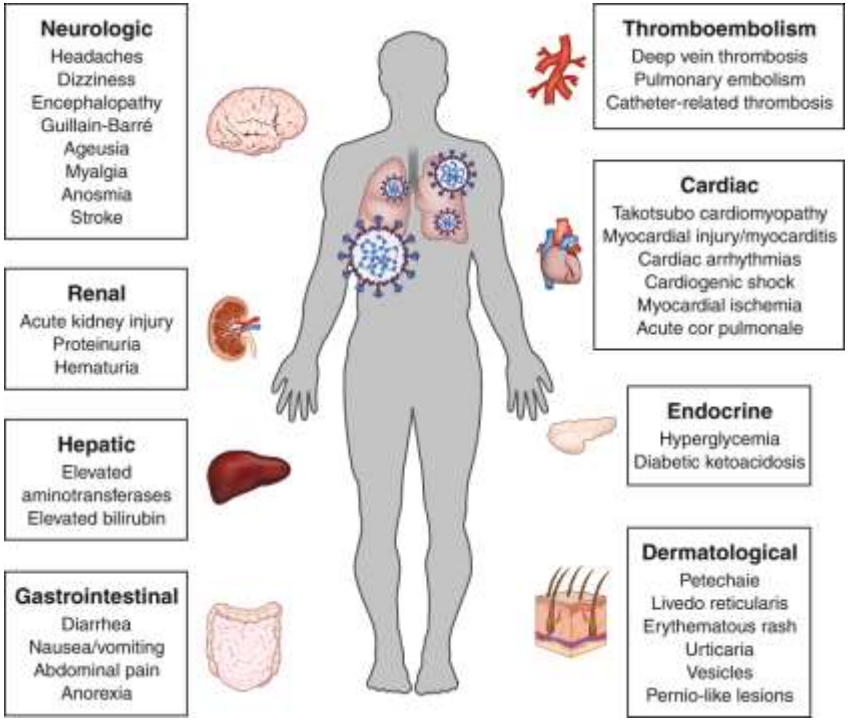
- Pneumonia, Respiratory failure, Acute respiratory distress syndrome
- Metabolic acidosis and internal environment disorders
- Acute kidney injury
- Acute cardiac injury
- ……



——Viral Sepsis

Ren L et al. Chin Med J 2020; 133(9):1015-1024
Huang C et al. Lancet 2020; 395(10223): 497-506
Li H et al. Lancet. 2020;395(10235):1517-1520

Multiple organ dysfunction and complications in hospitalized patients



Complications	Prevalence
Pneumonia	75%
Acute respiratory distress syndrome	15%
Acute liver injury	19%
Cardiac injury	7%-17%
Thromboembolic events	10%-25%
Acute kidney injury	9%
Neurologic manifestations	8%
Acute cerebrovascular disease	3%
Shock	6%

Gupta A, et al. Nat Med. 2020; 26(7):1017-1032
Wiersinga WJ, et al. JAMA. 2020; 324(8)

Clinical questions

- Will the multiple organ dysfunctions persist or new onset damage post-acute occur?
- What are the clinical picture of the aftermath of COVID-19?

Yelin D. Lancet Infect Dis 2020; 20: 1115–17.

- Objectives
  - Describe the health consequences of patients with COVID-19 who have been discharged from hospital at 6 months after symptom onset.
  - Identify the potential risk factors associated with the consequences, in particular disease severity.

Huang et al. Lancet. 2021.

Inclusion & Exclusion criteria

- Inclusion criteria
  - All laboratory confirmed COVID-19 patients who were discharged from Jin Yin-tan Hospital (Wuhan city, China) from January 7, 2020 to May 29, 2020
- Exclusion criteria
  - Dead before this follow-up visit
  - For whom follow-up would be difficult because of psychotic disorder, dementia, or re-admission to hospitals
  - Unable to move freely due to concomitant osteoarthropathy disease or immobile before or after discharge due to diseases such as stroke or pulmonary embolism
  - Declined to participate
  - Unable to be contacted
  - Living outside of Wuhan or in nursing or welfare homes

Huang et al. Lancet. 2021.

Schedule

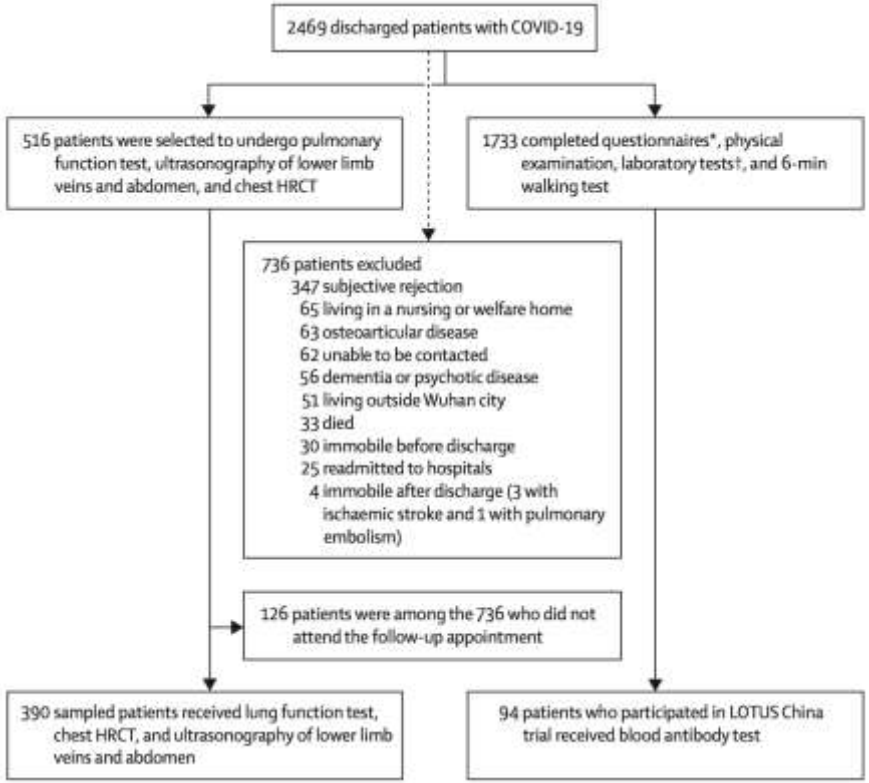
- The appointment for the follow-up visit was set by trained medical staff via telephone
- Follow-up was conducted in the outpatient clinic of Jin Yin-tan Hospital
- Examination items

  - ✓ Physical examination
  - ✓ Self-reported symptom questionnaire
  - ✓ mMRC dyspnea scale
  - ✓ EQ-5D-5L questionnaire & EQ-VAS
  - ✓ 6-min walking test
  - ✓ Blood test (include antibody test*)
  - ✓ Chest HRCT #
  - ✓ Pulmonary function test#
  - ✓ Ultrasonography of lower limbs vein and abdomen#

*: Participants who had been previously enrolled in the Lopinavir Trial for suppression of SARS-CoV-2 in China[1].
#: A stratified disproportional random sampling procedure according to severity scale was used to select patients to undergo special tests.

[1]Cao et al. N Engl J Med 2020; 382: 1787–99.
Huang et al. Lancet. 2021.

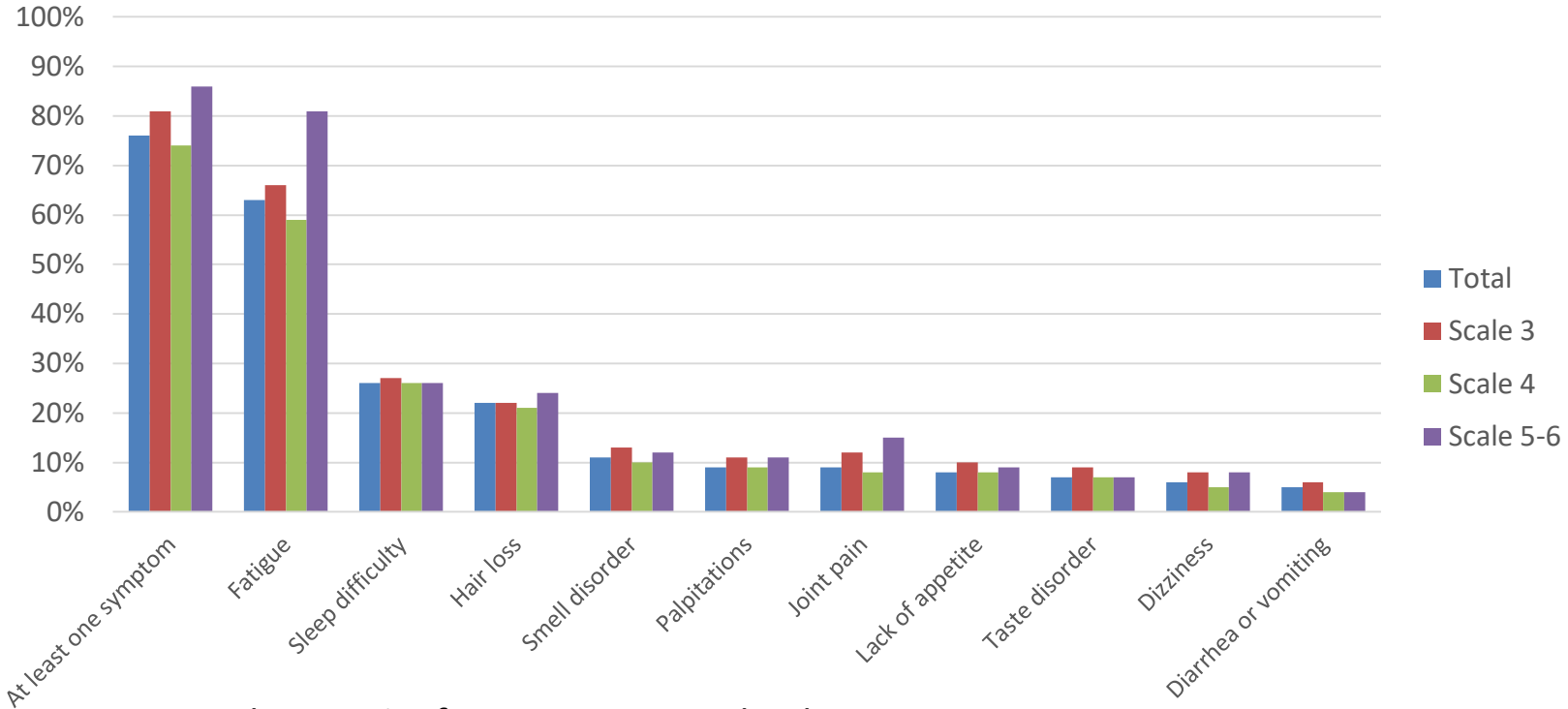
Flow chart of COVID-19 patients discharged from Jin Yin-tan hospital during January 7, 2020 and May 29, 2020



- 1733 enrolled
  - scale 3: 439
  - scale 4: 1172
  - scale 5-6: 122
- Median age: 57 years
- Median follow-up time
  - after symptom onset: 186 days
  - after hospital discharge: 153 days
- mortality after discharge: 1.3% (33/2469)

Huang et al. Lancet. 2021.

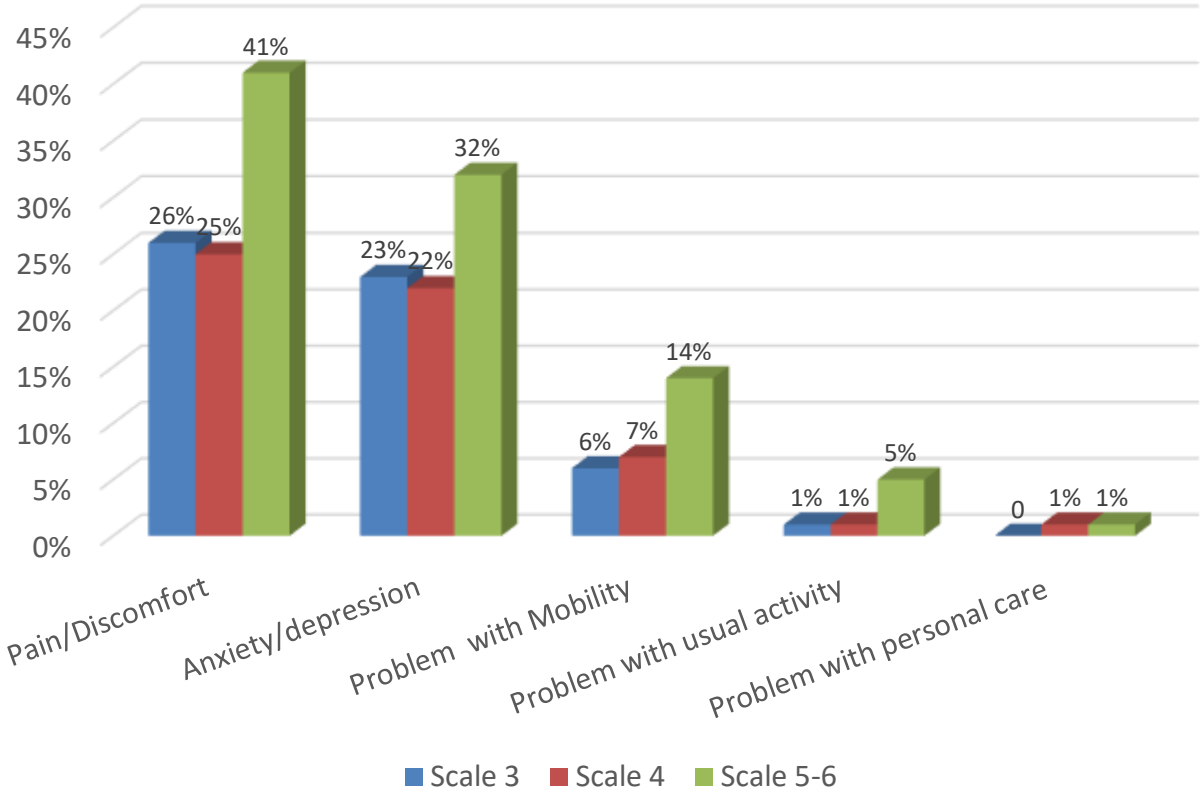
Persisting symptoms at follow-up



- More than 70% of patients reported at least one symptom.
- The most common symptoms are fatigue/muscle weakness(63%) and sleep difficulty(26%).

Huang et al. Lancet. 2021.

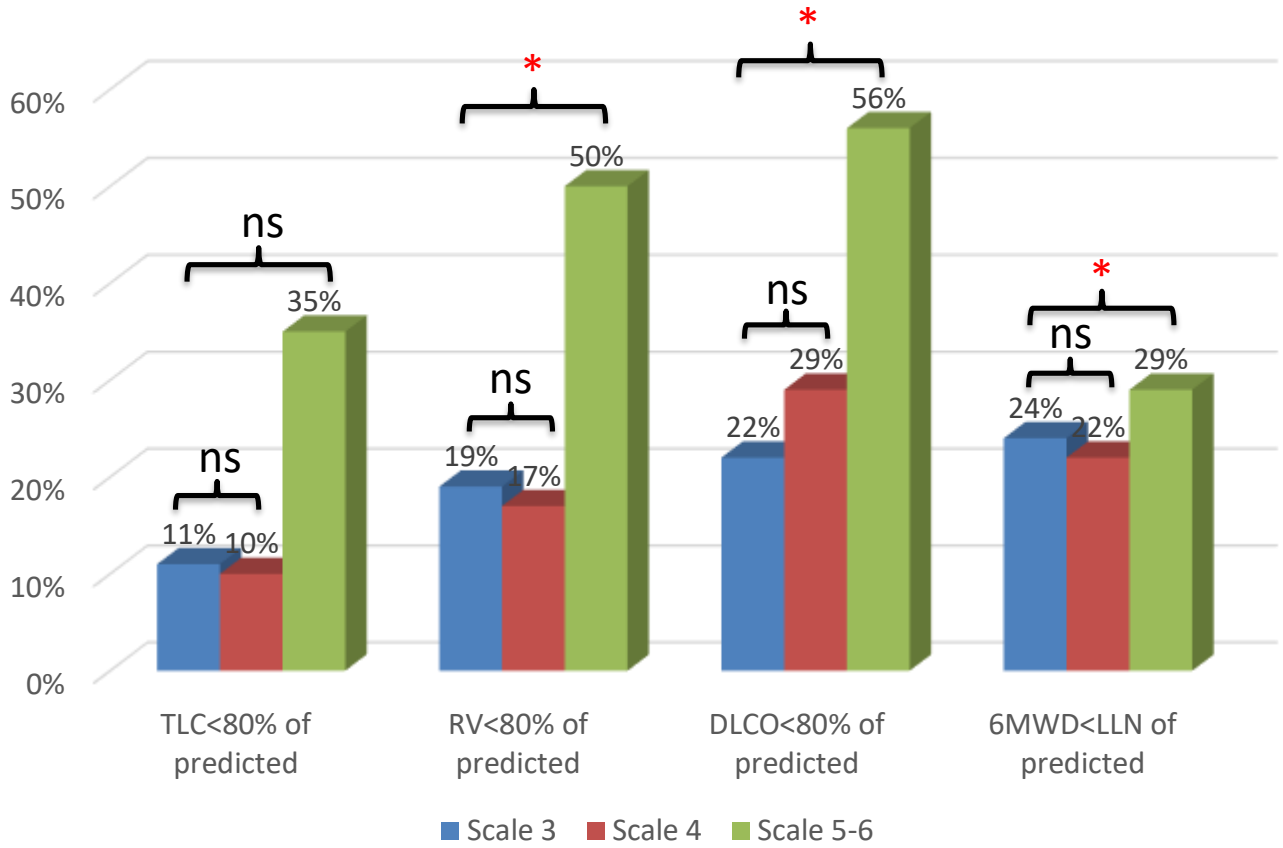
EQ-5D-5L questionnaire



- More severe patients endorsed more problems
- More than 20% reported psychological complications
- More than 90% had no problems in mobility, usual activity and personal care at follow-up.

Huang et al. Lancet. 2021.

Impaired lung function and exercise capacity



ns: no significant, *: $p<0.05$,LLN: lower limit of normal range.

Huang et al. Lancet. 2021.

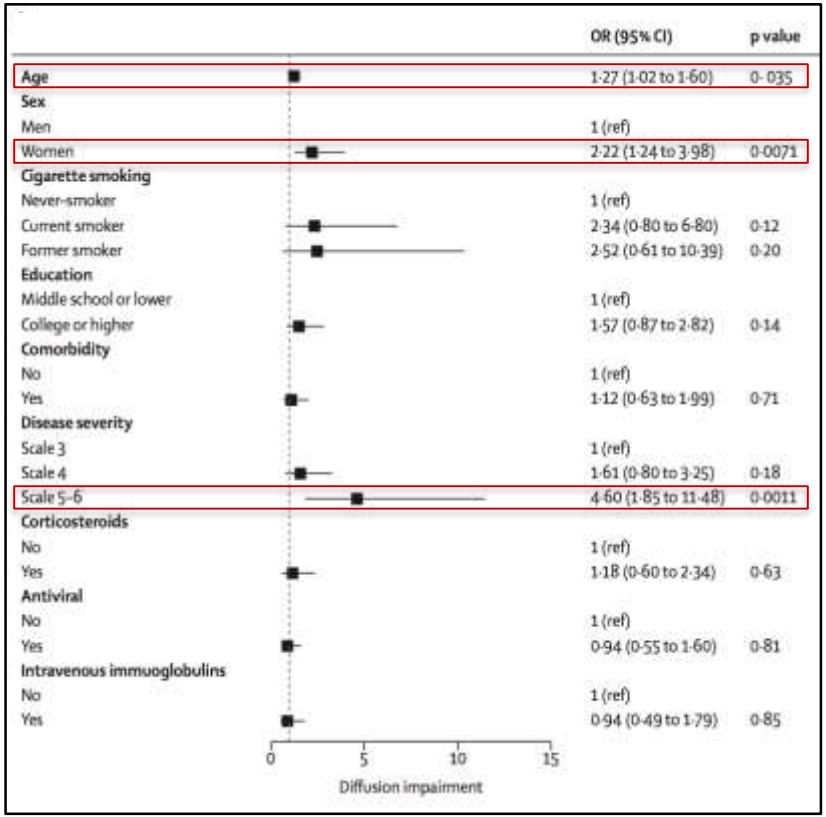
Lung CT image at follow-up

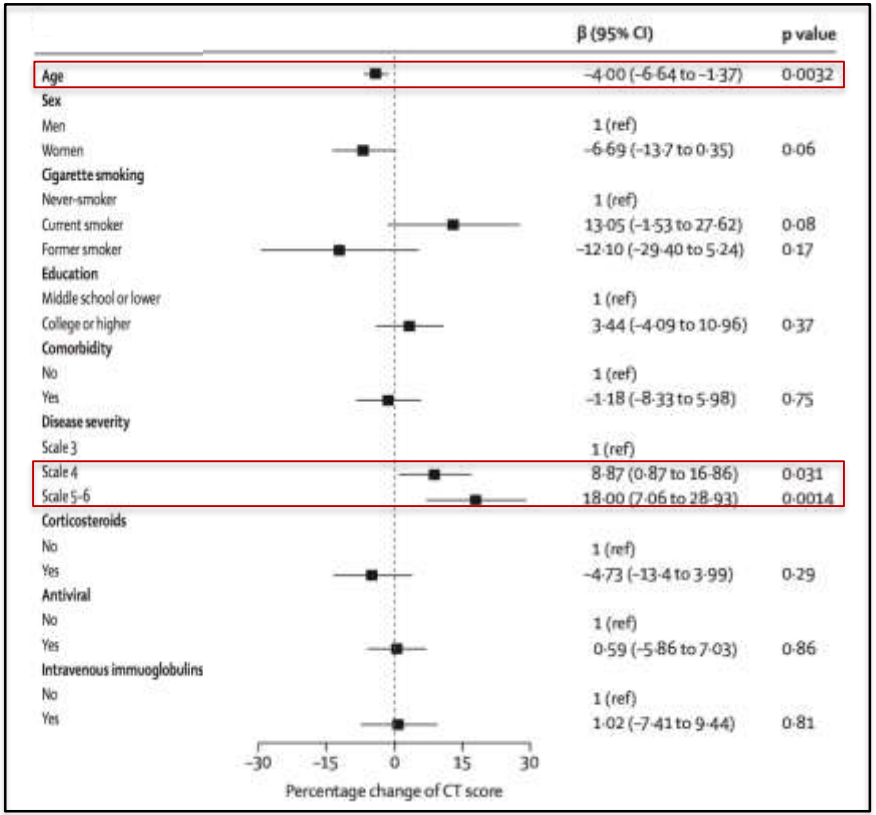
Characteristics	Scale 3	Scale 4	Scale 5-6
Number of patients	95	163	95
At least one abnormal CT pattern	49 (52%)	87/161 (54%)	50/92 (54%)
GGO	39 (41%)	78/161 (48%)	41/92 (45%)
Irregular lines	10 (11%)	24/161 (15%)	22/92 (24%)
Consolidation	0	4/161 (2%)	0
Interlobular septal thickening	1 (1%)	2/161 (1%)	0
Subpleural line	6 (6%)	5/161 (3%)	4/92 (4%)
Reticular pattern	0	1/161 (1%)	1/92 (1%)
Volume of lung lesions, cm^3	1.6 (0.6-5.6)	3.3 (0.8-12.4)	29.1 (4.6-77.3)
Volume of consolidation, cm^3	0.2 (0.1-0.4)	0.3 (0.1-1.0)	1.6 (0.2-4.4)
Volume of GGO, cm^3	1.4 (0.6-4.7)	2.9 (0.7-10.0)	26.3 (4.3-73.3)
Volume ratio of lung lesion to total lung, %	0.0 (0.0-0.1)	0.1 (0.0-0.3)	0.7 (0.1-2.2)
Volume ratio of consolidation to total lung, %	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.1)
Volume ratio of GGO to total lung, %	0.0 (0.0-0.1)	0.1 (0.0-0.2)	0.6 (0.1-1.9)
CT score	3.0 (2.0-5.0)	4.0 (3.0-5.0)	5.0 (4.0-6.0)

- At six-month after symptom onset, around half patients still have at least one abnormal CT pattern, GGO is the most common pattern.

Huang et al. Lancet. 2021.

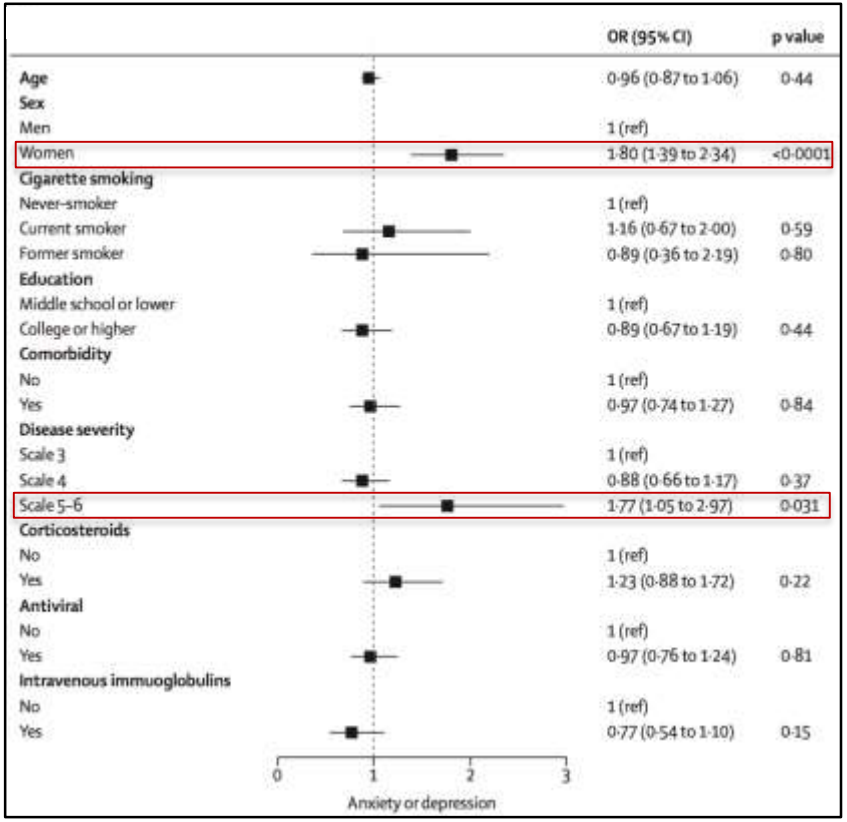
Risk factors of diffusion impairment and CT score

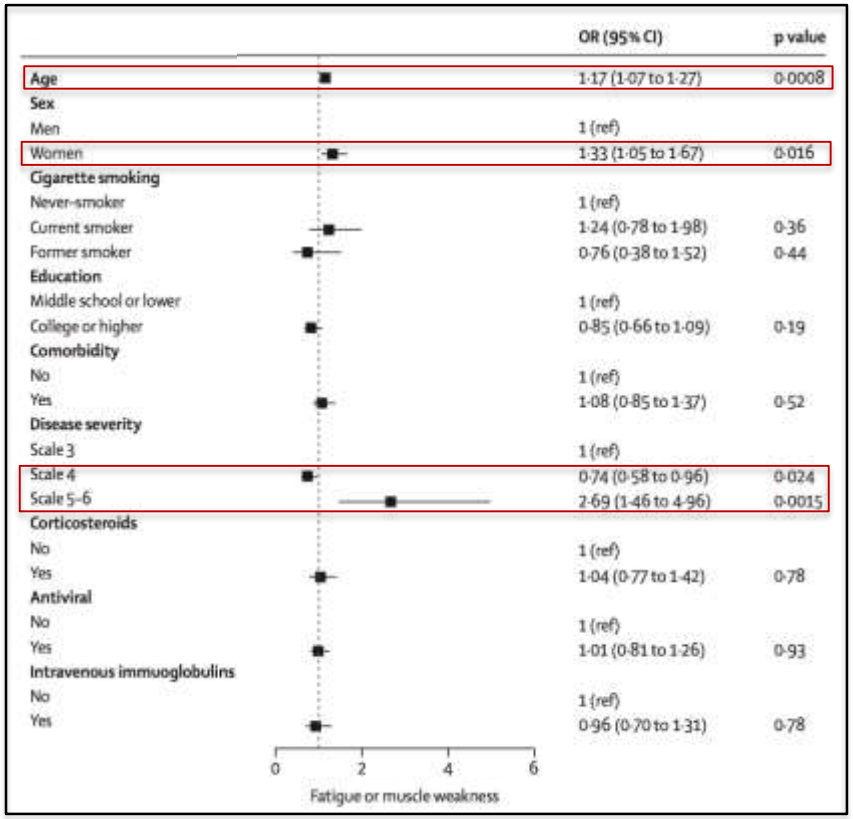




Huang et al. Lancet. 2021.

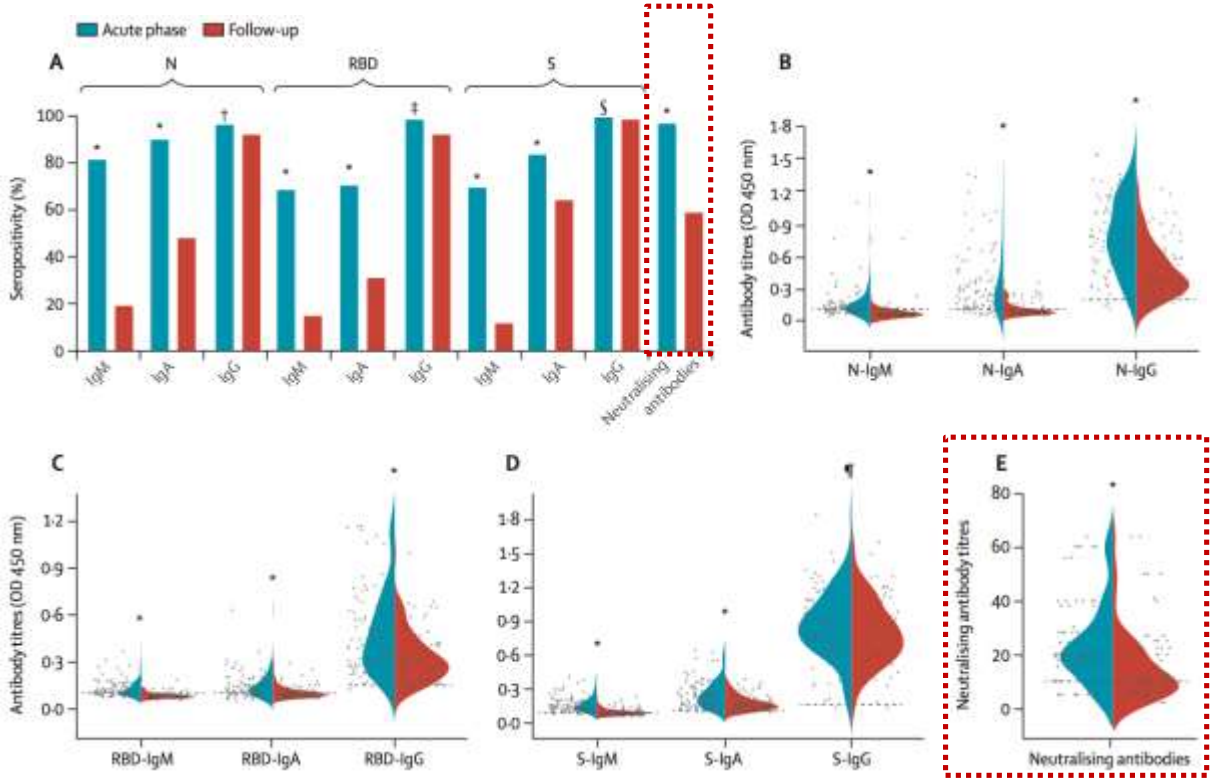
Risk factors of anxiety/depression and fatigue/muscle weakness





Huang et al. Lancet. 2021.

Temporal changes of seropositivity and antibody titers against SARS-CoV-2



- The seropositivity and titer of neutralizing antibody are significantly lower compared with that at acute phase.
- The decline of neutralising antibodies raises concern for SARS-CoV-2 re-infection.

Huang et al. Lancet. 2021.

Extrapulmonary organ manifestations

- For patients with lymphocyte count less than $0{\cdot}8\times10^9$/L at acute phase, 97% had lymphocyte counts $0{\cdot}8\times10^9$/L or more at follow-up.
- No deep venous thrombosis was observed in 390 patients who underwent ultrasonography at follow-up.
- 58 patients were newly diagnosed with diabetes at follow-up.
- 13% (107 of 822) of the patients who did not develop AKI during their hospital stay and presented with normal renal function, exhibited a decline in eGFR (<90 mL/min*1·73 m^2) at follow-up.

Huang et al. Lancet. 2021.

Summary

- At 6 months after illness onset, most patients had at least one symptom, with fatigue or muscle weakness being the most frequently reported symptom
- More severe patients during hospitalization had more severe lung diffusion capacity deterioration and chest imaging anomaly
- Critically ill patients deserve more attention during hospitalization and after discharge
- Longer and larger follow-up study are necessary to understand the full spectrum of health consequences of COVID-19, ranging from non-hospitalized patients, hospitalized patients to ICU survivors.
- Multidisciplinary, multicentre, and multinational collaborations are needed to face up the long COVID.

Huang et al. Lancet. 2021.

Cortinovis M. The Lancet, 2021.

Facing up to long COVID. Lancet 2020.

Acknowledgements

China-Japan Friendship Hospital
Chen Wang; Yeming Wang; Lixue Huang; Xiaoying Gu; Min Liu; Guohui Fan; Yong Li; Jiuyang Xu

Wuhan Jin-yintan Hospital
Dingyu Zhang; Chaolin Huang; Xia Li; Liang Kang; Li Guo; Xing Zhou; Jianfeng Luo; Zhenghui Huang; Shengjin Tu; Yue Zhao; Li Chen; Decui Xu; Yanping Li; Caihong Li; Lu Peng

CAMS&PUMC
Chen Wang； Jianwei Wang; Lili Ren; Li Guo; Geng Wang; Ying Wang; Jingchuan Zhong

Cooperators:

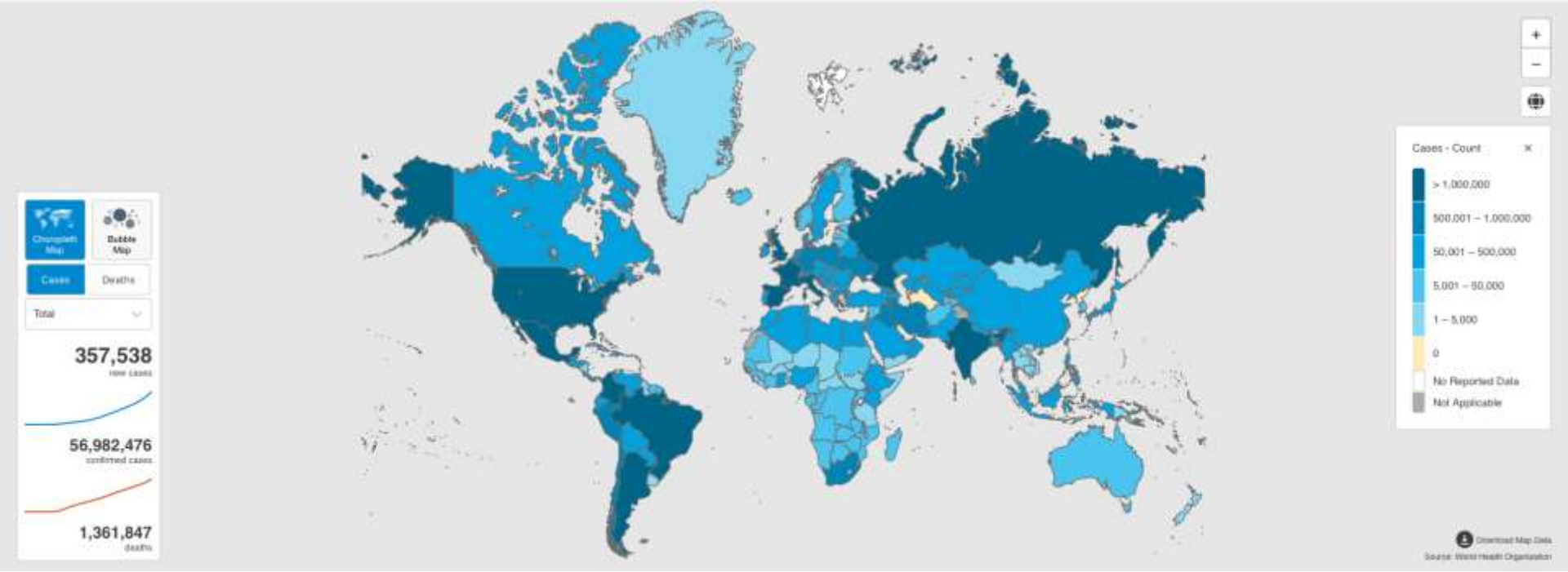
Wuhan Jin-yintan Hospital

Key Laboratory of Respiratory Disease Pathogenomics, Chinese Academy of Medical Sciences and Peking Union Medical College

All patients who participated in this study and their families
All health-care workers involved in the diagnosis and treatment of patients
All staff of this follow-up study team

中国工程院 Chinese Academy of Engineering
马云公益基金会 JACK MA FOUNDATION
World Health Organization
国家自然科学基金委员会 National Natural Science Foundation of China
中国肺炎研究 CAP-China

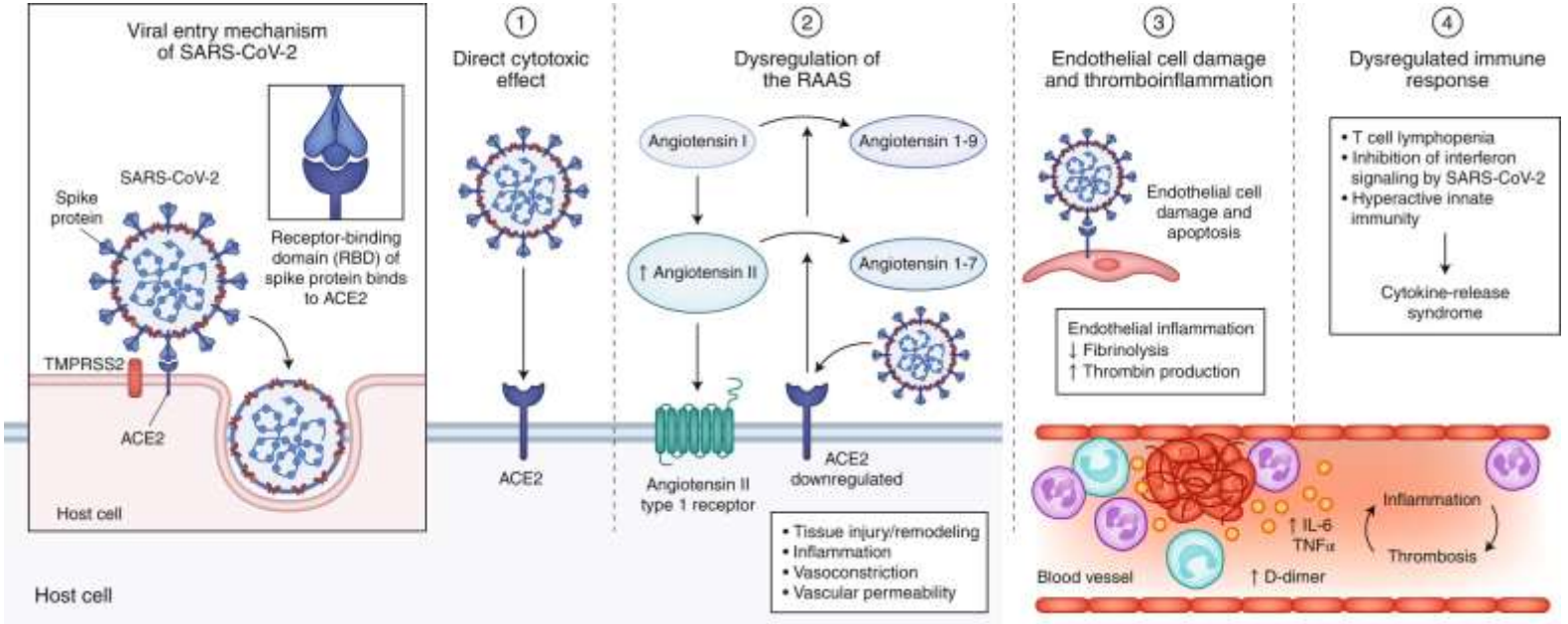
The ongoing COVID-19 Pandemic



As of 2021/2/2, there has been more than 102 million cases with more than 2.2 million death

World Health Organization, https://covid19.who.int, data as of 2021/02/02, 10:00am CET

Key pathophysiological mechanisms of COVID-19



- Direct virus-mediated cell damage;
- Dysregulation of the RAAS as a consequence of downregulation of ACE2 related to viral entry;
- Endothelial cell damage and thrombo-inflammation
- Dysregulation of the immune response and hyperinflammation caused by inhibition of interferon signaling by the virus, T cell lymphodepletion, and the production of proinflammatory cytokines, particularly IL-6 and TNFα

Gupta A, et al. Nat Med. 2020; 26(7):1017-1032