# What we learned from COVID-19 outbreak in Wuhan?

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# Disclosure

- Intensivist/medical researcher

- No COI to declare

# Contents

- Preparing the outbreak of COVID-19

- General characteristics of COVID-19

- Diagnosing the COVID-19

- Managing the critically ill patients with COVID-19

- Outcome of the patients with COVID-19
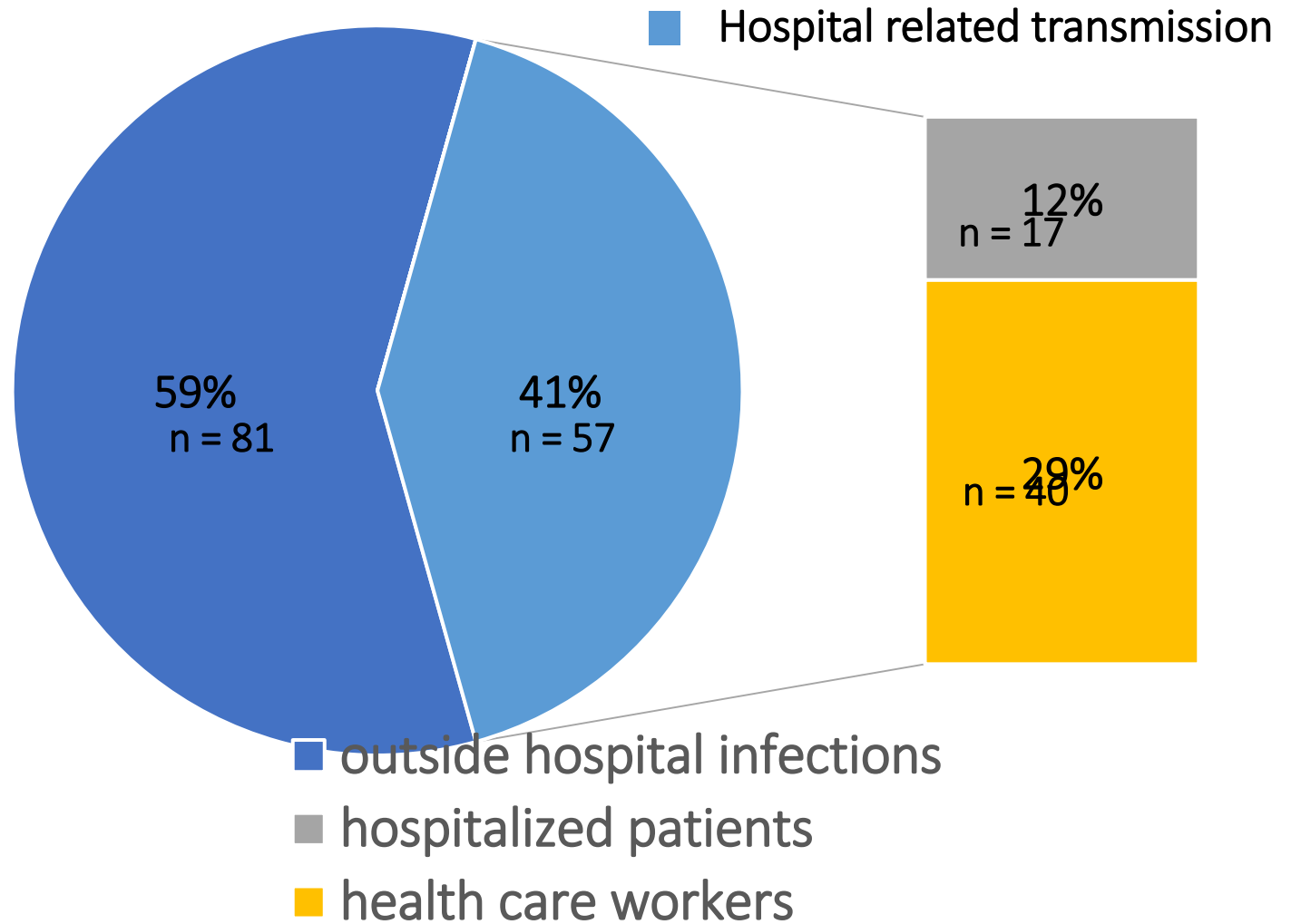
# Prepare the additional medical resources

- Lack of medical/ICU beds

- Lack of human resources

- Mobilizing the medical resource

- Organizing new teams

# Top priority: Personal protection

- PPE: cap, surgical gloves, fluid-resistant gowns/protective suits, fit-tested respirator(N95 or FFP3), goggles(anti-fog ), face shield/full hood

- Setting the different levels of  precautions for droplet, close contact or airborne

- Protocols for wearing PPE and taking off PPE

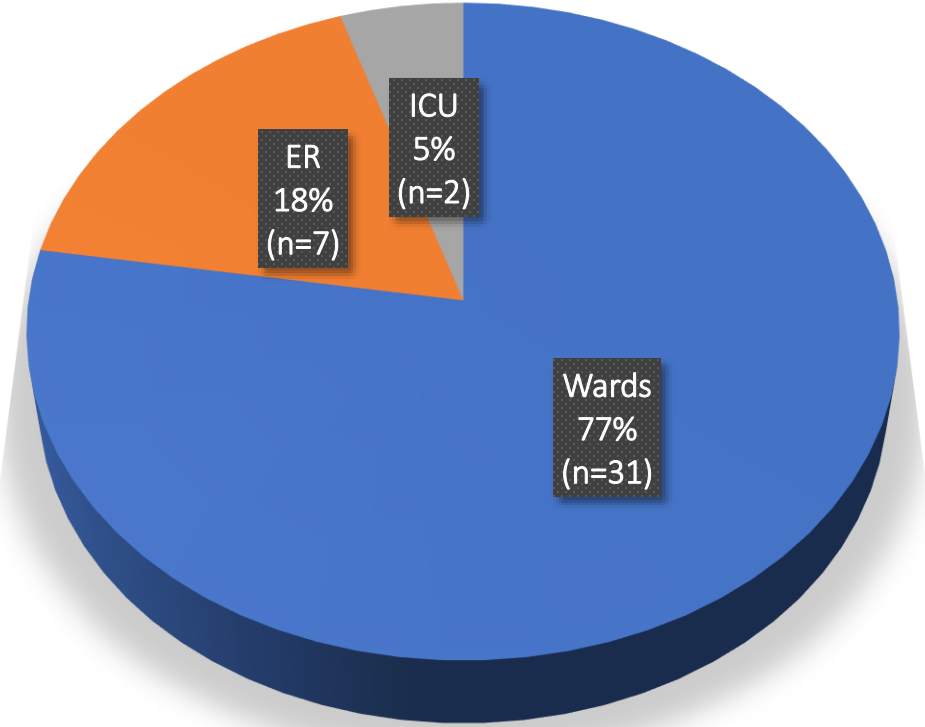- Environment monitoring for possible virus pollution

# Feature of transmission

- The human-to-human transmission was frequent, especially in hospitals.
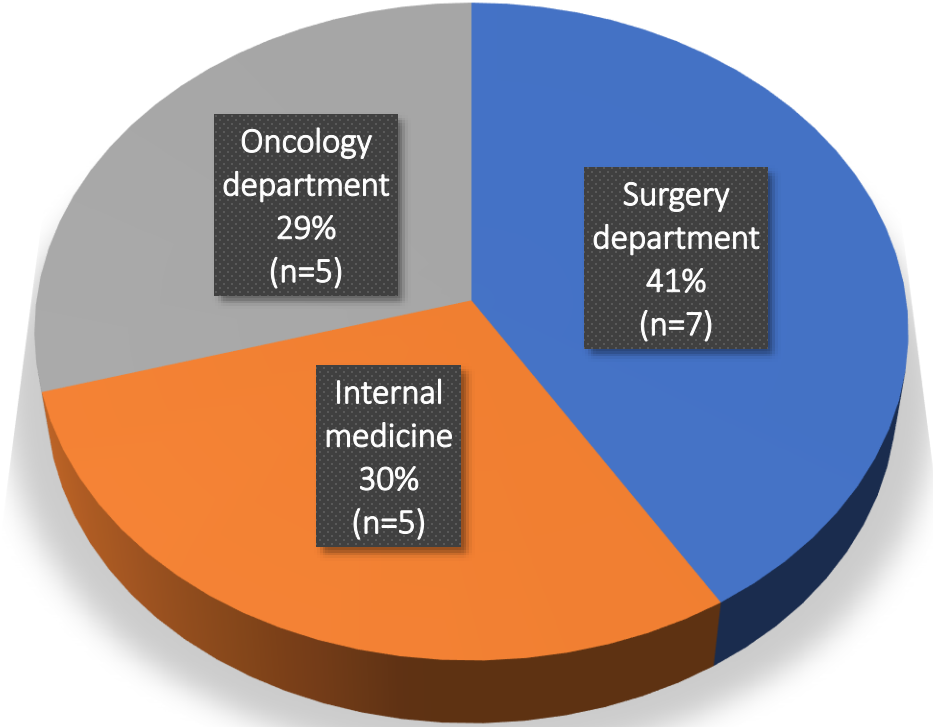


Hospital related transmission

59%
n = 81

41%
n = 57

12%
n = 17

29%
n = 40

outside hospital infections

hospitalized patients

health care workers

Wang D, et al. JAMA 2020;Feb7.

# Hospital related transmission

Health care workers (70%, n=40)



ICU
5%
(n=2)

ER
18%
(n=7)

Wards
77%
(n=31)

Hospitalized patients (30%, n=17)



Oncology
department
29%
(n=5)

Surgery
department
41%
(n=7)

Internal
medicine
30%
(n=5)

Wang D, et al. JAMA 2020;Feb7.

# Set up the policy for triage

- Unknown fever clinics
- ER
- Isolated wards
- ICU

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# Basic Characteristics of COVID-19

| | Total (n=138) | ICU (n=36) | Non-ICU (n=102) | *P* value |
|---|---|---|---|---|
| Age, years | 56(42-68) | 66(57-78) | 51(37-62) | <0.001 |
| Gender, Male | 75(54.3%) | 22(61.1%) | 53(52.0%) | 0.343 |
| **Comorbidities** | 64(46.4%) | 26(72.2%) | 38(37.3%) | <0.001 |
| Hypertension | 43(31.2%) | 21(58.3%) | 22(21.6%) | <0.001 |
| Diabetes | 14(10.1%) | 8(22.2%) | 6(5.9%) | 0.009 |
| Cardiovascular disease | 20(14.5%) | 9(25.0%) | 11(10.8%) | 0.037 |
| Cerebrovascular disease | 7(5.1%) | 6(16.7%) | 1(1.0%) | 0.001 |
| COPD | 4(2.9%) | 3(8.3%) | 1(1.0%) | 0.054 |
| CKD | 4(2.9%) | 2(5.6%) | 2(2.0%) | 0.279 |
| Chronic liver disease | 4(2.9%) | 0(0%) | 4(3.9%) | 0.573 |
| Malignancy | 10(7.2%) | 4(11.1%) | 6(5.9%) | 0.287 |
| HIV infection | 2(1.4%) | 0(0%) | 2(2.0%) | 1.000 |

**It was likely to infect older persons with comorbidities**
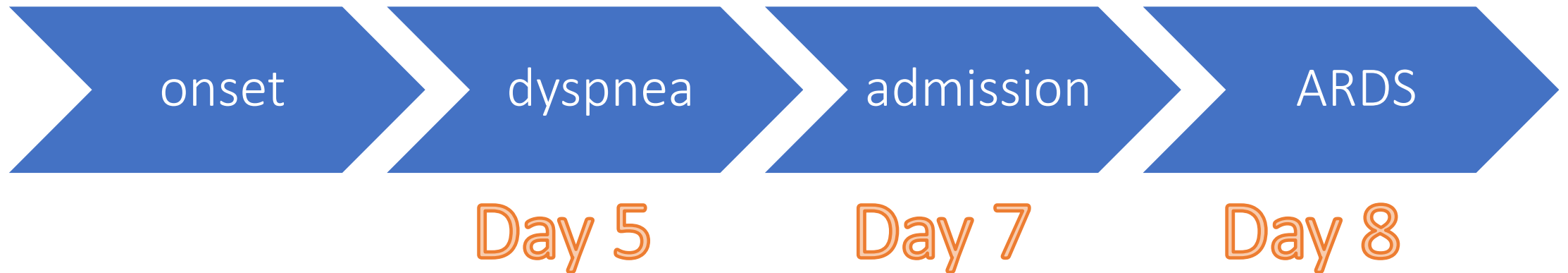
Wang D, et al. JAMA 2020;Feb7.

# Symptoms and signs

- Most common symptoms at onset

  fever (98.6%), fatigue (69.6%),

dry cough (59.4%), myalgia

(34.8%), and dyspnea (31.2%).

- About 10% of patients presented

  initially with diarrhea 1-2 days

  prior to development of fever

  and dyspnea.

- Dyspnea, dizzy, abdominal pain

  and anorexia  frequently

  occurred in ICU patients.

| Signs and symptoms | Total (n=138) | ICU (n=36) | Non-ICU (n=102) | P value |
|---|---|---|---|---|
| Fever | 136(98.6%) | 36(100%) | 100(98.0%) | 1.000 |
| Dry cough | 82(59.4%) | 21(58.3%) | 61(59.8%) | 0.877 |
| Expectoration | 37(26.8%) | 8(22.2%) | 29(28.4%) | 0.346 |
| Myalgia | 48(34.8%) | 12(33.3%) | 36(35.3%) | 0.832 |
| Fatigue | 96(69.6%) | 29(80.6%) | 67(65.7%) | 0.096 |
| Dyspnea | 43(31.2%) | 23(63.9%) | 20(19.6%) | <0.001 |
| Dizzy | 13(9.4%) | 8(22.2%) | 5(4.9%) | 0.007 |
| Abdominal pain | 3(2.2%) | 3(8.3%) | 0(0%) | 0.017 |
| Diarrhea | 14(10.1%) | 6(16.7%) | 8(7.8%) | 0.195 |
| Vomiting | 5(3.6%) | 3(8.3%) | 2(2.0%) | 0.127 |
| Anorexia | 55(39.9%) | 24(66.7%) | 31(30.4%) | <0.001 |

Wang D, et al. JAMA 2020;Feb7.

# Clinical Process

- The time from onset to dyspnea was 5.0 days, 7.0 days to hospital admission, and 8.0 days to ARDS.

| onset | dyspnea | admission | ARDS |
|:-----:|:-------:|:---------:|:----:|
|       | Day 5   | Day 7     | Day 8 |

Wang D, et al. JAMA 2020;Feb7.

# laboratory parameters

| | Normal range | Total (n=138) | ICU (n=36) | Non-ICU (n=102) | *P* value |
|---|---|---|---|---|---|
| White blood cell count, $\times 10^9$/L | 3.5-9.5 | 4.5(3.3-6.2) | 6.6(3.6-9.8) | 4.3(3.3-5.4) | 0.003 |
| Neutrophil count, $\times 10^9$/L | 1.8-6.3 | 3.0(2.0-4.9) | 4.6(2.6-7.9) | 2.7(1.9-3.9) | <0.001 |
| Lymphocyte count, $\times 10^9$/L | 1.1-3.2 | 0.8(0.6-1.1) | 0.8(0.5-0.9) | 0.9(0.6-1.2) | 0.033 |
| Monocyte count, $\times 10^9$/L | 0.1-0.6 | 0.4(0.3-0.5) | 0.4(0.3-0.5) | 0.4(0.3-0.5) | 0.955 |
| Platelet count, $\times 10^9$/L | 125-350 | 163(123-191) | 142(119-202) | 165(125-188) | 0.775 |
| Prothrombin time, s | 9.4-12.5 | 13.0(12.3-13.7) | 13.2(12.3-14.5) | 12.9(12.3-13.4) | 0.373 |
| Activated partial thromboplastin time, s | 25.1-36.5 | 31.4(29.4-33.5) | 30.4(28.0-33.5) | 31.7(29.6-33.5) | 0.093 |
| D-dimer, mg/L | 0-500 | 203(121-403) | 414(191-1324) | 166(101-285) | <0.001 |
| Creatine kinase, U/L | <171 | 92(56-130) | 102(62-252) | 87(54-121) | 0.076 |
| Creatine kinase-MB, U/L | <25 | 14(10-18) | 18(12-35) | 13(10-14) | <0.001 |
| Lactate dehydrogenase, U/L | 125-243 | 261(182-403) | 435(302-596) | 212(171-291) | <0.001 |
| Alanine aminotransferase, U/L | 9-50 | 24(16-40) | 35(19-57) | 23(15-36) | 0.007 |
| Aspartate aminotransferase, U/L | 15-40 | 31(24-51) | 52(30-70) | 29(21-38) | <0.001 |
| Total bilirubin, mmol/L | 5-21 | 9.8(8.4-14.1) | 11.5(9.6-18.6) | 9.3(8.2-12.8) | 0.016 |
| Urea, mmol/l | 2.8-7.6 | 4.4(3.4-5.8) | 5.9(4.3-9.6) | 4.0(3.1-5.1) | <0.001 |
| Creatinine, μmol/L | 64-104 | 72(60-87) | 80(66-106) | 71(58-84) | 0.037 |
| Hypersensitive troponin I, pg/mL | <26.2 | 6.4(2.8-18.5) | 11.0(5.6-26.4) | 5.1(2.1-9.8) | 0.004 |

Wang D, et al. JAMA 2020;Feb7.

# Typical chest CT: ground-glass opacity
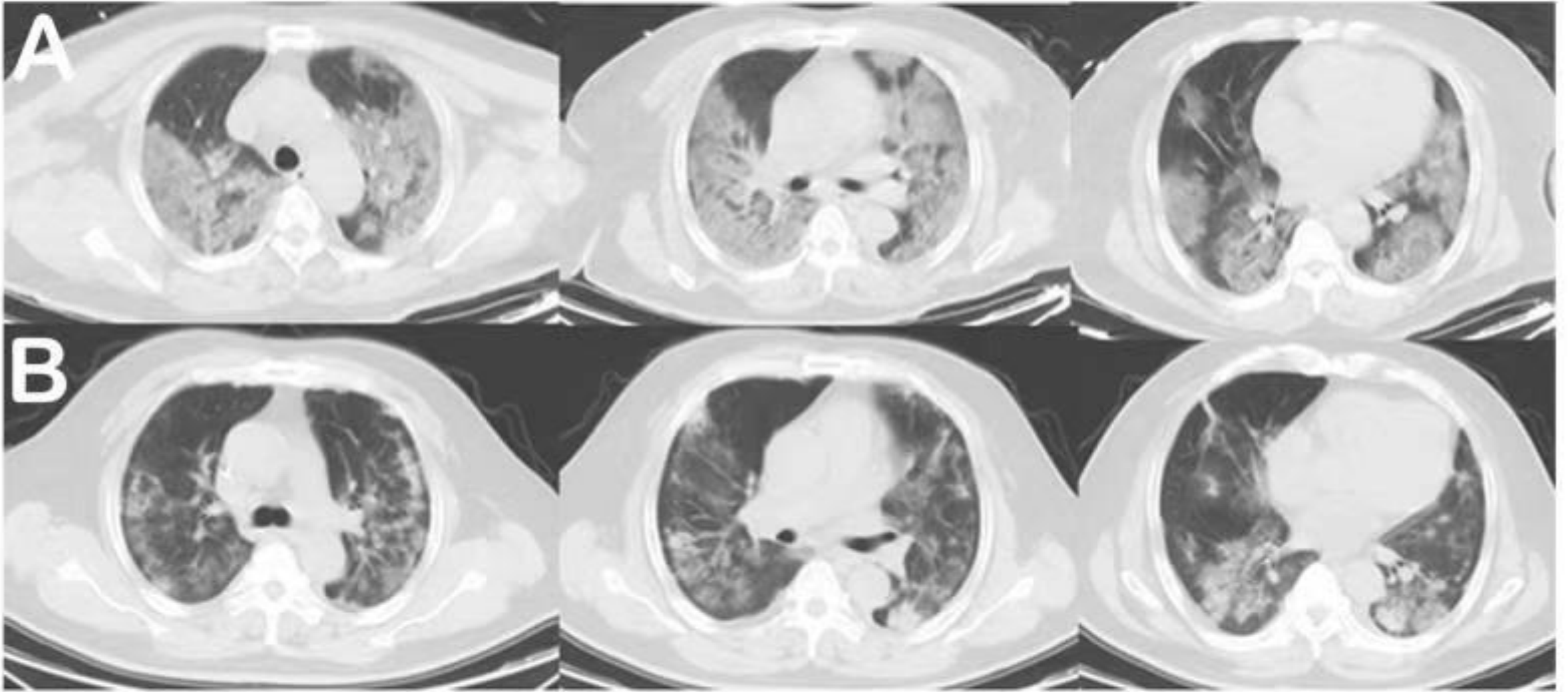


**Chest CT images of a 52-year-old patient infected with 2019-nCoV**

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# Diagnosis criterion

- Exposure history

- Typical symptoms/signs: febrile/fatigue /dyspnea

- Lab: lymphopenia, flu/RSV-test (-)

- Typical Chest CT: multiple patches peripheral distribution>50%

- Virus Rt-PCR test: low sensitivity

- Serology test: suspect if negative virus test

- <u>Confirmed diagnosis</u>: symptoms/signs+Lab test+typical chest

  CT+positive viral test

- <u>Clinical diagnosis</u>: symptoms/signs+Lab test+typical chest CT

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# Characteristics of ICU patients

| | Normal range | ICU (n=36) |
|---|---|---|
| Onset of symptom to ICU admission (d) | NA | 10 (6-12) |
| GCS | NA | 15 (9-15) |
| APACHE II | NA | 17 (10-22) |
| SOFA | NA | 5 (3-6) |
| PH | 7.35-7.45 | 7.43 (7.39-7.47) |
| Lactate, mmol/l | 0.5-1.6 | 1.3 (0.7-2.0) |
| PaO2, mm/Hg | 83-108 | 68 (56-89) |
| PaO2/FiO2, mm/Hg | 400-500 | 136 (103-234) |
| PaCO2, mm/Hg | 35-48 | 34 (30-38) |

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# Organ injury & Complications

- ICU patients had higher incidence of complications
- The common complications were ARDS, cardiac injury and shock.

| Complications | Total (n=138) | ICU (n=36) | Non-ICU (n=102) | P value |
|---|---|---|---|---|
| Shock | 12(8.7%) | 11(30.6%) | 1(1.0%) | <0.001 |
| Acute cardiac injury | 10(7.2%) | 8(22.2%) | 2(2.0%) | <0.001 |
| Arrhythmia | 23(16.7%) | 16(44.4%) | 7(6.9%) | <0.001 |
| ARDS | 27(19.6%) | 22(61.1%) | 5(4.9%) | <0.001 |
| AKI | 5(3.6%) | 3(8.3%) | 2(2.0%) | 0.111 |

Wang D, et al. JAMA 2020;Feb7.

# Ventilation supports

| Treatment | Total (n=138) | ICU (n=36) | Non-ICU (n=102) |
|---|---|---|---|
| High-flow Oxygen | 106(76.81%) | 4(11.11%) | 102(100%) |
| NIV | 15(10.9%) | 15(41.7%) | 0(0.0%) |
| IMV | 17(12.32%) | 17(47.22%) | 0(0.0%) |
| ECMO | 4(2.9%) | 4(11.1%) | 0(0.0%) |

Half of the critically ill patients needed invasive ventilation and four of them switched to ECMO

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# Data from current patients (Feb 7- March 6)

| Treatments and outcomes | Patients (number with percentage, n=50) | |
|---|---|---|
| **Parameter measured at ICU admission (median with IQR)** | | |
| PaO2/FiO2 (mmHg) | 115(87-190) | |
| Cstat (ml/cmH$_2$O) | 22.5(17.0-40.5) | |
| IL-6 (pg/ml ) | 62.2(18.2-129.5) | |
| Lymphocyte count (✕ 10$^9$/L ) | 0.59(0.32-0.85) | |
| **Modes of respiratory supports** | | |
| HFNC+NIMV | 14(28.0) | **Very sick with severe lung injury** |
| IMV | 19(38.0) | **28% patients recovered with only NIMV** |
| IMV+ECMO | 17(34.0) | **72% requiring IMV, and half of them switched to ECMO** |
| IMV+Prone ventilation | 15(30.0) | **64% patients complicated with heart problems** |
| **Medications** | | |
| Antiviral therapy | 37(74.0) | |
| Glucocorticoid therapy | 38(76.0) | |
| Antibiotics | 45(90.0) | |
| **Complications** | | |
| ARDS | 47(94.0) | |
| Shock | 22(44.0) | |
| Arrhythmia | 19(38.0) | |
| Acute cardiac injury | 13(26.0) | |
| AKI | 11(22.0) | |
| Secondary infection | 17(34.0) | |

# Key points for ventilation supports

- Lung protective approach is extremely important

- Prone the patients as early as possible

- Evaluate the mode/parameters set frequently, and switch/change if not appropriate

- Titrate PEEP and tidal volume based on the transpulmonary pressure or driving pressure. Keep driving pressure<15 , and Pplat<28

- Prevent acute CorPulmonale

- Be careful of lung Recruitment Maneuver. Set highest PEEP at 20

# When to switch the modes of ventilation

- **HFNC**: recommend in the room with negative-pressure

- If P/F 200-300mmHg, set flow rate at 40-50L/min, FiO2 100%, for 2 hr

- Evaluate the efficacy based on the ROXI[RR-(SpO2/FiO2)]

- If SpO2>93% and RR<25, or ROXI>3.85, continue HFNC; if SpO2<93% and RR>30, or ROXI<2.85, stop HFNC, and the go to NIV (if conscious) or intubation

- If the values between the ranges, continue for another 2 hr, and the re-evaluate

# NIV

- If P/F 150-200, start NIV, however BiPAP may worsen the lung injury,

- High RR or/ and tidal volume will increase trans-pulmonary or driving pressure, worsen lung injury and pulmonary edema and induce pulmonary fibrosis

- Initial set IPAP 12, EPAP 5-8,FiO2 80-100% for 2 h, follow the tidal volume (TV), if TV<9ml/kg, continue;  if TV>12, intubate

# IMV

- IF P/F< 150, go to IMV

- First, test if RM is available , set the highest PEEP at 20 , if not and driving pressure>15, then paralyze the patients with prone position

- Follow the lung compliance

- If FiO2>60, P/F<150 or Ppleuto>35, PaCO2>50 and PH<7.25, go to ECMO

# Case report

- F/64 yr, transferred to ICU from outside hospital due to severe dyspnea, and tachycardia.

- Diagnosed with COVID-19 in outside hospital

- Previously healthy.

- Tx in outside hospital:

  Antiviral & antibiotics for 5 days

  corticosteroids for 7 days

  NIV for 9 days

# NIV in the last 9 days

| NIV | FiO$_2$ | PS(cmH$_2$O) | PEEP (cmH$_2$O) | SPO$_2$ | RR (n/min) |
|-----|---------|--------------|-----------------|---------|------------|
| -D9 | 60% | 14 | 5 | 93% | 33 |
| -D8 | 55% | 16 | 5 | 92% | 32 |
| -D7 | 50% | 16 | 5 | 92% | 32 |
| -D6 | 50% | 16 | 5 | 92% | 30 |
| -D5 | 60% | 18 | 5 | 92% | 28 |
| -D4 | 50% | 18 | 8 | 93% | 32 |
| -D3 | 55% | 18 | 8 | 92% | 32 |
| -D2 | 60% | 18 | 8 | 90% | 44 |
| -D1 | 60% | 23 | 8 | 88% | 42 |

- Vital sign at the ICU admission:  HR 130bpm, $SpO_2$ 82% (with 6L/min), RR 46/min, NBP 130/82mmHg.

- We gave her NIV with $FiO_2$ 100% immediately, and prepared for intubation

- ABG：pH 7.26，$PaCO_2$ 55 mmHg，$PaO_2$ 49mmHg，($FiO_2$ 100%)。

- Intubated and supported with V-SIMV mode, tidal volume 400mL, FiO2 90%, PEEP 5cmH$_2$O, PS 12cmH$_2$O, (detected Pplat 26cmH$_2$O and Compliance 20ml/cmH$_2$O).

- Subsequently paralyzed with prone position ventilation for 12 hrs

- Not improved , P/F<60 for 4 hrs with hypercapnia,  and hypotension requiring vasopressors,  then switched to v-v ECMO

# Pt complicated with acute Cor Pulmonale
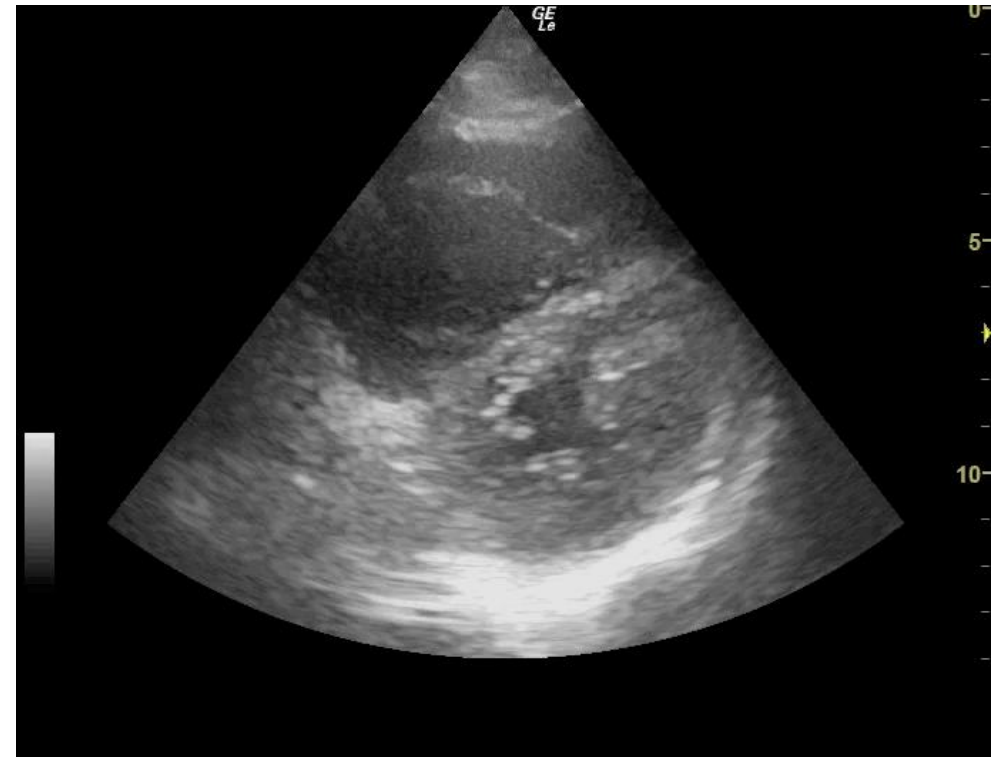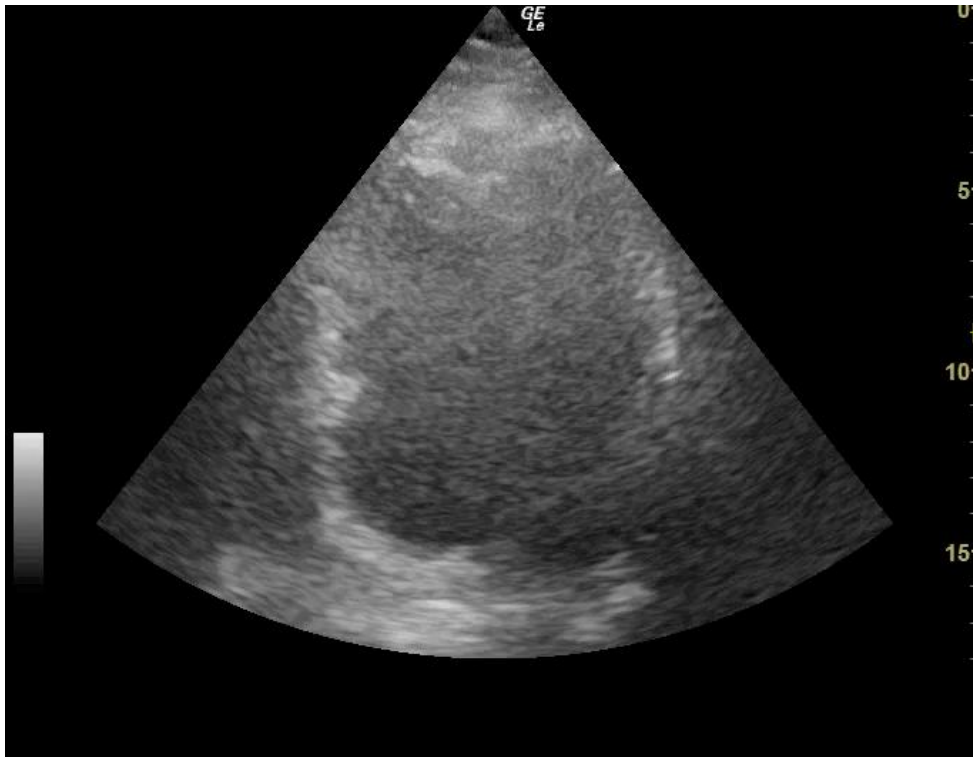


Before VV-ECMO support, NE 1μg/min kg

# Acute Cor Pulmonale improved with adequate oxygenation
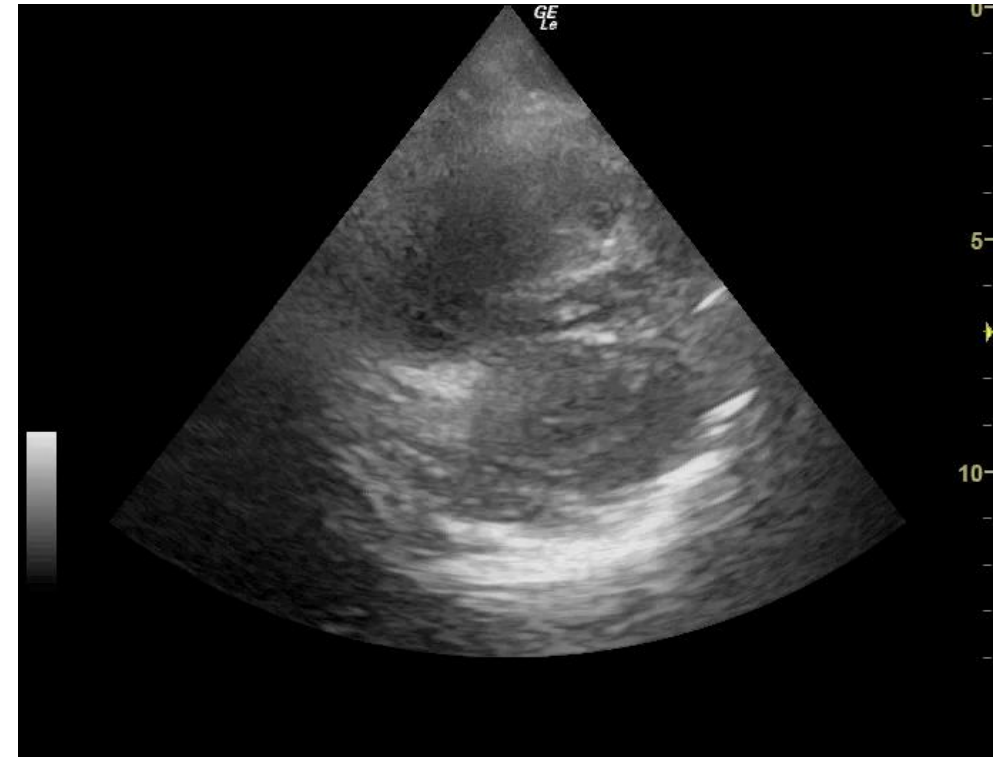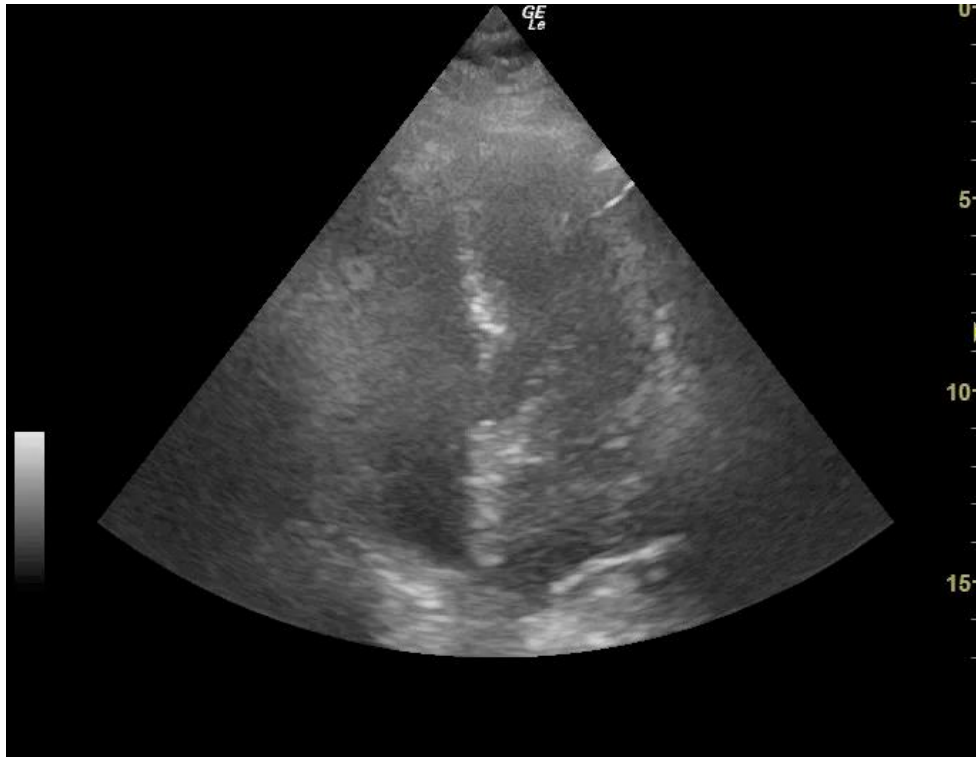


10 hr after ECMO, NE 0.3μg/min kg

# Detailed treatments from ECMO

| VV-ECMO | Rotation speed (r/min) | Blood flow(L/min) | Sweep rate (L/min) | FiO$_2$ |
|---|---|---|---|---|
| D1 | 3000 | 3.5 | 3.5 | 100% |
| D2 | 3400 | 3.8 | 3.5 | 80% |
| D3 | 3370 | 3.7 | 3.5 | 80% |
| D4 | 3360 | 3.7 | 3.5 | 70% |
| D5 | 3400 | 3.9 | 3.5 | 70% |
| D6 | 3400 | 3.8 | 3.5 | 50% |
| D7 | 3065 | 3.3 | 3.5 | 40% |
| D8 | 3100 | 3.4 | 3.5 | 30% |
| D9 | 2500 | 2.5 | 2.5 | 21% |

# Weaning ECMO and switched to SIMV

| V-SIMV | FiO$_2$ | PS (cmH$_2$O) | PEEP (cmH$_2$O) | Pplat (cmH$_2$O) | Compliance (ml/cmH$_2$O) | Prone position | Tidal volume (mL/kg) |
|--------|---------|---------------|-----------------|------------------|--------------------------|----------------|----------------------|
| D10 | 55% | 10 | 5 | 20 | 24 | Yes | 6 |
| D11 | 40% | 10 | 5 | 20 | 24 | Yes | 6 |
| D12 | 40% | 10 | 5 | 20 | 28 | Yes | 7 |
| D13 | 40% | 8 | 4 | 22 | 35 | Yes | 8 |
| D14 | 30% | 8 | 4 | 22 | 36 | No | 8 |

# Lessons learned from this case

- Long term of NIV worsens lung

- Set low PEEP

- Prevent acute Cor Pulmonale induced by severe hypoxemia

# Flowchart for ventilation supports

**Critically ill patients with COVID-19**

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**200 mmHg ≤ P/F < 300**

HFNC: 40 ~ 50 L/min, $FiO_2$ 100%, 2h

- ROXI≥3.85 or $SpO_2$≥93%, RR<25 rpm continue HFNC
- 2.85≤ROXI<3.85 or $SpO_2$≥93% but 25 < RR<30 rpm, continue HFNC and observe for 6h
- ROXI < 2.85 or $SpO_2$ < 93%, RR≥30rpm, Stop HFNC

- ROXI > 4.88 or $SpO_2$≥93%, RR<25 rpm continue HFNC
- ROXI≥3.85 or $SpO_2$≥93%, RR<25 rpm continue HFNC
- Altered mental status; Malignant arrhythmia; Severe shock [NE > 0.1 μg/(kg·min)]; Acute respiratory acidosis (PH < 7.25); Airway drainage difficulty

- ROXI < 3.85 or $SpO_2$ < 93%, RR > 30rpm,

**No** / **Yes**

---

**150 mmHg ≤ P/F < 200**

NIV, IPAP 8 ~ 12cm $H_2O$; EPAP 5 ~ 8 $cmH_2O$, $FiO_2$ 100%, 2h

- Vt ≤ 9ml/kg, continue NIV
- 9ml/kg < Vt < 12ml/kg, continue NIV, observe for 6h
- Vt ≥12ml/kg

Vt > 9 ml/kg

---

**P/F < 150 mmHg**

Intubation and mechanical ventilation: Vt 6 ml/kg (IBM), PEEP 8 ~ 10 cm $H_2O$, RR 20 rpm, $FiO_2$ 100%, monitor Pplat < 30 $cmH_2O$; If Pplat > 30 $cmH_2O$, decrease Vt by 1 ml/kg to Vt 4ml/kg. For every 1ml/kg reduction in Vt, RR increases by 5 rpm until RR reaches 30 rpm. Maintain $SpO_2$ 88% ~ 95%, PEEP selection according to ARDSnet low compliance

Evaluate lung recruitment ability: Increase PEEP from 5 $cmH_2O$ to 15cm $H_2O$. Meets two of the following three criteria: P/F increased; $PaCO_2$ decreased; improved lung compliance.

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Lung recruitment maneuver through PEEP titration: start from 20 $cmH_2O$, decreased by 2 cm $H_2O$/30sec. Continue lung recruitment if $SpO_2$ decreased, PEEP set as the value before $SpO_2$ decreased

Measure DP, if DP > 15 cm $H_2O$, use neuromuscular blocker

No recruitment ability

$FiO_2$ > 60%, P/F≤10 mmHg or Pplat > 35 $cmH_2O$, $PaCO_2$ > 50 mmHg and PH<7.25

$FiO_2$ > 60%, P/F < 150 mmHg → Prone position, observe for 24 h

VV-ECMO

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# Prognosis

- At the end of Feb 8, 2020, 58(42.03%) patients were still in hospitalization, 72 (52.17.10%) patients had been discharged and 8 (5.79%) patients had died, and ICU mortality 18%

# Updated information from Feb 8 to march 7

- More than 50 patients admitted in ICU from Feb 8 to March 7

- More severe patients, as some transferred from other hospitals

- Seventy percent needed IMV, half of them switched to ECMO, and

  7 of them weaned off ECMO

- The predicted overall ICU mortality 25-30%

# Dynamic changes of laboratory tests in survivors and non-survivors in hospitalized Pts



Wang D, et al. JAMA 2020;Feb7.
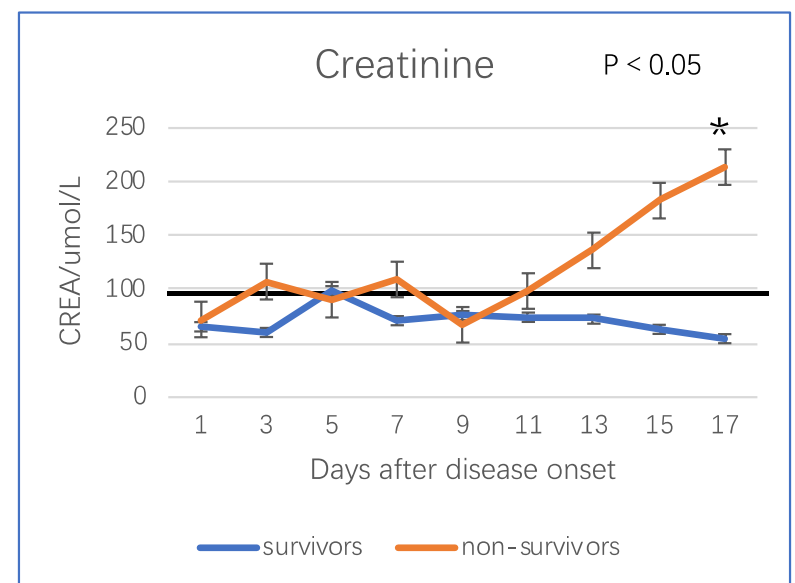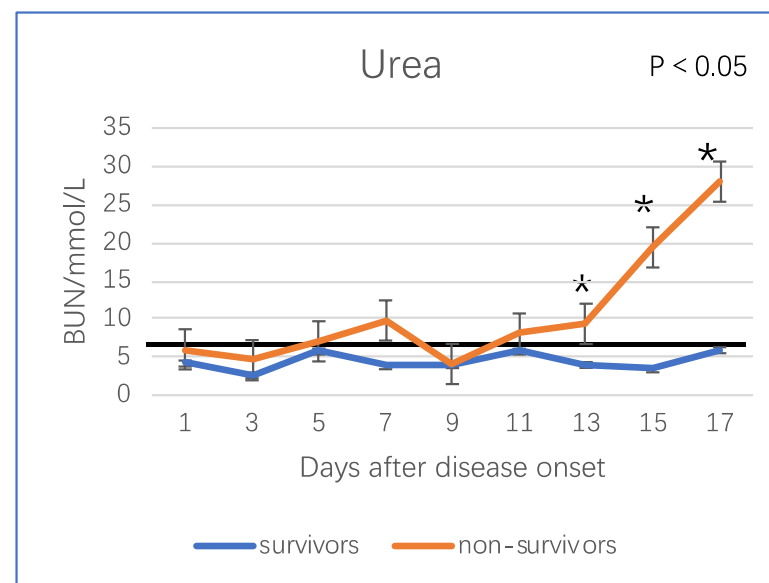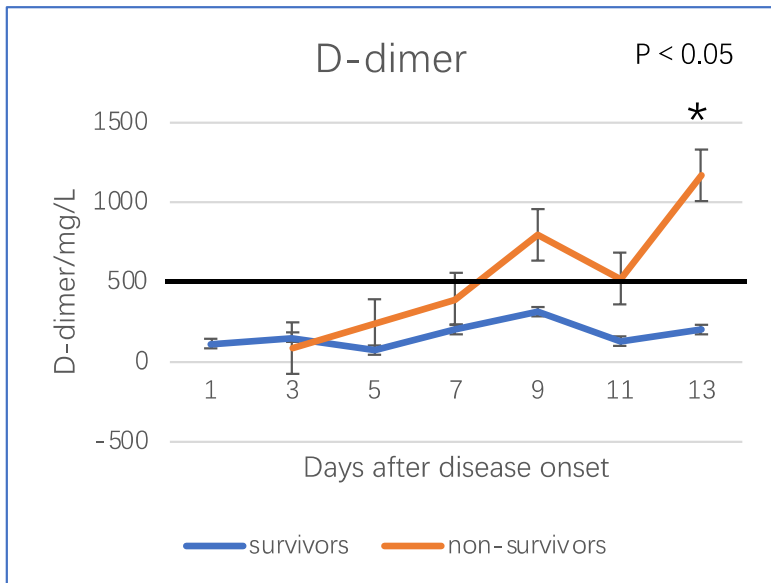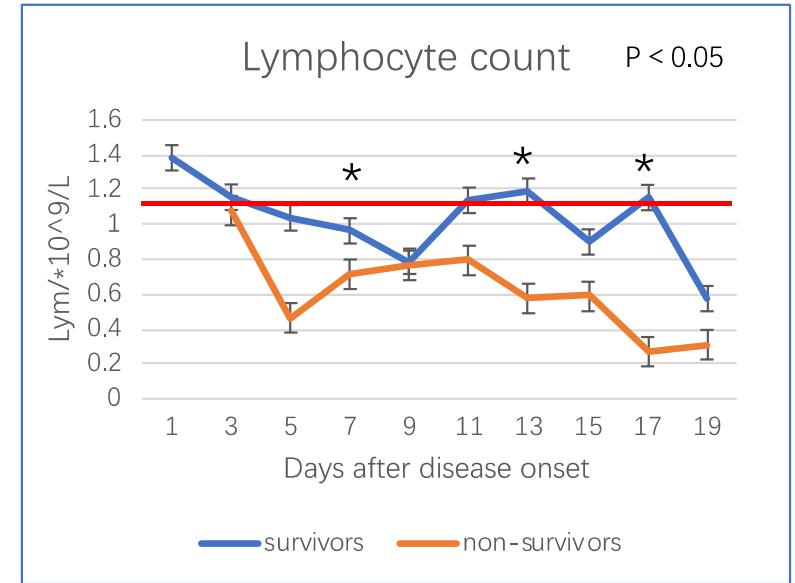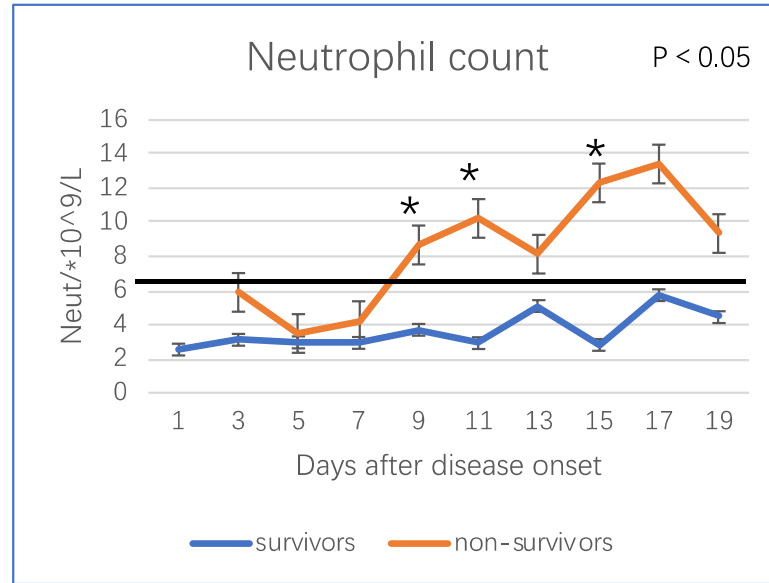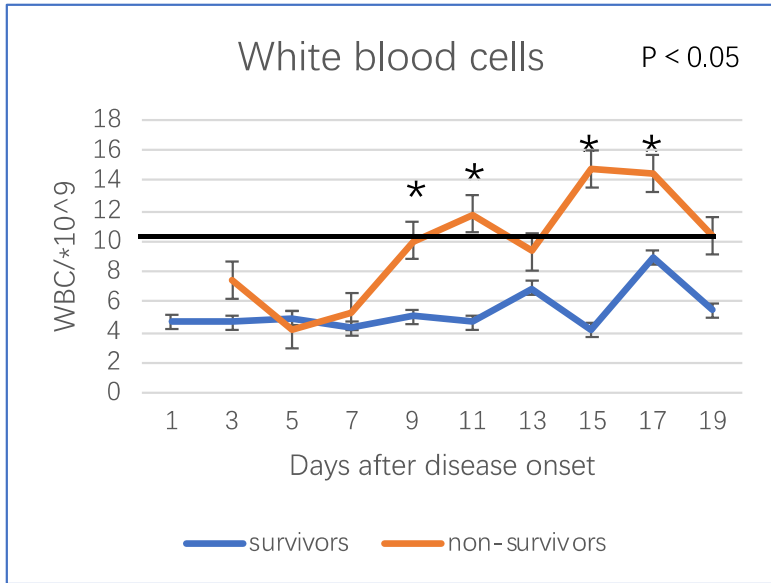
# Dynamic changes of survivors and non-survivors in ICU



Hu B, et al. Under review.
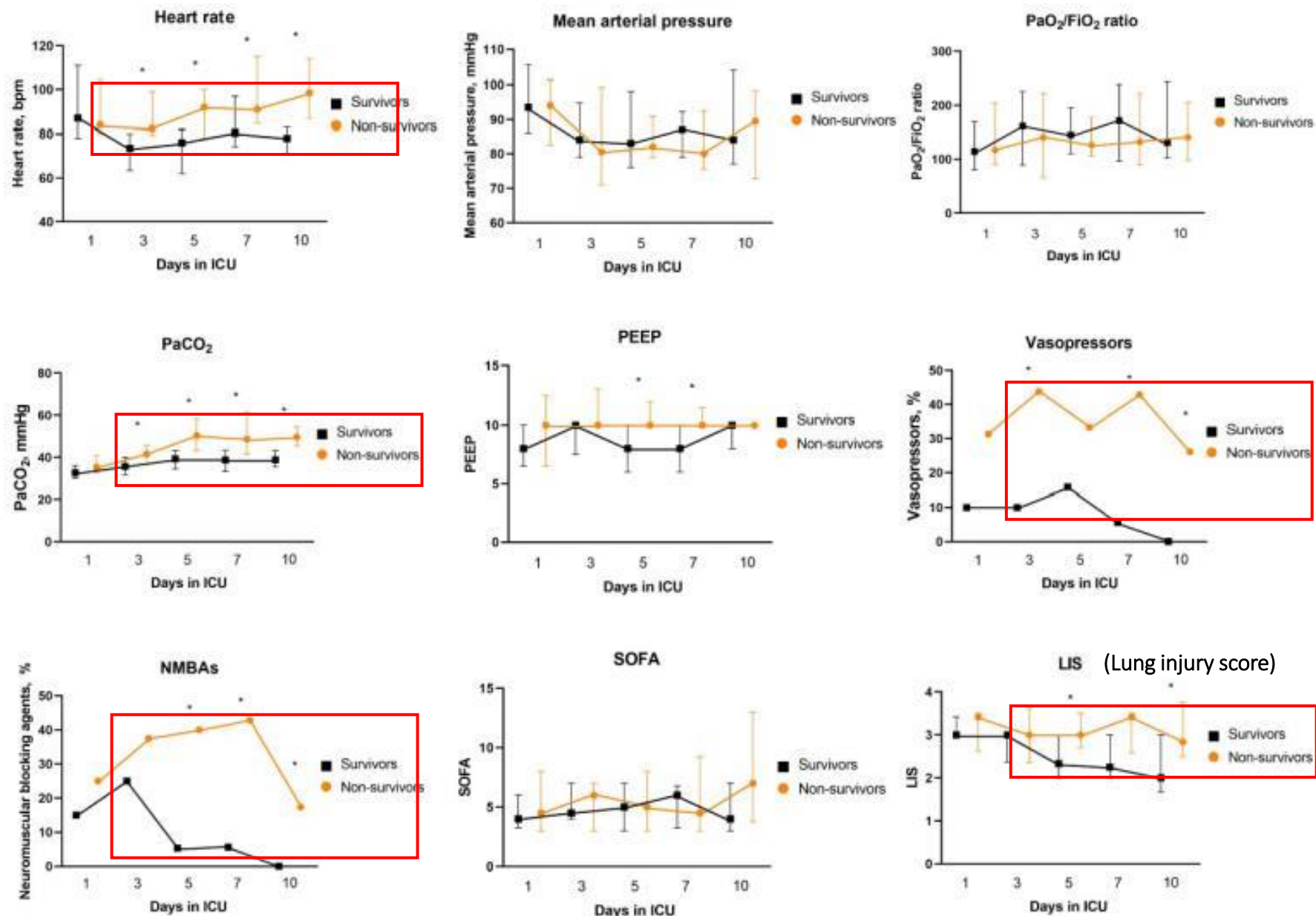
# Predictors at ICU admission for ICU mortality

| Variable | Univariable | | Multivariable | |
|---|---|---|---|---|
| | OR (95% CI) | P Value | OR (95% CI) | P Value |
| Age, years | 1.04(1.00-1.08) | 0.05 | 1.04(0.99-1.09) | 0.11 |
| APACHE II | 1.10(1.02-1.19) | 0.02 | 1.13(1.001-1.26) | 0.04 |
| LIS | 1.48(0.64-3.43) | 0.366 | | |
| Cstat | 0.923(0.87-0.99) | 0.02 | 0.92(0.86-0.98) | 0.02 |
| White blood cell count, $\times 10^9$/L | 1.05(0.96-1.16) | 0.25 | | |
| Blood urea nitrogen, mmol/L | 1.18(1.02-1.36) | 0.026 | 1.12(0.91-1.40) | 0.28 |
| IL-6, pg/mL | 1.01(1.00-1.02) | 0.15 | | |

# CONCLUSIONS

- The preparation for the outbreak of COVID-19 is important, as medical resource are always limited.

-  The transmission was frequent, characterized with hospital related infection but low mortality. The atypical patients were probably the main source of transmission.

- Critically ill patients tended to be older with comorbidities, specific symptoms and laboratory abnormalities.

- Titrating modes/parameters of ventilation supports with lung-protective approach is crucial.

- The most common complication was ARDS, arrhythmia and septic shock. Nearly half of the critically ill patients needed invasive ventilation.

- The lung compliance at ICU admission and persistently elevated $PaCO_2$ predicted poor outcome.

筑牢防线，坚决遏制疫情蔓延

加油，武汉！

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