Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China

2019中国武汉新型感染冠状病毒感染者的临床特征

Chaolin Huang*, Yeming Wang*, Xingwang Li*, Lili Ren*, Jianping Zhao*, Yi Hu*, Li Zhang, Guohui Fan, Jiuyang Xu, Xiaoying Gu, Zhenshun Cheng, Ting Yu, Jiaan Xia, Yuan Wei, Wenjuan Wu, Xuelei Xie, Wen Yin, Hui Li, Min Liu, Yan Xiao, Hong Gao, Li Guo, Jungang Xie, Guangfa Wang, Rongmeng Jiang, Zhancheng Gao, Qi Jin, Jianwei Wang†, Bin Cao†

Summary

Background **A recent cluster of pneumonia cases in Wuhan, China, was caused by a novel betacoronavirus, the 2019 novel coronavirus (2019-nCoV). We report the epidemiological, clinical, laboratory, and radiological characteristics and treatment and clinical outcomes of these patients.**

背景： 中国武汉最近一次的肺炎爆发源于一种新型的冠状病毒（2019-nCoV）。我们将从流行病学、临床、实验、放射影像、治疗方案及患者的治疗结果来对此进行描述。

Methods **All patients with suspected 2019-nCoV were admitted to a designated hospital in Wuhan. We prospectively collected and analysed data on patients with laboratory-confirmed 2019-nCoV infection by real-time RT-PCR and next-generation sequencing. Data were obtained with standardised data collection forms shared by the International Severe Acute Respiratory and Emerging Infection Consortium from electronic medical records. Researchers also directly communicated with patients or their families to ascertain epidemiological and symptom data. Outcomes were also compared between patients who had been admitted to the intensive care unit (ICU) and those who had not.**

方法：所有疑似感染新型冠状病毒的病例都在武汉的专门医院进行收治。我们对证实感染新型冠状病毒的病例预先进行了RT-PCR（逆转录聚合酶链反应）及新一代基因测序。数据采用国际严重急性呼吸道和新型感染联合会电子医疗记录格式收集。研究者也通过直接联系病人或家属确认流行病学及症状数据。我们也比对了需要进行深切治疗的病患和普通病患之间的数据。

Findings **By Jan 2, 2020, 41 admitted hospital patients had been identified as having laboratory-confirmed 2019-nCoV infection. Most of the infected patients were men (30 [73%] of 41); less than half had underlying diseases (13 [32%]), including diabetes (eight [20%]), hypertension (six [15%]), and cardiovascular disease (six [15%]). Median age was 49·0 years (IQR 41·0–58·0). 27 (66%) of 41 patients had been exposed to Huanan seafood market. One family cluster was found. Common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), haemoptysis (two [5%] of 39), and diarrhoea (one [3%] of 38). Dyspnoea developed in 22 (55%) of 40 patients (median time from illness onset to dyspnoea 8·0 days [IQR 5·0–13·0]). 26**

(63%) of 41 patients had lymphopenia. All 41 patients had pneumonia with abnormal findings on chest CT. Complications included acute respiratory distress syndrome (12 [29%]), RNAaemia (six [15%]), acute cardiac injury (five [12%]) and secondary infection (four [10%]). 13 (32%) patients were admitted to an ICU and six (15%) died. Compared with non-ICU patients, ICU patients had higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNFα.

发现：2020年1月2日，41名收治病人被确证感染新型冠状病毒。绝大多数病例为男性（30人/41人[75%]）；三分之一病例有带有基础疾病，（13人/41人[32%]），包括糖尿病（8人/41人[20%]），高血压（6人/41人[15%]），心血管疾病（6人/41人[15%]）。平均年龄位49岁，IQR（四分位间距）为41-58岁。27人（66%）曾经在华南海鲜市场活动。其中有一个家族病例。

普通发病症状为发烧（40人/41人[98%]），咳嗽（31人/41人[76%]），肌肉酸痛或无力（18人/41人[44%]）；少数发病症状为多痰（11人/39人[76%]），头痛（3人/38人[8%]），咳血（2人/39人[5%]），腹泻（1人/38人[3%]），40人中的22人发展为呼吸困难（55%，从发病开始的病程平均为8天，四分位间距为5-13天）41人中的26人（63%）出现淋巴减少症状。

所有41人都在胸部CT造影发现肺部异常炎症。并发急性呼吸窘迫综合症12人（29%），RNA贫血6人（15%），急性心脏损伤5人（12%），继发感染4人（10%）。13人（32%）需要进行深切治疗，6人（15%）死亡。对照没有进行深切治疗的病患，采取了深切治疗的病患血液中检出高水平的IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, TNFα.

Interpretation The 2019-nCoV infection caused clusters of severe respiratory illness similar to severe acute respiratory syndrome coronavirus and was associated with ICU admission and high mortality. Major gaps in our knowledge of the origin, epidemiology, duration of human transmission, and clinical spectrum of disease need fulfilment by future studies.

解释：新型冠状病毒导致的呼吸系统症状与非典型肺炎类似，并且一旦恶化具有高死亡率。我们目前对病毒起源、流行病学、人传人周期、临床治疗还存在盲区，需要进一步的研究。

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Introduction

Coronaviruses are enveloped non-segmented positive- sense RNA viruses belonging to the family Coronaviridae and the order Nidovirales and broadly distributed in humans and other mammals.[1] Although most human coronavirus infections are mild, the epidemics of the two betacoronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) [2,4] and Middle East respiratory syndrome coronavirus (MERS-CoV),[5,6] have caused more than 10000 cumulative cases in the past two decades, with mortality rates of 10% for SARS-CoV and 37% for MERS-CoV.7,8 The coronaviruses already identified might only be the tip of the iceberg, with potentially more novel and severe zoonotic events to be revealed.

冠状病毒是 *非分段*、*正向封装* RNA病毒，属于冠状病毒科巢病毒目，在人类和其他哺乳动物中广泛存在。尽管多数的人类冠状病毒感染是温和的，但非典型肺炎病毒（SARS-CoV）和中东呼吸综合征（MERS-CoV）两种冠状病毒在过去20年里造成了超过10000人的感染，非典型肺炎具有10%的死亡率，中东呼吸综合征的死亡率则高达37%。已经发现的冠状病毒只是冰山一角，未来预计将有更多的新型冠状病毒出现，并造成严重的人、畜公共卫生事件。

In December, 2019, a series of pneumonia cases of unknown cause emerged in Wuhan, Hubei, China, with clinical presentations greatly resembling viral pneumonia.9 Deep sequencing analysis from lower respiratory tract samples indicated a novel coronavirus, which was named 2019 novel coronavirus (2019-nCoV). Thus far, more than 800 confirmed cases, including in health-care workers, have been identified in Wuhan, and several exported cases have been confirmed in other provinces in China, and in Thailand, Japan, South Korea, and the USA.10–13

2019年12月，中国湖北省武汉市出现了一系列的未知原因肺炎病例，临床表现高度类似病毒性肺炎。通过深度测序分析，在病例的下呼吸道样本中发现了一种新型的冠状病毒，命名为2019新型冠状病毒（2019-nCoV）。迄今为止在武汉已经造成了包括医务工作者在内的超过800人感染，在其他中国省份以及泰国、日本、韩国及美国都出现了输出的病例。

Research in context

Evidence before this study

Human coronaviruses, including hCoV-229E, OC43, NL63, and HKU1, cause mild respiratory diseases. Fatal coronavirus infections that have emerged in the past two decades are severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus. We searched PubMed and the China National Knowledge Infrastructure database for articles published up to Jan 11, 2020, using the keywords “novel coronovirus”, “2019 novel coronavirus”, or “2019-nCoV”. No published work about the human infection caused by the 2019 novel coronavirus (2019-nCoV) could be identified.

人类冠状病毒包括hCoV-229E, OC43, NL63及HKU1，会导致轻微的肺部疾病。曾在过去20年爆发的冠状病毒有非典型肺炎病毒（SARS-CoV）及中东呼吸综合征病毒。我们检索了PubMed及中国知网截止2020年1月11日所有包含“新型冠状病毒”、“2019新型冠状病毒”或“2019-nCoV”。没有已经发表的研究提及导致人感染的2019新型冠状病毒。

Added value of this study

We report the epidemiological, clinical, laboratory, and radiological characteristics, treatment, and clinical outcomes of 41 laboratory-confirmed cases infected with 2019-nCoV.

我们研究了41个确认感染新型冠状病毒的案例的流行病学、临床、实验、放射造影、治疗方案及治疗结果。

27 (66%) of 41 patients had a history of direct exposure to the Huanan seafood market. The median age of patients was 49·0 years (IQR 41·0–58·0), and 13 (32%) patients had underlying disease. All patients had pneumonia. A third of patients were admitted to intensive care units, and six died. High concentrations of cytokines were recorded in plasma of critically ill patients infected with 2019-nCoV.

41名患者中的27人（66%）曾经在华南海鲜市场活动。他们的平均年龄为49岁。（四分位间距IQR为41-58），13人（32%）具有基础疾病。所有的病例都有肺部炎症。三分之一的病例进入了深切治疗，六人死亡。在严重病例的血液中检出高浓度的细胞因子。

Implications of all the available evidence

2019-nCoV caused clusters of fatal pneumonia with clinical presentation greatly resembling SARS-CoV. Patients infected with 2019-nCoV might develop acute respiratory distress syndrome, have a high likelihood of admission to intensive care, and might die. The cytokine storm could be associated with disease severity. More efforts should be made to know the whole spectrum and pathophysiology of the new disease.

新型冠状病毒的严重病例表现出与非典型肺炎高度的相似性。患者可能发展为急性呼吸窘迫综合症，具有较高比例需要进行深切治疗，并且可能死亡。严重病患将产生细胞因子风暴。为了认识这种新型疾病的病理学全貌，需要更多的努力。

We aim to describe epidemiological, clinical, laboratory, and radiological characteristics, treatment, and outcomes of patients confirmed to have 2019-nCoV infection, and to compare the clinical features between intensive care unit (ICU) and non-ICU patients. We hope our study findings will inform the global community of the emergence of this novel coronavirus and its clinical features.

我们的目标是描述对感染新型冠状病毒的病人进行流行病学、临床、实验以及放射影像、治疗及效果的研究，并对比需要深切治疗和不需要深切治疗的病人的情况。我们希望我们的研究发现能将新型冠状病毒的临床特征给予全球社区以应对可能的公共危机。

Methods

Patients

Following the pneumonia cases of unknown cause reported in Wuhan and considering the shared history of exposure to Huanan seafood market across the patients, an epidemiological alert was released by the local health authority on Dec 31, 2019, and the market was shut down on Jan 1, 2020. Meanwhile, 59 suspected cases with fever and dry cough were transferred to a designated hospital starting from Dec 31, 2019. An expert team of physicians, epidemiologists, virologists, and government officials was soon formed after the alert.

根据武汉不明肺炎病例报告曾经到访过华南海鲜市场的经历，2019年12月31日，当地健康管理机构发布了一个疫情警告，并在2020年1月1日关闭了该市场。同时，从2019年12月31日开始，59个具有发烧和干咳的疑似案例被转移到专门医院。之后，成立了一个由医生、流行病学家、病毒学家和政府官员组成的专家组。

Since the cause was unknown at the onset of these emerging infections, the diagnosis of pneumonia of unknown cause in Wuhan was based on clinical characteristics, chest imaging, and the ruling out of common bacterial and viral pathogens that cause pneumonia. Suspected patients were isolated using airborne precautions in the designated hospital, Jin Yin- tan Hospital (Wuhan, China), and fit-tested N95 masks and airborne precautions for aerosol-generating procedures were taken. This study was approved by the National Health Commission of China and Ethics Commission of Jin Yin-tan Hospital (KY-2020-01.01). Written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases.

因为这些症状发生时，致病原因未明，对于武汉不明肺炎的检测基于临床特征、胸片及对常见肺炎病菌、病毒病原的排查。疑似病例在专门医院（金银潭医院）治疗过程中进行了空气隔离，出于对突发感染疾病的考虑，医院伦理委员会放弃了签署书面知情同意书。

Procedures

Local centres for disease control and prevention collected respiratory, blood, and faeces specimens, then shipped them to designated authoritative laboratories to detect the pathogen (NHC Key Laboratory of Systems Biology of Pathogens and Christophe Mérieux Laboratory, Beijing, China). A novel coronavirus, which was named 2019-nCoV, was isolated then from lower respiratory tract specimen and a diagnostic test for this virus was developed soon after that.14 Of 59 suspected cases, 41 patients were confirmed to be infected with 2019-nCoV. The presence of 2019-nCoV in respiratory specimens was detected by next- generation sequencing or real-time RT-PCR methods. The primers and probe target to envelope gene of CoV were used and the sequences were as follows: forward primer 5'-TCAGAATGCCAATCTCCCCAAC-3'; reverse primer 5'-AAAGGTCCACCCGATACATTGA-3'; and the probe 5'CY5-CTAGTTACACTAGCCATCCTTACTGC-3'BHQ1. Conditions for the amplifications were 50°C for 15 min, 95°C for 3 min, followed by 45 cycles of 95°C for 15 s and 60°C for 30 s.

本地疾控中心收集了病人的呼吸道、血液和粪便样本，并运送专门的实验室检测病原体（中国，北京，NHC病原体系统生物学重点实验室和Christophe Mérieux 实验室）。一种被命名为2019-nCoV的新型的冠状病毒从下呼吸道样本中被检出。对这种病毒的检测手段也迅速被开发出来。在59个疑似病例中，41人被确诊为感染新型冠状病毒。呼吸道样本中的新型冠状病毒是通过新一代基因测序及实时RT-PCR（逆转录聚合酶链反应）方法完成的。冠状病毒的检测指针使用的是：正向引导：5'-TCAGAATGCCAATCTCCCCAAC-3'; 逆向引导：5'-AAAGGTCCACCCGATACATTGA-3'; 探针：5'CY5-CTAGTTACACTAGCCATCCTTACTGC-3'BHQ1. 检测条件是50°C 15分钟, 95°C 3分钟,以及45 周期以后的95°C下15秒，60°C 30秒.

Initial investigations included a complete blood count, coagulationprofile,and serumbio chemical test(including renal and liver function,creatinekinase,lactatedehydro- genase, and electrolytes). Respiratory specimens, including nasal and pharyngeal swabs, bronchoalveolar lavage fluid, sputum, or bronchial aspirates were tested for common viruses, including influenza, avian influenza, respiratory syncytial virus, adenovirus, parainfluenza virus, SARS-CoV and MERS-CoV using real-time RT-PCR assays approved by the China Food and Drug Administration. Routine bacterial and fungal examinations were also performed.

最初的调查内容包含了完整的血计数、凝血图以及血清化验（包括肝肾功能、肌酸酶、乳酸脱氢-基因酶和电解质）包含鼻咽拭子、支气管肺泡吸液、痰或支气管吸液的呼吸道样本，用于经过中国食药监局批准的检测常见病毒，包括流感、禽流感、呼吸道合胞病毒、腺病毒、副流感病毒、非典型肺炎病毒以及中东呼吸系统综合征病毒检测，同时还进行了常规细菌和真菌检测。

Given the emergence of the 2019-nCoV pneumonia cases during the influenza season, antibiotics (oral and intravenous) and oseltamivir (orally 75 mg twice daily) were empirically administered. Corticosteroid therapy (methylprednisolone 40–120 mg per day) was given as a combined regimen if severe community-acquired pneumonia was diagnosed by physicians at the designated hospital. Oxygen support (eg, nasal cannula and invasive mechanical ventilation) was administered to patients according to the severity of hypoxaemia. Repeated tests for 2019-nCoV were done in patients confirmed to have 2019-nCoV infection to show viral clearance before hospital discharge or discontinuation of isolation.

因为新型冠状病毒是在流感季节爆发，所以对于相关病例给予了治疗规程知道的抗生素（口服和静脉注射）奥司他韦（每天口服75mg两次）治疗。在专门医院，对于严重的社区感染病例，采用激素治疗（甲基苯丙酮每天40-120mg）作为联合方案。根据病例的低氧血症严重程度给进行人工输氧（例如鼻管及侵入性通气）。对于确诊新型冠状病毒的病例，在出院或结束隔离前，还进行了重复的检测，以观

察病毒的活动 。

Data collection

We reviewed clinical charts, nursing records, laboratory findings, and chest x-rays for all patients with laboratory- confirmed 2019-nCoV infection who were reported by the local health authority. The admission data of these patients was from Dec 16, 2019, to Jan 2, 2020. Epidemiological, clinical, laboratory, and radiological characteristics and treatment and outcomes data were obtained with standardised data collection forms (modified case record form for severe acute respira- tory infection clinical characterisation shared by the International Severe Acute Respiratory and Emerging Infection Consortium) from electronic medical records. Two researchers also independently reviewed the data collection forms to double check the data collected. To ascertain the epidemiological and symptom data, which were not available from electronic medical records, the researchers also directly communicated with patients or their families to ascertain epidemiological and symptom data.

我们复核了所有确诊感染新型冠状病毒的病人临床图表，护理记录，实验结果以及胸部x光片。收治数据从2019年12月16日至2020年1月2日。流行病学、临床、实验以及放射影像及治疗和结果电子医疗数据通过标准数据集格式收集（国际严重急性呼吸道和新兴感染联合会严重急性呼吸道感染临床特征修正表格）。两个研究者也独立的检查复核了这些数据。为了确定流行病学和症状数据，研究者直接联系了病人或他们的家属以确认流行病学和病症数据。

Cytokine and chemokine measurement 细胞因子和趋化因子测量

To characterise the effect of coronavirus on the production of cytokines or chemokines in the acute phase of the illness, plasma cytokines and chemokines (IL1B, IL1RA, IL2, IL4, IL5, IL6, IL7, IL8 (also known as CXCL8), IL9, IL10, IL12p70, IL13, IL15, IL17A, Eotaxin (also known as CCL11), basic FGF2, GCSF (CSF3), GMCSF (CSF2), IFNγ, IP10 (CXCL10), MCP1 (CCL2), MIP1A (CCL3), MIP1B (CCL4), PDGFB, RANTES (CCL5), TNFα, and VEGFA were measured using Human Cytokine Standard 27-Plex Assays panel and the Bio-Plex 200 system (Bio-Rad, Hercules, CA, USA) for all patients according to the manufacturer's instructions. The plasma samples from four healthy adults were used as controls for cross- comparison. The median time from being transferred to a designated hospital to the blood sample collection was 4 days (IQR 2–5).

为了弄清楚冠状病毒在病症急性期产生细胞因子或趋化因子的作用，对于血浆细胞因子和趋化因子(IL1B, IL1RA, IL2, IL4, IL5, IL6, IL7, IL8 (也叫CXCL8), IL9, IL10, IL12p70, IL13, IL15, IL17A, Eotaxin (也叫CCL11), basic FGF2, GCSF (CSF3), GMCSF (CSF2), IFNγ, IP10 (CXCL10), MCP1 (CCL2), MIP1A (CCL3), MIP1B (CCL4), PDGFB, RANTES (CCL5), TNFα, VEGFA)使用人类细胞因子标准27-Plex检测面板和Bio-Plex 200系统，根据厂家指引进行了检测。四个健康成人的血浆样本用于做交叉对比。将样本从收治到提取样本平均需要4天（四分位间距IQR2-5）

Detection of coronavirus in plasma 在血浆中检测冠状病毒

Each 80 μL plasma sample from the patients and contacts was added into 240 μL of Trizol LS (10296028; Thermo Fisher Scientific, Carlsbad, CA, USA) in the Biosafety Level 3 laboratory. Total RNA was extracted by Direct-zol RNA Miniprep kit (R2050; Zymo research, Irvine, CA, USA) according to the manufacturer's instructions and

50 μL elution was obtained for each sample. 5 μL RNA was used for real-time RT-PCR, which targeted the *NP* gene using AgPath-ID One-Step RT-PCR Reagent (AM1005; Thermo Fisher Scientific). The final reaction mix concentration of the primers was 500 nM and probe was 200 nM. Real-time RT-PCR was performed using the following conditions: 50°C for 15 min and 95°C for 3 min, 50 cycles of amplification at 95°C for 10 s and 60°C for 45 s. Since we did not perform tests for detecting infectious virus in blood, we avoided the term viraemia and used RNAaemia instead. RNAaemia was defined as a positive result for real-time RT-PCR in the plasma sample.

Definitions

Acute respiratory distress syndrome (ARDS) and shock were defined according to the interimguidance of WHO for novel coronavirus.9 Hypoxaemia was defined as arterial oxygen tension (PaO2) over inspiratory oxygen fraction (FIO2) of less than 300 mm Hg.15 Acute kidney injury was identified and classified on the basis of the highest serum creatinine level or urine output criteria according to the kidney disease improving global outcomes classification.16 Secondary infection was diagnosed if the patients had clinical symptoms or signs of nosocomial pneumonia or bacteraemia, and was combined with a positive culture of a new pathogen from a lower respiratory tract specimen (including the sputum, transtracheal aspirates, or bron- choalveolar lavage fluid, or from blood samples taken ≥48 h

after admission).17 Cardiac injury followed the definition used in our previous study in H7N9 patients.18 In brief, cardiac injury was diagnosed if serum levels of cardiac biomarkers (eg, troponin I) were above the 99th percentile upper reference limit, or new abnormalities were shown in electrocardiography and echocardiography.

Statistical analysis 统计分析方法

Continuous variables were expressed as median (IQR) and compared with the Mann-Whitney U test; categorical variables were expressed as number (%) and compared by χ2 test or Fisher's exact test between ICU care and no ICU care groups. Boxplots were drawn to describe plasma cytokine and chemokine concentrations.

连续变量将以平均数（IQR）表示，并与Mann-Whitney U测试进行比对。分类变量以百分比表示，并通过χ2测试和确切概率法进行比对深切治疗病患和普通病患的情况。方块图用于描述血浆细胞因子和趋化因子浓度。

A two-sided α of less than 0·05 was considered statis- tically significant. Statistical analyses were done using the SAS software, version 9.4, unless otherwise indicated.

Role of the funding source 资金提供者的角色

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

研究的资助者没有参与研究设计、数据采集、数据分析、数据解释或者撰写报告。合作撰稿人有完整的权限访问所有数据并对提交给公众的结论负责。

Results

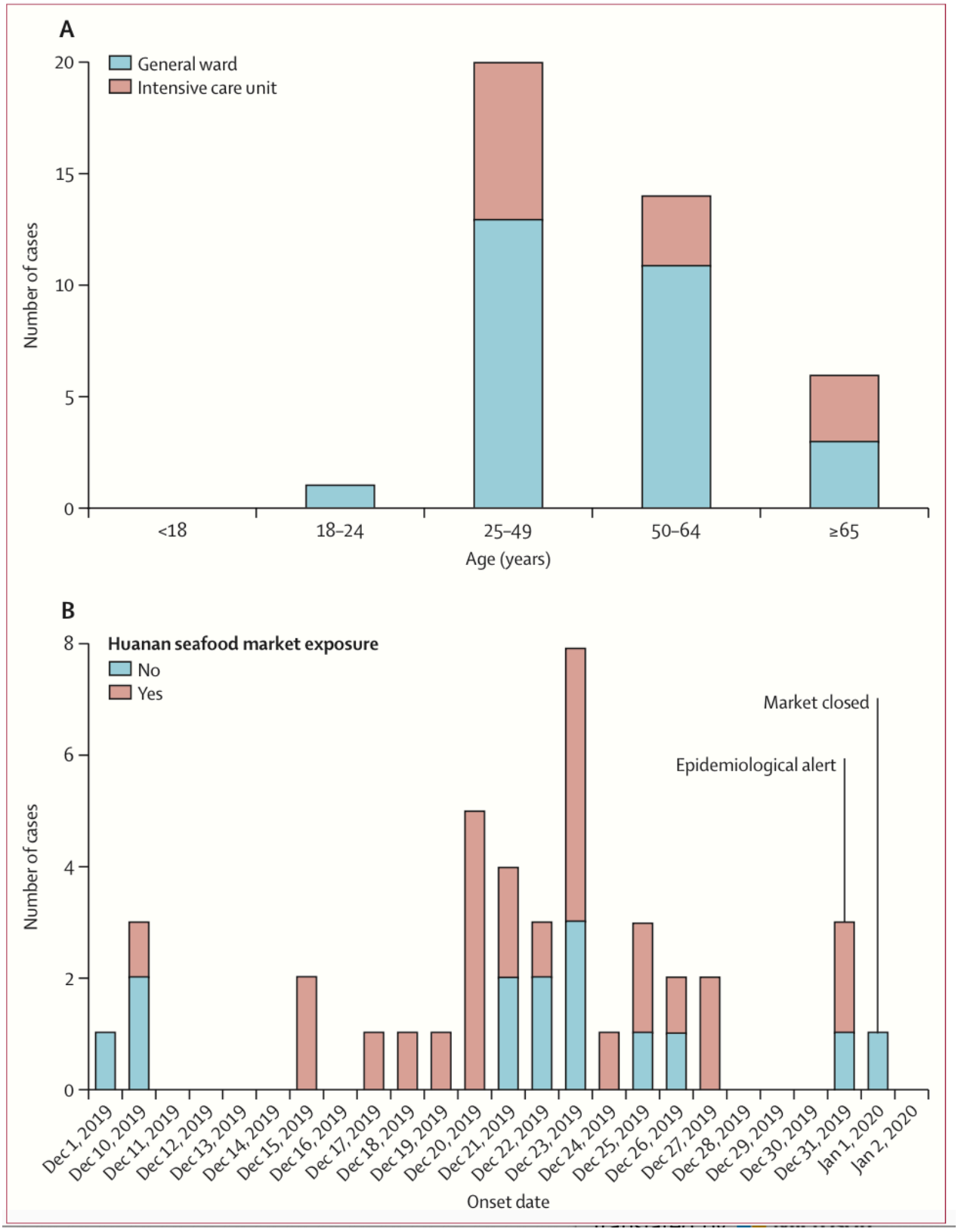

Figure 1: Date of illness onset and age distribution of patients with laboratory-confirmed 2019-nCoV infection (A) Number of hospital admissions by age group. (B) Distribution of symptom onset date for laboratory-confirmed cases. The Wuhan local health authority issued an epidemiological alert on Dec 30, 2019, and closed the Huanan seafood market 2 days later.

图1:确诊病人发病日期和年龄分布

(A)医院收治年龄组的人数. (B) 确诊病例的发病日期分布. 2019年12月30日，武汉卫生部门宣布疫情警示，两天后关闭了华南海鲜市场。

By Jan 2, 2020, 41 admitted hospital patients were identified as laboratory-confirmed 2019-nCoV infection in Wuhan. 20 [49%]) of the 2019-nCoV-infected patients were aged 25–49 years, and 14 (34%) were aged 50–64 years (figure 1A). The median age of the patients was 49·0 years (IQR 41·0–58·0; table 1). In our cohort of the first 41 patients as of Jan 2, no children or adolescents were infected. Of the 41 patients, 13 (32%) were admitted to the ICU because they required high-flow nasal cannula or higher-level oxygen support measures to correct hypoxaemia. Most of the infected patients were men (30 [73%]); less than half had underlying diseases (13 [32%]), including diabetes (eight [20%]), hypertension (six [15%]), and cardiovascular disease (six [15%]).

2020年1月2日，武汉41名收治病人被确诊为新型冠状病毒感染。20人[49%]年龄介于25-49岁，14人（34%）年龄介于50-64岁（图1A）患者平均年龄为49岁（四分位间距41-58 表1）。在41名患者中没有儿童或青少年被感染。13人（32%）因为需要高通量的鼻管或者输氧以应对低血氧症进行了深切治疗。绝大多数病例为男性（30[73%]）;三分之一具有基础疾病（13[32%]）, 糖尿病（8人/41人[20%]），高血压（6人/41人[15%]），心血管疾病（6人/41人[15%]）

	All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
Characteristics				
Age, years	49·0 (41·0–58·0)	49·0 (41·0–61·0)	49·0 (41·0–57·5)	0·60
Sex	..	..	..	0·24
Men	30 (73%)	11 (85%)	19 (68%)	..
Women	11 (27%)	2 (15%)	9 (32%)	..
Huanan seafood market exposure	27 (66%)	9 (69%)	18 (64%)	0·75
Current smoking	3 (7%)	0	3 (11%)	0·31
Any comorbidity	13 (32%)	5 (38%)	8 (29%)	0·53
Diabetes	8 (20%)	1 (8%)	7 (25%)	0·16
Hypertension	6 (15%)	2 (15%)	4 (14%)	0·93
Cardiovascular disease	6 (15%)	3 (23%)	3 (11%)	0·32
Chronic obstructive pulmonary disease	1 (2%)	1 (8%)	0	0·14
Malignancy	1 (2%)	0	1 (4%)	0·49
Chronic liver disease	1 (2%)	0	1 (4%)	0·68
Signs and symptoms				
Fever	40 (98%)	13 (100%)	27 (96%)	0·68
Highest temperature, °C	..	..	..	0·037
<37·3	1 (2%)	0	1 (4%)	..
37·3–38·0	8 (20%)	3 (23%)	5 (18%)	..
38·1–39·0	18 (44%)	7 (54%)	11 (39%)	..
>39·0	14 (34%)	3 (23%)	11 (39%)	..
Cough	31 (76%)	11 (85%)	20 (71%)	0·35
Myalgia or fatigue	18 (44%)	7 (54%)	11 (39%)	0·38
Sputum production	11/39 (28%)	5 (38%)	6/26 (23%)	0·32
Headache	3/38 (8%)	0	3/25 (12%)	0·10
Haemoptysis	2/39 (5%)	1 (8%)	1/26 (4%)	0·46
Diarrhoea	1/38 (3%)	0	1/25 (4%)	0·66
Dyspnoea	22/40 (55%)	12 (92%)	10/27 (37%)	0·0010
Days from illness onset to dyspnoea	8·0 (5·0–13·0)	8·0 (6·0–17·0)	6·5 (2·0–10·0)	0·22
Days from first admission to transfer	5·0 (1·0–8·0)	8·0 (5·0–14·0)	1·0 (1·0–6·5)	0·002
Systolic pressure, mm Hg	125·0 (119·0–135·0)	145·0 (123·0–167·0)	122·0 (118·5–129·5)	0·018
Respiratory rate >24 breaths per min	12 (29%)	8 (62%)	4 (14%)	0·0023

Data are median (IQR), n (%), or n/N (%), where N is the total number of patients with available data. p values comparing ICU care and no ICU care are from χ^2 test, Fisher's exact test, or Mann-Whitney U test. 2019-nCoV=2019 novel coronavirus. ICU=intensive care unit.

Table 1: **Demographics and baseline characteristics of patients infected with 2019-nCoV**

27 (66%) patients had direct exposure to Huanan seafood market (figure 1B). Market exposure was similar between the patients with ICU care (nine [69%]) and those with non-ICU care (18 [64%]). The symptom onset date of the first patient identified was Dec 1, 2019. None of his family members developed fever or any respiratory symptoms. No epidemiological link was found between the first patient and later cases. The first fatal case, who had continuous exposure to the market, was admitted to hospital because of a 7-day history of fever, cough, and dyspnoea. 5 days after illness onset, his wife, a 53-year-old woman who had no known history of exposure to the market, also presented with pneumonia and was hospitalised in the isolation ward.

27人（66%）直接到过华南海鲜市场活动（图1B）。此行为比例在深切治疗组（9 [69%])和普通组（18 [64%])中相似。第一例病人发病日期为2019年12月1日。他的家人没有发烧或呼吸道症状。没有找到此病例和后继病例的流行病学联系。第一例死亡病例曾经连续在海鲜市场暴露，在发烧、干咳7天后被收治。发病5天后，他的妻子，53岁的妇女在没有接触过海鲜市场的情况下，同样也出现了肺炎，并被收治在隔离病房。

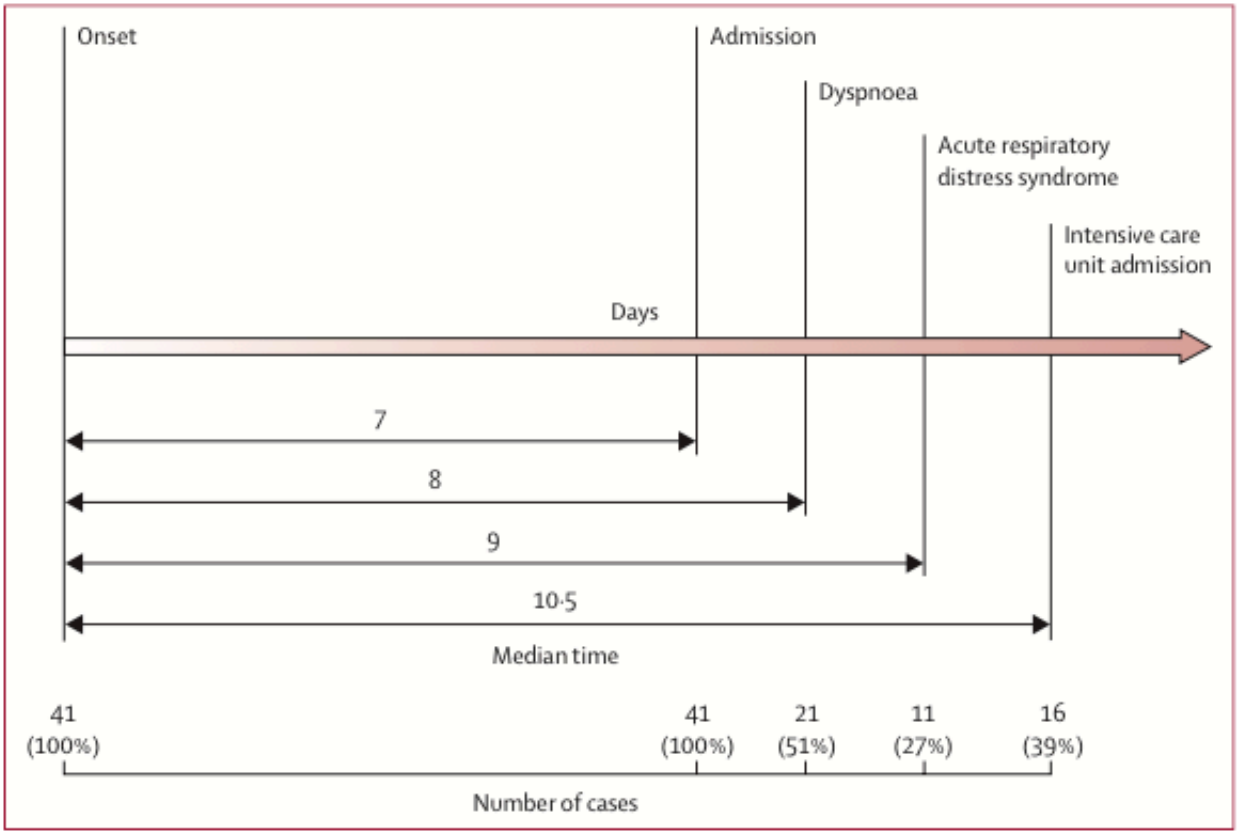

Figure 2: Timeline of 2019-nCoV cases after onset of illness

图2:新型冠状病毒发病时间线

The most common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), haemoptysis (two [5%] of 39), and diarrhoea (one [3%] of 38; table 1). More than half of patients (22 [55%] of 40) developed dyspnoea. The median duration from illness onset to dyspnoea was 8·0 days (IQR 5·0–13·0). The median time from onset of symp- toms to first hospital admission was 7·0 days (4·0–8·0), to shortness of breath was 8·0 days (5·0–13·0), to ARDS was 9·0 days (8·0–14·0), to mechanical ventilation was 10·5 days (7·0–14·0), and to ICU admission was 10·5 days (8·0–17·0; figure 2).

确证病例中最普遍的症状为发烧(40 [98%])、咳嗽(31 [76%]、肌肉酸痛或无力(18 [44%]，少数发病症状为多痰（11人/39人[76%]），头痛（3人/38人[8%]），咳血（2人/39人[5%]），腹泻（1人/38人[3%]）表1。超过一半的病例（22人/40人[55%]）发展为呼吸困难。从发病开始的病程平均为8天，四分位间距为5-13天）。从发病到入院的平均时间为8天（5-13）到出现急性呼吸窘迫症为9天（8-14），需要外部通气为10.5天（7-14），进入深切治疗为10.5天（8-17，图2）

The blood counts of patients on admission showed leucopenia (white blood cell count less than 4×109/L; ten [25%] of 40 patients) and lymphopenia (lymphocyte count <1·0×109/L; 26 [63%] patients; table 2). Pro- thrombin time and D-dimer level on admission were higher in ICU patients (median prothrombin time 12·2 s [IQR 11·2–13·4]; median D-dimer level 2·4 mg/L [0·6–14·4]) than non-ICU patients (median prothrombin time 10·7 s [9·8–12·1], p=0·012; median D-dimer level 0·5 mg/L [0·3–0·8], p=0·0042). Levels of aspartate aminotransferase were increased in 15 (37%) of 41 patients, including eight (62%) of 13 ICU patients and seven (25%) of 28 non-ICU patients. Hypersensitive troponin I (hs-cTnI) was increased substantially in five patients, in whom the diagnosis of virus-related cardiac injury was made.

入院病人的血液计数显示白细胞（40人中的10人[25%]白细胞数<4×109/L）和淋巴细胞（26人[63%]淋巴细胞<1·0×109/L）减少。深切治疗的病例在入园时的凝血酶时间（平均12.2秒[11.2-13.4]）和D-二聚体水平（平均2.4mg/L[0.6-14.4]高于普通病例（平均凝血时间10.7秒[9.8-12.1],p=0.012;，D-二聚体水平0.5mg

/L[0.3-08],p=0.0042)。 天冬氨酸转氨酶水平在15例[37%]病例升高，包含8例[62%]深切治疗病例he 7例[25%]普通病例。高敏肌钙蛋白I在5个被诊断为病毒引起心脏损伤病例中升高。

Most patients had normal serum levels of procalcitonin on admission (procalcitonin <0·1 ng/mL; 27 [69%] patients; table 2). Four ICU patients developed secondary infec- tions. Three of the four patients with secondary infection had procalcitonin greater than 0·5 ng/mL (0·69 ng/mL, 1·46 ng/mL, and 6·48 ng/mL).

大多数病例在入院时有正常的血清降钙素原水平（<0·1 ng/mL; 27 [69%]表2）。4个深切治疗病人出现了继发感染。其中三人的血清降钙素原水平超过了0.5ng/mL（0.69ng/mL，1.46ng/mL，6.48ng/mL）

	All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
White blood cell count, ×10⁹/L	6·2 (4·1–10·5)	11·3 (5·8–12·1)	5·7 (3·1–7·6)	0·011
<4	10/40 (25%)	1/13 (8%)	9/27 (33%)	0·041
4–10	18/40 (45%)	5/13 (38%)	13/27 (48%)	..
>10	12/40 (30%)	7/13 (54%)	5/27 (19%)	..
Neutrophil count, ×10⁹/L	5·0 (3·3–8·9)	10·6 (5·0–11·8)	4·4 (2·0–6·1)	0·00069
Lymphocyte count, ×10⁹/L	0·8 (0·6–1·1)	0·4 (0·2–0·8)	1·0 (0·7–1·1)	0·0041
<1·0	26/41 (63%)	11/13 (85%)	15/28 (54%)	0·045
≥1·0	15/41 (37%)	2/13 (15%)	13/28 (46%)	..
Haemoglobin, g/L	126·0 (118·0–140·0)	122·0 (111·0–128·0)	130·5 (120·0–140·0)	0·20
Platelet count, ×10⁹/L	164·5 (131·5–263·0)	196·0 (165·0–263·0)	149·0 (131·0–263·0)	0·45
<100	2/40 (5%)	1/13 (8%)	1/27 (4%)	0·45
≥100	38/40 (95%)	12/13 (92%)	26/27 (96%)	..
Prothrombin time, s	11·1 (10·1–12·4)	12·2 (11·2–13·4)	10·7 (9·8–12·1)	0·012
Activated partial thromboplastin time, s	27·0 (24·2–34·1)	26·2 (22·5–33·9)	27·7 (24·8–34·1)	0·57
D-dimer, mg/L	0·5 (0·3–1·3)	2·4 (0·6–14·4)	0·5 (0·3–0·8)	0·0042
Albumin, g/L	31·4 (28·9–36·0)	27·9 (26·3–30·9)	34·7 (30·2–36·5)	0·0066
Alanine aminotransferase, U/L	32·0 (21·0–50·0)	49·0 (29·0–115·0)	27·0 (19·5–40·0)	0·038
Aspartate aminotransferase, U/L	34·0 (26·0–48·0)	44·0 (30·0–70·0)	34·0 (24·0–40·5)	0·10
≤40	26/41 (63%)	5/13 (38%)	21/28 (75%)	0·025
>40	15/41 (37%)	8/13 (62%)	7/28 (25%)	..
Total bilirubin, mmol/L	11·7 (9·5–13·9)	14·0 (11·9–32·9)	10·8 (9·4–12·3)	0·011
Potassium, mmol/L	4·2 (3·8–4·8)	4·6 (4·0–5·0)	4·1 (3·8–4·6)	0·27
Sodium, mmol/L	139·0 (137·0–140·0)	138·0 (137·0–139·0)	139·0 (137·5–140·5)	0·26
Creatinine, µmol/L	74·2 (57·5–85·7)	79·0 (53·1–92·7)	73·3 (57·5–84·7)	0·84
≤133	37/41 (90%)	11/13 (85%)	26/28 (93%)	0·42
>133	4/41 (10%)	2/13 (15%)	2/28 (7%)	..
Creatine kinase, U/L	132·5 (62·0–219·0)	132·0 (82·0–493·0)	133·0 (61·0–189·0)	0·31
≤185	27/40 (68%)	7/13 (54%)	20/27 (74%)	0·21
>185	13/40 (33%)	6/13 (46%)	7/27 (26%)	..
Lactate dehydrogenase, U/L	286·0 (242·0–408·0)	400·0 (323·0–578·0)	281·0 (233·0–357·0)	0·0044
≤245	11/40 (28%)	1/13 (8%)	10/27 (37%)	0·036
>245	29/40 (73%)	12/13 (92%)	17/27 (63%)	..
Hypersensitive troponin I, pg/mL	3·4 (1·1–9·1)	3·3 (3·0–163·0)	3·5 (0·7–5·4)	0·08
>28 (99th percentile)	5/41 (12%)	4/13 (31%)	1/28 (4%)	0·017
Procalcitonin, ng/mL	0·1 (0·1–0·1)	0·1 (0·1–0·4)	0·1 (0·1–0·1)	0·031
<0·1	27/39 (69%)	6/12 (50%)	21/27 (78%)	0·0029
≥0·1 to <0·25	7/39 (18%)	3/12 (25%)	4/27 (15%)	..
≥0·25 to <0·5	2/39 (5%)	0/12	2/27 (7%)	..
≥0·5	3/39 (8%)	3/12 (25%)*	0/27	..
Bilateral involvement of chest radiographs	40/41 (98%)	13/13 (100%)	27/28 (96%)	0·68
Cycle threshold of respiratory tract	32·2 (31·0–34·5)	31·1 (30·0–33·5)	32·2 (31·1–34·7)	0·39

Data are median (IQR) or n/N (%), where N is the total number of patients with available data. p values comparing ICU care and no ICU care are from χ^2, Fisher's exact test, or Mann-Whitney U test. 2019-nCoV=2019 novel coronavirus. ICU=intensive care unit. *Complicated typical secondary infection during the first hospitalisation.

Table 2: Laboratory findings of patients infected with 2019-nCoV on admission to hospital

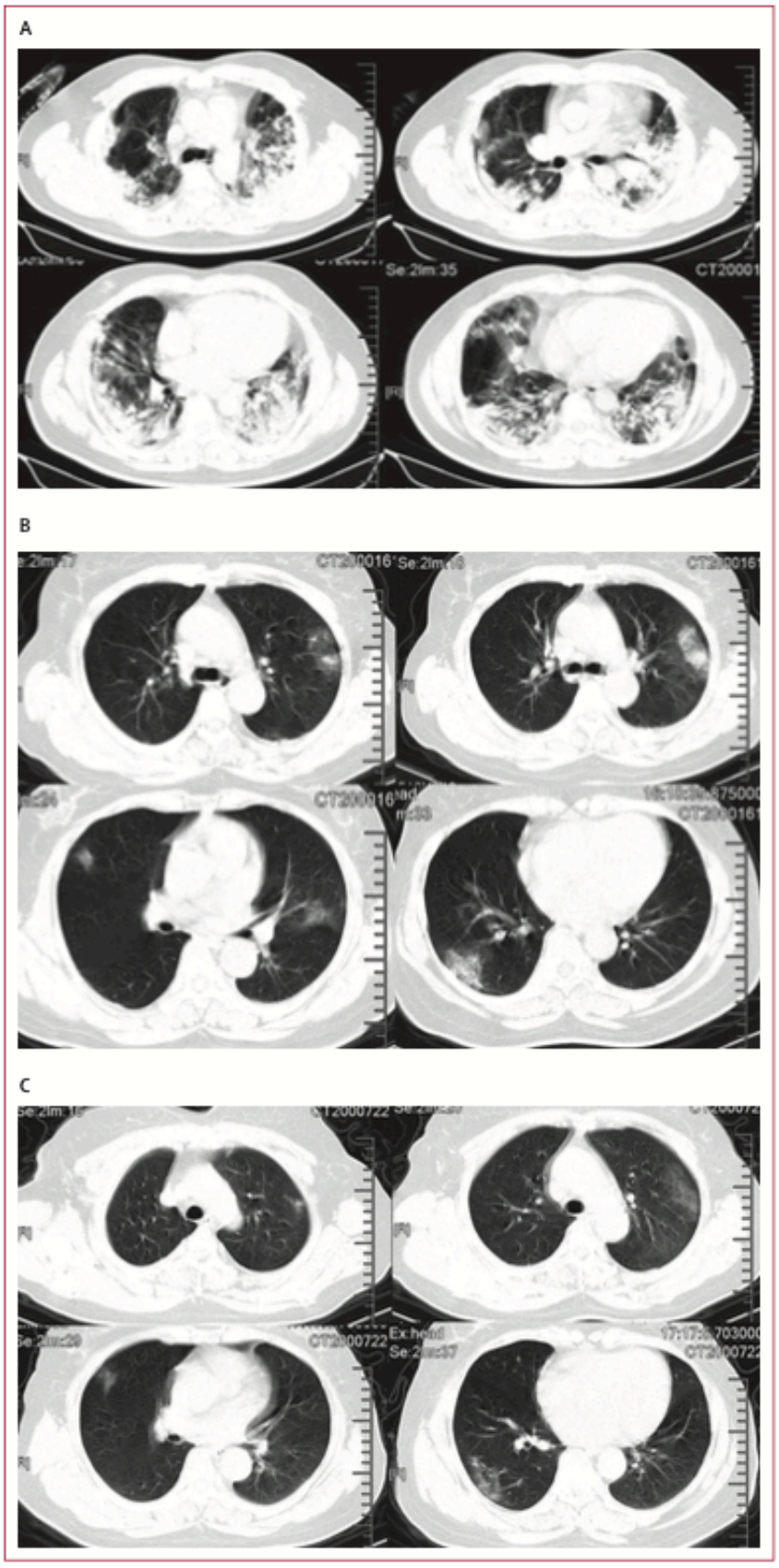

Figure 3: Chest CT images 图3:胸部CT影像

(A) Transverse chest CT images from a 40-year-old man showing bilateral multiple lobular and subsegmental areas of consolidation on day 15 after symptom onset. Transverse chest CT images from a 53-year-old woman showing bilateral ground-glass opacity and subsegmental areas of consolidation on day 8 after symptom onset (B), and bilateral ground-glass opacity on day 12 after symptom onset (C).

On admission, abnormalities in chest CT images were detected among all patients. Of the 41 patients, 40 (98%) had bilateral involvement (table 2). The typical findings of chest CT images of ICU patients on admission were bilateral multiple lobular and subsegmental areas of consolidation (figure 3A). The representative chest CT findings of non-ICU patients showed bilateral ground- glass opacity and subsegmental areas of consolidation (figure 3B). Later chest CT images showed bilateral ground-glass opacity, whereas the consolidation had been resolved (figure 3C).

入院时，所有病人的胸部CT影像都显示了异常，40（98%）累及双侧（表2）。胸部CT影像的典型发现为深切治疗病例在入院时为？？？(图3A)。普通病例的典型胸部CT影像显示？？？(图3B)。晚些时候的胸部CT影像显示？？？，然而这些固结已经被解决了（图3C）

Initial plasma IL1B, IL1RA, IL7, IL8, IL9, IL10, basic FGF, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1A, MIP1B, PDGF, TNFα, and VEGF concentrations were higher in both ICU patients and non-ICU patients than in healthy adults (appendix pp 6–7). Plasma levels of IL5, IL12p70, IL15, Eotaxin, and RANTES were similar between healthy adults and patients infected with 2019-nCoV. Further comparison between ICU and non-ICU patients showed that plasma concentrations of IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNFα were higher in ICU patients than non-ICU patients.

初始血浆中IL1B, IL1RA, IL7, IL8, IL9, IL10, basic FGF, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1A, MIP1B, PDGF, TNFα, VEGF深切治疗病例和普通病例的浓度相对健康人都很高。病人血浆IL5, IL12p70, IL15, Eotaxin, RANTES浓度与健康人类似。比对发现，深切治疗病例血浆中的IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, TNFα比普通比例要高。

All patients had pneumonia. Common complications included ARDS (12 [29%] of 41 patients), followed by RNAaemia (six [15%] patients), acute cardiac injury (five [12%] patients), and secondary infection (four [10%] patients; table 3). Invasive mechanical ventilation was required in four (10%) patients, with two of them (5%) had refractory hypoxaemia and received extracorporeal mem- brane oxygenation as salvage therapy. All patients were administered with empirical antibiotic treatment, and 38 (93%) patients received antiviral therapy (oseltamivir). Additionally, nine (22%) patients were given systematic corticosteroids. A comparison of clinical features between patients who received and did not receive systematic corticosteroids is in the appendix (pp 1–5).

所有病例出现肺炎症状。普通并发症包括急性呼吸窘迫症(12人[29%])，其次是RNA贫血症(6人 [15%])，急性心脏损伤(5人[12%])，继发感染(4人[10%]表3)，4人（10%）需要有创机械通气，其中两人（5%）出现了严重的低氧血症需要接受体外膜氧合抢救治疗。所有的病例都进行了经验抗生素治疗，38人（93%）接受了抗病毒治疗（奥司他韦）。此外，9人（22%）进行了系统皮质类固醇治疗。接受了类固醇治疗和未接受类固醇治疗的病例对比在附录中。

	All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
Duration from illness onset to first admission	7·0 (4·0–8·0)	7·0 (4·0–8·0)	7·0 (4·0–8·5)	0·87
Complications				
Acute respiratory distress syndrome	12 (29%)	11 (85%)	1 (4%)	<0·0001
RNAaemia	6 (15%)	2 (15%)	4 (14%)	0·93
Cycle threshold of RNAaemia	35·1 (34·7–35·1)	35·1 (35·1–35·1)	34·8 (34·1–35·4)	0·3545
Acute cardiac injury*	5 (12%)	4 (31%)	1 (4%)	0·017
Acute kidney injury	3 (7%)	3 (23%)	0	0·027
Secondary infection	4 (10%)	4 (31%)	0	0·0014
Shock	3 (7%)	3 (23%)	0	0·027
Treatment				
Antiviral therapy	38 (93%)	12 (92%)	26 (93%)	0·46
Antibiotic therapy	41 (100%)	13 (100%)	28 (100%)	NA
Use of corticosteroid	9 (22%)	6 (46%)	3 (11%)	0·013
Continuous renal replacement therapy	3 (7%)	3 (23%)	0	0·027
Oxygen support	..	..	..	<0·0001
Nasal cannula	27 (66%)	1 (8%)	26 (93%)	..
Non-invasive ventilation or high-flow nasal cannula	10 (24%)	8 (62%)	2 (7%)	..
Invasive mechanical ventilation	2 (5%)	2 (15%)	0	..
Invasive mechanical ventilation and ECMO	2 (5%)	2 (15%)	0	..
Prognosis	..	..	..	0·014
Hospitalisation	7 (17%)	1 (8%)	6 (21%)	..
Discharge	28 (68%)	7 (54%)	21 (75%)	..
Death	6 (15%)	5 (38%)	1 (4%)	..

Data are median (IQR) or n (%). p values are comparing ICU care and no ICU care. 2019-nCoV=2019 novel coronavirus. ICU=intensive care unit. NA=not applicable. ECMO=extracorporeal membrane oxygenation. *Defined as blood levels of hypersensitive troponin I above the 99th percentile upper reference limit (>28 pg/mL) or new abnormalities shown on electrocardiography and echocardiography.

Table 3: **Treatments and outcomes of patients infected with 2019-nCoV**

As of Jan 22, 2020, 28 (68%) of 41 patients have been discharged and six (15%) patients have died. Fitness for discharge was based on abatement of fever for at least 10 days, with improvement of chest radiographic evidence and viral clearance in respiratory samples from upper respiratory tract.

截止2020年1月22日，41人中的28人（68%）已经出院，其中6人死亡。出院的指标是至少10天没有发烧，并且胸部影像改善，以及上呼吸道样本中的病毒消失。

Discussion

We report here a cohort of 41 patients with laboratory- confirmed 2019-nCoV infection. Patients had serious, sometimes fatal, pneumonia and were admitted to the designated hospital in Wuhan, China, by Jan 2, 2020. Clinical presentations greatly resemble SARS-CoV. Patients with severe illness developed ARDS and required ICU admission and oxygen therapy. The time between hospital admission and ARDS was as short as 2 days. At this stage, the mortality rate is high for 2019-nCoV, because six (15%) of 41 patients in this cohort died.

我们在此报告，2020年1月2日，41位在中国武汉医院已经确证的新型冠状病毒（2019-nCoV）感染病例，病人出现严重，甚至致命的肺炎。临床表现高度类似非典型肺炎（SARS-CoV）。患者存在多项急性呼吸系统窘迫综合症（ARDS）的并发症状，需要进行深切治疗及输氧。从入院到出现ARDS症状最短病例为2日。在此阶段，新型冠状病毒的死亡率是高的，41名病例有15%死亡。

The number of deaths is rising quickly. As of Jan 24, 2020, 835 laboratory-confirmed 2019-nCoV infections were reported in China, with 25 fatal cases. Reports have been released of exported cases in many provinces in China, and in other countries;

死亡数字正在攀升，截止2020年1月24日，中国报告了835位确认患者及25例死亡。更多的病例正在中国其他省份及其他国家被发现。

some health-care workers have also been infected in Wuhan. Taken together, evidence so far indicates human transmission for 2019-nCoV. We are concerned that 2019-nCoV could have acquired the ability for efficient human transmission.19 Airborne precautions, such as a fit-tested N95 respirator, and other personal protective equipment are strongly recommended. To prevent further spread of the disease in health-care settings that are caring for patients infected with 2019-nCoV, onset of fever and respiratory symp- toms should be closely monitored among health-care workers. Testing of respiratory specimens should be done immediately once a diagnosis is suspected. Serum antibodies should be tested among health-care workers before and after their exposure to 2019-nCoV for iden- tification of asymptomatic infections.

中国武汉的一些医务工作者亦被感染。综上，迄今为止的证据显示新型冠状病毒存在人之间传播。我们担心新型冠状病毒已经具备有效人传人的能力。我们强烈建议采取空气传播预防措施，例如佩戴合格的N95口罩，以及其他个人防护装置。为了阻止新型冠状病毒在收治相关患者的医疗机构传播，医务工作者的发热及呼吸症状应该得到监控，疑似病例的呼吸系统标本应该立即被进行检测。同时还应该检测在他们被暴露在确证患者之前和之后的血清抗体。

Similarities of clinical features between 2019-nCoV and previous betacoronavirus infections have been noted. In this cohort, most patients presented with fever, dry cough, dyspnoea, and bilateral ground-glass opacities on chest CT scans. These features of 2019-nCoV infection bear some resemblance to SARS-CoV and MERS-CoV infections.20,21 However, few patients with 2019-nCoV infection had prominent upper respiratory tract signs and symptoms (eg, rhinorrhoea, sneezing, or sore throat), indicating that the target cells might be located in the lower airway. Furthermore, 2019-nCoV patients rarely developed intestinal signs and symptoms (eg, diarrhoea), whereas about 20–25% of patients with MERS-CoV or SARS-CoV infection had diarrhoea.21 Faecal and urine samples should be tested to exclude a potential alternative route of transmission that is unknown at this stage.

我们也注意到了新型冠状病毒与之前发现的冠状病毒在临床特征上的相似性。在此次的样本中，大多数病例都出现了发热、干咳、呼吸困难和肺部CT影像毛玻璃化症状表现。这些特征体现了一些与非典型肺炎及中东呼吸系统综合症（MERS-CoV）的相似性。但是，少量患者没有突出的呼吸系统症状（例如流鼻水、打喷嚏及喉咙痛），显示感染细胞位于下呼吸道。此外，新型冠状病毒患者很少出现肠道症状（例如腹泻），但是20-25%的非典型肺炎及中东呼吸系统综合症缓则出现了腹泻症状。粪便及尿液样本应该被检测用以排除潜在的人传人途径。

The pathophysiology of unusually high pathogenicity for SARS-CoV or MERS-CoV has not been completely understood. Early studies have shown that increased amounts of proinflammatory cytokines in serum (eg, IL1B, IL6, IL12, IFNγ, IP10, and MCP1) were associated with pulmonary inflammation and extensive lung damage in SARS patients.22 MERS-CoV infection was also reported to induce increased concentrations of proinflammatory cytokines (IFNγ, TNFα, IL15, and IL17).23 We noted that patients infected with 2019-nCoV also had high amounts of IL1B, IFNγ, IP10, and MCP1, probably leading to activated T-helper-1 (Th1) cell re- sponses. Moreover, patients requiring ICU admission had higher concentrations of GCSF, IP10, MCP1, MIP1A, and TNFα than did those not requiring ICU admission, suggesting that the cytokine storm was associated with disease severity. However, 2019-nCoV infection also initiated increased secretion of T-helper-2 (Th2) cytokines (eg, IL4 and IL10) that suppress inflammation, which differs from SARS-CoV infection.22 Further studies are necessary to characterise the Th1 and Th2 responses in 2019-nCoV infection and to elucidate the pathogenesis. Autopsy or biopsy studies would be the key to understand the disease.

非典型肺炎及中东呼吸系统综合症异常高的致病性的病理学研究至今依然没有完全清晰。早期研究显示血清促炎细胞因子与非典型肺炎的肺部伤害相关。中东呼吸系统综合症也同样表现出诱导增加促炎细胞因子的水平。我们注意到感染新型冠状病毒的患者同样具有高水平的相同促炎细胞因子，并且可能导致Th1细胞响应。此外，需要深切治疗的患者比其他患者具有更多种类的高水平的促炎细胞因子，这显示细胞因子风暴（感染者细胞因子和免疫系统之间的致命的正反馈现象）与病情严重程度相关。然而，新型冠状病毒感染同样增加了抑制炎症的Th2细胞因子的分泌，这是与非典型肺炎不同的地方。未来对于新型冠状病毒Th1和Th2响应的研究能够进一步厘清其致病机理。尸检及活检将是理解这种疾病的关键。

In view of the high amount of cytokines induced by SARS-CoV,22,24 MERS-CoV,25,26 and 2019-nCoV infections, corticosteroids were used frequently for treatment of patients with severe illness, for possible benefit by reducing inflammatory-induced lung injury. However, current evidence in patients with SARS and MERS suggests that receiving corticosteroids did not have an effect on mortality, but rather delayed viral clearance.27–29 Therefore, corticosteroids should not be routinely given systemically, according to WHO interim guidance.30 Among our cohort of 41 laboratory-confirmed patients with 2019-nCoV infection, corticosteroids were given to very few non-ICU cases, and low-to-moderate dose of corticosteroids were given to less than half of severely ill patients with ARDS. Further evidence is urgently needed to assess whether systematic corticosteroid treatment is beneficial or harmful for patients infected with 2019-nCoV.

因应非典型肺炎、中东呼吸综合征和新型冠状病毒高水平细胞因子的情况，类固醇通常用于减少炎症诱发的肺部伤害。然而，非典型肺炎及中东呼吸系统综合征的治疗显示接受类固醇治疗并不能降低死亡率，反而会延长病毒清除的时间。因此，根据世卫组织指引，类固醇并不应该作为经常性的系统用药。在我们研究的41个病例中，类固醇只在极少数非严重病例中使用，不到一半的呼吸系统窘迫综合症的病例使用了低到中剂量的类固醇。未来迫切需要评估类固醇治疗在新型冠状病毒治疗过程中的利弊。

No antiviral treatment for coronavirus infection has been proven to be effective. In a historical control study,31 the combination of lopinavir and ritonavir among SARS-CoV patients was associated with substantial clinical benefit (fewer adverse clinical outcomes). Arabi and colleagues initiated a placebo-controlled trial of interferon beta-1b, lopinavir, and ritonavir among patients with MERS 32 infection in Saudi Arabia. Preclinical evidence showed the potent efficacy of remdesivir (a broad-spectrum antiviral nucleotide prodrug) to treat MERS-CoV and SARS-CoV infections.33,34 As 2019-nCoV is an emerging virus, an effective treatment has not been developed for disease resulting from this virus. Since the combination of lopinavir and ritonavir was already available in the designated hospital, a randomised controlled trial has been initiated quickly to assess the efficacy and safety of combined use of lopinavir and ritonavir in patients hospitalised with 2019-nCoV infection.

我们没有发现抗病毒治疗在冠状病毒治疗过程中被证明有效。在对照试验中，洛匹那韦和利托那韦联合用药对于非典型肺炎治疗起到了作用。来自阿拉伯的同行也对沙特阿拉伯的病患进行了洛匹那韦和利托那韦联合用药方案的双盲对照试验。有证据显示remdesivir（一种广谱抗病毒核苷酸药物）在对于中东呼吸综合征综合症和非典型肺炎具有疗效。但新型冠状病毒作为一种新出现的病毒，目前还没有成熟的相关治疗方案，但洛匹那韦和利托那韦联合用药方案已经被相关医院采用，并且进行了针对有效性和安全性的随机对照试验。

Our study has some limitations. First, for most of the 41 patients, the diagnosis was confirmed with lower respiratory tract specimens and no paired nasopharyngeal swabs were obtained to investigate the difference in the viral RNA detection rate between upper and lower respiratory tract specimens. Serological detection was not done to look for 2019-nCoV antibody rises in 18 patients with undetectable viral RNA. Second, with the limited number of cases, it is difficult to assess host risk factors for disease severity and mortality with multivariable- adjusted methods. This is a modest-sized case series of patients admitted to hospital; collection of standardised data for a larger cohort would help to further define the clinical presentation, natural history, and risk factors. Further studies in outpatient, primary care, or community settings are needed to get a full picture of the spectrum of clinical severity. At the same time, finding of statistical tests and p values should be interpreted with caution, and non-significant p values do not necessarily rule out difference between ICU and non-ICU patients. Third, since the causative pathogen has just been identified, kinetics of viral load and antibody titres were not available. Finally, the potential exposure bias in our study might account for why no paediatric or adolescent patients were reported in this cohort. More effort should be made to answer these questions in future studies.

我们的研究具有局限性。首先，41名病例中的大多数，下呼吸道样本的检测并没有对应的上呼吸道鼻咽拭子样本来研究两个部位的病毒RNA差异。18名没有检测到病毒RNA的患者没有完成抗体的血清检测。其次，受到样本数量限制，通过多变量调整方法很难评估宿主风险因素对于致病和死亡率的影响。这里只有一个中等规模的病例样本，大规模的样本将对与临床表现、生物学和风险因子的定义具有具有更多的帮助。未来基于门诊、基层及社区医疗机构的研究将建立更完整的病理图谱。同时，统计测试和P值的发现应该被谨慎的解释，非显著性的P值不能揭示重症及非重症病例之间的必然规律。第三，虽然病原体已经被识别，但病毒荷载动力学和抗体效价还不明。最后，不同的病毒暴露条件可能导致此次样本中没有儿童及青少年病例的情况。未来需要更多的研究来得出答案。

Both SARS-CoV and MERS-CoV were believed to originate in bats, and these infections were transmitted directly to humans from market civets and dromedary camels, respectively.35 Extensive research on SARS-CoV and MERS-CoV has driven the discovery of many SARS-like and MERS-like coronaviruses in bats. In 2013, Ge and colleagues36 reported the whole genome sequence of a SARS-like coronavirus in bats with that ability to use human ACE2 as a receptor,

thus having replication potentials in human cells.37 2019-nCoV still needs to be studied deeply in case it becomes a global health threat. Reliable quick pathogen tests and feasible differential diagnosis based on clinical description are crucial for clinicians in their first contact with suspected patients. Because of the pandemic potential of 2019-nCoV, careful surveillance is essential to monitor its future host adaption, viral evolution, infectivity, transmissibility, and pathogenicity.

非典型肺炎和中东呼吸系统综合征都被确信来源于蝙蝠，并且分别通过果子狸和骆驼传播给人类。关于这些疾病的深入研究发现了更多来寄生于蝙蝠的类似冠状病毒。来自GE的同行报告，与非典型肺炎病毒类似存在于蝙蝠体内的冠状病毒的基因测序显示，它们都具有采用人类ACE2作为受体，进而在人体内大量复制的能力。作为一个全球健康威胁，新型冠状病毒依然需要进行深入研究。可信赖的快速病原体测试对于一线医务工作者来说是非常重要的。基于这种病毒的爆发潜力，我们必须小心监控它的宿主变化、病毒进化、传染性、遗传性和致病性。

Contributors BC and JW had the idea for and designed the study and had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. YWa, GF, XG, JiXu, HL, and BC contributed to writing of the report. BC contributed to critical revision of the report. YWa, GF, XG, JiXu, and HL contributed to the statistical analysis. All authors contributed to data acquisition,data analysis, or data interpretation, and reviewed and approved the final version. ***Declaration of interests*** All authors declare no competing interests. ***Data sharing*** The data that support the findings of this study are available from the corresponding author on reasonable request. Participant data without names and identifiers will be made available after approval from the corresponding author and National Health Commission. After publication of study findings, the data will be available for others to request. The research team will provide an email address for communication once the data are approved to be shared with others. The proposal with detailed description of study objectives and statistical analysis plan will be needed for evaluation of the reasonability to request for our data. The corresponding author and National Health Commission will make a decision based on these materials. Additional materials may also be required during the process. ***Acknowledgments*** This work is funded by the Special Project for Emergency of the Ministry of Science and Technology (2020YFC0841300) Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences (CIFMS 2018-I2M-1-003), a National Science Grant for Distinguished Young Scholars (81425001/H0104), the National Key Research and Development Program of China (2018YFC1200102), The Beijing Science and Technology Project (Z19110700660000), CAMS Innovation Fund for Medical Sciences (2016-I2M-1-014), and National Mega-projects for Infectious Diseases in China (2017ZX10103004 and 2018ZX10305409). We acknowledge all health-care workers involved in the diagnosis and treatment of patients in Wuhan; we thank the Chinese National Health Commission for coordinating data collection for patients with 2019-nCoV infection; we thank the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) for sharing data collection templates publicly on the website; and we thank Prof Chen Wang and Prof George F Gao for guidance in study design and interpretation of results.
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