

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

#### JID: YJINF

# **ARTICLE IN PRESS**

Journal of Infection xxx (xxxx) xxx

[m5G;March 27, 2020;15:30]



Review

Contents lists available at ScienceDirect

## Journal of Infection



journal homepage: www.elsevier.com/locate/jinf

# Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients

Kai Liu<sup>a,1,\*</sup>, Ying Chen<sup>b,1</sup>, Ruzheng Lin<sup>c</sup>, Kunyuan Han<sup>c</sup>

<sup>a</sup> Hainan General Hospital, Geriatric center, China

<sup>b</sup> Hainan General Hospital, Medical Laboratory, China

<sup>c</sup> Hainan General Hospital, General Practice, China

#### ARTICLE INFO

Article history: Accepted 4 March 2020 Available online xxx

Keywords: Clinical feature COVID-19 Elderly patients Young and middle-aged patients

#### SUMMARY

*Background:* Due to the general susceptibility of new coronaviruses, the clinical characteristics and outcomes of elderly and young patients may be different.

*Objective:* To analyze the clinical characteristics of elderly patients with 2019 new-type coronavirus pneumonia (COVID-19).

*Methods:* This is a retrospective study of patients with new coronavirus pneumonia (COVID-19) who were hospitalized in Hainan Provincial People's Hospital from January 15, 2020 to February 18, 2020. Compare the clinical characteristics of elderly with Young and Middle-aged patients.

*Results*: A total of 56 patients were enrolled 18 elderly patients (32.14%), and 38 young and middleaged patients (67.86%). The most common symptoms in both groups were fever, followed by cough and sputum. Four patients in the elderly group received negative pressure ICU for mechanical ventilation, and five patients in the young and middle-aged group. One patient died in the elderly group (5.56%), and two patients died in the young and middle-aged group (5.26%). The PSI score of the elderly group was higher than that of the young and middle-aged group (P < 0.001). The proportion of patients with PSI grades IV and V was significantly higher in the elderly group than in the young and middle-aged group (P < 0.05). The proportion of multiple lobe involvement in the elderly group was higher than that in the young and middle-aged group (P < 0.001), and there was no difference in single lobe lesions between the two groups. The proportion of lymphocytes in the elderly group was significantly higher in the young and middle-aged group (P < 0.001), and the C-reactive protein was significantly higher in the young group (P < 0.001). The Lopinavir and Ritonavir Tablets, Chinese medicine, oxygen therapy, and mechanical ventilation were statistically different in the elderly group and the young and middle-aged group, and the P values were all <0.05.

*Interpretation:* The mortality of elderly patients with COVID-19 is higher than that of young and middleaged patients, and the proportion of patients with PSI grade IV and V is significantly higher than that of young and middle-aged patients. Elderly patients with COVID-19 are more likely to progress to severe disease.

© 2020 The British Infection Association. Published by Elsevier Ltd. All rights reserved.

Since December 2019, some hospitals in Wuhan City, Hubei Province have successively found multiple cases of unexplained pneumonia with a history of South China seafood market exposure, which have now been confirmed as a new type of acute respiratory infection caused by a coronavirus infection. The coronavirus isolated from the lower respiratory tract of patients with unexplained pneumonia in Wuhan this time is a new type of coronavirus belonging to the genus  $\beta$  and named as a new type of coronavirus disease (COVID-19). As of March 2, COVID-19 has confirmed 80,175 cases in mainland China, and a total of 2915 deaths nationwide, with a case crude fatality rate of 3.63%. From the existing data, the mortality rate of new coronavirus pneumonia is lower than SARS-CoV (9.6%). And pneumonia caused by MERS-Cov (34%). New coronavirus populations are generally susceptible, but elderly people with underlying diseases are more susceptible. The underlying diseases are diabetes, hypertension, cardiovascular disease, and cerebro-vascular disease.<sup>1</sup> The elderly are more susceptible to severe illness and are admitted to the intensive care unit (ICU), and

0163-4453/© 2020 The British Infection Association. Published by Elsevier Ltd. All rights reserved.

<sup>\*</sup> Corresponding author.

E-mail address: hmliukai@126.com (K. Liu).

<sup>&</sup>lt;sup>1</sup> Contributed equally

https://doi.org/10.1016/j.jinf.2020.03.005

2

## **ARTICLE IN PRESS**

the mortality of elderly patients is higher.<sup>2</sup> A study of 1099 patients with confirmed new type of coronavirus pneumonia found that 15.1% of the population is 60 years old and above, and 27.0% of those who are severely aged 60 years and above.<sup>3</sup> Another large study analyzed 4021 confirmed cases, and the results showed that 1 052 (26.2%) were 60 years of age or older. In terms of mortality, the mortality rate of patients aged 60 years and over (5.3%) is significantly higher than that of patients under 60 years (1.4%).<sup>4</sup>

The purpose of this study was to compare the clinical features of elderly and non-elderly (young and middle-aged) patients with COVID-19.

#### Materials and methods

#### Study population

A total of 56 confirmed cases of neo-pneumococcal pneumonia treated in Hainan General Hospital from January 1, 2020 to February 15, 2020 were collected. According to the age, it is divided into the elderly group ( $\geq$ 60 years old) and the young and middle-aged group (<60 years old).

#### Research methods

#### New diagnostic criteria for coronavirus pneumonia

Suspected cases are determined in two cases. The first is "have any one of the epidemiological history, and meet any two of the clinical manifestations (fever and/or respiratory symptoms; with the imaging characteristics of the pneumonia mentioned above; the total number of white blood cells in the early stage of disease is normal or decreased, and the lymphocyte count is reduced). The second is "without a clear epidemiological history and conforms to 3 of the clinical manifestations (fever and/or respiratory symptoms; with the aforementioned imaging characteristics of pneumonia; the total number of white blood cells in the early stage of disease is normal or decreased, and the lymphocyte count is reduced). Confirmed cases need to have a positive result of pathogenic evidence (real-time fluorescent RT-PCR detection of new coronavirus nucleic acid positive; or viral gene sequencing, highly homologous to known new coronavirus).

#### Evaluation of clinical results

Compare the symptoms characteristics, antiviral and antibiotic use, admission to the intensive care unit (ICU), and mechanical ventilation requirements of the two groups. Compare the two groups of patients with Pneumonia Severity Index (PSI). PSI: age (direct scoring, such as 50 years old, direct 50 points), gender (no increase for males, minus 10 for females), and staff in nursing facilities (plus 10 Points), tumor (plus 30 points), liver disease (plus 20 points), congestive heart failure (plus 10 points), cerebrovascular disease (plus 10 points), kidney disease (plus 10 points), mental state changes (plus 20 points), respiratory frequency  $\geq$  30 / min (plus 20 points), systolic blood pressure <90 mmHg, body temperature <35 °Cor  $\geq 40$  °C, pulse  $\geq 125$  beats / min, blood gas analysis PH <7.35 (plus 30 points), blood urea Nitrogen  $\geq$ 11 mmol / L (plus 20 points), blood sodium <130 mmol/L (plus 20 points), blood glucose  $\geq$  14.0 mmol/L (plus 10 points), hematocrit < 30%, PO<sub>2</sub><60 mmHg (plus 10 points)), Pleural effusion (plus 10 points), the scores of the above 20 parameters are added up to calculate the total score, the higher the score, the worse the condition. PSI grades I (no score required), II ( $\leq$ 70), III (71–90), IV (91–130), and V (> 130).

Comparison of imaging and laboratory results between the symptoms and characteristics, hospital stay, disease outcome, and laboratory (leukocyte, neutrophil ratio, lymphocyte ratio, C response) Protein, procalcitonin); compare the difference between the two groups of patients based on chest 128-slice computed tomography(CT).

#### Statistical analysis

Continuous variables are represented by median and quartile ranges (P<sub>25</sub> and P<sub>75</sub>), and categorical variables are represented by numbers (percentages). Student, *t*-test is used for normal distribution variables and Mann–Whitney *U* test is used for non normal distribution variables.  $\chi^2$  test or Fisher exact test were used to analyze the classified variables. The statistical software package of Social Sciences (SPSS 25.0) was used for analysis, and *P* value < 0.05 was considered statistically significant.

#### Results

#### Comparison of basic clinical characteristics between the two groups

During the study period, a total of 56 patients were evaluated, 18 elderly patients (32.14%), and 38 young patients (67.86%). The median age of the elderly group was 68 years (interquartile range [IQR]65.25–69.75), while the median age of the young and middle age group was 47 years (IQR 35.75–51.25), showing a statistically significant difference between the two groups Significance (P < 0.001). The most common symptoms in both groups were fever, followed by cough and sputum. The PSI score of the elderly group was higher than that of the young and middle-aged group (P < 0.001). The proportion of patients with PSI grade IV and V was significantly higher in the elderly group than in the young and middle-aged group (P < 0.05).

# Comparison of chest CT and laboratory results between the two groups of patients

During the hospitalization period, 128 lung CT scans of 56 patients were performed. The proportion of multiple lobe involvement in the elderly group was higher than that in the young and middle-aged group (P < 0.001), and there was no difference in single lobe lesions between the two groups. The proportion of lymphocytes in the elderly group was significantly lower than that in the young and middle-aged group (P < 0.001), and the C-reactive protein was significantly higher than in the young and middle-aged group (P < 0.001). There were no significant differences in white blood cell count, neutrophil ratio, procalcitonin, hemoglobin level, hemoglobin, platelet, and serum creatinine in the two groups.

#### Complications after admission and treatment measures

The ARDS in the elderly group (4 of 18 patients [22.22%]) was higher than that in the young and middle-aged group, and acute heart, liver, and kidney function injuries were higher than those in the young and middle-aged group. The Lopinavir and Ritonavir Tablets, Chinese medicine, oxygen therapy, and mechanical ventilation were statistically different in the elderly group and the young and middle-aged group, and the *P* values were all <0.05. (Table 3)

#### Discussion

This is an extended descriptive study of the clinical characteristics of elderly COVID-19 patients, including data on elderly patients with severe referrals from other hospitals to the Hainan General Hospital. The differences between elderly COVID-19 patients and young and middle-aged patients were analyzed, and information on in-hospital deaths was added.

In the 56 patients with 2019-nCoV infection, we observed that more men than women in elderly patients, and more men

# **ARTICLE IN PRESS**

#### K. Liu, Y. Chen and R. Lin et al./Journal of Infection xxx (xxxx) xxx

#### 3

#### Table 1

compares the general situation and clinical manifestations of the two groups.

Variable	Elderly $(n = 18)$	Young and middle-aged $(n=38)$	Р
Age (years)	68.00 (65.25-69.75)	47.00 (35.75-51.25)	< 0.001
Male (n,%)	12(66.67%)	19(50.00%)	0.198
Smoking history (n,%)	8(44.44%)	14(36.84%)	0.667
Past medical history (n,%)			
Liver disease	1(5.56%)	0(0)	-
Chronic kidney disease	0(0)	1(2.63%)	-
Hypertension	5(27.78%)	5(13.16%)	0.782
Dabetes	3(16.67%)	1(2.63%)	0.246
Coronary heart disease	2(11.11%)	0(0)	-
Persistent atrial fibrillation	1(5.56%)	0(0)	-
Clinical symptoms			
Cough and sputum	6(33.33%)	15(39.47%)	0.284
Chest tightness, Difficulty breathing	2(11.11%)	2(5.26%)	0.351
Fever	14(77.78%)	30(78.95%)	0.008
Fatigue	2(11.11%)	3(7.89%)	0.385
Nasal congestion, runny nose	1(5.56%)	2(5.26%)	0.786
Sick and vomit	3(16.67%)	7(18.42%)	0.558
Pneumonia severity index			
PSI score	121 (95-148)	79 (55–107)	< 0.001
PSI grades IV and V	4(22.22)	2(5.26)	< 0.001

#### Table 2

Differences between 128-slice CT and laboratory indicators in the chest.

Variable	Elderly $(n = 18)$	Young and middle-aged $(n = 38)$	Р
CT results			
Multiple lobe Lesion	16(88.89%)	24(63.16%)	< 0.001
Single lobe Lesion	2(11.11%)	14(36.84%)	0.284
Laboratory indicators at admission			
White blood cell count ( $\times$ 109 / L)	5.38(4.33-6.13)	4.48(3.74-5.88)	0.365
Total white blood cells increased, n (%)	2(11.11%)	2(5.26%)	0.284
Total white blood cells decreased, n (%)	3(16.67%)	8(21.05%)	0.175
Neutrophil proportion,%	68.3(63.01-78.13)	61.80(56.25-66.45)	0.683
Increased neutrophil proportion, n (%)	7(38.89%)	6(15.79%)	0.333
Lymphocyte ratio,%	19.15(10.58-26.93)	28.95 (24.45-33.58)	< 0.001
Lymphocyte ratio decreased, n (%)	9(50.00%)	8(21.05%)	0.174
C-reactive protein (mg/L)	22.74(13.33-34.82)	6.49(1.26-17.6)	< 0.001
Procalcitonin (ng/mL)	0.04(0.02-0.09)	0.04(0.02-0.06)	0.921
Blood albumin (mg/L)	33(29-38)	39(36-42)	0.087
Hemoglobin (g/L)	107.35(92.13-120.35)	125.21(114.23-140.15)	0.568
Platelets ( $\times$ 10 <sup>9</sup> / L)	207(159-287)	215(180-287)	0.109
Serum creatinine( $\mu$ mol /L)	106.44(79.83-150.79)	88.71(79.83-106.44)	0.476

#### Table 3

Complications and treatment measures after admission in the two groups.

Variable	Elderly $(n = 18)$	Young and middle-aged $(n=38)$	Р
Comorbidities			0.337
Acute respiratory distress syndrome	4 (22.22%)	2 (5.26%)	
Acute heart injury	3 (16.67%)	4 (10.53%)	
Acute liver and kidney injury	7 (38.89%)	3 (7.89%)	
Secondary infection	4 (22.22%)	5 (13.16%)	
Shock	1 (5.56%)	2 (5.26%)	
Antiviral			
Lopinavir and Ritonavir Tablets	16(83.33%)	37(86.84%)	0.025
Interferon inhalation	6 (33.33%)	15 (39.47%)	0.584
Not anti-virus	3 (16.67%)	1 (2.63%)	0.387
Traditional Chinese medicine	14(77.78%)	32(84.21%)	< 0.00
Antibiotic	12(66.67%)	28(73.68%)	0.167
Immunoglobulin	4(22.22%)	5(13.16%)	0.241
Thymopentin	14(77.78%)	32(84.21%)	0.176
Continuous renal replacement therapy	2 (11.11%)	3 (7.89%)	0.299
Oxygen therapy	17 (94.44%)	37 (97.37%)	< 0.00
Mechanical ventilation <0.001			
Non-invasive (ie mask)	1 (5.56%)	2 (5.26%)	
Invasive	4 (22.22%)	3 (7.89%)	
Extracorporeal Membrane Oxygenation	1 (5.56%)	1 (2.63%)	0.387
Prognosis			0.316
Healed and discharged	17 (94.44%)	36(94.74%)	
Death	1 (5.56%)	2 (5.26%)	

4

K. Liu, Y. Chen and R. Lin et al./Journal of Infection xxx (xxxx) xxx

than women infected by MERS-CoV and SARS-CoV.<sup>5</sup> In addition, there are 12 elderly patients with chronic basic diseases with 2019-nCoV infection, which is much higher than the young and middle-aged patients, mainly cardiovascular and cerebrovascular diseases and diabetes, which is similar to MERS-CoV.<sup>6</sup> Our results suggest that 2019-nCoV is more likely to infect adult men with chronic comorbidities due to their weaker immune function.

In terms of laboratory tests, the proportion of patients with an increased number of white blood cells and neutrophils in elderly patients was significantly higher than that in the young and middle-aged group, suggesting that elderly 2019-nCoV infected patients are more likely to have bacterial infection. In addition, the proportion of lymphocytes decreased in 9 of the elderly patients, which was much higher than that of the young and middle-aged patients. It may be due to changes in the elderly's lung anatomy and muscle atrophy leading to changes in the physiological functions of the respiratory system, reduced airway clearance,<sup>7</sup> reduced lung reserve,<sup>8</sup> and reduced defense barrier function,<sup>9</sup> The level of C-reactive protein in elderly patients is significantly higher than that in the young and middle-aged group, which is similar to MERS-CoV.<sup>10</sup> In terms of imaging, the incidence of multilobe lesions in elderly patients is significantly higher than in young and middle-aged patients. CT examination is the most direct and rapid examination method, which can quickly confirm the diagnosis and grasp the changes of the patient's condition to guide the clinical update of the treatment plan. Judging the severity, severity, and severity of the disease by occupying the corresponding lung lobe area and scoring images can help early attention to the tendency to severe illness.<sup>11</sup>

In our study, there was 1 death in the elderly group (5.56%) and 2 deaths in the young and middle age groups (5.26%). Although the death rate in the elderly group was higher than that in the young and middle age groups, the death rate in the young and middle age group was significantly higher than the other two. Large sample study.<sup>12–13</sup> The reason may be that our hospital is the severe treatment base in Hainan Province, which has caused a significant increase in the proportion of severe illness in our hospital and caused an increase in the mortality rate of young people. But the mortality of elderly patients is basically consistent with domestic research.<sup>14</sup> Antiviral is particularly important in the treatment of COVID-19, but there are currently no drugs targeting new coronaviruses.<sup>15</sup> In this study, the elderly population also received Lopinavir and Ritonavir Tablets, and the proportion was not significantly different from the young and middle-aged group. At present, from the clinical point of view, the benefit of Lopinavir and Ritonavir Tablets tablets in the treatment of coronavirus is not obvious. The course of treatment is long and prone to liver and kidney damage. Those with respiratory symptoms were treated with interferon nebulized inhalation and Chinese medicine antiviral treatment. We observed that after using inhaled interferon, the cough symptoms of the elderly patients were relieved faster, and the effect seems to be better than that of the young and middle-aged people.

The new type of coronavirus mainly causes lung infections. Lung infections increase the burden on the heart. At the same time, it can lead to high blood sugar, which makes infection control difficult. The characteristics of multi-system disease coexisting in the elderly lead to complicated and complex diseases. Multiple diseases affect each other. Treatment The difficulty factor is greatly increased. Because elderly patients are prone to multi-system organ dysfunction and even failure, other systemic complications should be prevented, including gastrointestinal bleeding, renal failure, disseminated intravascular coagulation (DIC) or deep vein thrombosis, delirium, For secondary infections, a multidisciplinary team approach is recommended.

There are several limitations to our study: we included all confirmed cases in Hainan Province, some of them were referred to our hospital for severe cases, and the results may be biased; followed by 56 patients with a small sample size. Finally, more detailed patient information was not available during the analysis, especially about clinical outcomes.

#### Contributors

**Kai Liu** conceived the study, designed the study and obtained ethics approval. **Ying Chen** gave clinical advice on the study subject and methodology. **Ruzheng Lin** supervised the conduct of the study and data related issues. **Kunyuan Han** provided statistical advice and analysed the data.Kai Liu drafted the manuscript, and all authors contributed substantially to its revision. Kai Liu takes responsibility for the paper as a whole.

#### Patient consent

Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

#### **Ethics approval**

The Hainan General Hospital Review Board granted approval for this research.

**Provenance and peer review** Not commissioned; externally peer reviewed.

#### **Declaration of Competing Interest**

None declared.

#### Funding

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-forprofit sectors.

#### References

- 1. Li J-Y, You Z, et al. The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future. *Microbes Infect* 2020 In press, journal pre-proof Available online 20 February 2020.
- Guan W.J., Ni Z.Y., Zhong N.S., et al. Clinical characteristics of 2019 novel coronavirus infection in China. Med Rxiv, 2020, [Epub ahead of print]. https://doi.org/ 10.1101/2020.02.06.20020974.
- Yang Y., Lu Q.B., Liu M.J., et al. Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China. Med Rxiv, 2020, [Epub ahead of print]. DOI: https://doi.org/10.1101/2020.02.10.20021675
- Liu Y, Gayle AA, Wilder-Smith A, et al. The reproductive number of COVID-19 is higher compared to SARS coronavirus. J Travel Med 2020 [Epub ahead of print]. doi:10.1093/jtm/taaa021.
- Prompetchara E, Ketloy C, Palaga T. Immune responses in COVID-19 and potential vaccines: lessons learned from SARS and MERSepidemic. Asian Pac J Allergy Immunol 2020. doi:10.12932/AP-200220-0772.
- 6. Park M, Thwaites RS, Openshaw PJM. COVID-19: lessons from SARS and MERS. Eur J Immunol 2020. doi:10.1002/eji.202070035.
- Yao TT, Qian JD, Zhu WY, et al. A systematic review of lopinavir therapy for sars coronavirus and mers coronavirus-a possible reference for coronavirus disease-19 treatment option. J Med Virol 2020. doi:10.1002/jmv.25729.
- Zuo MZ, Huang YG, Ma WH, et al. Expert recommendations for tracheal intubation in critically ill patients with noval coronavirusdisease 2019. *Chin Med Sci J* 2020. doi:10.24920/003724.
- Xu J, Zhao S, Teng T, et al. Systematic comparison of two animal-to-human transmitted human coronaviruses: SARS-CoV-2 and SARS-CoV. *Viruses* 2020 Feb 22;12(2) pii: E244. doi:10.3390/v12020244.

## ARTICLE IN PRESS

- Peeri NC, Shrestha N, Rahman MS, et al. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? *Int J Epidemiol.* 2020 pii: dyaa033. doi:10.1093/ ije/dyaa033.
- Lin C, Ding Y, Xie B, et al. Asymptomatic novel coronavirus pneumonia patient outside Wuhan: the value of CT images in the course of the disease. *Clin Imaging* 2020;63:7–9. doi:10.1016/j.clinimag.2020.02.008.
- Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* 2020;**368**:m606. doi:10.1136/bmj.m606.
- 13. Liu W, Tao ZW, Lei W, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novelcoronavirus disease. *Chin Med J* 2020. doi:10.1097/CM9.00000000000775.
- 14. Wang NL, Jie Y, Tao FB. Precautions in ophthalmic practice in the prevention and control of the novel coronaviruspneumonia epidemic. *Zhonghua Yan Ke Za Zhi* 2020;**56**(0):E007. doi:10.3760/cma.j.cn112142-20200224-00102.
- Tian S, Hu W, Niu L. Pulmonary pathology of early phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. J Thorac Oncol 2020 pii: S1556-0864(20)30132-5. doi:10.1016/j.jtho.2020.02.010.