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.
Original article
C-reactive protein levels in the early stage of COVID-19
L. Wang
Department of Intensive Care Unit, People’s hospital of Qiandongnan Miao and Dong Autonomous Prefecture, Kaili Guizhou 556000, China

INFO ARTICLE
Historique de l’article :
Reçu le 26 mars 2020
Accepté le 30 mars 2020
Disponible sur Internet le 31 March 2020

Keywords :
COVID-19
C-reactive protein
Lung CT scan

ABSTRACT
Background. – COVID-19 is a new infectious disease, for which there is currently no treatment. It is therefore necessary to explore biomarkers to determine the extent of lung lesions and disease severity.
Objective. – We aimed to assess the usefulness of CRP levels in the early stage of COVID-19 and to correlate them with lung lesions and severe presentation.
Methods. – Confirmed cases of COVID-19 were selected at the Fever Unit in two regions of Guizhou, China. On admission CRP levels were collected, and the diameter of the largest lung lesion was measured in the most severe lung lesion by lung CT scan. Differences in the diameter and CRP levels were compared in the following groups of patients: mild group, moderate group, severe group, and critical group.
Result. – CRP levels and the diameter of the largest lung lesion in the moderate group were higher than those in the mild group (Mann-Whitney test = −2.647, P < 0.05), those in the severe group were higher than those in the moderate group (Mann-Whitney test = 0.693, −2.171, P < 0.05), and those in the critical group were higher than those in the severe group (Mann-Whitney test = −0.068, −1.549, P < 0.05). The difference was statistically significant. CRP levels were positively correlated with the diameter of lung lesion and severe presentation (correlation coefficient = 0.873, 0.734, P < 0.001).
Conclusion. – In the early stage of COVID-19 CRP levels were positively correlated with lung lesions and could reflect disease severity.
© 2020 L’auteur. Publié par Elsevier Masson SAS. Cet article est publié en Open Access sous licence CC BY-NC-ND (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Background

New coronavirus pneumonia (COVID-19) is a health emergency due to its high infectiousness [1] and high case fatality in critically ill patients. The pathological and physiological processes and diagnostic methods of COVID-19 are still in the exploratory stage. Clinical monitoring and appropriate treatment strategies were essential to improve case fatality. CT scan played an important role in assessing the disease [2]. Other sensitive indicators able to reflect lung lesion changes and disease severity had to be explored. C-reactive protein (CRP) levels can be used in the early diagnosis of pneumonia [3], and patients presenting with severe pneumonia had high CRP levels. We assessed the correlation between CRP levels, lung lesions, and disease severity to provide reference for clinical treatment.

2. Subjects and methods

From January 23, 2020 to February 29, 2020, a total of 27 patients admitted to the Fever Unit were selected (11 mild cases, 12 moderate cases, two severe cases, and two critical cases). Ten patients were from the people’s hospital of Qiandongnan Miao and Dong autonomous prefecture. Seventeen patients were from Qiannan Miao and Buyi autonomous prefecture. We included 13 males and 14 females, aged from 5 months to 59 years with a mean age of 33.23 ± 13.21 years.

Early definition of COVID-19: within 7 days of clinical symptoms, and within 7 days of positive viral nucleic acid test for asymptomatic patients.

Inclusion criteria: the criterion for confirming COVID-19 was a positive viral nucleic acid test [4].

Exclusion criteria: patients with bacterial infection, patients with onset more than 7 days before, and patients with incomplete data were excluded.

3. Methods

We performed a retrospective study. On admission CRP levels were collected, and the diameter of the largest lung lesion was measured in the most severe lung lesion by lung CT scan. Differences in the diameter and CRP levels were compared in the following groups of patients: mild group, moderate group, severe group, and critical group. We observed a correlation between CRP levels, lung lesion diameter, and disease severity.

Adresse e-mail : 463082910@qq.com

https://doi.org/10.1016/j.medinmal.2020.03.007
0399-077X/© 2020 The Author. Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Table 1
Comparison of CRP levels and lung lesions on admission in each group.

| Parameter         | Gender (male/Female) | Age (years)       | CRP (mg/L)          | Diameter of the largest lung lesion (cm) |
|-------------------|----------------------|-------------------|---------------------|----------------------------------------|
| Mild group        | 2/9                  | 30.55 ± 10.46     | 1.52 ± 1.56         | 1.23 ± 1.43                           |
| Moderate group    | 8/4                  | 33.29 ± 14.97     | 16.76 ± 8.38        | 2.94 ± 1.91                           |
| Severe group      | 2/0                  | 40.50 ± 4.95      | 54.15 ± 1.06        | 9.15 ± 1.20                           |
| Critical group    | 1/1                  | 41.00 ± 25.46     | 105.00 ± 12.73      | 17.00 ± 4.24                          |

Mild group: moderate group
χ²/degrees of freedom = 2.292
P-value = 0.051

Moderate group: severe group
χ²/degrees of freedom = 0.931
P-value = 0.549

Severe group: critical group
χ²/degrees of freedom = 1.000
P-value = 0.667

4. Statistical analysis

The statistical analysis was performed using the SPSS 24.0 software. Measurement data with normal distribution are expressed as mean ± standard deviation (mean ± SD), and comparisons among the groups were performed using the one-way analysis of variance (ANOVA) followed by LSD test (homogeneity of variance was determined) or Tamhane's T2 test. Numeration data was analyzed by chi-square test. Correlation was analyzed by Spearman correlation analysis. A P value below 0.05 was considered statistically significant.

5. Results

Symptom onset was 1–7 days, with a mean of 3.62 ± 2.78 days. We observed 22 cases (81.48%) of ground glass lesions in the lungs.

As shown in Table 1 and Fig. 1, CRP levels and the diameter of the largest lung lesion on admission in the moderate group were higher than those in the mild group (Mann-Whitney test = −2.647, −2.171, P < 0.05), those in the severe group were higher than those in the moderate group (Mann-Whitney test = 0.693, −2.177, P < 0.05), and those in the critical group were higher than those in the severe group (Mann-Whitney test = −0.068, −1.549, P < 0.05). The difference was statistically significant. Both CRP levels and diameter of the largest lung lesion increased with disease progression. CRP levels were positively correlated with lung lesions and severe presentation (correlation coefficient = 0.873, 0.734, P < 0.001).

![Fig. 1. Relation between CRP levels, clinical severity, and lung lesions.](image-url)

6. Discussion

The number of patients with COVID-19 is currently rapidly increasing globally, and asymptomatic patients are also the source of infection [5]. COVID-19-related case fatality is also rapidly increasing. COVID-19 is a new threat for populations [6–8], and treatment options need to be evaluated [9]. Early monitoring of key indicators was an important basis to guide treatment strategies, and early assessment of the severity of patients’ condition was of great value [10]. The main pathological changes of COVID-19 are lung and immune system damage [4]. Seros, fibrin exudate and clear membrane form in the alveolar cavity and congestion and edema appear in the lung [11]. CT dynamic monitoring may be used to identify the characteristic imaging of lung changes: multiple small patch shadows and stromal changes are observed in the early stage and the lung exudate is obvious [12], which then develops into multiple ground-glass shadows and infiltrating shadows in both lungs [13]. CT scan examination, as a quick and simple method to screen for pulmonary infection, cannot only determine the presence of pulmonary infection but it can also provide a reference for determining the type of pathogen, with unique diagnostic advantages. According to Zhong Nanshan’s latest research, the sensitivity of COVID-19 diagnosis with CT scan alone was 76.4%, and the application of CT scan in COVID-19 was evaluated as useful [14]. A 50% increase in lung X-ray findings within 24 to 48 hours was considered an early warning indicator of impending conversion to critical disease. The CT scan can sometimes predict the prognosis of patients [15]. Studies by Chen Lin et al. all suggested the value of the CT scan in the diagnosis and evaluation of COVID-19 [2]. Shortcomings of CT scan are the additional special protection required by medical personnel during examination of COVID-19 patients, the cost of protective equipment, and risks associated with the transportation and examination of critical patients. CT dynamic monitoring of lung lesions was limited. A simple index with good correlation with pulmonary pathological changes is required.

CRP levels are correlated with the level of inflammation, and its concentration level is not affected by factors such as age, sex, and physical condition [16]. CRP levels can activate the complement and enhance phagocytosis, thus clearing the pathogenic microorganisms invading the body. CRP levels can be used for early diagnosis of pneumonia [3], and patients with severe pneumonia had high CRP levels. It is an important index for the diagnosis and assessment of severe pulmonary infectious diseases [17]. Matsumoto’s study also showed the value of CRP levels in severe pneumonia [18]. This study showed that CRP levels and the diameter of the largest lung lesion increased as the disease progressed. CRP levels were positively correlated with lung lesion and disease severity. This suggests that in the early stage of COVID-19, CRP levels could reflect lung lesions and disease severity.
7. Conclusions

At the early stage of COVID-19, CRP levels were positively correlated with lung lesions. CRP levels could reflect disease severity and should be used as a key indicator for disease monitoring.

Ethical approval and consent to participate

This study was approved by the ethics committee of the people’s hospital of Qiandongnan Miao and Dong Autonomous Prefecture.

Funding

The study was funded by the researchers themselves, with no other funding.

Author’s contributions

Wang Ling did all the work on the manuscript. Only have one author.

Disclosure of interest

The author declares that he has no competing interest.

Acknowledgements

The authors are grateful to Professor Xianqing Shi, Professor Feng Shen, Professor Xiaoyun Fu, who helped with the topic development and with improving the article.

Références

[1] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395(10223):507–13, http://dx.doi.org/10.1016/S0140-6736(20)30185-9.

[2] Lin C, Ding Y, Xie B, Sun Z, Li X, Chen Z, et al. Asymptomatic novel coronavirus pneumonia patient outside Wuhan: the value of CT images in the course of the disease. Clin Imaging 2020;63(3):7–9, http://dx.doi.org/10.1016/j.clinimag.2020.02.008.

[3] Warusawithana A, Karunatilake D, Sim J, Smith C, Roffe C. Early diagnosis of pneumonia in severe stroke: clinical features, the diagnostic role of C-reactive protein. PLoS one 2016;11(3):e0150269, http://dx.doi.org/10.1371/journal.pone.0150269.

[4] General office of the national health commission of China. Covid-19 diagnostic and therapeutic regimen (trial 7th, edition). J Cardiopulm Rehabil Prev 2020;39(02):103–7, https://kns.cnki.net/KCMS/detail/detail.aspx.

[5] Machase E, China coronavirus: mild but infectious cases may make it hard to control outbreak. Report warns. BMJ 2020;368:m325, http://dx.doi.org/10.1136/bmj.m325ed.

[6] Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet 2020;395(10223):470–3, http://dx.doi.org/10.1016/S0140-6736(20)30185-9.

[7] Bassetti M, Vena A, Giacobbe DR. The novel Chinese coronavirus (2019-ncov) infections: challenges for fighting the storm. Eur J Clin Invest 2020;50(3), http://dx.doi.org/10.1111/eci.13209 [1320913213].

[8] Xu X, Chen P, Wang J, Feng J, Zhou H, Li X, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci China Life Sci 2020;63(3):457–60, http://dx.doi.org/10.1007/s11427-020-1637-5.

[9] Kruše R, Therapeutic strategies in an outbreak scenario to treat the novel coronavirus originating in Wuhan, China. F1000Research 2020;9:72, http://dx.doi.org/10.12688/f1000research.22111.2.

[10] Li C, de Clercq E. Therapeutic options for the 2019 novel coronavirus (2019-ncov). Nat Rev Drug Discov 2020;19(3):149–50, http://dx.doi.org/10.1038/s41573-020-00016-0.

[11] Xu Z, Shi I, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8(4):420–2, http://dx.doi.org/10.1016/S2213-2600(20)30076-X.

[12] Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT imaging features of 2019 novel coronavirus (2019-ncov). Radiology 2020;295(01):202–7, http://dx.doi.org/10.1148/radiol.2020200230.

[13] Pan F, Ye T, Sun P, Gu S, Liang B, Li L, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology 2020;283(06):20370–3, http://dx.doi.org/10.1148/radiol.2020200370.

[14] Wu JN, Shen J. Emphasis and scientific evaluate the role of CT in the diagnosis and treatment of novel coronavirus pneumonia. J Dalian Med Univ 2020;42(01):1–4 https://kns.cnki.net/KCMS/detail/41.1390.R.20200310.0917.002.html.

[15] Lee KS. Pneumonia associated with 2019 novel coronavirus: can computed tomographic findings help predict the prognosis of the disease? Korean J Radiol 2020;21(3):257–8, http://dx.doi.org/10.14345/kjr.2020.0096.

[16] Bilgir O, Bilgir F, Calan M. Comparison of pre-and post-levothyroxine high-sensitivity C-reactive protein and fetuin-A levels in subclinical hypothyroidism. Clinics 2015;70(2):97–101, http://dx.doi.org/10.6061/clinics/2015/02/05.

[17] Chalmers S, Khawaja A, Wieruszewski PM, Gajic O, Odeyemi Y. Diagnosis and treatment of acute pulmonary inflammation in critically ill patients: the role of inflammatory biomarkers. World J Crit Care Med 2019;8(5):59–71, http://dx.doi.org/10.5492/wjccc.v8.i5.59.

[18] Matsumoto H, Kasai T, Sato A, Ishiwata S, Yatsu S, Shitara J, et al. Association between C-reactive protein levels at hospital admission and long-term mortality in patients with acute decompensated heart failure. Heart Vessels 2015;34(12):1961–8, http://dx.doi.org/10.1007/s00380-019-01435-9.