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.
Mediastinal lymphadenopathy may predict 30-day mortality in patients with COVID-19

Celal Satici a,*, Ferhat Cengel b, Okan Gurkan b, Mustafa Asim Demirkol a, Elif Sargin Altunok c, Sinem Nihal Esatoglu d

a Department of Chest Diseases, Gaziosmanpasa Training and Research Hospital, University of Health Sciences, Istanbul, Turkey
b Department of Radiology, Gaziosmanpasa Training and Research Hospital, University of Health Sciences, Istanbul, Turkey
c Department of Infectious Disease and Clinical Microbiology, Gaziosmanpasa Training and Research Hospital, University of Health Sciences, Istanbul, Turkey
d Department of Rheumatology, Gaziosmanpasa Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

ARTICLE INFO

Keywords: Mediastinal lymphadenopathy Radiological findings COVID-19 Mortality

ABSTRACT

Purpose: There is scarce data on the impact of the presence of mediastinal lymphadenopathy on the prognosis of coronavirus-disease 2019 (COVID-19). We aimed to investigate whether its presence is associated with increased risk for 30-day mortality in a large group of patients with COVID-19.

Method: In this retrospective cross-sectional study, 650 adult laboratory-confirmed hospitalized COVID-19 patients were included. Patients with comorbidities that may cause enlarged mediastinal lymphadenopathy were excluded. Demographics, clinical characteristics, vital and laboratory findings, and outcome were obtained from electronic medical records. Computed tomography scans were evaluated by two blinded radiologists. Univariate and multivariate logistic regression analyses were performed to determine independent predictive factors of 30-day mortality.

Results: Patients with enlarged mediastinal lymphadenopathy (n = 60, 9.2%) were older and more likely to have at least one comorbidity than patients without enlarged mediastinal lymphadenopathy (p = 0.03, p = 0.003). There were more deaths in patients with enlarged mediastinal lymphadenopathy than in those without (11/60 vs 45/590, p = 0.01). Older age (OR:3.74, 95% CI: 2.06–6.79; p < 0.001), presence of consolidation pattern (OR:1.93, 95% CI: 1.09–3.40; p = 0.02) and enlarged mediastinal lymphadenopathy (OR:2.38, 95% CI:1.13–4.98; p = 0.02) were independently associated with 30-day mortality.

Conclusion: In this large group of hospitalized patients with COVID-19, we found that in addition to older age and consolidation pattern on CT scan, enlarged mediastinal lymphadenopathy were independently associated with increased mortality. Mediastinal evaluation should be performed in all patients with COVID-19.

1. Introduction

The novel coronavirus disease 2019 (COVID-19) pandemic still remains a major health problem and threatens the entire world with high number of deaths. After the first cases detected in Wuhan, China, COVID-19 has begun to spread rapidly. As of September 21, 2020, World Health Organization reported 30.6 million confirmed cases and 950.000 deaths across more than 200 countries.1

COVID-19 presents with a wide range of clinical scenarios including asymptomatic infection, mild to severe pneumonia or involvement of various organs and systems. Older age,2 male gender,3 presence of comorbidities,4 higher C-reactive protein levels (CRP)5 and higher pneumonia severity index (PSI) scores6 are among the well-known predictors of a worse outcome. However, none of these are sufficient alone, there is an ongoing need to investigate another prognostic biomarkers for progressive disease.

Radiological findings are of interest since the extent of radiological involvement is highly correlated with CRP which is one of the best...
prognostic factors for COVID-19. Ground-glass opacity is the most common radiological finding followed by air bronchogram, crazy-paving pattern, consolidation and pleural thickening. Among these, consolidation on initial chest computed tomography (CT) was reported as a predictor of clinical deterioration. On the other hand, pleural effusion, cavitary lesions, tree-in-bud sign and mediastinal lymphadenopathy were reported to be atypical radiologic findings of COVID-19 and their impact on the prognosis of COVID-19 has not been well known. Among these, enlarged mediastinal lymphadenopathy was observed in up to 29% of patients with COVID-19. Sardanelli et al. reported that in-hospital COVID-19 mortality rate was higher in patients with enlarged mediastinal lymphadenopathy compared to those without and suggested that the presence of enlarged mediastinal lymphadenopathy needs to be investigated as a prognostic factor. Interestingly, a relationship between the presence of enlarged mediastinal lymphadenopathy and disease severity has been demonstrated in patients with idiopathic pulmonary fibrosis (IPF) and the presence of enlarged mediastinal lymphadenopathy is thought to be a result of a higher degree of chronic inflammation. Similarly, there may be a possible link between the presence of enlarged mediastinal lymphadenopathy and the severity of COVID-19 in where inflammation plays a key role.

In this study, we aimed to investigate whether the presence of enlarged mediastinal lymphadenopathy is associated with an increased risk of 30-day mortality in 650 adult hospitalized patients with COVID-19.

2. Material and methods

2.1. Study design and setting

We performed a retrospective cross-sectional study at Gaziosmanpasas Training and Research Hospital, University of Health Sciences, Istanbul, Turkey. Our study was conducted in line with the Declaration of Helsinki tenets and our institutional ethics committee approved it (Approvement protocol number: 145-2020).

2.2. Study population

The first coronavirus case was registered in Turkey on March 11, 2020. Immediately, Turkish Ministry of Health has prepared a COVID-19 guideline for healthcare providers which has been updated several times according to scientific developments. Since favipiravir has become a mainstay therapy as of April 2, 2020, we included all adult patients who were hospitalized due to COVID-19 between April 2 and May 15, 2020. Patients with active malignancy, or heart failure were excluded due to the fact that these conditions may cause enlarged mediastinal lymphadenopathy.

According to the Turkish Ministry of Health COVID-19 guideline, any suspected patient who is older than 50 years, or have any comorbidities including cardiopulmonary disease, diabetes mellitus, hypertension, chronic kidney disease, immunosuppression or malignancy, or with tachycardia (heart rate > 125/min), tachypnea (respiratory rate > 30/min), hypotension (<90/60 mmHg), or hypoxemia (SpO2 < 92%) should be hospitalized. Severe cases are defined as those with respiratory distress (>30 breaths/min), and/or oxygen saturation lower than <90% at rest, and/or arterial partial pressure of oxygen/fraction of inspired oxygen <300 mmHg.

2.3. Data collection

Demographic features, comorbidities, presenting symptoms, vital signs at admission including heart rate, blood pressure, oxygen saturation and respiratory rate, initial systemic inflammatory markers including CRP, ferritin and procalcitonin were obtained from electronic medical records.

2.4. Definitions and measurements

2.4.1. Imaging protocol and techniques

The chest CT scans in the present study were obtained using the standard dose protocol of our hospital with a 128-slice multi-detector CT scanner (Optima; General Electric Healthcare, Wisconsin, USA). All CT scans were performed during a single breath-hold without contrast administration. The imaging parameters used were as follows; tube voltage; 120 kVp, tube current (regulated by automatic dose modulation); 80–200 mAs, slice thickness; 5 mm, matrix; 512 × 512, field of view; 350 mm × 350 mm. The scans were retrospectively reconstructed in the sagittal and coronal planes (1.25-mm thickness, 0.625-mm spacing).

Mediastinal lymphadenopathy was considered as pathological if the short-axis of mediastinal lymphadenopathy ≥ 10 mm. Mediastinal lymph nodes were evaluated and measured in the routine axial plane. If the lymph node was considered to be larger in any other plane, the short axis of mediastinal lymphadenopathy was measured and recorded. Mediastinal lymph node stations were classified according to a new international lymph node map. CT images of a COVID-19 patient with enlarged mediastinal lymphadenopathy are shown in Figs. 1 and 2. CT images were evaluated for distribution (unilateral/bilateral, apical predominance/basal predominance), lesion attenuation (ground-glass opacity, consolidation and crazy paving) and other radiological findings (bronchiectasis, subpleural band, reversed halo sign). The radiographic findings were defined in line with the Fleischner Society guidelines.

2.4.2. Imaging analysis

All CT images were reviewed by two radiologists with 9 and 12 years of experience in interpreting chest CT imaging [FC and OG, respectively], on a in Picture Archiving and Communication System (PACS) imaging workstation (Infinitt PACS; Infinitt Healthcare, Seoul, Korea). Each radiologist was blinded to demographic features, clinical, vital and laboratory findings of the patients. An almost perfect interobserver reliability with 0.89 Cohen Kappa coefficient was established for the presence of enlarged mediastinal lymphadenopathy. High interobserver reliability was also maintained for the distribution of enlarged mediastinal lymphadenopathy (>0.8 for all stations). The discrepancies were resolved by discussion.

2.4.3. Treatment

According to the COVID-19 Diagnosis and Treatment guideline published by Turkish Ministry of Health (20), the recommended hydroxychloroquine regimens for all hospitalized patients was a loading dose of 400 mg twice on day 1, followed by 400 mg daily for 4 more days. In addition, azithromycin at a dose of 500 mg on day 1 and then 250 mg daily for 4 additional days was also used with caution by monitoring the QT interval. Favipiravir was initiated in patients with severe pneumonia or in those with ongoing fever, despite hydroxychloroquine and/or azithromycin treatment, at a loading dose of 1600 mg twice on day 1, followed by 600 mg twice a day for additional 4 days. Favipiravir was available for outpatients with a high risk for progressive disease after this study was conducted. Tocilizumab was recommended at a dose of 8 mg/kg in patients with high inflammatory markers and ongoing hypoxemia despite favipiravir therapy. In patients with poor clinical response, a second dose of tocilizumab was considered within 24–48 h after the first dose. A prophylactic dose of enoxaparin was initiated in all patients unless there were contraindications. A therapeutic dose of enoxaparin was used in cases of severe pneumonia, D-dimer level ≥ 1000 ng/mL, body mass index ≥ 40 kg/m², and acute venous thromboembolism.

2.4.4. Outcome

The primary outcome was to assess whether if the presence of
enlarged mediastinal lymphadenopathy is associated with increased risk for 30-day mortality.

2.4.5. Statistical analysis

Descriptive statistics were used to define variables. Categorical data were reported as proportions and counts, and continuous data was presented as mean and standard deviation (SD) if the data was normally distributed. Median and interquartile range were indicated for not normally distributed continuous data. Chi-square test was used for comparing categorical variables. Student t-test was performed for comparison of two groups in terms of normally distributed continuous parameter and if not normally distributed, Mann Whitney U test was performed. Significant variables obtained from univariate analysis were analyzed by multivariate logistic regression analysis to determine independent predictors of mortality. If there is a strong correlation between two significant variables, only the parameter which was considered more clinically relevant was included in multiple logistic regression analysis which was tested for goodness of fit with Hosmer-Lemeshow test.

3. Results

A total of 650 patients with a mean ± SD age of 56.9 ± 14.9 were included in this study. The majority of them were male (333, 51.2%), 297 patients (45.7%) had at least one comorbidity and 208 patients (32%) had a severe disease.

Enlarged mediastinal lymphadenopathy was detected in 60 patients (9.2%). The characteristics of the patients with and without enlarged mediastinal lymphadenopathy are summarized in Table 1. Patients with enlarged mediastinal lymphadenopathy were significantly older and more likely to have at least one comorbidity than those without enlarged mediastinal lymphadenopathy (p = 0.03, p = 0.003 respectively). Gender, presenting symptoms and vital signs at admission, the severity status and radiological findings except the presence of crazy paving pattern were similar across two groups. Crazy-paving pattern was more common in patients with enlarged mediastinal lymphadenopathy than in those without (17 (21.3%) vs 57 (9.7%), p < 0.001) (Table 1). CRP level was higher in patients with enlarged mediastinal lymphadenopathy than in those without (80.6 ± 82.7 vs 54.6 ± 61.5, p = 0.02), while ferritin and procalcitonin levels were similar across the groups (p = 0.46, p = 0.16, respectively). Forty-five (7.6%) of 590 patients without enlarged mediastinal lymphadenopathy had died, while 11 (18.3%) of 60 patients with enlarged mediastinal lymphadenopathy had died (p = 0.01).

3.1. Patients with enlarged mediastinal lymphadenopathy vs those without

Among 650 patients, 56 (8.6%) had died. The univariate analysis revealed that the patients who died were older (p < 0.001) and more likely to have at least one comorbidity (p = 0.015). Patients with diabetes mellitus and hypertension were at increased risk for mortality (p = 0.001, p = 0.002, respectively). There were no significant differences regarding other radiological findings including pleural effusion.
After performing multivariate analysis; older age (OR: 3.74, 95% CI: 1.26–10.6) was an independent predictor of increased 30-day mortality. The presence of mediastinal lymphadenopathy was an independent predictor of 30-day mortality (Table 2). This finding was explained by a relationship between mediastinal lymphadenopathy and exaggerated host response due to SARS-COV-2 and recommended the investigation of this possible link in a larger cohort. In line with these studies we showed that enlarged mediastinal lymphadenopathy may predict 30-day mortality in a larger group of patients with COVID-19 by performing multivariate analysis. In addition, although mediastinal lymphadenopathy was considered as an atypical feature of COVID-19, it may not be a ‘atypical’ feature of COVID-19 as we and others have observed.

### 3.3. Number and distribution of enlarged mediastinal lymphadenopathy

Among the 60 patients with enlarged mediastinal lymphadenopathy, the distribution and the median number of enlarged mediastinal lymphadenopathies were similar between dead and alive patients (Table 3). The most common localization of enlarged mediastinal lymphadenopathy was the regional station 7 (37%), followed by station 4R (29%) and station 6 (12%) (Table 3).

| Variable                      | Patients with mediastinal lymphadenopathy (n = 60) | Patients without mediastinal lymphadenopathy (n = 540) | p value |
|-------------------------------|--------------------------------------------------|------------------------------------------------------|---------|
| Age (years) (mean ± SD)       | 63.3 ± 12.8                                       | 56.6 ± 12.0                                          | 0.03    |
| Female n (%)                  | 27 (45)                                          | 290 (49.2)                                           | 0.58    |
| Comorbidities n (%)           |                                                  |                                                      |         |
| Any comorbidity               | 44 (73.3)                                        | 309 (52.4)                                           | 0.003   |
| Hypertension                  | 26 (43.3)                                        | 200 (33.9)                                           | 0.15    |
| Diabetes mellitus             | 21 (35)                                          | 153 (25.8)                                           | 0.16    |
| COPD                          | 3 (5)                                            | 21 (3.6)                                             | 0.47    |
| Asthma                        | 6 (10)                                           | 36 (6.1)                                             | 0.26    |
| Ischemic heart disease        | 9 (15)                                           | 48 (8.1)                                             | 0.09    |
| Hypertension                  | 4 (6.7)                                          | 25 (4.2)                                             | 0.33    |
| Chronic renal disease         | 4 (6.7)                                          | 20 (3.4)                                             | 0.26    |
| Symptoms n (%)                |                                                  |                                                      |         |
| Cough                         | 39 (65)                                          | 430 (72.9)                                           | 0.22    |
| Fever                         | 22 (36.7)                                        | 183 (31)                                             | 0.38    |
| Dyspnea                       | 22 (36.7)                                        | 155 (26.3)                                           | 0.09    |
| Myalgia                       | 2 (3.3)                                          | 66 (11.2)                                            | 0.07    |
| Nausea and/or diarrhea        | 2 (3.3)                                          | 40 (6.8)                                             | 0.41    |
| Headache                      | 2 (3.3)                                          | 24 (4.1)                                             | N/A     |
| Physical findings n (%)       |                                                  |                                                      |         |
| Respiratory rate ≥ 30/min     | 3 (5)                                            | 24 (4.1)                                             | 0.73    |
| Heart rate ≥ 125/min          | 0 (0)                                            | 18 (3.1)                                             | 0.39    |
| SBP <90 mmHg or DBP <60 mmHg  | 2 (3.3)                                          | 9 (1.5)                                              | 0.27    |
| Radiologic findings n (%)     |                                                  |                                                      |         |
| Bilateral lung involvement    | 55 (91.7)                                        | 536 (90.8)                                           | N/A     |
| Ground-glass opacity          | 58 (96.7)                                        | 570 (96.6)                                           | N/A     |
| Consolidation                 | 36 (60)                                          | 281 (47.6)                                           | 0.07    |
| Crazy paving                  | 17 (21.3)                                        | 57 (9.7)                                             | <0.001  |
| Basal predominance            | 33 (55)                                          | 368 (62.4)                                           | 0.37    |
| Bronchiectasis                | 8 (13.3)                                         | 57 (9.7)                                             | 0.36    |
| Subpleural band               | 20 (33.3)                                        | 174 (29.5)                                           | 0.55    |
| Reversed halo sign            | 5 (8.3)                                          | 54 (9.2)                                             | N/A     |
| Pleural effusion              | 1 (1.7)                                          | 15 (2.5)                                             | N/A     |
| Inflammatory blood markers    |                                                  |                                                      |         |
| CRP (mg/L)                    | 54 (16.5–119.5)                                  | 29 (10–80.2)                                         | 0.006   |
| Ferritin (mg/mL)              | 179.6 (86.8–459.9)                               | 171.5 (85.9–371.8)                                  | 0.5     |
| PCT (ng/mL)                   | 0.12 (0–0.22)                                    | 0.11 (0–0.15)                                       | 0.13    |
| Disease status n (%)          |                                                  |                                                      |         |
| Non-severe                    | 35 (58.3)                                        | 407 (69)                                             | 0.11    |
| Severe                        | 25 (41.7)                                        | 183 (31)                                             |         |
| Mortality n (%)               |                                                  |                                                      |         |
| Survived                      | 49 (81.7)                                        | 545 (92.4)                                           | 0.01    |
| Deceased                      | 11 (18.3)                                        | 45 (7.6)                                             |         |

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease, SBP: systolic blood pressure, DBP: diastolic blood pressure, CRP: C-reactive protein, PCT: procalcitonin.

p values in bold indicate statistically significant results.

Bronchiectasis, subpleural band, reversed halo sign, ground-glass opacity and basal predominance among dead and alive patients (p > 0.05). However, the presence of consolidation, enlarged mediastinal lymphadenopathy and bilateral lung involvement were more likely to be present in patients who died (p = 0.04, p = 0.099, p = 0.03 respectively). After performing multivariate analysis; older age (OR:3.74, 95% CI: 2.06–6.79; p < 0.001), the presence of enlarged mediastinal lymphadenopathy (OR:2.38, 95% CI:1.13–4.98; p = 0.02) and consolidation on CT scan (OR:1.93, 95% CI: 1.09–3.40; p = 0.02) were found to be independent predictors of 30-day mortality (Table 2).
luphadenopathy was found to be associated with clinical worsening. This may explained by the fact that lymphangiogenesis and lymphatic remodeling resulted by chronic ongoing inflammation lead to progressive fibrosis. In this line, enlargement of mediastinal lymphadenopathy may also reflect increased inflammation in patients with COVID-19.

In our study, enlarged lymph nodes were more frequently found to be located in station 7 and station 4R, similar to observed in patients with IPF. The lung lesions showed right sided and basal predominance in patients with IPF as observed in those with COVID-19. This may be the reason for the similarity. In patients with IPF, increased number of enlarged mediastinal lymph node was found to be associated with mortality. In our study, although deceased patients tended to have increased number of enlarged mediastinal lymph nodes, there was no significant difference when compared with alive patients. It should be noted that our small sample size may not allow us to detect a significant difference.

Among other CT manifestations, crazy paving pattern is defined as combination of ground-glass opacity, intralobular and interlobular septal thickening. Based on previous data, crazy-paving pattern was associated with a worse outcome. However, we found no significant association between crazy-paving pattern and 30-day mortality. The possible explanation might be that diabetes mellitus, which is associated with a poor COVID-19 outcome, was more common in patients without crazy-paving pattern than in those with crazy paving pattern. In line with the previous studies, we also found consolidation pattern as a predictor of mortality. The extent of parenchymal involvement was not performed in patients with COVID-19, coexisting bacterial, fungal and mycobacterial infections could not be ruled out. Third; we cannot be sure that patients had already an enlarged mediastinal lymphadenopathy previously. Finally; it would be interesting to perform a biopsy to exclude other causes of enlarged mediastinal lymphadenopathy such as sarcoidosis and malignancy, and demonstrate the pathological findings of enlarged mediastinal lymphadenopaties in COVID-19 patients. However, our strength was that radiological findings on standardized chest CT scan were blindly evaluated by two experienced radiologists and interobserver reliability was almost perfect.

### Table 2

Univariate and multivariate analysis for 30-day mortality.

| Variable                        | Category      | Univariate analysis | Multivariate analysis |
|---------------------------------|---------------|---------------------|-----------------------|
|                                 |               | n OR CI (95%) p     | n OR CI (95%) p       |
| Gender                          | Male          | 333 1.09 0.64–1.84  | 0.79                  |
|                                 | Female        | 317 1 Ref           |                       |
| Age                             | <65           | 200 3.58 2.09–6.11  | <0.001                |
|                                 | ≥65           | 450 1 Ref           |                       |
| Comorbidity                     | Present       | 353 2.03 1.15–3.56  | 0.015                 |
|                                 | Absent        | 297 1 Ref           |                       |
| Radiologic pattern              | Consolidation | 317 1.75 1.02–2.99  | 0.04                  |
|                                 | (-)           | 333 1 Ref           |                       |
| Bilateral/unilateral lung       | Bilateral     | 591 6.67 0.9–49.0   | 0.03                  |
| involvement                     | Unilateral    | 59 1 Ref            |                       |
| Mediastinal lymphadenopathy     | Present       | 60 2.7 1.3–5.4     | 0.009                 |
|                                 | Absent        | 590 1 Ref           | 2.38 1.13–4.98 0.02   |

p values in bold indicate statistically significant results.

### Table 3

Comparison of the number and the distribution of enlarged mediastinal lymph nodes between deceased and survived patients.

| Lymph node station | Deceased patients (n = 12) | Survived patients (n = 48) | p value |
|--------------------|----------------------------|---------------------------|---------|
| 7                  | 7 (58.3)                   | 32 (66.7)                 | 0.73    |
| 4R                 | 7 (58.3)                   | 27 (56.3)                 | N/A     |
| 6                  | 4 (33.3)                   | 10 (20.8)                 | 0.44    |
| 4L                 | 2 (16.7)                   | 10 (20.8)                 | N/A     |
| 2R                 | 3 (25)                     | 4 (8.3)                   | 0.13    |
| 3                  | 1 (8.3)                    | 2 (4.2)                   | N/A     |
| 5                  | 0 (0)                      | 2 (4.2)                   | N/A     |
| 2L                 | 0 (0)                      | 1 (2.1)                   | N/A     |
| 8                  | 1 (8.3)                    | 0 (0)                     | 0.2     |
| Median number of enlarged mediastinal lymph nodes | 1.5 (1.0–2.7) | 1 (1–2) | 0.42 |

In conclusion, along with older age and consolidation pattern, enlarged mediastinal lymphadenopathy was found to be an independent predictor of 30-day mortality in patients with COVID-19. Although enlarged mediastinal lymphadenopathy was reported as an atypical radiological finding, mediastinum should be evaluated for the presence of enlarged mediastinal lymphadenopathy and it may be useful as a biomarker for progressive disease.

### Author contributions

Celal Satici: Conceptualization, Methodology, Formal analysis, Investigation, Writing - original draft
Erhat Cengel: Investigation, Resources
Okan Gurkan: Investigation, Resources
Mustafa Asim Demirkol: Investigation, Resources
Elif Sargin Altunok: Investigation, Resources
Sinem Nihal Esatoglu: Methodology, Writing - Review & Editing, Supervision.

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
Declaration of competing interest

None.

References

1. WHO (World Health Organization). Coronavirus disease (COVID-19) global epidemiological situation. n.d.

2. Shang Y, Liu T, Wei Y, et al. Scoring systems for predicting mortality for severe patients with COVID-19. EclinicalMedicine 2020;24. https://doi.org/10.1016/j.eclinm.2020.100426.

3. Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. J Infect 2020;91:e16–25. https://doi.org/10.1016/j.jinf.2020.04.021.

4. Posso M, Comas M, Román M, et al. Comorbidities and mortality in patients with COVID-19 aged 60 years and older in a university hospital in Spain. Arch Bronconeumol 2020. https://doi.org/10.1016/j.arbej.2020.06.012.

5. Sahu BR, Kampa RK, Padhi A, Panda AK. C-reactive protein: a promising biomarker for poor prognosis in COVID-19 infection. Clin Chim Acta 2020;509:91–4. https://doi.org/10.1016/j.cca.2020.06.013.

6. Satici C, Demirkol MA, Sargin Altunok E, et al. Performance of pneumonia severity index and CURB-65 in predicting 30-day mortality in patients with COVID-19. Int J Infect Dis 2020;98:84–9. https://doi.org/10.1016/j.ijid.2020.06.038.

7. Tan C, Huang Y, Shi F, et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol 2020;92:856–62. https://doi.org/10.1002/jmv.25871.

8. Li Y, Yang Z, Ai T, Wu S, Xia L. Association of "initial CT" findings with mortality in older patients with coronavirus disease 2019 (COVID-19). Eur Radiol 2020. https://doi.org/10.1007/s00330-020-06969-5.

9. Li K, Li K, Chen D, et al. Predictors of fatality including radiographic findings in adults with COVID-19. Respir Res 2020;21:146. https://doi.org/10.1186/s12931-020-01411-2.

10. Zhu J, Zhong Z, Li H, et al. CT imaging features of 4121 patients with COVID-19: a meta-analysis. J Med Virol 2020;92:891–902. https://doi.org/10.1002/jmv.25910.

11. Rush Y, Kaeuffer C, Ohana M, et al. CT lung lesions as predictors of early death or ICU admission in COVID-19 patients. Clin Microbiol Infect 2020. https://doi.org/10.1016/j.cmi.2020.07.030.

12. Simpson S, Kay FU, Abbara S, et al. Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and KRSA. Radiol Cardiothorac Imaging 2020;2:e200152. https://doi.org/10.11077/txe.jrci.20200512.

13. Meiler S, Schaible J, Poschenrieder F, et al. Can CT performed in the early disease phase predict outcome of patients with COVID 19 pneumonia? Analysis of a cohort of 64 patients from Germany. Eur J Radiol 2020;131:109256. https://doi.org/10.1016/j.ejrad.2020.109256.

14. Li K, Wu J, Wu F, et al. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Invest Radiol 2020;55:327–31. https://doi.org/10.1097/RLI.0000000000002672.

15. Leonard A, Scipione R, Altieri G, et al. Role of computed tomography in predicting critical disease in patients with covid-19 pneumonia: a retrospective study using a semiautomated quantitative method. Eur J Radiol 2020;124. https://doi.org/10.1016/j.ejrad.2020.109202.

16. Valette X, du Cheyron D, Goursaud A. Mediastinal lymphadenopathy with COVID-19 prognosis. Lancet Infect Dis 2020;20:1133–4. https://doi.org/10.1016/s1473-3099(20)30310-8.

17. Kim H, Kataru RP, Koh GY. Inflammation-associated lymphangiogenesis: a double-edged sword? J Clin Invest 2014;124:936–42. https://doi.org/10.1172/JCI71607.

18. Zeng F, Huang Y, Guo Y, et al. Association of inflammatory markers with the severity of COVID-19: a meta-analysis. J Int J Infect Dis 2020;96:476–74. https://doi.org/10.1016/j.ijid.2020.05.055.

19. Liu F, Zhang Q, Huang C, et al. CT quantification of pneumonia lesions in early days predicts progression to severe illness in a cohort of COVID-19 patients. Theranostics 2020;10:5613–22. https://doi.org/10.7150/thno.45985.

20. Salehi S, Abedi A, Balakrishnan S, Gholamrezaezaad A. Coronavirus disease 2019 (COVID-19) imaging reporting and data system (COVID-RADS) and common lexicon: a proposal based on the imaging data of 37 studies. Eur Radiol 2020;30:4930–42. https://doi.org/10.1007/s00330-020-06863-0.

21. Pan F, Zheng C, Ye T, et al. Different computed tomography patterns of Coronavirus Disease 2019 (COVID-19) between survivors and non-survivors. Sci Rep 2020;10:11336. https://doi.org/10.1038/s41598-020-68057-4.

22. Meiler S, Schabbe J, Poschenrieder F, et al. Can CT performed in the early disease phase predict outcome of patients with COVID 19 pneumonia? Analysis of a cohort of 64 patients from Germany. Eur J Radiol 2020;131:109256. https://doi.org/10.1016/j.ejrad.2020.109256.

23. Hansell DM, Bankier AA, MacHown H, McLoud TC, Müller NL, Remy J. Fleischner lexicon: a proposal based on the imaging data of 37 studies. Clin Imaging 2020;2020. https://doi.org/10.1016/j.clinimag.2020.103019.

24. Liu F, Zhang Q, Huang C, et al. CT quantification of pneumonia lesions in early days predicts progression to severe illness in a cohort of COVID-19 patients. Theranostics 2020;10:5613–22. https://doi.org/10.7150/thno.45985.

25. Sardanelli F, Cozzi A, Monfardini L, et al. Association of mediastinal lymphadenopathy with COVID-19 prognosis. J Thorac Imaging 2020;35:25. https://doi.org/10.1016/j.jtho.2019.07.003.

26. IYONU) REHBER