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

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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) scores[6] 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

*Abbreviations:* COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CRP, C-reactive protein levels; CT, computed tomography; DBP, diastolic blood pressure; IPF, idiopathic pulmonary fibrosis; PCT, procalcitonin; PSI, pneumonia severity index; SBP, systolic blood pressure.

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prognostic factors for COVID-19.[7] Extensive distribution of radiological involvement was found to be associated with increased mortality[8,9] Ground-glass opacity is the most common radiological finding followed by air bronchogram, crazy-paving pattern, consolidation and pleural thickening.[10] Among these, consolidation on initial chest computed tomography (CT) was reported as a predictor of clinical deterioration.[8,11] 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.[12] Among these, enlarged mediastinal lymphadenopathy was observed in up to 29% of patients with COVID-19.[13–17] Sardanelli et al.[18] 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.[19] 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 Gaziosmanpasa 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,[20] 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 ($<$90/60 mmHg), or hypoxemia ($SpO_2 < 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 $\geq$ 10 mm. Mediastinal lymph nodes were evaluated and measured in the routine axial plan. If the lymph node was considered to be larger in any other plan, the short axis of mediastinal lymphadenopathy was measured and recorded. Mediastinal lymph node stations were classified according to a new international lymph node map.[21] 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.[22]

#### 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 regimen 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 $\geq$ 1000 ng/mL, body mass index $\geq$40 kg/m$^2$, and acute venous thromboembolism.

#### 2.4.4. Outcome

The primary outcome was to assess whether if the presence of

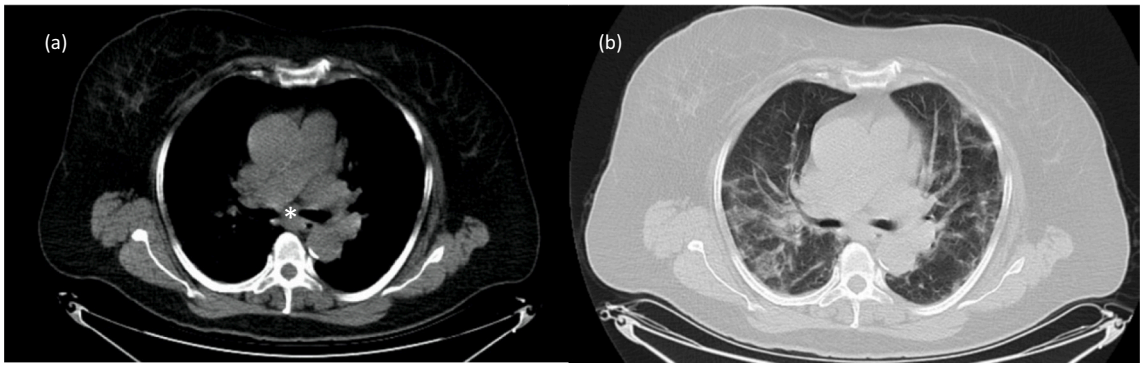


**Fig. 1.** Axial unenhanced chest CT images of a 63 year-old woman with laboratory-confirmed COVID-19 pneumonia. (1a): Mediastinal window showing enlarged lymph node station 7 (1b): Lung window shows mainly peripherally located multiple patchy ground-glass opacities.

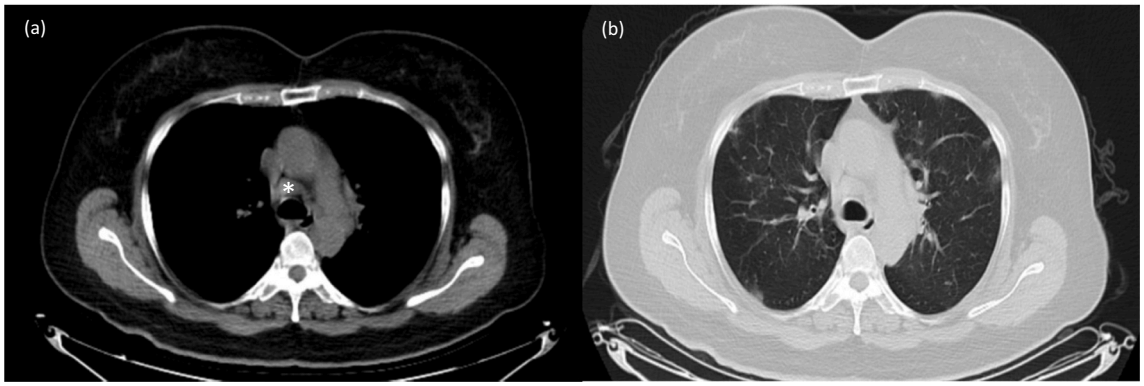


**Fig. 2.** Axial unenhanced chest CT images of a 61 year-old woman with laboratory-confirmed COVID-19 pneumonia. (2a): Mediastinal window showing enlarged lymph node station 4R (2b): Lung window shows peripherally located multiple round ground-glass opacities.

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.

### 3.1. Patients with enlarged mediastinal lymphadenopathy vs those without

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 ($p = 0.01$).

### 3.2. Deceased vs survived patients

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,

**Table 1**
Comparison of baseline characteristics, clinical and radiological findings of the patients with and without enlarged mediastinal lymphadenopathy.

| Variable | Patients with mediastinal lymphadenopathy ($n = 60$) | Patients without mediastinal lymphadenopathy ($n = 590$) | $p$ value |
|---|---|---|---|
| Age (years) (mean ± SD) | 60.3 ± 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 |
| Hyperlipidemia | 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 (ng/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 ($p = 0.04$, $p = 0.009$, $p = 0.03$ 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).

### 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).

## 4. Discussion

In our study, we aimed to assess the prognostic role of enlarged mediastinal lymphadenopathy in a large group of patients with COVID-19. In addition, we summarized the number and the distribution of enlarged mediastinal lymphadenopathy in patients with COVID-19. Our data showed that older age, the presence of consolidation and enlarged mediastinal lymphadenopathy on CT scan were independently associated with increased 30-day mortality. The distribution and the median number of enlarged mediastinal lymphadenopathies did not differ between dead and alive patients, however patients who died tended to have more lymph nodes than those who survived.

Since the course of the disease is still unpredictable and has different consequences for each patient, more reliable predictors are still needed to be studied. Systemic inflammatory markers have been reported to be one of the best predictors of a poor outcome in COVID-19.[23] On the other hand, extension of COVID-19 on CT scan has been considered as a good indicator and even superior in predicting progression to severe illness compared to clinical biomarkers.[24] Typical radiological findings denote a high level of suspicion for COVID-19 pneumonia, while atypical findings suggest the opposite.[25] Typical radiological findings include ground-glass opacity with or without consolidation, linear opacities and crazy paving pattern and these are sensitive but not specific for the diagnosis of COVID-19 pneumonia. Among them, consolidation and crazy paving pattern were found to be highly associated with increased mortality.[8,26,27] Although atypical radiological findings are less taken into account, enlarged mediastinal lymphadenopathy may be useful in predicting outcome. Kunhua et al. found that patients with enlarged mediastinal lymphadenopathy were more likely to deteriorate. However, their sample size was limited and there were only 7 patients with mediastinal lymphadenopathy among a total of 83 patients.[28] Similarly, a study including 189 patients reported that enlarged mediastinal lymphadenopathy was significantly more frequent in critically ill patients ($n = 27$) than in non-critically ill patients ($n = 162$) (51.9% vs 18.5%, $p < 0.05$).[29] Additionally, Xavier et al. found that enlarged mediastinal lymphadenopathy was seen in 66% of 9 critically ill patients who were admitted to intensive care unit.[30] Sardanelli et al. also suggested a possible link between enlarged mediastinal lymphadenopathy and a worse outcome in COVID-19 patients. The authors indicated that enlarged mediastinal lymphadenopathies were more frequent in patients who died than in those who survived (27% of 136 vs. 14% of 274 ($p = 0.001$)). 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.[18] 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.

Since lymphangiogenesis is one of the most crucial findings of inflammation,[31] enlarged mediastinal lymphadenopathy is a considerable finding in inflammatory diseases. In patients with IPF, characterized by chronic inflammation, the presence of enlarged mediastinal

**Table 2**
Univariate and multivariate analysis for 30-day mortality.

| Variable | Category | Univariate analysis | | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|---|
| | | n | OR | CI (95%) | p | 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** | 3.74 | 2.06–6.79 | **<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** | 1.93 | 1.09–3.40 | **0.02** |
| | Consolidation (−) | 333 | 1 | Ref | | | | |
| Bilateral/unilateral lung involvement | Bilateral | 591 | 6.67 | 0.9–49.0 | **0.03** | | | |
| | Unilateral | 59 | 1 | Ref | | | | |
| Mediastinal lymphadenopathy | Present | 60 | 2.7 | 1.3–5.4 | **0.009** | 2.38 | 1.13–4.98 | **0.02** |
| | Absent | 590 | 1 | Ref | | | | |

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.

| | Deceased patients ($n = 12$) | Survived patients ($n = 48$) | p value |
|---|---|---|---|
| Lymph node station | | | |
| 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) | 0.49 |
| 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 |

lymphadenopathy was found to be associated with clinical worsening.[19,32] This may explained by the fact that lymphangiogenesis and lymphatic remodeling resulted by chronic ongoing inflammation lead to progressive fibrosis.[33,34] 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.[19] The lung lesions showed right sided and basal predominance in patients with IPF[35] 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.[19] 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.[26] 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 reported to be correlated with a higher systemic inflammatory response.[36] Previous researches investigating potential predictors of the disease severity mainly focused on chest CT score, measuring how much lung parenchyma is involved. These studies had concluded that chest CT scoring system is helpful to grade the lung involvement and higher scores were found to be associated with a worse outcome in patients with COVID-19.[11,24,36] We found no significant difference between unilateral and bilateral lung involvement in terms of mortality. Although we did not calculate chest CT score, we may suggest that solely evaluation of unilateral or bilateral involvement is not helpful in the assessment of the extent of the disease.

Our study has several limitations. First of all; it has a cross-sectional design and longitudinal assessment of CT scans at different stages was not performed. Second; data on smoking status, which may cause enlarged mediastinal lymphadenopathy, was not available. Since invasive microbiological sampling 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 lymphadenopathies 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.

## 5. Conclusions

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 **Ferhat 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.

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## Declaration of competing interest

None.

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