



# Thoracosurgical treatment of pleural complications in patients with coronavirus disease 2019 (COVID-19): A cross-sectional study

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## ABSTRACT

**Introduction:** Pleural complications in coronavirus disease 2019 (COVID-19) are relatively uncommon findings. Pleural involvement in these patients may directly correlate to disease severity and overall prognosis. We aimed to review clinical features and treatment approaches for pleural complications (accumulation of fluid/air inside the pleural cavity) in 45 patients with COVID-19, who were treated at our institution between April 2020 and October 2021.

**Methods:** Our study was designed as single-center, observational, cross-sectional study of 45 patients with COVID-19 and at least one radiologically verified pleural complication. Demographic data, radiological findings, as well as type and number of thoracosurgical intervention(s) were recorded for every patient. We included patients of both genders and various age groups, with positive RT-PCR assay for COVID-19 and radiologic features of pleural complications, which required single or multiple thoracosurgical interventions.

**Results:** Unilateral pleural complications were more common, right-sided pleural complications were found in 44.4% of patients. Right-sided pneumothorax was reported in 26.7% of patients. Almost one-fourth of our patients required invasive mechanical ventilation. Tube thoracostomy was performed in 84.4% of patients with unilateral pleural complications. A fatal outcome was most common in patients over 60 years old. More than half of patients with bilateral pleural complications died in our study.

**Conclusions:** Pleural complications are a rare finding in patients with COVID-19. Tube thoracostomy is the mainstay of treatment for most symptomatic patients with pleural complications. Future research should be directed toward investigation of long-term pulmonary consequences in patients with COVID-19.

**Keywords:** COVID-19; pneumothorax; pleural effusion; emphysema; pleural cavity

## INTRODUCTION

Severe acute respiratory syndrome - coronavirus 2 (SARS-CoV-2) is caused by a member of the *Coronaviridae* family, a broad family of viruses that usually cause mild to moderate upper-respiratory tract illnesses in humans (1). Pleural involvement in patients with coronavirus disease 2019 (COVID-19) may be associated with disease severity and overall prognosis. Common initial radiologic findings include localized pleural thickening and pleural retraction, whereas pleural effusion and pneumothorax are considered late features of disease progression (2). Increased interstitial

fluid content due to diffuse alveolar injury and endothelial damage promotes the permeability of pleural surfaces and a direct invasion of the pleural space by the virus, as revealed by several post-mortem studies of the pleural fluid (3). The overall incidence of pleural effusion among patients with COVID-19 ranges from 2-11%, whereas a small pediatric study even reported the incidence of pleural effusion to be as high as 63% (4). The occurrence of pneumothorax, pneumomediastinum, and subcutaneous emphysema, may represent a different degree of disease severity. The incidence of pneumothorax in patients with COVID-19 amounts up to 1% (5). The severity of pleural complications may depend on certain factors (age, gender, and/or comorbidities); moreover, some patients will eventually require mechanical ventilation. We wanted to investigate clinical features that could contribute to the severity of the disease and review our experience with thoracosurgical treatment of pleural complications as a consequence of the primary disease.

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## METHODS

The study was designed as a retrospective cross-sectional study, in which we collected data on particular patient variables to investigate how they could affect the severity of the disease and the need for thoracoscopic intervention. Ethical approval issued from Ethical board of Clinical center of Sarajevo University was obtained before the study was enrolled. A total of 45 patients admitted to the Clinical Center University of Sarajevo between April 2020 and October 2021 who tested positive for COVID-19 and demonstrated pleural complications that required a thoracoscopic intervention were included in the study. Accumulation of air (pneumothorax), fluid (pleural effusion), as well as other conditions that required immediate thoracoscopic intervention, i.e. pneumomediastinum and subcutaneous emphysema, were documented for each patient, as well as the side of the complication and mean of intervention. Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assays of specimens collected by a nasopharyngeal swab were used to confirm a COVID-19.

Demographic data, radiological findings, and thoracoscopic intervention(s) (one or more pleural taps, tube thoracostomies and incisions for emphysema) were recorded for every patient. Patients of both genders and various age groups, who had positive RT-PCR assay for COVID-19 and radiologic features of pleural complications, which required single or multiple thoracoscopic interventions, were included in the study. Patients with negative RT-PCR assay, as well as patients with so-called post-acute COVID-19 syndrome with pleural complications, did not meet the inclusion criteria and were excluded from the study. Patient data included in this study was properly anonymized and was obtained using the already available medical history of patients.

Descriptive and inferential statistical analyses were applied. Categorical variables were expressed as counts and percentages. Continuous variable with normally distributed data was presented as means and standard deviation and continuous variable with non-normally distributed data was presented with median and interquartile range (IQR) values. *Independent t-tests* were performed to compare the mean of continuous variables with normally distributed data, and *the Mann-Whitney test* was applied to compare the distribution of non-normally distributed data. *The  $\chi^2$  test* was applied to compare the proportion of categorical variables. Statistical analysis was performed by using the *SPSS software package version 20.0*. A *p-value* less than 0.05 ( $p < 0.005$ ) was considered statistically significant.

## RESULTS

In total, 4520 patients with positive RT-PCR assay for COVID-19 were admitted to the Clinical Center University of Sarajevo between April 2020 and October 2021. Among them, 45 patients (1%) with COVID-19 had at least one radiologically verified pleural complication and were enrolled in this cross-sectional study.

Overall, there were 28 (62.8%) male and 17 (37.2%) female patients enrolled in our study. The most common pleural complication altogether was pneumothorax, which was reported in 21 (46.7%) patients, followed by pleural

effusion in 19 (42.2%) patients, and other complications that required immediate thoracoscopic intervention, i.e. pneumomediastinum and subcutaneous emphysema, etc. in five (11.1%) patients. More than half of 19 patients with pleural effusion and three-fifths of 21 patients with other pleural complications, 12 (63.0%) and 4 (80.0%), respectively, were over 60 years old, while almost half of patients with pneumothorax, i.e. 10 (48.0%) patients, were in the age group 31-60 years. The median (IQR) age of all observed patients was 61 (49 to 72) years. Regarding the groups presented in Table 1., the median (IQR) age of patients with COVID-19 who had pleural effusion, pneumothorax and other complications that required immediate thoracoscopic intervention was 64 (58 to 72), 69 (42 to 74), and 66 (48-68), respectively.

Right-sided pleural complications were most common, i.e. they were found in 20 (44.4%) patients. The most common complication was right-sided pneumothorax, reported in 12 (26.7%) patients, followed by left-sided pneumothorax in 8 (17.8%) patients.

More than two-thirds of patients with COVID-19 who had pleural effusion and pneumothorax first visited a doctor within five days from the onset of symptoms, while half of the other group of patients (other complications that required immediate thoracoscopic intervention) first visited a doctor within six to ten days from the onset of symptoms. Moreover, 34 (77.0%) patients were admitted to the hospital within five days after the first visit to the physician. The median (IQR) days from the onset of symptoms to hospital admission were 6 (1.5 to 10) days. Regarding pleural effusion, pneumothorax, and other complications, the mean (SD) of time from the initial onset of symptoms to the hospital admission was  $3.72 \pm 3.28$ ,  $8.75 \pm 9.54$ , and  $15.8 \pm 9.54$  days, respectively. In total, 18 patients (44.0%) were admitted to the hospital within less than five days from the onset of symptoms. The following data is presented in Table 2. Altogether, out of 45 patients, 11 (24.4%) of them had to be placed on mechanical ventilation.

Chest-tube drainage (tube thoracostomy) was the mainstay of treatment in patients with COVID-19, who had pleural complications. This procedure was performed in 38 (84.4%) patients with unilateral pleural complications, whereas in five (11.1%) patients, chest tubes needed to be placed on both sides. On the other hand, thoracentesis was performed in eight (17.8%) patients and pectoral incisions in four (8.9%) patients with extensive subcutaneous emphysema.

Regarding the outcome, 18 (40.0%) patients with pleural complication(s) died. In terms of gender, eight of 17 (47.0%) female patients died and ten of 28 (35.7%) male patients had the same outcome. We found no statistical significance between these two groups ( $p = 0.451$ ). Concerning age groups, a fatal outcome most commonly occurred in patients that were over 60 years old, i.e. in 14 (56.0%) out of 25 patients in this age group. Out of 21 patients with pneumothorax and pneumothorax with either subcutaneous emphysema, pleural effusion, pneumomediastinum, cystic lungs, pleural empyema, serial rib fracture, 12 (57.0%) patients died. More than half of patients with bilateral pleural complications had a fatal

**TABLE 1.** Gender, age and location of pleural complications in patients with COVID-19 (n=45)

Diagnosis	Pleural effusion (N=19)		<sup>a</sup> Pneumothorax (N=21)		<sup>b</sup> Other (N=5)		Total (N=45)	
Variable	N	%	N	%	N	%	N	%
Gender								
Female	10	52.0	6	28.6	1	20.0	17	37.8
Male	9	47.4	15	71.4	4	80.9	28	62.2
Age group								
≤30	0	0.0	2	9.5	1	20.0	3	6.7
31-60	7	36.8	10	47.6	0	0.0	17	37.8
>60	12	63.2	9	42.9	4	80.0	25	55.6
Age (years)								
Me (IQR)	64.00 (58.00-72.00)		59.00 (42.50-74.5)		66.00 (38.50-68.50)		61.00 (49.00-72.00)	
Location								
Right	6	31.6	12	57.1	2	40.0	20	44.4
Left	7	36.8	8	38.1	1	20.0	16	35.6
Bilateral	6	31.6	1	2.2	2	40.0	9	20.0

<sup>a</sup>Pneumothorax and pneumothorax with either subcutaneous emphysema, pleural effusion, pneumomediastinum, cystic lungs, pleural empyema, and/or serial rib fracture; <sup>b</sup>Other include the following diagnosis: other cases of hydrothorax, exudative pleuritis

**TABLE 2.** The timeline of disease progression in patients with COVID-19 with pneumothorax, pleural effusion and other pleural complications (n=45)

Diagnosis	Pleural effusion (N=19)		<sup>a</sup> Pneumothorax (N=21)		<sup>b</sup> Other (N=5)		Total (N=45)	
Variable	N	%	N	%	N	%	N	%
Time from onset of symptom to first visit doctor (days)								
≤5	15	83.3	14	77.8	1	25.0	30	75.0
6-10	3	16.7	3	16.7	2	50.0	8	20.0
>10	0	0.0	1	5.6	1	25.0	2	5.0
Time from first visit a doctor to admission of hospital (days)								
≤5	19	100.0	11	55.0	4	80.0	34	77.3
6-10	0	0.0	8	40.0	0	0.0	8	18.2
>10	0	0.0	1	5.0	1	20.0	2	4.5
Time from onset of symptoms to admission to hospital (days)								
	13	72.2	5	26.3	0	0.0	18	43.9
6-10	4	22.2	8	42.1	2	50.0	14	34.1
>10	1	5.6	3	15.8	0	0.0	9	22.0
$\bar{x} \pm SD / Me (IQR)$	3.72±3.28		8.75±6.8		15.8±9.54		6.0 (1.5-10)	
Mechanical ventilation								
Yes	1	5.3	9	42.9	1	20.0	11	42.9
No	18	94.7	12	57.1	4	80.0	34	57.1

<sup>a</sup>Pneumothorax and pneumothorax with either subcutaneous emphysema, pleural effusion, pneumomediastinum, cystic lungs, pleural empyema, and/or serial rib fracture; <sup>b</sup>Other include the following diagnosis: other cases of hydrothorax, exudative pleuritis

outcome as well, i.e. in 5 (55.5%) of 9 patients. Moreover, almost half of patients with two pleural complications died, i.e. 3 (43.0%) out of 7 patients, as seen in Table 3.

## DISCUSSION

COVID-19 represents an ongoing pandemic of international concern, which causes a wide range of clinical presentations. Hallmark findings of respiratory infection caused by this virus include bilateral patchy ground-glass opacities with a predominantly peripheral distribution, whereas pleural complications are still considered uncommon.

45 patients (1%) among the total number of 4520 RT-PCR positive patients admitted to the Clinical Center University of Sarajevo between April 2022 and October 2022, had at least one radiologically verified pleural complication and were enrolled in this observational study. According

to several case series and meta-analyses, the incidence of pleural effusion in patients with COVID-19 varies between 2-11% (6), even though some authors have reported an incidence of up to 20% (7). The overall incidence of pneumothorax was even lower, i.e. Chong et al. reported an incidence of 0.3% among all hospitalized patients with COVID-19 (8). Our study concluded that the most common pleural complication was pneumothorax, which was reported in 46.7% of patients, followed by pleural effusion in 42.2% of patients, whereas 11.1% of patients had other complications that required immediate thoracosurgical intervention, i.e. pneumomediastinum and subcutaneous emphysema.

There was a predominance of male to female patients in our study, 62.8% of our patients were males and 37.2% females, whereas, in terms of age, the median (IQR) age of patients

**TABLE 3.** Outcome of treatment in patients with COVID-19 with pneumothorax, pleural effusion and other pleural complications (n=45)

Outcome	Died (n=18)		Recovered (n=27)		P value	Total (n=45)	
Variable	n	%	n	%		n	%
Gender							
Female	8	47.1	9	52.9	<sup>c</sup> 0.451	17	37.8
Male	10	35.7	18	64.3		28	62.7
Age group							
<30	0	0.0	3	100.0		3	6.7
31-60	4	23.5	13	76.5	-	17	37.8
≥60	14	56.0	11	44.0		25	55.6
Age							
$\bar{x} \pm SD / Me (IQR)$	67.3±12.3		54.52±20.49		<sup>c</sup> 0.022*	61 (49-72)	
Pleural complication							
Pleural effusion	5	26.3	14	73.7		19	42.27
<sup>a</sup> Pneumothorax	12	57.1	9	42.9	-	21	46.7
<sup>b</sup> Other	1	20.0	4	80.0		5	11.1
Location							
Right	9	45.0	11	55.0	<sup>c</sup> 0.270	20	44.4
Left	4	25.0	12	75.0		16	35.6
Bilateral	5	55.6	4	44.4		9	20.0
Number of pleural complications							
1	13	36.1	23	63.9		36	80.0
2	3	42.9	4	57.1	-	7	15.6
3	2	10.0	0	100.0		2	4.4

<sup>a</sup>Pneumothorax and pneumothorax with either subcutaneous emphysema, pleural effusion, pneumomediastinum, cystic lungs, pleural empyema, and/or serial rib fracture; <sup>b</sup> Other include the following diagnosis: other cases of hydrothorax, exudative pleuritis;

<sup>c</sup>Chi Square test; <sup>d</sup> T-test for Equality means

\*The significance level is 0.05

with COVID-19 who had pleural effusion, pneumothorax and other complications that required immediate thoracoscopic intervention was 64, 69, and 66, respectively. One retrospective study by *Majidi et al.*, which included 552 patients with symptomatic COVID-19, reported that patients older than 50 years had a higher incidence of pleural effusion and that the presence of pleural effusion did not necessarily correspond to the severity of the disease itself (9). Unilateral pleural complications were more common, right-sided pleural complications were found in 44.4% of patients, and the most common complication was right-sided pneumothorax, reported in 26.7% of patients, followed by left-sided pneumothorax in 17.8% of patients and left-sided pleural effusion in 15.5% of patients. This finding is consistent with reports of *Saha, Chong, Malik et al.*, who reported a higher incidence of unilateral pleural complications (10).

Several epidemiologic studies have demonstrated that rates of invasive mechanical ventilation among patients admitted to intensive care unit settings range from 29.1% to 89.9% (11, 12). In our study, 11 (24.4%) patients out of 45 enrolled had to be placed on mechanical ventilation during their hospital stay.

The chest drainage approach is successful in the non-operative management of excess fluid and air in patients with unilateral or bilateral pleural complications. Most critically ill patients (most notably mechanically ventilated) with pneumothorax require tube thoracostomy, even though researchers have raised concerns regarding the

possibility of aerosol generation and dissemination through the chest tube and water seal drainage system. Thoracostomy was the mainstay of treatment in our patients and was performed in 84.4% of patients with unilateral pleural complications, whereas in 11.1% of patients, chest tubes needed to be placed on both sides.

According to a study conducted by *Zhan et al.*, pleural effusion should be used as a potential predictor for the progression to severe or critical conditions in patients with COVID-19. In other words, it may be a sign of severe inflammation and can indicate a poor prognosis (13). Our study demonstrated that 40% of patients with pleural complications had a fatal outcome, most commonly that was the case in patients that were over 60 years old. More than half of patients with bilateral pleural complications and 43% of patients with COVID-19 with two pleural complications had a fatal outcome. More studies are needed to determine whether and to what extent pleural complications play a role in the determination of disease severity in these patients.

Pleural complications are relatively uncommon findings in patients with COVID-19. It remains unclear whether the presence of pneumothorax, pleural effusion, and/or other complication that requires thoracoscopic intervention, is a reliable predictor of poor outcome. Tube thoracostomy remains the mainstay of treatment for most symptomatic patients and non-operative management may be a definite treatment for many patients with pleural complications, as mentioned previously in our study.

Our research was cost effective, generalizable and versatile. Nevertheless, this study has potential limitations, such as sample size, the unavailability of complete patient data (incomplete medical records, partially filled-out surveys, etc.), relatively short-term follow up of patients, as well as lack of previous large-scale research studies on the topic. The outbreak of COVID-19 has proven to be an unprecedented disaster for the whole world, with a broad spectrum of mild to critical respiratory symptoms in various patients. Pleural complications strongly influence the severity of the disease and should be promptly managed. Future research should be directed toward the assessment of long-term pulmonary consequences in patients who had COVID-19, with the development of strategies to withstand and treat potential consequences of similar viral infections in the future. The number of scientific articles related to COVID-19 increases, therefore the knowledge and experience in treating the devastating consequences of this viral infection increase. From the thoracoscopic point of view, it is of paramount importance to recognize a pleural complication related to COVID-19 and to treat it promptly, even in the intensive-care unit setting. Since there were no strict guidelines in the management of pleural complications, especially at the beginning of the pandemic, we wanted to share our experience and reflect on our results in treating these potentially life-threatening conditions.

## CONCLUSIONS

Even though pleural complications still represent an uncommon finding among patients with COVID-19, future research should be directed toward investigation of long-term pulmonary consequences and suitable treatment options.

## DECLARATION OF INTERESTS

The authors declare no conflicts of interests.

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