Reduced survival in patients requiring chest tubes with COVID-19 acute respiratory distress syndrome

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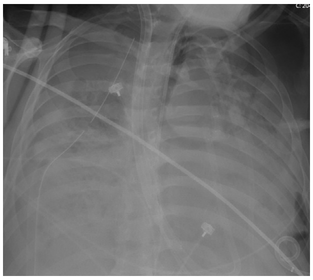
ABSTRACT

Background: Numerous complications requiring tube thoracostomy have been reported among critically ill patients with COVID-19; however, there has been a lack of evidence regarding outcomes following chest tube placement.

Methods: We developed a retrospective observational cohort of all patients admitted to an intensive care unit (ICU) with confirmed COVID-19 to describe the incidence of tube thoracostomy and factors associated with mortality following chest tube placement.

Results: In total, 1705 patients with laboratory confirmed COVID-19 patients were admitted to our ICUs from March 7, 2020, to March 1, 2021, with 69 out of 1705 patients (4.0%) receiving 130 chest tubes. Of these, 89 out of 130 (68%) chest tubes were indicated for pneumothorax. Patients receiving tube thoracostomy were much less likely to be alive 90 days post-ICU admission (52% vs 69%; $P < .01$), and had longer ICU (30 vs 5 days; $P < .01$) and hospital (37 vs 10 days; $P < .01$) lengths of stay compared with those without tube thoracostomy. Patients who received tube thoracostomy and survived at least 90 days post-ICU admission had shorter times to first chest tube insertion (8.5 vs 17.0 days; $P = .01$) and a nonsignificantly higher static compliance (20.0 vs 17.5 mL/cm H_2O; $P = .052$) at the time of chest tube placement than those who had expired. Logistic regression analysis demonstrated an association between time to first chest tube and decreased survival when adjusted for covariates.

Conclusions: Requiring a chest tube in COVID-19 is a negative prognostic end point. Delayed development of chest tube requirement was associated with a decreased survival and could reflect a poor healing phenotype. (JTCVS Open 2022;10:471-7)



Case example of severe ARDS requiring both surgical chest tube and percutaneous pigtail.

CENTRAL MESSAGE

Patients with COVID-19 ARDS have a high incidence of chest tube placement. Patients who receive a chest tube with COVID-19 ARDS have a worse outcome and a higher incidence of mortality.

PERSPECTIVE

The natural arc of severe COVID-19 ARDS lung pathology progresses from a highly compliant lung to stiff noncompliant fibrotic lung. Pneumothorax, pleural effusion, and empyema are significant occurrences in COVID-19 ARDS. This study is a retrospective cohort study of 1705 patients with COVID-19 ARDS who required a total of 130 chest tubes for any indication during their ICU stay.

Video clip is available online.

The novel coronavirus SARS-CoV-2 was first reported in Wuhan, China, in December 2019 and has since become a global pandemic.[1,2] COVID-19 is the clinical syndrome caused by infection with SARS-CoV-2 and is associated with significant morbidity and mortality, including acute

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Received for publication July 19, 2021; revisions received Feb 23, 2022; accepted for publication March 30, 2022; available ahead of print May 12, 2022.

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2666-2736

https://doi.org/10.1016/j.xjon.2022.03.008

Abbreviations and Acronyms
ARDS = acute respiratory distress syndrome
ICU = intensive care unit

respiratory failure requiring admission to an intensive care unit (ICU) and advanced respiratory support.[3,4] Among critically ill patients with COVID-19, several sequelae have been reported that may necessitate tube thoracostomy, including pneumothorax and pleural effusions.[5,6] These complications are not rare, with 1 report describing a 5.9% incidence rate of pneumothorax within 24 hours of intubation among critically ill patients with COVID-19.[7]

There have been numerous reports of tube thoracostomy in COVID-19 for pneumothorax and pleural effusion, yet these populations have been limited in size and included noncritically ill patients.[6-17] Furthermore, there has been scant evidence regarding incidence and postprocedure outcomes for critically ill patients with COVID-19 with tube thoracostomy. Among other globally important respiratory illnesses, one series of H1N1 pandemic influenza ICU patients reported a 14% tube thoracostomy rate and 1 small series of patients with SARS reported that 3 out of 6 patients with pneumothorax received tube thoracostomy.[18,19] Current guidance regarding chest tube management in COVID-19 has been limited and mostly centered on avoiding potential provider exposure.[20]

Patients with COVID-19 receiving mechanically ventilation are at unique risk for lung injury. The clinical course for so-called COVID-19 acute respiratory distress syndrome (ARDS) is dynamic and is believed to progress from a high-compliance phenotype to a low-compliance phenotype.[21] Failure to adequately appreciate how COVID-19 ARDS differs from so-called typical ARDS and recognize its transition from the compliant to stiff phenotype could expose patients to underappreciated barotrauma and resultant pneumothorax. The increased risk for secondary bacterial infections in patients with COVID-19 may also contribute to increased lung injury.[22] Furthermore, there is a lack of consensus on ventilator management and lung rest in COVID-19 ARDS and how to prevent further lung injury. Despite this unique potential for serious lung injury in COVID-19 ARDS, there is scant evidence regarding the clinical course of patients following tube thoracostomy.[23] In this study, we sought to characterize the clinical course of critically ill patients with COVID-19 with chest tubes to better understand the implications on morbidity and mortality. We present a retrospective cohort study describing all COVID-19 patients admitted to our ICU who underwent tube thoracostomy in a large multihospital health care system.

METHODS

Study Design and Population

This retrospective observational cohort study was performed within the University of Pennsylvania Health System, composed of several hospitals, including the Hospital of the University of Pennsylvania, a 776-bed teaching hospital; the Penn Presbyterian Medical Center, a 365-bed teaching hospital; and Penn Princeton Medical Center, a 245-bed community hospital, all caring for adult patients (older than age 18 years) primarily living in Southeastern Pennsylvania and Southern New Jersey. Patients with COVID-19 were treated in a variety of ICU settings and were managed by intensivists with backgrounds in anesthesiology critical care, pulmonary and critical care medicine, surgical critical care, and emergency medicine critical care.

We identified all patients admitted to 1 of our ICUs diagnosed with COVID-19 from March 7, 2020, to March 1, 2021, based on nasopharyngeal swab reverse-transcriptase polymerase chain reaction testing.[1] This study was reviewed and approved on May 20, 2020 by the University of Pennsylvania Institutional Review Board (No. 842836) and the requirement for informed consent was waived due to minimal risk to subjects and retrospective chart review only.

Data Collection and Outcomes

We queried our local electronic health record database (EPIC) for all patients with a laboratory confirmed active SARS-CoV-2 infection admitted to an ICU in our health system. Demographic information, past medical history, chest tube presence, number, output, and duration, mechanical ventilation parameters, and mortality were collected for all patients. The last recorded mechanical ventilation parameters within 48 hours before chest tube insertion were collected. Tidal volume was standardized according to predicted body weight. A team of trained medical researchers performed manual chart review to record the indications for each chest tube. Data collection ended June 1, 2021.

Patients were divided into 2 cohorts based on the presence of absence of at least 1 tube thoracostomy during the first COVID-related admission to the ICU. The primary end point was survival at 90 days after their first ICU admission (90-day survival). Secondary end points included in-hospital mortality, length of hospital stay, length of ICU stay, and presence and duration of mechanical ventilation.

Study Definitions

Patients with tube thoracostomy were defined by the presence of a tube thoracostomy procedure code or output measurement in the electronic health record. Patients who had tube thoracostomy for trauma with an incidental COVID-19 diagnosis or as a routine part of a surgical procedure were excluded from this study (n = 34). When investigating mortality by chest tube indication, patients with multiple chest tubes with different indications were included in all matching indication groups.

Past medical history was categorized according to the Charlson comorbidity index with ICD-10 codes present at admission.[24] The first ICU admission date was selected for patients with multiple ICU admissions. Ventilator data were collected retrospectively at the time of chest tube placement. Ventilator settings immediately before chest tube placement as well as compliance recorded in the 24 hours before chest tube placement were recorded among those receiving mechanical ventilation. Driving pressure was defined as plateau airway pressure minus positive end-expiratory pressure during an inspiratory pause and used to determine the static compliance of the lung. Patients not receiving mechanical ventilation or missing a ventilator parameter value were not included in analyses of the parameter of interest.

Statistical Analysis

All descriptive statistics are presented as medians with interquartile ranges (IQR) or absolute numbers with proportions. All continuous variables were compared using the Student 2-sample *t* test or the Mann-Whitney *U* test, depending on the underlying distribution. All categorical variables were compared using Fisher exact test with SE.

Statistics were computed by custom Python (version 3.7.6; Python Software Foundation) scripts using the pandas (version 1.0.1), NumPy (version 1.18.1), Stata 17, Statsmodels (version 0.11.0), and SciPy (version 1.4.1) libraries. Multivariable logistic regression models were created to examine the relationships between presence of time to first chest tube and 90-day survival. Univariate logistic regression was performed between demographic and clinical variables and 90-day survival, and any covariate with $P < .50$ was selected for inclusion into the model. Lasso regularization was performed to minimize overfitting. Coefficients are reported as odds ratios (ORs).

RESULTS

Patient Characteristics

We found 1705 patients with laboratory confirmed COVID-19 admitted to 1 of our center's ICUs from March 7, 2020, to March 1, 2021, with 69 patients (4.0%) receiving 130 chest tubes (Video Abstract). Demographic factors for patients with and without tube thoracostomy are presented in Table 1. Patients undergoing tube thoracostomy were more likely to be younger, male, have lower body mass index, and self-identify as Black or have an unspecified race. No significant differences in rates of comorbid conditions were found.

Clinical characteristics for patients with tube thoracostomy are presented in Table 2. Most chest tubes were placed due to pneumothorax (89 out of 130; 68%). Most patients required a single chest tube and the median time to chest tube placement was 13 days (IQR, 5-23 days) following ICU admission. The median duration of chest tube placement being 10 days (IQR, 4-21 days).

Ventilator Parameters

Seventy-two percent of patients receiving tube thoracostomy often were on volume control before chest tube insertion. Of note, immediately before chest tube insertion patients had a median driving pressure of 20.4 cm H_2O (IQR, 18.0-26.0 cm H_2O), and a median static compliance of 19.0 mL/cm H_2O (IQR, 12.0-25.8 cm H_2O) (See Table 3). 90% (62 out of 69) of patients with tube thoracostomy required mechanical ventilation during admission, a significantly increased incidence than among patients without tube thoracostomy (See Table 4).

Patient Outcomes

Patients with tube thoracostomy had higher mortality rates at 90 days post-ICU admission, at time of discharge, or the end of the study follow-up period. Patients with chest tubes had significantly longer lengths of stay in both the ICU and hospital (See Table 4). Among patients with chest tubes, patients with at least 1 chest tube indicated for

TABLE 1. Characteristics of patients with and without tube thoracostomy

Characteristic	Tube thoracostomy	Without tube thoracostomy	*P* value
Patients	69	1636	–
Median age (y)	59 (46-71)	65 (53-75)	<.01
Female	21 (30)	730 (45)	.01
Median body mass index	28.1 (23.5-31.6)	28.7 (24.5-34.7)	.73
Race			
White	33 (48)	709 (43)	.46
Black	18 (25)	774 (47)	.01
Asian/Pacific Islander	8 (12)	97 (6)	.07
Native American/American Indian	0 (0)	2 (0)	1.0
Other/unknown	11 (16)	87 (5)	<.01
Hispanic of any race	9 (13)	150 (9)	.29
Comorbidities			
Congestive heart failure	2 (3)	71 (4)	.77
Chronic pulmonary disease	2 (3)	27 (2)	.33
Diabetes without complications	9 (13)	339 (21)	.13
Peripheral vascular disease	1 (1)	67 (4)	.52
Myocardial infarction	0 (0)	14 (1)	1.0
Renal disease	2 (3)	43 (3)	.70
Cancer	0 (0)	49 (3)	.26
Mild liver disease	1 (1)	44 (3)	1.0
Moderate or severe liver disease	0 (0)	4 (0)	1.0
Connective tissue disease/rheumatic disease	0 (0)	6 (0)	1.0
Paraplegia or hemiplegia	0 (0)	8 (0)	1.0

Values are presented as n, n (%), or median (interquartile range).

TABLE 2. Clinical parameters for patients with chest tubes (n = 130)

Parameter	Result
Listed indications for all chest tubes	
Pneumothorax	89 (68)
Pleural effusion	19 (15)
Hemothorax	6 (5)
Empyema	4 (3)
Other	12 (9)
No. of tubes per patient	1.88 (1-3)
Output in first 24 h for first tube (mL)	345.0 (130.0-800.0)
Total output per patient (mL)	1740.0 (540.0-4566.0)
Time to first chest tube from ICU admission (d)	13 (5-23)
Time to first chest tube from initiation of mechanical ventilation (d)	9 (1-18)
Chest tube duration (d)	10 (4-21)
Time to first chest tube from ICU admission (d)	13 (5-23)

Values are presented as n (%) or median (interquartile range). *ICU*, Intensive care unit.

pneumothorax had lower 90-day survival rates compared with those who did not (51% ± 5.3% vs 78% ± 4.4%; $P < .01$) as well as survival at 60 days by Kaplan-Meier analysis (Figure 1). Among all patients with chest tubes, patients who were alive 90 days post-ICU admission had a shorter median time to initial chest tube (8.5 days; IQR, 1-18.0 days vs 17.0 days; IQR, 8.0-25.0 days; $P = .01$), with a nonsignificantly higher static compliance (20.0 mL/cm H_2O; IQR, 12.8-25.0 mL/cm H_2O vs 17.5 mL/cm H_2O; IQR, 11.3-28.3 mL/cm H_2O; $P = .052$) at time of chest tube insertion. To further characterize the relationship between time to first chest tube and mortality, we developed a multivariable logistic regression model to account for several prespecified demographic and clinical covariates. Our model demonstrated a significant decrease

TABLE 3. Last recorded mechanical ventilation parameters before patients' first tube thoracostomy

Ventilation parameter	Result
F_{IO_2} (n = 57)	0.80 (0.50-1.00)
Respiratory rate (breaths/min) (n = 57)	27 (22-32)
Tidal volume (mL/kg) (n = 56)	5.7 (4.3-6.4)
PEEP (cm H_2O) (n = 57)	10.0 (7.5-12.0)
Driving pressure (cm H_2O) (n = 57)	20.4 (18.0-26.0)
Compliance (mL/cm H_2O) (n = 46)	19.0 (12.0-25.8)

Values are presented as median (interquartile range). F_{IO_2}, Inspired oxygen fraction; *PEEP*, positive end-expiratory pressure.

TABLE 4. Outcomes for patients with and without tube thoracostomy

Outcome measure	Tube thoracostomy (n = 69)	Without tube thoracostomy (n = 1636)	*P* value
90-Day post-ICU survival	36 (52)	1131 (69)	<.01
In-hospital survival	38 (55)	1192 (73)	<.01
Hospital length of stay (d)	37 (20-56)	11 (5-21)	<.01
ICU length of stay (d)	30 (15-46)	5 (2-12)	<.01
On mechanical ventilation	62 (90)	707 (43)	<.01
Length of mechanical ventilation (d)	33 (12-54)	10 (3-18)	<.01

Values are presented as median (interquartile range) or n (%). *ICU*, Intensive care unit.

in 90-day survival with increased time to chest tube (OR, 0.93; $P = .03$), when accounting for male sex (OR, 1.2; $P = .86$), age (OR, 0.94; $P = .02$), body mass index (OR, 0.93; $P = .22$), self-reported Black race (OR, 0.97; $P = .97$), self-reported Asian race (OR, 0.69; $P = .80$), mechanical ventilation requirement during hospitalization (OR, 60.7; $P = .04$), and inspired oxygen fraction (OR, 0.97; $P = .03$), driving pressure (OR, 0.94; $P = .20$), and positive end-expiratory pressure (OR, 0.88; $P = .22$) immediately before chest tube insertion.

DISCUSSION

This data highlights that patients who require a chest tube for pneumothorax represent a diseased lung, in which those patients with pneumothorax will have higher mortality in critically ill patients with COVID-19 (Figure 2). Patients who receive chest tubes have increased mortality, long duration of mechanical ventilation, and hospital and ICU length of stay compared with those patients who did not develop a pneumothorax requiring chest tube placement. Additionally, we were able to estimate the prevalence of tube thoracostomy (4.0%) in COVID-19 ICU patients and describe the indications for chest tube placement. Our work also suggests a novel metric to aid in prognostication among patients with COVID-19 who require tube thoracostomies. That is prolonged ICU stay before requiring tube thoracostomy may reflect worse underlying lung pathology than patients with requirement of chest tube early in their ICU stay.

The 90-day-post-ICU admission mortality rate for our population of patients (31% vs 31%) was similar to another large European ICU cohort.[25] Furthermore, our work is concordant with previous literature suggesting that pneumothorax is a common and distinct risk in patients with COVID-19, with pneumothorax representing the majority of our indications for chest tube.[26,27] Although previous studies suggested that pneumothorax was not a negative prognostic sign in COVID-19 patients, our work shows this finding may not extend to critically ill populations as

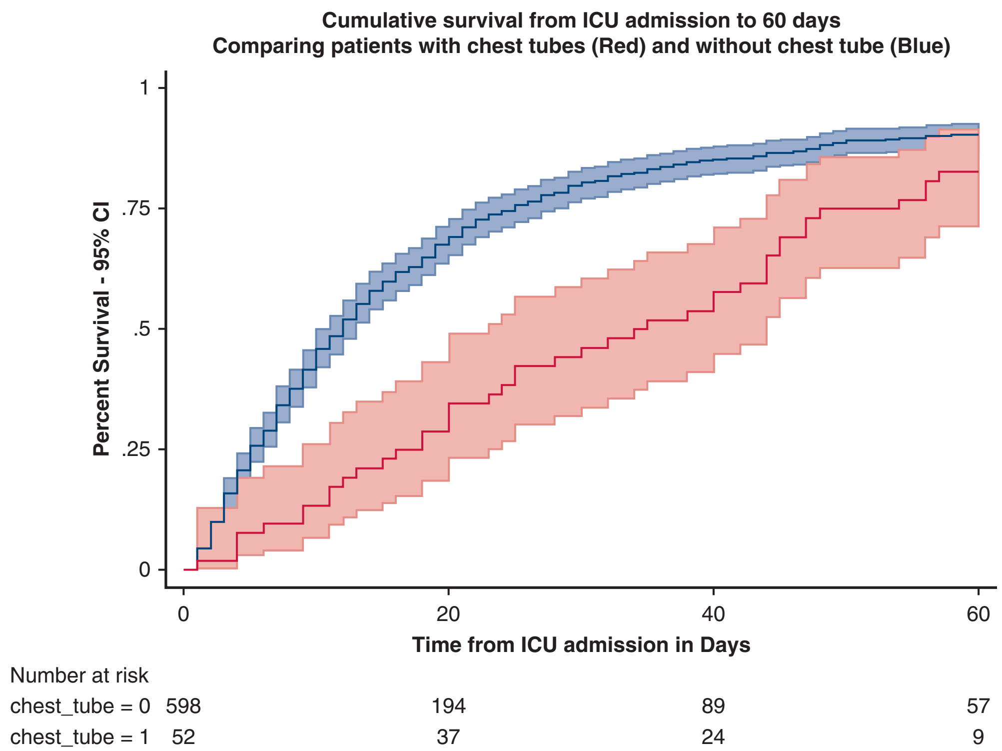

FIGURE 1. Cumulative survival from intensive care unit (ICU) admission to 60 days by comparing the chest-tube cohort versus the nonchest-tube cohort from day 0 to day 60 of ICU admission.

our patients with pneumothorax had lower survival rates at 90 days.[6,28]

This relationship between delayed development of a chest tube requirement was not wholly unexpected. Many reports have discussed the potential for significant change in lung pathophysiology over the course of COVID-19 ARDS, and the development of a low-compliance, fibrotic lung.[21,29,30] Failure to appreciate these changes in lung dynamics and adjust ventilation parameters accordingly may lead to barotrauma and significant pneumothorax requiring chest tube placement. Moreover, ventilator-induced lung injury may be particularly difficult to repair in stiff noncompliant COVID-19 ARDS leading to prolonged ICU courses and increased mortality seen in patients with non-COVID–19 ARDS.[31] Prior reports of bronchopleural fistulas developing in patients with COVID-19 following prolonged ICU stays suggest that a poor healing ARDS physiology may exist in a subset of patients with an advanced disease course. Mechanical ventilation data just before chest tube insertion seems to support the existence of a brittle phenotype among our patients requiring tube thoracostomy with our reported compliances lower (19 vs 27-41 mL/cm H_2O) and driving pressures higher (20.4 vs 9.5-15 cm H_2O) than reported in other published mechanically ventilated COVID-19 populations.[32] Driving pressure is a key predictor of ventilator-induced lung injury, and our observed driving pressure before tube thoracostomy was elevated compared with prior published cohorts of patients with ARDS and may be contributing to our patients' chest tube requirement.[33-35]

This work underscores the importance of recognizing the potential for ventilator-associated lung injury and a poor healing phenotype in critically ill patients with COVID-19. It also suggests that if lung injury does occur, delayed development of a chest tube requirement with decreased compliance may indicate a poor outcome and should be factored into decisions surrounding chest tube placement and management.

Our work is not without limitations. Because this was a retrospective observational analysis on a large, incomplete dataset we cannot eliminate the possibility of nonrandom missing or incorrectly labeled observations. We were unable to include a measure of disease severity as Sequential Organ Failure Assessment and Acute Physiology, Age, and Chronic Health Evaluation II scores were not readily available or calculable for many of our patients. Furthermore, the relationship between time to first chest tube and mortality is potentially complicated by unmeasured confounders.

CONCLUSIONS

Tube thoracostomy is a procedure with a low (4%) but significant frequency in critically ill patients with COVID-19, and may be a negative prognostic sign. Time to first chest tube is associated with worse mortality. Larger,

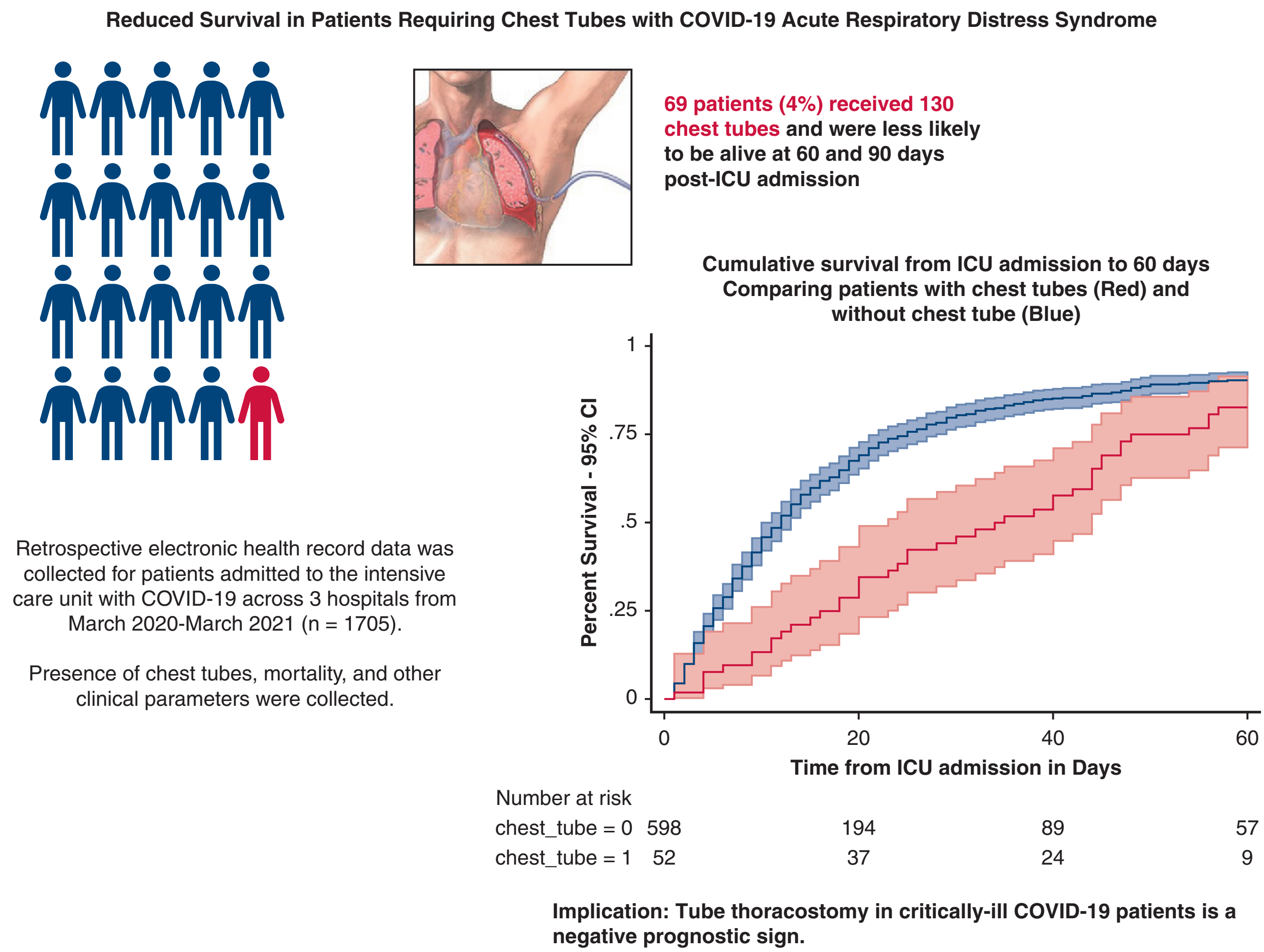

FIGURE 2. Depiction of the study's methods, results, and implications.

prospective studies are needed to further examine these relationships.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

The authors thank the Clinical Research Informatics Core the University of Pennsylvania Health System for the querying and collection of patient information from our electronic health records. The mapping of ICD-10 codes to Charlson comorbidity index values was adapted from https://github.com/chvlyl/Comorbidity_Index.

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Key Words: critical care, mechanical ventilation, COVID-19, tube thoracostomy