INTRODUCTION

Viral infections can cause severe respiratory failure, requiring specialized medical care. Coronaviruses are responsible for three conditions that have spread widely over the past two decades: severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and now COVID-19 (coronavirus disease 2019). The etiological factor of COVID-19 is the second severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first patients to develop symptoms of the disease were residents of Wuhan, a city in China's Hubei Province. Later, there was a violent human-to-human transmission of the virus, contributing to the intercontinental incidence of SARS-CoV-2, and the World Health Organization (WHO) in March 2020 designated a series of subsequent cases as a pandemic. Although SARS-CoV-2 appears to have a lower lethality than the viruses that cause SARS or MERS, its infectivity is higher.1

SARS-CoV-2 uses angiotensin converting enzyme 2 (ACE2) to enter the cell, and host proteases (transmembrane serine protease type 2-TMPRSS2, cathepsin L, furin) participate in the proteolytic processing of the S protein, which is necessary for the activation of the endocytic pathway. TMPRSS2 has been shown to be co-expressed with ACE2 in nasal epithelial cells, lung, and bronchi, which explains some SARS-CoV-2 tissue tropism. The virus binds to epithelial cells in the airways and then migrates...
down to the alveoli. Rapid replication of SARS-CoV-2 can cause cytokine storm syndrome, which leads to acute respiratory distress syndrome. In some cases, COVID-19 may even lead to multi-organ failure.²

Türk et al. retrospectively assessed the pleural complications of COVID-19 pneumonia in hospitalized patients, such as pneumothorax, pneumothorax, pleural effusion, and empyema. The analyzed data come from the period from March to December 2020. The study included 33 people aged 30–90 years, including 11 women and 20 men. Pneumothorax was diagnosed in the greatest number of patients (i.e., 20, 65%), and only one case of empyema. The Staphylococcus aureus was isolated from the culture.³

Tracheo-esophageal fistula is pathological communication between the posterior wall of the trachea or bronchus with the adjacent esophagus. It can be congenital or acquired. It occurs in 75% of patients undergoing long-term invasive mechanical ventilation (MV).⁴ The formation of TEF is favored by low pressure and a large volume of the endotracheal cuff.⁵ The average time it takes for a fistula to develop is 42 days.⁶ Due to the current epidemiological situation, an increase in the number of intubated patients is expected, and hence, more frequent occurrence of TEF.

Treatment of a tracheo-esophageal fistula is problematic. It is influenced by factors such as difficulties in the patient’s ventilation resulting from the location of the TEF, loss of tidal volume followed by gastric dilation, the possibility of atelectasis, and the need to treat other comorbidities.⁵,⁶

On the contrary, parapneumonic pleural effusion is a common complication of pneumonia. It can lead to an empyema, which depending on the stage, is only treated with antibiotics and drainage or in combination with thoracic surgery.⁷ Less commonly, 20%–30% of the empyema is caused by trauma, chest surgery, esophageal ruptures, cervical infections, and the remaining cases are not related to an earlier cause and are known as primary pleural empyema.⁸ Pleural empyema following COVID-19 pneumonia occurs in less than 5% of cases where SARS-CoV-2 is detected.⁹ The presence of pleural empyema is associated with higher mortality and increased morbidity. 20%–30% of patients with empyema die or will require further surgery only 1 year after its occurrence.⁸

2 | CASE REPORT

On June 22, 2020, a 49-year-old patient was transferred to the Intensive Care Unit (ICU) of the Clinical Hospital No. 1 in Zabrze after prior treatment in a facility dedicated to COVID-19 patients. The patient was admitted with chronic respiratory failure and esophageal-tracheal fistula in the course of severe SARS-CoV-2 pneumonia, acute circulatory and respiratory failure, bacteremia, bacterial and fungal pneumonia, right lung abscess, right pleural empyema, pneumothorax of the right pleural cavity, acute liver failure, acute renal failure, protein and energy wasting, critical state polyneuropathy. The chest X-ray from April 26, 2020, showed a right-sided pneumothorax up to 45 mm thick. Single drainage of the right pleural cavity was performed. In the control chest X-ray after drainage, almost complete regression of pneumothorax but bilateral congestive-inflammatory pulmonary densities were observed. Two abscesses were detected in computed tomography (CT) of the chest, and again on April 28, 2020, the right pleural cavity was drained. Chest X-ray performed on April 30, 2020, showed the enlarging chambers of the empyema of the right pleural cavity. After thoracic surgery consultation, it was decided to perform a right-sided thoracotomy (April 30, 2020). During the operation, a small amount of purulent blood was visible in the pleural cavity and two holes in the lower lobe of the right lung, probably after perforated abscesses. Cultures of pus showed the presence of Pseudomonas aeruginosa bacteria and fungi Aspergillus sp. Mechanical ventilation was used from April 11, 2020, to July 16, 2020. On May 19, 2020, gastroscope revealed the presence of a tracheo-esophageal fistula 15 cm from the incisor line, which was confirmed by a CT scan (Figure 1). On June 9, 2020, a nutritional intestinal fistula was placed on the second intestinal loop from the Treitz ligament. At the same time, pharmacotherapy was modified based on the current condition of the patient and the obtained results of bacteriological, morphological, and biochemical tests. CVVHDCiCa (Continuous Veno-Venous Hemodialysis with citrate anticoagulation) renal replacement therapy was started temporarily.

FIGURE 1 Image of the tracheoesophageal fistula in computed tomography, 23/06/2020
After stabilization of the patient’s condition and optimal preparation for surgery, on July 16, 2020, cervicotomy, segmental tracheal resection, esophageal-tracheal fistula excision, and esophagus stitching were performed. After treatment and rehabilitation, the patient began to recover (Figure 2). On July 27, 2020, the patient was transferred to the Thoracic Surgery Ward of the Clinical Hospital No. 1 in Zabrze, from where he was discharged on July 30, 2020, in good general condition. In September 2020, the patient was re-admitted to the thoracic surgery ward for a control gastrofiberoscopy. The examination did not reveal any abnormalities. On March 9, 2021, a chest CT scan was performed, which revealed a slight decrease in the aeration of the left upper lobe and fibrous changes in its apex, in segments 4 and 5 of the left lung, fibrous changes with bronchiectasis, small interstitial densities and small fibrous changes in the peripheral part of the left lung, elevation of the right diaphragm dome.

3 | DISCUSSION

So far, several cases of TEF have been documented in patients with COVID-19. One of the first is described by Marzban-Rad et al. as the case of a 25-year-old patient who was admitted to the hospital in December 2019 after a suicide attempt by hanging. Prolonged MV led to TEF with incomplete subglottic constriction. The patient underwent unilateral repair of the trachea to avoid damage to the left recurrent laryngeal nerve. Then, the stenosis site was widened endoscopically with a balloon. Unfortunately, as a result of the patient’s critical condition and infection with SARS-CoV-2, the patient died. Rosati et al. describe a 52-year-old patient with severe respiratory failure in the course of COVID-19, long-term mechanically ventilated, who also developed a tracheoesophageal fistula. The authors suggest that the formation of TEF in patients with SARS-CoV-2 infection may be related to the direct attack of the virus on the cells of the upper respiratory tract, causing inflammatory infiltration on the mucosa and submucosa, which may further weaken the structure of the trachea. Consequently, the risk of creating a connection between the posterior wall of the trachea and the anterior wall of the esophagus, pinched between the cuff of the orotracheal tube and the nasogastric tube (NGT), increases.

The above-described proposed mechanism of TEF formation may also confirm our observations of changes in the image of the tracheobronchial mucosa in patients suffering from COVID-19. In the described case, the mucosa was red with characteristic inflammatory lesions, which could be one of the causes of TEF formation.

Descriptions of four consecutive TEF cases were documented by Granata et al. The article concerns three men and one woman (55–61 years old) infected with SARS-CoV-2, who, due to respiratory failure, received venous-venous extracorporeal membrane oxygenation (V-V ECMO). The treatment strategy was to replace the tracheotomy cannula under endoscopic guidance, perform percutaneous endoscopic gastrojejunostomy, and insert endoluminal sutures of the esophagus. The technique that was used was successful in all patients. One relapsed within 4 weeks. According to the authors, the use of less invasive TEF treatments in patients on V-V ECMO may be a safe therapeutic option.

Roomi et al. describe a 53-year-old woman who also developed severe respiratory failure in the course of COVID-19. The patient was intubated and at the end of MV Week 3 she was diagnosed with a tracheoesophageal fistula. The patient suddenly developed hypoxemia, gastric distension, and a drop in peak pressure from 35 to 22 cm H₂O with the ventilator’s operating settings unchanged. CT of the neck confirmed the presence of a tracheoesophageal fistula. The fistula was temporarily bypassed.

FIGURE 2  Comparison of the regression of changes in the lungs (after COVID-19) over 3 months (from the left: June 22, 2020—before drain replacement in the right pleural cavity and before cervicotomy, July 16, 2020—after drain replacement in the right pleural cavity and after cervicotomy, excision of the fistula and suturing of the esophagus, 05/09/2020—control chest X-ray)
with a tracheostomy tube and treatment with the surgical team was planned.\textsuperscript{13}

Pereira et al. present the case of a 62-year-old woman treated for SARS-CoV-2 pneumonia. Initially, a high-flow nasal cannula (HFNC) was used for 2 days. The therapy turned out to be insufficient and a decision was made to intubate. On the 18th day of MV, leakage of the endotracheal tube cuff was observed, and a CT scan was performed due to suspected osteomalacia. Tracheal dilation was observed, and TEF was diagnosed. The fistula did not heal spontaneously, so after 84 days of stay in the ICU, the patient was transferred to surgical treatment of TEF. According to the authors, numerous pathophysiological mechanisms related to COVID-19 may contribute to the complication of TEF. They indicate that the use of the prone position, regularly used in intubated patients infected with SARS-CoV-2, increases the risk of damage to the trachea by increased pressure of the cuff on the wall of the trachea and displacement of the tracheal tube during the maneuver. In addition, the systemic inflammatory response in COVID-19, severe hypoxemia with a low oxygenation index, or the pro-thrombotic state contribute to microcirculation damage, tissue ischemia, and subsequent necrosis. The supply of high doses of corticosteroids in the therapy of the severe form of COVID-19 may impair wound healing, further increasing the risk of TEF.\textsuperscript{14}

Negaresh et al. and also Cuaño et al. described cases of patients with a tracheo-esophageal fistula treated conservatively. In the case of the patient described by Negaresh et al., a jejunostomy was used, and the fistula was healed. The use of tracheostomy in combination with jejunostomy described by Cuaño et al. proved unsuccessful and the patient died.\textsuperscript{15,16}

The described cases clearly indicate the lack of a single TEF treatment method with proven effectiveness, which certainly prompts a broad debate on this topic. In the case of a TEF, conservative or operative therapy may be considered depending on the patient’s clinical condition. In the treatment of TEF, in some patients, it is possible to use an endotracheal tube sealed with a balloon below the fistula and jejunostomy or gastrostomy, which may provide optimal healing conditions. However, this approach is associated with a high risk of failure. Therefore, in the opinion of the authors of this study, this approach is the optimal bridging therapy allowing to prepare the patient for surgery. As the above publications show, many surgical methods are possible, ranging from the least invasive endoscopic methods, but the assessment of their effectiveness is impossible due to the low number of individual groups.

During the treatment, our patient developed a pleural empyema in addition to the formation of a tracheoesophageal fistula. In the first stage of a pleural empyema, the optimal treatment may be appropriate antibiotic therapy and pleural drainage.\textsuperscript{3} This approach in the treatment of a pleural empyema in the course of SARS-CoV-2 infection has proven effective in the patients described by Zavin et al. and Silalahi et al.\textsuperscript{17,18}

Regarding the surgical approach, video-assisted thoracic surgery (VATS) is considered the “gold standard for the surgical management of an empyema.”\textsuperscript{19} VATS enables the proper decorcation of an empyema as effectively as thoracotomy, and is associated with less pain and, at the same time, greater patient acceptance.\textsuperscript{20} VATS is an alternative to thoracotomy, which is a more extensive surgical procedure in the early stages of an empyema.\textsuperscript{21} In the patient described above, the pleural empyema was very extensive, therefore, the decision was made to treat with classic thoracotomy.

Yarlagadda et al. described the effective use of the VATS technique in the treatment of a pleural empyema in the course of SARS-CoV-2 infection.\textsuperscript{22} Tessitore et al. in turn, describe the use of classic thoracotomy in the treatment of pleural empyema on the example of 3 patients diagnosed with COVID-19, emphasizing the role of decor In the treatment of empyema and suggest its superiority over inoperable management in people in severe general condition.\textsuperscript{23} In our experience in treating a pleural empyema, the most important is to conduct appropriate antibiotic therapy and early decompression of the pleural cavity from exudate or purulent contents—then, the surgical treatment may be limited to drainage of the pleural cavity, while in more advanced cases, it is necessary to use more extensive procedures (VATS or thoracotomy) and lung decortication.

4 | CONCLUSIONS

1. Both long-term intubation and the long-term use of medical devices supporting respiration in a bacterial hospital environment contribute significantly to the risk of the development of a tracheoesophageal fistula and the occurrence of a pleural empyema in patients diagnosed with COVID-19.

2. The therapeutic management should consider the possibility of developing these complications in long-term hospitalized, mechanically ventilated, and infected with SARS-CoV-2.

3. It is necessary to implement adequate prophylaxis, and when it turns out to be ineffective, immediately treatment.

4. In the case of patients with multiple comorbidities, the approach of staging TEF treatment seems to be an insulting approach ensuring greater chances of success in treatment.
AUTHOR CONTRIBUTIONS
Hanna Kubik edited the introduction, contributed to editing of the discussion, developing the conclusions, and collecting the bibliography, and edited the final text of the manuscript. Wiktoria Smyła and Mikołaj Herba contributed to editing the case report and the discussion, developing the conclusions, and collecting the bibliography. Szymon Białka provided content supervision and contributed to proofreading of the article. Mateusz Rydél provided content supervision, contributed to concept, critical revision, and proofreading of the article.

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CONFLICT OF INTEREST
None.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICAL APPROVAL
There are no ethical concerns relating to this case report.

CONSENT
Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy.

PERMISSION TO REPRODUCE MATERIALS FROM OTHER SOURCES
No other sources were used.

CLINICAL TRIAL REGISTRATION
No clinical trial was conducted.

ORCID
Hanna Kubik https://orcid.org/0000-0002-5129-0365
Wiktoria Smyła https://orcid.org/0000-0002-5662-6497
Mikołaj Herba https://orcid.org/0000-0002-8292-261X
Mateusz Rydél https://orcid.org/0000-0002-7876-2423

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