







Original Thoracic

Outcome of Emergency Pulmonary Lobectomy under ECMO Support in Patients with COVID-19

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Abstract

Background Not much is known about the results of nonelective anatomical lung resections in coronavirus disease 2019 (COVID-19) patients put on extracorporeal membrane oxygenation (ECMO). The aim of this study was to analyze the outcome of lobectomy under ECMO support in patients with acute respiratory failure due to severe COVID-19. Methods All COVID-19 patients undergoing anatomical lung resection with ECMO support at a German university hospital were included into a prospective database. Study period was April 1, 2020, to April 30, 2021 (first, second, and third waves in Germany). **Results** A total of nine patients (median age 61 years, interquartile range 10 years) were included. There was virtually no preexisting comorbidity (median Charlson score of comorbidity 0.2). The mean interval between first positive COVID-19 test and surgery was 21.9 days. Clinical symptoms at the time of surgery were sepsis (nine of nine), respiratory failure (nine of nine), acute renal failure (five of nine), pleural empyema (five of nine), lung artery embolism (four of nine), and pneumothorax (two of nine). Mean intensive care unit (ICU) and ECMO days before surgery were 15.4 and 6, respectively. Indications for surgery were bacterial superinfection with lung abscess formation and progressive septic shock (seven of nine) and abscess formation with massive pulmonary hemorrhage into the abscess cavity (two of nine). All patients were under venovenous ECMO with femoraljugular configuration. Operative procedures were lobectomy (eight) and pneumonectomy (one). Weaning from ECMO was successful in four of nine. In-hospital mortality was five of nine. Mean total ECMO days were 10.3 ± 6.2 and mean total ICU days were 27.7 ± 9.9 . Mean length of stay was 28.7 \pm 8.8 days.

Keywords

- ► COVID-19
- ► ECMO
- ► thoracic surgery
- ► lung abscess

Conclusion Emergency surgery under ECMO support seems to open up a perspective for surgical source control in COVID-19 patients with bacterial superinfection and localized pulmonary abscess.

received December 11, 2022 accepted after revision April 14, 2023

DOI https://doi.org/ 10.1055/s-0043-1770738. ISSN 0171-6425.

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Introduction

In February 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV 2) and the resultant coronavirus disease 2019 (COVID-19) pandemic hit Europe and caused an unprecedented number of patients with acute respiratory symptoms. A considerable share of these patients developed acute respiratory distress syndrome (ARDS) requiring intensive care and eventually mechanical ventilation. Despite maximal intensive therapy and extensive medical management, some patients proofed to be refractory to ventilator support and were at some point considered for extracorporeal membrane oxygenation (ECMO) application. While the role of ECMO in non-COVID-19 ARDS is well established, there was initially no experience with the use of ECMO in ARDS caused by COVID-19.^{1,2} Meanwhile several studies have convincingly demonstrated that ECMO is useful as a rescue therapy for selected critical ill patients with ARDS related to COVID-19 pneumonia.^{3,4} While the application of ECMO for eligible COVID-19 patients has been established to overcome failure of ventilator support, there exists only limited data regarding the outcome of thoracic surgery interventions in these patients. As a growing number of COVID-19 patients receives ECMO support, it can be assumed that thoracic surgeons will be more and more confronted with the task to provide operative treatment in this challenging situation. By now several case series covering mostly minor operative interventions for conditions such as pneumothorax, pleural empyema, and hemothorax were reported.⁵⁻⁷ In contrast, there is hardly any knowledge about the results of anatomical lung resections in COVID-19 patients put on ECMO. To fill this gap, we decided to report our experience with major thoracic surgery in COVID-19 patients while on ECMO. The aim of this study was to analyze indications and outcome of nonelective lobectomy and pneumonectomy under ECMO support in patients with acute respiratory failure due to severe COVID-19.

Patients and Methods

Ethics Statement

A local ethics committee approved the study (Az. 22-190) and the need for individual written consent was waived because of the retrospective study design. Moreover, at our institution, all hospitalized patients with COVID-19 infection, or rather their legal representatives, had routinely consented to the scientific use of their case history in anonymized form for research regarding the COVID-19 pandemic. The study complied with the Declaration of Helsinki.

In a retrospective study from a prospectively collected database, all cases of COVID-19 patients undergoing emergency anatomical lung resections under ECMO support at a German university hospital were analyzed. The University Hospital Carl Gustav Carus (Dresden, Germany) serves as only ECMO center for a population of approximately 2 million people in the South and East of Saxony including the state capital Dresden. During the third wave, Saxony was one of Germany's most severely affected regions.

ECMO Configuration

In the present study, ECMO was required to support the lung function in patients with respiratory failure and ARDS caused by COVID-19 infection. As cardiocirculatory support was not needed, venovenous ECMO (vv-ECMO) with peripheral vascular access in double-site configuration was applied in all cases. Double-site vv-ECMO was preferred over singlesite vv-ECMO because it allows higher extracorporeal blood flow resulting in better oxygenation. ECMO was established with the help of the Maquet Cardiohelp System (GETINGE AB, Göteborg, Sweden). HLS cannulae (GETINGE AB, Göteborg, Sweden) with a variety of sizes and insertion lengths were used for individual peripheral cannulation. Percutaneous cannulation under ultrasound guidance in Seldinger technique was accomplished either at the intensive care unit (ICU) or in the operation room immediately prior to thoracotomy. In general, the right internal jugular and the right femoral vein were cannulated and the cannulae were placed in the superior and inferior vena cava. Transesophageal echocardiography was performed to assist in the optimal placement of the cannulae and to monitor cardiac function during surgery. Percutaneous cannulation was always carried out by a specialized team of anesthesiologists and nurses (ECMO team).

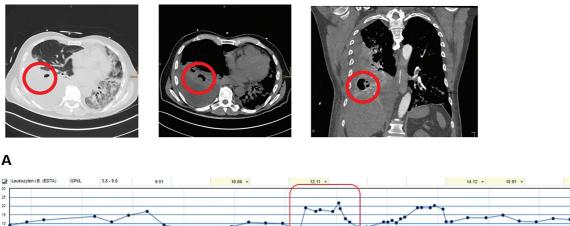
Anticoagulation Management

As severe COVID-19 is associated with substantially increased risk for lung artery embolism, all patients received already prior to ECMO application systemic anticoagulation with unfractionated heparin. Following ECMO placement, anticoagulation was continued with a target activated partial thromboplastin time (aPTT) between 60 and 70 seconds. During the immediate postoperative period, the aPTT was adjusted between 50 and 60 seconds to reduce the risk for massive postoperative hemorrhage.

Indications for Lobectomy/Pneumonectomy

At a multidisciplinary consensus conference, participants from anesthesiology, critical care medicine, thoracic surgery, and ECMO specialists discussed possible indications for pulmonary lobectomy and agreed on the following points.

Indications for surgery were bacterial superinfection with localized abscess formation and persistent septic disease despite the full range of nonoperative medical and interventional treatment (Fig. 1). Surgery was only considered when all nonoperative and interventional means had failed. Interventional treatment included all forms of endoscopic or image-guided interventions such as percutaneous drainage into abscess cavities, pleural space, or fluid collections. Bacterial superinfection was defined as a second infection with a bacterial agent after or on top of an earlier SARS-CoV 2 infection. As a prerequisite for making the diagnosis, bacterial superinfection had to be confirmed by microbiology samples obtained during bronchoscopy (►Table 1). Diffuse infectious lesions and multiple abscesses in both lungs were not considered to be amendable by surgery and were therefore ruled out as indications for operative management.



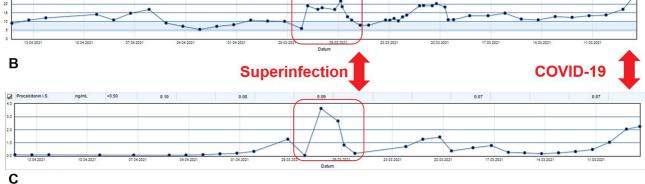


Fig. 1 Bacterial superinfection as second hit. Bacterial superinfection results in localized pulmonary abscess formation with pleural empyema (A) and second hit sepsis with clearly visible new elevation of white blood cell count (B; timeline from right to left) and procalcitonin (C; timeline from right to left).

Furthermore, pulmonary hemorrhage into an abscess cavity or massive endobronchial bleeding from a localized abscess formation was viewed as indications for pulmonary resection. As functional operability was not assessable in the acute situation, good pre-COVID-19 condition and performance status were mandatory for patients to be considered suitable and fit for surgery.

Operative Technique

The series comprises only cases of anatomical lung resection as lobectomy and pneumonectomy. All procedures were carried out exclusively with vv-ECMO support. Following establishment of high-flow extracorporeal circulation (at least 5 L/min), patients were placed in lateral decubitus position for thoracotomy. Standard surgical equipment and commercial stapling devices were used. As all patients were on ECMO and received relevant anticoagulation, there was an increased bleeding tendency. Therefore, packing of the thoracic cavity with gauze strips was routinely performed after pulmonary resection. Following stabilization of the patient at the ICU, rethoracotomy was carried out approximately 48 hours after the initial surgery. If the bleeding situation was controlled, the packing material was removed and the thorax was definitively closed. In case of continuing diffuse

Table 1 Microbiology finding in each patient

Patient no.	Infectious agents responsible for superinfection	COVID-19 variant of concern				
1	Candida albicans	No				
2	Staphylococcus aureus, Streptococcus anginosus	No				
3	Pseudomonas aeruginosa, E. coli, Candida albicans	No				
4	Klebsiella pneumoniae, Candida albicans	No				
5	Klebsiella oxytoca, E. coli	No				
6	Staphylococcus epidermidis, Klebsiella oxytoca, Candida albicans	No				
7	Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae	No				
8	Staphylococcus aureus, E. coli, Candida lusitaniae	B.1.1.7 (Alpha)				
9	Proteus mirabilis, E. coli	No				

Notes: Infectious agents identified from preoperative bronchial lavage and intraoperative samples (lung tissue, content of the abscess cavity, pleural empyema fluid).

bleeding, packing with gauze strips was renewed and a third procedure was scheduled again 48 hours later. Reinforcement of the bronchial stump was only carried out at the final rethoracotomy to prevent bleeding from the donor site as well as damage to the flap by the packing material. Following pneumonectomy, the bronchial stump was routinely covered with a large and viable muscle flap. In case of lobectomy, the decision for reinforcement of the bronchial stump was based on the intraoperative findings as the extent of pulmonary destruction and pleural empyema.

Team Safety in the Operating Room

With regard to team safety, personal protective equipment (PPE) was routinely used at the ICU as well as in the operating room⁵ (**Fig. 2**). All procedures were performed by the same team and every team member had received detailed instructions about the proper use of PPE. Fluid-resistant gown, gloves, FFP3 mask and a helmet with face shield, and air delivery unit (3M Versaflo M-Series, 3M, Bracknell, UK) were routinely used during all procedures.

Postoperative Care

Postoperatively, all patients were treated at the anesthesiology ICU and received the full range of sepsis therapy including hemodynamic monitoring and management, antibiotic therapy, hemofiltration in case of renal failure, and differentiated mechanical ventilation. Tracheotomy was performed early in the postoperative period. ECMO treatment was routinely managed and monitored by the specialized ECMO team. Intensive physiotherapy was applied on a daily basis.

Weaning from ECMO

Weaning from extracorporeal respiratory support was attempted as soon as sufficient recovery of the lung function with improved carbon dioxide clearance and oxygenation was observed. 10 ECMO blood flow as well as sweep gas were gradually turned back. Extracorporeal

blood flow was successively reduced to about 1.5 L/min and sweep gas flow was eventually switched off. If blood gases remained stable and no respiratory problems occurred, the decision to remove the system was made. Heparin treatment was briefly paused and aPTT, platelet count, and international normalized ratio were tested. If there were no objections, the system was finally removed. Decannulation was always carried out by the specialists of the ECMO team. As vascular access was peripheral, percutaneous, and venous only, decannulation took place at the ICU with manual compression of the access sites. ¹⁰ Vascular surgical intervention was not routinely intended.

Statistical Analysis

The following data concerning initial presentation, treatment, clinical course, and outcome were collected: demographic characteristics, preexisting comorbidity, date of first positive COVID test result, date of hospital and ICU admission, COVID-19 infection-related complications (e.g., pneumothorax), date of ECMO application, date of surgery, operative procedure, postoperative course, and outcome. All data were collected using a uniform data collection sheet. Statistical analysis was performed using R language and environment (R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org).

Data Availability Statement

All relevant data are within the article.

Results

During the study period (April 1, 2020–April 30, 2021), there were 26,645 confirmed cases of COVID-19 in Dresden (Saxony, Germany). Of these, 2,327 were admitted to several hospitals within the city of Dresden. In fact, most of them received inpatient treatment at the University Hospital Dresden (1,474 of 2,327; 63.34%) (Fig. 3). Of these 1,474





Fig. 2 (A, B) Team safety in the operating room. Personal protective equipment as fluid-resistant gown, gloves, FFP3 mask and a helmet with face shield, and air delivery unit were routinely used during all procedures.

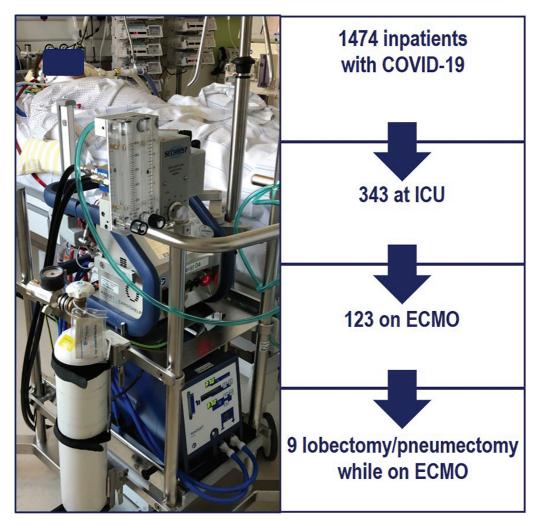


Fig. 3 Patient flow diagram. A total of 1,474 patients with COVID-19 were hospitalized during the study period. Out of these, 343 were admitted to the ICU, 123 needed ECMO treatment, and 9 eventually underwent lobectomy for lung abscess while on ECMO. COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

patients, 343 (23.27%) required critical care at the anesthesiology ICU and 123 of them finally needed vv-ECMO therapy for ventilatory support. Eventually, nine of them underwent lobectomy or pneumonectomy while on ECMO (**Fig. 3**).

Characteristics of Surgical Patients

The surgical group comprises a total of nine patients (two females and seven males) with confirmed COVID-19 infection (\succ **Table 2**). Median age was 61 years (quartile 1 55, quartile 2 65, interquartile range 10 years), and there was virtually no preexisting comorbidity (mean Charlson score of comorbidity 0.2). Following evaluation of the patients by the anesthesiology team at the time of surgery, the mean American Society of Anesthesiologists score amounted to 4.22. All patients were under vv-ECMO with femoral-jugular configuration. Mean ECMO days before surgery were 6 ± 7.07 days, mean ICU days before surgery were 15.4 ± 5.17 days, and the mean interval between the first positive COVID-19 test and surgery was 21.9 days (range 9–37 days) (\succ **Table 2**).

At the time of surgery, all patients suffered from severe sepsis (nine of nine) and ARDS with respiratory failure (nine of nine). Further symptoms were acute renal failure (five of nine) with the need of hemodialysis, lung artery embolism (four of nine) confirmed by CT pulmonary angiography, spontaneous intrapulmonary bleeding (two of nine) while on ECMO, pneumothorax (two of nine), mediastinal emphysema (one of nine), and pleural empyema (five of nine) (\succ **Table 2**). The mean RAPID score for pleural infection was 3.44 ± 1.26 .

Indications for Surgery, Operative Procedures, and Outcome

Indications for surgery were bacterial superinfection with localized lung abscess formation and either progressive septic shock (seven of nine) (**Fig. 1**) or massive pulmonary hemorrhage (two of nine) into the abscess cavity. Operative procedures were lobectomy (eight) and pneumonectomy (one) (**Table 3**). Packing of the thoracic cavity with gauze strips was routinely carried out in all cases. ¹³ Planned rethoracotomy took place in seven patients, while two died from therapy refractory septic shock at the ICU before the scheduled time of reoperation. Among the seven remaining patients, the average number of thoracotomies including the initial procedure and all planned rethoracotomies were

Table 2 Patients' characteristics

Patient no.		2	3	4	5	6	7	8	9	Mean (percentage)
Demographic characteristics										
Male		1	1	1	1	1	1	1		7/9 (78%)
Female									1	2/9 (22%)
Age (y)		66	65	56	70	61	65	54	47	59.9
Charlson score of comorbidity		0	0	0	1	1	0	0	0	0.2
Coronary heart disease					1					1/9 (11%)
Arterial hypertension				1	1	1				3/9 (33%)
Diabetes mellitus						1				1/9 (11%)
Hospital events prior to operation										
Acute renal failure		1			1	1	1	1		5/9 (55%)
Lung artery embolism		1		1			1	1		4/9 (45%)
Pleural empyema		1		1			1	1		5/9 (55%)
Pneumothorax						1		1		2/9 (22%)
Mediastinal emphysema						1				1/9 (11%)
Spontaneous bleeding						1			1	2/9 (22%)
Days between first positive PCR test and surgery		16	15	22	17	36	23	22	37	21.9 d

Abbreviation: PCR, polymerase chain reaction.

Notes: Other comorbidities were not observed. Acute renal failure was defined as acute impairment of renal function with need for hemodialysis. Spontaneous bleeding meant bleeding occurred suddenly without external cause such as percutaneous, endoscopic, or operative interventions.

Table 3 Operative procedure and outcome

Patient no.		2	3	4	5	6	7	8	9	Mean (percentage)
Lobectomy		1	1	1	1	1	1	1	1	8/9 (89%)
Pneumonectomy										1/9 (11%)
ECMO days before surgery		0	1	4	1	21	1	3	16	6 ± 7.07
ECMO day after first operation in survivors					2		5	5		
Total number of operations		2	1	1	2	2	3	2	4	
Total ECMO days		10	6	7	3	23	6	8	19	10.3 ± 6.2
Weaning off from ECMO					1		1	1		4/9 (45%)
Length of stay (d)		26	20	25	33	32	29	19	24	28.7 ± 8.8
In-hospital death		1	1	1		1			1	5/9 (55%)
Cause of death: septic shock			1	1		1			1	
Cause of death: basal ganglia infarction		1								
Transfer to rehabilitation					1		1	1		4/9 (45%)

Abbreviation: ECMO, extracorporeal membrane oxygenation.

three (range 2–5). Out of these seven patients, two more died from therapy refractory septic shock. Another patient sustained massive basal ganglia infarction and treatment was discontinued following consultation with his family. The combined in-hospital mortality was five of nine (\succ **Table 3**). Weaning from ECMO was successfully achieved in four of nine. For the whole group, mean total ECMO days were 10.3 ± 6.2 , mean total ICU days were 27.7 ± 9.9 , and the average length of stay was 28.7 ± 8.8 days. All four patients

who were successfully weaned off from ECMO were eventually discharged to rehabilitation facilities, and all were still alive at the end of the study period.

Discussion

To the best of our knowledge, we report one of the first substantial case series of pulmonary lobectomy and pneumonectomy under ECMO support in COVID-19 patients. Up to now, only a handful of single case reports regarding nonelective anatomical lung resections in COVID-19 patients has been published and except for one case, there was no ECMO application. ^{14,15} In general, the literature on thoracic surgery in COVID-19 patients with ongoing ECMO treatment is rather scarce. For the most part, simple interventions as tracheostomy, chest tube insertion, and video-assisted thoracoscopic surgery for hemothorax or pleural empyema are reported. ⁵⁻⁷ Therefore, we wanted to share our experience with nonelective major thoracic surgery in COVID-19 patients under ongoing ECMO therapy.

The Dresden ECMO Center is a major ECMO provider in East Germany for many years and has extensive experience with the application of ECMO for ARDS in non-COVID-19 cases. When the SARS-CoV 2 pandemic first appeared in Saxony and East Germany in March 2020, there existed virtually no experience regarding the use of ECMO in patients with ARDS caused by COVID-19.^{1,2} Nevertheless, ECMO therapy in COVID-19 patients with ARDS and ventilatory refractory respiratory failure was started at the University Hospital Dresden as soon as March and April 2020. The exceptional situation at the begin of the SARS-CoV 2 pandemic was worldwide seen as justifying the use of ECMO despite the lack of evidence at that time. In the meantime, single-center experience as well as large national or even supranational register studies have been reported. 16-21 Recently published data clearly substantiated the use of ECMO for COVID-19-induced ARDS.^{4,22}

In parallel with the increased utilization of ECMO during the pandemic, it was to be expected that thoracic surgeons would sooner or later be confronted with the task to provide surgery for COVID-19 patients while on ECMO. In this matter, it is important to distinguish between minor surgical interventions for ECMO-related complications and major thoracic surgery such as anatomical lung resections in COVID-19 patients while on ECMO. Over the past several years, experienced ECMO centers have reported case series for mostly minor thoracic surgical interventions for ECMO-related complications as hemothorax or pleural empyema in non-COVID-19 patients. Similar ECMO-associated complications could be anticipated for COVID-19 patients. In the meantime, some institutions have actually published reports on the surgical management of these complications precisely.^{6,7} On the other hand, it was obvious that major thoracic surgery would play no role in the first-line therapy of COVID-19 but was rather reserved for late effects of SARS-CoV 2 infection as massive pulmonary hemorrhage or bacterial superinfection.

In case of viral pneumonia, bacterial superinfection is a well-known phenomenon since the 1918–1919 "Spanish Flu" pandemic.²³ In case of SARS-CoV 2 infection, coinfection as well as bacterial superinfection has been described. Bacterial coinfections at the time of the first positive polymerase chain reaction test are quite common (7.1–9.1%)^{24,25} and have to be addressed in the initial antimicrobial therapy to prevent complications. Bacterial superinfection, however, usually occur later during COVID-19. Several studies have shown significant rates of bacterial superinfection between 16 and 41%.^{26,27} In COVID-19 patient, receiving intensive

care bacterial superinfection is even more common. An analysis from the University Hospital Eppendorf (Hamburg, Germany) identified bacterial superinfection in 74 out of 102 (72.5%) COVID-19 patients with mechanical ventilation at the ICU between March and November 2020.²⁸

All patients of our study had microbiological confirmed bacterial superinfection. The specimens were routinely obtained by bronchoscopy from the deep respiratory tract. Computed tomography showed that bacterial superinfection leads to lung abscess formation and pleural empyema. In COVID-19 patients, who survived the first period of COVID-19, the occurrence of bacterial superinfection with lung abscess formation constitutes a dangerous second hit and may ultimately result in renewed sepsis and septic shock associated with enormous mortality (►Fig. 2). Previous work of our group regarding the operative management of infectious lung abscess has clearly shown the benefit of timely surgical intervention before the onset of severe sepsis and septic complications.²⁹ This is also true for ECMO patients.³⁰ Therefore, we assumed that septic source control by means of removal of the affected pulmonary lobe would be favorable to overcome the acute situation.

We limited the indications for surgery to cases of localized lung abscess formation as diffuse lesions are generally not amendable by operative intervention. Lobectomy or even pneumonectomy of the affected lung was viewed as ultima ration to save the patient's life after all nonoperative treatment had failed. The absolute prerequisite for considering anatomical lung resection in ECMO patients was that post-operative weaning from ECMO was not rendered difficult or even impossible by the extent of pulmonary resection. Moreover, we had to take into account that in contrast to non-COVID-19 patients, the remaining lung was also severally damaged by the effects of SARS-CoV 2 infection. As a consequence, we only included patients with good pre-COVID-19 performance status and no serious preexisting comorbidity.

Our approach was successful in four out of nine patients. In a fifth patient, therapy was discontinued from reasons unrelated to the performed lobectomy and this case, therefore, should not be considered as actual failure of the operative management of lung abscess caused by bacterial superinfection. The intraoperative management of ECMO was unproblematic. Including planned rethoracotomy, we carried out 20 procedures in nine patients and experienced no technical problems or any difficulties with cannula position, ECMO flow, or gas exchange. The approach of thoracic packing and planned rethoracotomy was successful in dealing with the increased bleeding tendency. Postoperatively, we encountered no hemorrhagic shock and no need for mass transfusion.

Meanwhile several studies regarding the outcome of ECMO in COVID-19 patients have been published. At this, single institution experience is often more favorable than multicenter studies. Mortality rates of selected single-center reports are 38% (6 of 16 patients) Charité Berlin (Germany), ¹⁸ 22% (2 of 9) University Hospital Zürich ¹⁶ (Switzerland), and only 10% (3 of 30) NYU Langone Health (New York, United

States).¹⁹ On the other hand, a recent multi-institutional analysis from the United States showed a mortality of 50% (50 of 100).¹⁷ The ECMOVIBER study,²⁰ which included 338 COVID-19 patients on ECMO at 24 centers in Spain and Portugal, indicated a mortality rate of 49% and a national analysis comprising all hospitals in Germany revealed a mortality rate of 65.9% (2,552 of 3,875) in case of vv-ECMO.²¹

Although all participants of these studies received ECMO therapy for COVID-19, none of them underwent major thoracic surgery, let alone anatomical lung resection while on ECMO. Therefore, we feel that our results are well in line with the currently available experience. In our series, non-elective lobectomy/pneumonectomy did not lead to elevated mortality. On the contrary, it helped achieve the outcome to be expected from COVID-19 ECMO patients without operative intervention.^{20,21} We may assume that the outcome would have been worse otherwise.

Limitations

The main limitation is that our study constitutes a single-center experience with a limited study population. A multi-institutional research project is needed to obtain more evidence. On the other hand, it is the first substantial case series to report on lobectomy/pneumonectomy in COVID-19 patients while on ECMO. Therefore, we feel that our conclusions are an important contribution to the scientific debate about the use of ECMO in case of SARS-CoV 2 infection.

Conclusion

In conclusion, pulmonary lobectomy under ECMO therapy opens up a perspective for successful surgical management of COVID-19 patients with bacterial superinfection and localized lung abscess.

Note

This study was presented at the 30th European Conference on General Thoracic Surgery in The Hague, The Netherlands, June 19–21, 2022. Also, presented at the SCTS Annual Meeting in Belfast (Northern Ireland, United Kingdom), May 8–10, 2022.

Funding

None.

Conflict of interest

None declared.

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