Original Paper

Perfusion

Thoracic surgery in patients on veno-venous extracorporeal membrane oxygenation for COVID-19 associated acute respiratory distress syndrome

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Abstract

Objectives: The COVID-19 pandemic has generated a new type of acute respiratory distress syndrome (ARDS) arising as a complication of COVID-19 pneumonia. Extreme cases require the support of extracorporeal membrane oxygenation (ECMO). Here we present the outcomes of patients that underwent surgical tracheostomy or thoracic surgery at a single tertiary centre whilst on ECMO support for COVID-19 related ARDS.

Methods: 18 patients requiring thoracic input whilst on ECMO support during the first wave of COVID-19 (March–June 2020) were included. Thoracic surgery was required both for performing surgical tracheostomies in the operating theatre and for treating emergencies arising under the ECMO treatment such as bleeding complications.

Results: Thirteen patients underwent a surgical tracheostomy, whilst five patients had an invasive thoracic procedure. Anticoagulation was withheld for at least 12 h in the perioperative setting regardless of the indication. One patient was re-operated for haemothorax immediately after the end of the primary operation. 94.5% of the patients were successfully decannulated from ECMO support. Overall 30-day mortality in the cohort was 5.5% (1/18).

Conclusions: Thoracic surgeons can play a valuable role in supporting an ECMO unit during the COVID pandemic, by treating ECMO related complications and by safely performing surgical tracheostomies. Withholding anticoagulation in the perioperative window was not associated with increased thromboembolic events and is desirable when interventions or surgery is indicated in this patient cohort to avoid excessive bleeding.

Keywords

Thoracic surgery; ECMO; COVID-19; ECMO-complications

Introduction

The COVID-19 pandemic has led to unprecedented pressure on national healthcare systems requiring a significant restructuring of services. Elective cardiothoracic procedures were stopped in many countries in order to accommodate the new needs of the healthcare system, increase the availability of intensive care unit beds and protect the cardiothoracic patients from the COVID-19 related hospital morbidity. In the United Kingdom, most elective cardiothoracic surgery was suspended during the first wave of the pandemic as the country was severely affected.

Patients with COVID-19 pneumonia that develop respiratory failure often require non-invasive or invasive

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ventilation. Extreme deterioration which leads to acute respiratory distress syndrome (ARDS) requires more advanced respiratory support. The WHO, the Extracorporeal Life Support Organisation (ELSO) and other major health organisations have proposed the use of extracorporeal membrane oxygenation (ECMO) in patients with COVID-19 that fulfil specific criteria.

COVID-19 pneumonia has been associated with increased risk of thrombosis, especially pulmonary embolism or pulmonary thrombosis.[1] Patients needing ECMO support require systemic anticoagulation for the maintenance of the ECMO circuit and prevention or treatment of thrombotic events. However, anticoagulation in COVID-19 patients is associated with an increased risk of developing bleeding complications,[2] such as haemothorax, that require thoracic surgical intervention. Furthermore, in order to support the weaning of sedation, a percutaneous or surgical tracheostomy is often required. The risks of bleeding with complex peri-procedural anticoagulation and the risk to staff from aerosol generating procedures particularly with a percutaneous approach need to be carefully assessed on a case by case basis.

In this study, we review the outcomes of patients who underwent thoracic surgery while on ECMO for COVID-19 related ARDS with a specific focus on handling the anticoagulation agents in the perioperative window.

Materials and methods

18 consecutive patients that underwent surgical tracheostomy or thoracic surgical intervention at the Royal Brompton Hospital while on ECMO support for COVID-19 related ARDS between March and June 2020 were retrospectively evaluated. All procedures were performed with full PPE (personal protective equipment) gear and FFP3 masks. The study was approved by the local ethics committee (REC reference: 20/EM/0204).

Criteria for ECMO referral

There are five NHS (National Health Service) commissioned ECMO centres in England and one in Scotland, with each centre providing care within a specified area. Eligibility for ECMO support was based on the following criteria published by NHS England on 27th March. Patients were not considered for ECMO in cases of refractory multiorgan failure.

- Potentially reversible severe respiratory failure
- Lung Injury Score (Murray score [3]) $\geqslant 3$
- Failed trial of ventilation in prone positioning $\geqslant$ 6h (unless contraindicated)
- Failed Airway Pressure Release Ventilation (ARPV) or 'High PEEP ventilation strategy' $\geqslant$ 6h (unless contraindicated)
- Clinical Frailty Scale category $\leqslant 3$ (see below)
- If RESP score $\leqslant 3$ ECMO should be considered only after agreement across at least two centres.[4]

The decision for decannulation from ECMO was based on patients' lung ability to maintain adequate gas exchange for at least 24 h without ECMO support. After a successful ECMO trial of 24 h, patients were decannulated and stepped down for further treatment. The ECMO management in our centre is described in detail elsewhere.[5]

Data analysis

Clinical data were documented on ICCA (IntelliSpace Critical Care and Anaesthesia information system, Philips Healthcare Solutions) throughout the period that the patient was treated on the intensive care unit. Data were then entered in a prospective database which was formed for service evaluation and research purposes. Continuous data are presented as median and range (min–max). We reported the 30-day mortality (counting from the admission to the Royal Brompton Hospital) or in-hospital mortality when the 30-day data were not available.

Results

18 consecutive patients (12 male) underwent surgical tracheostomy or thoracic surgery while on veno-venous ECMO for COVID-19 related ARDS between March and June 2020. The median body mass index was 29.9 kg/m^2 (range 21.9–44.1 kg/m^2) and the median age at the time of admission was 47 years (range 33–65). Patient characteristics are summarized in Table 1. All 18 patients were non-smokers.

The median time between confirmation of the COVID-19 positivity and intubation was 5 days (range 1–13 days). The chronological diagram of the ICU treatment is presented in Figure 1. In 5 cases the patient was intubated without having direct confirmation of COVID-19 positivity which could only be confirmed several days later. Patients referred for ECMO treatment had been ventilated for a median of 3 days (range 1–14 days). All patients were cannulated for ECMO support on admission to the RBH or the day after.

The median time that the patients spent on ECMO was 28 days (range 5–63 days) before being decannulated. After an 11-day successful ECMO treatment course, one patient was repatriated but had to be readmitted 13 days later with deterioration and spent another 41 days on ECMO before being weaned off.

Table 1. Patient demographics and surgical procedures.

N	Age	Sex	PMH	Procedure	Complications
1	36	M	-	Tracheostomy	None
2	65	M	RF, HTN, Asthma	Tracheostomy	None
3	64	M	-	Tracheostomy	None
4	46	M	-	Tracheostomy	None
5	53	M	HTN, OSA	Tracheostomy	None
6	55	M	RF, Obesity, SCD	Tracheostomy	None
7	39	M	HTN	Haematoma evacuation	Bleeding[a]
8	47	M	-	Pericardial window	Deceased
9	46	F	RF	Tracheostomy	None
10	50	F	HTN	Tracheostomy	None
11	33	M	-	Tracheostomy	None
12	40	F	Asthma, DM, FLD	Tracheostomy	None
13	49	M	Asthma, DM	Bronch. Haemostasis	None
14	37	F	DM, Obesity	Haematoma evacuation	None
15	44	F	-	Microlaryngeal tubes and surgical chest drain	None
16	48	M	Alcoholism	Tracheostomy	None
17	55	M	-	Tracheostomy	Air leak
18	40	F	Obesity, Asthma, Schiz	Tracheostomy	None

PMH: past medical history, DM: diabetes mellitus, RF: renal failure, HTN: hypertension, OSA: obstructive sleep apnoea, FLD: fatty liver disease, SCD: Sickle cell disease, Schiz.: Schizophrenia.

[a]Preoperative fibrinogen: 2.5 g/L, Platelet count 82x109/L.

Perioperative anticoagulation management

It is our standard practice to give unfractionated heparin with a target heparin anti-Xa level of 0.2–0.3 for patients receiving VV-ECMO without thrombosis. The target anti-Xa level is increased to 0.3–0.5 if there is evidence of thrombosis but no evidence of major bleeding.

Nine of 18 patients developed thrombotic events during their treatment. Four patients were diagnosed with a type 2 heparin–induced thrombocytopaenia with

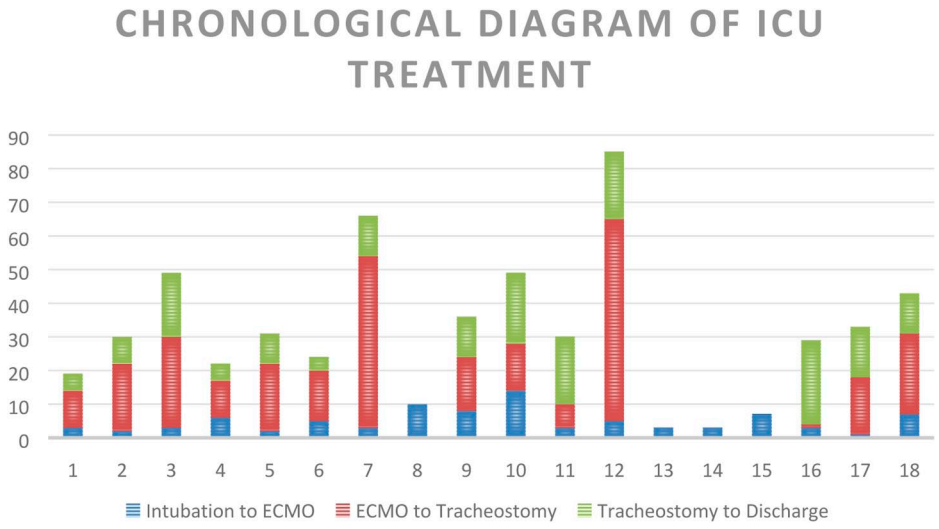

Figure 1. Chronological diagram of the ICU treatment phases. The *y*-axis represents the days and the *x*-axis the individual patient number. Patient eight did not receive a tracheostomy, patients 13 and 14 were repatriated without tracheostomy and patient 15 received the tracheostomy after being repatriated but was readmitted for a second ECMO treatment course.

Table 2. Thrombembolic events, anticoagulation management and ECMO related bleeding complications.

N	VTE	Anticoagulation	Target Anti-Xa or APTT	Complications
1	PE	Argatroban	aPTT 40–80 s	None
2	None	UFH	1.1–0.3 IU/mL	GI bleeding
3	None	Argatroban	aPTT 40–80 s	None
4	None	UFH	0.2–0.3 IU/mL	None
5	None	UFH	0.2–0.3 IU/mL	None
6	DVT	UFH	0.3–0.5 IU/mL	None
7	None	Argatroban	aPTT 40–80 s	None
8	PE	UFH	n.a[a]	GI bleeding
9	Prev. PE	UFH	0.3–0.5 IU/mL	None
10	DVT	UFH	0.3–0.5 IU/mL	None
11	None	UFH	0.2–0.3 IU/mL	None
12	PE	UFH	0.3–0.5 IU/mL	None
13	PE	UFH	0.2–0.3 IU/mL	Bronchial bleeding
14	PE	UFH	0.2–0.3 IU/mL	Intra-thoracic bleeding
15	PE	UFH	0.3–0.5 IU/mL	None
16	PE	UFH	0.2–0.3 IU/mL	None
17	PE	Argatroban	aPTT 40–80 s	None
18	None	UFH	0.2–0.3 IU/mL	None

VTE: thromboembolic events, PE: pulmonary embolism, DVT: deep vein thrombosis, UFH: unfractionated heparin, aPTT: activated partial thromboplastin time.

[a]anticoagulation was withheld due to ongoing gastrointestinal bleeding.

thrombosis (HITT, Table 2), two of which had evidence of thrombosis and two did not. Patients who developed HIT with or without thrombosis were treated with argatroban with a target activated partial thromboplastin time (APTT) of 40–80 s. In all cases, anticoagulation was stopped at least 6 h before the surgical procedure and was restarted 4–6 h after unless there was an ongoing bleeding complication.

Thoracic surgery was indicated for the treatment of spontaneous bleeding complications, but there were no cases where revisional surgery was required to treat postoperative bleeding. In one case (patient 7), the patient received a thoracoscopic haematoma evacuation for spontaneous haemothorax. Intraoperatively there was diffuse bleeding from the parietal pleura which could not be stopped surgically. During the transfer from the theatre back to the intensive care unit a significant amount of blood was drained, so the patient was returned to the theatre for re-exploration and control of the bleeding.

Patient eight developed a hemopericardium during ECMO cannulation which was initially treated with a pericardial drain. Due to continuous obliteration of the drains, the patient required a pericardial window which was achieved through a subxyphoid approach. During further treatment and after recovering from the hemopericardium, the patient developed intestinal bleeding leading to multiorgan failure from which the patient did not survive. Five patients required perioperative transfusion (patients 10, 13, 14, 15 and 17). Patient 14 required five red blood cell units, patient 17 required three units, while the other 3 patients less than two units. Patient 6 required 3 units of fresh frozen plasma, patient 14 received one pool of platelets and patient 18 received two pools of cryoprecipitates. There were no emergency ECMO circuit changes in the perioperative window, the average number of circuit changes was 0.45 (standard deviation 0.74).

The median time between ECMO cannulation and tracheostomy insertion was 16.5 days (range 1–60 days) and the median time between tracheostomy and discharge or repatriation to the local hospital was 12 days (range 4–25 days). 13 patients were repatriated to the initially referring hospital and three patients could be directly discharged home. The patient that was readmitted for a second ECMO treatment could be discharged home after spending almost 4 months in the RBH. None of the patients developed thrombotic event as results of perioperative withholding of anticoagulation. The in-hospital mortality rate (median of 40 days, range 12–115 days) was 5.5%.

Discussion

The implications of the COVID-19 virus to our health system have necessitated the review of many treatment pathways. Over 190.000 papers from every medical speciality have been published on COVID-19 in Medline since 2019 including several guidelines which have been

modified based on the needs of the new patient population. The WHO and the ELSO have published guidelines for the use of ECMO on COVID-19 patients.[6]

The Royal Brompton Hospital is one of the five commissioned ECMO centres in England. During the first wave of the COVID-19 pandemic, elective cardiothoracic surgical services were stopped in order to focus on the care of COVID-19 patients that required ECMO support. Thoracic surgical care during this period constituted of insertion of surgical tracheostomies, when there were concerns about airway bleeding complications in the coagulopathic COVID-19 patient on ECMO and the risk to staff of aerosol generating procedure from percutaneous tracheostomy. Occasionally, severe pleural disease was encountered and required thoracic surgical input.

We treated a total of 18 patients, 13 with a surgical tracheostomy and 5 with more invasive thoracic procedures. Two of these patients had a thoracoscopic or open haematoma evacuation, one patient a pericardial window for haemopericardium, one patient underwent a rigid bronchoscopy with evacuation of clots for severe intrabronchial bleeding and one patient rigid bronchoscopy with insertion of microlaryngeal tubes for tracheomalacia with a proximal tracheal injury. All patients that we operated on were on therapeutic or subtherapeutic anticoagulation which was discontinued 6 h before surgery and was restarted 4–6 h after unless there was a contraindication.

One patient died 1 month after admission and ECMO cannulation and 18 days after the cardiothoracic procedure. The main cause of death was not directly related with the procedure performed. The overall in-hospital mortality rate in our study was 5.5%, which is rather low for this specific patient cohort. The high survival rate can probably be explained by the high volume of patients and therefore the high expertise of the centre. Furthermore, careful patient selection and the fact that during the first wave we only treated treatment-naïve disease might have also contributed to the very low mortality. The high survival rate was similar between the surgical and the non–surgical patient cohort from our institution.[5]

What is certainly reasonable is to suggest that performing thoracic surgical procedures in COVID-19 patients on ECMO is possible but not without significant risk. Withholding the anticoagulation is feasible and is associated with low thrombotic complications. In order to achieve the best possible results, it is essential to have a multidisciplinary team approach with an optimal workflow and communication channel between the critical care team, the anaesthetic team, haematologist, perfusionists and surgeons.

The median time between ECMO cannulation and tracheostomy in this patient cohort was 16.5 days and the time between tracheostomy and discharge or transfer to the local hospital was 12 days in an overall treatment duration of 40 days in the RBH. The long interval between tracheostomy and discharge was mainly triggered by four patients, each of whom required almost 3 weeks of ECMO following the tracheostomy before they could be safely decannulated. Matsuyoshi et al. recommended to avoid tracheostomies in patients with severe COVID under ECMO support due to increased bleeding complications.[7] In our series, we did not experience bleeding complications after the surgical tracheostomies but the timing of the procedure has to be carefully chosen and correlated with the overall course of the disease.

Limitations

The collection of the data in this study was performed prospectively but the interpretation and process of the information was performed retrospectively, encompassing a certain possibility of selection bias. However, despite the retrospective nature of the study, all relevant information was available. Furthermore, although this is a large cohort of patients with a very specific disease profile, the surgical procedures performed, the comorbidities of each patient and the relevant differences in the cardiopulmonary support make the sample heterogeneous, which limits the generalizability of the conclusions. For this purpose, we present the results only as a report of the outcomes and not as a formal study with a control group in order to avoid further increasing the bias.

Conclusion

Thoracic surgeons can play a valuable role in supporting an ECMO unit during the COVID-19 pandemic. In the first instance dealing with intra-thoracic bleeding is a vital part of the management of patients on ECMO. Despite relatively high transfusion requirement perioperatively no patients died as a direct result from bleeding from their thoracic intervention and no patient suffered thrombotic complications directly due to stopping anticoagulation peri-operatively. Furthermore safe insertion of surgical tracheostomies can support early weaning off sedation and can potentiate liberation from ECMO and then from mechanical ventilation in carefully selected patients. The surgical approach allows control of bleeding and can potentially reduce the risk to staff of aeorosol generating procedures inherent in the percutaneous approach.

Author contributions

IK conceived of the presented idea, collected and analysed the data and drafted the manuscript.

AS collected and analysed the data.

PH conceived of the presented idea, collected and analysed the data.

MP collected and analysed the data.

DRJA conceived of the presented idea and reviewed the manuscript for important intellectual content.

SJ has reviewed the manuscript for important intellectual content.

LT conceived of the presented idea and reviewed the manuscript for important intellectual content.

BG supervised the data collection and has reviewed the manuscript for important intellectual content.

SL supervised the data collection and has reviewed the manuscript for important intellectual content.

SB conceived of the presented idea and reviewed the manuscript for important intellectual content.

Data availability

The datasets generated during the current study are not publicly available since the main part is included in this article. The complete database is available from the corresponding author on reasonable request.

Declarations

These data were collected for service evaluation purposes and not during a formal research project. All co-authors had full access to the data presented here. Data collection for this purpose was approved by the Adult Intensive Care Unit Research Committee. However, due to the severity of the ongoing pandemic, result dissemination is mandatory.

Declaration of conflicting interests

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References

1. Bompard F, Monnier H, Saab I, et al. Pulmonary embolism in patients with COVID-19 pneumonia. *Eur Respir J* 2020; 56.
2. Aubron C, DePuydt J, Belon F, et al. Predictive factors of bleeding events in adults undergoing extracorporeal membrane oxygenation. *Ann Intensive Care* 2016; 6: 97.
3. Murray JF, Matthay MA, Luce JM, et al. An expanded definition of the adult respiratory distress syndrome. *Am Rev Respir Dis* 1988; 138: 720–723.
4. Schmidt M, Bailey M, Sheldrake J, et al. Predicting survival after extracorporeal membrane oxygenation for severe acute respiratory failure. The Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score. *Am J Respir Crit Care Med* 2014; 189: 1374–1382.
5. Garfield B, Bianchi P, Arachchillage D, et al. Six month mortality in patients with covid-19 and non-covid-19 viral pneumonitis managed with veno-venous extracorporeal membrane oxygenation. *ASAIO J* 2021; 67: 982–988.
6. Shekar K, Badulak J, Peek G, et al. Extracorporeal life support organization coronavirus disease 2019 interim guidelines: a consensus document from an international group of interdisciplinary extracorporeal membrane oxygenation providers. *ASAIO J* 2020; 66: 707–721.
7. Matsuyoshi T, Shimizu K, Kaneko H, et al. Optimal timing of tracheostomy in patients on veno-venous extracorporeal membrane oxygenation for coronavirus 2019: a case series. *Acute Med Surg* 2021; 8: e662.