

# Video-assisted thoracic surgery in critically ill COVID-19 patients on venovenous extracorporeal membrane oxygenation

Perfusion  
2022, Vol. 0(0) 1–7  
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DOI: 10.1177/02676591221119319  
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## Abstract

**Introduction:** Coronavirus disease 2019 (COVID-19) leads to thoracic complications requiring surgery. This is challenging, particularly in patients supported with venovenous extracorporeal membrane oxygenation (VV-ECMO) due to the need for continuous therapeutic anticoagulation. We aim to share our experience regarding the safety and perioperative management of video-assisted thoracic surgery for this specific population.

**Methods:** Retrospective, single-center study between November 2020 and January 2022 at the ICU department of a 1.061-bed tertiary care and VV-ECMO referral center during the COVID-19 pandemic.

**Results:** 48 COVID-19 patients were supported with VV-ECMO. A total of 14 video-assisted thoracic surgery (VATS) procedures were performed in seven patients. Indications were mostly hemothorax (85.7%). In eight procedures heparin was stopped at least 1 h before incision. A total of 10 circuit changes due to clot formation or oxygen transfer failure were required in six patients (85.7%). One circuit replacement seemed related to the preceding VATS procedure, although polytransfusion might be a contributing factor. None of the mechanical complications was fatal. Four VATS-patients (57.1%) died, of which two (50%) immediately perioperatively due to uncontrollable bleeding. All three survivors were treated with additional transarterial embolization.

**Conclusion:** (1) Thoracic complications in COVID-19 patients on VV-ECMO are common. (2) Indication for VATS is mostly hemothorax (3) Perioperative mortality is high, mostly due to uncontrollable bleeding. (4) Preoperative withdrawal of anticoagulation is not directly related to a higher rate of ECMO circuit-related complications, but a prolonged duration of VV-ECMO support and polytransfusion might be. (5) Additional transarterial embolization to control postoperative bleeding may further improve outcomes.

## Keywords

Video-assisted thoracic surgery, COVID-19, venovenous extracorporeal membrane oxygenation, thoracoscopy, hemostasis

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## Introduction

Patients with refractory acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19) can be supported with venovenous ECMO (VV-ECMO).<sup>1</sup> Pulmonary disease due to COVID-19 may lead to thoracic and pulmonary complications such as pneumothorax, pleural effusion, and empyema, which might be resolved by drainage but sometimes requires surgery.<sup>2</sup> In patients on VV-ECMO, this can be challenging due to the need for continuous anticoagulation to inhibit circuit-induced activation of the clotting cascade.<sup>3</sup> Experience-based papers on handling these issues mostly predate the COVID-era.<sup>3</sup> As COVID-19 is a prothrombotic condition, small trials emphasize anticoagulating these patients more stringently.<sup>4</sup> This makes perioperative management even more difficult. To date, there is only minimal evidence regarding the safety and the perioperative hemostatic management of video-assisted thoracic surgery (VATS) for this specific population. This report aims to share our experience about safety and feasibility of VATS in this population at Ghent University Hospital in Belgium, a 1.061-bed tertiary care and VV-ECMO referral center during the COVID-19 pandemic.

## Methods

This retrospective, single-center study was carried out between November 2020 and January 2022 at the intensive care department of Ghent University Hospital, Belgium. Data were collected based on the hospital's ECMO registry, approved by the local ethical committee (BC-09806). All COVID-19 patients treated with VV-ECMO and scheduled for VATS between 23 March 2020 and 31 December 2021 were included. All demographics, pre-existing comorbidities, coagulation parameters, and surgical information were abstracted from the electronic health records. All patients were treated with unfractionated heparin (UFH) or bivalirudin (in case of heparin-induced thrombocytopenia, HIT) according to the local anticoagulation protocol, based on 4-hourly visco-elastic functional analysis with Sonoclot Analyzer<sup>®</sup> (Sienco Inc, Arvada, CO, USA) (clot rate (CR) target 7.5–10 Units per min) and hourly bedside kaolin activated clotting time (ACT, Istat<sup>®</sup>, Abbott Point of Care, Princeton, NJ, USA). The desired range for the Istat<sup>®</sup> ACT was defined by the ACT taken at the same time the Sonoclot CR was within its expected range, plus-minus 10 s. UFH dosage was adjusted according to the Istat ACT and this target

range. Platelet function (PF) was monitored using the same Sonoclot Analyzer<sup>®</sup>. In the Sonoclot Analyzer PF is a calculated value, derived by using an automated numeric integration of changes in the Sonoclot signature after fibrin formation has been completed. The nominal range of values for the PF goes from 0, representing no PF (no clot retraction and flat Sonoclot signature after fibrin formation), to approximately 5, representing strong PF (clot retraction occurs sooner and is very strong, with clearly defined, sharp peaks in the Sonoclot signature after fibrin formation). All statistical analyses were performed using R statistical software (R Foundation for Statistical Computing, Vienna, Austria. 2021, version 4.1.1). The Shapiro Wilk's test was used to test the normality of the distribution of continuous variables. Categorical variables are shown as frequencies, and continuous variables as mean (standard deviation) or median (interquartile range) based upon normality of distribution. Comparison of variables was performed using Chi-squared test for categorical and the Wilcoxon rank-sum test for continuous variables.

## Results

A total of 48 COVID-19 patients were supported with VV-ECMO with a median duration of 16 days. The median duration of VV-ECMO support in patients requiring VATS was significantly longer than those not requiring VATS (resp. 35 days and 14 days,  $p < .001$ ). VATS was required in seven patients (15%), and seven were re-explored due to recurrence of hemothorax, resulting in a total of 14 VATS procedures. Five of the 14 procedures (35%) were performed in one patient. Indications were empyema (2/14 or 14.3%) and hemothorax (12/14 or 85.7%). Hemothorax was secondary to another pleural intervention in five patients. These pleural interventions were in all cases performed to drain pleural effusion in order to improve ventilation in view of potential weaning of ECMO. One patient had a spontaneous hemothorax due to lung necrosis. Demographics, circuit- and VATS-related parameters for both patient groups are presented in [Tables 1](#) and [2](#). The median age of VATS patients was 47 years. Most of them were male (71.4%). The median time of the first VATS was 40 (IQR 27–44) days after PCR-positivity.

Six patients (85.7%) were treated with UFH, one with bivalirudin because of HIT antibodies. In 57.1% of cases, aspirin was associated to the standard anticoagulation protocol due to high platelet activity. During the first VATS procedure, UFH was continued throughout the procedure. In eight procedures, UFH was stopped for at

**Table 1.** Comparison of demographics, circuit related parameters and survival rates between the cohort of patients supported with venovenous extracorporeal membrane oxygenation requiring video assisted thoracic surgery (VATS), compared to those not requiring VATS.

Characteristic	Overall, N = 48 <sup>a</sup>	Non-VATS, N = 41 <sup>a</sup>	VATS, N = 7 <sup>a</sup>	p-value <sup>b</sup>
Age	50.5 (42.8, 57.2)	52.0 (43.0, 58.0)	47.0 (44.5, 49.5)	.46
Sex				>.99
Female	16/48 (33.3%)	14/41 (34.1%)	2/7 (28.6%)	
Male	32/48 (66.7%)	27/41 (65.9%)	5/7 (71.4%)	
Height	170.0 (165.0, 180.0)	170.0 (165.0, 177.5)	177.0 (163.5, 180.0)	.95
Weight	90.0 (81.2, 107.2)	90.0 (81.8, 108.2)	89.5 (82.2, 97.5)	.81
Body mass index (kg/m <sup>2</sup> )	30.4 (27.1, 33.8)	29.6 (26.9, 33.7)	31.1 (28.3, 35.9)	.78
Days of mechanical ventilation before ECMO	5.0 (3.0, 8.5)	5.0 (3.0, 7.2)	4.0 (2.0, 13.5)	.79
Days of ECMO support	16.0 (11.0, 28.8)	14.0 (10.0, 25.0)	35.0 (32.5, 48.0)	<.001
Circuit exchange incidence	17/48 (35.4%)	11/41 (26.8%)	6/7 (85.7%)	.005
Circuit lifespan (if exchanged)	16.0 (12.0, 28.0)	16.0 (9.8, 29.5)	15.0 (12.5, 21.2)	>.99
Survival (60 days)	32/48 (66.6%)	29/41 (70.7%)	3/7 (42.9%)	.20

ECMO: extracorporeal membrane oxygenation; VATS: video assisted thoracic surgery.

<sup>a</sup>Median (25%, 75%); n/N (%).

<sup>b</sup>Wilcoxon rank sum test; Fisher's exact test.

**Table 2.** Data on demographics, comorbidities, ECMO-circuit changes, VATS-procedures and overall survival of all patients included.

Comorbidities						ECMO circuit changes		VATS procedures			TAE	Survival
Asthma or COPD	AHT	DM2	CAD	CKD	Nr	Urgent?	Nr	Side	Indication		N	N
Pt 1	N	N	N	N	0	n/a	2	Right	Hemothorax (lung necrosis)		N	N
Pt 2	N	N	N	N	1	N	2	Right	Hemothorax (Tx drain)		Y	Y
Pt 3	N	N	N	N	2	N	1	Right	Hemothorax (pigtail)		N	N
Pt 4	N	Y	N	N	1	Y	1	Right	Hemothorax (attempt pleural puncture)		N	N
Pt 5	N	N	N	N	3	N	2	Right	Hemothorax (attempt pleural puncture)		Y	Y
Pt 6	N	Y	N	N	1	N	1	Right	Empyema (lung necrosis)		N	N
Pt 7	N	Y	N	N	2	Y	2	Right	Both (1st empyema; 2nd bleeding)		Y	Y

N: no; Y: yes; n/a: not applicable; M: male; F: female; BMI: body mass index; AHT: arterial hypertension; DM2: type 2 diabetes mellitus; CAD: coronary artery disease; CKD: chronic kidney disease, defined as an estimated glomerular filtration rate of less than 60 mL/min; TAE: transarterial embolisation; Tx: thorax; VATS: video-assisted thoracic surgery.

least 1 h before incision, of which the two most recent procedures were performed with a prolonged interruption of UFH (> 6 h). In the other procedures, UFH was discontinued just before the incision. Perioperative UFH and aspirin dosage and coagulation parameters are summarized in Table 3. Data on pre-, peri- and post-operative transfusion as well as use of prothrombin complex concentrate (PCC) are summarized in Table 4. Fibrinogen concentrate was administered in none of the patients. Full flow ECMO was maintained during the procedure (Pump Flow Index 2.4 L/min/m<sup>2</sup>).

A total of 10 circuit exchanges due to clot formation or oxygen transfer failure were required in six patients (85.7%) in the VATS group, of which two occurred

urgently, compared to 15 non-urgent system exchanges in 11 of 41 non-VATS COVID-19 patients (26.8%). Five circuit exchanges occurred before any VATS procedure, four after the VATS procedure, and one right before the start of surgery. Only one circuit replacement (patient 5) seemed to be related to the preceding VATS procedure with an increasing oxygenator resistance a few hours after VATS. However, this patient also received perioperative polytransfusion with more than 10 units of packed cells, 7 units of fresh frozen plasma and 1 vial of PCC (Table 4). This circuit had a lifespan of 6 days. The median lifespan of the circuits, if exchanged, was 15 days (IQR 12–21) in the VATS group which was comparable to non-VATS. None of these mechanical complications was fatal.

**Table 3.** Heparin and aspirin dose perioperatively and preoperative parameters of hemostasis for each video assisted thoracic surgery-procedure.

	Heparin dose (IE/kg/h) perioperatively with T <sub>0</sub> = time of incision (hours)											Aspirin dose (mg)		Platelet function	Preoperative parameters of hemostasis					Before heparinisation	
	-5	-4	-3	-2	-1	0	1	2	3	4	5	Preoperative	Postoperative		PT (%)	aPTT (s)	Platelet count (/μL)	Fibrinogen (mg/dL)	ACT (s)	CR (U/min)	aPTT (s)
VATS 1	10	10	10	9	9	9	9	9	8	8	8	100	100	0,5	70	72	352	547	142	7	29
VATS 2	5,5	5,5	5,5	5,5	5	0	0	0	5,5	5,5	5,5	0	0	2,2	76	43	104	450	142	10	29
VATS 3	13	13	13	13	13	0	13	13	13	13	13	100	100	3,4	73	47	172	338	131	10,4	31
VATS 4	11,5	11,5	11,5	11,5	11,5	0	0	0	11,5	11,5	11,5	100	0	4	84	56	253	532	136	9,5	37
VATS 5	8	8	10	10	10	0	10	10	10	10	10	0	0	3,4	74	54	107	300	136	9,3	37
VATS 6	bivalirudin 60 μg/kg/h											100	†	NA	53	92	233	NA	180	NA	47
VATS 7	0	0	0	0	0	0	0	0	0	0	0	100	0	3,2	104	72	197	485	136	8	30
VATS 8	7,5	8,5	8,5	0	0	0	0	0	0	0	0	50	50	1,2	88	55	130	177	136	18	30
VATS 9	7	7	0	0	0	0	0	0	0,5	0,5	10	100	100	NA	112	38	317	968	NA	NA	34
VATS 10	6,5	6,5	6,5	6,5	0	0	0	0	0	†	†	0	†	0,4	72	57	164	864	186	9,8	37
VATS 11	5	5	5	0	0	0	0	0	3	3	3	0	0	1	90	40	178	600	142	14,7	34
VATS 12	15	15	15	0,5	0	0	0	0	1	3	3	100	100	0,5	92	61	218	679	153	5,7	34
VATS 13	0	0	0	0	0	0	0	0	0	0	0	0	0	NA	77	76	119	166	131	11,3	34
VATS 14	0	0	0	0	0	0	0	0	1	1	1	0	0	2,9	82	45	136	346	147	25	34

VATS: video assisted thoracic surgery; PT: prothrombin time; aPTT: activated partial thromboplastin time; ACT: activated clotting time; CR: clot rate; NA: not applicable.

Procedures are ranked chronologically. Red color indicated duration of each procedure. As to the ninth procedure, no ACT or CR was available as this patient was put on VV-ECMO after the surgical procedure.

**Table 4.** Overview of the pre-, peri- and postoperative amounts of transfusion (packed cells, fresh frozen plasma, platelet concentrate and prothrombin complex concentrate, from 24 h before until 24 h after each video assisted thoracic surgery procedure).

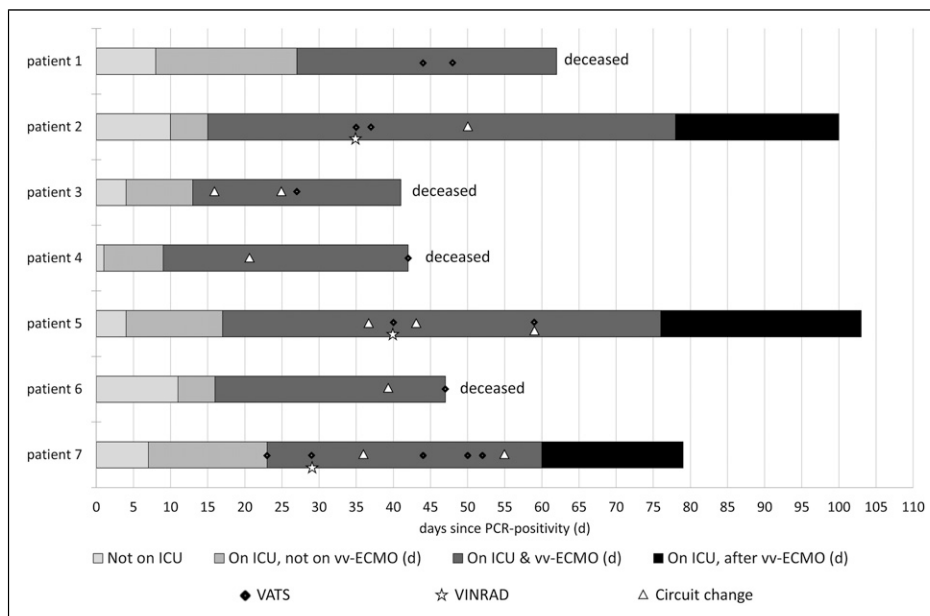
	Packed cells (U)			Fresh frozen plasma (U)			Platelet concentrate (pool)			PCC (vial)			
	Pre	Peri	Post	Pre	Peri	Post	Pre	Peri	Post	Pre	Peri	Post	
VATS 1 (patient 1)	1	1	2	0	0	0	0	0	0	0	0	0	0
VATS 2 (patient 1)	5	0	0	0	0	0	0	0	1	0	0	0	0
VATS 3 (patient 3)	1	0	1	0	0	0	0	0	0	0	0	0	0
VATS 4 (patient 2)	3	8	5	7	2	0	1	0	0	0	0	1	0
VATS 5 (patient 2)	5	2	2	0	0	0	0	0	0	1	0	0	0
VATS 6 (patient 4)	1	2	2	0	2	2	0	0	0	0	2	0	0
VATS 7 (patient 5)	1	4	5	0	4	8	0	1	0	0	0	1	0
VATS 8 (patient 5)	2	12	4	0	3	4	0	0	0	0	0	0	0
VATS 9 (patient 7)	0	2	3	0	0	0	0	0	0	0	0	0	0
VATS 10 (patient 6)	5	10	0	0	0	0	0	0	0	0	0	0	0
VATS 11 (patient 7)	4	2	2	2	2	0	0	0	0	0	0	0	0
VATS 12 (patient 7)	0	2	2	0	2	2	0	0	0	0	0	0	0
VATS 13 (patient 7)	2	4	2	2	4	0	0	3	1	0	0	0	0
VATS 14 (patient 7)	1	2	0	0	2	0	0	1	0	0	0	0	0

One unit packed cells = ~ 250–300 mL; one unit of fresh frozen plasma = ~ 200 mL; One pool platelet concentrate = ~8 units; One vial of PCC = 250 U factor IX. VATS: video assisted thoracic surgery; PCC: prothrombin complex concentrate.

The overall 60 days survival in the total COVID-19-ECMO-cohort was 66.6% (32/48). Out of seven patients with VATS, four patients (57.1%) ultimately died, of which two (50%) died immediately after a procedure due to uncontrollable bleeding. All three survivors were treated with additional transarterial embolization to control bleeding perioperatively. A timeline summary is presented in [Figure 1](#).

## Discussion

The perioperative management of COVID-19 patients on VV-ECMO is challenging due to the difficult balance between hemostasis and thrombosis. This is the first report evaluating the safety and feasibility of VATS procedures in critically ill COVID-19 patients supported with VV-ECMO. Our results demonstrate several important findings.



**Figure 1.** Timeline summary of included COVID-19 patients requiring VATS while on VV-ECMO. ICU: intensive care unit; VV-ECMO: venovenous extracorporeal membrane oxygenation; VINRAD: vascular and interventional radiology; VATS: video-assisted thoracic surgery.

First, thoracic complications which require VATS in this specific populations were common (15% of COVID-19 ECMO patients) and mostly consisted of hemothoraces and, to a lesser extent, empyema. Comparable data about pleural complications in critical COVID-19 are scarce. One series reports an incidence of 3.8% in hospitalized COVID-19 patients, of which only 8% was due to hemothorax (compared to 85.7% in our cohort).<sup>5</sup> However, this series cannot be extrapolated to the presented cohort as these patients were not critically ill, not supported on VV-ECMO and mostly not on full anticoagulation, which might explain the relative lower number of hemothoraces. Besides this, most hemorrhagic incidents occurred secondary to percutaneous intervention in the context of pleural effusion or pneumothorax. These data show that performing such percutaneous procedures should be considered carefully in patients at high risk of developing bleeding complications.

Second, the immediate perioperative mortality due to uncontrollable bleeding was high, as was the total in-hospital mortality. 60 days mortality in the total COVID-19-ECMO-cohort was 33.4%, irrespective of the need for surgery, which was similar to the reported rate by ELSO.<sup>1</sup> In the patients undergoing VATS, however, in-hospital mortality was as high as 57%. In another series of 18 patients on VV-ECMO requiring thoracotomy in the pre-COVID-19-era, the in-hospital mortality was 39%.<sup>3</sup> Yet our VATS cohort was on

ECMO for 35 days and admitted to the ICU for several weeks, illustrating this population's long and complicated course.

Third, all survivors were successfully treated with additional transarterial embolization to control bleeding postoperatively. Transarterial embolization is known to be a highly efficient therapy to stop the postoperative bleeding definitively.<sup>6</sup> In this study, transarterial embolization was mainly performed as a rescue strategy when uncontrollable bleeding with an arterial blush on contrast enhanced computed tomography (CT) scan was present. We believe this endovascular technique should be readily available in hospitals taking care of ECMO patients. The indications for transarterial embolization and its place as bail out versus pre-emptive strategy together with VATS should be further explored. Furthermore, VATS was necessary in all cases to allow lung expansion in order to facilitate potential weaning of ECMO. Other adjunctive therapeutic options, such as intrapleural tissue plasminogen activator (TPA) and DNase, were not used but might be of additional value. In the MIST2-study, intrapleural TPA and DNase in patients with pleural infection showed promising results with significantly improved radiographic clearance compared to all other groups and reduced surgical referrals and hospital stays.<sup>7</sup> However, its use and indication in critically ill COVID patients has not yet been clearly defined.

Fourth, a prolonged duration of VV-ECMO support and transfusion of blood products, rather than the interruption of heparin perioperatively, might be important contributing factors to higher need for circuit exchanges. In this matter, it is important to note that perioperative anticoagulation management was heterogeneous in this cohort. As no clear guidelines were available, it changed throughout the pandemic, focusing on short interruptions of UFH administration during the first six procedures, evolving to a more restrictive anticoagulation policy in the latter eight procedures. Literature from the pre-COVID era about thoracoscopy in patients supported on VV-ECMO already showed that heparin could be safely omitted during and shortly after thoracic interventions and a consensus document from the Society of Cardiovascular Anesthesiologists recommends withholding heparin for approximately 6 h before major noncardiac or airway surgery if the thrombotic risk is low, which depends on several factors such as baseline coagulation status, presence of active infection and ECMO blood flow >3.5 L/min.<sup>8-11</sup> In this context, it is important to note that six out of seven patients in the current cohort underwent a circuit exchange, which is however similar to a recent study that described at least one in all COVID-19 patients on VV-ECMO.<sup>1,12</sup> On the other hand, comparable to other reports, in the non-VATS COVID-19 VV-ECMO cohort ( $n = 41$ ), circuit exchanges occurred only in 26.8% of patients.<sup>1</sup> One could hypothesize that the discrepancy between VATS and non-VATS patients could result from withdrawing anticoagulation before the surgical procedure. However, we observed that only one out of 10 circuit exchanges was directly related to a VATS procedure. The five exchanges that occurred before any VATS were clearly not associated with these procedures. In the four other, the exchanges occurred after a median oxygenator life span of 17.5 days, exceeding the average circuit life span reported in COVID-19 patients.<sup>13</sup> Additionally, we observed a significantly longer median duration of ECMO support in VATS patients than non-VATS patients (35 vs 14 days,  $p < .001$ ). Furthermore, it is important to note that the patient in which the circuit change seemed related to the VATS procedure had received an important load of blood products (packed cells, but more importantly also fresh frozen plasma and PCC) and that no other patient had received equal amounts of transfusion. Thus, a prolonged period of VV-ECMO support and perioperative transfusion of blood products, rather than the abrupt withdrawal of anticoagulation, might be responsible for the increased incidence of circuit-related complications. However further research is needed to better

elucidate the contributing factors to circuit exchanges in this population.

This study is limited due to the small number of included patients, the small amount of interventions and its monocentric retrospective design. Furthermore it is important to note that 5 of 14 VATS procedures were performed in one patient. However, the presented data might be of interest for several reasons. First, there is no previous research available describing VATS in critically ill COVID-19 patients supported with VV-ECMO. Second, as COVID-19 patients often present with a prothrombotic state, results of previous research on thoracic surgery during VV-ECMO cannot be extrapolated to this specific population. Third, rather than providing firm conclusions on patient management, the primary goal of this study is to share our experience and express the need for further large-scale research since no clear management strategy has been described in literature.

## Conclusion

COVID-19 patients on VV-ECMO may require thoracic surgery. Finding the right balance between preventing thrombotic complications and avoiding uncontrollable bleeding is challenging. In this series, intra-thoracic bleeding complications were frequent and ECMO circuit-related complications seemed to be linked to a prolonged period of VV-ECMO support and polytransfusion, rather than the short preoperative withdrawal of anticoagulation. As such, we believe a perioperative interruption of anticoagulation might be considered to reduce bleeding complications. Additional transarterial embolization to control postoperative bleeding may further improve outcomes and should be available in ECMO centers. Further research is needed to enhance perioperative management in this specific population.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

## Ethical approval

Institutional Review Board (IRB) Approval: The study was approved by the local ethical committee (BC-09806), which waived informed consent. Ghent University Hospital, C. Heymanslaan 10, Ghent, Belgium.

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**Appendix****Abbreviations**

ARDS	acute respiratory distress syndrome
COVID-19	coronavirus disease 2019
VV-ECMO	venovenous extracorporeal membrane oxygenation
VATS	video-assisted thoracic surgery
UFH	unfractionated heparin
ACT	activated clotting time
CR	clot rate
PCR	polymerase chain reaction