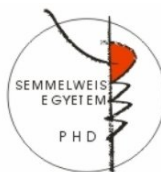


Anaesthesia and Intensive Therapy in Modern Thoracic Surgery

PhD Thesis

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1. Introduction

According to the WHO's projection, the incidence of lower respiratory infections will decrease by 2030 while COPD will be the 3. and lung cancer will be the 6. most frequent cause of death in the world. Hungary has the highest rate of lung cancer in men as well as in women. Complete surgical resection performed in time followed by complex oncotherapy is the most successful treatment of this disease. While the beginning of modern surgery originates from Morton's "ether day", the spread of anaesthesia performed with tracheal intubation made modern thoracic surgery possible. We are entitled to say that the second half of the 20. century is the "half century of the thoracic surgery". The interdependence of anaesthesia and thoracic surgery is characterised by the fact that the milestones of modern thoracic surgery are based on technical developments either in surgery or in anaesthesiology. By the end of thoracic surgery's half century pulmonary resections became low morbidity and mortality procedures. The modern thoracic – except robotic - surgery of the 21. century is present in Hungary

wedded to modern anaesthesiology and intensive therapy. Between 30-45% of lung cancer cases are operated with VATS in our modern thoracic centres. The implementation of the national lung transplantation program meant not only the realization of the only missing solid organ transplantation in Hungary, but anaesthetist and intensive therapists got also a new technique in their hands: the extracorporeal membrane oxygenation machine, the ECMO. Just as in the past, thoracic surgery, anaesthesiology and intensive therapy are inciting each other and as a result ECMO has appeared in the operating room, possessed mutually by thoracic surgeons and anaesthetists not only at lung transplantations but also at complex tracheobronchial resections for oncologic reasons. Today the non-sustainable intraoperative oxygenation is only a technical limitation of thoracic procedures. This includes difficult airways or insufficient parenchyma for the intraoperative single-lung ventilation. The postoperative respiratory insufficiency is particularly frequent after thoracic procedures, and it is an important task for the intensive therapists, this is why thoracic surgery the intra-, and perioperative suppliers have to work

end-to-end. The realisation of the national lung transplantation program enabled the National Institute of Oncology (NIO) AITO to use its ECMO capacity to treat not only patients with respiratory insufficiency before and after transplantation, but also that of other origin.

2. Objectives

The aim of this essay is to analyse the use of ECLS, particularly the different modalities of ECMO in modern thoracic surgery and anaesthesiology- intensive therapy as a working unit with the following questions:

2.1 The ECMO technique's role, significance, safety and effect on morbidity and mortality in lung transplantation

2.2 The role and significance of EMCO modality according to cardiorespiratory function before lung transplantation

2.3 The role and significance of EMCO modality according to cardiorespiratory function after lung transplantation

2.4 The role and significance of high frequency JET ventilation in lung transplantation

2.5 The role and significance of ECMO in respiratory insufficiency except lung transplantation

2.6 Retrospective analysis of our elective thoracic operations with the use of veno-venous ECMO to assess the indication, safety, perioperative morbidity and mortality.

2.7 The role and significance of VV-ECMO in extending the technical operability in modern anaesthesiology for modern thoracic surgery

3. Methods

We retrospectively analysed our data between 28. 04. 2014 – 30. 04. 2019 and found that the ECMO was used 107 cases in the NIO (table 1.). The study was permitted by the Regional Ethical Committee for Research of Semmelweis University under SE-RKEB 13/2019. Data were collected anonymously in a SPSS table. Ninety-one patients got

either VV or VA ECMO support for their operation, 66 of them were central VA, and we bridged 7 of them to transplantation, successful transplantation could be done in 4 cases. We also supported 4 patients after lung transplantation, 3 of them had PPH, and in one case the reason was the recipient's circulatory instability as well as PGD.

Table 1. ECMO supports in NIO between 28.04.2014-30. 04. 2019 grouped according to indication, modality and site of cannulation

n=107			LUTX		non-LUTX			
			V A	VV	V V	V A	VV → VA	
o p	preop	perif.	1	3				91
	IOP	centr.	66					
		perif.	2		13			
	postop	perif.	4		2			
non-op		perif.		3	11			1
all together			79		28			107

For non-operational reason additional 16 patients were supported by ECMO, 13 of them were transferred to our ICU because of severe acute respiratory distress caused by infection. One of them was reanimated with the aid of VA-ECMO, and by another VV to VA change was necessary.

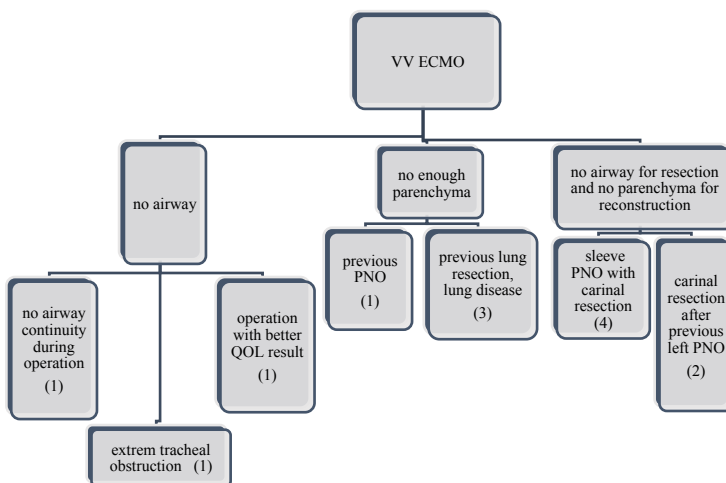


Figure 1. Indications of VV-ECMO supported lung resections except lung transplantation

In 2015 the infrastructure of lung transplantation was financed by the Hungarian government and as a result the NIO was supplied by 4 portable, compact multimodal

ECMOs (Cardiohelp System, Maquet, Getinge) issued with bilevel alarm and built in pressure control. We used these ECMOs by all 107 patients either in VV or VA modalities depending on the indication, and when it was necessary the patients were transferred with these machines inside the hospital or abroad. We used heparine coated (Bioline Coating) HLS 5.0 or 7.0 Advanced (Maquet, Getinge) premounted pump-oxygenator-line systems according to the patient's cardiac output. The system was filled up with 350-600 ml saline. All 4 ECMOs were mounted by a Heater Unit 35 (Maquet Getinge). The priming, operating, controlling and if necessary the adjusting of the machine, and also the problem shooting in the operating theatre and in the ICU were done by anaesthetist-intensive specialists, experts in ECMO technique. The machine was the same in each case, but according to driving and returning cannulae position we used them either VA or VV, and in case of VA either peripheral, or central.

Introducing narcosis since its cardio-depressive effect can lead to hemodynamic disaster by patients with severe pulmonary hypertension. Following the protocol in

Vienna by patients with IPAH at the beginning of lung transplantation we introduced peripheral VA-ECMO supported by conscious sedation which was in our practice sustained at low flow through the whole operation parallel to the central VA-ECMO providing cardio-hemodynamic stability. Our aim was to avoid the risk of changing from peripheral to central setting and to retain the possibility of postoperative peripheral VA-ECMO support. In those cases when the postoperative prolonged ECMO support was not presumably required we used HFJV at the beginning of anaesthesia until the starting of central VA-ECMO.

4. Results

We retrospectively collected data in our institute between 28. 04. 2014 and 30. 04. 2019 and found that we used ECMO support in 107 cases during 5 years. I describe the results according these three indications: 1. ECMO use in lung transplantation and its perioperative phase, 2. ECMO use in thoracic surgery except lung transplantation, 3. ECMO use in severe respiratory insufficiency caused by severe ARDS.

1. ECMO use in lung transplantation and its perioperative phase

During the 3.5 years since December 2015 we performed 69 lung transplantations. In 2017, the first patient with primer pulmonary hypertension (IPAH/PPH) was transplanted in Hungary and also the first combined (lung-kidney) transplantation was performed with the cooperation of the Transplantation and Surgery Department of Semmelweis University. The first lung transplantation in a child and also the first re-transplantation was done in 2018. Four patients were bridged to transplant. In one case peripheral VA-ECMO was used in a patient with secondary severe pulmonary hypertension. One CF patient was bridged with femoral-jugular VV-ECMO, another with single-site bicaval VV-ECMO in rapid progressive interstitial lung disease. We transferred one patient to Vienna with single-site jugular bicaval VV-ECMO for re-transplantation, where the operation was successfully performed. We experienced no “first lung syndrome”. The incidence of primer graft dysfunction (PGD) was low, there was no need to re-

implant the ECMO. PGD was grade 1 in three, grade 2 in one, and grade 3 in two cases. Hematoma evacuation was done in 5 cases because of bleeding and early decortication in 2 cases. The Kaplan-Meier 1-year survival of the patients was 82.96%. We had no intraoperative death. In the early postoperative period - 30 days - 3 patients died.

2. ECMO use in thoracic surgery except lung transplantation

The 13 patients spent average 7.4 days (2-18) in ICU and left the hospital after average of 12 days (4-35). In our cases the cannulation and the VV-ECMO support were uneventful. The average time of apnoe was 142 minutes (25-310). We had no neurological complication in the early postoperative period. We had to reopen the chest in one case because of bleeding from an intercostal vein. In one case reintubation and ventilation became necessary on the 3. postoperative day because of newly appeared pulmonary infiltrates. On postoperative 18 day this patient died on the base of sepsis and multiorgan failure.

3. ECMO use in severe respiratory insufficiency caused by severe ARDS

The 13 ECMO supported patients' mean age was 44.15 (10-68) years, the average Horowitz index at admission was $53 \pm 8,68$, and the length of previous ventilation was $5 \pm 2,62$ days. The average length of ECMO support 16.1 days (<1-44). At 8 patients we experienced bleeding, in 6 of them from the throat, mouth and beside the tracheotomy, in 2 cases only from the throat. By one patient the bleeding beside the tracheotomy necessitated surgical solution. Turning an extreme obese patient to the side, the previous vein puncture site on its lower arm bleed under the pressure so much that a compartment syndrome developed requiring surgery and open treatment. Pathological examination revealed intracranial bleeding in posterior scala. All patients got transfusion, $15,7 \pm 7,6$ units in average. Seven patients were weaned off the ECMO, 6 patients died on ECMO. All 7 patients were on VV-ECMO, they needed only respiratory support. Five of the 7 patients went home. Two patients died, both of them had new onset of fulminant sepsis caused by multi-

resistant bacterium. All five patients regained their full ability to daily life by the end of the study period.

5. Conclusions

1. The use of central VA-ECMO support during lung transplantation is outstanding. It is safe, we did not experience morbidity and mortality related to ECMO use. We did not have intraoperative death, the one-year survival was over 80%. Due to the intraoperative cardio-respiratory stability provided by ECMO our primer graft insufficiency incidence was low and no renal replacement therapy was required.

2. Before lung transplantation either VA or VV ECMO can be used to bridge the deteriorating patient on waiting list to transplantation. In cases of non-evaluated patients the indication of ECMO use can be bridge to decision.

3. The planned, prolonged peripheral VA-ECMO support after lung transplantation has a significant role. It enables the heart to adjust to the altered pressures after the

transplantation. Patients after transplantation with primer graft dysfunction can be supported with VV-ECMO.

4. Subglottic open-system HFJV can successfully ventilate the patients with low lung compliance before the transplantation as a bridge to transplantation. It has significant role during introducing anaesthesia to avoid the further elevation of pulmonary pressure. Using Jet ventilation the adverse cardio-depressive effect of positive pressure ventilation can be dismissed, which is of utmost importance during transplantation of patients with end-stage lung disease combined with pulmonary hypertension. In these cases it can be an alternative of peripheral pre- and intraoperative VA-ECMO bridge, before starting the intraoperative central VA-ECMO.

5. Based on our experience with the ECMO support in severe ARDS patients we think that is important to provide the possibility of ECMO support in respiratory insufficiency. In the prevention of a potential flu pandemic it may be as important to establish and organise the national ECMO support network, as the other prevention

aims declared previously in connection with 2009/2010 H1N1 pandemic.

6-7. In modern thoracic surgery the VV-ECMO has significant role in case of correct indication, and it is the first choice instead of CPB or VA-ECMO. In case of technical inoperability, when there is no airway or insufficient parenchyma for gas exchange, but pulmonary vascular bed is enough and there is no need for great-vessel resection, VV-ECMO can safely replace the complete gas exchange for several hours without further risk of bleeding. The use of VV-ECMO did not increase the perioperative morbidity and mortality. Previously inoperable patients can be operated with VV-ECMO.

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