Complex pulmonary resections using extracorporeal membrane oxygenation

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Background: The use and effect of extracorporeal membrane oxygenation (ECMO) in general thoracic surgery patients is still not clear. Although ECMO is being routinously used in lung transplantation patients, it's benefits in oncological patients are still to be defined.

Methods: In a period of 8 years, a total of 24 patients underwent complex lung resections under ECMO in our institution. In cases of carinal resection, percutaneous veno-venous, jugular-femoral cannulation was considered suitable. For combined resection of lung a descending aorta a percutaneous femoral veno-arterial cannulation was used. In cases of extended left atrial resection, a percutaneous jugular-femoral veno-venous-arterial cannulation was favoured.

Results: Carinal resections and reconstruction (n=8), resections of the descending aorta and left lung (n=7), resections of lung and left atrium (n=9). No intraoperative deaths occurred. Overall 30-day mortality was 25%. A complete resection was achieved in 18 patients.

Conclusions: In conclusion, the present study shows that intraoperative use of ECMO in oncological general thoracic surgery patients is feasible, with minimal intraoperative complications allowing surgeons increased operating-field safety. Perioperative mortality is high, but this is rather an attribute of local extended disease and patient comorbidities.

Keywords: Extracorporeal membrane oxygenation (ECMO); lung surgery; veno-venous (VV); veno-arterial (VA); aortic surgery; left atrial resection; carinal resection

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Introduction

Since the first reports of use of extracorporeal membrane oxygenation (ECMO) in the 1970's the role of extracorporeal life support systems for non-cardio/thoracic surgery patients has been expanding rapidly in the last decades (1,2). Up to now, beside its successful use in coronary artery bypass surgery and beyond (3,4), in thoracic surgery, utilization of veno-venous ECMO (VV-ECMO) or veno-arterial ECMO (VA-ECMO) is mainly established for patients undergoing lung transplantation (5,6). However, although ECMO is routinously used in this setting, only few data exist suggesting a beneficial effect for ECMO in non-lung-transplantation thoracic surgery. At least from a theoretical point of view, ECMO support might be helpful to achieve high radicality in cases of central tumor infiltration or higher intraoperative safety in salvage operations i.e., after definitive chemoradiotherapy.

Typically, surgical therapy of centrally located tumors with extensive infiltration of the left atrium, the descending aorta or the tracheal bifurcation is associated with challenging intraoperative conditions making the use of an extracorporeal support attractive for thoracic surgeons (7).

From a surgical perspective VV-ECMO offers the advantage for surgical procedures without or a minimum of mechanical ventilation. The abundance of mechanical ventilation allows safe and secure resection and anastomosis with an optimal surgical field. Furthermore, infiltration of the left atrium or the descending aorta sometimes require heart lung support for safe resection. In this situation VA-ECMO might offer an alternative to conventional heart/lung machines without using cardioplegia.

The aim of our study was therefore to summarize our single-center experience with intra- or perioperative use of VV- or VA-ECMO as respiratory and/or circulatory support in patients undergoing lung surgery.

Methods

Between June 2011 and August 2019, a total of 24 patients underwent combined complex lung, tracheobronchial, aortal or left atrial resections under ECMO. In cases of carinal resection, percutaneous veno-venous, jugular-femoral cannulation (VV-ECMO) was considered suitable. For combined resection of lung a descending aorta a percutaneous femoral veno-arterial cannulation was used (VA-ECMO). In cases of extended left atrial resection, a percutaneous jugular-femoral veno-venous-arterial ECMO (VV-A-ECMO) was favoured. In all patients ECMO was established at the beginning of the procedure. No central cannulation or cardioplegia was necessary in any of the patients. Decannulation was conducted immediately postoperatively when possible. Arterial femoral cannulation-sites were surgically closed through exposure of the artery and arterial-wall suture to avoid late aneurysmatic complications.

ECMO settings

Standard configuration of the VV-ECMO system consisted of a 23 Fr/38 cm femoral-draining cannula and a 19 Fr/15 cm inlet-flow cannula (Maquet, Rastatt, Germany). Standard configuration of the VA-ECMO system consisted of a 23 Fr/55 cm femoral-draining cannula or two single draining cannulas (jugular and femoral) placed in the right atrium, and a 15–17 Fr/15 cm inlet-flow cannula in the A. femoralis (Maquet, Rastatt, Germany). All VV- and VA-ECMO runs were performed with the Cardiohelp system (HLS set advanced 7.0). Standard anticoagulation with heparin was used with an initial bolus to target an aPTT of 1.5-fold of the normal range.

Surgical technique

In cases of tracheal carinal resection, we used a VV-ECMO as total respiratory support. In all cases of elective carinal resection complete interruption of ventilation was possible. In all cases we favored a jugular-femoral vein cannulation for sufficient flow in order to achieve longer periods of interrupted ventilation time. No jet-ventilation or operating field intubation was required. In one complex case of left sided postpneumonectomy empyema with oesophageal-left bronchial stump fistula, the use of a VV-ECMO respiratory support facilitated a right anterolateral approach of the carinal space with carinal and esophageal reconstruction. The operation was performed without ventilation of the right lung. Tracheobronchial anastomosis was completed using a continuous 4-0 monofilament absorbable polyester suture (PDS).

In cases of descending aorta resection, we favoured a femoral vein-contralateral femoral artery cannulation for circulatory support of the lower body. Aorta was clamped in the descending part of the thoracic aorta and above the diaphragm. Polyester grafts (Gelsoft) were used in most of the cases except two cases of local infection for which an aortic homograft was indicated.

In cases of combined lung and left atrial resection, we preferred a double venous cannulation (jugular and femoral) to drain the blood and empty the right atrium as much as possible and a femoral artery retrograde perfusion. Left atrial resections represent the most challenging surgical procedure in our study. We indicated a VV-A-ECMO-assisted left atrial resection in cases of tumor invading the pulmonary vein with visible polypoid tumor thrombi in the left atrium in computer tomography, magnetic resonance tomography and echocardiography. The superior and inferior vena cava were mobilized intrapericardial and both vessels were cross clamped using tourniquets during the cardial resection. This manoeuvre was easily conducted also for left-sided tumors through an anterolateral thoracotomy due to the reduced blood flow in the left ventricle under full circulatory support, allowing the surgeon a complete manual heart luxation and intrapericardial caval exposure. After intrapericardial caval clamping, a beating-heart atriotomy was performed and major left atrial resections were facilitated without the use of atrial clamping or cardiopulmonary bypass and cardioplegia with acceptable intraoperative blood loss.

Table 1 Patients' characteristics

Characteristics	Desc. aorta group, n=7	Left atrium group, n=9	Carina group, n=8
Men	5	2	6
Women	2	7	2
Age (mean in years)	60.8	58.8	54.6
FEV1 (mean in %)	73	64	64
KCO (mean in %)	63	51	58
Neoadj. chemotherapy	1	2	1
Neoadj. radiochemotherapy	4	4	6
Operating time (mean in min)	377	263	289
Lobectomy/Bilob.	2	9	4
Pneumonectomy	4	0	3
Bronchial or tracheal sleeve	1	4	8
Elective surgery	5	8	7
Radicality (R0-resection)	5	7	6

FEV1, forced expiratory volume in the first second; KCO, carbon monoxide transfer coefficient.

Ethics

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Individual Informed consent was waived due to the retrospective nature of the study. The Ethic Committee of the University of Witten Herdecke approved the above retrospective analysis.

Results

Patients and ECMO indication

Between 2011 and 2019, n=24 patients underwent thoracic surgery procedures with ECMO. The study included 13 women and 11 men. Surgical procedures were divided into three groups. Carinal resections and reconstruction (n=8), resections of the descending aorta and left lung (n=7), resections of lung and left atrium with reconstruction (n=9). Patients' characteristics are summarized in *Table 1*.

Indications were mainly because of underlying NSLC. Most of the procedures after definitive chemoradiotherapy were salvage operation of residual disease. Additional indication was fungal infection of an aortic prosthesis after combined resection of lung and aorta for lung cancer. The indications, type of ECMO and procedures are given in *Table 2*. Two patients in the aortic group were operated on as a matter of urgency. Also, two cases in the left atrium group and another two in the carinal group were indicated as emergency operations.

Complications

In the aorta and left atrium group all patients were intraoperatively weaned from ECMO. Two patients were re-operated on for bleeding at the operating site on the first postoperative day. In the carinal and aortic groups, two patients developed early anastomotic insufficiency, but only one required reoperation and revision of the anastomosis. Postoperative mechanical ventilation found place in four cases of the aortic group and four cases of the carinal group. No cannulation-site complications occurred. In cases of V-A or VV-A-ECMO, although no reperfusion cannula for the distal limb was used, there was no ischaemia of the lower extremity. Neurological complications could be documented in one patient of the aortic group (cerebral infarction on the fifth postoperative day). In one case of carinal resection the patient was weaned from ECMO on the 14^{th} postoperative day. Perioperative complications and 30-day-mortality are summarized in *Table 3*. There was no intraoperative change of the planned type of ECMO found place.

Resectability

A complete resection was achieved in 18 patients (78.2%). Pathology revealed one case of the aortic group having microscopical tumor involvement on the resection line of the pulmonary parenchyma. In two carinal resections microscopic invasion of the distal bronchus was confirmed on final pathology; however, in one of these cases, R1-resection was anticipated but accepted by intention in the emergency setting of esophageal-bronchial fistula after left sided pneumonectomy and local recurrence. In two cases of atrial resection final pathology revealed microscopic invasion of pericardium and of the oesophageal muscularis propia. Pathological examination of the resected myocardium was positive for tumor infiltration and negative for resected margins (R0) for all patients of the atrial group.

Short-term mortality

No intraoperative deaths occurred in the three groups. Overall 30-day mortality was 25% (6/24). In the aortic group three patients died during the first 30 postoperative

Table 2 Operating indication, types of ECMO and procedure performed

Indication	Type of ECMO and cannulation	Procedure
NSCLC of the left lower lobe infiltrating the desc. aorta (elective)	V-A; Femoral vein and artery	Pneumonectomy with *en bloc* resection of the aorta
NSCLC of the left lower lobe infiltrating the desc. aorta (elective)	V-A; Femoral vein and artery	Lobectomy with *en bloc* resection of the aorta,
NSCLC of the left main bronchus infiltrating the desc. aorta (elective)	V-A; Femoral vein and artery	Pneumonectomy with *en bloc* resection of the aorta
NSCLC of the left lower lobe infiltrating the desc. aorta with oesophagobronchial fistula after definitive chemoradiotherapy (emergency)	V-A; Femoral vein and artery	Pneumonectomy with *en bloc* oesophageal resection and reconstruction with gastric pull and aorta resection, homograft aorta
Fungal infection of the aortic graft after combined lower lobe-des. aorta resection without prior ECMO (emergency)	V-A; Femoral vein and artery	Replacement of the aortic graft with a homograft aorta, pedicled latissimus dorsi flap
NSCLC of the left lower lobe infiltrating the aorta desc. (elective)	V-A; Femoral vein and artery	Pneumonectomy with *en bloc* resection of the aorta
NSCLC of the left lower lobe infiltrating the desc. aorta (elective)	V-A; Femoral vein and artery	Left lower lobe bronchial sleeve lobectomy with angioplasty and *en bloc* resection of the aorta
NSCLC of the right upper lobe with left atrial infiltration (elective)	VV-A; Femoral and jugular vein, femoral artery	Upper bilobectomy with left atrial resection and reconstruction with bovine pericard
Sarcoma of the right lower lobe with left atrial infiltration (elective)	VV-A; Femoral and jugular vein, femoral artery	Lower lobectomy with left atrial resection and reconstruction with bovine pericard
Sarcoma of the right lower lobe with left atrial infiltration (elective)	VV-A; Femoral and jugular vein, femoral artery	Lower lobectomy with left atrial resection
NSCLC of the left main bronchus with left atrial infiltration, prior chemoradiotherapy (elective)	VV-A; Femoral and jugular vein, femoral artery	Upper Lobectomy with left atrial resection
NSCLC of the left lower lobe with left atrial infiltration (elective)	VV-A; Femoral and jugular vein, femoral artery	Lower Lobectomy with left atrial resection
NSCLC of the left upper lobe with left atrial infiltration and haemoptysis due to venous infarction (emergency)	VV-A; Femoral and jugular vein, femoral artery	Upper double Sleeve lobectomy with left atrial resection
NSCLC of the left upper lobe with left atrial infiltration, prior chemoradiotherapy (elective)	VV-A; Femoral and jugular vein, femoral artery	Upper double sleeve lobectomy with left atrial resection, reconstruction of the pulmonary artery with tailored bovine pericard conduit
NSCLC of the left upper lobe with left atrial infiltration, prior chemoradiotherapy, prior futile thoracotomy (elective)	VV-A; Femoral and jugular vein, femoral artery	Upper double sleeve lobectomy with left atrial resection
NCLC of the left upper lobe with left atrial infiltration, prior chemoradiotherapy and immunotherapy (elective)	VV-A; Femoral and jugular vein, femoral artery	Upper double sleeve lobectomy with left atrial resection and reinsertion of the left lower pulmonary vein in the left cardial appendix
NSCLC of the right main bronchus with carinal infiltration, prior radiotherapy (elective)	V-V; Femoral and jugular vein	Sleeve pneumonectomy
NSCLC of the right upper lobe with carinal infiltration, prior chemoradiotherapy (elective)	V-V; Femoral and jugular vein	Sleeve pneumonectomy
NSCLC of the right upper lobe with carinal infiltration, prior chemoradiotherapy (elective)	V-V; Femoral and jugular vein	Upper sleeve bilobectomy with carinal resection and neocarina

Table 2 (*continued*)

Table 2 (*continued*)

Indication	Type of ECMO and cannulation	Procedure
NSCLC of the right upper lobe with carinal infiltration, prior chemoradiotherapy (elective)	V-V; Femoral and jugular vein	Upper sleeve lobectomy with carinal resection and neocarina
NSCLC of the right upper lobe with carinal infiltration, prior chemoradiotherapy (elective)	V-V; Femoral and jugular vein	Upper sleeve bilobectomy with carinal resection and neocarina
Recurrent NSCLC of the right main bronchus with carinal infiltration after prior lower lobe lobectomy (elective)	V-V; Femoral and jugular vein	Sleeve Pneumonectomy
Oesophageal-bronchial fistula of the left main bronchus stump after chemoradiotherapy and salvage left pneumonectomy with pleural empyema (emergency)	V-V; Femoral and jugular vein	Right sided thoracotomy, isolated carinal resection, oesophageal resection and reconstruction via gastric pull
NSCLC of the right upper lobe with carinal and caval infiltration, prior chemoradiotherapy (elective)	V-V; Femoral veins	Upper sleeve lobectomy with carinal resection and superior vena cava resection, neocarina, reconstruction of the SVC with double PTFE conduits

ECMO, extracorporeal membrane oxygenation; NSCLC, non-small cell lung cancer; V-A, veno-venous; VV-A, veno-venous-arterial; SVC, superior vena cava; PTFE, polytetrafluoroethylene.

Table 3 Postoperative morbidity and mortality rates

Complications	Desc. aorta group, n=7	Left atrium group, n=9	Carina group, n=8	Total, n=24 (%)
30-day mortality	3	0	3	6 (25.0)
In-hospital mortality				
Mechanical ventilation postoperatively	4	0	4	8 (33.3)
Atrial fibrillation	1	2	2	5 (20.8)
Prolonged air leakage >7 days	0	1	0	1 (4.1)
Reoperation	2	0	1	3 (12.5)
Pneumonia	2	0	3	5 (20.8)
Bronchial anastomotic insufficiency	1	0	1	2 (8.3)
Bleeding requiring revision	2	0	0	2 (8.3)
Cerebral infarction	1	0	0	1 (4.1)
Pulmonary embolism	1	0	0	1 (4.1)
ARDS	0	0	3	3 (12.5)
Sepsis	2	0	0	2 (8.3)

ARDS, acute respiratory distress syndrome.

days. One of the patients died on day 3 due to massive pulmonary embolism without having thromboembolic events at the cannulation sites (autopsy result). The two following patients died from sepsis. None of the three patients in the aortic group were under ECMO postoperatively. We had no perioperative deaths in the left atrium group. In the carinal group, three patients died postoperatively from adult respiratory distress syndrome (ARDS), one of them still being under ECMO postoperatively. In this case the patient was intraoperatively weaned from ECMO and was extubated but due to an anastomotic air leakage on the first postoperative day surgical revision was indicated. Revision was performed again under ECMO but after the second procedure the patient could not be weaned and eventually died from ARDS.

Discussion

Our current single-centre experience demonstrates for the first time the feasibility of major lung resection in locally advanced tumors and salvage operations after definitive chemoradiotherapy facilitated by VV- and VA-ECMO, which had otherwise been inoperable. These preliminary results may indicate that acceptable survival rates by otherwise fatal underlying disease can be achieved.

The concept of ECMO assisted non-cardiac thoracic procedures is becoming more and more attractive (8). While conventional cardiopulmonary bypass systems can provide an ideal operative environment for challenging cases, ECMO circuits cause less coagulopathy, inflammation and vasoplegia due to the absence of cardioplegia, a reservoir outside the body and flexible approaches (9,10). Complex tracheobronchial, atrial or combined lung-aortic resections constitute a challenging operating field for the thoracic surgeon and the use of an extracorporeal assistance as respiratory or circulatory support could facilitate stable intraoperative conditions for fulfilling the main goal of complete (R0) resection (11).

Use of ECMO as total respiratory support for complex tracheobronchial resections has been described previously (8,11,12). Klepetko *et al.* reported a series of 10 patients undergoing complex carinal, tracheobronchial resections utilizing VA-ECMO with excellent results in terms of mortality (0%) and complete resection (89%). In our collective of carinal resections (n=8) complete resection (R0) rate was lower (78%) and 30-day mortality was higher (25%). A higher rate of pneumonectomy and prior radiochemotherapy and two emergency cases in our study significantly influenced perioperative mortality and morbidity. Under standard conditions, resections of the main carina can be safely performed with jet ventilation or *in situ* intubation, without requirement of ECMO. The use of VV-ECMO for total respiratory support facilitated in our collective excellent surgical exposure without interruption for mechanical ventilation. None of the patients required a VA cannulation for additional circulatory support. Extracorporeal support was in some cases mandatory (i.e., broncho-oesophageal fistula after left sided pneumonectomy) or individually indicated considering the complexity of the procedure (expected long operating time, resection of major vessels or organs, prior radiochemotherapy, large tracheobronchial resections >4 cm). Our intention was not only to increase safety in the operating field but also to decrease intraoperative ventilation trauma in a cohort of patients with high risk for postoperative ARDS, which is a common complication in this group of patients (13). Klepetko *et al.* also reported patients with postoperative ARDS requiring prolonged ECMO for 8 or 14 days. Two cases in our retrospective study required prolonged ECMO after primary operation. Under such circumstances, ECMO provided the additional advantage to minimize ventilator-induced lung injury.

In cases of combined lung and descending aorta resection, we favoured a VA-ECMO setting for partial circulatory support (approx. 50% of the cardiac output). None of the patients had involvement of the aortic arch. Ohta *et al.* reported 16 surgical cases of lung cancer with infiltration of the thoracic aorta with a mortality rate of 12.5% and a morbidity rate of 31% (14). In this series, cardiopulmonary bypass (CPB) or temporary bypass graft was used for cross clamping the aorta. In our aortic group 30-day-mortality for all cases was at highest (42%) comparing to the other ECMO groups; however, two cases were operated on an emergency basis. Mortality in our elective cases was 20%. We favoured a VA ECMO over CPB or temporary bypass graft for aortic resection because of the benefits of half body circulatory support (kidney, bowel perfusion) and the advantages of low dose heparin administration. We experienced no intraoperative complications regardless of the extent of the operation. Marulli *et al.* reported a series of 35 patients undergoing combined lung resections in four European centres (15). Perioperative morbidity was statistically significantly higher for pneumonectomy (52%) compared to lobectomy (18.7%). A high rate of pneumonectomies, in some cases combined with esophageal resections in our aortic group (57%) and additionally two emergency-indication cases could have significantly influenced morbidity and mortality. Considering that most of our cases were salvage operations after definitive chemoradiotherapy, a high mortality rate was expected. No spine-related neurological complications or perfusion-related abdominal complications were documented in our collective.

In cases of left atrial tumor invasion, we favoured a VV-A-ECMO setting for total circulatory support. The indication for this hemodynamically and technically challenging procedure was endoluminal growth of polypoid tumor in the left atrium in such a degree, that clamping of the atrium without extracorporeal support would lead to major neurological complications and incomplete resection (dissemination of tumor clots in the left ventricle and major cerebral or upper body embolism). To our knowledge, this is the first report of the above technique describing ECMO support and "beating heart"—no clamping atrial resection with *en-bloc* lung resection. Galvaing *et al.* reported in 2014 excellent results on lung cancer surgery with left atrial involvement without the use of CPB and direct clamping after dissection of the interatrial septum (16). The experienced group of authors clearly stated that following contraindications for direct clamping of the left atrium should be considered: invasion of both atria, the presence of an intra-atrial thrombi or a polypoid tumor inside the atrium. All eight cases of our collective met the above-mentioned criteria. Though most surgeons would favour CPB and cardioplegia over ECMO for such complex cases, we considered the setting described above as feasible. The use of two venous cannulas [superior vena cava (SVC) and inferior vena cava (IVC)] and the intrapericardial clamping of SVC and IVC above the level of the cannulas allowed sufficient flow for the ECMO and minimal blood filling of the left atrium (rest blood mainly due to coronary sinus venous flow) after atriotomy in all cases. Aortic valve insufficiency was ruled out by means of echocardiography preoperatively in all cases. In fact, VV-A-ECMO facilitated stable intraoperative conditions also in two cases of large atrium defect after resection requiring longer period of suturing using bovine pericardium as reconstruction material. In one case, VV-A-ECMO allowed sequential resection of left atrium and left pulmonary artery without clamping. Interestingly, the left atrial group of our collective had the lowest 30-day-mortality (0%) and morbidity rate (22.2%). No neurological complications, air or tumor embolism was documented. Dartevelle *et al.* reported on left atrial resections on CPB (bicaval cannulation, beating heart atriotomy) with a mortality rate of 5.5%. Left atrial resections series without CPB report 5-year survival rates of 0–43% (7,16-18). In our collective median survival was 18 months and 5-year survival 26.2%. A lower rate of pneumonectomy in the atrial group (0%) compared to the other two groups had assumably a positive effect on mortality and survival.

This study has some limitations that need to be addressed: (I) retrospective character, (II) limited number of patients, (III) high rates of prior definitive chemoradiotherapy, (IV) high rates of pneumonectomies, (V) absence of homogeneity in terms of tumor entity. Considering the rarity of the indication for the above procedures, a prospective analysis of large, homogenous cohorts is not an elementary goal. A retrospective analysis of 34 ECMO centres in France reported 36 cases of intraoperative ECMO-use for non-transplantation thoracic surgery procedures in a period of 3 years (19).

In conclusion, the present study shows that intraoperative use of ECMO for extended carinal, aortic or atrial resections is feasible with minimal intraoperative complications allowing surgeons increased operating-field safety. Perioperative mortality is high, but this is rather an attribute of local extended disease and patient comorbidities. Centres with extensive experience in ECMO and major thoracic resections could consider this setting as an alternative to CPB respiratory or circulatory support.

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Footnote

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