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Predictors of using extracorporeal membrane oxygenation in lung transplantation

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Rationale. *Lung transplantation is the only definitive treatment in end-stage pulmonary disease. Extracorporeal membrane oxygenation (ECMO) has been used during surgery in recent years as a replacement for respiratory function; ECMO,* however, *has some drawbacks: the presence of an extracorporeal circuit, the need for heparinization, potential thrombogenicity that underlies the risks of developing specific complications that worsen the transplantation prognosis. In this regard, it is relevant to study the factors that make it possible to predict the need in intraoperative ECMO in order to avoid its unjustified use.*

Purpose. *To identify predictors for intraoperative use of ECMO in lung transplantation.*

Material and methods. *The medical records of patients who underwent lung transplantation in the Sklifosovsky Research Institute for Emergency Medicine from May 2011 to July 2017 were retrospectively*

reviewed. Forty nine bilateral lung transplantations were made where 15 patients (30.6%) had lung transplantation performed without ECMO, and 34 (69.4%) underwent lung transplantation and ECMO. A central veno-arterial connection was used in all patients. The study analyzed various factors of patient condition at baseline and identified the most significant of them that enabled to predict the need of ECMO use at surgery with a high degree of probability, avoiding episodes of gas exchange and hemodynamic impairments, the prolongation of surgery, and, therefore, the graft ischemia time.

Results. *As assessed in this study, pulmonary hypertension was the only predictor of an increased likelihood of using ECMO. The probability of connection to ECMO statistically significantly increased in the patients with systolic pulmonary artery pressure higher 50 mmHg ($p<0.05$).*

Conclusion. *The presence of pulmonary hypertension > 50 mm Hg determines the preventive use of ECMO during lung transplantation, which should reduce the number of uncontrolled emergencies during the main stages of surgical intervention; in all other cases, ECMO should be connected basing either on the pulmonary artery compression test results or when indicated.*

Keywords: ECMO, lung transplantation, pulmonary arterial hypertension

Conflict of interests. Authors declare no conflict of interests

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LVC, lung vital capacity

AC, artificial circulation

BMI, body mass index

ABS, acid-base status

PAP_{Syst}, systolic pressure in the pulmonary artery

GFR, glomerular filtration rate

LVEF, left ventricular ejection fraction

ECMO, extracorporeal membrane oxygenation

DLCO, diffusing lung capacity

PaO_2, partial pressure of oxygen

$PaCO_2$, partial pressure of carbon dioxide

Rationale

Lung transplantation is the only definitive treatment in end-stage diseases [1, 2]. Nosological spectrum of indications for lung transplantation includes chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, cystic fibrosis, idiopathic pulmonary hypertension, pulmonary lymphangioleiomyosis, histiocytosis X, interstitial pneumonia with fibrosis, and other diseases [3]. The cardiorespiratory system status in these patients is characterized by severe impairments in gas exchange, which can be aggravated during surgical intervention. The use of artificial blood circulation (AC) for the correction of gas exchange disorders improves the safety of surgery, but a high degree of heparinization increases the risk of bleeding [4]. In recent years, extracorporeal membrane oxygenation (ECMO) has been used as an alternative method of respiratory function prosthetics, which also has some drawbacks: the presence of an

extracorporeal circuit, the need for heparinization (albeit less intense than with AC), potential thrombogenicity that underlie the risks of specific complications worsening the transplantation prognosis. In this regard, it is relevant to study the factors that make it possible to predict the need in intraoperative ECMO for using it only for those patients in whom lung transplantation without prosthetics is impossible.

Study objective

The study aimed at identifying the predictors for intraoperative ECMO use in lung transplantation.

Material and Methods

The medical records of the patients who had undergone lung transplantation in the Sklifosovsky Research Institute for Emergency Medicine from May 2011 to July 2017 were retrospectively reviewed. Forty nine bilateral lung transplantations were performed, including 34 (69.4%) patients having ECMO, and 15 patients (30.6%) without ECMO during their lung transplantation surgery. A central veno-arterial ECMO was used in all patients (Fig. 1).

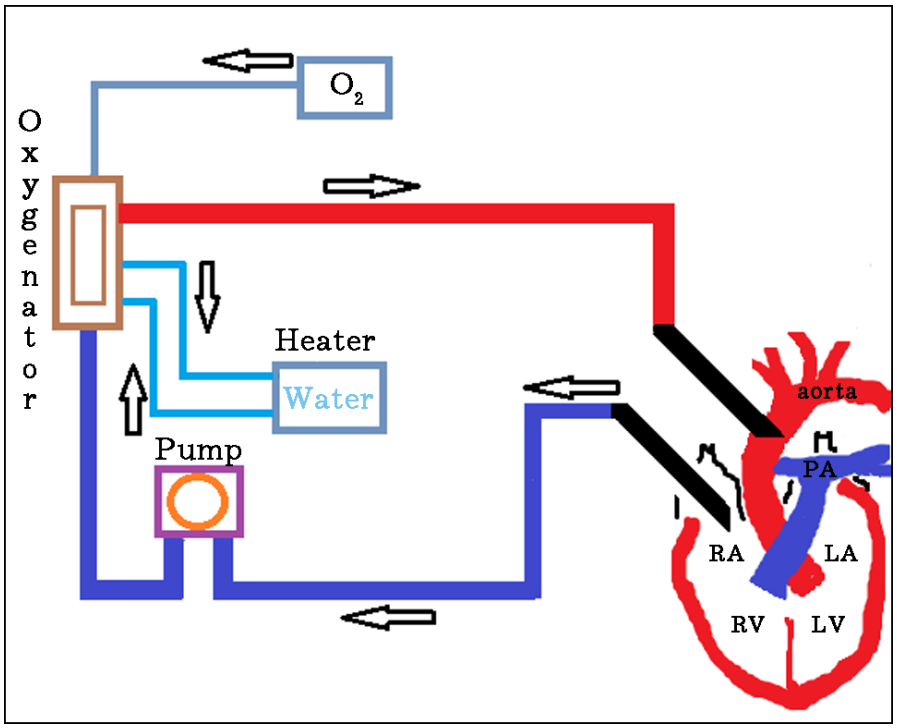

Fig. 1. The scheme of the connected extracorporeal membrane oxygenation circuit

The ECMO circuit connection was undertaken either in case of uncontrolled gas exchange or hemodynamic impairments (uncontrolled hypotension, arrhythmia, including fibrillation) as an emergency measure, or according to the results of the pulmonary artery clamping test. After obtaining an access to the heart and roots of the lungs, the pulmonary artery was isolated: a common trunk and anterior and descending trunks were isolated separately. A ligature on a common trunk was used as a tourniquet that was tightened to perform the pulmonary artery clamping test. The time of pulmonary artery clamping was recorded, the test lasted for at least 7 minutes, after which the hemodynamics status and the pulmonary gas exchange function were assessed by anesthesiologic monitor parameters and oxygen and carbon dioxide pressure in arterial blood (the decrease in

oxygenation index lower than 100 units; pH <7.2 caused by deteriorated CO_2 elimination) [5].

Various baseline factors of patient status were analyzed in the study, including the body mass index (BMI), partial pressure of oxygen (PaO_2) and partial pressure of carbon dioxide ($PaCO_2$) in arterial blood, lung vital capacity (LVC), diffusing lung capacity (DLCO), left ventricular ejection fraction (LVEF), systolic pressure in the pulmonary artery (PAP_{Syst}), glomerular filtration rate (GFR), the history of previous thoracic surgery for various nosologic groups: obstructive diseases (group A), vascular diseases (group B), cystic fibrosis and immune deficiency syndrome (group C), restrictive diseases (group D). We indentified the most significant of them for predicting with a high degree of probability the need of ECMO use during surgery, avoiding the episodes of gas exchange impairments and hemodynamic disorders and without increasing the surgery duration and, hence, the graft ischemia time.

We did not study other heart function parameters, since they were within the reference range, and the deviations in sizes of the right cardiac chambers correlated with the changes in the pulmonary artery pressure.

Results

Having made the analysis, we found that neither the respiratory failure type (hypoxemic, hypercapnic), nor respiratory function parameters, i.e. the predominance of broncho-obstructive or restrictive component among the respiratory failure causes did not correlate with the need for intraoperative ECMO. Neither nosological group, nor the previous history of thoracic surgical interventions had a significant impact on making the decision to use extracorporeal systems of hemodynamics and oxygenation support.

Table 1. Comparing the quantitative variables between the patient groups where the extracorporeal membrane oxygenation was used or was not used during surgery

Parameter	Without using ECMO (n = 15)	Using ECMO (n = 34)	P value
Age (years)	35.1 ± 9.3	35.5 ± 11.4	0.9307
BMI, kg/m ^{2}	20.5 ± 4.9	20.3 ± 3.9	0.8198
PaO_2, mm Hg	54.7 ± 17.4	44.4 ± 17.3	0.0668
$PaCO_2$, mm Hg	50.7 ± 14.1	53.2 ± 16.5	0.4655
Forced expiration volume in the first second, % of the reference value	21.0 ± 9.8	30.1 ± 21.6	0.0890
LVC,% of the reference value	44.9 ± 9.6	43.1 ± 20.5	0.3919
DLCO,% of reference value	24.9 ± 14.0	22.7 ± 19.5	0.3424
LVEF, %	64.7 ± 8.1	64.0 ± 6.6	0.9913
PAP_{Syst}, mm Hg	37.1 ± 8.5	58.4 ± 36.1	0.1329
GFR, ml/min/1.73 m^2	97.1 ± 16.0	98.9 ± 23.3	0.4671

Table 2. Comparing the binary variables between the patient groups where the extracorporeal membrane oxygenation was used or was not used during surgery

Indicator	Without using ECMO (n = 15)	Using ECMO (n = 34)	Total (%)	P value (df = 1)
Gender (% male)	9 (60.0%)	15 (44.1%)	24	0.3054
Nosological group A	8 (53.3%)	10 (29.4%)	18	0.1094
Nosological group B	0 (0.0%)	3 (8.8%)	3	0.2351
Nosological group C	4 (26.7%)	12 (35.3%)	16	0.5528
Nosological group D	3 (20.0%)	9 (26.5%)	12	0.6274
GFR (%GFR2)*	4 (26.7%)	6 (17.6%)	10	0.4703

Group PaO_2-$PaCO_2$ (%ABS2)**	2 (13.3%)	9 (26.5%)	11	0.3097
Group PaO_2 -$PaCO_2$ (%ABS3)***	6 (40.0%)	20 (58.8%)	26	0.2237
PAP_{Syst} (%PAP_{Syst}2)#	11 (73.3%)	8 (23.5%)	19	0.0010
PAP_{Syst} (%PAP_{Syst} 3)##	1 (6.7%)	14 (41.2%)	15	0.0157
Chronic systemic diseases	2 (13.3%)	5 (14.7%)	7	0.8993
Previous history of category 1 surgery*#	6 (42.9%)	10 (33.3%)	16	0.5408
Previously history of category 2 surgery#*	3 (21.4%)	4 (13.3%)	7	0.4941

Notes:
ABS, Acid-base status
* Patients with a reduced GFR <90 ml/min/1.73 m^2
** Patients who had the following results of the arterial blood gases: $PaO_2 \leq 60$ mm Hg, $PaCO_2 \leq 46$ mm Hg.
*** patients who had the following results of the arterial blood gases: any value of PaO_2, $PaCO_2 > 46$ mm Hg.
#, Patients who had PAP_{Syst} from 31–50 mm Hg.
##, Patients who had $PAP_{Syst} > 50$ mm Hg
*#, drainage, diagnostic video-assisted thoracoscopy, lung biopsy, lung volume reduction surgery
#*, chemical pleurodesis, pleurectomy, segmentectomy, lobectomy, lung transplantation

Pulmonary hypertension was the only factor that, when assessed, correlated with an increased likelihood of using ECMO. The likelihood of ECMO circuit connection significantly increased in patients with PAP_{Syst} higher 50 mm Hg ($p<0.05$). In the group of study patients with a pulmonary artery pressure higher 50 mm Hg, the surgery without ECMO circuit connection was possible only in one patient; in other cases, ECMO was provided intraoperatively (Fig. 2), and was necessary to be continued in 47.06% of those patients in the postoperative period.

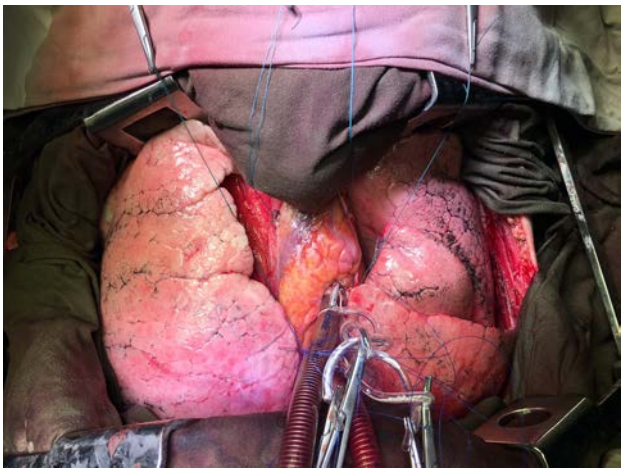

Fig. 2. Connection of peripheral veno-arteriovenous circuit of the extracorporeal membrane oxygenation machine (intraoperative photo)

Discussion

In cases of intraoperative hemodynamic impairments and gas exchange disorders, an artificial blood circulation machine is used to stabilize patient's condition. However, some studies [6–9] demonstrated better results of lung transplantation with using ECMO versus AC. Thus, in the group of patients who underwent lung transplantation using AC, a primary graft dysfunction often developed [10, 11]. The indications for ECMO occur considering the results of the pulmonary artery clamping test and in surgical emergencies (desaturation, uncontrolled hypotension). The studies of factors predicting the ECMO use are available in literature. According to studies by Hoechter D.J., Hinske L.C. [4, 12, 13], the likelihood of using ECMO was estimated by two factors: the mean pulmonary artery pressure and the LAS [lung allocation score], a parameter to determine the relative priority of allocating donor lungs for transplantation; and the PAP_{Syst} of 35 mm Hg [7, 14] has been defined as the threshold value, above which the intraoperative ECMO is indicated, which is

corresponding to the data obtained in our study of bilateral lung transplantations[1]. However, some studies confirmed better survival results in patients who underwent lung transplantation with the ECMO use "on default" [15]. In the study by Pettenuzzo T. [16], the patients who underwent lung transplantation under ECMO conditions received a larger volume of transfusions, but the patient survival was not significantly different from the group of patients without the intraoperative extracorporeal support. Considering the diverse data on the results of transplantation performed with ECMO and without it, we consider it necessary to use a differentiated approach to the choice of the extracorporeal support.

Conclusion

The presence of pulmonary arterial hypertension >50 mm Hg determines the use of preventive extracorporeal membrane oxygenation during lung transplantation, which should reduce the number of uncontrolled emergency situations at the main stages of surgical intervention; in all other cases, extracorporeal membrane oxygenation should be provided based on the results of the pulmonary artery clamping test, or if indications arise.

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