Original Article

Management of Anesthesia during Lung Transplantations in a Single Turkish Center

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Abstract

Aim: The aim of this study is to present our institutional experience during the management of anesthesia in lung transplantation (LT) surgeries as a definitive surgical treatment option in end-stage lung diseases.

Methods: From a total of 15 patients, lung transplantation was performed as single LT (SLT) in 4 patients (n = 4) and as sequential bilateral LT (BLT) in 11 patients (n = 11). The anesthetic management included; for induction; intravenous ketamine, midazolam at doses of 2 mg/kg, 0.05 mg/kg, respectively or propofol, fentanyl at doses of 1 mg/kg, 3 mcg/kg, respectively. For maintenance, all patients received; 100% O_2 and total intravenous infusion of propofol and remifentanil at doses of 0.02 mcg/kg/min and 0.1–0.25 µg/kg/min, respectively. All patients received intravenous rocuronium bromide for induction and maintenance. Hemodynamic stability was maintained with appropriate and adequate administration of vasodilators (intravenous Prostaglandin (PGI2) (0.5–1 ng/kg/min), inhaled nitric oxide (10–40 ppm), dopamine (2 mcg/kg/min) and vasopressors (intravenous dobutamine (5–15 mcg/kg/min), norepinephrine (0.05–1 mcg/kg/min),ephedrine (5 to 10 mg bolus doses) to keep mean arterial blood pressure above 50 mmHg.

Results: Cardiopulmonary bypass (CPB) was performed in five patients who underwent sequential BLT and one SLT case. Venoarterial (VA) extracorporeal membrane oxygenation (ECMO) was used in four cases of sequential BLT and in two cases of SLT. Neither ECMO nor CPB was performed in two BLT and in one SLT patient. One SLT patient who underwent CPB was admitted to the intensive care unit with support of intra-aortic balloon pump (IABP) and ECMO. Intraoperative death did not occur.

Conclusion: During SLT or BLT, management of anesthesia with propofol and remifentanil provides a stable hemodynamic and medical support. Although our experience with VA ECMO was limited, our experience shows that this support system is a valuable tool to provide hemodynamic stability for patients undergoing LT.

Keywords: Anesthesia, hemodynamics, lung transplantation

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Introduction

Lung transplantation (LT) is a well-established and definitive treatment option for patients with end-stage congenital or acquired lung diseases. The first single lung transplantation (SLT) in human was performed in 1963. The development of immunosuppressive drugs, improvements in anesthetic drug and methods, developments in surgical modalities and establishment of multidisciplinary specialist care in intensive care units have increased survival rates for lung transplantation patients.[1–4]

Anesthetic management of lung transplantation requires a thorough understanding of end-stage lung disease. Furthermore, there is a need for extensive knowledge on specific pharmacologic and technical considerations that may not be applicable in any other part of anesthetic practice. Critical periods include induction of anesthesia, initiation of positive pressure ventilation, establishment and maintenance of one-lung ventilation (OLV), pulmonary artery clamping, pulmonary artery unclamping, and reperfusion of the transplanted lung.

The use of remifentanil and propofol infusions in lung transplantation has been reported previously.[4–6,9] The comparison of the effects of propofol or inhalational agents (sevoflurane) on arterial oxygenation during OLV showed small increase in pulmonary shunt fraction thus no statistical differences in arterial oxygenation with the maintanance doses of propofol and there are studies that support that both drugs demonstrate similar effects on hemodynamical data including mean arterial pressure and heart rate. [7-9]

During the surgical procedure, patients may require conventional cardiopulmonary bypass (CPB), venoarterial (VA) or venovenous (VV) extracorporeal membrane oxygenation (ECMO). During ECMO, an artificial circuit carries venous blood to oxygenator for gas exchange and carbon dioxide removal. The return of blood to the venous system provides a veno-venous ECMO (VV-ECMO), whereas the return of blood to the arterial system provides a veno-arterial ECMO (VA-ECMO). VV-ECMO is considered for acute respiratory failure with good cardiac function, while VA-ECMO is used in cardiac failure with or without respiratory failure. For this reason, VA ECMO helps support the cardiac output and deliv-

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ers higher levels of oxygenation support than does VV ECMO. However, VA ECMO carries a higher risk of systemic emboli in comparison to ECMO.[10–12]

We aim to share our experience during the management of anesthesia of patients undergoing LT in a single center. This study is an original prospective observational study and provides valuable information on anesthetic management of patients undergoing lung transplantation. This information is needed for colleagues, both surgeons and anesthesiologists, during their experiences in lung transplantation. In addition we have provided detailed explanation on how we manage one lung ventilation during surgery by sharing the parameters including vital signs, arterial blood gas and venous catheterization values that we have followed during the study.

Materials and Methods

The patients enrolled into the study include; four single-lung transplantations (SLT) and eleven sequential bilateral lung transplantations (BLT) that were performed between January 1, 2012 and May 31, 2013 in Kartal Koşuyolu Specialty Education and Research Hospital, Istanbul, Turkey.

Anesthesia and Monitoring

Preoperative medications were continued prior to the operation and included bronchodilators, antibiotics and pulmonary vasodilators. Sedation was not administered to any patient prior to the operation.

All patients were monitored prior to induction. Monitoring included 12-lead ECG, pulse oximetry, body temperature with esophageal probe, urine with bladder probe, invasive blood pressure via radial artery cannula and cerebral oxygenation with non-invasive near infrared spectroscopy (NIRS) monitor (INVOS™, Somanetics/Covidien, Boulder, CO, U.S.A.) Thoracic epidural catheter was not placed in any of the patients considering the possibility of cardiopulmonary bypass (CPB). Both left or right jugular internal central venous catheters and pulmonary artery catheters over the right jugular internal sheet were inserted after induction of anesthesia. Using the Seldinger technique, data of cardiac output were monitored with cold thermodilution method from the right internal jugular vein. Patients received a pulmonary artery catheter (Swan-Ganz, Baxter Healthcare Corporation, Irvine, CA) with an 8.5 F Arrow introducer (Arrow International, Reading, PA) for measurement of cardiac output (CO), pulmonary arterial mean pressure (mPAP), pulmonary capillary wedge pressure (PAWP), and central venous pressure (CVP), right arterial pressure (RAP) as well as cardiac index (CI) and peripheral vascular resistance index (PVRI). We placed a radial artery line, a central venous line, and a Swan-Ganz catheter in each patient for serial monitoring. Data of CO was monitored with cold thermodilution method.[13] Systolic, diastolic and mean arterial pressures were followed during operation via radial artery catheter. A double-lumen endotracheal tube was placed to allow isolated lung ventilation.

The anesthetic management include; for induction; intravenous ketamine and midazolam at doses of 2 mg/kg and 0.05 mg/kg, respectively or propofol and fentanyl at doses of 1 µg/kg and 3 µg/kg, respectively. For maintenance, all patients received 100% O_2 and total intravenous infusion of propofol and remifentanil at doses of 0.02 µg/kg/min and 0.1–0.25 µg/kg/min. All patients received intravenous rocuronium bromide for induction and maintenance. The induction and maintenance doses for rocuronium bromide were 0.07 mg/kg and 0.04 mg/kg, respectively. Following neuromuscular blockage, in one case with cystic fibrosis, the patient was intubated with single lumen tube (SLT) initially and left side double-lumen tube (DLT) was placed following bronchial toilet. Double-lumen Robert Shaw (Broncho-catch-Mallincrodt Medical, Athlone, USA) Endotracheal tube (ETT) 35 French (Fr) was used in two cases, and 37 to 39 Fr was used in the others. Correct positioning of DTL was ascertained with the help of fiberoptic bronchoscopy. Left sided double-lumen ETT was the preferred choice in our patients; however, the right-sided double-lumen ETT was used safely and the use of right sided tube is performed due to the preference of the surgical team.[14]

During mechanical ventilation, each patient was considered individually. Respiratory parameters were adjusted accordingly based on the degree of underlying disease and lung damage, arterial blood gas values [pH, partial arterial oxygen pressure (Pa02), partial arterial carbon dioxide pressure (PaC02) and arterial oxygen saturation (Sp02)], capnography and peak airway pressures (Peak AP), tidal volume (TV): 6-8ml/kg, respiratory rate (RR = 12–20) (to maintain end-tidal carbon dioxide (ETCO2) between 35 and 45), inspiratory/expiratory ratio was 1:2 (I/E = 1/2), the fraction of inspired oxygen (FIO2) = 1, peak end expiratory pressure (PEEP) of 5 to 8 cmH2O were applied. The peak inspiratory pressure was up to 40 mmHg and plateau pressure was less than 35 mmHg. In hypercapnia control, the inspiration/ expiration ratio (I/E) ratio was maintained between 1/3 – 1/5, allowing moderate hypercapnia and acidosis in all patients.

During the operations, alterations were made in catheter positioning. Prior to pneumonectomy, the pulmonary artery catheter was withdrawn to the right ventricle if pulmonary artery catheter was located in the pneumonectomy side, and was repositioned in the contralateral lung after pneumonectomy. This maneuver was repeated in case of sequential BLT. For all patients, in whom we induced hypovolemia, pharmacologic support with norepinephrine (0.05–1 mcg/kg/min) was required to obtain good hemodynamic stability. At the same time, hemodynamic stability was maintained by appropriate and adequate administration of intravenous Prostaglandin (PGE1) (0.5–1 ng/kg/min), inhaled nitric oxide (10–40 ppm) and vasopressors (intravenous dobutamine (5–15 mcg/kg/min) and ephedrine (5 to 10 mg bolus doses) to keep mean arterial blood pressure above 50 mmHg. IV Furosemide at a dose of 0.3 to 0.5 mg/kg was administered to increase urine output as needed. In all patients, inhaled nitric oxide (iNO) was administered via inspiratory loop of the circuit (10–40 ppm). Administration of INO was achieved with the help of special nitric oxide delivery equipment that included a one-way conduction and this was synchronized inspiratory phase of the ventilation. Inhaled prostacyclin was not administered to any of the cases. Repeated hilar manipulation and cardiac compression resulted in a drop in CO and in hypotension. Vasopressor support was administered to keep adequate perfusion pressure in all cases.

The use of transesophageal echocardiography (TEE) was planned only for diagnosing right ventricular heart failure, assessment of the surgical anastomotic sites, and significant stenosis of pulmonary vein anastomoses. The use of preoperative medications of LT patients were continued prior to the operation and included bronchodilators, antibiotics and pulmonary vasodilators. Sedation was not administered to any patient prior to the operation. Before induction, inotropic agents (dobutamine), vasopressors (norepinephrine, phenylephrine), and vasodilators (nitroglyc-

erin) or direct pulmonary vasodilators (prostacyclin, inhaled nitric oxide) were kept ready for patients with severe pulmonary hypertension or any degree of heart failure.[13]

Cerebral monitoring was performed in all patients. Data obtained from the intraoperative hemodynamic parameters are shown in Tables 2 and 3 for SLT and sequential BLT, respectively. Hemodynamic data, blood gas, data regarding hemodynamical data, arterial blood gas values and the mean administered concentration values of PGE1, iNO, norepinephrine and dobutamine were compared and the results were analyzed.

Surgery Procedure

The single-lung transplant surgery was performed through posterolateral thoracotomy in four cases. Sequential bilateral-lung transplantation was performed using the sequential single lung implantation technique for 11 cases through bilateral anterolateral thoracotomy without transverse incision of the sternum. Once the donor lung was present in the operating room, the recipient pneumonectomy was completed. During implantation, the donor lung was cooled by ice slush. The bronchial anastomosis was accomplished first and was generally followed by vascular pulmonary artery and left atrial cuff anastomoses. De-airing was done thoroughly through the atrial cuff anastomosis. During this period, the systemic and pulmonary artery pressures, oxygen saturation, and arterial blood gas values were monitored.

Before the pulmonary artery clamp was removed, one patient was cannulated through the right atrium and ascending aorta for VA (veno-arterial) ECMO. Five patients underwent successful femoral VA cannulation. During ECMO, activated coagulation time (ACT) was maintained at 180–200 seconds. Nasopharyngeal temperature was kept at 35°C during ECMO, rewarming to 37°C when the transplantation procedure was completed; and 500 mg of methylprednisolone was administered before pulmonary artery clamp removal. After implantation of single or both lungs, the patients were gradually weaned from ECMO if hemodynamically stable and the following arterial blood gas parameters were obtained; 1- PaO_2 of 90 to 100 mm Hg, 2- $PaCO_2$ of 35 to 45 mm Hg, 3- Saturation of mixed venous blood (SvO_2) of 65 to 75% , 4- adequate ventilator settings including; normal tidal volume 8-10 mL/kg and within normal range for respiratory rate and positive end-expiratory pressure (10 cmH_2O), no signs of pulmonary infiltrates, poor lung compliance or right ventricular failure, patients were gradually weaned from ECMO, otherwise ECMO support was directly extended into the post-operative period and patients were weaned in the intensive care when the new lungs performed an adequate amount of ventilation and oxygenation.

In the study, femoral arteries and veins were cannulated for CPB in six patients. This provides an undisturbed and unobstructed surgical field at the lung hilum structures. Cardiopulmonary bypass circulation was provided by a roller pump. Systemic blood flow during CPB was maintained between 2 to 2.5 L/min/m^2 and systemic blood pressure was kept between 50 to 80 mmHg. Arterial blood gas values were followed every 60 minutes to keep the levels asat PaO_2 greater than 180 mmHg, $PaCO_2$ between 35 to 45 mmHg, pH between 7.35 to 7.40, hematocrit between 22% to 28 %, blood glucose between 100 to 180 mg/dL. After rewarming with a 37 °C maximal heat-exchanger temperature, CPB was discontinued. Reversal of heparin was achieved with 1.0 to 1.5 mg protamine per 100 IU heparin.

Statistics

All statistical analyses were performed using SPSS Statistical Package 15.0 (SPSS Inc. California, USA). The power analysis is performed using PASS 11 statistical program (NCSS Inc. Utah, USA). Data are presented as mean and standard deviation (SD) or as frequencies and percentages. Differences were assessed using Chi-square or Fisher exact test for categorical variables. Mann Whitney U-test was used for continuous or non-parametric data. After testing for normal distribution, data were compared using two-way analysis of variance (ANOVA) for repeated measurements. *P* values less than 0.05 were considered statistically significant.

Results

A total of 15 lung transplantations, including four SLT and eleven sequential BLT, were performed in the Kartal Kosuyolu Specialty Education and Research Hospital between January 2012 and March 2013.

The preoperative baseline characteristics of all patients are shown in Table 1. One SLT and two sequential BLT cases were successfully performed without the aid of conventional CPB or ECMO.

In this study, CPB was done because of uncontrollable hemorrhage or not tolerating the clamping of pulmonary artery in 4 cases with sequential-BLT after the first lung reperfusion and in 1 case during the second lung implantation. One SLT case underwent emergency cardiopulmonary bypass and was taken into the intensive care unit with IABP and ECMO to support hemodynamics in the postoperative period. Two days after surgery the patient died from multiple organ failure.

Especially during the initial stage of lung transplantation, VA ECMO was used to support gas exchange and hemodynamics without the need for high-dose heparin administration and anticoagulation therapy in six cases.

The average lung implantation procedure time was 304 minutes for SLT (ranging between 273 and 482 min) and 450 min for sequential BLT (ranging between 410 and 540 min).

Intraoperatively, the patients undergoing CPB required increased amount of packed red blood cell transfusions (11.6 ± 3 , 7.3 ± 2, 7 ± 1 U; $P < .01$) in comparison to ECMO applied or untreated CPB or ECMO patients, respectively (Table 1).

Hypercarbia can be seen without cardiac instability during mechanical ventilation in LT. A statistically significant decrease in pH and a statistically significant increase in $PaCO_2$ were found during the first lung pneumonectomy and prior to implantation, in which single lung ventilation was performed, in both groups. In sequential BLT and SLT cases, systemic blood pressure decreased statistically significantly compared to before induction (Tables 2 and 3).

Analyses of the data of each phase of transplantation in SLT and sequential BLT cases are depicted in Tables 2 and 3. In all patients, a decrease in MAP and HR was observed after mechanical ventilation in comparison to after induction values in both SLT and BLT groups ($P < 0.05$). An increase in PaO_2/FiO_2 values during MV and in CL1, RPL1 and final time points in comparison to after induction values were reported in both SLT and DLT patients ($P < 0.05$).

A statistically significant increase was noted in mPAP, CVP, PAWP, CI, and PVRI values after clamping of pulmonary artery

Table 1. Patient Characteristics and Perioperative Data.

Patient ECMO Transfusion*	Sex	Age	Body Surface Area	Diagnosis	SLT / BLT	CPB	ECMO	PRB
1	M	15	1.53	Bronchiectasis	BLT	-	+	6
2	M	48	2.01	Idiopathic pulmonary fibrosis	BLT	+	-	12
3	M	46	1.39	Bronchiectasis	BLT	-	+	7
4	M	18	1.71	Cystic fibrosis	BLT	+	-	11
5	F	28	2.06	Emphysema	BLT	-	-	7
6	M	34	1.61	Bronchiectasis	BLT	-	+	6
7	M	57	1.98	Interstitial lung disease	SLT	+	-	12
8	F	30	2.06	Emphysema	SLT	-	-	6
9	M	45	1.80	Silicosis	SLT	+	-	11
10	M	64	2.02	Bronchiectasis	BLT	-	+	7
11	M	47	1.55	Sarcoidosis and bronchiectasis	BLT	+	-	14
12	M	45	1.08	Bronchiolitis obliterans	BLT	+	-	10
13	M	37	1.44	Emphysema	SLT	-	-	5
14	M	47	1.84	Bronchiectasis	BLT	-	+	6
15	M	46	1.74	Bronchiectasis	BLT	-	+	7

(*) per unit; BLT = bilateral lung transplantation, SLT = single lung transplantation; M = male; F = female.

Table 2. Hemodynamics during SLT, blood gas changes and administered drugs.

Parameter	SS (n = 4) Mean ± SD	MV(n = 3) Mean ± SD	CL1(n=3) Mean ± SD	RPL1(n = 3) Mean ± SD	FINAL(n = 3) Mean ± SD
HR (b.min^{-2})	117.8 ± 51.4	86.5 ± 9.4*	103 ± 13*	97.3 ± 11.6	95.0 ± 8.7
MAP (mmHg)	102.5 ± 9.6	82.2 ± 4.2*	85.6 ± 9.8	84.3 ± 12.0	82.6 ± 1.5
mPAP(mmHg)	-	36.5 ± 12	44.6 ± 18*	25.3 ± 11*	21 ± 3.6
CVP (mmHg)	-	9.7 ± 2.3	15.6 ± 2.0*	9.3 ± 2.5	7.6 ± 3.0
PAWP (mmHg)	-	18.7 ± 10	24.3 ± 9*	15.3 ± 5*	13.0 ± 6
CI (L.min^{-1} . m^{-2})	-	3.2 ± 0.5	3.4 ± 0.6	4.1 ± 0.4*	3.3 ± 0.3*
PVRI (dynes.sec.cm^{-5}.m^{-2})	-	315.4 ± 88	392.2 ± 76.7*	213.8 ± 43*	240.6 ± 77.7
pH	7.35 ± 0.02	7.25 ± 0.03*	7.18 ± 0.03*	7.27 ± 0.06*	7.37 ± 0.1*
PaO2/FiO2 (mmHg)	140 ± 22	337 ± 43*	340 ± 55	263 ± 51*	247 ± 32
PaCO2 (mmHg)	56 ± 11	65 ± 16*	73 ± 14*	56 ± 11	53 ± 9
iNO (ppm)	-	-	30 ± 10	30 ± 10	25 ± 10
PGI2 (ng / kg / min)	-	-	1 ± 0.1	0.7 ± 0.2	0.5 ± 0.2
Norepinephrine (mcg/kg/min)	-	0.3 ± 0.2	0.8 ± 0.4*	0.4 ± 0.2*	0.2 ± 0.15
Dobutamine (mcg/kg/min)	-	-	5.9 ± 0.64	5.6 ± 2.14	4.5 ± 3.0

*= $P < 0.05$ when compared with each step of the previous phase. Abbreviations: MV = Mechanical ventilation, Sd = Standard deviation, SLT = Single lung transplantation. The parameters include; HR (b.min -2) = Heart Rate, MAP (mmHg) = Mean Arterial Presure, mPAP(mmHg) = Mean Pulmonary Arterial Pressure , CVP (mmHg) = Central Venous Pressure, PAWP (mmHg) = Pulmonary Arterial Wedge Pressure,
CI (L.min -1 . m -2) = Cardiac Index, PVRI (dynes.sec.cm-5.m-2) = Pulmonary Vascular Resistance Index, iNO = Inhaled Nitric Oxide, PGI2 = Prostaglandin I2, The parameters were obtained at time periods including; SS = spontaneously breathing patient, VM = during mechanical ventilation, after induction of anesthesia, CL1 = After clamping of pulmonary artery during first pneumonectomy, RPL 1 = After the first implanted lung reperfusion, for 30 minutes, Final; End of surgical intervention.

during first pneumonectomy (CL1 period) in comparison to MV period in both SLT and BLT patients ($P < 0.05$). There was also a remarkable increase in $PaCO_2$ in CL1 period in comparison to MV and after induction values in both SLT and BLT patients ($P < 0.05$). In addition, a statistically significant rise in CL1 period was recorded in both SLT and BLT patients in comparison to other time points ($P < 0.05$).

Discussion

Lung transplantation is the last therapeutic option for patients with end-stage lung disease due to a wide variety of end-stage lung disorders. The majority of single and sequential bilateral single lung transplantation surgeries are performed with extracorporeal circulatory support (CPB or ECMO).[10,11] Recently, transplantation

Table 3. Hemodynamics during BLT, blood gas changes and administered drugs.

Parameter	SS(n = 11) Mean ± SD	VM(n = 11) Mean ± SD	CL1(n = 11) Mean ± SD	RPL1(n = 9) Mean ± SD	CL2(n = 7) Mean ± SD	RPL2(n = 11) Mean ± SD	FINAL(n = 11) Mean ± SD
HR (b.min $^{-2}$)	121 ± 16	85 ± 24*	105 ± 11*	103 ± 14	105 ± 12	87 ± 15*	83 ± 15
MAP (mmHg)	104 ± 11	81 ± 15 *	80 ± 12	81 ± 12	83 ± 6	84 ± 12	82 ± 11
mPAP(mmHg)	-	35 ± 11	45 ± 9 *	32 ± 13 *	40 ± 9*	23 ± 7*	21 ± 11
CVP (mmHg)	-	9 ± 5	15 ± 6 *	15 ± 7	16 ± 5	9 ± 4*	9 ± 7
PAWP (mmHg)	-	18 ± 7*	26 ± 9 *	21 ± 7 *	25 ± 8*	17 ± 6*	17 ± 10
CI (L.min $^{-1}$. m $^{-2}$)	-	3.0 ± 0.2	3.8 ± 0.9*	4.6 ± 0.9*	3.3 ± 0.5*	3.9 ± 0.8*	3.6 ± 1.1
PVRI (dynes.sec.cm $^{-5}$. m $^{-2}$)	7.36 ± 0.03	320 ± 98	430 ± 165*	278 ± 95 *	442 ± 122*	280 ± 89*	244 ± 90
pH	150 ± 85	7.36 ± 0.2 *	7.20 ± 0.1*	7.41 ± 0.04*	7.36 ± 0.1*	7.38 ± 0.04	7.39 ± 0.03
PaO2/FiO2 (mmHg)	54.7 ± 13.1	343 ± 121 *	321 ± 106	331 ± 104	451 ± 104*	344 ± 96*	309 ± 112
PaCO2 (mmHg)	-	53.4 ± 12.5	68.9 ±16*	55.3 ± 11*	44.1 ± 13*	42.9 ± 6.6	45.2 ± 8
iNO (ppm)	-	-	30 ± 10	30±10	35 ± 10	20 ± 10*	20 ± 10
PGI2 (ng / kg / min)	-	-	0.91 ± 0.2	0.81±0.4	0.8 ± 0.2	0.7 ± 0.4	0.5 ± 0.2*
Norepinephrine (mcg/kg/ min)	-	-	0.4 ± 0.2	0.9 ± 1.4*	0.5 ± 0.2*	0.4 ± 0.3	0.4 ± 0.1
Dobutamine (mcg/kg/min)	-	-	5.9 ± 0.9	8.3 ± 2.4*	9.6 ± 3.6	9.4 ± 3.1	6.9 ± 3.1*

*= $P < 0.05$ when compared with each step of the previous phase. Abbrevations: BLT = Bilateral lung transplantation, MV = Mechanical ventilation, Sd = Standard deviation. The parameters include; HR (b.min -2) = Heart Rate, MAP (mmHg) = Mean Arterial Presure, mPAP(mmHg) = Mean Pulmonary Arterial Pressure , CVP (mmHg) = Central Venous Pressure, PAWP (mmHg) = Pulmonary Arterial Wedge Pressure, CI (L.min -1 . m -2) = Cardiac Index, PVRI (dynes.sec.cm-5.m-2) = Pulmonary Vascular Resistance Index, iNO = Inhaled Nitric Oxide, PGI2 = Prostaglandin I2. The parameters were obtained at time periods including; SS = spontaneously breathing patient, VM = during mechanical ventilation, after induction of anesthesia, CL1 = After clamping of pulmonary artery during first pneumonectomy, RPL 1= After the first implanted lung reperfusion, for 30 minutes, Final = End of surgical intervention.

is carried out without CBP and ECMO in some centers. When the pulmonary artery is clamped, pulmonary artery pressure increases dramatically leading to deterioration of right ventricular function so that CPB support is required in lung transplantation.[2,15] The use of CPB can further lead to increased blood product transfusions, increasing the release of cytokines, and activation of the systemic inflammatory response syndrome.[16,17]

In this study, one SLT and two BLT patients did not require the use of either ECMO or cardiopulmonary bypass (CPB). Preoperative and intraoperative evaluation of the recipient's respiratory and cardiac condition was of prime importance for these patients. The first graft implantation in sequential-BLT was quite similar to a SLT. After first graft, function was satisfactory and the second graft was implanted without ECMO or CPB. In these patients, especially in patients with mild preoperative pulmonary hypertension, there is a need for adequately protected right ventricular function and removal of the less well-perfused lung and in this way sequential BLT can be performed successfully.

The use of VA-ECMO was preferred instead of CPB due to fewer bleeding issues and faster time to discharge from intensive care.[18,19] In a series of 92 lung transplant recipients, ECMO was associated with reduced postoperative complications and a reduced mortality of 13% compared with 39%for CBP.[19]

Blood transfusion of ECMO and non ECMO non CPB groups were significantly lower than the CBP group ($P < 0.01$) (Table 1). A comparison of peri-operative blood transfusion requirements between double lung transplantation with and without CPB support by Gammie *et al.*[20] showed that the CPB group required significantly more blood transfusions (11.4 vs. 6.0 units.) Transfusion-related lung injury is a thoroughly described phenomenon and clinically similar to the adult respiratory distress syndrome.[21]

Right ventricular function should be monitored with PAB, SVB and if possible, with transesophageal echocardiography.[22] We did not use TEE whole the patients; therefore TEE, parameters were not taken into consideration. TEE is very useful in assessing venous anastomoses but it is extremely difficult to assess left-sided pulmonary arterial anastomoses. There is often a significant pressure gradient across the arterial anastomoses and TEE is more accurate in determining preload and filling status compared to pulmonary artery catheter.[23]

Recently, it has been reported that, total intravenous anesthesia may be beneficial in lung volume reduction surgery, lung transplantation and thymectomy. Total intravenous anesthesia is safer and propofol, dexmedetomidine, ketamine and remifentanil may be used in combination with anesthetic depth monitoring to administer an effective total intravenous anesthesia regimen during LTx surgeries.[24,25] In our study, we used remifentanil and propofol infusions with stable hemodynamic parameters during induction and during one lung ventilation throughout the surgical procedure.

We chose to use the cerebral oximeter in this study because of

cerebral oxygen saturation (ScO_2) monitoring by near-infrared spectroscopy is being increasingly used for assessing the delivery to demand in patients undergoing cardiac and non-cardiac surgery. Prolonged episodes of hypoxia may cause an increased risk for cognitive deficit in after surgery (i.e. cardiac surgery). Cerebral oximetry monitoring has shown to improve outcome after major cardiac surgery.[26,27] A relative decrease of intraoperative ScO_2 to less than 80% of the preoperative baseline or to absolute levels lower than 50% has been associated with postoperative cognitive dysfunction. One of the limitations of this study is not evaluating the postoperative cognitive function.

Pulmonary hypertension (PH) represents a major risk factor for increased perioperative morbidity. The perioperative management of patients with severe PH undergoing lung transplantation requires continuous monitoring of mean arterial pulmonary pressure and measurement of pulmonary capillary wedge pressure. INO prevents right to left shunt by dropping pulmonary vascular resistance.[28] Besides, it regulates oxygenation by directing the blood flow from poorly ventilated and diseased lung areas towards better ventilated regions (microselective effect). Myles *et al*. qualified the efficiency of iNO management in order to prevent CPB use during lung transplantation.[29] In this study, fluid restriction, direct pulmonary artery relaxants such as inhaled nitric oxide (iNO) and prostaglandin I2 were used for decreasing the pulmonary arterial pressure. According to our experience, the use of inhaled nitric oxide provides more stable hemodynamic response without simultaneous decrease in systemic blood pressure and helps to diminish the shunt.

Pulmonary edema should be avoided in lung transplantation due to ischemia-reperfusion injury and lymphatic interruption. Large volumes of fluid were avoided to keep the lungs "dry" in patients during LT because lymphatic drainage of the transplanted lung is deteriorated. Uncontrolled reperfusion poses a greater risk, especially in sequential BLT procedure because the newly implanted first lung has to receive overperfusion and hyperinflation to maintain hemodynamic stability during implantation of the second lung.

Our intraoperative fluid management strategy was fluid restriction with inotropic support and/or vasopressor and diuretic usage so that urine output was closely monitored to avoid the risk of renal hypoperfusion.

None of the cases died during the operation; one case who underwent CBP was taken into intensive care unit with support of IABP and ECMO at the end of the operation upon failing to stabilize the hemodynamics.

In conclusion, beside the experience of the surgical team, the anesthesia team should also have knowledge and experience as much as the surgical team in lung transplantation, and the anesthesia team should manage every step regarding induction, positioning, single lung ventilation, PA clamping, graft implantation, graft reperfusion and fluid resuscitation. Lung protective strategies, pulmonary artery catheterization, cardiopulmonary bypass, inhaled nitric oxide, and inhaled prostacyclin are all important tools for the anesthesiologist to optimize patient care.

Providing adequate pharmacologic support with positive inotropic, vasodilators and systemic vasoconstrictors during the transplantation allows control over most of the intraoperative hemodynamic changes. We aimed to present our anesthesia experiences, even though our number of cases of lung transplantation, a procedure with a very short history in Turkey, is not quite sufficient.

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