Pulmonary hypertension – intra- and early postoperative management in patients undergoing lung transplantation

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Abstract

Background: Single lung transplantation, bilateral lung transplantation and combined heart-lung transplantation are the procedures currently being performed in patients with arterial pulmonary hypertension and pulmonary hypertension as a result of end-stage lung disease. In patients with severe pulmonary hypertension, regardless of its aetiology, general anaesthesia and mechanical ventilation could precipitate the onset of cardiac failure and the necessity of extracorporeal circulation employment.

Aim: To assess the clinical and prognostic value of the pulmonary artery pressure (PAP) measured during the intra- and early postoperative period in patients undergoing lung transplantation.

Methods: We analysed 20 patients undergoing lung transplantation in the Silesian Centre for Heart Disease in Zabrze, of whom 13 suffered from pulmonary hypertension before the operation. The PAP was measured using Swan-Ganz catheters.

Results: Pulmonary artery pressure markedly decreased after transplantation (systolic, diastolic and mean PAP values were 31/19/23 mmHg, respectively) but in 3 recipients the mean PAP exceeded 25 mmHg (45/23/30 mmHg). In all 3 cases a cardiopulmonary bypass was required and single-lung transplantation was performed. Pulmonary hypertension immediately after the operation was the potential marker of lung dysfunction (pulmonary oedema, ischaemia-reperfusion injury, infection) – all 3 patients with increased PAP developed complications.

Conclusions: Lung transplantation is associated with a significant reduction in pulmonary artery pressures immediately after graft implantation. The persistence of pulmonary hypertension in the early postoperative period suggests temporal allograft dysfunction and affects the post-operative outcome.

Key words: pulmonary hypertension, lung transplantation, right heart failure

Kardiol Pol 2009; 67: 989-994

Introduction

Transplantation of one lung, two lungs or heart and lungs are established methods of treatment of pulmonary arterial hypertension (PAH) and end-stage pulmonary diseases with coexisting pulmonary hypertension [1]. Transplantation of one lung gives admittedly more organs for transplantation, which is important because the number of patients waiting for transplantation is currently increasing logarithmically. However, the consequence of a single lung transplantation is flow mismatch. Blood is preferentially distributed to the transplanted lung, which may cause acute hyperaemia of the allograft. As a result, reperfusion pulmonary oedema may occur in the early postoperative period [2, 3].

Pulmonary vasoconstriction due to hypoxia is an adaptive mechanism which enables blood redistribution to normally ventilated pulmonary segments. By this mechanism optimisation of blood flow occurs and intrapulmonary shunt is reduced. Vasoconstriction as a result of hypoxia can cause an increase of vascular resistance by 50-300%. Pressure in the pulmonary artery decreases immediately after transplantation.

The aim of the study was to assess the clinical and prognostic value of pulmonary artery pressure (PAP) measured in the periprocedural period in patients undergoing pulmonary transplantation.

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Received: 10 July 2008. **Accepted:** 01 July 2009.

Methods

The analysis included 20 patients (diagnosis and type of procedure are given in Table I), who underwent lung transplantation in the Silesian Centre for Heart Diseases in Zabrze between 11 December 2004 and 15 March 2008. In 13 patients pulmonary hypertension before the procedure was present (diagnosed on the basis of international criteria), including 2 patients with PAH.

Premedication was not given immediately before the surgery. Passive oxygen supplementation was supplied in all patients. fentanyl, hypnomidate, pancuronium and dormicum were used for induction of anaesthesia. In addition, propofol and temporarily isoflurane were used for anaesthesia maintenance. Ventilation of one lung was performed with 100% oxygen using a left endobronchial tube. In cases of hypoxaemia nitric oxide inhalation was administered (5-40 PPM). The ventilation schema was changed after release of the pulmonary artery clamp and the lowest possible oxygen concentration was used ($FiO_2 \leq 35\%$), positive end expiration pressure (PEEP) up to 15 cm H_2O and low tidal volume (V_T 5 ml/kg). During the transplantation procedure the following parameters were monitored with direct methods: blood pressure in radial and femoral artery, central venous pressure, 5-lead ECG and PAP (the final result was a mean of 4 to 6 measurements performed during 24 h). Invasive measurement of PAP was performed with a Swan-Ganz catheter.

During the surgery fluid restriction was implemented, especially concerning crystalloids. Colloids were administered, diuresis was forced in order to achieve diuresis of 0.5 ml/kg/h and blood osmolarity was monitored and maintained at the upper reference range. When a systemic blood pressure drop occurred, levonor infusion was used.

Extracorporeal circulation was used when there were problems with obtaining acceptable arterial blood gasometry parameters during ventilation of one lung, when haemodynamic destabilisation after clamping of the pulmonary artery branch occurred, and when technical difficulties in the operative area occurred.

Statistical analysis

Continuous variables are presented as median with ranges, categorical variables as number and percentages. Blood pressure measured at different time points in patients was compared using ANOVA Friedman rank test, with acceptable post-hoc analysis. Data were collected and processed using STATISTICA StatSoft. A p value < 0.05 was considered statistically significant.

Table I. Clinical characteristics (including primary disease and type of procedure) of patients undergoing lung transplantation

Number	Age [years]	Gender	Primary diagnosis	Type of procedure
1	54	M	fibrosis	right lung
2	34	M	sarcoidosis	right lung
3	51	M	ATT	both lungs
4	47	F	fibrosis	left lung
5	45	M	fibrosis	left lung
6	43	M	fibrosis	left lung
7	41	M	fibrosis	right lung
8	31	M	emphysema, fibrosis	both lungs
9	50	F	COPD	right lung
10	23	F	pulmonary arterial hypertension	both lungs
11	47	M	fibrosis	left lung
12	60	M	COPD	left lung
13	56	M	fibrosis, bronchiectasis	left lung
14	46	M	emphysema, fibrosis	right lung
15	30	F	bronchiolitis	left lung
16	59	K	fibrosis	left lung
17	34	F	silicosis	right lung
18	51	M	fibrosis	right lung
19	25	F	pulmonary arterial hypertension	right lung
20	58	M	COPD	left lung

Abbreviations: ATT – α_1 antitrypsin deficiency, COPD – chronic obstructive pulmonary disease; right, left or both lungs describe transplanted organs, M – male, F – female

Results

Detailed clinical and procedural characteristics of 20 analysed patients are presented in Table II. In 13 patients pulmonary hypertension (including 2 patients with PAH) was present preoperatively. 3 patients received transplant of two lungs, in 8 patients the right lung was transplanted, and in the remaining 9 patients the left one was transplanted. Eleven surgeries were performed using cardio-pulmonary bypass. Analysis of systolic, diastolic and mean pulmonary artery pressure measurements revealed a statistically significant decrease of all values in the early postoperative period (immediately after surgery and in the first 24 h after surgery) when compared to pressure values during anaesthesia induction (Table III, Figure 1 A).

In 3 patients mean PAP exceeding 25 mmHg in the postoperative period was observed and 2 patients had pulmonary hypertension before the surgery (Figure 1 B). In all patients from this group postoperative complications occurred. In a female patient with pulmonary hypertension as a consequence of idiopathic pulmonary fibrosis massive

Table II. Characteristics of transplant recipients including 3 patients with increased pulmonary artery pressure after the procedure

		Studied population	Recipients with pulmonary hypertension after transplantation	Recipients without pulmonary hypertension after transplantation
Gender, n (%)	F	7 (35)	1 (33.3)	6 (35.3)
	M	13 (65)	2 (66.7)	11 (64.7)
Age [years] (min-max)		46.5 (23-60)	50 (47-54)	45 (23-60)
NYHA class, n (%)	II	1 (5)	0	1 (5.9)
	III	4 (20)	1 (33.3)	3 (17.7)
	IV	15 (75)	2 (66.7)	13 (76.5)
Pulmonary hypertension,	no	7 (35)	1 (33.3)	6 (35.3)
before transplantation, n (%)	yes	13 (65)	2 (66.7)	11 (64.7)
Type	right lung	8 (40)	2 (66.7)	6 (35.3)
of transplantation,	both lungs	3 (15)	0 (0.0)	3 (17.6)
n (%)	left lung	9 (45)	1 (33.3)	8 (47.1)
Cardiopulmonary	no	9 (45)	0	9 (52.9)
bypass, n (%)	yes	11 (55)	3 (100)	8 (47.1)
Cardiopulmonary bypass time [min] (min-max)		190 (110-405)	152 (136-344)	220 (110-405)
Pulmonary hypertension	no	17 (85)	0	17
after transplantation, n (%)	yes	3 (15)	3	0

Table III. Median values of pulmonary artery pressures (systolic – S PAP, diastolic – D PAP, mean – M PAP) measured at 3 time points (1 – after anaesthesia induction; 2 – after the end of the surgery; 3 – during the first 24 h after transplantation)

	Studied population		Recipients with pulmonary hypertension after transplantation		Recipients with normal pulmonary pressure after transplantation	
	median	min-max	median	min-max	median	min-max
S PAP 1 [mmHg]	40.5	(27-80)	70	(38-70)	40	(27-80)
D PAP 1 [mmHg]	23	(10-50)	28	(23-45)	21	(10-50)
M PAP 1 [mmHg]	31	(21-60)	47	(26-53)	31	(21-60)
S PAP 2 [mmHg]	35	(28-55)	47	(45-55)	35	(28-46)
D PAP 2 [mmHg]	20	(15-35)	31	(30-35)	20	(15-21)
M PAP 2 [mmHg]	24.5	(19-40)	38	(35-40)	24	(19-28)
S PAP 3 [mmHg]	31	(26-48)	45	(45-48)	30	(26-36)
D PAP 3 [mmHg]	19	(15-30)	23	(20-30)	19	(15-21)
M PAP 3 [mmHg]	23.5	(18-35)	30	(29-35)	23	(18-26)

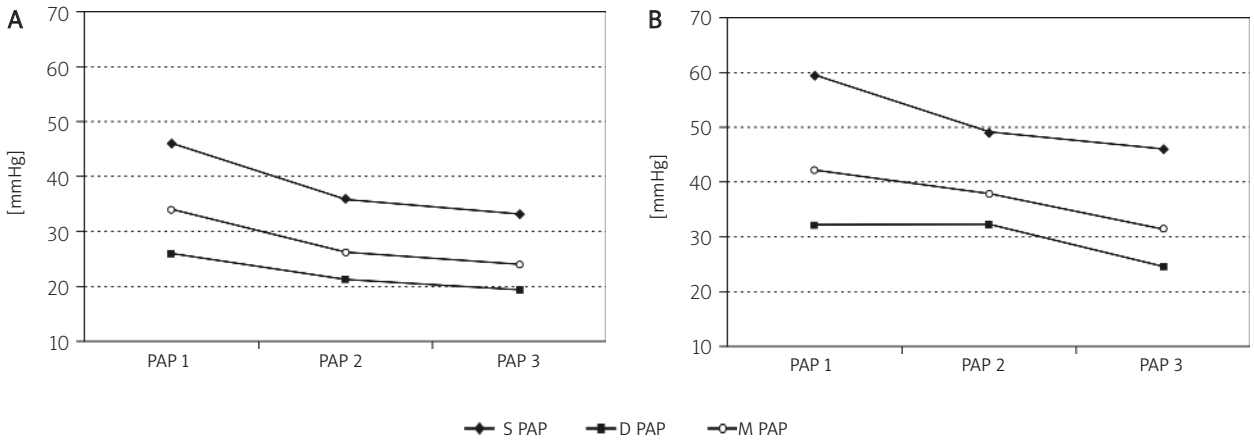

Figure 1. Graph representing pulmonary artery pressure measurements at 3 time-points in the studied population (**A**), and in patients with elevated pulmonary artery pressure after the procedure (**B**)

PAP 1 – after anaesthesia induction, PAP 2 – after the end of surgery, PAP 3 – during the first 24 hours after transplantation, S PAP – systolic pulmonary artery pressure, D PAP – diastolic pulmonary artery, M PAP – mean pulmonary artery pressure

pulmonary oedema occurred after transplantation of the right lung, which withdrew gradually, enabling termination of mechanical ventilation after 106 h. Another patient with increased PAP after the procedure had pulmonary changes demonstrated on chest X-ray with characteristics of parenchymatous consolidation. The changes were qualified as ischaemia-reperfusion injury, and dissapeared after two weeks of ventilation and enabled extubation. Infection as a cause of complication was excluded. In the third patient bleeding from the transplanted lung occurred, manifesting as a massive haemorrhage from the tracheal tube. It required resection of a segment of the transplanted lung in order to stop the bleeding. In bronchoscopy, multiple small thrombi in the bronchial tree were observed and the mucous membrane was susceptible to bleeding during attempts at their removal. Chest X-ray revealed pneumothorax at the site of the transplanted lung. The patient required tracheotomy in the period of weaning from mechanical ventilation. In all 3 of these patients cardio-pulmonary bypass was used during surgery and in all patients one lung was transplanted.

In 2 out of 17 (12%) patients with normal PAP complications in the early postoperative period occurred. One patient required re-thoracotomy due to excessive blood loss. In another patient left ventricular failure with recurrent arrhythmias (pulseless ventricular tachycardia) was observed.

No deaths occurred in the early postoperative period (30 days). In the first year after transplantation 6 patients died (30% of the studied population) at the mean time of 102 days after surgery (range 40-191 days).

Discussion

The priority in perioperative management is avoiding hypoxia and cardiovascular system destabilisation. Mechanical ventilation during surgery is unavoidable. Ventilation with positive end expiration pressure leads to an increase of intrathoracic pressure and pressure in the right atrium, which causes a decrease of pressure gradient, responsible for venous return. Reduction of preload is a dominant result of low PEEP values, and increased afterload together with diminished right ventricular compliance are consequences of utilising PEEP values exceeding 10 cm H_20 [4, 5].

The technique of the procedure has a substantial effect on the transplanted organ's function. Extracorporeal perfusion guarantees correct gas exchange and haemodynamic stability and enables limitation of over-flow through the lung which is transplanted first. [7]. There are the following disadvantages of using cardio-pulmonary bypass: the need for anticoagulation, release of systemic inflammatory response mediators with all its consequences, and increased use of blood and blood-based products.

In patients with severe pulmonary hypertension and right ventricular dysfunction, lung transplantation leads to normalisation of heart function and morphology [8]. Also right ventricular diameter decreases due to diminished volume overload as a result of reduction of tricuspid regurgitation and restoration of the normal position of the intraventricular septum [9]. A beneficial haemodynamic effect regarding right ventricular function is seen immediately after transplantation, whereas muscle mass reduction is a slow process which lasts several months [10].

An essential mechanism influencing lung function after transplantation is inflammatory response activation during surgery, which has a comprehensive character and which is caused by different factors (surgical trauma, ischaemia and reperfusion, cardio-pulmonary bypass) [11, 12]. Mechanical

ventilation induces mechanical lung injury (volume and pressure injury). Biotrauma is a result of release of inflammatory response mediators in pulmonary tissue as a response to mechanical ventilation. The main source of cytokines is atelectasis caused by repeated collapsing and opening of pulmonary alveoli. By using acceptable transpulmonary pressure (30 cm H_20), the pressure value which causes opening of these fragile structures reaches up to 140 cm H_20 [13]. The presence of inflammatory response mediators in pulmonary tissue makes its vulnerable to harmful effects of mechanical ventilation [14].

Based on the experience of multi-site clinical trials concerning mechanical ventilation with acute respiratory distress syndrome (ARDS), we used a protective model of ventilation in transplanted lungs [15]. It is based on using low tidal volume (Vt), high PEEP and, additionally, alveolar recruitment manoeuvres. By this strategy alternating opening and collapsing of pulmonary alveoli is eliminated. This strategy of ventilation promotes reduction of functional residual capacity (FRC) in the early postoperative period [16]. Also, lower concentration of interleukin 8 (produced by pulmonary macrophages) is observed, which causes strong neutrophil activation. Concentration of interleukin 10 represents the same changes, which indicates limitation of the primary inflammatory response by protective ventilation when compared to the conventional one [17, 18]. The strategy of pulmonary ventilation used in the current study prevents the occurrence of acute lung injury, caused by high pressure controlled ventilation.

It can be assumed that using extracorporeal perfusion leads to activation of a severe inflammatory response, which can be conducive for occurrence of complications in the early postoperative period. It can also be hypothesised that a donor with advanced systemic inflammatory response syndrome gives an organ with high potential for failure in the postoperative period [19].

In conclusion, PAP in patients with pulmonary hypertension of different aetiologies decreases to physiological values immediately after pulmonary artery clamp release, both in a single lung transplantation and in sequential double-lung transplantation. Increased PAP in the early postoperative period may be a result of organ failure (ischaemia-reperfusion injury, oedema, atelectasis, infection) and is associated with higher rate of perioperative complications.

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Nadciśnienie płucne – problem okresu okołooperacyjnego u chorych poddawanych zabiegom transplantacji płuc

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Streszczenie

Wstęp: Przeszczepy jednego płuca, obu płuc oraz serca i płuc są uznanymi metodami leczenia tętniczego nadciśnienia płucnego i schyłkowej postaci choroby płuc współistniejącej z nadciśnieniem płucnym. Przeszczep jednego płuca pozwala na zwiększenie puli narządów w czasach, kiedy lista oczekujących na transplantację rośnie wykładniczo. U chorych z ciężkim nadciśnieniem płucnym, niezależnie od jego etiologii, obserwuje się objawy destabilizacji funkcji serca w czasie operacji, co zmusza do zastosowania krążenia pozaustrojowego.

Cel: Ocena ciśnienia w tętnicy płucnej w okresie okołooperacyjnym u chorych poddawanych zabiegom przeszczepu płuc. Monitorowanie prowadzono na podstawie rejestracji ciśnienia w tętnicy płucnej mierzonego inwazyjnie przy użyciu cewnika Swana-Ganza.

Metody: Badaniem objęto 20 chorych, u których wykonano przeszczep płuc w Śląskim Centrum Chorób Serca w Zabrzu. Sekwencyjny przeszczep obu płuc wykonano u trzech chorych, pozostałym biorcom przeszczepiono jedno płuco. Jedenaście operacji wykonano z użyciem krążenia pozaustrojowego.

Wyniki: Analiza wykazała znamienne statystycznie obniżenie wartości ciśnień skurczowego, rozkurczowego i średniego w tętnicy płucnej we wczesnym okresie pooperacyjnym (ME 31/19/23 mmHg) w stosunku do ciśnień mierzonych po indukcji znieczulenia. Podwyższone ciśnienie w tętnicy płucnej (ME 45/23/30 mmHg) we wczesnym okresie pooperacyjnym stwierdzono u trzech chorych. W tej grupie przeprowadzono zabieg przeszczepu pojedynczego płuca z użyciem krążenia pozaustrojowego. U wszystkich chorych z podwyższonym ciśnieniem w tętnicy płucnej po zabiegu rozpoznano odwracalną dysfunkcję przeszczepionego narządu. W grupie badanej nie odnotowano zgonu w ciągu pierwszych 30 dni pobytu w szpitalu (wczesna śmiertelność).

Wnioski: Nadciśnienie płucne we wczesnym okresie pooperacyjnym jest objawem przejściowej dysfunkcji przeszczepionego płuca. Podwyższone ciśnienie w tętnicy płucnej we wczesnym okresie pooperacyjnym jest objawem dysfunkcji narządu (uraz niedokrwienno-reperfuzyjny, obrzęk, niedodma, infekcja). W grupie chorych z ciężkim nadciśnieniem płucnym charakterystyczny jest dramatycznie trudny przebieg okresu śródoperacyjnego. Dysfunkcja prawej komory, okresowo wentylacja mechaniczna jednego płuca i zamknięcie światła gałęzi tętnicy płucnej powodują destabilizację hemodynamiczną, w niektórych przypadkach tak gwałtowną, że konieczne jest zastosowanie krążenia pozaustrojowego w trybie pilnym.

Słowa kluczowe: nadciśnienie płucne, przeszczep płuc, niewydolność prawej komory serca

Kardiol Pol 2009; 67: 989-994

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Praca wpłynęła: 10.07.2008. **Zaakceptowana do druku:** 01.07.2009.