

LUNG TRANSPLANTATION PROGRAMME IN CROATIA

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Summary

Lung transplantation was first performed in 1963, but the real increase in performed transplantations occurred in the last twenty years. Leading indications for lung transplantation are: chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, cystic fibrosis, pulmonary arterial hypertension, and sarcoidosis. Careful selection of donors is extremely important for prognosis after transplantation. Physicians should consider lung transplantation as a therapeutic option and follow the guidelines on the indications for transplantation so patients could be sent on time to a referral center for all the necessary examinations and preparation for recruiting to the waiting list. Department for Lung Diseases Jordanovac, University Hospital Centre Zagreb, is a referral center for lung transplantation in Croatia. The Department is performing processing and preparing patients for transplantation as well as follow them during post-transplantation period.

Keywords: transplantation; lung; referral center.

Introduction

Lung transplation is today indicated like last therapeutic option for patients with end-stage lung diseases in which all conservative options are exhausted. First lung transplantation was performed in 1963. [1]. However, further twenty years were needed to get some modest clinically significant survival benefit after the procedure. With these encouraging results, in the last twenty years significant increase in number of lung transplantation was noticed. Today, more than 32 000 procedures were performed in the World [2]. Lung transplantation from rare medical procedure has become a standard of care in patients with terminal stage of lung disease.

Indications for lung transplantation

In the last decade indications for lung transplantation significantly broadened and include large spectrum of airway, lung parenchymal and pulmonary vasculature diseases. Nowadays, most common indication for lung transplantation is chronic obstructive pulmonary disease (COPD) and represents around one third of all procedures [3], (*Figures 1 and 2*).



Figure 1. X ray of COPD patient before transplantation



Figure 2. X ray of COPD patient after transplantation

Idiopathic pulmonary fibrosis (IPF) is the second most common indication, with constant increase in number of transplanted patients. IPF has become the most common reason for lung transplantation in the United States [4], (*Figures 3 and 4*).

Cystic fibrosis (CF) is responsible for 15% of all transplantations. Less common indications are emphysema of the lung due to $\alpha 1$ – antitrypsin deficiency, sarcoidosis, bronchiectasis and lymphangioleiomyomatosis (LAM), [3]. Idiopathic pulmonary arterial hypertension (IPAH) used to be the most common indication for lung transplantation, but today is cause of only 2% of all transplantations [2]. Significant decrease in number of transplantations in these patients is clear indicator of great improvement in conservative treatment of patients with IPAH (*Figures 5 and 6*).

Some indications are still largely debatable. Lung transplantation in patients with lung diseases associated with connective tissue diseases can lead to significant post – transplantation mortality because of a large spectrum of extra – pulmonary



Figure 3. X –ray of patient with idiopathic pulmonary fibrosis before transplantation

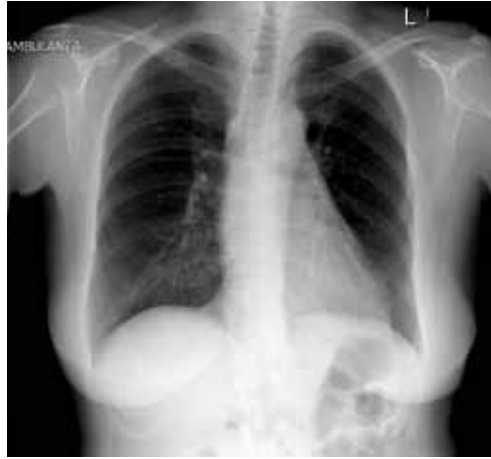


Figure 4. X –ray of patient with idiopathic pulmonary fibrosis after transplantation



Figure 5. X ray of patient with pulmonary arterial hypertension before transplantation

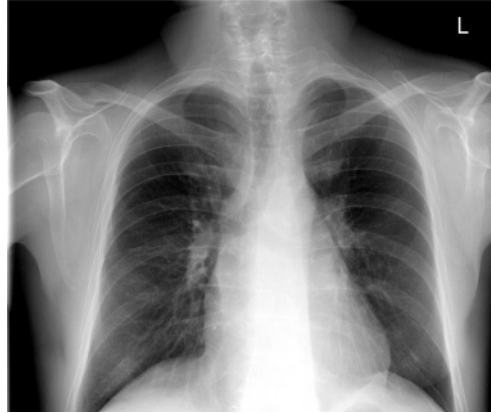


Figure 6. X ray of patient with pulmonary arterial hypertension after transplantation

manifestations in these patients. After thorough medical checkup, in selected patients with little or no extra-pulmonary manifestation lung transplantation can be performed [5]. Attempts to treat very early stages of lung cancer resulted in high rate of recurrence. Therefore, lung cancer is nowadays considered to be a contraindication for lung transplantation [6].

Contraindications for lung transplantation

There is surprisingly small number of absolute contraindications for lung transplantation. Absolute contraindications are: recent malignancy (except carcinoma of the skin), active hepatitis B and C with liver damage, active smoking, alcohol and drugs abuse, severe psychiatric disorder, non – compliance with medical procedures, poor social status and HIV infection [3]. Controlled diabetes, osteoporosis and coronary artery disease are not considered absolute contraindications [6].

In majority of transplantation centers, upper age limit for the procedure is 65 years. In some centers, attempts are done to move the upper limit according to functional status and not only age. Greatest improvement is achieved in the United States where almost 20% of all transplanted patients were older than 65 [4].

Mechanically ventilated patients were for a long time considered not to be candidates for lung transplantation due to high post-transplantation morbidity and mortality. However, improvements in technology and introduction of extra – corporeal membranous oxygenation (ECMO) have removed that as contraindication and patients on oxygenation support can be successfully transplanted in experienced centers [8].

Chronic infections of sinuses and lower respiratory tract are great problem in patients with cystic fibrosis. Chronic infections with vast majority of pathogens (like *Pseudomonas aeruginosa*) are nowadays not a contraindication for transplantation. Only chronic infection with *Burkholderia* is the contraindication for transplantation due to high post – operative mortality [3,9].

When to list patients for transplantation?

When to put patient on transplantation waiting list is not easy to determine. Patients became candidates for transplantation in the late stage of their disease when survival is more likely better with transplantation comparing to conservative treatment [3]. But it is extremely important to estimate a moment when patients are still capable of undergoing the procedure. It is really important to sensitize patients, their families and physicians not to hesitate to refer patients to expert center to estimate the right indication and ideal timing for putting patients on the waiting list [3].

Criteria for referring patient to referral center are shown on *Table 1* [10].

Table 1. Criteria for lung transplantation in most common indications

Chronic obstructive pulmonary disease
BODE index 7-10
Frequent exacerbations
pCO ₂ >50mmHg at rest
Oxygen dependent
Pulmonary hypertension, cor pulmonale
FEV ₁ <20%, DLCO <20%, emphysema
6-MWT 300 m
BMI
Pulmonary arterial hypertension
NYHA III-IV
Progression regardless of treatment
Walking distance <300 m on 6-MWT
Cardiac index <2L/min/m ²
Right atrial pressure >15mmHg
Cystic fibrosis and bronchiectasis
FEV ₁ <30% or fast decrease in FEV ₁ , especially in younger age
Exacerbations, ICU days
Frequency of exacerbations, antibiotic treatment
Pneumothorax
Haemoptysis
BMI
Oxygen dependent
Hypercapnia
Pulmonary hypertension
Idiopathic pulmonary fibrosis
UIP – histological or radiological finding
DLCO <35%
Decrease in FVC >10% in the last 6 months
SHbO ₂ <88% during 6-MWT
Honeycombing HRCT (fibrosis score > 2)
Histological NSIP:
- DLCO < 35%
- FVC of 10% or DLCO of 15%

Lung transplantation programme in Croatia

First lung transplantation was performed in Croatia in year 2003. After that, programme wasn't continued due to lack of specific surgical equipment. That was the reason why we started co-operation with Professor Walter Klepetko from University Hospital AKH in Vienna. He is recognized as one of the World leading surgeons in the field of thoracic surgery, and especially lung transplantation. Until now, his center performed around 3000 transplantations with one year survival of more than 90%, and 5-year survival of around 70%. Our collaboration started formally in 2011 and consisted of four different procedures: lung transplantation, lung transplantation with reconstructive cardiac surgery, lung and heart transplantation and pulmonary endarterectomy (PEA), (Figure 7).



Figure 7. Surgical specimen obtained by pulmonary endarterectomy

AKH Vienna is responsible for surgical procedures, early post-operative care and regular post – transplantation evaluations. Head of post-transplantation evaluation team in Vienna is dr Peter Jaksch. Croatian part of the programme is located at Department for Respiratory Diseases Jordanovac, University Hospital Centre Zagreb. Head of that part of the programme is Professor Miroslav Samaržija, his team consists of 5 physicians and 3 nurses who are responsible for screening, pre-transplantation evaluation, recruitment of patients to Vienna and Euro-Transplant active list, transport of patients, rehabilitation and comprehensive post-transplantation care.

After start of collaboration until now 157 patients were enrolled in the programme. Lung transplantation was performed in 34 patients, lung and heart transplantation in two patients and PEA in 8 patients. Detailed number of patients in the programme is shown in *Table 2 and Table 3*.

Table 2. Number of patients in lung transplantation programme

Total number - 118
Performed - 34 (1 re-LuTx)
Waiting list - 5
Accepted from AKH - 10
Patients in screening - 26
Screening failures - 7
Patients died after transplantation - 6
Patient died on waiting list - 1
Patients died in screening period - 18

Table 3. Number of patients in pulmonary endarterectomy programme

Total number - 29
Performed - 8
Patients in screening - 6
Screening failure - 3
Died after PEA - 2
Died in screening period - 2

Survival and rate of complications of Croatian patients is similar to whole Vienna cohort. Huge improvement was done when ECMO was introduced as essential part of pre- and post-transplantation support. Indications for ECMO are shown in *Table 4*.

Table 4. Indication for extracorporeal life support

CO ₂ removal
Bridge to recovery
Bridge to transplantation (lung ± heart)
Post transplantation support

Another step forward was done in last year when first successful re-transplantation of the lung was done in patient with chronic rejection. Programme is also expanded to children with end-stage lung diseases.

Conclusion

Lung translation program which started 4 years ago is fully implement in regular medical care of severe respiratory diseases. This program significantly reduced mortality and improved quality of life of these patients. At the same time development of this programme enables introduction of new diagnostic and therapeutic methods and improved general knowledge in the field of respiratory medicine, especially in the treatment of critically and severely ill patients. The collaboration with AKH enables Croatian physicians to get specific education as well as to improve scientific collaboration between the two institutions.

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Sažetak

Transplantacija pluća u Hrvatskoj

Transplantacija pluća prvi puta je učinjena 1963. godine, no pravi uzlet doživjela je tek unazad dvadeset godina. Vodeće indikacije za transplantaciju pluća su: kronična opstruktivna plućna bolest, idiopatska plućna fibroza, cistična fibroza, plućna arterijska hipertenzija te sarkoidoza. Pažljiv odabir donora iznimno je važan za prognozu i ishod postupka. Liječnici bi trebali razmišljati o transplantaciji pluća kao terapijskoj opciji te pratiti smjernice o indikacijama za transplantaciju kako bi bolesnike na vrijeme uputili u referalni centar radi pripreme i obrade. Klinika za plućne bolesti Jordanovac, Kliničkog bolničkog centra Zagreb, referalni je centar za transplantaciju pluća u Hrvatskoj. U Klinici se provodi obrada i priprema bolesnika za transplantaciju te posttransplantacijsko liječenje i praćenje.

Ključne riječi: transplantacija; pluća; referalni centar.

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