CURRENT STATUS OF LUNG TRANSPLANTATION IN POLAND: EXPERIENCE OF THE SILESIAN CENTER FOR HEART DISEASES

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Until the year 2001, lung transplantation was not available in Poland, as the only one among other kinds of solid organs transplantation. In 2001, in the Silesian Center for Heart Diseases the first successful combined heart-lung-one-block transplantation was performed. In 2003 and 2004, a successful single lung transplantation in Poland was performed in our center. Here the authors presented their experience with lung transplantation including the indications for specific types of transplantation, the immunosuppressive regimen, the management of early and late stages after lung transplantation, the infection complications, and the current problems with lung transplantation progress.

Key words: immunosuppression, infection, lung transplantation, rejection

INTRODUCTION

In Poland, lung transplantation remains the only solid organ transplantation that is not widely available. Difficulties involving the recognition and proper medical management of potential lung donors, organ preservation, and a clinically challenging postoperative course have introduced a long time barrier to achieve success in the field. Clinical difficulties come mainly from the susceptibility of lung transplant patients to infection and the need for a more aggressive immunosuppression regimen due to a higher rate of rejection than in case of other organs transplants.
In the Silesian Center for Heart Diseases in which a successful large heart transplant program has been continued since 1985, several attempts of heart-lung (HLT) one-block transplantations remained unsuccessful for a long time. Eventually, in 2001, a good result was achieved with HLT performed in a patient with post-myocarditis cardiomyopathy and pulmonary hypertension. In 2003 and 2004, two consecutive single lung transplantations (SLT) were performed with good results in patients with respiratory insufficiency due to lung diseases. These patients have remained alive and the follow-up has been from 7 months to 4 years. Despite the initial success, the number of lung transplantations has not shown an increasing trend. Paradoxically, the main obstacle has been a very low number of patients on the waiting list. A lack of awareness in the Polish community of chest physicians of the availability of HLT treatment creates a situation in which patients are not directed to a transplant center.

MATERIAL AND METHODS

The study was approved by a local Ethics Committee. In the Silesian Center for Heart Diseases the following criteria and guidelines have been established for the purpose of patients' selection for lung transplantation. In the majority, those guidelines are similar to those approved by the International Society for Heart and Lung transplantation.

Lung recipient criteria

1. predicted time of survival 18-24 months
2. significantly decreased quality of life
3. no response to medical treatment
4. need for home oxygen therapy
5. age below 55 years if HLT is necessary and below 65 years for single or double lung transplantation

Selection criteria for specific types of lung transplantation

1. Single lung transplantation:
   - restrictive pulmonary diseases:
     - idiopathic pulmonary fibrosis
     - sarcoidosis
     - silicosis
     - lymphangioleiomyomatosis
     - histiocytosis
   - obstructive pulmonary diseases:
     - emphysema
   - pulmonary vessels diseases:
     - primary pulmonary hypertension
2. Double lung transplantation
   - Cystic fibrosis
   - Pulmonary diseases with bronchiectasis
3. Heart-lung transplantation
   - Eisenmenger's syndrome
   - primary pulmonary hypertension
   - chronic pulmonary thromboembolism

**Immunosuppression**

Every patient after lung transplantation needs to be treated with immunosuppressive drugs. Immunosuppressive regimen can be divided into two kinds: to prevent organ rejection or to treat a rejection being underway. For the former purpose usually a triple drug therapy is used. That, in majority, consists of a combination of a calcineurin inhibitor, cyclosporin or tacrolimus, a steroid, prednisone or prednisolone, and a purine metabolism inhibitor, azathioprine or mycophenolate mofetil. There is also an increasing role of rapamycin, a relatively new drug in transplant armamentarium. For our patients, as a main set of drugs in lung recipients we employ the following combination (Zabrze modification): cyclosporine, rapamycin, and steroids. Additionally, in the direct post-operative period we use two kinds of immunoglobulins. One that is directed against the interleukin 2 receptor (IL-2R) and the other belonging to cytotoxic immunoglobulins that create T lymphocytes lysis. For treatment of a rejection underway the first line therapy is a bolus of methylprednisolone given for three consecutive days. Cytotoxic immunoglobulins can also be used for this indication, given separately or in combination with steroids.

Recognition of an episode of acute rejection is mainly based on a clinical judgment. Symptoms of dyspnea, decreased arterial oxygen saturation, increased respiratory effort, tiredness, and a moderate fever should draw attention to the possible rejection of a transplant, particularly when infection is not apparent in clinical or laboratory tests. In unclear situations, when infection and rejection are to be differentiated a transbronchial lung biopsy is performed and specimens are examined histopathologically.

**Infection**

Infection is always feared, since immunosuppression decreases the recipient's ability to fight against it. Bacterial infection is responsible for 50% of infections following lung transplantation and in some cases is particularly dangerous. The Pseudomonas and Burholderia species are of special importance. Also, such opportunistic infection as those caused by cytomegalovirus and pneumocystis carinii are truly dangerous for lung transplant recipients. In our center, routine prophylactic treatment is introduced against those pathogens.

Patients remain on co-trimoxazole for their life time. A two-three week treatment with ganciclovir is routinely given to every patient and then antigen pp65 is checked on a regular basis, as a marker for the introduction of preemptive therapy with ganciclovir infusions. Fungal infections are extremely dangerous after lung transplantation. Particularly, the aspergillus species is. In our practice, every patient receives short-term prophylaxis with vorikonazol and if the control of sputum is negative, the patient remains on prophylaxis of inhaled amphoterycin B. We advise to provide such antifungal strategy even for two years post-transplantation.

**Physiotherapy**

The value of physiotherapy in a lung transplant team cannot be underestimated. In a model of post-transplant care that we introduced in our department, the physiotherapy team stays with the patient for 24 h a day for the first week, even if the course remains without complications. Decreased level of surfactant due to ischemia, a lack of cough reflexes as result of denervation, the absence of ciliary transport in the bronchial tree all must be replaced by extensive physiotherapy.
RESULTS AND DISCUSSION

From 2001 to 2004, two combined HLT one-block and two single lung transplants were performed in our institution. One of the HLT patients suffered from post-myocarditis cardiomyopathy complicated by pulmonary thromboembolism with pulmonary hypertension. His pulmonary vascular resistance was above 14 Woods' units. At the time of transplantation he was bed-ridden and dependent on catecholamine infusions. Hyperuricemia and deep sacral lesion were his main co-morbidities. The second HLT patient was with end-stage pulmonary emphysema with right heart failure due to pulmonary hypertension. His most serious co-morbidity was advanced cachexia (BMI <18). At the time of transplantation he was bed-ridden and oxygen-dependent. His time on the waiting list was 18 months.

Our first SLT patient was transplanted due to emphysema. His condition forced him to live an armchair life, fully dependent on oxygen therapy. Diabetes and advanced prostate hypertrophy were main his co-morbidities. He spent 2.5 years on the waiting list. The second SLT patient suffered from end-stage idiopathic pulmonary fibrosis. His life style was home-restricted and oxygen-dependent. His breathing frequency was, on average, 30 breaths/min. As it happened, his waiting time for the transplant was just a day.

Three of the patients mentioned remain alive. The cachexic patient died shortly after transplantation due to a massive intestinal bleeding from a Meckel diverticulum, which was followed by a transverse colon perforation and peritonitis. The follow-up time of the living patients is, at the time of writing of this article, from 7 months to nearly 4 years. Two patients (one HLT and one SLT) are listed as NYHA class I. The other SLT patient is in NYHA class II due to partial dysfunction of the phrenic nerve caused by tissue damage during surgery. All the patients report a definite improvement in the quality of life. They do not require oxygen therapy, perform everyday tasks, and the HLT patient works a full-time job. All of them were diagnosed for rejection during the hospital post-operative time and were successfully treated.


There is no answer to the question what the real demand for lung transplantation is in Poland. Why is it unknown? Because patients are not directed for transplantation. There are two reasons for this situation: the lack of awareness that the treatment is already available in the country and that the treatment is an option for end-stage pulmonary diseases. This fact leads to a paradoxical situation where there are only a few patients on the waiting list for a lung transplant. Beside, strict body size matching criteria in lung transplantation make it often impossible to utilize recognized, suitable donors. Currently, there are 6 patients on our waiting list.

We wish to announce that our center is full ready to start a regular lung transplant program. We have extensive experience with immunosuppression, based on a large heart transplant program, experience with patients already
transplanted, available bronchofiberoscopy, experience with transbronchial lung biopsy, and physiotherapeutic and nursing teams with experience in lung transplant patients. We are looking for patients.

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