An 18-year follow-up after the first successful heart-lung transplant in Poland. Authors' tribute to the pioneers of heart and lung transplantation

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Introduction Heart-lung transplant (HLTx) is the procedure of choice in patients with concomitant advanced cardiopulmonary failure. For the first time, it was successfully carried out by Bruce A. Reitz in 1982 in patients with pulmonary vascular diseases.[1] According to the registry of the International Society of Heart and Lung Transplantation (ISHLT), more than 4000 patients have underwent HLTx from that time.[2] Thoracic organ transplant programs could be initiated thanks to James Hardy who performed the first single lung transplant, Christiaan Barnard who conducted the first heart transplant, and Joel D. Cooper—the father of the first successful single and double lung transplants.[3]

In Poland, the first attempts to conduct HLTx to save patients with cardiopulmonary failure were started in 1986, but turned out to be ineffective. The first successful combined heart-lung transplant in Poland was performed in 2001. So far, it has been the only successful HLTx carried out there. According to the archives of the Silesian Center for Heart Diseases (SCHD), more than 200 lung and 1200 heart transplants have been performed in our center so far.

In this short communication, we describe the case of the first patient in Poland who underwent combined heart-lung transplant due to dilated cardiomyopathy complicated with severe pulmonary embolism and pulmonary hypertension. The patient has survived over 18 years in good general condition.

Methods The analyzed medical records included findings obtained during the 18-year follow-up of this patient. Detailed data on the medical test results of the study patient are presented in the Supplementary material and include spirometry (*Figures S1* and *S2*), echocardiography (*Table S1*), laboratory test (*Table S2*), and magnetic resonance imaging (*Table S3*). The patient's written consent was required for participation in the study. The study obtained the ethics committee approval. No statistical analysis was performed.

Results and discussion A 37-year-old man underwent HLTx due to end-stage dilated cardiomyopathy complicated with severe pulmonary embolism and pulmonary hypertension. The disease onset was difficult to determine because of lack of medical records and incomplete patient's history. To our best knowledge, the patient had a 16-year history of cigarette smoking and no family history of cardiac or pulmonary disease. He worked as a metal press operator. At the age of 35 years, the patient started complaining of chest pain, dyspnea, and poor exercise capacity. Symptoms occurred after severe bacterial pneumonia and myocarditis was suspected. Due to progressive heart failure, the patient was admitted to

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Received: May 21, 2020.
Revision accepted: June 5, 2020.
Published online: June 5, 2020.
Kardiol Pol. 2020; 78 (7-8): 773-775
doi:10.33963/KP.15420

the SCHD for diagnostic workup. Coronary catheterization showed no abnormalities in the coronary arteries, and myocardial biopsy revealed dilated cardiomyopathy. Based on clinical status, the patient was considered as a potential heart transplant recipient. Since August 2001, the patient presented heart failure exacerbation due to pulmonary embolism complicated with pulmonary hypertension. For this reason, he was deemed eligible for heart-lung transplant. Twenty days thereafter, uncomplicated, orthotopic HLTx was performed. The procedure was conducted with sternotomy access. Both the heart and the lungs were very carefully dissected and excised. Then, the donor's heart was implanted with the Reitz technique. The trachea, the aorta, and the right atrium were fused. The procedure lasted 9 hours 20 minutes, the cardiopulmonary bypass time was 4 hours 38 minutes, and the organ ischemic time was 3 hours 57 minutes. In the postoperative course, acute rejection of transplanted organs occurred twice. The patient received the following immunosuppression therapy: cyclosporine (400 mg/d reaching 371.5 ng/ml of blood concentration), sirolimus (4.5 mg/d), and prednisolone (4 mg/d). The man was discharged from the hospital on postoperative day 86. A year after HLTx, during a follow-up visit in the SCHD, the patient's clinical status was improving. Immunosuppression therapy was modified—prednisolone was discontinued. During the first decade after transplant, the patient was hospitalized a few times due to bronchiolitis; however, he remained in a good general condition. Unfortunately, 10 years after HLTx, the patient had a single serious, life-threatening infection. He was urgently admitted to the SCHD because of symptoms of severe pneumonia. The dominant manifestations were high fever, cough with expectoration, and sore throat. High-resolution computed tomography showed consolidations in segment 6 of the right lung and less severe consolidations in the left lung. Ground glass opacities were present at the bases of both lungs. Bronchoalveolar lavage was performed and *Aspergillus* species and carbapenem-resistant *Pseudomonas aeruginosa* were detected. Infection was treated based on the microbiological test results, with amphotericin and caspofungin, which were continued for a month and a half. Immunosuppressive therapy was further modified: cyclosporine was discontinued, and sirolimus was maintained (1 mg every 4 days). After 2 months of treatment, the patient was discharged in a good general condition.

Currently, the patient is 18 years after the HLTx procedure. The post-transplant time has been complicated by type 2 diabetes, dyslipidemia, and arterial hypertension. During the last follow-up hospitalization in the SCHD, the patient achieved the distance of 535.4 m (3 points according to the Borg scale, without desaturation) in a 6-minute walk test. At present, the patient's condition is stable.

According to the ISHLT registry, 4054 heart-lung transplants were performed in adults in June 2017. The registry also included 1- and 5-year occurrence rates of comorbidities: diabetes, 17.1% and 26.5%; arterial hypertension, 59.1% and 87.2%; and hyperlipidemia, 28% and 70.4%, respectively. The cumulative incidence of severe renal dysfunction in 5-year survivors was 13.7%.[2] Our patient developed diabetes, arterial hypertension, and hyperlipidemia 2 years after HLTx, but kidney function was stable after almost 2 decades after surgery. These comorbidities could be related to post-transplant immunosuppressive therapy.[4]

Harringer et al[5] and Moffatt-Bruce at al[6] assessed 1- and 5-year survival rates after HLTx and showed 77% versus 87% and 64% versus 63%, respectively. According to a literature review, the survival rate after HLTx compared with single or double lung transplant is comparable, similar to the values cited above.[7-10] The authors of the 2018 ISHLT registry investigated the survival rate of all HLTx recipients from 1982 to June 2016. One-year survival was reached by 63% of the patients, 5-year survival by 45%, and 10-year survival by 32%.[11]

Postoperative management after HLTx is similar to that after lung transplant.[9,10] Early complications occurring after surgery are much more common to lung graft than the cardiac one. Yusen et al[11] showed that obliterative bronchiolitis occurs more frequently than coronary vasculopathy (28.7% vs 8.2%). Obliterative bronchiolitis and chronic lung allograft dysfunction are also the major causes of mortality at 1-year follow-up.[11] Maintenance immunosuppression and blood concentrations of immunosuppressive medications, which should be reached, are comparable to those used after lung transplant, being greater than after orthotopic heart transplant alone. Immunosuppression can be decreased 1 year after transplant, depending on the patient's history of rejection episodes and adverse effects from the medications. In recipients who remain stable, doses of calcineurin inhibitors and corticosteroids may be reduced.[12] Additionally, persistent or virulent infections require reduction of immunosuppression more quickly. The man described in this short communication received cyclosporine, prednisolone, and sirolimus during the first year after transplant. Then, corticosteroids were discontinued and blood concentrations of cyclosporine were reduced. Severe infection, which occurred after the first decade after HLTx, forced a modification in drug therapy. Currently, the patient receives only sirolimus and no signs of graft rejection are observed.

In summary, HLTx is an effective therapeutic option for patients with end-stage cardiac and

pulmonary disease. Although it is a risky procedure, burdened with high mortality and a low survival rate, it sometimes may be the only life-saving method. Proper patient care both before and after the surgery can significantly extend the patient's life and help achieve good quality of life.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

HOW TO CITE Zembala M, Religa Z, Large S, et al. An 18-year follow-up after the first successful heart-lung transplant in Poland. Authors' tribute to the pioneers of heart and lung transplantation. Kardiol Pol. 2020; 78: 773-775. doi:10.33963/KP.15420

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