

Case Report

Heart – lung Transplantation in Iran: A Case Report

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Abstract

We report our initial experience with a heart-lung transplant operation performed on a 12-year-old girl with Eisenmenger syndrome at Masih Daneshvari Teaching Hospital in Tehran, in 2009. We also outline the operative indications, anesthetic management, and postoperative complications of heart-lung transplantation. We hope that this issue on transplantation may provide an encouraging prospect for patients with end-stage cardiopulmonary disorders in Iran.

Keywords: Anesthesia, Eisenmenger syndrome, heart – lung transplantation, postoperative complications

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Introduction

A heart–lung transplant (HLT) is a procedure performed to replace both heart and lungs in a single operation. Since the first successful human HLT in 1981,¹ it has become an accepted therapy for patients with end-stage cardiopulmonary disease for which no therapeutic options exist except combined heart- lung replacement.^{2,3} The most common indications for HLT are irreversible Eisenmenger syndrome (ES) or primary pulmonary hypertension with end-stage biventricular failure and very limited reserves.⁴⁻⁷

According to the 2008 Registry Report of the International Society for Heart and Lung Transplantation (ISHLT), more than 3300 of HLT have been carried out worldwide since 1981.⁸ However, the annual number of HLT performed in Asia is extremely small. Although 60% of the world's population lives in Asia, very few of Asian countries perform thoracic organ transplantations. According to the Registry Report of the Asian Society of Transplantation, between 1997 and 2001, only 22 HLTs were performed in Asia. Among them, 13 cases were operated in Thailand, three in Korea, two in PR China, and four in Pakistan while the number of Asia's HLTs has declined from five in 1997 to three in 2001. The likely causes are the lack of medical, legal, social, and finan-

cial infrastructure; lack of trained staffs; low priority compared to other health problems; and cultural barriers and public beliefs.^{9,10} In Iran, to the best of our knowledge, there have been three other combined HLT operations in Imam Khomeini Hospital in Tehran, the first one was done in 2002.^{11,12} However, no published report of these HLT cases and their outcomes was found.

This is the first full report on a HLT in Iran, which was performed in 2009, on a pediatric case of complex congenital heart disease with ES at Masih Daneshvari Teaching Hospital in Tehran. We also outline the operative indications, anesthetic management, and postoperative complications of HLT patients.

Case Report

A 12-year-old girl, weighing 24 kg, height 137 cm, who had been diagnosed with ES due to Type I truncus arteriosus (TA) and a large ventricular septal defect (VSD) at the age of four, was referred to our hospital for HLT. Progressive deterioration in her cardiopulmonary function over the previous 12 months, led to persistent class IV symptoms despite medical treatment. Cardiac catheterization showed a mean pulmonary artery pressure of 90 mmHg and a mean aortic pressure of 110 mmHg. Preoperative electrocardiogram showed ischemic changes and right bundle branch block (Figure 1). The donor was a 12-year-old boy with a brain tumor and the same blood group.

The recipient was not premedicated. Cyclosporine 5mg/kg was given before arrival in the operating room. Before induction of anesthesia, in addition to standard monitoring, a radial arterial catheter was inserted with local anesthesia and conscious sedation with intravenous midazolam 0.2 mg and fentanyl 10 ug for continuous measurement of arterial blood pressure and frequent blood gas samplings. While, central venous line through the left subclavian vein was placed after induction of anesthesia. Baseline blood pressure was 120/74 mmHg, heart rate 120/min, respiratory rate 26/min, and SPO₂ 90% while breathing O₂ via face mask.

The heart and lungs of the donor were harvested en block in the other operating room of our hospital. Modified UW and Perfadex solutions were used to preserve the donor heart and lungs, respectively. The donor received prostaglandin E₁ intravenously before

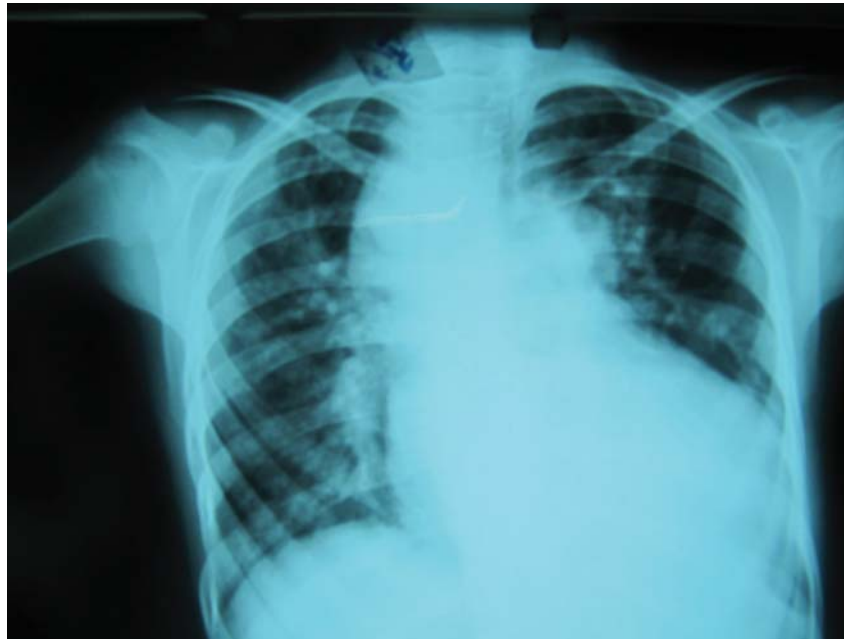
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Table 1. Arterial blood gas and hemodynamic data during and post-HLT

Time	FIO ₂	PH	PaO ₂	PaCO ₂	SaO ₂	HCO ₃	MAP	HR
Preinduction	0.6	7.40	61	41.5	91	25.8	86	120
During CPB	1.0	7.46	405	25	99.9	18.6	82	□
1 h post-transplant	1.0	7.27	103	45	96	20	77	137
4 h post-transplant	1.0	7.41	116	30	98	19.7	81	118
14 h post-transplant	0.5	7.40	73	40	94.7	21.2	85	111
24 h post-transplant	0.5	7.43	113.2	37.5	98.8	22.6	85	104
48 h post-transplant	0.5	7.41	128	34.6	98.8	21.6	82	105
7th post-transplant day	0.3	7.40	135	45	99	22.5	90	105

CPB: cardiopulmonary bypass; MAP: mean arterial pressure.

**Figure 1.** Chest x- ray before transplantation. Cardiomegaly with right- sided aortic arch, increased vascularity, and mild alveolar edema.

flushing the pulmonary artery with Perfadex solution.

When the donor organs' suitability was confirmed, the recipient was anesthetized with fentanyl 500 ug and midazolam 4 mg followed by pancuronium 4 mg to facilitate tracheal intubation with a 5.5 cuffed endotracheal tube. Anesthesia was maintained with isoflurane in 100% oxygen, remifentanyl, and atracurium infusion in conjunction with increments doses of midazolam.

HLT was performed through a median sternotomy with hypothermic full cardiopulmonary bypass (CPB), bicaval cannulation, and aortic cross-clamping. During CPB, anesthesia was maintained with infusion of remifentanyl, midazolam, and atracurium and bolus doses of fentanyl.

After removing the failing heart and both lungs of the recipient, the donor heart and lungs were implanted en block without incident. The patient's blood gases and hemodynamics are listed in Table 1. The graft ischemic time was 275 minutes. A bolus of methylprednisolone 10 mg/kg was given before aortic cross-clamp removal.

After unclamping the aorta, because of ascending aorta damage and major hemorrhage secondary to size mismatch between the donor and recipient aorta, a period of 20 minutes of total circulatory arrest with profound hypothermia (18°C) was commenced for aortic interposition grafting (Vascutek vascular graft). Thereafter, the patient was rewarmed. Hemodynamic stability was main-

tained by adjusting the anesthetic concentrations and infusion of epinephrine and dobutamine before termination of CPB. Once the donor organs were functioning normally, the patient successfully separated from CPB, the chest was closed, and she transferred to the intensive care unit (ICU). Upon arrival in the ICU, mechanical ventilation was set and invasive and noninvasive monitoring done in the operating room, as well as infusion of epinephrine was continued. Intensive care against infection and rejection was made after operation. The immunosuppressant drugs used to prevent and treat rejection involved three different classes of drugs including cyclosporine, methylprednisolone, and Cellcept with cyclosporine as the main immunosuppressive therapy. A bolus of methylprednisolone 10 mg/kg was given intraoperatively and continued at 5 mg/kg postoperatively. After extubation of the trachea, prednisolone was started at 30 mg /day and was tapered to 20 mg/day by two weeks. Cellcept 500 mg/kg BD was also given orally, adjusted to white cell counts greater than 5,000 cells/ mm³. Intravenous cyclosporine was loaded preoperatively with 5mg/kg, and postoperatively with 1 mg/kg and was continued orally at 100 mg BD. Doses were titrated to target blood levels of 102 to 307 ng/mL. The patient also received tazocin, ciprofloxacin, and itraconazole as antibacterial and antifungal medications.

The immediate postoperative period was complicated by mediastinal hemorrhage which required exploration at six and 12



Figure 2. Chest x-ray two days after transplantation shows infiltration in the left lower lobe, mild cardiomegaly, and mediastinal widening with right-sided aortic arch.

post-transplantation hours. In total, seven units of compatible packed red blood cells, 18 of platelets, four of whole blood, and eight of fresh frozen plasma were transfused throughout. Inotropic support was discontinued gradually by the second postoperative day (Figure 2). The patient was extubated on the postoperative day 4 after hemodynamics were stable and satisfactory gas exchange was present.

Follow-up fiberoptic bronchoscopy and bronchoalveolar lavage (BAL) was carried out at routine intervals. Diagnostic rigid bronchoscopy with BAL and transbronchial biopsy performed under general anesthesia five and six days after surgery. Serial cultures of BAL fluids and tissue biopsies were positive for *Candida* species and showed resolving rejection. Postoperative echocardiography revealed a normal left ventricle, normal ejection fraction, mild mitral regurgitation, and slight right atrium enlargement. Over the next 14 days, the recipient had a notable improvement in functional capacity compared to her preoperative condition (Figure 3). She developed an intermittent low-grade fever after the fourteenth day following surgery. Fiberoptic bronchoscopy and chest x-ray showed no sign of airway complication and lung infection. The presence of an aneurysm adjacent to aortic arch was detected by CT scan obtained on postoperative day 18.

On post-transplant day 19, during cycling exercise, she complained of an acute severe abdominal pain and following an unexpected very sudden massive bleeding via chest tube, irreversible cardiac arrest occurred in a few minutes. No tissue biopsy and autopsy was performed afterward due to her parents' refusal.

Discussion

The most common indications for HLT are primary pulmonary hypertension, congenital heart disease (including ES), and cystic fibrosis with end-stage biventricular failure and pulmonary hypertension.^{7,8} While more patients with pulmonary hypertension

and cystic fibrosis are treated with isolated lung transplantation, it is expected that the indications for HLT will be limited to severely symptomatic ES patients when optimum medical therapy fails and surgical repair of congenital cardiac defects seems unlikely to succeed.¹³ However, outcome has remained poorer than for other solid organ transplants. The survival after lung and HLT is approximately 50% at five years, but it continues to decrease thereafter.¹⁴⁻¹⁵

ES is the most advanced form of pulmonary arterial hypertension secondary to congenital heart defects with a significant morbidity and mortality. The cardiac defects most common to ES are VSD, atrial septal defect, atrioventricular septal defect, and patent ductus arteriosus. Patients with ES may also present with more complex underlying lesions, such as TA, and transposition of great vessels with VSD which is associated with increase in mortality. During the past 50 years, the incidence of ES in the Western world has reduced by an estimated 50%, due to advances in pediatric cardiology, surgery, anesthesia, and proper medical treatment. Continuing advances in management of these patients will likely reduce the numbers of those requiring HLT in the future.^{13,16}

Complexity of the HLT procedure and early complications are the major factors that limit frequent use of HLT treatment strategy. Technical complications, graft failure, hemorrhage, and infections account for most of the deaths during the first 30 days, whereas midterm and late deaths are mainly due to infections and obliterative bronchiolitis. Most recipients have at least one acute rejection episode despite adequate immunosuppression.^{3,7,13,17} Infectious complications are common in transplant patients because of immunosuppressive regimens and invasive fungal infections. *Candida* and *Aspergillus* are the important sources of infection among these immunocompromised patients.¹⁸

Aortic interposition grafting is widely accepted in the management of thoracic aortic aneurysm and dissection; however, complications including anastomotic dehiscence and graft infection have been reported.¹⁹ In our patient, concerning CT finding and

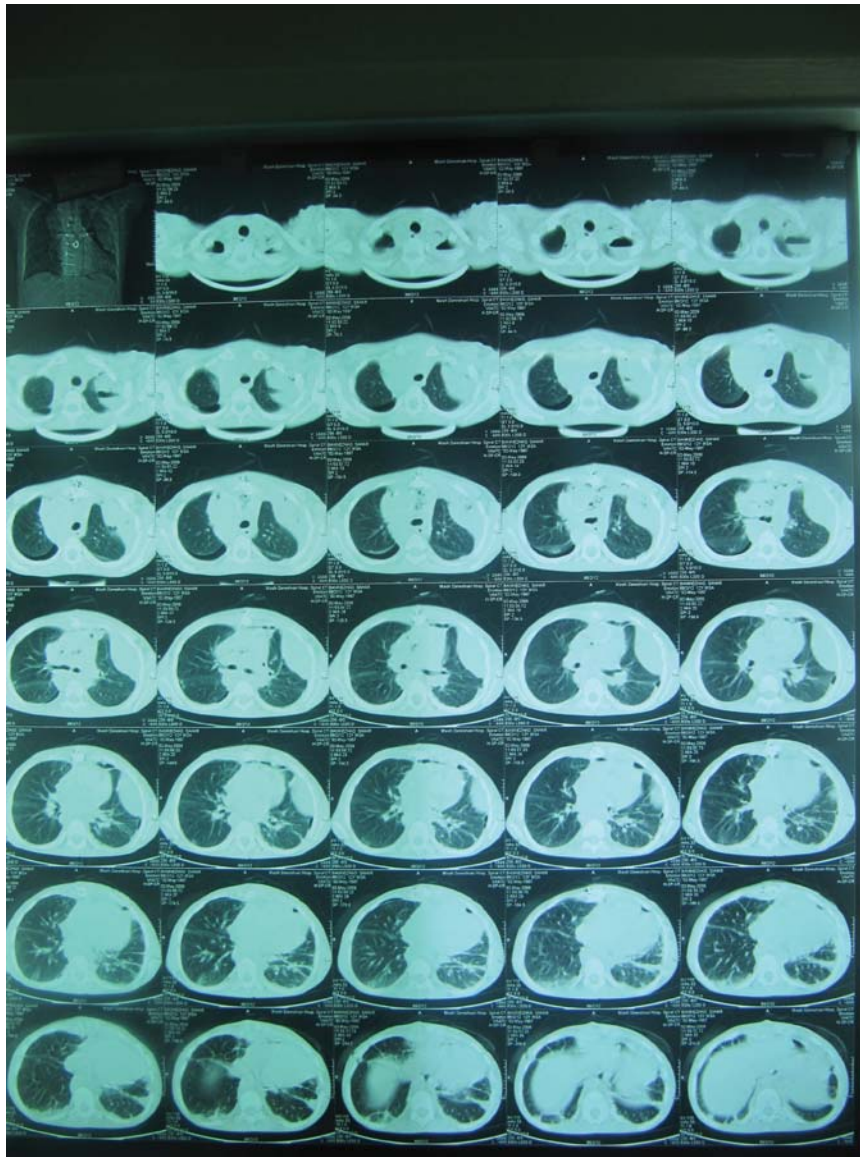


Figure 3. CT scan 18 days post-transplant shows cardiomegaly with pseudoaneurysm adjacent to the right- sided aortic arch, and mild loculated pleural effusion.

clinical presentation, we believe that rupture of aortic pseudoaneurysm was the most probable cause of lethal bleeding and the aneurysm originated from an area of dehiscence of the suture line at the site of aortic interposition graft. Furthermore, with regard to detection of *Candida* in the BAL fluid and tissue cultures of our patient, we think that in addition to technical complications, fungal infection was also a major contributing factor in postoperative dehiscence of the applied sutures. In the study of Katsumata, et al. intermittent or persistent low-grade fever was the only symptom in patients with mediastinal false aneurysm.²⁰ Aortic graft infections are actually associated with high morbidity and mortality rate; those involving the thoracic aortic grafts are the most catastrophic, with mortality rates ranging from 25% to 75%.²¹ Without reoperation for aortic repair and removing infection, aortic aneurysms progressively expand, compress, and erode the surrounding structures, or are a source of persistent infection and systemic embolism. However, reoperation is also associated with significant mortality.²⁰

Postoperative adhesions in the mediastinum are another factor that can contribute to considerable bleeding after HLT. Autopsy results of HLT patients in the study of Tazelaar, et al. showed that a major contributing factor in postoperative deaths of these patients was pleural hemorrhage from adhesions of prior chest surgery.²² However, regarding our patient's clinical picture, this factor seemed an unlikely cause of life-threatening massive hemorrhage.

Despite the complexity of management and high perioperative mortality, HLT is, nowadays, the only option for severe ES patients to return to a normal life.^{5,12} Donor-recipient matching in size, proper removal and protection of the donor lung and heart, and proper post-transplant management are the key features of survival for these patients.^{6,7} Furthermore, the success of HLT is related to careful patient selection, recipient status, recipient age and gender, donor age, ischemic time, type of cardiac defects, and appropriate surgical plan.^{4,5}

There is no single anesthetic technique recommended for HLT. The ultimate goal in anesthesia management is hemodynamic

control. A high-dose narcotic technique with fentanyl or sufentanil in conjunction with midazolam or a low inhaled concentration of isoflurane is a good choice to minimize hemodynamic instability. CPB should be started early to maintain acceptable hemodynamic conditions. During surgery, episodes of hemodynamic compromise must be treated promptly. Low doses of inotropes and vasopressors preserve hemodynamic stability and appropriate organ function. Catecholamine administration is usually maintained several days after surgery. Judicious fluid administration is often necessary to reduce reperfusion pulmonary edema.^{2,23}

Our experience in HLT may provide an encouraging prospect for patients with end-stage cardiopulmonary disorders in Iran. More effort needs to improve the long-term results.

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