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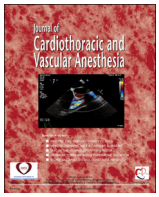

REVIEW ARTICLE

The Evolution of Anesthesia for Lung Transplantation

Daniel Sellers, MBBS, FRCA[1], Wilfred Cassar-Demajo, MD, FRCA, FRCPC, Shaf Keshavjee, MD, MSc, FRCSC, FACS, Peter Slinger, MD, FRCPC

Toronto Western Hospital, Toronto, Ontario, Canada

Key Words: thoracic anesthesia; lung transplant anesthesia; transesophageal echocardiography; ex vivo lung perfusion; primary graft dysfunction; immunosuppression; extracorporeal membrane oxygenation; ketamine; right ventricular failure; reperfusion injury

THE YEAR 2016 marked the 30th anniversary of the report of the first patient to undergo lung transplantation and experience long-term survival and the performance of the first clinically successful double-lung transplantation, both at Toronto General Hospital. During that time, enormous growth in the understanding and ability to deliver anesthetic care for this group of patients, not to mention an explosion in the amount of lung transplantation activity taking place, have occurred. The authors describe the evolution of anesthetic management for patients undergoing lung transplantation in the context of 2 representative cases. The first case details the first patient who experienced long-term survival; the surgery was performed at the authors' institution (anesthesiologist, W. D.). This case is compared and contrasted with a contemporary case that highlights the evolution in the areas of perioperative care, such as immunosuppression; hemodynamic management, including extracorporeal membrane oxygenation (ECMO); anesthetic drugs; fluid management; reperfusion; and transesophageal echocardiography. The review is concluded by a discussion of the potential for ex vivo lung perfusion techniques to increase transplantation activity and the changes to anesthetic delivery this may represent.

First Lung Transplantation With Long-Term Survival

A 58-year-old man presented with a 3-year history of fatigue and progressive exertional dyspnea due to idiopathic pulmonary fibrosis, which was confirmed with open-lung biopsy. He was treated with courses of prednisolone and penicillamine, but his condition continued to deteriorate; he had to quit work and required home oxygen. His pulmonary function tests showed a severe restrictive deficit with forced expiratory volume in 1 sec of 1.4 L/min, forced vital capacity of 1.6 L, and diffusing capacity of the lung of 48% predicted. Resting partial pressure of oxygen was 50 mmHg, with partial pressure of carbon dioxide 40 mmHg. Heart catheterization revealed a pulmonary artery (PA) pressure of 21 mmHg. After discussion with the institutional review board, permission was granted to proceed with lung transplantation. Three months later a donor organ was found from a young donor after brain death (DBD) who was a victim of cerebral gunshot trauma.

The patient received oral cyclosporine preoperatively but no corticosteroids, and a radial arterial line, PA catheter, and central venous catheter were placed. Fentanyl, thiopental, and pancuronium were used for induction of anesthesia, and isoflurane in oxygen was used for maintenance. He underwent ventilation on a volume-control mode at 6-to-8 mL/kg. There

S. Keshavjee is a founding partner and chief scientific officer of Perfusix Canada, Perfusix USA, and XOR Labs Toronto Inc. Has also has received research and clinical trial support from XVIVO Perfusion and United Therapeutics.

[1]*Address reprint requests to* Daniel Sellers, Toronto General Hospital, 200 Elizabeth Street, Toronto, Canada, M5S 2X1.

E-mail address: daniel.sellers@uhn.ca (D. Sellers).

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was very little blood loss during the initial dissection, and the right PA was test-clamped with no hemodynamic instability.

A right-sided single-lung transplantation was performed, with end-to-end anastomosis of the bronchus and PA, and a pulmonary venous anastomosis was performed as an atrial cuff. A small laparotomy was performed to mobilize a vascular pedicle of omentum, which was pulled up through the diaphragm and then wrapped around the bronchial suture line to protect and revascularize the bronchial anastomosis. A technique of cold atelectatic immersion was used for preservation of the lung. Essentially, a bronchial blocker was placed in the donor right main bronchus and the right lung, which was maintained in a deflated state. The donor lung was heparinized systemically, and topical cooling with iced saline slush was performed before extraction. No special technique was used for reperfusion of the implanted lung. The total fluid given was approximately 2 L of crystalloid, and no blood products were used.

The patient was transferred intubated to the intensive care unit (ICU), where an immunosuppressive regimen of cyclosporine and azathioprine was initiated. His airway was extubated on the third postoperative day, but he developed acute "rejection episodes" requiring reintubation on days 6 (3 days ventilated) and 16 (2 days ventilated). These episodes were treated with pulses of methylprednisolone and antilymphocyte globulin. Oral prednisolone was initiated at 3 weeks, which was reduced slowly over subsequent months. He spent a total of 6 weeks in the hospital and was discharged for further inpatient rehabilitation. His chest x-rays are shown in Figure 1.[1]

A Contemporary Case

A 50-year-old woman presented with a 7-year history of worsening bronchiectasis after a reactivation of multidrug-resistant tuberculosis, with which she was first infected 35 years previously. Her cultures had grown a number of antibiotic-resistant organisms including *Pseudomonas* and *Myobacterium avium*. Over the past 2 years, she had been hospitalized several times for hemoptysis, hypercapnic respiratory failure, and a tension pneumothorax.

A computed tomography scan of the chest revealed severe bronchiectasis and pleural inflammatory disease, with air-fluid levels. Her ventilation/perfusion (V/Q) scan showed differential perfusion of 69% to the left lung and 31% to the right, with matched ventilation deficits. Her echocardiogram results were normal, with no significant pulmonary hypertension and a cardiac stress test was normal. She managed 347 m on a 6-minute-walk test, but her oxygen saturation on air dropped from 96% to 85%. A resting arterial blood gas on air showed a partial pressure of oxygen in arterial blood of 68 mmHg, with a partial pressure of carbon dioxide of 40 mmHg. Her pulmonary function, blood gases, and other biochemical tests had remained stable in the 6 months before transplantation (Table 1), but the increasing frequency of hospitalizations for hemoptysis, decrease in functional ability, and a pulseless electrical activity arrest secondary to tension pneumothorax motivated the decision to offer lung transplantation in 2015.

She was quoted a 2% to 4% perioperative mortality, and she underwent a thorough multidisciplinary review process, including input from thoracic surgery, respirology, anesthesia, nursing, social work, physiotherapy, nutrition, and occupational therapy. Her lung allocation score was 31 at listing.

Lungs from a brain-dead multiorgan donor, matched by blood group and recipient predicted total lung capacity, were offered by the organ procurement agency. The donor team evaluated and examined the lungs and then flush cooled them with a low-potassium dextran flush solution (Perfadex; XVIVO Perfusion, Denver CO) and stored them cold and inflated for transportation to the authors' hospital. Based on the quality of the donor organs, the retrieving surgeons believed that the lungs required advanced evaluation before implantation, so they were placed on the Toronto Ex Vivo Lung Perfusion (EVLP) System and perfused and ventilated normothermically for 5 hours. Evaluation of serial gases, compliance, pulmonary vascular resistance (PVR), and x-ray

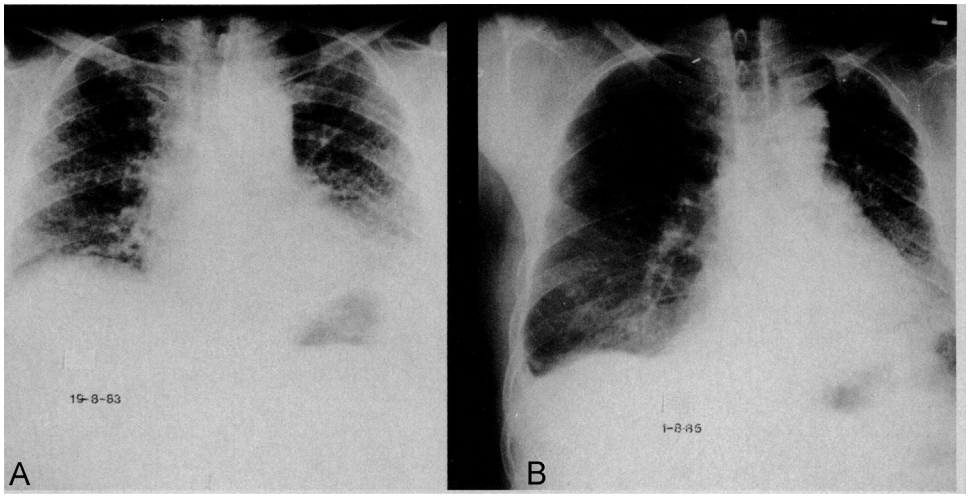

Fig 1. First lung transplantation recipient. (A) Before surgery. (B) Two months after transplantation. (From Unilateral lung transplantation for pulmonary fibrosis.[1] Reprinted with permission).

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