Lung Transplantation in Humans, with Emphasis on en Bloc Technique for Simultaneous Bilateral Transplantation without the Heart

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THE FIRST lung transplantation procedure in a human was performed by James D. Hardy and colleagues at the University of Mississippi Medical Center in 1963.[1] The transplant functioned for 18 days before death occurred from nonimmunologic complications. Even though the basic technique was well established,[2] numerous other attempts since have failed to produce long-term survivors. Although heart-lung transplantation became clinically feasible with the advent of cyclosporine, lung transplantation itself remained unsuccessful. J.D. Cooper and colleagues at Toronto introduced crucial modifications to the procedure, including use of an omental flap to wrap the bronchial anastomosis.[3,4] Several single lung[3,5] and fewer double lung transplants[4] have been successfully performed since. This report describes our experience with five double lung transplantation procedures.

PATIENTS AND METHODS

The technique described by the Toronto group[4] with modifications was used. Donor selection is based on blood group compatibility and close approximation of chest size between the donor and the recipient. A maximum of 15% in chest size disparity can be tolerated. The donor should have a clear chest x-ray without infiltrates and demonstrate an arterial Po_2 of over 300 mm Hg at 100% FIo_2, and 5 mm of PEEP. Tracheal aspirate should be free of purulence and pathogens by Gram stain. Distant procurement with a maximum travel time of up to 2.5 hours is feasible. The heart can be harvested separately from the lung for use in another recipient.

Preliminary lung dissection involves minimal handling of both lungs, elevation of large pleural pericardial flaps bilaterally, and digital separation of mediastinal pleura from the esophagus. Both pulmonary arteries are dissected out in the mediastinum, dividing the ligamentum and carrying the dissection on the left side well into the hilum extrapericardially. The trachea is divided five rings above the carina. As soon as the heart is excised, following cardioplegia, both lungs are topically cooled with Euro-Collins solution at 4°C. The heart is harvested with the left atrium incised in such a way that a generous cuff remains around the four pulmonary veins. The harvested lung is packed in ice-cold Euro-Collins solution and transported.

The recipient procedure is carried out with cardiopulmonary bypass. The pulmonary veins are mobilized retrocardially, stapled, and divided. The pulmonary artery bifurcation is excised, removing as much of the right and left pulmonary arteries as feasible and taking care to preserve the left recurrent laryngeal nerve. The trachea is divided above the bifurcation, approaching it between the vena cava and ascending aorta. The vagi should be preserved. Both lungs can be removed by cauterizing right and left hili. The tracheal/bronchial remnant distal to the tracheal division can then be extracted by cautery behind the superior vena cava into the right chest and removed. The donor trachea is trimmed to two or three rings above the carina and anastomosed to the recipient with a continuous 3-0 Prolene suture. With the heart cold and decompressed, the left atrial cuff is sewn to the left atriotomy of adequate length and the donor pulmonary artery to the recipient vessel using 3-0 and 4-0 Prolene sutures, respectively. Before closure of sternotomy, the tracheal anastomosis is wrapped with an omental pedicle brought up behind the xiphoid.

Immunosuppression consists of induction by Imuran and rabbit antithymocyte serum (ATG) at 1 to 2 mg/kg each daily, adjusted for WBC and platelet count. Cyclosporine is added (6 to 10 mg/kg daily) at 5 to 7 days after transplantation. When satisfactory serum levels are achieved, the ATG is withdrawn (usually around 10 to 12 days). Prednisone (7.5 to 10 mg daily) is added at three weeks postoperatively.

RESULTS

To date, five candidates ranging in age from 30 to 60 have received double lung transplantation at our institution. Primary pathology has been varied, including emphysema, infective bronchiolitis, cystic fibrosis and alpha-1 antitrypsin deficiency. Cold ischemia time varied from 2.5 to 5.5 hours. There was distant procurement in three of five instances, and the heart was shared with another team in a similar number. There was one operative mortality, traceable to a short pulmonary artery in the donor organ that required prolonged surgery, resulting in irreversible warm ischemic damage to the lung. The patient died on the sixth postoperative day from Candida sepsis, the organism having been present in the donor sputum. Two other patients have died at six weeks and four months postoperatively, respectively, the former from a donor-transmitted Pseudomonas pneumonia progressing to lung abscess and empyema, and the latter from an anesthetic complication during bronchoscopic resection of a tight stenosis at the tracheal suture line. Two other patients are alive at one year one month, and three months, respectively, after surgery. The surviving patients have normal arterial Po_2 on room air and have achieved a remarkable restoration of their exercise tolerance and activity levels since surgery.

The postoperative course has been smooth in only one of five patients transplanted. In the remaining four, prolonged intensive care was required owing to a variety of problems and complications in the postoperative period. One of five patients required "take back" for bleeding within a few hours after surgery. A space problem from a disproportionately small lung for the recipient chest was present in two patients but eventually resolved without incident. "Storage lung,"

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manifested by pulmonary edema, was present in all five patients. It was particularly severe in two, with excessive pleural drainage (up to 300 ml/hour). This vexatious complication, which appeared to be unrelated to cold storage time itself, was managed by fluid restriction, administration of colloids, diuresis, maintenance of low wedge pressure, cautious administration of prostaglandin E1 through a pulmonary catheter, and ventilator support with PEEP. The ventilator settings were adjusted to maintain the lowest possible peak pressure. The pulmonary edema, which usually became manifest within 24 hours after surgery, generally resolved in three to seven days with the above supportive measures. Three patients have suffered from early postoperative pneumonitis, with an organism identified in the donor sputum. Despite specific antibiotic therapy, two of these patients eventually died from the infection, and one was salvaged despite a serious sternal wound infection that required debridement and reclosure. The offending organisms in each instance were Candida, Pseudomonas, and Staphylococcus, respectively. Another patient had two episodes of pneumonitis at three months and nine months postoperatively that resolved easily with specific antibiotic therapy. Klebsiella and H-influenzae were isolated on one occasion and streptococcus during the second episode in this patient.

Two or more rejection episodes occurred in each of four patients who survived beyond a week after surgery. No rejection episodes were seen after two months postoperatively. A rejection episode was diagnosed when there was a significant fall in arterial Po_2 and one or more of the following features were present: hilar "flaring," vascular congestion or infiltrates on chest x-ray, leukocytosis, low-grade fever, desaturation on exercise detected by transcutaneous oximetry, and malaise. Rapid restoration of arterial Po_2 within a few hours of administration of 500 mg of Solu-Medrol intravenously was confirmation of the diagnosis of rejection. A daily pulse dose of Solu-Medrol for three days was uniformly successful in reversing individual rejection episodes.

Hypercarbia in the perioperative period is common in these patients until the central mechanisms and chemoreceptor centers readjust to the gas exchange capabilities of the newly transplanted undiseased lungs. A sense of suffocation and oxygen deprivation may episodically present during the first few months after surgery, even though arterial blood gases are entirely within normal limits during these episodes.

Long-term complications have included hemolytic uremic syndrome resulting in end-stage renal failure and chronic hemodialysis in one patient. This rare complication is thought to be related to cyclosporine administration. Two of five patients exhibited suture line tracheal stenosis, the cause of which remains unknown. In the first patient, who survives at 13 months after surgery, the lesion became evident at four months but stabilized after endoscopic resection of constricting granulation tissue at the suture line. A second patient, who exhibited this complication at four months postoperatively, underwent Gruntzig balloon dilatation of the stricture, which failed due to the rubbery nature of the stenosis. A subsequent attempt at endoscopic resection resulted in death during the procedure from an anesthetic complication.

In the course of our experience, it has become clear that chronic disease had resulted in long-standing nutritional and physical impairment in these patients. An intensive nutritional program with careful monitoring of caloric intake is necessary. Without a regular regimen of physical therapy and exercise, restoration of normal activity is seldom achieved because of chronic muscle wasting and long-standing physical inactivity. Having been near death and dependent on continuous oxygen prior to surgery, almost all surviving patients exhibit varying degrees of emotional and psychosocial problems postoperatively that require careful attention and support. With the passage of time, these problems appear to resolve satisfactorily.

Double lung transplantation is a more attractive alternative to heart/lung transplantation for certain pulmonary diseases in which the heart of the recipient is undiseased. One advantage is that the donor heart may be used for another patient. Heart-related rejection problems are avoided in the recipient since it is now known that pulmonary and cardiac components of heart-lung transplants may separately exhibit rejection. It appears that the bronchiolitis obliterans commonly evidenced after heart-lung transplantation has not been observed in the limited experience following double lung and single lung transplantation at our own institution or in Toronto.[6]

In conclusion, double lung transplantation provides a viable alternative to heart-lung transplantation. While the results reported herein will undoubtedly improve with increasing experience, an institution undertaking the procedure should be prepared for an intensive program of postoperative care both in the early postoperative period and over the long term.

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