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Special Article

Anesthesia for Lung Transplantation in Cystic Fibrosis: Retrospective Review from the Irish National Transplantation Centre

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Cystic fibrosis (CF) is an autosomal recessive disorder affecting approximately 1 in 2,500 live births worldwide, with double this estimated frequency in Ireland. CF is characterized by a genetic defect of the CF transmembrane regulator protein, causing impairment of chloride ion transportation. This has multisystem consequences, particularly in the lungs, where it results in intensely mucoid secretions, which increases susceptibility to infection. Lung transplantation is indicated in CF when there is progressive decline in a patient's functional reserve. In this report, the authors present a 6-year case review of allograft lung transplantations in 41 CF patients from the Irish National Centre for Lung Transplantation from 2010 through 2015. Preoperative risk factors for morbidity and major mortality are discussed. The authors' experience with intraoperative anesthetic challenges and management options are outlined, and postoperative complications are discussed.

Key Words: cystic fibrosis; lung transplantation; anesthesia

THE REPUBLIC OF Ireland has the highest incidence of cystic fibrosis (CF) in the world, at 1 in 1,461 live births, with a carrier rate for the genetic mutation of 1 in 19.[1] In developed European countries, the number of adults with CF has been predicted to increase by around 70% by 2025.[2] The median predicted survival for individuals with CF is now 36 years; yet, despite tremendous advances in its management, progressive respiratory failure remains the primary source of morbidity and mortality.[3]

Background

CF is a classic Mendelian autosomal recessive disorder, whereby a 230 kb gene on the long arm of chromosome 7, which encodes a 1,480 amino acid protein called CF transmembrane regulator (CFTR), is deficient, resulting in defective function of this protein.[1] In populations with northern European ancestry, the predominant mutation is Phe508del.[4] The CFTR protein is widespread throughout the body (lungs, salivary glands, liver, kidney, pancreas, sweat ducts, and reproductive tract) and acts as a chloride channel and regulator of sodium, chloride, and bicarbonate transport. Abnormal chloride transport, as a result of the defective functioning of the CFTR, causes increased water and sodium transport across the affected membranes and abnormally viscous secretions/mucus. In the lungs, this abnormal mucus compromises cilial function and impairs host defenses against bacteria. Mucus plugging, chronic chest infections, and bronchiectasis result, and over time, these chains of events cause a gradual decrease in respiratory function and eventual respiratory failure.

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Lung transplantation for CF was first performed using a combined heart-lung transplantation in 1983,[5] with the first double lung transplantations (DLTs) for CF performed by a French group 6 years later.[6] DLT has become an important therapeutic option for CF patients with end-stage lung disease. According to the 2011 report of the International Society for Heart and Lung Transplantation, patients with CF comprise the third largest group undergoing lung transplantation.[7,8]

The first and most widely referenced data on prognosis after transplantation are from the Toronto Lung Transplant Program.[9] This group identified patients with a risk of death $>50\%$ at 2 years (based on the estimated waiting time for transplantation).[9] The authors found that in patients with a forced expiratory volume in 1 second (FEV_1) of 20% of predicted, there was a 70% chance of death within 2 years, but the chance of death halved for every 10 percentage-point increase in FEV_1.[9] The authors concluded that "patients with cystic fibrosis should be considered candidates for lung transplantation when the FEV_1 falls below 30% of the predicted value. Female and younger patients may need to be considered for transplantation at an earlier stage".[9]

Subsequently the CF criteria for transplantation were developed by the American Thoracic Society as follows:

- FEV_1 $<30\%$ predicted or rapid progressive respiratory deterioration with FEV_1 $>30\%$ predicted
- Partial pressure of carbon dioxide >6.7 kPa and/or partial pressure of oxygen <7.3 kPa resting arterial blood gases on room air

These criteria are associated with 50% survival at 2 years. Young female CF patients whose condition deteriorates rapidly have a poor prognosis and should be evaluated on a case-by-case basis, regardless of physiologic criteria. However, by using these criteria, up to 30% of listed patients with CF will die before transplantation. High waiting list mortality data may reflect the inaccuracy of identifying the transplantation window or may highlight the limitations of waiting time–based donor allocation.[10]

The median survival after DLT in the international registry for patients with CF is 8.3 years. More current figures suggest that patients with CF who survive beyond the first postoperative year have a median survival of 10.5 years.[11,12] Therefore, DLT can extend and substantially improve quality of life in properly selected patients.[13]

Study Purpose

Ireland has the highest incidence of CF in the world. The Mater Misericordiae University Hospital (MMUH) is the national lung transplantation unit, and the aim of this review is to present the authors' experience of the provision of anesthesia and perioperative management for the CF patient for DLT from 2010 to 2015. The authors have reviewed the considerations applicable to the provision of anesthesia, the implications of the multisystemic nature of the disease, and how they influence technique and perioperative care.

Methods

After receiving Institutional Review Board approval, the authors examined all available data from a retrospective chart review to include preoperative assessment, intraoperative management, and postoperative anesthesia care of lung transplantation recipients in the CF cohort at the MMUH for the calendar years 2010 through 2015.

Results

Preoperative

This is the first reported series of its kind from a country with the highest prevalence of CF. The overall survival at the authors' institution is 97.6% at 1 year, 76.1% at 5 years, and 44.7% at 10 years (Fig 1).

Forty-one patients with CF underwent DLT at MMUH over the 6-year period; 28 were male and 13 were female. The average age at time of transplantation was 28 years (18-43 y). Thirty-seven recipients (90%) had a documented FEV_1 $<30\%$ (17%-30%) at the time of transplantation. Four recipients had an FEV_1 $>30\%$, and their consideration for transplantation was accounted for by increasing hospitalizations, low body mass index (BMI), and elevated baseline partial pressure of carbon dioxide >7 kPa. Of these 4, 3 were female recipients.

The average BMI in the cohort was 20.6 kg/m^2 (14-30.4 kg/m^2). Five recipients had a BMI <18.5 kg/m^2. Twenty-eight patients (68%) were on nutritional supplementation, and 20 of those patients had percutaneous endoscopic gastrostomy (PEG) tubes. One recipient also had a diagnosis of short gut syndrome and as a result was underweight despite supplementation. There was no difference in serum albumin concentration between patients who had received nutritional supplementation compared with those who had not. The average serum albumin level in both groups was 34 g/L. Of the underweight cohort, 4 of 5 transplantations were completed using cardiopulmonary bypass (CPB). Complications reported in the cohort with BMI <18.5 kg/m^2 included nerve injuries

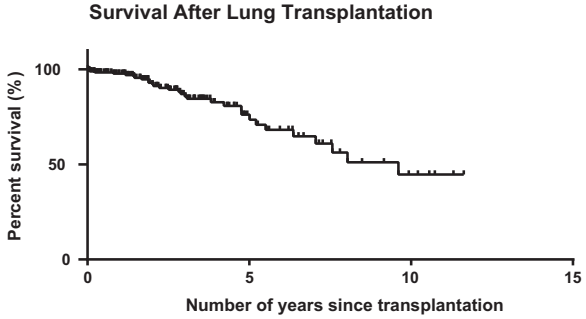

Fig. 1. Kaplan-Meier survival curve, Mater Misericordiae University Lung Transplantation Group.

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