The Role of Bronchial Artery Revascularization in Lung Transplantation

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KEYWORDS

• Bronchial artery revascularization • Lung transplantation • Bronchiolitis obliterans syndrome • Obliterative bronchiolitis

KEY POINTS

- Long-term survival of lung-transplant patients is 53% at 5 years and 31% at 10 years, which continues to lag behind the survival of other solid organs recipients.
- The modern era of lung transplantation has seen a shift from early mortality and complications related to the bronchial anastomosis to late mortality secondary to progressive organ dysfunction; the complex disease process may include elements of bronchiolitis obliterans syndrome, obliterative bronchiolitis, chronic rejection, or chronic lung allograft dysfunction.
- Although the initial goal of bronchial artery revascularization (BAR) was to reduce the incidence of airway ischemia and to improve bronchial healing, the benefits of restored bronchial artery circulation may extend beyond bronchial healing alone.
- Advantages of BAR include dramatically improving airway healing, decreasing airway complications, possibly better long-term survival compared with bilateral lung transplant, decreases in postoperative infection, less early rejection, and possibly delayed onset of progressive organ dysfunction.
- Disadvantages of BAR include being technically challenging, limited worldwide experience, extended surgical time and possibly ischemic time, increased risk of bleeding.

INTRODUCTION

The dual blood supply to the lungs consists of the pulmonary arterial tree and the small bronchial arteries (BAs). Although the bronchial circulation is known to be an important source of nutritive blood to the bronchial tree, most current techniques of lung transplantation do not restore the bronchial blood supply. Early in the clinical experience with lung transplantation, the primary barrier to clinical success, and the leading cause of mortality, was dehiscence or necrosis of the bronchial anastomosis.

The concept of bronchial artery revascularization (BAR) was known; however, the technically demanding nature of the procedure led surgeons to pursue alternative strategies to avoid bronchial complications. The lung transplant group at University of Toronto pioneered the method of wrapping the bronchial anastomosis with omentum,

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which was demonstrated in animal studies to augment bronchial healing.[1,2] Subsequently, on November 7, 1983, Dr Joel Cooper performed the first successful single-lung transplantation on a 58-year-old Canadian dying of pulmonary fibrosis. In contrast to the success achieved in single-lung transplantation, en bloc double-lung transplantation (DLTX) performed with a tracheal anastomosis was plagued by a bronchial complication rate of 40%, even with omental wrapping.[3]

As a result of this experience, techniques for DLTX evolved to sequential implantation of the lungs with a very distal bronchial anastomosis at the hilum of the lung, with which wrapping was no longer necessary.[4] This technique was widely adopted by the lung transplant community, and DLTX performed en bloc was largely replaced with sequential bilateral lung transplantation (BLTX), and the interest in BAR waned. Unfortunately, bronchial ischemia and the resultant complications continued, albeit to a lesser extent. In the authors' practice, the bronchial complication rate remains in the 15% range, and in the current literature is between 3% and 25%.[5–12] Of note, there is emerging evidence that airway ischemia promotes airway fibrosis and *Aspergillus* invasion, and conversely, that improved microvascular circulation at the anastomosis site, mediated by exogenous angiogenesis promoting compounds, is able to attenuate this process.[13,14] Such studies add weight to the existing evidence that methods to promote normal airway perfusion and healing deserve ongoing attention from surgeons.

Direct BAR is the obvious solution to help ensure a normally healing and healthy airway. The technique was first described in dogs by Metras in 1950[15]; however, the first series of BA anastomoses in humans was not reported until the early 1990s by the group from Bordeaux, France in 1992, Harefield Hospital in United Kingdom in 1993, and Mayo Clinic, United States, and Copenhagen in 1994.[16–19] Although the early and midterm results of these studies were extremely favorable for bronchial healing, BAR did not gain wide acceptance in the lung transplant community secondary to increased technical difficulty, prolongation of ischemic and operative times, and increased risk of bleeding. In addition, most lung transplant programs were happy with their results using decreased steroid doses and distal bronchial anastomoses at the secondary carina. Consequently, en bloc DLTX was largely abandoned in favor of BLTX.

The modern era of lung transplantation has seen a shift from early mortality and complications related to the bronchial anastomosis to late mortality secondary to progressive organ dysfunction, the complex disease process that may include elements of bronchiolitis obliterans syndrome (BOS), obliterative bronchiolitis (OB), chronic rejection, or chronic lung allograft dysfunction.[20] Long-term survival remains close to 50% at 5 years, which is lower than that for other solid organ transplants. In 2005, long-term outcomes from the Copenhagen BAR series were published demonstrating excellent 5- and 10-year survival, superior to that of sequential lung transplant without BAR.[21] This article inspired one of the authors (G.B.P.) and the Cleveland Clinic lung transplant group to revisit BAR and to begin a pilot study to compare safety and efficacy compared with standard therapy and to study "teachability" of this more technically demanding procedure. The recent results are presented under "Long term results".

ANATOMY AND PHYSIOLOGY OF BRONCHIAL ARTERY SUPPLY

The BA circulation represents a small portion of the cardiac output, estimated to be 3% to 5% of total cardiac output during lung injury and inflammation, and perhaps less in the normal lung. It is considered important for airway defense, fluid balance, and lung metabolism because it delivers nutritive supply to airways, lung parenchyma, and lymph nodes and forms bronchopulmonary anastomoses along the alveoli.[22–24]

The anatomy of the BA is quite varied. Variations in bronchial arterial origin and course were well studied by Schreinemakers and colleagues[25] and have been confirmed by the authors' clinical experience with BAR.[26] The BAs, 1 to 4 in number, arise from the descending aorta and are among or medial to the upper right intercostal arteries (**Fig. 1**). The authors have previously described the anatomic variations and named the different arteries.[26] The most frequent and largest BA is the right intercostobronchial artery (RICBA), which arises as the first or second right intercostal artery and courses behind the esophagus, giving off the intercostal artery branch 1 to 2 cm after its origin from the aorta (**Fig. 2**). It then passes under the azygos vein and continues on the membranous portion of the right main bronchus. An RICBA can be found and secured in up to 90% of donor specimens according to Schreinemakers and colleagues.[25] In the authors' clinical experience, this figure is probably 75% to 80%. Left BAs have a direct route from the aorta to the left bronchus. It is unusual that no BA can be identified; this, however, may be the case when severe aortic atherosclerosis is present or when the BAs are inadvertently severed during harvest.