Editorial

Revascularisation of the bronchial arteries in pulmonary transplant; does it ever have a role?

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The lung is unique amongst solid organ transplants in being implanted without a systemic arterial blood supply. It also differs in other respects. There is a huge endothelial surface, making the lung prone to reperfusion injury. But ischaemia is probably a small component of this injury; inflation allows aerobic metabolism to continue in the absence of any blood supply and the intrinsic metabolic activity is low. However, there is a clear link between this injury and reduced short and mid-term survival.

Another problem singular to the lung, and perhaps of most significance, is the poorer medium- and long-term survival, compared with other organ transplants, because of the early occurrence of chronic lung allograft dysfunction (CLAD). The dominant manifestation of CLAD is narrowing and then occlusion of small, intra-parenchymal airways—bronchiolitis obliterans syndrome (BOS).

The bronchial arteries are tiny, and the convention was to ignore them. A very early consequence was the catastrophic incidence of airway ischaemia at the dawn of the speciality (1). Only with the introduction of the omental pedicle, and then the adoption of a short donor bronchus, close to the lung parenchyma and nourished by pulmonary to bronchial collaterals (admittedly with desaturated blood) could the speciality start and then flourish (2).

Have we ignored the bronchial arteries to our peril? There was a phase, in the early years of pulmonary transplantation, almost entirely driven by cardiac surgeons to whom anastomosing 1–2 mm vessels were second nature, of bronchial artery revascularisation (BAR). This experience was reported in a sporadic manner, but not pulled together. The group of Ahmad and colleagues have now reviewed this area in considerable detail (3) and are to be congratulated on the thoroughness of their approach. However, there do seem to be some misconceptions and, at least from a surgeon's point of view, the paper is not entirely encouraging.

From a historical standpoint, much of the early work on BAR was done to reduce the problem of airway complications and post-ischemia airway healing. The emphasis was not on reduction of CLAD, but to reduce the risk of necrosis of the tracheal anastomosis and of the carinal area. It was thought by some that better airway vascularization might have a benefit, particularly for the BOS as a by-product.

As outlined in the article the documented experience of BAR in clinical lung transplantation is not current, but dates to the experiences of Professors Couraud, Yacoub and Pettersson in the 1980–1990s. All the included studies

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describe BAR used in either single lung transplantation (LTx) or double LTx performed with *en-bloc* implantation wherein both lungs are sewn in with a single tracheal anastomosis on cardiopulmonary bypass (CPB) support, as compared to the routine single sequential double lung transplant (SSLTx) the standard technique used in LTx today. Bronchial blood flow is particularly important in an *en-bloc* setting having a central airway anastomosis and full main donor bronchi, remote from the intra-parenchymal pulmonary to bronchial collaterals, in need of preservation. BAR has also been shown to improve tracheal anastomotic healing when compared to the initial *en-bloc* technique for double LTx without BAR (4).

However, none of these centers (Harefield, Cleveland Clinic, Mayo Clinic, Bordeaux, Copenhagen) now perform BAR as a standard of care any longer to the best of our knowledge. The Copenhagen group who reported some of the more contemporary results switched to SSLTx via bilat thoracotomies without BAR in 1998. They have not seen higher rates of CLAD since the change of practice and have not looked back (5).

BAR in combination with SSLTx where the bronchial anastomoses are as distal as the secondary carina might very well be redundant. Indeed, Yun and colleagues stated in a review in this journal from 2019 that not only would this in many cases not be achievable, but most likely also not essential. In their unmatched experience, revascularization of both a right single and left single lung with BAR is feasible in only less than half of cases and state that with distal bronchial anastomosis, the consequences of BAR failure are minimal (6).

It is notable, that many of the reports are from over 20 years ago, and this perspective is important. We need to know if lung preservation techniques, donor selection and use of CPB (routine for most of these patients) is going to affect both overall lung injury and the likelihood of airway problems. In the article with pooled data from these high-performance centres championing BAR, the airway anastomotic complications were considerably higher (17% airway ischaemia and 13% anastomotic complications) than what we would expect from routine SSLTx in our high-volume centres today. As an example, Schweiger and colleagues from the Vienna group reviewed their experience of bronchial anastomoses using a continuous running PDS SSLTx technique in 2020. From 1999 to 2017 they performed 1,555 lung transplants including 2,941 bronchial anastomoses with an overall anastomotic complication rate of 1.56%. In the more recent era of 2014–2017 the airway complication rate after LTx was 0.89% (7).

An example of another change with time, is the widespread adoption of a retrograde flush as a standard part of lung preservation. It has a benefit in both cooling and washout of donor-derived toxins (8) and this adds to the limitations of comparing historical data with current experience.

There is also very little evidence to support a causal relationship between bronchial artery blood flow, airway anastomotic problems, and CLAD. An important piece of evidence comes from combined heart and lung transplantation. In parallel to the *en bloc* BAR population, there is very reliable airway healing in this setting, as a consequence of coronary to bronchial collaterals. These same collaterals provide oxygenated blood to the larger airways in the lung. Nonetheless, these recipients have an equal ~40% risk of developing CLAD within the first 5-year post-transplant when compared to routine SSLTx recipients without BAR according to the International Society for Heart and Lung Transplantation (ISHLT) lung and heart-lung registry (9).

In the pooled analysis, Dr. Ahmad and colleagues reference a 5-year survival of 71% and an incidence of BOS at 3-year of 33% in the BAR population, arguing that their results might indicate that offsetting the period of early ischemia following transplantation can reduce BOS and improve survival times. However, the reported follow ups simply do not support those conclusions. With a mean follow-up of only 21 months (less than 2 years) and a stated median onset of BOS of 2.3 years there is not the data to predict long-term outcomes in the BAR population.

From the Danish BAR experience where the follow-up in fact was longer than 5 years, the incidence of BOS was 40% in surviving patients at 5 years and equal between BAR and SSLTx patients. The median onset of BOS was 2 years.

There is absolutely no doubt that early events after lung transplant can affect long term outcome. There is a clear link between primary graft dysfunction (PGD) and BOS/CLAD (10). The deleterious early events have features of ischemia/reperfusion, although ischemia alone is probably a small component. It is incorrect to link airway ischemia in a mechanistic way to early graft dysfunction and ischemia/reperfusion injury; the two are very different, and this is an important distinction.

In conclusion, bronchial artery revascularization was a fascinating idea in its time. It solved the issue of tracheal and central airway healing for the *en-bloc* double lung transplant. It was one of a number of steps taken to manage the problem of bronchial healing in single and bilateral lung transplants. But other advances—better preservation, for instance—and the adoption of distal bronchial anastomosis close to the lung parenchyma, resulted in the sort of very low bronchial complication results seen in major centres such as Vienna. For the bronchial anastomosis, BAR has become, like bronchial omentopexy, a chapter in history.

The putative link to reducing CLAD, perhaps by affecting ischaemia/reperfusion injury, is interesting. It is, as we have pointed out, very difficult to prove, but more importantly, intuitively incorrect. The phenomenon of PGD is a reperfusion injury with a large inflammatory element, affecting predominantly the pulmonary endothelium, but actually, the whole lung. It is not going to be improved by steps to improve the perfusion of a few centimetres of the larger airways.

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Footnote

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