Editorial

Airway complications—lung transplantation's Achilles' heel

Alan M. Carew[1,2], **John A. Mackintosh**[1]

[1]Queensland Lung Transplant Service, Department of Thoracic Medicine, The Prince Charles Hospital, Brisbane, QLD, Australia; [2]Faculty of Medicine, University of Queensland, Brisbane, QLD, Australia

Correspondence to: John A. Mackintosh. Queensland Lung Transplant Service, Department of Thoracic Medicine, The Prince Charles Hospital, Rode Road, Brisbane, QLD 4032, Australia. Email: John.mackintosh@health.qld.gov.au.

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From the earliest days of lung transplantation, the airway anastomosis has been an Achilles' heel. Between the first lung transplant in 1963 and 1978, 80% of recipients who survived for more than 7 days post-operatively experienced major complications relating to the bronchial anastomosis (1). Numerous refinements have since been attempted or established, including abandonment of the tracheal anastomosis in bilateral transplants, avoidance of telescoped bronchial anastomoses, use of an omental pedicle wrap, minimizing the donor bronchus length, and bronchial artery revascularisation. Despite innovative and meticulous surgical technique, the overall reported incidence of airway complications remains in the range of 10–15% (2).

The transplant airway anastomosis is vulnerable for several reasons. Arterial blood is supplied to the native airway by the bronchial circulation which is interrupted during retrieval of the donor organ and rarely reconstructed. The donor bronchus therefore relies on retrograde perfusion via the pulmonary circulation until the bronchial arteries are re-established after 2–3 weeks (3). Bronchial arterial revascularisation is technically challenging, and is not routinely performed in most centres due to concerns regarding operative and ischaemic times and higher rates of re-operation for bleeding from the bronchial artery anastomosis. Centres with experience in this technique, however, report normal airway healing and even improved long-term survival with reduced rates of infection and allograft dysfunction (4). In the absence of direct revascularisation, the ischaemic anastomosis may be subject to necrosis or dehiscence in the early stages, and stenosis or malacia as a later consequence. Those who experience these complications may require bronchoscopic interventions, including balloon or rigid dilation, airway ablative therapy and stent placement.

Fortunately, the survival of lung transplant recipients in the current era is considerably longer than at its inception. The expectation of long-term survival means that the treatment of airway complications must have a long-term horizon in mind. Airway stenting, frequently a tool applied in malignant central airway obstruction with its dismal associated prognosis, must be adapted to this expectation.

The practice of airway stenting for transplant anastomotic complications varies from institution to institution, and is limited by a lack of randomized evidence to guide practice. Most publications consist of single centre retrospective case series with relatively few patients overall.

Airway stents are imperfect, with inherent risks of migration, and obstruction with mucous or granulation tissue. Metallic stents are easily inserted with flexible bronchoscopy, are flexible and conform reasonably well to airway anatomy, and are less prone to migration. However, with time uncovered stents epithelialize and become challenging or impossible to safely remove, while covered or hybrid stents risk obstructing lobar or segmental airways when the target lesion is adjacent to the secondary carina or in the bronchus intermedius. Straight and bifurcated silicone stents may be customized by the bedside to accommodate airway anatomy and branching, and are relatively straightforward to reposition or remove. However, they require rigid bronchoscopy and general anaesthesia to insert, have a narrower internal diameter than size-matched

metallic stents, and may be more prone to migration.

As it is for the surgical aspect of the transplant airway anastomosis, the approach to stenting in this area must undergo innovation and refinement. An uncovered metal stent when left *in situ* long-term in this population has reported complication rates of 80% (5), but the vigorous early granulation tissue response may be used to the patient's advantage in sealing anastomotic dehiscence prior to early elective removal (6). Durable responses following removal of silicone stents used for anastomotic stenosis or malacia have been reported in 69–88% of patients (7-9). Notably, these authors reported a median duration of stent placement of between 6–12 months prior to definitive removal, perhaps encouraging remodelling of the airway wall around the stent in a lasting fashion. Biodegradable stents provide a tantalizing promise of a single airway implant which dissolves, avoiding both long-term adverse effects and additional procedures to remove the stent. The data in transplant recipients is limited to small numbers overall, though repeat stent insertion or dilation were common upon degradation suggesting longer-lasting biodegradable implants may be required (10). Ideally, the best airway stent is no stent at all.

In this issue of *Journal of Thoracic Disease*, the Temple University Hospital, Philadelphia Lung Transplant Program detail their experience with airway stenting for transplant airway complications (11). As one of the highest volume lung transplant programs, this report on their approach in this under-published area is much appreciated. Over a 5-year period, 50/645 lung recipients required stent placement, invariably for bronchial stenosis. Given this describes only the tip of the airway compromise iceberg, these data suggest that despite significant improvements in surgical technique over many decades, there remains an unacceptably high rate of airway complication post-transplant. The fact that ~1 in 13 recipients of this high volume centre required stenting will provide some comfort to those smaller centres who encounter airway complications on what might seem a far too frequent basis.

The main aim of the study was to confirm the safety of their covered metallic stent approach given previous black box warnings against metallic stents in benign airway disease. Sinha *et al.* (11) achieve their aim by demonstrating a low rate of mortality following a stenting procedure with only one death occurring across 376 stents, 15,711 stent days and 774 bronchoscopies. However, what is perhaps most palpable in this report is the morbidity associated with airway complications in lung transplant recipients. While patient reported outcomes were not assessed in this study, it stands to reason, that the 50 patients who required stents experienced a degree of morbidity. Beyond the risks and discomfort of undergoing an invasive procedure, a frequent requirement for bronchoscopy also imposes a significant financial and time burden upon patients. How these 50 patients came to needing a stent is not entirely clear, however in the case of bronchial stenosis they are likely to have experienced a degree of discomfort (e.g., dyspnoea, frequent infections) as the initial indication for stent insertion. Following their initial stent insertion, any relief was subsequently compromised by a frequent requirement for stent removal and replacement for secretions and excess granulation over the course of their post-transplant life. The fact that more than half of the cohort were single lung recipients is likely to have amplified the impact of this complication. What is not entirely clear from the data is how successful the covered metallic stent strategy was in terms of achieving a durable response in the airway.

We thank Sinha *et al.* (11) for detailing their approach to this often buried complication of lung transplantation. Their recent experience highlights that airway complications are not confined to lung transplants of the past. Airway complications remain a very real obstacle to regaining a normal life after lung transplantation. This study adds to the previous study of stenting for lung transplant airway complications provided by Ma *et al.* (12) in this journal. While a silicone stent approach was favoured by Ma *et al.* (12) there would appear to be a similar degree of morbidity associated with airway complications, with a requirement for relatively frequent bronchoscopic interventions after stent placement. In the wake of these two publications, we call on the International Society for Heart and Lung Transplantation to strongly consider collecting data on airway complications and its management in a standardised fashion with a view to a future registry report focused on this post-transplant scourge. Only through our collected experience will it be possible to identify the best strategies to prevent and cure airway complications.

Airway stenting for anastomotic complications of lung transplantation has been born out of necessity. However, this should not be viewed as an exemption to a requirement for robust evidence. The incidence of stenting in this paper, would suggest that the management of anastomotic complications is imminently suited to a multi-centre clinical trial. Off the back of this paper by Sinha *et al.* (11) the lung transplant community should collaborate towards

a well-designed clinical trial to generate an evidence-based approach to treating airway complications after lung transplantation. Key to the success of such a trial will be the inclusion of patient reported outcome measures. The time has come to solve lung transplantation's Achilles' heel.

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