

has not been the case in the majority of published literature on the subject and thus limits its applicability and reproducibility. In the present article by Davidson and colleagues,<sup>9</sup> the authors have amassed available data correlating antireflux surgery with preservation of allograft function. As expected, although they were able to confirm the beneficial effect of antireflux surgery, the available data were extremely variable and did not provide any of the above-mentioned context.

To make progress in the study of GERD and its effect on native or allograft lung dysfunction, we have to address the 2 major limitations discussed: (1) We need a reproducible marker of gastric contents that can be measured in BAL; and (2) we need to report GERD and antireflux procedure outcomes in the context of the organ proximal to the gastroesophageal junction and the one distal to it and not be oblivious to their dysfunction.

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## Commentary: The burning questions of reflux management in lung transplantation

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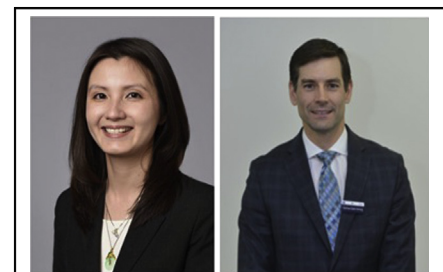
Our knowledge of the complex mechanisms leading to chronic allograft rejection after lung transplantation is evolving. Early studies indicated non-alloimmune injury such as gastroesophageal reflux disease (GERD) poses risk by potentiating inflammation in the small airways

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### CENTRAL MESSAGE

Surgical management of gastroesophageal reflux disease may prolong allograft function in lung transplant patients.

leading to bronchiolitis obliterans syndrome and eventually contributing to diminished allograft function. Multiple single-institution series over the past decades have suggested the potential benefit of an antireflux surgical procedure on minimizing the progression of chronic lung allograft dysfunction (CLAD). However,

evidence was not strong enough to recommend fundoplication according to the clinical practice guidelines issued by the International Society for Heart and Lung Transplantation. Davidson and colleagues<sup>1</sup> have now summarized all current available data and provide continued measured evidence that fundoplication confers protection against CLAD. Although there is still no randomized evidence to suggest superiority of fundoplication versus medical management, this study provides a structure to measure results and develop risk stratification.

The experiences at many transplant centers, including ours, have shown that fundoplication safely leads to improved allograft function.<sup>2</sup> However, the optimal timing and type of antireflux procedure in lung transplant patients have yet to be determined. This is, in part, due to the variable clinical stability post-transplantation and presence of acute rejection episodes or other illnesses that preclude elective surgical procedures. However, for the subset that can and have undergone surgical correction, this work suggests that CLAD progression may be stabilized when acid exposure is minimized. We can speculate that if surgical intervention is performed early in the process, CLAD from GERD may be prevented, and the current study allows for some meaningful interpretation of the rate of change of forced expiratory volume in 1 second (FEV1) in the settings of reflux and allograft function.<sup>1</sup> However, because of its retrospective nature, the study was unable to determine how early, how often, and how long to surveil FEV1 before determining that an antireflux procedure is needed, leaving important questions such as “who is truly

at risk?” and “are all recipients with reflux created equal?” It is also unclear what degree of change should trigger surgical considerations and what rate of change signifies irreversibility. What about patients with stable or rate of change that suggest improvement in FEV1 despite known gastroesophageal reflux? There are a scarcity of long-term data to assess the effects of antireflux surgeries on allograft function, chronic rejection, and ultimately survival. The lack of consistency in timing and type of antireflux measures in the current literature further confuses our understanding of this common disease and its impact on allograft function following lung transplantation. Additional GERD therapies have entered the market since the original studies were performed, such as LINX, TIF, or Stretta, with unknown results in this patient population and further muddying already murky waters. There are many confounders and variabilities that have not been addressed, seemingly increasing the number of burning questions GERD-induced allograft dysfunction raises, but this work marks an important additional step to establish a measurement criterion to base future research.

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