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,[9] 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.

References

1. Parikh S, Brownlee IA, Robertson AG, Manning NT, Johnson GE, Brodlie M, et al. Are the enzymatic methods currently being used to measure bronchoalveolar lavage bile salt levels fit for purpose? *J Heart Lung Transplant*. 2013;32:418-23.
2. Neujahr DC, Uppal K, Force SD, Fernandez F, Lawrence C, Pickens A, et al. Bile acid aspiration associated with lung chemical profile linked to other biomarkers of injury after lung transplantation. *Am J Transplant*. 2014;14:841-8.
3. Reder NP, Davis CS, Kovacs EJ, Fisichella PM. The diagnostic value of gastroesophageal reflux disease (GERD) symptoms and detection of pepsin and bile acids in bronchoalveolar lavage fluid and exhaled breath condensate for identifying lung transplantation patients with GERD-induced aspiration. *Surg Endosc*. 2014;28:1794-800.
4. Griffin SM, Robertson AG, Bredenoord AJ, Brownlee IA, Stovold R, Brodlie M, et al. Aspiration and allograft injury secondary to gastroesophageal reflux occur in the immediate post-lung transplantation period (prospective clinical trial). *Ann Surg*. 2013;258:705-11.
5. Murthy SC, Nowicki ER, Mason DP, Budev MM, Nunez AI, Thuita L, et al. Pretransplant gastroesophageal reflux compromises early outcomes after lung transplantation. *J Thorac Cardiovasc Surg*. 2011;142:47-52.e3.
6. Davis RD Jr, Lau CL, Eubanks S, Messier RH, Hadjiliadis D, Steele MP, et al. Improved lung allograft function after fundoplication in patients with gastroesophageal reflux disease undergoing lung transplantation. *J Thorac Cardiovasc Surg*. 2003;125:533-42.
7. Raghu G, Pellegrini CA, Yow E, Flaherty KR, Meyer K, Noth I, et al. Laparoscopic anti-reflux surgery for the treatment of idiopathic pulmonary fibrosis (WRAP-IPF): a multicentre, randomised, controlled phase 2 trial. *Lancet Respir Med*. 2018;6:707-14.
8. Bodet-Milin C, Querellou S, Oudoux A, Haloun A, Horeau-Llanglard D, Carlier T, et al. Delayed gastric emptying scintigraphy in cystic fibrosis patients before and after lung transplantation. *J Heart Lung Transplant*. 2006;25:1077-83.
9. Davidson JR, Kumar S, Franklin D, Eaton S, Curry J, De Coppi P, et al. Fundoplication to preserve allograft function after lung transplant: systematic review and meta-analysis. *J Thorac Cardiovasc Surg*. 2020;160:858-66.

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Commentary: The burning questions of reflux management in lung transplantation

Hai Salfity, MD, MPH, and Matthew Hartwig, MD

Hai Salfity, MD, MPH, and Matthew Hartwig, MD

CENTRAL MESSAGE

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

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 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,

From the Department of Surgery, Duke University School of Medicine, Durham, NC.
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Address for reprints: Matthew Hartwig, MD, Department of Surgery, Duke University School of Medicine, DUMC Box 3863 Med Ctr, Durham, NC 27710 (E-mail: Matthew.hartwig@duke.edu).
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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[1] 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.[2] 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.[1] 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.

References

1. Davidson JR, Franklin D, Kumar S, Mohammadi B, Dawas K, Eaton S, et al. Fundoplication to preserve allograft function after lung transplant: systematic review and meta-analysis. *J Thorac Cardiovasc Surg*. 2020;160:858-66.
2. Hartwig MG, Anderson DJ, Onaitis MW, Reddy S, Snyder LD, Lin SS, et al. Fundoplication after lung transplantation prevents the allograft dysfunction associated with reflux. *Ann Thorac Surg*. 2011; 92:462-8.