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Mechanical pleurodesis is not a contraindication to lung transplantation

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ABSTRACT A critical appraisal and clinical application of Shigemura N, Bhama J, Gries CJ, et al. Lung transplantation in patients with prior cardiothoracic surgical procedures. *American Journal of Transplantation*. 2012;12(5):1249-1255. doi: 10.1111/j.1600-6143.2011.03946.x.

Keywords: pleurodesis, lung transplantation

Clinical Context

A 64-year-old male with a history of emphysema and interstitial lung disease was transferred for definitive management of a left upper lobe bronchopleural fistula, attributed to spontaneous apical bleb rupture, which was complicated by persistent air leak for over two weeks. Following successful endobronchial valve placement by Interventional Pulmonology (IP), there was interval resolution of the air leak for 24 hours before a severe coughing fit precipitated not only leak recurrence, but also an increased oxygen requirement. The IP team was reluctant to place a second valve given the failure of the first, so Thoracic Surgery was consulted for alternative interventions. Due to concern that pleurodesis would leave the patient ineligible for future lung transplant, Thoracic Surgery recommended against acute intervention given his end-stage lung pathology and potential for transplant. However, when the patient developed subcutaneous emphysema of his left chest wall the following day, the situation was re-evaluated. At this point, the Pulmonary Transplant team became involved and, upon their review of the case, determined that the patient's lung disease was not yet severe enough to qualify him for transplant. Contrary to prior understanding, the Transplant team shared that pleurodesis was a viable option and not a contraindication for future transplant. They specifically recommended that a mechanical, rather than chemical, pleurodesis be performed, to which the Thoracic Surgery team was agreeable. The patient subsequently underwent mechanical pleurodesis without complication and was safely discharged home within a week. However, his case raises the question of whether prior cardiothoracic surgery will affect his outcome after future lung transplantation.

Clinical Question

Does prior cardiothoracic surgery affect outcomes of lung transplantation?

Research Article

Shigemura N, Bhama J, Gries CJ, et al. Lung transplantation in patients with prior cardiothoracic surgical procedures. *American Journal of Transplantation*. 2012;12(5):1249-1255. doi: 10.1111/j.1600-6143.2011.03946.x.

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Related Literature

Literature review began with a PubMed search using keywords "pleurodesis" and "lung transplant." Six relevant studies evaluating lung transplant outcomes following pleurodesis in specific populations were returned, two of which address the issue in patients with a history of cystic fibrosis, and three of which focus on patients with lymphangioleiomyomatosis—two lung diseases with a predilection for recurrent pneumothoraces. ¹⁻⁵ An UpToDate search with similar keywords yielded general guidelines for lung transplant recipient selection, including special considerations such as previous cardiothoracic surgery. One cited article was a consensus for the selection of lung transplant candidates from the Pulmonary Transplantation Council of the International Society of Heart and Lung Transplantation, which lead to discovery of two additional large-volume, single-institution studies on lung transplantation in patients having previously undergone cardiothoracic surgical procedures. ⁶⁻⁸ All of the aforementioned studies are retrospective and conclude that lung transplantation is a viable option following various cardiothoracic surgeries, although they cite varying technical difficulties and challenges due to differences in measured outcomes.

The clinical research selected for appraisal in this manuscript originates from one of the largest lung transplant centers in the United States, where 40-50% of patients who undergo lung transplant have a history of prior cardiothoracic surgery. Additionally, this study used radiographic assessment to identify 39 of 129 (30%) cases with moderate to severe pleural adhesions with predicted technical and surgical difficulties. Of these identified cases, the pleurodesis subgroup made up the largest number of patients, which is fitting for this paper's clinical context.

Critical Appraisal

This research is a comparative retrospective study of outcomes after lung transplantation in 554 patients divided into two groups — patients who had undergone prior cardiothoracic surgery and those who had not. The study was designed to discover whether there is a difference between groups in long-term survival, as well as multiple secondary endpoints related to perioperative complications. Data was collected from the University of Pittsburgh Medical Center Transplant Patient Management System, which documents intraoperative details, postoperative complications and long-term follow-up results. In this study, the primary endpoint was overall survival 3 years after transplantation, while secondary endpoints included the incidence of major complications including reexploration due to post-operative bleeding, phrenic nerve injury, prolonged ventilation, tracheostomy rate, renal insufficiency, primary graft dysfunction and ICU length of stay.

Despite no significant difference in long-term survival, the incidence of perioperative complications was higher in individuals with prior cardiothoracic procedures. Subgroup analysis demonstrated that such complications were most common in those who had undergone previous pleurodesis. One particular weakness in methodology was the application of a backward stepwise regression model in an attempt to identify significant risk factors for death after lung transplant, which may have underestimated combinations of variables and in turn deviated from reality. It is therefore possible that factors beyond chemical pleurodesis, cardiopulmonary bypass time and high transfusion requirements negatively influence lung transplant outcomes.

Strengths of the study include a large sample size and the standardization of procedures in a single institution study, allowing for analysis of multiple outcomes. Given the retrospective nature of the study, limitations include selection bias, inability to measure key data points and reliance on accurate record keeping. The authors address such limitations by referencing utilization of standardized and established protocols throughout "the entire process, from candidate selection to post-operative care." While patient distribution among the cardiothoracic surgery group (n=238) and non-surgery group (n=316) was consistent with the institution's noted 40-50% of transplant cases occurring in patients with prior cardiothoracic surgery, there is a question of whether those fulfilling the cardiothoracic surgery description are entirely representative of the population. For instance, transplant recipients with prior combined heart and lung surgery were entirely excluded from the study. Additionally, distribution among subtypes of cardiothoracic procedure was skewed in favor of those with chest tube insertion alone (115 of 238 patients, 48%). The significance of this may be demonstrated by the fact that, unlike for other subgroups, outcomes in patients with chest-tube insertion only did not differ significantly from outcomes in patients without prior cardiothoracic surgery. Finally, given that this single-institution study was performed in a renowned lung transplant center, the external validity of results remains to be seen in centers with less expertise and experience.

This retrospective cohort study meets criteria for level 2 evidence using the SORT Criteria.⁹



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The risk difference was calculated as the absolute reduction in risk attributed to lung transplant without prior cardiothoracic surgery. It is the three-year probability of survival in the control group minus the same statistic in the group exposed to prior cardiothoracic surgery. Number needed to treat (NNT) was computed as the reciprocal of the risk difference, or 17.9. Thus, approximately one death is prevented at three years for every 18 patients who do not undergo prior cardiothoracic surgery.

Clinical Application

When providing informed consent to patients with the decision of whether or not to pursue cardiothoracic surgery before the prospect of future lung transplant, it is important to note that the types and distribution of prior procedures described in this study may not be representative of the patient's actual situation. For instance, the findings in this study may be more relevant for an individual who may undergo chest tube insertion, as this made up the largest number of pre-transplant procedures. The patient described above specifically underwent mechanical pleurodesis. Since the study does not differentiate between chemical and mechanical pleurodesis, the conclusions should be extrapolated with caution. Still, the particularly troublesome situation of pleurodesis before lung transplant, as highlighted by the greater number of complications in the pleurodesis subgroup, should be shared with the patient.

This paper is valuable to patients in that it offers insight into the impact of prior cardiothoracic surgery on lung transplant outcomes, something that had not been elucidated in prior literature. Based on this study, patients should be made aware of not only the increased incidence in perioperative lung transplant complications after prior cardiothoracic surgery, but also the lack of significant difference in long-term survival.

Finally, this study offers reassurance to potential transplant candidates who must undergo cardiothoracic surgery for immediate management of a medical problem. They should have a better understanding that such intervention is unlikely to affect their acceptance for future lung transplantation and their long-term survival. The study holds particular clinical relevance as the number of lung transplant candidates who have had previous cardiothoracic surgeries continues to increase. This uptrend in post-cardiothoracic surgery referrals is especially likely as minimally invasive surgical techniques become more commonplace. Evaluation of the outcomes in lung transplant recipients with and without prior cardiothoracic procedures not only facilitates understanding of the unique challenges associated with prior intervention, but also allows for the development of strategies to prevent complications in the future.

Take-home points:

- 1. There is no significant difference in long-term survival between patients who undergo cardiothoracic surgery prior to lung transplantation and those who do not.
- 2. Retrospective cohort studies are prone to many biases, including sampling bias that may undermine the external validity of findings.
- 3. Decisions that demand immediate action should be made based on available evidence and with sensitivity to a patient's short and long-term goals.

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