# From Research to Clinical Practice

## Cognitive Trajectory after Lung Transplantation

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Cognitive impairment is a feared complication of aging and a significant threat to functional independence and health-related quality of life. In many ways, the same is true of advanced lung disease, a disease process that exacts a toll both physically and neuropsychologically. Lung transplantation is an effective means to restore functional independence and health-related quality of life, yet the trajectory of cognitive function after transplantation remains largely unknown.

If unrecognized, cognitive impairment after lung transplantation could undermine the goals of lung transplantation. As we recently learned, these are salient questions to patients, who must weigh the potential risks and benefits of a surgery intended to improve their quality of life as well as their length of life (1). To address this critically important question, Smith and colleagues (pp. 1520–1527) conducted a longitudinal cohort study of 47 lung transplant recipients, presented in this month's issue of *AnnalsATS* (2).

The authors examined patients before lung transplantation, at the time of hospital discharge after transplant, and again as an outpatient 3 months after transplant. Cognitive function was assessed using a comprehensive battery, the Repeatable Battery for the Assessment of Neuropsychological Status, and a specific executive function test, the Trail Making Test Parts A and B. To complement the more extensive battery, cognition was also assessed using a practical screening tool, the Montreal Cognitive Assessment. Postoperatively, the presence and severity of delirium were assessed daily using well-validated instruments, the Confusion Assessment Method and Confusion Assessment Method for the Intensive Care Unit.

Pretransplant, cognitive impairment was identified in 45% of patients, according to the Montreal Cognitive Assessment, and the more comprehensive battery of tests confirmed the screening test results. Perioperatively, 34% of patients experienced delirium, with a median duration of 2.0 days. Consistent with the longitudinal study conducted by Saczynski and colleagues, which examined cognitive function after cardiac surgery (3), Smith and colleagues observed that an initial decline was common and, importantly, modified by the presence of delirium. The dramatic effect of postoperative delirium highlights both the importance of delirium management, including minimization of benzodiazepines, early mobilization, and patient interaction with family and support system, as well as our lack of proven, effective therapies (4). Cognitive decline, and executive dysfunction in particular, was more frequently observed among non–cystic fibrosis lung transplant recipients than those with cystic fibrosis. Over time, cognitive impairment on average improved from pretransplant to the outpatient follow-up, most significantly in the patients with cystic fibrosis. However, 57% of post-transplant subjects were at least mildly impaired 3 months after transplant, confirming the recent work by Cohen and colleagues (1). Furthermore, 39% of cognitively intact subjects pretransplant were impaired at hospital discharge post-transplant, confirming the work of Hoffman and colleagues (5).

In counseling patients for what to expect after lung transplantation, and for designing effective postdischarge strategies, these are fundamentally important findings. During our recent study, one patient described that their "brain was mush" after returning home post-transplant. Moving forward, as a result of the work by Smith and colleagues and others, the opportunity exists for clinicians to prepare patients for what to expect post-transplant from a neuropsychological perspective. At the patient level, the time has come to examine patients serially to identify cognitive decline post-transplant and to implement strategies to compensate and rehabilitate identified cognitive impairment. Although evidence reveals that the transplant population is a resilient one (1), information and strategies such as these will only aid in the process to achieve a sustained recovery.

Despite its many strengths, there are several limitations that warrant discussion. First, with the exception of delirium development post-transplant, it is unclear what mechanisms mediate cognitive decline post-transplant. Future studies, designed to examine the independent association between perioperative (e.g., allograft ischemic time, primary graft dysfunction, time on mechanical ventilation, intensive care unit length of stay) and postoperative (e.g., post-transplant physical function gain through rehabilitation, acute rejection, changes in immunosuppressive dosing) risk factors and cognitive function are required. Second, there needs to be a correlation of

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neurocognition as it pertains to complex planning and executive function (e.g., adherence with medication regimens) with other important outcomes associated with lung transplant, including acute and chronic rejection and overall patient survival. Finally, this is a single-center assessment in a limited population of transplant recipients. Previous literature has highlighted the wide variation across U.S. transplant centers with respect to patient selection criteria, time to transplantation, and surgical volume and mortality (6–8). Future investigations need to build on the evaluation of neurocognitive changes in patients receiving lung transplants with larger, multicenter cohort studies.

In conclusion, Smith and colleagues provide a guide to patients, their caregivers, and their providers for what to expect post-transplant with regard to cognitive function and how to operationalize these processes into routine clinical care. The work by Smith and colleagues also highlights the important role played by social workers and psychiatrists in the management of lung transplant recipients. There is a need for expanded assessment of neurocognition as part of pretransplant transplant candidate assessment, as well as post-transplant care. The findings presented in this study complement the robust literature on survival and functional status post-transplant and highlight the need to understand how these patient-centered outcomes interact and which factors can be modified to optimize long-term outcomes. ■

**Author disclosures** are available with the text of this article at www.atsjournals.org.

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