Lung Transplant May Dramatically Improve Survival for Patients With Terminal Lung Cancer

Transplantation may be an option for some people with terminal NSCLC confined to the lungs who are out of other treatment options.

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A landmark Northwestern Medicine study published in JAMA suggests lung transplantation can significantly extend survival in select patients with advanced lung cancer.

In a study of patients with medically refractory, lung-limited Stage IV non-small-cell lung cancer (patients with terminal lung cancer confined to the lungs who are out of treatment options), Northwestern Medicine physicians and scientists at the Northwestern Medicine Canning Thoracic Institute found that lung transplantation was associated with substantially better early survival than medical management (chemotherapy, radiation, immunotherapy, etc.) alone.

The study evaluated outcomes from the Double Lung Transplant Registry for Lung-Limited Malignancies – known as the DREAM registry – a pioneering Northwestern Medicine program designed to test whether replacing lungs overtaken by treatment-resistant cancer can remove organ-confined disease and rescue patients dying of respiratory failure. Northwestern Medicine is currently the only known health system in the country with a dedicated lung transplant program (DREAM) for patients with advanced lung cancers who have failed all other treatment options.

“This work changes what we can imagine for a highly selected group of patients who were previously considered beyond the reach of curative-intent intervention,” said co-corresponding author Ankit Bharat, MD, chief of Thoracic Surgery in the Department of Surgery and director of the Canning Thoracic Institute. “We are not saying lung transplant is appropriate for every patient with Stage IV lung cancer. We are saying that when the cancer is rigorously proven to be confined to the lungs, when standard therapies have been exhausted, and when the lungs themselves have become the life-limiting organ, transplantation may offer a new path forward.”

A Devastating Form of Stage IV Lung Cancer

Cancers of the lung are the leading cause of cancer-related deaths in the United States with more

people dying of lung cancer than colon, breast and prostate cancers.

Most patients with Stage IV lung cancer have disease that has spread beyond the lungs. But a subset develops advanced non-small-cell lung cancer that remains confined to the lungs, even as it progresses throughout both lungs and causes respiratory failure. These patients may exhaust targeted therapy, immunotherapy, chemotherapy and clinical trial options, yet still have no evidence of cancer outside the lungs. For these patients, the immediate cause of death is often not widespread systemic cancer, but progressive failure of cancer-filled lungs.

“This is a biologically distinct clinical scenario. These patients have Stage IV cancer, but the disease remains anatomically limited to the lungs,” said co-corresponding author Young Kwang Chae, MD, MPH, professor of Medicine in the Division of Hematology and Oncology and a thoracic medical oncologist with the Robert H. Lurie Comprehensive Cancer Center of Northwestern University at Northwestern Memorial Hospital. “In these rare select group of patients, DREAM provides us a disciplined, scientifically rigorous way to ask whether removing the organ containing all visible disease can change the natural history of an otherwise fatal condition.”

What the Study Found

The study included 404 adults treated or evaluated at Northwestern Medicine from September 2021 through June 2025 for end-stage pulmonary disease.

Among 98 patients with Stage IV lung cancer confined to the lungs, 17 underwent lung transplant and 81 met transplant eligibility criteria but didn’t undergo transplant because of nonbiologic barriers such as logistical, financial or geographic factors, and were treated with medical management alone.

The results showed 100% one-year survival among the 17 patients with Stage IV lung cancer who received a lung transplant, compared to 41% one-year survival among the 81 patients with Stage IV lung cancer who were treated with medical therapies alone.

The investigators also compared the lung cancer transplant recipients with 306 patients without cancer who underwent lung transplant for end-stage pulmonary disease such as cystic fibrosis, COPD or pulmonary hypertension. Between those two groups of patients, one-year posttransplant survival was 100% among the patients transplanted for Stage IV lung cancer, versus 88% among lung transplant recipients without cancer.

“Any time we consider expanding the use or donor lungs, organ stewardship must be central. These results suggest that, in carefully selected patients and in the right multidisciplinary setting, lung transplantation for lung-limited malignancy can achieve early outcomes that are comparable to accepted noncancer transplant indications,” said Bharat, who is also the Harold L. and Margaret N. Method Professor of Surgery.

Why This Approach is Different

Lung cancer has long been considered a relative contraindication to lung transplantation due to

the concern that lung cancer would rapidly recur in the transplanted lung. The Northwestern Medicine team designed the DREAM trial to determine whether modern cancer detection methods could identify patients whose cancer was limited to the lung, limiting the chances of recurrence.

Patients underwent comprehensive contemporary staging to confirm that disease was confined to the lungs, including advanced imaging and systematic invasive mediastinal evaluation to reduce the risk of missing cancer spread outside the lungs. Transplant was considered only after patients had medically refractory disease despite available systemic therapies and consideration for clinical trials.

The surgical strategy was also redesigned to minimize the risk of cancer dissemination during the operation.

“This innovative technique involves putting the patient on heart and lung bypass, delicately taking both cancer-ridden lungs out at the same time along with the lymph nodes, washing the airways and the chest cavity to clear the cancer, and then putting new lungs in,” Bharat said. “These patients can have billions of cancer cells in the lungs, so we must be extremely meticulous to not let a single cell spill into the patient’s chest cavity or blood stream. We believe this technique can help reduce the risk of recurrence, which we learned through our experience with pioneering COVID-19 lung transplants in 2020.”

The team also used single-cell transcriptomic analyses to study tumor regions across the removed lungs and investigate mechanisms of treatment resistance.

“Using state-of-the-art single-cell analysis of individual cancer cells from multiple regions of both cancer-filled lungs, we saw tumors that were profoundly resistant, with different cancer-cell populations relying on different resistance pathways. That helps explain why chemotherapy, immunotherapy and other systemic therapies could no longer meaningfully control the disease and why replacing the diseased lungs may be the only realistic option to extend life for these carefully selected patients,” Bharat said.

“The paradigm shift is not simply that transplant was performed for lung cancer. The shift is that transplantation was embedded within a complete scientific framework—rigorous staging, proof of lung-limited disease, transplant-specific operative innovation, intensive surveillance and molecular analysis of the explanted tumors. That is what makes this a new model of transplant oncology,” said co-corresponding author G.R. Scott Budinger, MD, chief of pulmonary and critical care medicine at the Canning Thoracic Institute.

Recovery, Recurrence and Next Steps

Postoperative outcomes among the transplant recipients with cancer were generally similar to those among transplant recipients without cancer. Median hospital length of stay was 14 days for patients transplanted for Stage IV lung cancer and 16 days for transplant recipients without cancer.

During follow-up, four of the 17 transplant recipients saw their cancer return and they were treated with local and systemic therapies (ex: surgery, radiation, chemotherapy, immunotherapy, etc.). By the end of the study in January 2026, two of the 17 transplant recipients had died.

The authors emphasize that longer follow-up is needed to define the durability of disease control, the risk of late recurrence and long-term quality of life after transplant.

“This is not a claim that transplant restores normal life expectancy, and it’s not a blanket indication for Stage IV lung cancer. It’s evidence that a carefully selected group of patients facing otherwise poor near-term survival may have an opportunity for meaningful additional life – that’s why this work matters,” Bharat said.

About the DREAM Program

To date, Northwestern Medicine surgeons have performed more than 50 lung transplants for patients with advanced lung cancers.

Since Northwestern Medicine’s Lung Transplant Program first started in 2014, they’ve performed more than 700 lung transplant procedures for patients with end-stage lung diseases such as COVID, lung cancer, cystic fibrosis, chronic obstructive pulmonary disease (COPD) and more. Northwestern Medicine has one of the shortest wait times for a lung transplant in the U.S. with a median wait time of three days.

Patients interested in being evaluated for a lung transplant can contact the 24-hour referral line at 312.695.5864 or 844.639.5864. For more information about the Lung Transplant Program or lung cancer screenings, visit nm.org.

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http://beta.docker.cancerhealth.com/article/lung-transplant-may-dramatically-improve-survival-patients-terminal-lung-cancer