Cleveland Clinic’s lung and heart-lung transplant program has long been one of the nation’s largest and most active of its kind. The program performed 98 lung transplants (both single and double lung procedures) in 2013. This activity ranks Cleveland Clinic among the four largest-volume lung transplant programs in the nation and the largest in Ohio.

The program’s patient survival rates compare well with national norms and expected rates, as detailed in the graph on the next page. Notable program data from the January 2014 report of the Scientific Registry of Transplant Recipients (SRTR) include:

- 87.85 percent one-year adult patient survival (vs. expected rate of 85.71 percent and national average of 86.11 percent)
- 4.5-month median time to transplant, shorter than the regional (OPTN Region 10) median of 6.9 months and the national median of 4.6 months (see graph, p. 47)

These strong clinical outcomes are achieved despite the program’s large number of high-acuity cases and high-risk transplant candidates from far reaches of the nation and the globe, including those with:

- Chronic obstructive pulmonary disease/emphysema
- Fibrotic lung disease
- Primary or secondary pulmonary hypertension
- Cystic fibrosis/bronchiectasis
- Congenital cardiac disease requiring combined heart-lung transplant
- Serious comorbid cardiac disease, requiring concomitant heart surgery in many patients
Points of distinction

The program offers special expertise in a number of areas, including:

**Multiorgan transplants**, including heart-lung and liver-lung,

**Retransplantation** for chronic rejection or bronchiolitis obliterans syndrome.

**Lung transplant with bronchial artery revascularization (BAR).** The world’s first BAR procedure in lung transplantation was performed in 2007 by Cleveland Clinic’s Gösta Pettersson, MD, PhD, who continues with the program today. Cleveland Clinic is one of a small number of centers in the world that perform BAR in the setting of lung transplant, which restores bronchial arterial circulation to transplanted lungs (see images below). Current evidence suggests that BAR may lower early biopsy rejection grades, postpone the onset of bronchiolitis obliterans syndrome and improve long-term survival.

**Without BAR.** The anastomotic site one week after lung transplant using a standard surgical approach, with evidence of necrosis and ischemia.

**With BAR.** Normal-appearing tracheal anastomosis one week after lung transplant using the BAR surgical technique.

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Image: The difference that bronchial artery revascularization (BAR) can make in selected cases.

**Source:** Scientific Registry of Transplant Recipients (SRTR), January 2014
Ambulatory/awake extracorporeal membrane oxygenation (ECMO). Cleveland Clinic was one of the first U.S. centers to use ambulatory ECMO to allow for reconditioning and successful transplant in critically ill patients with respiratory failure.

Use of donation-after-cardiac death (DCD) lungs. Cleveland Clinic is among the few U.S. centers with considerable experience in DCD lung transplants, which represent about 5 percent of the program’s transplants in recent years. The lung transplant team recently published its early and midterm experience with DCD lung transplant (Ann Thorac Surg. 2012;94:406-412), which demonstrated that recipient survival and early graft function with DCD lungs are excellent when standardized selection, procurement and implantation techniques are followed.

Leadership in the development of normothermic ex vivo perfusion to better preserve, assess and even enhance donor lungs, promising to substantially increase the number of usable donor lungs (see sidebar, p. 49).

Expanded options and flexibility for patients

The program’s embrace of options such as DCD and normothermic ex vivo perfusion is part of its commitment to expanding the pool of high-quality donor lungs and trimming wait times for transplant candidates. Not only is its wait time shorter than that of many other centers (see graph above), but Cleveland Clinic’s program allows patients to live at home while awaiting transplant and accepts patients who live within 1,000 miles of Cleveland, enabling patients to avoid the need to relocate.

Because many lung transplant candidates have high-acuity conditions, a good number benefit from the services of Cleveland Clinic’s Critical Care Transport team (see patient profiles, pp. 50 and 51), which deploys specially trained critical care physicians, nurses and paramedics to transfer the most critically ill patients to Cleveland Clinic by mobile ICU vehicles, helicopter or fixed-wing aircraft (see p. 83 for more on Critical Care Transport services).
Comprehensive approach to evaluation and care

When a patient is referred for lung transplant evaluation, he or she is assigned a dedicated multidisciplinary team that includes:

- One or more physicians from the program’s staff of eight pulmonologists and five lung transplant surgeons
- A pretransplant coordinator
- A transplant pharmacist
- A transplant social worker
- A financial team

The team creates a tailored care plan for each patient, which involves determining the timing of transplant listing, testing and addressing specific patient needs. Once a patient is listed, outpatient and inpatient transplant educational programs are started to prepare both the patient and his or her caregiver(s) for all aspects of the waiting and transplant experience.

Because treatment adherence in the post-transplant period is vital to ultimate transplant success, the program supplements standard one-on-one patient education with pretransplant outpatient education on medication regimens and with inpatient group instruction for patients and their caregivers. The inpatient instruction is offered each week in two group sessions led by a post-transplant coordinator on the lung transplant unit. The popular classes have resulted in greater patient knowledge about their medications and post-transplant health issues in general.

Destination program for end-stage lung disease

The comprehensiveness of this management approach is matched by the program’s equally comprehensive approach to end-stage lung disease in general.

For patients who are not yet ready for lung transplant, whose conditions deteriorate while waiting for donor lungs, or who may not be appropriate transplant candidates, the transplant team can partner with colleagues in Cleveland Clinic’s Respiratory Institute, which has been ranked among the nation’s top 3 pulmonology programs for more than a decade by U.S. News & World Report, to offer other advanced therapies for end-stage lung disease. These options, which are considered solely in collaboration with the patient’s referring physician, include:

- Lung volume reduction surgery, which is now performed via a video-assisted thoracoscopic approach to reduce morbidity
- Enrollment in an advanced clinical trial of novel medical therapy for the patient’s underlying condition, such as idiopathic pulmonary fibrosis
- Leading-edge management of patients with primary or secondary pulmonary hypertension via Cleveland Clinic’s premier Pulmonary Hypertension Program
Approximately 80 percent of donated lungs cannot be transplanted, due to infection, fluid accumulation or other damage. With thousands of Americans on the lung transplant waiting list, Cleveland Clinic specialists are proud to be engaged in leading-edge research to address these unmet needs by using normothermic ex vivo perfusion to make more donor lungs suitable for transplant. (See p. 6 for a profile of Cleveland Clinic’s normothermic ex vivo perfusion efforts across multiple organs.)

Normothermic ex vivo perfusion involves use of a miniature heart-lung machine that shoots a proprietary solution through a hose into donor lungs hooked up to the machine (see photo). The solution provides nutrients and extracts excess water from the lungs, potentially resuscitating them to function anew. After this “lung washing,” a ventilator mechanically fills the lungs with oxygen via another tube to allow assessment of lung function and prolong the time the lungs can be preserved for potential transplant.

Based on experience in Europe and Canada, where normothermic ex vivo perfusion systems have been approved for use for several years, the technology appears to make a large share — from 40 to 75 percent — of previously untransplantable lungs fit for transplant, functioning as well as donor lungs that didn’t require the treatment.

Normothermic ex vivo lung perfusion remained experimental in the U.S. in 2013, but in August 2014 the FDA approved XVIVO Perfusion’s XPS™ system and STEEN Solution™ for preserving donor lungs that do not initially meet standard criteria for transplant but may be deemed transplantable with more time to evaluate the organs’ function.

Though Cleveland Clinic was not involved in clinical trials of the XVIVO system, it is one of eight U.S. centers participating in the international INSPIRE trial that involves transplanting donor lungs preserved with a similar system (from TransMedics) into human recipients. As of the end of 2013, Cleveland Clinic had transplanted one patient with a lung preserved using that system.

As part of their preclinical preparation and to increase knowledge about ex vivo perfusion strategies, Cleveland Clinic researchers have conducted extensive research on nontransplantable human lungs using various ex vivo perfusion systems. They have presented this work at numerous national and international meetings, including the 2013 and 2014 meetings of the International Society for Heart and Lung Transplantation.

Following the recent FDA approval of the XPS system, Cleveland Clinic plans to implement clinical use of normothermic ex vivo perfusion as soon as possible with systems that have been utilized in the laboratory of lung transplant surgeon Kenneth McCurry, MD, who has led Cleveland Clinic’s lung perfusion efforts. Dr. McCurry says that FDA approval and ultimate use of normothermic ex vivo perfusion systems promise to increase the center’s lung transplant volume by 50 to 100 percent.

Equally exciting are the additional uses to which normothermic ex vivo perfusion might be put, such as to deliver antibiotics or other drugs to donor lungs to thwart rejection. “We might be able to change the lung in some way so that the recipient’s immune system responds to it less vigorously, reducing rejection risk,” Dr. McCurry says.

**FUTURE OF TRANSPLANTATION:**

**LEADERSHIP IN NORMOTHERMIC EX Vivo LUNG PERFUSION**

- Versatile medical and surgical approaches for patients with various congenital diseases offered collaboratively by the heart and pulmonary teams within Cleveland Clinic’s Adult Congenital Heart Disease Center

The result is an agile and highly multidisciplinary approach to care dictated by the patient’s unique needs.

**Forceful lung transplant research**

Cleveland Clinic’s lung transplant team is active in a diverse group of innovative research programs. Major studies that were active in 2013 include:

**INSPIRE trial of ex vivo lung perfusion.** Cleveland Clinic is one of eight U.S. centers in this global trial comparing the TransMedics OCS™ Lung normothermic ex vivo perfusion technology with cold storage techniques for preserving and assessing donor lungs for transplantation in human recipients (see sidebar).
HLA Antibodies After Lung Transplantation (HALT I) study. Cleveland Clinic is one of six U.S. centers participating in this NIH-funded study evaluating long-term outcomes after early development of donor-specific HLA antibodies (DSAs) following lung transplant and the potential benefit of preemptive DSA depletion.

Immune Mechanisms of Rejection in Human Lung Allografts study. Cleveland Clinic is collaborating with Washington University in St. Louis on this NIH-sponsored trial to determine whether downregulation of autoimmune responses by depletion of autoantibodies to self-antigens prior to lung transplant will prevent primary graft dysfunction and reduce the risk of bronchiolitis obliterans syndrome.

Lung Transplant Clinical Trials Network (LT-CTN). Cleveland Clinic is one of five academic centers taking part in this NIH-funded study within the Clinical Trials in Organ Transplantation (CTOT) program. This multicenter trial is addressing two of the most important contemporary graft-limiting problems, cytomegalovirus infection and chronic lung allograft dysfunction, and aims to yield better understanding of the risks, phenotypes and mechanisms of chronic allograft dysfunction to reduce long-term graft loss rates.

TERRY PERROTTA: RECIPIENT OF A DOUBLE LUNG TRANSPLANT AFTER CRITICAL CARE TRANSFER FOR A RARE LUNG CONDITION

Pulmonary veno-occlusive disease (PVOD) accounts for only a small number of cases of pulmonary hypertension, and Terry Perrotta’s case was one of them. Severe deterioration of the condition sent the 53-year-old Rhode Island resident and former professional figure skater into right-sided heart failure in January 2013, and soon she was comatose in the ICU of her local hospital. Terry’s doctors said her only chance was a double lung transplant, and they arranged her transfer to Cleveland Clinic to have it performed.

After undergoing venoarterial extracorporeal membrane oxygenation (ECMO) as a bridge to transplant to increase chances she’d survive the flight, Terry was rushed to Ohio by Cleveland Clinic’s Critical Care Transport team. She underwent a successful bilateral sequential lung transplant by Cleveland Clinic surgeons. When Terry woke up four days later, a nurse was testing her oxygen level. “It was 100 percent,” she recalls. “I thought it was a dream.”

Lung transplant is the only therapy that appears to significantly prolong the lives of patients with PVOD, but the cumulative transplant experience for the condition is small.

In Terry’s case, it’s been a success. She was discharged home after several weeks of close monitoring and rehabilitation at Cleveland Clinic. “On the drive back to Rhode Island, I walked on a treadmill at a hotel gym for 45 minutes,” she says. “Before the surgery I could barely climb a set of stairs.”

Today Terry says she can breathe as well as before her PVOD developed. “I’ve been able to return to ice skating, and I’m working again. All is well.”

clevelandclinic.org/transplant
Other studies that the lung transplant team is leading or taking part in include:
• A prospective study of the incidence, prevalence and risk factors for neurocognitive impairment in a cohort of lung transplant recipients
• A multicenter trial assessing gastroesophageal reflux as a contributor to chronic lung allograft rejection
• A single-center prospective investigation to determine the utility of pCLE (probe-based confocal laser endomicroscopy), an optical tool allowing in vivo microscopic imaging of lung tissue during standard bronchoscopy, for detecting rejection after transplant

Pediatrics: Enhancing offerings for an underserved population

Fewer than 100 pediatric lung transplants are performed annually worldwide. Several factors explain this low volume:
• The relatively few diagnoses leading to end-stage lung disease in children
• Limited availability of suitable donor lungs for pediatric patients
• An inferior survival rate relative to other solid organ transplant types

Only a few centers perform pediatric lung transplants, and Cleveland Clinic is among them, having completed 25 lung transplants and seven heart-lung transplants in the pediatric population since 1991. It is one of the world’s only centers offering the BAR procedure for pediatric patients undergoing lung transplant.

Cleveland Clinic is now looking to build its volume and expertise in this underserved clinical area with the 2013 arrival of its first dedicated medical director for pediatric lung transplant, Nathan Kraynack, MD, an expert in pediatric cystic fibrosis. Dr. Kraynack is leveraging his background in the medical management of pediatric lung transplant recipients to better position Cleveland Clinic to offer transplant to more children with end-stage lung disorders.

The result is a newly formalized pediatric lung transplant program combining the deep experience of Cleveland Clinic’s lung and heart-lung transplant surgeons with the expertise of Cleveland Clinic Children’s five pediatric pulmonologists, who are skilled in the care of children with conditions such as:
• Cystic fibrosis
• Pulmonary hypertension
• Childhood interstitial lung disease
• Genetic disorders of surfactant dysfunction

The program draws on this collective expertise to make the critical judgment in most pediatric lung transplant decisions: pinpointing the time when a young patient is sick enough to need transplantation yet still well enough to tolerate the surgery. In doing so, the program aims to contribute to knowledge gains to help accelerate progress in outcomes for this underserved population.

KATHERINE RUSSELL: BACK TO HER CELLO AFTER A DOUBLE LUNG TRANSPLANT WITH BAR

“I used to wake up coughing ferociously every morning,” recalls Katherine Russell, a 23-year-old from Amherst, New York. “I would hesitate to go out on the dance floor, and I used to struggle not to cough through classical concerts — a challenge for a performing cellist.”

After battling cystic fibrosis since birth, Katherine experienced rapid health deterioration in 2012 following a bout of influenza that led to pneumonia. Just two weeks after being airlifted to Cleveland Clinic, Katherine was listed for transplant and a pair of donor lungs was identified. She underwent lung transplant with bronchial artery revascularization (BAR), a challenging surgical technique pioneered at Cleveland Clinic to restore bronchial arterial circulation to her transplanted lungs.

“Now my coughing difficulties are all lifted,” Katherine reflects. “The lung transplant has brought more than comfort — it has raised my quality of life.”