September 20, 2017



CTS INSPIRATIONS

CTS NEWS

President's Letter

We have a few exciting updates for our upcoming UCSD Multidisciplinary COPD Advanced Skills Training Symposium on Saturday September 30 and 2-day Ultrasound skills course on Saturday September 30 and Sunday October 1 at the beautiful UCSD MET center in La Jolla CA: We have also extended the early bird rate and are promoting a '3 registrations for the price of 2 for each conference. Only one CTS member is needed to get the member discount for group registration.



Discount details:

3 for 2 group rate – Three registrations for the price of two: Either Ultrasound Skills Two day hands on course at \$2600 for 3, or Advanced Clinical Training in COPD at \$250 for 3.

https://calthoracic.org/cts-2017-fall-symposium-and-educational-conference-new-discounted-group-rate/

To register for the group rate, either email info@calthoracic.org or call 415-536-0287.

More information on both courses can be found at the following link:

https://calthoracic.org/events/fall-symposium-educational-conference/

Our sincere thanks to Philippe Montgrain, Shazia Jamil, Dan Sweeney, Trina Limberg, Ni-Cheng Liang, Bill Stringer, the members of CTS planning, multidisciplinary and education committees, and our outstanding administrative leads Phil Porte, Vickie Parshall, Dave Eubanks and Karen Lui. **We hope to see you there!**

Thanks to our sister societies for your partnership and collaboration including the California Society for Respiratory Care, the American Lung Association of California, the National Association of Medical Directors of Respiratory Care, and California Society for Pulmonary Rehabilitation, ATS and thanks to Rick Robbins for generously sharing the outstanding Southwest Journal of Pulmonary and Critical Care. We thank all of our colleagues and sister societies for your collaboration and improving pulmonary care in CA and beyond.

The ATS joins <u>Forum of International Respiratory Societies</u> in the call to recognize Sept. 25 as World Lung Day, an annual event dedicated to respiratory disease that helps focus attention and resources on an often overlooked, but very real threat to global health. <u>We urge you to join the cause</u> and add your name to the petition at <u>www.firsnet.org</u>.

Update on Lung Transplantation



By Nicholas A. Kolaitis, MD and Steven R. Hays, MD

Lung transplantation is an important therapeutic option for patients suffering from advanced lung disease to extend survival and improve quality of life ^{1–3}. While overall success has improved, challenges remain that span from donor supply and patient selection through the post-transplant period.

Access to sufficient and quality organs remains one of the most significant challenges in lung transplantation. It is estimated that only 15% of lungs are deemed suitable for transplantation from multiorgan donors ⁴. To combat this limitation, there are increased efforts to procure organs from donation after cardiac death (DCD) donors as well as to use novel technologies such as ex vivo lung perfusions systems ^{5–7}. The ex vivo lung perfusion (EVLP) system is a very promising tool that will hopefully expand the supply of viable donor lungs. Commonly referred to as "lung in a box", EVLP provides perfusion and ventilation of marginal donor lungs for prolonged periods of time, without the need for traditional cold preservation ⁸. This process may provide a period of observation and even rehabilitation of marginal lungs so that these can become suitable for transplantation. In early clinical trials, transplants performed after using the EVLP devices had similar outcomes to transplants performed using traditional cold preservation ^{7,9}. In the United States the EVLP system is approved under the Humanitarian Device Exception. Ongoing trials, including one with UCSF as an investigative center, are underway for full device approval.

Expanding the donor pool is also important because despite overall higher rates of transplantation, wait list mortality has risen over the last several years ⁵ In fact, wait list mortality is nearly twice the rate it was prior to implementation of the lung allocation score in 2005. This may be in part related to a sicker cohort of patients being considered for lung transplantation ¹⁰. This is driven predominantly by the lung allocation scoring system itself that prioritizes patients who have the highest risk of dying on the waiting list. Fortunately, the use of life support technologies such as extracorporeal membrane oxygenation (ECMO) has provided a viable bridge to transplantation for patients with severe hypoxemic respiratory failure and/or pulmonary hypertension. Since 2000, there has been a 28 fold increase in the utilization of ECMO as a bridge to transplantation ^{11,12}. The most recent retrospective studies show that at centers with expertise in the use ECMO, the short and long term outcomes are similar in patients who are bridged to transplant using ECMO compared to those who do not require ECMO as a bridge to transplantation.

Appropriate recipient selection continues to evolve. One area that has shifted in recent years relates to the use of lung transplantation in connective tissue disease (CTD). Traditionally, transplant centers have been reluctant to offer lung transplant to these patients, specifically scleroderma, because of the concern for complications related to extra pulmonary involvement leading to decreased survival ^{1,13,14}. Specialized centers, including UCSF and UCLA, have experience with transplantation for scleroderma and have demonstrated these patients can have similar outcomes as other transplant recipients ^{15–17}. Another area of recent interest in recipient selection relates to how frailty is being considered. Frailty is a concept of increased susceptibility to stressors that

occurs due to multiple physiologic deficits. A recent study demonstrated that frailty is independent risk factor for delisting and death on the wait list ¹⁸. Future studies to incorporate more objective measures in selection of transplant recipients would be beneficial to help maximize transplant success.

Overall, success following lung transplantation has continued to slowly improve. The most recent international transplant registry data has demonstrated that median survival increased from 4.2 years for those transplanted between 1990-1998 to 6.1 years for those transplanted from 1999-2008 ¹⁹. Despite advances, long term survival continues to be limited by the development of chronic rejection, also known as Chronic Lung Allograft Dysfunction. This has recently been further characterized into two phenotypes, a restrictive form called restrictive allograft syndrome and an obstructive form called bronchiolitis obliterans syndrome ²⁰. The two syndromes are distinct in terms of pathophysiology, treatments and prognosis.

With continued focus on improving donor supply, recipient selection and support, and post transplant care, lung transplantation will continue to evolve as an important therapeutic option for our patients with advanced lung disease.

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Lung Allocation Score System (Updated Sept 2017)

George E. Chaux, M.D., Medical Director, Lung and Heart-Lung Transplant Program, Cedars-Sinai Medical Center

Lung transplantation is now considered to be a standard of care therapeutic intervention for end-stage lung disease that has a poor prognosis and that is refractory or progressive in spite of exhaustive medical therapy. Prior to 2005, donor lungs were allocated to recipients on the basis of seniority on the lung transplant wait list. Under this old system, the waiting time for a suitable lung donor was

extensive and averaged more than two years resulting in excessive waitlist mortality especially amongst patients with idiopathic pulmonary fibrosis. In May of 2005 the Lung Allocation Score (LAS)

system was implemented by the United Network for Organ Sharing in the United States in which donor lungs are allocated to recipients on the basis of priority as determined by the lung allocation score which is a normalized value between 0 and 100 calculated based on probability of death while on the waitlist and likelihood of benefit after transplantation. These probabilities were calculated based on data collected in the five years prior to implementation of the LAS system and have since undergone some revision. Under this new system a patient could be transplanted at any time after listing since seniority no longer plays any role in allocation of donor lungs to recipients. The intent was to allocate donor lungs preferentially to patients on the waiting list with the highest probability of death while waiting and highest likelihood of benefit after lung transplantation. During the past decade since the LAS system was instituted, it appears that the system has had the intended immediate effect of reducing wait list times for patients at highest risk of mortality but many unanswered questions remain.

Following implementation of the current LAS system, there has been a significant decrease in wait-list mortality by 40% and the number of lung transplants performed has increased, with most of the organs allocated to patients with idiopathic pulmonary fibrosis. (1) In addition, the median age of recipients has increased which is consistent with more IPF patients undergoing transplantation than before the LAS system went into effect. One of the first major concern after implementation of the LAS system was that if we were to transplant the patients at highest risk of dying while on the lung transplant wait list first, would we potentially increase post-transplant graft loss and recipient mortality by virtue of transplanting sicker patients. Fortunately, a study by Egan et al published recently in the Journal of Heart and Lung Transplantation actually found that 1-year survival after lung transplantation had a small but significant increase after introduction of the LAS system. They concluded that "allocating lungs for transplant based on urgency and benefit instead of waiting time was associated with fewer waitlist deaths, more transplants performed, and a change in distribution of recipient diagnoses to patients more likely to die on the waiting list." In the end, the LAS system seems to have had a net positive effect.

Some remaining concerns include the possibility that some patient diagnostic groups may have been disadvantaged by the LAS system. For example, patients listed for lung transplantation with a diagnosis of Pulmonary Arterial Hypertension (PAH) tend to be awarded lower LAS scores by virtue of the fact that they tend to have relatively preserved lung function as measured by spirometry and they tend to have lower supplemental oxygen requirements. However, Schaffer et al, found that following implementation of the LAS system patients with PAH actually enjoyed a higher rate of transplantation with a lower wait-list mortality. (2) Similarly, although patients with COPD now make up a smaller proportion of patients being transplanted in the post-LAS era, the absolute number of patients with COPD that are transplanted has increased without adverse effect on survival. (1) Unfortunately, the same cannot be said of patients with cystic fibrosis who are listed and transplanted with high lung allocation scores. In an analysis by Braun et al, CF patients with higher lung allocation scores had a lower 90-day, 1-year and 2- year survival rate than did CF patients with lower lung allocation scores. (3) This may be in part due to a greater burden of suppurative lung disease with resistant organisms which is unique to this patient population compared to the other prevalent patient diagnostic groups. Although 1- year survival appears to be improved in the LAS era, there is still uncertainty of the effect on long term survival beyond a year. One recent study published by Maxwell et al in the American Journal of Transplantation suggests that the long term outcomes may not be as good. (4) The same group has also pointed out that since the LAS system went into effect, lung transplant recipients seem to have a greater degree of resource utilization during the index hospitalization compared to other solid organ transplant recipients again reflecting the greater severity of disease amongst these patients. (5)

On balance, the relatively new but now 12-year-old LAS system seems to be working well. It has had the intended effect of allocating donor lungs to sicker recipients thereby decreasing the waitlist mortality which was unacceptably high prior to the system's implementation. In addition, the system seems to have resulted in a greater number of transplants being performed without a significant negative impact on short term survival after transplantation. Based on this experience, lung allocation systems in other parts of the world are now being modeled after the LAS system developed in the United States. In Germany, for example, a new LAS type system was introduced in December 2011 with similar impact on waitlist mortality and outcomes as observed in the United States. (6) One of the biggest challenges still facing the lung allocation system is a method for better sharing of organs across larger areas beyond 500 or 1,000 miles as is done with kidney transplantation. Lung allocation across a large geographic area is limited primarily by the lung's inability to tolerate long cold ischemic times but new innovations such as ex-vivo lung perfusion may change that and allow for more equitable sharing of organs across larger regions of the country.

For more information of the LAS system and organ donation in general please visit the United Network for Organ Sharing web site at UNOS.org. This site contains very useful information for both healthcare professionals and organ transplant recipients and can serve as a very helpful resource for individuals considering organ donation. I want to conclude by reminding readers that the great success of organ transplantation would not be possible if it were not for the tremendous generosity of organ donors and their families.

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CALIFORNIA LUNG TRANSPLANT PROGRAMS

1. Cedars-Sinai Medical Center

MEDICAL DIRECTOR: GEORGE CHAUX, MD

When to Refer Patients for Lung Transplantation

If you are a physician with a patient who has lung disease, the following guidelines may help you determine whether the patient should be evaluated for transplantation.

When a patient is referred to the Cedars-Sinai Lung Transplant Center, an initial phone call will be needed to gather medical and insurance information. Following that, a visit will be scheduled for the patient to meet with a pulmonologist, transplant surgeon, transplant coordinator and a finance coordinator for an initial evaluation.

The following are intended to serve as guidelines. Each patient's situation is different, the transplant team at Cedars-Sinai Medical Center is always available for consultation. Specific criteria are available for:

Inclusion and exclusion criteria
Single lung transplant referral guide
Double lung transplant referral criteria
Heart and lung transplant referral criteria
Retransplant indications
Contraindications for lung transplantation

For physician-to-physician consultations:

Lung Transplantation Center Women's Guild Lung Institute Cedars-Sinai Medical Center

Phone: 310-423-4685 Fax: 310-423-0129

Email: grouplungtransplantcontact@cshs.org

2. UCSD

MEDICAL DIRECTOR: GORDON YUNG, MD

https://health.ucsd.edu/specialties/surgery/transplant/areas-expertise/pages/lung-transplant.aspx

For more information, please call:

Toll-Free: 888-UCSD-LNG

Other Transplant Pulmonolgists:

Dr. Kamyar Afshar and Dr. Timothy Floreth.

Office number: (858) 657-5050

3. UCLA

MEDICAL DIRECTOR: David Ross, MD

Transplant coordinator: Jay Onga 310-825-6068 or 310-267-8294

jonga@mednet.ucla.edu

https://www.uclahealth.org/transplants/lung

UCLA Lung Transplant Program 200 UCLA Medical Plaza Los Angeles, CA 90095 (310) 825-6068

4. USC

MEDICAL DIRECTOR: Sivagini Ganesh MD

RN Coordinators Roya Sadeghi Maria Bembi Phone 3234426077 Fax 3234426201

http://transplant.keckmedicine.org/lung/

Contact us at (800) USC-CARE (800-872-2273) http://www.cts.usc.edu/lungtransplantprogram.html

5. UCSF

MEDICAL DIRECTOR: STEVEN HAYS. MD

https://www.ucsfhealth.org/clinics/lung_transplant/

Lung Transplant Program

400 Parnassus Ave., Fifth Floor San Francisco, CA 94143 Phone: (415) 353-4145 Fax: (415) 353-4166

Hours: Thursday 8 a.m. – 5 p.m. (exact times vary depending on number of physicians in clinic)

24 hour physician line (for referring MDs) (415) 433-UCLT

6. STANFORD

MEDICAL DIRECTOR: Gundeep Dhillon, M.D.

Pre-Transplant Coordinator: Lisa Levin, RN, MS

https://stanfordhealthcare.org/medical-treatments/l/lung-transplant.html

https://stanfordhealthcare.org/health-care-professionals/referring-physicians.html

Stanford Referral Center Phone: 877-254-3762 Fax: 650-320-9443

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Center for Advanced Lung Disease

300 Pasteur Drive Stanford, CA 94305 Phone: 650-723-3633

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Volume 15, Issue 2							
Title (Click on title to be taken to the manuscript, CME in Bold)	Journal Section	First Author	Year	Vol	Issue	Pages	Date Posted
Medical Image of the Week: The Atoll Sign in Cryptogenic Organizing	Imaging	Frankl J	2017	15	2	92-3	8/30/17
<u>Pneumonia</u>							
Medical Image of the Week: Cannon V Waves	Imaging	Raschke RA	2017	15	2	90-1	8/23/17
<u>Disclosures for All</u>	Editorial	Robbins RA	2017	15	2	87-9	8/19/17
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