# DAILY LINKS

34th Annual Meeting & Scientific Sessions

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@ISHLT



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## Review: *I Think We Need A Bigger Boat*

**Saturday's Plenary** session featured some keynote presenter's focusing on the dire shortage of organs that, unfortunately, remains an ongoing theme of these ISHLT meetings. Well, this morning, Dr. Lynne Stevenson presented further data to distress even the most hungover of us in the audience (come on, that Thoratec group put on a good party last night, we all know that). While the Department of Health and Human Services is still tabulating how many cocktail shrimp you ate courtesy of big pharma to place on their Sunshine website today, Dr. Stevenson jumped right into the biggest problem we face today. Too many sick patients, and not enough hearts.

She took a unique perspective, starting off with an analogy of the sinking ship with a small lifeboat that can only hold so many patients to drive home the point that the sharks are circling our patients if we don't figure out a better way to allocate the limited resources we have. One point she continued to drive home is that the way we list our patients on UNOS for transplant is inefficient and makes the list look artificially large. She points out that almost no Status 2 patients get transplanted anymore (particularly on the east coast) and that not all 1A patients are created equal. She drove this home by quoting her father, Stanley L. Warner, who said, "Anyone who has reached the age of 21 and thinks that life is fair has a learning disability."

She also keenly pointed out that reducing just 20% of those patients listed every year would provide a more reasonable wait list and would provide better access to those who needed hearts. Clearly there are no easy ways to do this, but re-evaluating borderline patients with too many risk factors and ensuring patients with higher chances of good outcomes could be a start. She also points out the psychological toll the list takes on patients, especially those who are so-called "bridge to decision" and are kept in limbo with an LVAD with no clear end in site, whether it be destination therapy, or in fact a transplant.

In an effort perhaps to expand the donor pool, Dr. Ardehali offered data on the PROCEED II trial. Using an Organ Care System (OCS), which can keep a harvested heart "alive and beating" before implantation, his group hopes not only to expand the donor pool, but eliminate such concerns such as cold ischemic times from the equation that are always an issue with the old fashioned "ice chest"


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method of transporting organs." This novel device provides blood flow, oxygenation nutrients, and inotropes to the explanted donor heart while it is in transit. It also monitors continuously hemodynamic parameters and biochemical markers of ischemia and damage. It could potentially exponentially expand heart transplants in a multitude of ways.

The study was set up as a non-inferiority and safety trial, and luckily it seemed to meet all its primary and secondary endpoints. Most interestingly, I found, is that five potential donor hearts in the study that were in the OCS were found to have abnormally high lactate levels during monitoring which led to pathologic review. All five hearts had significant pathology that would have limited graft survival had they been used. It is not hard to see the usefulness of this device in future evaluation and harvesting of organs. Perhaps this device can one day be used to evaluate resuscitated hearts before implanting into a new host as Dr. Ardehali pointed out.

From there, the Plenary session focused on lung transplantation, so for that. So I turn it over to my esteemed pulmonary friend to continue coverage...

Cardiac transplants since Barnard have flashed on the cover of Time Magazine (and presumably much earlier than that) have been regarded as something close to science fiction. However, since Professor Shaf Keshavjee gave his iconic talk at TED a few years back, the lung has had its much desired revenge as the audience awed at the possibility of perfusing and ventilating a pair of lungs outside of the human body.

As organ perfusion has become one of the "hot topics" in all fields of transplantation, ex-vivo lung perfusion (EVLP) continues to lead its progression and is featured in over 40 presentations at this year's Annual Meeting. The available EVLP methods are being investigated in four ongoing multicenter trials (NOVEL, DEVELOP-UK, EXPAND, and INSPIRE), and the full safety, cost effectiveness and potential impact on graft availability would shortly be revealed. In the well-visited Plenary Session on Saturday, the one-year outcome of the NOVEL lung trial was presented as a featured abstract by the now established front figure Dr. Pablo Sanchez.

The NOVEL trial was the first prospective multicenter trial designed to evaluate the safety of EVLP as a method to screen and identify good quality grafts from the donor pool of lungs rejected for transplantation. It is a non-randomized open label study, where 84 lung transplant recipients were enrolled with the start in August 2011. 42 EVLP transplants with lungs initially found unusable for transplant and rejected by multiple centers (median of 39 times according to Dr. Sanchez) and 42 standard controls. The early outcomes have been very promising, and the primary endpoint of 30-day survival was not significantly different between patients that received EVLP or standard criteria lungs (98% vs. 100%, p=1).

Dr. Sanchez said, "We are excited with the results and believe that the NOVEL trial has helped in establishing the rationale to extend the donor pool and permit the acceptance of donor organs that might have otherwise been not transplanted".

This has, for obvious reasons, also been received with great excitement in the camp of the study sponsor XVIVO Perfusion AB, which has recently had the trial EVLP machine, XPSTM, CE marked for EU distribution and has progressed in the FDA approval process.

Many congratulations to the trial investigators for managing to complete this important multicenter trial. "He who waits gets a tailwind, and he who rows, a harbor"…right!?

## Review: *Natural Born Killers (Cells)*

It's early, I hit the snooze, and didn't have time for coffee for this a.m.'s **Sunrise Symposium 10: Exploring Interactions Between Cellular and Humoral Immunity in Cardiac Allograft Rejection**, but luckily this highly complex topic got the brain juices flowing faster then Woody Harrelson can pull a gun on Route 666.

Dr. Esme Dijke opened the session with a great review of all the major players in innate immunity, and the role innate immunity plays in ACR and AMR. Macrophages and Neutrophils and NK cells, oh my! It became readily apparent from Dr. Dijke's talk that our well-balanced immune system provides both good and bad feature that aid and hinder transplant medicine. Unfortunately for every good these cells provide, like aiding wound healing and suppressing allogenic immune responses, these cells can also infiltrate graft tissue and co-stimulate allo-reactive T cells.

Next up, Dr. Annalisa Angelini reviewed the overlap between CMR and AMR, deemed the gray zone (though more like the Twilight Zone for us clinicians trying to help these patients), and reviewed histologic features that may help or hinder deciding which treatment pathway to follow. Staining for CD markers may be one tool that can help the pathologist and clinical team help decide what is going on. Particularly noteworthy, Dr. Angelini pointed out that most "mixed rejection" samples demonstrate a proclivity towards CD4 cells, while acute cellular rejection mostly demonstrates CD8 cells. She also interestingly pointed out varying degrees of inflammation in the endothelial layers of vessels, a capillary predominant vasculitis and a more diffuse vasculitis affecting all vessels, and proposed that perhaps differentiating which components of the vasculature are inflamed may help differentiate AMR, ACR and mixed rejection into more readily identifiable classes of rejection.

Dr. A. G. Kfoury then finished the session by outlining the ramifications of this "mixed rejection" picture and what it may really mean. He proposed several different pathways including the possibility that this mixed rejection is a unique pathophysiologic pathway of rejection, or that perhaps it is some combination of AMR and ACR or perhaps that each of these pathways may devolve into a mixed picture. In terms of treatment options, a confluence of factors including most importantly graft dysfunction, biopsy and antibody screening, donor antibody status and time from transplant should all play a role in deciding the aggressiveness of treatment.

Now I'm no Wayne Gale (another shameless Natural Born Killers movie reference, if you're not familiar with the movie), but that's some pretty good coverage of a 7 a.m. session without caffeine.

## Review: *Third Time's the Charm*

As part of the mission, ISHLT aims to provide and update international guidelines, consensus documents, standards statements, and policy statements regarding end-stage heart and lung disease and cardiothoracic transplantation. The first edition of international guidelines for the selection of lung transplant candidates was published in 1998, and this was last updated in 2006. Given the continued evolution of the field, the Pulmonary Transplantation (Cont'd)

Council now presents a **Third Edition of the Consensus Report for the Selection of Lung Transplant Candidates.**

The goal is to assist physicians, both those who refer candidates and those who work in the lung transplant field, in properly identifying patients who are the most likely to benefit from lung transplantation. The new consensus document follows the current trend of more open selection terms adhering less strictly to age limitation, co-morbidities, type and severity of concurrent infection and support the conditional acceptance of patients supported with mechanical lung ventilation or extracorporeal life support. Importantly, an updated list of absolute contraindications include untreatable or significant dysfunction of another major organ system, malignancy, and acute medical instability.

"We've had a unique opportunity to pull together physicians and surgeons who are considered to be experts in their field, to come up with these guidelines to assist both patients and non-patients," stated a satisfied Chair of the Writing Group, Dr. David Weill. With 14 invited thoracic physicians and surgeons having taken part in the writing process, there is good hope for a broad agreement on these updated guidelines for lung transplant recipient selection.

A complete list of ISHLT Guidelines and Consensus Reports can be found at: https://www.ishlt.org/publications/guidelines.asp

## Preview: *On The Road Again*

"Goin places that I've never been, Seein' things that I many never see again, and I can't wait to get on the road again," ah, Willie Nelson had it right. Sadly this is the last update you'll be receiving from your humble roving cardiology reporter at this year's ISHLT, but fear not, France is but a year away. The meeting's been great, the sessions incredible, plus you get to reunite with friends and colleagues from around the world.

In one of the last **Sunrise Symposium's 11: VAD Teams working Across Different Countries: How To Do It several presenters will review some more novel aspects of caring for the VAD patient.** Neil Wrightson will review driveline options for patients supported on long-term VAD therapy, drawing on his experience from Newcastle, England. Desiree Robson will then review travel options for patients with a VAD, and review how coordinators can help prepare and aid patients from living a normal life (which must include a vacation!). Dr. Pamela Combs will then review the nursing guidelines for Heart Failure and for VADs that may be applicable to the VAD patient as he/she enters into the community at large and what role these may have in helping our VAD patients adjust to a normal everyday life.

In another **Sunrise Symposium 15: High-Risk Donor: Extending Our Criteria in Times of Organ Shortage**, an extensive review of high-risk donors will be discussed. Dr. Piedad Usetti will explain some of the limitations of current HIV, Hep B and Hep C testing has in organ donation. He will review the prevalence of these diseases and potential advances in screening tests such as nucleic acid testing which can solve these problems. (Cont'd)

Dr. Valentina Stosor will then discuss the use of Hepatitis B core antibody positive donors and the use of these organs in transplant. He will focus on the interpretation of Hepatitis B screening, the risk of transmission, further testing that can be performed to the donor prior to harvesting and ultimately how to manage patients in which transmission does occur.

Dr. Paolo Grossi will then change gears a bit and talk about Hepatitis C and its role in thoracic organ transplant. While there is a significant amount of data in the renal transplant literature revolving around hepatitis C, little exists in heart and lung literature. He will review the data out there, and the role of new Hepatitis C therapies may have in advancing Hepatitis C positive donor into Hepatiticx C naive patients. He will also propose that there is no reason to turn down a Hepatitis C donor in a naive recipient due to the extreme shortage of organs that exists already.

Finally, Dr. Fernanda Silveira will review the current guidelines on accepting donors with documented infections and review data and offer insight as to whether these organs can be safely used. And with that, my duties are done. It's been great providing you with daily summaries of the all the hottest sessions at this year's ISHLT Annual Meeting, and I hope you've enjoyed the articles (and the cheesiness as my wife would say of some of my analogies and side comments). Perhaps if you are lucky, you will get to read more of these literary masterpieces next year in Nice, France. Au revoir et Bon Voyage! Vous voir l'annee prochaine.

## The Year in Review

At this year's **Concurrent Symposium 28: JHLT at ISHLT: The Year in a Capsule**, a "who's who" of transplant medicine presented summaries of the most intriguing and novel publications put out this year in the Journal of Heart and Lung Transplant.

The session started off with Dr. Schwieger reviewing some of the biggest articles in MCS and Heart Transplants this year. He focused first on the interesting Heartware trial, HVAS Bridge to Transplant, which featured outstanding survival data and some promising hope for this new device that featured over 84% survival with use at one year. He then reviewed a retrospective review of the UNOS registry, which addressed organ allocation for those with congenital heart disease. Sadly as we are confronted with a greater number of these end stage patients, ventricular assist devices are often not feasible due to anatomical or physiologic factors that would otherwise provide a viable bridge to transplant. Unfortunately, our current procurement system does not make allowance for these patients to move higher on the list, and thus time waiting can seriously impede survival. On a similar topic, he reviewed findings of the European experience with the Cardiac Allocation Score to help address several deficits in transplant waiting lists. Using a combination of urgency, wait time and evaluating outcome/survival odds after transplant, this system may better help predict who will benefit most from a transplant. Finally, further addressing donor shortages, he reviewed a fascinating review of the UNOS registry from 1994-2012 to evaluate whether there were any significant differences in outcomes using "marginal hearts" from post-CPR donors. Using a sample size of over 1300 patients, which represented nearly 5% of all donor hearts, there was no significant difference in outcome post

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transplant. While there were different features between CPR and non-CPR donors (regarding alcohol use, drug use, smoking, etc.), all recipients did quite well regardless. What should further allay fears to all of us in the transplant community, was that the amount of time CPR was administered had no bearing on outcomes either, with some donor hearts receiving upwards of 50 minutes of CPR, and a mean time of nearly 20 minutes for all CPR donors.

Dr. Heather Ross then took to the stage to congratulate Dr. Shwieger on his review of cutting edge literature, and echoed many of his sentiments from these articles, raising concerns from the Heartware trial that pump thrombosis remains a critical limiting step in the use of MCS. She also agreed with many of the limitations of the UNOS criteria for transplant waiting lists, and pointed out that many of these articles reviewed should further discussion on how better to improve the system.

After several reviews on the pulmonary literature that my colleague will cover, the session concluded with a review of pertinent Infectious Disease literature in the last year of transplant medicine.

Dr. Me-linh Luong reviewed three articles dealing with CMV, C diff and hepatitis E. While several of her topics pertained more to lung transplantation, her review of the emerging threat hepatitis E plays in all of our transplant patients was of significant concern. Emerging case series are demonstrating that hepatitis E, common in undercooked pork products and various other sources can activate in immuno-compromised hosts. In a single center review six patients were found to have this virus. Fortunately if it is caught relatively early in its course it can be easily treated with medication and augmentation of immunosuppression. Dr. Husain then reviewed this topic further, and it is clear that appropriate screening in transplant patients with abnormal liver function tests and/or evidence of fibrosis and cirrhosis should trigger immediate testing.

Curious about the award winners? Check out the 2014 Award's Presentation on the ISHLT website by clicking here.

# As heard on Twitter…

**Chesney Castleberry** @chesneydc · 19h
Packed house at Controversies in Listing the Ped Patient... Such a hard topic, thanks to the society for providing the forum **#ishlt2014**
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**Eugene DePasquale** @DrDePasquale · Apr 12
Proceed II Int'l #HeartTransplant Trial Results: OCS Effective as Standard Method bit.ly/PZXEQX **#ishlt2014** @UCLAHealth via @ISHLT
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At **#ishlt2014** fantastic talk on upcoming tech. Looking forward to the future
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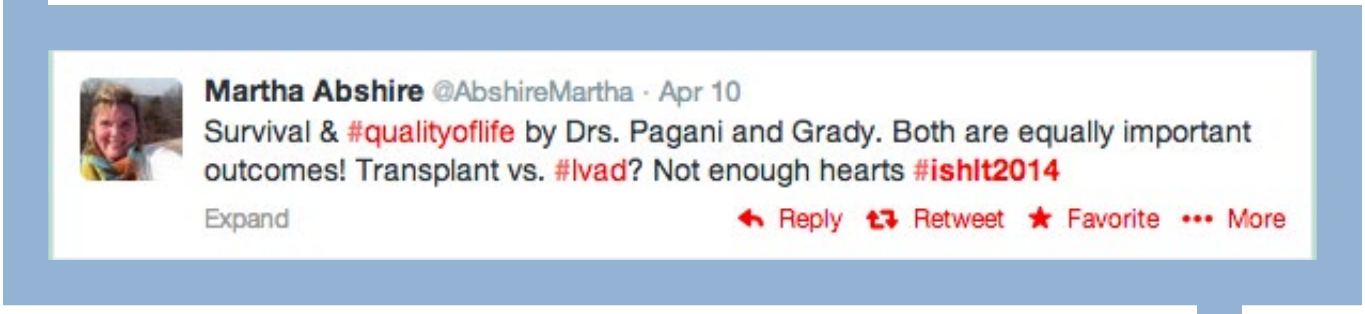
Martha Abshire @AbshireMartha · Apr 10
Survival & #qualityoflife by Drs. Pagani and Grady. Both are equally important outcomes! Transplant vs. #lvad? Not enough hearts #ishlt2014
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**Martha Abshire** @AbshireMartha · Apr 9

Standardizing social support is key for #lvad and transplant outcomes #ishlt2014 #hopkinsnursing

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**Bryan Boling** @bryanboling · 3h

Poster up. Now I fret as people silently judge our work. :-) #ishlt2014

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**Anders Andreasson** @anders_si · 2h

Packed session with audience standing all along the walls in Seaport H, JHLT @ishlt: The Year in a Capsule! #ishlt2014

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**Henrik Bergenfeldt** @HBergenfeldt · 7h

Excited about presenting: "ABO-incompatible adult heart transplantation. A registry study." @ the #ISHLT2014 today.

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**dipesh shah** @dr_dipkshah · 3h

Interesting talk by Prof. Alvin Roth, Nobel laureate-economics-Donor organ allocation policy.#ishlt2014

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