



April 28, 2016

DAILY Links

36th Annual Meeting & Scientific Sessions Marriott Wardman Park, Washington, DC

Current innovations and future of EVLP –“Lords of the Rig” ‘The best way to predict the future is create it’ – Abraham Lincoln

What a start to ISHLT! Christine Lau opened by describing the potential therapeutic target A2aR receptor predominantly expressed on iNKT cells, which, may moderate donor derived neutrophilic infiltration contributing to ischaemic reperfusion injury. EVLP, may be the ideal platform to allow administration of large doses of medications with minimal systemic side effects. Dr Shaf Keshavjee (Toronto) also suggested that EVLP provides a platform not only for administration of large doses but also for advanced biological repair gene and cell therapies. John Dark from Newcastle started his ‘Lord of the Rig’ talk with data showing that 43% of donors had less airway colonization. He went on to show impressive reductions in BAL bacterial load following administration of meropenem during EVLP. Echoing a theme suggested by a previous presenter, John suggested that airway resistance and other biomarkers might be better parameters for determining suitability than the ubiquitously used PO2.

The much-anticipated debate started with Frank D’Ovidio (Columbia) arguing that EVLP is an essential component of lung transplant medicine to improve donation rates. Helen Whitford (Melbourne) countered by highlighting the results of their EVLP devoid program, which in terms of organ utilization and 1 year survival are comparable. It certainly did not answer the question posed from the floor earlier – when will EVLP become standard of care?

From the BSTR Council Meeting on Wednesday



17-Month Tyler, bottle in hand, led the afternoon session, supporting mom, Sonja Schrepfer, MD, PhD.

It Takes Two Baby, It Takes Two Baby... Or does it?

Walter Klepetko (Vienna) engaged the interactive symposium by suggesting that RV performance is never the limiting factor for success in PAH transplants. He went on to say that the only indication for combined heart lung transplant should be complex cardiac defects. Daniel Chambers (Brisbane), asked the question "how bad does the liver have to be". He started by tackling a frequent clinical quandary - the CF patient with severe compensated liver disease. Although reported outcomes post combined lung liver are comparable to lung transplantation, he highlighted the high waitlist mortality in patients listed for combined lung / liver transplants. He concluded that given this high mortality only very severe liver disease would warrant combined upfront lung/liver. John Dunning (Papworth) followed by looking at the same subject from a surgical perspective highlighting the staged or combined technical approaches. The talk highlighted how techniques are evolving with subsequent floor discussion regarding transplant order – lung or liver first? Moving down the body, Greg Snell (Melbourne) discussed the lung and kidney. Combined lung kidney and late kidney were both reviewed, regarding wait time, "jumping the kidney que" and relative allograft survival (lung determined). He concluded that a patient requiring a late kidney unquestionably benefits although the renal allograft usually outlives the lungs. Underpinning the session is the issue of organ utility and equality – why should a patient receive more than one organ and how should they be allocated? Through confronting these examples, he explored and illustrated the issues of justice and utility. Mark Greer (Hanover) concluded the session discussing immune tolerance in multi-organ recipients. He explained using animal and human data an improved survival and reduced cellular rejection where more than one organ (heart / kidney) were transplanted.



Anticoagulation and MCS: Can We Do Better? Yes We Can!

This fascinating symposium provided a wealth of information on current practices, trends and future directions for optimal management of anticoagulation in MCS. Dr. Jorde set the tone with the opening lecture, which focused on bleeding and clotting with the take home message that "early intervention is key" and to use device specific approaches for thrombosis. Dr. Jennings presented the effect of inherited coagulopathies on LVAD patients, indicating that data on this topic is minimal. "Who should monitor INR?" was the question that Dr. Meyer asked and the surprising answer was: patients. Dr. Hayward challenged the status quo on Heparin monitoring with compelling data on the discordance between aPTT and Factor Xa results when monitoring heparin. However, there are limiting factors in changing our practices including costs, ease of use and "clinical inertia". Antiplatelet monitoring was the next topic on the docket. Dr. Page

admitted that we are not quite there yet as there is an array of antiplatelet monitoring with variability in reliability and precision among tests. The session concluded with Dr. Uriel who, aptly stated that we need to focus our efforts on *why* our patients bleed. This session did answer the question it asked and the answer seems to be: that with continued focus on this subject, *yes, we can do better!*

Tissue Engineering – What is it Good For?



Bio or Ghost scaffolding and allotransplantation tolerance, are we there yet?

Not! We are still a long way off in the goal of organ's made to order in transplantation especially for heart and lungs. The main obstacles are the vast numbers of stem cells, sources of extracellular matrix and types of cells needed. Smaller patches (CORMATRIX) and the clinical trials to watch which are looking to demonstrate dECM safety are Ventrix trial and AUGMENT-HF trial. How about regenerating damaged tissue? Regenerative efficacy with regenerative cell therapy and injecting CDC's is promising, not only in the post MI patient for improvement in structural damage load in grams but also in LV function. The ALLSTAR trial is one to watch. However, even if we stay with the old and continue to perform allogenic transplantation, desensitization and promotion of tolerance to transplant immunogenically is occurring in animal models and in human kidney transplantation with promising results.

As heard in Wednesday morning session:

'I wish I could trade my heart in for another liver. That way I could drink more and care less'

Joint thinking on pulmonary hypertension - Weight gain is too late, what's the LAP?



Since the World Health Organization Pulmonary Hypertension Group 2: Pulmonary Hypertension due to Left Heart Disease in the Adult published its summary statement in 2012. The dilemma of PVH is challenging and this session was all about our underdiagnosis and the need for protocol driven algorithms to treat pulmonary hypertension from left sided heart disease, group two. Continuous physiological monitoring teases out problems before pulmonary edema develops detected by radiofrequency transmission from implanted defibrillators or directly implanted monitors in the atrial septum. Essentially prevalence of PH in left sided heart disease is 60% with an incremental risk of death. The type of PH matters in terms of survival, therefore, we need to monitor and treat, not only LAP, but LV disease and PH together in a three pronged approach.

Between a Rock and a Hard Place: Debating Treatment Decisions for Marginal Psychosocial Candidates Let the Battle Begin!

Several psychosocially challenging case reports were presented during the session that included recurrent challenging themes of substance abuse, non-adherence, homelessness, anxiety and depression. After the initial presentations, there was a pro con debate as to whether these three patients could be considered as suitable candidates for VAD and/or heart transplant. While past behavior is often used to predict future behavior, there is very little convincing evidence to support which if any psychosocial risk factors have an impact on long-term outcomes in this population. Arguments for and against include morality, social judgments and resource scarcity just to name a few. All rounds ended in a draw for the fighters. The crowd was asked to weigh in on the decision by raising their dukes to a series of questions at the end of each round.

Round 1: Fabienne Dobbels (Pro) vs Luke Burchill (Con) with head judge Michael McDonald presenting.

Round 2: Quincy Young (Pro) vs Jeremy Kobulnik with head judge Finn Gustafsson presenting.

Round 3: Mary Amanda Dew (Pro) vs Jay Baumwol (Con) with head judge Nancy Blumenthal presenting.

Let's go crazy!



Coming Attractions

Is it Raining Complications? (Concurrent Session 1)

We never mean to cause our patients any sorrow. We never meant to cause them any pain. We only want to see them laughing in the purple rain. But unfortunately, complications (even minor ones) after LVAD insertion are more common than we'd like. In this session, a variety of abstracts covering common post implant complications will be discussed. Dr. Milano will review results after changes made in the HVAD pump during the ENDURANCE trial. The next two talks will discuss the dreaded complication of stroke, Dr. Acharya presents predictors of stroke during LVAD based on INTERMACS registry data and Dr. Wong will examine hemorrhagic conversion of strokes in a retrospective study. Dr. Grandin's presentation will review the spectrum of early right heart failure post LVAD. The session will conclude with two abstracts on difficult problems. Dr. Maninveld will cover the incidence of ventricular arrhythmias after LVAD

and its impact on survival. This is followed by Dr. Pstoka presentation on infection rates after tunneling the driveline through an alternative exit site. Hopefully this session will give us all some ideas on how to decrease the bad and increase the good, as we only want to see our patients bathing in the **Purple Rain**.

Bringing sexy back – what’s up in Heart Failure (Concurrent Session 5)

This session will be all about pills, procedures and sex, which is sure to wake up the audience after the conference dinners the night before! The session will be in good hands, chaired by Christopher Hayward and Jose Gonzalez-Costello, as we go from looking at renal blood flow with intrarenal doppler flow velocity as a novel approach in blood flow dynamics. Bojan Vrtovec from Stanford will examine renal function reversibility with an inotrope as a predictor of heart transplant outcomes. Luiz Moreira will take us to sympathetic ablation in the treatment of left ventricular remodeling in rats and tells us that a two sided approach is better. For its climax, we will explore patient’s concerns on how heart failure influencing their libido and why they want us to talk about it more. Why not!

Quality over Quantity? Quality of Life in MCS (Concurrent Session 8)

Quality is more important than quantity.

One home run is much better than two doubles. – Steve Jobs

Joseph Rogers will discuss results from the ENDURANCE trial which compared safety and effectiveness of the HeartWave® VAD in end-stage heart failure for patients ineligible for heart transplant. Connie White-Williams will discuss results from a health related quality of life (HRQOL) study looking at patients from pre-implant to 2 years post transplant. Geetha Bhat will highlight the potential effects of LVAD implementation on depression and anxiety. Josef Stehlik will discuss the prospective observational ROADMAP study and how treatment assignment may have influenced patient reported outcomes. Roxana Ghashghaei will highlight results from a study of VAD caregivers having significantly less caregiver burden or demand than caregivers of patients with other chronic diseases, such as heart failure. Matthew Inra will discuss causes and temporal trends in LVAD readmissions.



All against the graft (Concurrent Session 11)

CS 11, 2-3.30pm is the heartbreak of rejection, chaired by Maryjane Farr and Kumud Dhital. In this session we look at capillary damage and fibrin in heart transplantation with Deborah Budge who will show us that we need to look closer at our endomyocardial biopsies with interstitial fibrin evaluation. Jose Vazquez de Prada will argue that we don't need biopsies with his work on using echo alone in post-transplant surveillance. We will also cover a new biomarker, dd-cfDNA (plasma) as we strive to spot and treat rejection early.

Improving Outcomes: Body and Soul (Concurrent Session 19)

The body heals with play, the mind heals with laughter and the spirit heals with joy. - Proverb

This session will feature a multidisciplinary presentation covering a variety of topics including BMI and other body composition measurements, nutritional support on ECMO, the impact of physical activity and vocal cord palsy. James Tatum will present an abstract on change in body mass index over time after continuous flow LVAD implementation and the effect on conditional survival. Eleanor Capel will discuss if pre-lung transplant body composition and its associations will affect post transplant outcomes. Rupal Patel will present the results of a single center study on adequacy and tolerance of nutrition support during the first 7 days of ECMO as bridge to lung transplant. James Walsh will discuss their abstract on the impact of lung transplant on daily activity in the setting of improved respiratory function and exercise capacity. Finally, Patel will look at the results of a multi-center study on the effects of Iyengar yoga on health related quality of life in patients with PH.

Joint ISHLT / PVRI symposium: exploring combination therapy in PAH "We are all in!" (Concurrent Session 29)

Combination therapies – widely used and accepted in many disciplines of medicine. Targeting parallel pathways to synergistically reduce a common effector- it certainly makes rationale sense and is commonly practiced within PAH. Yet our ambition to help patients resulted in practice surpassing the evidence, which is now catching up. Paul Corris (Freeman hospital) will evaluate current evidence of variable outcomes with different combinations. Perhaps Martin Wilkins (Imperial College, London) will explain differences in the pharmacology of common drug classes and their potential interactions. Ardeschir Ghofrani (University of Glessen) will review soluble guanylyl cyclase stimulants – the newest class of PAH therapy in our arsenal. Finally, Mardi Gomberg-Maitland (University of Chicago) will explore optimal timing for prescribing combination – upfront or at clinical decline?

Ch Ch Changes

What's in a name? We met *paecilomyces* and got to know the mold. Now it's **purpureocillium**. Why the name change?

Identity crisis? First *Lichtheimia corymbifera*. Then *Absidia corymbifera*. And now, back to *Lichtheimia corymbifera*. Was this a divorce? Or a conscious uncoupling.

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