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MAY 2026 | Early Career and Trainee Studies

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Anesthesiology & Critical Care Professional Community
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International cooperation in cardiogenic shock is key to improving outcomes: Cardiogenic Shock Working Group impacts a single center in a developing country

Ortega-Hernández JA, González-Pacheco H, Hernández-Montfort J, Araiza-Garaygordobil D, et al. *JHLT,* 2025; 44(7):1165-1171 | DOI: 10.1016/J.HEALUN.2025.03.003

Study Highlights

Objective: To evaluate whether adoption of Cardiogenic Shock Working Group (CSWG) standards and international collaboration was associated with changes in care processes and improved in-hospital outcomes in patients with cardiogenic shock (CS) at a single tertiary referral center in a middle-income country.

Methods: Retrospective single-center analysis of 9,430 patients with CSWG-SCAI stage B–E CS identified from 28,054 CCU admissions between 2005 and 2023. Outcomes were compared across the historic pre-CSWG era, contemporary pre-CSWG era, and CSWG era using multivariable Cox regression and propensity score matching.

Results: After CSWG implementation, pulmonary artery catheter use increased from 4.2% to 7.9%, and overall mechanical circulatory support use increased from 8.1% to 10.3%. In-hospital mortality declined from 22.3% in the historic pre-CSWG era and 20.5% in the contemporary pre-CSWG era to 15.3% in the CSWG era. Pre-CSWG eras remained associated with higher mortality risk in adjusted and propensity score–matched analyses.

Conclusions: International collaboration and adoption of standardized CS team principles were associated with improved care processes and lower mortality, supporting the value of global CS networks even in resource-constrained settings.

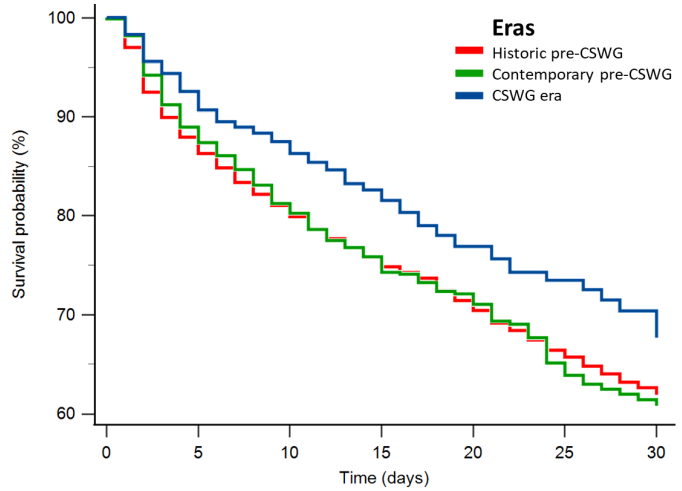

Figure 1. Survival according to era of care.

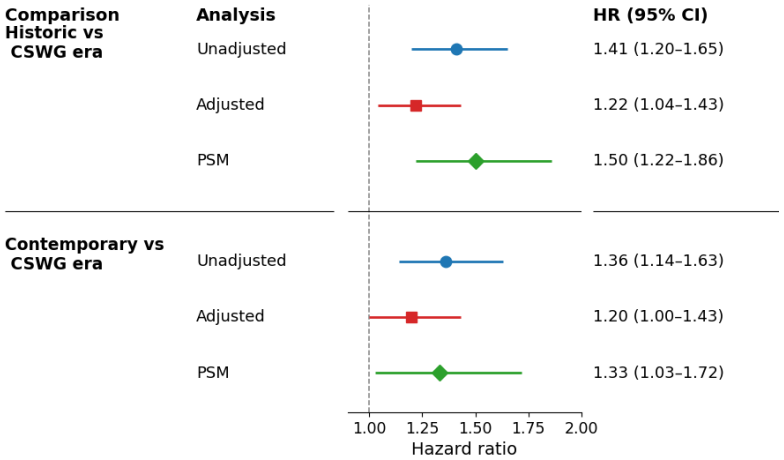

Figure 2. Hazard ratios for mortality by era.

Author's Comments

- This study suggests that international CS collaborations can translate into meaningful survival gains outside high-income healthcare systems.
- Standardized shock protocols, earlier recognition, and greater use of invasive hemodynamic assessment may improve real-world care delivery.
- These findings are especially relevant for developing countries, where system-level organization may have a major impact even before broader access to advanced therapies.
- The study also highlights that global research networks can improve not only academic collaboration, but also clinical implementation and outcomes.

Limitations

- This was an observational, retrospective, single-center study and remains vulnerable to residual confounding despite adjustment and propensity score matching.
- The CSWG era covered a relatively short period, limiting assessment of long-term sustainability.
- Temporal changes in patient mix, referral patterns, provider preferences, and shock management may have influenced the observed differences.
- Limited availability of advanced heart failure therapies, including durable LVAD and heart transplantation, may reduce generalizability.

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Mitigating Post-operative Right Ventricular Dysfunction After Left Ventricular Assist Device: The RV Protection Study

Kanelidis AJ, Gozdecki L, Belkin MN, Kalantari S, Nguyen A, Chung BB, et al. *JCF* 2025; 32, 46-57 | DOI: 10.1016/j.cardfail.2025.01.017

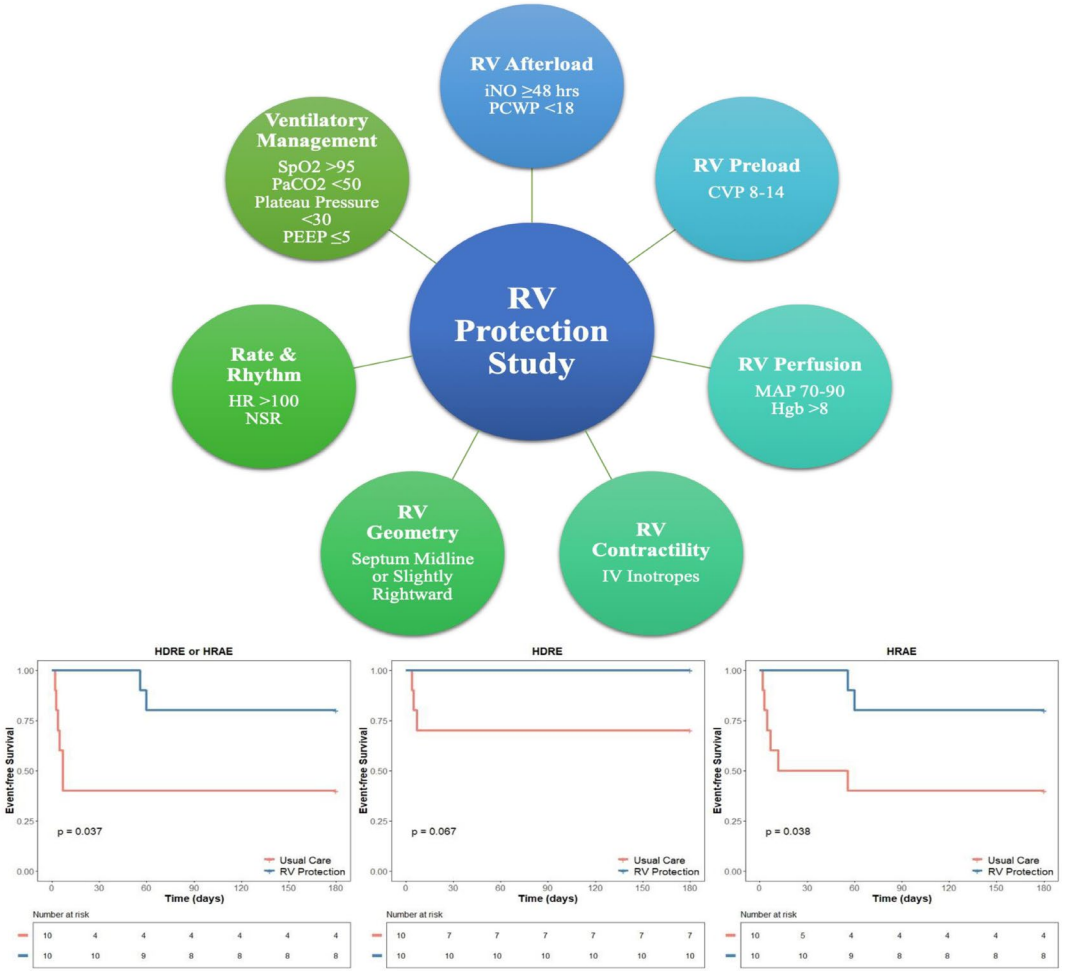
Study Highlights

Objective: Investigate a comprehensive, upfront RV protection strategy combining hemodynamic, ventilatory and pharmaceutical optimization to mitigate right ventricular failure (RVF).

Methods: Prospective randomized controlled trial (RV protection strategy vs usual care) for post-operative LVAD management. The primary outcome was survival free from any hemodynamic-related events (HDREs), i.e. RVF and aortic insufficiency, or hemocompatibility-related adverse events (HRAEs) at 24 weeks.

Results: Twenty participants were randomized (10 in each arm). The RV protection strategy showed significantly greater survival rates free from HDREs or HRAEs compared to usual care (80% vs 40%; P=0.04), including no RVF.

Conclusions: Participants receiving a novel, comprehensive, upfront RV protection strategy post-LVAD implantation had significantly greater survival rates free from HDREs or HRAEs at 24 weeks.



The RV protection strategy showed significantly greater survival rates free from HDREs or HRAEs (left), with no HDREs vs 3 (30%) RVF with usual care (middle), and significantly greater survival rates free from HRAEs (right).

Author's Comments

- This is the first RCT to demonstrate an upfront, multifaceted intervention can reduce the risk of RV failure post-LVAD implantation.
- Isolated interventions and simplified risk scores are likely insufficient to tackle the challenge that RVF poses.
- The RV Protection Study puts together best practices for optimization post-LVAD implantation – these upfront therapies can help mitigate RVF.

Limitations

- The RCT was conducted at a single center, with 20 patients enrolled, as a proof of concept.
- Patients were standard risk (INTERMACS profiles 3-4), with normal pre-operative RV hemodynamics, which may not be generalizable to INTERMACS 1-2. Thus, upfront RVAD was not assessed for patients at high risk of RVF.

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Lack of association between donor left ventricular hypertrophy and graft survival in the contemporary era of heart transplantation

Mahar JH, Wayda B, Weng Y, Zhang S, Zaroff JG, Khush KK. *Am J Transplantation,* 21 January 2026 | DOI: 10.1016/j.ajt.2026.01.013

Study Highlights

Objective: To evaluate whether donor left ventricular hypertrophy (LVH) is associated with graft survival in contemporary adult heart transplantation.

Methods:

- Retrospective analysis of 14,584 adult heart transplants from the Scientific Registry of Transplant Recipients (SRTR,2015–2022)
- Secondary analysis of 2,168 donors from the Donor Heart Study (DHS) with blinded core echocardiographic measurements
- Donor LVH defined by posterior wall thickness:
  - Mild: 1.2–1.3 cm
  - Moderate–severe: ≥1.4 cm
- Primary outcome: composite of death, graft failure, or retransplant.

Results:

- Donor LVH was common (12.5% in SRTR; 23% in DHS)
- Donors with LVH were older and more likely to have hypertension
- No significant difference in graft survival by LVH severity:
  - 1- and 3-year graft survival similar across all LVH groups
  - Multivariable-adjusted analyses showed no association between donor LVH and adverse outcomes
  - Post-transplant length of stay was similar regardless of LVH presence

Conclusions:

Donor LVH was not associated with worse graft survival in contemporary heart transplant recipients.

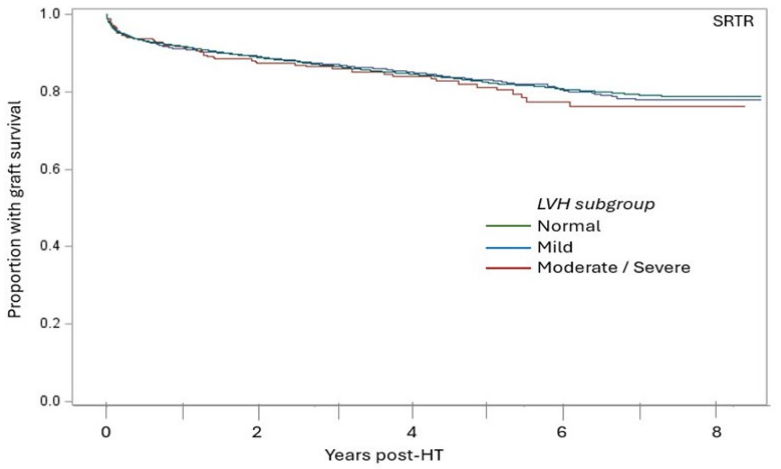

Figure 3A: Kaplan-Meier analysis of the graft survival by LVH subgroup, in the SRTR cohort

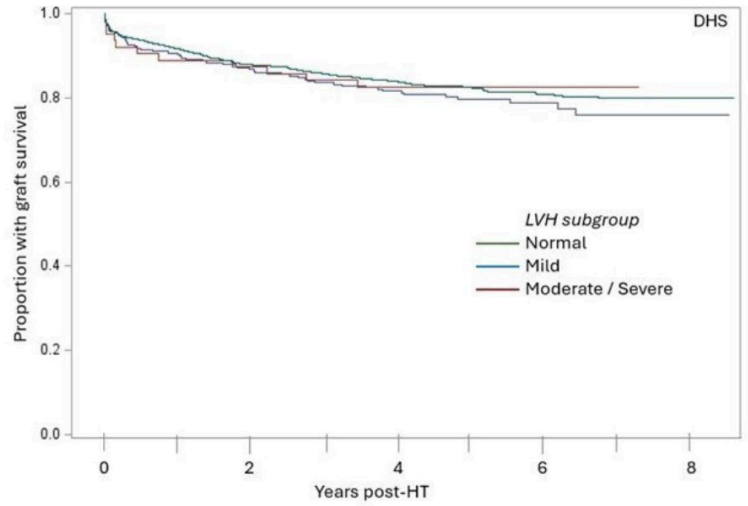

Figure 3B: Kaplan-Meier analysis of graft survival, by LVH subgroup, in the DHS cohort

Author's Comments

- Donor LVH remains a frequent reason for organ non-use despite limited contemporary evidence of harm
- This is the largest modern analysis evaluating donor LVH using both national registry data and a prospectively phenotyped cohort
- Findings suggest LVH alone should not preclude donor heart acceptance, particularly in the setting of ongoing donor scarcity
- Broader utilization of donor hearts with LVH may safely expand the donor pool without compromising outcomes
- Results support reconsideration of LVH thresholds in donor selection guidelines.

Limitations

- Limited number of donors with moderate-to-severe LVH, reducing power to define an upper safe threshold
- Inability to assess primary graft dysfunction, as PGD data were not available during the study timeframe
- Findings do not include DCD donors or reflect the impact of newer organ perfusion technologies.

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Determining an optimal central cannulation strategy for ambulatory veno-venous extracorporeal life support

Kumpfbeck AR, Woo Y, Petrovic M, Simon V, Cortelli M, Adjei E, et al. *JHLT* 7 April 2026| DOI: 10.1016/j.healun.2026.02.1682

Study Highlights

Objective: To develop a durable cannulation strategy for use with chronic respiratory support systems utilizing veno-venous ECMO.

Methods:

- Four custom central cannulation configurations were constructed: single site (SS) or dual site (DS) with drainage from the RA and reinfusion into the RA (-RA-RA) or RV (-RA-RV) and for use with custom grafts (dacron base and PTFE cannula sleeve(s) sealed with low density silicone).
- Acute sheep studies of configuration performance consisted of a right thoracotomy, graft affixation to the RA, and central cannulation through the grafts via a modified-Seldinger technique.
- For configurations SS-RA-RV and DS-RA-RV, the reinfusion cannula tip was directed through the tricuspid valve into the RV.
- Sheep were placed on VV-ECMO for at least 5 hours at 2 L/min flow and 2 LPM of 100% O_2 sweep gas flow.
- Pressure/Flow, hemolysis (plasma free hemoglobin), recirculation, and blood gas analyses were performed.

Results:

- SS-RA-RV had a 50% attrition rate due to sheep mortality or cannula tip migration/misplacement.
- DS-RA-RV had the lowest recirculation (22.8±16.7%, p=0.016) and plasma free hemoglobin (1.7±0.3mg/dL, p=0.459).
- DS-RA-RA had the lowest cumulative pressure drop (p<0.001), but its reinfusion and drainage pressure drops were not significantly different from those of DS-RA-RV (p=0.767 & p=0.076, respectively).

Conclusions: This work suggests a DS cannulation configuration with RA drainage and RV reinfusion may be optimal for durable ambulatory VV-ECMO. Future studies will evaluate the cannula in longer-duration, ambulatory models.

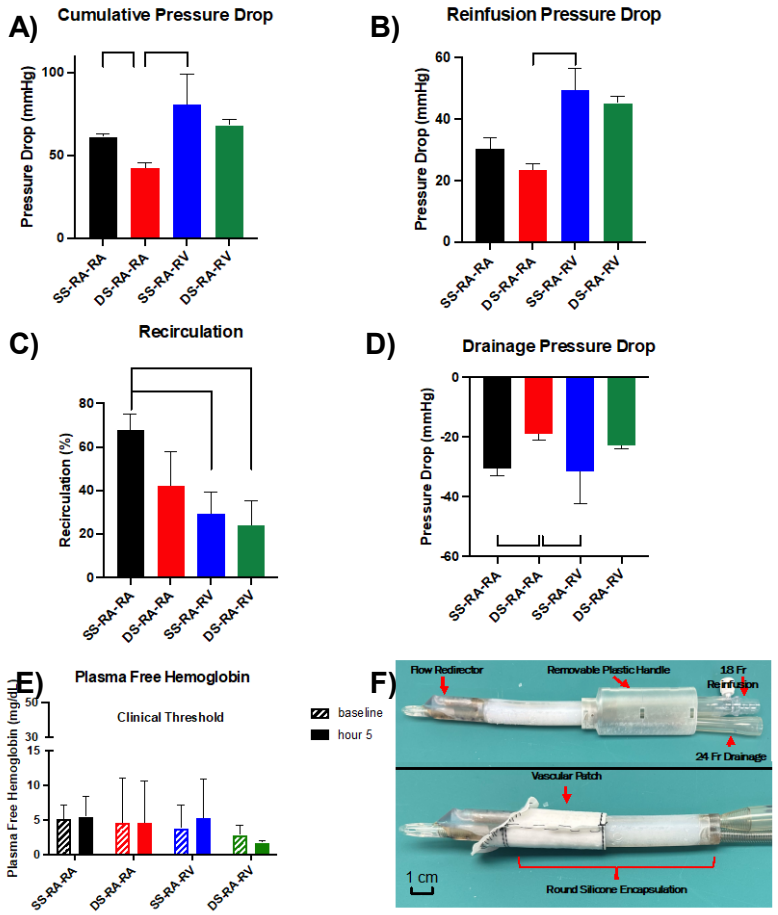

Figure 1 A) cumulative pressure drop, B) reinfusion cannula pressure drop, C) average hourly recirculation, D) drainage cannula pressure drop, E) baseline plasma free hemoglobin and after 5 h of circuit flow by cannulation configuration, and F) example of SS-RA-RA cannula with custom graft.

Author's Comments

- Medical treatments for end stage lung disease do not delay disease progression, and lung transplantation is plagued by donor scarcity and a short medial survival
- Artificial lung therapies and chronic respiratory support systems utilizing VV-ECMO have the potential to treat patients with chronic respiratory failure, but the development of a durable, ambulatory system has not yet been achieved.
- This study is the first propose a central cannulation configuration, with custom cannulae and vascular attachment grafts for further long term testing.
- These acute studies demonstrated the technical feasibility of central cannulation and characterized their performance with physiologic relevant parameters of cannula pressure/flow, hemolysis via plasma free hemoglobin, and recirculation.

Limitations

- Small sample size of n=4-6 sheep per configuration
- High attrition rate of configuration SS-RA-RV (50%) limits robustness of statistical testing
- This acute study did not focus on cannula tunnelling or long term gas exchange, which are relevant to system durability
- Tricuspid regurgitation was not directly assessed in –RA-RV configurations, though their low recirculation values suggest it may not be significant
- Sheep body habitus can propose a technical challenge for cannula tunnelling which may make ambulatory assessment of our system difficult.

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Serum Ammonia Screening and Donor Mollicutes Detection for Hyperammonemia Syndrome Post-Lung Transplantation: A Prospective Observational Study

Walti LN, Ng CF, Kaur S, Almansour S, Mazzulli T, Bitterman R, et al. *Clinical Infectious Diseases* 2025; 81(5):998-1004. | DOI: 10.1093/cid/ciaf078

Study Highlights

Objective: Hyperammonemia Syndrome (HS) is a serious complication after lung transplantation (LT). Optimal screening is unknown. We investigated daily serum ammonia screening (SAS) and compared it with polymerase chain reaction (PCR) for Mollicutes (Urease-producing bacteria).

Methods: We included all LT recipients from 07/2019-02/2020 and 10/2021-11/2022 with available donor bronchial wash samples. Mollicutes PCR was done using commercially available kits. Daily serum ammonia was measured for the first 14 days; recipients were followed for HS for 30 days. HS was defined by new neurological symptoms and elevated serum ammonia levels >70umol/l. In case of HS suspicion, treatment was started (**Figure 1**).

Results: 5/241 (2%) LT recipients developed HS. All HS was diagnosed within 14 days post-LT (median time to HS was 8 days (IQR 5-10)). Confirmed elevated serum ammonia was found in 9/241 (4%): either related to HS (5/9) or liver disease (4/9). At transplant, donor and recipient Mollicute PCR was positive in 8% (19/241) and 1% (1/72) respectively. Positive donor Mollicute PCR was associated with HS but only in 2 of the 5 HS cases (**Figure 2**); in both patients *Ureaplasma urealyticum* was detected. 17/19 with positive donor Mollicute PCR did not develop HS, however 9/17 received antimicrobials covering Mollicutes for unrelated reasons in the first 30 days post-LT. No HS patient died within 90 days post-LT.

Conclusions: HS was rare. Daily ammonia screening might add to early HS diagnosis and treatment as well as improved outcome. Donor PCR screening had limited predictive value for HS post-LT.

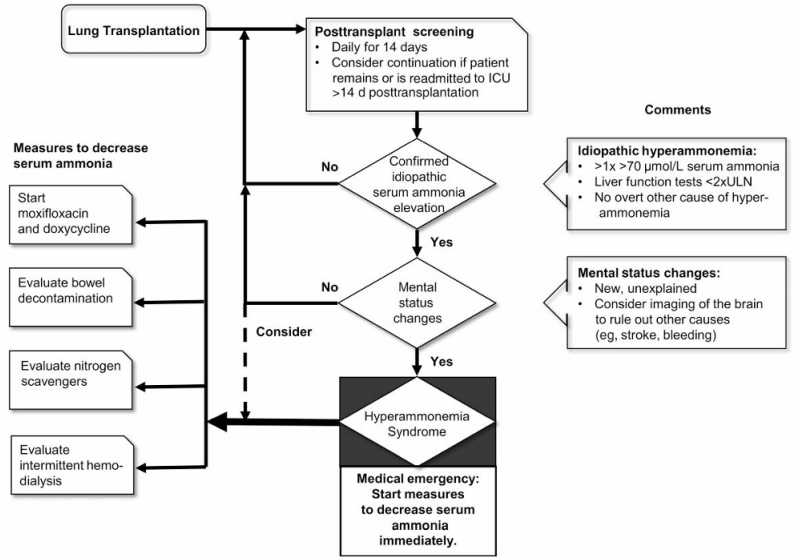
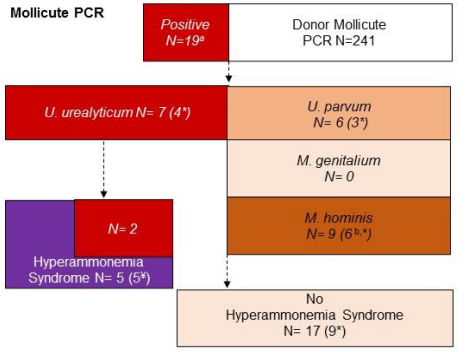


Figure 1: Algorithm for Serum Ammonia Screening

Figure 2: Donor Mollicute PCR in 241 lung transplant recipients.



* Indicates recipients who received any antimicrobial substance with Mollicute coverage in the first 30 days post-transplant for other reasons than Hyperammonemia Syndrome.
[a]) Mollicute PCR was positive in 19 recipients, thereof 4 had positive PCR for more than one Mollicute (1 *U. urealyticum/M. hominis*, 3 *U. parvum/M.hominis*)
[b]) In two recipients donor cultures were positive for *M. hominis*, they therefor received respective antimicrobial prophylaxis post-transplant.

Author's Comments

- This is one of the largest prospective studies investigating HS screening approaches in LT.
- Our study provides evidence that daily serum ammonia screening is able to diagnose HS in a timely manner.
- Moreover, serum ammonia level measurement is inexpensive and readily available and is eventually able to diagnose HS outside of Mollicute infection.
- Furthermore, few patients (n=4) outside of HS received antimicrobial treatment for elevated ammonia levels, mainly for liver-related hyperammonemia.
- Early diagnosis with immediate multi-modal treatment is potentially associated with improved outcomes: no patient in our cohort died from HS.

Limitations

- No definitive diagnostic criteria for HS are available.
- Single centre study.
- We did not perform Mollicute PCR in the context of HS suspicion, precluding us from elucidating the potential causes of HS.

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Detection of lung allograft injury through a comprehensive multidisciplinary analysis of donor-derived cell-free DNA in plasma and bronchoalveolar lavage: a real-world single center experience

Calabrese F, Pezzuto F, Vedovelli L, De Chellis C, Lunardi F, Loy M, et al. *Frontiers in Immunology* 2025; 16:4 Sep 2025. | DOI: 10.3389/fimmu.2025.1619771

Study Highlights

Objective: To assess plasma dd-cfDNA for detecting lung allograft injury in a real-world surveillance setting and to evaluate the added diagnostic value of BAL dd-cfDNA.

Methods: Plasma dd-cfDNA was measured by NGS in 127 surveillance samples from consecutive lung transplant recipients and interpreted with lung allograft standardized histological analysis (LASHA)-based biopsy assessment, BAL microbiology/cytology, and immunological data within a multidisciplinary team framework.

Results: Plasma dd-cfDNA was highest in immunological injury, with a median value of 2.67% and 100% sensitivity. Its sensitivity was lower for non-immunological injury, detecting 28% of cases. In paired samples, adding BAL dd-cfDNA increased sensitivity for non-immunological injury from 28% to 71%. Random forest analysis ranked plasma dd-cfDNA >1% among the most important variables associated with death and CLAD.

Conclusions: Plasma dd-cfDNA is a strong marker of immune-mediated graft injury, while BAL dd-cfDNA improves detection of non-immunological complications, supporting integrated compartment-based surveillance.

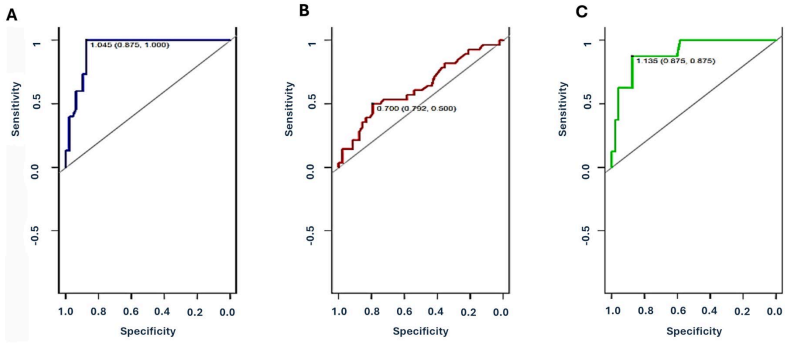

Figure 1. ROC curves for plasma dd-cfDNA by injury category: (A) immunological injury, (B) non-immunological injury, and (C) mixed injury. Performance was high for immunological and mixed injury (AUC 0.93 and 0.90) but limited for non-immunological injury (AUC 0.63).

Injury type	Threshold [median (CI 95%)	Sensitivity	Specificity	PPV	NPV	Overall accuracy
Immunological injury	1.045 (0.870,1)	100	87	71	100	90
Non-immunological injury	0.7 (0.702,0.5)	28	87	57	67	65
Mixed immunological and non-immunological injury	1.135 (0.875,0.875)	87	87	53	97	87

Table 1. Diagnostic performance for plasma dd-cfDNA by injury type.

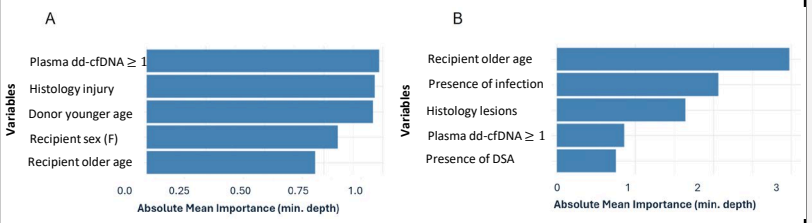

Figure 2. Random forest variable-importance plots showing the top predictors associated with (A) death and (B) CLAD. Plasma dd-cfDNA >1% ranked among the most relevant variables in both models.

Author's Comments

- The strength of this study is the integration of dd-cfDNA within a structured multidisciplinary assessment.
- Plasma dd-cfDNA is most useful for immune-mediated injury when interpreted with LASHA-based pathology and immunological data.
- BAL dd-cfDNA adds a compartment-specific perspective for non-immunological injury, such as infection or aspiration.
- Pathology remains central for classifying graft injury and guiding biomarker interpretation.
- Future studies should define how plasma and BAL dd-cfDNA can be incorporated into routine surveillance algorithms.

Limitations

- Single-center observational study.
- BAL processing within 2 hours may limit real-world feasibility.
- Few cases of acute cellular rejection.
- Incomplete immunological data in some patients.
- Limited sample size may affect performance estimates.

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Association of Neutropenia With Valganciclovir Prophylaxis Dosing Practices Within Pediatric Solid Organ Transplant Recipients

Gerthoffer E, Pozderac A, Darland L, Yasechko S, et al. *Pediatric Transplantation* 2025; 29:e70098. | DOI: 10.1111/petr.70098

Study Highlights

Objective: We evaluated whether valganciclovir cytomegalovirus (CMV) prophylaxis dosing strategy was associated with neutropenia in pediatric solid organ transplant (SOT) recipients at a single academic center using a novel glomerular filtration rate (GFR) estimation approach.

Methods: We performed a retrospective review of pediatric SOT recipients and compared patients who did and did not develop neutropenia. Multivariable regression was used to evaluate whether valganciclovir dosing strategy was associated with post-transplant neutropenia.

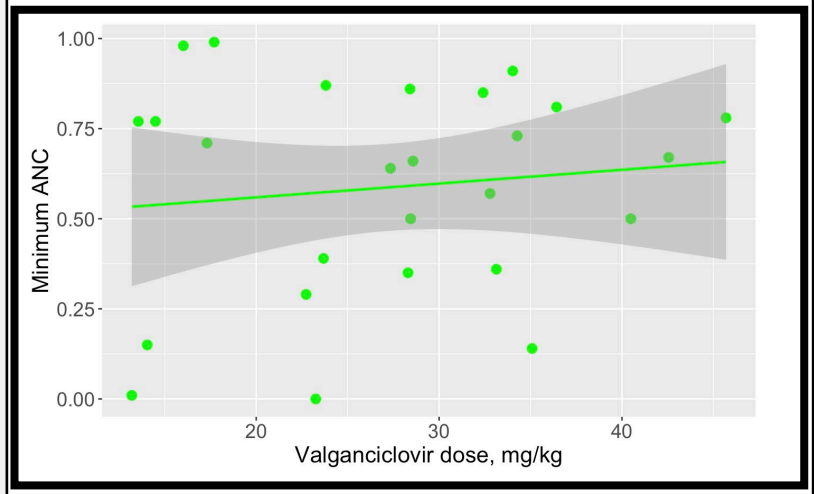
Results: Among pediatric SOT recipients, approximately one-third developed neutropenia while receiving valganciclovir. Concomitant myelosuppressive therapy was common, particularly sulfamethoxazole-trimethoprim and mycophenolate. Use of cystatin C-based GFR estimates to guide dosing did not differ between neutropenic and non-neutropenic patients, and CMV DNAemia remained rare in both groups. While valganciclovir dose alone did not predict neutropenia, higher kidney function-adjusted dosing was associated with increased odds of neutropenia.

Conclusions: BSA-based dosing guided by age-adjusted renal function was associated with lower neutropenia rates than previously reported in the literature. Neutropenia risk correlated with kidney function-adjusted valganciclovir exposure, not milligram (mg)/kilogram (kg) dose alone, highlighting the importance of renal-informed dosing strategies.

Valganciclovir Dosing

$$Dose\ (mg) = 7 \times BSA \times GFR$$

GFR calculation: Cystatin C-based or Bedside Schwartz
GFR maximum:
<1 year of age = 100 mL/min/1.73m2
1-18 years = 120 mL/min/1.73m2



Valganciclovir dose (mg/kg) not predictive of rate, odds, or degree of neutropenia

Author's Comments

- This study highlights that valganciclovir exposure incorporating kidney function and BSA (not mg/kg dose alone) drives neutropenia risk supporting more individualized dosing in pediatric SOT recipients.
- Lower neutropenia rates compared with prior reports suggest that careful renal function estimation (including cystatin C use and age-appropriate GFR maximum) may improve safety without compromising efficacy of CMV prophylaxis.
- Future studies integrating pharmacokinetic targets (e.g., AUC-guided dosing) are needed to better define optimal prophylactic exposure thresholds that balance efficacy and safety across pediatric age groups.

Limitations

- Single-center, retrospective design with a modest sample size
- Variability in transplant organ type, prophylaxis duration, and concomitant myelosuppressive therapies
- Pharmacokinetic measures (e.g., valganciclovir AUC) not assessed

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Pharmacy Professional Community
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Belatacept-Based Immunosuppression in Lung Transplant Recipients with Calcineurin Inhibitor Renal Toxicities

Walter K, Chen A, Hagopian J, Belloli E, Combs M, Lyu D, Sagana R. *Transplantology* 2025; 6(4), 31. | DOI: 10.3390/transplantology6040031

Study Highlights

Objective: Determine if belatacept, as an alternative to a calcineurin inhibitor (CNI)-based maintenance regimen, ameliorates the effects of CNI-related nephrotoxicity in lung transplant recipients (LTR) while preserving graft function.

Methods: Retrospective case series of adult LTR initiated on belatacept for any indication at a single center between 2020-2023

- **Efficacy outcomes:** estimated glomerular filtration rate (eGFR, calculated by CKD-EPI 2021), pulmonary function tests (PFTs), mortality, donor specific antibodies (DSA), rejection (biopsy proven ACR, AMR) and CLAD stage
- **Safety outcomes:** infection (viral, fungal, bacterial), malignancy, therapy discontinuation

Results: 5 LTR converted (median follow-up 3.49 years) at median of 575 days post-transplant

- eGFR improved (+18 ml/min/1.73 m^2) at 12 months and last follow-up (+18 ml/min/1.73m^2)
- FEV1 declined (-0.53L) from baseline to last follow-up; 60% treated ACR episode
- 80% (4/5) discontinued belatacept, primarily due to graft dysfunction (3/4) at median of 199 days post conversion
- No CLAD, DSA, malignancy, or mortality occurred on belatacept
- Infection, primarily pulmonary bacterial or fungal, occurred in all on belatacept

Conclusions: Belatacept with complete CNI elimination in LTR resulted in a sustained improvement in renal function in this series but was accompanied by a high discontinuation rate due to worsening graft function.

Patient	1	2	3	4	5
Indication for Belatacept	Renal insufficiency	Renal insufficiency	Renal insufficiency	Renal insufficiency	Microangiopathic hemolytic anemia
ISN Before Belatacept	Tac (8–12 ng/mL) MPS 180 mg BID Pred 5 mg daily	Tac (4–6 ng/mL) EVL (3–8 ng/mL) Pred 5 mg daily	Tac (3–5 ng/mL) MPS 720 mg BID Pred 5 mg daily	Tac (8–12 ng/mL) AZA 150 mg daily Pred 5 mg daily	Tac (10–14 ng/mL) MMF 500 mg BID Pred 20 mg daily
Belatacept Dosing Schedule	5 mg/kg day 1, 15, 29, 43, 57, then 5 mg/kg monthly	5 mg/kg day 1, 15, 29, 43, 57, 71, then 5 mg/kg monthly	5 mg/kg day 1, 15, 29, 43, 57, 71, then 5 mg/kg monthly	5 mg/kg day 1, 15, 29, 43, 57, then 5 mg/kg monthly	10 mg/kg day 1, 7, 14, 28, 56, 84, then 5 mg/kg monthly
Management of Tac	Tapered off	Tapered off	Tapered off	Tapered off	Immediate discontinuation
ISN on Belatacept	MPS 180 mg BID and Pred 5 mg daily	MPS 720 mg BID and Pred 5 mg daily	MPA 720 mg BID and Pred 5 mg daily	AZA 150 mg daily and Pred 5 mg daily	MMF 500 mg BID and Pred 20 mg daily
Time on Belatacept, days	121	104	276	512	Remains on belatacept therapy

Table 1: Immunosuppression at Time of Belatacept Initiation and Belatacept Conversion Dosing

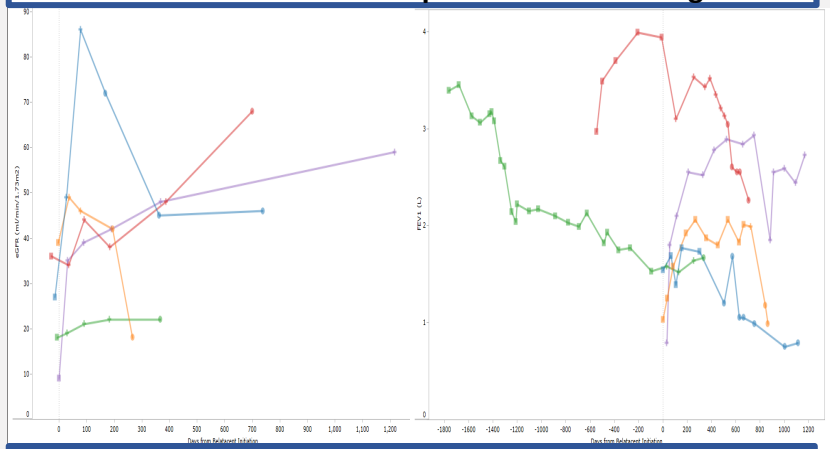

Figure 1: eGFR Post-Belatacept Initiation

Figure 2: FEV1 (L) Post-Belatacept Initiation

Author's Comments

- Belatacept is as an alternative to CNI in LTR improved/stabilized kidney function
- Improvements in kidney function were sustained post-belatacept discontinuation after CNI therapy was resumed
- The high rate of treated rejection and high discontinuation rate of belatacept due to graft dysfunction warrants caution with use of this agent in the setting of CNI withdrawal
- Future studies are needed to determine if alternative belatacept dosing and concurrent maintenance immunosuppressive regimens, such as use in combination with low-dose CNI, may preserve renal function and maintain adequate graft function

Limitations

- This case series is limited by retrospective study design, small sample size, and lack of a control group
- LTR were converted at varying times post-transplant
- Concurrent maintenance immunosuppressive regimens varied between patients
- Adjustments to maintenance immunosuppressive regimens throughout study period were not captured

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MAY 2026 | Early Career and Trainee Studies

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Abnormal spirometry one year after lung transplantation may identify patients at risk for chronic lung allograft dysfunction in a multicenter cohort

Graham AR, Grau-Sepulveda MV, Todd JL, Neely ML, Snyder LD. *JHLT Open* 2025; 11:100473. | DOI: 10.1016/j.jhlto.2025.100473

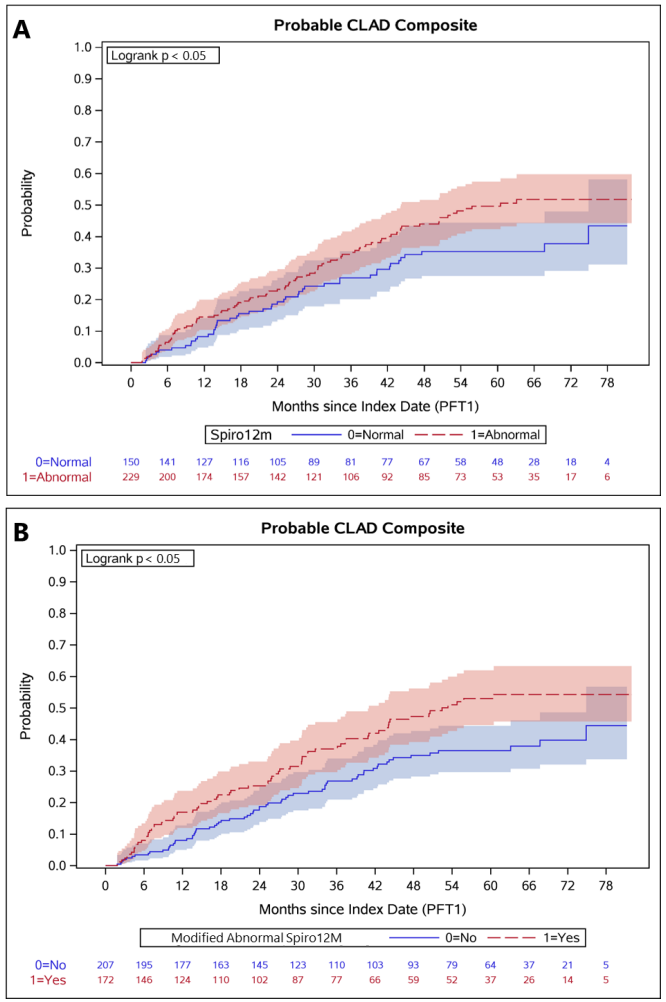
Study Highlights

Objective: To evaluate the association of abnormal spirometry at 12 months post-transplant (Spiro12M), an early definition of baseline lung allograft dysfunction (BLAD), with post-transplant graft loss and chronic lung allograft dysfunction (CLAD) in a multicenter cohort.

Methods: This was a cohort from the multicenter prospective CTOT-20/ES study across 5 North American centers. Spiro12M was defined as the average of two forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) values closest to 12 months post-transplant, taken at least 3 weeks apart. Abnormal Spiro12M was defined as FEV1<80%, FVC<80%, or FEV1/FVC<70% predicted. A modified abnormal Spiro12M required at least 2 of FEV1, FVC, or FEV1/FVC to be abnormal. Multivariable Cox models were used to assess the association of abnormal Spiro12M with graft loss (death or retransplantation), probable CLAD, and a probable CLAD composite outcome (probable CLAD or CLAD-related death or retransplant).

Results: 517 patients met inclusion criteria, 229 (60.4%) bilateral (BLTx) and 109 (79%) single lung (SLTx) transplants had normal Spiro12M. In BLTx, abnormal Spiro12M was associated with an increased risk of probable CLAD composite (HR, 1.58; 95% CI, 1.09, 2.29; p=0.015). In BLTx, modified abnormal Spiro12M was associated with probable CLAD (HR, 1.70; 95% CI, 1.15, 2.52; p=0.008), probable CLAD composite (HR, 1.82; 95% CI, 1.25, 2.65; p=0.002), and graft loss (HR, 1.68; 95% CI, 1.14, 2.48; p=0.009). In SLTx, abnormal Spiro12M was not associated with probable CLAD, probable CLAD composite, or graft loss.

Conclusions: Spiro12M and modified Spiro12M are reproducible, clinically relevant definitions that can prospectively identify BLTx at risk for CLAD.



Abnormal Spiro12M (A) and modified abnormal Spiro12M (B) was associated with Probable CLAD composite

Author's Comments

- Our results suggest that Spiro12M is an objective measure of lung function after lung transplantation that can help identify BLTx recipients at risk for CLAD.
- Abnormal Spiro12M may be useful for enriching studies that evaluate the development of CLAD or preventative interventions as it can be measured prospectively.
- These findings do not support using the abnormal Sprio12M definition in SLTx recipients, which given the concomitant contributions of donor and native lungs as well as changes in chest wall mechanics would likely have a different relationship with lung function over time.

Limitations

- Unable to further define CLAD phenotypes due to missing lung volume and/or imaging data.
- Follow up period of only 5.8 years for evaluation of our outcomes, where the original study had a longer follow up.
- Limited information on potential alternative causes of reduced spirometry.
- Patients excluded for not having FEV1 and FVC at 12 months, which may increase the risk of selection bias.
- Further evaluation with the ISHLT consensus BLAD definition is needed.

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Tiling 16S rRNA Gene Amplicon Sequencing Identifies Bacterial Species Soon After Lung Transplant That Predict Acute Cellular Rejection

Jesudasen S, Haghnazari D, Minsik K, Brenner LN, et al. *Transplantation* 2026; 110(4):p e923-e928. | DOI: 10.1097/TP. 0000000000005599

Study Highlights

Background

- Lung transplant (LTx) alters the pulmonary microbiome with subsequent associations to outcomes such as primary graft dysfunction, acute cellular rejection (ACR), and chronic lung allograft dysfunction
- Most pulmonary microbiome studies are limited to genus-level identification through 16S rRNA sequencing methods, due to limitations from bacterial biomass and human DNA contamination

Objective

To assess a tiling amplicon sequencing method to discriminate the post-LTx pulmonary microbiome to the species-level, and determine association of specific taxa with ACR

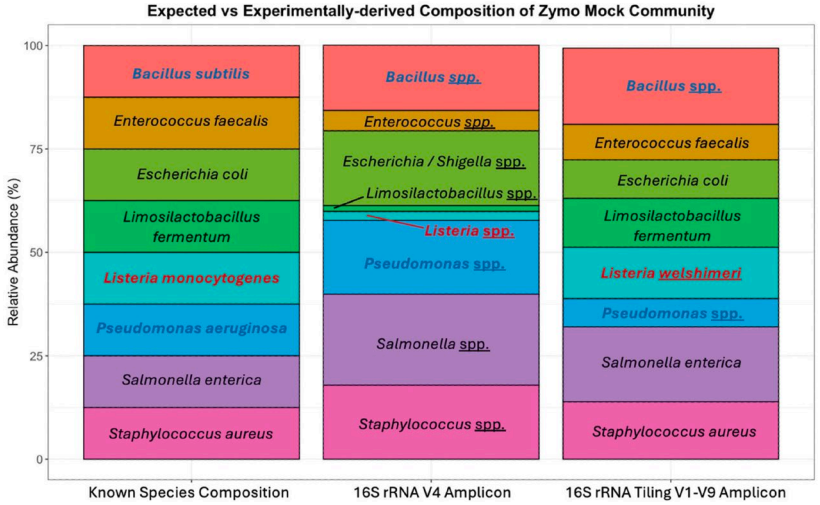
Methods

- N = 23 LTx performed at single USA center 2017-2021
- Zymo mock community control to validate tiling methodology
- Tiling sequencing performed on Zymo community control and bronchoscopy samples collected on average 1 day post-LTx
- ACR defined by grade ≥A2 on any biopsy in first year post-LTx

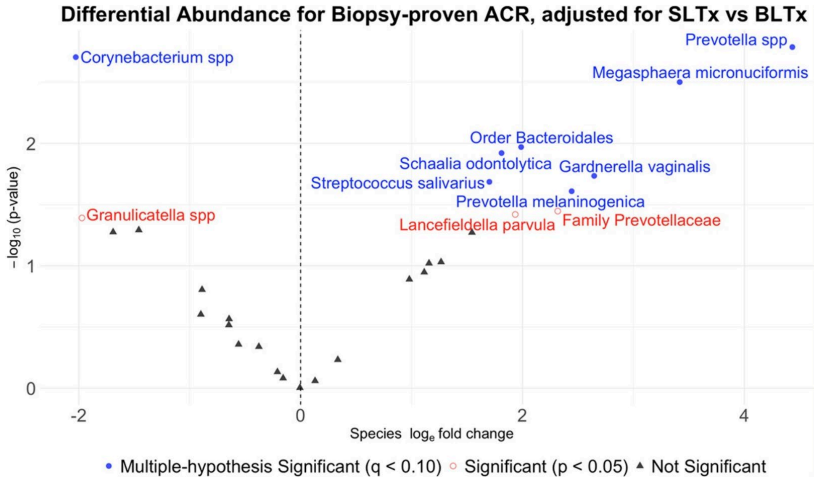
Results

- Tiling method identified 8/8 genera and 5/8 species from Zymo mock community
- Increased oral anaerobes such as *Schaalia odontolytica, Streptococcus salivarius*, and *Prevotella* species, as well as reduced *Corynebacterium* species, were associated with ACR

Tiling Sequencing Recapitulates Positive Control



Oral anaerobes associated with +ACR



Author's Comments

- Species-level identification of the pulmonary bacteriome may distinguish pathogenic species from protective or commensal species
- This paper builds on prior work that identified ↑ Corynebacterium species associated with ↓ ACR, and ↑ Prevotella species associated with ↑ ACR
- Samples were collected prior to initial extubation (on average 1 day post-LTx). Thus, findings that oral anaerobes in the pulmonary bacteriome are associated with ACR may implicate pre-LTx aspiration as a risk factor for ACR
- A sensitivity analysis with a minimum read threshold identified increased Schaalia odontolytica and Prevotella species, and reduced Corynebacterium, were associated with ACR
- Inclusion of contamination analysis (with bronchoscope prewash negative controls), enhances the robustness of the study's findings.

Limitations

- The tiling method recapitulated species in the mock community, though it did mis-identify *Listeria monocytogenes* as *Listeria welshimeri*
- Sample size of n=23 in a single-center study limits power; analysis of a larger cohort across multiple centers would increase generalizability, and may capture additional significant taxa associated with ACR