

Supplementary Online Content

Ghadimi K, Cappiello J, Cooter-Wright M, et al; INSPIRE-FLO Investigators. Inhaled pulmonary vasodilator therapy in adult lung transplant: a randomized clinical trial. *JAMA Surg*. Published online November 17, 2021. doi:10.1001/jamasurg.2021.5856

eMethods. Protocols and Additional Information

eTable 1. Multivariable Model

eTable 2. Adverse Events Separated by Allocated Treatment.

eTable 3. Primary Outcome by Randomization Strata

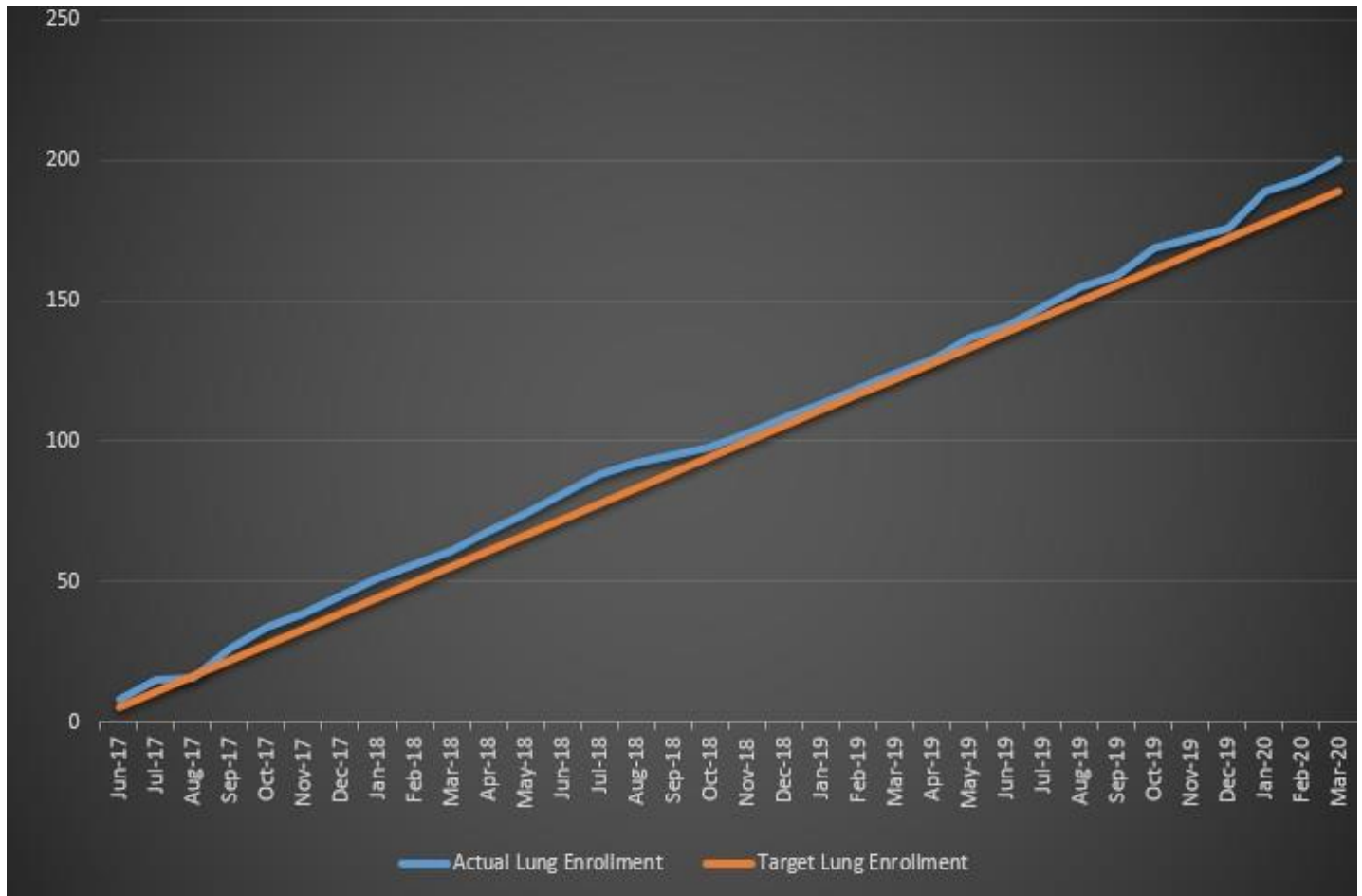
eFigure 1. Time-to-Event Analysis for Duration of Mechanical Ventilation

eFigure 2. Daily Mean Pulmonary Arterial Pressure Values According to Treatment Groups

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Protocols and Additional Information

201 Lung Transplant Recipients



Standard care in Lung Transplantation

Important aspects of standard care that are relevant to this investigation include intraoperative prophylaxis against reperfusion injury through administration of intravenous methylprednisolone 500 mg and mannitol 25 grams prior to reperfusion of each lung allograft. Inhaled pulmonary vasodilation is initiated. Reperfusion is performed in a controlled fashion over a period of 10-15 minutes. Ventilation and lung recruitment are then performed once the organ has been allowed to rewarm along with continued administration of inhaled pulmonary vasodilator treatment. The newly implanted lung is suction-lavaged and placed on mechanical ventilation. Ventilation management is standardized where by pressure-controlled ventilation is utilized to achieve a tidal volume of 4-6ml/kg (predicted body weight). Fraction of inspired oxygen is set at 0.40 with PEEP of 8 cm H₂O, ensuring driving pressures remain below 15 cm H₂O and peak pressures remain less than 30 cm H₂O. Serial arterial blood gas measure allows for monitoring of P:F ratios (PaO₂:FiO₂). Before transport to the ICU, a bronchoscopy is performed to evacuate airway debris, blood and mucous. In the majority of cases, FiO₂ is reduced to 0.30 before leaving the operating on mechanical ventilatory support and inhaled pulmonary vasodilator treatment.

In the event that P:F ratio falls below 300, the FiO₂ is increased by 5% and the PEEP is increased to 10cm H₂O with additional blood gas measures to determine improvement in P:F ratios. In patients with progressive PGD, the FiO₂ requirements will be increased until a maximum of 0.60 is reached. If no improvement in oxygenation is observed after bronchoscopy, then the decision is made by the operating surgeon to initiate ECMO support to augment systemic oxygenation. After ECMO initiation, the FiO₂ delivered from the mechanical ventilator is decreased to 0.21 to minimize oxygen exposure to the airways. Tidal volumes are reduced to 4 ml/kg with PEEP remaining at 10 cm H₂O. The rate is decreased to 10 breaths per minute and the lungs are allowed to rest and recover. Similar protocols and criteria exist for both the operating room and ICU settings. **ECMO management protocols are included in this supplement.**

Sample Adverse Events Log for INSPIRE-FLO Lung Transplant Cohort up to 90-days.

AEs were reviewed each quarter by the PI, research team and the Pharmacy & Therapeutics committee of Duke University Hospital given that both medications were on formulary and were not new drugs under investigation. We remained blinded to assignment, reviewed overall AEs and ensured AEs were comparable with non-study patients each quarter. A DSMB was not required by our IRB as these medications were on formulary and used as part of standard care in non-study patients undergoing lung transplantation.

	Lungs
N	200
In Hospital	200
Atrial Fibrillation	89
Upper GI Bleed	7
Lower GI Bleed	5
Mesenteric Ischemia	2
Intestinal Perforation	3
Pulmonary Hemorrhage	4
Day 30	200
DVT	28
Pulmonary Embolism	6
Other Venous Thromb Disease	14
TIA	2
Stroke	5
Myocardial Infarc	3
Mesenteric Ischemia	2
Other Arterial Thromb Disease	2
^a COVID-19	0
Influenza	1
Day 90	198
DVT	13
Pulmonary Embolism	6
Other Venous Thromb Disease	7
TIA	0
Stroke	0
Myocardial Infarc	3
Mesenteric Ischemia	3
Other Arterial Thromb Disease	0
^a COVID-19	0
Influenza	0

^aCOVID-19 diagnosis added January 2020.

Modified KDIGO Criteria for INSPIRE-FLO Trial

Acute Kidney Injury (AKI) definition

Any time within 7-days after surgery:

- Increase in Serum Creatinine (Cr) by ≥ 0.3 mg/dL within 48 hours; or
- Increase in Cr to ≥ 1.5 times baseline
- Urine output is not included as urine could be under-captured after Foley catheter removal

Modified KDIGO Criteria for INSPIRE-FLO Trial

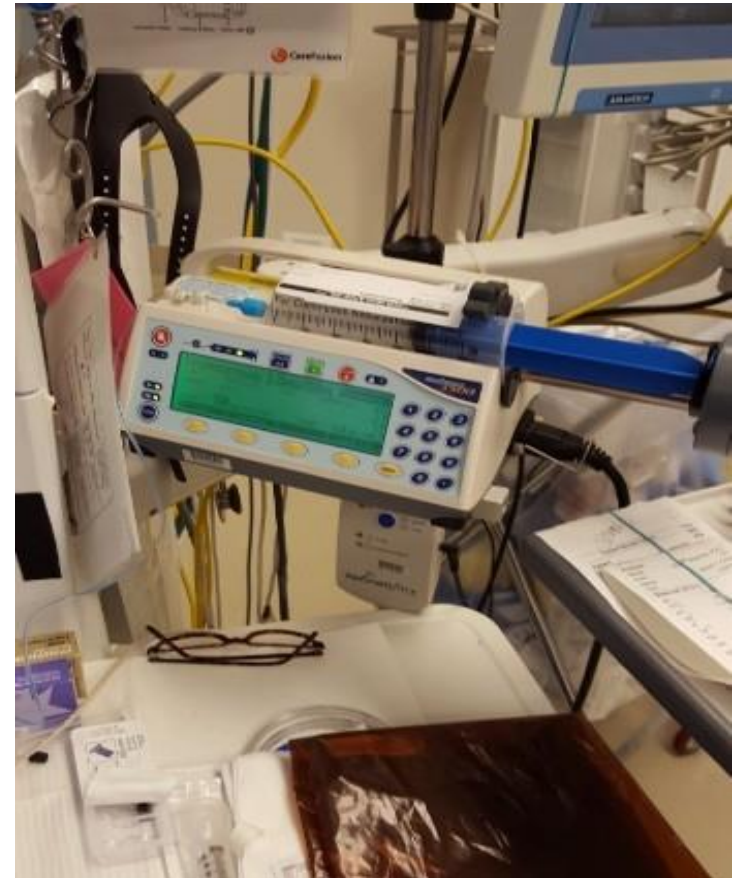
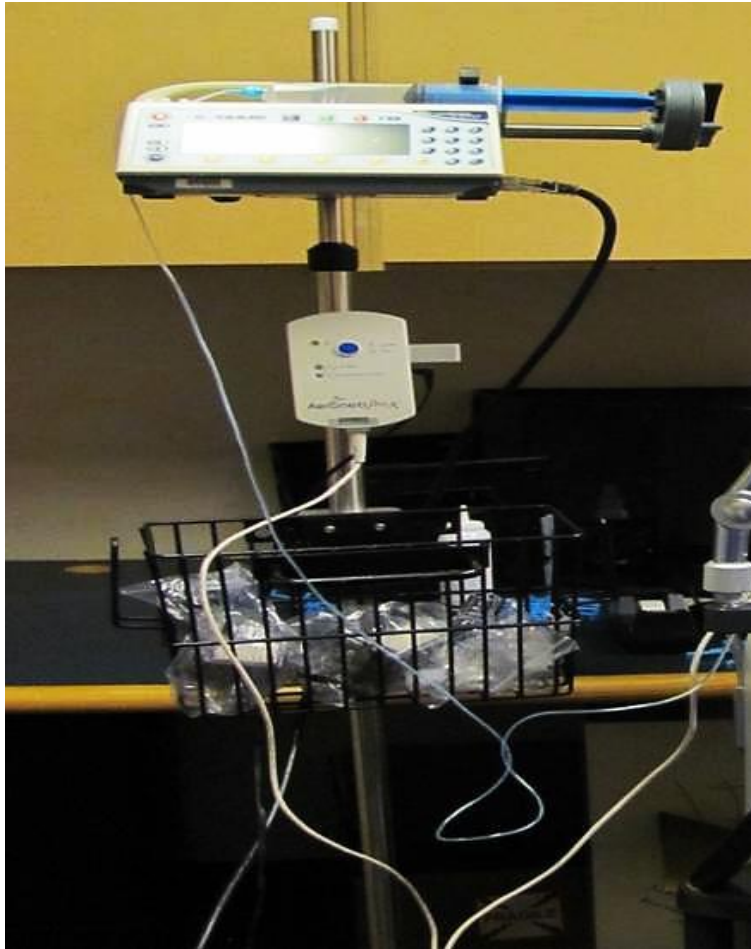
Acute Kidney Injury (AKI) Staging (Age > 18)

Any time within 7-days after surgery:

<u>Stage</u>	<u>Serum Creatinine (Cr)</u>
1	1.5 – 1.9 times baseline Cr <i>or</i> <u>≥0.3 mg/dL increase</u>
2	<u>2.0 – 2.9 times baseline</u>
3	3.0 times baseline <i>or</i> Cr increases to ≥4.0 mg/dL <i>or</i> <u>Initiation of Renal Replacement Therapy</u>

From: *Kidney International Supplements*, OpenArchive,
Volume 2, Issue 1, pp.19-36; Chapter 2.1: Definition and Classification of AKI
<http://dx.doi.org/10.1038/kisup.2011.32>

Intra-operative Epoprostenol



Medfusion Syringe Pump

Components



Aerogen Nebulizer (or Aerosolizer), Tee and power cable



Aerogen Infusion Tubing



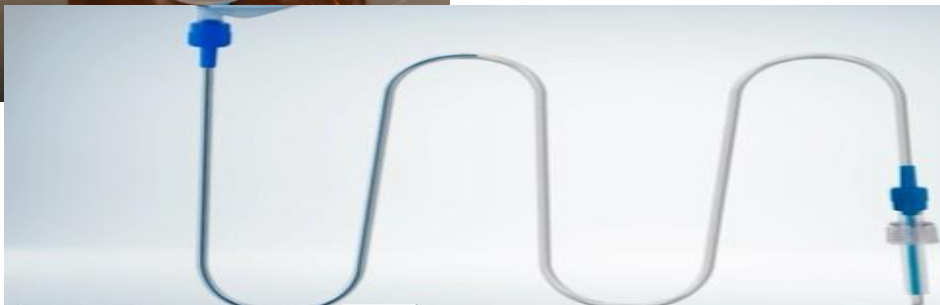
Aerogen Controller



Epoprostenol Syringe (Aerogen Specific)

System set-up

1



Attach Epo syringe to Aerogen tubing and prime (3.5 ml)

2



Place syringe barrel in pump

Infusion Start-up



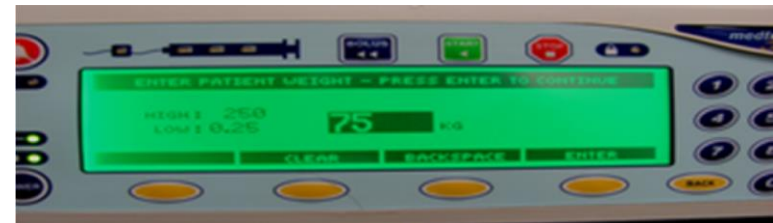
On prompt, press “1” for Respiratory Folder



Press “1” for Epoprostenol Menu



Press yes for concentration (prepared by Pharmacy/label check)



Enter **Ideal Body Weight**

IBW (males) = $50 + 2.3 (\text{height inches} - 60)$

IBW (females) = $45.5 + 2.3 (\text{height inches} - 60)$

Not Actual Weight

Nebulization



Enter starting dose (Always 50 ng/kg/min) Device will not allow a higher dose.



Press Bolus twice. On second press, hold it down to remove mechanical slack of system



Press "Start" to begin drug delivery

Nebulization

Observe nebulization



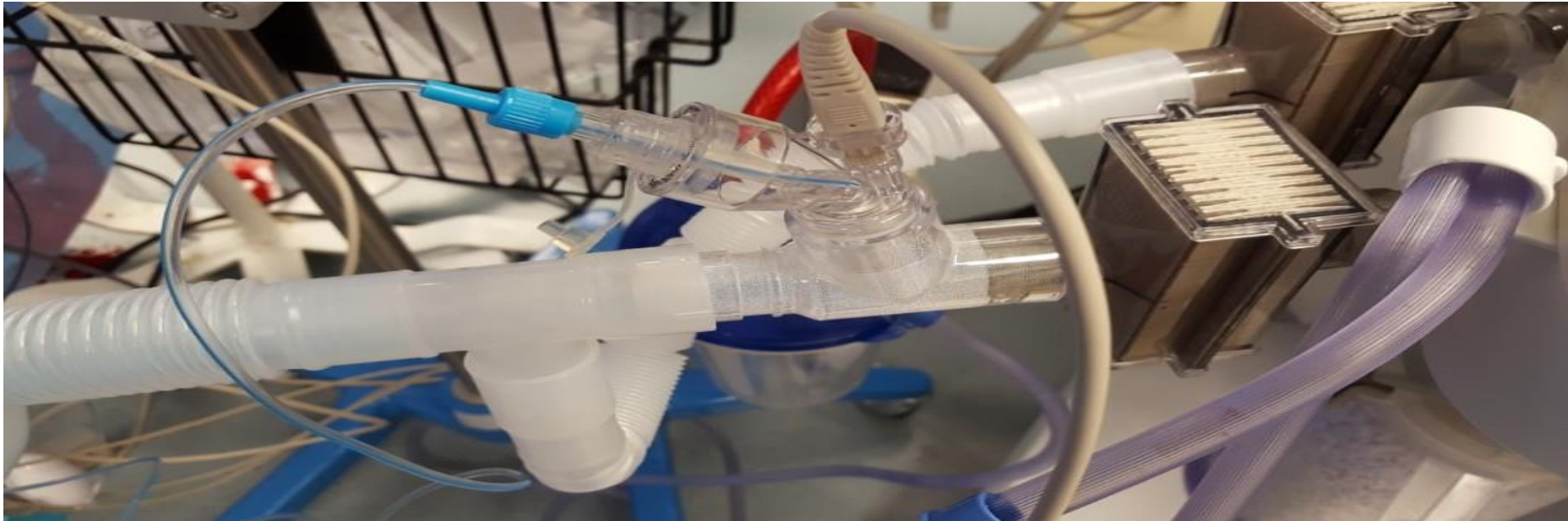
Press and hold “**Blue**” button for 3 seconds. Light for Continuous mode will illuminate



In Circuit



Remove Heat & Moisture Exchange (HME) Filter from the circuit during set up in the operating room



Place device on “Inspiratory Limb” as shown

Trouble-shooting



Yellow Light on Front panel:

Nebulizer chord not communicating with nebulizer

Fix:

- Check connections of chord to nebulizer and unit
- Change nebulizer

30 Min mode light on:

AC power disconnected or unit not placed in Continuous mode

Fix:

- Check AC power connected
- Turn off unit and restart into continuous mode by holding Blue button for three seconds

Troubleshooting



AC Power light not illuminating

- Check AC connection

**Unit will only deliver 30 minute mode if no AC connection. Internal battery life is 30 minutes when fully charged.

Trouble-shooting



Fluid Level in Continuous Aerosolization:
-There should never be more than 0.75-1 ml of fluid in nebulizer. Build-up of this level means there is no nebulization.....Trouble-shoot system.

Trouble-Shooting Review

If No Aerosolization/Nebulization....

- Connections secure?
- Power on? Power cable?
- Continuous mode?
- Change Nebulizer Components

In a quality assurance study (abstract below), we evaluated and optimized our vibrating mesh setup in preparation for iEPO-related protocols implemented during

Continuous Aerosol Medication Therapy in an *in vitro* High-Flow System
Using Wire Mesh Technology

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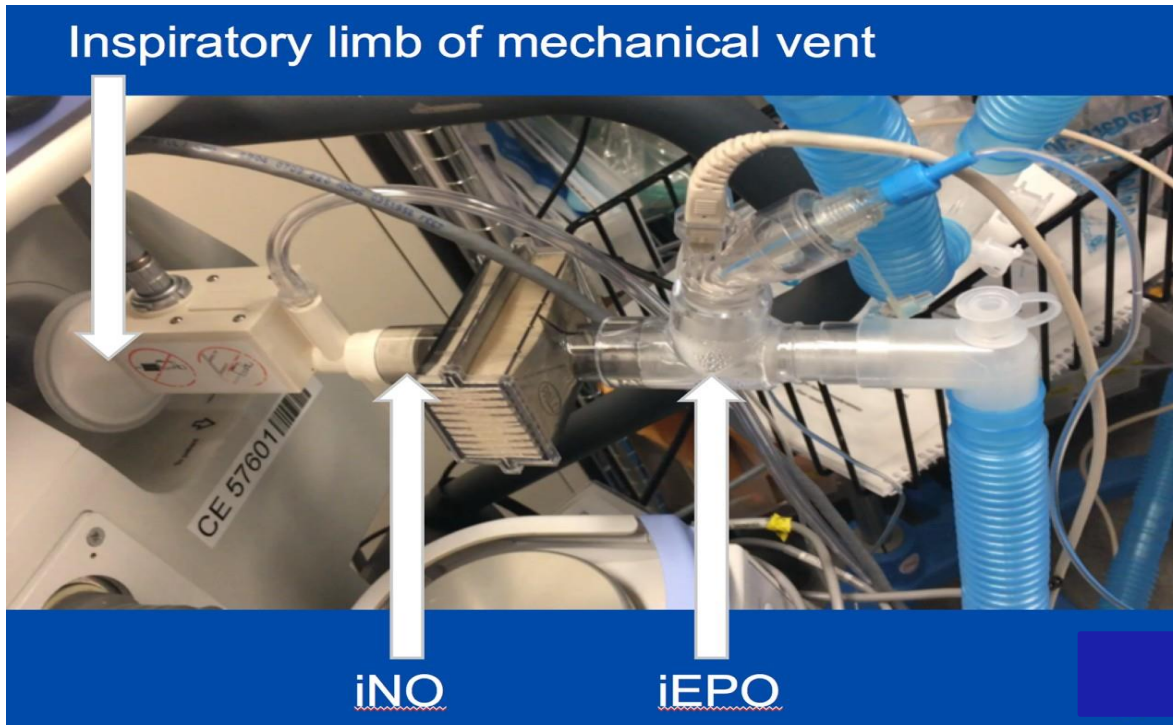
Abstract

BACKGROUND: Jet nebulizers are commonly used to provide continuous aerosolized medication therapy (CAMT). We observed the function of our CAMT system that utilizes the Aeroneb Solo nebulizer system (Aerogen Ltd, Galway, Ireland). **METHODS:** An observational study was performed on 2 CAMT systems with 15 Aeroneb nebulizers for each system. CAMT was simulated for 1, 2 and 3 hours. Continuous nebulization was monitored and residual volumes were recorded at the end of each simulation. Our primary endpoint was established as intermittent nebulization observed by nebulizer filling of > 1 ml during CAMT simulation. Secondary endpoint was a residual volume of < 0.1 ml. **RESULTS:** Out of 30 simulations in two arms, a fluid level was observed to accumulate intermittently in three nebulizers with a residual volume of 0.7 mls in one of these three. This produced a total success rate of 90%, Arm-A 80%, Arm B-100%, for our primary endpoint. Our secondary endpoint was achieved in 29 of the 30 nebulizers for an overall 97% success rate, Arm A-93%, Arm B-100%. **CONCLUSION:** Our Aerogen Solo CAMT system successfully emitted the set dose with 90% accuracy.

Key Words: *continuous albuterol; continuous epoprostenol; residual volume; nebulizer.*

Blinding of Medication Delivery

Blinding of medication delivery for LT patients required injector ports of the iNO delivery device (iNOMax®, Mallinkrodt Pharmaceuticals) and iEPO injector ports from the vibrating mesh aerosolizer (Aerogen Pro-X®, Galway, Ireland) to be placed in series, separated by filter, and attached to a mechanical ventilator (VELA™, Vyair Medical, Mettawa, Illinois) at the inspiratory port (**Figure**). This design was developed and tested in our



facility prior to trial commencement. The screen of the iNO delivery device was masked with a locking mechanism (**red circle**) while the syringe pump (Medfusion 3500, Smiths Medical, Inc., Minneapolis, Minnesota) for delivery of the blinded solution to the vibrating mesh aerosolizer did not have a medication label



and was dialed to deliver 50 nanograms/kg/min of aerosolized blinded solution using ideal body weight. **See separate protocol in this supplement for syringe pump use and dialing medication delivery.**

VV ECMO post-BOLT/SOLT Management Protocol

ECMO Blood Flow

- **Adjust flow to minimum needed to achieve SpO₂ >92% (PaO₂ 70-90), >2LPM ECMO flow**
- **If having sustained flow decreases AND signs of hemodynamic or respiratory instability:**
 - *Adjust patient position*
 - *Assess cannula position*
 - *Consider intravenous fluid (IVF) bolus for sustained low flows resulting in desaturation when patient and cannula malposition ruled out:*
 - IVF bolus with minimum volume required to improve flow, packed red blood cells (PRBC) for Hb<8 or ongoing bleeding

ECMO Sweep Gas

- Sweep gas: 100% FiO₂
- Primary goal is to maintain pH 7.35-7.45. pCO₂ should be titrated to meet this goal
- Secondary goal pCO₂ of 35-45, but may tolerate hypercapnia with pCO₂ up to 60 if pH is within target range

Ventilator Settings

- **Rest ventilator settings:**
 - Pressure-controlled mode ventilation
 - Keep FiO₂ minimum needed
 - Utilize ECMO to increase oxygenation as able
 - Maximum ventilator FiO₂ 60%
 - Goal SpO₂ >92% (PaO₂ 70-90)
 - Starting PEEP = 8 cm H₂O
 - Starting respiratory rate = 8 breaths per minute (BPM)
 - Apply inspiratory pressures to achieve tidal volumes of 4-6ml / kg ideal body weight
 - Inspiratory pressure should not exceed 20 cm H₂O, even if target tidal volumes can not be achieved and total volumes should not exceed 6 ml / kg ideal body weight
 - Plateau pressures should not exceed 30 cm H₂O
- **If unable to achieve goals with specified ventilator and ECMO parameters, contact attending lung transplant surgeon**

VV ECMO post-BOLT/SOLT Management Protocol

Sedation

- Closed Chest: ICU sedation to maintain RASS 0 to -1, wean as tolerated
- Daily sedation vacation
- If sedation or anxiolytics are required for patient comfort, first line agents should be propofol
 - IV narcotic for pain until epidural catheter is placed
- Benzodiazepines should be avoided

Anticoagulation and Transfusion

- per ECMO Anticoagulation policy (see post-op section)
- Population Specific Transfusion Targets:
 - Hemoglobin goal >8.0
 - Plt > 50 (75 for bleeding patient)
 - Fibrinogen >100 (150 for bleeding patient)

Sweep Trial

- Initiate first sweep trial 8 hours after protocol initiation and continue Q8 hr sweep trials x 72 hours
- If a wean trial is deferred, must be discussed with attending and documented
- Ventilator settings during sweep trial to consider decannulation:
 - FiO2 40%
 - Vt 4-6ml/kg ideal body weight
 - Adjust rate to maintain pH and pCO2 goals
 - Inspiratory pressure should not exceed 20 cm H2O, even if tidal volume is < 4 ml/kg
 - Plateau pressure should not exceed 30 cm H2O
- Monitor the following parameters during sweep trial
 - SpO2 > 90%
 - pH 7.35 - 7.45
 - Target pCO2 of 35 - 45, but may tolerate hypercapnia with pCO2 up to 60 if pH is within target range
 - Perform ABG at baseline prior to starting sweep trial but on above vent settings then hourly for a total of 4 hours or at point of failure by other indicators. ABG's drawn more frequently if clinically indicated.
 - Continue sweep trial as tolerated, consider decannulation if tolerated greater than 4 consecutive hours

Venovenous ECMO Management after Bilateral or Single Lung Transplantation

Admission to ICU status-post BOLT/SOLT on VVECMO

Is there ongoing evidence of **bleeding** or **active resuscitation effort**?

NO

YES

Chest X-ray shows extensive infiltrates involving the lung allograft?

NO

YES

- Check PT, APTT, Fibrinogen, platelets and correct with blood products as necessary to achieve goals above
- Assess the need for operative re-exploration
- Assess bleeding and resuscitation effort every 2hrs

Bleeding stopped

Patient adequately resuscitated

- Begin to wean ventilator to rest settings
- Assess daily for ability to liberate from the ventilator and manage patient with prolonged ambulatory VV ECMO
- Consider upper body VVECMO configuration (eg. Left subclavian Avalon cannula) if not already in place
- Tracheostomy no later than ECMO day 3; ASAP for patients entering from protocol arm

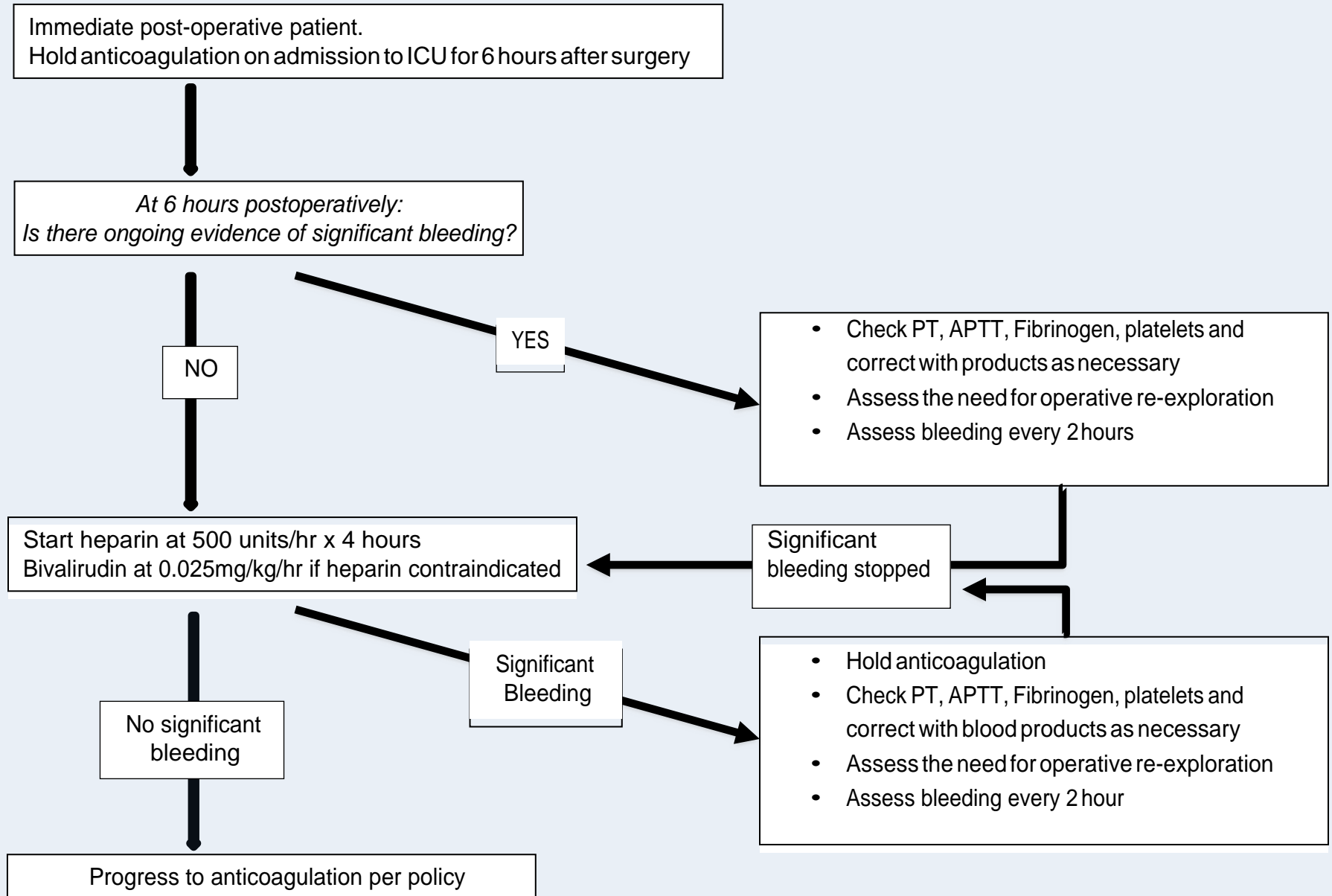
VVECMO management per s/p BOLT/SOLT VV ECMO Protocol (see pages 1-2)

Patient decannulated from VV ECMO

Sweep trials unsuccessful at 72 hours post-protocol entry

Initiate daily sweep trials when evidence of improved allograft function and patient stability

Flowchart 1: Adult ECMO Anticoagulation Algorithm for Immediate Postoperative Patients:



Anticoagulation during Extracorporeal Membrane Oxygenation

Definitions	
ECMO	Extracorporeal Membrane Oxygenation; aka ECLS or Extracorporeal Life Support
Pediatric Patient	A pediatric patient will be defined as any patient being cared for in Children's Services regardless of age.
Adult Patient	An adult patient will be defined as any patient being cared for by an Adult Service regardless of age. In the non-cardiac operating room, a patient cared for by Adult Services Surgeon or Adult Services Anesthesia team who will be transferred to a pediatric area post-operatively will be defined as a pediatric patient.
Initiation of ECMO	
<ul style="list-style-type: none"> • *Prior to cannulation on the order of the Cannulating Surgeon, 50units/kg of heparin administered to the patient up to a total max dose of 5000 units of heparin for adult patients. CONFIRM DOSE AND ADMINISTRATION WITH SURGEON AND PERFUSIONIST/ECMO SPECIALIST. • 100 units of heparin will be administered to the ECMO prime for blood primed circuits. • DO NOT HEPARINIZE SURGICAL IRRIGATION FOR NEONATAL/INFANT ECMO CANNULATION. • If HITT positive, 0.5mg/kg Bivalirudin bolus 	
Neonatal and Pediatric Anticoagulation	Adult Anticoagulation
<p>IMMEDIATELY POST-INITIATION:</p> <ul style="list-style-type: none"> • Start Heparin: <25kg= 25units/kg/hour; ≥25kg= 15units/kg/hour unless otherwise ordered. • Start platelet transfusion 20ml/kg for all patients less than 12 months old • Send full coagulation labs: aPTT, PT/INR, ATIII, heparin level, fibrinogen, platelet (CBC) <ul style="list-style-type: none"> –If Fibrinogen <100 give 10ml/kg Cryo. –If Platelets <75 in patients >12mo old, give 20ml/kg Platelets (max 1 unit). –If Fibrinogen and platelets normal and INR>2, give 20ml/kg FFP (max 1 unit). –If INR <2 and ATIII<50% give one vial Thrombate. • If any replacement given, resend coags in 1 hour. Recheck for neonates/infants after platelet infusion complete. • For surgical ECMO cases, hold heparin infusion up to 6 hours. Discuss and document criteria to be met prior to starting ECMO anticoagulation. Assess patient Q2 hours until criteria met <ul style="list-style-type: none"> ○ Start anticoagulation per above when criteria met <p>COAG LAB SCHEDULE FIRST 24 HOURS:</p> <ul style="list-style-type: none"> • aPTT, Heparin Level, STAT Platelet Q6 <p>ROUTINE ECMO COAG LABS</p> <ul style="list-style-type: none"> • Q6- aPTT • Q12- platelet count (CBC or HCT/Plat) • Q24- Heparin Level, PT/INR, Fibrinogen, ATIII STAT (x2 and PRN), PFHB 	<p>IMMEDIATELY POST-INITIATION:</p> <ul style="list-style-type: none"> • Start Heparin: 15 units/kg/hr (max starting dose 1200 units/hr) if no bleeding contra-indication • Correct known factor and platelet deficiencies • Send full coagulation labs: aPTT, PT/INR, ATIII, heparin level, fibrinogen, platelet (CBC) <ul style="list-style-type: none"> –If Fibrinogen <100 consider Cryo transfusion. –If Platelets <75 consider Platelet transfusion. –If Fibrinogen and platelets normal and INR remains>2, consider ROTEM testing and potentially FFP transfusion. –If INR <2 and AT<50% and evidence of heparin resistance consider Thrombate administration. • If any products/replacement given, resend coags in 1 hour. • For surgical ECMO cases see FLOWCHART 1: Adult ECMO Anticoagulation Algorithm for Immediate Postoperative Patients. <p>ROUTINE ECMO COAG LABS</p> <ul style="list-style-type: none"> • Q6- aPTT • Q12- platelet count (CBC or HCT/Plat)

ROUTINE HEPARIN TITRATION 15-50units/kg/hr

- Neonates/Infants: aPTT 80-100sec
- >12months: aPTT 60-80sec
- INCREASE OR DECREASE HEPARIN DRIP BY 10-20% TO ACHIEVE aPTT GOAL
- Ideal Heparin Level (anti-Xa): 0.4-0.7
- Fibrinogen>100 (150 for high bleed risk); If Fibrinogen low give 10ml/kg Cryo.
- Platelets>75 (100 for high bleed risk); If platelets low give 20ml/kg Platelets.
- Hb>8; if Hb low give 20ml/kg RBC (for every two RBC transfusions, give one FFP transfusion (20ml/kg))
- INR<2; If high, give 20ml/kg FFP.
- ATIII>50%, if ATIII low and aPTT low discuss FFP vs. ATIII.
- PFHb <300; if PFHB high, recheck and consult perfusion regarding possible pump change

HEPARIN RESISTANCE: >40units/kg/hr + aPTT low + HEP LEV low + INR<2+ ATIII<70% = GIVE 1 VIAL THROMBATE;
–if above and INR>2, give 20ml/kg FFP and recheck prior to THROMBATE administration

COAG DISCREPANCY: aPTT>100 + HEP LEV <0.3 = GIVE 20ml/kg FFP
–Recheck LABS in 1 hour after Thrombate or product administration
–Send **ROTEM** if above algorithm not working, to evaluate platelet function, confirm aPTT results, and distinguish coagulopathy from surgical bleeding and consult ROTEM expert for interpretation.
–*Hep levels can be falsely *depressed* by hyperbilirubinemia and high PFHB.

HEPARIN TITRATION ADULT ARDS VV ECMO: SEE ADULT ARDS VV ECMO PROTOCOL.

- aPTT 40-50s

HEPARIN TITRATION REMAINING ADULT ECMO PATIENTS

- Target aPTT 50-70sec unless otherwise ordered
- Titrate heparin gtt in 10% increments Q6 hours to achieve aPTT goals
- Send "Heparin Level" AntiXa as warranted, goal range 0.4- 0.7
- Hemoglobin goal ≥ 7.0 g/dL, plt goal ≥ 75 , fibrinogen goal ≥ 100 , INR <2.0 unless otherwise ordered; see specific patient population ECMO protocols
- Send STAT ATIII level if heparin resistance suspected, treat with Thrombate or FFP if ATIII <50% and clinically warranted after discussion with attending physician.

Additional Information

- Heparin Alternatives
 - Consider Heparin Alternatives in patients with demonstrated heparin resistance.
 - For acute drop in platelet count of 50% or greater not as a result of hemodilution, consider HITT and send HITT panel. (Consider consult with Pediatric Hem/Onc 970-6491 or Adult Coagulation Service 970-1526). If highly suspicious of HITT, stop heparin, start DTI.
- Bivalirudin
 - Titrate based on aPTT to goal. DC Heparin level and ATIII labs.
 - Bolus dose for cannulation/initiation of ECMO is 0.5mg/kg
 - Consult pharmacist and coagulation service for continued use.
 - Maintenance infusion rate 0.05mg/kg/hr and titrate in 10% increments to achieve desired aPTT. DC Heparin Level and ATIII labs.
- Argatroban
 - Consider as a heparin alternative for patients with renal dysfunction.
 - Consult pharmacist and coagulation service for use.
 - Titrate based on aPTT to goal. DC Heparin level and ATIII labs.
- Thrombate Dosing:
 - Round dosing up to full vials
- Antifibrinolytic Therapy
 - Aminocaproic acid and tranexamic acid use has been safely reported in ECMO patients.
- Platelet administration
 - Do not increase heparin infusion for platelet administration
- Plasmapheresis and CVVHD
 - Do not arbitrarily increase/decrease heparin for plasmapheresis or CVVHD.
 - If coag labs due during plasmapheresis, hold and draw one hour after completion.
 - Only citrate should be used for plasmapheresis and CVVHD anticoagulation.

- Consider ATIII replacement if plasmapheresis replacement volume used was Albumin.
- Bleeding
 - Consider sending ROTEM to distinguish sources of coagulopathy
 - Bleeding patients may require a cooler of blood at the bedside
 - Cannula and wound site bleeding should be assessed by surgical team
 - DO NOT USE HEMOSTATIC AGENTS ON CANNULA SITE
- Factor VII and PCC Replacement:
 - Indication- life threatening hemorrhage unresponsive to more conventional therapies
 - The coagulation service must be notified prior to administering this drug. Page Peds Heme/Onc 970-6491 or Coagulation Service 970-1526. The coagulation service must approve the use of this drug and will recommend proper dosing- notify that patient is on ECMO- typical dosing is in slow, small increments.
 - Prior to administering clotting factors, the following steps must be taken:
 - Have back up ECMO pump at bedside.
 - For pediatric patients order blood products sufficient for re-initiating ECMO to a cooler: 2 units PRBCs, 1 unit FFP (in cooler), 20 ml/kg of platelets (minimum 50 ml: max 1 unit)
 - An ECMO surgeon and perfusionist must be in the hospital and available to respond in case an emergency arises.
 - ICU attending physician must be present at bedside.
 - Do not administer this medication to the ECMO pump.
 - Continuously monitor patient and ECMO pump for signs and symptoms of clotting.

Safety

Blood Product Administration Safety

- **Two licensed professionals (MD, RN, LPN/MLPN, CRNA, NP, PA, Respiratory Therapist [ECMO], or Perfusionist) may verify and/or administer blood. In the OR, the 2nd person verifying blood (not administering) may be an anesthesia technician.**
- **Discuss all transfusion triggers and potential exposures for transplant candidates and post-transplant patients with primary team.**
- **Recommended massive transfusion blood product ratio: (1 dose PRBC : 1 dose FFP) x4 then 1 dose cryo + 1 dose platelets**

Heparin Administration Safety

- **ECMO Heparin Drip**
 - **Only standard heparin infusion bag for ECMO (25,000 unit heparin in 250 ml D5W pre-mix) will be used.**
 - **The site of the heparin infusion may be:**
 - **ECMO circuit for neonatal/pediatric patients with limited access.** Heparin administration via ECMO access FOR NEONATAL/PEDIATRIC PUMPS:
 - Only an ECMO Specialist or Perfusionist will attach drips to the ECMO Circuit, RN will prepare drip, set infusion rate, and document
 - **Patient access for all other patients.**
 - Heparin administration via patient access per unit policy.
 - See Nursing Standards.
 - *Heparin titration only by provider order
 - *A new provider order is required to hold heparin or restart heparin.
 - During ECMO, all intravenous fluids given to the patient are typically changed to non-heparinized solutions including the patient's arterial line(s).

Organ Procurement and Transplantation Network

LAS Calculator

Home » Resources » Allocation Calculators » LAS Calculator

Patient Safety

Allocation Calculators

CPRA Calculator

EPTS Calculator

KDPI Calculator

LAS Calculator

MELD Calculator

PELD Calculator

By Organ

Kidney & Pancreas

Liver & Intestine

Heart & Lung

Vascular Composite Allograft

Organ Transport

Living Donation

Pediatric transplant

Informing Patients

Ethics

Guidance

Calendar of Events

Calendar archive

Glossary

COIIN

This calculator uses the same formula as the UNet system which is used by transplant centers to calculate lung allocation scores for patients in need of a lung transplant.

How the calculator should be used

The LAS calculator is a tool that can be used to estimate each lung candidates' medical urgency and expected post-transplant survival rate relative to other patients on the waiting list for a lung transplant.

What the calculator isn't...

The LAS calculator cannot accurately predict how long any patient will live with or without a transplant. It is not a definitive measure of life expectancy on the waiting list or post-transplant survival. It does not include all factors that influence survival and does not take into account any quality-of-life benefit patients may receive from transplantation.

Talk to your physician or your transplant team about your specific situation.

How to calculate an approximate lung allocation score (LAS)

Enter as much data as you can. If you do not know the value for an entry, leave the field blank and a policy default value will be used when calculating the LAS.

Did You Know?

Access more lung allocation system resources on the United Network for Organ Sharing (UNOS) website.

[Go](#)

i LAS results should not be considered definitive; they are merely a snapshot based upon the values entered and can vary daily.

Date of Birth * (mm/dd/yyyy)

Height * ft in cm Weight * lbs kg

Lung diagnosis code *

Functional status

Diabetes

Assisted ventilation

Requires supplemental O₂

Predicted FVC Percentage (%) 6-minute walk distance (feet)

Pulmonary Artery Systolic Pressure (mmHg) Mean Pulmonary Artery Pressure (mmHg)

Cardiac index (CI) (L/min/m²) Central venous pressure (CVP) (mmHg)

i If using a central venous test value for PCO₂ subtract 6 mmHg before entering the value.

PCO₂ (mmHg)

Current

Highest

Lowest

Serum Creatinine (mg/dL)

Current

Highest

Lowest

Total Bilirubin (mg/dL)

Current

Highest

Lowest

[Reset](#)



Electronic Health Record at Duke Health

<https://medschool.duke.edu/research/clinical-and-translational-research/duke-office-clinical-research/clinical-research-resources-and-applications/docr-maestro-care-training>

Maestro Care (Epic) is the unified electronic medical record and clinical care application for Duke Health. Epic go-live deployment for all of Duke Health was completed in June 2013 and is the primary health record application at Duke University Hospital, Duke Children's Hospital, Duke Regional Hospital, Duke Raleigh Hospital, Duke Primary Care Physicians Network, and all affiliates of Duke Health.

The goal of Maestro Care at Duke Health is to provide one system unifying all health record information for the patient and accessible to all members of the Duke Health care team. One patient, one record and one bill for each patient at all locations to improve efficiency and information sharing for our providers and staff to ensure the best possible care for our patients.

In May 2018, Maestro Care integrated with OnCore as the system-wide CRMS (Clinical Research Management System). Clinical research data relevant to patient care should be in Maestro Care and viewable by the extended care team just like other clinical data.



Citing REDCap

Please cite the publication below in study manuscripts when using REDCap for data collection and management. We recommend the following boilerplate language:

Study data were collected and managed using REDCap electronic data capture tools hosted at Duke University.¹ REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

¹Paul A. Harris, Robert Taylor, Robert Thielke, Jonathon Payne, Nathaniel Gonzalez, Jose G. Conde, Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support, *J Biomed Inform.* 2009 Apr;42(2):377-81.

Link to article: <http://www.sciencedirect.com/science/article/pii/S1532046408001226>.

Multivariable Model including variables with P<0.15 from Table 1 and Table 2.

eTable 1. Multivariable Model

Multivariable Model	Full Model		Selected Model	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Effect				
Group iEPO vs iNO	1.27 (0.67, 2.25)	0.508	1.22 (0.67, 2.20)	0.518
Preop Creatinine	2.71 (0.68, 11.18)	0.161	--	
Preop Cardiac Index	1.19 (0.68, 2.08)	0.543	--	
Preop Mean PAP	1.01 (0.97, 1.05)	0.613	--	
Donor Recip Sex Mismatch M to F vs Matched	3.42 (1.31, 9.50)	0.014	2.86 (1.12, 7.69)	0.031
Donor Recip Sex Mismatch F to M vs Matched	1.40 (0.62, 3.16)	0.411	1.46 (0.66, 3.19)	0.346
Delayed Chest Closure YES v NO	^a 2.48 (0.95, 6.85)	0.069	^a 2.95 (1.17, 7.91)	0.025
Model AIC	275.411		273.046	

^aIndicates Odds Ratio of delayed chest closure occurrence for the development of the primary outcome in our cohort.

Baseline Characteristics (from Table 1) with p-values

	iNO (N=98)	iEPO (N=103)	Total (N=201)	p-value
Patient Demographics and History				
Age	64 [54, 68]	64 [51, 69]	64 [52, 68]	0.561 ¹
Gender (Male)	59 (60.2%)	70 (68.0%)	129 (64.2%)	0.252 ²
Race				0.715 ²
Caucasian/White	83 (84.7%)	91 (88.3%)	174 (86.6%)	
African American	12 (12.2%)	9 (8.7%)	21 (10.4%)	
Other	3 (3.1%)	3 (2.9%)	6 (3.0%)	
BMI	25.0 [22.1, 26.7]	26.0 [22.8, 27.3]	25.5 [22.5, 27.0]	0.286 ¹
Previous Sternotomy for Cardiac Surgery	4 (4.1%)	2 (1.9%)	6 (3.0%)	0.373 ²
Previous Lung Transplantation	6 (6.1%)	4 (3.9%)	10 (5.0%)	0.466 ²
HTN	48 (49.0%)	43 (41.7%)	91 (45.3%)	0.303 ²
PH Diagnosis	42 (42.9%)	54 (52.4%)	96 (47.8%)	0.175 ²
Severity of PH				0.552 ²
Mild	6 (14.3%)	7 (13.0%)	13 (13.5%)	
Moderate	29 (69.0%)	33 (61.1%)	62 (64.6%)	
Severe	7 (16.7%)	14 (25.9%)	21 (21.9%)	
Diabetes Mellitus	17 (17.3%)	25 (24.3%)	42 (20.9%)	0.227 ²
COPD	34 (34.7%)	45 (43.7%)	79 (39.3%)	0.192 ²
Preoperative LVEF (%)				0.394 ²
Normal >50	94 (100.0%)	100 (98.0%)	194 (99.0%)	
Mild Dysfunction (40-49)	0 (0.0%)	1 (1.0%)	1 (0.5%)	
Moderate Dysfunction (30-39)	0 (0.0%)	1 (1.0%)	1 (0.5%)	
Primary Indication for Transplant				0.660 ²
Obstructive lung disease	21 (21.4%)	21 (20.3%)	42 (20.9%)	
Pulmonary vascular disease	2 (1.9%)	1 (1.0%)	3 (1.3%)	
Infectious lung disease	8 (8.2%)	15 (14.6%)	23 (11.4%)	
Restrictive lung disease	63 (64.2%)	63 (61.2%)	126 (62.3%)	
Other	4 (4.1%)	3 (2.9%)	7 (3.4%)	
Preoperative Labs				
eGFR*	85 [70, 98]	88 [75, 100]	87 [73, 98]	0.158 ¹
Hemoglobin	12.30 (1.65)	12.57 (1.73)	12.44 (1.69)	0.269 ³
Creatinine	0.9 [0.7, 1.0]	0.9 [0.7, 1.0]	0.9 [0.7, 1.0]	0.087 ¹

Right Heart Catheterization Variables				
CI	2.8 [2.5, 3.2]	2.9 [2.7, 3.3]	2.9 [2.6, 3.3]	0.085 ¹
Mean PAP	22.8 [18.3, 27.7]	24.7 [20.0, 29.7]	23.7 [19.7, 28.7]	0.086 ¹
Donor Characteristics				
Age (years)	35 [26, 46]	35 [27, 47]	35 [27, 46]	0.944 ¹
Sex donor-recipient mismatch				0.065 ²
Matched	78 (79.6%)	69 (67.0%)	147 (73.1%)	
F Donor – M Recipient	6 (6.1%)	16 (15.5%)	22 (10.9%)	
M Donor – F Recipient	14 (14.3%)	18 (17.5%)	32 (15.9%)	
Race				0.944 ²
Caucasian/White	72 (73.5%)	74 (71.8%)	146 (72.6%)	
African American/Black	16 (16.3%)	17 (16.5%)	33 (16.4%)	
Other	10 (10.2%)	12 (11.7%)	22 (10.9%)	
BMI donor-recipient % mismatch	-4.5 [-20.4, 10.0]	-7.5 [-20.3, 7.2]	-6.6 [-20.3, 7.9]	0.348 ¹
Donor P:F ratio	443 [396, 494]	425 [378, 495]	430 [388, 494]	0.588 ¹
Donor cigarette use >20 pack years	11 (11.5%)	10 (9.7%)	21 (10.6%)	0.688 ²
DCD Donor	10 (10.2%)	13 (12.6%)	23 (11.4%)	0.591 ²
Cause of Death				0.665 ²
Anoxia	33 (33.7%)	30 (29.1%)	63 (31.3%)	
CVA/Stroke	26 (26.5%)	29 (28.2%)	55 (27.4%)	
Head Trauma	37 (37.8%)	41 (39.8%)	78 (38.8%)	
CNS Tumor	1 (1.0%)	0 (0.0%)	1 (0.5%)	
Other	1 (1.0%)	3 (2.9%)	4 (2.0%)	
Ischemia time – Single OLT only	325 [304, 353]	325 [261, 340]	325 [293, 350]	0.462 ¹
Ischemic time – 2 nd Lung BOLT only	395 [349, 489]	432 [352, 495]	415 [349, 492]	0.346 ¹
Use of Transmedics Device/EVLP	4 (4.1%)	3 (2.9%)	7 (3.5%)	0.652 ²
Transplant Characteristics				
LAS score	42.0 [36.9, 51.9]	42.8 [37.2, 52.4]	42.8 [37.1, 52.2]	0.433 ¹
Class 1 PRA > 0	17 (17.3%)	17 (16.5%)	34 (16.9%)	0.874 ²
Class 1 PRA % (among those >0)	17 [7, 75]	29 [17, 57]	28 [7, 62]	0.629 ¹
Class 2 PRA > 0	13 (13.3%)	13 (12.6%)	26 (12.9%)	0.892 ²
Class 2 PRA % (among those >0)	38 [26, 49]	30 [22, 40]	35 [22, 43]	0.280 ¹
Transplant Type				0.887 ²
BOLT	84 (85.7%)	89 (86.4%)	173 (86.1%)	
SOLT	14 (14.3%)	14 (13.6%)	28 (13.9%)	
Randomization Strata Diagnosis				0.9565 ²
SOLT Restrictive Lung Disease	14 (14.3%)	14 (13.6%)	28 (13.9%)	
BOLT Obstructive Lung Disease	26 (26.5%)	31 (30.1%)	57 (28.4%)	
BOLT Restrictive Lung Disease	52 (53.1%)	53 (51.5%)	105 (52.2%)	
BOLT Pulmonary arterial hypertension	2 (2.0%)	1 (1.0%)	3 (1.5%)	
BOLT Other	4 (4.1%)	4 (3.9%)	8 (4.0%)	
Concurrent Cardiac Surgery	7 (7.1%)	7 (6.8%)	14 (7.0%)	0.923 ²
Intraoperative CPB used	19 (19.4%)	19 (18.4%)	38 (18.9%)	0.865 ²
Intraoperative ECMO Used	33 (33.7%)	27 (26.2%)	60 (29.9%)	0.248 ²
*preop EGFR calculated via formula for CKD Epi Creatinine				
P-Value Key: 1Wilcoxon 2Chi-Square 3Equal Variance T-Test				

eTable 2. Adverse Events Separated by Allocated Treatment

	iNO (N=98)	iEPO (N=103)	Total (N=201)	<i>P</i> value
In Hospital				
Any Adverse Event in hospital	45 (45.9%)	55 (53.4%)	100 (49.8%)	0.324
Pulmonary Hemorrhage while on iPVD	2 (2.0%)	2 (1.9%)	4 (2.0%)	>0.999
^a Maximum MetHb within 72h (%)	2.2 [2.0, 2.5]	1.7 [1.6, 2.0]	2.0 [1.7, 2.3]	<0.001 ^b
^a Median MetHb within 72h (%)	1.5 [1.3, 1.7]	1.1 [0.9, 1.3]	1.3 [1.1, 1.6]	<0.001 ^b
Post-op Atrial Fibrillation	39 (39.8%)	50 (48.5%)	89 (44.3%)	0.256
Recurrent Atrial Fibrillation	27 (29.7%)	32 (32.7%)	59 (31.2%)	0.754
Upper GI Bleeding	2 (2.0%)	5 (4.9%)	7 (3.5%)	0.446
Lower GI Bleeding	1 (1.0%)	4 (3.9%)	5 (2.5%)	0.370
Mesenteric Ischemia	2 (2.0%)	0 (0.0%)	2 (1.0%)	0.237
Intestinal Perforation	0 (0.0%)	3 (2.9%)	3 (1.5%)	0.247
30-Day Follow-Up				
Venous Thromboembolic disease (DVT/PE)	20 (19.4%)	14 (8.7%)	28 (13.9%)	0.259
^c Venous Thromboembolic disease (Other)	10 (10.2%)	4 (3.9%)	14 (7.0%)	0.099
Arterial Thromboembolic disease (TIA)	0 (0.0%)	2 (1.9%)	2 (1.0%)	0.498
Arterial Thromboembolic disease (CVA/Stroke)	4 (4.1%)	1 (1.0%)	5 (2.5%)	0.203
Arterial Thromboembolic disease (MI)	1 (1.0%)	2 (1.9%)	3 (1.5%)	>0.999
Arterial Thromboembolic disease (Mesenteric Ischemia)	1 (1.0%)	1 (1.0%)	2 (1.0%)	>0.999
Arterial Thromboembolic disease (Other)	0 (0.0%)	2 (1.9%)	2 (1.0%)	0.498
90-Day Follow-up				
Venous Thromboembolic disease (DVT/PE)	11(7.3%)	10(6.9%)	14 (7.1%)	0.819
^c Venous Thromboembolic disease (Other)	3 (3.1%)	4 (3.9%)	7 (3.5%)	>0.999
Arterial Thromboembolic disease (TIA)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Arterial Thromboembolic disease (CVA/Stroke)	0 (0.0%)	1 (1.0%)	1 (0.5%)	>0.999
Arterial Thromboembolic disease (MI)	1 (1.0%)	2 (2.0%)	3 (1.5%)	>0.999
Arterial Thromboembolic disease (Mesenteric Ischemia)	2 (2.1%)	0 (0.0%)	2 (1.0%)	0.234
Arterial Thromboembolic disease (Other)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

^aMethemoglobin levels by percent. Levels in the iNO group are expected to be greater than those in the iEPO group given the mode of iNO action. In both groups, levels do not exceed clinically important threshold of 10% to be concerning for impact on systemic oxygenation.

^bp-value from Wilcoxon Rank sum test, all other p-values are from Fisher Exact tests.

^cIncludes diagnosis of superficial venous thrombosis

CVA, Cerebrovascular accident; DVT, Deep vein thrombosis; GI, Gastrointestinal; iPVD, Inhaled pulmonary vasodilator; MetHb, Methemoglobin; MI, Myocardial infarction; PE, Pulmonary embolus; TIA, Transient ischemic attack

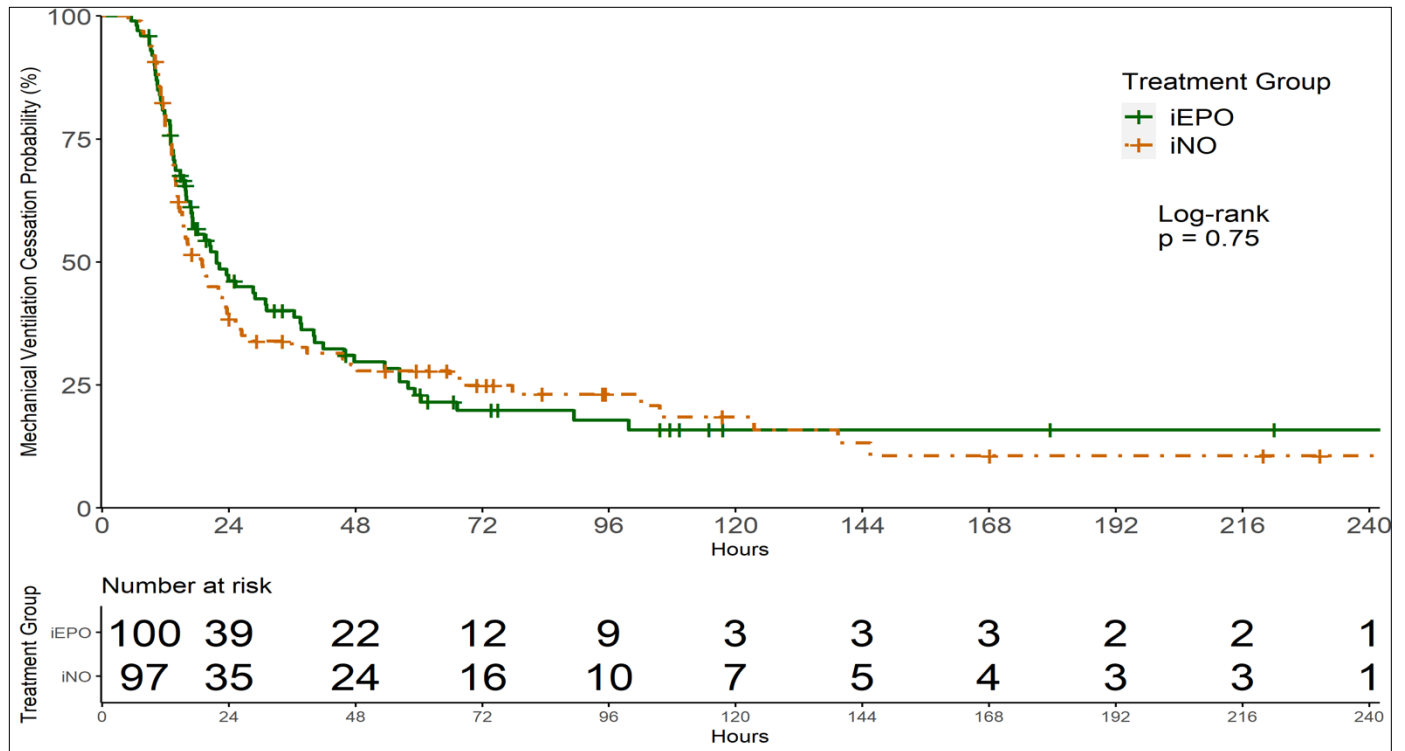
eTable 3. Primary Outcome by Randomization Strata

Randomization Stratum	iNO N Event (% Event)	iEPO N Event (% Event)	Total N Event (% Event)
^a Bilateral LT Obstructive	6/26 (23.1%)	11/31 (35.5%)	17/57 (29.8%)
Bilateral LT Restrictive	26/52 (50.0%)	27/53 (50.9%)	53/105 (50.5%)
Bilateral LT Pulmonary Vascular Disease	1/2 (50.0%)	0/1 (0.0%)	1/3 (33.3%)
Bilateral LT Other	1/4 (25.0%)	2/4 (50.0%)	3/8 (37.5%)
Single LT Restrictive	5/14 (35.7%)	6/14 (42.9%)	11/28 (39.3%)

^aiNO group diagnosis: COPD without A1AD (N=2), COPD with A1AD (N=1), Cystic Fibrosis (N=3)

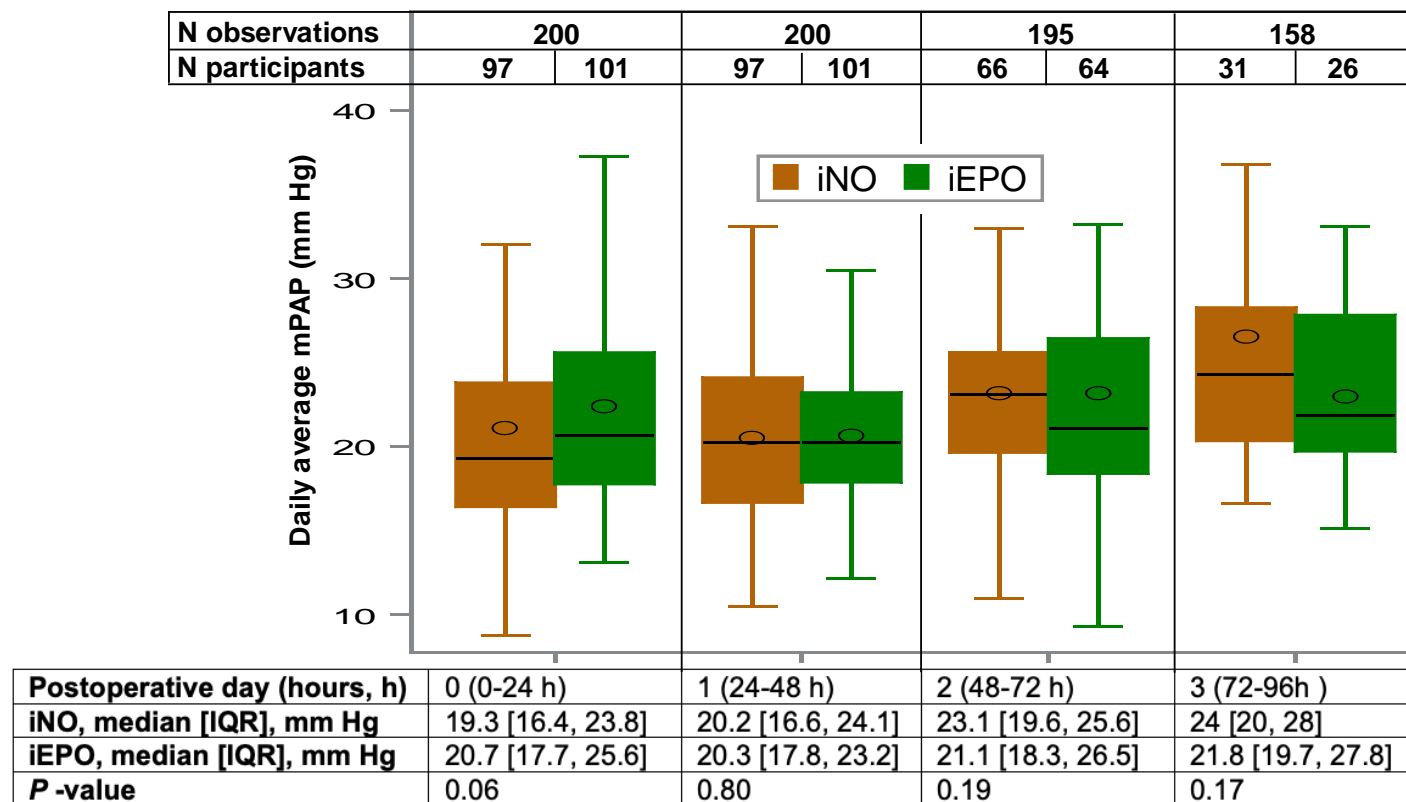
iEPO group diagnosis: COPD without A1AD (N=6), Cystic Fibrosis (N=5)

A1AD, Alpha-1 Antitrypsin Deficiency; iEPO, Inhaled epoprostenol; iNO, Inhaled nitric oxide; LT, Lung transplantation



eFigure 1. Time-to-Event Analysis for Duration of Mechanical Ventilation

For those that underwent postoperative tracheostomy placement (iEPO group, N= 29; iNO group, N = 22), time-to-extubation interval was censored (as indicated with “+” on the Kaplan-Meier curve) at the time of tracheostomy placement to avoid underestimating the distribution of time-to-end of mechanical ventilation. Number at risk for continued mechanical ventilation are indicated across the duration of the entire cohort that did not have a tracheostomy on ICU arrival after lung transplantation (iEPO group, N=100; iNO group, N=97). The KM median (95% CI) estimates of mechanical ventilation duration were 19.0 hours (95% CI: 14.8, 23.7) in the iNO group and 21.7 hours (95% CI: 16.9, 36.4) in the iEPO group ($P = 0.75$). iEPO, Inhaled epoprostenol; iNO, Inhaled nitric oxide.



eFigure 2. Daily Mean Pulmonary Arterial Pressure Values According to Treatment Groups

Box plots are displayed from postoperative day 0 to 3 with corresponding median (IQR) values for mean pulmonary arterial pressures for each group and *P*-values for comparisons of the medians. At the top panel of the image, the number (N) of mPAP observations included for the postoperative day are indicated along with the number (N) of participants that contributed to the observations, separated by treatment group. On POD 3, the number of patients becomes appreciably fewer due to removal of pulmonary arterial catheter.

iEPO, Inhaled epoprostenol; iNO, Inhaled nitric oxide; mPAP, Mean pulmonary arterial pressure; N, number