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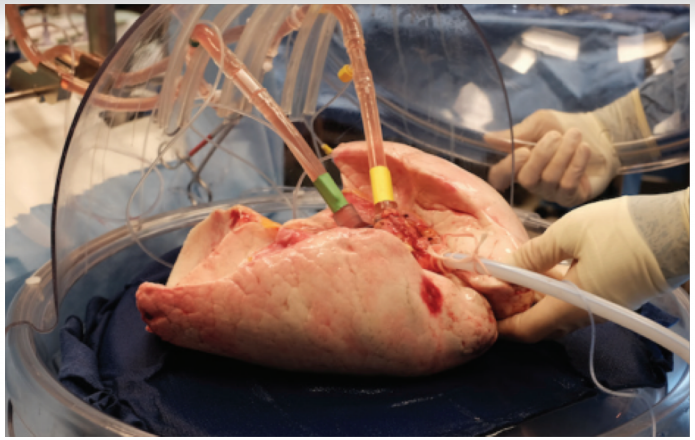

A Breath of Fresh Air: Approaches to Doubling Lung Utilization

April 9, 2019| 2-3pm ET

Speakers: Samir Latifi, MD

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WEBINAR SPEAKERS

Moderator:

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A Breath of Fresh Air: Approaches to Doubling Lung Utilization

April 9th, 2019, 2-3 pm EST
ODT-Alliance Webinar

Samir Latifi, MBBS, FRCPH, FAAP
Chair Department of Pediatric Critical Care
Associate Medical Director Lifebanc

Cleveland Clinic

DONATE LIFE Lifebanc

I have no financial
or conflicts of interest
disclosures

The Ideal Lung Donor

- PaO_2/ FiO_2 (P/F) ratio > 300 mmHg
- A clear chest radiograph
- Minimal, non-infected tracheal secretions

Nalk PM, Angel LF: Special Issues in the Management and Selection of the Donor for Lung Transplantation. Semin Immunopath; 2011,33(2) 201-210

Lung Transplantation – 2018 Data

- 36,530 transplants
- 2530 were lung
- 10,721 donors
- 23.7% were lung donors
- But as of 4/6/19 there are still 1,463 people on the wait list, 20% of whom will die waiting

https://optn.transplant.hrsa.gov/data

Objectives

- Develop an understanding of the inflammatory and pathophysiological changes in lung function of the neurologically deceased donor
- Develop an approach to treat all donors as potential lung donors by utilizing a structured approach to lung recruitment
- Become familiar with the use particularly of APRV (airway pressure release ventilation) for lung recruitment

Reasons for suboptimal donor lung function

- Preexisting conditions
  - Asthma, smoking, infection, etc
- Cause of death related
  - Aspiration, contusions, fractures, pneumothorax, infection
  - Head injury – neurogenic pulmonary edema
  - Ventilator induced injury / infection
- Brain death related

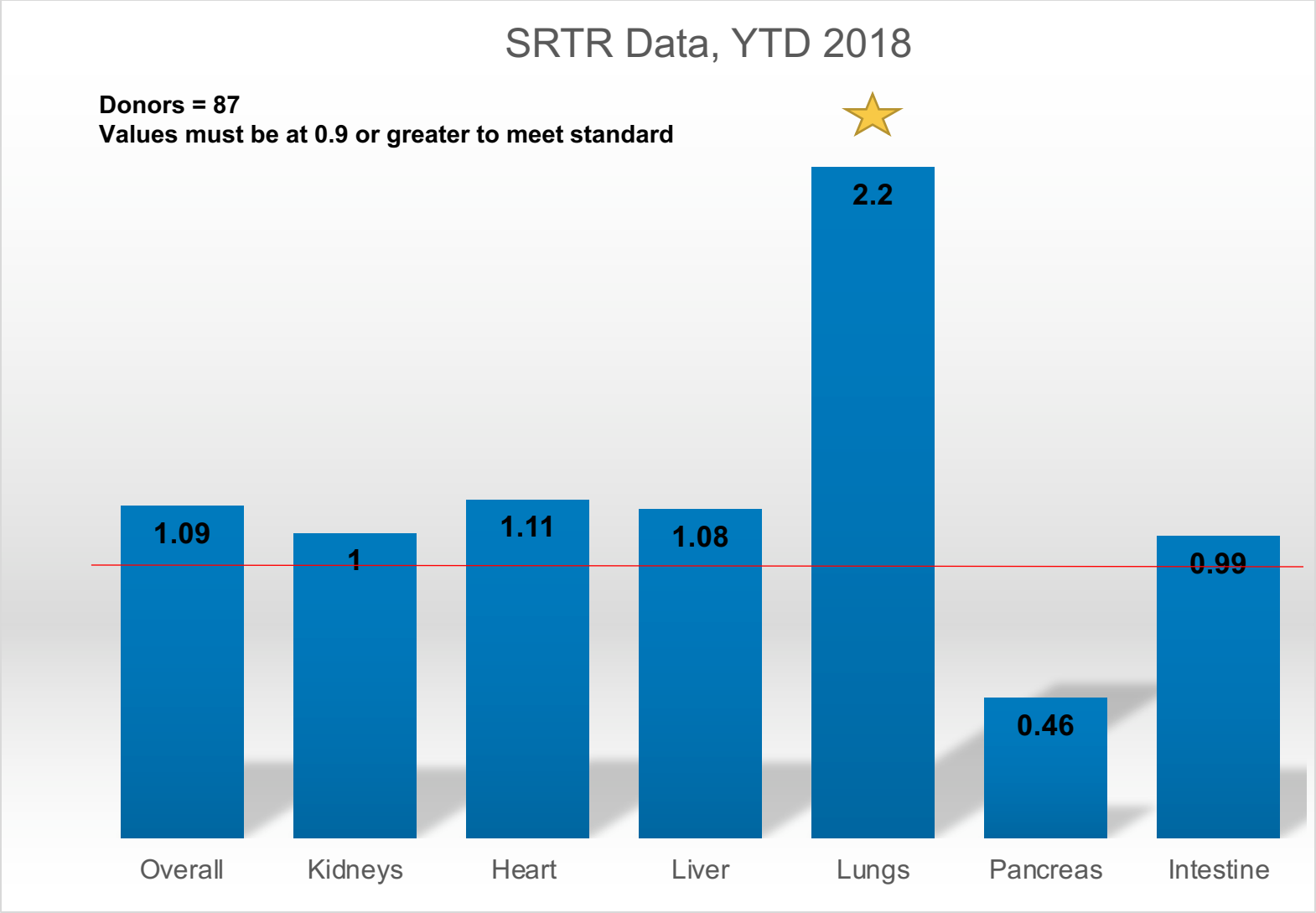
Effect of Brain Death Physiology on Lung Function

- The catecholamine storm, dysregulation of neurohumoral factors, and proinflammatory mediator release lead to increased vascular endothelial permeability promoting neurogenic, cardiogenic and noncardiogenic ***pulmonary edema***
- No spontaneous respirations, no cough, no gag leads to pooling of secretions promoting ***atelectasis***
- Leads to hypoxemia and poor lung compliance

So…

How do we overcome these issues during donor management, and can we really double our lung utilization?

Lifebanc O/E Data



We Have Done This Before: Some History

- San Antonio Lung Transplant (SALT) donor management protocol reported in 2006 improving their proportion lung donors from 11.5% to 25.5%
- Key feature was recruitment maneuver of PC 25, PEEP 15 for 2 hours

Angel LF et al: Impact of a lung transplantation donor-management protocol on lung donation and recipient outcomes. Am J Respir Crit Care Med. 2006 Sep 15;174(6):710-6

Respiratory Goals – Getting There

- ***Mindset: All donors are lung donors until proven not***
- Head up 30º, ETT cuff inflated to prevent aspiration
- Early and repeated bronchoscopy – with minimal saline lavage
- Albuterol, Mucomyst, chest physiotherapy, suctioning, positioning
- Adjunct meds: corticosteroids, ~~naloxone~~
- Fluid Status - euvolemia, loop diuretics

Dhar R et al: A Randomized Controlled Trial of Naloxone for Optimization of Hypoxemia in Lung Donors after Brain Death. Transplantation; 2018, Nov epub

Ventilator, Blood Gas Goals

- Normal ventilation and oxygenation
  - pH 7.35-7.45, $PaCO_2$ 35-45, O_2 sats >95%
- Limit Ventilator Associated Complications
  - Oxygen toxicity
    - <= 40% oxygen, the lower the better
  - Barotrauma
    - Plateau <30-35, PIP<35-40, MAPs<20-25
    - Generally need PIPs in mid 20s for acceptance for transplantation
  - Volutrauma
    - TV 6-8 ml/kg of ideal body weight

Protocolize Your Donor Lung Management

Ventilator Management		
Evaluate Oxygenation Status		
P / F Ratio > 350	P / F Ratio 200 - 350	P / F Ratio < 200
Maintain MAP 15 – 20	Maintain MAP 20 – 25	Maintain MAP 25 – 28
• Incrementally increase PEEP from 5 to 10 cmH20 as tolerated. *(Monitor HR and BP and maintain WNL. Administer fluids as directed.)* • Maintain current PC mode with I: E of 1:1 ratio. • Adjust drive pressure to achieve Vt 6 - 8ml/kg of IBW. • Monitor Vt as compliance changes and adjust drive pressure to maintain desired Vt. • Set respiratory rate to adjust CO2 between 35 - 45 mmHg to achieve pH 7.35 - 7.45. *(See ABG Interpretation and Interventions pages 34 - 35)*	• If PIP ≤ 30 and if CXR not hyper inflated (> 6 anterior ribs): Incrementally increase PEEP from 10 to 15 cmH20 as tolerated. *(Monitor HR and BP and maintain WNL. Administer fluids as directed.)* • If PIP > 30, initiate APRV. • If P/F ratios remain 200 - 350 after reaching PEEP 15 cmH2O, begin to inverse I: E ratio. *(Decrease PEEP when inversing.)* • Adjust drive pressure to achieve Vt 6 - 8ml/kg of IBW. • Monitor Vt as compliance changes and adjust drive pressure to maintain desired Vt. • Set respiratory rate to adjust CO2 between 35 - 45mmHg to achieve pH 7.35 - 7.45. *(See ABG Interpretation and Interventions pages 34 - 35)*	• Change to or maintain APRV mode of ventilation. *(See pages 32 - 33 for APRV settings and adjustments.)* • Prior to changing modes, note plateau pressure (PP) in volume control (VC) mode or PIP in pressure control (PC) mode. • Assess fluid status prior to changing to APRV. Patient will not tolerate APRV until fluid resuscitated. *(See Fluids page 10 - 12)*
• Obtain ABG in two hours then reevaluate oxygenation status following the above guidelines. • If P / F ratios are stable, repeat ABG in four hours and reevaluate oxygenation status following the above guidelines.		

What's APRV or Extreme PCIRV?

- Airway Pressure Release Ventilation is basically a PC mode of mechanical ventilation
- Uses a P high and a P low
- Allows for an inverse ratio ventilation
- Short release time (or P low) prevents PEEP from returning to zero (to avoid de-recruitment)
- Time triggered, pressure limited, time cycled

Extreme PCIRV

In spontaneously breathing ventilation is spontaneous as well an additional washout of CO_2 during the P_{low} Phase

In the non breathing patient like DBD donors, CO_2 production is low and so the time in P_{low} is enough for clearance, but the high overall MAP allows for sustained lung recruitment

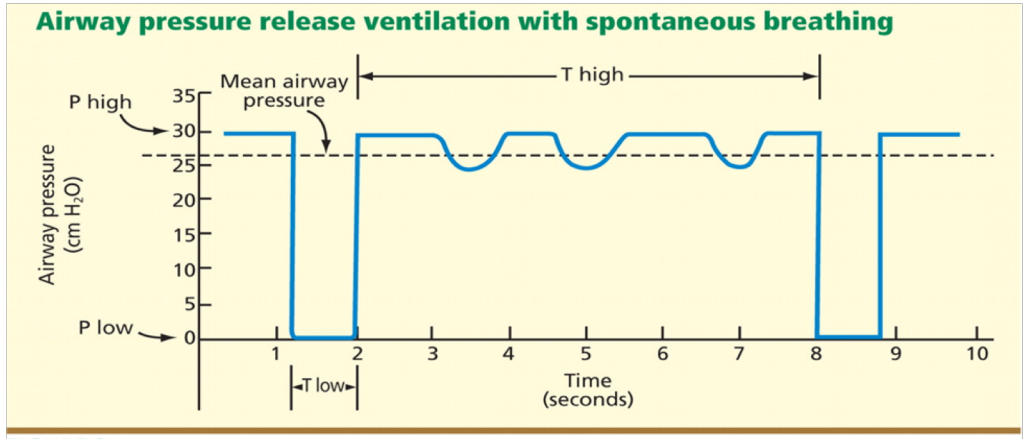


FIGURE 2

REPRINTED FROM FRAWLEY PM, HABASHI NM. AIRWAY PRESSURE RELEASE VENTILATION: THEORY AND PRACTICE. AACN CLINICAL ISSUES 2001; 12:234–246, WITH PERMISSION FROM WOLTERS KLUWER HEALTH/LIPPINCOTT, WILLIAMS & WILKINS.

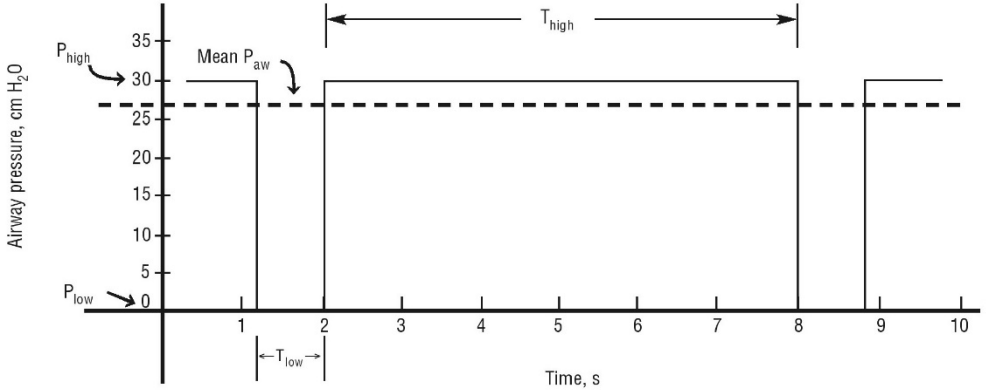


Figure Schematic representation of airway pressure release ventilation relating airway pressure to the times of continuous positive pressure and pressure-release episodes. See text for discussion of primary variables. In this illustration, P_{high} = 30 cm H_2O, T_{high} = 6 seconds, P_{low} = 0 cm H_2O, T_{low} = 0.8 seconds, and mean airway pressure (mean P_{aw}) = 26 cm H_2O.

Modified with permission from Frawley et al.[6]

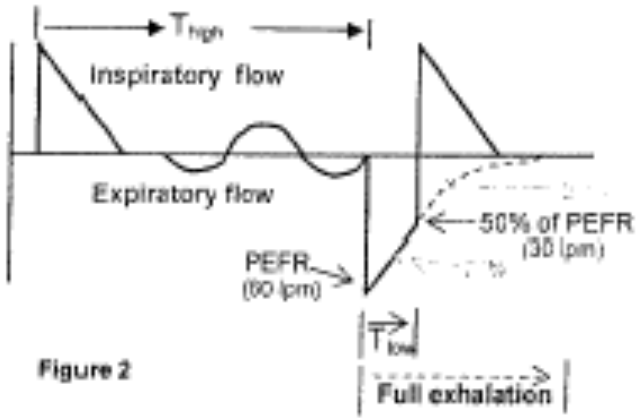
APRV Settings

Setting Airway Pressure Release Ventilation (APRV)

1. Set P High using the peak inspiratory pressure (PIP) of the previous PC mode or at the peak plateau pressure (pPlat) of the previous VC mode.
    a. *A plateau pressure is obtained by performing an inspiratory hold.*
    b. *Set to a minimum of 20 cmH20 but avoid exceeding 35 cmH2O.*
    c. *Make adjustments in 2 cmH2O increments to maintain MAP 25 – 28.*
2. Set P Low to 0.
3. Set T High initially between 4 - 6 seconds.
4. Set T Low initially between 0.5 - 0.8 seconds.
    a. *Set to achieve an expiratory flow rate termination that is 50% of the peak expiratory flow. (See Expiratory Flow Waveform page 26)*
    b. *Consult RT for assistance.*
5. Recheck ABG in 2 hours after initial change and then every 4 hours and make adjustments as needed to obtain optimal oxygenation and a normal pH.

The first ABG in APRV may be worse than baseline. Keep in mind full recruitment may take 4 – 6 hours.

Expiratory Flow Waveform

Expiratory Flow Waveform	 Figure 2	• During APRV, adjust T Low to cut off the expiratory flow during a release at about 50% of the peak expiratory flow rate (PERF). • Never allow the termination of expiratory flow to go < 25% of the PERF. This intentional intrinsic PEEP allows P Low to be set at 0 cmH2O without causing de-recruitment.

Our Vents Don't Do That…

- Don't worry when your RT says that:

Puritan Bennett 840 (Covidien)– Bilevel
Servo U and I (Maquet) – Bivent
Drager Evita/Infinity – APRV
Carefusion Avea (Viasys) – Biphasic

Relative Contraindications for PCIRV

- Hypotension, hemodynamic instability
- Untreated pneumothorax, or known bronchopleural fistula
- Unilateral lung disease
- Severe COPD

Advantages for PCIRV

- Improves oxygenation by increasing MAP
- Increases/maintains MAP without increasing PIP
- Lower minute ventilation, which equates to less ventilation of dead space
- Recruits collapsed alveoli, and for DBD donors who are not spontaneously breathing, this means nearly constant recruitment

Lifebanc Experience
Aggressive Lung Recruitment Protocol Increases Lungs for Transplantation with No Adverse Effect in Recipients

Presented August 18, 2010 at the International Transplant Congress

Dan Lebovitz, MD

Medical Director – Lifebanc - Cleveland, Ohio, USA

Hypothesis

- Introduction of an aggressive lung management protocol (ALMP) using advanced mechanical ventilator recruitment would increase P/F ratio and therefore increase lung acceptance rate by transplanting surgeons

Methods

- Reviewed current donor management and aggressive ventilator recruitment strategies
  - Reviewed current literature
  - Discussed with high performing OPOs
  - Discussed with ICU Ventilator “experts”
- Developed Aggressive Lung Management Protocol (ALMP)
- Discussed with local lung transplant physicians for input

Successful Lung Management Implementation Strategies

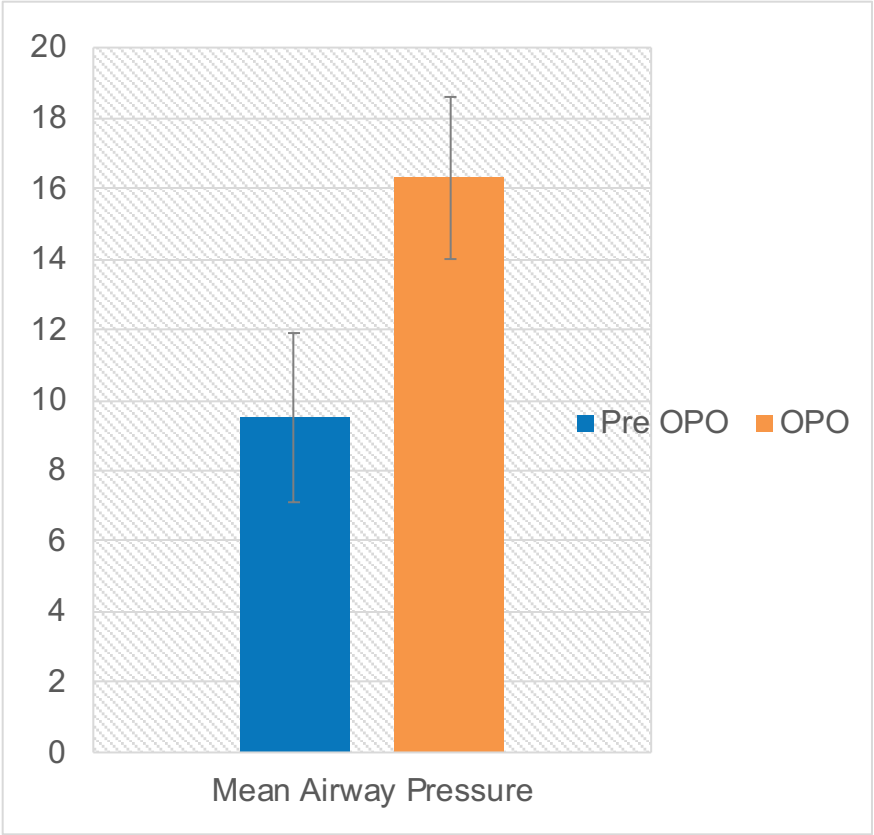
COOPERATION AND COLLABORATION

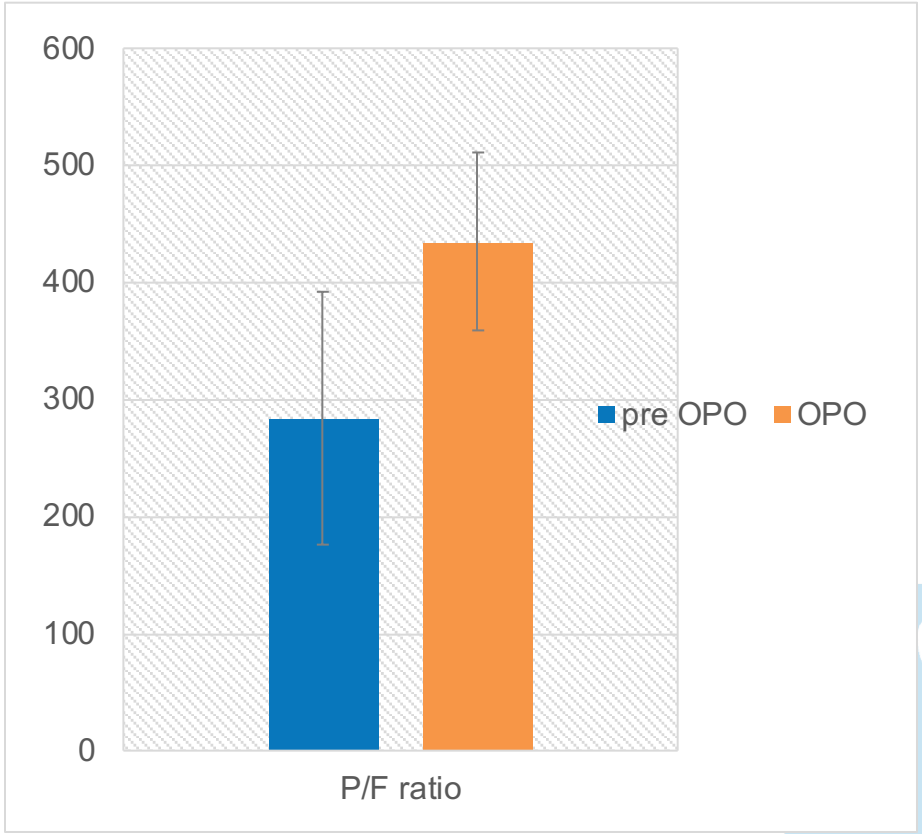
- Pro-active Approach
- Education
  - Organ Procurement Staff
  - Donor Hospital Staff – MDs, Nurses, Resp therapists
  - Transplant Teams
- Expanded Criteria
  - Right recipient for the right donor

Aggressive Lung Management Protocol

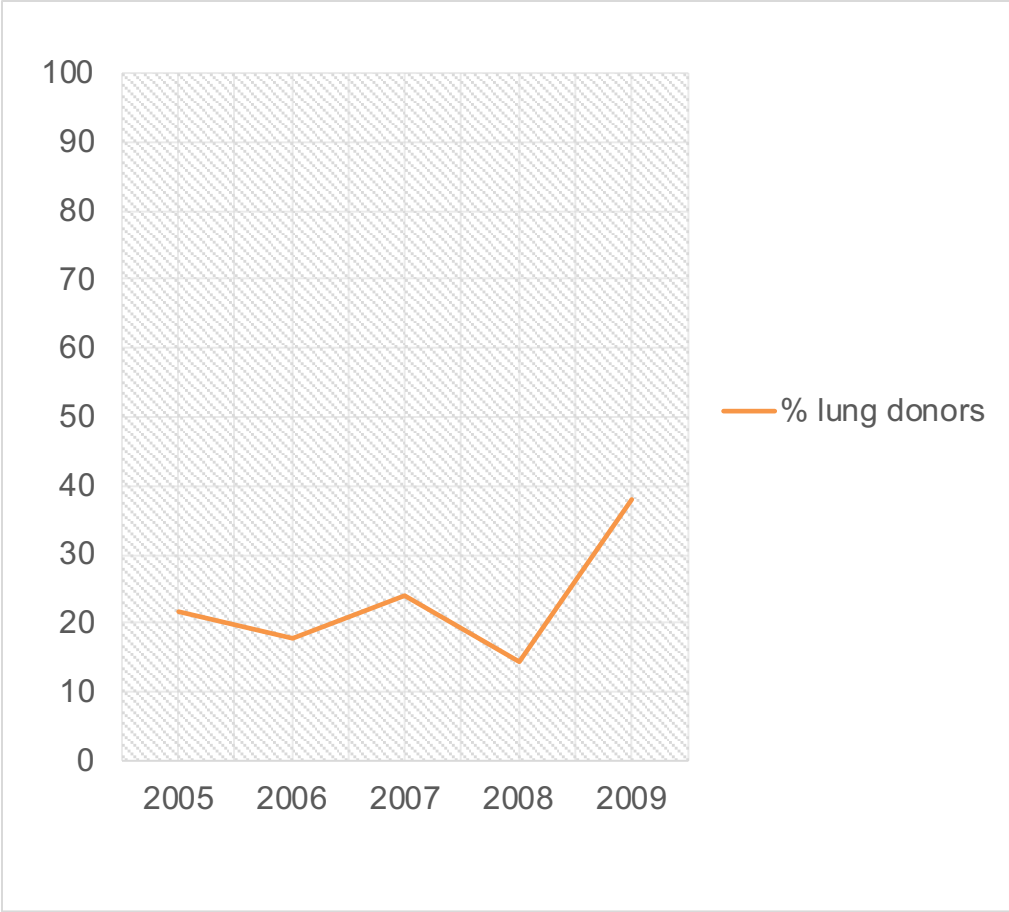
- Mindset: All donors are lung donors (until proven otherwise)
- Protocolized donor lung management
- When lungs felt fully recruited: change to PCV, I:E of 1:1, PEEP 5 and FiO2 of 100% for 30 min obtain ABG for lung offers – ***then return to PCIRV***

Pre and Post OPO ALMP Implementation





Data from Lifebanc



Recipient Donor Outcome Data Cleveland Clinic - 2009 Local vs Imported Lungs

Lung Donors	N	ICU days	Survival at 30 days	PGD 0	PGD 24	PGD 48	PGD 72
Local	38	25+/-37	37/38 (97.4%)	1.13 ± 1.18	1.09 ± 1.25	1.41 ± 1.24	1.22 ± 1.26
Import	119	21 +/-44	111/119 (93.3%)	1.15 ± 1.18	1.02 ± 1.03	1.11 ± 1.05	0.92 ± 0.92
p-value		NS	NS	NS	NS	NS	NS

Study Conclusions

- Utilization of an aggressive lung management protocol incorporating extreme PCIRV can double your lung donor rates
- With no apparent effect on recipient outcomes as compared to lungs from “standard” donor management

Supported by Further Studies

- Hanna et al showed in 2011 a significantly higher lung donation rate for donors managed with APRV(84%) versus ACV (18%)
- Recipient survival was also not significantly different between groups

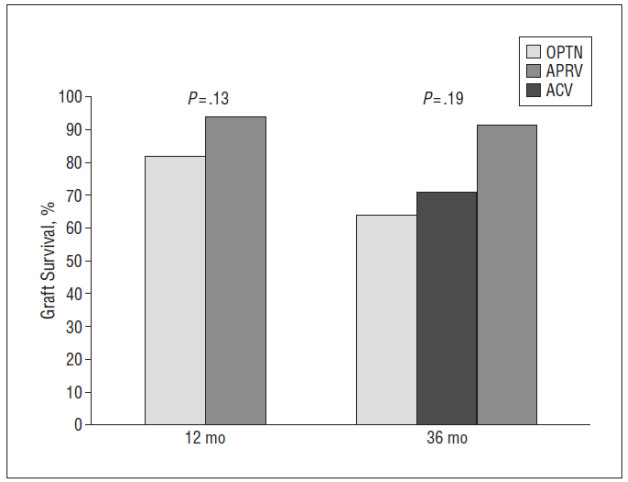


Figure 2. Survival of grafts managed with airway pressure release ventilation (APRV) at 12 months and 36 months and assist/control ventilation (ACV) at 36 months compared with national data from the Organ Procurement and Transplantation Network (OPTN).

Hanna et al: APRV and Successful Lung Donation. Arch Surg; 2011,146(3) 325-328

Is Taking the Extra Time for Lung Management Worth it?

- Retrospective review: 400 consecutive donors where lungs were transplanted
- Mechanism of donor brain death had no effect
- Donor management longer than 10 hrs results in ***better lung recipient survival*** (69% vs 58% at 5 years, 51% vs. 42% at 10 years, $p < .05$)
- Longer and better donor management is better for recipients

Wauters et al. Eur J Cardiothoracic surgery 2011; 39; e 68-e76

Meta-analysis: Lung Management Protocols vs. No Protocol

- 10 articles eligible for inclusion
- Implementation of lung management protocols led to an OR 2.56 for recovery and transplantation
- And recipient survival was also significantly higher at one year with an OR 1.82 when a protocol was used

Raios, C et al: Lung management protocols increase the incidence of lung procurement and organ transplantation: A meta-analysis. Physiother Theory Pract; 2018, Jul 17, 1-10

Other Opportunities

- Lung donation among DCDD is only around 2%
- In this situation of course though the OPO is not able to actively manage lung recruitment strategies
- However potential DCDD donors with borderline PF ratio's may be suitable candidates for ex vivo lung perfusion (EVLP)

Mooney et al: Lung Quality and Utilization in Controlled Donation After Circulatory Determination of Death Within the United States. Am J Transpant; 2016,16; 1207-1215

An Interesting Observation…

- Lifebanc noticed that as one of our local lung transplant centers became an EVLP center that the recovery surgeons have sometimes determined at the time of recovery that the lungs were suitable for immediate transplantation without the need for EVLP
- This was particularly so for those donors who were obese

Obesity Amongst Deceased Donors

- The OPTN database for 2018 showed that 34% of deceased donors were obese (BMI > 29)
- Higher BMI is associated with a lower PF ratio
- It could be that instituting aggressive lung management helps particularly in obese donors to turn marginal into potential lungs, and now with the option of EVLP gets a recovery surgeon to come assess these lungs thus improving overall lung utilization

Okamoto et al: High Body Mass Index in Organ Donor is Significantly Correlated to Low PF Ratio in SRTR Database. Am J Transpant; 2017,17(suppl 3)

Hepatitis C and Lung Transplant

- 36 lung recipients received HCV+ lungs
- Treatment started within hours, for 4 weeks
- Recipients all doing well with no evidence for infection
- EVLP team from Toronto also reported on 10 patients in June 2018
- This could lead to potentially another 1000 lungs for transplantation annually in North America

Woolley et al: Heart and Lung Transplant from HCV-Infected Donors to Uninfected Recipients. NEJM; 2019 Apr 3. epub

Key Takeaways

- We have the potential to easily double lung donors and eliminate the wait list for lung transplantation
- OPO's in collaboration with their transplant centers need to treat every donor as a potential lung donor
  - Utilize an aggressive lung management protocol incorporating the use of extreme PCIRV (APRV)
- The increasing use of EVLP and utilization of HCV+ donors will help achieve this goal

THANK YOU

Cleveland Clinic

Every life deserves world class care.