Pediatric Artificial Lung: Improving a Large Animal Model of ESLF

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The pediatric artificial lung (PAL) may serve as a bridge to lung transplantation for children with end-stage lung failure (ESLF). An animal model of pediatric ESLF is needed to evaluate a PAL's. Previously a Hem-o-lok ® ligation system was used to clamp the right pulmonary artery (rPA) with success in lambs, but was associated with high mortality (65%) in the first 12hrs. This study aims to improve the ESLF model by decreasing mortality in the first 24 hours. Five anesthetized lambs underwent a left thoracotomy to ligate the left upper lobe pulmonary artery and to place a perivascular band around the rPA. Animals were monitored for up to 14 days. Mean pulmonary arterial pressure (MPAP), respiratory rate (RR), venous oxygen saturation (SvO_2%), and blood gases (PaO_2, $PaCO_2$) were collected. Dead space fraction (VD/VT) was measured at baseline and at the end of the study. All five animals survived >5 days. Data was analyzed from baseline to the 5th post-operative day. MPAP and VD/VT had a significant increase (15.2±3.2 vs 29.0±6.3mmHg, p=0.004) and (38±5.6% vs 57.0±6.0%, p=0.001) respectively. However, no significant changes were observed in RR (81.9±27.5 vs. 95.8±34.6BPM, p=0.447), PaO_2 (77.3±19.9 vs 72.1±20.5mmHg, p=0.075), and $PaCO_2$ (35.7±6.6 vs 35.0±4.3mmHg, p=0.419). Although, SvO_2% decreased (78.2±6.2 vs. 56.8±3.7%, p=0.007) its value did not have clinical significance. All lambs were induced with ESLF and weaned from mechanical ventilation without fatality in the first 24hrs. However, criteria for ESLF were not achieved because of lack of changes in RR, arterial blood gases, and SvO_2.

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BACKGROUND

Current treatments for chronic lung disease raise clinical concerns

•Mechanical ventilation has been shown to cause inflammatory responses, infection, and barotrauma

•Lung transplantations have long waiting lists due to organ scarcity

The pediatric artificial lung (PAL) may serve as a bridge to lung transplantation for children with end-stage lung failure (ESLF)

•An animal model of pediatric ESLF is needed to evaluate a PAL's efficacy.

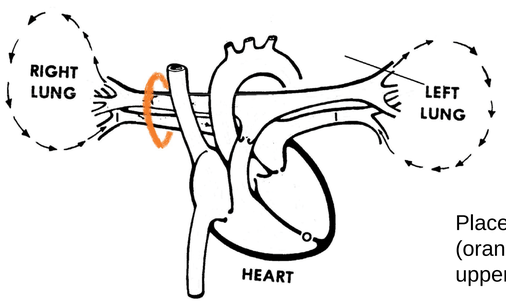
HYPOTHESIS

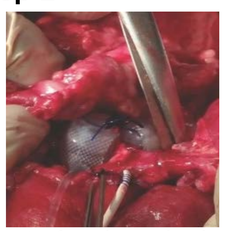
This study aims to improve the ESLF model developed in our laboratory by decreasing mortality in the first 24 hours

METHODS

All animals received humane care in accordance with the NIH Guide for the Care and Use of Laboratory Animals. Animal protocol was approved by the University of Michigan Committee on Use and Care of Animals. Healthy 40-50Kg sheep were used for this model

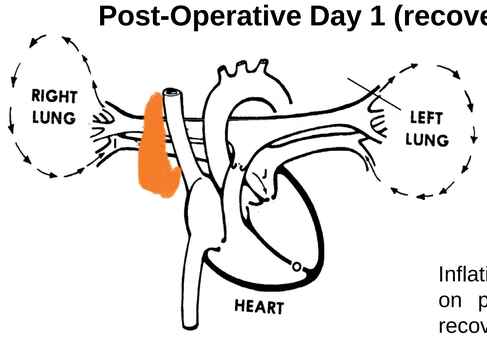
Surgical Procedure: Step 1

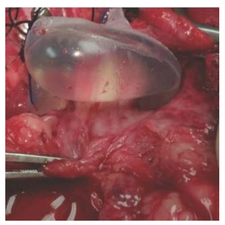




Placement of perivascular band (orange) + ligation of the left upper pulmonary artery (black)

Post-Operative Day 1 (recovery): Step 2





Inflation of the perivascular band on post-operative day 1, after recovery from anesthesia

DATA COLLECTION

TABLE 1. DATA COLLECTION

VARIABLE	NORMAL RANGE	CRITERIA FOR ESLF	FREQUENCY OF MONITORING
Mean Pulmonary Artery Pressure (MPAP)	12-18 mmHg	≥ 25 mmHg	Hourly
Respiratory Rate (RR)	50-60 BPM	> 60 BPM	Hourly
Venous Oxygen Saturation (SvO_2%)	70-80%	< 70 mmHg without Supplemental O_2	Every 2 or 4 hours
Partial Pressure of O_2 (PaO_2)	80-100 mmHg	< 70 mmHg	Every 2 or 4 hours
Partial Pressure of CO_2 ($PaCO_2$)	40±5 mmHg	> 45 mmHg	Every 2 or 4 hours
Dead space fraction (VD/VT)	N/A	N/A	Baseline & End of Study

RESULTS

- **All lambs survived the surgical procedure and recovered from anesthesia**
- **All lambs tolerated without complications rPA ligation for >24 hours**

Survival rates: All (n=5) lambs survived for at least 7 days. Between 7-14 days, animals died due to unrelated complications (pneumonia, sepsis, and intravascular line problems). One animal survived 14 days

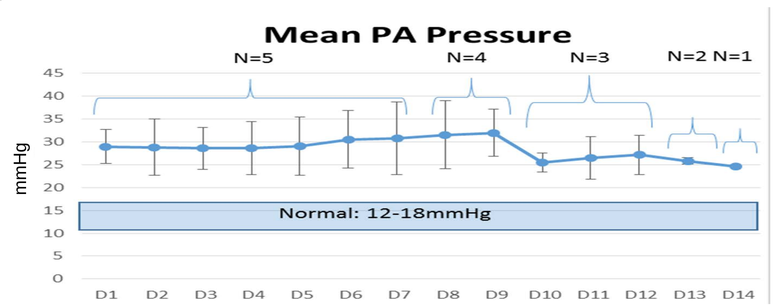


Figure 1. Mean Pulmonary Artery Pressure (MPAP). Baseline results compared to the 5th day MPAP had a significant increase (15.2±3.2 vs 29.0±6.3mmHg, p=0.004)

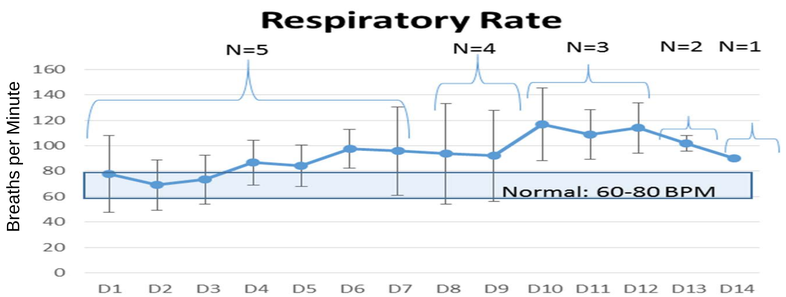


Figure 2. Respiratory Rate (RR). Baseline results compared to the 5th day RR had no significant change (81.9±27.5 vs. 95.8±34.6BPM, p=0.447)

RESULTS

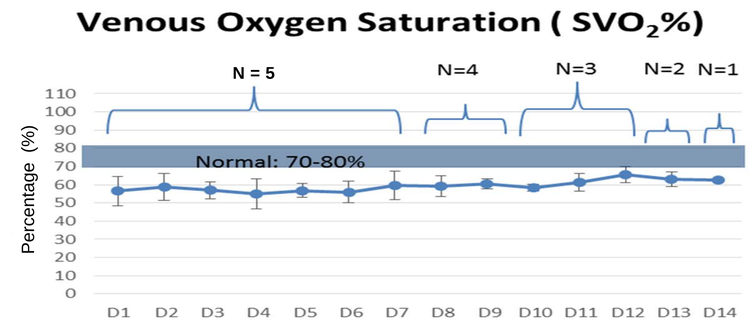


Figure 3. Venous Oxygen Saturation (SvO_2). Baseline results compared to the 5th day SvO_2% decreased (78.2±6.2 vs. 56.8±3.7%, p=0.007).

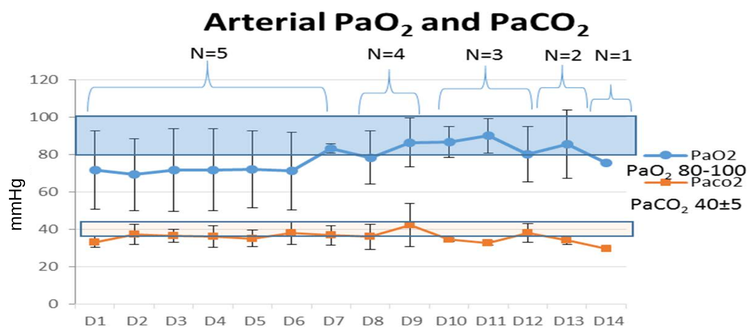


Figure 4. Arterial PaO_2 and $PaCO_2$. Baseline results compared to the 5th day Pao_2 and $PaCo_2$ didn't change significantly (77.3±19.9 vs 72.1±20.5mmHg, p=0.075) (35.7±6.6 vs 35.0±4.3mmHg, p=0.419) respectively.

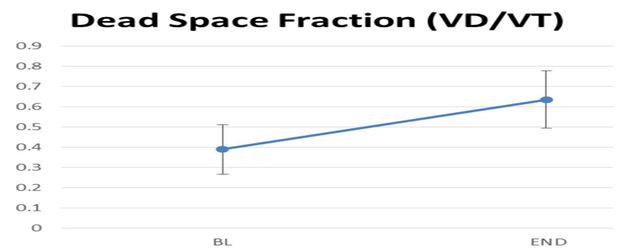


Figure 5. Dead Space Fraction (VD/VT). Baseline results compared to the 5th day VD/VT had a significant increase (38±5.6% vs 57.0±6.0%, p=0.001)

CONCLUSIONS

1. Using the perivascular band allowed a **successful recovery of all animals after surgery**. They were weaned from mechanical ventilation without fatality in the first 24hrs
2. Only a **mild clinical ESLF was induced** based on the lack of changes in RR, arterial blood gases, and SvO_2
3. **A leakage in the band may have allowed blood to pass through into the right lung**. Further studies are required to improve the disease model