Lung Protective Mechanical Ventilation in Pediatric Acute Respiratory Distress Syndrome

Study by PACCMAN collaboration

Background

- Acute respiratory distress syndrome (ARDS) is recognized as the most severe form of lung injury with oxygenation failure
- The only available treatment is supportive MV
- MV in itself has the potential to initiate and aggravate lung injury
- Led to development of lung-protective mechanical ventilation (LPMV) strategies which aim to minimize ventilator induced lung injury

Background

- PARDS mortality in Asia (30%) is higher than global mortality rates (17%)
- Pediatric Acute Lung Injury Consensus Conference (PALICC) recommendations were developed in 2015
- Compliance to recommendations is poor:
  - 25% with PIP>28cmH2O
  - >75% with TV>6ml/kg
  - >50% do not observe permissive hypoxia
  - >50% do not observe permissive hypercarbia
- Could this account for the high mortality rate?

Aims and Hypothesis

- **Aim 1**: to determine if a pragmatic LPMV protocol applied to patients with PARDS over the first 7 days of disease reduces mortality

- **Hypothesis 1**: LPMV deployed in the form of a pragmatic ventilation protocol in the first 7 days of PARDS reduces mortality by one-third

Aims and Hypothesis

- **Specific aim 2:** To determine if the level of adherence to LPMV elements is greater after the implementation of the LPMV protocol

- **Hypothesis 2:** The level of adherence to LPMV elements in the first 7 days of PARDS as measured by an adherence score, is greater after the implementation of the LPMV protocol

Aims and Hypothesis

- **Specific aim 3:** To determine if the level of adherence to LPMV elements applied to patients with PARDS over the first 7 days of disease reduces mortality

- **Hypothesis 3:** The level of adherence to LPMV elements in the first 7 days of PARDS as measured by an adherence score, is associated with reduced mortality.

Significance

- This study will determine the impact of a PARDS MV bundle on mortality and other clinical outcomes **(RESEARCH)**
- This study will improve adherence to PARDS MV guidelines advocated by international authorities **(QUALITY)**
- This study will standardize MV practices in PARDS laying the foundation for more comparable trials in the future **(FUTURE RESEARCH)**

Methodology

- Multi-center, before-and-after comparison study
- Recruitment of patients with PARDS will be based on the PALICC definition
- **Recruitment period approximately 4years:**
  - Baseline (control) data can be collected retrospectively/prospectively in the **2-year** period prior to bundle implementation
  - Bundle implementation with 1-month wash in period
  - Prospective data collection for the next **2-years** post-implementation

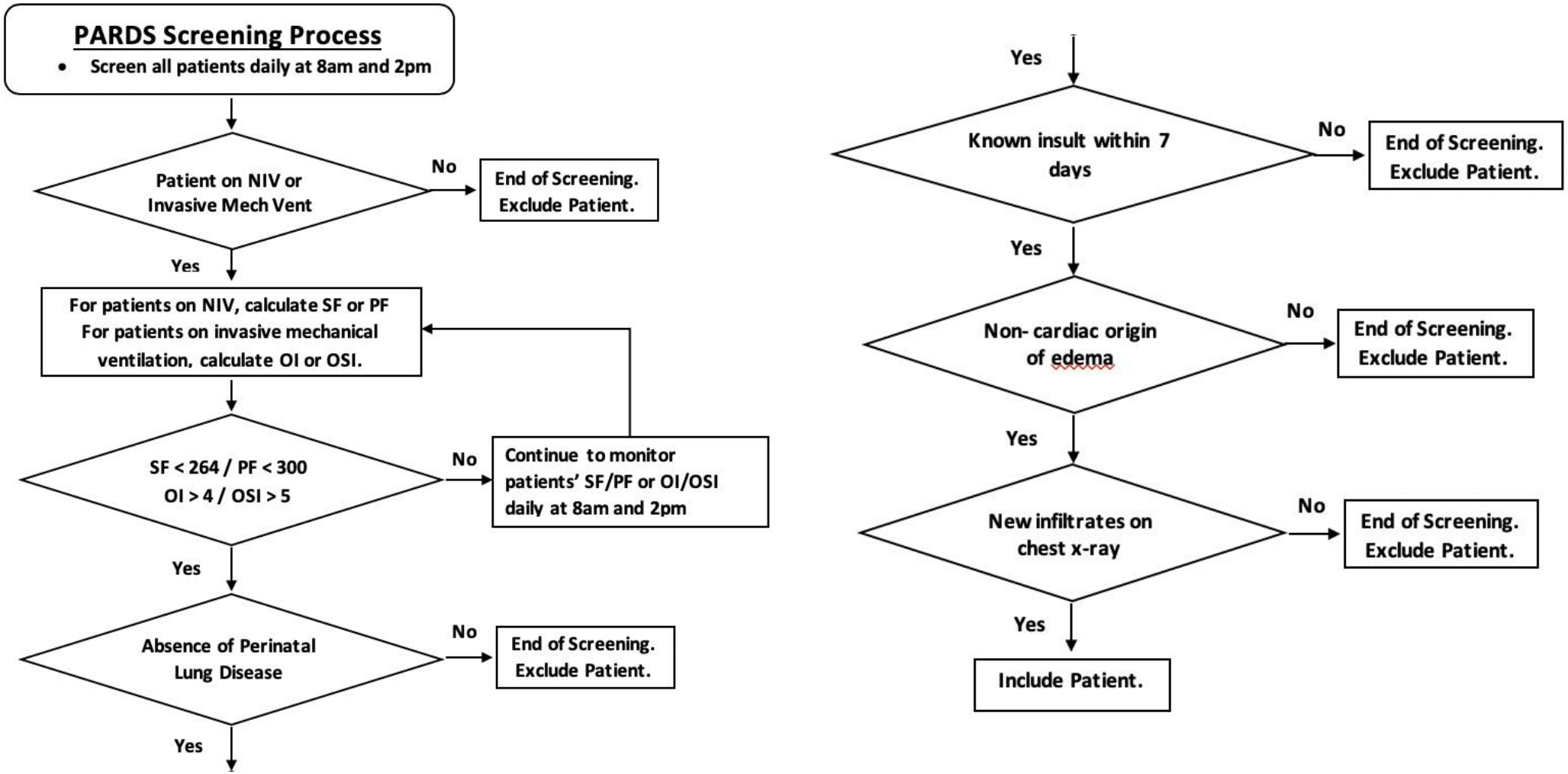
Methodology

- Seek approval by PICU medical and nursing **stakeholders**
- **Championed** by intensivist and respiratory therapist/nurse
- **Training**/ education sessions for all PICU staff
- Posters and **reminders** in the unit and at patient bedside
- Regular **updates** at administrative meetings

LPMV team

- Medical
  - Site-PI
  - Team member
- Respiratory Therapist representative (optional)
  - Team member
  - Team member
- Nursing representative
  - Team member
  - Team member

Screening


PARDS Screening Process
• Screen all patients daily at 8am and 2pm
Patient on NIV or Invasive Mech Vent
No
End of Screening. Exclude Patient.
Yes
For patients on NIV, calculate SF or PF
For patients on invasive mechanical ventilation, calculate OI or OSI.
SF < 264 / PF < 300
OI > 4 / OSI > 5
No
Continue to monitor patients' SF/PF or OI/OSI daily at 8am and 2pm
Yes
Absence of Perinatal Lung Disease
No
End of Screening. Exclude Patient.
Yes
Known insult within 7 days
No
End of Screening. Exclude Patient.
Yes
Non- cardiac origin of edema
No
End of Screening. Exclude Patient.
Yes
New infiltrates on chest x-ray
No
End of Screening. Exclude Patient.
Yes
Include Patient.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LPMV targets

Ventilation		Targets
Tidal volume	All patients	3-6ml/kg predicted body weight
Peak/ plateau pressure	All patients	Max 29-30cm H_2O
Permissive hypercapnia		pH 7.20-7.30*
Oxygenation		Targets
Permissive hypoxia	Mild PARDS	SpO_2 92-97%
	Moderate/severe PARDS	SpO_2 88-92%*
Positive end expiratory pressure	Incremental FiO2/PEEP combinations	

FiO_2	.30	.40	.40	.50	.50	.60	.70
PEEP	5-7	5-7	8	8	10	10	10
FiO_2	.70	.70	.80	.90	.90	.90	1.0
PEEP	12	14	14	14	16	18	18

Preliminary Data from KKH

- **Lung Protective Mechanical Ventilation Strategies in Pediatric Acute Respiratory Distress Syndrome; single centre (completed)**

Outcomes	Total (N = 132)	No LPMV (N=69)	LPMV (N=51)	p value
Mortality	28 (21.2)	18 (26.1)	10 (15.9)	0.152
Ventilator-free days	17.5 (0.0, 23.0)	19.0 (0.0, 23.0)	16.0 (2.0, 23.0)	0.697
PICU-free days	14.0 (0.0, 21.0)	16.0 (0.0, 22.0)	13.0 (0.0, 21.0)	0.233

Preliminary Data – PACCMAN collaboration

- **Risk Stratification in Pediatric Acute Respiratory Distress Syndrome: A Multicenter Observational Study (completed)**
- Study design: Retrospective multicenter (n=10 sites)
- Patients: PARDS
- Intervention: NA
- Outcome: Mortality

Demonstrated variability in management and outcomes

Outcomes	Total (n=373)	Mild (n=89)	Moderate (n=149)	Severe (n=135)	P value
Ventilator free days	16 (0, 23)	22 (17, 25)	16 (0, 23)	6 (0, 19)	< 0.001
Duration of MV	9 (4, 16)	6 (3, 9)	10 (5, 16)	11 (5, 21)	< 0.001
PICU free days	14 (0, 22)	19 (11, 24)	15 (0, 22)	5 (0, 20)	< 0.001
Duration of PICU stay	11 (6, 22)	9 (5, 16)	12 (7, 24)	13 (6, 25)	0.010
PICU mortality	113 (30.3)	11 (12.4)	046 (30.9)	056 (41.5)	< 0.001
100-day mortality	126 (39.7)	14 (18.7)	50 (39.1)	62 (54.4)	<0.001

PARDSProAsia study

Phase I (in progress)

- Study design: Prospective observational multicenter (n=16 sites)
- Patients: PARDS
- Intervention: **NA (standard care)**
- Outcome: Mortality

- Aims:
  - Establish reliable screening process for 100% identification
  - Determine recruitment rate
  - Establish feasibility of data collection tool
  - Confirm baseline ventilation management

Phase II (current proposal)

- Study design: Before-after comparison design
- Patients: PARDS
- Intervention: **LPMV bundle**
- Outcome: Mortality

- Aims:
  - Hypothesis testing

Potential Challenges

- Adherence to protocol elements in the pre-bundle arm?
  - If this is high, comparison will be difficult
- Data Quality
  - Pre and post data need to be comparable
- Secular Trend
  - The longer the study, the greater the risk of secular trend biasing results
  - Staggering the protocol start time in each center will help
- Large sample size
  - Assuming 1/3 risk reduction (from 25% to 17%), 16 centers with variability i number of subjects and mortality, approximately 500 in each pre/post arm

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