Improved Ventilation - Modeling

P Jouvet MD PhD – Sainte-Justine Hospital

PALISI Pediatric Acute Lung Injury & Sepsis Investigators
Financial disclosures

- Relationship with commercial interests:
  - Consultancies: none.
  - Equipment:
    - Drager Medical
    - Philips Medical
    - Maquet
    - Hamilton Medical
  - Grants: Hamilton Medical
  - Invitation to meetings:
    - Hamilton Medical
- Operating grants without commercial interest:
  - CIHR
  - NSERC
  - FRQ-S

Please notice that ePalive and SimulResp are Offlabel products
Plan

- Introduction
- Research on clinical decision support system to ventilation modeling.
- Validation of a virtual patient
- Preliminary results
- Conclusion
Actual management of mechanical ventilation

There is a lack of agreement between and within PICUs on ventilator management of P-ARDS.

- M Santschi et al. ICM 2007
- S Erickson et al. PCCM 2007
- R Khemani et al. AJCCCM 2010
Written protocols in mechanical ventilation

Experience in clinical practice

- Time consuming
- Instructions not explicit enough (ex: if patient stable …)
- Specific of an organization of care

↓ compliance
Variability in the interpretation
Difficult to transfer from an institution to another
Clinical decision support systems (CDSS)

Explicit computerized protocols in closed loop (ECP-CL)
Hypothesis - Objective

- **Hypothesis**: The lack of agreement in the ventilation management of P-ARDS results in significant differences in length of mechanical ventilation (LMV).

- **We planned to develop an explicit computerized protocol to decrease this LMV in P-ARDS.**

- **Goal**: To personalize and standardize mechanical ventilation management in P-ARDS with an explicit computerized protocol.
PALISI Workshop Since 2009

Financial support

PALISI Pediatric Acute Lung Injury & Sepsis Investigators
Creation of explicit computerized protocol(s) for P-ARDS patients

- **Intent of the protocol:** to create and validate an explicit computerized protocol for P-ARDS in children

- **Protocol development:** we will adapt a protocol already developed in adults (ARDS Network)

- **Applicable to what type of ventilation?** Pressure assist control mode and HFOV. ECMO will be considered as a rescue therapy

- **Stepwise validation process:** the protocol will be created as a closed-loop system, but will be initially validated using an open-loop system
Course of mechanical ventilation in pediatric ALI

- **Acute phase**
- **Weaning phase**

**NIV**

**e-protocol**

**IMV course**

**IMV Weaning phase**

Intubation

End of weaning

Extubation

End time

**ALI criteria**

Weaning Readiness test

Extubation Readiness test

Weaning & extubation failure
Next step: Clinical decision points

Acute phase | ? | Weaning phase

IMV course

VHFO

IMV Weaning phase

End of weaning

Intubation | Extubation | End time

Definitions

- ALI criteria
- VMC to VHFO criteria
- VMC to VHFO criteria
- Stabilization criteria
- Weaning Readiness test
- Extubation Readiness test
- Extubation criteria
- End NIV criteria
- Weaning & extubation failure
For the medical knowledge, need for INPUT

- Evidences
  - Littérature
- Practice pattern
  - Databases
- Stated practice
  - Survey
- Expert Opinion
- Decision points
For the medical knowledge, need for INPUT

- PALICC data on mechanical ventilation
  International experts group

- Development of non-invasive markers of ventilation & oxygenation
  Robinder Khemani

- Survey on clinical Decision points
  G Loron

- Translating an Adult Ventilator Computer Decision Support Tool to a Pediatric Version
  Christopher Newth/Kathy Sward

- Observational study on the ventilation setting modifications practice: Pifometric study
  Allen Eddington

- Chest X-Ray clinical decision support for ARDS diagnosis
  N Zaglam

- ...
What is the Current Medical Knowledge on P-ARDS

Pediatric Acute Lung Injury Consensus Conferences

Organizing committee: Philippe Jouvet, Neal Thomas, Doug Willson
Expert group
Now
Preparation
1st meeting
Starting meeting
1st draft
Recommendation Creation
2nd meeting
Recommendations review
Rating
(2 rounds)
Rand/UCLA
3rd meeting
Finalization
4th step
Diffusion

Organizing committee (n=3)
Define the methodology
Define the agenda
Define the organization
Topic selection (n=9)
Expert selection (n=27)

1st experts meeting
Presentation of the methodology to the experts
Validation of the topics
Validation of the working agenda

Experts group work
Standardized literature review
1st draft of the recommendations
1st draft of the argumentations

2nd experts meeting
Harmonization of the recommendations with the whole group of experts

3rd experts meeting
Presentation of agreed recommendations
Discussion on disagreements
3rd rating round if necessary
Finalization of the Recommendations (short text) with argumentations (9 long texts)
Priorization of research

Dates
Since March 14th 2012 (PALISI meeting)
Chicago October 2nd 2012
Montreal April 18th-19th 2013
Paris (ESICM) October 9th 2013
1st presentation at PALISI meeting March 2014

Completed
Completed
Completed
Completed
Completed
Completed
Completed
Pending

Presentations:
PALISI, SCCM, ESPNIC, ANZICS, GFRUP, CCCTG & WFPICS meetings

Publications:
Pediatr Crit Care Med online ± paper (according to fundings) & other journals
VentilExpert working page
(Platform to develop CDSS rules)

Output data

Rules
Example of rule

VentilExpert working page
(Platform to develop CDSS rules)
Clinician researcher

Computer scientist

e-PALIVE team: members of the PALISI network

e-PALIVE website
Platform to develop and virtually validate the CDSS

**Virtual patient**

<table>
<thead>
<tr>
<th>Input</th>
<th>Controller</th>
<th>Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient characteristics</td>
<td>Data Analyzer</td>
<td>Physiological parameters</td>
</tr>
<tr>
<td>Physiological parameters</td>
<td>Processing engine</td>
<td></td>
</tr>
<tr>
<td>Ventilation</td>
<td>Implementation</td>
<td></td>
</tr>
</tbody>
</table>

**Graphic interface**

<table>
<thead>
<tr>
<th>Output</th>
<th>Controller</th>
<th>Input</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation</td>
<td>Data analyzer</td>
<td>Patient characteristics</td>
</tr>
<tr>
<td></td>
<td>Processing engine</td>
<td>Physiological parameters</td>
</tr>
<tr>
<td></td>
<td>Implementation</td>
<td>Ventilation</td>
</tr>
</tbody>
</table>
Development of a virtual patient

- To validate the CDSS
- To train caregivers on CDSS
- To develop the ventilation forecast
<table>
<thead>
<tr>
<th>Different simulators</th>
<th>Teaching</th>
<th>Ventilation</th>
<th>Ventilator performance</th>
<th>Aim</th>
<th>Research and development</th>
<th>Adult</th>
<th>Child</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanics simulators</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homemade [8–11]</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PneuView*</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>ASL5000**</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Series 101***</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Ventilator simulators</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virtual ventilator [17]</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>Purchasing decision tool</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>EVita_trainer*</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>simulator</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Physiology cardiorespiratory simulators</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MacPuf [18]</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HUMAN [19]</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>VentSim [20]</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>SimuVent [22]</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>***Nottingham physiology simulator (NPS) [24]</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>Intelligent ventilator [29]</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>VO2.htm [23]</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>SOPAVent [21]</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>NPS + Matlab [25]</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>NA</td>
</tr>
<tr>
<td>ARDS simulator [26]</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>SimulResp [33]</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>High-fidelity patient simulators</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SimMan*</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Human patient simulator</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Physiological model of SimulResp (Virtual Patient)

C Dickinson, 1977
SimulResp
(Virtual patient)
SimulResp  
(Virtual patient)

### ePALIVE - Version 2011.02.19.02 | SimulResp - Version 2011.06.28.01

#### Control of SimulResp session

<table>
<thead>
<tr>
<th>Action</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pause</td>
<td></td>
</tr>
<tr>
<td>Start</td>
<td></td>
</tr>
<tr>
<td>Stop</td>
<td></td>
</tr>
</tbody>
</table>

#### Time compression

<table>
<thead>
<tr>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

#### Patient data

- **Age**: 12 (Years) 0 (Months) 0 (Days)
- **Weight**: 30 (kg)
- **Gender**: Male
- **Height**: 120 (cm)
- **Patient disease**: Normal

#### ePALIVE/SimulResp

- **Link SimulResp to ePALIVE**: 
- **Natural ventilation**: 
- **Mechanical ventilation**: 

---

**Note**: The screenshot shows the interface for controlling a virtual patient scenario in SimulResp, with options for adjusting patient data and clinical scenarios.
<table>
<thead>
<tr>
<th>Patient disease (details)</th>
<th>General</th>
<th>Cardiovascular</th>
<th>Brain</th>
<th>Mechanical ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Environment</td>
<td>Exercise: 100</td>
<td>CO: 100</td>
<td>Breath cap: 100</td>
<td>FiO2: 20.93</td>
</tr>
<tr>
<td>Patm 760</td>
<td>Volume EC: 12</td>
<td>CO max: 35</td>
<td>PaO2 resp: 100</td>
<td>FiCO2: 0.03</td>
</tr>
<tr>
<td>Lungs</td>
<td>Ht: 45</td>
<td>R-L shunt: 0</td>
<td>pH resp: 100</td>
<td>PEEP: 0</td>
</tr>
<tr>
<td>Shunt effect: 3</td>
<td>2-3 DPG: 3.8</td>
<td>L-R shunt: 0</td>
<td>Resp drive: 100</td>
<td></td>
</tr>
<tr>
<td>FRC 3000</td>
<td>Temperature: 37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elastance: 5</td>
<td>PVO2 min: 33</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vd + 0</td>
<td>RQ: 0.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VC 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I/E ratio: 0.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Virtual patient debug tool

To change value of one or many parameters, enter the new values in boxes, then click on 'Update'.
For more accuracy, suspend SimuResp during this operation.

ACPR: 35.71 | ADDC: 0.00 | AGE: 24.00 | AN2MT: 2334.97 | AO2MT: 381.34 | AO2PR: 95.15
AVENT: 331.38 | AZ: 100.00 | BAPR: 760.00 | BC2CT: 61.67 | BC2PR: 53.68 | BC3AW: 0.00
BC3CT: 22.00 | BO2AD: 1.00 | BO2CT: 7.47 | BO2PR: 22.30 | BPH: 7.34 | BULLA: 0.00
BZ: 100.00 | CBF: 41.00 | C0: 100.00 | COADJU: 5.60 | COMAX: 27.22 | CONOH: 5.13
CONSO: 263.27 | CZ: 100.59 | DSPAC: 143.05 | DVENT: 6.32 | EJAST: 4.01 | EN2CT: 0.77
EO2CT: 19.50 | FADM: 0.00 | FEV: 4.20 | RC2: 0.03 | FIO2: 21.00 | FITNS: 33.00
FT: 0.08 | FVENT: 4.42 | HB: 14.80 | HT: 175.00 | PC: 0.62 | PC2CT: 48.69
PCV: 45.00 | PD: 100.00 | PEEP: 0.00 | PR: 100.00 | PW: 2.65 | Q4: 21.52
Q8: 13.41 | RC2MNT: 407.44 | RCPP: 35.60 | RC2CT: 24.75 | RLCCT: 0.98 | RN2MT: 7.65
R2MNT: 194.37 | RO2PR: 86.01 | RPH: 7.46 | RATE: 13.30 | RVADM: 0.00 | SHUNT: 0.00
SNI2MT: 966.09 | SNO2PR: 554.25 | SPACE: 0.40 | SVENT: 6.32 | TC2CT: 52.19 | TC2MNT: 13.60
TC2PR: 40.53 | TC3RF: 40.53 | TEMP: 37.00 | TIDVL: 474.43 | TLAMT: 36.06 | TN2PR: 1258.35
TC3CT: 14.46 | TDDMT: 170.32 | TO2PR: 37.67 | TPH: 7.43 | TRQ: 0.80 | TVOL: 12.20
UN2MT: 0.00 | VADM: 3.14 | VBLVL: 3040.11 | VC: 5.00 | VC2CT: 52.01 | VC2MNT: 1581.05
VC3MT: 79.20 | VLUFS: 3462.00 | VO2CT: 14.96 | VO2MNT: 442.63 | VPH: 7.43
XDI:PA: 0.00 | XMALE: 1.00 | XRESP: 12.02 | XVENT: 326.75

Decreasing values: 

Increasing values:

Click on a printed value above to view the history of previous breaths.

[001] Breaths: 42
[002] evalMain (v0) | [003] y = Arc2RCT = 0.054 = 1.09 | increases Cardiac Output if DO supplied is too low
...... y (before damping) = 0.054 = 1.09 | increases Cardiac Output if DO supplied is too low
...... y (after damping) = 0.054 = 1.09 | increases Cardiac Output if DO supplied is too low
...... y (before damping) = 0.054 = 1.09 | increases Cardiac Output if DO supplied is too low
...... y (after damping) = 0.054 = 1.09 | increases Cardiac Output if DO supplied is too low

Enable line trace

Clear output after each breath

Enable debug

08:24
Virtual patient model modification
Validation of a virtual patient
Methodology (1)

Step 1: Validation with physiological knowledge

Step 2a: Validation on a clinical database (methodology similar to R Khemani et al. Intensive Care Med 2011;37:1840)

Step 2b: Validation with a panel of experts

Step 3: Validation on a prospective clinical study (observational study)

Step 4: Validation on a prospective clinical study (interventional study)
Validation of a virtual patient
Methodology (2)

Validation

Virtual Patient model improvement
Validation of a virtual patient

Results

**Step 1:** Validation with physiological knowledge

**Step 2a:** Validation on a clinical database (methodology similar to R Khemani et al. Intensive Care Med 2011;37:1840)

**Step 2b:** Validation with a panel of experts

**Step 3:** Validation on a prospective clinical study (observational study)

**Step 4:** Validation on a prospective clinical study (interventional study)
Spontaneous ventilation with SimulResp, accuracy for PaO2 and PaCO2 in boys

O Flechelles et al. 2013
Simulated and observed blood gazes during exercise in healthy men

Validation of a virtual patient

**Step 1:** Validation with physiological knowledge

**Step 2a:** Validation on a clinical database (methodology similar to R Khemani et al. Intensive Care Med 2011;37:1840)

**Step 2b:** Validation with a panel of experts

**Step 3:** Validation on a prospective clinical study (observational study)

**Step 4:** Validation on a prospective clinical study (interventional study)
Validation on a clinical database (Step 2a)

**Data collection system**

- Electronic Medical Record
- Research server connected to e-Palive
Sainte-Justine Hospital Pediatric Intensive Care EMR*

- Interface Oacis*
  - Profiles – SSO (AD) Biometry

Clinical gate Oacis

- Interface Ingenio
  - MSSS

- Interface Prim
  - March 2012

- Interface Oacis
  - May 2012

- Laboratory application
  - Labo
  - Laboratories equipments

- Intensive Care Application
  - PC & virtual PC
  - Notebooks
  - Infusion pumps
  - Monitor
  - Ventilator
  - Other devices

- ICCA
  - R&D

- Prescription sent by Fax to Radiology Dietetist

- R&D Gespharx

- Pediatric Transport

*EMR: electronic medical record, ** Fax sent to pharmacy
Database:
Mechanically ventilated children for more than 4 days
(criteria from V Payen et al. PCCM 2012)
Conclusion : Here we are!

Plateform for rules implementation
Done

Virtual patient to test the rules and for training
Done, validation in process …

First set of rules will be based on the expert recommendations
On going …

Database creation for preclinical validation of the CDSS
In process …

Clinical validation of the CDSS
Coming …

Training on scenarios
Coming
Hybrid computerized decision support protocol

- Acute phase
  - NIV
  - eVentilator protocol
  - SmartCare or Intellivent or …

- IMV course
  - HFOV
  - IMV Weaning phase

- Weaning phase
  - NIV
  - End of weaning
  - Extubation

- ALI criteria
- Weaning Readiness test
- Extubation Readiness test

- Weaning & extubation failure
- End time
Clinical research team of Sainte-Justine hospital


PALISI Research members involved (alphabetical)

I Cheifetz, A Doctor, D Hamel, R Kelly, A Lia Graciano, D McKinley, A Morris, C Ozment, C Newth, N Thomas, A Randolph, K Rehder, R Khemani, D Tellez, E Williams, D Willson, A Wratney, …

Research grants and award

- Researcher award
- Respiratory Research Network FRSQ
- Réseau Mère-Enfant de la Francophonie
- Natural Sciences & Engineering Research Council of Canada
Equipe des Soins Intensifs Pédiatriques
Hôpital Sainte-Justine

1er rang : Catherine Litalien, Geraldine Pettersen, Marisa Tucci, Guillaume Emeriaud, Catherine Farrell
2nd rang : François Proulx, Baruch Toledano, Karen Harrington, France Gauvin, Jean-Sebastien Joyal
3ème rang : Jacques Lacroix, Philippe Jouvet,