Management of Severe ARDS: Current Canadian Practice

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Disclosures

I have no conflicts of interest to declare.
1. Canadian contributions to knowledge of ARDS
2. Timeline of landmark trials in ARDS
3. Current Canadian ARDS management
4. Adoption and application of evidence in ARDS
How have Canadian patients, clinicians and researchers contributed to our knowledge of ARDS?


Redefining ARDS: Slutsky et al. JAMA 2012.
What informs current management of ARDS in Canada?
Timeline of landmark RCTs in ARDS

- 2000: ARDSNET
- 2002: Low tidal volume ventilation
- 2004: ALVEOLI
- 2006: Higher PEEP
- 2008: Neuromuscular blocking agents
- 2010: LOVS EXPRESS
- 2012: Prone positioning
- 2014: High frequency oscillation
- 2016: Oscar OScillate PRoseva AcurasyS
Several therapies improve oxygenation not mortality

- **Pulmonary vasodilators**
  no mortality benefit with iNO in meta-analyses

- **Airway pressure release ventilation**
  No RCTs

- **Esophageal manometry guided PEEP titration**
  1 RCT (EPVent) with improved oxygenation

- **ECMO**
  1 RCT (CESAR) evaluated transfer to ECMO centre
Rescue therapies?
Refractory hypoxemia

- No precise definition of life-threatening hypoxemia, but as clinicians we all recognize it

- Has been described as PaO2 < 60 mmHg or SpO2 < 88% on FiO2 1.0

- Limited evidence to guide rescue therapy

- Patients underrepresented in RCTs, and observational studies haven't shown survival benefit with any specific therapies or strategy
What is current management of ARDS in Canada?
Study Objective

To provide a benchmark for current clinical care for intensive care clinicians in a new era of ARDS management following the publication of landmark clinical research.

a) describe **mechanical ventilation strategies** and **treatment adjuncts** that clinicians employ routinely for adults with **moderate-to-severe ARDS**

b) and those with **refractory hypoxemia**
Design

• Prospective observational cohort of consecutive mechanically ventilated adults

• **Moderate-to-severe ARDS** (Berlin definition) 
  \((\text{PaO}_2/\text{FiO}_2 < 200 \text{ mmHg}, \text{PEEP} > 5 \text{ cm H}_2\text{O})\) requiring \text{FiO}_2 \geq 0.50

• 12 months (Mar 1/14 to Feb 28/15)
Patients

All patients (moderate-to-severe ARDS) n=664 (96% [n=637] in Canada)

Severe ARDS n=442

Refractory Hypoxemia n=138
defined as… sustained PaO2 < 60 mmHg on FiO2 1.0
Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (n=664)</th>
<th>Refractory Hypoxemia (at any point during study) (n=138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>58.6 (16.3)</td>
<td>56.17 (16.6)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>392 (59.0%)</td>
<td>82 (59.4%)</td>
</tr>
<tr>
<td>APACHE II Score, mean (SD)</td>
<td>25.8 (9.1)</td>
<td>28.84 (9.9)</td>
</tr>
<tr>
<td>Risk factor n, (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>433 (65.2%)</td>
<td>90 (65.2%)</td>
</tr>
<tr>
<td>Non-pulmonary sepsis</td>
<td>144 (21.7%)</td>
<td>29 (21.0%)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>120 (18.1%)</td>
<td>33 (23.9%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>32 (4.8%)</td>
<td>4 (2.9%)</td>
</tr>
<tr>
<td>Multiple transfusion</td>
<td>25 (3.8%)</td>
<td>3 (2.2%)</td>
</tr>
<tr>
<td>Vasculitis/pulmonary hemorrhage</td>
<td>18 (2.7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Multiple fractures</td>
<td>15 (2.3%)</td>
<td>3 (2.2%)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>15 (2.3%)</td>
<td>3 (2.2%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>11 (1.7%)</td>
<td>4 (2.9%)</td>
</tr>
<tr>
<td>Other</td>
<td>59 (8.9%)</td>
<td>1 (0.7%)</td>
</tr>
</tbody>
</table>
Outcomes

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<tr>
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<th>All patients (n=664)</th>
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<tbody>
<tr>
<td>ICU mortality</td>
<td>291 (43.8%)</td>
<td>83 (60.1%)</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>323 (48.6%)</td>
<td>88 (63.8%)</td>
</tr>
</tbody>
</table>

If pt developed refractory hypoxemia:
• Adj OR for ICU mortality: **2.07** (95%CI 1.36, 3.14)
• Adj OR for hospital mortality **2.10** (1.37, 3.22)
  (Adjusted for age and APACHE II score)
Day 1
Mode of conventional ventilation

- CPAP + PSV
- Volume-target, pressure-regulated
- Volume control
- Pressure control

Bar chart showing distribution:

- All patients (n=652):
  - CPAP + PSV: 23%
  - Volume-target, pressure-regulated: 24%
  - Volume control: 41%

- Refractory Hypoxemia (n=135):
  - CPAP + PSV: 19%
  - Volume-target, pressure-regulated: 24%
  - Volume control: 44%
Day 1 of study

**Tidal volume**

- mean Vt: 7.5 (SD 2.1) ml/kg PBW

**PEEP**

- mean PEEP: 10.5 (3.7) cmH₂O

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>FIO₂</td>
<td>0.74 (0.21)</td>
</tr>
<tr>
<td>Plateau pressure (cmH₂O)</td>
<td>25.8 (6.7), 525</td>
</tr>
<tr>
<td>Δ P (cmH₂O)</td>
<td>15.0 (5.7), 525</td>
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Day 1 of refractory hypoxemia

Tidal volume

- Mean Vt: 7.3 (SD 1.8) ml/kg PBW

PEEP

- Mean PEEP: 11.5 (4.3) cmH_2O

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<tr>
<td>FIO2</td>
<td>0.88 (0.18)</td>
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<tr>
<td>Plateau pressure (cmH_2O)</td>
<td>26.9 (6.7), 112</td>
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<tr>
<td>ΔP (cmH_2O)</td>
<td>15.4 (6.1), 112</td>
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Utilization of ARDS adjuncts

Mean FiO\textsubscript{2} at initiation:
- 0.70-0.79
- 0.80-0.89
- ≥0.90

- Corticosteroids: 26%
- Esophageal manometry: 6%
- APRV: 5%
- NMBAs: 42%
- ECLS: 4%
- Prone positioning: 10%
- Pulmonary vasodilators: 18%
- HFOV: 13%

All patients n=664
After refractory hypoxemia n=138
Utilization of ARDS adjuncts

NMBA:
- continuous infusion 76.7% of NMBA-days
- median 3 days of NMBA (SD 1, 5)
- cisatracurium 70.5% of NMBA-days
- rocuronium 36.6%

Mean FiO₂ at initiation:
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Utilization of ARDS adjuncts

- All patients n=664
- After refractory hypoxemia n=138

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Utilization of ARDS adjuncts

**Pulmonary vasodilators:**
- iNO 83.5% of vasodilator-days
- inhaled epoprostanol 15.6%
- IV epoprostanol 3.0%

**Mean FiO₂ at initiation**
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Utilization of ARDS adjuncts

Mean FiO\textsubscript{2} at initiation

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Utilization of ARDS adjuncts

70%

Prone positioning:
- Median 12 hours daily (Q1, Q3 7, 16)
- Regular bed 91.4% of prone-days

Adjuncts used prior to prone:
- NMBA 47.7%
- Pulmonary vasodilators 26.8%
- Corticosteroids 20.9%
- Esophageal manometry 9.0%
- APRV 4.5%
- HFOV or ECLS 0%

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All patients n=664
After refractory hypoxemia n=138
Mean FiO$_2$ at initiation:

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Utilization of ARDS adjuncts

**ECLS:**
- VV ECMO 88.7% of ECLS days
- VA ECMO 8.8%
- VVA or VAV ECMO 2.3%
- No patients received exclusively ECCO$_2$R

Mean FiO$_2$ at initiation:
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ECLS:
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Mean FiO$_2$ at initiation

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Why is there an apparent discordance between evidence and practice?
Adoption of evidence & Application of evidence

- physiologic rationale
- certainty in the evidence
- endorsement of evidence
- guidelines and knowledge translation
- individual patient factors
- perception of risks and benefits
- availability and resources
- clinician experience
What are the key messages for Canadian clinicians?
Take home messages

• Canadians have contributed significantly to the understanding of ARDS management

• Current Canadian management of severe ARDS (2014-15):
  • 66% receive initial low tidal volumes, 11% higher PEEP
  • 42% receive NMBA, 10% prone, 4% HFO, 18% vasodilators

• Refractory hypoxemia is associated with higher mortality and more ARDS adjunct usage

• Further guidelines, knowledge translation, quality improvement initiatives and qualitative studies are needed
Thank you!

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