Predicting Outcomes in ECMO Patients...

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Conflict of interest

• Principal Investigator: EOLIA trial
  • VV ECMO in ARDS
  • NCT01470703
  • Sponsored by MAQUET, Getinge Group

• Received honoraria from
  • MAQUET, XENIOS, GAMBRO, ALUNG
Facts...
In 2016....

- Evidence to support widespread use of ECMO
  - Still lacking
- Outcomes of VV/VA-ECMO patients
  - Not extensively evaluated
  - Survival
  - Functional outcomes
- Need for tools to help physicians
  - In the decision process
ELSO Registry, Cardiac ECMO
Temporal Trends in Post-Cardiotomy ECMO
How to improve the outcomes?
Better select patients suitable for ECMO
Survival predictive models to help in the decision?

*To identify pre-ECMO mortality risk factors...*
Predicting the Outcomes of Respiratory ECMO Patients
Predictive survival model (VV ECMO)

Predicting mortality risk in patients undergoing venovenous ECMO for ARDS due to influenza A (H1N1) pneumonia: the ECMOnet score

Pappalardo et al, ICM 2013

The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome

Schmidt et al, ICM 2013

Outcome of acute respiratory distress syndrome patients treated with extracorporeal membrane oxygenation and brought to a referral center

Roch et al, ICM 2013

Prediction of mortality in adult patients with severe acute lung failure receiving veno-venous extracorporeal membrane oxygenation: a prospective observational study

Enger et al, Crit Care 2014

Predicting Survival after Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Failure
The Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) Score

Schmidt et al, AJRCCM 2014
Predicting mortality risk in patients undergoing venovenous ECMO for ARDS due to influenza A (H1N1) pneumonia: the ECMOnet score

Intensive Care Med (2013)

PreECMO hospital length of stay (days)

<table>
<thead>
<tr>
<th>Length of Stay</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3 days</td>
<td>0.5</td>
</tr>
<tr>
<td>4-7</td>
<td>1</td>
</tr>
<tr>
<td>8-11</td>
<td>1.5</td>
</tr>
<tr>
<td>&gt;11</td>
<td>2</td>
</tr>
</tbody>
</table>

Bilirubin (mg/dl)

<table>
<thead>
<tr>
<th>Bilirubin Level</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.15</td>
<td>0</td>
</tr>
<tr>
<td>0.16-0.65</td>
<td>0.5</td>
</tr>
<tr>
<td>0.66-1.15</td>
<td>1</td>
</tr>
<tr>
<td>1.16-1.65</td>
<td>1.5</td>
</tr>
<tr>
<td>1.66-2.15</td>
<td>2</td>
</tr>
<tr>
<td>&gt;2.15</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Creatinine (mg/dl)

<table>
<thead>
<tr>
<th>Creatinine Level</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.5</td>
<td>0</td>
</tr>
<tr>
<td>0.51-0.80</td>
<td>0.5</td>
</tr>
<tr>
<td>0.81-1.10</td>
<td>1</td>
</tr>
<tr>
<td>1.11-1.40</td>
<td>1.5</td>
</tr>
<tr>
<td>1.41-1.70</td>
<td>2</td>
</tr>
<tr>
<td>1.71-2.00</td>
<td>2.5</td>
</tr>
<tr>
<td>2.01-2.30</td>
<td>3</td>
</tr>
<tr>
<td>&gt;2.30</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Hematocrit (%)

<table>
<thead>
<tr>
<th>Hematocrit Level</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;40</td>
<td>0.5</td>
</tr>
<tr>
<td>36-40</td>
<td>1</td>
</tr>
<tr>
<td>31-35</td>
<td>1.5</td>
</tr>
<tr>
<td>≤30</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Mean arterial pressure (mmHg)

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90</td>
<td>0</td>
</tr>
<tr>
<td>61-90</td>
<td>0.5</td>
</tr>
<tr>
<td>≤60</td>
<td>1</td>
</tr>
</tbody>
</table>
Outcome of acute respiratory distress syndrome patients treated with extracorporeal membrane oxygenation and brought to a referral center

Parameter | Partial score $p_{i}$
---|---
SOFA
<9 | 0
9–11 | 1
≥12 | 2
Age
<45 years | 0
≥45 years | 1
Influenza pneumonia
Yes | 0
No | 1
Total score | 0–4

n=85
The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome

ECMO-ARDS Patients
n=140

50 patients died in the ICU after 27 (17-50) days of ECMO

Alive at ICU discharge
n=90 (64%)

6 patients died 61 [20-76] days after ICU discharge

Alive >6 months after ICU discharge
n=84 (60%)
The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>0</td>
</tr>
<tr>
<td>45–55</td>
<td>2</td>
</tr>
<tr>
<td>&gt;55</td>
<td>3</td>
</tr>
<tr>
<td>Body mass index &gt;30</td>
<td>-2</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>2</td>
</tr>
<tr>
<td>SOFA &gt;12&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
</tr>
<tr>
<td>MV &gt;6 days</td>
<td>1</td>
</tr>
<tr>
<td>No prone positioning before ECMO</td>
<td>1</td>
</tr>
<tr>
<td>PEEP &lt; 10 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>2</td>
</tr>
<tr>
<td>Plateau pressure &gt;30 cm H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>2</td>
</tr>
<tr>
<td>Total score&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0–14</td>
</tr>
</tbody>
</table>
The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome

Intensive Care Med 2013

$P < 0.001$, Log-rank test

Days after ECMO initiation

Cumulative probability of survival

0.0 0.2 0.4 0.6 0.8 1.0

PRESERVE 0-2
PRESERVE 3-4
PRESERVE 5-6
PRESERVE ≥7

La Pitié Paris Cardiology Institute alain.combes@aphp.fr www.paris-tcsecmo.org
Prediction of mortality in adult patients with severe acute lung failure receiving veno-venous extracorporeal membrane oxygenation: a prospective observational study

Tone Bull Enger⁴, Alois Philipp¹, Vibeke Videm⁴, Matthias Lubnow², Alexander Wahba⁵, Marcus Fischer², Christof Schmid¹, Thomas Bein³ and Thomas Müller²

Methods: Established mortality risk scores were validated to assess their usefulness in 304 adult patients undergoing vV-ECMO for refractory lung failure at the University Medical Center Regensburg from 2008 to 2013. A parsimonious prediction model was developed based on variables available before ECMO initiation using logistic regression modelling. We then assessed whether addition of variables available one day after ECMO implementation enhanced mortality prediction. Models were internally validated and calibrated by bootstrapping (400 runs). Predictive ability, goodness-of-fit and model discrimination were compared across the different models.

Results: In the present study population, existing mortality prediction tools for vV-ECMO patients showed suboptimal performance. Evaluated before vV-ECMO initiation, a logistic prediction model comprising age, immunocompromised state, artificial minute ventilation, pre-ECMO serum lactate and hemoglobin concentrations showed best mortality prediction in our patients (area under curve, AUC: 0.75). Additional information about norepinephrine dosage, fraction of inspired oxygen, C-reactive protein and fibrinogen concentrations the first day following ECMO initiation further improved discrimination (AUC: 0.79, P = 0.03) and predictive ability (likelihood ratio test, P < 0.001). When classifying patients as lower (<40%) or higher (>80%) risk based on their predicted mortality, the pre-ECMO and day1-on-ECMO models had negative/positive predictive values of 76%/82% and 82%/81%, respectively.
Prediction of mortality in adult patients with severe acute lung failure receiving veno-venous extracorporeal membrane oxygenation: a prospective observational study

Tone Bull Enger, Alois Philipp, Vibeke Videm, Matthias Lubnow, Alexander Wahba, Marcus Fischer, Christof Schmid, Thomas Bein and Thomas Müller

Table 2 Comparison of mortality prediction models in the study population (number = 304)

<table>
<thead>
<tr>
<th>Model</th>
<th>Valid n</th>
<th>AUC</th>
<th>P-value</th>
<th>Hosmer-Lemeshow test P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-ECMO prediction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFA score</td>
<td>303</td>
<td>0.611 (0.544-0.678)</td>
<td>0.027</td>
<td>&lt;0.0001(^b)</td>
</tr>
<tr>
<td>ECMOnet score</td>
<td>280</td>
<td>0.604 (0.537-0.671)</td>
<td>0.009</td>
<td>0.0002(^b)</td>
</tr>
<tr>
<td>PRESERVE</td>
<td>289</td>
<td>0.685 (0.623-0.748)</td>
<td>0.12</td>
<td>0.004(^b)</td>
</tr>
<tr>
<td>Model 1</td>
<td>284</td>
<td>0.746 (0.689-0.804)</td>
<td>Reference</td>
<td>0.50</td>
</tr>
</tbody>
</table>

Table 3 Performance of the PRESERVE score in the original and validation cohorts

<table>
<thead>
<tr>
<th>PRESERVE score class</th>
<th>Original study population</th>
<th>UKR ECMO registry</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%)</td>
<td>Mortality rate up to six months post-ICU</td>
</tr>
<tr>
<td>0 to 2</td>
<td>34 (25.0%)</td>
<td>3%</td>
</tr>
<tr>
<td>3 to 4</td>
<td>38 (27.9%)</td>
<td>21%</td>
</tr>
<tr>
<td>5 to 6</td>
<td>26 (19.1%)</td>
<td>46%</td>
</tr>
<tr>
<td>≥7</td>
<td>38 (27.9%)</td>
<td>84%</td>
</tr>
<tr>
<td>Total</td>
<td>136 (100.0%)</td>
<td>40%</td>
</tr>
<tr>
<td>PSEP</td>
<td>81%(^a)</td>
<td></td>
</tr>
</tbody>
</table>
Prediction of mortality in adult patients with severe acute lung failure receiving veno-venous extracorporeal membrane oxygenation: a prospective observational study

[Graph of sensitivity and 1-specificity for different models: Model 2 (Day 1), Model 1 (Pre-ECMO), PRESERVE, ECMOnet, SOFA]
Predicting Survival after ECMO for Severe Acute Respiratory Failure: the Respiratory ECMO Survival Prediction (RESP)-Score

Matthieu Schmidt, Michael Bailey, Jayne Sheldrake, Carol Hodgson, Cecile Aubron, Peter T. Rycus, Carlos Scheinkestel, D. Jamie Cooper, Daniel Brodie, Vincent Pellegrino, Alain Combes, and David Pilcher

Corresponding Author: Matthieu Schmidt, Email: matthieuschmidt@yahoo.fr
The RESP Score

The RESP Score has been developed by ELSO and The Department of Intensive Care at The Alfred Hospital, Melbourne. It is designed to assist prediction of survival for adult patients undergoing Extra-Corporeal Membrane Oxygenation for respiratory failure. It should not be considered for patients who are not on ECMO or as substitute for clinical assessment.


Age (years):
- 18-49
- 50-59
- ≥60

Immunocompromised

Mechanical ventilation prior to initiation of ECMO
- <48 hours
- 48 hours - 7 days
- >7 days

Acute Respiratory diagnosis group
- Viral pneumonia
- Bacterial pneumonia
- Asthma
- Trauma/burn
- Aspiration pneumonitis
- Other acute respiratory diagnosis
- Non-respiratory and chronic respiratory diagnoses

Central nervous system dysfunction

Acute associated (non-pulmonary) infection

Neuro-muscular blockade before ECMO

Nitric oxide use before ECMO

Bicarbonate infusion before ECMO

Cardiac arrest before ECMO

PaCO₂ 275 mmHg / 10kpa

Peak inspiratory pressure ≥242 cmH₂O
External Validation on the PRESERVE Cohort

(A) Observed survival

(B) Occurrence of death or re-intubation (RESP-score)
Predicting the Outcomes of Cardiac ECMO Patients
Latest series of VA-ECMO for AMI

The ENCOURAGE mortality risk score and analysis of long-term outcomes after VA-ECMO for acute myocardial infarction with cardiogenic shock

Grégoire Muller¹, Erwan Flecher³, Guillaume Lebreton², Charles-Edouard Luyt¹, Jean-Louis Trouillet¹, Nicolas Bréchet¹, Matthieu Schmidt¹, Ciro Mastroianni², Jean Chastre¹, Pascal Leprince², Amedeo Anselmi³ and Alain Combes¹*

Intensive Care Med 2016
Latest case series of VA-ECMO for CS-AMI

Intensive Care Med 2016

138 Patients

65 ICU survivors

73 In-ICU deaths:
- 47 Under ECMO
- 20 Bridged to another device
- 6 Weaned

44 Weaned

- 12 LVAD
- 4 Heart transplants

- 36 Alive
- 3 Died
- 5 Lost to follow-up

21 Not weaned

- 4 Heart transplants
- 1 BiVAD
- 1 Impella 5.0
- 3 Centralized ECMO

- 12 Alive
- 4 Alive
- 1 Heart transplant
- 1 Alive
- 3 Alive (1 heart transplant)

6-month follow-up

41% survival
Latest case series of VA-ECMO for CS-AMI

Intensive Care Med 2016

47% ICU survival

138 Patients

73 In-ICU deaths:
- 47 Under ECMO
- 20 Bridged to another device
- 6 Weaned

65 ICU survivors

12 LVAD
- 36 Alive
- 3 Died
- 5 Lost-to-follow-up

4 Heart transplants
- 12 Alive

1 BiVAD
- 4 Alive

1 Impella 5.0
- 1 Heart transplant

3 Centralized ECMO
- 3 Alive (1 heart transplant)

6-month follow-up
41% survivors
Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock


Encourage cohort

Control

IABP

Mortality (%)

Days since Randomization

0 5 10 15 20 25 30

0 10 20 30 40 50
Latest case series of VA-ECMO for CS-AMI

Intensive Care Med 2016

138 Patients

65 ICU survivors

44 Weaned

21 Not weaned

73 In-ICU deaths:
47 Under ECMO
20 Bridged to another device
6 Weaned

32% successful weaning

36 Alive
3 Died
5 Lost-to-follow-up

12 Alive

4 Alive

1 Heart transplant

1 Alive

3 Alive (1 heart transplant)

41% surviving 3-month follow-up
# The ENCOURAGE cohort

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 138)</th>
<th>Survivors (n = 65)</th>
<th>Non-survivors (n = 73)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobile ECMO retrieval</td>
<td>33%</td>
<td>33%</td>
<td>33%</td>
<td>0.940</td>
</tr>
<tr>
<td>Pre-ECMO cardiac arrest</td>
<td>57%</td>
<td>57%</td>
<td>58%</td>
<td>0.940</td>
</tr>
<tr>
<td>Thrombolysis for AMI</td>
<td>12%</td>
<td>9%</td>
<td>14%</td>
<td>0.410</td>
</tr>
<tr>
<td>ECMO pre-PCI</td>
<td>10%</td>
<td>12%</td>
<td>8%</td>
<td>0.460</td>
</tr>
<tr>
<td>Post-PCI ECMO</td>
<td>90%</td>
<td>88%</td>
<td>92%</td>
<td>0.660</td>
</tr>
</tbody>
</table>
Emergency circulatory support in refractory cardiogenic shock patients in remote institutions: a pilot study (the cardiac-RESCUE program)

Sylvain Beurtheret¹*, Pierre Mordant¹†, Xavier Paoletti², Eloi Marijon³,⁴,⁵, David S. Celermajer⁶, Philippe Léger¹, Alain Pavie¹, Alain Combes⁷, and Pascal Leprince¹

The Mobile ECMO rescue team at La Pitié: 2005-2009 experience for refractory cardiac failure...
Comparison with in-house patients

• In the multivariate analysis
  • Adjusted for the inotrope score
  • Stratified for diagnosis and CPR at ECMO start

• Mortality at hospital discharge in the Cardiac-RESCUE Program group was not statistically different between groups
  • OR 1.48, 95% CI 0.72–3.00, p=0.29
## The ENCOURAGE cohort

<table>
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<tr>
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<th>All patients (n = 138)</th>
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<th>Non-survivors (n = 73)</th>
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<td>12%</td>
<td>8%</td>
<td>0.460</td>
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<tr>
<td>Post-PCI ECMO</td>
<td>90%</td>
<td>88%</td>
<td>92%</td>
<td>0.660</td>
</tr>
</tbody>
</table>
The ENCOURAGE cohort

Days after ECMO initiation

Lactate < 2 mmol/l

Lactate 2-8 mmol/l

Lactate > 8 mmol/l

P <0.005, log-rank

0 25 50 75 100 125 150 175 200

0 0.2 0.4 0.6 0.8 1
The ENCOURAGE cohort

P = 0.04, log-rank

Age < 60

Age > 60

Days after ECMO initiation
**ENCOURAGE SCORE to predict the outcomes of CS-AMI VA-ECMO....**

*Intensive Care Med 2016*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>Component score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;60 years</td>
<td>2.63 (1.01–6.85)</td>
<td>0.048</td>
<td>5</td>
</tr>
<tr>
<td>Female</td>
<td>4.35 (1.29–14.72)</td>
<td>0.018</td>
<td>7</td>
</tr>
<tr>
<td>Body mass index &gt;25 kg/m²</td>
<td>3.10 (1.21–7.92)</td>
<td>0.018</td>
<td>6</td>
</tr>
<tr>
<td>Glasgow Coma Score &lt;6</td>
<td>3.09 (1.19–8.05)</td>
<td>0.021</td>
<td>6</td>
</tr>
<tr>
<td>Creatininemia &gt;150 mmol/L</td>
<td>2.60 (1.05–6.49)</td>
<td>0.04</td>
<td>5</td>
</tr>
<tr>
<td>Serum lactate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 mmol/L</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2–8 mmol/L</td>
<td>4.71 (1.31–17.01)</td>
<td>0.02</td>
<td>8</td>
</tr>
<tr>
<td>&gt;8 mmol/L</td>
<td>8.71 (1.76–43.10)</td>
<td>0.004</td>
<td>11</td>
</tr>
<tr>
<td>Prothrombin activity &lt;50%</td>
<td>2.80 (1.01–7.77)</td>
<td>0.049</td>
<td>5</td>
</tr>
</tbody>
</table>
ENCOURAGE SCORE to predict the outcomes of CS-AMI VA-ECMO....

Intensive Care Med 2016

![Graph showing cumulative probability of survival over days after ECMO initiation for different score ranges.]

- **SCORE 0–12**
- **SCORE 13–18**
- **SCORE 19–22**
- **SCORE 23–27**
- **SCORE ≥28**

**Cumulative Probability of Survival**

**Days after ECMO Initiation**

*P* < 0.001, log-rank test
Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score

Matthieu Schmidt¹,²*, Aidan Burrell¹,³, Lloyd Roberts³, Michael Bailey¹,³, Jayne Sheldrake³, Peter T. Rycus⁴, Carol Hodgson¹,³, Carlos Scheinkestel³, D. Jamie Cooper¹,³, Ravi R. Thiagarajan⁴,⁵,⁶, Daniel Brodie⁷, Vincent Pellegrino¹,³, and David Pilcher¹,³
The patient's SAVE Score is

**Diagnosis:**
- Myocarditis
- Refractory VT/VF
- Post heart or lung transplantation
- Congenital heart disease
- Other diagnoses

**Age (years):**
- 18-38
- 39-52
- 53-62
- ≥63

**Weight (kg):**
- <65
- 65-89
- ≥90

**Cardiac:**
- Pulse pressure pre ECMO ≤20 mmHg
- Diastolic BP pre ECMO ≥40 mmHg
- Pre-ECMO cardiac arrest

**Respiratory:**
- Peak inspiratory pressure ≤20 cmH₂O
- Intubation duration pre ECMO (hrs)
  - ≤10
  - 11-29
  - ≥30

**Renal:**
- Acute renal failure
- Chronic renal failure
- HCO₃ pre ECMO ≤15 mmol/L

**Other organ failures pre ECMO:**
- Central nervous system dysfunction
- Liver failure

**Additional Information:**
- The SAVE Score has been developed by ELSO and The Department of Intensive Care at The Alfred Hospital, Melbourne. It is designed to assist in the prediction of survival for adult patients undergoing Extra-Corporeal Membrane Oxygenation for refractory cardiogenic shock. It should not be considered a substitute for clinical assessment.
- For more information, see: [Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE) score](http://www.save-score.com)
External Validation of the SAVE score
ENCOURAGE SCORE to predict the outcomes of CS-AMI VA-ECMO....

Intensive Care Med 2016
Usefulness of such scores

• To help clinicians identify “good” and “bad” candidates for ECMO with a simple tool at the beside
Usefulness of such scores

• To help clinicians identify “good” and “bad” candidates for ECMO with a simple tool at the bedside
Usefulness of such scores

• To help clinicians identify “good” and “bad” candidates for ECMO with a simple tool at the beside
Usefulness of such scores

• To help clinicians identify “good” and “bad” candidates for ECMO with a simple tool at the beside
Usefulness of such scores

• To allow institutions to
  • Appropriately allocate resources

• To facilitate risk-adjusted comparison
  • Of center-specific outcomes (benchmarking)

• To help to inform family members
  • On the prognosis of the disease
Limitations of these scores

• Should not be considered a substitute
  • For clinical judgment

• Developed on patients already on ECMO +++
  • Not validated for prediction of survival in a general population of severe ARF patients where ECMO has not (yet) been instituted

• More useful to identify patients...
  • For whom ECMO should not be used???

• Very few scoring systems have external validation
Conclusions

• Survival after VV-ECMO
  • Constantly >60% in latest series of patients
  • Improves if adequate patients’ selection

• Scoring systems...
  • Easy tool at the beside
  • Better than “classical” ICU scoring (SAPS, APACHE, SOFA...)
  • May help in the decision to deny ECMO support?
  • Not a “Magic Crystal Ball”
  • All have yet to be prospectively validated
“Prediction is very difficult, especially about the future”

Niels Bohr 1885-1962  
Physics Nobel Price - 1922