Neurally Adjusted Ventilatory Assist as an alternative to Pressure Support Ventilation – A multicentre randomized trial

A Demoule, M Clavel, C Rolland-Debord, S Perbet, N Terzi, A Kouatchet, F Wallet, H Roze,
F Vargas, C Guerin, J Dellamonica, S Jaber, L Brochard, T Similowski

Online supplement
### Table E1. Main differences between Pressure Support Ventilation (PSV) and Neurally Adjusted Ventilatory Assist (NAVA)

<table>
<thead>
<tr>
<th></th>
<th>PSV</th>
<th>NAVA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ventilator triggering</strong></td>
<td><strong>Principle</strong></td>
<td>The ventilator is triggered when flow or pressure at airway opening exceed a preset value.</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Preset value is set in l.s(^{-1}) or cmH(_2)O.</td>
<td>Preset value is set in µV.</td>
</tr>
<tr>
<td><strong>Airway pressurization</strong></td>
<td><strong>Principle</strong></td>
<td>Airways are pressurized at the preset “pressure support level”.</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Pressure support level, expressed in cmH(_2)O.</td>
<td>NAVA level : factor by which the Edi signal is multiplied to adjust the amount of assist delivered to the patient.</td>
</tr>
<tr>
<td><strong>Relationship between the level of assistance and the intensity the patient inspiratory effort.</strong></td>
<td>The level of assistance is constant, irrespective of the intensity of the patient inspiratory effort.</td>
<td>The level of assistance is proportional to the EAdi, a surrogate of the intensity of the patient ventilatory drive.</td>
</tr>
<tr>
<td><strong>Ventilator cycling-off</strong></td>
<td><strong>Principle</strong></td>
<td>Airway insufflation by the ventilator ends when the inspiratory flow falls below a set proportion of the maximal inspiratory flow.</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Cycling-off can be adjusted. In most ventilators, cycling-off value is set between 25% and 30% by default.</td>
<td>Fixed (70% of EAdi peak value) cannot be adjusted</td>
</tr>
</tbody>
</table>

*EAdi*, electrical activity of the diaphragm.
### Table E2. Definition of the five main asynchronies and the asynchrony index

<table>
<thead>
<tr>
<th>Asynchronies</th>
<th>Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ineffective effort (n.min⁻¹)</strong></td>
<td>Presence of a characteristic EAdi activity not followed by a ventilator-delivered pressurization</td>
</tr>
<tr>
<td><strong>Late cycling (n.min⁻¹)</strong></td>
<td>Duration of pressurization at least twice as long as the patient’s neural inspiratory time</td>
</tr>
<tr>
<td><strong>Double triggering Type (n.min⁻¹)</strong></td>
<td>Two respiratory cycles due to a biphasic EAdi signal</td>
</tr>
<tr>
<td><strong>Premature cycling (n.min⁻¹)</strong></td>
<td>Duration of pressurization at least twice shorter than the patient’s neural inspiratory time</td>
</tr>
<tr>
<td><strong>Auto-triggering (n.min⁻¹)</strong></td>
<td>A cycle delivered by the ventilator in the absence of EAdi signal</td>
</tr>
<tr>
<td><strong>Asynchrony index (%)</strong></td>
<td>[(auto-triggering + ineffective efforts + late cycling + premature cycling +double triggering) / (ineffective effort + breath rate)] x 100</td>
</tr>
</tbody>
</table>

_EAdi_, electrical activity of the diaphragm.

The number of each type of asynchrony was reported as the total number of each event per minute (n.min⁻¹).
Table E3. Volume of patients per year and enrolment rate per centre

<table>
<thead>
<tr>
<th>Centre</th>
<th>Volume of patients admitted per year, n</th>
<th>Enrollment rate per year, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centre 1</td>
<td>569</td>
<td>6.7</td>
</tr>
<tr>
<td>Centre 2</td>
<td>568</td>
<td>1.1</td>
</tr>
<tr>
<td>Centre 3</td>
<td>406</td>
<td>2.7</td>
</tr>
<tr>
<td>Centre 4</td>
<td>646</td>
<td>0.8</td>
</tr>
<tr>
<td>Centre 5</td>
<td>732</td>
<td>1.6</td>
</tr>
<tr>
<td>Centre 6</td>
<td>516</td>
<td>0.8</td>
</tr>
<tr>
<td>Centre 7</td>
<td>744</td>
<td>0.3</td>
</tr>
<tr>
<td>Centre 8</td>
<td>462</td>
<td>3.0</td>
</tr>
<tr>
<td>Centre 9</td>
<td>698</td>
<td>1.3</td>
</tr>
<tr>
<td>Centre 10</td>
<td>889</td>
<td>2.8</td>
</tr>
<tr>
<td>Centre 11</td>
<td>666</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Table E4. Causes of respiratory failure

<table>
<thead>
<tr>
<th></th>
<th>PSV (n = 66)</th>
<th>NAVA (n = 62)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>De novo. n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia. n (%)</td>
<td>38 (58)</td>
<td>34 (55)</td>
</tr>
<tr>
<td>Aspiration. n (%)</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td>Extra pulmonary sepsis. n (%)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Other. n (%)</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td><strong>Postoperative. n (%)</strong></td>
<td>13 (20)</td>
<td>13 (21)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Extrapulmonary sepsis</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>ARDS following cardiothoracic surgery</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Hemorrhagic shock. trauma</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Acute-on-chronic. n (%)</strong></td>
<td>12 (18)</td>
<td>12 (19)</td>
</tr>
<tr>
<td>Acute cardiogenic pulmonary oedema. n (%)</td>
<td>3 (5)</td>
<td>3 (5)</td>
</tr>
</tbody>
</table>
Table E5. Main reasons for switch to controlled mechanical ventilation

<table>
<thead>
<tr>
<th>Reason</th>
<th>PSV (n = 60)</th>
<th>NAVA (n = 58)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory distress, hypoxaemia or hypercapnic acidosis despite optimization of ventilator settings. n (%)</td>
<td>8 (13)</td>
<td>5 (9)</td>
<td>0.414</td>
</tr>
<tr>
<td>Severe hypotension, shock or arrhythmias. n (%)</td>
<td>1 (2)</td>
<td>2 (3)</td>
<td>0.378</td>
</tr>
<tr>
<td>Increased need for sedation for agitation or patient-ventilator asynchrony. n (%)</td>
<td>1 (2)</td>
<td>2 (3)</td>
<td>0.378</td>
</tr>
<tr>
<td>Investigation requiring an increase of sedation for (gastrointestinal endoscopy, transoesophageal echocardiography, surgery). n (%)</td>
<td>10 (17)</td>
<td>9 (16)</td>
<td>0.865</td>
</tr>
<tr>
<td>Other. n (%)</td>
<td>2 (3)</td>
<td>1 (2)</td>
<td>0.579</td>
</tr>
</tbody>
</table>
Table E6. Comparison of patients’ characteristics and baseline variables between failure and success patients

<table>
<thead>
<tr>
<th></th>
<th>Failure of partial ventilatory mode n=39</th>
<th>Success of partial ventilatory mode n=79</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age. years</td>
<td>61 (58-71)</td>
<td>72 (58-78)</td>
<td>0.172</td>
</tr>
<tr>
<td>Sex. male. n (%)</td>
<td>30 (38)</td>
<td>48 (62)</td>
<td>0.081</td>
</tr>
<tr>
<td>SAPS 2</td>
<td>44 (34-63)</td>
<td>43 (34-58)</td>
<td>0.610</td>
</tr>
<tr>
<td>Blood gases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO₂/FiO₂, mmHg</td>
<td>233 (187-280)</td>
<td>226 (190-280)</td>
<td>0.811</td>
</tr>
<tr>
<td>PaCO₂, mmHg</td>
<td>40 (34-45)</td>
<td>39 (34-48)</td>
<td>0.806</td>
</tr>
<tr>
<td>Dyspnoea-VAS, from 0 to 10</td>
<td>1 (0-3)</td>
<td>1 (0-3)</td>
<td>0.945</td>
</tr>
<tr>
<td>Duration of mechanical ventilation prior to inclusion. days</td>
<td>4 (3-8)</td>
<td>5 (3-9)</td>
<td>0.401</td>
</tr>
<tr>
<td>Cause of acute respiratory failure</td>
<td></td>
<td></td>
<td>0.420</td>
</tr>
<tr>
<td>Acute-on-chronic n (%)</td>
<td>8 (53)</td>
<td>7 (47)</td>
<td></td>
</tr>
<tr>
<td>Acute cardiogenic pulmonary edema. n (%)</td>
<td>1 (20)</td>
<td>4 (800)</td>
<td></td>
</tr>
<tr>
<td>De novo. n (%)</td>
<td>22 (33)</td>
<td>44 (67)</td>
<td></td>
</tr>
<tr>
<td>Postoperative. n (%)</td>
<td>7 (27)</td>
<td>19 (73)</td>
<td></td>
</tr>
<tr>
<td>Study group. NAVA. n (%)</td>
<td>19 (49)</td>
<td>39 (49)</td>
<td>0.663</td>
</tr>
</tbody>
</table>

SAPS, simplified acute physiology; NAVA, neurally adjusted ventilatory assist.
Continuous data are reported as median (interquartile range [IQR]) and categorical data are reported as number of events (percentages).
Table E7. Time spent in each mechanical ventilation mode during the first 48 hours following inclusion

<table>
<thead>
<tr>
<th>Mode</th>
<th>PSV (n = 66)</th>
<th>NAVA (n = 62)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure support ventilation (PSV). h</td>
<td>47.1 (39.8-48.0)</td>
<td>2.5 (0.8-12.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PSV-Pressure control. h</td>
<td>1.5 (0.5-2.4)</td>
<td>0 (0-0)</td>
<td>ND</td>
</tr>
<tr>
<td>Neurally adjust ventilator assist (NAVA). h</td>
<td>NA</td>
<td>44.1 (33.0-47.8)</td>
<td>NA</td>
</tr>
<tr>
<td>NAVA-PSV. h</td>
<td>NA</td>
<td>0.7 (0.3-2.2)</td>
<td>NA</td>
</tr>
<tr>
<td>NAVA-Pressure control. h</td>
<td>NA</td>
<td>0.85 (0.4-1.2)</td>
<td>NA</td>
</tr>
<tr>
<td>Assist-control ventilation. h</td>
<td>3.0 (1.0-10.5)</td>
<td>2.1 (0.6-25.5)</td>
<td>0.812</td>
</tr>
<tr>
<td>Pressure-regulated volume control. h</td>
<td>4.5 (1.8-8.5)</td>
<td>1.3 (0.8-7.3)</td>
<td>0.330</td>
</tr>
<tr>
<td>Pressure control ventilation. h</td>
<td>1.2 (0.6-1.8)</td>
<td>0 (0-0)</td>
<td>ND</td>
</tr>
</tbody>
</table>

(a) PSV-Pressure control. pressure control ventilation as back-up mode of PSV.

(b) NAVA-PSV. PSV as a primary back-up mode in NAVA.

(c) NAVA-Pressure control. pressure control ventilation as secondary back-up mode in NAVA.
Table E7. Respiratory variables at three time points during the first 5 days of treatment

<table>
<thead>
<tr>
<th></th>
<th>24 hours</th>
<th></th>
<th></th>
<th>48 hours</th>
<th></th>
<th></th>
<th>Day-5</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PSV (n = 66)</td>
<td>NAVA (n = 60)</td>
<td>P</td>
<td>PSV (n = 66)</td>
<td>NAVA (n = 58)</td>
<td>P</td>
<td>PSV (n = 25)</td>
<td>NAVA (n = 22)</td>
<td>P</td>
</tr>
<tr>
<td>Dyspnoea, n (%)</td>
<td>19 (66)</td>
<td>9 (28)</td>
<td>0.03</td>
<td>13 (52)</td>
<td>14 (50)</td>
<td>0.54</td>
<td>6 (46)</td>
<td>3 (30)</td>
<td>0.67</td>
</tr>
<tr>
<td>ATICE score</td>
<td>16.5 (13-19)</td>
<td>16 (11-19)</td>
<td>0.66</td>
<td>16.5 (11-20)</td>
<td>18 (12-20)</td>
<td>0.68</td>
<td>17 (14-19)</td>
<td>16 (11-20)</td>
<td>0.66</td>
</tr>
<tr>
<td>PEEP level, cmH₂O</td>
<td>6 (5-8)</td>
<td>6 (5-8)</td>
<td>0.52</td>
<td>6 (5-8)</td>
<td>6 (5-8)</td>
<td>0.97</td>
<td>6 (5-8)</td>
<td>6 (5-8)</td>
<td>0.67</td>
</tr>
<tr>
<td>PSV level, cmH₂O</td>
<td>12 (10-14)</td>
<td>NA</td>
<td>NA</td>
<td>12 (10-12)</td>
<td>NA</td>
<td>NA</td>
<td>10 (8-12)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>NAVA level, cmH₂O.μV⁻¹</td>
<td>NA</td>
<td>1.8 (1.0-2.5)</td>
<td>NA</td>
<td>NA</td>
<td>1.9 (1.0-2.8)</td>
<td>NA</td>
<td>NA</td>
<td>1.3 (1.0-3.0)</td>
<td>NA</td>
</tr>
<tr>
<td>Tidal volume, ml</td>
<td>461 (400-530)</td>
<td>455 (410-550)</td>
<td>0.69</td>
<td>456 (386-549)</td>
<td>444 (380-535)</td>
<td>0.65</td>
<td>467 (425-587)</td>
<td>439 (380-572)</td>
<td>0.33</td>
</tr>
<tr>
<td>Tidal volume, ml.kg⁻¹</td>
<td>7.2 (6.3-8.3)</td>
<td>7.2 (6.4-8.2)</td>
<td>0.92</td>
<td>7.2 (6.4-8.3)</td>
<td>7.15 (6.3-8.3)</td>
<td>0.53</td>
<td>7.1 (6.6-9.2)</td>
<td>6.8 (5.9-8.7)</td>
<td>0.34</td>
</tr>
<tr>
<td>Minute ventilation, l.min⁻¹</td>
<td>10.0 (8.9-12.4)</td>
<td>11.7 (10-13)</td>
<td>0.045</td>
<td>11.0 (9.4-13.4)</td>
<td>10.4 (8.5-12.4)</td>
<td>0.44</td>
<td>11.5 (9.95-13.0)</td>
<td>11.0 (8.7-14.0)</td>
<td>0.57</td>
</tr>
<tr>
<td>Respiratory rate, min⁻¹</td>
<td>23 (20-26)</td>
<td>26 (20-29)</td>
<td>0.09</td>
<td>24 (18-29)</td>
<td>24 (19-28)</td>
<td>0.95</td>
<td>25 (22-28)</td>
<td>25 (23-30)</td>
<td>0.53</td>
</tr>
<tr>
<td>PaO₂/FiO₂, mmHg</td>
<td>217 (166-293)</td>
<td>237 (179-305)</td>
<td>0.66</td>
<td>247 (189-320)</td>
<td>262 (198-305)</td>
<td>0.68</td>
<td>197 (170-277)</td>
<td>261 (186-51)</td>
<td>0.11</td>
</tr>
<tr>
<td>pH</td>
<td>7.43 (7.39-7.47)</td>
<td>7.45 (7.40-7.47)</td>
<td>0.29</td>
<td>7.43 (7.39-7.46)</td>
<td>7.44 (7.39-7.47)</td>
<td>0.74</td>
<td>7.42 (7.40-7.43)</td>
<td>7.44 (7.37-7.46)</td>
<td>0.87</td>
</tr>
<tr>
<td>PaCO₂, mmHg</td>
<td>40 (36-46)</td>
<td>39 (33-48)</td>
<td>0.41</td>
<td>40 (34-46)</td>
<td>41 (34-51)</td>
<td>0.71</td>
<td>42 (37-49)</td>
<td>41 (39-48)</td>
<td>0.88</td>
</tr>
</tbody>
</table>

PSV, pressure support ventilation; NAVA, neurally adjust ventilator assist; ATICE, adaptation to intensive care environment (evaluates comfort, ranges from 0 to 20).

*Respiratory rate was computed based on ventilator breaths.
Continuous data are reported as median (interquartile range [IQR]) and categorical data as number of event (percentages).