Future of Automated Ventilation

patient vs. healthcare provider
Disclosures

• Xenios/Fresenius, Germany
• Hamilton Medical AG, Switzerland
Agenda

• history of ventilation
• history of automated ventilation
• benefits of automated ventilation
• need for automated ventilation?
• wrap–up
Agenda

• history of ventilation
• history of automated ventilation
• benefits of automated ventilation
• need for automated ventilation?
• wrap–up
Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation
Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation
QUESTION Does the use of a lower tidal volume ($V_T$) with mechanical ventilation affect important clinical outcomes in ARDS patients?

CONCLUSION Ventilation with a lower $V_T$ than is traditionally used results in decreased mortality and increases the number of days without ventilator use.

POPULATION

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
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<tbody>
<tr>
<td>344</td>
<td>516</td>
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</table>

344 Women, 516 Men

patients with ARDS

mean age: 52 years

LOCATION

ICUs in the USA

VENTILATION STRATEGIES

861 patients with mild, moderate or severe ARDS

432 patients lower $V_T$ (6 ml/kg) [~ 400 to 500 ml]

429 patients traditional $V_T$ (12 ml/kg) [~1000 to 1200 ml]

(PRI) PRIMARY OUTCOME

hospital mortality and duration of invasive ventilation

FINDINGS

QUESTION For patients in the ICU who are ventilated for reasons other than ARDS, is low tidal volume superior to intermediate tidal volume?

CONCLUSION Among ICU patients receiving invasive ventilation, a strategy with a low tidal volume was not superior to using intermediate tidal volume.

**POPULATION**

621 Men 340 Women

ICU patients without ARDS expected to be intubated for more than 24 hours

Median age: 68 years (IQR, 59-76)

**LOCATIONS**

6 ICUs in the Netherlands

**INTERVENTIONS**

961 Patients randomized

477 Randomized
475 Analyzed

484 Randomized
480 Analyzed

**Low tidal volume**

Started at tidal volume of 6 mL/kg; tidal volume then decreased in steps of 1 mL/kg predicted body weight

**Intermediate tidal volume**

Started at tidal volume of 10 mL/kg; if plateau pressure exceeded 25 cm H₂O, tidal volume was decreased in steps of 1 mL/kg predicted body weight

**FINDINGS**

**PRIMARY OUTCOME**

Number of ventilator-free days and alive at day 28

Writing Group for the PReVENT Investigators. Effect of a low vs intermediate tidal volume strategy on ventilator-free days in intensive care unit patients without ARDS: a randomized clinical trial [published online October 24, 2018]. JAMA. doi:10.1001/jama.2018.14280
**QUESTION** What is the impact of mechanical power on mortality in patients with ARDS as compared with that of primary ventilator variables such as the ΔP, Vₜ, and RR?

**CONCLUSION** Mechanical power was associated with mortality during controlled mechanical ventilation in ARDS, but a simpler model using only the ΔP and RR was equivalent.

**POPULATION**

1728 Women  2821 Men

Patients with ARDS

Mean Age: 55 years

**LOCATION**

6 RCTs and 1 observational study

**VENTILATION PARAMETERS**

4549 patients with mild, moderate or severe ARDS

MP 0.32 J/min/kg

ΔP 15 cm H₂O

RR 26 breath/min

**(PRIMARY) OUTCOME**

Mortality at 28 or 60 days

during spontaneous vs non–spontaneous ventilation, note:

- the position of diaphragm
- the aerated lung size
- presence of atelectasis
- presence of overdistension
Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation
QUESTION Does use of a lung recruitment maneuver associated with PEEP titration according to the best respiratory-system compliance reduce 28-day mortality of patients with moderate to severe ARDS, compared with a conventional low-PEEP strategy?

CONCLUSION A strategy using a lung recruitment maneuver and titrated PEEP increased mortality of patients with moderate to severe ARDS.

POPULATION

379 Women 631 Men

Consecutive patients with moderate to severe ARDS

Mean Age: 51 years

LOCATION

120 ICUs from 9 countries

VENTILATION STRATEGIES

1010 patients with moderate or severe ARDS

501 patients titrated (high) PEEP [>15 cm H₂O] with RM

509 patients standard (low) PEEP [< 12 cm H₂O] without RM

FINDINGS

Better oxygenation, but worse outcomes, and more pneumothorax and barotrauma with high PEEP

(PRIMARY) OUTCOME

28-day mortality; length of ICU and hospital stay; VFD28; pneumothorax requiring drainage or barotrauma within 7 days
QUESTION Is there heterogeneity in treatment effects in patients enrolled in the ART, using a machine learning approach?

CONCLUSION Recruitment maneuvers and titrated PEEP may be harmful in ARDS patients with pneumonia or requiring vasopressor support. Driving pressure appears to modulate the association between the ART study intervention, etiology of ARDS, and mortality.

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Mean Age: 51 years

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120 ICUs from 9 countries

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FINDINGS

OUTCOME OF THE BAYESIAN ANALYSIS

28–day mortality

**QUESTION** Does a mechanical ventilation strategy that is personalized to individual patients’ lung morphology improve the survival of patients with ARDS when compared with standard of care?

**CONCLUSION** Personalization of ventilation decreased mortality in patients with ARDS [in the posthoc analysis]; a ventilator strategy misaligned with lung morphology substantially increases mortality.

**POPULATION**

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
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<tbody>
<tr>
<td>114</td>
<td>286</td>
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</table>

114 Women, 286 Men

Patients with ARDS for less than 12 hours

Median Age: 62 years

**LOCATION**

20 ICUs in France

**INTERVENTION**

400 patients with moderate to severe ARDS

204 standard care

- V<sub>T</sub> 6 ml/kg PBW
- low PEEP

196 personalized care

- non-focal V<sub>T</sub> 6 ml/kg PBW high PEEP with RM
- focal V<sub>T</sub> 8 ml/kg PBW low PEEP and prone positioning

**FINDINGS**

**(PRIMARY) OUTCOME**

- mortality at day 90; ventilator–free days,
- ARDS resolution; LOS in ICU; barotrauma

**Graph**

- Personalised group (n=196)

- Standard care vs personalised care
  - Focal correctly classified
  - Focal misclassified or misaligned
  - Non-focal correctly classified
  - Non-focal misclassified or misaligned

- Time after inclusion (days)

- HR 1.39, 95% CI 1.18-1.64; p=0.001
- HR 2.03, 95% CI 1.58-2.63; p=0.001

**LITERATURE**

QUESTION In ICU patients who received invasive ventilation for reasons other than acute respiratory distress syndrome (ARDS), is a strategy with lower positive end-expiratory pressure (PEEP) noninferior to higher PEEP with respect to ventilator-free days at day 28?

CONCLUSION This clinical trial found that among ICU patients receiving invasive ventilation, a strategy with lower PEEP was noninferior to a strategy using higher PEEP for the outcome of ventilator-free days, supporting the use of lower PEEP in patients without ARDS.

POPULATION 623 Men 346 Women
Adults without ARDS expected not to be extubated within 24 hours of intubation
Median age: 66 years

INTERVENTION
980 Patients randomized
969 Patients analyzed

476 Lower PEEP strategy
Lowest level between 0-5 cm H₂O

493 Higher PEEP strategy
Lowest level of 8 cm H₂O

PRIMAR Y OUTCOME
Number of ventilator-free days by study day 28 (noninferiority margin of −10%)

Writing Committee for the RELAx Collaborative Group. Effect of a lower vs higher positive end-expiratory pressure strategy on ventilator-free days in ICU patients without ARDS: a randomized clinical trial. JAMA. Published online December 9, 2020. doi:10.1001/jama.2020.23517
Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation
QUESTION Is $\Delta P$ an index more strongly associated with survival than $V_T$ or PEEP in patients who are not actively breathing?

CONCLUSION $\Delta P$ is the ventilation variable that best stratified risk; decreases in $\Delta P$ owing to changes in ventilator settings may be strongly associated with increased survival.

### POPULATION

- ~40% Women
- ~60% Men

Patients with ARDS included in RCTs

Mean Age: from 34 to 60 years

### SOURCE

9 trials worldwide

### METHODS

Multilevel mediation analysis of individual patient data from 3562 patients

- Prediction model
  - Univariate
  - Multivariate

Mediation analysis

Risk priority of $\Delta P$, $V_T$ and PEEP

### FINDINGS

(PARTIAL) OUTCOME

60-day mortality

QUESTION What is the association between exposure to different intensities of mechanical ventilation over time and intensive care unit (ICU) mortality in patients with acute respiratory failure?

CONCLUSION Cumulative exposure to higher intensities of mechanical ventilation was harmful, even for short durations.

POPULATION

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
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<tbody>
<tr>
<td>5141</td>
<td>8267</td>
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patients receiving ventilation for 4 hours or more

Median Age: 62 years

LOCATION

9 ICUs in Toronto, Canada

FINDINGS

<table>
<thead>
<tr>
<th>Exposure to high driving pressure</th>
<th>Exposure to high mechanical power</th>
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<tbody>
<tr>
<td>Baseline variables</td>
<td></td>
</tr>
<tr>
<td>PaO₂/FIO₂, mm Hg</td>
<td>0.945 (0.896-0.994)</td>
</tr>
<tr>
<td>Age</td>
<td>1.098 (1.048-1.160)</td>
</tr>
<tr>
<td>APACHE III score</td>
<td>1.692 (1.256-1.689)</td>
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<tr>
<td>APACHE pH</td>
<td>0.832 (0.809-0.859)</td>
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Time-varying variables

Days with driving pressure ≥15 cm H₂O 1.049 (1.023-1.076) <0.0001

Days with mechanical power ≥17 l/min 1.069 (1.047-1.092) <0.0001

1622 (20.6%) of 7876 patients died; 64,281 daily observations were recorded. HRs were the adjusted HRs associated with a 1-SD increment in the given variable. Values higher than 1 indicate increased mortality. The values used for SDs were as follows: PaO₂/FIO₂, ratio 115; pH 10; age 17 years; and APACHE III score 29. The effects of the number of days with either driving pressure greater than or equal to 15 cm H₂O or mechanical power greater than or equal to 17 l/min were estimated using Quasi-Poisson models in the joint model analyses. HR= hazard ratio. CI= credible interval. PaO₂= partial pressure of oxygen. FIO₂= fraction of inspired oxygen. APACHE= Acute Physiology and Chronic Health Evaluation.

Table 3: Cumulative effect on HRs of exposure to high intensities of mechanical ventilation for 7876 patients with available data

QUESTION Does the intensity of ventilation, reflected by the mechanical power of ventilation (MP), has an association with outcome in invasively ventilated patients without ARDS.

CONCLUSION In ICU patients without ARDS, MP has an independent association with mortality. This finding suggest that MP holds an added predictive value over its individual components, making MP an attractive parameter to monitor and target in these patients.

POPULATION

1962 Patients

ICU patients without ARDS, expected to need invasive ventilation > 24 hours

Median Age: 67 years

LOCATION

8 ICUs in the Netherlands

van Meenen D, for the NEBULAE–, PReVENT– and RELAx–investigators. Effect of Intensity of Ventilation on Outcome in Invasively Ventilated ICU patients without ARDS—An IPD–analysis of Three Randomized Clinical Trials. [Eur J Anaesth 2022; Nov 21; doi:10.1097/EJA.0000000000001778]
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Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation
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Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation
A History of Automated Ventilation

Despite years of research in mechanical ventilation many settings remained to be set by hand. Here is when the ventilators became smarter.

1. 1992: PAV+
   - PAV+ monitors flow and volume inspiratory assist in proportion to patient’s effort

2. 1998: ASV
   - ASV automated selection of $V_t$ and RR according to the least WOB (Otis)

3. 2002: NAVA
   - NAVA monitors diaphragm activity inspiratory assist in proportion to diaphragm activity

4. 2006: SmartCare
   - SmartCare automated weaning mode monitors $V_t$, RR, and $etCO_2$ reduction of PS and performs SBT

5. 2016: INTELLIVENT–ASV
   - INTELLIVENT–ASV automated selection of $V_t$ and RR according to the least WOB (Otis) and FOB (Mead)
     - monitors $V_t$, RR, $etCO_2$, and $SpO_2$
     - automated titrations of AMV, PEEP, and $FiO_2$
     - reduction of AMV via reduction of PS, performs SBT
**QUESTION** Is the amount of mechanical power of ventilation (MP) under adaptive support ventilation (ASV) different from that under nonautomated pressure–controlled ventilation?

**CONCLUSION** This study suggests ASV may have benefits compared with pressure–controlled ventilation with respect to the MP transferred from the ventilator to the respiratory system in passive invasively ventilated critically ill patients.

**POPULATION**

- 7 Women
- 15 Men

Patients expected to need invasive ventilation for the next 24 hours

Median Age: 67 years

**LOCATION**

1 ICUs in The Netherlands

**QUESTION** In patients receiving post–operative ventilation after cardiac surgery, does INTELLiVENT–ASV improve the quality of breathing compared with conventional ventilation?

**CONCLUSION** Fully automated ventilation in patients after cardiac surgery optimized lung–protective ventilation during postoperative ventilation, with fewer episodes of severe hypoxaemia and an accelerated resumption of spontaneous breathing.

**POPULATION**

- **67** Women
- **153** Men

Patients after uncomplicated cardiac surgery

Median Age: 62–76 years

**LOCATION**

1 ICU in the Netherlands

**INTERVENTION**

- **220** patients after surgery
  - **111** conventional ventilation
  - **109** automated ventilation

**FINDINGS**

**PRIMARY) OUTCOME**

Proportion of breath within predefined optimal, acceptable, and critical ranges ($V_T$, $P_{max}$, $SpO_2$ and $etCO_2$); severe hypoxaemia ($SpO_2 <85\%$) and resumption of spontaneous breathing

**POSITiVE investigators. Fully automated postoperative ventilation in cardiac surgery patients: a randomized clinical trial. [BJA 2021; 125:739; doi: 10.1016/j.bja.2020.06.037]**
QUESTION In COVID–19 patients with ARDS, does INTELLiVENT–ASV reduce the driving pressure and mechanical power of ventilation compared with conventional ventilation?

CONCLUSION INTELLiVENT–ASV reduces the intensity of ventilation in COVID–19 patients with ARDS.

POPULATION
12 Women 39 Men
COVID–19 with moderate to severe ARDS
Median Age: 63 years

LOCATION
2 ICUs in the Netherlands

INTERVENTION
51 patients intubated in the ICU for acute hypoxemia
conventional ventilation automated ventilation crossover

FINDINGS
ΔP and MP before and after converting from conventional ventilation to INTELLiVENT–ASV

**QUESTION** In COVID–19 patients with ARDS, does INTELLiVENT–ASV reduce the driving pressure and mechanical power of ventilation compared with conventional ventilation?

**CONCLUSION** INTELLiVENT–ASV reduces the intensity of ventilation in COVID–19 patients with ARDS.

**POPULATION**

12 Women 39 Men

COVID–19 with moderate to severe ARDS

Median Age: 63 years

**LOCATION**

2 ICUs in the Netherlands

**QUESTION** What is the effect of automated closed–loop oxygen control, compared to automated ventilation with manual oxygen titrations, on time spent in predefined pulse oximetry (SpO₂) zones in pediatric critically ill patients?

**CONCLUSION** In this randomized crossover trial in pediatric critically ill patients under invasive ventilation with ASV, the percentage of time spent within in optimal SpO₂ zones increased with the use of closed–loop oxygen control.

**RESULTS**

- **37 patients under ASV for acute hypoxemia**
  - 2 hours manual or automated FiO₂ control
  - 2 hours automated or manual FiO₂ control

**INTERVENTION**

**POPULATION**

- 37 Pediatric Patients
- 1 ICU in Turkey
- Median Age: 1 year
  - children with or without ARDS under invasive ventilation

**LOCATION**

- 1 ICU in Turkey

**(PRIMARY) OUTCOME**

- FiO₂ settings and SpO₂ readings

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**QUESTION** What is the efficacy of a closed-loop oxygen control in critically ill patients with moderate to severe acute hypoxemic respiratory failure (AHRF) treated with high flow nasal oxygen (HFNO).

**CONCLUSION** Closed-loop oxygen control improves oxygen administration in patients with moderate-to-severe AHRF treated with HFNO, increasing the percentage of time in the optimal oxygenation range and decreasing the workload of healthcare personnel.

### POPULATION

| 45 patients under HFNO |
---|---|
| patients with moderate to severe ARF, including patients with COVID-19 |
| Median Age: 49 year |

### LOCATION

| 1 ICU in Spain |

### INTERVENTION

- 45 patients under HFNO
- 4 hours manual or automated FiO$_2$ control
- 4 hours automated or manual FiO$_2$ control

### RESULTS

<table>
<thead>
<tr>
<th>100%</th>
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<tr>
<td>75%</td>
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<tr>
<td>50%</td>
</tr>
<tr>
<td>25%</td>
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</tbody>
</table>

**PRIMARY OUTCOME** percentage of time spent in the individualized optimal SpO$_2$ ranges

Roca O. Closed–loop oxygen control improves oxygen therapy in acute hypoxemic respiratory failure patients under high flow nasal oxygen (HILOOP): a randomized cross-over study. [Crit Care 2022; 26:108; doi10.1186/s13054-022-03970-w]
QUESTION What is the effect of HFNO with closed–loop control of the fraction of inspired oxygen (FiO₂), compared to HFNO with manual titrations of the FiO₂, on time spent in predefined pulse oximetry (SpO₂) zones in pediatric critically ill patients?

CONCLUSION In this randomized crossover trial in pediatric critically ill patients under HFNO, the percentage of time spent within in optimal SpO₂ zones increased with the use of closed–loop FiO₂ control.

POPULATION
23 Pediatric Patients
children with acute hypoxemic respiratory failure under HFNO
Median Age: 1 year

LOCATION
3 ICUs in Turkey

INTERVENTION
23 patients under HFNO for acute hypoxemia
manual or automated FiO₂ control
crossover
automated or manual FiO₂ control

(PRIMARY) OUTCOME
FiO₂ settings and SpO₂ readings; alarms and manual adjustments

RESULTS

Lung Protective Ventilation during ECMO

**how to set the ventilator (and adjust ECMO) by hand and the potential role of automation**

**PAV+**
- inspiratory assist in proportion to patient's effort

**ASV**
- automated selection of VT and RR according to the least work of breathing

**NAVA**
- inspiratory assist in proportion to diaphragm activity

**SmartCare**
- automated weaning: reduction of support and performs spontaneous breathing trials

**INTELLiVENT–ASV**
- automated selection of VT and RR according to the least work of breathing and force of breathing (power), automated titrations of AMV, PEEP and FiO₂, and automated weaning: reduction of support, performs spontaneous breathing trials

1. Cannulation for ECMO
   - **Initiation**
     - Start on time, to prevent unnecessarily long use of harmful ventilation
   - **Blood flow**
     - Use sufficiently high blood flows, to provide optimal oxygenation
   - **Initial sweep gas flow**
     - Use sufficiently high gas flows, to provide good decapneization
   - **Sweep gas flow**
     - Adjust to allow use of even lower VT and RR, to keep the energy transfer low

2. Tidal Intubation
   - **Tidal volume**
     - Target a low VT, from 4 to 8 ml/kg PBW
   - **Positive end-expiratory pressure**
     - Use PEEP levels that prevent too much alveolar collapse (with ECMO PEEP is suggested to be set > 10 cm H₂O)
   - **Respiratory rate**
     - Target an alveolar minute volume that fits patient’s need, and use permissive hypercapnia
   - **Driving pressure**
     - Adjust VT and titrate PEEP, so that ΔP stays low
   - **Mechanical power**
     - Titrate ventilator settings and use permissive hypercapnia, so that the energy transferred to the lung stays low

3. Automated modes (but studies that support their use during ECMO remain lacking)
   - **PAV+**
   - **ASV**
   - **NAVA**
   - **SmartCare**
   - **INTELLiVENT–ASV**

4. Decannulation
   - **Cannulation for ECMO**
   - **Initiation**
   - **Blood flow**
   - **Initial sweep gas flow**
   - **Sweep gas flow**

5. Extubation
   - **Cannulation for ECMO**
   - **Initiation**
   - **Blood flow**
   - **Initial sweep gas flow**
   - **Sweep gas flow**
Agenda

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• wrap–up
Agenda

- effectiveness
- safety
- efficacy?
Agenda

• history of ventilation
• history of automated ventilation
• benefits of automated ventilation
• need for automated ventilation?
• wrap–up
Daily confirmed new cases (5-day moving average)

Outbreak evolution for the current 10 most affected countries
Potential gap between supply and demand of NHS doctors (FTE)

Gap between projected trend growth and required growth to meet expected growth in activity level.
**QUESTION** What is the precise amount of oxygen consumption with high–flow nasal oxygen (HFNO) and with mechanical ventilation in patients with acute hypoxemic respiratory failure due to COVID–19?

**CONCLUSION** Actual oxygen consumption, hourly oxygen consumption, and total oxygen consumption are substantially higher in COVID–19 patients that start with HFNO compared with patients that start with mechanical ventilation.

**POPULATION**

275 Patients

COVID–19 patients with acute hypoxemic failure receiving respiratory support

Median Age: 63 year

**LOCATION**

2 ICUs in Europe

**COMPARISON**

275 acute hypoxemic patients

147 started with HFNO

128 started with mechanical ventilation

**FINDINGS**

oxygen consumption per minute during the first 2 full calendar days of ICU admission; oxygen consumption per hour and total oxygen consumption in the same time frame

QUESTION What is the safety, efficacy and workload for the health care team of INTELLiVENT–ASV versus conventional modes over a 48-hour period?

CONCLUSION INTELLiVENT–ASV requires less manual intervention and delivered more variable PEEP, while delivering ventilation safe and effective ventilation in terms of $V_T$, RR, $SpO_2$ and $etCO_2$.

POPULATION

86 Patients

patients expected to need ventilation for more than 48 hours

Median Age: 59 year

LOCATION

1 ICU in Belgium

RESULTS

Bialais E. Closed-loop ventilation mode (INTELLiVENT–ASV) in intensive care unit: a randomized trial. [Minerva Anestesiologica 2016; 82:657]
QUESTION Does INTELLiVENT–ASV reduce the number of manual ventilator setting changes compared to conventional ventilation modes like volume assist control and pressure support in ICU patients?

CONCLUSION For mechanically ventilated ICU patients, INTELLiVENT–ASV significantly reduces the number of manual ventilator setting changes with the same number of arterial blood gas analysis and sedation dose, and is easier to use.

POPULATION

60 Patients

patients with an expected duration of ventilation of at least 48 hours

Median Age: 65 year

LOCATION

1 ICU in France

RESULTS

Arnal JM. Closed loop ventilation mode in Intensive Care Unit: a randomized controlled clinical trial comparing the numbers of manual ventilator setting changes. [Minerva Anestesiologica 2018; 84:58; doi:10.23736/S0375-9393.17.11963-2]
**QUESTION** How does INTELLiVENT–ASV perform, in terms of lung–protective ventilation, compared to conventional mechanical ventilation in the resource–constrained setting of the COVID–19 pandemic?

**CONCLUSION** During an early highpoint of the pandemic, mechanical ventilation using INTELLiVENT–ASV was associated with a higher degree of lung–protective ventilation than was conventional mechanical ventilation.

**POPULATION**

40 Patients

COVID–19 ARDS patients receiving mechanical ventilation

Median Age: 63 year

**LOCATION**

1 ICU in Switzerland

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2.8 [2.3–3.6] automatic adjustments per minute

4 [2–7] vs. 7 [3–12] manual adjustments per hour

Wrap-up

• ventilation can be complex and time-consuming
• automated modes are increasingly available
• effectiveness, safety, effectivity
• workload reductions