Utilization of the PAV+™ software has been demonstrated to reduce asynchrony and improve respiratory mechanics. Yet, the implications of implementing the PAV+™ software in a clinical setting may be unfamiliar to many providers.

Use this guide for additional information on the evidence describing the clinical application of the PAV+™ software in mechanically ventilated patients.
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<td>An introduction to implementing the PAV+™ software at the bedside.</td>
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INTRODUCTION

Patient-controlled breath delivery with the PAV+™ software

Two objectives of modern mechanical ventilation include reducing patient-ventilator asynchrony and preventing respiratory muscle weakness, resulting from either respiratory muscle loading or inactivity. (See Table 1). Both of these issues may be mitigated by providing the patient greater control over his or her breathing through assisted or spontaneous breathing modes. The PAV+™ software is a spontaneous breath type that has been demonstrated to assist patients in breathing more naturally, engaging and strengthening the respiratory muscles and minimizing the adverse effects of patient ventilator asynchrony.

The PAV+™ software delivers support directly proportional to the patient’s inspiratory effort. In doing so, the PAV+™ software allows the patient to control the delivery of support provided by the ventilator. If the patient initiates or ends inspiration, the ventilator triggers or cycles accordingly. If the patient increases or decreases his or her effort, the support provided by the ventilator increases or decreases accordingly. The PAV+™ software enables the patient to determine when inspiration begins, how deeply to breathe, and when the breath ends.

### TABLE 1. Definition and consequences of patient-ventilator asynchrony and respiratory muscle weakness

<table>
<thead>
<tr>
<th>Patient-ventilator asynchrony</th>
<th>Respiratory muscle weakness</th>
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<tr>
<td>Definition</td>
<td>Reduction or loss of respiratory muscle capacity related to passive mechanical ventilation or respiratory muscle overload</td>
</tr>
<tr>
<td>Consequences</td>
<td>• Increased mortality</td>
</tr>
<tr>
<td></td>
<td>• Increased duration of mechanical ventilation</td>
</tr>
<tr>
<td></td>
<td>• Delayed weaning</td>
</tr>
</tbody>
</table>
INTRODUCTION (cont’d.)

Utilizing the PAV+™ software to facilitate spontaneous breathing

- Evidence suggests that earlier transition from controlled to spontaneous ventilatory modes (see figure 1) may encourage earlier weaning and reduce the adverse effects of sedative administration, patient-ventilator asynchrony, diaphragmatic atrophy and respiratory muscle fatigue associated with controlled modes.\(^1\)
- Though pressure support ventilation (PSV) is the most commonly used spontaneous breath type to transition patients from controlled ventilation to weaning,\(^10\) it is associated with several drawbacks including the potential for respiratory muscle passivity after triggering and increased patient-ventilator asynchrony.\(^11\)
- Compared to PSV, the PAV+™ software has been demonstrated to improve patient performance by:
  - Increasing the portion of respiratory workload shared by the patient, which may aid in strengthening the respiratory muscles\(^2\)
  - Reducing respiratory distress and patient-ventilator asynchrony\(^2\)
  - Reducing the likelihood that patients revert back to a controlled mode due to respiratory distress, hypoxemia, hypercapnia, severe hemodynamic instability, or increased need for sedation (For more info, see Xirouchaki et al.)\(^12\)

Implementing a spontaneous breathing protocol with the PAV+™ software to transition patients from controlled ventilation to extubation

- Bosma et al. performed a randomized controlled trial implementing a spontaneous breathing protocol in ICU patients to facilitate weaning from mechanical ventilation.\(^2\)
- After fulfilling a clinical stability criteria for transition from controlled to spontaneous ventilation, patients were randomized to receive the PAV+™ software or PSV and managed via an algorithm to minimize respiratory distress and transition patients to extubation.
- Time to ICU discharge was significantly reduced in patients receiving the PAV+™ software.
- Patients on the PAV+™ software shared a greater portion of the respiratory workload which aided in strengthening the respiratory muscles with fewer episodes of respiratory distress and patient-ventilator asynchrony compared to patients on PSV. (For more info, see Bosma et al.)

**FIGURE 1.** Proposed process for early implementation of spontaneous breathing in mechanically ventilated patients via the PAV+™ software
INTRODUCTION (cont’d.)

Procedure for placing patients on the PAV+™ software

Because the PAV+™ software delivers ventilatory assistance in proportion to patients’ respiratory effort, it does not require the clinician to set traditional parameters on the ventilator. Consequently, the PAV+™ software has been demonstrated to require fewer ventilator manipulations than PSV \[\text{For more information, see Xirouchaki et al.}^\text{13}\]. Nonetheless, manipulations of PEEP and percentage of support may be necessary to optimize the delivery of respiratory support upon commencing the PAV+™ software \(\text{See Adjusting level of assist and PEEP in the PAV+™ software}\).

Steps for Initiating the PAV+™ software\(^\text{14}\):

1. Correctly enter predicted body weight, tube type, tube size, and maximum airway pressure
2. Set FiO₂, per usual criteria
3. Set initial PEEP value ≥ 5 cmH\textsubscript{2}O and level of assist at 70%. Consider using the PAV+™ software provided compliance measurement \(C_{aw}\) to titrate PEEP \(\text{see Adjusting level of assist and PEEP in the PAV+™ software}\).
4. If the patient was over-assisted or asynchronous in the previous mode, the patient response to being placed on the PAV+™ software may be dramatic. Wait a minute or more for the patient’s respiratory pattern to settle.
5. Evaluate the patient’s breathing patterns (see below), adjust PEEP or percentage of support accordingly \(\text{see Adjusting level of assist and PEEP in the PAV+™ software}\).

Assessing breathing patterns in patients on the PAV+™ software

Because breathing pattern on the PAV+™ software is reflective of patient respiratory drive, it may be variable. Likewise, a lower tidal volume, higher respiratory rate pattern may be reflective of the patient’s desired pattern.\(^{14}\) Therefore, additional signs of respiratory distress (i.e., extremes of HR or BP, diaphoresis, abdominal paradox, dyspnea) should be considered in addition to respiratory rate when evaluating patients for respiratory distress.\(^{14}\) If a patient’s respiratory rate decreases with increasing the PAV+™ software assist level, this is indicative of the patient compensating with rate due to an inability to achieve the desired minute ventilation.\(^{14}\) However, if rate is insensitive to the PAV+™ software support level, it should be viewed as the patient’s intrinsic breathing pattern.\(^{14}\)
INTRODUCTION (cont’d.)

Adjusting level of assist and PEEP in the PAV+™ software

The level of assist setting determines the percentage of support provided by the ventilator during inspiration, with the remaining effort being provided by the patient. Therefore, the intent of setting the assist is to target a degree of respiratory effort that engages the respiratory muscles as much as possible while avoiding respiratory distress. The algorithm below developed by Georgopolous et al. is intended to guide clinicians in setting the level of assist and PEEP level in patients on the PAV+™ software. For more information on setting assist at the bedside, see the methodology for adjusting assist according to patient respiratory effort (see section 2) described in Carteaux et al. or the protocol for resolving respiratory distress in patients on the PAV+™ software as described in Bosma et al.

FIGURE 2. Procedure for setting PEEP and assist when placing a patient on the PAV+™ software (Adapted from Georgopolous et al.)

- Set assist to 70%
- Is RR > 35 b/min and/or VT < 5 mL/kg?
  - Yes: Increase PEEP 2-3 cmH₂O
  - No: Distress or RR, C, or R deteriorating?
    - Yes: Increase % assist incrementally up to 90%
    - No: Reduce assist 10-20% every 2 hours if: No respiratory distress and RR, C, and R improve
    - Distress at > 20%, or ↓ C or R ↑?
      - Yes: Increase assist to previous value
      - No: Distress continues: Switch to another mode
- No distress at 10-20%, PEEP ≤ 5 cm H₂O
- Wean slowly
- Observe 5-10 minutes

* Increase PEEP until compliance no longer increases. Other factors may need to be considered in determining how high PEEP can be increased.
INTRODUCTION (cont’d.)

Limitations of the PAV+™ software

Respiratory Drive
As the PAV+™ software requires the patient effort to drive the ventilator, it must be used with caution in patients with very low respiratory efforts.

Leaks
As the flow provided by the ventilator is proportional to the patient demand, the existence of leaks may undermine the relationship between pressure provided by the ventilation and pressure provided by the patients.

Runaway
Runaway (when leaks or overestimations of lung resistance or elastance cause inaccurate feedback resulting in overinflation or overpressurization) is an issue unique to the PAV+™ software. If assist is high (85% or greater) and estimates for tidal volume and/or elastance are greater than actual, the inflating pressure may exceed the recoil pressure, causing runaway. Flow limited patients, such as COPD patients, may be at greater risk for runaway. The occurrence of runaway is rare and only occurs when assist approaches 90%.

Intrinsic PEEP
The presence of intrinsic PEEP may adversely affect coordination of support with neural inspiration in the PAV+™ software. Because the PAV+™ software does not initiate support until the patient draws air from the ventilator, the patient must overcome dynamic hyperinflation before support is provided, causing a significant proportion of inspiratory effort to go unsupported in patients with air trapping. Similarly, work of breathing estimates may be inaccurate in the presence of intrinsic PEEP. Careful application of external PEEP and increased trigger sensitivity should be considered when intrinsic PEEP is suspected.
BOSMA 2016


STUDY INFORMATION

<table>
<thead>
<tr>
<th>PURPOSE</th>
<th>Evaluate the safety and efficacy of the PAV+™ software or PSV in coordination with daily spontaneous breathing trials to facilitate weaning from mechanical ventilation.</th>
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<td>STUDY DESIGN</td>
<td>Pilot, randomized-controlled trial</td>
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| ARMS | **PAV+™ software group:** Upon meeting eligibility requirements, patients were placed on the PAV+™ software (initial assist set at 70%).  
**PSV group:** Upon meeting eligibility requirements, patients were placed on PSV (initial support setting: 15 cmH2O). |
| PATIENTS | Included adult mechanically ventilated patients intubated > 36 hours, eligible for partial ventilatory support, and not eligible for extubation. |
| METHODS | After randomization, patients were placed on either the PAV+™ software or PSV. Level of assist and PEEP were adjusted per a protocol to limit respiratory distress or acidosis. If respiratory distress or acidosis could not be resolved on the PAV+™ software or PSV, patients were placed on controlled ventilation and reassessed daily for eligibility to return to the PAV+™ software or PSV. Both arms underwent gradual reduction of support coupled with spontaneous breathing trials. |
| RESULTS | • Patients in both groups had similar requirements for being switched to controlled ventilation  
• Patients in PSV group required increases in the level of support resulting from distress more frequently than the patients in the PAV+™ software group. (0.002)  
• Adjusted for baseline measurements, patients in the PAV+™ software group received significantly less ventilator assistance (p<0.0001) and increased their tidal volume more than the PSV group (p<0.001)  
• Asynchrony index decreased significantly post randomization in the PAV+™ software group  
• Time to ICU discharge was significantly less in the PAV+™ software group (P=0.03) |
| CONCLUSION | Patients on the PAV+™ software shared a greater proportion of respiratory workload with fewer episodes of respiratory distress and patient-ventilator asynchrony than patients on PSV. Further research is required to determine whether this improvement in respiratory mechanics will lead to improved outcomes. |
# CARTEAUX 2013


## STUDY INFORMATION

<table>
<thead>
<tr>
<th>PURPOSE</th>
<th>Evaluate the feasibility of titrating level of assist to target a predefined range of respiratory effort in patients receiving the PAV+™ software.</th>
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<tr>
<td>STUDY DESIGN</td>
<td>Prospective, multicenter, clinical observational study.</td>
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<tr>
<td>PATIENTS</td>
<td>Mechanically ventilated ICU patients who fulfilled a predefined criteria for removal from controlled ventilation and initiation of partial ventilatory assist.</td>
</tr>
<tr>
<td>METHODS</td>
<td>Upon recruitment, patients were placed on the PAV+™ software and remained until extubation or they were required to be switched back to controlled ventilation. Gain was adjusted according to protocol to maintain peak respiratory muscle pressure (derived from PEEP, gain, and peak airway pressure), a surrogate of respiratory muscle pressure-time product, between 5 and 10 cmH₂O, while minimizing alkalosis/acidosis, extremes of tidal volume, or respiratory distress.</td>
</tr>
</tbody>
</table>
| RESULTS | ▪ Providers adjusted the gain setting 1.0 times per day.  
▪ The reason for adjusting gain was peak respiratory muscle pressure outside of range in 91% of cases and hypoventilation/hyperventilation in 9% of cases.  
▪ Patients spent 79% of their time within an acceptable level of respiratory effort (PTP(mus) 50-150 cmH₂O).  
▪ The protocol succeeded in titrating peak respiratory muscle pressure within the target range in 98% of patients. |
| CONCLUSION | Protocolized adjustment of gain in PAV+™ software ventilated patients to target a predefined level of respiratory effort is feasible. Often, this ventilation strategy was adequate to safely ventilate patients until withdrawal and extubation. |
KONDILI 2006


### STUDY INFORMATION

<table>
<thead>
<tr>
<th>PURPOSE</th>
<th>Elastance and resistance may change considerably over time in mechanically ventilated patients. This variation may lead to dramatic shifts in support in patients receiving pressure support and result in increased respiratory effort from over or under-assist. The intent of the study is to compare the ability of the PAV+™ software and PS to prevent under or over-assist under artificially imposed increases in resistance and compliance.</th>
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<tbody>
<tr>
<td>STUDY DESIGN</td>
<td>Single cohort, crossover</td>
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<tr>
<td>PATIENTS</td>
<td>10 mechanically ventilated ICU patients</td>
</tr>
<tr>
<td>METHODS</td>
<td>At the time of study initiation, patients were receiving pressure support under propofol sedation. In randomized order, patients were ventilated with the PAV+™ software or PS in 30 minute increments with and without increased respiratory load. Additional respiratory load was induced via sand bags placed on the patient’s chest to increase elastance (as measured by the PAV+™ software) by 30%.</td>
</tr>
</tbody>
</table>
| RESULTS | • Without additional respiratory load, PS and the PAV+™ software provided similar support.  
• With load, respiratory rate and pressure-time product of the diaphragm per breath, per minute, and per liter of ventilation increased significantly more with PS compared to the PAV+™ software.  
• With load, tidal volume decreased significantly less with the PAV+™ software than with PS.  
• Unlike PS, neuroventilatory coupling remained relatively unaffected by the application of respiratory load. |
| CONCLUSION | With additional respiratory load, patients ventilated with the PAV+™ software were able to maintain minute ventilation with significantly less inspiratory effort compared to patients ventilated with PS. |
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- Introduction
- BOSMA 2016
- CARTEAUX 2013
- KONDILI 2006
- XIROUCHAKI 2009
- XIROUCHAKI 2008
- References

## Introduction


## Study Information

| Purpose | Compare the influence of the PAV+™ software and pressure support ventilation on mechanical ventilated patients’ requirements for adjustments to the ventilator and adjustments to the administration of sedative or vasoactive agents. |
| Study Design | Randomized, controlled trial |
| Arms | **PAV+™ software group:** Randomized to receive the PAV+™ software upon meeting eligibility criteria  
**PSV group:** Randomized to receive PS ventilation upon meeting eligibility criteria |
| Patients | ICU patients ventilated for at least 36 hours with controlled ventilation and who met eligibility criteria for assisted ventilation |
| Methods | Patients in both groups were managed according to pre-defined algorithms in order to determine ventilator settings. The PAV+™ software or PSV was administered for 48 hours unless patients were liberated from MV or met the predefined failure criteria and returned to controlled ventilation. |
| Results | • The mean number of changes to ventilator settings was significantly lower in patients receiving the PAV+™ software  
• Of the changes made to ventilator settings, a significantly higher percentage of changes in patients receiving the PAV+™ software were made to facilitate weaning  
• Of changes related to clinical deterioration, a significantly higher percentage of changes in patients receiving PSV were related to patient-ventilator asynchrony  
• Clinicians more frequently adjusted the administration of sedatives due to clinical deterioration and to facilitate weaning in patients receiving pressure support  
• Clinicians more frequently adjusted the administration of vasoactive agents to facilitate weaning in patients receiving pressure support. |
| Conclusion | The PAV+™ software may be a more user-friendly mode. Compared to pressure support ventilation, patients on the PAV+™ software required fewer adjustments to the ventilator and adjustments to the administration sedative and vasoactive agents. |
STUDY INFORMATION

**PURPOSE**
Evaluate the effectiveness of the PAV+™ software to prolong the ability of mechanically ventilated patients to remain on assisted ventilation and reduce the need for controlled mechanical ventilation compared to pressure support.

**STUDY DESIGN**
Randomized, controlled trial

**ARMS**
- **PAV+™ software group:** Randomized to receive the PAV+™ software upon meeting eligibility criteria
- **PS group:** Randomized to receive PS ventilation upon meeting eligibility criteria

**PATIENTS**
ICU patients ventilated for at least 36 hours with controlled ventilation and who met eligibility criteria for assisted ventilation

**METHODS**
Patients in both groups were managed according to pre-defined algorithms to minimize respiratory distress. The PAV+™ software or PSV was administered for 48 hours unless patients were liberated from MV or met the predefined failure criteria and returned to controlled ventilation.

**RESULTS**
- The PAV+™ software group was significantly less likely to meet failure criteria and returned to controlled ventilation (OR 0.443, P=0.04)
- The PAV+™ software group was significantly less likely to exhibit patient-ventilator asynchrony (OR=0.1, P=0.001)

**CONCLUSION**
Compared to pressure support, the PAV+™ software increased the ability of mechanically ventilated patients to remain on assisted ventilation and reduced the need for controlled mechanical ventilation.


