



## Adaptive high flow oxygen therapy: New concept

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DOI: <https://doi.org/10.53097/JMV10112>

Cite: Ongsupankul S, Dhupa A, Daoud EG. Adaptive high flow oxygen therapy: New concept. J Mech Vent 2024; 5(4):127-132.

### Abstract

#### Background

High-flow oxygen therapy (HFOT) is increasingly utilized in clinical settings due to its potential to improve oxygenation, patient comfort and possibly outcomes in different respiratory failure states. The potential benefits of HFOT include matching the patients' flow to reduce the work of breathing, creating airway pressure, humidification, and reducing dead space.

However, it has some shortcomings including the difficulty of setting the flow to match patients' efforts, the continuous flow does not represent normal physiologic spontaneous breathing, and the lack of traditional airway pressure monitoring.

We are testing a new adaptive high-flow oxygen delivery technique "Auto Positive Airway Pressure" (Auto-PAP) where the flow delivered from the ventilator adapts to patients' efforts taking into consideration the patients' dead space

#### Methods

A bench study using ASL 5000 simulator, we created a single-compartment active model of a male with IBW 70 kg, with compliance of 40 ml/cmH<sub>2</sub>O and resistance of 10 cmH<sub>2</sub>O/L/s. The respiratory rate was set at 20 bpm, with inspiratory time of 1 second. Muscle pressure (P<sub>mus</sub>) was gradually increased by increments of 5 cmH<sub>2</sub>O from 5 to 50. Adaptive high flow mode (Auto PAP) using a Bellavista 1000e ventilator (Zoll MA, USA) using a large bore nasal cannula to an adult-sized mannequin nose that was connected to the lung simulator. Pearson correlation coefficient was used in correlating the P<sub>mus</sub> to the maximum, mean flow and pressure, and the simulator to the ventilator flow.

#### Results

There was significant strong correlation between the P<sub>mus</sub> and the maximum flow R: 0.949, CI (0.794, 0.988) P < 0.001, and mean flow R: 0.955, P < 0.001, CI (0.816, 0.989). There was a significant strong correlation with P<sub>mus</sub> and the maximum pressure R: 0.972, P < 0.001, CI (0.883, 0.993) and mean pressure R: 0.942, P < 0.001, CI (0.768, 0.986). There was significant strong correlation between the simulator and the ventilator flow R: 0.961, P < 0.001. There was significant strong correlation between the simulator and the ventilator mean pressure R: 0.951, P < 0.001, CI (0.799, 0.988). There was significant strong correlation between the mean flow from the ventilator to the mean airway pressure measured at the simulator R: 0.936, P < 0.001 CI (0.747, 0.985).

#### Conclusion

Results suggest a significant correlation between the flow and pressure from adaptive HFOT and the patient muscle effort, indicating that the flow and pressure increase in response to the patients' effort. This may reduce respiratory muscle workload compared to traditional high flow oxygen therapies and reduce the need for multiple manual adjustment of the flow. These findings underscore the potential of this technology to enhance respiratory support while minimizing patient effort.

Further research is warranted to validate these findings in real patient cohorts in diverse clinical scenarios.

**Keywords:** High flow oxygen therapy, mean flow, mean pressure

**Acknowledgment:** Special thanks to Mr. Matthias van der Staay, Mr. Christian Remus from IMT analytics and Mr. Robert Cabbat from Kuakini Medical Center for their help and support conducting the study.

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Conflict of interest/Disclosures: None

## Introduction

High-flow oxygen therapy (HFOT) has many physiological beneficial effects that prompted its indications and inclusion in multiple societies guidelines<sup>1,2</sup> in patients with acute hypoxic and hypercarbic respiratory failure and post extubation management. Among those benefits are improved carbon dioxide clearance and reduced dead space. The creation of positive airway pressure<sup>3,4</sup> by the high flow along the reduced room air entrainment by the high flow<sup>5</sup> leads to improved oxygenation in acute respiratory failure conditions.<sup>6</sup> Additionally, the high flow delivered attempting to match the patients' flow might lead to improved comfort and respiratory efforts.<sup>7</sup>

Despite all the benefits of HFOT, clinicians find themselves in a dilemma of how to set the flow rate during initiation and weaning it, and what pressures are delivered as the results of their settings.

An adaptive flow algorithm named Auto-PAP was developed bearing in mind those challenges. The mode estimates the volume of the dead space based on the patient gender and height (2.2 ml/kg IBW) to calculate the minimal flow for CO<sub>2</sub> washout and delivers flow in a cyclical high flow during inspiration, lower flow during exhalation targeting a mean flow level that is hypothesized to adapt to the patients' own flow instead of the traditional linear flow rate thus eliminating the guesswork from the clinicians. The flow during exhalation is kept at a minimum based on exhalation time and dead space to account for carbon dioxide clearance. The inspiratory flow is mainly driven by the patient's estimated airway pressure, while Auto PAP tries to keep the airway pressure as constant as possible. The airway pressure is estimated with delivered flow and the resistance of the circuit/filter/cannula.

## Methods

Bench study using ASL 5000, we created an active single compartment active model of a male with IBW 70 kg with compliance 40 ml/cmH<sub>2</sub>O and resistance of 10 cmH<sub>2</sub>O/L/s. Respiratory rate was set at 20 bpm, with inspiratory time of 1 second. Patients' effort

(P<sub>mus</sub>) was gradually increased by increments of 5 cmH<sub>2</sub>O from 5 to 50. Adaptive high flow mode (Auto PAP) using a Bellavista 1000e ventilator (Zoll MA, USA) using a large bore nasal cannula to an adult sized mannequin nose that was connected to the lung simulator, the mouth of the mannequin was open. The correlations were analyzed using Pearson correlation coefficients.

## Results

### Correlation of ventilator output with P<sub>mus</sub>

Flow:

Maximum Flow: A strong significant correlation was observed between P<sub>mus</sub> and the maximum flow from the ventilator, with a correlation coefficient (R) of 0.949 and a 95% confidence interval (CI) of 0.794 to 0.988 (P < 0.001).

Mean Flow: The mean flow from the ventilator also showed a strong significant correlation with P<sub>mus</sub>, R: 0.955, with a CI of 0.816 to 0.989 (P < 0.001).

Pressure:

Maximum Pressure: The maximum pressure delivered by the ventilator correlated strongly with P<sub>mus</sub>, R: 0.972, CI 0.883 to 0.993 (P < 0.001).

Mean Pressure: Similarly, mean pressure displayed a strong correlation, R: 0.942, with a CI 0.768 to 0.986 (P < 0.001).

### Correlation between simulator and Ventilator

Flow:

A strong significant correlation was found between the simulated flow demands and the actual flow delivered by the ventilator, R: 0.961 with CI 0.839, 0.991 (P < 0.001).

Pressure:

A strong significant correlation was found between the simulated flow demands and the actual flow delivered by the ventilator, R: 0.951 with CI 0.799, 0.988 (P < 0.001).

### Correlation of Mean flow to mean airway pressure

There was significant strong correlation between the mean flow from the ventilator to the mean airway pressure measured at the simulator R: 0.936 with CI 0.747, 0.985 (P < 0.001).



Figure 1 Setup of the experiment. On the left is the adaptive high-flow machine, while the right displays the ASL 5000 and mannequin.

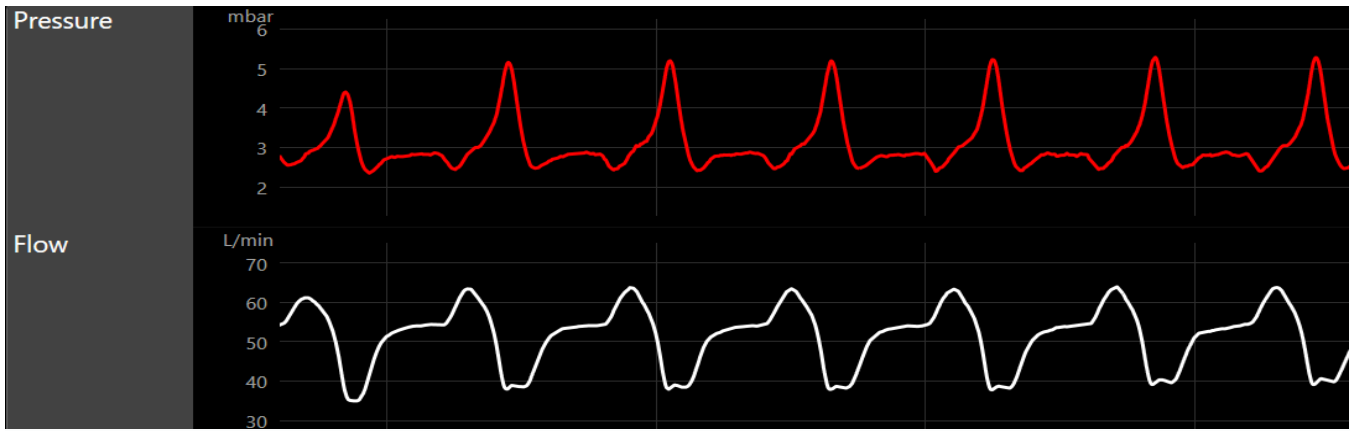


Figure 2: example of the maximum, minimum and mean pressure (red) and flow (white) curves

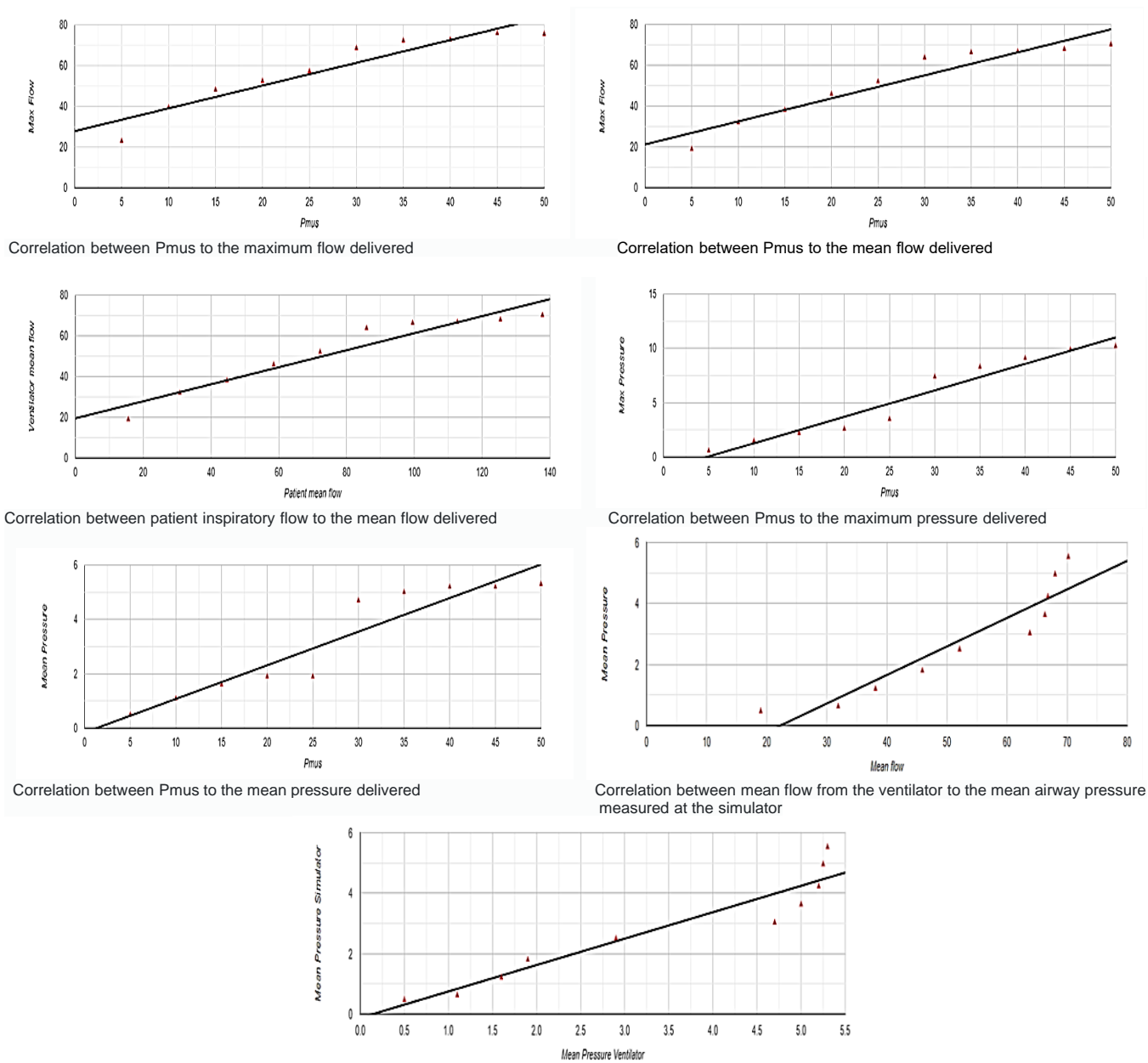


Figure 3: Correlations results. Pmus: muscle pressure.

Table 1: Correlation of ventilator flow and pressure output with Pmus. R: correlation coefficient, CI: confidence interval

	<b>R</b>	<b>CI</b>	<b>P value</b>
<b>Max flow-Pmus</b>	0.949	0.79, 0.98	< 0.001
<b>Mean flow-Pmus</b>	0.95	0.81, 0.98	< 0.001
<b>Max pressure-Pmus</b>	0.97	0.88, 0.99	< 0.001
<b>Mean pressure-Pmus</b>	0.94	0.76, 0.98	< 0.001

Table 2: Correlation between simulator and ventilator variables. R: correlation coefficient, CI: confidence interval

	<b>R</b>	<b>CI</b>	<b>P value</b>
<b>Flow</b>	0.96	0.83, 0.99	< 0.001
<b>Pressure</b>	0.95	0.79, 0.98	< 0.001

## Discussion

This pioneering study establishes the efficacy of the new Adaptive High Flow (Auto-PAP) system, demonstrating its potential to revolutionize high-flow oxygen therapy. Our findings reveal significant correlations between patient muscle effort (Pmus) and both flow and pressure (mean and maximum) outputs from the ventilator. Additionally, the significant correlation between patient flow demands and machine flow underscores the system's ability to precisely match ventilatory support with patient requirements.

The adaptivity of the Auto-PAP system addresses a critical limitation in traditional high-flow therapy: the generation of excessive flow, which can compromise patient comfort and tolerability. <sup>1</sup> If the ventilator can ensure that the flow remains above the patient's peak tidal inspiratory flow by a certain degree, this could translate into a reduced chance of HFOT failure, as calculated by the ROX index. <sup>2</sup> This capability suggests that Auto-PAP could enhance patient comfort and reduce the odds of intubation, which in turn may increase the chances of successful treatment with HFOT.

The ventilator's ability to automatically adjust the flow based on the patient's effort can eliminate the need for the clinician to estimate the initial flow settings and manage the weaning process. Li and colleagues <sup>2</sup> tried to set the flow after measuring the patient peak inspiratory flow with a different device then placing them on the HFOT. This is impractical in the clinical setting and highlights the difficulty of setting the flow and the weaning of the flow as patients' condition changes.

There are some hypothetical benefits of cyclical flow during Auto-PAP versus the conventional linear flow:

- **Enhanced synchronization with breathing:** Cyclical flow can better synchronize with the patient's natural breathing pattern. By increasing flow during inspiration, the patient receives more support when they need it most, and by decreasing flow during exhalation, it reduces unnecessary resistance.
- **Improved comfort:** patients may find cyclical flow more comfortable because it mirrors their natural breathing rhythm, reducing the sensation of pressure or air resistance during exhalation.
- **Potential for reduced work of breathing:** by matching the flow to the patient's effort, cyclical flow may decrease the work of breathing, particularly during inspiration, potentially making it easier for the patient to breathe.
- **Optimized oxygen delivery:** Increasing flow during inspiration can enhance the delivery of oxygen to the alveoli when the demand is highest, potentially improving oxygenation. <sup>8</sup> This may be explained by the ability of the ventilator to maintain positive airway pressure even during inspiration as the mechanism of work of breathing reduction in HFOT use is postulated to be from generation of positive airway pressure.
- **Reduce paradoxical increase work of breathing in COPD patients.** In some studies, <sup>9</sup> increasing flow rate beyond a certain threshold can paradoxically increase patients' work of breathing, likely due to dynamic hyperinflation. Auto-PAP could allow clinicians to achieve higher flow during inspiration while maintaining adequately low flow during expiration which

could avoid this adverse effect. A study by Vierra<sup>10</sup> and colleagues found that the expiratory resistance increase by HFOT, and the reduction of respiratory rate might be secondary to increase resistive load and expiratory work rather than improved clinical condition.<sup>11</sup>

- Reduced risk of airway dryness and irritation: A cyclical flow pattern may reduce the overall amount of flow delivered, lowering the risk of airway dryness and irritation that can occur with constant high flows.

Similar to a study by Ritchie and colleagues,<sup>12</sup> our study demonstrated that the airway pressures (peak and mean pressures) are increased as the flow increases. The measurement of patients' airway pressures in clinical practice is difficult and non-practical. The new mode offers monitoring of the delivered pressure from the ventilator. Our findings of strong correlation between those measured pressures and the mean pressures at the simulator confirms the precision of this monitoring technique.

The adaptive features of this new mode, combined with continuous pressure monitoring, represent a significant advancement in high-flow oxygen therapy. These improvements address a gap that has been previously noted by experts in the field.<sup>13</sup>

While the correlations observed are promising, the translation of these in vitro results to in vivo settings remains speculative. The dynamic nature of patient breathing patterns affected by factors such as clinical status changes, talking, coughing, hiccupping, or emesis may alter the efficacy of the flow and pressure correlations observed in a controlled environment. Thus, while the bench model provides a foundational understanding, the clinical applicability of these findings needs careful evaluation.

It is worth noting that the advancement in machine learning (ML) and artificial intelligence (AI) has made it possible to predict respiratory outcomes in patients receiving HFOT.<sup>14</sup> Studies using ML and AI to predict flow patterns that would be best suited for a particular patient should yield findings that will ultimately further decrease the limitations of HFOT.<sup>15</sup>

The primary limitation of this study is its in vitro nature, which may not fully capture the complex interplay of factors affecting respiratory therapy in clinical settings. Future research should focus on in vivo studies to determine whether the adaptability of the Auto-PAP system can effectively improve oxygenation and ventilation, reduce respiratory effort, and ultimately enhance patient outcomes in real world scenarios. It is

crucial to assess whether the theoretical benefits observed under controlled conditions hold true in the variable and unpredictable realm of human pulmonary physiology.

## Conclusion

This study validates the concept of adaptive high-flow oxygen therapy through the Auto-PAP system. By aligning ventilator output more closely with patient specific respiratory demands, the Auto-PAP system holds the promise of enhancing the efficacy and tolerability of oxygen therapy. Further research is imperative to confirm these benefits in clinical practice and to explore the full potential of Auto-PAP.

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