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# Patient-Ventilator Interaction using Autoencoder derived Magnitude of Asynchrony Breathing

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**Abstract**: The occurrence of asynchronous breathing (AB) is prevalent during mechanical ventilation (MV) treatment. Despite studies being carried out to elucidate the impact of AB on MV patients, the asynchrony index (*AI*), a metric to describe the patient-ventilator interaction, may not be sufficient to quantify the severity of each AB fully in MV patients. This research investigates the feasibility of using a machine learning-derived metric, the ventilator interaction index (*VI*), to describe a patient's interaction with a mechanical ventilator. *VI* is derived using the magnitude of a breath's asynchrony to measure how well a patient is interacting with the ventilator. 1,188 hours of hourly *AI* and *VI* for 13 MV patients were computed using a convolution neural network and an autoencoder. Pearson's correlation analysis between patients' *AI* and *VI* versus their levels of partial pressure oxygen ($PaO_2$) and partial pressure of carbon dioxide ($PaCO_2$) was carried out. In this patient cohort, the patients' median *AI* is 38.4% [Interquartile range (IQR): 25.9-48.8], and the median *VI* is 86.0% [IQR: 76.5-91.7]. Results show that high *AI* does not necessarily predispose to low *VI*. This difference suggests that every AB poses a different magnitude of asynchrony that may affect patient's $PaO_2$ and $PaCO_2$. Quantifying hourly *VI* along with *AI* during MV could be beneficial in explicating the aetiology of AB.



*Keywords*: Asynchronous breathing, Magnitude of asynchrony, Asynchrony index

## 1. INTRODUCTION

Asynchronous breathing (AB) is a spontaneous event during mechanical ventilation (MV) treatment. AB often occurs when there is a mismatch between ventilatory support with the patient's demand (Moorhead et al., 2013, Mellott et al., 2014). Different phenotypes of AB can be caused by patient-related factors such as excessive patient respiratory effort or inadequate MV settings (de Haro et al., 2019). Frequent occurrence of AB may predispose patients to adverse outcomes (Epstein, 2011, Blanch et al., 2015). However, the implementation of monitoring tools to automatically classify and quantify AB is still limited. This limitation obscures the elucidation of the aetiology and the impact of AB on patient outcomes (Georgopoulos et al., 2006, Dres et al., 2016). Therefore, multiple efforts using machine learning algorithms or models have been proposed for automated AB detection (Loo et al., 2018, Chatburn and Mireles-Cabodevila, 2020, Gutierrez, 2020, Zhang et al., 2020, Rehm et al., 2020).

The asynchrony index (*AI*) is a metric commonly applied in a clinical setting to assess patient-ventilator interaction (PVI) by determining the frequency of AB occurrence within a breathing period (de Wit et al., 2009b). While the relationship between *AI* and patient outcomes has been investigated (Thille et al., 2006, de Wit et al., 2009b, de Wit et al., 2009a, Blanch et al., 2015, Rué et al., 2017), the actual impact of AB on a patient's condition remains uncertain. For example, Blanch et al. and Martos-Benítez et al. found that severe AB occurrence (*AI* > 10%) is associated with high mortality and lower $PaO_2/FiO_2$ ratio (Blanch et al., 2015, Martos-Benítez et al., 2020). However, a study by Rolland et al. found that severe AB occurrence is not associated with adverse outcomes (Rolland-Debord et al., 2017). Such contradiction may suggest that counting *AI* alone may not be able to fully reflect the actual impact of AB.

We hypothesise that the magnitude of patient effort induced in AB might play a deterministic role in affecting the patient's outcome. Chiew et al. proposed the idea of measuring the magnitude of patient effort induced in AB by reconstructing it to a presumably normal breathing cycle (Chiew et al., 2018b). This enables the magnitude of AB quantification by computing the differences between an AB versus a presumably normal breathing cycle (Kannangara et al., 2016, Chiew et al., 2018b, Arunachalam et al., 2020, Damanhuri et al., 2016, Loo et al., 2021, Ang et al., 2022).

In this study, we investigate the feasibility of a metric, a ventilator interaction index (*VI*) derived using a machine learning autoencoder with a focus placed on inspiratory airflow and triggering-based asynchrony. *VI* describes a patient's 'receptivity' to ventilatory support by measuring the asynchrony 'element' in each AB. The *VI* aims to quantify how well a patient interacts with the ventilator with consideration of the severity of AB during MV treatment. A study comparing


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the relationship between the *AI* and *VI* metrics with the patient's arterial partial pressure oxygen ($PaO_2$) and carbon dioxide ($PaCO_2$) level is also carried out.

## 2. METHODS

### *2.1 Patients*

13 mechanically ventilated respiratory failure patients from an observational trial were included in this study (Chiew et al., 2018a). The patients were ventilated using Puritan Bennet 980 ventilators, with synchronous intermittent mandatory ventilation (SIMV) volume-controlled (VC) mode. The ventilator waveform data were collected using the CURE data acquisition system (Szlavecz et al., 2014, Davidson et al., 2014). The patient's information, such as sex, age, APACHE II score, SOFA score and arterial blood gases ($PaO_2$ and $PaCO_2$) were collected. Informed consent was obtained from family members of patients. The study was approved by the International Islamic University Malaysia, Research Ethics Committee (IREC) with the approval number IREC666.

### *2.2 Asynchronous and Ventilator-Interaction Index (VI)*

This work analyses inspiratory airflow asynchrony which is characterised by strong patient inspiratory effort due to insufficient inspiratory airflow provided by the ventilator and also triggering-based AB (de Haro et al., 2019, Loo et al., 2021). Triggering-based AB are classified into: early, reverse, and late triggering, all described by negative inflections on the airway pressure waveform due to patient inspiratory effort. The asynchrony index (*AI*) is computed using a deep learning (DL) algorithm (convolutional neural network) (Loo et al., 2018). The patient's hourly *AI* is computed using (1):

$$AI = \frac{Number\ of\ AB\ in\ an\ hour}{Total\ breathing\ cycle\ in\ an\ hour} \times 100\% \quad (1)$$

The *AI* effectively describes the prevalence of asynchronous events as a percentage of the total breaths in an hour. The magnitude of an AB is obtained using a convolutional autoencoder (CAE) proposed by Loo et al. (Loo et al., 2021). The method of computing the magnitude of asynchrony, $M_{asyn}$ is shown in **Fig. 1**. The calculation is shown in (2) (Chiew et al., 2018b):

$$M_{asyn} = \frac{|AUC_{Rec} - AUC_{Asyn}|}{AUC_{Rec}} \times 100\% \quad (2)$$

where $AUC_{Rec}$ and $AUC_{Asyn}$ are the area under the curve of the reconstructed and original AB airway pressure wavform respectively. The area difference between $AUC_{Rec}$ and $AUC_{Asyn}$ as shown in **Fig. 1a** (shaded black area) defined as $M_{asyn}$. A larger shaded area or higher $M_{asyn}$ indicates more 'severe' asynchrony.

The proposed ventilator-interaction index (*VI*) is a metric aimed at measuring how well a patient interacts with the ventilator with consideration of AB 'severity' during MV. A higher *VI* indicates better PVI and less asynchrony. From (2), the hourly *VI* can be calculated using (3) as the average percentage of how well a patient interacts with the ventilator.

$$VI = \frac{\sum(100\% - M_{asyn})}{Total\ breathing\ cycle\ in\ an\ Hour} \quad (3)$$

The calculation of $M_{asyn}$ and subsequently *VI* requires for $AUC_{Rec}$ to be determined. However, given an asynchronous patient breath, it would not be possible to know the true "asynchrony-free" breath. Thus, DL models trained with sufficient data can reconstruct these "asynchrony-free" breaths for the calculation of $M_{asyn}$ in an automated process.

Pearson's correlation test was carried out between *AI* and *VI* to determine the relationship between these two metrics. As AB can disrupt the normal breathing process and lead to haemodynamic disturbances, therefore it is possible that large asynchrony magnitudes and prevalence (described by $M_{asyn}$ and *VI* respectively) may affect the balance of arterial blood gases. Therefore, Pearson's correlation test was also performed between *AI*, *VI* with $PaO_2$ and $PaCO_2$ to determine if either *AI* or *VI* can directly reflect the patient's condition during MV. All statistical analyses in this study were performed using MATLAB 2017b (Natick, MA).

## 3. RESULTS

**Fig. 1** depicts an example of computing $M_{asyn}$. **Fig. 2 (a)-(c)** shows 5 consecutive breathing cycles experienced in a patient sample. The shaded black region indicates the magnitude of the breathing cycle encapsulated by the reconstructed airway profile. **Fig. 2 (a)-(c)** shows that different AB may impose dissimilar magnitudes of AB. **Fig. 2 (d)-(f)** shows three patient samples (Patient P1, P10 and P13) experiencing different AB magnitudes.

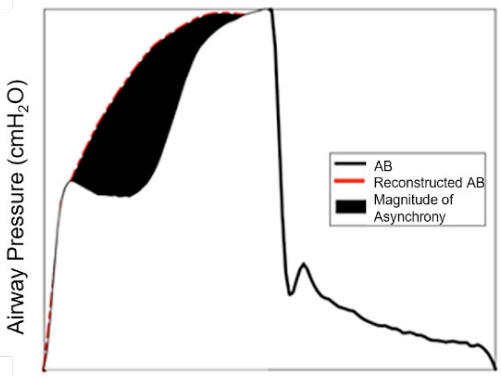


Fig 1. An example of how to compute the $M_{asyn}$ for a breath. The area under the curve between the reconstructed AB-free and AB (shaded black) waveform is the magnitude of AB.

**Table 1** summarises the patient's demographics, and **Table 2** shows the patient's *AI* and *VI*. 11 of 13 patients were mechanically ventilated due to pneumonia. The MV patients' median [interquartile range (IQR)] *AI* and *VI* are 38.4% [25.9–48.8] and 86.0% [76.5–91.7] respectively. The range of *AI* is wider compared to the *VI* range. **Fig. 3** shows a scatter plot of *VI* versus *AI* for this patient cohort. A Pearson's coefficient of correlation $R$ = -0.34 was found between *VI* and *AI*, indicating a weak negative relationship between these two metrics. The result is expected as *VI* is opposed to *AI*, as a measure of how well a patient interacts with the ventilator. **Table 3** shows the correlation coefficient, $R$ of *AI* and *VI* when tested against $PaO_2$ and $PaCO_2$. A positive correlation ($R$>0) between *VI* and $PaO_2$ together with a negative correlation ($R$<0) $PaCO_2$ may

suggest a good PVI which leads to improved patient oxygenation and carbon dioxide expulsion.

As shown in **Table 3**, a total of 6 patients (Patients P4-7, P11 and P12) exhibited this aforementioned trend, whereas only

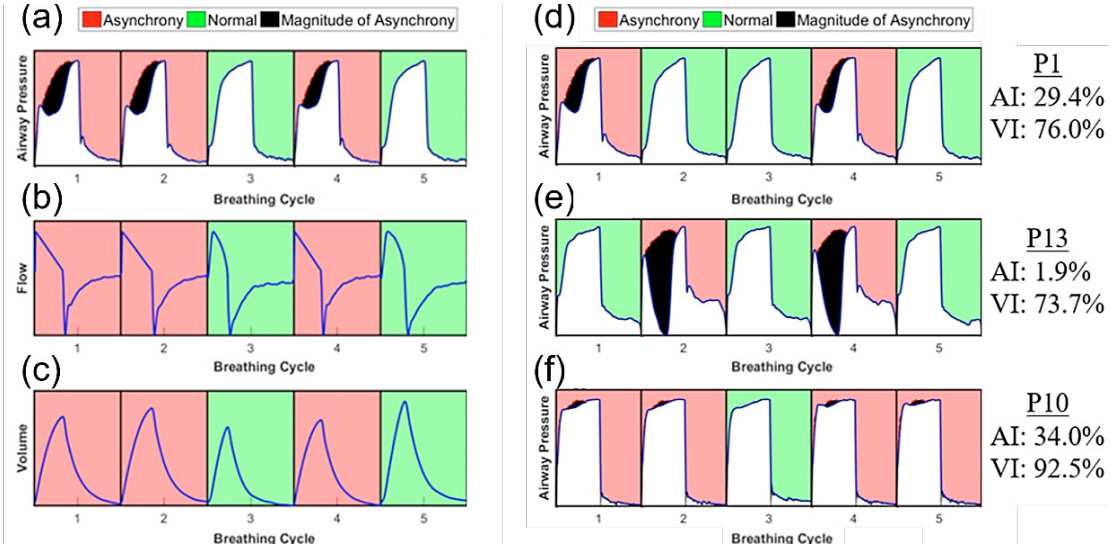


Fig 2. (a)-(c) shows 5 consecutive breathing cycles, where (a), (b) and (c) are the airway pressure, flow and volume waveforms respectively. AB and normal breathing cycles are shaded red and green respectively. Figures (d), (e) and (f) shows samples of patients' $AI$ and $VI$ for 5 breathing cycles in three different patients (P1, P10 and P13). The $AI$ and $VI$ are values throughout the treatment duration. (a) Patient P1 had $AI$ of 50% with average $M_{asyn}$ of 14.78% and $VI$ of 85.23%. P1 achieved a median $AI$ of 29.4% and median $VI$ of 76.0% throughout the treatment. (b) Patient P13 experienced $AI$ of 50% with average $M_{asyn}$ of 46.26% and $VI$ of 53.73. Although P13 attained the lowest $AI$ among the three patients with only 1.9%, P13 also experienced the lowest $VI$ with 73.7% during treatment. (c) Patient P10 experienced $AI$ of 90% with average $M_{asyn}$ of only 3.45% and $VI$ of 96.66%. Overall, P10 achieved a median $AI$ of 34.0% with 92.5% $VI$ throughout the treatment.

**Table 1: Summary of Patients' Demographic**

| Patient No. | Age | Sex | Clinical Diagnosis | APACHE II | SOFA | Initial P/F Ratio | MV Mode |
|---|---|---|---|---|---|---|---|
| P1 | 43 | F | Thyroid Carcinoma | 6 | 1 | 150 | SIMV |
| P2 | 54 | M | Pneumonia | 21 | 6 | 202 | SIMV |
| P3 | 64 | M | HAP | 22 | 16 | 238 | SIMV |
| P4 | 63 | F | Klebsiella Sepsis | 25 | 10 | 146 | SIMV |
| P5 | 64 | F | Pneumonia | 14 | 4 | 117 | SIMV |
| P6 | 48 | M | CAP | 18 | 6 | 128 | SIMV |
| P7 | 53 | M | HAP | 10 | 7 | 133 | SIMV |
| P8 | 34 | F | Pneumonia | 15 | 4 | 155 | SIMV |
| P9 | 43 | M | Acute Pancreatitis | 14 | 1 | 157 | SIMV |
| P10 | 61 | F | Right Lobar Pneumonia | 14 | 10 | 92 | SIMV |
| P11 | 48 | M | CAP | 31 | 11 | 350 | SIMV |
| P12 | 66 | M | HAP | 16 | 9 | 119 | SIMV |
| P13 | 53 | M | HAP | 4 | 3 | 246 | SIMV |

**Table 2: Summary of Patient *AI* and *VI***

| Patient No. | MV Hours | No. of BC | $PaO_2$ (mmHg) | $PaCO_2$ (mmHg) | *AI* (%) | *VI* (%) |
|---|---|---|---|---|---|---|
| P1 | 168 | 270,580 | 89.4 [81.2-93.6] | 38.4 [32.9-41.0] | 29.4 [3.6-42.9] | 76.0 [70.0-81.0] |
| P2 | 59 | 61,785 | 95.7 [81.5-153.5] | 43.2 [40.4-46.1] | 64.5 [25.0-93.8] | 88.5 [78.1-98.7] |
| P3 | 20 | 21,286 | 133.0 [130.8-142.8] | 31.3 [30.0-34.1] | 26.1 [19.3-53.3] | 91.4 [83.8-94.5] |
| P4 | 139 | 152,464 | 175.0 [141.5-186.3] | 38.8 [31.0-41.6] | 38.4 [24.6-49.8] | 89.5 [84.6-97.1] |
| P5 | 34 | 38,865 | 92.2 [79.7-126.0] | 32.0 [31.4-34.3] | 45.8 [40.8-58.4] | 76.6 [63.3-85.9] |
| P6 | 35 | 36,566 | 95.8 [87.9-109.0] | 44.9 [42.3-45.4] | 74.2 [58.4-87.6] | 75.4 [74.6-77.4] |
| P7 | 49 | 38,908 | 107.0 [103.0-130.8] | 47.1 [45.9-48.3] | 25.3 [4.5-44.4] | 92.7 [87.3-99.4] |
| P8 | 112 | 120,172 | 86.7 [73.3-95.1] | 37.9 [36.7-40.7] | 41.4 [5.4-60.6] | 86.0 [82.5-93.4] |
| P9 | 42 | 52,960 | 117.0 [103.0-130.8] | 36.4 [34.2-37.3] | 40.3 [9.0-56.5] | 83.7 [71.0-87.6] |
| P10 | 64 | 62,145 | 65.9 [61.4-79.5] | 63.1 [58.6-85.7] | 34.0 [6-65.9] | 92.5 [78.2-97.4] |
| P11 | 303 | 368,689 | 76.8 [66.5-110.0] | 34.4 [26.2-38.8] | 57.7 [45.3-68.0] | 82.1 [52.7-93.0] |
| P12 | 114 | 149,158 | 82.1 [76.2-91.0] | 46.2 [46.2-49.1] | 14.2 [1.0-36.8] | 97.0 [94.4-98.6] |
| P13 | 49 | 56,227 | 89.1 [80.5-132.5] | 39.6 [37.7-41.2] | 1.9 [0.9-3.3] | 73.7 [68.2-83.6] |
| | | | 95.7 [85.6-109.5] | 38.8 [35.9-45.2] | 38.4 [25.9-48.8] | 86.0 [76.5-91.7] |

*APACHE II – Acute Physiology and Chronic Health Evaluation II; BC – Breathing Cycle; BiPAP – Bilevel Positive Airway Pressure; CAP – Community-Acquired Pneumonia; HAP – Hospital Acquired Pneumonia; IQR – Interquartile Range; SIMV – Synchronized Intermittent-Mandatory Ventilation; SOFA – Sequential Organ Failure Assessment; SPONT – Spontaneous Breathing; SVC – Superior Vena Cava

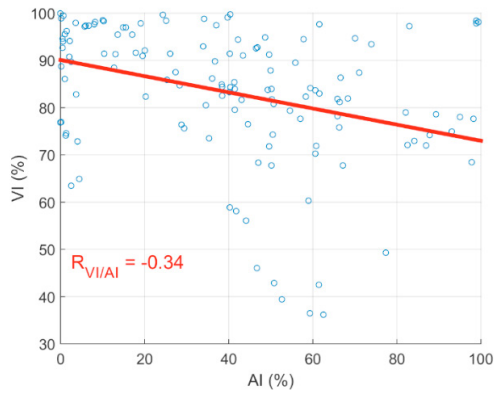


Fig 3. Patients' *VI* versus *AI* scatter plot.

As shown in **Table 3**, a total of 6 patients (Patients P4-7, P11 and P12) exhibited this aforementioned trend, whereas only one patient (Patient P1) showed the opposite trend. The rest of the patients manifested a mixed coefficient of correlation in *VI* versus $PaO_2$ and *VI* versus $PaCO_2$. **Fig. 4** depicts the trend of *VI* and *AI* metrics versus all 13 patients' $PaO_2$ and $PaCO_2$. The result shows that, in general, *AI* indicated a negative trend. As *AI* increases, the $PaCO_2$ decreases and vice versa with *AI* versus $PaO_2$. However, *VI* showed a positive trend when assessing both $PaCO_2$ and $PaO_2$.

## 4. DISCUSSION

A CAE model trained with 400,000 unique AB-NB (normal breath) pairs is used to quantify the $M_{asyn}$ (Loo et al., 2021). The CAE model receives an AB waveform as an input (**Fig. 1** black line) and reconstructs/ predicts the AB-free pressure waveform (**Fig. 1** red line), subsequently determining $M_{asyn}$ (**Fig. 1** shaded area).

We found that AB occurrence is prevalent among this patient cohort with a median *AI* of 38.4% [IQR: 25.9-48.8], consistent with literature-reported values where *AI* > 10% in several patients (Vignaux et al., 2009, Mellott et al., 2014, Rolland-Debord et al., 2017). However, the proposed *VI* is also high, with a median of 86.0% [IQR: 76.5-91.7]. In one instance, an *AI* of > 90.0% within an hour was observed, but the *VI* is equally high at 98.2%. This high *AI* could indicate that patient AB was common, but $M_{asyn}$ was low most of the time. In other words, the patient's resistance to ventilator support is minimal, possibly due to the mismatch between the MV supply and patient demand. However, the $M_{asyn}$ is insufficient to deform the patient's airway waveform, a marker of asynchrony incidence (Yoshida et al., 2018, Baedorf Kassis et al., 2021).

A Pearson's coefficient of correlation $R$ = -0.34 was observed between *VI* and *AI*, suggesting that as *AI* increases, the *VI* decreases. However, not all high hourly *AI* lead to lower *VI* because *VI* also accounts for breath-specific $M_{asyn}$. This is illustrated in **Fig. 2(f)**, where patient P10 experienced frequent occurrence of AB, but $M_{asyn}$ was minimal at 3.45%; whereas Patient P2 experienced a less prevalent AB but exhibited an average $M_{asyn}$ of 46.26%. This result shows that measuring *AI* alone may be insufficient to access PVI, and it is important to quantify the 'severity' of each asynchrony.

A high *VI* suggests that patients are receptive to ventilatory support, with lesser occurrences of 'severe' AB, however it does not truly reflect the patient's condition in several cases. Confounding factors such as patient condition, level of MV support, MV settings and sedation may influence the quality of MV treatment (Blackwood et al., 2006, Guo et al., 2018, Aragón et al., 2019). We speculate that high *VI* indicates good PVI and should predispose the patient to high $PaO_2$ and low $PaCO_2$ during treatment, but **Fig. 4** shows otherwise. However, it is important to note that $PaO_2$ and $PaCO_2$ measurements are intermittent and based on clinical decision or need (**Table 3**), and thus may not indicate real-time patient

**Table 3 Pearson's Correlation Coefficient when testing AI or VI with $PaO_2$ or $PaCO_2$**

| Patient No. | No. of ABG Data | *VI* | | *AI* | |
|---|---|---|---|---|---|
| | | $PaO_2$ | $PaCO_2$ | $PaO_2$ | $PaCO_2$ |
| | | ***R*-value** | ***R*-value** | ***R*-value** | ***R*-value** |
| P1$^+$ | 13 | -0.48 | 0.18 | 0.44 | -0.17 |
| P2 | 4 | -0.56 | -0.05 | 0.64 | 0.24 |
| P3 | 3 | 0.41 | 0.91 | -0.50 | -0.85 |
| P4* | 15 | 0.17 | -0.57 | -0.25 | 0.57 |
| P5* | 4 | 0.84 | -0.25 | 0.90 | 0.27 |
| P6* | 4 | 0.65 | -1.0 | -0.11 | -0.36 |
| P7* | 7 | 0.32 | -0.52 | -0.49 | 0.32 |
| P8 | 19 | 0.16 | 0.24 | 0.04 | 0.23 |
| P9 | 7 | -0.37 | -0.04 | 0.57 | 0.08 |
| P10 | 10 | 0.45 | 0.56 | -0.43 | -0.48 |
| P11* | 28 | 0.51 | -0.24 | 0.46 | -0.47 |
| P12* | 14 | 0.30 | -0.20 | -0.47 | 0.06 |
| P13 | 4 | -0.28 | -0.82 | 0.87 | 0.96 |
| Median | 7 | 0.30 | -0.20 | 0.04 | 0.08 |
| IQR | [4–14] | [-0.30–0.47] | [-0.53–0.20] | [-0.44–0.59] | [-0.39–0.28] |

Patients with * indicate attaining a positive *VI* correlation with $PaO_2$ but a negative correlation with $PaCO_2$. Patients with $^+$ indicate attaining a negative *VI* correlation with $PaO_2$ but a positive correlation with $PaCO_2$

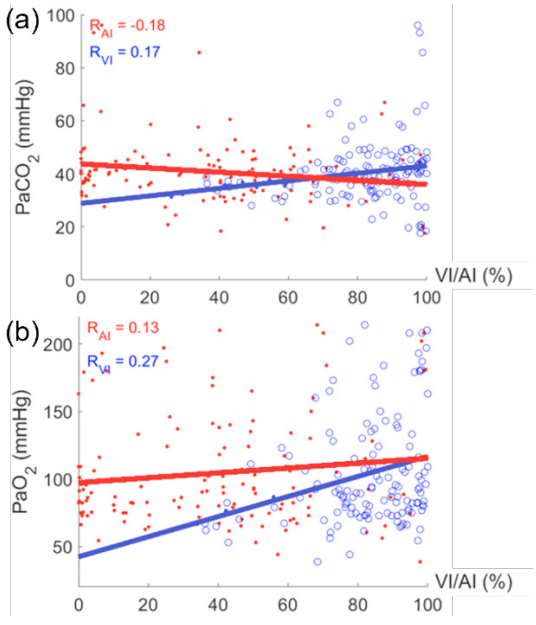


Fig 4. Scatter plots of combined patient's *AI* (red solid dot) and *VI* (blue circle) versus $PaCO_2$ (a) and $PaO_2$ (b). In Fig (a) VI shows a positive correlation whereas AI shows a negative correlation. In Fig (b), VI shows a greater correlation of $R_{VI}$ = 0.27 (line with steeper gradient) as compared to AI.

responses towards AB. The sporadic measurement frequency of $PaO_2$ and $PaCO_2$ may also lead to statistically underpowered results. Hence, further studies are necessary to elucidate the prevalence of $AI$ and $VI$ towards patients' $PaO_2$ and $PaCO_2$.

One of the limitations in this study is that $VI$ is currently limited to reconstructing airway pressure asynchronies observed in a VC ventilation mode. The calculation of $VI$ can be extended to include airway flow asynchrony during any form of pressure support or controlled ventilation. One potential method is to calculate $M_{asyn}$ via the difference between a missed tidal volume to their supposed tidal volume, as proposed by Kannangara et al. and Ang et al. (Kannangara et al., 2016, Ang et al., 2022). Besides that, the DL algorithm used is trained with limited and unspecified types of AB data, potentially affecting AB detection and $AI$ calculation performance particularly when presented with cases of AB not within the training dataset (Loo et al., 2018). Furthermore, the CAE model is also limited to the reconstruction of pressure waveforms exhibiting flow starvation or triggering-based AB. Future work warrants the diversification of AB phenotypes within the training dataset while extending application to other MV modes or respiratory waveforms.

Finally, a lack of additional clinical data such as sedation levels which might cause AB occurrence may affect the quality of this study (de Wit et al., 2009b). Further studies are required to relate a $VI$ metric towards assessing the quality of PVI. For example, an observational trial with continuous breath-by-breath airway pressure and flow data of MV patients (Ng et al., 2021, Ng et al., 2022) for quantification of $AI$ and $VI$, together with an hourly collection of arterial blood gas $PaO_2$ and $PaCO_2$ can be carried out for better correlation studies.

## 5. CONCLUSION

In this study, the automated calculation of $AI$ using machine learning methods has shown the potential to provide additional insight into a patient's response to MV treatment that is previously unavailable. In addition, the feasibility of $VI$ for PVI has been carried out. $VI$ can potentially be used alongside $AI$ to quantify the severity of each asynchronous breathing on top of the frequency of AB occurrence. It could be beneficial in understanding the quality of patient-ventilator interaction in the quest to better manage MV treatment.

## 6. ACKNOWLEDGEMENT

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