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Real-Time Breath-to-Breath Asynchrony Event Detection using Time-Varying Respiratory Elastance Model

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Abstract: Asynchronous events (AE) occur during mechanical ventilation (MV) therapy when the patient's breathing is not synchronised with the ventilator support. Frequent AE indicates sub-optimal ventilation therapy and may lead to further complications. Asynchrony Index (AI) gives the percentage of AEs as a percentage of total breaths, but is only assessed via manual scrutiny. Thus, there is a need to automate AE detection in real-time. A model-based approach using time-varying elastance to detect AEs is developed and retrospectively assessed in MV patients. Data from 14 mechanically ventilated respiratory failure patients, enrolled in an observational study in Christchurch Hospital, New Zealand were used to investigate the performance of the method. Patient data is sorted according to the ventilation mode used, and AI is calculated for each episode separately. The model-based approach accurately identifies AEs, and shown not to give false positive readings when compared to manual detection (gold standard). None of the ventilation modes give significantly different AI levels ($P > 0.05$). AI decreases when ventilation mode changes and increases overall time indicate worsen patient-ventilator interaction. The model-based method is able to successfully and accurately calculate AI. Real time use of this metric will enable patients with sub-optimal ventilator settings to be automatically identified for the first time and the settings adjusted as necessary, improving the efficacy of mechanical ventilation therapy, and providing a quantified metric to help guide MV care.

1. INTRODUCTION

A ventilation asynchronous event (AE) occurs when the patient's breathing effort is not synchronised with mechanical ventilator's breathing support. The frequent occurrence of AEs results in poor patient-ventilator interaction, leading to increase in work of breathing and other adverse effects (Chao et al., 1997, Sassoon and Foster, 2001, Dasta et al., 2005, Thille et al., 2006, Epstein, 2011). Asynchrony events can occur anytime during partially or fully controlled ventilation. However, it is more frequent during non-invasive ventilation or partially assisted modes where the patient is breathing spontaneously and the ventilator support is triggered by patient respiratory effort (Tobin et al., 2001, Vignaux et al., 2009, Epstein, 2011).

Currently, the standard method of evaluating patient-ventilator interaction is through assessing the asynchrony index (AI). AI is a measure of the asynchronous events as a percentage of total number of breathing cycles (Chao et al., 1997, Epstein, 2011, Colombo et al., 2011). However, AI is calculated retrospectively by detecting asynchrony events using manual inspection of the patient's airway and/or oesophageal pressure and flow waveforms (Fabry et al., 1995, Chao et al., 1997, Thille et al., 2006, Epstein, 2011, Colombo et al., 2011). This method is arduous and is not clinically practical to assess patient-ventilator interaction in real-time. Thus, the ability to identify asynchrony events in real-time could be a useful clinical marker of patient-ventilator interaction. An increase in the total number of asynchrony events within a time frame could also indicate the need to change ventilation mode, or adjust sedation (Bennett and Hurford, 2011).

One method that was proposed to automate asynchronous event detection is through spectral analysis of the airway flow profile (Gutierrez et al., 2011). However, this method focuses only at the airway flow profile and not the airway pressure changes, neglecting the matching of pressure and flow that defines AE (Colombo et al., 2011). Detecting asynchrony should include analysis of both pressure and flow.

This research presents a model-based method to identify AEs using both airway pressure and flow in for MV patients. In particular, a time-varying respiratory elastance derived from a lung model describing the respiratory mechanics of a mechanically ventilated patient is used (Chiew et al., 2011). Quantifying breath-to-breath time-varying respiratory system elastance, has the ability to track AEs in real-time.

2. METHODOLOGY

2.1 Study and Patients

This observational study was carried out in the intensive care unit (ICU) of Christchurch Hospital, New Zealand. Patients requiring mechanical ventilation because of respiratory failure were eligible for the study. 14 patients were included for the study and had their airway pressure and flow profile recorded. 7 of the 14 patients included for the study had multiple episodes of data recorded. The study and use of the data was approved by the New Zealand South Regional Ethics Committee.

2.2 Ventilator and Settings

Patients were ventilated using a Puritan Bennett 840 (PB840) (Covidien, Boulder, CO, USA) under different ventilation modes as determined by attending clinicians. The modes of ventilation and period of data recording were not specified as they were patient-specific. In this study cohort, three ventilation modes were used: 1) Bi-Level pressure ventilation (BL), 2) Synchronised intermittent mandatory ventilation (SIMV) and 3) Spontaneous breathing (SPONT).

2.3 Model-based Asynchrony Detection

Asynchrony detection was carried out using the time-varying respiratory elastance parameter from the model described by Chiew et al (Chiew et al., 2011). This model was extended from a first order model and is defined as:

$$P_{aw}(t) = E_{drs}(t) \times V(t) + R_{rs} \times Q(t) + P0 \qquad (1)$$

Where P_{aw} is the airway pressure, t is time, E_{drs} is time-varying elastance, V is tidal volume, R_{rs} is conducting airway resistance, Q is flow and $P0$ is the offset pressure or PEEP.

For each breathing cycle, the inspiratory time (t_i) is normalised to its maximum time for the inspiratory cycle, allowing fair comparison between each breathing cycle. The area under the curve of E_{drs} ($AUCE_{drs}$) for every breathing cycle is then calculated. When the $AUCE_{drs}$ over a breath cycle was ±50% of the median within a 5 minutes window for the given patient, an AE was declared. Model-based declared asynchrony events are compared to matching of the patients' airway pressure and flow curve through manual inspection (Colombo et al., 2011). The asynchrony index (AI) for each observation episode is calculated (AI = 100% × total AE/total breathing cycle per episode).

2.4 Statistical Analysis

The results are reported as median and interquartile range (IQR), where appropriate. Non-parametric Kruskal-Wallis one way analysis of variance (K-W ANOVA) test was used to assess the difference of location (median) of the distribution of the asynchrony index for each ventilation mode. P-values < 0.05 are considered statistically significant.

3. RESULTS

Table 1 shows the data analysed for the 14 patients included for the study. Several patients (Patients 2, 4, 6, 7, 8, 10 and 11) had data in multiple episodes. Every recorded episode is also separated according to the ventilation mode for analysis. Table 2 and Fig. 1 shows the summary of analysis.

Table 1. Asynchronous event analysis for each patient

Patient	Episodes	Ventilation Mode	Time [minute]	Breathing Cycles	No. of AE*	AI*(%)	PEEP (cmH2O)
1	1	BL	15	265	7	2.6	15
		SPONT	122	2699	34	1.3	15
2	1	SIMV	63	1112	142	12.8	12.5-25 (up to 45 during RM*)
	2	BL	1340	28007	2106	7.7	12.5
3	1	SPONT	1000	11899	21	0.2	20
4	1	BL	455	7346	635	8.6	10
	2	BL	547	7394	2730	36.9	8-10
5	1	SIMV	1442	22928	36	0.2	10
6	1	SPONT	783	16113	413	2.6	5
	2	SPONT	596	15126	1124	7.4	5
7	1	SPONT	934	23000	225	1.0	12.5
		BL	838	20635	102	0.5	12.5-18
	2	BL	1378	34112	2511	7.4	12
8	1	SIMV	38	560	74	13.2	10 (up to 22 during RM)
		BL	416	7251	116	1.6	15 (up to 22 during RM)
		SIMV	346	5999	29	0.5	15
	2	BL	267	5367	56	1.0	12.5
	3	BL	470	9347	330	3.5	12.5
9	1	SIMV	29	500	155	31.0	10
		SPONT	59	1041	554	53.2	10
		SIMV	1263	23839	4306	18.1	10-15 (up to 37 during RM)
10	1	SIMV	1001	23714	2459	10.4	25
	2	SPONT	202	4500	2305	51.2	15
		BL	273	6255	377	6.0	18
11	1	SPONT	214	2470	8	0.3	10
		BL	953	17503	1388	7.9	12.5-14
	2	SIMV	340	7255	989	13.6	14
12	1	SIMV	3132	69880	8348	12.0	15
13	1	BL	180	3300	686	20.8	15
		SPONT	858	12483	647	5.2	12.5-15
14	1	BL	1085	25034	1248	5.0	10 - 17

*AE - Asynchronous Events, AI - Asynchrony Index, RM - Recruitment Manoeuvre

Table 2. Summary of results

Ventilation Modes	Breathing Cycles Median [IQR]	No. of AE Median [IQR]	AI (%) Median [IQR]
BL	7394 [6033-21735]	635 [113-1581]	6.1 [2.4-8.2]
SIMV	7255 [974-23745]	155 [65-2921]	12.8 [7.9-14.8]
SPONT	11899 [2641-15373]	413 [31-766]	2.6 [0.8-18.5]

Note: No significant difference was found in the number of AI comparing each ventilation mode using automated model-based method.

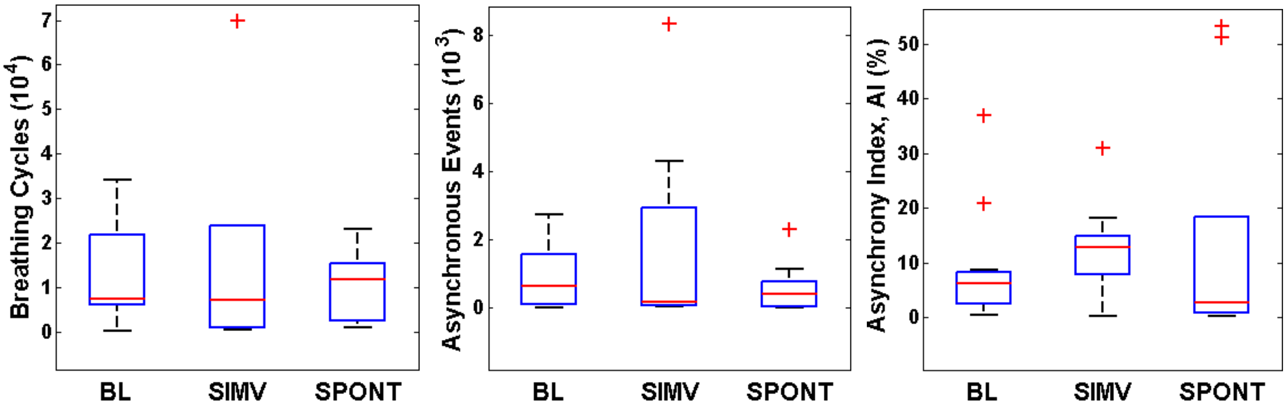

Fig. 1. Boxplot for total analysed breathing cycles (Left), total AEs (Middle) and AI (Right) for each ventilation mode.

Figs. 2-4 are examples of model-based asynchrony detection ($AUCE_{drs}$) with respect to observation using airway pressure (P_{aw}) and flow (Q) profile. Fig. 2 shows a section of Patient 5 for P_{aw}, Q and $AUCE_{drs}$ when ventilated using SIMV volume controlled mode. A smooth and transient $AUCE_{drs}$ is observed when there is no pressure and flow mismatch and thus no AEs.

Fig. 3 shows the P_{aw}, Q and $AUCE_{drs}$ for Patient 11 episode 2 when ventilated using BL. Occasional $AUCE_{drs}$ spikes were observed indicating that asynchronous events may occur at any time throughout the ventilation period. Fig. 4 show the P_{aw}, Q and $AUCE_{drs}$ for Patient 1. At the time of data recording, Patient 1 was initially ventilated using BL and was changed to SPONT mode.

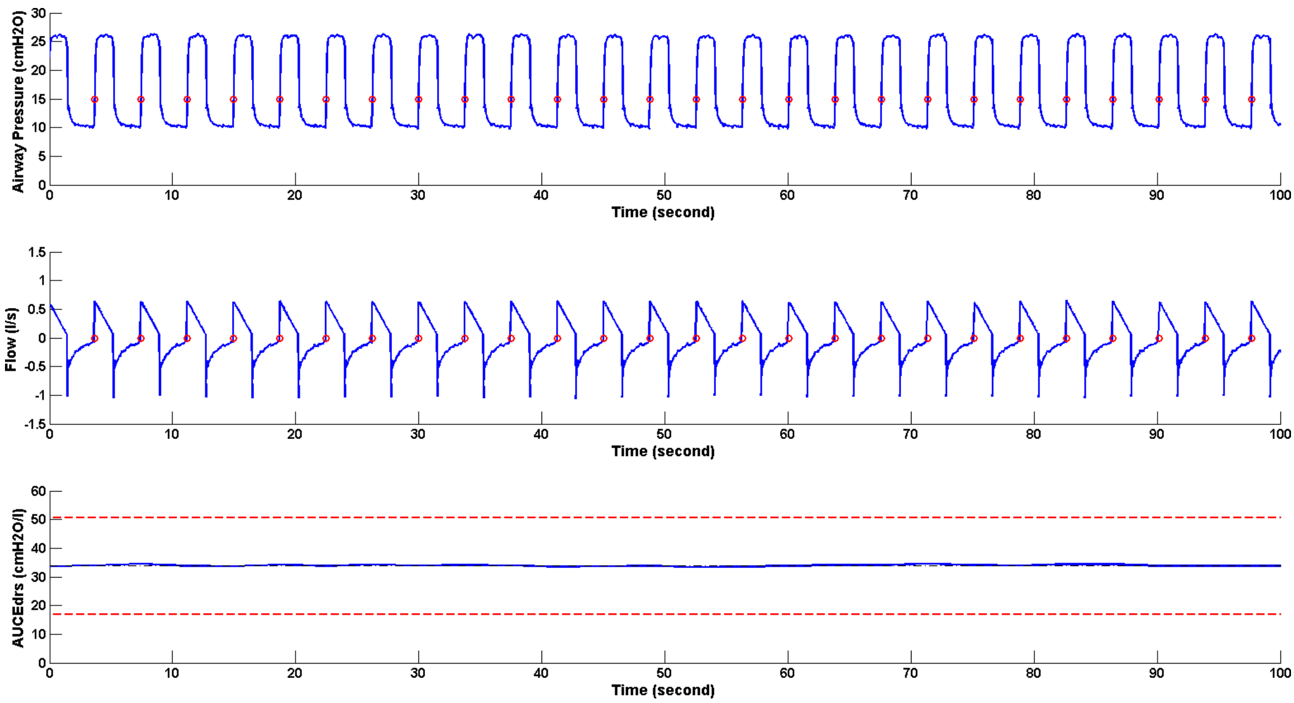

Fig. 2. Section of P_{aw}, Q and $AUCE_{drs}$ for Patient 5 episode 1. There is no pressure and flow mismatch, resulting in a smooth and transient $AUCE_{drs}$. The red markers indicate the start of a breathing cycle. The dashed lines in $AUCE_{drs}$ are the ±50% of the median $AUCE_{drs}$. No $AUCE_{drs}$ exceed the ±50% AE boundary, indicating no AE.

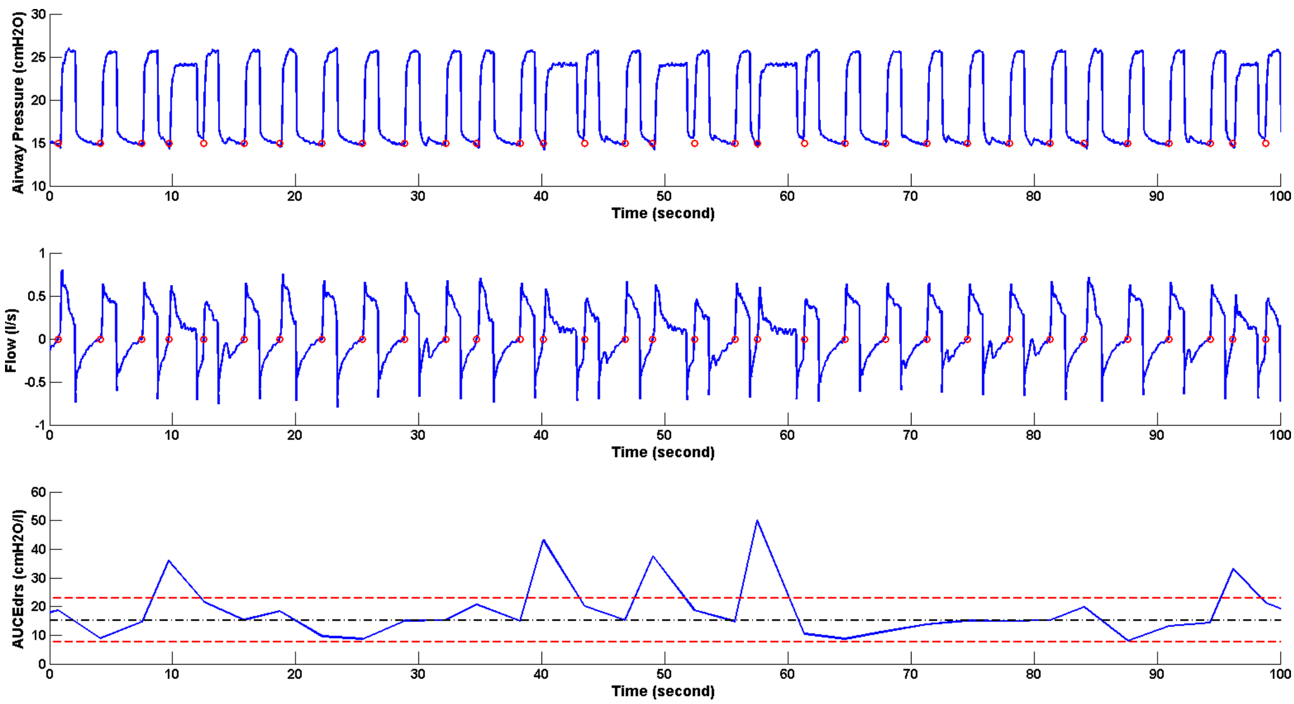

Fig. 3. Section of P_{aw}, Q and $AUCE_{drs}$ for Patient 11 episode 2. Pressure and flow mismatch resulted in sudden change of $AUCE_{drs}$ indicating an asynchrony event has occurred. The red markers indicate the start of a breathing cycle. The dashed lines in $AUCE_{drs}$ are the ±50% of the median $AUCE_{drs}$. 5 $AUCE_{drs}$ spikes exceeded ±50% AE boundary, indicating there were 5 AEs within this time frame.

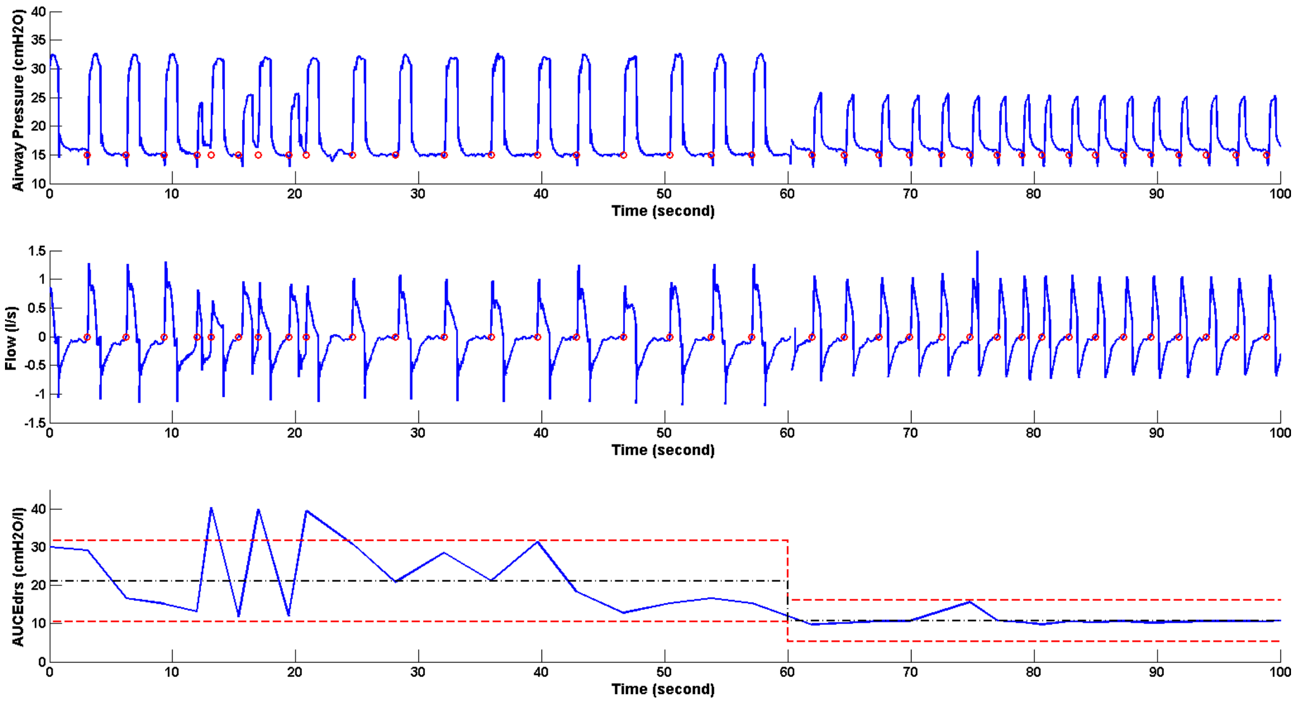

Fig. 4. Section of P_{aw}, Q and $AUCE_{drs}$ for Patient 1 when the ventilation mode is changed from BL to SPONT. The red markers indicate the start of a breathing cycle. The dashed lines in $AUCE_{drs}$ are the ±50% of the median $AUCE_{drs}$. The median and ±50% of $AUCE_{drs}$ shifts when ventilation mode changes. There were 3 $AUCE_{drs}$ exceeded the ±50% AE boundary during BL in this time frame.

4. DISCUSSION

4.1 $AUCE_{drs}$ as an Asynchronous Event (AE) Marker

Pressure and flow waveforms were manually scrutinised to identify AEs and compared to the results obtained using the model-based asynchrony detection method ($AUCE_{drs}$). Figs. 2

to 4 showed that every breathing cycle with pressure and flow mismatch corresponds to a spike in $AUCE_{drs}$. The results showed that $AUCE_{drs}$ can be used as an automated AE indicator using simple thresholds.

From Table 1, it was found that Patient 5 data was recorded for 1442 minutes when the patient was ventilated in SIMV. During this ventilation period, the model-based detect asynchronous event is only 36 out of 22928 breathing cycles. The low asynchronous breaths result in AI of only 0.2%. A section of consistent $AUCE_{drs}$ for Patient 5 is shown Fig. 2. Comparatively, Patient 11 during episode 2 (Fig. 3) is also ventilated with SIMV but there are occasional $AUCE_{drs}$ 'spikes', resulting in a higher AI of 13%. This results shows that AE can occur at any time throughout the ventilation period. An occasional AE may be a patient coughing, or misfiring of the ventilator. These particular AEs are often masked by the total ventilation period and are neglected as a whole. However, an accumulation of these AEs or snowballing AEs may have adverse effect (Sassoon and Foster, 2001, Dasta et al., 2005, Epstein, 2011, Gutierrez et al., 2011) and it is important to have real time AE detection.

4.2 Effect of Ventilator Settings on $AUCE_{drs}$ and AEs

Fig. 4 shows the P_{aw}, Q and $AUCE_{drs}$ for Patient 1 transitioning from BL to SPONT. At the start of the data collection, Patient 1 had relatively little AE that slowly increased with time. The increasing occurrence of AE may be due to the patient regaining spontaneous breathing effort and thus starting to 'fight' the ventilator support. In this data, the ventilation mode is later changed to SPONT at time = 60 s. After BL is changed to SPONT, the incidents of $AUCE_{drs}$ is reduced as shown in Fig. 4 after 60 s, resulting in consistent $AUCE_{drs}$ profile. Overall, the AI was reduced from 2.6% to 1.3% in changing modes (Table 1). This result is a positive indication of how AEs might be reduced by changing ventilation mode.

Equally, as shown in Fig. 4, the peak airway pressure (PIP) during SPONT is ~25 cmH2O, lower than for BL with a PIP = ~33 cmH2O. In addition, the inspiratory time is lower, resulting in lower tidal volume. It is observed that the combination of both these reductions have resulted in lower $AUCE_{drs}$ magnitude. $AUCE_{drs}$ is a non-invasive model-based method to estimate respiratory system elastance. Thus, $AUCE_{drs}$ not only captures AEs, but it can also be a useful metric to estimate respiratory system elastance in real time without additional clinical protocol.

4.3 The Need of Real-Time AI Assessment

Transition from BL to SPONT in Patient 1 resulted in reductions in AI, suggesting better patient-ventilator interaction. This reduction can also be observed in other patients with multiple ventilation mode in each data recording episode. In particular, 5 of 7 patients (Patients 1, 7, 8, 10 and Patient 13) have shown decrease in AI, and 2 patients (Patients 9 and 11) have increase in AI after changing the ventilation modes. Changing ventilation mode by attending clinicians to adapt to patients breathing is generally intended to improve patient-ventilator interaction and care. Thus, the main issue highlighted by this study is that there is no practical way to identify these AEs in real time. Clinicians thus lack the tools to objectively assess thus aspect of patient ventilator interaction. This lack of clinical diagnostic tools further exposes patients to the risk of prolonged ventilation and other adverse outcomes (Chao et al., 1997, Sassoon and Foster, 2001, Dasta et al., 2005, Thille et al., 2006, Epstein, 2011).

Overall, this study has shown that the $AUCE_{drs}$ metric can successfully identify AEs in ventilated patients, and thus determine the AI in an automated fashion. Currently, the AE and the AI can only be determined by manual inspection of the pressure waveforms, a tedious exercise that is not regularly performed. By making the AI an accessible metric for clinical use, this study has the potential to improve the efficacy of mechanical ventilation therapy. As well as providing quantitative feedback that can be examined over time to assess overall MV care.

4.4 Clinical Implications

MV settings, in particular breath triggering and breathing frequency, affect the quality of patient-ventilator interaction. However, this interaction is also highly dependent of the patient disease state and amount of sedation used. More severely ill patients will often be administered higher sedation dose to reduce the work of breathing and aid recovery. These patients will be fully ventilated and have relatively little spontaneous breathing effort, resulting in lower AI. However, regardless of the mode, this approach can detect AEs as shown in Table 1, and as noted, may serve as an objective, quantified measure of when to change mode or MV approach.

The summary of asynchrony index for BL, SIMV and SPONT is shown in Fig. 1 (Right). The K-W ANOVA test showed that there were no significant difference in the location of the AI distribution when comparing these three tested ventilation mode ($P > 0.05$). In this study, it was found that no ventilation mode is universally 'better' in terms of preventing or reducing asynchrony events. In addition, this study focuses on investigating a physiological relevant method to detect asynchronous events automatically. Thus, concluding a ventilation mode that will result in higher or lower AI is not the intention of this observational study. Furthermore, the patients' variability and disease progression during mechanical ventilation was not able to provide clearly information to distinguish which ventilation mode is better in reducing asynchronous events.

4.5 Study Limitations

An important consideration in the development of any new metric is the incidence of false positive readings. The model-based AE detection proposed in this study incorporates an arbitrary time frame of 5 minutes for to assess the AEs. This arbitrary time frames thus limits the overall accuracy of proposed metric. For example, within a 5 minute window, 60% of the analysed breathing cycles had $AUCE_{drs}$ exceeding ±50% of the median $AUCE_{drs}$ and are 'true AEs'. However, this model will instead declared 40% of the breathing cycles as 'false AEs' because the median $AUCE_{drs}$ is now shifted towards the true AEs. However, these extreme cases are unlikely to happen and will still indicate high numbers of AE and AI. Equally, the sudden change of overall $AUCE_{drs}$ may also be contributed by the change of patient's disease state and variability.

$AUCE_{drs}$ is area under the curve for normalised time-varying elastance and is effectively the respiratory system elastance at each breathing cycle. Carlucci et al. reported that the incidence of asynchronous events has no relation to the any parameters of respiratory mechanics (Carlucci et al., 2013) which somehow contradicts to the finding of this research. However, the results reported by Carlucci focuses patients' overall respiratory mechanics and not breath-to-breath respiratory mechanics evaluation. Thus, the AE detection proposed by this research remains viable and valid. Results have shown that a breathing cycle that has a ±50% difference of the median $AUCE_{drs}$ correspond to a breathing cycle with significant pressure and flow mismatch, suggesting an asynchronous breathing cycle.

Another limitation of this study is that this is an observational study and there were no specific protocol or ventilator setting required during data collection. Patients' airway pressure and flow data were recorded at any time during MV once they meet the inclusion criteria. Thus, there is no specific clinical trend, or related outcome that can be drawn for this analysis. However, as pointed out in discussion section, AE can occur at any time during mechanical ventilation. Thus, an observational study without a specific protocol further demonstrates the ability of the model-based method to capture AEs at any time during MV.

5. CONCLUSION

The proposed $AUCE_{drs}$ metric can be reliably used as a measure of AI for both fully controlled ventilation and spontaneously breathing patients. Investigation of the effect of ventilation mode on the AI has shown that no mode is significantly better or worse than another in terms of AI. However, changing the ventilator settings may improve or worsen patient-ventilator interaction. Thus, monitoring of the AI trend over time could be used as a clinical marker to assess patient-specific patient-ventilator interaction at different ventilation settings. The ability of this real time metric will help clinicians to ensure that the ventilator settings chosen are optimal for the patient, and to improve the efficacy of mechanical ventilation therapy.

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7. CONFLICT OF INTEREST

The authors declared that they have no conflict of interest.

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