

Predicting Mechanical Ventilation Duration Using the Asynchrony Index in ICU Patients

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Abstract:

Background: Mechanical ventilation is a supportive measure for patients with respiratory failure. Patient-ventilator interaction must be harmonious to achieve the goals of mechanical ventilation. Mismatch between patient's demand and ventilator's delivery results in Patient-ventilator asynchrony (PVA). Though PVA is associated with adverse outcomes, it is less recognized. PVA is quantified by Asynchrony index (AI). The largest body of literature has focused only on ineffective triggering in the calculation of AI. The effects of other pattern of asynchrony on patient's length of mechanical ventilation is not well-known.

Objectives: To predict the duration of mechanical ventilation by evaluating the asynchrony index following assessment of various asynchrony type prevalence among mechanically ventilated ICU patients.

Methods: This prospective, non-interventional cohort study was conducted in the Department of Anaesthesia, Analgesia, and Intensive Care Medicine at Bangladesh Medical University, Dhaka, over a one-year period from September 1, 2018, to August 31, 2019. Following approval by the Institutional Review Board, we enrolled seventy ICU patients receiving mechanical ventilation via orotracheal tube according to predefined inclusion and exclusion criteria. Each patient underwent a one-hour observation period during the first 24 hours of admission. We visually analyzed pressure-time and flow-time waveforms displayed on bedside mechanical ventilator monitors to identify various asynchrony types. The asynchrony index (AI) was calculated as the ratio of asynchronous events to total respiratory rate, expressed as a percentage. Patients were stratified into two groups based on AI: high asynchrony (AI $\geq 10\%$) and low asynchrony (AI $< 10\%$). All participants were followed for 28 days to assess the duration of mechanical ventilation. Data analysis was performed using SPSS version 25 (IBM Corp.) for Windows.

Results: Mean age of 70 study subjects were 57.66 ± 11 years. Among them 55.7% were male and 44.3% were female. Twenty-seven (38.57%) patients had AI $\geq 10\%$ and forty-three (61.4%) had AI $< 10\%$. Age and sex distribution were similar between two groups. About Nineteen percent of total breath were asynchronous. Identified asynchrony includes Ineffective triggering 40.55%, Flow asynchrony 37.14%, Premature termination 11.45%, Auto-triggering 5.42%, Double-triggering 4.92% and Delayed termination 0.5%. At least one type of asynchrony was present in 55% patients and two or more combined asynchrony were present in 12.85% patients. Patients with AI $\geq 10\%$ had 10 more days on mechanical ventilation than patients with AI $< 10\%$ [19 days (IQR 10-28) vs. 9 days (IQR 3-15), $p = 0.0001$]. At 28 days, 28% patients with AI $\geq 10\%$ were on mechanical ventilation in contrast to no patients belonging AI $< 10\%$ group.

Conclusion: Patients with a high asynchrony index (AI $\geq 10\%$) demonstrated significantly prolonged mechanical ventilation duration compared to findings in most comparable studies. Notably, our study identified flow asynchrony as a particularly prevalent form of patient-ventilator dyssynchrony, occurring frequently alongside ineffective triggering.

Keywords: Asynchrony Index (AI), Mechanical ventilation (MV), Patient Ventilator Asynchrony (PVA).

INTRODUCTION

Mechanical ventilation supports patients with respiratory failure by improving oxygenation, removing CO₂, reducing respiratory muscle workload, and facilitating recovery.¹ Effective treatment requires synchronized patient-ventilator interaction to minimize work of breathing (WOB) and avoid complications such as excessive sedation, prolonged ventilation, or lung injury.^{1,2} Patient-ventilator asynchrony (PVA) occurs when ventilator assistance fails to match patient effort, often due to improper timing or flow delivery.³ Despite affecting ~25% of ventilated patients, PVA remains underrecognized.³ Contributing factors include suboptimal ventilator settings, inappropriate sedation, or patient-related conditions.¹ Ventilator waveforms (pressure-time, flow-time, volume-time) enable bedside identification of PVA, yet are underutilized.⁴ There are four phases of a respiratory cycle-

1. Breath initiation (Trigger). 2. Flow and pressure delivery, 3. The transition from inspiration to expiration (Cycling off) and 4. Expiration. PVA can occur in all phases of the respiratory cycle.¹ There are at least three types of asynchrony described in literature associated with the breath initiation phase of respiratory cycle which are called Trigger asynchronies- 1. Ineffective triggering, 2. Double-triggering and 3. Auto-triggering. Flow asynchrony occurs in flow phase of respiratory cycle. Here ventilator flow does not match with the patient flow. Termination asynchrony occurs at Cycling off phase of respiratory cycle. It is of two types – Premature termination and Delayed termination.⁴ The asynchrony events will be quantified by Asynchrony index (AI). It is defined as the number of asynchrony events divided by the total respiratory rate.^{2,5} The purpose of the study is to evaluate the prevalence of six major types of asynchrony in mechanically

ventilated patients in Intensive Care Unit (ICU) and to predict the duration of mechanical ventilation by Asynchrony Index.

Limited studies have evaluated PVA prevalence and its clinical impact, primarily in high-resource settings. In resource-limited countries like Bangladesh, ICU populations are heterogeneous, often comprising transferred patients with prolonged mechanical ventilation via endotracheal tube (ETT) or tracheostomy. There is a paucity of structured research on PVA in resource limited ICU settings. Existing studies have predominantly examined only trigger asynchrony when predicting ventilation duration. Our study advances this field by evaluating flow and cycling asynchronies in addition to trigger events, while also implementing a more comprehensive 60-minute waveform analysis period compared to the standard 30-minute observation window.

Our objective was to determine the prevalence of six major asynchrony types (ineffective triggering, double-triggering, auto-triggering, flow asynchrony, premature termination, and delayed termination) in newly admitted mechanically ventilated patients on ICU Day 1; and to predict the duration of mechanical ventilation by assessing the Asynchrony Index (AI).

METHODOLOGY

This prospective cohort study was done in the department of Anesthesia, Analgesia and Intensive Care Medicine, Bangladesh Medical University (BMU) from 1st September, 2018 to 31st August, 2019. Patients were enrolled after the date of IRB clearance. Purposive sampling was done in all newly admitted ICU patients requiring invasive mechanical ventilation during the study period. Written informed consents were obtained from guardians of patients' after full disclosure of study procedures, risks/benefits, and confidentiality measures (secure data storage with password protection).

Sample size calculation

Sample size calculation is based on the study conducted by de Wit et al. (2009a). They estimated that the median duration of mechanical ventilation for low asynchrony index (<10%) is 4

days and for high asynchrony index ($\geq 10\%$) is 10 days. Assuming a constant hazard ratio between two groups leading to an exponential hazard distribution, a one sided log rank test will be used for comparison of two groups. The estimated sample size is 72 as calculated below:

$$m = (C+E)/2 = (4+10)/2 = 7$$

$$pa = 1 - \frac{\exp(-\frac{\ln(2)A}{m})}{\frac{\ln(2)A}{m}} = 1 - \frac{\exp(-\frac{\ln(2)180}{7})}{\frac{\ln(2)180}{7}} = 0.99$$

$$p = 1 - pa \cdot \exp(-\ln(2)F/m) \\ = 1 - 0.99 \cdot \exp(-\ln(2)28/7) \\ = 0.94$$

$$n = (z_{\alpha/2} + z_{\beta})^2 \left(\frac{1 + \frac{1}{m}}{\ln(r)^2} \right) p$$

$$n = (1.96 \cdot 2 + 0.842)^2 \left(\frac{1 + \frac{1}{7}}{\ln(2.5)^2} \right) \cdot 0.94 = 29.8 = 30$$

(approx.)

Assuming both group sizes are equal, Total number of patients to be enrolled is (30+30)= 60

Considering 20% drop-out, Patients need to be enrolled {60+ (60x0.2)}= 72

C: Median duration of mechanical ventilation for low asynchrony index group = 4 days

E: Median duration of mechanical ventilation for high asynchrony index group = 10 days

r: Hazard ratio = E/C = 10/4= 2.5

A: Accrual time during which subjects are recruited to the study= 180 days

F: Additional follow-up time after the end of recruitment = 28 days

At $\alpha=0.05$, $z_{\alpha/2} = 1.96 \times 2$ (single sided)

At Power 80%, $z_{\beta}=0.842$

n= sample size per group

Subject selection criteria

Inclusion criteria:

1. All newly admitted ICU patients undergoing invasive mechanical ventilation via endotracheal tube.
2. Age more than 18 years.

Exclusion criteria:

1. Mechanical ventilation duration <24 hours (as the minimum duration in this study was one day)
2. Inability to initiate spontaneous breaths (including cases due to neuromuscular blocking agents or apnea)
3. Chronic neuromuscular disorders (e.g., myasthenia gravis, Guillain-Barré syndrome)
4. Ventilation via tracheostomy tube or T-piece
5. Patients undergoing spontaneous breathing trials.

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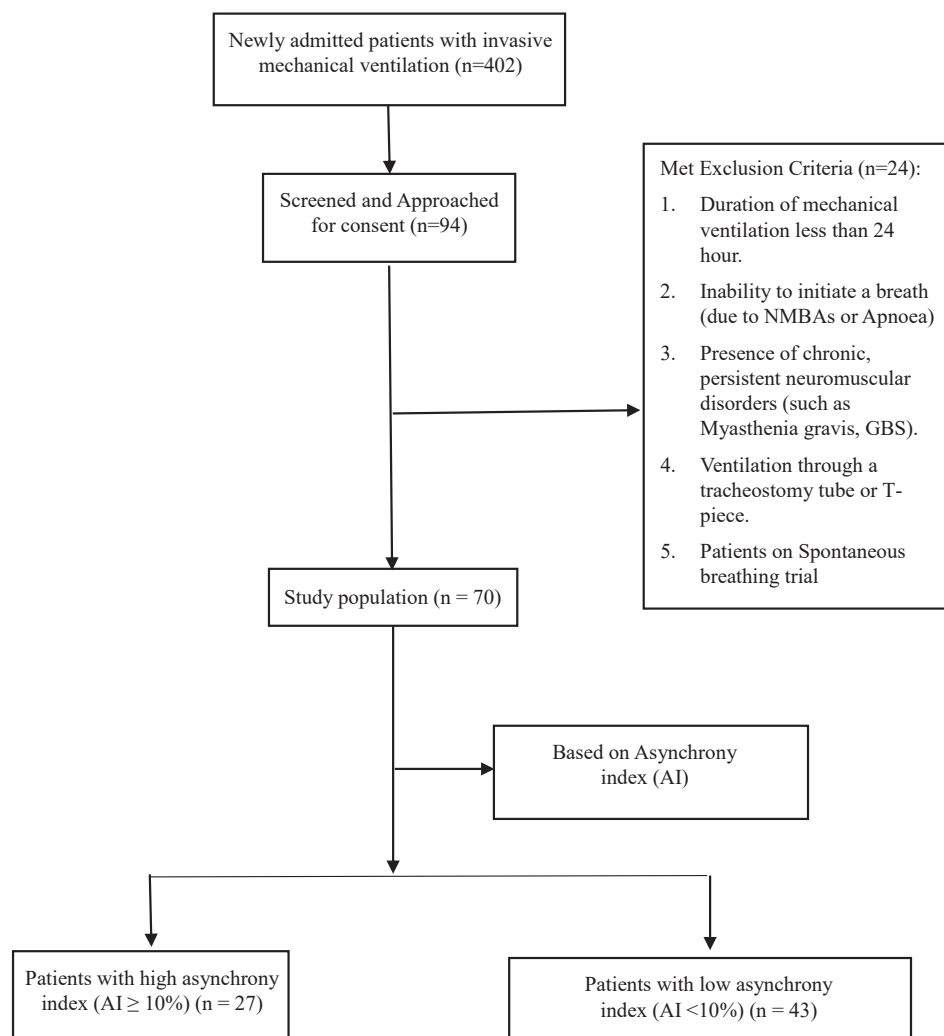


Fig 1: Cohort derivation and Study plan

Study procedure: Enrolled patients underwent a 1-hour observation period within the first 24 hours of invasive mechanical ventilation. Ventilator waveforms (pressure-time and flow-time) were analyzed at the bedside using SERVO-s (Maquet), iTERNIS (HEYER), and Newport™ e360 (Medtronic) ventilators to identify asynchrony types and frequency. A study guide assisted in difficult cases. Asynchrony Index (AI) was calculated as: (Number of asynchrony events/Total respiratory rate) × 100%. Patients were stratified using the established 10% threshold: AI ≥ 10% (high asynchrony group) and AI < 10% (low asynchrony group).⁵⁻⁷ Patients were followed for 28 days to assess the duration of mechanical ventilation (from enrollment, including post-tracheostomy ventilation time). Day 0 was defined as the start of invasive ventilation via endotracheal tube in any ICU.

Statistical analysis: Categorical variables (Breath types, Asynchrony types, Age and sex distribution of patients, Ventilatory status prior to admission to current ICU, Reason

for ICU admission, Admission source, Reason for intubation, Co-morbidities, Mode of mechanical) were reported as count and percentage. Normally distributed continuous data (Patient's age) were presented as mean with 95% confidence interval whereas non-normally distributed data (Length of mechanical ventilation) were reported as median with interquartile range. To determine any association between two categorical variables Chi-square test or Fisher's exact test was used. Quantitative data (Length of mechanical ventilation) was compared using Mann-Whitney U test. Spearman correlation was used to find out the correlation between Asynchrony index and length of mechanical ventilation. Kaplan-Meier time to event curve was produced for length of mechanical ventilation of both groups and a one-sided log-rank test was used to compare the duration. All p value at or below 0.05 was considered as significant. The statistical analysis was performed using the Windows based statistical software package SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.)

Operational Definitions

Asynchrony Index (AI): Asynchrony index is a way of quantifying Patient-ventilator asynchrony. It is defined as the number of asynchrony events divided by the total respiratory rate. Total respiratory rate is computed as the sum of number of ventilator cycles (triggered or non-triggered) and of wasted efforts. So, Asynchrony index (expressed in percentage) = Number of asynchrony events/Total respiratory rate (ventilator cycles + wasted efforts) x 100.⁶

Ineffective triggering: It occurs when the patient's inspiratory effort fails to trigger a ventilator breath. It results from a weak inspiratory effort and presence of intrinsic positive end-expiratory pressure (PEEPi).⁴

Double-triggering: It happens when two breaths occurs in interval less than half mean inspiratory time. Here patient's demand outlasts set inspiratory time resulting in ventilator triggering second breath. Patients risk factor includes high ventilatory demand, high PaO₂/FiO₂ ratio whereas the ventilator inspiratory time is too short.⁴

Auto-triggering: Here ventilator triggers unscheduled breath in the absence of patient's effort and it can be generated by cardiogenic oscillation, leak in the ventilator circuit, flow triggering and low triggering threshold.⁴

Flow asynchrony: Here ventilator flow does not match with the patient flow. Ventilator flow setting is the most frequent incorrectly-set ventilator parameter.⁴

Premature termination: It occurs when patient's inspiratory time exceeds ventilator set inspiratory.⁴

Delayed termination: It is the result when ventilator set inspiratory time exceeds patient's inspiratory.⁴

RESULTS

Four hundred and eighty-eight patients were admitted to the ICU of BMU during the period of January, 2019 to July, 2019. Four hundred and two patients were mechanically ventilated. Ninety-four patients were screened and approached for consent. Twenty-four patients were excluded. Seventy patients were enrolled in the study.

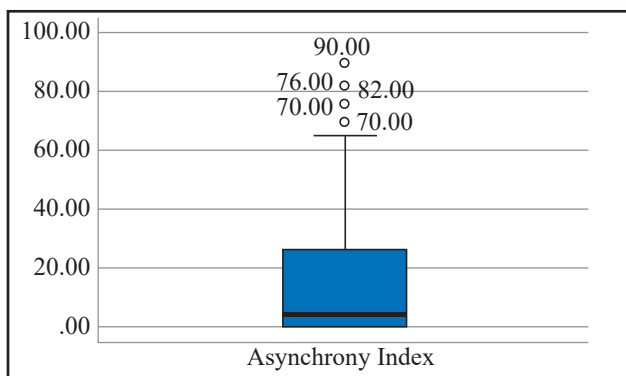


Figure 2: Box and Whisker plot diagram of Asynchrony index of study population

Patients were studied for one hour to identify Patient-ventilator asynchrony. The median Asynchrony index

of the study population was 3.80%. Interquartile range 0.00 – 26.50%. Minimum Asynchrony index was 0.00% and maximum 90.00%.

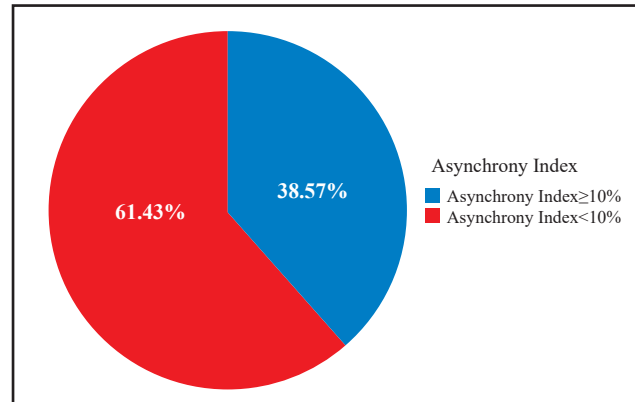


Figure 3: Distribution of patients according to Asynchrony index

Of 70 patients, twenty-seven (38.57%) had Asynchrony index $\geq 10\%$ and forty-three (61.4%) had $< 10\%$.

Table I: Age distribution of patients (N=70)

Age group (year)	Asynchrony index		Total (N=70) N (%)	p* value
	$\geq 10\%$ (n=27) N (%)	$< 10\%$ (n=43) N (%)		
≤ 40	1 (3.7)	5 (11.6)	6 (8.6)	0.216
41-50	3 (11.1)	5 (11.6)	8 (11.4)	
51-60	9 (33.3)	22 (51.2)	31 (44.3)	
61-70	12 (44.4)	10 (23.3)	22 (31.4)	
≥ 71	2 (7.4)	1 (2.3)	3 (4.3)	
Mean $\pm$ SD	61.37 $\pm$ 8.20	55.33 $\pm$ 11.95	57.66 $\pm$ 11.00	

* p value determined by Pearson Chi-Square test

Mean age of the patients was 57.66 $\pm$ 11.00 years ranging from 22 to 80 years. Majority patients were aged 51 to 60 years (44.3%). Asynchrony index $\geq 10\%$ was mostly prevalent in 61-70 year age group (44.4%). However, age distribution was statistically similar between two groups ($p > 0.05$).

Table II: Sex distribution of patients

Gender	Asynchrony index		Total (n=70) N (%)	p* value
	$\geq 10\%$ (n=27) N (%)**	$< 10\%$ (n=43) N (%)		
Male	18 (66.7)	21 (48.8)	39 (55.7)	0.144
Female	9 (33.3)	22 (5.2)	31 (44.3)	

*p value determined by Pearson Chi-Square test

**Values are expressed in Number and Percentage of total patients in parenthesis

Of all patients, thirty-nine were male (55.7%) and thirty-one were female (44.3%). Statistically similar gender distribution was noted ($p > 0.05$).

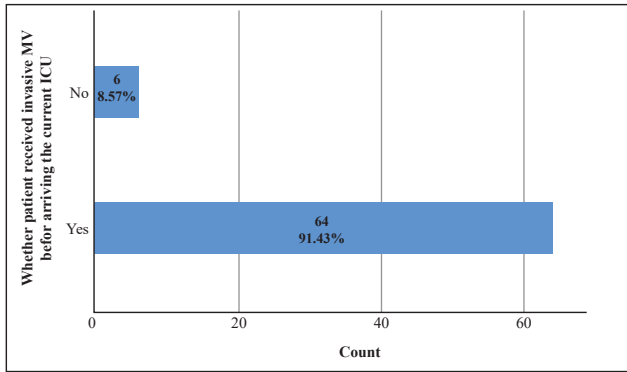


Figure 4: Ventilatory status before arriving the current ICU

Sixty-four (91.43%) patients received invasive mechanical ventilation prior to admission to current ICU (fig 4). Figure 5 showed that fifty-two (74.29%) patients were admitted due to medical conditions. Twelve (17.14%) patients required ICU admission after planned surgery. Trauma was the cause for admission in five (7.14%) patients. Only one (1.43%) patient admitted for Emergency surgery.

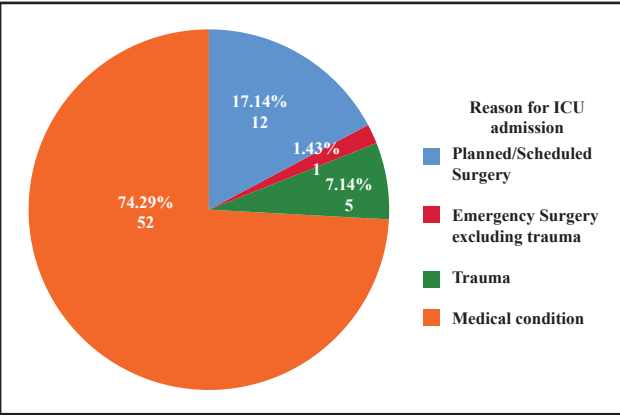


Figure 5: Reason for ICU admission (n=70)

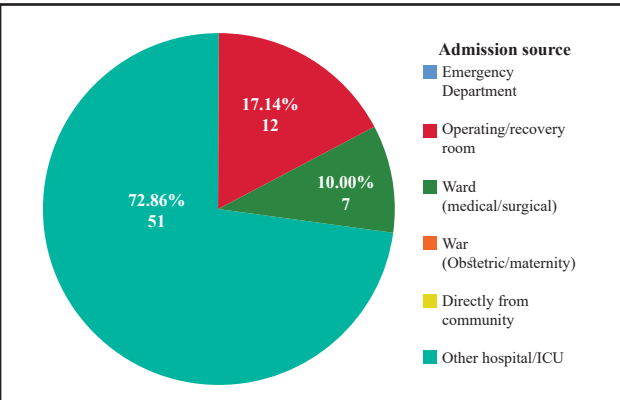


Figure 6: Admission source of patients (N=70)

Out of 70 patients, fifty-one (72.86%) patients were admitted as a transfer case from another hospital / ICU (fig 6). Twelve (17.14%) patients were from operating room. Only seven (10.00%) patients were shifted from medical/surgical ward. No patients were admitted directly from community. Figure 7

showed that most common reason for endotracheal intubation was depressed level of consciousness. It was present in fifty (37.04% of intubation) patients. Acute respiratory failure was the second cause (34.81%). Other reasons for intubation included haemodynamic instability (18.52%), planned post-operative mechanical ventilation (8.89%) and post-cardiac arrest (0.74%)

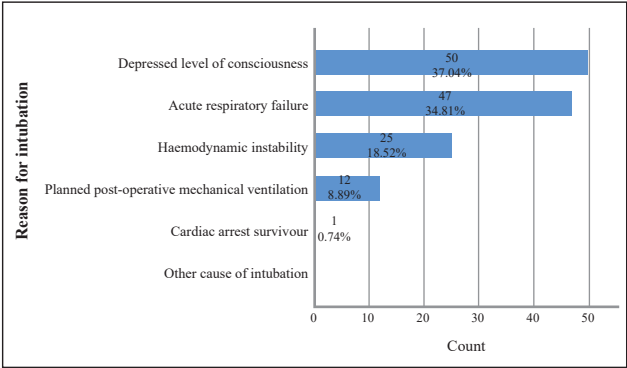


Figure 7: Reason for intubation (N=70)

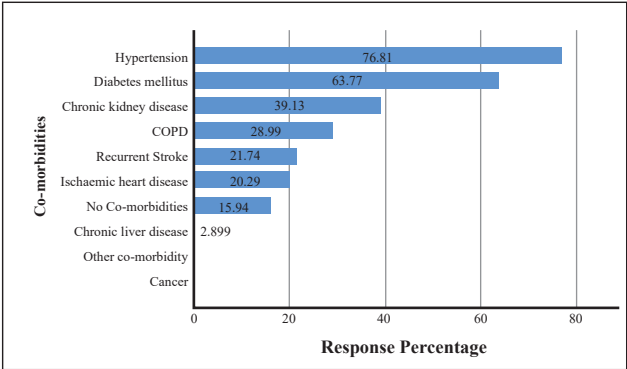


Figure 8: Co-morbidities among study population
Hypertension (76.81%) and Diabetes mellitus (63.77%) were the major co-morbidities among study population (fig 8). Other co-morbidities included CKD (39.13%), COPD (28.99%), Recurrent stroke (21.74%), Ischaemic heart disease (20.29%) and CLD (2.90%). All co-morbidities were similarly distributed between patients with Asynchrony index $\geq 10\%$ and $< 10\%$ (table III). However, patients without co-morbidities had a significant difference ($p=0.041$)

Table III: Comparison of co-morbidities between two group of patients (N=70)

Co-morbidities	Asynchrony index		p*
	$\geq 10\%$	$< 10\%$	
	N	N	
Hypertension	23	30	0.118
Diabetes mellitus	21	23	0.335
Chronic kidney disease	12	15	0.458
COPD	8	12	0.543
Recurrent stroke	7	8	0.554
Ischaemic heart disease	7	7	0.248
Chronic liver disease	2	1	0.626
Cancer	0	0	
No co-morbidity	1	10	0.041

*p value determined by Pearson Chi-Square test.

Table IV: Breath categories observed in study population (N=70)

Breath category	Frequency during observation period (one hour)*	% of total breaths
Normal	72492	81.35
Asynchronous	16617	18.65
Total	89109	100

*Values are expressed as number of breaths in one hour

Pressure-time and Flow-time curves displayed on the monitor of bedside mechanical ventilator were observed for one hour for each patient (N=70) (table IV). Total breath observed during the study period was 89109 and mean respiratory rate was 21.22 ± 3.75 /min. Minimum and maximum rate of study population were 16/min and 30/min respectively. 18.65% breath were asynchronous and 81.35% breath were normal.

Table V: Patient ventilator asynchrony (PVA) frequency

Identified asynchrony	Frequency in one hour*	% of PVA
Ineffective triggering	6739	40.55
Double-triggering	818	4.92
Auto-triggering	900	5.42
Flow asynchrony	6172	37.14
Premature termination	1904	11.45
Delayed termination	84	0.5
Total	16617	100

* Values are expressed as number of asynchronous breaths in one hour

The most common identified asynchrony in the sample was Ineffective triggering (40.55% of all asynchronous breath) (table V). The second most common category was Flow asynchrony (37.14%). Other asynchronies included Premature termination (11.45%), Auto-triggering (5.42%), Double-triggering (4.92%) and delayed termination (0.5%).

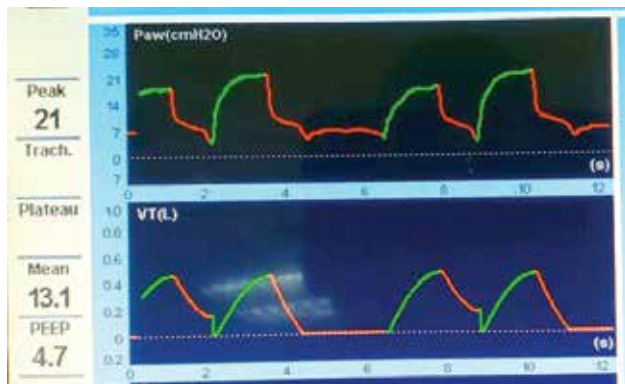


Figure 9: This Pressure-time waveform (upper) shows 2 ineffective triggering & 3 delayed termination among 6 total breaths in 12 seconds.

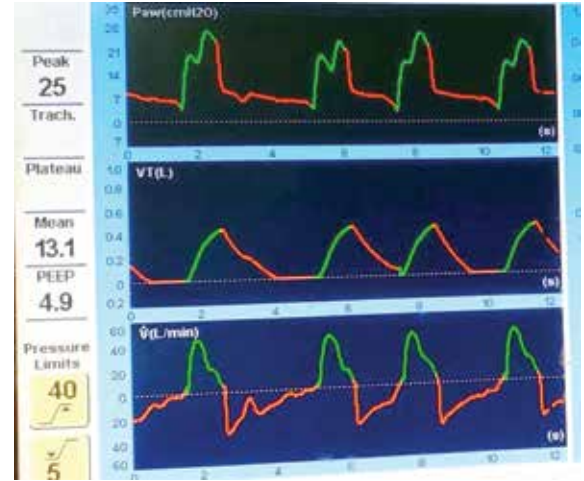


Figure 10: Pressure-time waveform (upper) and Flow-time waveform (lower) shows 4 breaths with flow asynchrony and 1 ineffective triggering among 5 total breaths in 12 seconds

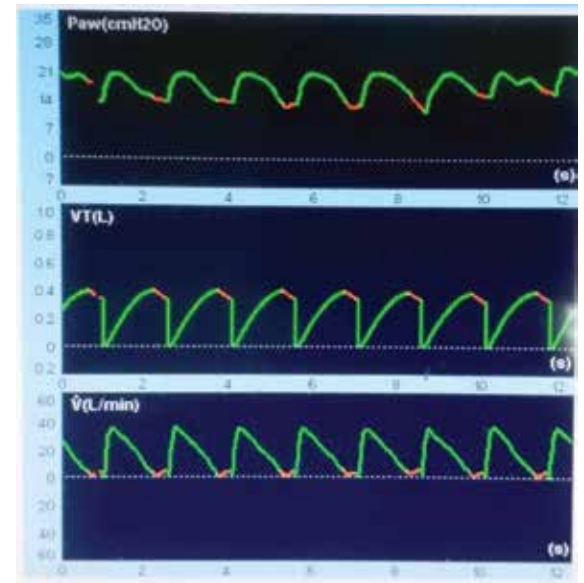


Figure 11: All 8 breaths were auto-triggered in 12 seconds.

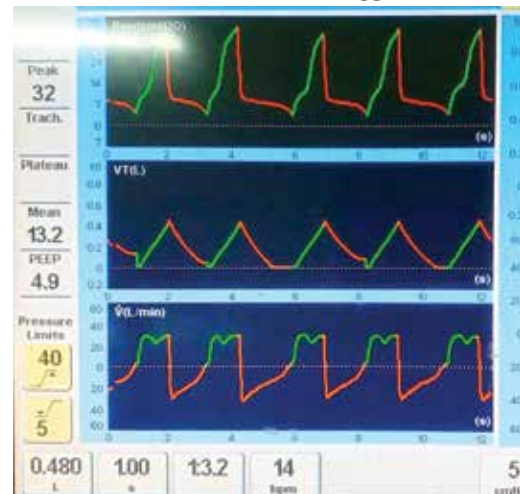


Figure 12: Flow asynchrony were present on all 5 breaths in 12 seconds. Flow-time curve showed flow hunger.



Figure 13: All three breath shows premature termination.



Figure 14: Multiple asynchrony present. Delayed termination 2, Double-triggering 2 & Ineffective triggering 2.

Table VI: Prevalence of asynchrony in study sample (N=70)

Types of asynchrony	Prevalence N (%) [*]
Ineffective triggering	24 (34.3)
Double-triggering	3 (4.3)
Auto-triggering	1 (1.4)
Flow asynchrony	15 (21.4)
Premature termination	13 (18.6)
Delayed termination	3 (4.3)
At least one type of asynchrony	39 (55)
No identified asynchrony	31 (45)

* Values are expressed as number of patients experiencing the specific types of asynchrony and Percentage of total patients experiencing that particular asynchrony are shown in parenthesis

Table VI showed thirty-one (45%) patients had no identified asynchrony. Thirty-nine (55%) patients exhibited at least one type of asynchrony. Ineffective triggering was observed in twenty-four (34.3%) patients. Prevalence of other asynchrony in descending order Flow asynchrony 15 (21.4%), Premature termination 13 (18.6%), Delayed termination 3 (4.3%), Double-triggering 3 (4.3%), Auto-triggering 1 (1.4%). At least two or more combined asynchronies were present in nine (12.85%) patients. The median length of mechanical ventilation for patients with Asynchrony index $\geq 10\%$ was 19 days (IQR 10–28 days) and for patients with AI $< 10\%$ was 9 days (IQR 3–15 days) (table VII). Patients with AI $\geq 10\%$ had 10 more days on mechanical ventilation than patients with AI $< 10\%$ ($p < 0.05$).

Table VII: Comparison of Length of mechanical ventilation (days) by Asynchrony Index (AI)

Asynchrony Index	Length of mechanical ventilation (days) Median (IQR ^{**})	p [*]
$\geq 10\%$	19.00 (10.00 – 28.00)	< 0.001
$< 10\%$	9.00 (3.00 – 15.00)	

*p value determined by Mann-Whitney U test

** Values are expressed in Median and Interquartile range (IQR)

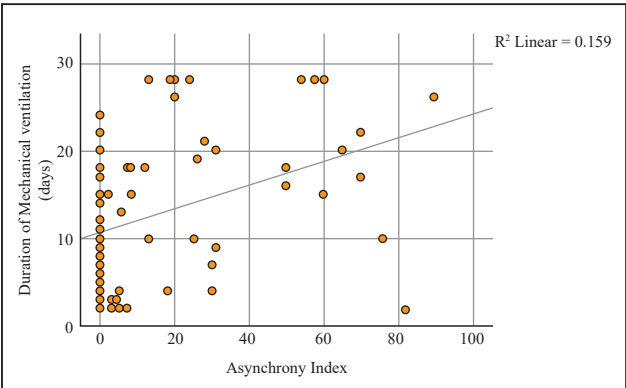


Figure 15: Scatter plot between Asynchrony index and Duration of mechanical ventilation

Figure 15 showed that Spearman rho correlation coefficient, $r = 0.39$ indicating a positive low correlation. It means increase in Asynchrony index might result in an increase in length of mechanical ventilation and vice versa. However, only 15.9% variation in length of mechanical ventilation was related to the variation in Asynchrony index. In figure 16, one sided log rank test revealed $p < 0.0001$. At 10 days, 82% patients with AI $\geq 10\%$ was still receiving mechanical ventilation whereas only 50% patients with AI $< 10\%$ receiving mechanical ventilation. At 28 days, 28% patients with AI $\geq 10\%$ still receiving mechanical ventilation whereas no patients belonging AI $< 10\%$ group receiving it.

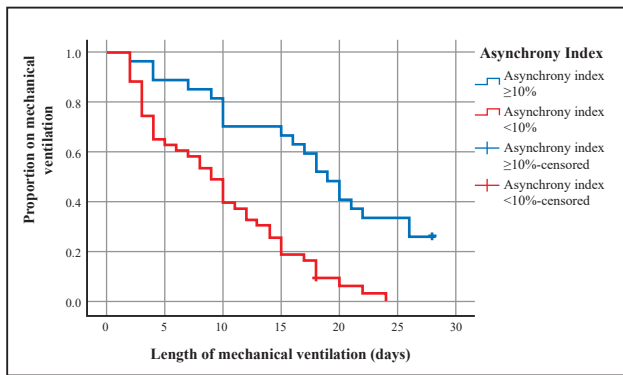


Figure 16: Kaplan-Meier plot illustrating the difference of length of mechanical ventilation between patients with Asynchrony index $\geq 10\%$ (blue line) and Asynchrony index $< 10\%$ (red line). Target event was whether the patient still receiving mechanical ventilation at 28 days or not.

Table VIII: Comparison among different modes of ventilator in relation to Asynchrony Index

Ventilator Modes	Asynchrony Index		Total (n=70) N (%)	p
	$\geq 10\%$ (n=27) N (%)	$< 10\%$ (n=43) N (%)		
A/CMV – VC	26 (96.3)	21 (48.8)	47 (67.1)	<0.001
A/CMV – PC	0	0	0	
SIMV – VC with PSV	1 (3.7)	17 (39.5)	18 (25.7)	
SIMV – PC with PSV	0 (0)	0 (0)	0	
PSV – Spontaneous	0 (0)	5 (11.6)	5 (7.1)	

p value determined by Pearson Chi-Square test.

ACMV-VC was the most frequently (67.1%) used ventilator mode in our study population, followed by SIMV – VC with PSV (25.7%) and PSV – Spontaneous (7.1%). No patient received A/CMV-PC and SIMV – PC with PSV modes. 96.3 % patients with AI $\geq 10\%$ were ventilated by A/CMV – VC mode. Patients with AI $< 10\%$ were ventilated by A/CMV – VC (48.8%), SIMV – VC with PSV (39.3%), and PSV – Spontaneous (11.6%) modes. ACMV-VC is associated with AI $\geq 10\%$ ($p < 0.05$), whereas SIMV – VC with PSV with AI $< 10\%$ ($p < 0.05$).

DISCUSSION

A total of seventy ICU-admitted patients receiving mechanical ventilation via orotracheal tube were included in the study. The mean age was 57.66 ± 11.00 years (range: 22-80 years), which was lower than the findings of Chao et al. Their study of 174 patients investigating trigger asynchrony in prolonged mechanical ventilation reported a mean age of 75 ± 6 years.⁸ Its prevalence, physiologic basis, and clinical implications in patients requiring prolonged mechanical ventilation (PMV). Similarly, Thille et al, who examined 62 patients for asynchrony incidence during assisted ventilation, reported a higher median age of 70 years (IQR: 48-77).² Whereas, de Wit

et al studied 60 mechanically ventilated patients and found a comparable mean age of 60 ± 8 years while investigating ineffective triggering as a predictor of prolonged ventilation.⁹ Mellott et al reported similar findings, with a mean age of 55 ± 13.3 years (range: 32-83) in their study of PVA frequency and types.¹⁰ These studies collectively demonstrate that the majority of ICU patients tend to be elderly.

Sixty-seven percent of patients were male and 33% were female. This finding was lower than that of Thille et al, who reported 76% male participants, but higher than the 56% male population reported by Mellott et al.^{2,3} De Wit et al found 57% male participants in their study.¹¹ Males predominated in all studies.

Ninety-one percent of patients in this study had received invasive mechanical ventilation before arrival at the current ICU, a finding that contrasts with other studies. Thille et al examined patients an average of 4.5 days (IQR: 3-7 days) after intubation, while Chao et al. assessed asynchrony in patients who had been ventilated for weeks.^{2,8} Its prevalence, physiologic basis, and clinical implications in patients requiring prolonged mechanical ventilation (PMV). De Wit et al studied patients within the first 24 hours of mechanical ventilation.⁹ All these previous studies evaluated patients receiving mechanical ventilation at the study site from ventilation onset. In contrast, only nine percent of patients in our study began mechanical ventilation at the study location. Although we included mechanically ventilated patients within 24 hours of ICU admission regardless of ventilation onset time, the median duration of pre-admission mechanical ventilation was six days. Consequently, this study examined patients at varying, non-uniform time points following intubation.

The ICU population in this study was heterogeneous. Seventy-three percent of patients were admitted as transfer cases from other hospitals/ICUs, 17% were post-operative cases, and 10% came from medical/surgical wards. This distribution differs from previous studies: Thille et al and de Wit et al exclusively studied medical ICU patients, while Chao et al investigated patients in a tertiary weaning center.^{2,8,11} Mellott et al reported a more similar distribution, with their ICU population comprising 52% medical ICU, 37% surgical trauma ICU, and 11% cardiac surgery ICU patients.³

In this study, the most common reason for endotracheal intubation was depressed level of consciousness (37%), followed by acute respiratory failure (35%), hemodynamic instability (18.5%), and planned postoperative mechanical ventilation (9%). These findings contrast with previous studies: De Wit et al exclusively studied patients intubated for acute respiratory failure, while Chao et al focused on patients who failed to wean.^{5,8} Thille et al did not specify the causes of intubation but investigated patients with respiratory failure.²

In this study, pressure-time and flow-time waveforms displayed on the bedside mechanical ventilator's monitor were visually analyzed for sixty minutes to identify asynchronous breaths. All ventilators used in this study could display these waveforms without external devices. This approach aligns

with Gogineni, Brimeyer, and Modrykamien, who also identified asynchrony through graphical analysis of ventilator-displayed waveforms.¹² However, methodological differences exist among other studies: Mellott et al utilized a cardiac output monitor to obtain waveforms for software-coded analysis, de Wit et al placed sensors between endotracheal tubes and ventilator circuits, whereas, Chao et al employed the invasive gold-standard method of esophageal catheter measurements.^{3,8,9}

This study utilized a 60-minute observation period for ventilator graphics analysis, contrasting with the shorter 10-minute period used by de Wit et al.⁵ Gogineni, Brimeyer, and Modrykamien employed brief 1-minute observations repeated over three consecutive days, while Thille et al conducted 30-minute assessments. The longest observation period was reported by Mellott et al, lasting up to 90 minutes.^{2,3,12}

The study population demonstrated a mean respiratory rate of 21.22 ± 3.75 breaths per minute (range: 16-30/min), resulting in 89,109 total breaths analyzed. The observed asynchrony rate of 18.65% was intermediate compared to previous studies: lower than the 23.30% reported by Mellott et al in their analysis of 43,758 breaths, yet higher than the 9% asynchrony rate found by de Wit et al in their examination of 11,482 breaths during a 10-minute observation period.^{5,10}

Ineffective triggering emerged as the most prevalent form of asynchrony in this study, accounting for 40.55% of all asynchronous events. This finding aligns with Mellott et al.'s comprehensive analysis, which reported ineffective triggering at 62.88% of asynchronous breaths.³ However, our study revealed a substantially higher rate of flow asynchrony (37.14%) compared to their reported 1%, potentially indicating suboptimal ventilator flow settings in our population. The distribution of other asynchrony types in our sample followed this descending frequency: premature termination (11.45%), auto-triggering (5.42%), double-triggering (4.92%), and delayed termination (0.5%). Mellott et al reported different proportions: premature termination (9.19%), double-triggering (0.74%), and delayed termination (0.09%). While their study did not document auto-triggering, they identified a newly described asynchrony type in 26.20% of cases.³ Notably, both double-triggering and auto-triggering were relatively prominent in our population. 55% of our study population exhibited at least one type of asynchrony, contrasting with Mellott et al.'s finding that 93% of their sample experienced at least one PVA incident during observation.

The study population demonstrated a median Asynchrony Index (AI) of 3.80% (IQR: 0.00–26.50), with minimum and maximum values of 0.00% and 90.00% respectively. While Thille et al reported a lower median AI of 2.1% (IQR: 0.7–8.6), their analysis exclusively considered trigger asynchrony, whereas our study incorporated both flow and termination asynchronies.² Notably, 38.57% of our population exhibited $AI \geq 10\%$, exceeding the proportions reported by Thille et al (24%) and de Wit et al (26.6%).^{2,5} This higher prevalence likely reflects our comprehensive inclusion of

multiple asynchrony types rather than solely trigger asynchronies.

The median duration of mechanical ventilation differed significantly between patient groups, with those showing $AI \geq 10\%$ requiring ventilation for 19 days (IQR 10-28) compared to just 9 days (IQR 3-15) for patients with $AI < 10\%$ ($p=0.0001$). These results closely mirror the findings of Thille et al. (2006), who reported 25 days (IQR 9-42) versus 7 days (IQR 3-20) for their respective high and low AI groups ($p=0.005$). Similar patterns emerged in other studies, though with varying durations: de Wit et al observed 6 days (95% CI 2.2-12.4) versus 2 days (1.6-3.8) using their Ineffective Triggering Index (ITI), which specifically measured trigger asynchrony, while Gogineni, Brimeyer, and Modrykamien reported 10 ± 3 days versus 4 ± 7 days for their high and low asynchrony groups respectively.^{2,5,12} During our 28-day follow-up period, a striking difference emerged: 28% of patients with $AI \geq 10\%$ remained mechanically ventilated at day 28, whereas none of the patients with $AI < 10\%$ required continued ventilation at this endpoint. This persistent ventilation requirement in high-AI patients aligns with the broader research consensus demonstrating prolonged mechanical ventilation durations in patients with elevated asynchrony indices, with our results showing particular similarity to Thille et al.'s earlier findings.

Assist-control mechanical ventilation with volume control (ACMV-VC) was the predominant ventilator mode in our study population (67.1%) and showed the strongest association with $AI \geq 10\%$. In contrast, only one patient (3.7%) receiving synchronized intermittent mandatory ventilation with volume control and pressure support ventilation (SIMV-VC+PSV) demonstrated high asynchrony. These findings differ from previous studies: Thille et al. reported pressure support ventilation (PSV) as the primary mode (82.25% of cases), with greater asynchrony observed in assist-control ventilation (ACV). Similarly, de Wit et al. found SIMV-PSV to be the most common mode (76%), noting increased asynchrony at higher pressure support levels.^{2,5}

Patient-ventilator asynchrony is common in mechanically ventilated patients. It required trained eye to detect them. In addition to Ineffective triggering, Flow asynchrony was very common in our study population. Asynchrony index $\geq 10\%$ was associated with more prolonged length of mechanical ventilation. This study has several strengths. It included patients belonging to medical, surgical and trauma patients. Flow asynchrony and Termination asynchrony were included to estimate the composite Asynchrony index. Most of the published literatures have focused on ineffective triggering only.

Limitations:

The interpretation of ventilator waveforms without esophageal pressure measurement may result in either overestimation or underestimation of asynchrony. Furthermore, waveform artifacts caused by airway secretions can potentially lead to misidentification of certain asynchrony

patterns. Three models of mechanical ventilators made by three different manufacturers were used to assess asynchrony due to lack of sufficient numbers of single ventilator in perfect working condition. This study focused exclusively on three ventilator modes: assist-control mandatory ventilation with volume control (ACMV-VC), synchronized intermittent mandatory ventilation with volume control and pressure support (SIMV-VC+PSV), and pressure support ventilation (PSV) for spontaneous breathing. No other ventilation modes were utilized in our patient population. It should be noted that our investigation did not examine ventilator parameters beyond these operational modes. Asynchrony can occur throughout the time. Only one hour observation in the first 24 hour after admission might not be enough time for the detection of persistent asynchrony. This study was performed in a single centre with small sample size. These limitations may reduce the validity and generalizability of the results.

CONCLUSION

More than half of MV patients experienced PVA; thus, recognition and management of PVA should be mandatory skills for ICU personnel. Patients with high asynchrony index had more prolonged length of mechanical ventilation than most of the other studies. Flow asynchrony was more prevalent in our cohort compared to global data, likely reflecting lower flow settings used during MV in our context. This highlights the importance of avoiding flow deprivation during ventilator setup. Whether optimizing the ventilatory setting would reduce the length of mechanical ventilation by reducing the flow asynchrony cannot be determined from the present study. Multi-centered study with large sample will be required for validation of the study. Effect of pattern specific asynchrony on patients' outcome should be the subject of further investigation.

Conflict of interest : The authors have no conflict of interest to declare.

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