Defining patient–ventilator asynchrony severity according to recurrence

Kay Choong See¹,²*, Juliet Sahagun³ and Juvel Taculod³

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Dear Editor,

Patient–ventilator asynchrony (PVA) is a mismatched interaction between the patient’s needs and the ventilator-delivered breath. Types of PVA include trigger asynchrony (problem with mechanical inspiration), flow asynchrony (problem with inspiratory flow delivery) and cycling-off asynchrony (problem with timing of mechanical expiration). Almost all mechanically ventilated patients experience PVA [1], though poor clinical outcomes have only been associated with severe PVA. Some authors define severe PVA using proportion (≥ 10% of breaths are asynchronous) [2], while others use clustering of PVA events [3]. However, these definitions do not allow ready selection of patients for personalized treatment. We therefore propose defining PVA severity based on recurrence and explored the association of recurrent PVA with clinical outcomes.

We studied patients who were intubated in the emergency department and directly admitted to the medical intensive care unit (ICU), from February 2017 to July 2017 (Figure E1, online ESM). Nurses titrated analgesia to achieve a Critical-Care Pain Observation Tool score of 0–2 and sedation to achieve a Richmond Agitation Sedation Scale score −2 to 0. Respiratory therapists also implemented a PVA protocol (reflecting our usual practice) for all mechanically ventilated patients upon ICU admission and twice daily (7 am, 7 pm), which involved bedside observation and management of PVA events for at least 2 min each time (Table E1, online ESM). During each PVA check, PVA was noted as a dichotomy (present versus absent) and was coded as present if the sum of asynchronous breaths exceeded 2 over 120 s. Recurrent asynchrony is defined as two or more PVA checks at two different times where asynchrony was coded as present. Logistic regression was used to examine the association of nonrecurrent and recurrent asynchrony with ICU/hospital mortality, adjusting for any factors that were statistically significant on univariate analysis.

One hundred twenty patients were studied (age 64.8 ± 12.5 years, 45/37.5% female, APACHE II score 26.7 ± 8.1, 116/96.7% on volume assist control initially); 1635 episodes of PVA checks were performed for 120 patients (median seven checks per patient, interquartile range 3–18.5), of whom 35 (29.2% of 120 patients) experienced 110 episodes of PVA. The most common PVA was double triggering (64 episodes/3.9%), and the most common actions taken were to increase inspiratory flow, tidal volume or sedation (35–38 times, respectively) (Tables E2 and E3, online ESM). Presence of ARDS, use of non-volume assist-control ventilation mode and use of dexmedetomidine were associated with asynchrony, though ventilation mode was only associated with nonrecurrent asynchrony. Recurrent asynchrony, but not nonrecurrent asynchrony, was associated with increased ICU and hospital mortality (Table 1).

The association of asynchrony recurrence with mortality suggests that it may be used to identify severe asynchrony. Using PVA recurrence as a severity criterion has several advantages compared to proportion or clustering of PVA events: It avoids the need for continuous monitoring, it can be done using simple bedside observation, and it can be applied prospectively to select patients for further treatment, e.g., neuromuscular blockade [4, 5]. Nonetheless, given our single-center design, our proposed concept of recurrent

*Correspondence: kay_choong_see@nuhs.edu.sg

¹ Division of Respiratory and Critical Care Medicine, University Medicine Cluster, National University Health System, 1E Kent Ridge Road, NUHS Tower Block Level 10, Singapore 119228, Singapore

Full author information is available at the end of the article

This work was performed at the National University Health System, Singapore.
Table 1 Characteristics and outcomes of patients with and without PVA

| Patient characteristics and outcomes | Patients without PVA | Patients with nonrecurrent PVA | Patients with recurrent PVA |
|--------------------------------------|----------------------|-------------------------------|-----------------------------|
| Number of patients                   | 85                   | 18                            | 17                          |
| Median number of asynchrony episodes | NA                   | 1                             | 3                           |
| IQR                                  | NA                   | NA                            | 2–5                         |
| Range                                | NA                   | NA                            | 2–21                        |
| Age (years)                          | 63.8 ± 13.4          | 66.5 ± 10.3                   | 67.7 ± 9.1                  |
| Female (%)                           | 33 (38.8)            | 7 (38.9)                      | 5 (29.4)                    |
| APACHE II score                      | 26.1 ± 8.6           | 27.2 ± 7.4                    | 29.1 ± 6.4                  |
| ARDS (%)                             | 24 (28.2)            | 6 (33.3)                      | 10 (58.8)*                  |
| Height (m)                           | 1.6 ± 0.11           | 1.57 ± 0.1                    | 1.61 ± 0.11                 |
| Weight (kg)                          | 63.5 ± 17.3          | 61.2 ± 13.8                   | 64.8 ± 17.5                 |
| Primary diagnosis (%)                |                      |                               |                             |
| Pneumonia                            | 25 (29.4)            | 7 (38.9)                      | 9 (52.9)                    |
| Other sepsis                         | 15 (17.7)            | 3 (16.7)                      | 3 (17.7)                    |
| COPD                                 | 3 (3.5)              | 0 (0)                         | 0 (0)                       |
| Asthma                               | 3 (3.5)              | 1 (5.6)                       | 1 (5.9)                     |
| Stroke                               | 8 (9.4)              | 3 (16.7)                      | 2 (11.8)                    |
| Othera                               | 31 (36.5)            | 4 (22.2)                      | 2 (11.8)                    |
| Comorbidity (%)                      |                      |                               |                             |
| Diabetes mellitus                    | 36 (42.4)            | 7 (38.9)                      | 4 (23.5)                    |
| Hypertension                         | 48 (56.5)            | 9 (50)                        | 11 (64.7)                   |
| Ischemic heart disease               | 18 (21.2)            | 4 (22.2)                      | 3 (17.7)                    |
| Chronic heart failure                | 3 (3.5)              | 1 (5.6)                       | 0 (0)                       |
| Asthma                               | 7 (8.2)              | 0 (0)                         | 2 (11.8)                    |
| COPD                                 | 4 (4.7)              | 1 (5.6)                       | 0 (0)                       |
| Chronic kidney disease               | 17 (20)              | 1 (5.6)                       | 3 (17.7)                    |
| Chronic liver disease                | 15 (17.7)            | 3 (16.7)                      | 3 (17.7)                    |
| Stroke                               | 3 (3.5)              | 1 (5.6)                       | 0 (0)                       |
| Cancer                               | 13 (15.3)            | 2 (11.1)                      | 4 (23.5)                    |
| ICU admission parameters             |                      |                               |                             |
| Temperature (Celsius)                | 36.9 ± 1.2           | 36.7 ± 1.3                    | 36.8 ± 1                    |
| Heart rate (beats/min)              | 99 ± 26              | 105 ± 27                      | 107 ± 20                    |
| MAP (mmHg)                           | 94 ± 23              | 91 ± 24                       | 97 ± 17                     |
| Respiratory rate (/min)             | 24 ± 6               | 25 ± 6                        | 24 ± 6                      |
| ICU admission ABG                    |                      |                               |                             |
| pH                                   | 7.33 ± 0.15          | 7.31 ± 0.18                   | 7.36 ± 0.14                 |
| pCO2 (mmHg)                          | 42.0 ± 19.2          | 34.0 ± 8.6                    | 46.4 ± 23.9                 |
| Bicarbonate (mmol/L)                 | 20.8 ± 6.1           | 18.8 ± 7.3                    | 23.5 ± 4.9                  |
| Ventilation mode on ICU admission (%)|                      |                               |                             |
| Volume assist control                | 84 (98.8)            | 16 (88.9)*                    | 16 (94.1)                   |
| Pressure assist control              | 0 (0)                | 2 (11.1)                      | 1 (5.9)                     |
| Pressure support                     | 1 (1.2)              | 0 (0)                         | 0 (0)                       |
| Ventilation parameters on ICU admission | N² | N² | N² |
| FIO2                                 | 0.68 ± 0.16          | 85 (N²)                       | 18 (N²)                     | 0.69 ± 0.2 | 17 |
| PEEP (cmH2O)                         | 5.8 ± 1.7            | 85 (N²)                       | 18 (N²)                     | 6.2 ± 2.2  | 17 |
| Tidal volume (ml/kg IBW)             | 7.2 ± 1.7            | 73 (N²)                       | 14 (N²)                     | 7 ± 0.8   | 12 |
| Driving pressure (cmH2O)             | 11.7 ± 4.7           | 59 (N²)                       | 13 (N²)                     | 11.1 ± 5.8 | 10 |
| Analgesia/sedation usec             |                      |                               |                             |
| Fentanyl (%)                         | 78 (91.8)            | 17 (94.4)                     | 17 (100)                    |
| Propofol (%)                         | 75 (88.2)            | 18 (100)                      | 17 (100)                    |
asynchrony as a severity marker for PVA requires broader validation.

Electronic supplementary material
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Author details
1 Division of Respiratory and Critical Care Medicine, University Medicine Cluster, National University Health System, 1E Kent Ridge Road, NUHS Tower Block Level 10, Singapore 119228, Singapore. 2 Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore. 3 Division of Critical Care – Respiratory Therapy, National University Hospital, Singapore, Singapore.

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Authors’ contributions
KCS was involved in study concept, design and drafting of manuscript. All authors conducted the study and were involved in data analysis and interpretation and critical revision of the manuscript for important intellectual content. All authors had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

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Availability of data and material
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Compliance with ethical standards

Conflicts of interest
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Consent for publication
Not applicable.

Ethics approval
Our Ethics Review Board (National Healthcare Group Domain-Specific Review Board) approved the study (approval number DSRB 2018/00223). Given the observational study design, the need for patient consent was waived.

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