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LETTER

Defining patient–ventilator asynchrony severity according to recurrence

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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

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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)	
Other[a]	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[b]		N[e]		N[e]		N[e]
FIO2	0.68 ± 0.16	85	0.74 ± 0.12	18	0.69 ± 0.2	17
PEEP (cmH2O)	5.8 ± 1.7	85	5.6 ± 1.6	18	6.2 ± 2.2	17
Tidal volume (ml/kg IBW)	7.2 ± 1.7	73	7.9 ± 2	14	7 ± 0.8	12
Driving pressure (cmH2O)	11.7 ± 4.7	59	12.7 ± 5.1	13	11.1 ± 5.8	10
Analgesia/sedation use[c]						
Fentanyl (%)	78 (91.8)		17 (94.4)		17 (100)	
Propofol (%)	75 (88.2)		18 (100)		17 (100)	

Table 1 (continued)

Patient characteristics and outcomes	Patients without PVA	Patients with nonrecurrent PVA	Patients with recurrent PVA
Midazolam (%)	5 (5.9)	1 (5.6)	1 (5.9)
Dexmedetomidine (%)	9 (10.6)	2 (11.1)	9 (52.9)*
Median fluid balance at 24 h after ICU admission (IQR) (ml)	669 (105–1600)	1415 (503–2300)	650 (305–1333)
Vasopressor use on ICU admission (%)	36 (42.4)	11 (61.1)	8 (47.1)
Median ventilator-free days through day 28 (IQR)	25 (23–26)	23.5 (21–25)*	18 (10–23)*
Median sedation-free days through day 28 (IQR)	26 (25–27)	25.5 (24–27)	22 (18–26)*
Median ICU LOS (IQR)	6 (4–9)	7.5 (4–11)	12 (7–18)*
Median hospital LOS (IQR)	14 (8–31)	12.5 (8–35)*	17 (12–28)
ICU mortality (%)	10 (11.8)	5 (27.8)	7 (41.2)*
Hospital mortality (%)	12 (14.1)	5 (27.8)	7 (41.2)*
ICU mortality (OR, 95% CI)			
Unadjusted	Reference	2.88 (0.85–9.81)	5.25 (1.62–16.91)
Adjusted[d]	Reference	2.51 (0.71–8.93)	4.35 (1.17–16.24)
Hospital mortality (OR, 95% CI)			
Unadjusted	Reference	2.34 (0.71–7.76)	4.26 (1.36–13.35)
Adjusted[d]	Reference	2.07 (0.6–7.17)	3.81 (1.05–13.82)

ABG, arterial blood gas; APACHE, acute physiology and chronic health evaluation; ARDS, acute respiratory distress syndrome; BP, blood pressure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; and IBW, IBW: ideal body weight. For males, IBW = 50 kg + 2.3 kg for each increment of 2.54 cm (1 inch) in length over 152.4 cm (5 feet). For females, IBW = 45.5 kg + 2.3 kg for each increment of 2.54 cm (1 inch) in length over 152.4 cm (5 feet); ICU, intensive care unit; IQR, interquartile range; LOS, length-of-stay; OR, odds ratio; NA, not applicable; and PVA, patient–ventilator asynchrony

* $P < 0.05$, compared to patients without PVA

[a] Includes myocardial infarction, bleeding gastrointestinal tract, status epilepticus, drug overdose, pulmonary embolism, diabetic ketoacidosis

[b] Done immediately after first application of the synchrony protocol

[c] Medication utilization over the course of each patient's ICU stay. A patient could be on more than one of these medications

[d] Adjusted for the presence of acute respiratory distress syndrome, use of volume assist-control mode of ventilation and use of dexmedetomidine

[e] Discrepancy in numbers between FIO2 and PEEP vs. tidal volume was because the tidal volume values were not recorded on admission for some patients. Discrepancy in numbers between FIO2 and PEEP vs. driving pressure was because plateau pressure was not measured on admission for some patients

asynchrony as a severity marker for PVA requires broader validation.

Electronic supplementary material
The online version of this article (https://doi.org/10.1007/s00134-020-05974-y) contains supplementary material, which is available to authorized users.

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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
The data that support the findings of this study are available from the corresponding author, KCS, upon reasonable request.

Compliance with ethical standards

Conflicts of interest
KCS has received honoraria and travel support from Medtronic. JS and JT have no conflicts of interest to declare.

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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