References

1 Shimatani T, Yoon B, Kyogoku M, Kyo M, Ohshimo S, Newth CJL, *et al.* Frequency and risk factors for reverse triggering in pediatric acute respiratory distress syndrome during synchronized intermittent mandatory ventilation. *Ann Am Thorac Soc* 2021;18:820–829.
2 Blokpoel RGT, Wolthuis DW, Koopman AA, Kneyber MCJ. Reverse triggering: a novel type of patient-ventilator asynchrony in mechanically ventilated children. *Am J Respir Crit Care Med* 2019;200:e4–e5.
3 Mortamet G, Larouche A, Ducharme-Crevier L, Fléchelles O, Constantin G, Essouri S, *et al.* Patient-ventilator asynchrony during conventional mechanical ventilation in children. *Ann Intensive Care* 2017;7:122.
4 Akoumianaki E, Lyazidi A, Rey N, Matamis D, Perez-Martinez N, Giraud R, *et al.* Mechanical ventilation-induced reverse-triggered breaths: a frequently unrecognized form of neuromechanical coupling. *Chest* 2013; 143:927–938.
5 Rodriguez PO, Tiribelli N, Fredes S, Gogniat E, Plotnikow G, Fernandez Ceballos I, *et al.*; Grupo Argentino de Estudio de Asincronías en la Ventilación Mecánica Study Group. Prevalence of reverse triggering in early ARDS: results from a multicenter observational study. *Chest* 2021; 159:186–195.
6 de Vries HJ, Jonkman AH, Tuinman PR, Girbes ARJ, Heunks LMA. Respiratory entrainment and reverse triggering in a mechanically ventilated patient. *Ann Am Thorac Soc* 2019;16:499–505.

Reply: Not All Breaths That Follow a Ventilator Cycle Are Reverse Triggering

From the Authors:

We thank Dr. Levy and colleagues for posing a debate about our definition of reverse triggering (RT) (1), contending that RT breaths should occur with minimal variability of neural respiratory time and phase difference, with a fixed mechanical/patient effort ratio (1:1, 1:2, or 1:3). We agree that RT should include a stable phase difference, but we do not believe that a fixed pattern of mechanical/patient effort should be used in RT definitions.

First, in most previous reports, Assist/Controlled (AC) was used (2), with a fixed pattern for breath delivery and cycling. This is more likely to produce RT with a predictable pattern of entrainment. Nevertheless, RT can still be irregular in AC because the reverse breaths lead to incomplete exhalation, air trapping, or double cycling. A recent study (3) in adult patients used a similar definition for RT as ours, using electrical activity of the diaphragm to confirm patient effort. Although these adult patients were mostly on AC, a consistent pattern of entrainment was not always present, with nearly 90% of patients having at least a few RT breaths and RT occurring in 2–8% of breaths. Although not a requirement for their definition, RT breaths without clear entrainment patterns had a stable phase angle (difference between timing of machine inflation and patient effort), which would argue against them being "premature triggering" of the ventilator.

In our study, synchronized intermittent mandatory ventilation pressure control–pressure support (SIMV PC-PS) was used, in which time cycled breaths (pressure control) are mixed with flow cycled breaths (pressure support), which may predispose to an even more irregular pattern of RT. In our cohort, the phase angle for RT breaths for patients with an "inconsistent" pattern of entrainment was nearly always constant within the patient with low coefficient of variation. Although the overall median phase angle from patient to patient with RT ranged from 20 to 140, the median coefficient of variation of the phase angle among RT breaths within a patient was 20.2 (interquartile range, 13.6–25.1). This demonstrates that patients with RT had internally consistent and minimally variable timing of respiratory effort after lung inflation.

Furthermore, RT with 1:1 entrainment had median tidal volume (V_T) of 9 ml/kg, inconsistent RT had V_T of 8.9 ml/kg, and no RT had V_T of 6.0 ml/kg. RT with 1:1 entrainment had a median difference between neural respiratory rate and set ventilator rate of 0 breathing per minutes (bpm), inconsistent RT 5.3 bpm, and no RT 13.5 bpm. It seems that risk factors for RT with an "inconsistent" pattern are very similar to RT with a consistent pattern.

We also believe set ventilator rate is integral to understand why RT does not always have consistent entrainment (4). We recently had cases of RT with consistent entrainment and modified the respiratory rate. Figure 1A1 is from a 2 year old on SIMV PC-PS with a set ventilator rate of 21 and RT with 1:1 entrainment with a positive phase angle of 48°. After reducing the ventilator rate to 15 (Figure 1A2), he continued to breathe 21 bpm with no RT and a negative phase angle of −16°. RT was abolished by lowering the ventilator rate. Figure 1B1 shows a 2-year-old girl with 1:1 entrainment with a phase angle of 68° and consistent double cycling. Interestingly, dropping the ventilator rate did not completely eliminate RT, but it did convert it from 1:1 entrainment to an irregular entrainment pattern (Figure 1B2). She still had irregular RT 24 hours later, but the phase angle of her RT breaths remained similar to the day before at 64° (Figure 1B3). It is hard to argue that irregular patterns of RT do not represent RT when we could convert RT with 1:1 entrainment to an irregular pattern of RT by manipulating the ventilator rate. However, we could not eliminate RT completely, speaking to its complex physiology.

Importantly, irregular RT can cause harm from breath stacking and eccentric contraction of the diaphragm with myotrauma, making it important to have clear definitions for RT to create targeted treatment strategies. These definitions should not mandate a consistent respiratory entrainment pattern given the multitude of variables that affect this and that risk factors for RT are similar between those with and without consistent entrainment. However, it is important to ensure a stable phase relationship in the timing of patient effort after ventilator insufflation to label a breath as an RT, and perhaps low coefficient of variation of phase angle within RT breaths should be required.

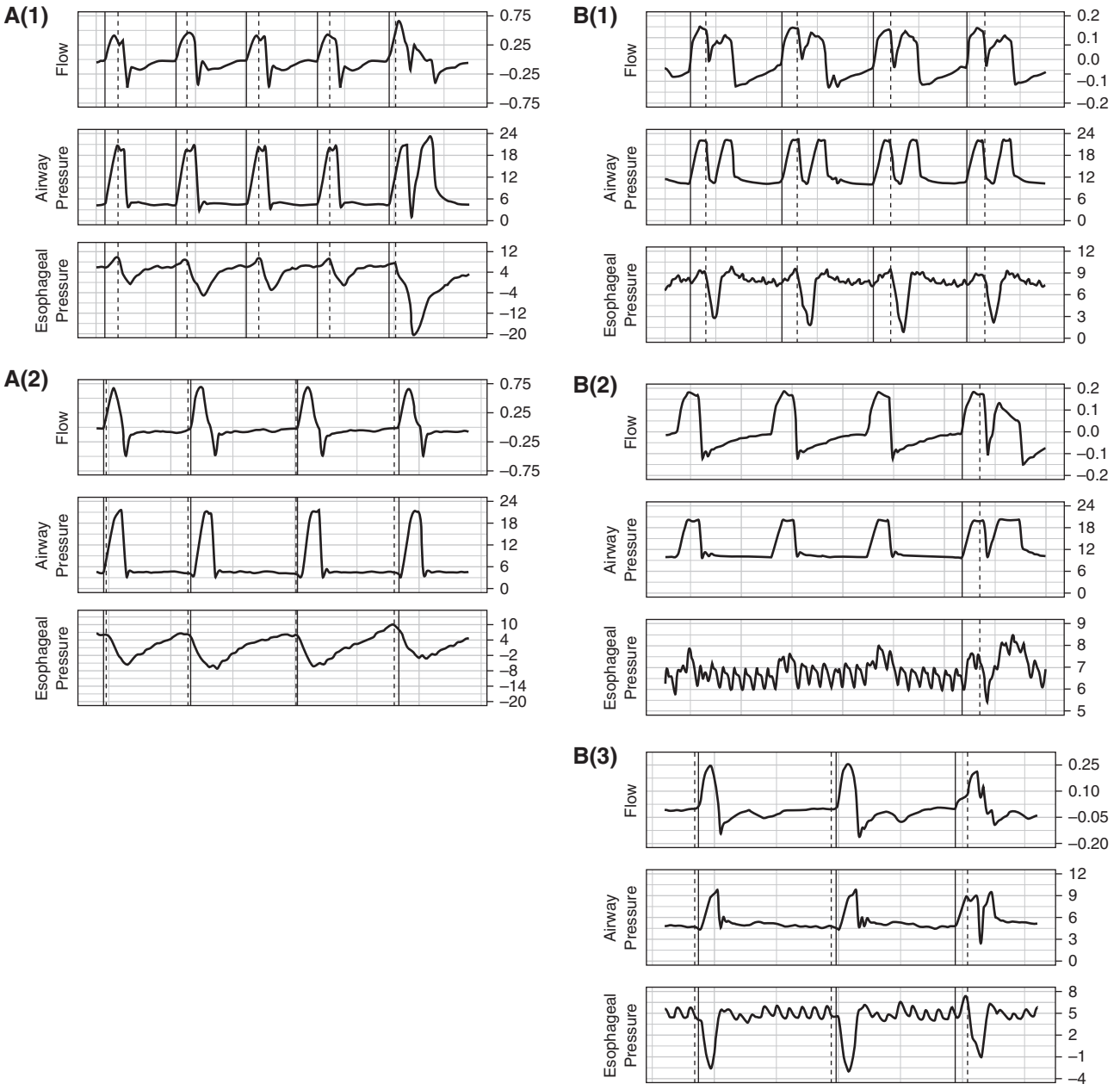

Figure 1. Left panel (*A1*) shows 1:1 entrainment pattern. (*A2*) After reducing the ventilator rate, reverse triggering (RT) was abolished. Right panel (*B1*) shows 1:1 entrainment pattern. (*B2*) After reducing the ventilator rate, the RT pattern converted to irregular. (*B3*) The irregular pattern of RT remained consistent 24 hours later, with a stable phase relationship between the timing of ventilator initiation and patient effort.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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References

1 Shimatani T, Yoon B, Kyogoku M, Kyo M, Ohshimo S, Newth CJL, et al. Frequency and risk factors for reverse triggering in pediatric acute respiratory distress syndrome during synchronized intermittent mandatory ventilation. *Ann Am Thorac Soc* 2021;18:820–829.
2 Akoumianaki E, Lyazidi A, Rey N, Matamis D, Perez-Martinez N, Giraud R, et al. Mechanical ventilation-induced reverse-triggered breaths: a frequently unrecognized form of neuromechanical coupling. *Chest* 2013;143:927–938.
3 Mellado Artigas R, Damiani LF, Piraino T, Pham T, Chen L, Rauseo M, et al. Reverse triggering dyssynchrony 24 h after initiation of mechanical ventilation. *Anesthesiology* [online ahead of print] 4 Mar 2021; DOI: 10.1097/ALN.0000000000003726.
4 Graves C, Glass L, Laporta D, Meloche R, Grassino A. Respiratory phase locking during mechanical ventilation in anesthetized human subjects. *Am J Physiol* 1986;250:R902–R909.

Check for updates

Erratum: Obesity in Pulmonary Arterial Hypertension: The Pulmonary Hypertension Association Registry

The authors would like to make a correction to an author's name in this article, published in the February 2021 issue of *AnnalsATS* (1). "Matthew Lammi" should be corrected to "Matthew R. Lammi". For the convenience of our readers, *AnnalsATS* is replacing the online version of the article with a corrected version.

Reference

1 Min J, Feng R, Badesch D, Berman-Rosenzweig E, Burger C, Chakinala M, De Marco T, Feldman J, Hemnes A, Horn EM, Lammi MR, Mathai S, McConnell JW, Presberg K, Robinson J, Sager J, Shlobin O, Simon M, Thenappan T, Ventetuolo C, Al-Naamani N; PHAR Investigators. Obesity in pulmonary arterial hypertension: the Pulmonary Hypertension Association Registry. *Ann Am Thorac Soc* 2021;18:229–237.

Check for updates

Erratum: Regional Variation in Methamphetamine-associated Pulmonary Arterial Hypertension: Who'd Better Call Saul?

There was a misspelling in this editorial published in the April 2021 issue of *AnnalsATS* (1) of the name of the lead author of the related article. "Koliatis" should be corrected to "Kolaitis". For the convenience of our readers, *AnnalsATS* is replacing the online version of the article with a corrected version.

Reference

1 Prohaska CC, Machado RF. Regional variation in methamphetamine-associated pulmonary arterial hypertension: who'd better call Saul? *Ann Am Thorac Soc* 2021;18:584–585.