[Critical Care Original Research]

CHEST

Prevalence of Reverse Triggering in Early ARDS

Results from a Multicenter Observational Study

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BACKGROUND: The prevalence of reverse triggering (RT) in the early phase of ARDS is unknown.

RESEARCH QUESTION: During early ARDS, what is the proportion of patients affected by RT, what are its potential predictors, and what is its association with clinical outcomes?

STUDY DESIGN AND METHODS: This was prospective, multicenter, and observational study. Patients who met the Berlin definition of ARDS with less than 72 h of mechanical ventilation and had not been paralyzed with neuromuscular blockers were screened. A 30-min recording of respiratory signals was obtained from the patients as soon as they were enrolled, and the number of breaths with RT were counted.

RESULTS: One hundred patients were included. ARDS was mild to moderate in 92% of them. The recordings were obtained after a median of 1 day (interquartile range, 1-2 days) of ventilation. Fifty patients had RT, and most of these events (97%) were not associated with breath stacking. Detecting RT was associated with lower tidal volume (V_T) and less opiate infusion. The presence of RT was not associated with time to discontinuation of mechanical ventilation (subdistribution hazard ratio, 1.03; 95% CI, 0.6-1.77), but it possibly was associated with a reduced hospital mortality (hazard ratio, 0.65; 95% CI, 0.57-0.73).

INTERPRETATION: Fifty percent of patients receiving assist-control ventilation for mild or moderate ARDS, sedated and nonparalyzed, demonstrate RT without breath stacking on the first day of mechanical ventilation. RT may be associated with low V_Ts.

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KEY WORDS: adult; artificial; hospital mortality; respiration; respiratory distress syndrome

ABBREVIATIONS: IQR = interquartile range; MV = mechanical ventilation; NMBA = neuromuscular blocking agent; Paw = airway pressure; RT = reverse triggering; V_T = tidal volume

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FLA 5.6.0 DTD ■ CHEST3486_proof ■ 26 October 2020 ■ 7:02 am ■ EO: CHEST-20-1749

ARDS is a type of diffuse, inflammatory lung injury leading to increased pulmonary vascular permeability, increased lung weight, and loss of aerated lung tissue clinically characterized by marked gas exchange abnormalities and reduced respiratory system compliance.[1] Hospital mortality is roughly 40% and has been related to the severity of the injury.[2,3] ARDS management requires the prompt identification and treatment of the primary causes of lung injury and physiologic support until recovery. The latter usually is achieved with invasive mechanical ventilation (MV). However, strong experimental and clinical evidence has confirmed that MV can induce further lung injuries in this setting.[4,5]

Patient-ventilator asynchrony has been found frequently during MV.[6] After the widespread use of low tidal volume (V_T) in ARDS MV, Pohlman et al[7] reported the finding of double triggering in patients who were heavily sedated, where asynchrony is unexpected. This finding has been called *breath stacking*. The authors postulated that a neural inspiratory time larger than ventilator inflation time is responsible for this finding. Reverse triggering (RT) is an asynchrony in which the inspiratory effort paradoxically is triggered by the mechanical insufflation. The underlying mechanism is the entrainment of the respiratory rhythm by the cyclic mechanical inflation of the lungs.[8] If the ventilator-triggering threshold is overcome by the RT, then a new ventilator cycle can be triggered (RT with breath stacking). Recent evidence suggests that one-third of the breath stacking in patients with mixed acute respiratory failure is related to RT.[9] This mechanism also has been described in animal models and anesthetized humans associated with respiratory entrainment of the respiratory rhythm by the ventilator.[8,10-17] The Hering-Breuer reflexes mediated by slowly adapting receptors and other potential pathways may be implicated.[11,15,17] Different types of entrainment patterns have been reported.[10,15,16]

Our main objective was to establish the frequency of RT during the early phase of treatment in nonparalyzed mechanically ventilated ARDS patients. Additionally, this study sought to determine potential predictors of the asynchrony and the association between early presence of RT and clinical outcomes. The preliminary results of this study were presented previously at the Sociedad Argentina de Terapia Intensiva Annual Meeting.[18,19] The study was registered with the ClinicalTrials.gov (Identifier: NCT02732041).

Methods

We conducted a prospective, multicenter, observational study in five medical-surgical ICUs from five hospital sites in Buenos Aires, Argentina. The study took place from May 2016 through November 2018. The study protocol was approved by the Centro de Educación Médica e Investigaciones Clínicas research ethics committee (approval no.: 1008; February 2016), and the informed consent forms were signed by the patients' next of kin before starting the procedures.

Patient Selection

Patients older than 18 years with ARDS, according to the Berlin definition, were included within 72 h of starting MV.[1] The exclusion criteria were as follows: neuromuscular blocking agent (NMBA) continuous infusion or having clinical signs of persistent neuromuscular blockade, any known severe neuromuscular disease, or poor prognosis according to the decision of the investigators.

Study Procedures, Detection of Asynchrony, and Variable Processing

Details about definitions (RT and breath stacking) (Fig 1), variable collection, and processing are available in the e-Appendix 1. After gathering the baseline data, a 30-min recording of airway pressure (Paw) time and flow time (V) signals was obtained from the circuit Y-piece. The duration of the recordings was selected to avoid interference with patient health care and has been carried out previously in other studies of patient-ventilator asynchrony.[6,20-22] The time point for the signal acquisition was established as soon as the selection criteria were verified, and the patient was accessible for the recordings. Then, the ventilator rate was increased sequentially and decreased by 5 breaths per 1 min for 3-min periods in a random order to evaluate a possible change in the entrainment response. Five minutes of ventilation with the baseline rate were performed between both periods.

The respiratory waveform files were processed using a custom program that detects RT using Paw time and flow time signals.[23] RT can start during the insufflation time (any time after the start of insufflation), during the short pause at end inspiration, or even during the early part of expiration (especially when the inspiratory time is short). It

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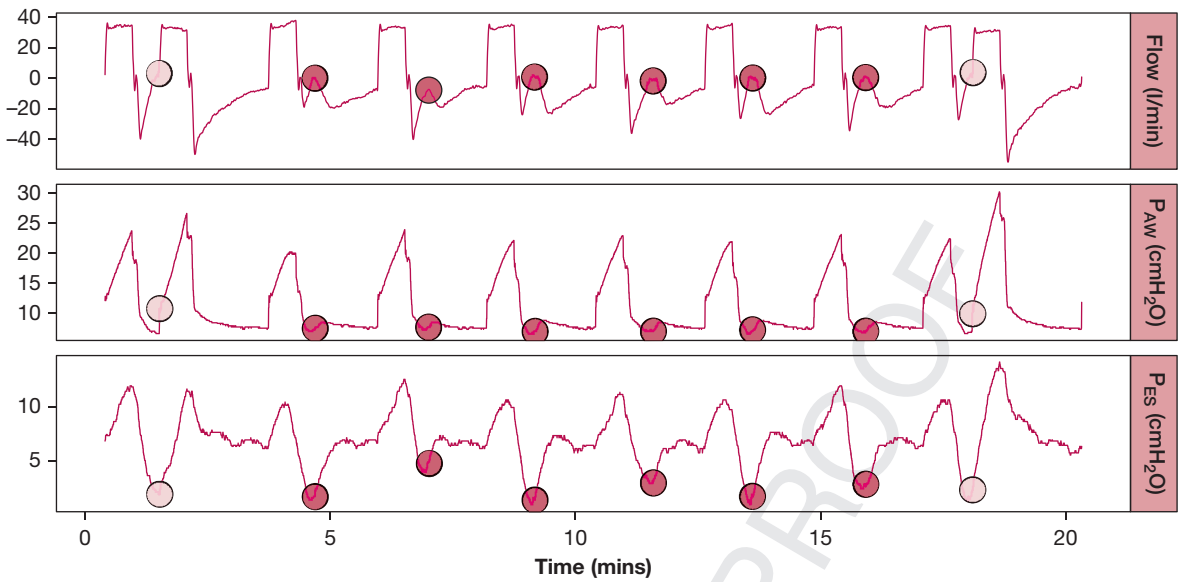

Figure 1 – *Examples of respiratory waveforms from a patient showing reverse-triggering asynchrony. Flow, airway pressure (Paw), and esophageal pressure (Pes) recordings from a patient with ARDS. The points denote the exact time when the reverse triggering is detected by the script based on flow and Paw. The ratio between the ventilator and the efforts of the patients is 1:1. Light gray points indicate reverse triggering-related breath stacking. Inspiratory efforts of patients that fail to trigger the ventilator back are indicated by dark gray points.*

can be associated with breath stacking, and this mostly depends on the magnitude of the effort at the end of the insufflation. Basically, the script classifies a respiratory cycle as RT when either a breath stacking or a patient effort (detected in the inspiratory time or during expiration) is preceded by a controlled insufflation. In the absence of breath stacking, the patient inspiratory effort may produce a sudden decrease in Paw during the insufflation, a distortion of the flow during the expiratory time, or both. The algorithm tracks these waveform distortions, but it does not establish the beginning of the patient effort. Thus, the delay between the initiation of the insufflation and the RT (phase angle) could not be computed. Furthermore, according to Akoumianaki et al,[8] RT was confirmed when a repetitive pattern was found, defined by a ratio between the efforts and the mandatory cycles of 1:1 in more than five consecutive breaths, or other ratios (1:2 or 1:3) in more than 10 cycles. Asynchrony was expressed as a rate (count per minute). The entrainment patterns, defined as the ratio between the patient effort and the mandatory cycles, from the baseline recordings were calculated every 30 s.

The patients were followed up until hospital discharge. Benzodiazepine and opiate doses were converted to midazolam and fentanyl equivalent doses.[24,25] The discontinuation from the MV was defined as the time point at which no further invasive MV was required by the patient.

Statistical Analysis

The sample size calculation and the detailed description of the statistical analysis can be found on the supplemental material. The quantitative data were expressed as mean ± SD or median (interquartile range [IQR]) according to the observed distribution. The comparisons of continuous variables were performed with a Student *t* test or a Wilcoxon signed rank test. A multiple binomial generalized linear model was used to assess the independent effect of potential predictors on RT findings. Some continuous variables were rescaled to obtain more meaningful estimates. A stepwise model selection was performed in both directions. A competing risk model was used to evaluate the effect of RT on the probability of successful discontinuation from MV, as has been done previously.[26] Death occurring during MV was used as the competing event. The patients who were transferred to another facility while receiving MV were censored. The cumulative incidence function and the Fine and Gray competing risks regression model subdistribution hazard ratios were computed with cmprsk in R software (R Foundation for Statistical Computing).[27] The effect of RT on 90-day hospital mortality was assessed with a Kaplan-Meier curve, and the probability of survival was modeled with Cox proportional hazards regression. Patients discharged alive from the hospital were censored. The analysis was performed with R version 3.6.1 software, and a *P* value of .05 or less was considered statistically significant.

Results

One hundred forty-five patients met the inclusion criteria, whereas 42 met at least one exclusion criterion. The respiratory signals from three patients could not be used, leaving a sample of 100 patients for the analysis (Fig 2). The median duration of recording was 30.3 min (IQR, 30.0-32.2 min) per patient. Table 1 summarizes the baseline characteristics of the patients. ARDS was graded by the investigators as mild in 35 patients, moderate in 57 patients, and severe in the remaining 8 patients. The most frequent cause of ARDS was pneumonia (67%). The length of stay in the ICU and the duration of MV before signal recording were 2 days (IQR, 1-4 days) and 1 day (IQR, 1-2 days), respectively.

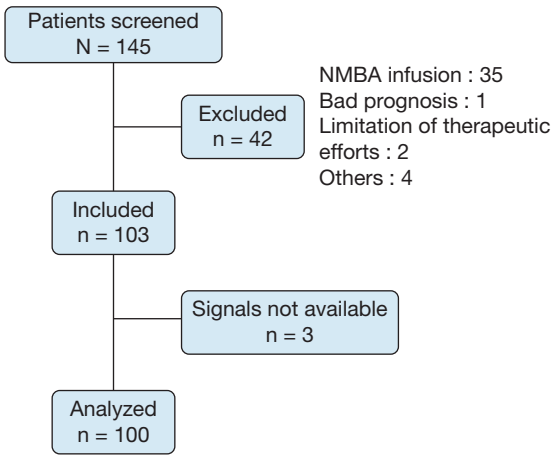

Figure 2 – *Flow chart showing selection of patients. NMBA = neuromuscular blocking agent.*

All the patients were ventilated in constant flow volume-controlled mandatory ventilation at the time of respiratory signal acquisition. Ventilator settings and respiratory monitoring measurements at the time of signal acquisition are summarized in Table 1. The patients were sedated deeply during signal acquisition (Table 1). The median Richmond Agitation Sedation Scale[28] score was -4 (IQR, -5 to -4). Propofol and midazolam were used as continuous infusion in 38 and 57 patients, respectively, and their median infusion rates were 110 mg/h (IQR, 100-200 mg/h) and 6.6 mg/h (IQR, 4.5-12 mg/h), respectively. Three patients were sedated with dexmedetomidine infusion. Seventy-six patients received fentanyl, whereas 22 and two patients received a remifentanil or a morphine infusion, and the median fentanyl equivalent dose infusion was 96 μg/h (IQR, 62.5-176 μg/h).

Reverse Triggering-Related Asynchrony

Fifty patients had at least one single RT event detected over the recording. In these patients, the median asynchrony rate was 4.8 per minute (IQR, 0.3-14.3 per minute) or 17.7% (IQR, 0.95%-49.5%) of the controlled respiratory rate. The rates of RT without breath stacking and RT with breath stacking were 4 per minute (IQR, 0-12 per minute) and 0 per minute (IQR, 0-1.5 per minute), respectively. RT without breath stacking represented 97.3% (IQR, 80.5%-100%) of these asynchronies. The most frequent entrainment ratios were 1:2 and 1:1 (Fig 3).

Median inspiratory V_T from breaths without breath stacking was 5.8 mL/kg (IQR, 5.4-6.4 mL/kg) of predicted body weight. Thirty-nine patients had RT with breath stacking, and the cumulative median V_T of breath stacking was 10.3 mL/kg (IQR, 9.5-11.6 mL/kg; $P < .001$). Furthermore, the median driving Paw values calculated using the baseline respiratory system elastance during normal and breath-stacking breaths were 9.8 cmH_2O (IQR, 8.5-11.8) and 16.9 cmH_2O (IQR, 13.5-20.2 cmH_2O; $P < .001$).

Table 2 presents the independent associations of ventilator settings and clinical variables, including severity scores, driving Paw, gas exchange, and sedation, on the probability of finding RT. RT was associated independently with lower V_T ($P = .019$) and lower fentanyl infusion rate ($P = .018$). Additionally, greater ARDS severity ($P = .08$), higher pH ($P = .053$), and lower Acute Physiology and Chronic Health Evaluation II score ($P = .052$) tended to decrease the probability of finding RT.

Effect of Changing the Ventilator Rate on Reverse Triggering

The rate of RT without breath stacking per minute decreased when the ventilator rate was reduced by five breaths per minute (difference from baseline, -1.9 ± 4.71 breaths/min; $P = .006$, paired t test), whereas the rate of breath stacking significantly increased by 0.63 ± 2.05 breaths/min ($P = .035$, paired t test). When the ventilator rate was increased by 5 breaths/min, no significant change in RT count was noted (Fig 4).

Outcomes

Thirty-five patients died in the ICU, and 9 (13.8% of survivors) were transferred from the ICUs to chronic rehabilitation facilities. Among them, 3 were discharged from the hospital before completing the weaning from MV. The median time from intubation to the last day of MV in the hospital was 10.5 days (IQR, 6-20.5 days). Figure 5 and Table 3 summarize the results of competing risk analysis for the time to the definitive discontinuation from MV or death as the competing event. The former was not affected by the detection of RT in the cumulative incidence analysis ($P = .378$, Gray's test). The adjusted subdistribution hazard ratio of the detection of RT for this event in the Fine and Gray model was 1.11 (95% CI, 0.65-1.91; $P = .710$).

The median time from admission to hospital discharge was 30 days (IQR, 17-57 days). Hospital mortality was 40%. e-Figure 1 illustrates the probability of 90-day hospital survival according to the detection of RT in the baseline recording. The between-groups comparison was not statistically significant ($P = .180$, log-rank test).

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TABLE 1] Baseline Characteristics of the Patients

Variable	Value (n = 100)
Age, y	66 (53.5-73)
Male sex	62 (62)
ARDS severity	. . .
Mild	35 (35)
Moderate	57 (57)
Severe	8 (8)
APACHE II score	18 (12-24)
SOFA	7 (5-9)
ARDS cause	. . .
Pneumonia	67 (67)
Aspiration	11 (11)
Trauma	5 (5)
Postoperative	5 (5)
Extrapulmonary	12 (12)
Other	3 (3)
Comorbidities	. . .
COPD	20 (20)
Cardiac failure	13 (13)
CNS disorders	9 (9)
Active cancer	15 (15)
Mechanical ventilation settings	. . .
V_T, mL/kg	6.1 (5.94-6.82)
Respiratory rate, bpm	25 (22-29)
Inspiratory time, s	0.71 (0.68-0.78)
Inspiratory flow, L/min	49 (36-56)
PEEP, cmH_2O	12 (10-15)
Respiratory monitoring, cmH_2O	. . .
Intrinsic PEEP	1 (0-1.8)
Plateau Paw	24 (21-27)
Driving Paw	10 (9-12)
Gas exchange	. . .
pH	7.36 (7.31-7.41)
P_{aCO_2}, mm Hg	40 (36-45)
P_{aO_2}/F_{IO_2}, mm Hg	197 (163-231)
Sedation	. . .
RASS	-4 (-5 to -4)
Midazolam (mg/h)	6.6 (4.5-12)
Propofol (mg/h)	110 (100-200)
Fentanyl (mcg/h)	96 (62-176)
Prior use of NMBA	28 (28)

Data are presented as No. of patients (%) or median (interquartile range). APACHE II = Acute Physiology and Chronic Health Evaluation II; Paw = airway pressure; PEEP = positive end-expiratory pressure; RASS = Richmond Agitation Sedation Scale; SOFA = sequential organ failure assessment; V_T = tidal volume.

After adjusting for other potential predictors, the hazard ratio of RT in the Cox regression model was 0.65 (95% CI, 0.57-0.73; $P < .001$) (Table 3).

Discussion

This multicenter study provides new epidemiologic data about RT in mechanical ventilation during the early phase of the ARDS treatment and its possible determinants. Our key findings can be summarized as follows: (1) one-half of patients showed detectable RT asynchrony soon after starting MV for ARDS based on a single 30-min recording; (2) most of the observed RT asynchrony was not associated with breath stacking; (3) breath stacking secondary to RT was associated with large V_T and driving Paw; (4) lower V_T and opiate dose increased the probability of RT prevalence; and (5) the early presence of RT was not related to the time to discontinuation of MV and, after adjustment for known predictors, possibly was associated with a reduced 90-day hospital mortality rate.

RT Asynchrony Frequency and Predictors

One-half of patients demonstrated RT asynchrony, which was not related to breath stacking in most of them. The most frequent entrainment patterns expressed as patient-to-ventilator ratio were 1:1 or 1:2 (Fig 3), which is consistent with the study of Akoumianaki et al.[8] Studies in humans showed the same pattern of phase locking when the mechanical stimulus is approximately the same as the intrinsic respiratory rate of patients.[10,15] Unfortunately, the phase angle of the entrainment, which represents the delay between the stimulus to the beginning of the effort of the patient, could not be measured directly in our study. RT usually occurs soon after machine inflation, which means that the phase angle is positive. The latter can be observed when the stimulation rate is more than the baseline respiratory rate in anesthetized and sleeping healthy people.[10,16] Breath stacking, which is the more striking consequence of RT, can be identified easily on ventilator tracings.[29] Pohlman et al[7] found a median breath-stacking rate of 0 per minute (IQR, 0-4 per minute) in patients with early ARDS, consistent with our findings. Moreover, de Haro et al[9] described a low frequency of these asynchronies, which were clustered temporally in patients with mixed acute respiratory failure ventilated with different methods of MV. Similar to our research, these studies demonstrated that breath stacking induces high V_T and Paw.[29] These findings may alert clinicians or even trigger high airway pressure alarms, prompting

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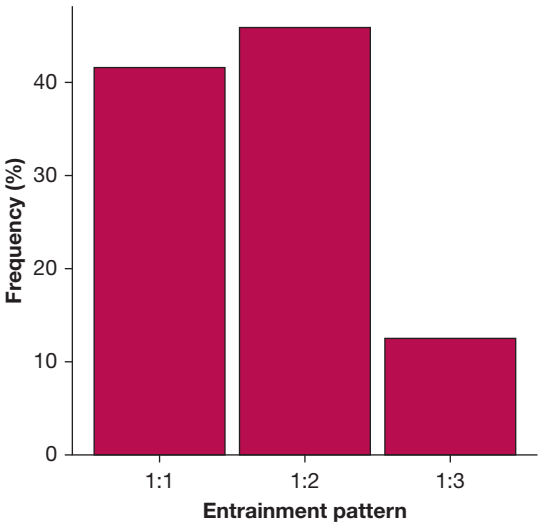

Figure 3 – *Histogram showing the ratio of ventilator to reverse-triggering asynchrony breath in patients with at least one asynchrony. The ratios were calculated every 30 s and rounded.*

the former to increase the sedation level, paralyze the patient, or adjust the ventilator.[30] In the early phase of the ARDS treatment, most clinicians may not feel comfortable with changing the setting of the ventilator; thus, increased sedation, NMBA use, or both may be the preferred options. Breath stacking requires a high inspiratory effort to overwhelm the respiratory system load during early expiration before triggering the ventilator. The effort should be sustained during the triggering phase of the ventilator and should reach the selected threshold. Thus, the use of ventilators with different triggering properties and different refractory periods can affect the likelihood of breath stacking. Our data suggest that the effort of patients during RT often may not be strong enough to produce breath stacking in most cases. Although patients with ARDS are expected to have a high respiratory drive during the acute phase of the disease, several chemical, pharmacologic, and mechanical signals may interact to modulate it. Most of the patients were still receiving heavy sedation during signals recording. P_{aCO_2} tightly correlates with the drive output, even if ARDS seems to shift this relationship.[31] The patients showed normal P_{aCO_2} values and received sedatives and opiates, which possibly reduced the respiratory drive activity, thereby decreasing the possibility of triggering breath stacking. Additionally, because RT usually is detected soon after starting passive lung inflation, the Hering-Breuer inhibitory inspiration reflex plausibly may decrease the neural inspiratory time, the magnitude of the effort, and the probability of breath stacking.[8,16]

TABLE 2] Predictors of Reverse Triggering-Related Asynchrony

Predictor	OR (95% CI)	*P* Value
APACHE II score	0.95 (0.9-1)	.052
ARDS severity[a]	. . .	. . .
Mild	Reference	. . .
Moderate	0.59 (0.21-1.66)	.315
Severe	0.12 (0.01-0.90)	.040
V_T (per 0.1 mL/kg)	0.91 (0.84-0.98)	.019
pH (per 0.1 units)	0.57 (0.32-1.007)	.053
Fentanyl (per 10 μm)	0.93 (0.88-0.99)	.018

Data are binominal generalized linear model coefficients (adjusted ORs). The dependent variable is the detection of reverse triggering. Tidal volume and fentanyl infusion dose were rescaled by 0.1 mL/kg of predicted body weight and 10 μm/min, respectively, to obtain meaningful estimates. APACHE II = Acute Physiology and Chronic Health Evaluation II; V_T = tidal volume.
[a]Likelihood ratio test for ARDS severity, $P = .080$.

Several potential predictors of RT asynchrony were evaluated. Ventilator respiratory rate is a determinant of the entrainment of the respiratory rhythm by MV. However, we did not find a significant effect of baseline ventilator rate setting on RT. When this parameter was decreased in 5 breaths/min, both a sudden reduction of RT without breath stacking and an increase in breath stacking rates were observed. The former was the expected response because of the entrainment. The increase in breath-stacking number may indicate a more favorable condition for triggering the ventilator associated with a reduction in intrinsic positive end-expiratory pressure or with a stronger effort. Conversely, the increase in the ventilator rate failed to entrain more RT. In this setting, high frequencies of stimulation may be beyond the capability of response of the respiratory drive. Interestingly, V_T clearly disclosed a significant effect on RT occurrence. Low V_Ts are associated with a higher prevalence of RT. P_{aCO_2} was unrelated to RT, but this variable was not altered markedly in patients, which agrees with the study of Simon et al,[16] in which small increases in end tidal P_{CO_2} failed to modify the respiratory drive entrainment behavior in healthy people during non-rapid eye movement sleep. Sedation depth measured with the Richmond Agitation Sedation Scale and the doses of midazolam and propofol did not affect the probability of detection of RT (these variables were excluded from the final regression model). By contrast, for every increase of 10 μm/min in the fentanyl equivalent infusion rate at the time of airway signal recording, an adjusted 7% decrease existed in the odds of finding RT. Pohlman et al[7] reported that the breath stacking rate increased when sedation was interrupted,

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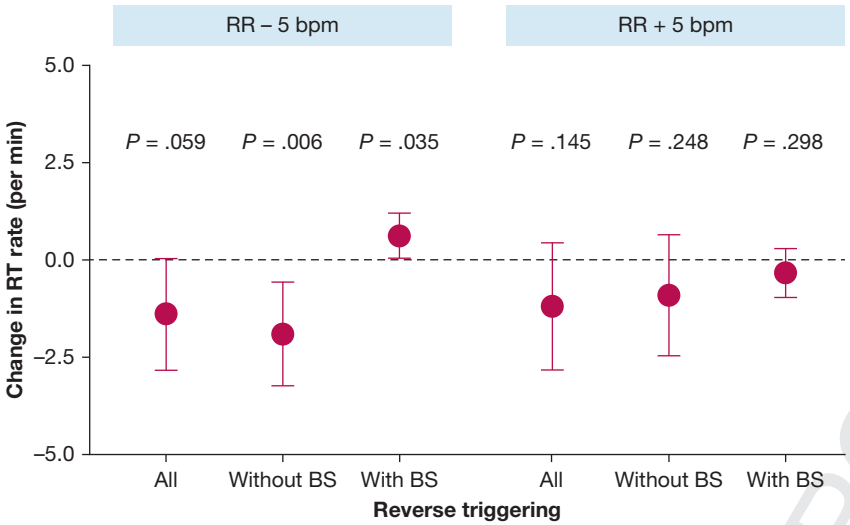

Figure 4 – *Box-and-whisker plot showing variation in reverse-triggering count per minute after increasing or decreasing the ventilator rate. Points represent the mean change from baseline. Error bars represent the 95% CI of the means. The P values correspond to paired t test comparisons. Panels refer to the change in ventilator rate. bpm = breaths per minute; BS = breath stacking; RT = reverse-triggering asynchrony; RR = respiratory rate.*

and Chanques et al[30] also reported a decrease in breath stacking frequency from 41% to 27% when sedation was increased in patients with a high asynchrony rate. However, these two studies did not provide information about specific drugs and doses involved in the sedation of the patients. Acute Physiology and Chronic Health Evaluation II scores tended to be associated to a lower probability of RT. The latter suggests that the entrainment response may be decreased indirectly in the most severe patients, possibly because of higher cumulative doses of respiratory drive depressants. Acidosis also may increase the probability of entrainment of the respiratory rhythm, although the association was not significant.

Clinical Outcome

The severity of lung injury manifest as gas exchange abnormalities and high lung elastance,[2,32] comorbidities, concomitant organ failure, and underlying lung disease severity all affect outcome. In this context, the potential predictive strength of a single variable in a prevalence study at day 1 of ventilation, such as RT rate for clinical prognosis, must be interpreted with great caution. RT asynchrony was unrelated to the time required to discontinue the MV in the competing risk analysis, but it was associated independently with a decrease in the 90-day hospital mortality. This result simply may reflect, despite multiple adjustments, a lower general severity and different clinical management. In a recent preliminary analysis, patients demonstrating RT were more likely to trigger the ventilator fully or to be extubated the next day than patients without RT.[33] The presence of RT thus may indicate that the patient is more likely to resume spontaneous activity rapidly, which in turn may be linked to a better outcome.

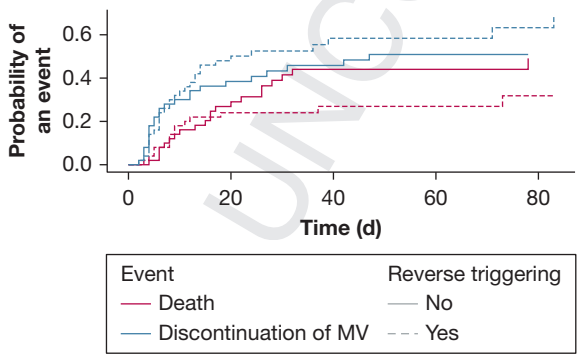

Figure 5 – *Cumulative incidence curves showing discontinuation of mechanical ventilation (MV; P = .378, Gray test) or death (P = .179, Gray test) as competing events over time according to the presence of reverse triggering.*

Considerable debate about the effect of spontaneous ventilation on ARDS exists.[34] The potential beneficial effects of spontaneous breathing, such as regional recruitment and preservation of inspiratory muscle activity, have been contrasted with deleterious effects, such as occult pendelluft, breath stacking, and strong diaphragmatic contractions responsible for muscle damage. The net effect may depend on the severity of the lung injury and the intensity of the inspiratory effort. RT, as we report herein, represents spontaneous breathing in a setting where controlled ventilation is expected. Most of the patients had mild to moderate ARDS, and RT without breath stacking largely was prevalent. Thus, some mild spontaneous breathing effort also may improve patient outcomes.

Our study has several limitations. We chose to perform a 30-min respiratory signal acquisition as soon as the

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TABLE 3] Clinical Outcomes

	Discontinuation of MV			90-Day Hospital Mortality		
	SHR	95% CI	*P* Value	HR	95% CI	*P* Value
Reverse triggering	1.11	0.65-1.91	.710	0.65	0.57-0.73	< .001
APACHE II	0.98	0.95-1.01	.150	1.02	1-1.05	.038
ARDS severity	. . .	. . .	. . .	. . .	. . .	. . .
Moderate	0.90	0.5-1.62	.740	0.83	0.49-1.42	.504
Severe	0.35	0.08-1.44	.140	0.50	0.24-1.03	.060
DP (cmH_2O)	0.90	0.82-1	.056	1.13	1.04-1.23	.003
RASS	1.00	0.83-1.2	.990	0.96	0.75-1.24	.774

Summary of coefficients from Fine and Gray competing risk and Cox proportional hazard regression models for time to discontinuation of mechanical ventilation and 90-day hospital mortality. Mild ARDS severity was used as reference in the model. DP = airway driving pressure; HR = hazard ratio; MV = mechanical ventilation; SHR = subdistribution hazard ratio. See Table 1 and 2 legends for expansion of other abbreviations.

selection criteria were confirmed. Whether this is good enough for acquiring sample data is uncertain, but it allowed us to detect several parameters potentially associated with RT. Previous studies regarding patient-ventilator interaction have used similar durations and also have provided interesting data about this topic.[6,20-22] Long periods of registry would provide more robust data regarding the frequency of the problem and the variability or potential clustering of the asynchrony.[9,35] The detection of the asynchrony was based on the flow and Paw signal analysis. This methodology potentially is insensitive to very small inspiratory efforts when compared with electromyography recordings. Therefore, even if we previously validated our detection script, our estimates of the real frequency of RT-related asynchrony would be less than its real value. Finally, NMBA was the most frequent exclusion criterion. Patients who met this criterion were certainly sicker than those who were finally included, and only 8% of patients had severe disease. Hence, our data provide little insight into RT in severe ARDS.

Conclusions

Our study showed that RT was found in one-half of mechanically ventilated patients with ARDS not receiving NMBA infusion soon after intubation. Acute Physiology and Chronic Health Evaluation II score, large V_T, and high doses of opiates were associated with a reduced risk of asynchrony. This observational study suggested that the early detection of RT may be a marker of favorable outcome in patients with mild to moderate ARDS. Whether specific interventions should be taken when RT is detected in this setting warrants further investigation.

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Additional information: The e-Appendix and e-Figure can be found in the Supplemental Materials section of the online article.

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