

Double-Triggering During Noninvasive Ventilation in a Simulated Lung Model

Robert D Sheehy, Brett Duce, Timothy P Edwards, Joseph A Churton, Rajiv Sharma, and Craig A Hukins

BACKGROUND: Double-triggering is a well-recognized form of patient-ventilator asynchrony in noninvasive ventilation (NIV). This benchtop simulated lung study aimed to determine under which patient and device-specific conditions double-triggering is more prevalent, and how this influences the delivery of NIV. **METHODS:** Two commonly used proprietary NIV devices were tested using a benchtop lung model. Lung compliance, airway resistance, respiratory effort, and breathing frequency were manipulated, and the frequency of double-triggering was assessed. A lung model of very low lung compliance (15 mL/cm H₂O) was then used to assess the frequency of double-triggering when breathing frequency and respiratory effort were varied, along with basic NIV settings, including inspiratory pressure and expiratory pressure. Minute ventilation and total inspiratory work (as calculated by the simulated lung model) were also correlated with frequency of double-triggering. **RESULTS:** In both devices, double-triggering was observed with reduced lung compliance ($P = .02$ and $P < .001$ for the two devices, respectively). Reduced airway resistance was associated with double-triggering with the one device only ($P = .02$). Respiratory effort and breathing frequency were not independent predictors of double-triggering across all lung models. In the lung model of very low lung compliance, both devices showed increased double-triggering at a lower breathing frequency ($P < .001$ and $P < .001$), higher respiratory effort ($P = .03$ and $P < .001$), and greater pressure support ($P = .044$, $P < .001$). Importantly, double-triggering was associated with reduced minute ventilation ($P = .007$) with one device and increased inspiratory work ($P < .001$) with the other device. **CONCLUSIONS:** Both simulated-patient and device characteristics influenced the frequency of double-triggering in NIV, resulting in meaningful consequences in a simulated lung model. *Key words:* double-triggering; patient-ventilator asynchrony; noninvasive ventilation; low lung compliance; simulated lung model; bench study. [Respir Care 2020;65(9):1333–1338. © 2020 Daedalus Enterprises]

Introduction

Noninvasive ventilation (NIV) is considered the standard of care for some forms of respiratory failure. Successful NIV therapy improves ventilatory efficiency, improves gas exchange, rests respiratory muscles, resets

central respiratory centers, and reduces cardiovascular strain.¹ Robust clinical evidence supports the use of NIV in patients with hypercapnia due to exacerbations of COPD.^{2,3} In addition, patients with chronic respiratory failure due to restrictive ventilatory deficits, such as in

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the context of neuromuscular disease, also benefit from long-term NIV.^{4,5}

The effective delivery of NIV relies, at least in part, on synchronous patient respiratory effort and ventilator insufflation. Despite the treating clinician's best efforts, patient-ventilator asynchrony is a common pitfall in the delivery of NIV. Asynchrony is associated with increased work of breathing, ineffective respiratory effort, impaired gas exchange, disruption of sleep, and reduced patient comfort.⁶⁻¹¹ Furthermore, optimization of ventilator settings to improve patient-ventilator asynchrony has been demonstrated to improve gas exchange parameters in select clinical scenarios.^{12,13}

Double-triggering is a well-recognized form of patient-ventilator asynchrony.⁷ Fundamentally, double-triggering can be defined as 2 ventilator insufflations corresponding with 1 patient inspiratory effort.¹⁴ There is variation in the morphology of double-triggering waveforms, but it is accepted that double insufflation will be separated by an expiratory time less than half of the mean inspiratory time.¹⁴⁻¹⁶ Anecdotally, factors such as high inspiratory demand, restrictive lung mechanics, mask leak, and device settings such as rise time or trigger sensitivity may play a role in the development of double-triggering, although robust data to confirm this are lacking. Many of these factors have been implicated in other forms of asynchrony, particularly in invasive mechanical ventilation.¹⁰ In this study, we used a simulated lung model with a physiological upper airway to investigate both the patient- and device-specific factors that contribute to the development of double-triggering.

Methods

The bench model consisted of an ASL5000 (IngMar Medical, Pittsburgh, Pennsylvania) computerized, piston-driven, lung simulator attached to a head manikin with a physiological upper airway. The upper airway remained patent, and upper airway air-flow resistance was not manipulated. The ventilation circuit was completed via smooth-bore tubing (20 cm × 22 mm internal diameter) and a Quattro Medium full-face mask (ResMed, Bella Vista, New South Wales, Australia). The mask was fitted to the manikin head and the cushion was sealed to the manikin with silicone sealant to ensure the absence of unintended leaks (Fig. 1).

In part one of the study protocol, lung simulator variables were altered to determine their influence on the frequency of double-triggering. A single-compartment lung model was used with an uncompensated residual volume of 300 mL. Lung compliance (mL/cm H₂O) and airway resistance (cm H₂O/L/s) were manipulated to simulate normal lung mechanics, restrictive, obstructive, and mixed ventilatory deficits. Values were altered in a graded fashion to simulate mild, moderate, and severe iterations of the above settings.

QUICK LOOK

Current knowledge

Noninvasive ventilation (NIV) relies on patient-ventilator synchrony to deliver effective therapy. In practice however, patient-ventilator asynchrony is common and has been implicated with suboptimal delivery of NIV. Although double-triggering is a well-recognized form of patient-ventilator asynchrony seen in NIV, the understanding of the precise device- and patient-specific factors that lead to increased frequency of double-triggering is limited.

What this paper contributes to our knowledge

Using a benchtop simulated lung model, two commonly used NIV devices were tested. Double-triggering was exclusively seen under conditions of low simulated lung compliance. Varying states of respiratory demand (eg, low breathing frequency and increased respiratory effort) along with increased pressure support also increased double-triggering frequency under conditions simulating low lung compliance. Double-triggering resulted in to potentially clinically meaningful consequences with reduced minute ventilation and increased inspiratory work observed under certain conditions.

Precise compliance and resistance parameters used are listed in Table 1 and are comparable to those used in prior benchtop studies.¹⁷ Two further parameters were also varied to simulate different physiological states of respiratory demand: breathing frequency (15, 20, and 25 breaths/min) and respiratory effort (2, 8, and 15 cm H₂O). In all, 90 iterations were created.

The frequency of double-triggering was then assessed with 2 commonly used NIV devices. The S9 VPAP Tx (ResMed, Bella Vista, New South Wales, Australia) and Omnilab (Philips Respironics, Murraysville, Pennsylvania) devices were used. Settings for both devices are included in Table 2. A standardized 100-breath algorithm was used.

In the second part of the study, a lung model of very low lung compliance (lung compliance 15 mL/cm H₂O, airway resistance 5 cm H₂O/L/s) was used. The aim was to determine which additional simulated lung characteristics affected the frequency of double-triggering under low lung compliance conditions while varying basic device settings. Simulator respiratory effort and breathing frequency were varied as in the first part of the study. Device sensitivity settings and rise times were unchanged. Unlike in the first part, however, expiratory positive airway pressure (PAP) settings of 5 cm H₂O, 10 cm H₂O, and 15 cm H₂O were used, and pressure support was varied at 5 cm H₂O, 10 cm H₂O, and 15 cm H₂O. The inspiratory and expiratory PAP

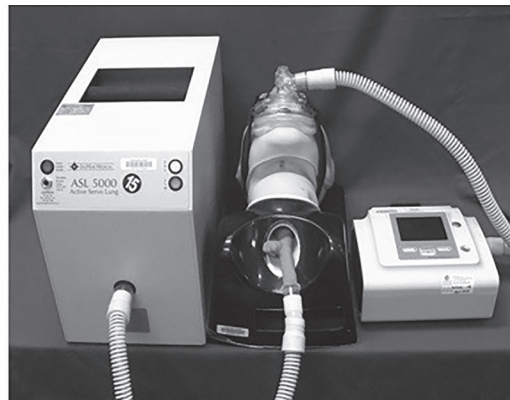
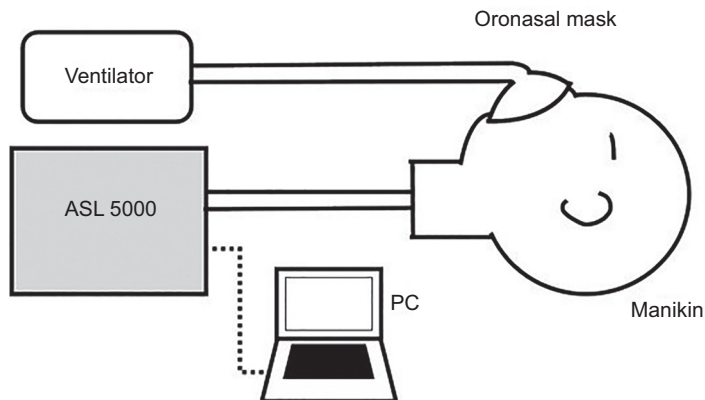


Fig. 1. Benchtop simulated lung model.

Table 1. Lung Compliance and Lung Resistance Settings to Simulate Various Ventilatory Deficits

Ventilatory Deficit Type	Lung Compliance, mL/cm H ₂ O	Airway Resistance, cm H ₂ O/L/s
Normal	60	5
Restrictive		
Mild	45	5
Moderate	30	5
Severe	15	5
Obstructive		
Mild	60	10
Moderate	60	20
Severe	60	30
Mixed		
Mild	45	10
Moderate	30	20
Severe	15	30

settings on each device determined the level of pressure support (with pressure support defined as the difference between inspiratory and expiratory PAP). This created 81 iterations across a standardized 100-breath protocol, where the frequency of double-triggering was assessed. The consequences of double-triggering were also evaluated with software-derived calculations of total inspiratory work (mJ) and minute ventilation (L/min).

Data Analysis

Simulation data were analyzed with the software built into the ASL5000. Pressure/flow waveforms were manually reviewed by 4 of the investigators (RS, TE, BD, CH) to determine the frequency of double-triggering. The effect of varying both simulated lung and device settings on double-triggering frequency was calculated as an η^2 statistic. The effect of double-triggering on inspiratory work and minute ventilation was assessed with linear

Table 2. Ventilator Settings Used to Test Physiological Lung Models

Setting	ResMed S9 VPAP Tx	Philips Omnilab
Inspiratory PAP, cm H ₂ O	15	15
Expiratory PAP, cm H ₂ O	5	5
Rise time	0.1*	1*
Trigger/cycle settings	Medium trigger and cycle†	Auto-Trak function‡
Inspiratory time (min–max), s	0.1–4.0	Auto-Trak function‡

* Denotes the shortest rise time available for each device.
 † ResMed Medium trigger: device will trigger to IPAP if it detects a minimum of 6 L/min of inspiratory flow. ResMed Medium cycle setting: cycles to EPAP when flow has decreased to 25% of peak inspiratory flow.
 ‡ Philips Respironics Auto-Trak is a proprietary algorithm that estimates patient flow on a breath by breath basis (while taking into account changes in circuit leak) and compares the estimated patient flow to the actual flow shape signal.
 PAP = positive airway pressure

regression techniques. SigmaPlot (Systat Software, San Jose, California) was used for statistical analysis. $P < .05$ was considered statistically significant (Fig. 2).

Results

In part one of the study protocol, both devices were tested across the 90 iterations. For both devices, double-triggering was exclusively seen when lung compliance was low (≤ 30 mL/cm H₂O), with 13.03% of breaths delivered to the restrictive model exhibiting double-triggering. Double-triggering in the ResMed (RM) device was only observed under conditions of very low lung compliance (15 mL/cm H₂O). Averaged over all lung model iterations, 2.27% of breaths delivered by the RM device exhibited double-triggering. The ResMed double-trigger waveform was compact, with the biphasic waveform separated by a very short expiratory time. When incorporated as part of a multivariate analysis, reduced lung compliance was the only

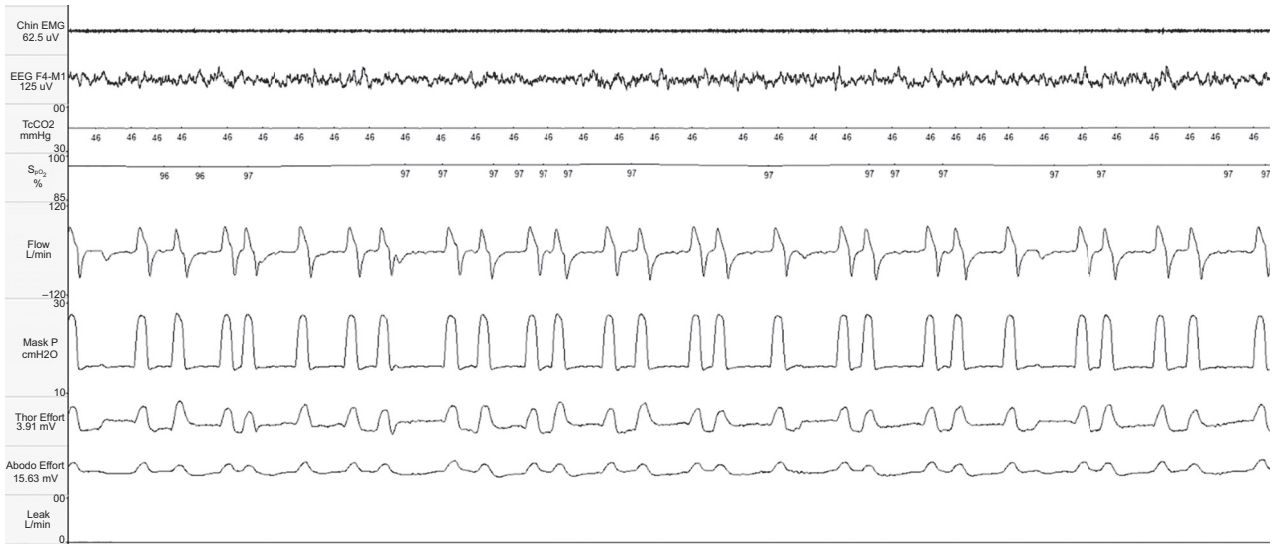


Fig. 2. Example of double-triggering during polysomnography. Chin EMG = mental-submental electromyogram; EEG F4-M1 = electroencephalogram; TcCO₂ = transcutaneous carbon dioxide; S_{pO₂} = oxygen saturation; Flow = device-derived air flow; Mask P = mask pressure; Thor/Abdo Effort = thoracic and abdominal effort as measured by inductance plethysmography; Leak = unintended leak.

significant association with double-triggering ($P = .02$). Breathing frequency ($P = .07$), respiratory effort ($P = .40$), and airway resistance ($P = .15$) were not significantly associated with double-triggering.

With the Philips Respironics (PR) device, double-triggering was also mostly observed under very low lung compliance conditions, although it was seen in one iteration at a higher compliance setting of 30 mL/cm H₂O (airway resistance = 5 cm H₂O/L/s). When averaged across all lung models, 5.54% of breaths delivered by the PR device exhibited double-triggering. The Philips Respironics double-triggering waveform was different in appearance from the RM device, with the second insufflation often following an expiratory time approaching 50% of mean inspiratory time. In a multivariate analysis, reduced lung compliance ($P < .001$) and, to a much lesser extent, reduced airway resistance ($P = .02$) were associated with increased frequency of double-triggering. Breathing frequency ($P = .067$) and respiratory effort ($P = .068$) were not statistically significant predictors of double-triggering. In both devices, the relative effect size of lung mechanics toward double-triggering frequency was small (Fig. 3; see detailed data in the supplementary materials at <http://www.rcjournal.com>).

In part two of the study both devices were tested across 81 iterations. Under simulated conditions of very low lung compliance, and by varying ventilator settings (inspiratory and expiratory PAP), more frequent double-triggering became apparent. When averaged across all iterations of the second part of the study, double-triggering was noted in 20.87% of breaths delivered by the RM device and in 39.77% of breaths delivered by the PR device. The RM device exhibited an increased propensity to

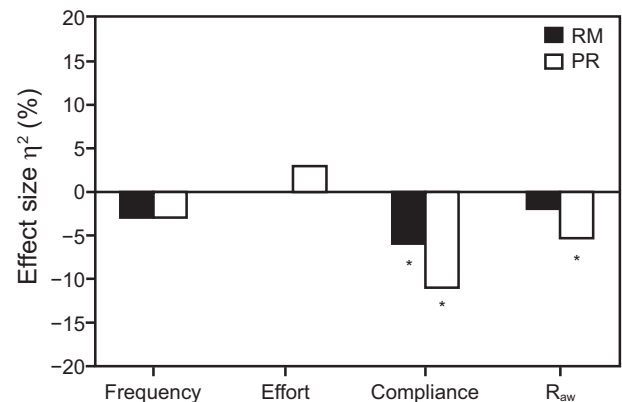


Fig. 3. Relative effect size of simulated patient characteristics on double-triggering frequency across all lung models. Effort = respiratory effort; compliance = lung compliance; R_{aw} = airway resistance. * $P < .05$.

deliver double-triggering with a lower breathing frequency ($P < .001$), higher respiratory effort ($P = .03$), and greater pressure support ($P = .044$). Expiratory PAP did not significantly influence double-triggering frequency ($P = .63$). The PR device similarly exhibited increased frequency of double-triggering with lower breathing frequency ($P < .001$), higher respiratory effort ($P < .001$), and greater pressure support ($P < .001$). Again, expiratory PAP did not affect double-triggering frequency ($P = .59$) (Fig. 4; see detailed data in the supplementary materials at <http://www.rcjournal.com>).

Although the multivariate analysis of both devices was similar, of note is the relative effect size of each variable. The lower breathing frequency had a more significant

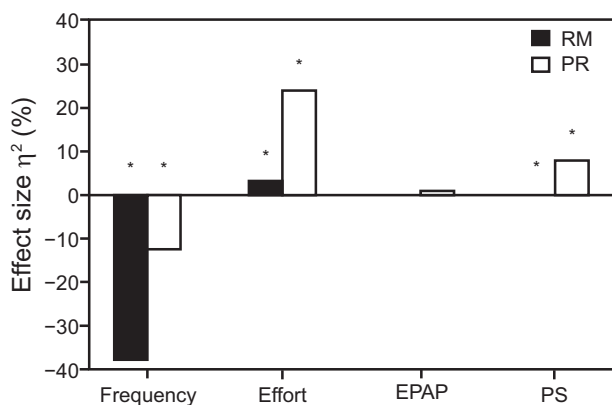


Fig. 4. Relative effect size of simulated patient and device characteristics on double-triggering frequency in the restrictive lung model. Effort = respiratory effort; EPAP = expiratory positive airway pressure; PS = pressure support. * $P < .05$.

influence on double-triggering with the RM device, whereas respiratory effort had a larger effect on the PR device in causing double-triggering. Pressure support, while statistically significant in the RM device, had a minimal effect size.

With the RM device, double-triggering was associated with reduced minute ventilation ($P = .007$); however, no association was found with total inspiratory work ($P = .89$). Conversely, with the PR device there was a significant association between double-triggering and increased simulated total inspiratory work ($P < .001$) but no relationship was found with minute ventilation ($P = .16$).

Discussion

In this study, the causes and consequences of double-triggering were explored in 2 commonly used NIV devices by testing simulated lung models of restrictive, obstructive, and mixed ventilatory deficits. In the 2 NIV devices tested, double-triggering was mostly observed under conditions of very low lung compliance. Airway resistance also had an association with double-triggering, but to a lesser extent (only with the PR device, and only with simultaneous low lung compliance). Further investigation of double-triggering in a model of very low lung compliance revealed additional patient- and device-specific factors that influenced the frequency of double-triggering. In the RM device, the development of double-triggering was most influenced by breathing frequency. In contrast, the PR device was most influenced by respiratory effort. The presence of double-triggering in this model was associated with increased inspiratory work in the PR device, whereas double-triggering was associated with decreased minute ventilation in the RM device.

With the proliferation of various NIV devices intended for both hospital and home use over the last 2 decades,

much interest has focused on improving patient-ventilator interaction.^{8,18-21} Patient-ventilator asynchrony is common in NIV, with some studies suggesting a clinical prevalence of 25–50%.^{8,22} In one study, 12% of breaths delivered to 53 subjects receiving invasive mechanical ventilation (for a variety of indications) showed evidence of double-triggering.¹⁴ This is in comparison to the data presented in this benchtop investigation, which exhibited an overall lower frequency of double-triggering, of 3.90%, across all lung models and devices tested. When the lung model was set to maximize the frequency of double-triggering by imposing conditions of very low lung compliance, however, double-triggering rates as high as 39.77% and 20.87% were noted in the PR and RM devices, respectively.

Modern NIV devices rely on air flow-dependent triggering and cycling to first initiate inspiratory pressure and then to cycle to a lower expiratory pressure in synchrony with patient respiration. Patient-ventilator asynchrony, in the form of double-triggering was observed in this study under conditions where the ventilator flow curve was profoundly altered by simulated lung or device settings. It is hypothesized that very low lung compliance is likely to flatten the flow curve delivered by the NIV device. Conversely, low air flow resistance may result in inspiratory overshoot delivered by the PR device, in turn leading to early initiation of the next respiratory cycle.

When ventilator and simulator settings were varied in a model of very low lung compliance, an increased pressure flux (created by higher respiratory effort or higher pressure support) is proposed to significantly destabilize the flow waveform and thus cause double-triggering. In addition, an extended cycling window (due to slower breathing frequency) is associated with increased frequency of double-triggering. The observed early cycling leading to double-triggering was not influenced by the maximum inspiratory time settings, which were held constant in this study. Finally, manual review of flow traces confirmed the shape of flow waveforms delivered by proprietary device algorithms vary, which may explain the slight variations between the 2 proprietary device algorithms tested in this study.

Ultimately, under each of these conditions where double-triggering became more prevalent (whether it was due to alterations in lung mechanics, increased pressure flux, or increased cycling window), the flow waveform delivered by the ventilator algorithm is distorted, resulting in asynchrony. This theory has been previously speculated upon, and the evidence from this study further supports this theory.²³

Regardless of the underlying mechanisms, the consequences of double-triggering are of significant clinical relevance. The association identified in this study between double-triggering, reduced minute ventilation, and increased patient inspiratory work (under certain conditions) further highlights the importance of this type of patient-ventilator asynchrony.

There are limitations to this study that need to be acknowledged. Benchtop simulations involving physiological lung models and NIV are an effective tool in improving our understanding of this technology, although the limitations of benchtop simulations are well recognized, particularly in the clinical application of findings.^{24,25} Further, double-triggering waveforms varied between devices in this study, although they did fit within accepted double-triggering definitions (as opposed to auto-triggering, for example).¹⁴ This does, however, raise an important limitation in that manually reviewed pressure flow waveforms are open to interobserver interpretation. Every attempt was made between the authors to standardize and agree upon waveform interpretation to maximize the sensitivity of the analysis. Finally, there are several device and simulator variables that were not evaluated as part of this study, including manipulating upper airway resistance, testing only 2 proprietary devices, and studying only one form of patient-ventilator asynchrony. The influence of these factors have been explored elsewhere.^{19,21}

Conclusions

This study successfully utilized a benchtop simulated lung model to investigate the underlying causes of the common type of patient-ventilator asynchrony known as double-triggering. Low lung compliance was noted to have the most profound effect of developing double-triggering. Importantly, under some circumstances, double-triggering was associated with increased inspiratory work and reduced minute ventilation. These associations have meaningful clinical implications if extrapolated to the patient bedside. Further investigation to elucidate specific device settings that minimize the frequency of double-triggering is warranted to guide clinician interventions when double-triggering is identified.

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