# Analysis of the mechanisms of expiratory asynchrony in pressure support ventilation: a mathematical approach

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Yamada, Yoshitsugu, and Hong-Lin Du. Analysis of the mechanisms of expiratory asynchrony in pressure support ventilation: a mathematical approach. J Appl Physiol 88: 2143-2150, 2000.-A mathematical model was developed to analyze the mechanisms of expiratory asynchrony during pressure support ventilation (PSV). Solving the model revealed several results. 1) Ratio of the flow at the end of patient neural inspiration to peak inspiratory flow (VTI/V<sub>peak</sub>) during PSV is determined by the ratio of time constant of the respiratory system ( $\tau$ ) to patient neural inspiratory time (TI) and the ratio of the set pressure support (Pps) level to maximal inspiratory muscle pressure (Pmusmax). 2) VTI/Vpeak is affected more by  $\tau/TI$  than by Pps/Pmus max.  $VTI/V_{peak}$  increases in a sigmoidal relationship to  $\tau/TI$ . An increase in Pps/ Pmus max slightly shifts the  $\dot{V}_{TI}/\dot{V}_{peak}$ - $\tau/TI$  curve to the right, i.e.,  $\dot{V}\mbox{TI}/\dot{V}_{peak}$  becomes lower as Pps/Pmusmax increases at the same  $\tau/TI$ . 3) Under the selected adult respiratory mechanics, VTI/V<sub>peak</sub> ranges from 1 to 85% and has an excellent linear correlation with  $\tau/TI$ . 4) In mechanical ventilators, single fixed levels of the flow termination criterion will always have chances of both synchronized termination and asynchronized termination, depending on patient mechanics. An increase in  $\tau/TI$  causes more delayed and less premature termination opportunities. An increase in Pps/Pmusmax narrows the synchronized zone, making inspiratory termination predisposed to be in asynchrony. Increasing the expiratory trigger sensitivity of a ventilator shifts the synchronized zone to the right, causing less delayed and more premature termination. Automation of expiratory trigger sensitivity in future mechanical ventilators may also be possible. In conclusion, our model provides a useful tool to analyze the mechanisms of expiratory asynchrony in PSV.

mechanical ventilation; patient-ventilator synchrony; mathematical modeling

PRESSURE SUPPORT VENTILATION (PSV) has been one of the most frequently applied modes for partial ventilatory support. Because patients under PSV have control of the ventilatory rate and the inspiratory assist time, they feel more comfortable with PSV than with other partial ventilatory support modes (e.g., synchronized intermittent mandatory ventilation) (11). Nevertheless, recent clinical studies have revealed that patients under PSV may frequently encounter patientventilator asynchrony. Ventilators may not be in synchrony with the onset of the patient inspiratory effort, which causes inspiratory asynchrony (or trigger asynchrony). Studies on inspiratory asynchrony have indicated that inspiratory asynchrony is related to a high patient work in breathing and difficulty in weaning patients from the mechanical ventilation (7, 8). In addition, patient-ventilator asynchrony may also be present during the onset of exhalation, i.e., expiratory asynchrony (9, 10, 14, 16). In this situation, the termination of the ventilator flow occurs either before or after patients stop their inspiratory efforts. Expiratory asynchrony not only causes discomfort to patients but costs patients unnecessary inspiratory and expiratory work as well (12). When the termination of the ventilator flow falls behind the end of the patient inspiratory effort (i.e., delayed termination), the patient recruits his expiratory muscles to "fight" against the ventilator flow, which increases expiratory workload (10). When the termination of the ventilator flow occurs before the end of the patient inspiratory effort (i.e., premature termination), inspiratory muscle work continues into or even throughout the ventilator's expiratory phase, thus resulting in inefficient inspiratory muscle work (16). Furthermore, a high lung volume caused by the previous breath with delayed termination may result in trigger failure of the subsequent inspiratory effort in patients with chronic obstructive pulmonary disease (COPD) (14). Premature termination in PSV, on the other hand, sometimes causes retriggering of inspiration and a stuttering pattern of ventilator assistance (16). Although expiratory asynchrony has been of clinical concern for years, there are very few studies exploring the mechanisms of expiratory asynchrony (20). Younes (20) used computer simulation to evaluate the effects of selected levels of respiratory mechanics and patient effort on the duration of ventilator assistance time during PSV. Because his presentation was limited to relatively few, selected levels of resistance, compliance, and patient effort, more general relationships governing expiratory asynchrony cannot be deduced.

Flow cycling is the primary method for intensive care ventilators to terminate their inspiratory flow delivery during PSV. The ventilator is cycled off when the inspiratory flow has decayed to a certain level (i.e., termination criterion). Most current ventilators use an arbitrary termination criterion to terminate the inspiratory flow delivery during PSV (e.g., 5% of the peak flow in the Siemens Servo 300, 25% of the peak flow in the Siemens Servo 900 and Bird 8400ST, 5 l/min in the Nellcor Puritan Bennett 7200ae). These arbitrary criteria have been shown to cause expiratory asynchrony in certain patient categories. Van de Graaff and co-workers (16) found that patients with prolonged and slow inspiratory efforts sometimes suffered premature termination under PSV with the Siemens Servo 900C ventilator. With this same ventilator, Jubran et al. (10) revealed delayed termination of ventilator flow in patients with a long time constant and a high support pressure level. In a mechanical simulation study evaluating expiratory synchrony during PSV in different ventilators (17), we identified a delayed ventilator flow termination with

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weak inspiratory effort and long time constant using the Siemens Servo300. Surprisingly, ventilator flow was never cycled off by the flow criterion with the Nellcor Puritan Bennett 7200ae in the tested conditions.

With the understanding that a single level of the flow criterion in a specific ventilator probably would not satisfy all patient categories and the chances of premature termination and delayed termination are always likely, some ventilator manufacturers have introduced user-selectable termination criteria into their newest model ventilators in an effort to improve expiratory synchrony (e.g., Nellcor Puritan Bennett 840, Hamilton Galileo). Clinicians can select a termination flow criterion (expiratory trigger sensitivity) to optimize the expiratory synchrony. This function, although it provides flexibility to clinicians, breaks the simplicity of the application of PSV and has been shown to be difficult even with visual observation of the bedside airway pressure waveform (4, 6). Part of the difficulty in using this function is attributed to lack of clarification of the mechanisms of expiratory asynchrony in different patient mechanic conditions during PSV.

To better understand the mechanisms of expiratory asynchrony caused by the flow termination criteria in PSV of mechanical ventilators, we developed a mathematical model. Solving this model revealed that expiratory synchrony is governed by two ratios: the ratio of the respiratory time constant ( $\tau$ ) to patient neural inspiratory time (TI) and the ratio of the ventilator set pressure support level (Pps) to patient inspiratory muscle pressure (Pmus). The use of this model for automation of expiratory trigger sensitivity in the development of future mechanical ventilators is also possible.

#### **METHODS**

## The Model

During partial ventilatory support, the motion of the respiratory system can be represented by the single first-order differential Eq. 1, with the assumption that inertial losses are negligible and that the pressure-flow and pressure-volume relationships are linear in the range of tidal ventilation.

$$Paw(t) + Pmus(t) = R \cdot \dot{V}(t) + E \cdot \Delta V(t)$$
(1)

where at any instant (t), the volume displacement  $[\Delta V(t)]$  from the end-expiratory level and the instantaneous flow  $[\dot{V}(t)]$  are determined by the total driving pressure applied to the respiratory system, i.e., the time varying airway pressure (Paw) and patient-generated Pmus. R and E represent the resistance and elastance of the respiratory system, respectively.

On the basis of this differential equation, the inspiratory flow waveform during PSV can be solved analytically by assuming the form of the input pressure signals Paw(t) and Pmus(t).

Paw(t) is simulated by assuming that the ventilator is triggered as soon as inspiratory effort succeeds in either generating inspiratory flow or reducing Paw below the baseline pressure level (here assumed to be zero). Once the ventilator is triggered, Paw is assumed to exponentially increase to the Pps level with a ventilator time constant ( $\tau_v$ ) and then maintain that level until the termination of inspiration (Fig. 1). Thus

$$Paw(t) = Pps(1 - e^{-t/\tau_v})$$
(2)



Fig. 1. Model-derived time courses of airway pressure (Paw; *top*) and inspiratory muscle pressure (Pmus; *bottom*). When the ventilator is triggered, Paw is assumed to exponentially increase to the set pressure support level (Pps) with a time constant of  $\tau_v$ . Pmus is approximated by a second-order polynomial function during neural inspiration time (T1). After the end of inspiration, Pmus decays exponentially during the entire expiration with a nearly linear decline (at a slope of  $\alpha$ ) during the first 0.1 s. Pmus max, maximal Pmus; *t*, time.

where  $t \ge 0$ . The time course of Pmus can be approximated by the following second-order polynomial function (13)

$$Pmus(t) = -d \cdot (t - TI)^2 + d \cdot TI^2$$

where *d* is a constant; TI is defined as the time between the onset of the increase in inspiratory Pmus and the start of its decline. It is assumed that Pmus reaches its maximum and becomes flattened at the end of the neural inspiratory effort (t = TI); thus the maximal Pmus (Pmus max) can be expressed as Pmus max =  $d \cdot TI^2$ . Substituting this into the above equation yields the expression

$$Pmus(t) = -Pmus \max\left(1 - \frac{t}{TI}\right)^2 + Pmus \max \qquad (3)$$

where  $0 \le t \le TI$ . Substituting *Eqs. 2* and *3* into *Eq. 1* and solving the resultant differential equation for the initial condition of  $\dot{V}(t = 0)$  yields

$$\dot{\mathbf{V}}(t) = \frac{\mathbf{Pps}}{\mathbf{R}} \cdot \frac{e^{-t/\tau} - e^{-t/\tau}}{1 - (\tau_{\mathrm{v}}/\tau)} + \frac{2\mathbf{Pmus}\max}{\mathbf{R}} + \frac{(4)}{(1 + \frac{\tau}{\mathrm{TI}})} \cdot \left[\left(1 + \frac{\tau}{\mathrm{TI}}\right)\left(1 - e^{-t/\tau}\right) - \frac{t}{\mathrm{TI}}\right]$$

where  $\tau$  is the time constant of the patient respiratory system ( $\tau = R/E$ ).

Rearranging the above equation to express  $\dot{V}(t)$  in terms of Pps/Pmus max and  $\tau/TI$  yields the equation

$$\frac{V(t)}{Pps/R} = \frac{1}{1 - (\tau_v/TI)(TI/\tau)} \cdot \left[e^{-(TI/\tau) \cdot (t/TI)} - e^{-(TI/\tau_v) \cdot (t/TI)}\right] \\
+ \frac{2}{Pps/Pmus max} \cdot \left(\frac{\tau}{TI}\right) \qquad (5) \\
\cdot \left\{\left(1 + \frac{\tau}{TI}\right) \cdot \left[1 - e^{-(TI/\tau) \cdot (t/TI)}\right] - \frac{t}{TI}\right\}$$

This is a fundamental equation describing the inspiratory flow profile during PSV, which implies that the flow profile as the function of normalized time (t/TI) is determined by Pps/Pmusmax,  $\tau/TI$ , and  $\tau_v/TI$ . Furthermore, this equation also implies that, during PSV at a given level of  $\tau_v/TI$ , the ratio of the flow at the end of patient neural inspiration to peak inspiratory flow ( $\dot{V}TI/\dot{V}_{peak}$ ) can be uniquely expressed and graphically plotted on the plane of Pps/Pmusmax vs.  $\tau/TI$ . This provides the framework for the following analyses.

Computation of  $\dot{V}TI/\dot{V}_{peak}$ . To simplify the calculations,  $\tau_V/TI$  is assumed to be 0.06. This  $\tau_V/TI$  value represents cases in which, for example, patient neural TI is 1.0 s and ventilator  $\tau_V$  is 0.06 s [ $\tau_V$  of 0.06 s corresponds to the flow acceleration percent setting of 90% in the Nellcor Puritan Bennett 840 ventilator (15)]. The inspiratory flow rates at *t* during PSV over the entire TI were then computed with *Eq. 5* by stepwise changing Pps/Pmusmax and  $\tau/TI$ .  $\dot{V}_{peak}$  and  $\dot{V}TI$  were determined in these calculations. In this study, Pps/Pmusmax was changed from 0.1 to 3.0 (at 0.1 intervals) and  $\tau/TI$  from 0.1 to 2.0 (at 0.1 intervals). In this way, we obtained 30  $\times$  20 matrices for  $\dot{V}_{peak}$  and  $\dot{V}TI$ , which yielded  $\dot{V}TI/\dot{V}_{peak}$  on the Pps/Pmusmax on  $\dot{V}TI/\dot{V}_{peak}$ ,  $\dot{V}TI/\dot{V}_{peak}$  values as a function of  $\tau/TI$  (ranging from 0.1 to 2.0 at 0.1 intervals) at five different levels of Pps/Pmusmax (i.e., 1/3, 2/3, 1, 2, 3) were also plotted.

 $VTI/V_{peak}$  at the ranges of adult respiratory mechanics. Because expiratory asynchrony has been experienced primarily in adult applications of PSV (9, 10, 14, 16), we calculated  $\dot{V}TI/\dot{V}_{peak}$  values at wide ranges of adult respiratory mechanics. The respiratory mechanics used were lung compliance of 0.08, 0.04, and 0.02 l/cmH\_2O; chest wall compliance of 0.2 l/cmH\_2O; respiratory resistance of 5 and 20 cmH\_2O·l^{-1}·s^{-1}; Pps of 10, 20, and 30 cmH\_2O; and Pmus max of 10 and 30 cmH\_2O. The patient neural TI was assumed to be 1.0 s and  $\tau_{v}/TI$  was the same as described above.

Expiratory synchrony with representative termination criteria. Two representative termination criteria were chosen in this study: 25 and 5% of peak inspiratory flow. This means that the ventilator is cycled off when the inspiratory flow decays to the level that is equal to the threshold level, i.e., 25 or 5% of peak inspiratory flow. With the use of these termination criteria, the ventilator will be in expiratory synchrony with the patient if  $\dot{V}_{TI}/\dot{V}_{peak}$  is equal to the threshold level. It is in asynchrony with the patient when  $\dot{V}_{TI}/\dot{V}_{peak}$  is higher than (delayed termination) or lower than (premature termination) the threshold level. When  $\dot{V}\mbox{TI}/\dot{V}_{peak}$  is higher than the threshold level at the end of patient neural inspiration, however, the decline in Pmus after neural inspiration augments the flow decay so as to decelerate flow to reach the threshold subsequently. Effect of the Pmus decline on the flow decay can be approximated as  $\Delta Pmus/R$ . Physiologically, the cessation of Pmus is not instantaneous; rather, the inspiratory muscle activity generally extends into the expiratory phase, resulting in residual inspiratory Pmus during neural expiration (13). In anesthetized humans and animals (2, 21), although the time course of the inspiratory Pmus during the entire expiration follows a curvilinear relationship, it is almost a linear decay during the first 0.1 s of the expiration. This is also supported by our data from the patients under mechanical ventilation with PSV (18). Taking this Pmus decay pattern into consideration, we designate the rate of the Pmus decline (in percent) during the first 0.1 s of expiration as  $\alpha$  (Fig. 1), i.e., Pmus is assumed to decay by  $\alpha \times Pmus \, max.$ Therefore, the contribution of the Pmus decline to the flow decay after the end of TI would be modified to  $\alpha \times Pmusmax/$ R. If we consider the delayed ventilator flow terminations of up to 0.1 s as synchronous terminations, the conditions of synchronous terminations can be written as

$$\frac{V_{TI}}{\dot{V}_{peak}} \ge 0.25 \text{ (or } 0.05)$$

 $\frac{\dot{V}_{TI}}{\dot{V}_{peak}} - \frac{1}{\dot{V}_{peak}} \cdot \frac{\alpha \cdot Pmus \max}{R} \le 0.25 \text{ (or } 0.05)$ 

Rearranging

and

$$0.25 \text{ (or } 0.05) \leq \frac{V_{TI}}{\dot{V}_{peak}} \geq 0.25 \text{ (or } 0.05) + \frac{Pps/R}{\dot{V}_{peak}} \cdot \frac{\alpha \cdot Pmus \max}{Pps}$$
(6)

The right side of *Eq.* 6 (upper limit) can be calculated using *Eq.* 5, generating a matrix distributed on the Pps/Pmus max- $\tau$ /TI plane. Comparing elements in VTI/V<sub>peak</sub> with both the lower limit (i.e., 0.25 or 0.05) matrix and the upper limit matrix, we obtained the zone for synchronous termination on the plane. The asynchronous zones were defined if VTI/V<sub>peak</sub> was higher than the upper limit (delayed termination) or lower than the lower limit (premature termination).

Although results from humans and animals with normal respiratory functions indicate that inspiratory Pmus decreases by  $\sim 25\%$  in the first 0.1 s (2, 21), the value of  $\alpha$  in this study was assumed to be 25 and 50% because a higher level of  $\alpha$  may represent the condition in which a sudden expiratory muscle activity augments the inspiratory flow decay (1).

## RESULTS

## Computation of $\dot{V}_{TI}/\dot{V}_{peak}$

 $V\rm{TI}/\dot{V}_{peak}$  is determined by two ratios:  $\tau/T\rm{I}$  and Pps/Pmus max (Fig. 2). At the same Pps/Pmus max,  $V\rm{TI}/\dot{V}_{peak}$  increases as  $\tau/T\rm{I}$  increases. When  $\tau/T\rm{I}$  remains the same,  $V\rm{TI}/\dot{V}_{peak}$  decreases as the Pps/Pmus max increases. Figure 3 reveals that  $V\rm{TI}/\dot{V}_{peak}$  is predominantly affected by  $\tau/T\rm{I}$ . The influence of  $\tau/T\rm{I}$  on  $V\rm{TI}/\dot{V}_{peak}$ 



Fig. 2.  $\dot{V}_{TI}/\dot{V}_{peak}$  plotted on the Pps/Pmus max- $\tau/T_{I}$  plane.  $\dot{V}_{TI}/\dot{V}_{peak}$ , ratio of the flow at the end of the patient neural inspiration to the peak inspiratory flow (in percent);  $\tau$ , time constant of the respiratory system.



Fig. 3.  $VTI/V_{peak}$  as a function of  $\tau/TI$  at different levels of Pps/Pmusmax. Levels of Pps/Pmusmax are 1/3 (*A*), 2/3 (*B*), 1 (*C*), 2 (*D*), and 3 (*E*).

follows a sigmoidal pattern. An increase in Pps/Pmusmax slightly shifts the  $VTI/V_{peak}$ - $\tau/TI$  curve to the right.

## *VTI/V<sub>peak</sub> at the Ranges of Adult Respiratory Mechanics*

Under adult respiratory mechanics,  $\dot{V}TI/\dot{V}_{peak}$  ranges from 1 to 85% (Table 1). It is affected more strongly by  $\tau/TI$  of the respiratory system than by Pps/Pmusmax. Analysis using linear regression reveals an excellent correlation between the  $VTI/\dot{V}_{peak}$  and  $\tau/TI$  within the selected mechanic ranges, with a correlation coefficient of  $\geq 0.96$  (Table 2).

## Expiratory Synchrony With Representative Termination Criteria

Expiratory synchronies with representative termination criteria are shown in Fig. 4. Single fixed levels of the termination criterion, no matter how much they are, always have chances of both synchronized termination and premature as well as delayed termination, depending on the Pps, Pmus,  $\tau$  of the respiratory system, and patient neural TI. An increase in  $\tau/TI$ causes greater opportunity of delayed termination and less chance of premature termination. An increase in Pps/Pmus max narrows the synchronized zone, making

Table 1.  $\dot{V}_{TI}/\dot{V}_{peak}$  at the ranges of adultrespiratory mechanics

		10 cmH <sub>2</sub> O Pmus max			30 cmH <sub>2</sub> O Pmus max		
	τ, s	10 Pps	20 Pps	30 Pps	10 Pps	20 Pps	30 Pps
R (20), C (0.08)	1.14	79	70	65	85	82	79
R (20), C (0.04)	0.66	58	48	43	70	64	58
R (20), C (0.02)	0.36	30	22	19	44	36	30
R (5), C (0.08)	0.29	21	15	12	34	26	21
R (5), C (0.04)	0.17	8	5	4	16	11	8
R (5), C (0.02)	0.09	3	2	1	6	4	3

Values for ratio of the flow at the end of patient inspiratory effort to peak inspiratory flow ( $\dot{V}TI/\dot{V}_{peak}$ ) are shown in %. Pmus max, inspiratory muscle pressure; Pps, set pressure support level (in cmH<sub>2</sub>O);  $\tau$ , mathematically calculated time constant of the respiratory system; R, resistance (in cmH<sub>2</sub>O·l<sup>-1</sup>·s<sup>-1</sup>); C, compliance (in l/cmH<sub>2</sub>O).

the inspiratory termination predisposed to be in asynchrony (delayed or premature termination). When the patient mechanics remain unchanged, increasing the expiratory trigger sensitivity of a ventilator shifts the synchronized zone to the right, in general causing less delayed termination and more premature termination. An increase in  $\alpha$  (indicating a faster Pmus decay or expiratory muscle activity) broadens the synchronous zone and narrows the delayed termination zone.

## DISCUSSION

Analysis of the mechanisms of expiratory asynchrony could be done with a mathematical model, computer simulation, mechanical model simulation, or even animal and/or human studies. Because it is difficult or unrealistic to manipulate the potentially involved parameters in animals and humans, animal and human studies do not fit well for this type of study. Mechanical model simulation and computer simulation have advantages because many parameters can be manipulated in a controlled manner and can be designed in a way that is mechanically closer to human physiology than mathematical models. However, the use of a mathematical model approach, with some assumptions and simplifications, allows easier elucidation of the basic rules behind expiratory asynchrony than the use of other approaches. In this study, we assumed the pressurevolume relationship to be linear in the range of tidal ventilation. We also assumed the pressure-flow relationship to be linear so that we could solve the mathematical model. This assumption, especially in intubated patients, is not true because the real pressure-flow relationship is more of nonlinearity. This nonlinearity will attenuate the peak flow and reduce VTI/V<sub>peak</sub>, thus, in general, shifting the results presented here toward delayed termination. We could incorporate trigger delay time ( $T_{delay}$ ) and trigger pressure ( $P_{trigger}$ ) into the model by changing TI, Pmus, and Pps to TI –  $T_{delay}$ ,  $Pmusmax - P_{trigger}$ , and  $Pps + P_{trigger}$ , predisposing to delayed terminations; however, in the model, we assumed that the ventilator is triggered as soon as the patient starts inspiratory efforts for the simplicity of data presentation. The airway pressure waveform in the model was characterized by an exponential curve with a variable rate constant  $(1/\tau_v)$ , which incorporated changes in the slope of the pressurization. To simplify the data presentation, we fixed  $\tau_v/TI$  at 0.06, which represents cases in which the patient T<sub>I</sub> is 1.0 s and the ventilator time constant is 0.06 s ( $\tau_v$  of 0.06 s corresponds to the flow acceleration setting of 90% in the Nellcor Puritan Bennett 840 ventilator). On the basis of *Eq. 5*, an increase in  $\tau_v/TI$  will reduce the peak flow and increase VTI/V<sub>peak</sub>. It means that an increase in  $\tau_v$  at a given TI will cause more delayed termination than what we presented in this study. This is consistent with the results from Bonmarchand et al. (3) who found that changing the pressurization time from 0.1 s to a maximum of 1.5 s greatly modified the ventilator TI, promoting delayed termination of inspiration. In the analyses of expiratory synchrony with the representative termination criteria (i.e., 25 and 5% of the peak

0.99

	I ···		0	-	v		
		10 cmH <sub>2</sub> O Pmus max			30 cmH <sub>2</sub> O Pmus max		
	10 Pps	20 Pps	30 Pps	10 Pps	20 Pps	30 Pps	
Equation	y = -1 + 75x	y = -4 + 68x	y = -5 + 64x	y = 9 + 75x	y = 3 + 76x	y = -1 + 75x	

Table 2. Correlation between  $V_{TI}/V_{peak}$  (y) and  $\tau/TI$  (x) at the range of adult respiratory mechanics

0.99

Pps values are shown in  $cmH_2O$ . TI, patient neural inspiratory time.

0.98

Correlation coefficient

flow), we arbitrarily defined a termination delay of up to 0.1 s as synchronized termination. These assumptions and simplifications can be easily criticized because they are not necessarily equivalent to those in



Fig. 4. Divisions of the synchronous zone (*A*), premature termination zone (*B*), and delayed termination zone (*C*) with the termination criterion of 5% peak flow (*top*) and 25% peak flow (*bottom*).  $\alpha$ , Slope of the Pmus decline in the first 0.1 s of expiration. *Left* vertical curve represents the flow termination criterion line. The synchronous zone (*A*) is between this curve and *middle* curve ( $\alpha$  25% curve), assuming that  $\alpha$  is 25%. The synchronous zone (*A*) would be extended to between the *left* and *right* curve ( $\alpha$  50% curve) if  $\alpha$  is 50%, suggesting a faster decay of Pmus or that the active expiratory effort broadens the synchronous zone and narrows the delayed termination zone. Note that increasing the expiratory trigger sensitivity (i.e., termination flow threshold) from 5 to 25% shifts the synchronized zone (*A*) to the right.

reality; however, they are helpful and allow an in-depth mathematical analysis of the mechanisms of expiratory asynchrony in PSV.

0.97

0.96

With these assumptions and simplifications being kept in mind, this mathematical model study reveals the following results during PSV. 1) The ratio of the flow at the end of patient  $\dot{V}\text{TI}/\dot{V}_{peak}$  during PSV is determined by two ratios,  $\tau/TI$  and Pps/Pmus max. 2) VTI/V<sub>peak</sub> is affected more by  $\tau$ /TI than by Pps/Pmusmax. Within the data ranges presented in the Fig. 3, VTI/V<sub>peak</sub> increases in a sigmoidal (s-shaped) relationship to  $\tau/TI$ . An increase in Pps/Pmusmax slightly shifts the VTI/ $V_{peak}$ - $\tau$ /TI curve to the right. 3) Under the selected adult respiratory mechanics, VTI/V<sub>peak</sub> ranges from 1 to 85% and has an excellent linear correlation with  $\tau/TI$ . 4) Single fixed levels of the flow termination criterion used in mechanical ventilators will always have chances of both synchronized termination and asynchronized (premature and delayed) termination, depending on the patient mechanics. An increase in  $\tau/TI$ causes greater opportunity of delayed termination and less chance of premature termination. An increase in Pps/Pmus max narrows the synchronized zone, leaving the inspiratory termination predisposed to be in asynchrony (premature or delayed termination). Increasing the expiratory trigger sensitivity of a ventilator shifts the synchronized zone to the right, causing less delayed termination and more premature termination. An increase in  $\alpha$  (indicating a faster Pmus decay or expiratory muscle activity) broadens the synchronous zone and narrows the delayed termination zone.

Although all factors, including Pps, Pmus, τ, and TI, influence VTI/V $_{peak}$ , the weight of the influence of  $\tau/TI$ is the most (Fig. 3, Table 1). VTI/V<sub>peak</sub> is affected by  $\tau/TI$ in a sigmoidal pattern across the full data ranges, as shown in Fig. 3. VTI/V<sub>peak</sub> rises as  $\tau$  becomes longer at a given TI, which implies that the expiratory trigger sensitivity should be set higher in the conditions of longer time constant. As an example of the results from this study,  $VTI/V_{peak}$  turns out to be higher than 60% in the conditions of 20 cmH<sub>2</sub>O $\cdot$ l<sup>-1</sup> $\cdot$ s<sup>-1</sup> resistance and 0.08 l/cmH<sub>2</sub>O compliance at a TI of 1.0 s (Table 1). This is consistent with the findings of the delayed inspiratory termination shown both in patients with COPD (10, 14) and in a mechanical lung model study (17) in which the ventilators with peak flows of 5 or 25% as the termination criterion were used [the Siemens 900C (10), Taema Cesar or Hamilton Amadeus (14), and Siemens 300 (17)]. In another study on COPD patients, Jubran and co-workers (10) showed that 5 of their 12 studied patients displayed expiratory effort before the cessation of inspiratory flow (i.e., delayed termination).

0.98

These five patients had an average time constant of 0.54 s compared with an average time constant of 0.38 s in the patients who displayed no expiratory effort during the inspiratory phase. The delayed termination at the long time constant can be explained because the inspiratory flow decay after the peak level is slower as a result of a longer time constant. The strong relationship between  $VTI/V_{peak}$  and  $\tau$  may also explain why expiratory synchrony can be achieved with the ventilator (Newport E200) in which expiratory time (17).

The direct effects of the Pps level and the magnitude of the patient inspiratory effort (Pmus) on  $V_{TI}/V_{peak}$ are not as important as those of  $\tau/TI$  (Fig. 3, Table 1); however, the higher the Pps/Pmusmax, the narrower the synchronized zone becomes with a certain flow criterion (Fig. 4). This means that the possibility of expiratory synchrony is reduced if a high level of pressure support is applied and/or the patient has a weak inspiratory effort (19). When the patient Pmus is predominant (compared with the ventilator support) in generating inspiratory flow, the ventilator is predisposed to be in synchrony with the patient in terms of the inspiratory termination and vice versa. These results are consistent with the findings in the abovementioned study done by Jubran and co-workers (10) because the delayed termination existed at PSV of 20  $cmH_2O$  but disappeared at PSV of 10 and 5  $cmH_2O$ .

It is surprising to find that, even under the adult respiratory mechanics,  $VTI/V_{peak}$  can vary in a very wide range, from 1 to 85%. This finding explains why expiratory asynchrony occurs frequently when mechanical ventilators with a fixed level of flow termination criteria are used. Contrary to a fixed level of flow termination criteria, user-selectable expiratory trigger sensitivity in some of the most recently released ventilators (e.g., Hamilton Galileo and Nellcor Puritan Bennett 840) provides flexibility, allowing clinicians to manually select the flow termination criteria to achieve good patient-ventilator synchrony. However, because VTI/V<sub>peak</sub> may change when any of the four parameters (Pps, Pmus,  $\tau$ , and TI) change, clinicians may need to readjust the expiratory trigger sensitivity setting very frequently. This is obviously unrealistic in routine clinical practices. Because expiratory asynchrony is a clinical concern primarily in adult applications (9, 10, 14, 16) and  $V_{TI}/V_{peak}$  has an excellent linear correlation with  $\tau/TI$  in the range of adult mechanics (with correlation coefficient  $\geq$  0.96, Table 2), the adjustment of expiratory trigger synchrony for the purpose of patient-ventilator synchrony, in theory, could easily be done automatically by the current computer technologies in mechanical ventilator applications.

Because of the assumptions and simplifications that we used in this mathematical model study, the results presented here may not be directly extrapolated to clinical application. It is especially true in terms of the data of expiratory synchrony with the representative termination criteria (Fig. 4), since our model did not take into account the role of the pressure criteria in the inspiratory termination. The divisions of the premature, synchronized, and delayed termination zones in Fig. 4 were based on the assumption that the ventilator has only flow criteria to terminate the inspiratory flow. Many mechanical ventilators, in reality, are also equipped with pressure criteria as a backup to terminate the inspiration. By pressure criteria, the ventilator flow is terminated when Paw rises a certain amount (e.g., +1.5, 2.0, 3.0, and 20.0 cmH<sub>2</sub>O in the Nellcor Puritan Bennett 7200ae, the Newport E200, the Siemens 900, and the Siemens 300 ventilators, respectively) above the Pps level. In fact, pressure criteria could become a primary method for terminating the ventilator flow in some ventilators (17) if they are strict (i.e., the ventilator is cycled off at a small supraplateau pressure). The addition of a strict pressure criterion may fundamentally narrow the delayed termination zone and widen the synchronized zone, especially in patients with active expiratory efforts (at the cost of the patient expiratory work). It should be kept in mind, however, that a strict pressure criterion may cause other problems, such as premature termination of inspiration in the case of pressure variation at the plateau level.

## Contribution to Already Published Work

Using computer simulation, Younes (20) evaluated the effects of patient respiratory mechanics and the level of patient inspiratory effort on the tidal volume and ventilator's TI during PSV by choosing a few levels of resistance, compliance, and Pmus. His results indicate that, for a given level of patient resistance and compliance, expiratory asynchrony is affected by the change in the patient inspiratory effort. Although his data help to explain, in part, the mechanism of expiratory asynchrony, his approach is less likely to elucidate the general rules governing expiratory synchrony. With our simple but comprehensive mathematical formulation, however, we were able to characterize, in a first-order approximation, the influence of  $\tau$  (and thus resistance and compliance) in dimensionless form as the ratio  $\tau/TI$ , incorporating the effect of TI. It means that expiratory synchrony is not affected by  $\tau$  alone but, rather, is affected by  $\tau/TI$ . Accordingly, we can conclude that changes in  $\tau$  could result in different levels of expiratory asynchrony dependent on the patient's adjustment of neural TI: if TI is changed proportionally to maintain a constant value of  $\tau/TI$ , there would be no change in expiratory asynchrony. In the same way, expiratory synchrony is governed by the balance in relative weight between patient effort magnitude (Pmus) and ventilator support level (Pps) in the manner of the ratio Pps/Pmus and not by the individual values of Pps or Pmus. As shown in Fig. 4, when the patient Pmus is predominant compared with the ventilator support pressure, the ventilator is predisposed to be in synchrony with the patient's expiration. In contrast, when ventilator support pressure overwhelms the patient inspiratory effort, expiratory asynchrony may easily occur. In addition, Younes' approach is

Table 3. Comparison of  $\dot{V}_{TI}/\dot{V}_{peak}$  computed from the mathematical formula and  $\dot{V}_{TI}/\dot{V}_{peak}$  read from the mechanical test lung model

			$\dot{V}_{TI}/\dot{V}_{peak}$ , %		
	τ, s	Pmus max, cmH <sub>2</sub> O	Mathematical model	Mechanical model	
R (20), C (0.08)	1.14	32.9	85	71	
R (20), C (0.04)	0.66	37.2	73	60	
R (20), C (0.02)	0.36	41.1	45	44	
R (5), C (0.08)	0.29	15.1	28	35	
R (5), C (0.04)	0.17	20.0	13	21	
R (5), C (0.02)	0.09	35.3	7	4	

Values for R are in  $cmH_2O \cdot l^{-1} \cdot s^{-1}$ ; values for C are in  $l/cmH_2O$ .

limited to a set of specific conditions: he only computed machine TI for a few selected levels of resistance, compliance, and Pmus. As a result, Younes' study only covers a range of  $\tau/TI$  values between  $\sim 0.3$  and 0.6. As shown in Fig. 4, this range of  $\tau/TI$  cannot reveal information about expiratory asynchrony in other common pathophysiological conditions outside of this limited range.

## Potential Applications of This Study

Although the assumptions used in this study preclude the direct extrapolation of our data to clinical applications, some basic rules that the study has revealed may be clinically helpful. In patients with a long time constant of respiratory system, such as COPD patients, clinicians may need to set a high level of expiratory trigger sensitivity to achieve expiratory synchrony. When a patient is stabilized with a good expiratory synchrony at a given expiratory trigger sensitivity level and if clinicians suction the patient's airway (i.e., reduction in the airway resistance) or increase the Pps level, for instance, clinicians should reassure expiratory synchrony due to the change in VTI/ V<sub>peak</sub>. More importantly, our study may indicate the possibility of development of a computer-automated expiratory trigger sensitivity feature in future mechanical ventilators.

#### APPENDIX

## Validation of the Mathematical Model Using a Mechanical Lung Model

A mechanical lung model setup was used to validate the appropriateness of our mathematical model. The mechanical model (Michigan TTL, model 1600) consisted of two compartments in drive-dependent relationship (17). One side of TTL was driven by a Bear 5 ventilator using a sinusoidal flow pattern. The other side of TTL was connected to a Siemens 300 ventilator through a parabolic resistor (R5 or R20). The two sides of TTL were connected completely by a metal connector, which allowed the two compartments to behave like compliances in series. The pressure at the driving compartment can therefore be taken as inspiratory Pmus when the compliance of the driving lung was set at 0.2 l/cmH<sub>2</sub>O to simulate the chest wall compliance. This mechanical model simulates the interactive relationship between a ventilator and a patient who does not exhibit active expira-

tory effort. The compliance of the dependent lung was set to 0.08, 0.04, or 0.02 l/cmH<sub>2</sub>O. The settings of the Siemens 300 were as follows: pressure support mode, pressure support of 10 cmH<sub>2</sub>O, positive end-expiratory pressure of zero, pressure trigger sensitivity of -0.5 cmH<sub>2</sub>O, rise time of 1%. The Bear 5 was set at continuous mandatory ventilation with Ti of 1.0 s and frequency of 10 breaths/min. The peak flow of the Bear 5 was set so that the peak flow at the airway of the dependent lung achieved 1 l/s when the Siemens 300 was not connected.

A hot wire flow transducer (model RF-L, Minato Medical Science, Osaka, Japan) and a pressure transducer (Heise 901A, Dresser Industries, Stratford, CT) were placed at the Y connector of the Siemens 300 to measure the patient Paw and flow. The same pressure and flow transducers were placed at the Y connector of the Bear 5 to measure Pmusmax and to identify the time when the driving lung completed inspiration. The signals from the transducers were digitized at 100 Hz and recorded on a computer recorder (model DT2831, Data Translation, Marlborough, MA). The flow rate at the patient airway was measured both at its peak value (V<sub>peak</sub>) and at the time when the driving lung completed inspiration (VTI). Dividing VTI by  $\dot{V}_{peak}$  generated VTI/ $\dot{V}_{peak}$  values at different levels of Pps/Pmus max and  $\tau/TI$  in the mechanical lung model.  $VTI/V_{peak}$  values were also calculated using Eq. 5 from the mathematical approach. Both VTI/Vpeak values calculated from the mathematical model and  $\ensuremath{\mathsf{VII}}\xspace/\ensuremath{\mathsf{V}}\xspace_{\text{peak}}$  values measured from the mechanical model were compared (Table 3). The data indicate a favorable consistency between the values from both models ( $r^2 = 0.98$ , P < 0.01, bias:  $8\% \pm 5\%$ ; means  $\pm$  SD).

In this study, the Siemens 300 was chosen because it has a very high pressure cycling criteria in PSV (i.e.,  $+20 \text{ cmH}_2\text{O}$  above the target Pps level) (5). Our previous study using the same mechanical lung model (17) showed that the pressure criteria in the Siemens 300 under the above test conditions has never been activated, which allowed us to evaluate the effects of only flow termination criteria.

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