Go with the flow—clinical importance of flow curves during mechanical ventilation: A narrative review

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INTRODUCTION

Measurements of flow, volumes, and pressures are of paramount importance during mechanical ventilation. New generation ventilators use different flow and pressure sensors for adequate pressure and gas flow to and from the ventilator to the patient. The flow sensors not only measure flow but they also act as trigger sensors for the patient’s spontaneous breathing. The flow signals then need to be sent to the ventilator to trigger it as per the required patient’s rate and pattern. The ventilator then works in closed-loop systems [1].

Most ventilators display the graph of flow (L/min), pressure (cmH₂O), and tidal volume (mL) in the waveform. The exact mechanisms and anatomical inhomogeneity of the expiratory flow to increase despite an increase in the expiratory peak flow rate (PEF) and expiratory flow time are dependent on the time constant (TC) that results in the Resistance X Compliance of the respiratory system. At each TC, the flow is estimated to decay to about 37.8% from its previous value [5]. At least four TCs are required for the lung to reach the resting terminal airway resistance [5, 6]. As the compliance and resistance become higher (e.g., cases of chronic obstructive airway disease (COPD)), the PEF is reduced and the expiratory TC is prolonged. If this expiratory time is not long enough for the new breath to start after expiration reaches baseline, hyperinflation (auto-positive end-expiratory pressure [PEEP]) will develop [7]. In addition to its well-known adverse hemodynamic affect, auto-PEEP worsens oxygenation and ventilation by increasing the dead space and work of breathing (WOB). The dead space causes ventilation-perfusion mismatch and with increased WOB will cause more oxygen consumption and CO₂ production [8]. Additionally, it places the diaphragm at a disadvantage causing diaphragmatic weakness, patient-ventilator asynchrony, or the inability to trigger the ventilator [9].

On the other hand, restrictive lung disease has very low TC, thus the PEF is high and the lungs tend to return to FRC rapidly [5].

A recent condition termed the expiratory flow limitation (EFL) is the inability of the expiratory flow to increase despite an increase in the expiratory driving pressure (the pressure difference between the alveoli and the airway opening during expiration) [10]. The exact mechanisms and anatomical location are not entirely clear but the most commonly cited mechanism is dynamic airway compression that occurs when the intraluminal pressure equals the pressure in the surrounding structure (pleural space) and there is

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Most clinicians pay attention to tidal volume and airway pressures and their curves during mechanical ventilation. On the other hand, inspiratory–expiratory flow curves also provide a plethora of information, but much less attention is paid to them. Flow curves show the velocity and direction of inspiration and expiration and are influenced by the respiratory mechanics, the patient’s effort, and the mode of ventilation and its settings. When the ventilator setting does not synchronize with the patient’s respiratory pattern, the patient can easily have worsening breathing effort, patient-ventilator asynchrony, which can lead to prolonged ventilator support or lung injury. The information provided by the flow curves during mechanical ventilation, such as respiratory mechanics, the patient’s effort, and patient–ventilator interactions, are very helpful when adjusting the ventilator setting. If clinicians can monitor and assess the flow curves information appropriately, it can be a useful diagnostic and therapeutic tool at the bedside. There may be association between inspiratory effort and flow, and this may further guide us, especially in the weaning process when patients are not synchronizing with the ventilator. In this review, we try to gather information about “flow” that is scattered around in the literature and textbooks in one place. We will summarize the different flow waveforms utilized in commonly used ventilator modes with their advantages and disadvantages, information gained by the flow curves (i.e., flow-time, flow-volume, and flow-pressure), how to detect and manage asynchronies, and some ideas for future use. Flow waveforms shapes and patterns are very beneficial for the management of patients undergoing mechanical ventilatory support. Attention to those waveforms can potentially improve patient outcomes. Clinicians should be familiar with this information and how to act upon them.

Key Words: flow curve, mechanical ventilation, ventilator synchrony, respiratory mechanics, ventilator weaning

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no pressure gradient. Dynamic collapse occurs from this point to the down-
stream segment. It is a relatively frequent phenomenon among critically ill
patients, and usually goes unrecognized especially in COPD patients, but it
can also occur in obesity, heat failure, and Acute Respiratory Distress
Syndrome (ARDS) patients. One of the methods to diagnose EFL is to alter
the expiratory driving pressure and compare the difference of flow in each
condition at the same lung volume. This method requires the operator to
manually reduce the PEEP while recording two consecutive flow-volume
loops. Reducing the PEEP will increase the expiratory driving pressure, and
this should generate higher expiratory flow if there is no EFL. Also, small
airway collapse occurs during exhalation and can cause auto-PEEP. However,
the auto-PEEP caused by EFL happens to be relatively refractory to changes
in expiratory time compared with auto-PEEP generated by insufficient expi-
ratory time and patients with EFL have greater auto-PEEP than patients
without EFL. Applied PEEP can help improve such occurrences [10].

A new ventilator mode termed flow-controlled ventilation that uses lin-
ear inspiratory and expiratory flow in contrast to the exponential expiratory
flow in the volume- and pressure-controlled modes has shown enhancement
of lung aeration in the dependent lung region and consequently improved
gas exchange and attenuation of lung injury in animal studies and may pro-
vide a novel option for lung-protective ventilation [9] (Figure 2).



**Inspiratory flow**

**Types of inspiratory waveforms**

Essentially there are five different inspiratory flow waveforms output
from the ventilator depending on the mode used (Figure 3).

Most pressure-controlled ventilator (PCV) modes use the decelerating or
descending waveform where the inspiratory flow rises fast and exponentially
decays down during the inspiratory cycle. The pressure in the lung increases
as it gets filled and pressure gradient diminishes, which drops the flow con-
tinuously during inspiration. The square or constant waveform is used
mainly on the volume-controlled ventilator (VCV) modes, the flow value
quickly rises linearly to the value set on the ventilator and then remains
constant during inspiration until the tidal volume ($V_T$) has been delivered
then falls rapidly before exhalation begins. Most new generation ventilators
can apply the descending waveform in the VCV mode as well to reduce the
peak inspiratory pressure [11, 12], which indicates that the influence of the
airway resistance is minimized in the descending waveform. A decelerating
waveform was also reported to reduce the dead space, the alveolar-arterial
gradient and the WOB [13, 14]. The accelerating or ascending waveform
starts with the low flow but steadily rises during inspiration, this has been
eliminated from most new ventilators for its unfavorable effects on the
patient’s WOB and asynchronies. It is rare but some ventilators still use the
sinusoidal waveform that reciprocates the normal spontaneous breathing
with an increase followed by a decrease during the inspiration.

The type of waveform used can affect the peak inspiratory airway
pressure (PIP) [11], mean airway pressure (Paw), and inspiratory time (I
time) [15], which can subsequently affect ventilation and oxygenation.
We will focus on the decelerating and constant waveforms as they are the
most commonly used by virtually all modes of mechanical ventilation.

**Factors affecting waveforms**

Multiple factors affect the inspiratory flow shape, peak inspiratory flow
(PIF), and flow (inspiratory) time. Particularly, the inspiratory time,
respiratory rate (RR), respiratory system mechanics (compliance, resis-
tance, and TC), rise time, and patients’ muscle efforts (Pmus).
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In the VCV modes using any flow waveforms, with a fixed flow rate, the PIF will remain constant while the inspiratory time will be variable according to the flow rate (higher with lower flow and vice versa), and the peak inspiratory pressure (PIP) will vary according to the respiratory mechanics (higher with high resistance and low compliance). On the other hand, when the Inspiratory:Expiratory ratio is fixed, the PIF and inspiratory time will be variable according to the RR (i.e., the PIF increases and the inspiratory time shortens with the higher RR and vice versa). The PIP will change similar to the fixed flow rate (Figure 4).

In the PCV modes, flow is variable as the ventilator constantly adjusts the flow to maintain preset pressure and inspiratory time. The PIF is higher with low compliance (e.g., ARDS) and conversely lower with high resistance and compliance (e.g., COPD) (Figure 4). The PIF will increase with a higher RR and vice versa.

The effect of patients’ Pmus on flow is not very well studied or reported, but based on the patient’s observation and simulator work, the higher Pmus, the higher the PIF and higher mean inspiratory flow [16] (Figure 5).

Effects of different flows on oxygenation, WOB, and outcomes

The effects of different inspiratory flow patterns on respiratory mechanics, oxygenation, ventilation, and WOB have been controversial and nonconclusive. Some studies showed improved oxygenation, respiratory mechanics, and dead space with the decelerating flow ramp, while others were not able to reproduce the same conclusions [11–13].

It is widely accepted that the decelerating waveforms can achieve higher mean airway pressures (surrogate for oxygenation) and alveolar recruitment with lower peak inspiratory flow, while a constant airflow ramp produces shorter inspiratory time with higher PIF [13]. Additionally, the decelerating waveform in PCV modes have been proposed to decrease WOB and patient-ventilator asynchrony due to the initial high flow in conditions of air hunger and due to the unrestricted flow according to patient’s efforts and respiratory mechanics as mentioned above. On the other hand, patient-ventilator asynchronies may happen more frequently in the constant flow ramp as the patients are only allowed to inhale with the same flow (Figure 5).

When compared together, sinusoidal waveforms and constant square waveforms did not show a significant difference in WOB or inspiratory pressure [13].

Effects of flows on ventilator-induced lung injury (VILI)

VILI has been increasingly understood and is usually related to volutrauma, baro-trauma, atelectrauma, and bio-trauma. The effect of high PIF was suggested to cause accelerated VILI in animal models using very high V<sub>e</sub> (20–30 mL/kg) [17]. The results of high PIF is unclear in human studies because it is unethical to prescribe such high tidal volumes.

Calculating tidal volumes

Most modern ventilators do not have a spirometer built-in to measure inhaled and exhaled tidal volumes. However, the displayed tidal volumes are obtained from integration of the flow rate divided by time (i.e., flow/time).

Trigger

Breaths trigger variable refers to starting the breath during mechanical ventilation. It is usually either time triggered (based on set respiratory rate) or patient triggered. Patient-triggered breaths may be either flow or pressure triggered. For most patients, pressure sensitivity settings from −0.5 cmH<sub>2</sub>O to −2.0 cmH<sub>2</sub>O are safe and effective. With the flow trigger, the typical flow trigger setting is 1–3 L/min [1]. Studies comparing pressure versus flow triggering have shown that flow triggering may be more comfortable than pressure-triggered breaths with resultant decreased WOB, though this has been challenged by some authors [18]. More recent studies did not show a significant difference in patient’s responses with flow and pressure triggering during pressure support ventilation (PSV) [19].

In the presence of auto-PEEP, the patient’s effort must overcome the whole amount of auto-PEEP before a pressure or flow change occurs at the proximal airway to trigger the ventilator. In this scenario, flow triggering showed superiority to pressure triggering [20]. Adjusting the trigger sensitivity or changing from the pressure to flow triggering may help with the trigger asynchrony. The neural trigger (diaphragmatic electromyogram) or the electrical activity of the diaphragm is not affected by auto-PEEP and therefore might be the most appropriate triggering mode for these patients.

Cycle

Breaths cycle variable refers to the end of inspiration and transitioning to expiration. The most common cycle variables are flow, time, or pressure. VCV modes usually use flow cycle where the breath ends after a set flow rate and tidal volume is applied. Pressure support mode is a common mode where the ventilator cycles when a predetermined percentage of the PIF is reached, it is usually called expiratory sensitivity or expiratory trigger sensitivity (historically around 25% but can be adjustable on most ventilators). Attention must be paid when adjusting this level as it can affect patients’ effort and comfort, respiratory mechanics, and asynchronies. If it is set too low, the ventilator will continue inspiration even after the respiratory muscles have relaxed. If it is set too high, the ventilator will stop delivering air even if the respiratory muscles are...
FIGURE 3.
Typical flow waveforms used by different modes of ventilators. Upper yellow curves are the airway pressures in cmH₂O, middle pink curves are flows in L/min, and lower green curves are tidal volumes in mL. (A) Constant or square flow waveform, (B) descending, (C) sinusoidal, (D) decelerating, and (E) ascending.

FIGURE 4.
Volume-controlled mode with constant square waveform in different clinical scenarios (A–C) and pressure-controlled mode showing different flow appearance in different clinical scenarios (D–F). (A) ARDS, (B) normal, (C) COPD showing missed effort (yellow arrow) and auto PEEP (red arrow), (D) normal resistance and compliance, (E) COPD with higher resistance and compliance, and (F) ARDS with normal resistance and low compliance. Upper yellow curves are the airway pressures in cmH₂O, middle pink curves are flows in L/min, and lower green curves are tidal volumes in mL.
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still contracted and can lead to double triggering, breath stacking, and lung injury (Figure 6).

Ideally, the ventilator should cycle to exhalation at the end of the neural inspiratory time. If breath terminates before the need for neural inhalation, the patient may double trigger the ventilator.

Automatic adjustment of ventilator settings in newer modes

Adaptive support ventilation is one of the newer and intriguing modes of mechanical ventilation that uses the closed-loop controlled ventilatory mode. It uses the decelerating flow waveform and it is based on the optimal or intelligent targeting scheme. The ventilator automatically adjusts its output (tidal volume, respiratory rate, flow time, and inspiratory time) based on the calculation of time constant of the expiratory flow. The ventilator analyzes the flow–volume curve and adjusts the I:E relation and the target rate to keep the target volume within a margin of safety and prevent auto-PEEP, volu-trauma, and baro-trauma [21, 22]. Proportional-assist ventilator is another ventilator mode that calculates the patient’s inspiratory effort and provides variable support (inspiratory flow and tidal volume) depending on the amplification setting of the patient’s effort (percentage support) to unload the respiratory muscles [23].

Calculation of respiratory mechanics

The traditional calculation of respiratory mechanics is described using both an inspiratory and expiratory flow that pauses maneuvers in the volume-controlled mode using the square waveform as below. The plateau pressure can be measured by inspiratory hold maneuver or the addition of an inspiratory pause on every breath (Table 1, Equations 1 and 2).

Another way of breath-to-breath automatic calculation of the dynamic respiratory mechanics (compliance, resistance, and auto-PEEP) without the need for any pause maneuvers is termed the least square fitting method, which uses regression analysis of the airway pressure, flow, and volume curves and applies it to the equation of motion (below). Those measurements are available in many new-generation ventilators [24]; however, those calculations might not be accurate in the actively
Hyperinflation and auto-PEEP can have deleterious effects during mechanical ventilation, including adverse hemodynamic effects, missed trigger, increased WOB, asynchronies, and delayed weaning. This more often occurs in obstructive airway diseases like asthma or COPD; however, it can happen in other conditions, such as ARDS, mucus plugs, and dynamic hyperinflation without airflow obstruction (inadequate expiratory time) [1, 26]. Higher V̇, RR, and shorter expiratory time contribute to this phenomenon. Early detection and correction of such a phenomenon are of paramount importance. These may be detected in the expiratory flow–time curve when it does not reach the baseline before the next breath or in the flow–volume curve (Figure 7) when expiratory flow does not reach the baseline.

Quantification of auto-PEEP is usually done via the end-expiratory pause maneuver. Corrections include reducing minute ventilation (tidal volume and respiratory rate) or increasing the expiratory time (by increasing inspiratory flow in VCV modes or reducing the I-time or I:E ratio in the pressure-controlled modes). Increasing applied PEEP to 70%–80% of total PEEP has been suggested for intrinsic expiratory flow obstruction such as COPD [19, 26]. Disconnecting from mechanical ventilation to allow adequate exhalation of the trapped air has been described, though the potential derecruitment of the lung is worrisome, especially in conditions of increased elasticity like ARDS. This maneuver should only be done only in extenuating circumstances [27].

**TABLE 1**

| Equation number | Equation |
|-----------------|----------|
| 1               | Total respiratory system compliance (C<sub>RS</sub>, mL/cmH<sub>2</sub>O) = V<sub>e</sub> (exhaled)/Plateau pressure – Total PEEP (applied + auto-PEEP) |
| 2               | Total airway resistance (R<sub>aw</sub>, cmH<sub>2</sub>O/L/s) = PIP – Plateau pressure/Flow in cmH<sub>2</sub>O/L/s [25] |
| 3               | P<sub>total</sub> = P<sub>vent</sub> + P<sub>mus</sub> = VT/CRS + Raw x V̇ + PEEP total |

Note: P<sub>Total</sub>, total pressure required to move tidal volume in cmH<sub>2</sub>O; P<sub>vent</sub>, airway pressure in cmH<sub>2</sub>O; P<sub>mus</sub>, patient’s muscle pressure, in cmH<sub>2</sub>O; VT, tidal volume in mL; CRS, respiratory system compliance in mL/cmH<sub>2</sub>O; Raw, airway resistance in cm H<sub>2</sub>O/L/s; V̇, flow in L/s; PEEP<sub>i</sub>, the intrinsic PEEP in cm H<sub>2</sub>O.
Setting inspiratory time
As described above, PCV modes use decelerating inspiratory flow ramps, if the inspiratory time is inadequately short, then the resultant $V_t$ will be lower, which can cause inadequate recruitment and result in hypoxia. If it is higher than optimal, no extra volumes will be gained, which can cause the patient-ventilator asynchrony [1]. Sometimes this strategy is needed, such as in cases of severe hypoxia in ARDS to increase Paw like in cases of inverse ratio ventilation or airway pressure release ventilation (APRV) [1] (Figure 8).

Setting expiratory time
As explained above, inadequate expiratory time can lead to auto-PEEP and an appropriate setting of expiratory time is essential. In APRV, the expiratory flow is important in setting the release time also known as time low or T-Low. It is usually set very low in the millisecond to intentionally create auto-PEEP, some research suggested setting the T-Low when the expiratory flow decreases to 50%–75% of the PEF [28] (Figure 8).

Rise time
Once the ventilator is triggered in a PCV mode, Paw increases exponentially to the driving pressure or pressure support level and then stays at the level until the termination of the inspiratory phase (cycling). The “rise time” is the slope until the inspiratory flow reaches the maximum and it should be adjusted to patient comfort (Figure 6). Fast and slow rise times are associated with high and slow flow at the onset of inhalation, respectively, and this should be tailored based on the patient’s respiratory drive [19]. For patients with COPD, and restrictive lung disease, faster rise time provided the lowest WOB. In one small study with 15 patients, fast rise time was as effective as increasing the level of pressure support [29].

Flow–volume loop
The flow–volume loop has been used in the outpatient pulmonary function tests as an objective measure of airway resistance. It differentiates whether the resistance is dynamic or fixed and whether its location is intra- or extra-thoracic. With the advanced computing of mechanical ventilators, they can display the flow–volume loops breath to breath. They provide some useful information, for example auto-PEEP can be identified when the flow does not return to zero before the next breath as described above. Additionally, the expiratory flow decay curve signifying effects of airway resistance. Clinicians can use the flow–volume curve as a tool to evaluate the response to bronchodilator (e.g., increased peak expiratory flow, faster decay of the expiratory curve, and resolution of auto-PEEP) or to assess the need for these treatments in patients with airway obstruction (Figure 7).

In addition, “saw tooth” artifacts on the flow–volume as well as flow–time curve signals the need of airway suctioning for the presence of mucus or water condensation in the circuit or within the large airways.

Flow–pressure loop
Some ventilators offer a flow versus pressure loop. Though the significance of this curve is not mentioned in the mechanical ventilation literature, it has been described in physics and engineering literature. For gas to flow from the ventilator to the patient during inspiration there should be a pressure gradient between the ventilator and the alveoli also known as the driving pressure.

The relation between pressure and flow was described by the Poiseuille law, it describes the pressure difference between two ends of a pipe that are proportional to the length, dynamic viscosity, and volumetric flow rate while inversely related to the radius of the pipe [30].
\[ \Delta p = \frac{8 \mu LQ}{\pi R^4} = \frac{8 \pi \mu LQ}{A^2} \]

where \( \Delta p \) is pressure difference between the two ends, \( L \) is the length of the pipe, \( \mu \) is the dynamic viscosity, \( Q \) is the volumetric flow rate, \( R \) is the pipe radius, and \( A \) is the cross-section of the pipe.

As described above, the airway resistance is the value of the airway pressure drop from the peak to plateau pressures over the flow rate, thus concluding that the flow-pressure loop basically describes airway resistance during inspiration and expiration (Figure 7).

Asynchronies

Patient–ventilator asynchronies are encountered frequently during mechanical ventilation [31]. There are many kinds and classifications of asynchronies. Most of the asynchronies, unfortunately, go unnoticed, but their existences have been linked to prolonged mechanical ventilation, difficult weaning, reduced patient comfort, increased risk of diaphragmatic damage, and potential increased morbidity and mortality [32]. Reviewing all asynchronies is beyond the scope of this article, we will review some of the asynchronies that can be detected by observing the flow-time curve. Figure 9 summarizes those asynchronies.

Trigger asynchronies usually happen at the beginning of the breath. The patient’s effort can be detected as a positive deflection on the flow curve even if still negative [33] (Superscripts 1 and 2 correspond to numbers used in Figure 9).

A) Delayed triggering occurs when the time between the patient’s effort to the delivery of the breath is prolonged. It is characterized by prolonged time from the positive deflection in flow1 to the ventilator-delivered breath2. It is usually caused by inappropriately high settings of trigger sensitivity, presence of auto-PEEP, weak effort, or low respiratory drive.

B) Missed triggering occurs when the patient’s inspiratory effort does not trigger a breath from the ventilator. It is characterized by a positive deflection in flow1 and not followed by a breath2. Causes are similar to the case of delayed triggering alongside high-pressure support settings, high tidal volumes, and high-set respiratory rate and inspiratory time.

C) Double triggering occurs when the ventilator cycles to exhalation while the patient’s continued inspiratory activity can retrigger the ventilator. It is characterized by two assisted breaths without expiration between them or with an expiration interval less than half the mean inspiratory time (two inspiratory peaks). This can be caused by early cycling of the breath, (e.g., high expiratory trigger sensitivity (ETS) in the pressure support modes, high level of pressure support, the very short time constant, or very high respiratory drive) [1]. Cycling asynchronies happen when there is...
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Future research

Resistance calculation

CONCLUSION

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