RESPIRATORY CARE

Research Article | *Original Research*

Multiplex Ventilation: A Simulation-based Study of Ventilating Two Patients with One Ventilator

https://doi.org/10.4187/respcare.07882

Cite as: RESPCARE 2020; 10.4187/respcare.07882

Received: 27 March 2020
Accepted: 15 April 2020

Multiplex Ventilation: A Simulation-based Study of Ventilating Two Patients with One Ventilator

Authors

Robert L. Chatburn MHHS, RRT-NPS, FAARC
Richard D. Branson, MS, RAARC
Umur Hatipoğlu, MD

Contributions

Literature Review: Chatburn
Data Collection: Chatburn
Study Design: Chatburn, Branson, Hatipoğlu
Data Analysis: Chatburn
Manuscript Preparation: Chatburn, Branson, Hatipoğlu
Manuscript Review: Chatburn, Branson, Hatipoğlu

Location of Study

Cleveland Clinic, Cleveland, OH, USA

Presentations

None

Financial Support

None

Conflicts of Interest

Robert L. Chatburn MHHS, RRT-NPS, FAARC
Consultant for IngMar Medical Inc, and Vyaire Medical Inc.
Rich Branson MS RRT
Consultant for Mallinckrodt, Ventec Life Systems, and Zoll

Key Words

Mechanical ventilation, ventilator modes, disaster medicine

Abstract

Background: The overwhelming demand for mechanical ventilators due to COVID-19 has stimulated interest in using one ventilator for multiple patients (multiplex ventilation). Despite a plethora of information on the Internet, there is little supporting evidence and no human studies. The risk of multiplex ventilation is that ventilation and PEEP effects are largely uncontrollable and depend on the difference between patient resistance, (R) and compliance (C). It is not clear whether volume control or pressure control is safer or more effective. We designed a simulation-based study to allow complete control over the relevant variables to determine the effects of various degrees of RC imbalance on tidal volume (V_T), end-expiratory lung volume (V_{EE}), and imputed pH. **Methods**: Two separate breathing simulators were ventilated with a ventilator using pressure control (PC) and volume control (VC) breaths. Evidence-based lung models simulated a range of differences in R and C (six pairs of simulated patients). Differences in V_T, V_{EE}, and imputed pH were recorded. **Results**: Depending on differences in R and C, differences in V_T ranged from 1% (equal R and C) to 79%. Differences in V_{EE} ranged from 2% to 109%. Differences in pH ranged from 0% to 5%. Failure due to excessive tidal volume (> 8 mL/kg) did not occur. Failure due to excessive V_{EE} difference (> 10%) was evident in 50% of patient pairs. There was no difference in failure rate between VC and PC. **Conclusions**: These experiments confirmed the potential for markedly different ventilation and oxygenation for patients with uneven respiratory system impedances during multiplex ventilation. Three critical problems must be solved to minimize risk: (1) partitioning of inspiratory flow from the ventilator individually between the two patients, (2) measurement of V_T delivered to each patient, and (3) provision for individual PEEP. We provide suggestions for solving these problems.

Quick Look

What is known

The use of one ventilator to ventilate more than one patient was suggested in 2006. To date, there are no published studies of actual use of multiplex ventilation in humans and only anecdotal short-term use in traumatic injury. There are several theoretical complications that must be considered before such use should be attempted.

What this study adds to our knowledge

This study confirmed the potential for markedly different ventilation and oxygenation for patients with very different respiratory system impedances during multiplex ventilation. Three critical problems must be solved to improve clinical management and minimize risk: (1) partitioning of inspiratory flow from the ventilator between the two patients for individualized V_T, (2) a means of measuring the V_T delivered to each patient, and (3) provision for individual PEEP, with the possibility of one patient having PEEP higher than the value set on the ventilator.

Striving to better, oft we mar what is well

King Lear Act 1

Shakespeare

Introduction

The notion that one ventilator could be used to ventilate more than one patient was suggested in 2006. We refer to this technique as multiplex ventilation because the word 'multiplex' is defined as a system or signal involving simultaneous transmission of several messages along a single channel of communication (analogous to transmitting gas destined to be more than one V_T from a single source). The original paper by Neyman and Irving [1] demonstrated ventilation of 4 simple test lungs using a single ventilator and four separate circuits. No scientific measurements were attempted. It was followed by a study by Paladino et al using four sheep.[2] This trial demonstrated that hourly blood gases were required to maintain adequate gas exchange in animals with normal lungs. They reported that normal animals had both hypercarbia and hypoxemia related to maldistribution of volumes These studies demonstrated severe limitations as noted by Branson et al.[3, 4] Yet, the idea has been resurrected by the recent COVID-19 pandemic due to the possibility of a shortage of mechanical ventilators. Indeed, social media has given this scheme a life of its own. One source claiming to allow ventilation of nine patients at once (https://interestingengineering.com/canadian-doctor-rigs-ventilator-to-treat-nine-patients-instead-of-just-one, accessed 3/23/30)!

To date, there are no published studies of actual use of multiplex ventilation in humans and only anecdotal short-term use in traumatic injury. This media report fails to report any meaningful data. There are several theoretical complications that must be considered before such use should be attempted. The two primary problems with any mode of ventilation are setting safe and effective values for tidal volume (V_T) and positive end-expiratory pressure (PEEP). These problems are exacerbated with multiplex ventilation because V_T and PEEP are not adjustable with the systems described in the literature.

When performing multiplex ventilation with two patients, they share the V_T output by the ventilator. Those shares are determined by the mechanical properties of their respective respiratory systems. They both get the same PEEP (set on the ventilator) but the effect on end expiratory lung volume (V_{EE}) depends on their individual compliances. Each respiratory system can be represented as a flow resistance (R, representing the natural and artificial airways) connected in series with a compliance (C, representing the lungs and chest wall), what we will call an RC circuit (the product of R and C also represents the respiratory system time constant). This is shown in Figure 1. These two RC circuits (and their individual time constants) are connected in parallel to the ventilator (i.e., they share the same pressure driving flow). The flow (and hence V_T) each patient receives depends on the relative flow impedances of their RC circuits; the higher the impedance, the lower the flow and V_T. Given that both patients share the same ventilatory frequency (i.e., the set breath rate on the ventilator), each patient receives a minute ventilation determined by their relative mechanical properties. Hence, as a rule of thumb, the patient with the lowest impedance will receive the largest V_T and highest minute ventilation (V_E). This could pose a risk of volutrauma to that patient and a risk of hypoventilation to the other patient.

PEEP is intended to increase end expiratory lung volume (V_{EE}), decrease intrapulmonary shunt, and improve oxygenation. But excessive PEEP (ie, intrathoracic pressure) has negative consequences. The risks of volutrauma and hemodynamic compromise appear to exceed the risk of atelectrauma.[5]

At end expiration, if flow is zero, each patient is exposed to the same level of PEEP. Hence, their end expiratory lung volumes will be determined by respiratory system compliance (i.e., volume = pressure × compliance). When patients have different compliances, they will experience different risks of both poor oxygenation (PEEP too low) and hemodynamic compromise (PEEP too high).

Finally, for multiplex ventilation to work at all, patients must be chemically paralyzed, otherwise random trigger efforts would invoke chaos in the ventilatory pattern leading to alarms and ventilatory compromise. Clearly one patient should not be allowed to determine the minute ventilation of the other by means of a higher ventilatory drive and trigger rate. It is also theoretically possible that the increased compliance of the

parallel ventilator circuits may defeat triggering efforts and gas may move between circuits (pendelluft), risking cross infection. Note that parallel compliances are additive, and this increased circuit compliance may be rejected by the ventilator during a pre-use operational verification procedure. If this is true, then compensation for patient circuit compressible volume during volume control ventilation must be performed manually.

While these risks of multiplex ventilation are patently obvious, their magnitudes (as functions of respiratory system RC) are not. Nor is it clear whether volume control, VC (ie, preset tidal volume and inspiratory flow[6]) or pressure control, PC (preset inspiratory waveform or inspiratory pressure proportional to inspiratory effort[6]) would be preferable. Therefore, we designed a simulation-based study to allow complete control over the relevant variables. Specifically, we sought to determine the effects of various degrees of RC imbalance on resultant imbalance in V_T, minute ventilation$\dot{V}_E$, V_{EE}, and imputed $PaCO_2$.

Methods

We restricted this study to the case of ventilating two patients with one ventilator for simplicity. The two patients were connected in parallel in two configurations. The first configuration was identical to that originally described by Neyman and Irving[1] (Figure 2). However, in this configuration, when the impedance of Patient 1 is higher than Patient 2 (imagine complete obstruction for clarity), gas is shunted from the y adapter of Patient 1, through the exhalation limb (containing CO_2 from the last exhalation) and into Patient 2.

On the other hand, to individualize V_T delivery, it is possible to balance the flows to the two patients by increasing the resistance of the inspiratory circuit of one patient. For example, if the need is to decrease the V_T of Patient 1, then increasing impedance in that circuit can accomplish that, but without one-way valves, it will cause some amount of CO_2 re-breathing to Patient 2 (Figure 3). Therefore, one way-valves should be placed in the expiratory limbs for both patients (Figure 4). Note that for some ventilators, such valves may interfere with patient triggering of inspiration as the pressure sensor for triggering is in the expiratory portion of the ventilator. However, as mentioned above, paralysis is required so patient initiated triggering is not an issue.

Mechanical ventilation was implemented with a Servo-i (Getinge Medical, Rastatt, Germany) using both volume control continuous mandatory ventilation with set-point targeting (VC-CMVs) or pressure control continuous mandatory ventilation with set-point targeting (PC-CMVs).[6] Settings used are shown in Table 1.

The ventilator was connected to 2 breathing simulators (ASL 5000, RespiSim sw v3.6, IngMar Medical). Simulation models created with this device are comprised of a lung model (respiratory system R and C) and an effort model (muscle pressure, P_{mus}, as function of time). Lung model parameters are shown in Table 3. The effort model was set to simulate a paralyzed patient (i.e., maximum $P_{mus} = 0$, representing no inspiratory trigger effort).

The design of the lung models (Table 2) was based on several considerations. First, the values for R and C have to be realistic.[7] This was assured by using values from the study by Arnal et al,[8] and by making sure they were similar to the values from a small number of patients ventilated for COVID-19 at Cleveland Clinic. Second, we wanted to evaluate the effects of RC imbalance for R separately from C, to determine which might have a largest effect on the distribution of V_T and minute ventilation ($\dot{V}_E$) Third, we wanted to define extreme cases in order to roughly define the performance envelope of multiplex ventilation.

Outcome Variables

The effects of unbalanced lung mechanics were characterized by three variables: tidal volume (V_T, both in mL and mL/kg, assuming a 70 kg ideal body weight for both patients), $\dot{V}_E$, end expiratory lung volume (V_{EE}) and imputed values for arterial carbon dioxide tension ($PaCO_2$) and pH. Tidal volume was reported by the simulator (as measured meaning uncorrected for temperature or humidity) and obtained from recordings using the Multi-Parameter Trend option of the Post-Run Analysis feature of the ASL software. Minute ventilation was calculated as the product of measured average V_T and breath rate set on the ventilator. V_{EE} was obtained from lung volume waveform recordings using the Multi-Parameter Waveforms option of the Post-Run Analysis feature of the ASL software ($V_{EE} = 0$ for PEEP = 0). Imputed $PaCO_2$ was calculated as follows:[9]

$$PaCO_2 = \frac{0.863 \times \dot{V}CO_2}{\dot{V}_E \times \left(1 - \frac{V_D}{V_T}\right)} \quad (1)$$

where $PaCO_2$ (mm Hg) is imputed arterial carbon dioxide tension, 0.863 is the factor to reconcile measurement units, VCO_2 is carbon dioxide output (assumed to be 200 mL/min), $\dot{V}_E$ is minute ventilation (L/min) and V_D/V_T is dead space fraction (assumed to be 0.5, an average of our COVID-19 patient).

Imputed pH was calculated as from the equation:[9]

$$pH = 6.1 + \log\left(\frac{24}{0.03 \times PaCO_2}\right) \quad (2)$$

where 24 is normal bicarbonate concentration.

Data Analysis

All data are reported as the mean of at least 10 breaths. The difference between simulated patients for any variable was calculated as the absolute difference of the two values for that variable divided by the average of the two values. Standard deviations are not given because they are very small with this type of simulation (eg, coefficient of variation for V_T was approximately 0.05 %). Hence, any statistical test for difference between means (eg a t-test) will almost always yield significant results for differences that are not clinically important. For example, in the case of VC-CMVs where both patients have identical V_T, the measured mean (standard deviation) V_T values were 396.179 (0.206) mL and 392.884 (0.194) mL. A t-test for difference between the means gives a P value of < 0.001. However, the difference amounts to only 1%, which is much less than the error of the ventilator's V_T control system. Hence we defined this *a priori* as not clinically important.

To interpret these data, we assumed the following arbitrary safe limits: acceptable tidal volume delivery = 4-8 mL/kg, acceptable difference in V_{EE} = 10%, acceptable pH = 7.20 – 7. 45. The lower limit on V_T is, in practice, determined by V_D, which was 200 mL in this simulation.

Results

Volume Control Ventilation - Circuits with no one-way valves

Experimental data for volume control ventilation are shown in Table 3. When the lung mechanics of the two simulated patients are identical, there was no important difference in outcome variables. However, with unequal compliance the distribution of ventilation was markedly different. Comparing a simulated patient with mild ARDS with one that has severe ARDS, there was a 32% difference in V_T (lower C resulted in lower V_T). The difference in C produced a 76% difference in V_{EE}, and a 2% difference in pH. The change in V_{EE} exceeded the safe limits. Extreme differences in compliance further exacerbated differences in the distribution of VT's. Comparing a simulated normal patient (eg, early in the progression of COVD-19) with one that has severe ARDS, there was a 54% difference in V_T (much lower C resulted in much lower V_T). The difference in C produced an 86% difference in V_{EE}, and a 3% difference in pH. The differences in V_{EE} and pH exceeded safe limits.

The impact of resistance was not as severe as compliance changes. The inequality in R of the simulated patient was modeled using the R of a patient with a heated humidifier (lower R) compared to one that has a heat and moisture exchanger (HME). We would probably only use HME in the practice of multiplex ventilation, and not mix the two types of humidification. There was a 23% difference in V_T (higher R resulted in lower V_T). The difference in R produced a 2% difference in V_{EE}, and a 1% difference in pH. None of the variables exceeded the safe limits. Comparing a simulated patient with mild ARDS to a simulated patient with both asthma and ARDS, there was a 79% difference in V_T (much higher R resulted in much lower V_T). The difference in R produced a 7% difference in V_{EE}, and a 5% difference in pH. The pH fell below the pre-defined safe limit.

The impact of extreme differences in time constant (τ) produced large changes in V_{EE}. Comparing a simulated patient with severe ARDS to a patient with COPD (early in the progression of COVD-19), there was a 6% difference in V_T (the longer time constant of the COPD patient resulted in lower V_T). The

difference in R produced a 108% difference in V_{EE}, and a 0% difference in pH. The V_{EE} far exceeded the safe limit.

Pressure Control Ventilation - Circuits with no one-way valves

As with volume control ventilation, we assumed the following arbitrary limits for delivering safe mechanical ventilation to patients with ARDS to interpret the data: acceptable V_T delivery = 4-8 mL/kg, acceptable difference in V_{EE} = 10%, acceptable pH = 7.20 – 7. 45. The lower limit on V_T is, in practice, determined by V_D, which was 200 mL in this simulation. Experimental data for pressure control ventilation are shown in Table 4.

When the lung mechanics of the two simulated patients are identical, there was no important difference in outcome variables. Unequal compliance resulted in changes in V_T distribution as predicted. Comparing a simulated patient with mild ARDS with one that has severe ARDS, there was a 59% difference in V_T (lower C resulted in lower V_T). The difference in C produced a 76% difference in V_{EE}, and a 4% difference in pH. The change in V_T and V_{EE} exceeded the safe limits. Extreme differences in compliance created greater differences. Comparing a simulated normal patient (e.g., early in the progression of COVD-19) with one that has severe ARDS, there was a 64% difference in V_T (much lower C resulted in much lower V_T). The difference in C produced an 86% difference in V_{EE}, and a 4% difference in pH. The differences in V_T, V_{EE}, and pH exceeded safe limits.

Changes in resistance resulted in less severe distribution of volumes. In the case of mildly different resistances there was a 21% difference in V_T (higher R resulted in lower V_T). The difference in R produced a 2% difference in V_{EE}, and a 1% difference in pH. None of the variables exceeded the safe threshold.

Comparing a simulated patient with mild ARDS to a patient with both asthma and ARDS (extreme R differences), there was a 69% difference in V_T (much higher R resulted in much lower V_T). The difference in R produced a 7% difference in V_{EE}, and a 4% difference in pH. The V_T and pH fell below the safe limits.

Extreme differences in τ produced large difference in V_{EE}. Comparing a simulated patient with severe ARDS to a patient with COPD (early in the progression of COVD-19), there was a 9% difference in V_T (the longer

time constant of COPD resulted in lower V_T). The difference in R produced a 106% difference in V_{EE}, and a 1% difference in pH. The V_{EE} far exceeded the safe limit.

Volume Control vs Pressure Control Ventilation - Circuits with no one-way valves

When the lung mechanics of the two simulated patients are identical, there was no important difference in outcome variables between VC and PC. When compliances are unbalanced, PC produced more difference in V_T than VC (59%-64%, vs 32%-54% respectively). When resistances are unbalanced, PC produced less difference in V_T than VC (21%-69% vs 23%-79%, respectively). Extreme differences in τ resulted in similar differences in volume distribution. Comparing a simulated patient with severe ARDS to a patient with COPD, PC produced a slightly greater difference in V_T than VC (9% vs 6%).

Circuits with One-way Valves Added

Experimental data for VC ventilation are shown in Table 5. Data for PC ventilation are shown in table 6. In comparison with the data for multiplex ventilation without one-way valves (Tables 3 and 4), several differences can be seen.

For VC ventilation, the use of one-way valves increased the difference between V_Ts for the case of unequal C (32% without valves vs 50% with valves). This effect was not seen in the case of extreme inequality in C. The use of one-way valves decreased the difference between V_Ts for the case of unequal R (23% without valves vs 24% with valves) and this was similar for the case of extreme inequality in R (79% without valves vs 72% with valves). The use of one-way valves increased the difference between V_Ts for the case of inequality in τ (6% without valves vs 8% with valves).

For PC ventilation (Table 6), the use of one-way valves had virtually no effect on the difference in tidal volumes for the case of unequal C (59% without valves vs 58% with valves). This was similar to the case of extreme inequality in C (64% without valves vs 63% with valves). This held true for inequality in R (21% without valves vs 22% with valves) and extreme inequality in R (69% without valves vs 69% with valves) as well as extreme inequality in τ (9% without valves vs 8% with valves).

Volume Control With Ramp Flow vs Constant Flow

We repeated the VC experiments (with one-way valves) using a descending ramp flow (RF) instead of constant flow (CF) because the latter is very popular among respiratory therapists in the United States. We kept the tidal volume and inspiratory time the same as for constant flow. Data are shown in Table 7. The overall pattern of failure (cells with red fill) was the same as for VC with CF and for PC.

When the lung mechanics of the two simulated patients are identical, there was no important difference in outcome variables between CF and RF (see above). When compliances are unbalanced, RF produced a greater difference in V_T than CF (59%-70% vs 50%-54%, respectively). RF results were similar to PC results in this regard.

When resistances are unbalanced, RF produced less difference in V_T than CF (19%-62% vs 24%-72%, respectively). RF results were similar to PC results in this regard (see above). Extreme difference in τ had a minor impact on volume distribution. Comparing a simulated patient with severe ARDS to a patient with COPD, RF produces a slightly lower difference in V_T than CF (7% vs 8%).

Discussion

This study confirms that during multiplex ventilation with two patients, major outcome variables for each patient, such as $\dot{V}_E$ (determinant of $PaCO_2$) and V_{EE} (determinant of PaO_2 in ARDS) are dependent on the distribution of lung mechanics (R and C) between patients. Lower compliance and higher resistance for one patient will decrease V_T, $\dot{V}_E$, and pH for that patient compared to the other. The patient with the highest C will get the largest V_T and greatest effect of PEEP (i.e., largest V_{EE}). For the case of extreme inequality in τ, (i.e., the simulated ARDS patient vs the one with both ARDS and COPD), the decrease in V_T due to increased resistance was partially balanced by the effect of increasing V_T by the higher compliance. Our comparison between normal mechanics and ARDS was done for theoretical and illustrative purposes only. However, we emphasize the importance of thorough screening to try and avoid pairing patients with co-

morbidities that complicate matching such as asthma or COPD. Importantly, matching patients simply by height or predicted body weight, as suggested by others[1] is unwise without knowledge of lung mechanics.

Volume control ventilation provides a more equal distribution of V_T than pressure control in the case of unequal compliances, but less equal distribution with differing resistances. These observed differences between VC and PC are supported by a previous theoretical study.[10] That study compared two hypothetical lung units with different impedances (analogous to two patients with different respiratory system impedances) during VC (constant inspiratory flow) and PC (constant inspiratory pressure). The results can be interpreted to suggest that for patients with equal impedances, both PC and VC result in equal distribution of volume between the patients. For patients with different compliances but equal resistances, VC gives more uniform V_T distribution than PC and possibly lower risk of either hypoventilation or volutrauma to one patient. For patients with different resistances but equal compliances, PC gives more uniform V_T distribution than VC.[10] Failure of ventilation (ie, imputed pH < 7.20) occurred during VC for the cases of extremely unequal C and extremely unequal R. Failure of ventilation occurred during PC for the same cases.

Failure of PEEP can be inferred from V_{EE} results. For VC, the set PEEP would be too low for one patient in the case of unequal C but not unequal R. On the other hand, set PEEP would be too high for one patient in the case of extremely unequal τ (ARDS versus ARDS + asthma). For PC, the PEEP effects were the same.

Finally, although not mentioned in the original studies of multiplex ventilation, from a theoretical standpoint (Figure 4) it appears that one-way valves are a necessary addition to the exhalation limbs of the circuits. Addition of one-way valves had minor effects on volume distribution in VC but not in PC. We cannot infer effects of rebreathing (i.e., inhaling previously exhaled CO_2) because we did not test this hypothesis (see Limitations section). Use of chemical paralysis is required for multiplex ventilation to avoid the effects on minute ventilation of one patient triggering at a different rate than the other. Use of one-way valves may pressure monitoring, depending on the design of the ventilator.

Problems and Directions for Further Research

As this study implies, matching subjects for both resistance and compliance at the initiation is prudent. However, as the disease evolves in each patient, disparities are almost certain to arise. Catastrophic failure in one subject (e.g., pneumothorax or plugged endotracheal tube) may result in injury to the contralateral patient. It follows that the extent of this injury may be mitigated by use of PC ventilation. The complexities of this technique require that it only be done following ethics board approval and family consent to treatment. Only experts in mechanical ventilation should attempt this technique under extreme duress of ventilator supply and demand.

Based on our data, it appears that use of multiplex ventilation without modification may be temporarily successful if patients are adequately matched for lung mechanics at initiation of ventilation. The question is how closely they must match. For example, when the difference in compliances was high enough (ie, mild vs severe ARDS) the resultant V_T and pH were within safe limits. But this was not true then the difference in compliances was 86%, when both V_T and pH were outside safe limits. This argues for the need of continuous V_T monitoring. Multiplex ventilation will fail to adequately support at least one patient as disease progresses and lung mechanics begin to differ to a great enough extent. Indeed, it appears that there are two major reasons for the failure: low V_T and either low or high PEEP.

We suggest that (aside from using one-way valves), pressure control ventilation is preferable when performing multiplex ventilation. In the first place, the vastly increased patient circuit compliance due to multiple parallel patients most likely will not allow the ventilator to pass a pre-use operation verification procedure. We found this to be a problem with only two patient circuits in parallel. Furthermore, volume control ventilation is not recommended because a sudden increase in flow impedance of one patient (eg, tube kinking or mucous plug, or advancement into the right main-stem bronchus) will create a sudden increase in tidal volume to the other patient, possibly to dangerous levels. The increase in total impedance seen by the ventilator will register as a sudden increase in airway pressure. If this exceeds the high pressure alarm setting, then inspiration will be cycled off and *both* patients will fail to be ventilated as long as the alarm condition remains. This sequence of

events cannot occur with pressure control ventilation. On the contrary, the patient whose flow impedance remains unchanged will continue to receive ventilation so long as the pressure waveform remains undisturbed. Note: It is incorrect to assume that alterations in one patient's respiratory mechanics will not affect the volume delivered to the other patient sharing the ventilator. For example, Table 6 shows that when simulated Patient-1 with mild ARDS was paired with another with mild ARDS, Patient-1 got a tidal volume of 5.3 mL/kg. However, when the same simulated Patient-1 was paired with one that had severe ARDS, Patient-1 then received an inadequate tidal volume of 3.9 mL/kg. The same effect was observed when Patient-1 was paired with a simulated patient with ARDS and asthma.

Three issues that must be addressed to make multiplex ventilation more manageable at the bedside and maximize safety. The first important issue is that because V_T distribution between patients depends on the distribution of respiratory system mechanics, then multiplex ventilation will fail if their impedances differ beyond some critical threshold due to the different time courses of disease (eg, extreme imbalance in R or C, see red filled cells in Tables 3-7). Hence, some means of diverting flow from one patient to the other is important to extend the time that multiplex ventilation is remains effective for both patients. Multiple sources have suggested placing flow restrictor valves in the patient circuit. Our experience suggests that it is not as simple as described. For some ventilators, the pressure waveform is controlled by a signal generated by a pressure sensor in the exhalation manifold. This means that any obstruction to flow in the patient circuit between the flow outlet of the ventilator and the exhalation manifold (eg, by placing adjustable valves) may alter the shape of the pressure waveform, ie, increasing the pressure rise time, and altering volume distribution.

Second, given the first issue, there is a need to monitor the two separate V_T's. Unfortunately, simple, inexpensive stand-alone monitors are not commercially available. This represents an opportunity for any manufacturer that can create and deploy such a device. Alternatively, preliminary results from our related research indicate that there is a way configure the patient circuit such that one patient exhales to atmosphere and one through the ventilator's exhalation manifold. If this can be accomplished, then the exhaled tidal

volume of one patient is displayed on the ventilator and the other is simply the difference between the displayed inhaled and exhaled values. More research in this area is imperative.

Third, our data show that there is a large difference in the effect of PEEP (i.e., V_{EE}) due to even a modest difference in compliance between the patients (see red filled cells in Tables 3 to 7). When this difference reaches some critical threshold there may be a situation where even after careful adjustment of the PEEP setting on the ventilator, adverse oxygenation or hemodynamic consequences remain for one patient. Again, solutions have been presented on the Internet, but without any supporting evidence of effective performance. We believe we have a solution for independent PEEP control using standard patient circuit parts, but it is still in testing.

The point of explaining these three issues is that by identifying the problem, an effective crowd sourced solution may emerge in a timely fashion. What we hope to avoid is failed attempts to improve multiplex ventilation due to a misunderstanding of the basic theory. Failure may come to light, perhaps catastrophically, only when used on patients if appropriate simulation-based research is not conducted first.

Multiplex Ventilation of More Than Two Patients

If you believe YouTube, ventilating 4, 9, or even 10 patients with one ventilator is just as easy as ventilating two. It might be reasonable to presume that the responses of, say, 4 patients would fall along the spectrum of extreme cases shown in this study. However, the practical problems with monitoring V_T and optimizing PEEP increase not linearly, but exponentially. We do not recommend multiplex ventilation unless some means of flow balancing, V_T monitoring, and customizing PEEP have been incorporated into the procedure and sufficient skill has been acquired in their use. These social networking demonstrations suggest a simple solution which in fact, is fraught with peril. It is clear the presenters have not thought beyond the simplest concepts of the physical connection of tubing. These ill-advised and academically inadequate demonstrations encourage a *laissez faire* approach to a serious challenge and should be taken down.

Limitations

The main limitations of this study are the same for any simulation-based research. We chose only a small set of mechanical lung parameters among an infinite variety that may be experienced in clinical practice. While we chose evidence-based values, there are as yet no published data on respiratory system mechanics for COVID-19 patients. Note that our results regarding use of one way valves test the hypothesis that these valves affect the distribution of tidal volume between the two patients. It does not test any hypothesis about rebreathing, which would have required a breathing simulator that exhaled carbon dioxide. Clinical experience and formal research of multiplex ventilation are necessary before this approach can be adequately evaluated.

Conclusions

These experiments confirmed the potential for markedly different ventilation and oxygenation for patients with uneven respiratory system impedances during multiplex ventilation. Therefore, ventilation of just two patients with one ventilator, presents substantial practical problems that may preclude its use in randomly selected pairs of patients. Even if patients are matched in terms of R and C, the initial values are likely to diverge as the disease progresses (for better or worse) to the point that one patient fails and endangers the other patient.

Results of this simulation-based study suggest that three critical problems must be solved to minimize risk: (1) partitioning of inspiratory flow from the ventilator between the two patients for individualized V_{TS}, (2) some means of measuring the V_T delivered to each patient, and (3) provision for individual PEEP, with the possibility of one patient having PEEP higher than the value set on the ventilator. These problems are ripe for innovative solutions.

Figure Legends

Figure 1 Electrical circuit equivalent of multiplex ventilator circuit. RRS = resistance of respiratory system, CRS = compliance of respiratory system.

Figure 2. Schematic of multiplex ventilation with two patients connected in parallel. No one-way valves. Potential CO_2 rebreathing due to increased impedance of Patient 1 relative to Patient 2.

Figure 3. Schematic of multiplex ventilation with two patients connected in parallel. No one-way valves. Potential CO_2 rebreathing due to increased impedance of the inspiratory limb of Patient 1.

Figure 4. Schematic of multiplex ventilation with two patients connected in parallel. One-way valve added to prevent re-breathing.

Figure 5. Electrical circuit equivalent of multiplex ventilator circuit with adjustable resistors in each inspiratory limb. RRS = resistance of respiratory system, CRS = compliance of respiratory system, Rvar = variable resistance (eg, pneumatic globe valve).

Figure 6. Electrical circuit equivalent of multiplex ventilator circuit with adjustable resistors in each inspiratory limb. RRS = resistance of respiratory system, CRS = compliance of respiratory system. The variable resistors are coupled such that increasing resistance in one decreases resistance in the other, hence proportioning flow to the two patients, ideally while maintaining the same total resistance to avoid altering the pressure waveform during PC ventilation.

References

1. Neyman G, Irvin CB. A single ventilator for multiple simulated patients to meet disaster surge. Acad Emerg Med 2006;13(11):1246-1249.
2. Paladino L, Silverberg M, Charchaflieh JG, Eason JK, Wright BJ, Palamidessi N, et al. Increasing ventilator surge capacity in disasters: ventilation of four adult-human-sized sheep on a single ventilator with a modified circuit. Resuscitation 2008;77(1):121-126.
3. Branson RD, Blakeman TC, Robinson BR, Johannigman JA. Use of a single ventilator to support 4 patients: laboratory evaluation of a limited concept. Respir Care 2012;57(3):399-403.
4. Branson R, L R. A single ventilator for multiple simulatd patients to meet disaster surge. Acad Emerg Med 2006;13(12):1352 (author reply 1353-1354).
5. Gattinoni L, Quintel M, Marini JJ. "Less is More" in mechanical ventilation. Intensive Care Med 2020.
6. Chatburn RL, El-Khatib M, Mireles-Cabodevila E. A taxonomy for mechanical ventilation: 10 fundamental maxims. Respir Care 2014;59(11):1747-1763.
7. Chatburn RL. Simulation-Based Evaluation of Mechanical Ventilators. Respir Care 2018;63(7):936-940.
8. Arnal JM, Garnero A, Saoli M, Chatburn RL. Parameters for Simulation of Adult Patients During Mechanical Ventilation. Respir Care 2017;63(2):158-168.
9. Chatburn RL, Mireles-Cabodevil E. Handbook of Respiratory Care 3rd Edition. Sudbury: Jones & Bartlett Learning; 2011.
10. Chatburn R, El-Khatib M, Smith P. Respiratory system behavior with constant inspiratory pressure and flow. Respiratory Care 1994;39(10):979-988.

Table 1. Ventilator settings.

Mode	VC-CMVs
V_T tot (L)	800
Freq (bpm)	20
T_I (s)	0.9
$T_{rise\ (s)}$	0.0
PEEP (cm H_2O)	15

Table 2. Experimental lung models. R = resistance, C = compliance, τ = time constant = R×C.

Experiment	A		B		C	
Use Case	Same RC		Unequal C		Unequal C (extreme)	
Patient	1	2	1	2	1	2
Diagnosis	ARDS-Mild	ARDS-Mild	ARDS-Mild	ARDS-Sev	Normal	ARDS-Sev
R (cm H_2O/L/s)	10	10	10	10	10	10
C (mL/cm H_2O)	45	45	45	20	50	20
τ (s)	0.45	0.45	0.45	0.2	0.6	0.2

Experiment	D		E		F	
Use Case	Unequal R		Unequal R (extreme)		Unequal τ (extreme)	
Patient	1	2	1	2	1	2
Diagnosis	ARDS-Mild	ARDS-Mild	ARDS-Mild	Asthma-ARDS	ARDS-Sev	COPD
R (cm H_2O/L/s)	10	15	10	30	10	25
C (mL/cm H_2O)	45	45	45	45	20	60
τ (s)	0.45	0.675	0.45	1.35	0.2	1.5

Table 3. Experimental data for volume control ventilation without one-way valves. Values shown in green are considered the most important clinical outcomes.
Red shading indicates that the value is outside pre-defined "safe" limits. R = resistance, C = compliance, τ = time constant = R×C. Sev = severe

Experiment	A			B			C		
Use Case	Same RC			Unequal C			Unequal C (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	ARDS-Sev		Normal	ARDS-Sev	
V_T (L)	0.396	0.392	1%	0.406	0.293	32%	0.467	0.267	54%
V_E (L/min)	7.9	7.8	1%	8.1	5.9	32%	9.3	5.3	54%
PaCO2	44	44	1%	43	59	32%	37	65	54%
V_T (mL/kg)	5.7	5.6	1%	5.8	4.2	32%	6.7	3.8	54%
V_{EE} (L)	0.7	0.7	0%	0.7	0.313	76%	0.793	0.316	86%
pH	7.36	7.36	0%	7.37	7.23	2%	7.44	7.19	3%

Experiment	D			E			F		
Use Case	Unequal R			Unequal R (extreme)			Unequal τ (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	Asthma-ARDS		ARDS-Sev	COPD	
V_T (L)	0.440	0.349	23%	0.499	0.216	79%	0.406	0.382	6%
V_E (L/min)	8.8	7.0	23%	10.0	4.3	79%	8.1	7.6	6%
PaCO2	39	49	23%	35	80	79%	43	45	6%
V_T (mL/kg)	6.3	5.0	23%	7.1	3.1	79%	5.8	5.5	6%
V_{EE} (L)	0.7	0.713	2%	0.713	0.766	7%	0.318	1.064	108%
pH	7.41	7.31	1%	7.46	7.10	5%	7.37	7.35	0%

Table 4. Experimental data for pressure control ventilation without one-way valves. Values shown in green are considered the most important clinical outcomes.
Red shading indicates that the value is outside pre-defined "safe" limits. R = resistance, C = compliance, τ = time constant = R×C. Sev = severe

Experiment	A			B			C		
Use Case	Same RC			Unequal C			Unequal C (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	ARDS-Sev		Normal	ARDS-Sev	
V_T (L)	0.421	0.417	1%	0.500	0.272	59%	0.485	0.250	64%
V_E (L/min)	8.4	8.3	1%	10.0	5.4	59%	9.7	5.0	64%
PaCO2	41	41	1%	35	63	59%	36	69	64%
V_T (mL/kg)	6.0	6.0	1%	7.1	3.9	59%	6.9	3.6	64%
V_{EE} (L)	0.700	0.700	0%	0.700	0.314	76%	0.789	0.316	86%
pH	7.39	7.39	0%	7.47	7.20	4%	7.45	7.16	4%

Experiment	D			E			F		
Use Case	Unequal R			Unequal R (extreme)			Unequal τ (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	Asthma-ARDS		ARDS-Sev	COPD	
V_T (L)	0.457	0.369	21%	0.493	0.241	69%	0.376	0.412	9%
V_E (L/min)	9.1	7.4	21%	9.9	4.8	69%	7.5	8.2	9%
PaCO2	38	47	21%	35	72	69%	46	42	9%
V_T (mL/kg)	6.5	5.3	21%	7.0	3.4	69%	5.4	5.9	9%
V_{EE} (L)	0.700	0.717	2%	0.719	0.769	7%	0.319	1.042	106%
pH	7.43	7.33	1%	7.46	7.15	4%	7.34	7.38	1%

Table 5. Experimental data for volume control ventilation with one-way valves. Values shown in green are considered the most important clinical outcomes.
Red shading indicates that the value is outside pre-defined "safe" limits. R = resistance, C = compliance, τ = time constant = R×C. Sev = severe

Experiment	A			B			C		
Use Case	Same RC			Unequal C			Unequal C (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	ARDS-Sev		Normal	ARDS-Sev	
V_T (L)	0.368	0.365	1%	0.451	0.271	50%	0.465	0.266	54%
V_E (L/min)	7.4	7.3	1%	9.0	5.4	50%	9.3	5.3	54%
PaCO2	47	47	1%	38	64	50%	37	65	54%
V_T (mL/kg)	5.3	5.2	1%	6.4	3.9	50%	6.6	3.8	54%
V_{EE} (L)	0.717	0.717	0%	0.717	0.316	78%	0.802	0.316	87%
pH	7.33	7.33	0%	7.42	7.20	3%	7.43	7.19	3%

Experiment	D			E			F		
Use Case	Unequal R			Unequal R (extreme)			Unequal τ (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	Asthma-ARDS		ARDS-Sev	COPD	
V_T (L)	0.408	0.321	24%	0.496	0.233	72%	0.369	0.342	8%
V_E (L/min)	8.2	6.4	24%	9.9	4.7	72%	7.4	6.8	8%
PaCO2	42	54	24%	35	74	72%	47	50	8%
V_T (mL/kg)	5.8	4.6	24%	7.1	3.3	72%	5.3	4.9	8%
V_{EE} (L)	0.721	0.739	2%	0.723	0.768	6%	0.326	1.074	107%
pH	7.38	7.27	1%	7.46	7.13	4%	7.33	7.30	0%

Table 6. Experimental data for pressure control ventilation with one-way valves. Values shown in green are considered the most important clinical outcomes.
Red shading indicates that the value is outside pre-defined "safe" limits. R = resistance, C = compliance, τ = time constant = R×C. Sev = severe

Experiment	A			B			C		
Use Case	Same RC			Unequal C			Unequal C (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	ARDS-Sev		Normal	ARDS-Sev	
V_T (L)	0.37	0.367	1%	0.496	0.273	58%	0.480	0.251	63%
V_E (L/min)	7.4	7.3	1%	9.9	5.5	58%	9.6	5.0	63%
PaCO2	47	47	1%	35	63	58%	36	69	63%
V_T (mL/kg)	5.3	5.2	1%	7.1	3.9	58%	6.9	3.6	63%
V_{EE} (L)	0.714	0.71	1%	0.715	0.314	78%	0.797	0.318	86%
pH	7.33	7.33	0%	7.46	7.20	4%	7.45	7.17	4%

Experiment	D			E			F		
Use Case	Unequal R			Unequal R (extreme)			Unequal τ (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	Asthma-ARDS		ARDS-Sev	COPD	
V_T (L)	0.406	0.326	22%	0.523	0.254	69%	0.351	0.38	8%
V_E (L/min)	8.1	6.5	22%	10.5	5.1	69%	7.0	7.6	8%
PaCO2	43	53	22%	33	68	69%	49	45	8%
V_T (mL/kg)	5.8	4.7	22%	7.5	3.6	69%	5.0	5.4	8%
V_{EE} (L)	0.721	0.733	2%	0.719	0.797	10%	0.321	1.089	109%
pH	7.37	7.28	1%	7.48	7.17	4%	7.31	7.35	0%

Table 7. Experimental data for control ventilation with ramp flow. Values shown in green are considered the most important clinical outcome Red shading indicates that the value is outside pre-defined "safe" limits. R = resistance, C = compliance, t = time constant (t = R×C).

Experiment	A			B			C		
Use Case	Same RC			Unequal C			Unequal C (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	ARDS-Sev		Normal	ARDS-Sev	
V_T (L)	0.337	0.334	1%	0.43	0.235	59%	0.457	0.219	70%
V_E (L/min)	6.7	6.7	1%	8.6	4.7	59%	9.1	4.4	70%
PaCO2	51	52	1%	40	73	59%	38	79	70%
V_T (mL/kg)	4.8	4.8	1%	6.1	3.4	59%	6.5	3.1	70%
V_{EE} (L)	0.717	0.717	0%	0.717	0.316	78%	0.802	0.316	87%
pH	7.29	7.29	0%	7.40	7.14	4%	7.43	7.11	4%

Experiment	D			E			F		
Use Case	Unequal R			Unequal R (extreme)			Unequal τ (extreme)		
Patient	1	2	Δ	1	2	Δ	1	2	Δ
Diagnosis	ARDS-Mild	ARDS-Mild		ARDS-Mild	Asthma-ARDS		ARDS-Sev	COPD	
V_T (L)	0.367	0.303	19%	0.442	0.234	62%	0.321	0.345	7%
V_E (L/min)	7.3	6.1	19%	8.8	4.7	62%	6.4	6.9	7%
PaCO2	47	57	19%	39	74	62%	54	50	7%
V_T (mL/kg)	5.2	4.3	19%	6.3	3.3	62%	4.6	4.9	7%
V_{EE} (L)	0.721	0.739	2%	0.723	0.768	6%	0.326	1.074	107%
pH	7.33	7.25	1%	7.41	7.14	4%	7.27	7.30	0%