External Jet Nebulization and Measured Ventilator Performance

Jeyanthan Jayakumaran, Gerald C Smaldone, and Ann D Cuccia

BACKGROUND: During invasive ventilation, external flow jet nebulization results in increases in displayed exhaled tidal volumes (V_T). We hypothesized that the magnitude of the increase is inaccurate. An ASL 5000 simulator measured ventilatory parameters over a wide range of adult settings: actual V_T, peak inspiratory pressure (PIP), and time to minimum pressure. METHODS: Ventilators with internal and external flow sensors were tested by using a variety of volume and pressure control modes (the target V_T was 420 mL). Patient conditions (normal, COPD, ARDS) defined on the ASL 5000 were assessed at baseline and with 3.5 or 8 L/min of added external flow. Patient-triggering was assessed by reducing muscle effort to the level that resulted in backup ventilation and by changing ventilator sensitivity to the point of auto-triggering. RESULTS: Results are reported as percentage change from baseline after addition of 3.5 or 8 L/min external flow. For ventilators with internal flow sensors, changes in displayed exhaled V_T ranged from 10% to 118%, however, when using volume control, actual increases in actual V_T and PIP were only 4%–21% ($P = .063, .031$) and 6%–24% ($P = .25, .031$), respectively. Changes in actual V_T correlated closely with changes in PIP ($P < .001$; $R^2 = 0.68$). For pressure control, actual V_T decreased by 3%–5% ($P = .031$) and 4%–9% ($P = .031$) with 3.5 and 8 L/min respectively, PIP was unchanged. With external flow sensors at the distal Y-piece junction, volume and pressure changes were statistically insignificant. The time to minimum pressure increased at most by 8% ($P = .02$) across all modes and ventilators. The effects on muscle pressure were minimal (~1 cm H_2O), and ventilator sensitivity effects were nearly undetectable. CONCLUSIONS: External flow jet nebulization resulted in much smaller changes in volume than indicated by the ventilator display. Statistically significant effects were confined primarily to machines with internal flow sensors. Differences approached the manufacturer-reported variation in ventilator baseline performance. During nebulizer therapy, effects on V_T can be estimated at the bedside by monitoring PIP. *Key words: aerosols; nebulizers and vaporizers; administration; inhalation; ventilators; mechanical; drug delivery; drug therapy; jet nebulizer; mechanical ventilation.* [Respir Care 2024;69(7):790–798. © 2024 Daedalus Enterprises]

Introduction

During mechanical ventilation, aerosolized medications have been traditionally delivered by using jet nebulizers.[1] Departments of respiratory therapy often define hospital protocols, which include device choice and methods of aerosol delivery. Factors involved in decision-making include cost, ease of use, and perception of device function. Jet nebulizers require a pressurized gas to generate aerosol. Many modern ventilators are equipped with an in-line nebulization option integrated with the ventilator flow sensor, providing control of delivered volume and pressure. However, these systems are not standardized and the combination of an unregulated pressure/flow source with a given nebulizer can affect drug delivery.[2] In addition, the integrated in-line systems cannot deliver continuous nebulization. Nebulizer driving pressure and flow can be standardized by using wall air or oxygen. Clinicians experienced in aerosol delivery know that external gas added to the circuit can affect the ventilator readout on some machines, with marked elevation in the displayed exhaled V_T.[3,4] We hypothesized that the magnitude of this increase is inaccurate.

However, although potential effects are often mentioned, there are few sources that report actual delivered volumes, pressures, and triggering behavior. Cuccia et al,[5] in a study of aerosol delivery by using a prototype jet nebulizer, the i-AIRE (InspiRx, Somerset, New Jersey), tested its effect on several ventilators by using different modes and breathing patterns. The i-AIRE was driven with wall air at a flow of 3.5 L/min 50 psig. They measured changes in delivered V_T by using an ASL 5000 (ASL) test lung (Ingmar Medical, Pittsburgh, Pennsylvania) and found small changes in

delivered V_T, much less than the indicated values on the ventilator monitor.[5] It is important to note that the study by Cuccia et al[5] tested the nebulizer in a "breath actuated" condition, which can reduce effects of added gases. Other reports, some in abstract form, report variable changes in delivered volumes and pressures.[6]

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Li et al,[7] in a recent comprehensive study, measured delivered volume and pressure by using several ventilators. They tested a single breathing pattern that represented a patient with COPD when using the ASL breathing simulator, which served as both a test lung and a ventilator trigger (similar to Cuccia et al[5]). In the volume control mode, they reported increases in V_T as well as increases in inspiratory pressures. The ASL also provided a measure of time to reach the lowest airway pressure after a patient-initiated effort (time to minimum pressure). Li et al[7] reported that the time to minimum pressure was increased and statistically significant, with the implication that this will further affect patient ventilation.

The present paper is designed to further explore this problem by following a similar protocol to that used by Li et al.[7] We tested a broader range of adult breathing patterns designed to reflect commonly used modern ventilator settings for different patient conditions and additional measures of patient-triggering, measuring changes induced by adding external flow to the circuit, duplicating the clinical use of continuous nebulization.

QUICK LOOK

Current knowledge

During invasive ventilation, ventilators equipped with an in-line nebulization option are not standardized. The combination of an unregulated pressure/flow source with a given nebulizer can affect drug delivery and cannot deliver continuous nebulization. External flow jet nebulization allows for standardization of driving pressure and flow by using wall air or oxygen; however, this results in increases in displayed exhaled tidal volume. Interactions between continuous external jet flow and mechanical ventilators are not well defined.

What this paper contributes to our knowledge

Actual tidal volume changes were significantly lower than those displayed by the ventilator. Analysis of our findings suggests that these changes are best monitored through associated changes in peak inspiratory pressure.

Methods

Three adult breathing patterns were evaluated to simulate normal physiology, COPD, and ARDS. Ventilators tested included Dräger V500 critical care ventilator (Dräger, Telford, Pennsylvania), Servo-i (Maquet, Getinge, Solna, Sweden), Bella Vista (Vyaire Medical Inc, Mettawa, Illinois), and Hamilton-C1 (Hamilton Medical, Bonaduz, Switzerland). The tested Dräger V500 and Servo-i ventilators use an internal flow sensor, whereas the Bella Vista 1000 and Hamilton-C1 machines use an external flow sensor located at the distal Y-piece of the circuit near the test lung.

The following ventilator modes were tested for each patient breathing pattern: VC-CMV (volume control continuous mandatory ventilation), VC-IMV (volume control intermittent mandatory ventilation), PC-CMV (pressure control continuous mandatory ventilation), PRVC (pressure regulated volume control), and CSV (continuous spontaneous ventilation), with APRV tested only in the ARDS patient model for all ventilators. VC-CMV and VC-IMV were not available for the Hamilton ventilator. Ventilator settings and patient breathing patterns were chosen to simulate common scenarios that could reasonably present to a clinician in the clinical setting (Table 1 & 2). V_T was chosen to simulate lung-protective ventilation of a 70-kg ideal body weight adult. Clinically relevant inspiratory times for patients who are critically ill and require invasive ventilation were selected. Pressure support settings were adjusted to achieve the target V_T. Default

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The State University of New York at Stony Brook holds patents in the fields of nebulizer development and inhaled drug delivery, which have been licensed to InspiRx.

Dr Smaldone is a consultant to InspiRx and is a member of the Advisory Board; Ms Cuccia serves as a consultant to InspiRx; and Dr Jayakumaran has disclosed no conflicts of interest. Hamilton Medical loaned equipment used in this study.

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Table 1. Experimental Conditions: Tested Ventilator Modes and ASL 5000 Settings

Patient Profile	Ventilator Settings						ASL 5000 Settings				
	Mode	V_T, mL*	T_I, s	I:E	Duty Cycle T_I/TCT	PEEP, cm H_2O	ASL Inspiratory Airway Resistance, cm H_2O/L/s	ASL Expiratory Airway Resistance, cm H_2O/L/s	ASL Compliance, mL/cm H_2O	ASL Rate, breaths/min	ASL Inspiratory Muscle Pressure, cm H_2O
Normal	VC-CMV (A/C)	420	0.7	1:4.7	0.18	5	6	6	50	15	9/0.5
	VC-IMV	420/340	0.7	NA	NA	5	6	6	50	15	9/0.5
	PC-CMV	420	0.5	1:7	0.13	5	6	6	50	15	9/0.5
	PRVC	420	0.5	1:7	0.13	5	6	6	50	15	9/0.5
	CSV	340	NA	NA	NA	5	6	6	50	15	9/0.5
COPD†	VC-CMV (A/C)	420	0.7	1:3.3	0.23	5	10	15	60	20	8/0.5
	VC-IMV	420/340	0.5	NA	NA	5	10	15	60	20	8/0.5
	PC-CMV	420	0.5	1:5	0.2	5	10	15	60	20	8/0.5
	PRVC	420	0.5	1:5	0.2	5	10	15	60	20	8/0.5
	CSV	340	NA	NA	NA	5	10	15	60	20	8/0.5
ARDS‡	VC-CMV (A/C)	420	0.5	1:3.8	0.21	5	11	16	30	25	12/0.5
	VC-IMV	420/340	0.5	NA	NA	5	11	16	30	25	12/0.5
	PC-CMV	420	0.5	1:3.8	0.21	5	11	16	30	25	12/0.5
	PRVC	420	0.5	1:3.8	0.21	5	11	16	30	25	12/0.5
	CSV	340	NA	NA	NA	5	11	16	30	25	12/0.5
ARDS‡			P_{high}, cm H_2O	P_{low}, cm H_2O	T_{high}, s	T_{low}, s	ASL Inspiratory Airway Resistance, cm H_2O/L/s	ASL Expiratory Airway Resistance, cm H_2O/L/s	ASL Compliance mL/cmH_2O	RR, breatds/min	ASL Inspiratory Muscle Pressure, cm H_2O
	APRV		25	0	4.4	0.6	11	16	30	25	12/0.5

*Set V_T or target V_T.
†From Reference 9.
‡From Reference 10.
V_T = tidal volume
T_I = inspiratory time
I:E = inspiratory to expiratory time ratio
TCT = total cycle time ($T_I + T_E$)
VC-CMV= volume control continuous mandatory ventilation
A/C = assist/control
VC-IMV = volume control intermittent mandatory ventilation
PC-CMV = pressure control continuous mandatory ventilation
PRVC = pressure regulated volume control
CSV = continuous spontaneous ventilation
ASL rate = rate set on ASL to trigger ventilator
ASL inspiratory muscle pressure = first number: muscle pressure used in each patient model (normal,COPD, ARDS), second number: lowest muscle pressure checked during ventilator triggering assessment.
APRV = airway pressure release ventilation
P_{high} = upper pressure
P_{low} = lower pressure
T_{high} = time at upper pressure
T_{low} = time at lower pressure

Table 2. Effect of Added Nebulizer Flow Separated by Ventilator Flow Sensor Type

Flow Sensor Ventilator	Effect of Added Nebulizer Flow											
	V_T, mL*	Mode	Total experiments, no.	Exhaled V_T, mL†	Δ Exhaled V_T 3.5 L, %; *P*‡	Δ Exhaled V_T 8 L, %; *P*‡	Actual V_T, mL§	Δ Actual V_T 3.5 L, %; *P*‖	Δ Actual V_T 8 L, %; *P*‖	PIP, cm H_2O¶	ΔPIP 3.5 L, %; *P***	ΔPIP 8 L, %; *P***
Internal flow sensor ventilators: Dräger, Servo	420	VC-CMV (A/C)	6	412 ± 4	50 ± 12; .031	114± 26; .031	420 ± 12	11 ± 2; .031	21 ± 9; .031	17 ± 3	12 ± 0; .031	19 ± 11; .031
	420	VC-IMV (IMV breaths)††	6	402 ± 11	54 ± 16; .031	118 ± 32; .031	413 ± 8	9 ± 4; .031	19 ± 6; .031	16 ± 3	10 ± 3; .031	24 ± 8; .031
	340	VC-IMV (PS breaths)§§	6	347 ± 14	50 ± 16; .031	110 ± 33; .031	360 ± 16	–5 ± 2; .031	–7 ± 4; .031	11 ± 3	ND	2 ± 4; >.99
	420	PRVC	6	410 ± 5	45 ±11; .031	107 ± 26; .031	423 ± 10	4 ± 4; .063	12 ± 9; .031	14 ± 3	6 ± 8; .25	14 ± 14; .13
	420	PC-CMV	6	399 ± 34	41 ± 11; .031	94 ±26; .031	413 ± 32	–3 ±2; .031	–4 ±3; .031	13 ± 3	ND	1 ±3; >.99
	340	CSV	6	367 ± 36	48 ± 16; .031	100 ± 30; .031	379 ± 26	–3 ± 1; .031	–9 ± 10; .031	12 ± 2	ND	–1 ± 2; >.99
		APRV	2	686 ± 56	10 ± 17	23 ± 38	709 ± 40	–3 ± 5	–13 ± 5	28 ± 1	ND	ND
External flow sensor ventilators: Hamilton, Bella Vista												
	420	VC-CMV (A/C)	3	415 ± 4	0 ± 1; >.99	1 ±1; .50	405 ± 5	0 ± 1; >.99	2 ± 2; .25	18 ± 4	2 ± 3; >.99	2 ± 3; >.99
	420	VC-IMV (IMV breaths)††	3	395 ± 8	9 ± 3; .25	11 ± 4; .25	385 ± 5	9 ±3; .25	12 ± 3; .25	16 ± 5	6 ± 0; .25	10 ± 7; .25
	340	VC-IMV (PS breaths)§§	3	350 ± 32	2 ± 3; .50	–2 ± 4; >.99	340 ± 26	2 ± 2; .25	–1 ± 3; .75	12 ± 2	ND	3 ± 5; >.99
	420	PRVC	6	416 ± 9	1 ± 3; .38	1 ± 2; .31	408 ± 7	1 ± 2; .30	1 ± 1; .031	16 ± 4	4 ± 3; .13	5 ± 16; .63
	420	PC-CMV	6	413 ± 9	–1 ± 3; .50	0 ± 7; .75	406 ± 14	1 ± 2; .25	0 ± 5; >.99	16 ± 4	–1 ± 3; >.99	–3 ± 3; .5
	340	CSV	6	352 ± 38	–3 ± 3; .16	–3 ± 9; .59	346 ± 39	–2 ± 2; .16	–2 ± 6; .43	13 ± 2	–3 ± 4; .5	–3 ± 8; .75
		APRV	2	609 ± 26	0 ± 5	–5 ± 1	624 ± 10	–3 ± 1	8 ± 6	27 ± 1	ND	ND

Data are presented as mean ± SD unless otherwise noted.

The effects of 3 patient profiles (normal, COPD, ARDS) averaged in each column, mean ± SD includes variation between waveforms and the error of measurement.

The column " V_T, mL" lists either set V_T (volume controlled) or target V_T (pressure controlled). Results are shown with mean ± SD baseline values without nebulizer flow reported for exhaled V_T, actual V_T, and PIP, followed by percentage change from baseline, with an added flow of 3.5 L/min and 8 L/min; the results are separated by flow sensor location and presented as percentage change compared with baseline.

* Set or target V_T.

† Displayed on the ventilator.

‡ The change in exhaled V_T (displayed on the ventilator) with the introduction of nebulizer flow.

§ V_T delivered displayed on the ASL 5000.

‖ The change in exhaled V_T (ASL) with the introduction of nebulizer flow (displayed on the ASL).

¶ PIP displayed on the ventilator.

** The change in PIP with the introduction of nebulizer flow.

†† IMV breaths: V_T measured from IMV breaths during the IMV mode.

§§ PS breaths: V_T measured from pressure supported breaths during the IMV mode.

V_T = tidal volume

PIP = peak inspiratory pressure

VC-CMV = volume control continuous mandatory ventilation

A/C = assist/control

VC-IMV = volume control intermittent mandatory ventilation

IMV = intermittent mandatory ventilation

ND = no data

PS = pressure support

PC-CMV = pressure control continuous mandatory ventilation

PRVC = pressure regulated volume control

CSV = continuous spontaneous ventilation

APRV = airway pressure release ventilation

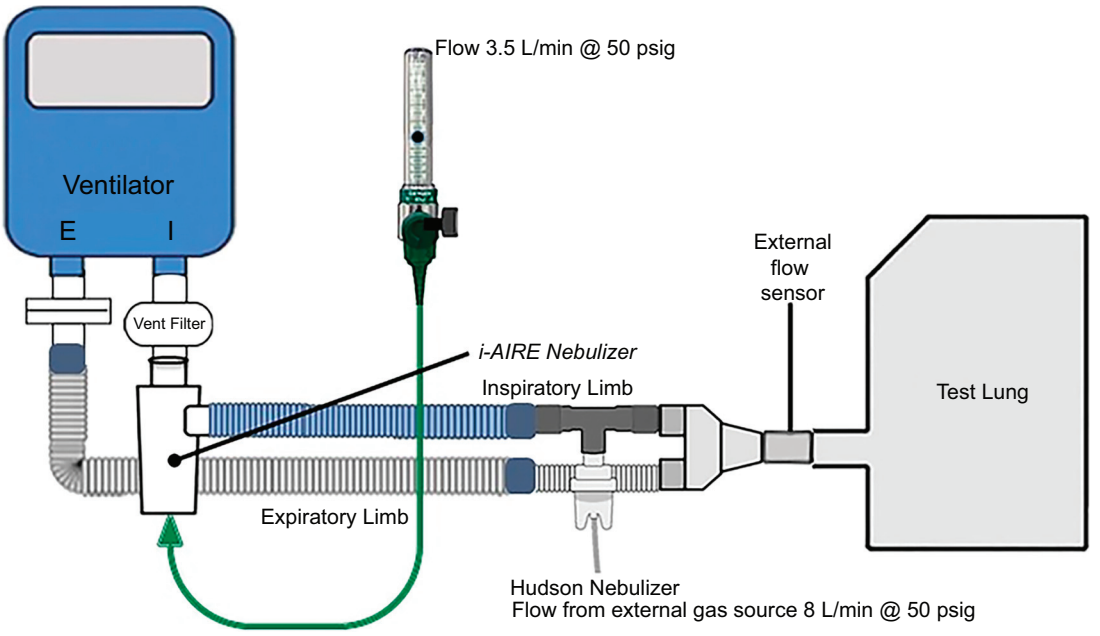

Fig. 1. Experimental setup for different nebulizer locations with only one nebulizer placed in the circuit at a time. The i-AIRE breath-enhanced jet nebulizer prototype located at the inspiratory outlet of the ventilator powered by 3.5 L/min air from flow meter. Hudson nebulizer placed in the inspiratory line proximal to the patient Y-piece powered by 8 L/min air from flow meter. External flow sensor shown at the distal Y-piece position for tested ventilators (Bella Vista and Hamilton).

bias flow for each ventilator was used: 2 L/min for the Dräger V500 and Servo-i, 3 L/min for the Hamilton-C1, and 6 L/min for the Bella Vista 1000. Complete ventilator settings are detailed in the supplementary file (see the supplementary materials at http://www.rcjournal.com).

The ASL test lung served to both monitor ventilatory parameters and simulate a variety of relevant patient scenarios, which consisted of set compliance, resistance, and rate. Different from other test lungs, the ASL can trigger the ventilator, through generation of negative inspiratory force that can be set and modified by the operator. Settings for each patient scenario in Table 1 were based on manufacturer recommendations as well as previously published literature.[8,9] Settings for the normal example were chosen from the ASL library. For the normal settings, inspiratory muscle force was decreased from the default settings to avoid double-triggering of the ventilator at the chosen set V_T.

Each ventilator was connected directly to the test lung, without active humidification. Two nebulizers were tested. They were chosen based on recommended flow and pressure settings. The experimental setup is illustrated in Figure 1. The i-AIRE, placed at the ventilator outlet port, operated at 3.5 L/min and air at 50 psig, and the Hudson RCI (Teleflex Medical, Research Triangle Park, North Carolina), placed in the inspiratory limb proximal to the Y-piece position, operated at 8 L/min and air at 50 psig. All the nebulizers were run with dry gas only. The ventilator and ASL were monitored during testing with and without added flow from the test nebulizer. Steady-state (after 5–10 breaths) readings were recorded of exhaled V_T measured by the ventilator and V_T delivered (actual V_T) measured by the ASL. Other recorded parameters included peak inspiratory pressure (PIP) from the ventilator readout as well as time to reach minimum pressure (time to minimum pressure, a parameter reported by Li et al,[7] from the ASL. To evaluate triggering, 2 maneuvers were performed; the first was tested by reducing inspiratory muscle force (muscle pressure, P_{mus}) (with ventilator sensitivity fixed at its default setting) until the ventilator defaulted to its backup rate, the second trigger function was tested by gradually increasing sensitivity (with the chosen P_{mus} fixed) until auto-triggering was observed.

The statistical significance of the effects of added external flow was assessed by using the Wilcoxon test (GraphPad Prism for Mac OS X, GraphPad Software, San Diego, California) to compare baseline measurements with no additional flow to those with added flows of 3.5 L/min and 8 L/min. Comparison data were grouped based on mode type across the tested ventilators and patient scenarios. Differences were reported between ventilator and ASL measurements with and without added flow. Data were separated for the internal and external distal Y-piece flow sensor ventilators. Data were reported as mean ± SD.

Results

A complete data set for all measurements is available in the supplementary files. Summary data are reported in

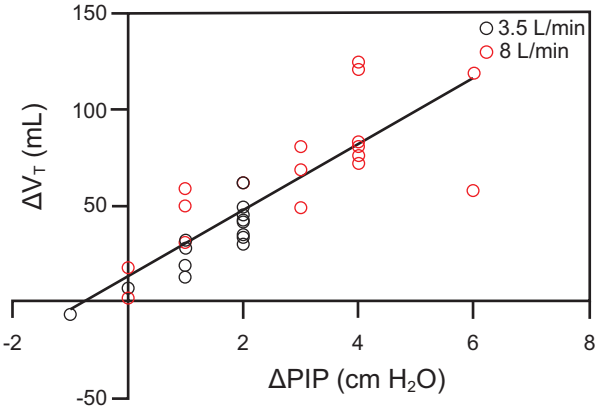

Fig. 2. Change in tidal volume delivered (Δ actual V_T) (mL) vs change in peak inspiratory pressure (ΔPIP) (cm H_2O) during volume control modes, internal flow sensor ventilators; 3.5 L/min external flow, 8 L/min external flow; y = 17.21x + 13.51, $P < .001$, $R^2 = 0.68$.

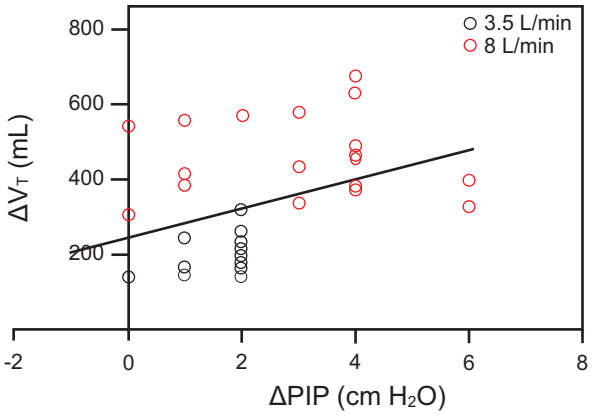

Fig. 3. Change in displayed exhaled tidal volume (V_T) (mL) vs change in peak inspiratory pressure (PIP) (cm H_2O) during volume control modes, internal flow sensor ventilators; 3.5 L/min external flow, 8 L/min external flow; y = 39.9x + 243.3; $P = .02$; $R^2 = 0.16$.

Table 2 and in the online supplement (see the supplementary materials at http://www.rcjournal.com). For internal flow sensor ventilators (Table 2) across volume control modes, changes measured by the ASL (actual V_T) were much lower than the changes in exhaled V_T displayed on the ventilator. exhaled V_T changes displayed on the ventilator ranged from 45 ± 11% to 118 ± 32%, whereas actual V_T delivered increased from 4 ± 4% to 11 ± 2% with the introduction of 3.5 L/min of external flow and 12 ± 9% to 21 ± 9% for 8 L/min of added flow. PIP changes were of similar magnitude (6 ± 8% to 12 ± 0% with 3.5 L/min, and 14 ± 14% to 24 ± 8% with 8 L/min). In pressure control modes, actual V_T decreased slightly (−3 ± 2% to −9 ± 10%) for both 3.5 L/min and 8 L/min added flow. All changes, although small, were statistically significant ($P = .031$). With added flow, PIP did not change significantly, with P values that ranged from $P = .031$ to $P > .99$. Despite the small, measured decreases in V_T, as assessed by actual V_T in pressure controlled modes, the ventilator monitor indicated marked false elevations in exhaled V_T of 41 ± 11% to 110 ± 33%. In APRV, V_T delivered decreased slightly, –3 ± 5%, with 3.5 L/min of added flow and –13 ± 5% with 8 L/min of added flow. These measured changes during APRV were different in magnitude and direction than the mean ± SD 10 ± 17% and 23 ± 38% increase in exhaled V_T reported on the ventilator monitor for 3.5 L/min and 8 L/min added flow, respectively.

Ventilators with the external flow sensors located in the distal Y-piece position behaved differently. As shown in Table 2, the measured changes in all the parameters were less than their internal flow sensor counterparts and largely statistically insignificant (outside of the changes noted with 8 L/min of added flow in PRVC with an average increase of 1% [$P = .031$]). Across the volume controlled modes, exhaled V_T usually mirrored actual V_T. With 3.5 L/min of external flow, exhaled V_T increased by 0 ± 1% to 9 ± 3%, while actual V_T increased by 0 ± 1% to 9 ± 3%. With 8 L/min of external flow, exhaled V_T increased by 1 ± 1% to 11 ± 4% and actual V_T increased by 2 ± 2% to 12 ± 3%. PIP changes were of similar magnitude, with an increase of 2 ± 3% to 6 ± 0% with 3.5 L/min, and 2 ± 3% to 10 ± 7% with 8 L/min.

In the pressure controlled modes, actual V_T ranged from –2 ± 6% to 2 ± 2% with added flow. These changes were similar to those displayed on the ventilator, with exhaled V_T that ranged from –3 ± 9% to 2 ± 3%. PIP did not change significantly in pressure controlled modes (–3 ± 8% to 3 ± 5%). In APRV, volume delivered decreased slightly with 3.5 L/min added flow, –3 ± 1% and increased slightly with 8 L/min added flow, 8 ± 6%. These changes were different than those displayed on the ventilator, with a negligible decrease in exhaled V_T of 0 ± 5% with 3.5 L/min and decreased by 5 ± 1% with 8 L/min.

Changes in actual V_T and PIP, for 3.5 L/min and 8 L/min added external flow when using volume controlled modes and internal flow sensor ventilators are described in Figure 2. For all data, the relationship is described by the linear correlation, y = 17.21x + 13.51 ($P < .001$, $R^2 = 0.68$). The coefficient of determination indicates that 68.2% of the variability is explained. The same analysis for changes in exhaled V_T versus changes in PIP is illustrated in Figure 3. The regression, although significant ($P = .02$), poorly explains the data ($R^2 = 0.16$).

The time to minimum pressure (Table 3) increased between 1 and 8% with 3.5 L/min external flow. At 8 L/min, unusually large changes were seen on the Dräger ventilator when using the normal patient ASL settings (eg, time to minimum pressure change from baseline 54 ms to 2,046 ms in VC-CMV); however, the ventilator continued to trigger with no dropped breaths or change in ventilator frequency. For all other measurements at 8 L/min flow, with the Dräger findings excluded, time to minimum pressure increased from 1 to 8%.

Results for measures of ventilator triggering via changes in patient muscle strength are summarized in Tables 4.

Table 3. Changes in Time to Minimum Pressure Reported as Percentage Change from Baseline*

Mode	Total experiments, no.	Time to Minimum Pressure, ms	Δ Time to Minimum Pressure 3.5 L, %; $P^{\dagger}$	Δ Time to Minimum Pressure 8 L, %; $P^{\dagger}$
VC-CMV (A/C)	9	97 ± 48	5 ± 5; .007	8 ± 9; .008
VC-IMV (IMV breaths)‡	9	104 ± 59	1 ± 5; .47	1 ± 16; .69
VC-IMV (PS breaths)§	9	75 ± 22	8 ± 8; .02	2 ± 27; .87
PRVC	12	78 ± 17	2 ± 13; .21	5 ± 19; .39
PC-CMV	12	76 ± 17	1 ± 11; .61	6 ± 14; .25
CSV	12	78 ± 17	3 ± 14; .08	4 ± 20; .47
APRV	4	77 ± 9	4 ± 5; .38	4 ± 11; .63

Data are presented as mean ± SD and no.
* Data for Dräger at 8 L/min in the normal patient model were excluded.
† The change in time to pressure minimum with the introduction of nebulizer flow.
‡ IMV breaths: the tidal volume measured from IMV breaths during the IMV mode.
§ PS breaths: the tidal volume measured from pressure supported breaths during the IMV mode.
VC-CMV = volume control continuous mandatory ventilation
A/C = assist/control
VC-IMV = volume control intermittent mandatory ventilation
IMV =intermittent mandatory ventilation
PS = pressure support
PRVC = pressure regulated volume control
PC-CMV = pressure control continuous mandatory ventilation
CSV = continuous spontaneous ventilation
APRV = airway pressure release ventilation

Table 4. Muscle Pressure at Failure to Trigger (initial set point 8–12 cm H_2O)

Mode	Total experiments, no.	P_{mus}, cm H_2O	P_{mus} 3.5 L, cm H_2O; *P*	P_{mus} 8 L, cm H_2O; *P*
VC-CMV (A/C)	9	1.0 ± 0.7	1.6 ± 0.70; .063	2.2 ± 1.5; .13
VC-IMV	9	0.8 ± 0.4	1.4 ± 0.9; .031	2.0 ± 1.1; .031
PRVC	12	1.0 ± 0.7	1.5 ± 0.8; .063	2.0 ± 1.5; .039
PC-CMV	12	1.0 ± 0.6	1.3 ± 0.7; .063	1.8 ± 1.2; .02
CSV	12	0.9 ± 0.67	1.4 ± 0.7; .031	2.0 ± 1.3; .008

Data are presented as mean ± SD.
P_{mus} = ASL inspiratory muscle pressure
VC-CMV= volume control continuous mandatory ventilation
A/C= assist/control
VC-IMV = volume control intermittent mandatory ventilation
PRVC = pressure regulated volume control
PC-CMV = pressure control continuous mandatory ventilation
CSV = continuous spontaneous ventilation

Muscle strength (P_{mus}) settings were lowered until the ventilator failed to trigger, defined by initiation of the backup rate. With added flow, differences in muscle strength (P_{mus}) required to trigger the ventilator were small, <1 cm H_2O with 3.5 L/min and at most by ~1 cm H_2O with 8 L/min. The independent measure, ventilator sensitivity, assessed by adjusting sensitivity to the most sensitive setting for both pressure and flow triggers, rarely induced auto-triggering, with failure observed 3 times with 8 L/min and 4 times with 3.5 L/min across a total of 104 trigger tests per flow.

Discussion

Although changes in ventilator performance with added flow to the circuit are real, they are predictable and often minimal. Changes in PIP, as shown in Figure 2, which can be measured without the ASL, paralleled the changes in actual V_T and indicate that a clinician at the bedside can easily assess real changes in delivered volume by looking at the magnitude of changes in PIP. For all settings, the changes in delivered volume measured by the ASL were markedly different from the readouts on the ventilator monitors for machines that used an internal flow sensor. The changes in exhaled V_T recorded by the ventilator did not correlate well with PIP (Fig. 3). Of note, during testing of the Dräger V500, a flow measurement alarm would be triggered with the addition of external flow. Despite the alarm, the ventilator continued to trigger and deliver the volumes reported. External flow sensors placed in the distal Y-piece readily compensated for any added external flow. Our measures of ventilator triggering (changing ventilator sensitivity and the ASL index for muscle activity) were minimally responsive to added flow. Preliminary data from earlier studies predicted that many results will be statistically significant because expected changes, no matter how minimal, will be in one direction and, therefore, significant, but small changes may not be clinically important.

Review of manufacturer specifications indicated that many repeated measurements of function might vary as much as 10% (8–10% volume, 4–6% pressure).[10-14] The ventilator manufacturer specifications for volume and

Table 5. Ventilator Manufacturer Specifications for Volume and Pressure Accuracy[10,11,13,14]

Ventilator Brand	Volume Accuracy, %	Pressure Accuracy, %
Bellavista 1000	±10	±4
Hamilton-C1	±10	±4
Servo-i	±8	±5
Dräger Infinity V-500	±10	±6
Average	9.5	4.8

pressure accuracy are summarized in Table 5, and the changes observed in this study are illustrated in Table 3. Changes to the actual V_T delivered with the introduction of nebulizer flow are reflected in the columns Δ actual V_T 3.5 L and Δ actual V_T 8L. With the introduction of 3.5 L/m nebulizer flow, the internal flow sensors showed a volume change of 4–11% in volume controlled modes; however, all other modes were ≤4%. External flow sensors showed a change of ≤9% across all modes. With the introduction of 8 L/m nebulizer flow, internal flow sensors showed a change of 12–21% in volume controlled modes and external flow sensors showed a change of ≤12% across all modes. Changes in PIP with the introduction of nebulizer flow are reflected in the columns: ΔPIP 3.5 L and ΔPIP 8 L. With the introduction of 3.5 L/m nebulizer flow, internal flow sensors showed a pressure change of ≤12%, while external flow sensors showed a change of ≤4% across all modes. With the introduction of 8 L/m nebulizer flow, internal flow sensors showed a change of ≤24% and, with external flow sensors, a change of ≤10% across all modes.

Li et al[7] also examined the influence of external flow, testing one breathing pattern (COPD) across several ventilators. Six ventilators were tested, 5 with internal flow sensors and one distal Y-piece sensor. Our findings for actual V_T and PIP for internal flow sensor ventilators were comparable with theirs. However, Li et al[7] recommend that the therapist should lower V_T settings based on the exhaled V_T displayed on the ventilator. This recommendation seems inconsistent with both our observations and the data reported by Li et al.[7] That is, the exhaled V_T changes displayed on the ventilators tested were much larger than the true increases in V_T. Making ventilator adjustments based on exhaled V_T could potentially lead to hypoventilation of the patient. Analysis of our results suggests that clinicians should simply monitor the PIP. For ventilators with internal flow sensors, measured changes in exhaled V_T are not accurate. True changes in delivered V_T can be assessed by observing PIP, which reflects actual volume changes delivered to the patient, and PIP is not subject to flow artifacts. This is best seen in Figure 2, which describes a strong linear relationship between changes in actual V_T and changes in PIP. For example, an addition of 3.5 L/min generally increased PIP by ~2 cm H_2O. The greatest changes (eg, 6 cm H_2O) were measured with the addition of 8 L/min in models with low lung compliance (ARDS model). Due to the weak correlation between exhaled V_T and PIP, it may be unsuitable to make ventilator adjustments based on this parameter.

Li et al[7] also examined "triggering performance" through the evaluation of variables displayed on the ASL, one of which was the time to reach the lowest airway pressure (time to minimum pressure). They reported significant increases and concluded that these changes may affect a patient's ability to reliably trigger the ventilator. Although we found much smaller changes in time to minimum pressure across most ventilators tested (except for Dräger at 8 L/min), no faulty triggering or dropped breaths were noted, even for Dräger, which suggested to us that this parameter is not related to measures of trigger function. measures of trigger function and changes in muscle force and ventilatory sensitivity were minimally affected.

Our study has limitations. Bench studies, including ours, may not reflect actual patient behavior but guide the initial approach to therapy as well as future directions in studies on patients who are critically ill. We did not evaluate all commercially available ventilators, nebulizer positions, and clinically relevant situations. In this study, we specifically used an adult patient model, it is unclear what the effects of external flow would be on smaller patients, such as pediatric or neonatal patients, by using lower V_T.

Conclusions

Based on our findings, clinicians should be aware that external flow affects ventilators differently based on the location of the flow sensor. Ventilators with the flow sensor in the distal Y-piece position include external flow into their exhaled V_T calculation after a few transient breaths, compensating for external flow with a quick return to baseline. For ventilators with internal flow sensors, external V_T readings are inaccurate. Our bench study indicates that, to estimate V_T changes, it is more reliable to monitor PIP, which increased in parallel to actual changes in V_T.

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