Development and Safety Trial of the OstreaVent2™ Prototype for Mechanically Ventilated Adult Patients

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ABSTRACT

Background. With the surge of COVID-19 infections, there were concerns about shortage of mechanical ventilator in several countries including the Philippines.

Objective. To transform a locally made, low-cost, neonatal ventilator into a volume- and pressure-controlled, adult ventilator and to determine its safe use among ventilated, adult patients at the Philippine General Hospital.

Methods. The modification of the neonatal ventilator (OstreaVent1) to the adult OstreaVent2 was based on the critical need for adult ventilators, in volume or pressure mode, in the Philippines due to the COVID-19 pandemic. The adult ventilator settings were calibrated and tested for two days to check for consistency and tolerance and then submitted to a third party for certification. Once certified, a safety trial of 10 stable adult patients on mechanical ventilator was conducted. The patients were placed on the OstreaVent2 for four hours while ventilator parameters, patient's vital signs, and arterial blood gases were monitored at baseline, during, and after placement on the OstreaVent2. A post-study chest radiograph was also done to rule out pulmonary complications, particularly atelectasis and pneumothorax.

Results. The prototype OstreaVent2 received an FDA Certification for Medical Listing after passing its third-party certification. Ten patients (60% male) recruited in the study had a mean age of 39.1 ± 11.6 years. Half of the patients had a diagnosis of non-COVID-19 pneumonia. During the 4-hour study period, the patients while on the OstreaVent2, had stable ventilator settings and most of the variabilities were within the acceptable tolerances. Vital signs were stable and arterial blood gases were within normal limits. One patient developed alar flaring which was relieved by endotracheal tube suctioning. No patient was withdrawn from the study. One patient who was already transferred out of the ICU subsequently deteriorated and died three days after transfer to the stepdown unit from a non-ventilator related cause.

Conclusion. The new OstreaVent2 is safe to use among adults who need ventilator support. Variabilities in the ventilator's performance were within acceptable tolerances. Clinical and blood gas measurements of the patients were stable while on the ventilator.

Keywords: adult ventilator, OstreaVent1, OstreaVent2

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INTRODUCTION

At the onset of the COVID-19 epidemic worldwide, there was a major concern that with an alarming increase in COVID-19 infections, the estimated number of available ventilators which ranged from 60,000 to 160,000 was considered insufficient to care for patients with severe COVID-19 infection. The recommendations, therefore, were to tap private companies, including automakers, to produce ventilators, optimize supply of raw materials and maximize the distribution of the ventilators. This concerted effort was aimed to provide the necessary life saving devices to avoid the painful decision on who should or should not receive ventilator support.[1]

Early in the COVID-19 pandemic from December 2019-January 2020, a review of 30 provinces in China showed that around 5% of patients with Covid-19 infections required ICU admissions with 2.3% requiring invasive mechanical ventilation, 5.1% non-invasive mechanical ventilation, and 6.1% requiring oxygen therapy.[2] Furthermore, in a retrospective study of 155 consecutive patients admitted in Wuhan, China from January to February 5, 2020, 45% had refractory pneumonia (no clinical and radiologic remission within 10 days after hospitalization), and required mechanical ventilation and adjunct therapy.[3]

In a review of admissions to the Adult Intensive Care Unit (ICU) of the Philippine General Hospital (PGH) from April 1 to May 31, 2020, majority of the patients had moderate level of hypoxemia on admission with 69% requiring invasive mechanical ventilation and 43% needing pressor support. Overall mortality among patients admitted at the ICU was 63%.[4]

In April 2020, the Department of Health has sent an alert for the possible shortage of ventilators with only 1,263 units available in the hospitals nationwide.[5] Subsequently, the Department of Science and Technology (DOST) issued a special call for proposals to develop ventilators and respirators to augment the health care system grappling with COVID-19 patients needing these medical devices.[6]

In the Philippines, a locally made, low-cost, neonatal ventilator (OstreaVent1) has already undergone animal and clinical trials which have proven its safety and effectiveness in the care of sick, newborn infants with significant respiratory problems.[7] Around 75 units have already been successfully distributed to neonatal intensive care units nationwide. Thus, with an impending need for more ventilators especially among COVID-19 patients, an emergency discussion among key members of the Breath of Life Foundation, the University of the Philippines Manila, Metals Industry Research and Development Center, and the Philippine Council for Health Research and Development-DOST, was held to modify the OstreaVent1 into an adult ventilator prototype which could provide high flow rate, high pressure, and operate in a volume-controlled mode.

Significance

The modification of the neonatal OstreaVent1 from a time cycled, pressure-limited ventilator to an adult pressure- and volume-controlled mechanical ventilator (OstreaVent2) will augment ventilator availability for adults in the Philippines.

Review of Literature

Mechanical ventilation remains the cornerstone in the treatment of adult respiratory distress syndrome (ARDS) with emphasis on preventing ventilator-induced lung injury. On a review of 31 articles detailing major advances in the diagnosis and treatment of ARDS, a sample algorithm recommended a target tidal volume of 6 ml/kg of predicted body weight, plateau pressure of ≤30 cmH_2O, and a higher PEEP of ≥5 cmH_2O in moderate to severe ARDS.[8] In a descriptive study of Chen in COVID-19 infected patients with ARDS, the ventilator mode was pressure-controlled, synchronous intermittent mandatory ventilation (P-SIMV) with the inhaled oxygen concentration ranging from 35-100% and the PEEP from 6-12 cmH_2O.[9]

There was an urgency to produce adult ventilators in anticipation of its shortage in the upcoming months of the COVID-19 pandemic. Institutions such as the Massachusetts Institutes of Technology and the Rice University have developed model ventilators that would add to ventilator availability. However, clinical trials were still pending.[10-13]

The OstreaVent1 has already undergone previous animal and clinical trials and has been distributed to many hospitals in the Philippines, but almost exclusively used for neonates. The conversion of the OstreaVent1 to OstreaVent2 would still preserve the basic concept in the OstreaVent1 of utilizing a non-moving piston to provide the tidal volume and pressure of the adult ventilator.

OBJECTIVES

1. To develop a low-cost adult mechanical ventilator prototype (OstreaVent2) which provides pressure and volume controlled, time-cycled, intermittent mandatory mechanical ventilation.
2. To determine the safety of using OstreaVent2 in mechanically ventilated adult patients.

METHODS

Development of the OstreaVent2 Prototype

A core group consisting of adult pulmonologists (MCJ, KT), pediatric (HGU, EVSF) and neonatal intensivists (EMO, MEVU), and engineers (ROD, APP) was convened to develop, using the OstreaVent1 as the model, a prototype pressure and volume controlled, time cycled, intermittent mandatory mechanical ventilator. Flow rate (FR), peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), and tidal volume (TV) settings would be made to conform with the requirements of the 2020 Association

for the Advancement of Medical Instrumentation (AAMI) consensus report for the development of ventilators for COVID-19 pneumonias.[14] A touch screen display was incorporated in the ventilator to set many of the ventilator parameters and to display their actual measurements. Safety features such as audio and visual alarms for parameter limits were set. Shutdown of the ventilator would be a two-step process to prevent an accidental switch off of the ventilator. An oxygen blender was not incorporated into the prototype OstreaVent2 but instead, mixing of flow rates of the oxygen and medical air was done to deliver the desired oxygen concentration. After the prototype OstreaVent2 was developed and tested for accuracy and consistency, it was submitted for certification by a DOST-recommended third-party accreditor.

Safety Clinical Trial of the OstreaVent2 Site

Study Site

Intensive Care Units of the Philippine General Hospital

Study Population

Ten adult patients on mechanical ventilator were recruited consecutively after an informed consent was obtained from their legally appointed representatives.

Inclusion Criteria

1. Ages 18 to 70 years old
2. Patient has stable blood pressure and oxygen saturations (≥93%)
3. Intubated for more than 1 day
4. Unchanged mechanical ventilator settings for the past 12 hours
5. Patient is neither a COVID suspect nor a COVID patient.

Exclusion Criteria

1. On double inotrope medications
2. In cardiogenic or distributive shock (sepsis)
3. No access to blood gas (venous or arterial)
4. Patients whose oxygenation ratio (PaO_2/FiO_2) ≤200

Intervention

After obtaining baseline data, the patient was placed on the OstreaVent2 for four hours. The OstreaVent2 was placed on the same settings as the previous ventilator the patient was on. Parameters set were the tidal volume (TV), the flow rate (FR), ventilator rate, and the positive end expiratory pressure (PEEP). The FiO_2 blending was external to the OstreaVent2 and was delivered through a mixture of different flow rates of the oxygen and air. The combined gas flow rates would be the Flow rate set on the ventilator. Actual measurements of the parameters (except the FiO_2) were displayed on the ventilator screen. The prototype OstreaVent2 could also measure the resultant peak inspiratory pressure (PIP), inspiratory time (Ti), and the calculated mean alveolar pressure (MAP). All measurements could be displayed on the screen and recorded.

The patient was placed on a cardiac monitor during the duration of the study. At baseline, ventilator parameters (15 mins before transfer) and vital signs (60 and 30 mins before transfer) were recorded. Subsequently, the patients' vital signs and ventilator parameters were monitored at 15, 30, 45, 60, 120, 180 and 240 minutes while on the OstreaVent2 and then 30 and 60 minutes after the patients' transfer back to the original ventilator. A blood gas was obtained 1 hour before, at 1 hour on the OstreaVent2, and 1 hour after return to the original ventilator. Pulmonary auscultatory examinations for wheezing, decreased breath sounds as well as signs of increase in respiratory distress were also monitored and managed accordingly. A chest radiograph was requested after the 4-hour study period to rule out atelectasis and pneumothorax.

Withdrawal Criteria

If at any time that the patient's vital signs would deteriorate while on the OstreaVent2, the patient would be removed from the OstreaVent2 and placed back on his previous ventilator after exclusion of extraneous events such as empty gas tanks, accidental detachment from the ventilator, pulmonary secretion, mucus plug and others. Clinical deterioration would be considered if the following conditions persisted for five minutes:

1. Decrease in the oxygen saturations by 5 points from baseline or an oxygen saturation <94%
2. A heart rate change of ± 10/min from baseline or a heart rate <70 or >120/min
3. Systolic blood pressure <90 mmHg or a change of ± 20 mmHg from baseline
4. An increase in respiratory distress such as increase in the RR to >30/min, deepening of the intercoastal retraction, gasping respiration, alar flaring or head bobbing.
5. Any life-threatening event would prompt an immediate transfer of the patient to the previous ventilator without waiting for a 5-minute observation period.

Ethical Considerations

This study was registered (RGAO-2020-0297) and approved by the UP Manila Ethics Review Board (2020-340-01). The OstreaVent2 has received an approval for the Philippine FDA Certificate for Medical Listing (CDRRHR-CMDL-2020-04) after having received a certification from an external third-party certifier for consistency of parameters. Once the safety trial was started, an informed consent was obtained by a trained, science research assistant. Data from the patient's medical record were extracted and encoded in a password-protected database. Patients' names were anonymous and identified only by an assigned code number. All forms were stored in a locked cabinet and would be destroyed by the primary investigator after five years from the termination of the study. The Data Privacy Act of 2012 was strictly observed.

RESULTS

Ostreavent2 Prototype Development

Pneumatic and Electrical Components

The OstreaVent2 adult ventilator has been assembled to permit the regulation of airflow, pressure, and tidal volume to the patient. Ventilation of the patient was achieved by the opening and closing of solenoid valves that alternate the flow of oxygen/air mixture through the machine between a high-pressure and low-pressure path. The rate of opening or closing of the solenoid valves were controlled by a microcontroller which could be set to determine the number of breaths per minute (bpm) and the length of inspiratory time or volume of oxygen/air mixture delivered to the patient. Peak Inspiratory Pressure (PIP) was adjusted by a throttling valve installed at the high-pressure path while the Positive End Expiratory Pressure (PEEP) was adjusted by a similar valve installed at the low-pressure path (Figure 1). Other ventilator parameters could be adjusted using the Human Machine Interface (HMI) installed in the device. For safety, a mechanical pressure relief valve and alarms were installed and integrated into the system. The ventilator has been made downstream to the patient and no medical gas from the machine flowed back into the patient at any time (Figure 2). The OstreaVent2 was tested continuously for two days using a linear test lung (IngMar Medical) to assess for consistency of the different ventilator parameters. Calibration was performed using the Certifier®

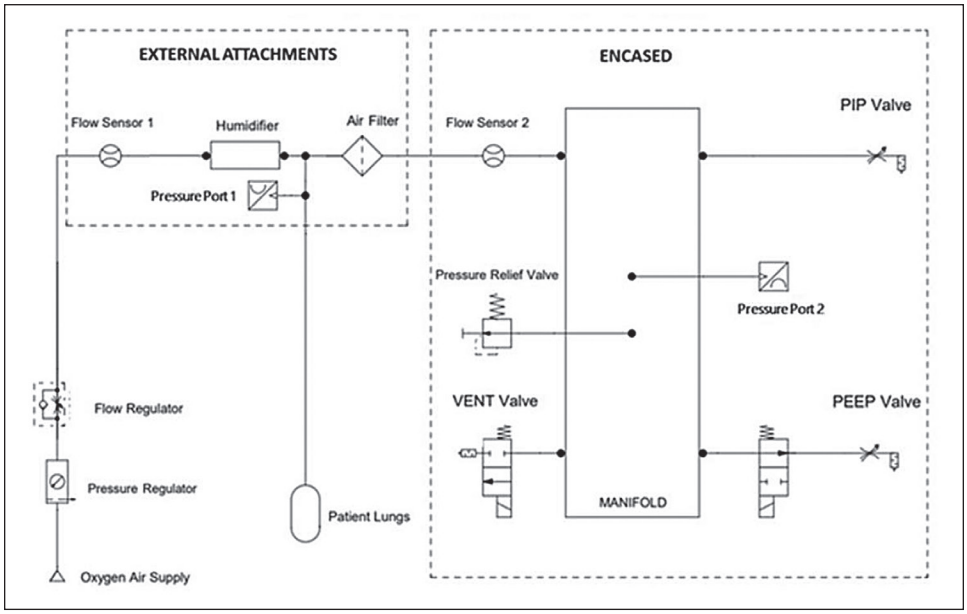


Figure 1. Pneumatic diagram of the OstreaVent2 prototype.

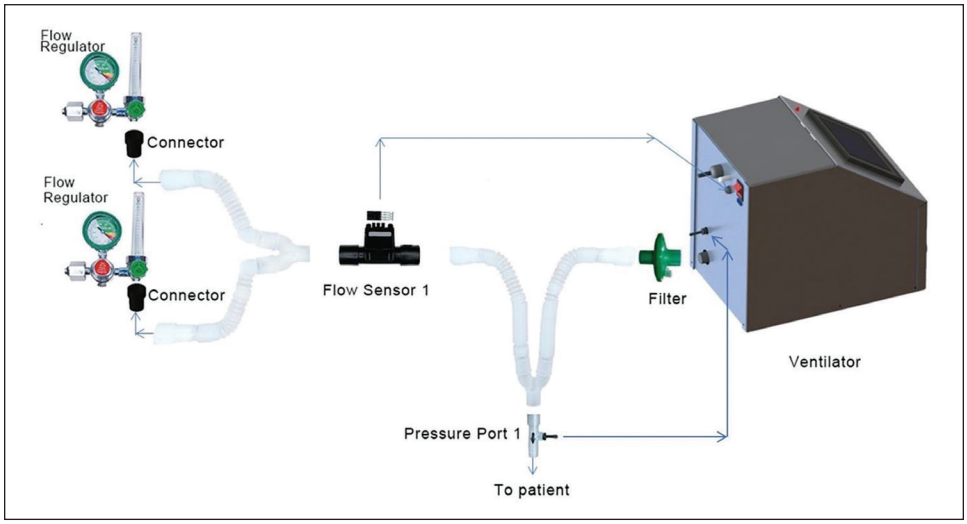


Figure 2. External hardware, ports, and accessories of the OstreaVent2.

Table 1. Performance Specifications and Tolerances of the OstreaVent2 Prototype

Parameters	Ranges	Tolerances
Tidal Volume	0-550 mL	Greater of ±50 mL or ±10%
Breath Rate	0-60 bpm	Greater of ±2 bpm or ±3%
PEEP	0-17 cmH_2O	±2.5 cmH_2O
PIP	0-40 cmH_2O	±2.5 cmH_2O
Over Pressure Relief	45-60 cmH_2O	±2.5 cmH_2O
Inspiratory Time	0.5-2 sec	±0.02 sec
High-Pressure Alarm Limit	5-45 cmH_2O	±2.5 cmH_2O
Low-Pressure Alarm Limit	3-20 cmH_2O	±2.5 cmH_2O
Alarm Volume	70 dB at 1 m	±5 dB

Flow Analyzer Plus 4080 Ventilator Test System (TSI). Thereafter, the prototype was submitted for certification by an external DOST-recommended third-party assessor to obtain a certificate of 24-hour consistency of its parameters.

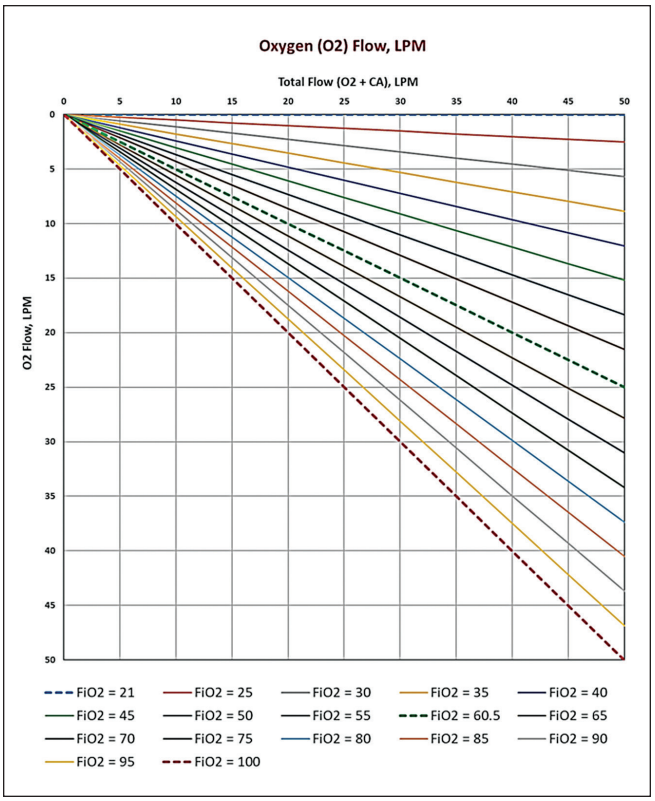
OstreaVent2 Performance Specifications and Tolerances

Table 1 shows the different parameters and tolerances of the OstreaVent2. These parameters were measured using the Certifier® Flow Analyzer Plus 4080 Ventilator Test System (TSI).

External features and accessories of the OstreaVent2

The OstreaVent2 hardware measured 43 x 27 x 36 cm in dimension and weighed 10kg. A 7" Touchscreen user interface with an 800 x 600 resolution was installed for ease of operation. An external port was placed for the expiratory arm of the ventilator tubing. A USB port was installed to allow a download of the previous 3,000 respiratory cycles to analyze the ventilator's performance. A stand could be attached at the bottom of the prototype. A red power button could be seen at the upper left corner (Figure 2).

Gas mixture was sourced from the combination of oxygen and medical air gas set at specific flow rates to deliver desired FiO_2. Oxygen blending was done using the graph below (Figure 3). Computation of gas mixture could also be done using the cellphone application: Respiratory Flow CALC (copyright pending) developed by APP and accessible using the link: https://webclient.openasapp.net/portal#!/client/app/705edd81-38b4-4291-845f-250a277255d0?invitationId=362c1faa-fb27-4f64-84a6-8f29293aa193&token=eyJhbGciOiJIUzI1NiIsInR5cCI6IkpXVCJ9.eyJvYWEuYWN0Lmludi51c2UiOiJ7XCJpbnZpdGF0aW9uSWRcIjpcIjM2MmMxZmFhLWZiMjctNGY2NC04NGE2LThmMjkyOTNhYTE5M1wifSIsImlhdCI6MTY4NTgwNDcyNSwiaXNzIjoidXJuOm9hYTpzZXJ2aWNlOnRva2VuIiwiYXVkIjoidXJuOm9hYTpzZXJ2aWNlOnRva2VuIn0.G0dhkCAEWYv7ZAFcucwfcmMITZNMl7ROI1A0b_zhzi0.



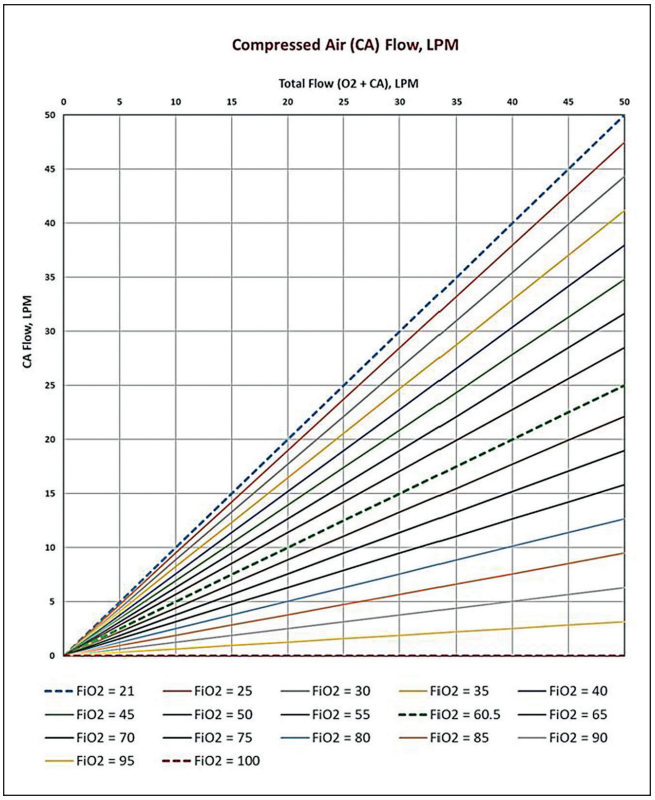


Figure 3. Blending of oxygen and compressed air depending on the desired oxygen delivery and flow rate. (Paran AP, 2021).

Screen Displays

The Touch Screen showed the actual pressures, tidal volume, flow rate, inspiratory time, I:E ratio, ventilator rate, and the calculated mean alveolar pressure (MAP). The screen could display moving bar graphs for the pressure and the volume delivered (Figure 4A). There is an option to display scalars of pressure versus time and volume versus time. Scalar displaying pressure versus time is shown in Figure 4B.

Parameter alarms

Minimum and maximum alarm settings could be inputted directly on the screen. A password would be needed to override the default alarm settings of the OstreaVent2.

Safety Shutdown

To avoid accidental shutdown of the OstreaVent2, a 2-step procedure was incorporated. To turn off the OstreaVent2, pressing the red power button icon on the home screen (Figure 4A) would lead to the first sub-screen prompt (Figure 5A). The next step was to click on the red power switch located at the upper right corner at the back of the OstreaVent2 (Figure 2) which would result into another sub-screen prompt (Figure 5B) to press on the SHUTDOWN command on the home screen.

Ventilator shutdown due to Power Interruption

In the event of an unexpected ventilator shut down due to power interruption, the OstreaVent2 has a built-in uninterrupted power supply for 30 mins.

Certification of the OstreaVent2

A third-party assessor accredited by the DOST tested the prototype OstreaVent2 for a 24-hour consistency test. The OstreaVent2 passed the accreditation test and was issued the Philippine FDA Certificate for Medical Listing which allowed the ventilator to proceed to the safety, clinical trial.

Safety Clinical Trial

An Institutional ethical board approval was obtained for a safety, clinical trial from the UP Manila Ethical Review Board. Ten patients were recruited in the study after an informed consent was obtained from their legally appointed representatives. Two patients were from the Pediatric ICU and eight were from the Adult ICU. The patients' mean age was 39.1 ± 11.6 years with 60% males. The most common diagnosis was pneumonia (50%) followed by acute respiratory failure from a central nervous system pathology (30%), bronchial asthma (10%), and neurogenic pulmonary edema (10%). The patients were recruited on their mean hospital

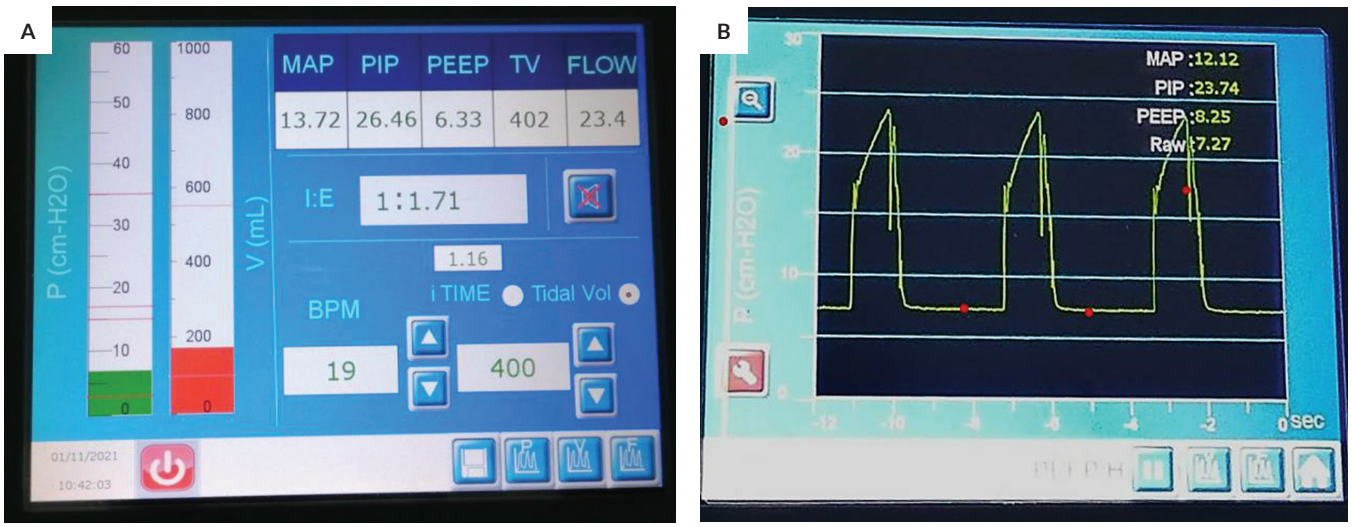


Figure 4. Screen display of the OstreaVent2 showing actual ventilator parameters, bar graph **(A)**, and Pressure-time scalar **(B)**.

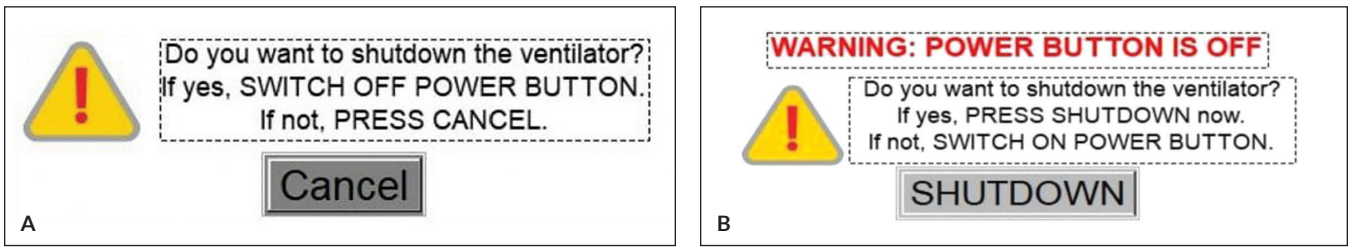


Figure 5. **(A)** First sub-screen display on safety shutdown of the OstreaVent2; **(B)** Second sub-screen display affirming shutdown of the OstreaVent2.

day of 15.3 ± 9.3 days and on their mean ventilator days of 13.3 ± 7.8 days. Majority of the patients were on the Puritan Bennet ventilator (90%). Mean baseline ventilator settings were: FiO_2 of 0.33 ± 0.05, PIP of 18.0 ± 3.6 cmH_2O, PEEP of 5.8 ± 1.4 cmH_2O, TV of 367.0 ± 76.1 ml, Ventilator rate of 15.2 ± 5.9 breaths per min and Flow rate of 42.2 ± 11.5 L/min (Table 2).

Table 2. Baseline Characteristics of the 10 Adult Participants

Patient Characteristics	Mean	SD
Age (years)	39.1	11.6
Days of hospitalization when patient was recruited	15.3	9.3
Days on the ventilator when patient was recruited	13.3	7.7
Initial Ventilator Support		
FiO_2	0.33	0.05
PIP	18.0	3.6
PEEP	5.8	1.4
Tidal volume	367.0	76.1
Ventilator rate	15.2	5.9
Flow rate	42.4	11.5
	No.	**%**
Sex		
Male	6	60
Female	4	40
Diagnosis		
Acute respiratory failure due to central cause	3	30
Pneumonia	5	50
Bronchial Asthma	1	10
Neurogenic Pulmonary Edema	1	10
Ventilator Brand		
Puritan Bennet	9	90
Mindray	1	10

Median Ventilator Settings

All patients were on volume-controlled mode. The parameters set by the clinician in the original ventilator were followed in the OstreaVent2, e.g., tidal volume (TV), positive end expiratory pressure (PEEP), ventilator rate (VR), and the flow rate (FR). During the 4-hour period on the OstreaVent2, there was no instance when the clinician needed to increase or decrease the ventilator settings due to patient intolerance or deterioration.

Results of volume-controlled ventilation of 10 patients on the OstreaVent2

Tidal Volume

The median tidal volumes of all 10 patients were stable throughout the study period (Figure 6). The values of the 1st and 3rd quartiles of the tidal volume were less than ± 50 mL from the tidal volumes set in the commercial ventilator at all time points during the 4-hour study period. The IQRs at different time points were narrow ranging from 40- 65 mL.

As can be noted in Figure 7, there was minimal variability among the tidal volume delivered to individual patients at different time points during the 4-hour period. There were only two transient tidal volume deviations beyond 50 mL on Patient 3 (-114 and -86 ml from median TV at 180 and 240 minutes, respectively) and Patient 10 (-140 and -80 ml from median TV at 15 and 240 minutes, respectively). Deviations were below the patients' median tidal volumes.

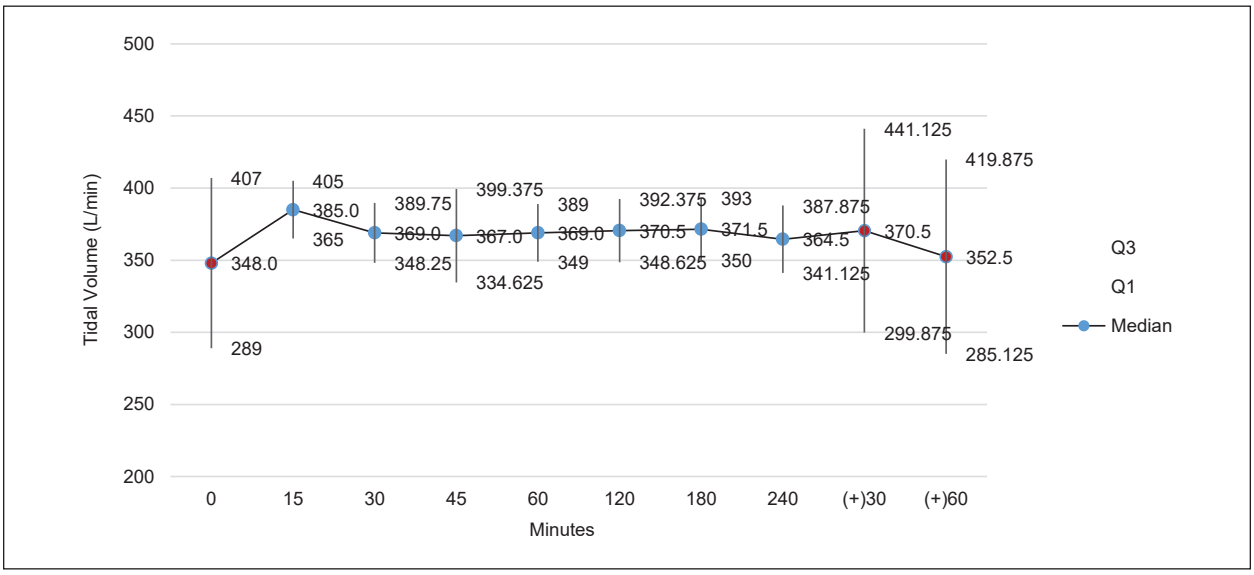


Figure 6. Median (±1 IQR) tidal volumes of the 10 adult patients before, during, and after placement on the OstreaVent2.

* *Blue circles are the actual tidal volumes delivered by the OstreaVent2 at 15-240 mins.*
** *Red circles are baseline (0) and +30- and +60-minutes values off the OstreaVent2 and on the commercial ventilator.*

PEEP

PEEP on the commercial ventilator was set at 5 cmH_2O. In the OstreaVent2, PEEPs were also set at 5 cmH_2O and the actual pressures displayed on the screen were recorded. The median PEEP ((blue dots) measured during the study period were relatively stable (Figure 8). Deviations of the median PEEPs recorded while on the OstreaVent2 during the trial period were within the acceptable tolerance of ± 2.5 cmH_2O except in two patients. Patient 8 had PEEPs which were -4.42 cm, -5.21 cm, +2.71 cm and +2.58 cmH_20 above the patient's median PEEP at 30-, 45-, 180- and 240-minute readings, respectively on the OstreaVent2. Patient 9 had a PEEP of 3.1 cmH_2O above the patient's median PEEP at 30 minutes on the OstreaVent2.

Considering the PEEP delivered by the OstreaVent2 to the individual patients, there was minimal PEEP variability as noted by the narrow IQR. The deviations (Figure 9) from the patients' median PEEP were < ±1.5 cm in all patients

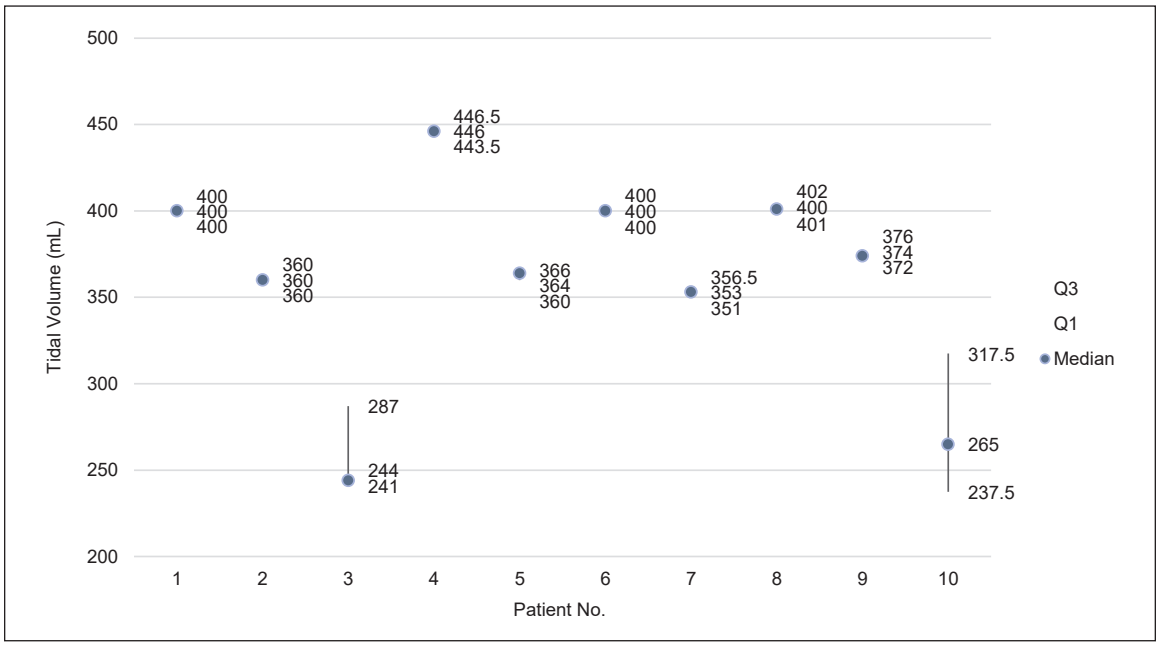


Figure 7. Median (±1 IQR) tidal volumes of individual patients during the 4-hour study period on the OstreaVent2.

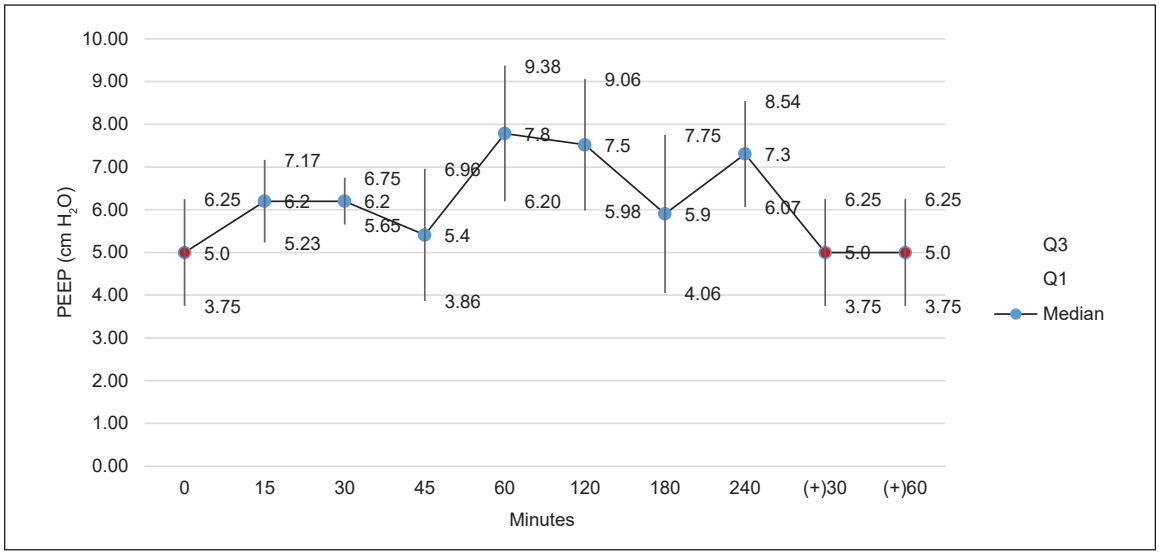


Figure 8. Median (±1 IQR) PEEP of the 10 patients before, during, and after placement on the OstreaVent2.

* *Blue circles are the actual tidal volumes delivered by the OstreaVent2 at 15-240 mins.*
** *Red circles are baseline (0) and +30 and +60 minutes values off the OstreaVent2 and on the commercial ventilator.*

except for two patients. For Patient 8, there were a -4.2 and -5.2 cmH_2O differences from the patient's median PEEP at the 30th and 45th minute on the OstreaVent2. Patient 9 had a transient increase of 3.1 cmH_2O from the patient's median PEEP at the 30th minute on the OstreaVent2.

Flow Rate

Flow rates were automatically set in the commercial ventilators to be able to provide the desired tidal volume. On the OstreaVent2, the flow rates were set from 30-40 L/min as an estimation of the flow rates in the commercial ventilators. External from the OstreaVent2, the total flow rate was the combination of the oxygen and medical air flow rates using the flow meters connected to the gas tank or central gas supply. A flow sensor was placed in the inspiratory limb of the patient's ventilator tubing to measure the actual flow rate provided. As can be noted, the flow rates were stable in most patients with a tolerance of <5 L/min during the 4-hour study period (Figure 10). Patient 1 had a flow rate of 7.8 L/min below the patient's median at 60 minutes on the OstreaVent2 after which all flow rates were <1 L/min from the median. Patient 6 had a flow rate of 5.7 L/min below the patient's median flow rate with all the other readings <3 L/min from the median. Patient 7 had flow rates which were

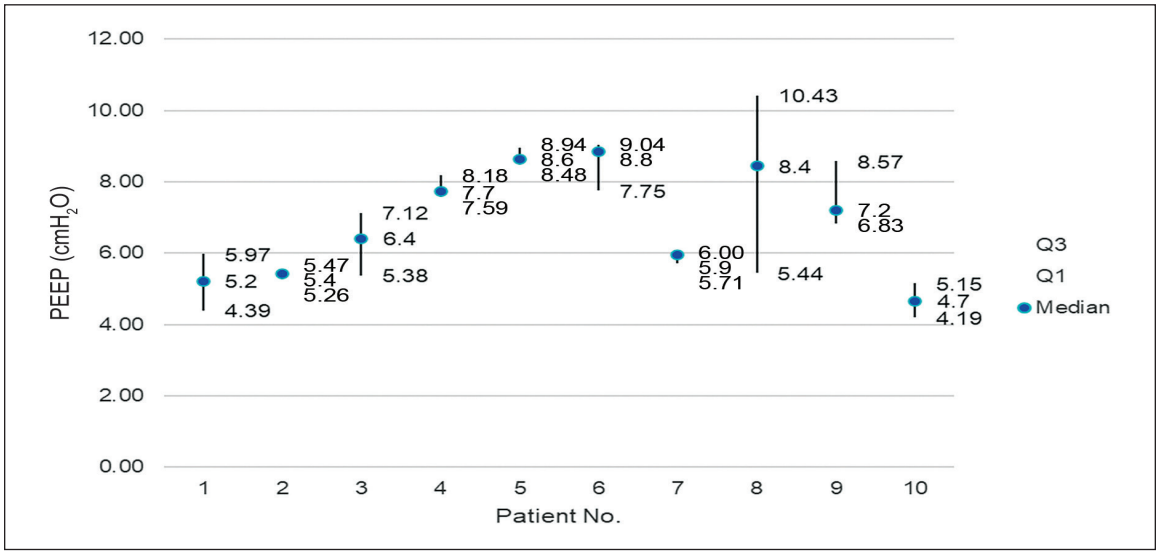


Figure 9. Median (IQR) PEEP of individual patients during study period on the OstreaVent2.

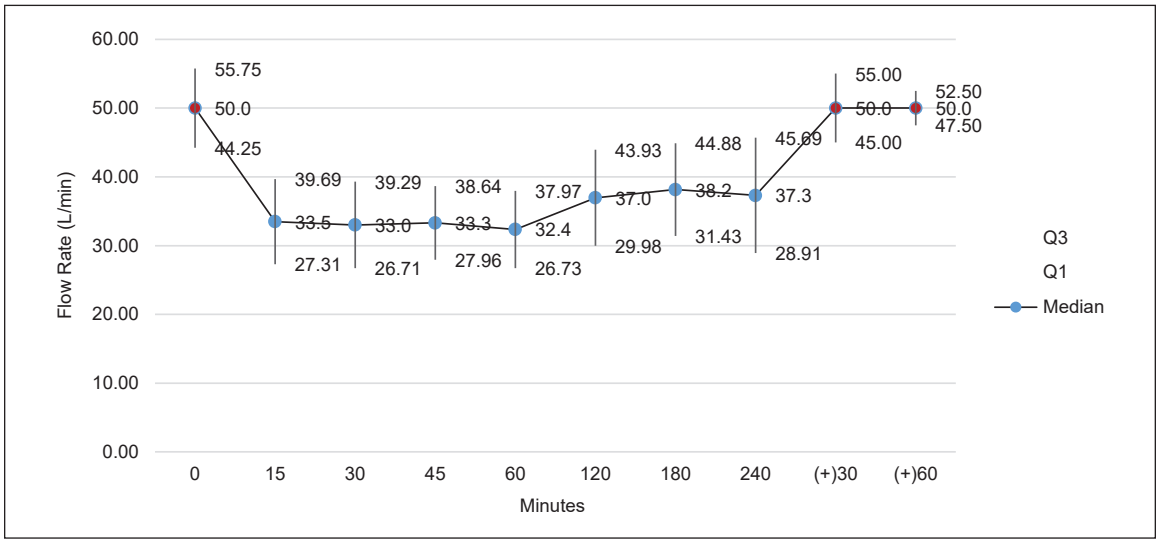


Figure 10. Median (1 IQR) flow rate of the 10 patients before, during, and after placement on the OstreaVent2.

* *Blue circles are the actual tidal volumes delivered by the OstreaVent2 at 15-240 mins*
** *Red circles are baseline (0) and +30 and +60 minutes values off the OstreaVent2 and on the commercial ventilator.*

10.6, 11.7, 11.3 L/min below the patient's median flow rate at 120, 180 and 240 minutes, respectively on the OstreaVent2, with the rest of the readings <3.6 L/min from the median. All deviations of flow rates were below the median FR.

The flow rates of individual patients were stable except for Patient 7 who had transient deviations of 10-11 cmH_2O below his median flow rate during the 4-hour study period (Figure 11). However, this was not associated with a decrease in the tidal volume delivered (Figure 7).

Ventilator Rate

The ventilator settings on the commercial ventilator varied from assist control, pressure support, synchronized intermittent mandatory ventilation so that the ventilator rate was variable since these were the patients' spontaneous breaths. The ventilator breaths of the OstreaVent2 were non-synchronous intermittent mandatory ventilation and were set at 10-20 breaths per minute (blue dots) following the patients' respiratory rate at baseline. As such, all ventilator

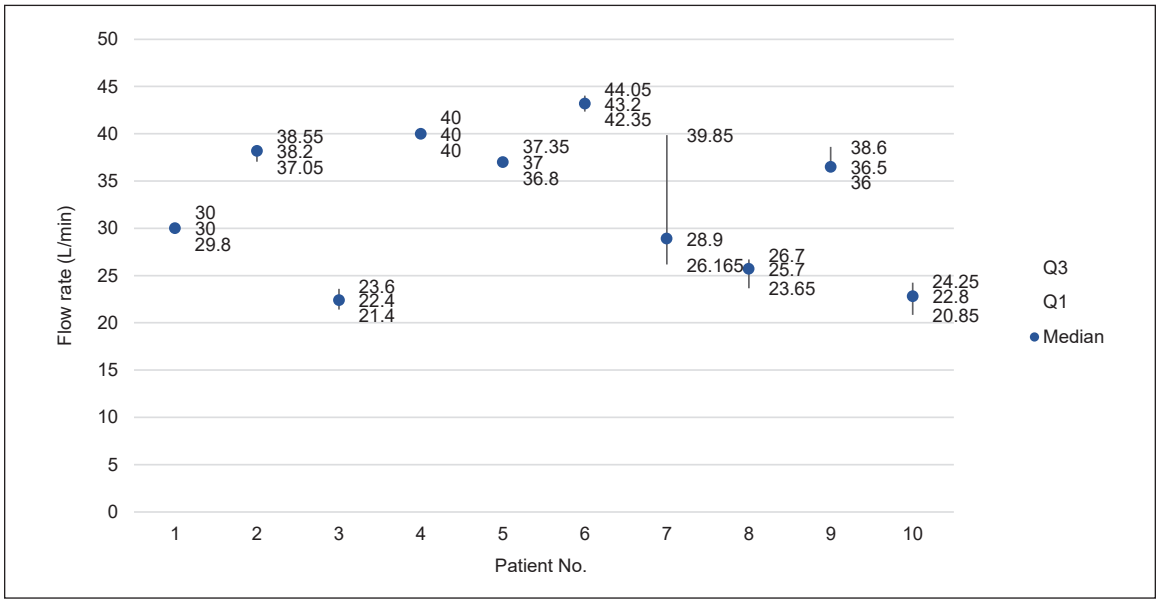


Figure 11. Median (IQR) flow rate of individual patients during the 4-hour study period on the OstreaVent2.

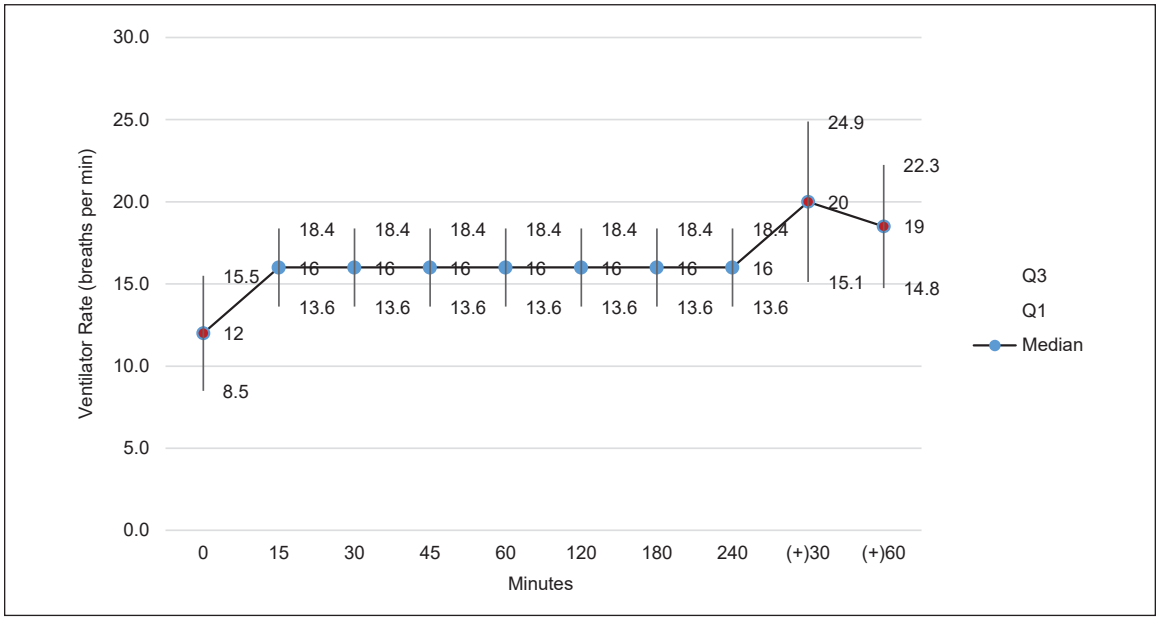


Figure 12. Median (IQR) ventilator rate of the 10 patients before, during, and after placement on the OstreaVent2.

* *Blue circles are the actual tidal volumes delivered by the OstreaVent2 at 15-240 mins.*
** *Red circles are baseline (0) and +30 and +60 minutes values off the OstreaVent2 and on the commercial ventilator.*

rates recorded were the same as the set mandatory breaths in the OstreaVent2 (Figure 12).

Dependent ventilator parameters

The following were ventilator parameters that were not set on the OstreaVent2.

FiO_2

The OstreaVent2 does not have an oxygen blender so that the FiO_2 was a mixture of different flow rates of the oxygen and compressed air (either from gas tanks or a central source). Throughout the study period from 30 minutes prior to transfer to the OstreaVent2 up to 60 minutes back on the original mechanical ventilator, the FiO_2 requirements of the patients remained the same.

PIP

Peak inspiratory pressures were not set during the study since all patients were on volume-control. The commercial and the OstreaVent2 ventilators have set maximum peak inspiratory pressure (Pmax) to avoid lung trauma with the latter setting a default Pmax at 45 cmH_2O. The PIP during volume mode ventilation would be dependent on the lung pathology which would affect its compliance and resistance. As can be seen, the variability was very low (<2.5 cmH_2O from the median) in the PIP measured in individual patients during the 4-hour period (Figure 13). There was a transient increase of 9.97 cmH_2O at the 60th minute on the OstreaVent2 on Patient 9 with the rest of the PIP with minimal variability.

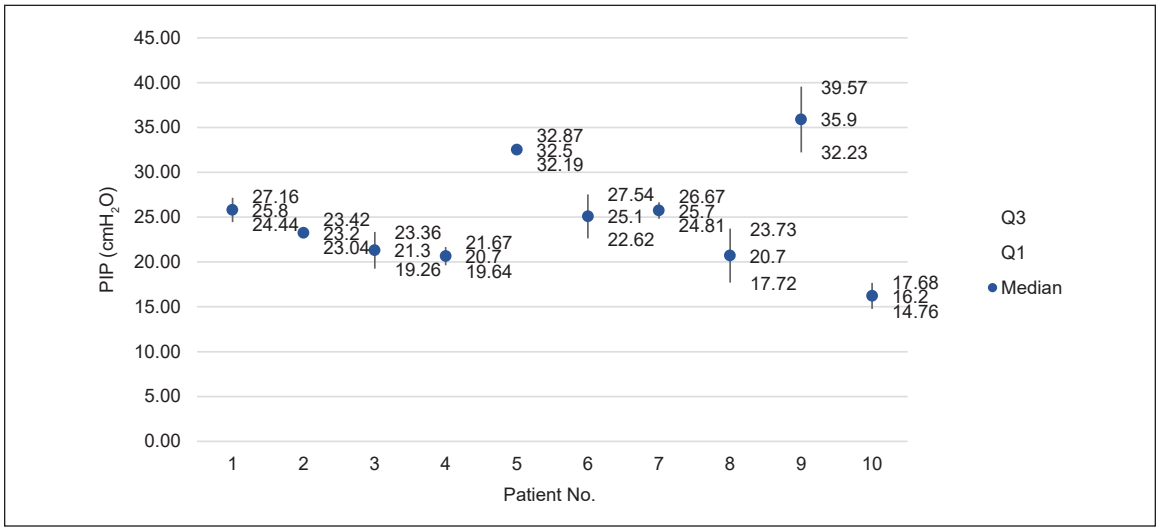


Figure 13. Median (IQR) PIP of individual patients during the 4-hour period on the OstreaVent2.

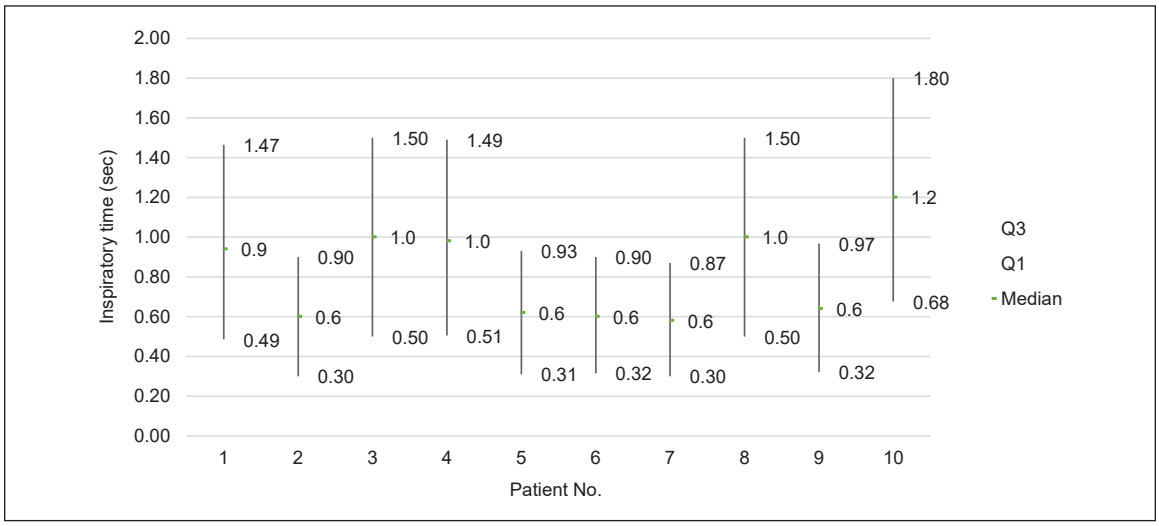


Figure 14. Median (1 IQR) inspiratory time of individual patients during the 4-hour OstreaVent2 study period.

Inspiratory time

Inspiratory time was measured on each breath of the patient. As can be seen, median inspiratory time ranged from 0.5 to 1.2 secs. Differences from 3rd quartile to median ranged from 0.27 to 0.6 second and differences from median to the 1st quartile were similar (Figure 14).

Vital Signs

Median vital signs (heart rate, respiratory rate, systolic and diastolic pressure, mean arterial pressure, axillary temperature, and peripheral oxygen saturations) were stable before, during, and after placing the patients in the OstreaVent2 (Figure 15). Interquartile ranges were narrow.

Arterial Blood Gas

Arterial blood gas was obtained at baseline (60 mins before), one hour after patients were placed on the OstreaVent2, and 60 mins after the patients were transferred back to the original mechanical ventilator.

Blood gas parameters were stable all throughout the study period. However, there was note of a lower but still within normal range of the median pO_2 one hour after placement on the OstreaVent2 (Figure 16). No concomitant desaturations were noted.

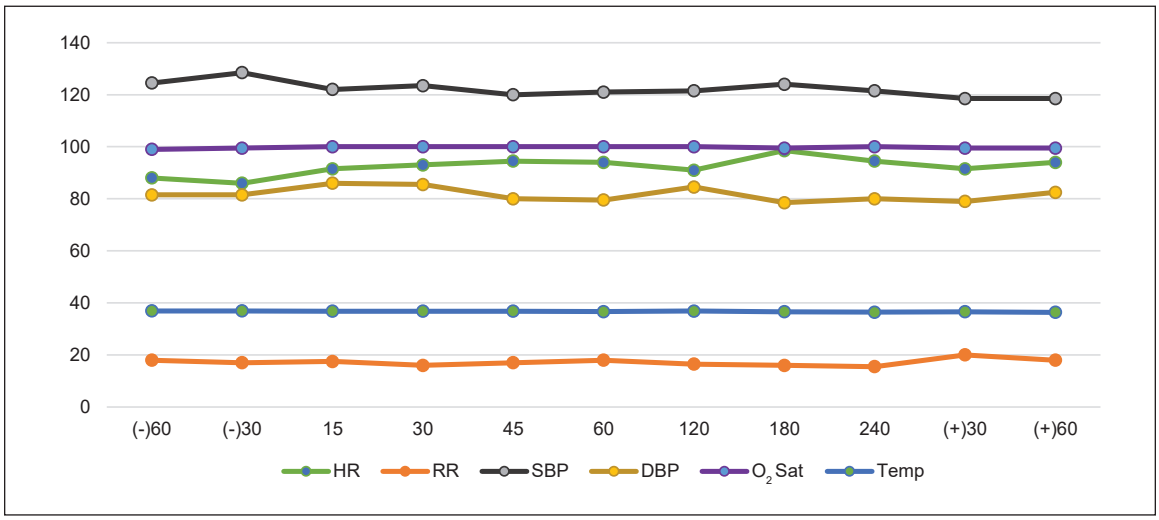


Figure 15. Median vital signs of the 10 patients before, during, and after placement on the OstreaVent2.

* *Minutes 15 to 240 were the time period the patients were on the OstreaVent2*
** *-60 and -30 were time periods prior to attaching to the OstreaVent2*
*** *+30 and +60 were 30 and 60 mins after removal from the OstreaVent2 and return to previous mechanical ventilator*

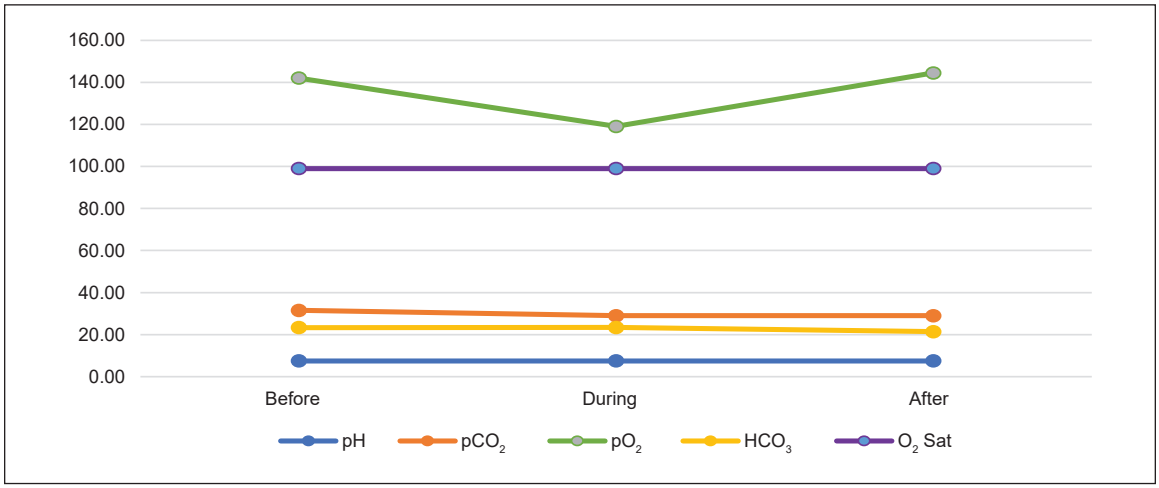


Figure 16. Median (IQR) arterial blood gases of the 10 patients 1 hour before, 1 hour after placement on the OstreaVent2, and 1 hour after return to commercial ventilator.

Patient Outcomes

All patients remained stable during and after the OstreaVent2 placement. There were no reported episodes of oxygen desaturations, intercoastal retractions or gasping during the study period. There was one episode of alar flaring in Patient 10 which was relieved by endotracheal tube suctioning. Post-study chest radiographs did not show worsening of lung pathology, atelectasis nor air leak. All the patients survived except one who died three days after she was transferred out of the ICU. This patient was a 63-year-old female who was on the mechanical ventilator for 40 days prior to recruitment to the study. She was transferred out of the ICU but subsequently deteriorated and died three days after the transfer to the step-down unit. Final diagnosis was acute respiratory failure, third degree atrio-ventricular block, and acute renal failure.

DISCUSSION

The results showed that the OstreaVent2 prototype fulfilled all the requirements set by the Association for the Advancement of Medical Instrumentation (AAMI) for an emergency ventilator during the COVID-19 pandemic.[14] Tolerances or variabilities within the ventilator parameters were within acceptable limits set by the AAMI taskforce. Although the OstreaVent2 was placed on the adult patients for only four hours, it has also passed the 24-hour consistency report by a DOST-accredited third-party assessor.

The OstreaVent2 is safe to use in adult patients needing ventilator support, as shown by the stable ventilator parameters set such as the PEEP, IT, tidal volume, and flow rates. Variations were within the acceptable tolerances. For the flow rates and the PEEP, the deviations observed were mostly below the median values and as such, there was no risk for lung injury. Furthermore, since the delivered parameters were continuously measured and displayed on the screen, the operator can adjust settings to achieve the desired parameter value. Also, the OstreaVent2 has alarms for high or low limit pressures so that any significant deviations will result in an audiovisual alarm.

Patients' vital signs were stable throughout the study period so there was no instance when the ventilator settings were changed, or a patient was withdrawn from the study. One patient had transient alar flaring which was resolved with endotracheal suctioning.

As of June 21, 2023, the Philippines had 4,159,310 cases with 66,482 deaths (1.6%).[15] From April 1, 2020 to June 30, 2022, a total of 93 patients were placed on a mechanical ventilator at the PGH. The average ventilator duration was 9.8 ± 8.10 days and with a range from <1 to 39 days.[16] This underscores the need for mechanical ventilators in highly affected countries, including the Philippines.

In the US, nearly 200,000 additional mechanical ventilators were deployed in different states.[17] There was a 31.5% increase in purchase of adult ventilator and a 16.5% increase in neonatal/pediatric ventilators from 2019 to 2020.[18] On a review of the current US SNS ventilators purchased and on order, approximately only half of the ventilators has the capability to support COVID-19 patients with severe hypoxic acute respiratory failure and adult respiratory distress syndrome.[19] Although focus of the control of the pandemic should be on the prevention of spread of the infection through immunization and behavior modification, ventilators capable of treating those with severe COVID-19 infection should be available.

In anticipation of the potential shortage of mechanical ventilators due to the COVID-19 pandemic, manufacture of adult ventilators was contemplated worldwide. One such ventilator was the ACUTE-19 ventilator developed in Spain which was a microprocessor-controlled, turbine-based ventilator which could provide non-assisted pressure-controlled and continuous positive airway pressure modes. It has undergone simulation testing with an artificial lung and bench comparison with the VIVO-50 commercial ventilator with promising results. Animal testing involved placement of the ACUTE-19 on a 60-kg. adult sheep for 8 hours.[20] Similar to the OstreaVent2, its oxygen blending was external to the mechanical ventilator. However, unlike the OstreaVent2, it did not have a volume-controlled mode and no human trial has been published.

The OstreaVent2 is a certified and safe mechanical ventilator which can be used among adults in respiratory failure whether due to SARS-CoV-2 virus or other pathogens. This will enable greater access to affordable adult ventilators. At present, other Philippine scientists are also developing low-cost adult ventilators. Testing of the prototypes are ongoing.

CONCLUSION

The OstreaVent2 adult mechanical ventilator, a pressure- and volume-controlled, time-cycled with intermittent mandatory ventilation, has been found to be safe for use in adult patients who need ventilator support.

FUTURE PLANS

There are plans to incorporate Assist Control and synchronized intermittent ventilation modes in the OstreaVent2. Internal oxygen blending is also contemplated.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

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