

PRESSURE & VOLUME - CONTROLLED MECHANICAL VENTILATION FOR COVID-19 PATIENT WITH ARDS

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ABSTRACT: Mechanical Ventilator is a machine that helps a patient breathe (ventilate) when they are having surgery or cannot breathe on their own due to critical illness. In the present situation of COVID-19, many people lose their life due to respiratory problems. In respiratory problems, human lungs get damaged & cavity creates in the lung. A mechanical ventilator is playing a vital role in tackling this situation. Ventilators needed for providing inspiration or expiration from the body. The simulator provides a monitoring window to observe the optimal respiratory waveform of instantaneous pressure, airflow, and lung volume. Through the use of virtual instruments, the optimized breathing, includes frequency, the pressure of CO₂, initial lung volume can be monitored. Ventilation process is implemented using LabVIEW tools and can be used to monitor the breathing per minute, TLC, Vt, pressure-volume control, and also in respiration and flow without any negative effect. LabVIEW provides virtual instruments like a PID controller, switches, mathematical components, counters, Timer, etc. The three basic modes of ventilation include volume-controlled ventilation (VCV), pressure-controlled ventilation (PCV), and pressure support ventilation (PSV). Acute respiratory distress syndrome (ARDS) is a syn-drome characterized by increased permeability pulmonary edema, lung inflammation, hypoxemia, and decreased lung compliance. Clinical criteria include bilateral opacities on chest imaging, hypoxemia with a PaO₂/FIO₂ ratio < 300 mm Hg with positive end-expiratory pressure (PEEP) ≥ 5 cm H₂O, and the respiratory failure cannot fully be explained by cardiac failure or fluid overload.

Keywords: (respiratory, COVID-19, Pressure-volume control, LabVIEW, ARDS, PCV, VCV)

I. INTRODUCTION: A Ventilator is a mechanical device that helps patients with their respiration. The ventilator for therapy is for the severely sick and asks for the ability to realize a variety of ventilations depending on the needs. A mechanical ventilator is a device that supports enough oxygen for patients with respiratory distress in an intensive care unit (ICU). Oxygen is important for human beings since it provides energy. Respiration can be defined as transportation of oxygen and carbon dioxide. It has two phases: inspiration and expiration. Inhalation or inspiration is defined as taking air into the lungs, and exhalation or

expiration is called the process of breathing it out. Ventilation can be done in three different types. These are negative pressure ventilation, positive-pressure ventilation and high-frequency ventilation. In the designing of intelligent mechanical ventilator prototype and user interface. Understanding mechanical ventilation must start with a review of the physiology and mechanics of normal spontaneous breathing. Spontaneous breathing is defined as movement of air into and out of the lungs as a result of work done by an individual's respiratory muscles. Positive pressure ventilation, on the other hand, is defined as movement of air into the lungs by the application of positive pressure to the airway through an endotracheal tube, tracheostomy tube, or noninvasive mask. It is frequently delivered to patients admitted to intensive care units (ICU). In most cases, the ventilator is set to completely control the patient's ventilation shortly after intubation. The objective is to improve the ability to inhale without causing any damage to the lungs and to put the respiratory muscles at rest. When a patient's condition starts to improve, his/her ventilation is favored by the ventilator until destination. There is no clear consensus about when, how, and at which level the patient's work of breathing should be reduced. Insufficient assistance may induce diaphragmatic fatigue or weakness and force the recruitment of accessory inspiratory muscles, sometimes leading to respiratory acidosis.

II. LITERATURE SURVEY:

BASIC TERMINOLOGY OF CONTROL MODES: Some functions have been used for controlling the function of ventilation.

1. PEEP (positive end-expiratory pressure): It stands for positive end-expiratory pressure which in layman's terms is the pressure at which the lungs must be after completing explorations, this is a crucial parameter as the all behind might collapse if the beep is too low causing inflammation and other complications. The basic function of PEEP is to increase the pressure.

2. Pmax (Maximum pressure): It is simply the maximum pressure of the lungs of their inspiration. It can be triggered by the system as per the requirements of breaths.

TLC (Total lung capacity): It is the total capacity of the lungs (airway) which takes the maximum volume of gas, it may be calculated as:

$$\text{TLC} = \text{Vital capacity} + \text{Respiratory volume}$$

4.VT (Tidal Volume): It stands for tidal volume of the lungs which is the difference of the volume between the breath.

5.VC (Volume Control): It is the specific mode in which our simulation will run is intermittent mandatory ventilation (IMV).

6. BPM (Breath per minute): It is quite self-explanatory which means the amount of air breathed per minute.

7. PAW (Airway Pressure): It is a pressure that is applied in positive pressure and can be calculated as the average pressure of the lung during inspiration and expiration.

8.Spontaneous Breathing: It is defined as movement of air into and out of the lungs as a result of work done by an Individual's respiratory muscles.

9. Pleural Space: The potential space between the lungs and the chest wall is known as the pleural space.

10.Pleural pressure (Ppl): The coupling of the lungs and the chest wall, pressure in the pleural space, known as Pleural pressure

11.Alveolar Pressure (Palv): The forces pushing the alveolar walls outward must equal the forces pushing the alveolar walls inward. The expanding outwards force is alveolar pressure

12.Transpulmonary pressure (Ptp): The difference between alveolar pressure and pleural pressure.

$$P_{tp} = P_{alv} - P_{pl}$$

13. Assist-Control: A patient trigger (assist) and a ventilator trigger (control) can be combined to create a hybrid trigger mode known as assist-control (A/C).

14. PSV: It is known as pressure support ventilation

15. ARDS: Acute respiratory distress syndrome (ARDS) is a syndrome characterized by increased permeability pulmonary edema, lung inflammation, hypoxemia, and decreased lung compliance

16. Breath Stacking: Mechanical ventilation in patients with inefficient exhalation can be challenging as patients may not achieve full exhalation prior to the triggering of another breath, a phenomenon known as breath stacking.

17. Shallow Breathing: The breathing pattern of low tidal volume with a high respiratory rate is referred to as rapid shallow breathing.

III. RESPIRATORY SYSTEM & MODEL: The flow of air in and out of the lungs can be model in a manner similar to an electrical circuit using Ohm's law, where the voltage (V) across a resistor is equal to the electric current (I) multiplied by the electrical resistance (R). The difference between proximal airway pressure (Pair) measured at the mouth and alveolar pressure (Palv) is analogous to the voltage difference within a circuit.

Similarly, flow (Q) and airway resistance (R) in the respiratory system are analogous to the electric current and electrical resistance in the circuit, respectively (Fig. 1). The equation for the respiratory system can be rearranged to solve for flow

$$Q = (P_{air} - P_{alv}) / R$$

By convention, flow into the patient (inspiration) is designated as positive, and flow out of the patient (expiration) is designated as negative. Note that when proximal airway pressure equals alveolar pressure, there is no flow present in either direction (Q = 0). Under normal conditions, this scenario occurs twice during the breathing cycle, at the end of expiration and at the end of inspiration

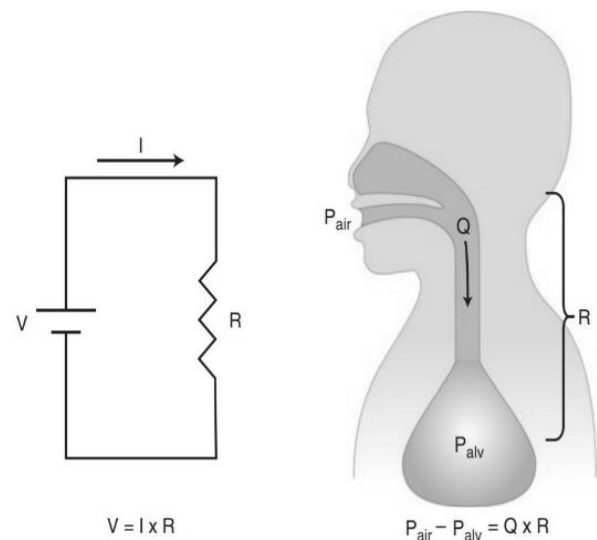


Figure 1: (The respiratory system modeled as an electrical circuit. I electric current; Pair proximal airway pressure; Palv alveolar pressure; Q flow; R resistance; V voltage)

IV. SEQUENCE OF VENTILATION EVENTS: With positive pressure ventilation, as occurs with mechanical ventilation, the ventilator increases proximal airway pressure during inspiration. This increase in proximal airway pressure relative to alveolar pressure results in a positive value for flow, causing air to flow into the patient. Expiration with positive pressure ventilation is passive and occurs in a manner similar to that which occurs in spontaneous breathing. The sequence of events for inspiration is different for spontaneous breathing than for positive pressure ventilation. In spontaneous breathing, increased intrathoracic volume leads to decreased alveolar pressure, which leads to air flowing into the patient because of the pressure gradient. With positive pressure ventilation, increased proximal airway pressure leads to air flowing into the patient, which, because of Boyle’s law, result in an increasing in lung volume.

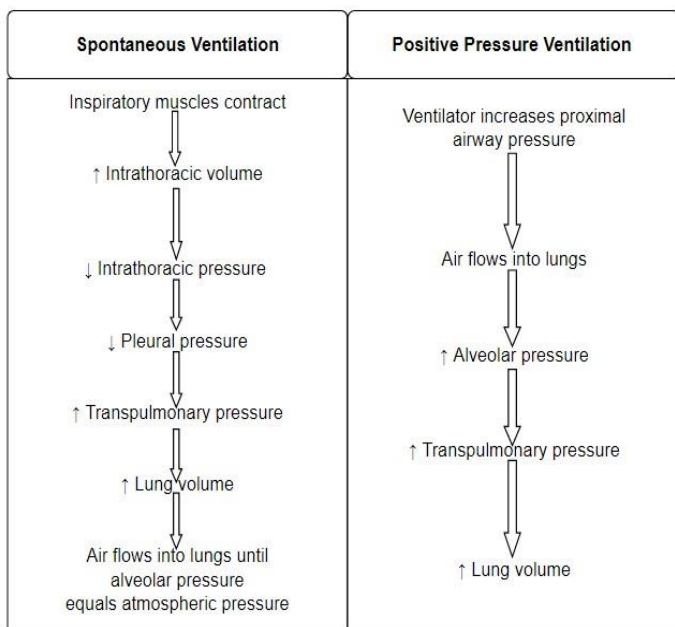


Figure 2: (Sequence of events during inspiration for spontaneous breathing and positive pressure ventilation)

V. PHASE VARIABLE: Breathing is a periodic event, composed of repeated cycles of inspiration and expiration. Each breath, defined as one cycle of inspiration followed by expiration, can be broken down into four components, known as phase variables. These phase variables determine

- when inspiration begins (**trigger**)
- how flow is delivered during inspiration (**target**)
- when inspiration ends (**cycle**) proximal airway pressure during expiration (**baseline**)

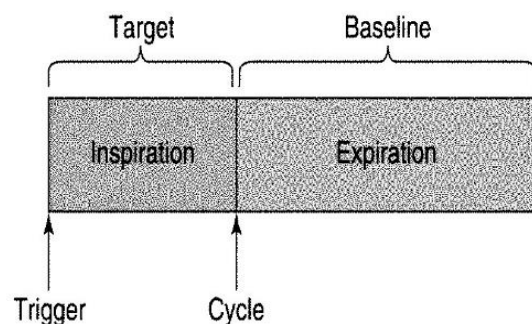


Figure 3: (Schematic of a breath cycle.)

The trigger variable determines when expiration ends and inspiration begins. The cycle variable determines when inspiration ends and expiration begins. The target variable determines flow during inspiration. The baseline variable determines proximal airway pressure during expiration.)

VI. MODES OF VENTILATION:

The three basic modes of ventilation:

- volume-controlled ventilation (**VCV**)
- pressure-controlled ventilation (**PCV**)
- pressure support ventilation (**PSV**)

Volume-controlled ventilation:

In volume-controlled ventilation, the target is flow, and the cycle is volume. Increasing flow reduces the time required to deliver the set tidal volume, which reduces inspiratory time for each breath. Decreasing inspiratory time for each breath will then increase expiratory time.

increasing flow will also increase proximal airway pressure:

$$P_{air} = Q \times R + (V/C)$$

C = compliance

Q = flow

P_{air} = proximal airway pressure

R = airway resistance

V = volume

However, most of this pressure is dissipated in the endotracheal tube and central airways, which can withstand this increased pressure. Alveolar pressure will not be affected if tidal volume remains the same. Decreasing tidal volume will also increase expiratory time. By decreasing

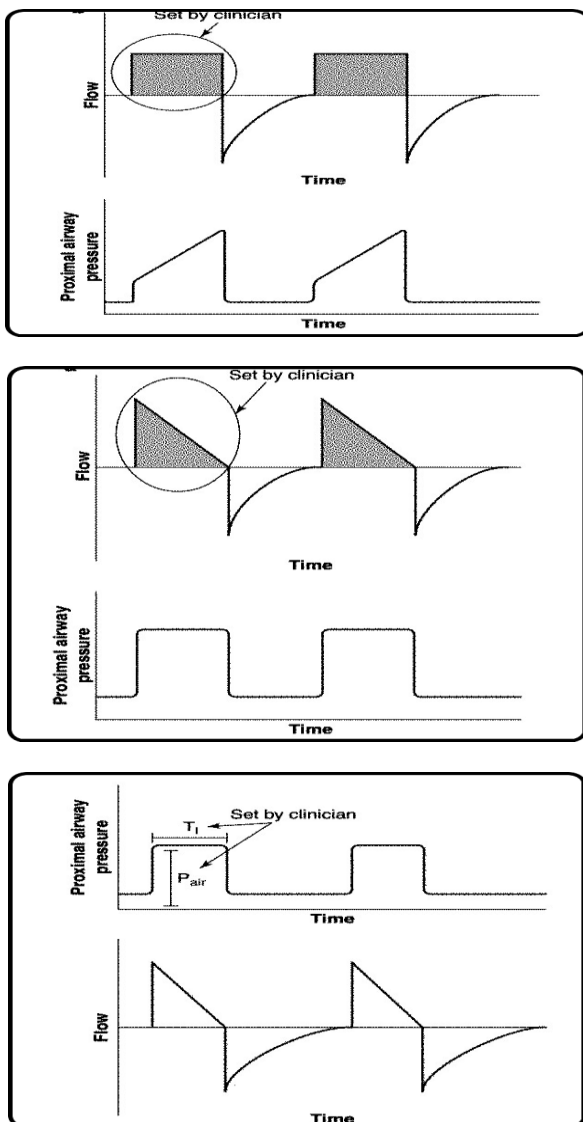


FIGURE 4: (Flow and pressure waveforms in PCV.

The target variable for PCV is pressure. The cycle variable for PCV is time. Proximal airway pressure and inspiratory time are set by the clinician. The flow waveform is a result of the interaction between the set variables (pressure-targeted and

volume, less time is needed for inspiration at a given flow, resulting in an increase in expiratory time. Additionally, with decreased tidal volume, less time is needed to fully expire the total administered tidal volume.

Pressure-Controlled Ventilation: In pressure-controlled ventilation, the target is proximal airway pressure, and the cycle is time. Inspiratory time can be directly reduced, leading to an increase in expiratory time. Tidal volume can be reduced by decreasing proximal airway pressure. With decreased tidal volume, less time is needed to fully expire the total administered tidal volume.

time-cycled) and the respiratory system. The resultant flow waveform in PCV is a decelerating ramp. (P_{air} proximal airway pressure; PCV pressure-controlled ventilation; T_i inspiratory time)

Pressure Support Ventilation: In pressure support ventilation, the target is proximal airway pressure, and the cycle is flow. Similar to pressure-controlled ventilation, proximal airway pressure can be reduced, which decreases tidal volume. Inspiratory time can be decreased by increasing the flow cycle threshold, which is the percentage of peak flow to which inspiratory flow must diminish in order for inspiration to be terminated. By increasing this threshold, flow does not have to reach as low a level, and inspiration will be terminated sooner, resulting in decreased inspiratory time. This decreased inspiratory time will also result in decreased tidal volume.

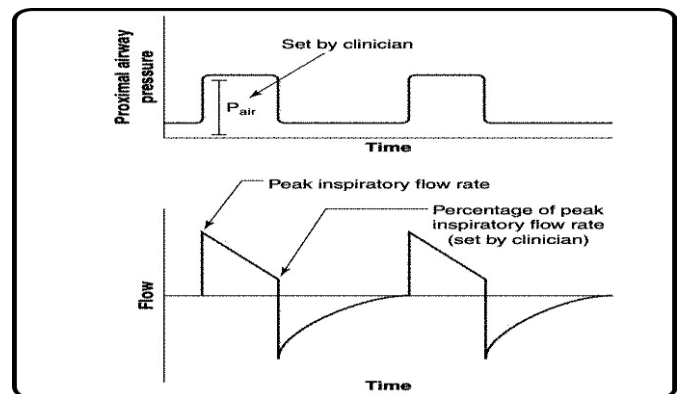


FIGURE 5: (Flow and pressure waveforms in PSV.

The target variable for PSV is pressure. cycle variable for PSV is flow. Proximal airway pressure and the percentage of peak inspiratory flow for cycling are set by the clinician. The flow waveform is a result of the interaction between the set variables (pressure-targeted and flowcycled) and the respiratory system. Similar to PCV, the resultant flow waveform in PSV is a decelerating ramp. With flow-cycling,

the breath terminates once flow depreciates to a set percentage of the peak flow, in this case 25%. Pair proximal airway pressure; PSV pressure support ventilation)

Mode of Ventilation	Trigger	Target	Cycle
VCV	Assist-control	Flow	Volume
PCV	Assist-control	Pressure	Time
PSV	Assist	Pressure	Flow

Table 1: Summary of the basic modes of ventilation

injury, leaky pulmonary capillaries, exudation of proteinaceous fluid into alveoli, and alveolar collapse. Patients with ARDS often require mechanical ventilation because of the increased work of breathing from decreased lung compliance and impaired gas exchange.

Three types of ventilator-induced lung injury have been described:

Volutrauma:

Tidal volume should be ≤ 6 mL per kg of ideal body weight to prevent volutrauma in ARDS

Barotrauma:

setting lower proximal airway pressure will ensure lower alveolar pressure and help prevent barotrauma.

Atelectrauma:

lung injury from repetitive opening and closing of alveoli, PEEP can minimize atelectrauma by preventing closure of open alveoli

PEEP IN ARDS:

- Repetitive opening and closing of alveoli cause further lung damage
- PEEP prevents open alveoli from closing
- Maintaining alveoli open will improve gas exchange

VII. ACUTE RESPIRATORY DISTRESS SYNDROME:

Acute respiratory distress syndrome (ARDS) is a syndrome characterized by increased permeability pulmonary edema, lung inflammation, hypoxemia, and decreased lung compliance. Clinical criteria include bilateral opacities on chest imaging, hypoxemia with a PaO₂ /FI O₂ ratio <300 mm Hg with positive end-expiratory pressure (PEEP) ≥ 5 cm H₂O, and the respiratory failure cannot fully be explained by cardiac failure or fluid overload. Causes of ARDS can be categorized into those resulting from direct injury to the lungs (e.g., pneumonia, aspiration, toxic inhalation, near-drowning) and those from indirect injury to the lungs (e.g., sepsis, trauma, pancreatitis, blood transfusions). Lung inflammation in ARDS causes alveolar

VIII. VENTILATOR SETUP AND ADJUSTMENT:

FiO ₂	0.3	0.3	0.4	0.4	0.5	0.5-0.8	0.9	1.0	1.0
PEEP	5	12	14	16	16	16	16	16	16

1. Calculate predicted body weight (PBW)

Males = 50+2.3 [height (inches)-60]

Females = 45.5+2.3 [height (inches) -60]

2. Select any ventilator mode

3. Set ventilator settings to achieve initial VT = 8 ml/kg PBW

4. Reduce VT by 1 ml/kg at intervals 2 hours until VT = 6ml/kg PBW.

5. Set initial rate to approximate baseline minute ventilation (not > 35bpm).

FiO ₂	0.3	0.4	0.5	0.6	0.7	0.8	0.9	0.9	1.0
PEEP	5	8	10	10	14	14	16	18	18-24

6. Adjust VT and RR to achieve pH and plateau pressure goals below.

PLATEAU PRESSURE GOAL: 30 cm H₂O

Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or VT.

- **If Pplat > 30 cm H₂O:** decrease VT by 1ml/kg steps (minimum = 4ml/kg).
- **If Pplat < 25 cm H₂O and VT < 6 ml/kg,** increase VT by 1 ml/kg until Pplat > 25 cm H₂O or Vr = 6 ml/kg.
- **If Pplat < 30 and breath stacking or dys-synchrony occurs:** may increase V. in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains < 30 cm H₂O.

OXYGENATION GOAL: PaO₂, 55-80 mmHg or SpO₂**88-95%**

- Use a minimum PEEP of 5 cm H₂O.
- Consider use of incremental FIO₂/PEEP combinations such as shown below (not required) to achieve goal.

process with NI's graphic interface, hardware and drivers. LabVIEW was developed by National Instruments as a workbench for controlling test instrumentation. However, its applications have spread well beyond just test instrumentation to the whole field of system design and operation. The LabVIEW environment consists of LabVIEW VI manager (project explorer), the programming tools, debugging features, templates and ready built sample examples, and an easy interface to the hardware drivers. LabVIEW uses a graphic interface that enables different elements to be joined together to provide the required flow. LabVIEW programs are called as virtual labs LabVIEW is a

LabVIEW KEY CONCEPT:

LabVIEW Environment: LabVIEW VI(project explorer), the programming tools, debugging features, templates and ready built sample examples.

Lower PEEP / Higher FiO₂**Table 2:** for Lower PEEP / Higher FiO₂**Higher PEEP/Lower FiO₂**

(Don't increase PEEP above 16 cm H₂O without guidance from a critical care Physician)

Table 3: Higher PEEP/Lower FiO₂

IX. SOFTWARE USED: LabVIEW: Laboratory Virtual Instrument Engineering Workbench (LabVIEW) offers a graphical programming approach that helps you visualize every aspect of your application, including hardware configuration, measurement data, and debugging. This visualization makes it simple to integrate measurement hardware from any vendor, represent complex logic on the diagram, develop data analysis algorithms, and design custom engineering user interfaces. National Instruments' (NI) LabVIEW is popularly deployed software for academic and industrial application. It is easy to control a real time visual programming language: it is a system-design platform and development environment that was aimed at enabling all forms of system to be developed. LabVIEW uses a graphic interface that enables different elements to be joined together to provide the required flow. LabVIEW is essentially an environment that enables programming in G – this is a graphical programming language created by National Instruments that was initially developed to communicate via GPIB, but since then it has been considerably updated. Nowadays, G can be used for automated test applications, general data acquisition, programming FPGA etc

LabVIEW VIs: Enables a user interface to be built and it contains the programming code.

LabVIEW G Programming: Graphical programming language where the functional algorithms are “built using drag and drop” techniques. Graphical programming determines the running order for the programme.

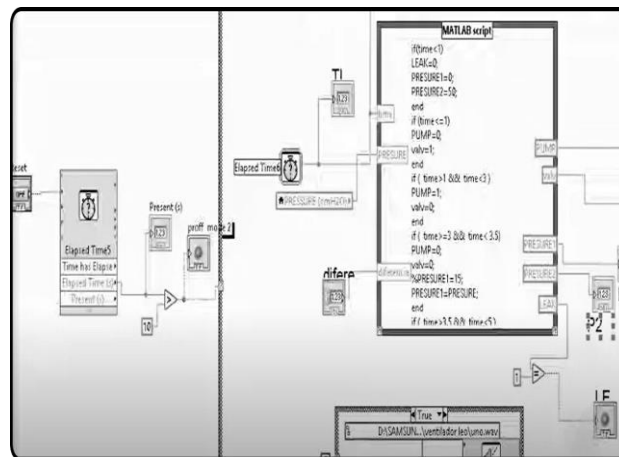


FIGURE 6: Virtual instruments of LabVIEW

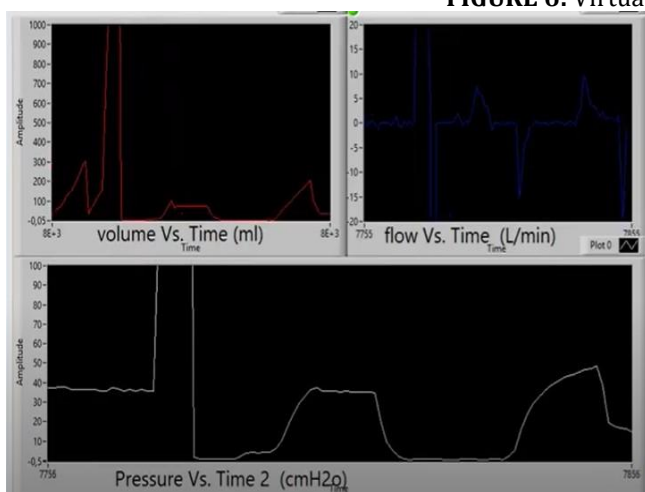


FIGURE 7:(Graphical Interface of Ventilation System in LabVIEW)

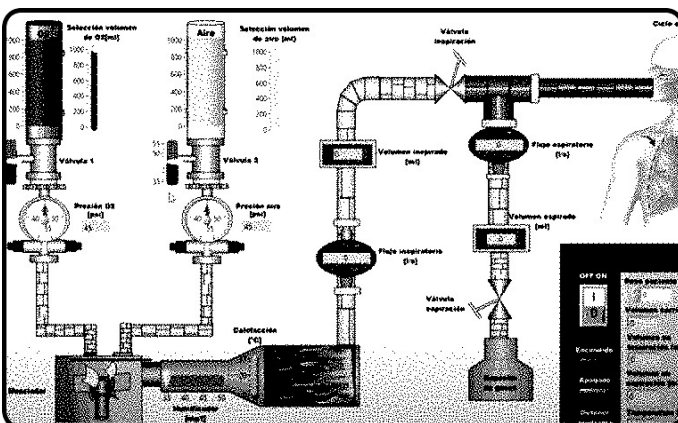


FIGURE 8:(Block diagram panel of Ventilation System)

IX. CONCLUSION: Patients on Mechanical ventilators have higher estimated needs. A good understanding of respiratory physiology is required for judicious mechanical ventilation. The equation of motion is the single most useful guide to understanding mechanical ventilation. A registered dietician is needed to make ample tube feeding recommendations for patients. Simulation process is carried

out by utilizing the graphical programming language of LabVIEW, the control strategy and signal monitoring can be observed in real-time. The expandable Plugins and GUI interface also enable the simulator to further be implemented on a web manner for e-learning without the need of installing LabVIEW on the user end. The ultimate goal of this study is to use the simulated process of the control model to human respiratory care.

In ventilator-triggered-

- control, variable is time & set respiratory rate (frequency = 1/time)
- RR12 bpm is one breath every 5 seconds

In patient-triggered-

- Assist
- Flow or pressure changes sensed by ventilator

Control respiratory rate

- 10 BPM
- Breath every 6 second

Neural respiratory rate

- 20 BPM
- Breath every 3 second

100 % of the breath will be assist & control rate clock reset after an “Assist” breath. The control respiratory rate 20 L/min & it is an actual respiratory rate. In flow control The Vmax would be 40 L/min & graph becomes decelerating ramp shape. The peak pressure would be 19. The tidal volume would be 330 ml so the high tidal volume in ARDS

causes lung stretch sedation, sometimes even paralysis and further lung damage. So, tidal volume ventilation is essential and set to 6 cc/kg of Ideal body weight.

For COVID-19 Patient Just got Intubated

- place on volume-controlled ventilation
- Set respiratory rate to 20 bpm
- Set tidal volume to 6 cc/kg of ideal body weight
- Set FiO₂ to 100%
- Set PEEP to 15 cm H₂O
- Check plateau pressure (Ppl)
- if Ppl > 30 cm H₂O, reduce tidal volume to 5 cc/kg
- If Ppl still > 30 cm H₂O, call for help
- ensure patient is well sedated
- check ABG or VBG 30 minutes after settings adjusted to ensure appropriate pH
- if pH < 7.2, increase RR (maximum of 35 bpm)
- Wean FiO₂ and PEEP as per the ARDS net ladder to ensure SpO₂ 88-95%.
- Wait at least 12 hours between changes in PEEP (equal to 16).

X. REFERENCES:

- [1] S. E. Morton, J. L. Knopp, P. D. Docherty, G. M. Shaw, and J. G. Chase, "Validation of a Model-based Method for Estimating Functional Volume Gains during Recruitment Manoeuvres in Mechanical Ventilation," IFAC-Papers on Line, vol. 51, no. 27, pp. 231-236, 2018.
- [2] K. T. Kim, S. Howe, Y. S. Chiew, J. Knopp, and J. G. Chase, "Lung Mechanics in Premature infants: Modelling and clinical validation," IFAC-Papers on Line, vol. 51, no. 27, pp. 225-230, 2018.
- [3] S. L. Howe et al., "Estimation of Inspiratory Respiratory Elastance Using Expiratory Data," IFAC Papers On Line, vol. 51, no. 27, pp. 204-208, 2018.
- [4] R. Langdon, P. Docherty, and J. Chase, "Basis function modelling of respiratory patients with high or low auto-PEEP," IFAC Papers on Line, vol. 50, no. 1, pp. 15121-15126, 2017.
- [5] D. P. Redmond, K. T. Kim, S. E. Morton, S. L. Howe, Y. S. Chiew, and J. G. Chase, "A Variable Resistance Respiratory Mechanics Model," IFAC- Papers on Line, vol. 50, no. 1, pp. 6660-6665, 2017.
- [6] M. J. Uddin, Y. Alginahi, O. A. Bég, and M. N. Kabir, "Numerical solutions for gyrotactic bioconvection in nanofluid-saturated porous media with Stefan blowing and multiple slip effects," Computers & Mathematics with Applications, vol. 72, no. 10, pp. 2562-2581, 2016.
- [7] M. N. Kabir, Y. M. Alginahi, and A. I. Mohamed, "Modeling and simulation of traffic flow: a case study first ring road in downtown Madinah," International Journal of Software Engineering & Computer Systems, vol. 2, pp. 89-107, 2016.
- [8] M. B. Amato et al., "Driving pressure and survival in the acute respiratory distress syndrome," New England Journal of Medicine, vol. 372, no. 8, pp. 747-755, 2015.
- [9] J. H. Bates, Lung mechanics: An inverse modeling approach. Cambridge University Press, 2009.
- [10] J. M. Halter et al., "Positive end-expiratory pressure after a recruitment maneuver prevents both alveolar collapse and recruitment / de recruitment," American journal of respiratory and critical care medicine, vol. 167, no. 12, pp. 1620-1626, 2003.
- [11] J. J. Liang, A. K. Qin, P. N. Suganthan, and S. Baskar, "Comprehensive learning particle swarm optimizer for global optimization of multimodal functions," IEEE Transactions on Evolutionary Computation, vol. 10, no. 3, pp. 281-295, 2006.
- [12] J. B. Odili and M.N.M. Kahar, "African buffalo optimization," International Journal of Software Engineering and Computer Systems, vol. 2, no. 1, pp. 28-50, 2016.
- [13] Stegmaier, P.A.; Brunner, J.X.; Tschichold, N.N.; Laubscher, T.P.; Liebert, W.: Fuzzy Logic Cough Detection: A First Step Towards Clinical Application. Fuzz Sys, IEEE W Cong on Comp Int, Proof the 3th IEEE Conf, pp. 1000-1005 (1994).
- [14] Kwok, H.F.; Linkens, D.A.; Mahfouf, M.; Mills, G.H.: SIVA: hybrid knowledge and model based advisory system for intensivecare ventilators. IEEE Trans. Inf. Tech. Biomed. 8(2), 161-171(2004).

- [15] Zhu, H.; Möller, K.: Ventilator control based on fuzzy-neural network approach. *Bioinf. Biomed. Eng. ICBBE* 747–750 (2008).
- [16] Tzavaras, A.; Weller, P.R.; Spyropoulos, B.: A neuro-fuzzy controller for the estimation of tidal volume and respiration frequency ventilator settings for copd patients ventilated in control mode. In: *Proceedings of the Annual International Conference of the IEEE MBS*, pp. 3765–3768 (2007) *Arab J Sci Eng* (2014) 39:4805–4813 4813.
- [17] Wang, S.; Shaw, D.; Jih, K.S.: An intelligent control system for ventilators. *Med. Eng. Phys.* 20, 534–542(1998).
- [18] Nelson, D.S.; Strickland, J.H.; Jannet, T.C.: Simulation of fuzzy control for management of respiratory rate in assist control mechanical ventilation. In: *Proceedings of 19th International Conference on IEEE/EMBS*, pp. 1104–1107 (1997).
- [19] Karakaya, A.; Karakas, E.: Performance analysis of PM synchronous motors using fuzzy logic and self-tuning fuzzy PI speed controls. *Arab. J. Sci. Eng.* 33, 153–177 (2008).
- [20] Tobin M. Principles and practice of mechanical ventilation. 3rd ed. Beijing: McGraw-Hill; 2013.
- [21] Cairo J. Pilbeam's mechanical ventilation: physiological and clinical applications. 5th ed. St. Louis: Mosby; 2012.
- [22] Gentile M. Cycling of the mechanical ventilator breath. *Respir Care.* 2011; 56:52–60.
- [23] Gilstrap D, MacIntyre N. Patient-ventilator interactions. Implications for clinical management. *Am J Respir Crit Care Med.* 2013; 188:1058–68.
- [24] MacIntyre N, Branson R. Mechanical ventilation. 2nd ed. Philadelphia: Saunders; 2009.
- [25] C. S. Poon, "Respiratory Models and Control," in: J. D. Bronzine (Ed.), *The Biomedical Engineering Handbook*, BocaRaton: CRC Press, 2404-2421, 1995.
- [26] C. S. Poon, S. L. Lin and O. B. Knudson, "Optimization character of inspiratory neural drive," *J. Appl. Physiol.*, 59:2005-2017, 1992.
- [27] S. L. Lin and C. C. Chiu, "Optimizing the neuro-mechanical drive for human respiratory system," *Biomed. Eng. Appl. Basis Comm.*, 6: 95-103, 1994.
- [28] F. T. Tehrani, "Mathematical analysis and computer simulation of the respiratory system in the newborn infant," *IEEE Trans. Biomed. Eng.*, 40: 475-481, 1993.
- [29] S. L. Lin, C. R. Pai, C. H. Yang and C. C. Chiu, "MATLAB based real-time signal simulator and monitor for human respiratory system," *Proc. 2nd Med. Eng. Week of the World*, 181-181, 1996.
- [30] A. M. Hernandez, M. A. Maanas and R. Costa-Castello, "Learning respiratory system function in BME studies by means of a virtual laboratory: Respi Lab," *IEEE Trans. on Education*, 51: 24-34, 2008.
- [31] J. Leatherman, "Mechanical ventilation for severe asthma," *Chest*, vol. 147, no. 6, pp. 1671-1680, 2015.
- [32] C. Schranz, T. Becher, D. Schädler, N. Weiler, and K. Möller, "Model based ventilator settings in pressure-controlled ventilation," *Biomedical Engineering/ Bio medizini sche Technik*, vol. 58, no. SI-1-Track-S, 2013