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DEFINING A META-MODEL FOR A COMMERCIAL PULMONARY MECHANICAL VENTILATOR

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Abstract. *The coronavirus disease 2019 (COVID-19) impacts the health infrastructure. In some places, people who need artificial ventilation suffer with the lack of equipment and health system overburden. While many initiatives seek solutions to overcome the lack of respiratory support equipment, it was necessary to understand the behavior of a commercial pulmonary ventilator, by characterizing the way in which some input variables such as required volume, admitted inspiratory flow, positive end-expiratory pressure, and the patient's lung condition contribute to the response of the equipment, according to the ventilation mode set. This study aims to build a meta-model for the behavior of a commercial pulmonary ventilator, when configured in the volume-controlled ventilation mode. The design considered three treatment-level for each factor resulting in a* 3^4 *full factorial design. The volume delivered by the ventilator (tidal volume) and the peak inspiratory pressure were defined as the response variable and, as factor variables, the patient pulmonary condition (low, medium, and high), the adjusted inspiratory flow (25, 35, and 45 l/min), the controlled inspiratory volume (400, 500 and 600 ml) and adjusted PEEP (5, 10, and 15 cmH2O). The three different pulmonary condition was emulated by varying the patient complacency and resistance in a simulated respiratory circuit and the three treatments for the others factor was adjusted in the equipment. Then, the analysis of variance (ANOVA) and fitting regression models for main and interactions effects of linear and quadratic order was conducted. In addition to the test for significance of regression at ANOVA, the adherence of the metamodeling was checked through the analysis of residuals and the standardized effects at 95 % confidence interval. For tidal volume, the controlled volume is the most significant factor, while for peak inspiratory pressure is the pulmonary condition. Also, PEEP has an important significance for both models. The reached results were preliminary, but essential to lead the process of design and characterization of an alternative pulmonary mechanical ventilator prototype, which aims to be applied in future unpredictable emergency situations, like observed in the COVID-19 crisis.*

Keywords: *biomedical equipment, system modeling, metamodel, covid-19*

1. INTRODUCTION

For Coropechi et al. (2020), the world is facing an unprecedented situation in which the medical system is placed in a critical situation regarding available intensive care unit (ICU) equipment, especially mechanical ventilation devices. According to Hao et al. (2021), mechanical ventilation is an effective medical means in the treatment of patients with critically ill, COVID-19 and other pulmonary diseases. Grasselli et al. (2020) reports a large proportion of patients with COVID-19 develop severe respiratory failure requiring ICU and about 80% of them need mechanical ventilation.

Due to this situation many research teams have designed and developed pulmonary mechanical ventilation (PMV) equipment (Oproescu *et al*., 2020, Ramos-Paz *et al*., 2020, Rehm *et al*., 2020, EPUSP, 2021, INESC TEC, 2020, INESC P&D BRASIL, 2020, MIT, 2020). But testing this equipment can be a challenge, some tests can be performed with a simple test lung, with known features like resistance and compliance. However, Coropechi et al. (2020) point that ventilator should respond to the various compliances and resistances a patient's lung can pose, but without an adjustable test lung and the ability to simulate patient efforts, it is impossible to sure the ventilators response is accurate.

While many initiatives seek solutions to overcome the lack of respiratory support equipment, it was necessary to understand the behavior of a commercial pulmonary ventilator, by characterizing the way in which some input variables such as required volume, admitted inspiratory flow, positive end-expiratory pressure, and the patient's lung condition contribute to the response of the equipment, according to the ventilation mode set. This study aims to build a meta-model for the behavior of a commercial PMV, when configured in the volume-controlled ventilation mode. The design considered three treatment-level for each factor resulting in a 3^4 full factorial design.

The next sections of this paper are organized as follows: initially the material and methods were presented in section 2, while section 3 shows the results and discussion. Then, some conclusions are summarized in section 4, followed by acknowledgment and references.

2. MATERIALS AND METHODS

2.1 Medical ventilator systems basics

The basic unit of mechanical ventilation is the mechanical breath, which is defined as a breath realized through a ventilator system. Mechanical ventilation can be viewed as a series of mechanical breaths. There are several mechanical breath types. The type of mechanical breath is determined by five essential variables (Lei, 2017):

1. Triggering: defines when inspiration begins;
2. Cycling: defines when inspiration ends;
3. Controlling: defines how delivery of inspiratory gas is controlled;
4. Targeting: defines the size of a mechanical breath;
5. Baseline: defines the baseline pressure at which mechanical breaths occur.

According to Lei (2017) various mechanisms are associated with these variables, as shown in Table 1, and every type of mechanical breath represents a unique combination of these variables.

Table 1. Essential variables and their common mechanisms (Lei, 2017).

Variable	Triggering	Cycling	Controlling	Targeting	Baseline
◆ Common mechanisms	◆ Time triggering ◆ Pressure triggering ◆ Flow triggering ◆ Manual triggering	◆ Time cycling ◆ Flow cycling	◆ Volume controlling ◆ Pressure controlling ◆ Adaptive controlling ◆ Hybrid controlling	◆ Tidal volume ◆ Inspiratory pressure ◆ Target tidal volume	◆ Positive end-expiratory pressure (PEEP)

For this first study, considering guaranteed of tidal volume, the proposal was the analysis of a commercial pulmonary ventilator performing a volume controlling breath type with time triggering, time cycling, V_T targeting, and PEEP baseline.

As highlighted by Lei (2017), the major perceived advantage of volume controlling is stable tidal and minute volumes, which makes clinicians more comfortable. In the other hand, in pressure controlling actively breathing patients may influence the inspiratory flow and tidal volume they receive, resulting in better patient-ventilator synchrony. Besides, with pressure controlling, when the system has a leak, causing circuit pressure to drop, the ventilator responds with an increased inspiratory flow, allowing the ventilator effectively to compensate a moderate leak.

Developing a new alternative PMV prototype (UFG, 2020, Alcântara *et al*., 2021), the volume controlling has been observed to have faster and easier logical implementation when using discrete command (on/off) inspiratory valves, more easily found in the Brazilian national marketing during the critical period of the COVID-19 pandemic. For this reason, it was necessary to better understand the behavior of a commercial PMV operating in volume-controlled ventilation (VCV) mode and an experimental planning to define a metamodel was then proposed.

2.2 Pulmonary ventilator equipment

Testing was performed with a commercial and calibrated PMV, model Inter7 Plus, manufactured by Intermed Equipamento Médico Hospitalar Ltda. The Inter7 Plus is a micro processed electronic ventilator, specifically developed for use in neonatal, pediatric, and adult intensive care patients. The equipment is registered and certified according to the standards NBR IEC 60601-1/1997, NBR IEC 60601-1-2/2006, NBR IEC 60601-1-4/2004, NBR IEC 60601-2-12/2004 and NBR ISO 14971/2004, and may be considered the gold standard for this type of device (INTERMED, 2007).

The ventilator was connected to a standard 22 mm diameter breathing circuit, composed of tracheas, connectors, and derivations. These accessories meet the specifications of the NBR13475 technical standard. Due to the absence of humidity in the circuit, no drain was used. To simulate the pulmonary behavior, it was used a test lung with specified compliance of 22± 3 mL/cmH2O, based on 500 ml of tidal volume, from VADI Medical Technology Co., Ltd. Other levels for the pulmonary condition were achieving using a calibrated pulmonary simulator, model LS2000, produced by Intermed Equipamento Médico Hospitalar Ltda. This simulator allows tests using different levels of compliance and airway resistance, using springs and restrictions to the air passage, thus allowing the characterization of the ventilator behavior under different "clinical" conditions of a supposed patient.

A medical air cylinder regulated at 3.5 kgf/cm^2 was used as the pneumatic power supply for the ventilator. Tests were performed with no oxygen supply, ensuring a fixed fraction of inspired oxygen (FiO2) of 21%. Figure 1 shows the schematic circuit assembled to perform the tests.

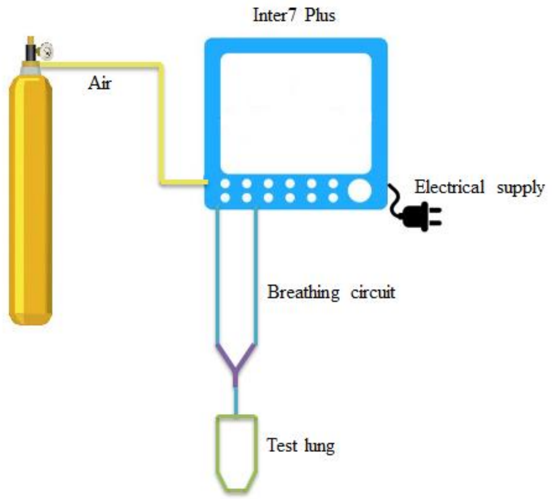

Figure 1. Schematic drawing of the experiment setup.

2.3 Experimental procedure

The tests were performed using the VCV mode. Different values of controlled volume, inspiratory flow, and positive end-expiratory pressure (PEEP) were adjusted, while other variables, such as inspiratory and expiratory times, peak pressure, plateau pressure, among others, were given as a function of the adjusted parameters and the system's respiratory mechanics response. The value of the respiratory rate was maintained at 10 cycles per minute for all the tests, as well as the constant inspiratory flow (square waveform). Since this is a controlled ventilation mode using an artificial lung, there is no external respiratory effort, so the ventilator sensitivity options were kept disabled (OFF mode). To avoid excessive pressures, the Inter7 Plus also allows setting a threshold pressure in VCV mode. The input parameters set in the ventilator and their respective values are shown in Table 2. In addition to the parameters set in the ventilator, the respiratory mechanics vary by using three different pulmonary conditions, regarding a qualitative variable, as listed in Table 3.

Table 2. Ventilator input parameters - VCV mode.

Parameter	**Value**		
Controlled volume, mL	400	500	600
PEEP, cmH_2O	5	10	15
Inspiratory flow, L/min	25	35	45
Threshold pressure, mH_2O	50		
Respiratory rate, cycles /min	10		
Inspiratory flow waveform	square		

Table 3. Pulmonary Conditions.

Condition	**Description**
High	Test lung Compliance: 22±3 mL/cmH_2O No additional resistance
Medim	Pulmonary simulator LS2000 Two tensioned springs Airway Resistance: 20 cmH_2O/L/s
Low	Pulmonary simulator LS2000 One tensioned spring Airway Resistance: 20 cmH_2O/L/s

After defining the ventilator and system parameters (pulmonary conditions), data acquisition was performed using different combinations to characterize the ventilator behavior in a broad manner. For each test, the ventilator was put into operation and waited until the system reach the steady state condition, i.e., until the measured quantities presented stable values at each cycle (variation ≤ 5%). Once stable, the values of each parameter were manually recorded. The response parameters analyzed were tidal volume (V_T), peak inspiratory pressure (PIP), inspiratory time (Ti), inspiration/expiration ratio (I:E), expiratory time (Te), and measured PEEP ($PEEP_m$), as presented in Table 4. The testing methodology can be visualized in the form of a flowchart, shown in figure 2:

Table 4. Response parameters.

Parameter	**Unit**
Tidal Volume (V_T)	mL
Peak Inspiratory Pressure (PPI)	cmH_2O
Inspiratory Time (Ti)	s
Expiratory Time (Te)	s
Inspiration/Expiration Ratio (I:E)	Non-dimensional
Measured PEEP ($PEEP_m$)	cmH_2O

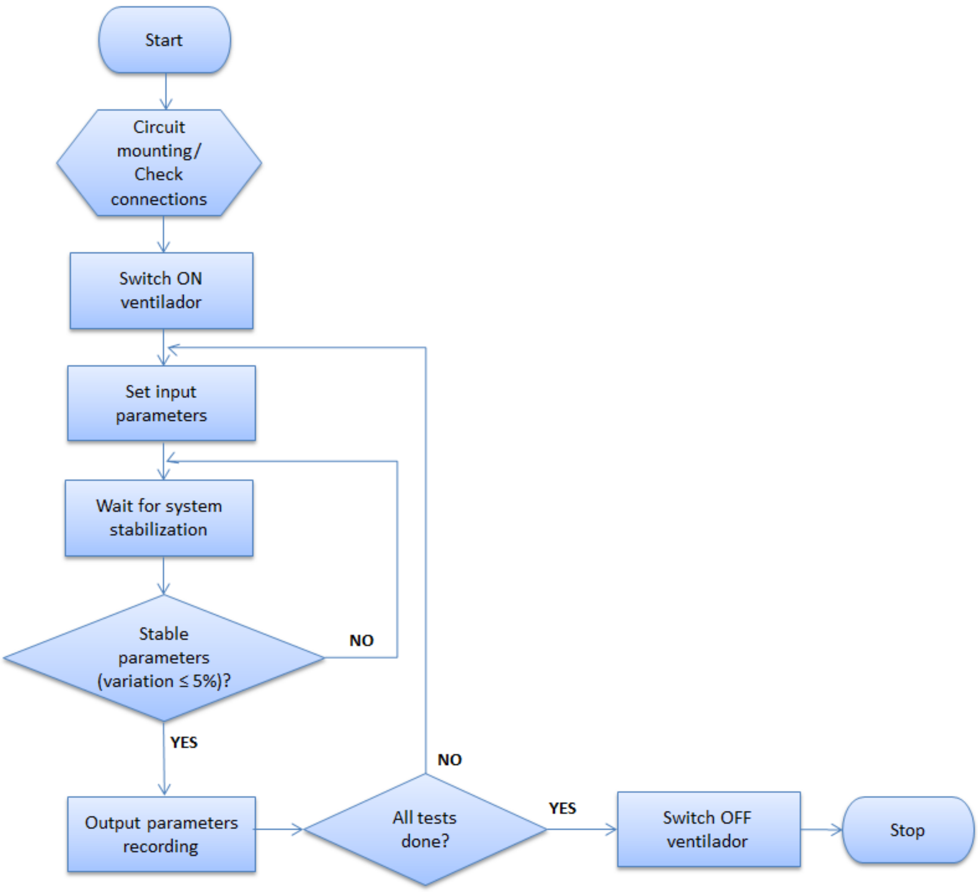

Figure 2. Test methodology.

2.4 Factorial design

Box *et al*., (2005) mentions that factorial design is the most efficient way to study the effect of two or more factors. By the factors, we mean the ventilator input parameters in Table 2 and the pulmonary condition in Table 3. Further, to investigate the factor effects, the response was evaluated at different levels (i.e., different values or condition of factors). For this paper, it was decided to investigate the input parameters and condition that have different values. There are four factors at three levels each, that results in 81 runs to perform all combinations. Table 5 shows the 3^4 factorial design.

Defining the metamodel variables of interest must be a cautious decision. In literature, some complications can become true with mechanical ventilation. Barotrauma and volutrauma are example of pulmonary injury that mechanical ventilation can lead. According to Gannon et al. (1998), barotrauma can be defined by pressure-induced pulmonary injury.

Webb and Tierney (1974) highlight that ventilation with high peak inspiratory pressures (PIP) can induce pulmonary edema formation, interstitial edema either alone or in combination with alveolar flooding, as function of the peak pressures used. Volutrauma is the term that describes ultrastructural lung injury due to overdistention occurring during mechanical ventilation. The two terms—barotrauma and volutrauma—reflect the two sides of the same phenomenon: the lung injury due to a large distending volume and/or to a high airway pressure (Ioannidis et al., 2015).

Then, it is important for this study evaluate the volume delivered by the ventilator (tidal volume) and the peak inspiratory pressure when working in the VCV ventilation mode.

Table 5 – The 3^4 factorial design for tidal volume (V_T) and peak inspiratory pressure (PIP).

Factor	Levels		
Controlled volume$^{(1)}$, mL	400	500	600
PEEP$^{(1)}$, cmH2O	5	10	15
Inspiratory flow$^{(1)}$, L/min	25	35	45
Pulmonary conditions$^{(2)}$	Low	Medium	High

$^{(1)}$ quantitative factor $^{(2)}$ qualitative factor

The effect of a factor is defined to be the average change in response produced by a change in the level of that factor (Montgomery, 2019). This source of variation in response can be caused by the main and/or interaction effect of the factors. To test the significance of one or more factors one can be use the analysis of variance (ANOVA), where the null hypothesis states that all factor level means are equal, while the alternative hypothesis states that at least one of that is different (Box *et al*., 2005 and Montgomery, 2019).

Additionally, a metamodeling can express the most significant factors by fitting a regression model to the response. The adherence of the metamodeling is checked through the analysis of residuals and the pareto chart of effects. Finally, the regression coefficient of the model is estimate by the least square method and verified with 95 % confidence interval. Equation (1) express a regression model representation.

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k + \epsilon, \quad (1)$$

where y is the response, the β's are regression coefficients whose values are to be determined, x_k is a variable that represent factor k. Notice that an interaction term $\beta_{12} x_1 x_2$ can be written as $\beta_3 x_3$ and likewise the quadratic term $\beta_{11} x_1^2$ as $\beta_4 x_4$.

3. RESULTS AND DISCUSSION

3.1 Tidal volume (V_T)

First the pulmonary condition ANOVA was conducted for the full regression model. Then, by evaluating the most significative factors, the reduced regression model is achieved and displayed in Table 6. Reports that the significant factor is chosen by the high values in the F-Value Column, also the P-Value allows us to get them, but for values smaller than 0,05 (95 % confidence).

So, the most significant factors are Controlled volume (linear term), PEEP (linear and quadratic terms), Pulmonary condition (linear term) and interaction between then. Notice that pulmonary condition has not quadratic term because is a qualitative or categorical factor. The R^2_{adj} statistic equal to 96,05% was reached, which explain almost the total variability by the size of the model. Finally, to assist interpreting the results, Figure 3 shows the pareto chart of the standardized effects.

Table 6 – Tidal volume ANOVA for the reduced regression model.

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Regression	10	520112	52011,2	195,68	0,000
Controlled volume	1	89856	89856,0	338,07	0,000
PEEP	1	14323	14323,3	53,89	0,000
Pulmonary condition	2	7421	3710,5	13,89	0,000
PEEP*PEEP	1	15941	15941,0	59,95	0,000
Controlled volume*PEEP	1	2162	2162,2	8,14	0,006
Controlled volume*Pulmonary condition	2	5493	2746,3	10,33	0,000
PEEP*Pulmonary condition	2	11300	5650,1	21,26	0,000
Error	70	18605	265,8		
Total	80				

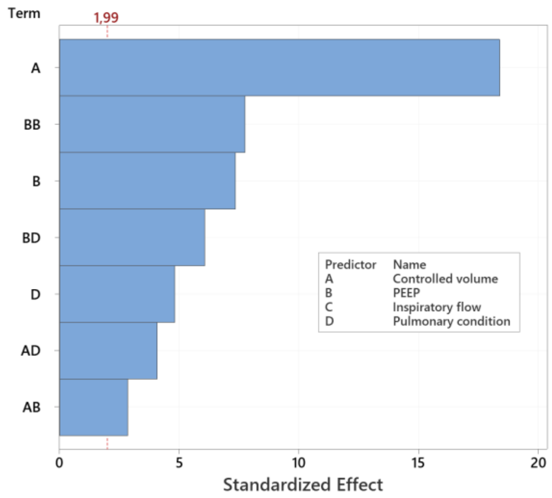

Figure 3 – Tidal volume pareto chart of the standardized effects for the reduced regression model. The red dashed line indicates the threshold for the factor to be significant.

In the reduced model, one can verify that the controlled volume factor is the most significant effect. This is because the tidal volume is the volume delivered by the ventilator. Therefore, the others significant factors – PEEP and pulmonary condition – may be associated to the dispersion around the controlled volume.

Figure 4 shows the surface plot of tidal volume for each pulmonary condition with the regression coefficients. Observe that in high pulmonary condition the surface response has smaller slope, while low and medium pulmonary condition have similar and larger slope. Furthermore, PEEP has a quadratic effect with downward concavity at 10 cmH2O.

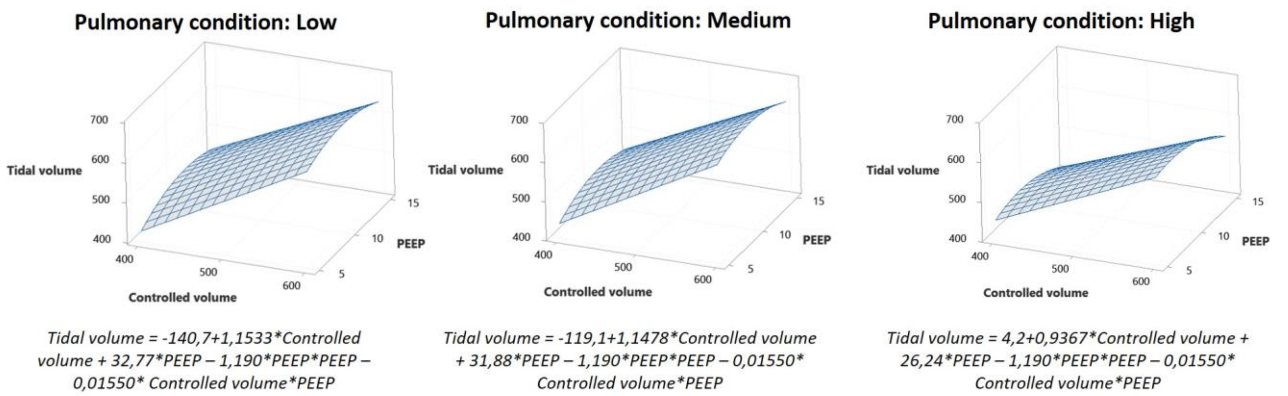

Figure 4 – Surface plot and regression model for tidal volume.

Although that, the adequacy of the underlying model should be checked by residual analysis shown in Figure 5. One can verify that the residual follows a normal distribution with zero mean and reveal some outlier – data with larger residual than any of the others. Also, these outliers in residual versus order are more expressive as they are at the run order end, suggesting fatigue of the experimenter. To better explore these outlier Figure 6 displays the residual versus factors.

For pulmonary condition, the highest residuals are present at high level, so the data has more dispersion. However, the model present better adequacy at medium pulmonary condition. This result indicates the difficult to reach the adjusted volume when performing the ventilation with a high pulmonary condition. Regardless of outliers at adjusted volume, the less dispersion data are observed for 500 mL and similar residuals for 400 and 600 mL. PEEP level at 15,0 cmH20 has most of the outliers and, despite an outlier at 10,0 cmH20, it has similar dispersion for 5,0 cmH20 level. This result indicates that the equipment suffers to reach the adjusted volume when operating with the higher PEEP level. Finally, the inspiratory flow has equivalent residuals at their levels.

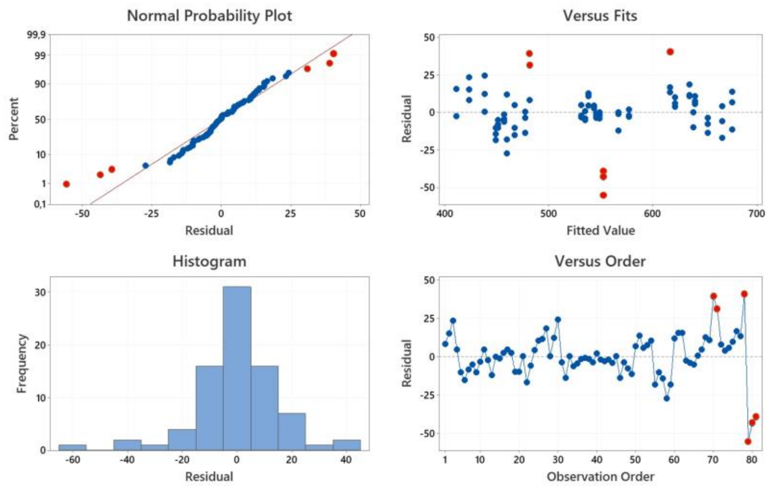

Figure 5 – Tidal volume residual analysis for model adequacy checking. The red dots are outliers.

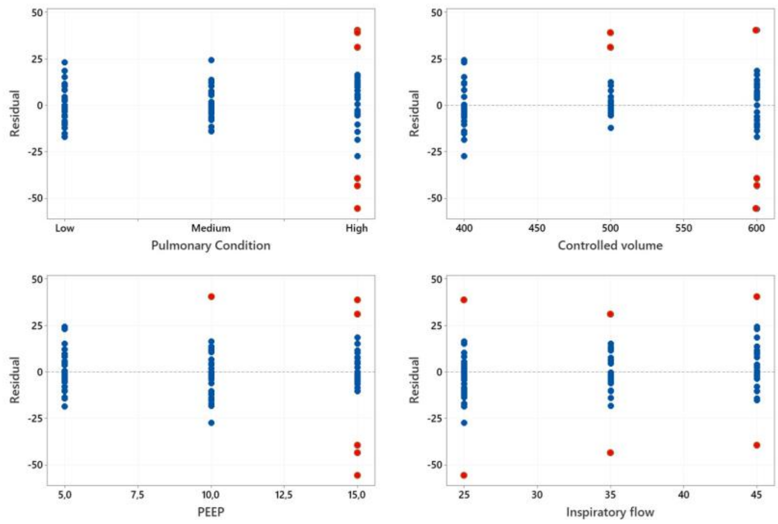

Figure 7 – Tidal volume residual versus factors. The red dots are outliers.

3.2 Peak Inspiratory Pressure (PPI)

Like tidal volume ANOVA analysis, Table 7 presents the peak inspiratory pressure ANOVA for the reduced regression model, with a R^2_{adj} statistical equal to 84,98 %, and Figure 8 shows the pareto chart. One can verify that the significant factors are pulmonary condition, PEEP, controlled volume, and their interactions. Although the linear controlled volume is lower than the threshold value, it is considered to maintain the hierarchical model. Finally, the most significant factor for peak inspiratory pressure is the pulmonary condition.

Table 7 – Peak inspiratory pressure ANOVA for the reduced regression model.

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Regression	8	4056,78	507,09	57,59	0,000
Controlled volume	1	0,21	0,21	0,02	0,876
PEEP	1	63,24	63,24	7,18	0,009
Pulmonary condition	2	827,22	413,61	46,97	0,000
PEEP*PEEP	1	78,82	78,82	8,95	0,004
Controlled volume*PEEP	1	72,25	72,25	8,21	0,005
PEEP*Pulmonary condition	2	234,78	177,38	13,33	0,000
Error	72	633,98	8,80		
Total	80				

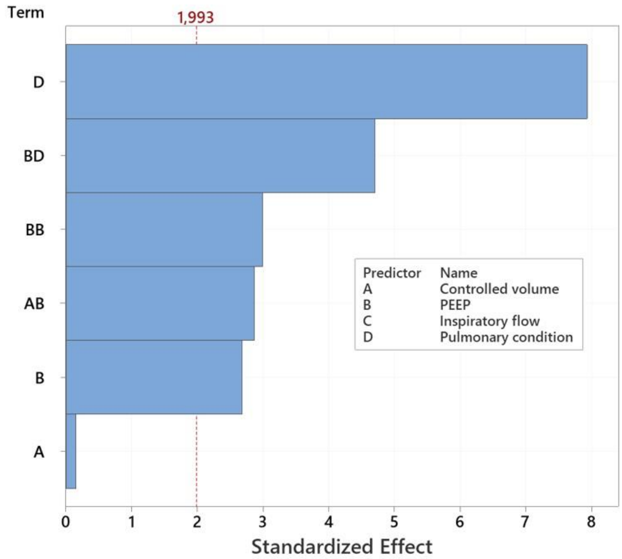

Figure 8 – Peak inspiratory pressure pareto chart of the standardized effects for the reduced regression model. The red dashed line indicates the threshold for the factor to be significant.

Figure 9 displays the surface plot for each pulmonary condition. One can notice that followed by pulmonary condition, PEEP factor has an important role for peak inspiratory pressure. The 600 mL and 15 cmH20 have the highest response. Also, the mean predicted response in medium pulmonary condition are higher than in low and high condition at all levels.

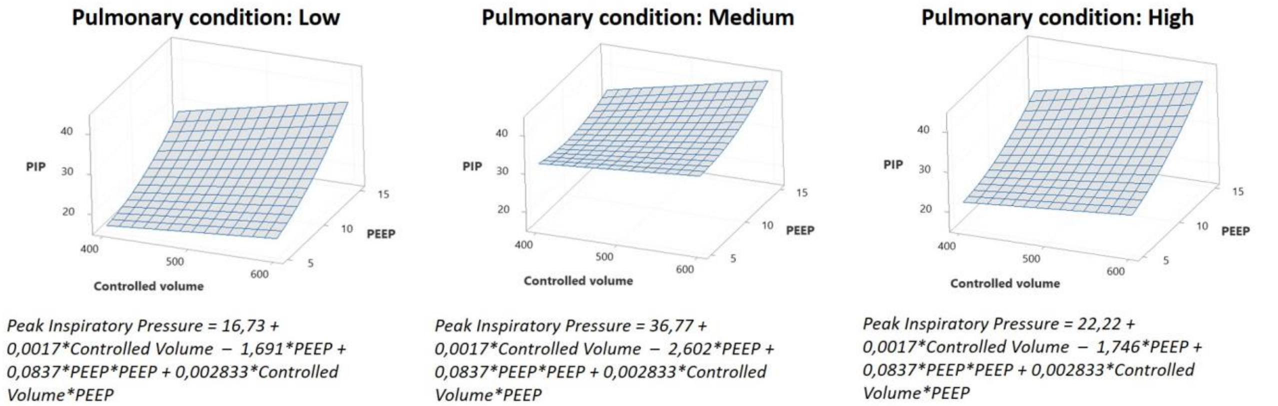

Figure 9 – Surface plot and regression model for peak inspiratory pressure.

Next, Figure 10 presents the peak inspiratory pressure residual analysis for model adequacy checking and Figure 11 show the residual versus factor. Besides the outliers, the error distribution is approximately normal. The residual versus observation order also revels experimenter fatigue because these outliers are at run order end. Also, these outliers are observed in the high pulmonary condition and 15 cmH20 of PEEP. These results show that pressure induced injury is more likely to patients with worrisome conditions and high levels of PEEP. However, for controlled volume and inspiratory flow these outliers are present at all levels. Finally, except for the inspiratory flow the residuals have similar dispersion at all levels and factors. The inspiratory flow residuals at 25 L/min are more negative and at 45 L/min are more positive.

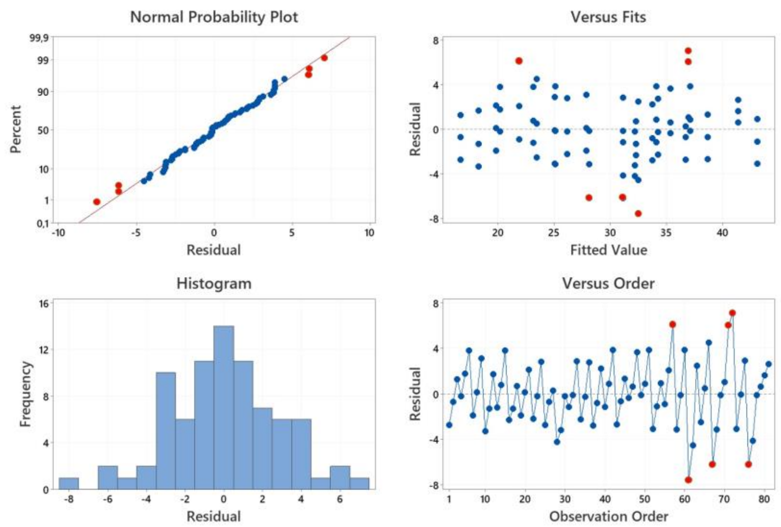

Figure 10 – Peak inspiratory pressure residual analysis for model adequacy checking. The red dots are outliers.

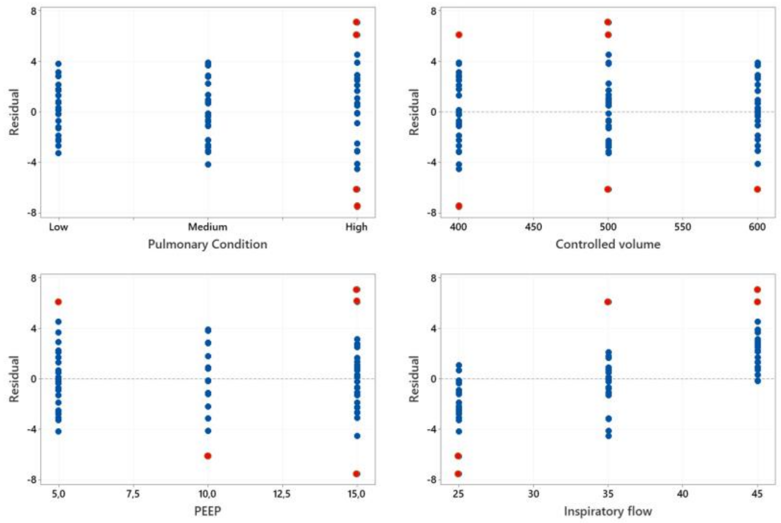

Figure 11 – Peak inspiratory residual versus factors. The red dots are outliers, some have equal residuals at level and are overlaid.

4. CONCLUSIONS

This paper highlights the procedure to obtain regression models for the behavior of a commercial PMV performing VCV ventilation mode, as well as the results and discussion about them. For the commercial and calibrated pulmonary ventilator, model Inter7 Plus, one can conclude that the significant factors for tidal volume and peak inspiratory pressure are controlled volume, PEEP and pulmonary condition, and almost total variability is explained by the regression models.

For tidal volume, the controlled volume is the most significant factor, while for peak inspiratory pressure is the pulmonary condition. Also, PEEP has an important significance for both models.

For tidal volume the high pulmonary condition, 600 mL of adjusted volume and 15 cmH20 of PEEP have higher residuals than other levels. For peak inspiratory pressure, the outliers are related to high pulmonary condition and 15 cmH20 of PEEP. They are the highest level for those factors, and likewise attention should be taken to then. It also indicates the characteristic of patients with worrisome conditions. Barotrauma and volutrauma are example of the lung injury due to a large distending volume and/or to a high airway pressure, whose require special clinician care.

Some outliers are observed in the experiment, on the observation order they are most present at run order end. Possibly the experimenter fatigue could be the cause and additionally care should be taken on. An automatically recorder process could mitigate this type of error. As further works, other ventilation modes, like PCV and PSV could be evaluated with the same procedure. Furthermore, a regression model should be evaluated for the others response parameters, such as Ti, I:E, Te, and PEEPm.

5. ACKNOWLEDGEMENTS

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6. REFERENCES

Alcântara, E., Júnior, S., Fonseca, J., Franco, L. and Rabahi, M., 2021. "Pre-Clinical Testing of a Mechanical Ventilation Prototype for Emergency Pandemic Situation, COVID-19". Revista da Sociedade Portuguesa de Anestesiologia, Vol. 30, No. 1, pp. 19-25.

Box, G. E. P., Hunter, J. S., Hunter, W. G. 2005. Statistics for Experimenters: Design, Innovation and Discovery. John Wiley & Sons, 2nd Edition.

Coropeţchi, I. C., Indreş, A. I., Moţa, F., and Vasile, A. 2020. "Mechanical Test Lung Simulation Device". 2020 International Conference on e-Health and Bioengineering (EHB), 2020, p. 1-4.

EPUSP, 2020. INSPIRE: Equipamento de Suporte Respiratório Emergencial e Transitório, Escola Politécnica da Universidade de São Paulo, https://www.poli.usp.br/inspire. Accessed 19 June 2021.

Gannon, C. M.; Wiswell, T. E.; Spitzer, A.R. 1998. Volutrauma, Paco2 Levels, and Neurodevelopmental Sequelae Following Assisted Ventilation. Clinics in Perinatology, Volume 25, Issue 1, Pages 159-175.

Grasselli, G., Zangrillo, A., Zanella, A., Antonelli, M., Cabrini, L., Castelli, A., et al. 2020. "Baseline characteristics and outcomes of 1591 patients infected with SARSCoV-2 admitted to ICUs of the Lombardy region, Italy". JAMA, Vol. 323, No. 16, pp. 1574–81.

Hao, L.M., Li, X., Shi, Y., CAI, M.L., REN, S., XIE, F., LI, Y.N., WANG, N., WANG, Y.X., LUO, Z.J., and XU, M. 2021. "Mechanical ventilation strategy for pulmonary rehabilitation based on patient-ventilator interaction". Sci China Tech Sci, Vol. 64, No. 4, pp. 869–878.

INESC P&D Brasil, 2020. Reanimador automatizado Vita Pneuma, Instituto de Engenharia de Sistemas e Computadores, Pesquisa e Desenvolvimento do Brasil, https://inescbrasil.org.br/produtos-disponiveis/. Accessed 19 June 2021.

INESC TEC, 2020. Projeto n. 082, PNEUMA - Sistema de ventilação com recurso a um balão autoinsuflável, Instituto de Engenharia de Sistemas e Computadores, Tecnologia e Ciência, https://pneuma.inesctec.pt/fct/. Accessed 19 June 2021.

Intermed, 2007, *Manual de operação - Ventilador Pulmonar Inter7 Plus* (in Portuguese), Intermed Equipamento Médico Hospitalar Ltda, São Paulo, pp. 10–13.

Ioannidis, G.; Lazaridis, G.; Baka, S.; Mpoukovinas, I.; Karavasilis, V.; Lampaki, S.; Kioumis, I.; Pitsiou,G.; Papaiwannou, A.; Karavergou, A.; Katsikogiannis, N.; Sarika, E.; Tsakiridis, K.; Korantzis, I.; Zarogoulidis, K.; Zarogoulidis, P. 2015. Barotrauma and pneumothorax. J Thorac Dis. Feb; 7(Suppl 1): S38–S43.

Lei, Y., 2017. Essential variables and breath types. in medical ventilator system basics: a clinical guide. Oxford, UK: Oxford University Press. Retrieved 18 Jun. 2021, from https://oxfordmedicine.com/view/10.1093/med/9780198784975.001.0001/med-9780198784975-chapter-7

Montgomery, D. C. 2019. Design and Analysis of Experiments. John Wiley & Sons, 10th edition.

MIT, 2020. MIT Emergency Ventilator Project, Massachusetts Institute of Technology, https://emergency-vent.mit.edu. Accessed 19 June 2021.

Oproescu, M., Iana, V. G., Bizon, N., Anghel, D. C., Sirghie, A., and NOVAC, O. C. 2020. "Mechanical ventilation device with adapted parameters to assist patients infected with the SARS-CoV-2 virus". 2020 12th International Conference on Electronics, Computers and Artificial Intelligence (ECAI), 2020, pp. 1-6.

Ramos-Paz, S., Belmonte-Izquierdo, R., Inostroza-Moreno, L. A., Velasco-Rivera, L. F., Mendoza-Villa, R. and Gaona-Flores, V. "Mechatronic Design and Robust Control of an Artificial Ventilator in Response to the COVID-19 Pandemic". 2020 IEEE International Autumn Meeting on Power, Electronics and Computing (ROPEC), 2020, pp. 1-6.

Rehm, G. B., Woo, S. H., Chen, X. L., Kuhn, B. T., Cortes-Punch, I., Anderson, N. R., Adams, J. Y., Chuah, C-N. 2020. "Leveraging IoTs and Machine Learning for Patient Diagnosis and Ventilation Management in the Intensive Care Unit". IEEE Pervasive Computing, vol. 19, no. 3, pp. 68-78, 1 July-Sept. 2020, doi: 10.1109/MPRV.2020.2986767.

UFG, 2020. *Jornal UFG*. Projeto Pneuma: Engenharia Mecânica a serviço da Saúde, Universidade Federal de Goiás, https://jornal.ufg.br/n/131332-projeto-pneuma-engenharia-mecanica-a-servico-da-saude. Accessed 12 June 2021.

Webb HH, Tierney DF: Experimental pulmonary edema due to intermittent positive pressure ventilation with high inflation pressures: Protection by positive end-expiratory pressure. Am Rev Respir Dis 110:556, 1974.

7. RESPONSIBILITY NOTICE

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