Modeling of FiO2 delivered by self-inflating ventilation device

Modelagem de FiO2 entregue por bolsa auto inflável

DOI:10.34117/bjdv8n11-003r

Recebimento dos originais: 24/10/2022
Aceitação para publicação: 22/11/2022

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ABSTRACT
During the COVID-19 pandemic, professionals in the medical field have been using bag resuscitators, also called bag valve masks, to provide respiratory support for patients for long periods. A relevant issue arising because of such use is the little information regarding the FiO_2 delivered by these devices, leading to toxic effects of O_2 and its waste. This paper presents a model that relates volume, respiratory frequency, and flow in an O_2 line with the FiO_2 delivered by bag resuscitators. The model was obtained based on a formal procedure and data from a 1500 ml Hsiner bag resuscitator collected in the literature, both presented in this paper. Then, we compared through Bland-Altman analysis the FiO_2 values estimated by our model with the ones from data considering different bag resuscitators to evaluate the amplitude of the errors it can generate. The average error for Hsiner and Laerdal bag resuscitators was less than 0.035 (or 3.5%) and less than 0.063 (or 6.3%) for Ambu devices. The maximum error found for Ambu bag resuscitators was high. The obtained model presented satisfactory errors, compatible with the uncertainty levels associated with FiO_2 measuring instruments and blenders, meaning the model can be used to estimate the delivered FiO_2 accurately. Additionally, the procedure presented in this paper can be used to obtain specific models for bag resuscitators of other companies, equipping professionals with tools that can accurately estimate FiO_2.

Keywords: fraction of inspired oxygen, FiO_2 modeling, bag resuscitator.

RESUMO
Durante a pandemia de COVID-19, profissionais da área médica têm usado bolsas auto infláveis, também chamadas reanimadores manuais, para fornecer suporte respiratório aos pacientes por longos períodos. Uma questão relevante decorrente desse uso é a pouca informação sobre a FiO_2 fornecida por esses dispositivos, levando a efeitos tóxicos do O_2 e seus resíduos. Este artigo apresenta um modelo que relaciona volume, frequência respiratória e fluxo em uma linha de O_2 com a FiO_2 fornecida por ressuscitadores de bolsa. O modelo foi obtido com base em procedimento formal e dados de um reanimador com bolsa Hsiner de 1500 ml coletados na literatura, ambos apresentados neste trabalho. Em seguida, comparamos através da análise de Bland-Altman os valores de FiO_2 estimados pelo nosso modelo com os dados de diferentes reanimadores de balão para avaliar a amplitude dos erros que ele pode gerar. O erro médio para ressuscitadores de bolsa Hsiner e Laerdal foi menor que 0,035 (ou 3,5%) e menor que 0,063 (ou 6,3%) para dispositivos Ambu. O erro máximo encontrado para ressuscitadores com bolsa Ambu foi alto. O modelo obtido apresentou erros satisfatórios, compatíveis com os níveis de incerteza

associados aos instrumentos de medição de FiO_2 e misturadores, o que significa que o modelo pode ser utilizado para estimar com precisão a FiO_2 fornecida. Além disso, o procedimento apresentado neste artigo pode ser utilizado para obter modelos específicos para ressuscitadores com bolsa de outras empresas, equipando os profissionais com ferramentas que possam estimar com precisão a FiO_2.

Palavras-chave: fração inspirada de oxigênio, modelagem de FiO_2, bolsa auto inflável.

1 INTRODUCTION

In the last months of 2019, distressing news about a novel coronavirus (SARS-CoV-2) with the potential to generate explosive outbreaks began to spread globally. Currently, the World Health Organization (WHO) statistics show the number of new cases and deaths due to the COVID-19 pandemic is still concerning in several countries, with more than 440 million confirmed cases and 5.97 million confirmed deaths in the entire world in February 2022 [1].

The SARS-CoV-2 spreads mainly through the droplet route, causing mild symptoms in most cases [2, 3]. However, there is a significant number of occasions in which the virus can cause acute respiratory distress syndrome (ARDS). In such cases, patients usually need some form of respiratory assistance [2, 4]. People with severe manifestations of ARDS often require treatment in the Intensive Care Unit (ICU), where they can have access to mechanical ventilation and specialized healthcare professionals [5, 6].

As SARS-CoV-2 is a rapidly spreading infectious virus, the number of COVID-19 patients can grow exponentially, especially during a new wave, leading countries' healthcare systems to collapse. In these situations, health professionals need to use all available resources to provide some form of assistance to patients, such as self-inflating bag resuscitators [7].

Bag resuscitators are usually employed to provide respiratory support for short periods, for instance, during patients' transportation and stabilization. However, during the COVID-19 pandemic, several patients have been kept on ventilation using bag resuscitators for longer periods, due to the shortage of mechanical ventilators. Still, using bag resuscitators for manual ventilation is an exhausting effort and prone to significant variations in tidal volume and fraction of inspired oxygen (FiO_2) [7, 8].

Several researchers and engineers addressed these issues by developing a variety of automated bag resuscitators devices [8-12] to provide an alternative to manual ventilation when better support, such as a mechanical ventilator, is not available. On the other hand, there is little information in the literature regarding FiO_2 control or estimation for both manual and automated self-inflating bag resuscitators.

Common knowledge among healthcare professionals states that bag resuscitators (with oxygen reservoir) can supply a FiO_2 close to 100% if the oxygen flowing in the supply line equals or exceeds minute ventilation [13]. However, several studies already show that the FiO_2 relation with O_2 flow, ventilation frequency, and tidal volume (from which derives minute volume) is not so simple [13-19].

The lack of accurate models that healthcare professionals could use to estimate the FiO_2 delivered is due to, in most cases, the use of manual ventilation for a short period, and high values of FiO_2 usually not generating significant levels of toxicity. However, the pandemic brought the need for prolonged use of bag resuscitators as well as the development and dissemination of their automatic versions. In this scenario, healthcare professionals should be able to adjust the delivered FiO_2 to reach specific peripheral oxygen saturation (SpO_2) levels, promoting rational use of O_2 with fewer collateral effects to the patient. Even when the therapist cannot regulate the FiO_2, a reliable FiO_2 estimation can become a relevant tool for redefining treatment and for better understanding the patient's evolution.

In this context, we propose in this paper a model to estimate the FiO_2 delivered by an adult bag resuscitator for different combinations of O_2 flow, respiratory frequency, and tidal volume, based on data presented by studies through the last two decades. The proposed model may be a relevant and reliable tool for estimating the FiO_2 value, aiding healthcare professionals during treatment protocols. Also, it can be used to define values of ventilation parameters, such as O_2 flow, to adjust FiO_2 and reach the desired SpO_2.

2 METHODS

This section presents how data was collected and analyzed to generate practical and reliable information on which we formulated the proposed model.

2.1 WORK METHODOLOGY

We performed a search through studies and reports regarding manual and automated use of self-inflating bag resuscitators to generate a model capable of accurately estimating the FiO_2 delivered by such devices. We aimed to identify papers addressing

FiO_2 modeling or investigating the influence of usual ventilation parameters on the inspired fraction value.

Several complications arose during such a search, mainly because there is no established standard for evaluating the FiO_2 delivered by bag resuscitators. For example, there is no common ground on volume, O_2 flow, and frequency ranges. Also, data entries or how authors present it differed considerably. Usually, they give little information about sampling rate and measurement uncertainties. For instance, some works did not consider the reservoir bag during tests, neither described the methodology used during such experiments or presented values of relevant parameters, such as tidal volume [14, 16, 20-27]. Further, other works had different goals, such as evaluating the time necessary for the FiO_2 to stabilize, usually neglecting parameters as tidal volume, giving only a rough approximation of its values [21, 23, 26, 27]. Besides, bag resuscitators from different models and companies can present different results.

Thereby emerged the challenge of identifying studies that consider similar setup and methodology during experiments and present the values of, at least, tidal volume, O_2 flow, and ventilation frequency corresponding to each FiO_2 data entry.

To enhance our investigation efficacy, we performed a review following a structured approach. First, we defined a "guiding question": *How different values of ventilation parameters, such as tidal volume, respiratory frequency, and O_2 flow, affect the FiO_2 delivered by self-inflating bag resuscitators for adult use?*. Based upon it, we defined keywords, databases, inclusion and exclusion criteria, and other relevant aspects we considered during such review. Subsections 2.2 and 2.3 present details about the data gathering and selection processes.

Only then, after collecting (and selecting) enough relevant information indicating how the ventilation settings (tidal volume, O_2 flow, and frequency) affect the FiO_2 value, we could use a formal procedure (presented in section 3.2) to obtain a suitable model.

2.2 DATA GATHERING

We selected our databases based on the Cochrane Collaboration recommendations. These were MEDLINE via PubMed, Embase, CENTRAL (Cochrane Central Register of Controlled Trials), ScienceDirect, Scopus, and CAPES (Coordination for the Improvement of Higher Education Personnel) Portal of Journals. English was the chosen language for investigation, and search strings were established based on the following combination: (FiO_2 OR inspired oxygen) AND ("self-inflating" OR "resuscitation bag") AND (frequency OR ((oxygen OR O_2) AND flow) OR "tidal volume" OR "volume minute"). We slightly adjusted the combination syntax to suit the query requirements of each database.

We used the advanced-search option of each selected database engine and chronologically filtered studies between 2000 and 2021. To avoid the influence of biological factors, we did not consider clinical or preclinical trials, although we did not restrict other types of references. For the initial selection, we read the title and abstract of each study. As a rule, we included any article that seemed somewhat related to the subject of interest.

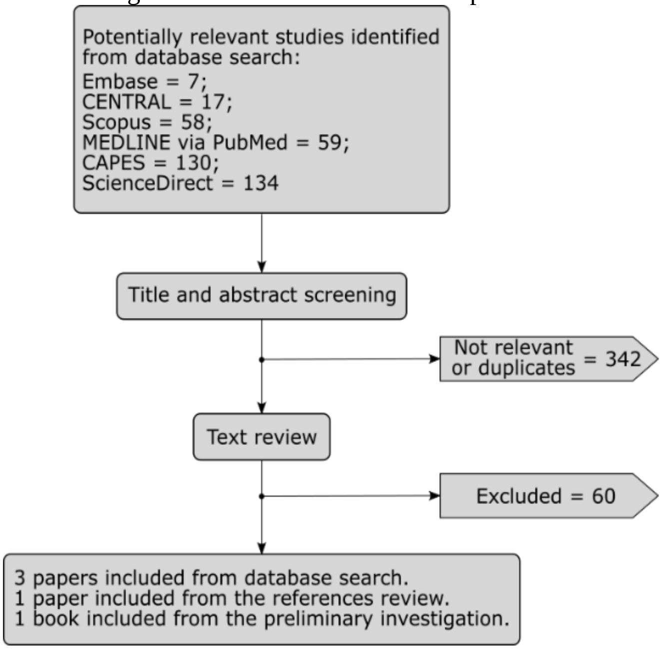
To advance the refinement of study selection, we established some exclusion criteria, meaning we withdrew references absent in:

- Quantifiable results (tables or graphs with FiO_2 values considering the different ventilation parameters, i.e., O_2 flow, frequency, and volume);
- Numerical data on any of the ventilation parameters;
- Information on the model/brand of the ventilation device;
- The methodology applied during the experiments (for example, when it did not report the number of repetitions of each test, or when there was a lack of rigor in the application or measurement of delivered volume);
- The use of O_2 reservoir (reservoir bag) in the setup considered during experiments.

Additionally, we excluded works that considered ventilation devices for infants or newborns since COVID-19 mainly affects adults, which is this work's focus. Another reason for establishing this criterion was that it's hard to found enough data to support a model for the infant or neonatal population. To draw our final list, we also checked the references of studies selected so far and of the preliminary investigation, both following the already described procedure.

Fig. 1 shows a flowchart of the review process. In total, we found four-hundred and five search results within all our selected sources, with sixty-three of them making it to our initial list. It is worth mentioning that we found some studies in more than one database. When it happened, we did not select the duplicates for examination. The first criteria analysis lowered the number of references to three, and then we added two more from the checking procedures described. Therefore, we picked five works for the final list.

Figure 1: Flowchart of the review process.



Source: Prepared by the authors.

2.3 DATA SELECTION

To help perform and manage the task of extracting pertinent information from selected studies, we used shared folders and a spreadsheet. Beyond that, we considered the following to be relevant information in our investigation: tables or graphs with FiO_2 values regarding the different volume, frequency, and O_2 flow ranges; measurement levels of uncertainty (when available); model and brand of the ventilation device; description of protocol applied during tests; and description of the experimental setup. During this process, we eliminated results related to experiments carried out without the reservoir bag.

Collected samples from the papers, to be used in the procedure to obtain the FiO_2 model, were stored as tuples <device, volume, frequency, O_2 flow, FiO_2>. Table 1 shows the selected studies and data review outcome, indicating the brand of the bag resuscitator device, ranges considered for each parameter, and the number of samples extracted from each work.

Table 1. Selected studies and data review outcome.

Device	Volume (ml)	Frequency (bpm)	O_2 flow (L/min)	Number of Samples	Reference
Laerdal	250-500	10-20	5-15	25	[20]
Laerdal **Ambu**	500-1000 250-1000	12-24 12	3-15 2-15	30 16	[28]
Laerdal **Marshal** **Intersurgical**	400-500 400-500 400-500	12-20 12-20 12-20	8 8 8-12	3 3 3	[13]
Ambu	400-800	10-30	2-25	150	[15]
Hsiner	300-900	10-30	0.5-15	45	[18]

Source: Prepared by the authors

Although we selected only five out of four hundred and five studies from the research sample space, they represent a suitable and satisfactory amount of information aligned with our modeling purpose. All data samples gathered from the review can be found here. By using those, we were to obtain the proposed model and analyze the behavior of the FiO_2 concerning the other relevant ventilation parameters, i.e., O_2 flow, respiratory frequency, and tidal volume.

3 PROPOSED MODEL

After preliminary analysis based on the collected data, we observed that we could use a hyperbolic function as a good approximation for FiO_2 delivery on self-inflating devices. Specifically, the relation between FiO_2 and tidal volume, respiratory frequency, and O_2 flow can be described by a hyperbolic tangent function with four parameters,

$$FiO_2 \; = \; a \cdot \tanh(b \cdot O_2 \; + \; c) + \; d, \qquad (1)$$

where O_2 corresponds to the oxygen flow from the hospital supply line, *a*, *c*, and *d* are constants, and *b* is a function that depends on the tidal volume and the respiratory frequency.

In this work, we propose a second-order function, presented in Eq. (2), to describe the relation between parameter b and the delivered volume and respiratory frequency.

$$b = b_0 + b_1 \cdot V + b_2 \cdot F + b_3 \cdot V^2 + b_4 \cdot F^2 + b_5 \cdot V \cdot F, \qquad (2)$$

where V is the tidal volume, F is the respiratory frequency, and b_k, with k = {0; 1; 2; 3; 4; 5}, are constants obtained from the data.

3.1 DATA PROCESSING

Since data was collected from different sources and we considered various self-inflating ventilation devices, we had to address two aspects before executing the procedure to determine the values of the constants.

The first aspect is related to the fact that each work retrieved through the review defined its own range of volume, respiratory frequency, and O_2 flow. Specifically, some studies considered a small range of O_2 flow, not indicating the FiO_2 behavior for flow values close to 0 L/min or showing the FiO_2 tendency to its upper limit (1 or 100%). Using data with such a narrow range to define the values of the constants can produce models that are unable to fit the data.

To handle this problem, instead of discarding data, we added two points in each (volume x frequency) configuration: (O_2 flow = 0 L/min, FiO_2 = 0.21)1 and (O_2 flow = 40 L/min, FiO_2 = 1.00). In collected data, FiO_2 converges to values close to 1 for O_2 flow values higher than 20 L/min. So, we doubled the value for insurance and assumed that FiO_2 converged to 1 at an O_2 flow of 40 L/min, for all (volume x frequency) configurations.

The second aspect is related to the fact that studies considered resuscitators from different models and companies [13, 15, 18, 20, 28]. Some studies already described significant changes in the relation between FiO_2 and O_2 flow, tidal volume, and respiratory frequency for different bag resuscitators.

Thus, we organized data based on the ventilation device considered in the study and considered data from a single device to obtain the values of the constants and generate a model. Then, the proposed model was analyzed and validated using data from different bag resuscitators. We can use the achieved results to verify if it is possible to obtain a reliable model to estimate FiO_2 delivered by a resuscitator. We can also use the outcome to investigate how the model's accuracy can deteriorate when we use it to estimate the FiO_2 for a different bag resuscitator.

To generate the model, we used data from Young et al. [18], which considered a 1500 ml Hsiner Manual Resuscitator with a 2500 ml reservoir bag during experiments.

Data presented by Young et al. [18] consider an ample range of volume, O_2 flow, and respiratory frequency and have low uncertainties associated with the FiO_2 measurements (lower than 5% for all data). By considering data from a single work, we also avoid the influence of different experimental methodologies in the generated model.

3.2 CONSTANTS ESTIMATION

From the analysis of the collected data, we noticed that parameters *a*, *c*, and *d* of Eq. (1) suffer little influence from volume and frequency. So, we considered them as constants. On the other hand, *b* was defined in Eq. (2) as a function of volume and frequency based on constants b_0, …, b_5.

Thus, to obtain the constants defined in both Eq. (1) and Eq. (2), we proposed a two-steps procedure. In the first step, we calculate the values of parameters *a*, *b*, *c*, and *d* that better fit the collected data. Then, the constants in Eq. (1) can be obtained as the average of values obtained for a, c, and d values in all configurations. The values of b are discarded and recalculated in the second step, considering the values obtained for *a*, *c*, and *d*. Then, based on the new values of *b*, we can estimate the values of constants b_0, …, b_5.

Algorithm 1: Obtaining best values for *a*, *c*, and *d*

Result: Arrays **A**, **C** and **D**

A = [ ]; **C** = [ ]; **D** = [ ];

load FiO2.data; //FiO2(V,F,O)

for *each (v,f) configuration in FiO2.data* **do**

  y = FiO2(v,f,:);

  x = all O2 flow considered in conguration (v,f);

  $[a\ b\ c\ d]$ = Random('normal', $\mu = 0, \sigma = 0.1$, len = 4);

  $\mathbf{y}^* = a \cdot \tanh(b \cdot \mathbf{x} + c) + d$;

  r = **y**-**y***;

  while max(r)> ϵ **do**

    $\mathbf{J} = \left[\frac{\partial y*}{\partial a}, \frac{\partial y*}{\partial b}, \frac{\partial y*}{\partial c}, \frac{\partial y*}{\partial d}\right]$;

    $\Delta = (\mathbf{J}^T\mathbf{J})^{-1}\mathbf{J}^T\mathbf{r}$;

    $\Delta = \Delta \cdot \alpha$;

    Δ= Saturation(Δ, Δ_{max});

    $[a\ b\ c\ d] = [a\ b\ c\ d] + \Delta$;

    $\mathbf{y}^* = a \cdot \tanh(b \cdot \mathbf{x} + c) + d$;

    r = **y**-**y***;

  end

  A(v,f) = a;

  C(v,f) = c;

  D(v,f) = d;

End

Specifically, in the first step, an algorithm based on Gauss-Newton (presented in Algorithm 1) is used to calculate the values of parameters a, c and d that better fit the FiO_2 for each (volume x frequency) configuration. Let n be the number of (volume x frequency) configurations in the selected data, Algorithm 1 generates three arrays, **A**, **C** and **D**, of length n, with the corresponding values of *a*, *c*, and *d* that better fitted the data for each configuration. Also, for the sake of simplicity, we will refer to (volume x frequency) as (*v*, *f*).

In the beginning of Algorithm 1, the selected data is loaded and the values of *a*, *b*, *c*, and *d* are defined randomly using Random('normal', μ = 0, σ = 0.1, len = 4) function, which generates an array of 4 elements, considering a normal (or Gaussian) distribution of mean μ and standard deviation σ (μ and σ were defined as 0 and 0.1, respectively, in the algorithm executions).

Then, for each (*v*, *f*) configuration, the difference between real FiO_2 values (from data) and currently estimated ones, **r**, and the Jacobian matrix of the approximated function, **J**, are calculated. Based on **J** and **r**, an increment Δ is calculated and added to parameters *a*, *b*, *c*, and *d* current values. To improve the algorithm convergence, a parameter α (with value between 0 and 1) is multiplied to Δ and its module is limited to a maximum value Δ_{max}, by Saturation(Δ,Δ_{max}) function. The execution for each (*v*, *f*) configuration ends when the errors between the FiO_2 real and estimated values are smaller than a limit ϵ. During the algorithm execution, we considered $\alpha = 1$, $\Delta_{max} = 1$ and $\epsilon = 10^{-10}$. These parameters are important for convergence, and we refer to specific works for further information about them [29].

At the end of Algorithm 1, we obtain arrays **A**, **C**, and **D**, and constants *a*, *c*, and *d* are defined as their respective mean values. The values for the parameter *b* are also calculated in Algorithm 1. However, since we choose, for simplicity, to use the mean value for the parameters a, c, and d, a new estimation for b parameter is necessary.

To accomplish that, a slightly different version from Algorithm 1 is executed in the second step. Considering the values of *a*, *c*, and *d* calculated in the first step, Algorithm 2 generates an array **B** with the values of parameter *b* that better fitted each (*v*, *f*) configuration.

Algorithm 2: Obtaining best values for $b_0 \cdots b_5$

```
Result: Array B
B = [ ];
load FiO2.data;                                        //FiO2(V,F,O)
load constants data;                                   //a, c, and d
for each (v,f) configuration in FiO2.data do
    y = FiO2(v,f,:);
    x = all O2 flow considered in conguration (v,f);
    b = Random('normal', μ = 0, σ = 0.1, len = 1);
    y* = a · tanh (b · x + c) + d;
    r = y-y*;
    while max(r)> ϵ do
        J = [∂y*/∂b];
        δ = (J^T J)^-1 J^T r;
        δ = δ · α;
        δ = Saturation(δ, Δ_max);
        b = b + δ;
        y* = a · tanh(b · x + c) + d;
        r = y-y*;
    end
    B(v,f) = b;
end
```

In Algorithm 2, *a*, *c*, and *d* are loaded from a file with the values calculated using Algorithm 1. Thus, only the parameter b is iteratively updated to find a value that reduces the error between FiO_2 real and estimated values below a limit ϵ.

At the end of Algorithm 2 execution, it generates the array **B** (of length n), which is used then to calculate the parameters of Eq. (2), named b_0, b_1, b_2, b_3, b_4, and b_5. To accomplish this, we use a simple Least Squares function approximation [29].

Let v_i and f_i be the values of volume and frequency of the i-th (v, f) configuration. From Eq. (2), we have that the i-th element of **B**, $\mathbf{B}_i$, corresponds to:

$$\mathbf{B}_i = b_0 + b_1 v_i + b_2 f_i + b_3 {v_i}^2 + b_4 {f_i}^2 + b_5 v_i f_i. \qquad (3)$$

Eq. (3) can be redefined, for all data in array **B**, as the matrix form shown in Eq. (4).

$$\mathbf{B} = \overbrace{\begin{bmatrix} 1 & v_1 & f_1 & {v_1}^2 & {f_1}^2 & v_1 f_1 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 1 & v_n & f_n & {v_1}^n & {f_1}^n & v_n f_n \end{bmatrix}}^{\mathbf{M}} \cdot [b_0 \cdots b_5]^T. \qquad (4)$$

Based on array **B** and matrix **M**, the values of b_0, b_1, b_2, b_3, b_4, and b_5 are obtained through the Least Squares method as:

$$[b_0 \cdots b_5]^T = (\mathbf{M}^T \cdot \mathbf{M})^{(-1)} \cdot \mathbf{M}^T \cdot \mathbf{B}. \qquad (5)$$

It's important to state that the presented method can only be applied in datasets where n is greater than 5, the number of free parameters in Eq. (2). By executing the presented procedures over the data from Hsiner's bag resuscitator, we obtained the values of the model constants presented in Table 2.

Table 2: Values of the function constants.

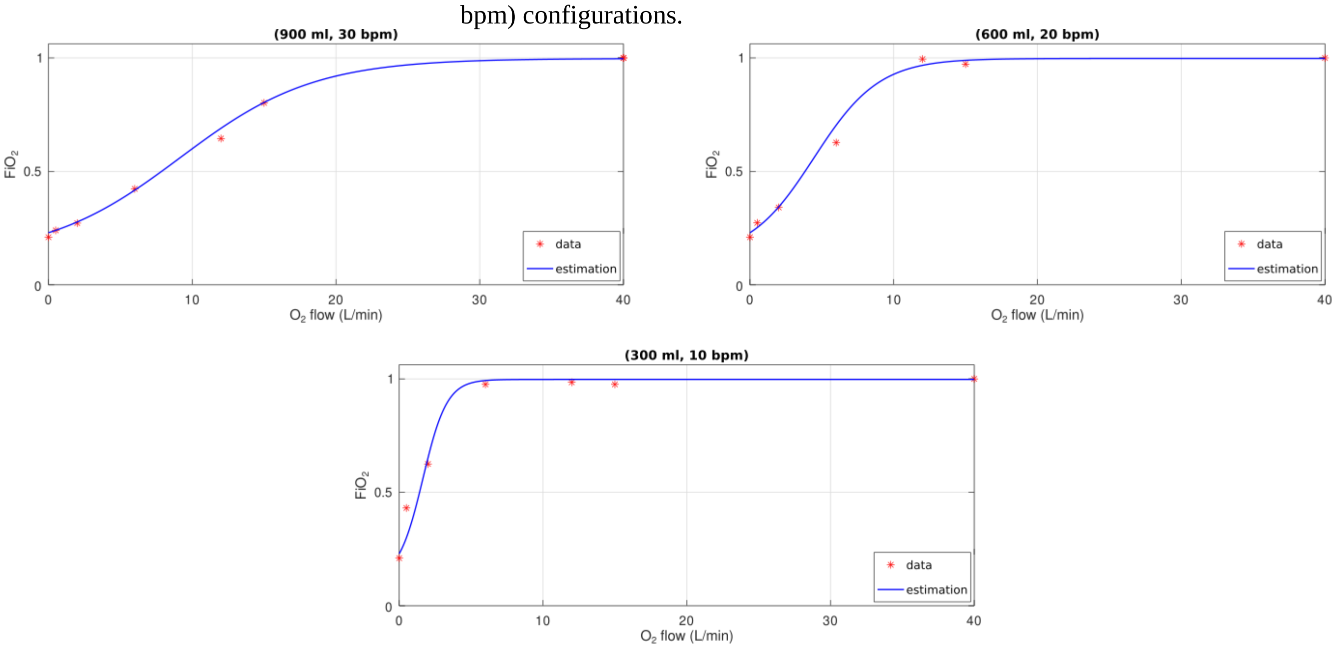
Constant	Value
a	0.437860
c	-0.982190
d	0.559790
b_0	1.23804202

b_1	-0.00109772
b_2	-0.04429894
b_3	0.00000028
b_4	0.00049656
b_5	0.00001907

Source: Prepared by the authors

Fig. 2 illustrates the FiO_2 curves generated by our model, considering the constants presented in Table 2, for different volume and respiratory rate configurations. Additionally, we present the data collected in the literature to help the reader understand how our model fits the data. In the next section, we analyze and validate the model considering the set with all the data selected during the review process.

Figure 2: FiO2 curves generated by our model for (900 ml, 30bpm), (600 ml, 20 bpm) and (300 ml, 10 bpm) configurations.



Source: Prepared by the authors

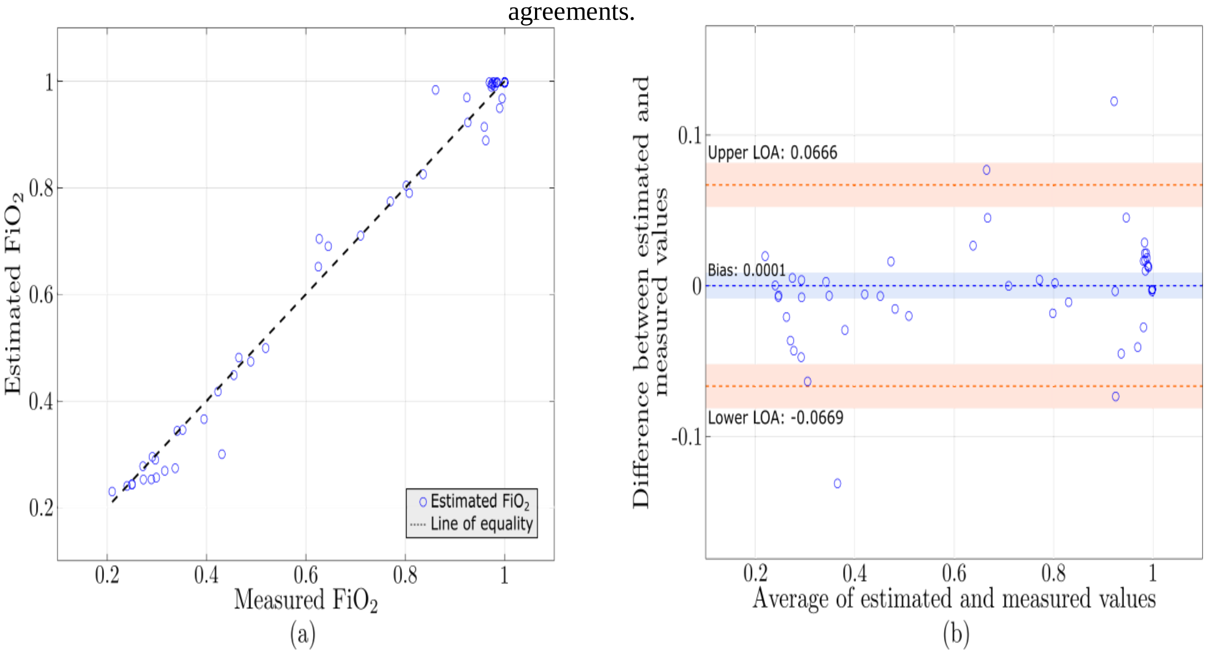
4 MODEL ANALYSIS AND VALIDATION

To evaluate the performance and validate the proposed model, we organized the data based on the model of the ventilation device. We compared our model estimations of FiO_2 with the experimental ones (from the original works of Nam et al. [20], Kulkarni et al. [28], Dimpel [13], Smith and Maguire [15], Young et al. [18]). To quantify the agreement between the estimated (by our model) and measured (collected from the literature) values of FiO2, we applied the Bland-Altman method [30] and obtained the mean bias, standard deviation, and limits of agreement (LOA) for each bag resuscitator considered. The analysis was carried out by using GNU Octave 5.2.0 and python library pyCompare [31].

To ensure statistical relevance during analysis, we discarded data on resuscitators with only a few collected samples. Thus, we only considered data associated with bag resuscitators from Hsiner, Laerdal, and Ambu. Results about the comparison between estimated and measured values of FiO2 are presented in Figs. 3, 4, and 5, which show the dispersion of the estimated over measured values of FiO2.

Let F_i and F_i^* be the measured and estimated values of FiO_2 for the i-th configuration, Figs. 3(a), 4(a), and 5(a) show graphs of F_i^* versus F_i. To make it easier to visually assess how well the estimated and measure values agree, we also present the line of equality, corresponding to the line where all points would lie if our model gave the same values measured in the original works.

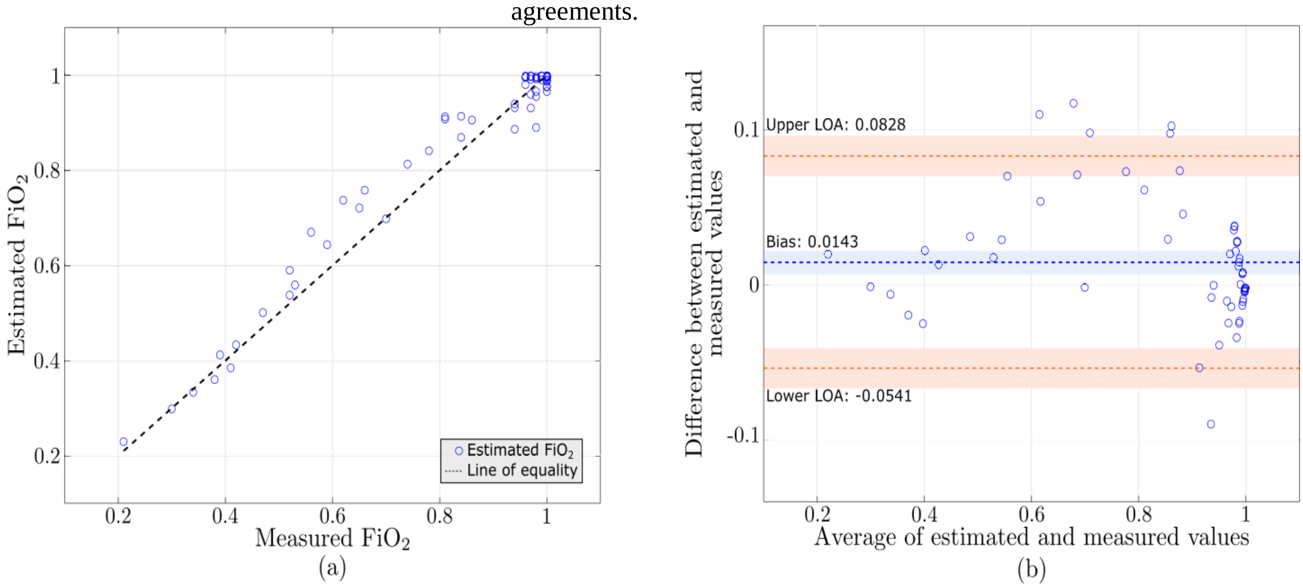
Figure 3: Additional information on validation with Hsiner bag resuscitator. (a) FiO2 estimated versus measured, with line of equality. (b) Difference (F_i^*- F_i) versus average values with bias and 95% limits of agreements.



Source: Prepared by the authors

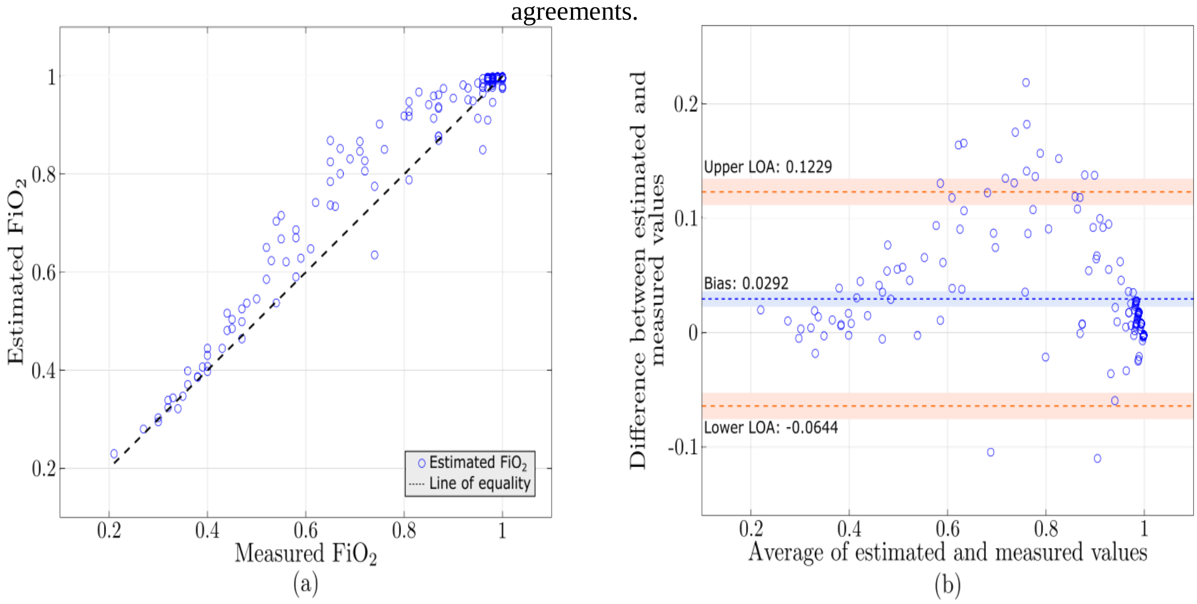
In turn, Figs. 3(b), 4(b), and 5(b) show graphs of the differences (F_i^* - F_i) versus the average (F_i^* + F_i)/2. The Figs. also show lines with mean bias, upper and lower limits of agreements, as well as their 95% confidence interval (indicated by the coloured boxes). These parameters were obtained through Bland-Altman analysis and are summarized in Table 3.

Figure 4: Additional information on validation with Laerdal bag resuscitator. (a) FiO2 estimated versus measured, with line of equality. (b) Difference ($F_i^* - F_i$) versus average values with bias and 95% limits of agreements.



Source: Prepared by the authors

Figure 5: Additional information on validation with Ambu bag resuscitator. (a) FiO2 estimated versus measured, with line of equality. (b) Difference ($F_i^* - F_i$) versus average values with bias and 95% limits of agreements.



Source: Prepared by the authors

Based on the data presented in Figs. 3 and 4, and in Table 3, we can observe that the mean bias was insignificant for data from Hsiner's device and small (less than 0.015 or 1.5%) for Laerdal. Considering the limits of agreement, our model estimated FiO_2 with errors below ±0.08 (or ±8%) in both cases.

Table 3: Bland-Altman analysis of FiO_2 estimated and measured values.

Device	Mean Bias	Lower LOA	Upper LOA
Hsiner	0.0001±0.0085	-0.0666±0.0146	0.0669±0.0146
Laerdal	0.0143±0.0076	-0.0541±0.0130	0.0828±0.0130
Ambu	0.0292±0.0067	-0.064±0.0114	0.1229±0.0114

Source: Prepared by the authors

Fig. 5 and Table 3 show that errors for data from Ambu devices are higher, with mean bias of 0.03 (or 3%) and limits of agreement of -0.06 (lower LOA) and +0.12 (upper LOA), which indicates errors of ±0.12 (or ±12%). Also, Fig. 5 shows a higher dispersion of point in the interval from 0.6 to 0.8 of FiO_2 values and that, in this interval, the difference could reach values of 20%.

Considering that oxygen gas blenders can produce a FiO_2 with errors of ±3% of the full scale [32], the level of errors generated by the proposed model are low enough for professionals to rely on its estimations, especially when considering Hsiner's and Laerdal's devices. We highlight that, although we did not consider data from Laerdal devices to obtain the constants in Table 2, the model fitted their data well.

It's also worth noticing that common knowledge among respiratory therapists says that bag resuscitators with oxygen reservoirs can supply a FiO_2 close to 100% if the oxygen flow in the supply line equals or exceeds minute ventilation [13]. Professionals also state that the FiO_2 varies from 80 to 100% regardless of volume minute, which is an even worse approximation [33]. Considering such empiric models and that errors associated with the model are lower than 10% in most cases, the model could be used with caution to estimate FiO2 values for different bag resuscitators.

We must call attention to two other aspects about the differences regarding Ambu's devices. First, we did not consider data from experiments with Ambu's devices to obtain the model constants (Table 2), so we already expected the model would produce worse estimations when compared to Hsiner bag resuscitators. Second, Fig. 3 shows a higher data density for FiO_2 values closer to 0.3 and 1, and the lack of a better distribution of points may harm the capacity of the model estimating FiO2 values in the central region of the scale. It's into this region where occurs the higher differences for both Laerdal's and, especially, Ambu's devices, as can be observed in Figs. 4(b) and 5(b).

The hyperbolic characteristic of FiO_2, shown in Fig. 2, can result in values changing significantly with small variations of the parameters (tidal volume, respiratory rate, and O_2 flow) in the central region of its scale. Thus, despite the experiments described by Young et al. [18] having considered well-spaced intervals for volume, respiratory rate, and O_2 flow, the values of FiO_2 measured were not well distributed. This issue indicates that experiments to collect data for FiO_2 modeling should pay closer attention to the configurations evaluated to generate data better distributed over the FiO_2 range.

5 CONCLUSIONS

This paper proposes a model relating FiO_2 delivered by bag resuscitators with tidal volume, frequency, and O_2 flow. It has an accuracy close to the ones considered by oxygen blender devices for other respiratory applications. In addition, we present the procedure used to obtain the model, which can be used by companies, for instance, to obtain new models to estimate the FiO_2 delivered by their products. Considering the lack of instruments that could allow healthcare professionals to assess the FiO_2 delivered by bag resuscitators, the model presents a pertinent contribution to the area.

Further, the model proposed in this paper could be implemented in a smartphone app or computer program, equipping professionals with software able to estimate FiO_2. Healthcare professionals can use such tools to adjust the FiO_2 (as an example, through O_2 flow) to reach specific SpO_2 levels, promoting rational use of O_2 with fewer collateral effects to the patient.

Finally, the model can also be used to estimate the FiO_2 when O_2 sources are too limited, and it is hard to use higher O_2 flows, as in a cylinder. In such cases, FiO_2 values can be hard to adjust, and estimation can be a piece of important information, for example, to review the initially proposed ventilation settings to compensate the FiO_2.

In future works, experiments considering configurations of volume, respiratory rate, and O_2 flow that generates a better distribution on the FiO_2 values could be performed to help in evaluating the influence of this aspect on the model's accuracy. Another relevant aspect that we could investigate in future works is the influence of using PEEP valves in FiO_2 values.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the support of the Institute of Systems and Computers Engineering, Research and Development of Brazil (INESC P&D Brasil).

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