A New Formula for Predicting the Fraction of Delivered Oxygen During Low-Flow Oxygen Therapy

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BACKGROUND: During O_2 therapy at low flow in patients who breathe spontaneously, the fraction of delivered O_2 (F_{DO_2}) is unknown. In recent years, F_{DO_2} prediction formulas have been proposed. However, they do not take into account the effect of inspiratory flow ($\dot{V}_I$) on the F_{DO_2}. The aim of this study was to validate a new F_{DO_2} prediction formula, which takes into account the $\dot{V}_I$ and compares it with other F_{DO_2} prediction formulas. METHODS: During a bench study, spontaneous breathing was generated with a mechanical test lung connected to a mechanical ventilator set to volume control mode. O_2 flow from a wall-mounted tube was delivered through a heat-and-moisture exchanger filter. A flow sensor recorded each breath of the $\dot{V}_I$ in ambient temperature and barometric pressure conditions. Three parameters [O_2 flow at 2, 3, 4, 5, 6 L/min; minute ventilation at 5, 10, 15, 20 L/min; and ratio of the inspiratory time (T_I) to the total breathing cycle time (T_{tot}) (T_I/T_{tot}) of 0.33 (T_I/T_{tot} value) and 0.50 (T_I/T_{tot} value)] were modified to generate many ventilatory patterns. An O_2 analyzer continuously examined the F_{DO_2}. RESULTS: When the O_2 flow and/or T_I/T_{tot} increased, the F_{DO_2} increased. When the minute ventilation increased, the F_{DO_2} decreased. The results of the Bland-Altman method for the F_{DO_2}, calculated by using our mathematical model and the measured F_{DO_2}, showed that the mean ± SD bias value was equal to 1.49 ± 0.84%, and the limits of agreement ranged from −0.17% to 3.14%. The intraclass correlation coefficients were 0.991 for $T_I/T_{tot} = 0.33$ and 0.994 for $T_I/T_{tot} = 0.50$, and the coefficient of variation was 2.1% for $T_I/T_{tot} = 0.33$ and 1.3% for $T_I/T_{tot} = 0.50$. The results of the Bland-Altman method for the F_{DO_2} calculated by using the Shapiro formula and the F_{DO_2} measured on the bench indicated that the bias value was 0.075 ± 8.66% and the limits of agreement ranged from −16.89% to 17.04%. For the Vincent formula, the bias value was 3.08% ± 8.56% and the limits of agreement ranged from −13.69% to 19.84%. CONCLUSIONS: The $\dot{V}_I$ has a major impact on F_{DO_2} during O_2 therapy at low flow. F_{DO_2} comparisons between frequently used prediction formulas and F_{DO_2} measured on the bench indicated greater differences. Uncritical use of these formulas should be used cautiously to predict F_{DO_2}. In this study, our prediction formula indicated a good accuracy for predicting F_{DO_2} during supplemental oxygenation through a heat-and-moisture exchanger in patients who breathe spontaneously. *Key words: oxygen; F_{DO_2}; low flow; oxygen therapy; prediction formula.* [Respir Care 2018;63(12):1528–1534. © 2018 Daedalus Enterprises]

Introduction

When trying to wean the patient from mechanical ventilation, spontaneous breathing trials assess the patient's ability to breathe while receiving no ventilatory support. In general, these patients receive oxygen to avoid hypoxemia. During this period, the fraction of delivered O_2 (F_{DO_2}) must be maintained within strict limits to avoid arterial

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oxygen variations. However, as reported by several studies, the F_{DO_2} varies according to the O_2 flow and/or the patient's respiratory pattern (eg, frequency, tidal volume).[1,2,3] This raises the question about F_{DO_2} prediction in patients who are intubated or tracheotomized oxygenated patients who breathe spontaneously with a Heat Moisture Exchanger (HME). In recent years, F_{DO_2}–validated formulas have been promoted.[4,5] However, they only take into account the administered O_2 flow and are only applicable in resting adult patients who breathe spontaneously and are oxygenated through a nasal cannula, transtracheal catheters, or a tracheostomy or endotracheal tube.[4-6]

Moreover, these formulas do not take into account the influence of the inspiratory flow ($\dot{V}_I$) on the variability of F_{DO_2} when the patient receives O_2 at low flow.[7-19] Our hypothesis is that the $\dot{V}_I$ has a major impact on F_{DO_2} during O_2 therapy at low flow and that these formulas are not accurate in clinical situations. The aim of this study was to validate a new F_{DO_2} prediction formula that takes into account the $\dot{V}_I$ and compares it with other formulas for use in patients who were tracheostomized or intubated and spontaneously breathing.

QUICK LOOK

Current knowledge

During O_2 therapy at low flow when using a heat moisture exchanger, the fraction of delivered O_2 (F_{DO_2}) can be estimated with prediction formulas. However, these formulas do not consider the effect of inspiratory flow on F_{DO_2}. The true F_{DO_2} delivered in these cases is not precisely known.

What this paper contributes to our knowledge

Comparisons with prediction formulas typically used by clinicians show major differences between the F_{DO_2} calculated and the F_{DO_2} measured on the bench. Indiscriminate use of prediction formulas exposes the practitioner to errors in O_2 administration assessment. Our study proposed a new prediction formula that takes into account minute ventilation and the ratio of the inspiratory time to the total breathing cycle time during oxygen delivery via a heat-and-moisture exchanger.

Methods

Part 1

The following F_{DO_2} prediction formula was developed (F_{DO_2} calculated [see the supplementary materials at http://www.rcjournal.com]) and compared with the F_{DO_2} measured in a bench study (F_{DO_2} measured).

$$F_{DO_2} = 0.21 + (x) \times \text{L/min } O_2$$

$$x = 1/(4 \times \dot{V}_E) \quad \text{for } T_I/T_{tot} = 0.33$$

$$x = 1/(2.5 \times \dot{V}_E) \quad \text{for } T_I/T_{tot} = 0.50$$

with O_2 flow in L/min, minute ventilation ($\dot{V}_E$) in L/min, inspiratory time (T_I) in seconds; and total inspiratory and expiratory time (T_{tot}) in seconds.

Model and Settings. Spontaneous breathing was generated in ambient temperature and barometric pressure conditions with a mechanical test lung (Model 5600i Dual Test Lung, Michigan Instruments, Grand Rapids, Michigan), which included 2 independent artificial lungs. With a special lung coupling clip, one lung was used to drive the second lung to achieve spontaneous breathing simulation. The settings of the artificial lung were as follows: resistance: ±5 cm H_2O/L/s and compliance of 0.06 L/cm H_2O. The first lung was driven by a mechanical ventilator, Servo-i (Maquet, Getinge group, Getingue, Sweden), set to volume control mode (continuous flow without auto-flow, time pause, and an inspiratory rise time at 0%; PEEP of 0 cm H_2O; the trigger was set at -10 cm H_2O to avoid self-triggering). The O_2 flow from a wall-mounted Thorpe Tube (0 to 15 L/min; Air Liquide RTM3, Technologie medicale, Noisy Le Sec, France) was delivered through an HME filter (dead space volume: 16 mL; Tracheolife I Filter HME Kendall-Covidien, 353U19004, Medtronic, Dublin, Ireland). The HME filter was directly fixed to a flow sensor. The flow sensor was directly connected to the entry of the lung port inlet of the second Dual Test Lung (Fig. 1). An O_2 analyzer port was located on the top plate of the second artificial lung. The 3 parameters were modified as followed:

1. O_2 flow: 2, 3, 4, 5, 6 L/min.
2. $\dot{V}_E$: 5, 10, 15, 20 L/min.
3. T_I/T_{tot}: 0.33 and 0.50.

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Supplementary material related to this paper is available at http://www.rcjournal.com.

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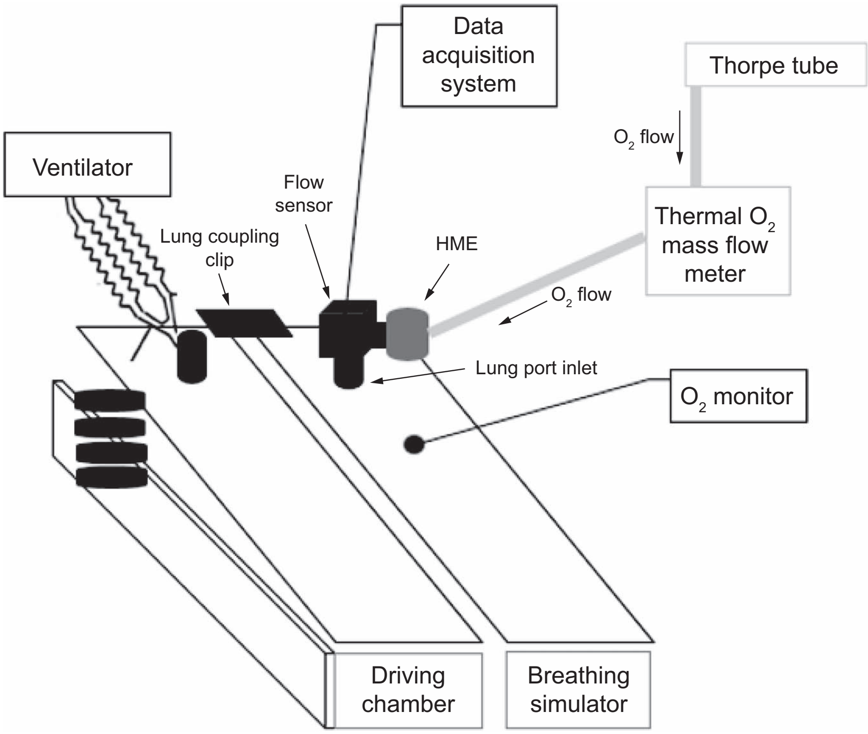

Fig. 1. Study schematic.

Table 1. Inspiratory flow value (L/min) as regard of Minute ventilation and T_I/T_{tot}

Variable	$\dot{V}_E$ and T_I/T_{tot} (L/min)			
$\dot{V}_E$	5	10	15	20
T_I/T_{tot} = .33	15	30	45	60
T_I/T_{tot} = .50	10	20	30	40

$\dot{V}_E$ = minute ventilation
T_I = inspiratory time
T_{tot} = total breathing cycle time

Note: With these $\dot{V}_E$ and T_I/T_{tot} values, $\dot{V}_I$ ranges from 10 to 60 L/min (Table 1).

Variables. The main measured variable was F_{DO_2} (expressed as the volumetric percentage of O_2 in the steady-state dual test lung). F_{DO_2} was measured with a Datex Ohmeda O_2 Monitor (Model 5120, Louisville, Kentucky) calibrated with room air (21%), then at 30%, 35%, and 50%, with certified O_2 gas (sensor type, galvanic fuel cell reference 0237–2034–700; accuracy, ±2% of full scale; response time, 9 s; measuring range, 0–100%). F_{DO_2} was measured as the mean of 15 breaths after a stabilization period of at least 1 min.

O_2 flow was measured continuously with a Thermal O_2 Mass Flow Meter (Red Y Vögtlin Instruments, Switzerland, Aesch) (accuracy, ±1.5% of full scale; repeatability, ±0.1% of full scale). The $\dot{V}_E$ and T_I/T_{tot} were measured with a data acquisition system IX-214 (iWorx Systems, New Hampshire), which included an SP-304 (iWorx Systems, New Hampshire) flow sensor and a data-acquisition hardware connected to a Software Labscribe 3 (Iworx). The flow sensor was calibrated by using a 1-L calibration syringe (Hans Rudolph, Inc., Shawnee, Kansas) and ambient air. During this step, the gap between the required value and read value was a maximum of ±30 mL. All measurements were done in triplicate.

Part 2

The calculated F_{DO_2} values were compared with the F_{DO_2} values obtained through the following 2 previously validated formulas:

The Shapiro formula,[4]

$$F_{DO_2} = 0.20 + (0.04 \times \text{L/min } O_2)$$

The Vincent formula,[5]

$$F_{DO_2} = 0.21 + (0.03 \times \text{L/min } O_2)$$

Statistical Analysis

Data were analyzed by using the Sigma plot software (Version 12.0 Systat Software Inc., San Jose, California).

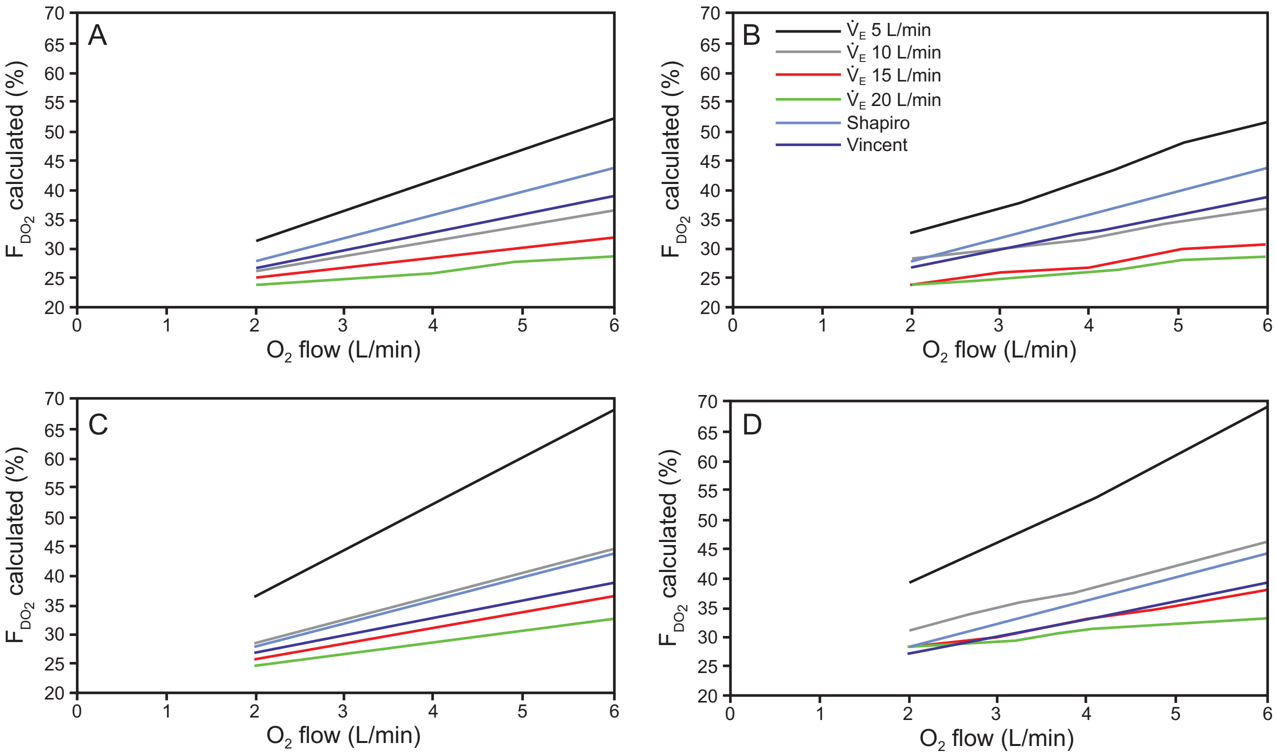

Fig. 2. Graphic values of the fraction of delivered O_2 (F_{DO_2}) calculated (A, C) and the F_{DO_2} measured (B, D) for O_2 flow, ranging from 2 to 6 L/min, Minute ventilation from 5 to 20 L/min for the ratio of the inspiratory time (T_I) to the total breathing cycle time (T_{tot}) (T_I/T_{tot}) = 0.33 (A, B) and T_I/T_{tot} = 0.50 (C, D), and between the F_{DO_2} obtained with the Shapiro and Vincent formulas. Inspiratory flow ($\dot{V}_I$), ranging from 10–60 L/min.

The values are expressed as mean ± SD. The agreement between F_{DO_2} calculated by the mathematical model and the F_{DO_2} measured during the bench test measurements was expressed as proposed by Bland and Altman.[20] As such, the bias and the limits of agreement were reported for each T_I/T_{tot} (95% CI for the difference between measurements). An intraclass correlation coefficient was calculated to measure the relationship between F_{DO_2} calculated and F_{DO_2} measured for each T_I/T_{tot}. To analyze the variability between the F_{DO_2} calculated with our formula and the F_{DO_2} measured, a coefficient of variation was calculated for each T_I/T_{tot}. Finally, an agreement between F_{DO_2} calculated by using the prediction formulas (Shapiro and Vincent), and the F_{DO_2} measured during the bench test measurements was calculated.

Results

In this bench study, when the O_2 flow and/or the T_I/T_{tot} increased, the F_{DO_2} increased. When the $\dot{V}_E$ increased, the F_{DO_2} decreased (Fig. 2).

Part 1

The results of the Bland-Altman method between F_{DO_2} calculated by using our mathematical model and the F_{DO_2} measured showed that the bias value was 1.49 ± 0.84%, and the limits of agreement ranged from −0.17% to 3.14% (Fig. 3). The intraclass correlation coefficient results were 0.991 for T_I/T_{tot} = 0.33 and 0.994 for T_I/T_{tot} = 0.50, and the coefficient of variations were 2.1% for T_I/T_{tot} = 0.33 and 1.3% for T_I/T_{tot} = 0 .50 (Fig. 3).

Part 2

The results of the Bland-Altman method for the F_{DO_2} calculated by the Shapiro formula and the F_{DO_2} measured on the bench showed that the bias value was 0.075 ± 8.66%,[4,20] and the limits of agreement ranged from −16.89% to 17.04%. For the Vincent formula, the bias value was 3.08 ± 8.56% and the limits of agreement ranged from −13.69% to 19.84% (Fig. 4).

Discussion

During O_2 administration through an HME in patients with tracheostomy and who breathed spontaneously, slight absolute differences were found between the F_{DO_2} calculated with our formula and the F_{DO_2} measured on the bench. The bias (with its limits of agreement), the intraclass correlation coefficient, and the coefficient of variation were

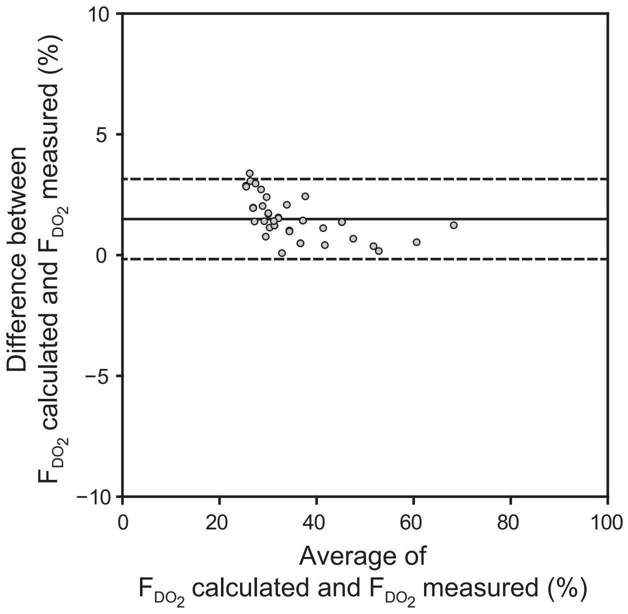

Fig. 3. Bland-Altman graph comparing the fraction of delivered O_2 (F_{DO_2}) calculated with our formula and the F_{DO_2} measured on the bench for an O_2 flow of 2–6 L/min, a minute ventilation that ranged from 5 to 20 L/min), and the ratio of the inspiratory time (T_I) to the total breathing cycle time (T_{tot}) (T_I/T_{tot}) of 0.33 (T_I/T_{tot} value) and 0.50 (T_I/T_{tot} value). Inspiratory flow ($\dot{V}_I$) that ranged from 10 to 60 L/min. The center line denotes mean, dashed lines show ±1.96 SD.

low between the F_{DO_2} measured and the F_{DO_2} calculated, which indicated the suitable validity of our prediction formula. However, when the F_{DO_2} increased, this bias varied, in an inversely proportional manner, and was probably due to the turbulence during high O_2 flow.[21] Bias between the F_{DO_2} calculated and the F_{DO_2} measured of both prediction formulas (Shapiro and Vincent) were small and showed slight differences (bias for the Shapiro formula, 0.075 ± 8.66%; and for the Vincent formula, 3.08 ± 8.56%). However, the SD of these biases and the limits of agreement were wider compared with the values obtained with our formula.

According to our calculations, both prediction formulas were well suited for a healthy adult patient breathing at rest ($\dot{V}_E = \pm 8$ L/min and $T_I/T_{tot} = 0.33$). This meant that these formula minute volumes were less suitable when the V_E values differed from this threshold. Therefore, the Shapiro and the Vincent formulas should be used cautiously. Indeed, not considering these facts could lead to an over-or underestimation of oxygenation. The $\dot{V}_I$ value is equal to the ratio between the minute volume and the T_I/T_{tot} ($\dot{V}_I = [f \times Vt]/[T_I/T_{tot}]$). According to our formula, the F_{DO_2} was roughly equal to the ratio between the O_2 flow and $\dot{V}_I$. So, in adult patients, because the $\dot{V}_I$ value was much higher than the O_2 flow value, the impact of $\dot{V}_I$ on F_{DO_2} was higher. However, in small patients, it was the opposite: the O_2 flow was higher than the $\dot{V}_I$. In this case, small variations of O_2 flow will have a major impact on F_{DO_2}. According to our research, this variation appears in several studies.[1,10,11,19,22] Thus, for instance, when taking into consideration two $\dot{V}_E$ values, the gap between both F_{DO_2} values increases when the O_2 flow increases (Fig. 2). Consequently, during O_2 therapy, if the ventilatory pattern was not constant, then the F_{DO_2} would not be constant either. When the O_2 flow is constant:

- If the $\dot{V}_I$ increases, then the F_{DO_2} will decrease, for example, under conditions of stress, hyperthermia, agitation, metabolic acidosis, pain, or exercise (eg, COPD rehabilitation).[1,23] Similar observations were found by Couser and Make[12] with subjects oxygenated through a transtracheal catheter. These investigators observed that a decrease in $\dot{V}_I$ increased P_{aO_2}.
- If the $\dot{V}_I$ decreases, then the F_{DO_2} will increase. For example, under some sedative medications and/or instances of drug abuse, as well as in reassuring and relaxing atmospheres, or when patients are in a deep sleep and are receiving O_2 by low flow.[11,15,24]
- If the $\dot{V}_I$ is small, then the F_{DO_2} value will be high, even with low O_2 flow (eg, during O_2 therapy in preterm infants).

These situations should encourage us to be cautious when $\dot{V}_I$ varies during oxygenation at low flow because this can lead to a risk of over or under oxygenation. Indeed, if hypoxemia (or hyperoxemia) is only due to ventilatory pattern variations, it is enough to modify the O_2 flow to adjust the value of arterial pressure in O_2. There are other considerations with regard to the dead space of the HME. Indeed, first, during spontaneous ventilation with HMEs, the mixture with expired air could affect the O_2 fraction of inspired air. However, the dead-space value of these devices generally varies from 9 to 29 mL[25] and was 16 mL in the HME used in our study.

Second, a tracheostomy tube reduces the upper-airway anatomic dead space by up to 150 mL, or 50%.[26] In these cases, the CO_2 contained in the anatomic dead space is lower than in normal physiologic ventilation. Therefore, the impact on the F_{DO_2} decrease would be limited. Third, during oxygenation with an O_2 administration device, during the expiratory phase, the continuous O_2 flow washout reduces the dead space, which limits the impact of CO_2 rebreathing.[14] The clinical utility of knowing the formula is that it could be helpful for the therapist to be aware of the initial setup for O_2 therapy for specific situations. For example, for small patients (or lower V_E), low O_2 flow can deliver high F_{IO_2}, for tall people (or high $\dot{V}_I$), high O_2 flow delivers less F_{IO_2} than with normal $\dot{V}_I$, and during high O_2 flow in adults, any variation of $\dot{V}_I$ will change the F_{IO_2} drastically.

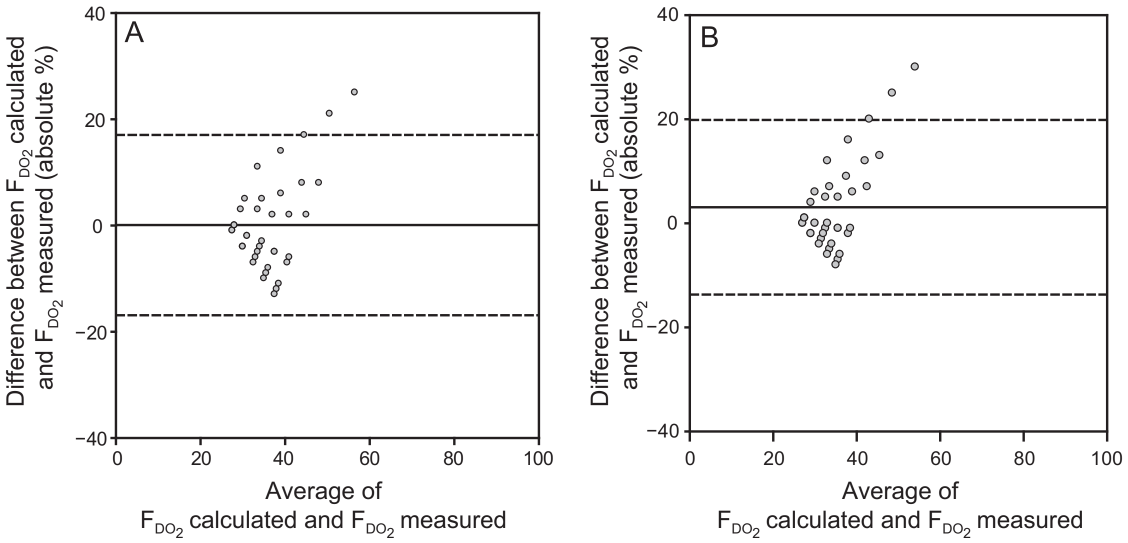

Fig. 4. Bland-Altman graph compares F_{DO_2} calculated with the Shapiro formula and the F_{DO_2} measured (A) and Vincent formula and the F_{DO_2} measured (B) for an O_2 flow that ranges from 2 to 6 L/min, minute ventilation that ranges from 5 to 20 L/min) and the ratio of the inspiratory time (T_I) to the total breathing cycle time (T_{tot}) (T_I/T_{tot}) of 0.33 and 0.50. Inspiratory flow ($\dot{V}_I$) range from 10 to 60 L/min.

The aim of this bench study was to validate a new formula to predict F_{DO_2} during oxygenation through an HME. The $\dot{V}_E$ and the analyzed O_2 flow ranged from 5 to 20 L/min (Table 1) and from 2 to 6 L/min, respectively. However, we draw attention to the risk of under humidification of inspired gas during high O_2 flow through an HME in patients who are able to breathe spontaneously.[25]

Study Limitations

The present study had some limitations. In practice, use of our prediction formula was difficult because the exact patient $\dot{V}_I$ value was unknown and O_2 flow meters have a low accuracy.[27-29] Moreover, in this study, the $\dot{V}_I$ used was continuous (rectangular form). However, the human $\dot{V}_I$ wave is not continuous (waveform). As such, determining the exact value of F_{DO_2} is difficult in clinical situations. In addition, our model had limitations because it did not reproduce anatomic dead space. Also, the HME used was Tracheolife I, other systems exist with different dead spaces, which could affect results.

Conclusions

During supplemental oxygenation at low flow in a model of spontaneous breathing with an artificial airway, the F_{DO_2} was influenced by the O_2 flow and the $\dot{V}_I$. According to our observations, the $\dot{V}_I$ had a substantial impact on the F_{DO_2} and, therefore, could lead to over or under oxygenation without careful monitoring. F_{DO_2} comparisons between the prediction formulas typically used by clinicians and F_{DO_2} measured on the bench had larger differences. Caution should be exercised when using these formulas for predicting F_{DO_2}. Indeed, during the calculation of the P_{aO_2}/F_{IO_2} with the Shapiro or Vincent formulas, there was a high risk of overestimating the F_{IO_2}, especially if the patient's inspiratory rate was high. This paper proposed a new prediction formula that takes into account O_2 flow and $\dot{V}_I$ values. Our prediction formula showed good accuracy when predicting F_{DO_2} during supplemental oxygenation at low flow through an HME.

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