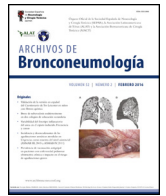




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Original Article

Protective Recommendations for Non-invasive Ventilation During COVID-19 Pandemic: A Bench Evaluation of the Effects of Instrumental Dead Space on Alveolar Ventilation

Mathieu Delorme^{a,*}, Karl Leroux^b, Ghilas Boussaid^a, Marius Lebret^c, Helene Prigent^{d,e}, Antoine Leotard^{d,e}, Bruno Louis^{f,◇}, Frédéric Lofaso^{a,d,◇}

^a Université Paris-Saclay, UVSQ, ERPHAN, 78000 Versailles, France

^b ASV Santé, 92230 Gennevilliers, France

^c Institut Universitaire de Cardiologie et de Pneumologie de Québec (IUCPQ), Québec, QC, Canada

^d Service de Physiologie – Explorations Fonctionnelles, Unité des Pathologies du Sommeil, AP-HP, Hôpital Raymond Poincaré, 92380 Garches, France

^e Université Paris-Saclay, UVSQ, INSERM U1179, Equipe 3, 78000 Versailles, France

^f INSERM, U955, Université Paris Est Créteil, Faculté de Médecine, CNRS ERL 7000, 94010 Créteil, France

ARTICLE INFO

Article history:

Received 8 September 2020

Accepted 2 January 2021

Available online 2 February 2021

Keywords:

Coronavirus

Infectious disease transmission

Non-invasive ventilation

Respiratory therapy

Respiratory dead space

ABSTRACT

Introduction: With the current COVID-19 pandemic, concerns have raised regarding the risk for NIV to promote airborne transmission. In case of hospital admission, continuation of therapy in patients undergoing chronic NIV is necessary and several protective circuit configurations have been recommended to reduce the risk of aerosol dissemination. However, all these configurations increase instrumental dead space. We therefore designed this study to evaluate their effects on the tidal volume (VT_E) required to preserve stable end-tidal CO_2 partial pressure ($P_{ET}CO_2$) with constant respiratory rate.

Methods: A bench consisting of a test lung connected to an adult-sized mannequin head was set up. The model was ventilated through usual domiciliary configuration (single limb circuit with facial vented mask) which was used as reference. Then, five different circuit configurations including non-vented facial mask with viral/bacterial filter, modification of leak position, and change from single to double-limb circuit were evaluated. For each configuration, pressure support (PS) was gradually increased to reach reference $P_{ET}CO_2$. Resulting VT_E was recorded as primary outcome.

Results: Reference $P_{ET}CO_2$ was 38(0) mmHg, with a PS set at 10 cmH₂O, resulting in a VT_E of 432(2) mL. Compared to reference, all the configurations evaluated required substantial increase in VT_E to preserve alveolar ventilation, ranging from +79(2) to +216(1) mL.

Conclusions: Modifications of NIV configurations in the context of COVID-19 pandemic result in substantial increase of instrumental dead space. Re-evaluation of treatment efficiency and settings is crucial whenever protective measures influencing NIV equipment are considered.

© 2021 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

Recomendaciones de protección para la ventilación no invasiva durante la pandemia de COVID-19: una evaluación con modelo experimental de los efectos del espacio muerto instrumental en la ventilación alveolar

RESUMEN

Introducción: Durante la actual pandemia de COVID-19 ha surgido la preocupación sobre el posible riesgo de que la ventilación no invasiva (VNI) promueva la transmisión aérea. En el caso de ingreso hospitalario, es necesario continuar con el tratamiento de aquellos pacientes tratados con VNI crónica y se han recomendado varias configuraciones protectoras de los circuitos para reducir el riesgo de diseminación por aerosoles. Sin embargo, todas estas configuraciones aumentan el espacio muerto instrumental. Así,

Palabras clave:

Coronavirus

Transmisión de enfermedades infecciosas

Ventilación no invasiva

Terapia respiratoria

Espacio muerto respiratorio

* Corresponding author.

E-mail address: mathieu.delorme.pt@gmail.com (M. Delorme).

◇ Both authors contributed equally to this manuscript.

<https://doi.org/10.1016/j.arbres.2021.01.012>

0300-2896/© 2021 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

diseñamos este estudio para evaluar los efectos de estas configuraciones sobre el volumen corriente (VCE) necesario para mantener estable la presión parcial de CO₂ al final del volumen corriente espirado (PETCO₂) con una frecuencia respiratoria constante.

Métodos: Se construyó un modelo experimental que constaba de un pulmón de prueba conectado a una cabeza de maniquí de tamaño adulto. El modelo recibió ventilación utilizando la configuración domiciliar habitual (circuito de rama única con máscara facial ventilada), lo que se utilizó como referencia. Después se evaluaron cinco configuraciones diferentes del circuito, incluidas la máscara facial sin ventilación con filtro antiviral/antibacteriano, la modificación de la posición de la fuga y el cambio de circuito de rama única a doble rama. Para cada configuración, la presión de soporte (PS) se incrementó gradualmente hasta alcanzar la PETCO₂ de referencia. El VCE resultante se registró como resultado primario.

Resultados: La PETCO₂ de referencia fue de 38(0) mmHg, con una PS fijada en 10 cmH₂O, lo que resultó en un VCE de 432(2) mL. En comparación con la referencia, todas las configuraciones evaluadas requirieron un aumento sustancial del VCE para preservar la ventilación alveolar, en un rango entre +79(2) mL y +216(1) mL.

Conclusiones: Las modificaciones de las configuraciones de VNI en el contexto de la pandemia de COVID-19 resultan en un aumento sustancial del espacio muerto instrumental. Reevaluar la eficacia y los ajustes del tratamiento es fundamental cuando se ponen en consideración unas medidas de protección que influyen en el equipo de VNI.

© 2021 SEPAR. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Introduction

Non-invasive ventilation (NIV) is the standard of care for the treatment of chronic hypercapnic respiratory failure.¹ It can be conducted through different configurations, single-limb circuits with facial masks being the most frequently met in the home setting.¹ This implies the presence of an intentional leak either at the mask or between the mask and circuit, preventing exhaled air to be rebreathed. However, substantial dissemination of exhaled particles into patients' environment has been documented.²

With the current COVID-19 pandemic, growing interest regarding the risk for NIV to promote airborne transmission has emerged.³ This concern has led by itself to discuss the indication of this therapy in patients requiring hospital admission for *de novo* SARS-CoV-2 infection or in situations of acute-on-chronic respiratory failure.^{4–6} In the latter situation, patients treated with chronic NIV may worsen with ventilation cessation and protective measures allowing for pursuing therapy in and out of the hospital setting are necessary.

Thus, several adaptations of circuit configuration in order to reduce the risk of NIV-related viral contaminations have been proposed worldwide.^{7–11} Most of these recommendations share the common aspect that they increase instrumental dead space (VD) and airway resistance compared to “usual” configuration. As a consequence, any modification of NIV circuit configuration when applying these protective recommendations may require NIV settings adjustments to preserve ventilation efficiency.

We therefore designed this bench study in order to evaluate the effects of circuit configurations recommended for NIV during COVID-19 pandemic on the pressure support (PS) and expired tidal volume (VT_E) modifications required to maintain treatment efficiency with respect to end-tidal CO₂ partial pressure (P_{ET}CO₂).

Methods

Respiratory System Model

A test lung was used to simulate the patient's respiratory mechanics (compliance: 60 mL/cmH₂O, resistance: 5 cmH₂O/L/s). These parameters were chosen to be central enough to be consistent both with respiratory mechanics of patients undergoing chronic NIV and patients eligible for NIV at hospital admission in the context of suspected SARS-CoV-2 infection.¹² In order to simulate

CO₂ production, a constant flow of 100% CO₂ (V'CO₂) was provided into the test lung (180 ± 5 mL/min).¹³

Ventilation of the test lung was performed with the Astral 150 (SR6; ResMed Ltd, Bella Vista, NSW, Australia) set with PS 10 cmH₂O and expiratory positive airway pressure (EPAP) 6 cmH₂O. Rise time was set to 150 ms, trigger medium, cycling 50% of peak inspiratory flow, minimum and maximum inspiratory times (TiMin and TiMax) set to offer a window from 1/4 to 1/2 of total breath cycle time, i.e. 0.6 and 1.2 s, respectively. The simulated patient was passively ventilated and respiratory rate was driven by the backup rate, set at 25 bpm.

Data Acquisition

Respiratory flow (V_{aw}), airway pressure (P_{aw}) and PCO₂ were continuously monitored between the mannequin head and the test lung (Supplementary Fig. 1). Partial pressure of end-tidal CO₂ (P_{ET}CO₂) was defined as the maximum PCO₂ value reached at the end of expiration. Steady state was determined as a period of at least 5 min of stable ventilation assessed by visual inspection of respiratory flow and pressure curves, and stable P_{ET}CO₂ (i.e. variations < 0.5 mmHg from breath to breath).

Data were analysed with a dedicated software. Inspiratory positive airway pressure measured between the mannequin and the test lung (IPAP_{aw}) was determined as the maximum P_{aw} reached during inspiratory time; positive end-expiratory pressure (PEEP_{aw}) was determined as mean P_{aw} during the last 200 ms of expiratory time. Inspiratory time (T_i) was defined as the duration in seconds from the onset of positive V_{aw} to the onset of negative V_{aw}. Peak inspiratory flow (PIF) was determined as the maximal V_{aw} value reached during inspiratory time. Expired tidal volume (VT_E) was calculated as the integral of V_{aw} over expiratory time. Additional measurements were performed to determine circuit compliance and resistances according to the different configurations evaluated, as detailed in the [supplementary material](#).

Protocol

Configuration A consisted in a single-limb circuit (Standard air tubing, ResMed Ltd, Bella Vista, NSW, Australia) and a facial mask with built-in intentional leak (Quattro Air – Medium size, ResMed Ltd, Bella Vista, NSW, Australia).¹ The mask was carefully fitted on the mannequin head to avoid non-intentional leaks. Calibration of

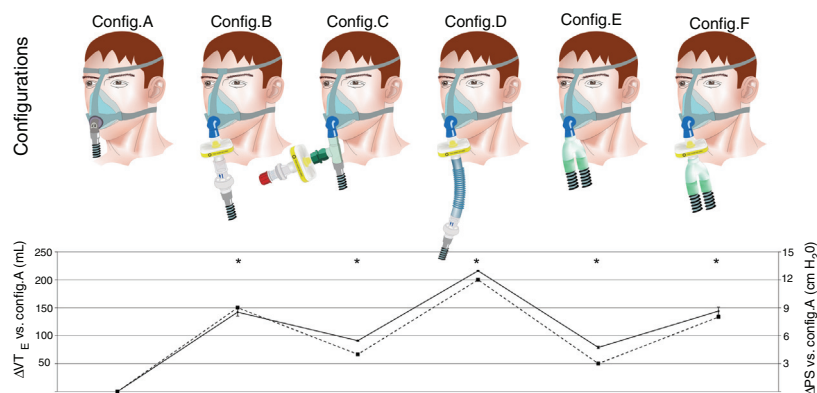


Fig. 1. PS and VT_E variations required to maintain iso-P_{ET}CO₂ according to the configurations evaluated.

Upper panel: configuration A: conventional domiciliary configuration; configuration B: from Ref. 7; configuration C: from Ref. 8; configuration D: from Ref. 9; configuration E: from Ref. 10; configuration F: from Ref. 11; for configurations E and F, two additional filters were placed both at the inspiratory and expiratory port of the ventilator (not shown).

Lower panel: data are expressed as mean (SD). ΔPS (cmH₂O, dashed line), difference between pressure support set for a given configuration and reference PS (configuration A; 10 cmH₂O). ΔVT_E (mL, solid line): difference between measured VT_E for a given configuration and reference VT_E (configuration A; 432 mL). *Clinically relevant variation compared to reference (configuration A). Note that ΔVT_E represents the increase in VT_E required to preserve alveolar ventilation with constant respiratory rate, i.e. the additional instrumental dead space in mL.

the device and circuit up to the end of the tubing was performed prior to data acquisition and remained unmodified throughout the protocol except for configurations E and F (double-limb circuit). Configuration B consisted in a serial connection of circuit (Standard air tubing, ResMed Ltd, Bella Vista, NSW, Australia), calibrated intentional leak (ResMed leak valve, ResMed Ltd, Bella Vista, NSW, Australia), viral/bacterial filter (Air-Guard™ Clear, Intersurgical Ltd, UK, internal volume: 120 mL), and non-vented facial mask (Quattro Air NV – Medium size, ResMed Ltd, Bella Vista, NSW, Australia).⁷ In configuration C the circuit (Standard air tubing, ResMed Ltd, Bella Vista, NSW, Australia) was connected to the mask (Quattro Air NV – Medium size, ResMed Ltd, Bella Vista, NSW, Australia) via a T-connector, to the remaining port of which was connected the filter (Air-Guard™ Clear, Intersurgical Ltd, UK), followed by the leak (ResMed leak valve, ResMed Ltd, Bella Vista, NSW, Australia) and an occlusion cap (Intersurgical Ltd, UK).⁸ Configuration D consisted in configuration B with a 15 cm flexible tubing with 22 mm inner diameter inserted between the filter and the leak.⁹ Configuration E consisted in a double-limb circuit (Smoothbore breathing system, Intersurgical Ltd, UK), connected to a non-vented facial mask (Quattro Air NV – Medium size, ResMed Ltd, Bella Vista, NSW, Australia), with two filters (Air-Guard™ Clear, Intersurgical Ltd, UK) placed both at the inspiratory and expiratory port of the ventilator.¹⁰ Configuration F consisted in configuration E with a filter placed between the Y-piece and the mask.¹¹

First, a baseline assessment was performed with the usual domiciliary configuration (Fig. 1, upper panel; configuration A). After steady state was reached, P_{ET}CO₂ was recorded and used as reference for the following experiments. Then, five additional configurations recommended for NIV during COVID-19 pandemic were successively evaluated (Fig. 1, upper panel; configurations B–F). With each of these configurations, resulting P_{ET}CO₂ and VT_E with baseline pressure support (10 cmH₂O) were recorded (iso-PS variables).

For each configuration, PS was manually incremented to reach reference P_{ET}CO₂ (configuration A), and therefore to determine the tidal volume variations required to maintain isocapnia (i.e. stable alveolar ventilation). The additional VD with the different configurations evaluated was calculated according to Bohr's equation (see supplementary material). P_{ET}CO₂ deviation from reference <1 mmHg was considered clinically acceptable. Data analysis was performed with a dedicated software on a breath by breath basis over 1 min of stable ventilation. Mean and standard deviation (SD)

were calculated for each variable of each configuration and used for between-groups comparison.

Statistical Analysis

VT_E difference (ΔVT_E) between reference configuration (A) and other configurations (n) was calculated as VT_E(n) – VT_E(A) and absolute value expressed in mL was used for analysis. The same calculation was performed to determine pressure support and dead space differences (respectively, ΔPS; in cmH₂O, and ΔVD; in mL) between reference and other configurations. Data were described as mean (SD). Given the simulation-based design of this study, standard variations for each variable was extremely small and any statistical analyses would have yielded significant results. Therefore, we arbitrarily chose a cut off set at ±10% above which variations from reference configuration's mean ± SD (config. A) would be considered clinically relevant.

Additional information regarding the methods is provided in the [supplementary material](#).

Results

For configuration A, reference P_{ET}CO₂ at steady state was 38(0) mmHg, with a PS set at 10 cmH₂O resulting in a VT_E of 432(2) mL. With the baseline ventilatory parameters, substantial variations in VT_E were observed, associated with a clinically relevant increase in P_{ET}CO₂ (Table 1; iso-PS variables). Consequently, all the configurations evaluated required higher PS to maintain stable P_{ET}CO₂ (Table 1; iso-P_{ET}CO₂ variables). V̇CO₂ remained within clinically acceptable range (180(5) mL/min) throughout the protocol. The absolute increase in PS (ΔPS, cmH₂O) to maintain iso-P_{ET}CO₂ for each configuration is depicted in Fig. 1, lower panel. This resulted in higher VT_E for all configurations evaluated compared to reference configuration (Fig. 1, lower panel), respectively +142(7), +91(1), +216(1), +79(2) and +144(7) mL with configurations B–F. The calculation of additional VD according to Bohr's equation yielded similar results, with an increase in VD by +143(7), +91(2), +216(2), +81(3) and +148(6) mL with configurations B–F, respectively. Ventilatory parameters measured in the condition of stable alveolar ventilation (iso-P_{ET}CO₂) are displayed in Table 2. The time course of P_{aw}, V̇_{aw} and PCO₂ for the reference configuration (A) and the configuration requiring the maximum PS and VT_E modifications to reach reference P_{ET}CO₂ (configuration D) is depicted in Fig. 2.

Table 1
Iso-PS and Iso- $P_{ET}CO_2$ Basic Monitoring According to the Different Configurations Evaluated.

Variables	Config. A	Config. B	Config. C	Config. D	Config. E	Config. F
<i>Iso – PS</i>						
Settings (PS/PEEP), cmH ₂ O	10/6	10/6	10/6	10/6	10/6	10/6
$P_{ET}CO_2$, mmHg	38 (0)	93 (1)*	64 (1)*	99 (0)*, ^a	53 (1)*	89 (1)*
VT _E , mL	432 (2)	379 (1)*	413 (2)	383 (2)*	449 (2)	394 (1)
<i>Iso – $P_{ET}CO_2$</i>						
Settings (PS/PEEP), cmH ₂ O	10/6	19/6*	14/6*	22/6*	13/6*	18/6*
$P_{ET}CO_2$, mmHg	38 (0)	38 (0)	38 (1)	37 (0)	38 (0)	39 (0)
VT _E , mL	432 (2)	574 (7)*	523 (1)*	648 (1)*	511 (2)*	576 (7)*

Iso-PS variables were recorded with PS set at 10 cmH₂O. Iso- $P_{ET}CO_2$ variables were recorded with $P_{ET}CO_2$ set at 38(1) mmHg.

Results were obtained with respiratory rate set at 25 breaths/min and V'CO₂ set at 180(5) mL. Other ventilatory settings remained unchanged for the various configurations evaluated.

Data are presented as mean (SD).

PS, pressure support; PEEP, positive end-expiratory pressure; $P_{ET}CO_2$, end-tidal CO₂ partial pressure; VT_E, expired tidal volume.

^a Upper limit of the capnograph's accuracy.

* Clinically relevant variation compared to reference (configuration A).

Table 2
Ventilatory Parameters Measured in the Condition of Stable Alveolar Ventilation According to the Different Configurations Evaluated.

Variables	Config. A	Config. B	Config. C	Config. D	Config. E	Config. F
IPAP _{aw} , cmH ₂ O	16.7 (0.0)	22.8 (0.3)*	19.8 (0.0)*	26.3 (0.0)*	19.0 (0.0)*	22.4 (0.3)*
PEEP _{aw} , cmH ₂ O	7.4 (0.1)	8.8 (0.0)*	8.0 (0.0)	9.5 (0.0)*	8.5 (0.2)*	9.6 (0.3)*
PIF, L/min	32 (1)	38 (1)*	36 (1)	43 (1)*	35 (1)	36 (1)
T _i , s	1.1 (0.0)	1.2 (0.0)	1.2 (0.0)	1.2 (0.0)	1.2 (0.0)	1.2 (0.0)

Results were obtained with respiratory rate set at 25 breaths/min, $P_{ET}CO_2$ set at 38(1) mmHg and V'CO₂ set at 180(5) mL.

Data are presented as mean (SD).

IPAP_{aw}, inspiratory positive airway pressure; PEEP_{aw}, airway positive end-expiratory pressure; PIF, peak inspiratory flow; T_i, inspiratory time.

* Clinically relevant variation compared to reference (configuration A).

Values reported were measured between the mannequin head and test lung.

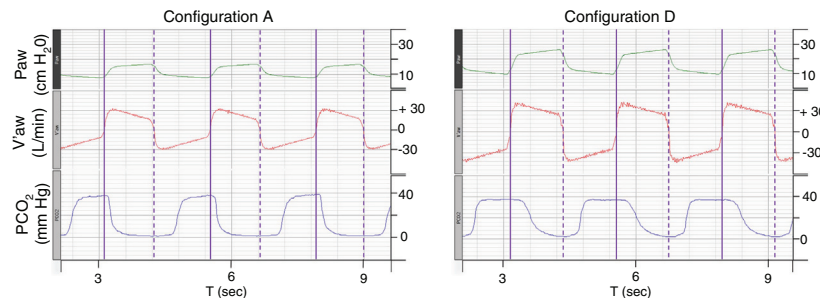


Fig. 2. Time course of P_{aw} , V_{aw} and PCO_2 for configurations A and D.

P_{aw} , airway pressure; V_{aw} , respiratory flow; PCO_2 , partial pressure of CO₂. Vertical purple lines: solid line, beginning of inspiration; dashed line, end of inspiration. The figure illustrates the need to increase pressure support and thus tidal volume to maintain isocapnia (38(1) mmHg). Note that the duration of PCO_2 decline during inspiration in configuration D is much longer than configuration A, suggesting higher volume of CO₂ rebreathed from additional instrumental dead space.

Compared to reference (config. A), circuit compliance was increased with all the configurations evaluated (see [supplementary Table 1](#)). Mean compliance ranged from 0.4 to 2.2 mL/cmH₂O with configurations A–F, respectively. At 0.5 L/s, the lowest (1.4 cmH₂O/L/s) and highest (3.3 cmH₂O/L/s) inspiratory resistances were encountered with configurations C and F, respectively. Configurations B, C and D resulted in substantially higher expiratory resistances than configurations A, E and F (see [supplementary Table 1](#)), with the lowest (2.2 cmH₂O/L/s) and highest (20.0 cmH₂O/L/s) values encountered with configurations E and D, respectively. [Supplementary Fig. 2](#) displays the pressure–flow relationship for each configuration during inspiration and expiration.

Discussion

In this study, we demonstrated that substantial adjustments in NIV settings are needed to maintain alveolar ventilation when modifications of circuit configuration are required to prevent NIV-related contaminations in the current context of COVID-19

pandemic. This is particularly relevant in patients chronically ventilated pursuing their therapy at home, or exhibiting acute-on-chronic exacerbation requiring hospital admission.^{7,10,14} Of note, even the change from configuration A–E which is often made when patient's condition requires switching to a life-support ventilator needed setting adjustments.

In contrast, this finding is less relevant in patients for whom NIV is initiated during an acute episode because treatment efficiency can be expected, in this context, to be carefully monitored and settings adapted whenever necessary. Moreover, in patients hospitalised for an acute lung injury related to coronavirus, the initiation of bilevel NIV is highly controversial.^{15–17} Most guidelines recommend NIV in patients with SARS-CoV-2 infection as a “default” option when oxygen therapy or constant positive airway pressure (CPAP) are not sufficient to improve patient's status, provided that appropriate personal protective equipment is available.^{10,14,18,19} Its indications in this context therefore remain restricted to situations in which access to invasive mechanical ventilation is limited, in patients not eligible to ICU admission, or in patients with

underlying respiratory disease or previously undergoing long-term NIV in which NIV cessation could worsen even more their condition and for whom the results of the present study apply as well.^{14,20}

Unexpectedly, we found discrepancies between values set on the ventilator and values measured between the mannequin head and the test lung even for baseline configuration (A) in which PEEP_{aw} was 1.4 cmH₂O above EPAP setting. Of note, as most ventilators do not control the pressure directly inside the mask, any additional material increasing resistances between the point of pressure measurement and the mask may affect the delivered pressure inside the mask during NIV. Advices from ventilators' manufacturers could be helpful in daily practice when unusual circuit configurations are considered in patients undergoing NIV.

In our experimental setup, the increased PEEP_{aw} could at least in part be explained by the elevated RR (25 bpm), which however is in line with clinical characteristics of severe patients and may promote dynamic hyperinflation (Fig. 2).²¹ This phenomenon was even more pronounced with other configurations (>3.5 cmH₂O with configurations D and F). From a theoretical point of view, increased expiratory resistances related to additional equipment (filters, tubing) might explain this observation. However, the highest PEEP_{aw} monitored for all configurations was encountered with configuration F which actually was one of the configurations providing the lowest expiratory resistance (Supplementary Fig. 2). Conversely, configuration D yielded similar PEEP_{aw} as configuration F, despite substantially higher expiratory resistances. It should be noted that for single with leak circuits (configurations A, B, C and D), expiratory resistances were measured with the circuit closed at ventilator's side, so that exhalation could only occur through the intentional leak. This may not accurately reflect clinical situations in which an important proportion of expired tidal volume may occur inside the circuit despite the presence of an intentional leak and contribute both to increasing CO₂ rebreathing and reducing expiratory resistance as previously demonstrated.²² Either way, a simple regression analysis showed a significant linear relationship between tidal volume and PEEP_{aw} ($R^2 = 0.76$ and $P = .014$) whereas no relationship was detected between expiratory resistance and PEEP_{aw}. This suggests that increased PEEP_{aw} observed in the condition of iso-P_{ET}CO₂ was most likely driven by the increase in VT (additional instrumental dead space) contributing, along with high respiratory rate, to hyperinflation of the model, rather than variations in circuit resistances.

Our study has several limitations.

First, in our experimental setup, driving pressure was generated by the device solely. Simulating patient's effort would have interestingly given the opportunity to evaluate the effects of circuit configurations with CPAP mode and to assess the variations in respiratory effort required to preserve alveolar ventilation in these different situations. Unfortunately, using one chamber of the Michigan test lung as a driving chamber to simulate patient's effort would have substantially reduced the end-expiratory lung volume of the model. With clinically relevant V'/CO₂, a parallel connection of the two chambers of the test lung was required to reach relevant P_{ET}CO₂. Another limitation to the evaluation of CPAP mode is that this study aimed to test all the circuits modifications proposed in the literature to prevent coronavirus contamination in subjects chronically ventilated, both with single and double limb circuits. Almost all adult patients treated with CPAP mode in the context of domiciliary usage are treated with devices with single with leak configuration only. The external validity of evaluating double limb circuit modifications (configurations E and F) in subjects undergoing long term CPAP would have been broadly questionable. Additionally, even though the use of CPAP mode has been widely described in COVID-19 patients,^{19,21} this ventilatory mode with constant pressure would not have allowed to determine the variations of driving pressure required to maintain isocapnia with

respect to the design of our bench and would also not have reflected the population of interest of our study. The results of the present study therefore do not apply to this mode. Finally, we therefore decided to use a controlled ventilation condition without patient effort in order to simplify the model, considering that modifications observed in this context were only attributable to the modifications of instrumental dead space and resistances that we wanted to evaluate. Consequently, we adjusted PS according to P_{ET}CO₂. In clinical practice it can be expected that patients, as long as their muscle capacities allows to do so, would increase their work of breathing – and obviously V'/CO₂ – in order to regulate PCO₂, as previously demonstrated with heat and moisture exchangers.²³ Instead of continuous monitoring of P_{ET}CO₂, adjusting PS according both to clinical signs of respiratory effort and to tidal volume would be less cumbersome and more appropriate in clinical routine.²⁴ Nevertheless, the aim of our bench study was limited to a simple comparison in tidal volumes keeping P_{ET}CO₂, respiratory rate and V'/CO₂ constant in order to consider that, in these conditions, the tidal volume differences would therefore represent the instrumental dead space differences according to Bohr's equation.²⁵

Second, we used a viral/bacterial filter with a large internal volume (120 mL). Even though this reference was found to be used by several other teams, such large internal volume deserves discussion.^{8,26} Along with the use of a non-vented mask, this resulted in an increase in VT_E required to reach isocapnia, i.e. in an increase of instrumental dead space, of 142(7) and 144(7) mL with configurations B and F, respectively, and in a PS (and in our situation driving pressure) nearly twice as big as with configuration A. Of note, because of fluid dynamics variations depending on circuit configuration (and particularly on the position of intentional leak), the internal volume of instrumental dead space in mL may not accurately reflect the absolute value of additional dynamic dead space as previously demonstrated by Saatci et al.²⁷ Nevertheless, as far as equipment is available, any reduction in instrumental dead space should be encouraged in order to reduce respiratory effort and prevent patient self-inflicted lung injury (P-SILI), especially in the context of acute lung injury related to COVID-19.²⁸

Conclusion

Large differences in additional VD exist between the recommended configurations. It is noteworthy that the configuration which induces the lowest increase of VD with single-limb circuit is configuration C, which proposes to laterally position the leak and filter with a T-piece placed immediately after the mask.⁸ This allows a bypass where the expiratory gas is blown in this lateral space, preventing from its reinhalation during the next insufflation. The need to re-evaluate treatment efficiency and settings is crucial whenever protective measures influencing NIV equipment are considered.

Authors' Contributions

All authors contributed substantially to study conception and design; MD, KL, BL and FL contributed to data acquisition; MD, GB, BL and FL contributed to data analysis and interpretation; MD, GB, ML, BL and FL drafted the manuscript. All authors revised the manuscript for important intellectual content, approved the final version, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding

None declared.

Conflict of Interests

MD is a former employee of ResMed SAS, which had no involvement in the current study. Other authors have no conflicts of interest to disclose.

Acknowledgements

The authors would like to thank Fatima Lebret and Adrian Morales Robles for their helpful contribution to Spanish translation.

Appendix A. Supplementary Data

Supplementary data associated with this article can be found, in the online version, at doi: [10.1016/j.arbres.2021.01.012](https://doi.org/10.1016/j.arbres.2021.01.012).

References

- Cantero C, Adler D, Pasquina P, Uldry C, Egger B, Prella M, et al. Long term noninvasive ventilation in the Geneva Lake area: indications, prevalence and modalities. *Chest*. 2020; [http://dx.doi.org/10.1016/j.chest.2020.02.064](https://doi.org/10.1016/j.chest.2020.02.064) [online ahead of print].
- Hui DS, Chow BK, Ng SS, Chu LCY, Hall SD, Gin T, et al. Exhaled air dispersion distances during noninvasive ventilation via different respirators face masks. *Chest*. 2009;136:998–1005, [http://dx.doi.org/10.1378/chest.09-0434](https://doi.org/10.1378/chest.09-0434).
- Guan L, Zhou L, Zhang J, Peng W, Chen R. More awareness is needed for severe acute respiratory syndrome coronavirus 2019 transmission through exhaled air during non-invasive respiratory support: experience from China. *Eur Respir J*. 2020;55, [http://dx.doi.org/10.1183/13993003.00352-2020](https://doi.org/10.1183/13993003.00352-2020).
- Arulkumaran N, Brealey D, Howell D, Singer M. Use of non-invasive ventilation for patients with COVID-19: a cause for concern? *Lancet Respir Med*. 2020; [http://dx.doi.org/10.1016/S2213-2600\(20\)30181-8](https://doi.org/10.1016/S2213-2600(20)30181-8).
- Baker JG, Sovani M. Case for continuing community NIV and CPAP during the COVID-19 epidemic. *Thorax*. 2020;75:368, [http://dx.doi.org/10.1136/thoraxjnl-2020-214913](https://doi.org/10.1136/thoraxjnl-2020-214913).
- Barker J, Oyefeso O, Koeckerling D, Mudalige NL, Pan D. COVID-19: community CPAP and NIV should be stopped unless medically necessary to support life. *Thorax*. 2020;75:367, [http://dx.doi.org/10.1136/thoraxjnl-2020-214890](https://doi.org/10.1136/thoraxjnl-2020-214890).
- Cao M, Katz S, Wolfe L. Care Recommendations for the Home-Based Ventilation Patient Undergoing Therapy for Known or Suspected Respiratory Viral Infection with COVID-19, CHEST Home-Based Mechanical Ventilation and Neuromuscular Disease NetWork, American College of Chest Physicians. Available from: <https://www.thoracic.org/professionals/clinical-resources/disease-related-resources/chest-care-recommendations-for-the-home-based-ventilation-patient-with-suspected-or-known-covid-19.pdf> [accessed 13.05.20].
- Gonzalez-Bermejo J, Maisonneuve J, Oranger M, Mendoza-Ruiz A. Appareillages respiratoires de domicile d'un malade suspect ou porteur de virus respiratoire. Available from: <https://splf.fr/wp-content/uploads/2020/04/LES-PROCEDURES-DU-GAVO2-ProtectionVirale2020-MAJ02avril2020.pdf> [accessed 13.05.20].
- Kryger M, Thomas R. Home PAP devices in COVID-19 infected patients. *J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med*. 2020; [http://dx.doi.org/10.5664/jcsm.8490](https://doi.org/10.5664/jcsm.8490) [online ahead of print].
- Cinesi Gómez C, Peñuelas Rodríguez Ó, Luján Torné M, Egea Santaolalla C, Masa Jiménez JF, García Fernández J, et al. Clinical consensus recommendations regarding non-invasive respiratory support in the adult patient with acute respiratory failure secondary to SARS-CoV-2 infection. *Arch Bronconeumol*. 2020; [http://dx.doi.org/10.1016/j.arbres.2020.03.005](https://doi.org/10.1016/j.arbres.2020.03.005).
- Respiratory Care Committee of Chinese Thoracic Society. Expert consensus on preventing nosocomial transmission during respiratory care for critically ill patients infected by 2019 novel coronavirus pneumonia. *Chin J Tuberc Respir Dis*. 2020;43:288–96, [http://dx.doi.org/10.3760/cma.j.cn112147-20200304-00239](https://doi.org/10.3760/cma.j.cn112147-20200304-00239).
- Rello J, Storti E, Belliato M, Serrano R. Clinical phenotypes of SARS-CoV-2: implications for clinicians and researchers. *Eur Respir J*. 2020; [http://dx.doi.org/10.1183/13993003.01028-2020](https://doi.org/10.1183/13993003.01028-2020).
- Lampotang S, Gravenstein N, Banner MJ, Jaeger MJ, Schultetus RR. A lung model of carbon dioxide concentrations with mechanical or spontaneous ventilation. *Crit Care Med*. 1986;14:1055–7, [http://dx.doi.org/10.1097/00003246-198612000-00013](https://doi.org/10.1097/00003246-198612000-00013).
- Rabec C, Gonzalez-Bermejo J. Respiratory Support Chronic Care Group AVO2 of the French Society of Respiratory Diseases SPLF, GAVO2 collaborators. Respiratory support in patients with COVID-19 (outside intensive care unit). A position paper of the Respiratory Support and Chronic Care Group of the French Society of Respiratory Diseases. *Respir Med Res*. 2020;78:100768, [http://dx.doi.org/10.1016/j.resmer.2020.100768](https://doi.org/10.1016/j.resmer.2020.100768).
- Namendys-Silva SA. Respiratory support for patients with COVID-19 infection. *Lancet Respir Med*. 2020;8:e18, [http://dx.doi.org/10.1016/S2213-2600\(20\)30110-7](https://doi.org/10.1016/S2213-2600(20)30110-7).
- James A, Verdonk F, Bougle A, Constantin J-M. Non-invasive ventilation for acute respiratory failure (in COVID-19 patients): the non-ending story? *Anaesth Crit Care Pain Med*. 2020; [http://dx.doi.org/10.1016/j.accpm.2020.08.004](https://doi.org/10.1016/j.accpm.2020.08.004).
- Karagiannidis C, Mostert C, Hentschker C, Voshaar T, Malzahn J, Schillinger G, et al. Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study. *Lancet Respir Med*. 2020; [http://dx.doi.org/10.1016/S2213-2600\(20\)30316-7](https://doi.org/10.1016/S2213-2600(20)30316-7).
- Italian Thoracic Society (AIPO – ITS) and Italian Respiratory Society (SIP/IRS). Managing the respiratory care of patients with COVID-19. Available from: <http://www.aiponet.it> [accessed 14.08.20].
- Nicholson TW, Talbot NP, Nickol A, Chadwick AJ, Lawton O. Respiratory failure and non-invasive respiratory support during the covid-19 pandemic: an update for re-deployed hospital doctors and primary care physicians. *BMJ*. 2020;369:m2446, [http://dx.doi.org/10.1136/bmj.m2446](https://doi.org/10.1136/bmj.m2446).
- Rochweg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J*. 2017;50, [http://dx.doi.org/10.1183/1399300302426-2016](https://doi.org/10.1183/1399300302426-2016).
- Haudebourg A-F, Perier F, Tuffet S, de Prost N, Razazi K, Mekontso Dessap A, et al. Respiratory mechanics of COVID-19 vs non-COVID-19 associated acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2020; [http://dx.doi.org/10.1164/rccm.202004-1226LE](https://doi.org/10.1164/rccm.202004-1226LE) [online ahead of print].
- Lofaso F, Brochard L, Touchard D, Hang T, Harf A, Isabey D. Evaluation of carbon dioxide rebreathing during pressure support ventilation with airway management system (BiPAP) devices. *Chest*. 1995;108:772–8, [http://dx.doi.org/10.1378/chest.108.3.772](https://doi.org/10.1378/chest.108.3.772).
- Lellouche F, Maggiore SM, Deye N, Taillé S, Pigeot J, Harf A, et al. Effect of the humidification device on the work of breathing during noninvasive ventilation. *Intensive Care Med*. 2002;28:1582–9, [http://dx.doi.org/10.1007/s00134-002-1518-9](https://doi.org/10.1007/s00134-002-1518-9).
- Fauroux B, Hart N, Luo YM, MacNeill S, Moxham J, Lofaso F, et al. Measurement of diaphragm loading during pressure support ventilation. *Intensive Care Med*. 2003;29:1960–6, [http://dx.doi.org/10.1007/s00134-003-1941-6](https://doi.org/10.1007/s00134-003-1941-6).
- Robertson HT. Dead space: the physiology of wasted ventilation. *Eur Respir J*. 2015;45:1704–16, [http://dx.doi.org/10.1183/09031936.00137614](https://doi.org/10.1183/09031936.00137614).
- Tonetti T, Zanella A, Pizzilli G, Irvin Babcock C, Venturi S, Nava S, et al. One ventilator for two patients: feasibility and considerations of a last resort solution in case of equipment shortage. *Thorax*. 2020;75:517–9, [http://dx.doi.org/10.1136/thoraxjnl-2020-214895](https://doi.org/10.1136/thoraxjnl-2020-214895).
- Saatci E, Miller DM, Stell IM, Lee KC, Moxham J. Dynamic dead space in face masks used with noninvasive ventilators: a lung model study. *Eur Respir J*. 2004;23:129–35, [http://dx.doi.org/10.1183/09031936.03.00039503](https://doi.org/10.1183/09031936.03.00039503).
- Brochard L, Slutsky A, Pesenti A. Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. *Am J Respir Crit Care Med*. 2016;195:438–42, [http://dx.doi.org/10.1164/rccm.201605-1081CP](https://doi.org/10.1164/rccm.201605-1081CP).