# Page Proof Instructions and Queries

Please respond to and approve your proof through the "Edit" tab, using this PDF to review figure and table formatting and placement. This PDF can also be downloaded for your records. We strongly encourage you to provide any edits through the "Edit" tab, should you wish to provide corrections via PDF, please see the instructions below and email this PDF to your Production Editor.

**Journal Title:** Clinical Nursing Research

**Article Number:** 1112745

Thank you for choosing to publish with us. This is your final opportunity to ensure your article will be accurate at publication. Please review your proof carefully and respond to the queries using the circled tools in the image below, which are available in Adobe Reader DC* by clicking **Tools** from the top menu, then clicking **Comment**.

Please use *only* the tools circled in the image, as edits via other tools/methods can be lost during file conversion. For comments, questions, or formatting requests, please use T. Please do *not* use comment bubbles/sticky notes.


*If you do not see these tools, please ensure you have opened this file with **Adobe Reader DC**, available for free at get.adobe.com/reader or by going to Help > Check for Updates within other versions of Reader. For more detailed instructions, please see us.sagepub.com/ReaderXProofs.

| No. | Query |
|---|---|
| GQ1 | Please confirm that all author information, including names, affiliations, sequence, and contact details, is correct. |
| GQ2 | Please confirm that the Funding and Conflict of Interest statements are accurate. |
| GQ3 | Please note that we cannot add/amend ORCID iDs for any article at the proof stage. Following ORCID's guidelines, the publisher can include only ORCID iDs that the authors have specifically validated for each manuscript prior to official acceptance for publication. |
| 1 | Please check that the article title is correct as set. |
| 2 | Please check that the affiliations and the corresponding author details are correct as set. |
| 3 | Please provide page number for reference "Ottestad et al. 2020" |
| 4 | Author biographies statement missing. please check and provide the same since it is mandatory. |

Clinical Nursing Research
1–7
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/10547738221112745
journals.sagepub.com/home/cnr
SAGE

# Safety Assessment of Low-Flow Oxygenation Device: Quasi-Experimental Study[AQ: 1]

**Francisca Sánchez-Ayllón, RN, PhD[1], Oscar Segura-Alba, RN[2], Manacés dos Santos-Bezerril, RN, MD[3], Andrés Rojo-Rojo, RN, PhD[1], Rafael Melendreras-Ruiz, PhD[1], Mireia Alcázar-Artero, MD[2], Maria José Pujalte-Jesús, RN, PhD[1], and José Luis Díaz-Agea, RN, PhD[1][GQ: 1]**

**Abstract**

The objective of this study was to verify the feasibility of using an Oxygenation Device with Reservoir and Positive End-Expiratory Pressure (ODRPEEP; DORPEEP in Spanish) and to analyze its safety with respect to mask leaks and carbon dioxide retention measured upon expiration. A quasi-experimental pilot study was designed with eight volunteers in two experiments to determine the degree of leaks from the device, according to the observation of water vapor particle diffusion, on the one hand, and of thermal images on the other. The results from this study showed that the mask from the DORPEEP© device at is tightest fit provided an adequate seal, although not fully airtight. In the thermal images and in the experiment with water vapor in our study, dispersions were mainly observed in the lower area in individuals with a beard. The DORPEEP© device was shown to have only slight leaks.

**Keywords**

oxygenation device, positive end-expiratory pressure, mask leaks, feasibility, safety

## Introduction

Acute Respiratory Failure (ARF) is a severe acute disease that is commonly found as a result of heart or respiratory diseases which lead to respiratory system failure for a few minutes to hours, in either or both gas exchange functions (oxygenation and carbon dioxide elimination; Braune et al., 2016). The common causes of ARF include heart failure, pneumonia, Chronic Obstructive Pulmonary Disease (COPD), pulmonary embolism and asthma, among others (Gattinoni et al., 2020). Non-invasive ventilation (NIV) has shown to be efficient in the treatment of various types of ARF (Bonnesen et al., 2021), leading to a significant improvement in vital signs, such as respiratory frequency, heart rate, blood pressure, and peripheral arterial or capillary oxygen saturation (Nielsen et al., 2016)

Continuous positive pressure in the airways is useful in Acute Hypoxemic Respiratory Failure (AHRF), as it recruits the collapsed alveoli and improves ventilation-perfusion compatibility and, therefore, oxygenation (Gattinoni et al., 2020). Given the characteristics of pneumonia caused by SARS-CoV-2 and Acute Respiratory Distress Syndrome (ARDS), it is reasonable to assume that COVID-19 patients would benefit from the therapy with Continuous Positive Airway Pressure (CPAP; Dobler et al., 2020; Gattinoni et al., 2020).

Even so, not enough evidence is available to determine if CPAP is associated with a greater risk of virus transmission as compared to the standard administration of oxygen through a nasal cannula or different types of masks, especially when relatively high oxygen flows are used (Dobler et al., 2020).

As an alternative to a CPAP system, some reports have suggested connecting a PEEP valve to a Bag-Valve-Mask (BVM) system (Mæhlen et al., 2021). However, a BVM with a PEEP valve cannot generate continuous positive pressure in the airways; it only applies positive pressure in the airways during expiration.

[1]Catholic University of Murcia, Spain[AQ: 2]
[2]Region of Murcia, Spain
[3]Federal University of Rio Grande do Norte, Natal, Brazil

**Corresponding Author:**
Manacés dos Santos-Bezerril, Federal University of Rio Grande do Norte, Campus Universitário—Lagoa Nova, Natal 59078-970, Brazil.
Email: manacesbezerril@hotmail.com

In this study, an Oxygenation Device with Reservoir and Positive End-Expiratory Pressure/PEEP valve (the Spanish acronym is DORPEEP©) was used for being a low-flow system (Supplemental Material I) for patients with spontaneous respiration, without it being equivalent to a CPAP method (Segura Alba et al., 2020). The idea is based on other certified CPAP devices during spontaneous respiration, Boussignac©, Pulmodyne©, and another one used for ventilation during application of anesthesia, Mapleson©, which is perhaps the most similar to DORPEEP©.

This is a low-flow device (up to 15 L/minutes) that allows using high oxygen concentrations by employing a reservoir bag with a one-way valve, with the addition of a passive braking system in the exhalation part (PEEP valve), along with a filter for the virus and bacteria (filtering efficiency >99.99%), and a mouth-nose mask without openings that is fitted with a strap. It is assumed that the device can avoid further dispersion of particles for the patients to recapture oxygen from such reservoir through their stable respiratory pattern.

The objective of this study was to verify the feasibility of using a hybrid ventilation system, the Oxygenation Device with Reservoir and Positive End-Expiratory Pressure (DORPEEP©) and to analyze its safety with respect to mask leaks and carbon dioxide retention measured upon expiration.

## Methods

### Design

A quasi-experimental study was designed following the instructions of Des Jarlais et al. (2004) in the checklist items for non-canonized studies, the Transparent Reporting of Nonrandomized Designs (TREND), and presenting two experiments to determine the level of device leakage following a measurement based on the observation of diffusion of water vapor particles, on the one hand, and using thermal images on the other.

### Participants

For the study, eight volunteers (four men and four women) with accessibility criteria were recruited, who belonged to the staff working at the university (convenience sampling). The criteria for their selection were that they were middle-aged people and that they had no medical history or illnesses. Once the procedures were explained to them (measurement of leaks by observation of dispersion with water vapor and measurement of dispersion/leakage of the mask with thermal images), they had to consent in writing by means of a form indicating their informed consent and authorizing recording of their image and dissemination of this recording for scientific purposes.

### Procedures

*Mask leak detection using steam.* The first experiment consisted of asking two volunteers (a short-haired bearded man and a woman who were users of a "vaping" device) to wear the mask, connected to a compressor with compressed air (not oxygen) at a flow of 15 L/minute for 2 minutes, in order to get used to the device. After a 2-minute break, they were asked to take a deep breath from their vaping devices and the mask was fitted to their faces. Subsequently, they were asked to exhale and breathe normally for 1 minute. This was repeated five times for each participant (the volunteer was first recorded exhaling without a mask, and the subsequent times, with different mask fit levels). On the first occasion, the mask was fitted using the least force, and in the last, with the highest force possible, without causing harms to the participants.

At first, we considered the possibility of using other data collection techniques such as gas detector cameras ($CO_2$) to detect leaks instead of using "vaping." The problem was the high cost of such devices. Before considering observation of water vapor by "vaping," tests were carried out with black light and adding pigmentation (Fluorescein) to the device connected to a nebulizer in a patient simulator, due to the high resolution and contrast photographic process for leak detection in healthy volunteers, as it is possible to see the color distinction and better visualize the air leak escape.

A black curtain suspended from a cyclorama was used for the experiment and, at the same time, the participants were asked to wear dark clothes. To illuminate the scene, cold-temperature (3,200 K) spotlights were used (Fresnel and Fluorlight, 1 kW and 300 W, respectively). To capture the images, a high-resolution video camera and a high-resolution photographic camera were used, placed on tripods; more specifically: Sony EX1, Full HD (1,920 × 1,080 pixels/image), and MILC Sony Alpha a6000 with a fixed 35 mm lens and F-stop of 1.8, in burst mode (11 shots/second), at a resolution of 24.3 MP. Figure 1 shows the sequence of images collected from both volunteers.

For the analysis of these images, an observation-based tool was used (Supplemental Material II) and built by consensus among the research team members after several deliberations in meetings and with a Content Validity Index of 1 (CVI = 1). The observers (10 healthcare professionals trained by the research team for this purpose) received a template with the high-resolution images and the assessment tool with instructions (Supplemental Material II). In this template, each image was evaluated on a scoring scale from 1 to 10 (1 = maximum dispersion, minimum tightness; 10 = minimum dispersion, maximum tightness).

*Mask leak detection with thermal imaging.* For the thermal imaging experiment, all eight participants (including those two that participated in the water vapor dispersion test) were

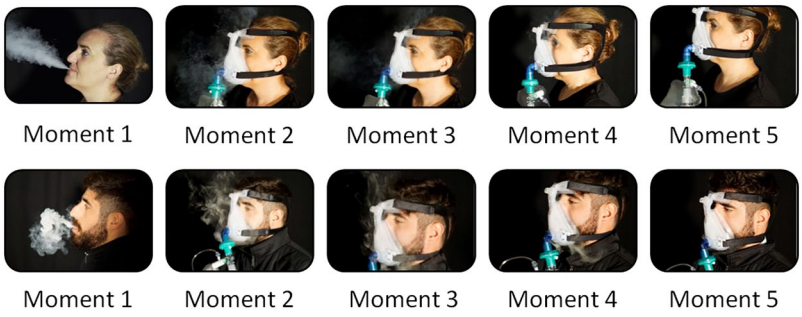


**Figure 1.** Images of the water vapor leak experiment with mask fit levels from least tight (Moment 1) to most tight (Moment 5).

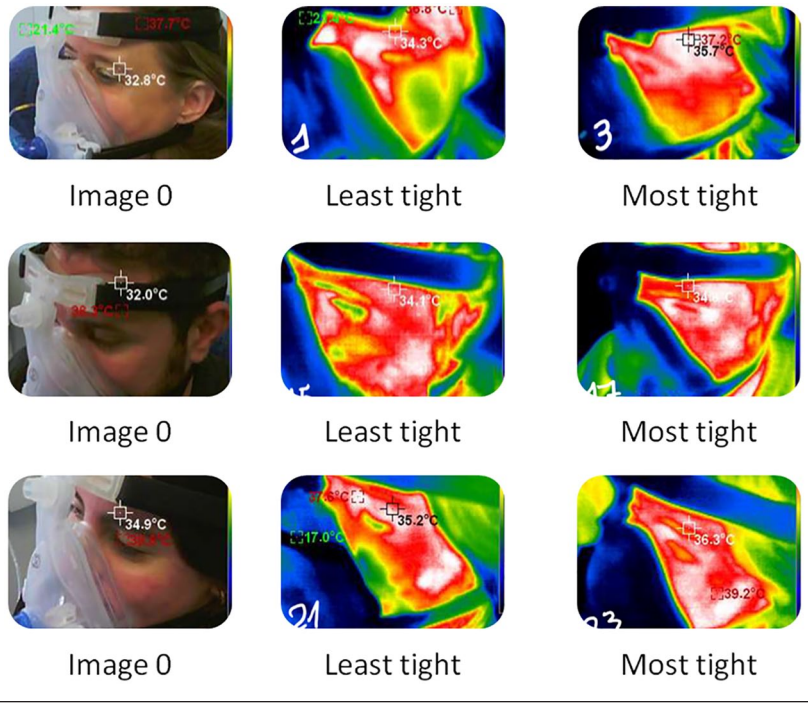


**Figure 2.** Thermal images with different levels of mask fit to the face.

asked to wear the mask while air (15 l pm) at a temperature of 8°C to 9°C was supplied. Previously, it had been possible to cool the air down through a circuit of mask connectors immersed in ice water with salt (at −2°C). In addition, measurements of physiological variables were made to the eight volunteers before and after wearing the device for 10 minutes.

The images (Figure 2) were taken at different levels of mask fit to the subjects' face. Each volunteer received pressurized cold air (8°C–9°C) through the device for 10 minutes. Ambient temperature was 27°C to 28°C during the experiment to obtain a good difference in temperature, which was detected by means of the thermal camera used to take images of the different volunteers and with different mask fits. The thermal camera used was a TC-33N model from PCE instruments, with a wavelength between 8 and 14 µm, resolution of 220 × 160 pixels and precision of ±2%, in a temperature range between −20°C and 300°C, and a sensitivity of less than 0.1°C.

For the analysis of the images, the same procedure as in the previous experiment (air vapor leak) was used with the same 10 observers. They received the template with the high-resolution images (a total of 26) and the assessment tool with instructions (Supplemental Material II). The observers were asked to identify leaks based on the color of the skin around the mask. If they saw leaks around the mask, these appeared as a cold tone (yellowish, greenish, and bluish), and a lower temperature as compared to the face would also be observed

(the face tends to be shown as reddish colors). A total of 26 images were evaluated.

*Carbon dioxide retention analysis.* To evaluate the changes in some of the physiological parameters, the following variables were measured in all eight volunteers at rest, as well as before and after wearing the mask for 10 minutes with an oxygen flow of 15 L/minute: heart rate, respiratory frequency, oxygen saturation, and $CO_2$ levels measured with a calibrated capnography (the sidestream capnography measurement technology was used, Microstream® variant). The probe used was the FilterLine $CO_2$ system, which drives a sample of the gases exhaled by the patient directly into the monitor to determine $CO_2$ concentration. Two monitors were employed which contained this technology in their capnography module, Philips MRX®, and LIFEPAK 15®.

### Data Analysis

To analyze the data, the following descriptive statistics were calculated: mean, standard deviation, and standard error for the quantitative variables, as well as frequencies and percentages for the categorical ones. The Student's *t*-test was used to assess statistical significance. To estimate reliability of the evaluation forms (and analyze agreement between the scores provided for the amount of dispersion or observed leak), the inter-observer agreement test was applied through calculation of the Intraclass Correlation Coefficient (ICC; Fleiss et al., 2013).

The ICC was interpreted as the variability percentage of the score that was only dependent on variability of the subjects evaluated. To interpret the ICC, the following classification was used: ICC > .90 indicated very good agreement, ICC [.71–.90] meant good agreement, ICC [.51–.70] represented moderate agreement, ICC [.31–.50] stood for mediocre agreement, and ICC < .31 indicated bad or very bad agreement. Statistical significance was set at $p < .05$. A sample simulation for 998 samples with bias corrected and accelerated (BCa) intervals was performed. Data processing and analysis were conducted through the creation of a database in the IBM SPSS® v.22 for Windows statistical package.

### Ethical Considerations

During the research process, all the institutional and governmental regulations applicable to the ethical use of human volunteers were followed. This study complied with the requirements set forth in the Declaration of Helsinki and was approved by the Ethics Committee. All the participants were informed regarding their participation and signed an informed consent form, which also authorized recording their image and dissemination of this recording for scientific purposes.

**Table 1.** Scores Corresponding to the Evaluation of the Images Regarding Mask Leakage at Maximum Fit.

| Images | *M* | *SD* |
|---|---|---|
| Water vapor #5 | 9.10 | 2.85 |
| Water vapor #10 | 8.50 | 2.72 |
| Thermal camera #3 | 7.00 | 2.11 |
| Thermal camera #7 | 7.60 | 2.67 |
| Thermal camera #10 | 5.90 | 2.85 |
| Thermal camera #14 | 6.30 | 3.13 |
| Thermal camera #17 | 7.90 | 2.18 |
| Thermal camera #20 | 6.70 | 3.09 |
| Thermal camera #23 | 8.30 | 2.21 |
| Thermal camera #26 | 8.20 | 2.70 |

**Table 2.** Scores Between the Masks' Minimum and Maximum Fit.

| Images | *t* | 95% CI | *p*-Value* |
|---|---|---|---|
| Water vapor #1–5 | 9.00 | 6.06–10.14 | .001 |
| Water vapor #6–10 | 8.16 | 5.28–09.32 | .001 |
| Thermal camera #1–3 | 3.62 | 0.98–04.22 | .006 |
| Thermal camera #4–7 | 1.96 | 0.39–05.39 | .082 |
| Thermal camera #8–10 | 1.47 | 0.70–03.30 | .175 |
| Thermal camera #11–14 | 0.15 | 2.89–03.29 | .890 |
| Thermal camera #15–17 | 2.06 | 0.15–02.06 | .070 |
| Thermal camera #18–20 | 2.35 | 0.09–05.51 | .043 |
| Thermal camera #21–23 | 5.22 | 5.45–02.16 | .001 |
| Thermal camera #22–26 | 3.92 | 1.56–05.83 | .004 |

*p-Value with simulation of a sampling of 998 samples with bias corrected and accelerated (BCa).

## Results

Regarding the participants' demographic variables, mean age of 45 years old ($SD = 11.15$), height of 169.38 cm ($SD = 9.91$), weight of 72.21 kg ($SD = 11.26$), and Body Mass Index (BMI) of 25.06 kg/cm$^2$ ($SD = 2.22$) were found.

The ICC obtained for the evaluation of leaks with water vapor was ICC = .974 [$p < .001$] (very good), with a Cronbach's alpha of .984. The ICC obtained for the evaluation of leaks with the thermal imaging camera in the case of maximum fit was ICC = .916 [$p < .001$] (very good), with a Cronbach's alpha of .929. Table 1 presents the mean scores assigned by the observers in terms of mask leakage for the best-fit images.

Statistically significant differences in leakage ($p < .05$) were found for images from participants who did not have a beard. Table 2 presents the results referring to the score assigned by the observers between the minimum and maximum fit of the masks.

Regarding the participants' physiological variables (Table 3) at the beginning and at the end of the experiment,

**Table 3.** Physiological Variables of the Participants Before and After the Experiments.

| Variables | Initial mean (*SD*) | Final mean (*SD*) | *t* | 95% CI | *p*-Value* |
|---|---|---|---|---|---|
| Respiratory frequency | 15.13 (4.94) | 11.38 (2.93) | 2.93 | 0.14–1.89 | .006 |
| Capnography | 37,75 (4.53) | 37.75 (6.84) | −0.38 | −0.78–0.61 | .824 |
| Heart rate | 71.38 (6.91) | 70.88 (6.53) | 0.186 | −0.66–0.63 | .857 |
| $SpO_2$ | 98.75 (11.17) | 100 (0.00) | −3.035 | −1.07–(−1.92) | .080 |

**p*-Value with simulation of a sampling of 998 samples with bias corrected and accelerated (BCa).

the only one that obtained a statistically significant difference was respiratory frequency.

## Discussion

The results of this study showed that the mask from the DORPEEP© device at is tightest fit provided an adequate seal, although not fully airtight. Nonetheless, Faraone et al. (2021) indicated that the orofacial devices used in non-invasive mechanical ventilation therapies under pressure (CPAP or double pressure levels), or non-mechanical devices such as Boussignac or Pulmodyne CPAP, among others, do not ensure airtightness of the system in any of the cases. These devices were argued against for patients with a high risk of infection, as they represented a risk for the workers' health (Takazono et al., 2021). Hui et al. (2009) measured dispersion of the particles in a piece of equipment that used two different pressure levels with an orofacial mask, finding that it was 0.5 to 0.95 m around the patient through the orifice where the leak took place, and the point where the mask meets the nasal bridge.

About the level of dispersion, Gaeckle et al. (2020) indicate that the aerosols generated by oxygen therapy devices (conventional masks, HFNC) or positive pressure mechanical equipment did not increase significantly. NIMV equipment, with a mouth-nose interface, generates more aerosols than the rest of the devices tested; however, the dispersion is limited. Situations such as coughing, speaking, and the mask fit level are the most important predictors to avoid particle dispersion in NIMV. Using filters in the NIPPV expiratory circuit in COVID-19 patients seems to be a safe treatment option (always with proper use of Personal Protective Equipment; Bonnesen et al., 2021; Gaeckle et al., 2020; Gattinoni et al., 2020; Segura Alba et al., 2020).

As for the leaks found in oronasal masks, different causes that were dependent on the patient were found (underbite, lack of teeth, presence of a beard, deviated nasal septum, etc.) and others that were dependent on the interface materials themselves (such as an inadequate mask size or bad fit). In the thermal images and in the experiment with water vapor in our study, dispersions were mainly observed in the lower area (mandibular) in individuals with a beard. With the mask fitted at its maximum, the leaks were scarce, as the device uses low flow, and the mask is not subjected to high pressures.

DORPEEP© ensured an acceptable level of air tightness, but at the expense of a high pressure level in the masks and the holding straps (although this pressure was not measured). However, Bonnesen et al. (2021) suggests that it should be taken into account that excessive tightness could imply the emergence of skin lesions associated with the area of friction between the face and the interface. Fit pressure of the face mask should oscillate between 2 and 3 mmHg above the pressure administered by the MV device (Custodero et al., 2021; Gattinoni et al., 2020; Segura Alba et al., 2020).

Above the pressure of 3 mmHg, and in shearing conditions, the risk of pressure ulcers multiply (Dobler et al., 2020; Gattinoni et al., 2020; Takazono et al., 2021). In any case, as an added complication, facial interfaces do not have systems in place to measure this pressure; therefore, the masks are fitted intuitively, with excessive pressure observed, increasing discomfort. The discomfort level associated with the use of these masks is notable (up to 20% of the users perceive discomfort, claustrophobia, mouth dryness, etc.; Bonnesen et al., 2021; Custodero et al., 2021). This discomfort is the reason behind some of the leaks observed in these devices (Gattinoni et al., 2020; Segura Alba et al., 2020; Takazono et al., 2021).

In addition, a deficient interface-mask fit can increase unintentional leakage and, thus, patient-ventilator asynchrony, increasing autocycling, and inefficient respiratory efforts (Dobler et al., 2020). Another aspect to consider is the time that the masks will remain on the face skin (if this is over 2 hours of pressure without protection measures, the patient's skin will become irritated, especially in the nose bridge area; Ottestad et al., 2020).

In view of all the above, the DORPEEP© device ensures minimum dispersion level, with the inconveniences typical of this type of masks. We recommend that it is firmly fixed but not excessively tight, and that the pressure points on the skin are evaluated before reaching 2 hours of use, as well as to place padding with protection bandages if necessary.

We believe that this device is perfectly adapted for its use in out-of-hospital settings, as it had the appropriate pieces of equipment and physical means to protect the skin, and care can be provided in a limited amount of time (from the emergency site to the hospital).

The vital signs analyzed did not deteriorate after the 10 minutes of mask use by the volunteers, and no $CO_2$

retention was observed. This provides evidence on its safe use with all the participants, as it ensures adequate air flow, which avoids retention. The interfaces for Non-Invasive Ventilation (NIV) and the ventilator connections represent an additional dead space which can increase the possibilities of $CO_2$ re-inhalation in proportion to the dead space volume (Gaeckle et al., 2020; Ottestad et al., 2020).

## Limitations

The main limitation of this study is the small sample used for the experiments. As this is a preliminary pilot study, we believe that it could serve as a basis for other studies which could confirm the results. Internal validity of the study could be improved through the use of a control group and randomization when selecting the sample, allocating the participants to the experimental conditions. External validity of the study (generalization of the results) could be improved if the research was conducted with individuals with respiratory failure, which would imply having the pertinent authorizations and permits to conduct an experimental study that complies with all the ethical guidelines.

Another limitation of this study is the failure to measure the degree of pressure exerted to ensure maximum air tightness and minimum leaks, which would imply conducting more studies in this regard. The measurement recorded by capnography in this study did not correspond to the arterial $PCO_2$ measurement when suffering from breathing alterations, as these are two different $CO_2$ measuring methods that are not equivalent in the case of presence of a breathing, metabolic, or perfusion alteration. Perhaps in future studies with real patients, the gas results found in arterial blood could be recorded.

## Contributions

In all, the current study presents significant contributions to the care activities for patients with respiratory difficulties in health services, as it allows for an initial proposal of a simple, low-cost device with possible positive results in the short- and/or long-term.

We believe that the DORPEEP© device is a safe piece of equipment for health workers who perform their duties in a closed environment, such as the back of an ambulance, as it is easy to use due to the simplicity of its parts, which are connected with recognizable materials, and which allows for its transport anywhere due to its low weight and dimensions. DORPEEP© could be useful in patients with spontaneous respiration who have difficulty breathing, especially among COVID-19 patients with or without pneumonia. It could also be employed as a preventive measure until mechanical ventilation becomes available. In addition, it might expand the possibilities of the devices for these patients and reduce the expenses related to the equipment intended for this type of treatment.

## Conclusions

The DORPEEP© device was shown to have only slight leaks in this preliminary study with healthy volunteers. The volunteers with beards showed greater gas dispersion, as evidenced from the observation of water vapor leaks and the thermal images. Changes were not observed in the healthy volunteers' vital signs measured before and after using the device. For being a pilot study, its results cannot be generalized or extrapolated to individuals with respiratory failure, without first conducting an experimental study with a large enough number of participants before it can be recommended for the clinical practice.

### Author Contributions

It is worth noting that the authors FSA, OSA, MSB, ARR, RMR, MAA, MJPJ, and JLDA presented substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; on drafting the work or revising it critically for important intellectual content; in final approval of the version to be published; and agreement 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.

### Declaration of Conflicting Interests[GQ: 2]

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work has been funded by a research project [PMAFI-COVID19/16] of the Catholic University of Murcia-UCAM (Spain), with an amount of €1,639.16

### ORCID iDs[GQ: 3]

Oscar Segura-Alba https://orcid.org/0000-0001-9044-3259
Manacés dos Santos-Bezerril https://orcid.org/0000-0002-9003-2334
Rafael Melendreras-Ruiz https://orcid.org/0000-0002-5404-6245
José Luis Díaz-Agea https://orcid.org/0000-0002-0818-0224

### Supplemental Material

Supplemental material for this article is available online.

### References

Bonnesen, B., Jensen, J. -U. S., Jeschke, K. N., Mathioudakis, A. G., Corlateanu, A., Hansen, E. F., Weinreich, U. M., Hilberg, O., & Sivapalan, P. (2021). Management of COVID-19-associated acute respiratory failure with alternatives to invasive mechanical ventilation: High-flow oxygen, continuous positive airway pressure, and noninvasive ventilation. *Diagnostics*, *11*(12), 2259. https://doi.org/10.3390/diagnostics11122259

Braune, S., Sieweke, A., Brettner, F., Staudinger, T., Joannidis, M., Verbrugge, S., Frings, D., Nierhaus, A., Wegscheider, K., & Kluge, S. (2016). The feasibility and safety of extracorporeal carbon dioxide removal to avoid intubation in patients with COPD unresponsive to noninvasive ventilation for acute hypercapnic respiratory failure (ECLAIR study): Multicentre case-control study. *Intensive Care Medicine*, *42*(9), 1437–1444. https://doi.org/10.1007/s00134-016-4452-y

Custodero, C., Gandolfo, F., Cell, A., Cammalleri, L. A., Custureri, R., Dini, S., Femi, R., Garaboldi, S., Indiano, I., Musacchio, C., Podestà, S., Tricerri, F., Pasa, A., Sabbà, C., & Pilotto, A. (2021). Multidimensional prognostic index (MPI) predicts non-invasive ventilation failure in older adults with acute respiratory failure. *Archives of Gerontology and Geriatrics*, *94*, 104327. https://doi.org/10.1016/j.archger.2020.104327

Des Jarlais, D. C., Lyles, C., & Crepaz, N.; TREND Group. (2004). Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: The TREND statement. *American Journal of Public Health*, *94*(3), 361–366. https://doi.org/10.2105/AJPH.94.3.361

Dobler, C. C., Murad, M. H., & Wilson, M. E. (2020). Noninvasive positive pressure ventilation in patients with COVID-19. *Mayo Clinic proceedings*, *95*(12), 2594–2601. https://doi.org/10.1016/j.mayocp.2020.10.001

Faraone, A., Beltrame, C., Crociani, A., Carrai, P., Lovicu, E., Filetti, S., Sbaragli, S., Alessi, C., Smith, M. C., Angotti, C., & Fortini, A. (2021). Effectiveness and safety of noninvasive positive pressure ventilation in the treatment of COVID-19-associated acute hypoxemic respiratory failure: A single center, non-ICU setting experience. *Internal and emergency medicine*, *16*, 1183–1190. https://doi.org/10.1007/s11739-020-02562-2

Fleiss, J. L., Levin, B., & Paik, M. C. (2013). *Statistical methods for rates and proportions*. John Wiley & Sons.

Gaeckle, N. T., Lee, J., Park, Y., Kreykes, G., Evans, M. D., & Hogan, C. J. Jr. (2020). Aerosol generation from the respiratory tract with various modes of oxygen delivery. *American Journal of Respiratory and Critical Care Medicine*, *202*(8), 1115–1124. https://doi.org/10.1164/rccm.202006-2309OC

Gattinoni, L., Coppola, S., Cressoni, M., Busana, M., Rossi, S., & Chiumello, D. (2020). COVID-19 does not lead to a "Typical" acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine*, *201*(10), 1299–1300. https://doi.org/10.1164/rccm.202003-0817LE

Hui, D. S., Chow, B. K., Ng, S. S., Chu, L., Hall, S. D., Gin, T., Sung, J., & Chan, M. (2009). Exhaled air dispersion distances during noninvasive ventilation via different Respironics face masks. *Chest*, *136*(4), 998–1005. https://doi.org/10.1378/chest.09-0434

Mæhlen, J. O., Mikalsen, R., Heimdal, H. J., Rehn, M., Hagemo, J. S., & Ottestad, W. (2021). Pre-hospital critical care management of severe hypoxemia in victims of Covid-19: A case series. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*, *29*, 16. https://doi.org/10.1186/s13049-021-00831-3

Nielsen, V. M., Madsen, J., Aasen, A., Toft-Petersen, A. P., Lübcke, K., Rasmussen, B. S., & Christensen, E. F. (2016). Prehospital treatment with continuous positive airway pressure in patients with acute respiratory failure: A regional observational study. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*, *24*(1), 121. https://doi.org/10.1186/s13049-016-0315-3

Ottestad, W., Seim, M., & Mæhlen, J. O. (2020). COVID-19 with silent hypoxemia. *Tidsskr Nor Laegeforen*, *140*(7). https://doi.org/10.4045/tidsskr.20.0299 **[AQ: 3]**

Segura Alba, O., Nieto Fernández-Pacheco, A., & Pardo Ríos, M. (2020). Oxygenation device with reservoir and PEEP (ODRPEEP) in patients with acute respiratory distress due to COVID-19. Dispositivo de oxigenación con reservorio y PEEP (DORPEEP) en pacientes con dificultad respiratoria aguda por COVID-19. *Medicina clinica*, *155*(3), 133–134. https://doi.org/10.1016/j.medcli.2020.04.010

Takazono, T., Yamamoto, K., Okamoto, R., Tashiro, M., Morimoto, S., Hosogaya, N., Miyazaki, T., Yanagihara, K., Izumikawa, K., & Mukae, H. (2021). Effects of surgical masks on droplet and aerosol dispersion under various oxygen delivery modalities. *Critical Care*, *25*, 89. https://doi.org/10.1186/s13054-021-03512-w

## Author Biographies

**[AQ: 4]**