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ORIGINAL RESEARCH

A new portable and ready-to-use device for out-of-hospital non-invasive treatment of acute respiratory failure: preclinical validation

Eleonora Salurso[1,†], Federica Ciceri Negri[1,†], Giacomo Monti[2,3], Tommaso Scquizzato[2,3], Glauco Bordoni[4], Luca Cabrini[5], Katia Donadello[6,7], Giuseppe Santarpino[8,9,10], Gianfranco Beniamino Fiore[1], Alberto Redaelli[1], Filippo Consolo[2,*], Giovanni Landoni[2,3]

[1]Department of Electronics, Information and Bioengineering, Politecnico Di Milano, 20133 Milan, Italy
[2]School of Medicine, Vita-salute San Raffaele University, 20132 Milan, Italy
[3]Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, 20132 Milan, Italy
[4]Elebor GB s.r.l., 20156 Milan, Italy
[5]Unit of General and Neurosurgical Intensive Care, Ospedale di Circolo, ASST Sette Laghi, 21100 Varese, Italy
[6]Anaesthesia and Intensive Care B Unit, AOUI-University Hospital Integrated Trust of Verona, 37126 Verona, Italy
[7]Department of Surgery, Dentistry, Gynecology and Pediatrics, University of Verona, 37134 Verona, Italy
[8]Department of Cardiac Surgery, Cittá di Lecce Hospital, GVM Care & Research, 73100 Lecce, Italy
[9]Department of Clinical and Experimental Medicine, Università degli Studi "Magna Graecia" di Catanzaro, 88100 Catanzaro, Italy
[10]Department of Cardiac Surgery, Paracelsus Medical University, 90419 Nürnberg, BY, Germany

***Correspondence**
consolo.filippo@unisr.it
(Filippo Consolo)

[†] These authors contributed equally.

Abstract

Background: Acute respiratory failure (ARF) remains a leading cause of emergency medical intervention and requires prompt management to prevent severe morbidity and mortality. Non-invasive ventilatory (NIV) support in the pre-hospital setting via Continuous Positive Airway Pressure (CPAP) can improve ARF outcomes. However, existing CPAP devices demand specialized technical expertise and require complex setup, thereby presenting usability barriers in emergency out-of-hospital scenarios. Aim of this study was to develop, and preclinically validate, a portable, ready-to-use CPAP device specifically designed for out-of-hospital emergency treatment of ARF. **Methods**: The device performance, efficacy and safety profile were evaluated using a high-fidelity lung simulator replicating various ARF conditions at different respiratory requirements. Positive End-Expiratory Pressure (PEEP) levels were monitored. Afterwards, usability was assessed by 15 operators of varying medical expertise, who applied the device on a manikin connected to the simulator. **Results**: In preclinical validation tests the device demonstrated reliable performance, consistently stabilizing PEEP around the target value of 5 cmH_2O across all simulated scenarios. In usability tests, 93% of operators successfully applied the device, achieving the target PEEP in the simulated manikin setting. The operators' feedback highlighted that the device provides respiratory support in a compact and user-friendly format and is of rapid and intuitive application with minimum effort. All operators expressed their willingness to use the device during real emergency situations. **Conclusions**: Our new CPAP device showed promise in preclinical simulation-based tests as a tool for improving pre-hospital emergency response to ARF, enabling timely, effective and safe respiratory support during critical early phases. Validation tests in humans are ongoing.

Keywords

Acute respiratory failure (ARF); Non-invasive ventilation (NIV); Continuous positive airway pressure (CPAP); Positive end-expiratory pressure (PEEP); Out-of-hospital; Emergency; Respiratory distress

1. Introduction

Acute respiratory failure (ARF) is a medical emergency that can rapidly lead to death if not promptly treated [1–3]. The worsening of ARF towards life-threatening conditions is indeed rapid and the delay in treatment is a cause of poor prognosis [1–3]. On the other hand, to date, the treatment of out-of-hospital ARF is often delayed till the arrival of the emergency team or patient's hospital admission. The first-line treatment of ARF consists in most cases in providing non-invasive respiratory support to increase blood oxygen levels and reduce respiratory fatigue. In particular, continuous positive airway pressure (CPAP) is a well-established, safe and effective therapy for ARF, which can reduce ARF progression, related complications and even mortality. Preventing airway collapse, facilitating alveoli recruitment thus promoting oxygenation, and reducing the respiratory effort are the main mechanisms of action [4].

Over the last few years, positive experiences on the use of CPAP by emergency medical services in the pre-hospital setting are accumulating [5–14]. Interestingly, Hensel *et al.* [13] suggested that pre-hospital CPAP should be administered

regardless of transport distances to the hospital, thus highlighting the clinical value of prompt pre-hospital respiratory support. A recent systematic review confirmed that early pre-hospital administration of CPAP therapy to ARF patients can prevent further deterioration and the need for invasive mechanical ventilation [15]. According to this growing body of evidence, in 2022 the American National Association of Emergency Medical Services Physicians (NAESMP) released a position statement that holds a strong recommendation for pre-hospital non-invasive ventilation (NIV) in patients with respiratory failure, including patients with chronic obstructive pulmonary disease (COPD), asthma, and pulmonary edema [16]. Safety of pre-hospital NIV applied by emergency medical technicians was also confirmed [16]. At present, unfortunately, the application of CPAP treatment in the pre-hospital setting remains limited by the lack of portable, user-friendly and "ready-to-use" devices that can be promptly deployed in emergency situations. Currently available CPAP systems are indeed designed for in-hospital use, or to treat sleep apnea at home, and features such as their size, the need for complex setting of ventilatory parameters, the need for electrical power supply or external oxygen source, as well as high costs, all represent important barriers for their routinary adoption in emergency pre-hospital settings.

In this paper, we describe the development and preclinical validation of a new portable, easy and ready-to-use CPAP device designed specifically for emergency pre-hospital treatment of ARF. The device owns indeed unique features—including small dimensions, no need for connection to external power or oxygen sources, intuitive switch-on and no need for settings to initiate the therapy—which might promote its prompt application in emergency out-of-hospital scenarios. Such a device might be applied by emergency medical services during patient transportation to the hospital or even placed in public and private areas and used by a lay bystander without any specific expertise while waiting for the ambulance to arrive. Our device could replicate, in the field of emergency ARF treatment, the use case model of automated external defibrillators (AEDs) in the pre-hospital management of cardiac arrest, by promoting widespread, decentralized delivery of early out-of-hospital emergency CPAP, thereby reducing treatment delays and improving ARF outcomes.

Our hypothesis is that the development of a new, intuitive and easy to use CPAP device could overcome limitations of currently available systems, enabling even individuals without specific technical skills or expertise in the treatment of respiratory failure to intervene promptly, thereby helping to bridge the gap between hospital-based care and early, pre-hospital treatment of ARF.

2. Methods

2.1 Design requirements

The design of the device was based on a combination of 5 main requirements strictly related to its intended use in out-of-hospital emergency situations, namely:

(i) Compact and lightweight design: an essential requisite to enhance easy transportation and/or placement in public areas and convenient deployment in emergency scenarios;

(ii) Standalone device: the device must function without reliance on external electrical or pneumatic source;

(iii) Intuitiveness and easiness of use: the device must enable immediate deployment also by an individual without specialized technical skills or medical expertise, with no need for setting configuration or parameters to be monitored and adjusted during its use;

(iv) Efficacy and safety: the device must deliver clinically relevant positive end-expiratory pressure (PEEP) to prevent airway collapse and ensure alveolar patency, together with avoiding the onset of potentially harmful pressure values;

(v) Affordability: low manufacturing costs are essential for broad accessibility and large-scale deployment of the device.

2.2 Description of the device

According to the described design requirements, we designed and developed a new highly compact CPAP system allowing one-handed operation and ensuring ergonomic usability for both right- and left-handed users. The device (Fig. 1) comprises the following components and features:

(i) External enclosure: it features ad-hoc indentations for an ergonomic grip, ensuring a comfortable and secure hold during the device application (Fig. 1A);

(ii) Power control: it relies on a single on/off button without any additional configuration settings or user interface; this allows to activate the system and immediately start the treatment in a simple and intuitive manner (Fig. 1A). When the system is activated a light-emitting diode (LED) indicator (Fig. 1B) further enhances usability and accessibility of the device displaying the battery charging status. In detail, the different colors of the LED indicator alert the operator that the batteries are properly charged, delivering the correct voltage supply (green color) or running at low charge (yellow color), allowing only limited operation time, or eventually fully depleted (red color), at which point the device cannot longer be used;

(iii) Patient interface: the device utilizes a standard nasal-oral mask for non-invasive ventilation to deliver the airflow generated by the system to the patient's airways (Fig. 1A). This design choice ensures familiarity on how to apply the device, aligning with widely recognized and commonly used practices for interfacing respiratory support systems with a patient's airways;

(iv) Air-handling system: it includes:

- A particulate hypoallergenic filter (S9/Air10 Hypoallergenic Filters, ResMed Pty. Ltd., Sydney, NSW, Australia; Fig. 1C) positioned upstream of the positive pressure generator (*i.e.*, the centrifugal fan), which ensures clean airflow preventing the inhalation of unwanted fine particles;

- A centrifugal fan (or blower) that generates the desired airflow (WS7040-12-X200N, Ningbo Wonsmart Motor Fan Co., Ltd, Ningbo, Zhejiang, China; Fig. 1C); the fan draws the air from an inlet, located upstream of the particulate filter (Fig. 1A) and directs it into the fluidic channel downstream;

- An airflow distribution chamber connected downstream of the fan (Fig. 1C), which acts as a buffer zone between the high-velocity airflow generated by the fan and the downstream patient interface (nasal-oral mask); in detail, it allows air to

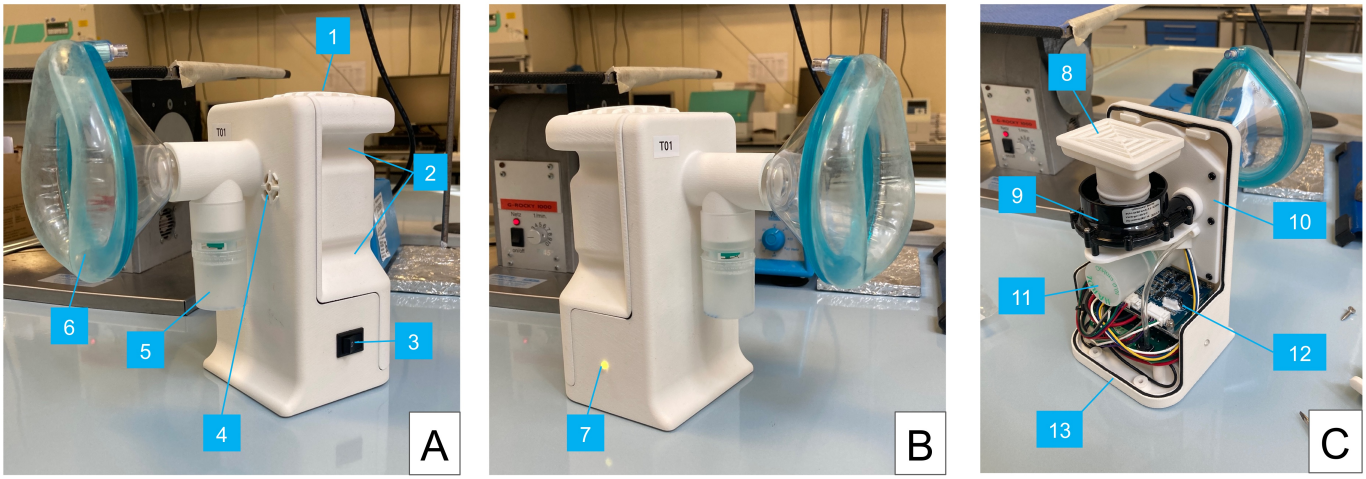

FIGURE 1. The miniaturized CPAP device. (A) front-left view showing the (1) air inflow located at the top of the enclosure, (2) the indentations on the external enclosure for a comfortable and secure hold during the device application, (3) the on/off button, (4) the anti-asphyxiation valve, (5) the 5 cmH_2O PEEP valve, and (6) the nasal-oral mask delivering the generated airflow to the patient airways; (B) front-right side view showing (7) the LED indicator of the battery pack charging status; (C) internal view showing (8) the particulate filter located on top of the (9) centrifugal fan, (10) the airflow distribution chamber located downstream of the fan, (11) the 10 cmH_2O PEEP valve, (12) the control system board, and (13) the lower compartment containing the battery pack.

decelerate and expand, smoothing the chaotic and turbulent flow patterns that develop downstream the fan, eventually leading to more uniform flow rate and pressure delivered to the patient's airways;

- Two mechanical PEEP valves opening at 5 and 10 cmH_2O, respectively (HAROL s.r.l., Italy; Fig. 1A,C); the use of the two valves grants, on the one hand, that the actual pressure delivered to the patient (P_{target}) is equal to 5 cmH_2O (efficacy) and, on the other hand, prevents the pressure from exceeding potential unsafe levels (safety limit, PEEP is always $<$10 cmH_2O); this design solution ensures the safe and effective device application across a broad spectrum of patients with heterogeneous anthropometric characteristics and/or varying pathological respiratory conditions. The 5 cmH_2O valve is opportunely positioned close to the nasal-oral mask (Fig. 1A): this helps ensuring the CO_2 exhaled by the patient exits the system so to minimize rebreathing of CO_2-rich air;

- An anti-asphyxiation valve (MiniValve Inc., The Netherlands; Fig. 1A) located in proximity of the nasal-oral mask, which ensures that the patient can still inhale air and breathe freely even in the event of a malfunction or obstruction of the air delivery system. The anti-asphyxiation valve is a flexible, dome-shaped membrane positioned over an exhaust port. Under normal device operation, positive pressure generated by the device keeps the valve closed, preventing ambient air entry and allowing proper pressurized breathing. Conversely, if for any reason the CPAP flow stops (*e.g.*, turbine fan failure/malfunction, inlet port obstruction or any obstruction in the fluidic circuit downstream the turbine fan), the valve opens passively upon patient's inhalation, allowing the patient to breathe room air, thereby preventing asphyxiation;

(v) Electrical system: it comprises a battery pack (Panasonic Energy Co., Ltd. Japan) providing a total power supply of 15 Volts, and the components sending the battery power to the fan and the control system. Autonomy specification of the battery pack was set at a minimum of 45 minutes at P_{target} (PEEP = 5 cmH_2O). Autonomy of the battery pack was empirically tested in n = 5 tests. Specifically, the device was connected to an active lung simulator (as described in the next "Performance testing" section) and operated at P_{target} until complete battery depletion. A duration of the battery pack of at least 45 minutes was always recorded. Potential issues related to challenging out-of-hospital environmental conditions, such as extreme temperature or high ambient humidity, were mitigated by the selection of commercial batteries certified by the manufacturer for performance stability in the temperature operating range −40/+85 °C and through the implementation of appropriate electrical circuit insulation, including battery compartments. This protective measure ensures the device's reliable operation and prevents moisture-induced malfunctions;

(vi) Control system: features a microcontroller assembly and a driver for operating the centrifugal fan and auxiliary electronics (Fig. 1C). It enables the operation of the centrifugal fan at a fixed preset level to deliver the P_{target} (5 cmH_2O) without the need for any user configuration/adjustments.

A schematic representation of the various components and their layout and interconnections within the device enclosure is depicted in Fig. 2.

2.3 Preclinical validation testing

To evaluate the device performance and validate the efficacy and safety requirements, we conducted an experimental study where the device was connected to a lung simulator able to replicate different respiratory conditions. The objective was to assess the device ability to maintain the P_{target} (5 cmH_2O) across various simulated scenarios.

To perform the tests, the device was connected to a high-fidelity active lung simulator (ASL 5000™ Lung Simulator, IngMar Medical Ltd., Pittsburgh, PA, USA) via a standard

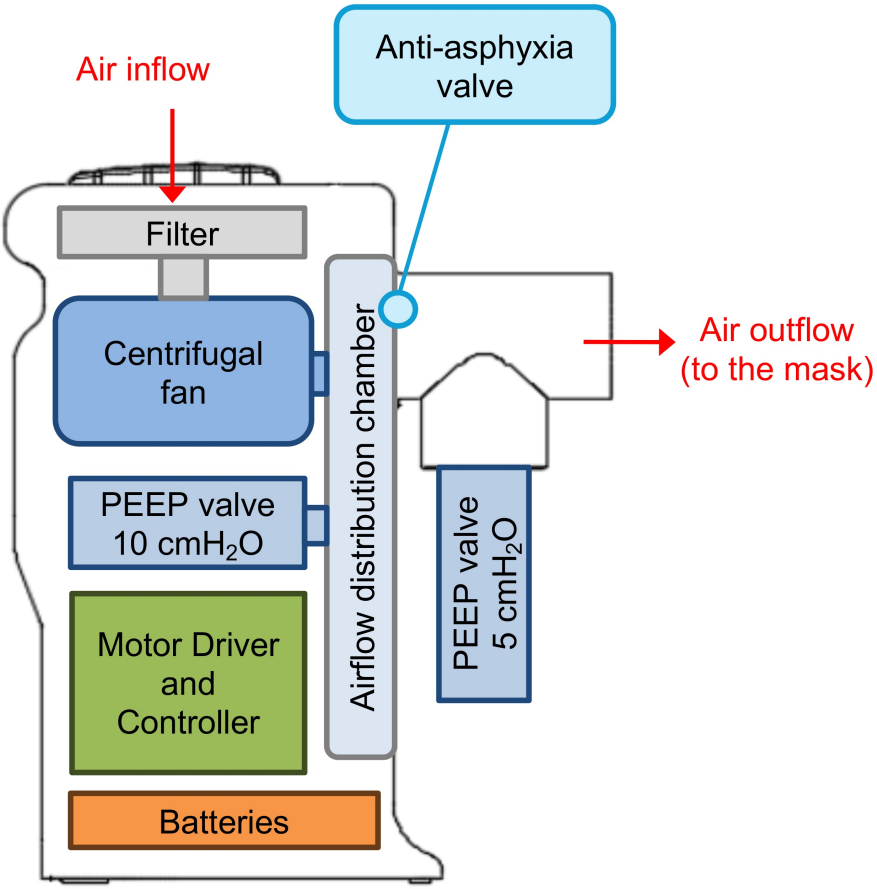

FIGURE 2. Schematics of the various components and their layout within the device enclosure. Red arrows indicate the direction of the air entering (air inflow) and exiting (air outflow) the device. PEEP: Positive end-expiratory pressure.

corrugated ventilator tube. This way we were able to evaluate the device performance (*i.e.*, generated flow and pressure) in an ideal, leakage-free pneumatic connection to the patient's airways, thereby eliminating any possible source of bias related to non-perfect fitting of the nasal-oral mask due to incorrect positioning. Ideal, leakage-free, condition tests were performed to establish baseline performance metrics for the device, serving as a benchmark for evaluating results in later usability tests performed under realistic conditions. The simulator software (ASL Software 3.6; IngMar medical LTd., Pittsburgh, PA, USA) enabled data recording and real-time monitoring of airflow and pressure dynamics during the tests.

We tested the device performance in 4 different simulated clinical scenarios: (i) normal, (ii) asthma, (iii) acute respiratory distress syndrome (ARDS), and (iv) chronic obstructive pulmonary disease (COPD).

The normal, healthy state served as a control scenario for evaluating the device performance under well-defined and predictable conditions. Within the normal, healthy scenario we simulated three different levels of respiratory requirements, corresponding to those of an individual breathing during rest, moderate and intense increase of respiratory needs.

Besides, the three pathological conditions (asthma, ARDS and COPD) represent typical and different respiratory conditions which are relevant for analyzing the effectiveness of CPAP systems as a supportive treatment [17, 18]. For each pathological condition, three different levels of severity were simulated (mild, moderate, severe), by appropriately adjusting key respiratory variables—namely (i) pulmonary compliance and (ii) resistance, (iii) breathing rate and (iv) respiratory effort—according to predefined values provided in the simulation software libraries for the different severity levels. Those values were configured by the software manufacturer according to data derived from the scientific literature (**Supplementary material**). Values set in our experiments for all the simulated scenarios are reported in Table 1.

The tests were conducted in the Simulation Lab of Vita-Salute San Raffaele University in Milan. A total of 36 test runs were performed: for each of the 4 simulated conditions (healthy, asthma, ARDS and COPD), and across the three levels of severity (mild, moderate and severe), the device was indeed tested under further three different operating conditions obtained modulating the fan maximum power, which was set equal to: (i) a rated or preset value (W_{set}), and then varied (ii) +5% (W_{high}), and −5% (W_{low}) of the preset value. The W_{set} condition represents the nominal power selected during the design stage as a compromise between delivering the desired P_{target} (5 cmH_2O) and energy consumption (autonomy of the batteries). The other two conditions (W_{low} and W_{high}) were chosen to account for potential power fluctuations (approximately +/−10% of the W_{set} condition) arising from uncertainties in the device performance when switching from prototype design to the device manufacturing (*e.g.*, manufacturing tolerances, variability in component effi-

TABLE 1. Software libraries parameters to simulate different severity of breathing conditions.

	Compliance (mL/cmH_2O)	Insp/Exp Resistance (cmH_2O/Lpm)	Breathing rate (breath/min)	Respiratory Effort (cmH_2O)
Normal				
Mild (rest)	50	13	8	5
Moderate increase of respiratory needs	50	13	15	10
Severe increase of respiratory needs (intense physical activity)	50	13	25	18
Asthma				
Mild	80	30/50	35	30
Moderate	60	40/70	25	20
Severe	40	50/90	15	10
ARDS				
Mild	40	8	25	25
Moderate	25	15	30	18
Severe	10	24	35	10
COPD				
Mild	50	12/14	30	30
Moderate	75	21/23	18	20
Severe	100	30/32	10	10

ARDS: Acute Respiratory Distress Syndrome; COPD: Chronic Obstructive Pulmonary Disease; Insp: inspiratory; Exp: expiratory.

ciency, environmental factors such as temperature or humidity, *etc.*). The evaluation of the device performance reliability and stability secondary to relative power setting variations has the role of validating the robustness of the design towards possible real-world applications.

To perform the tests, for each condition, the corresponding values listed in Table 1 were configured on the simulator's interface, the device was switched on and, following an initial stabilization period during which the system reached a steady state (approximately 5 s), data were recorded over a 30 s interval. Recorded pressure and flow data were used to derive PEEP values and tidal volume (V_T) for each respiratory cycle. For all the simulated scenarios, values were averaged over the characteristic breaths and reported as mean $\pm$ standard deviation (SD).

2.4 Usability tests

Following the experimental validation of the device performance, a usability test was performed to evaluate the intuitiveness and actual easiness of use of the device in a simulated real-life scenario, where the application of the device is performed by users with different expertise and/or technical skills. Intuitiveness and easiness of use were defined as the operator's ability to promptly and successfully apply the device. A successful application was defined as the delivery of the P_{target} (PEEP = 5 cmH_2O) in the recipient's airway during the test.

To replicate real-life usage conditions, operators were tasked with manual application of the device to a manikin (Laerdal Airway Management Trainer, Laerdal® Airway Management Trainer, Laerdal Medical, Bologna, Italy) via a nasal-oral mask (Ambu King Mask, Ambu A/S, Denmark) to simulate a patient receiving the CPAP (Fig. 3). The manikin's inner airways were connected to the active lung simulator (ASL 5000™ Lung Simulator, IngMar medical LTd., Pittsburgh, PA, USA). Real-time monitoring and recording of respiratory parameters were carried out via the lung simulator software, including measurement of the PEEP delivered by the operator during the device application. In all the tests, the device was configured to operate at the nominal preset operating conditions (W_{set}).

The tests were conducted in the Simulation Lab of Vita-Salute San Raffaele University in Milan and included a convenient sample of 15 voluntary operators (O1 to O15) selected on the basis of their varying levels of expertise in the management of devices for respiratory support and emergency care. In detail, the operators were categorized into 3 groups:

(1) Group 1: high expertise (n = 5): anesthesiologists/intensivists working in the intensive care unit of Ospedale San Raffaele (n = 3), residents in Anesthesia and Resuscitation at Vita-Salute San Raffaele University (n = 1), and medical students from Vita-Salute San Raffaele University (n = 1).

(2) Group 2: moderate expertise (n = 5): non-medical personnel recruited from the staff of Ospedale San Raffaele who had completed at least one Basic Life Support (BLS) course or have served/are serving in emergency medical services (*e.g.*, ambulance volunteers).

(3) Group 3: no expertise (n = 5): non-medical personnel recruited from the administrative staff of Ospedale San

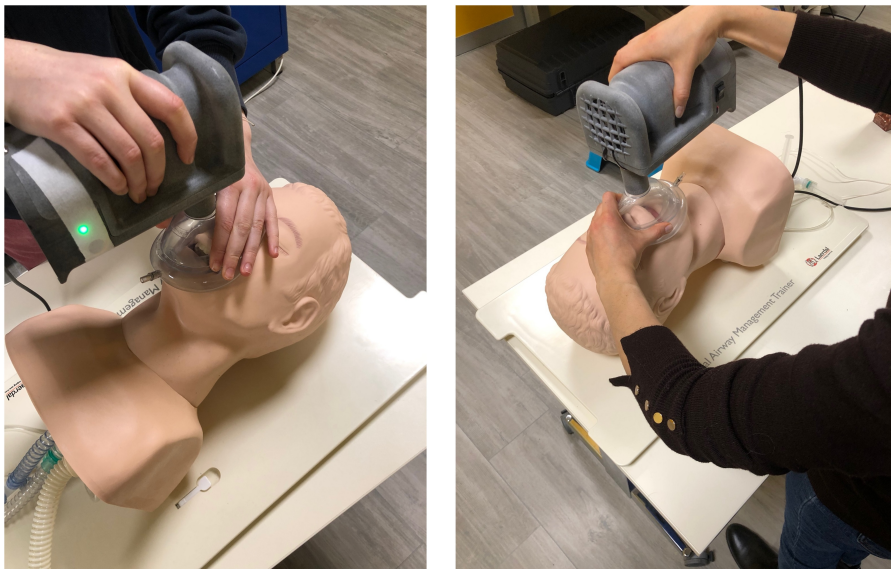

FIGURE 3. Representative pictures showing two operators applying the device to the manikin face during the usability tests.

Raffaele and Università Vita Salute San Raffaele with no medical training/knowledge or prior experience in either the management of devices for respiratory support or emergency care/BLS procedures.

Upon entering the laboratory, each operator was given the following oral instructions regarding the test:

"*This device is a non-invasive respiratory support device. To turn on the device, push the black on/off button at the bottom of the external case. Once the device is turned on, you will hear a fan generating an airflow, which exits through the mask. We ask you to please turn the device on and apply the mask to the manikin's face, so as to provide respiratory support. During the test, we will measure the pressure that will be delivered by the device to the mannequin lungs. We ask you to apply the device for 30 seconds (we will signal you when to start and stop). Afterward, we will ask you to remove the device from the manikin face, wait for about 10 seconds, and, upon our signal, apply again the device for 30 seconds (we will signal you when to stop).*"

Each operator thus performed 2 consecutive applications of the device (T1 and T2), each lasting 30 s, with a 10-s pause in between. This sequence was repeated four times per user—for a total of 8 applications lasting 4 minutes overall—changing the respiratory conditions on the lung simulator (normal, asthma, ARDS, and COPD). The different conditions were set in a random sequence. For each condition, the same parameters reported in Table 1 were set on the simulator. For each operator, the recorded PEEP values from each respiratory cycle were averaged separately for T1 and T2, for all the different simulated conditions. The standard deviation was then calculated.

After completing the tests, each operator was asked to report on their experience with the device by responding to a structured questionnaire. In detail, we asked the operators to assess their experience using the device in terms of (i) intuitiveness and ease of use, (ii) effort required to apply the device, and (iii) willingness to use the device in a real emergency scenario.

3. Results

3.1 Performance testing

Representative curves of the respiratory parameters measured with the active lung simulator during the performance tests are shown in Fig. 4.

Fig. 5 reports the airflow (Flow, Fig. 5A), tidal volume (V_T,) and PEEP (Fig. 5C) generated by the device at the nominal operating condition (W_{set}) as measured with the active lung simulator in the different simulated scenarios and respiratory requirements/pathology severity (mild, moderate and severe). In normal healthy conditions, the flow and V_T increased proportionally with increasing levels of respiratory requirements (Fig. 5A,B; **Supplementary material**), while the PEEP remains almost constant around the target value of 5 cmH_2O (Fig. 5C; **Supplementary material**; PEEP: mild = 5.27 $\pm$ 0.02 cmH_2O, moderate = 5.26 $\pm$ 0.08 cmH_2O, severe = 5.27 $\pm$ 0.07 cmH_2O).

In the pathological scenarios (asthma, ARDS and COPD), both the flow (Fig. 5A; **Supplementary material**) and V_T (Fig. 5B; **Supplementary material**) tend to decrease as the disease severity increases (from mild to severe), with the degree of flow reduction varying consistently by pathology, whereas the PEEP consistently stabilizes around the target value of 5 cmH_2O, with only minimal fluctuations (Fig. 5C; **Supplementary material**). PEEP: Asthma mild = 5.36 $\pm$ 0.05 cmH_2O; Asthma moderate = 5.32 $\pm$ 0.04 cmH_2O; Asthma severe = 5.29 $\pm$ 0.02 cmH_2O; ARDS mild = 5.23 $\pm$ 0.08 cmH_2O; ARDS moderate = 5.21 $\pm$ 0.07 cmH_2O; ARDS severe = 5.28 $\pm$ 0.03 cmH_2O; COPD mild = 5.37 $\pm$ 0.04 cmH_2O; COPD moderate = 5.29 $\pm$ 0.06 cmH_2O; COPD severe = 5.34 $\pm$ 0.03 cmH_2O).

In Fig. 6, the results of the performance tests performed at different levels of the device operating conditions (W_{set} *vs.* W_{low} *vs.* W_{high}) are shown; PEEP values are obtained by averaging across different respiratory needs or disease severities (mild, moderate, and severe). The results clearly indicate

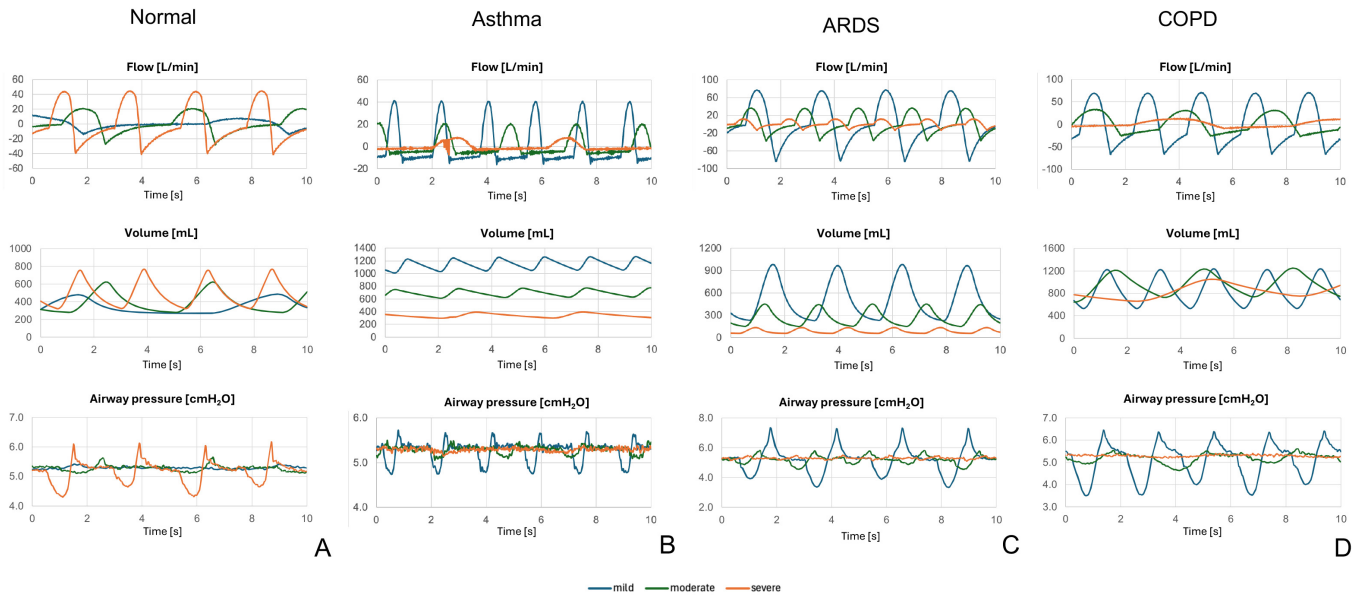

FIGURE 4. Representative curves of the respiratory parameters measured with the active lung simulator during the performance tests in the different simulated scenarios and respiratory requirements. (A) Normal; (B) Asthma; (C) ARDS; (D) COPD. ARDS: acute respiratory distress syndrome; COPD: chronic obstructive pulmonary disease.

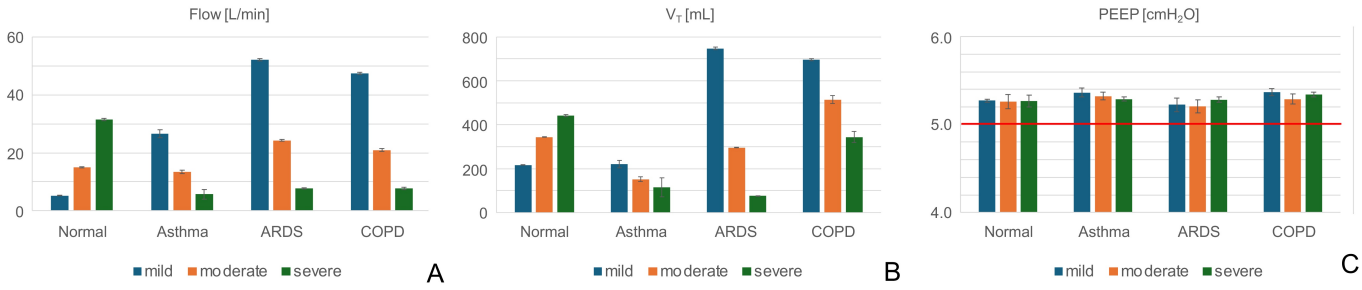

FIGURE 5. Airflow (Flow), tidal Volume (V_T) and positive end-expiratory pressure (PEEP) measured with the active lung simulator during the performance tests for each simulated scenario in mild, moderate and severe respiratory requirements. (A) Flow, (B) V_T and (C) PEEP. ARDS: acute respiratory distress syndrome; COPD: chronic obstructive pulmonary disease.

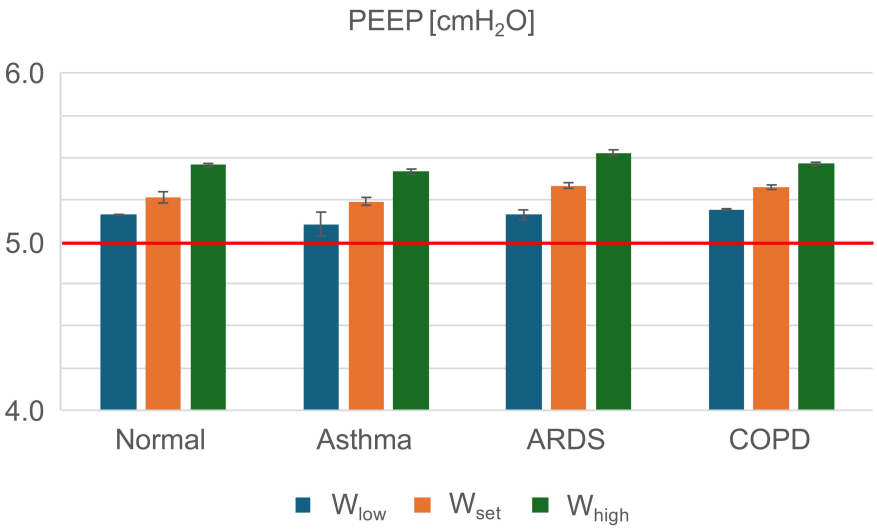

FIGURE 6. Positive end-expiratory pressure (PEEP) measured with the active lung simulator during the performance tests with the device operating at different operating conditions (W_{low}, W_{set}, W_{high}). ARDS: acute respiratory distress syndrome; COPD: chronic obstructive pulmonary disease.

that the PEEP consistently remains close to the target value (5 cmH_2O), with minimal fluctuations when the blower operates either at lower (W_{low}; PEEP: Normal = 5.16 ± 0.003 cmH_2O; Asthma = 5.19 ± 0.005 cmH_2O; ARDS = 5.10 ± 0.07 cmH_2O; COPD = 5.16 ± 0.03 cmH_2O; **Supplementary material**) or higher (W_{high}; PEEP: Normal = 5.45 ± 0.009 cmH_2O; Asthma = 5.46 ± 0.01 cmH_2O; ARDS = 5.42 ± 0.02 cmH_2O; COPD = 5.53 ± 0.01 cmH_2O; **Supplementary material**) power supply with respect to the values recorded at the nominal power setting (W_{set}; PEEP: Normal = 5.26 ± 0.003 cmH_2O; Asthma = 5.32 ± 0.01 cmH_2O; ARDS = 5.24 ± 0.02 cmH_2O; COPD = 5.33 ± 0.01 cmH_2O; **Supplementary material**).

3.2 Usability tests

The results of the usability test are reported in Fig. 7, where the mean PEEP values recorded during the two cycles of application of the device (T1 and T2) by each operator (O1 to O15) for each of the tested conditions (normal, asthma, ARDS and COPD) are shown.

Fourteen out of 15 operators (93%) were able to successfully apply the device, achieving the P_{target} (PEEP = 5 cmH_2O) in all the different simulated respiratory conditions. Of note, no major differences were observed between PEEP values achieved at T1 *vs.* T2 for all but one operator (O15, Fig. 7; **Supplementary material**).

The feedback on user-experience gathered from post-test questionnaires revealed that:

(1) Intuitiveness and ease of use:

- 14 out of 15 operators (93%) found the device intuitive and straightforward to apply;
- One operator (7%), although successfully applying the device (*i.e.*, correctly positioning the mask and achieving the target PEEP), highlighted would have preferred more comprehensive guidance and technical details on how to use the device;

(2) Effort required:

- 11 out of 15 operators (73%) of operators reported no fatigue or discomfort in handling the device while performing the test;
- Four operators (27%) experienced mild hand fatigue to hold the mask fitted against the manikin's face, but this fatigue was deemed acceptable.

(3) Willingness to use:

- All operators (100%) indicated they would use the device in a real emergency situation;
- However, 30% of them emphasized the importance of providing clear instructions on the application procedure and, possibly, receiving feedback on the proper functioning to enhance confidence in its use.

4. Discussion

We developed and described a new portable, miniaturized and easy-to-use CPAP device for out-of-hospital respiratory support. We documented that in a simulation setting a PEEP of 5 cmH_2O was always achieved under 36 different test runs including healthy, asthma, ARDS and COPD respiratory conditions, across three levels of severity (mild, moderate and severe). Professional and lay people users found the device intuitive and easy-to-use, confirming they would use it in a real emergency situation. The device was safe (a PEEP >6 cmH_2O was never reached) and the efficacy of CPAP has already been demonstrated over the decades. This device could therefore be applied in multiple out-of-hospital scenarios including (i) home, work, public places or street emergencies by lay bystanders; (ii) nursing homes, retirement homes, elder care facilities; (iii) ambulances not equipped with or do not have the expertise or time to initiate non-invasive ventilation; (iv) non-intensive hospital wards that do not have promptly available non-invasive ventilation devices or expertise, while waiting for the arrival of the medical emergency team.

CPAP is an established and safe treatment for ARF. Preliminary experiences of early CPAP administration in out-of-hospital settings demonstrated improved patient outcomes [5–

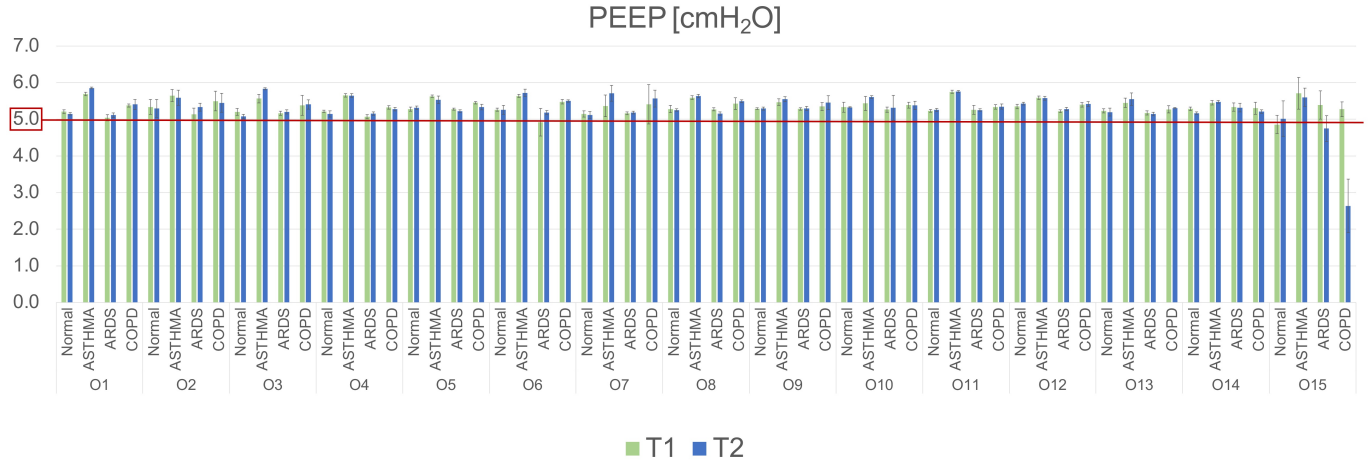

FIGURE 7. Mean positive end-expiratory pressure (PEEP) values recorded during the usability tests performed by the different operators (O1 to O15) over two consecutive cycles (T1: first application of 30 s and T2: second application of 30 s) in different simulated respiratory conditions (normal, asthma, ARDS, COPD). ARDS: acute respiratory distress syndrome; COPD: chronic obstructive pulmonary disease.

14, 18]. However, current CPAP devices present usability barriers in emergency out-of-hospital settings, related to required specialized technical expertise and complex setup. As a result, there is a lack of CPAP devices specifically matching the requirements for deployment in out-of-hospital emergencies.

To address this technological gap, we have developed a novel portable CPAP device which is compact and ready to use, thus rapidly deployable. To reach this goal, starting from a comprehensive analysis of currently available CPAP systems, we developed a design pathway focused on optimizing the device core function (the delivery of a continuous PEEP), while intentionally excluding ancillary features that are essential for in-hospital therapy (*e.g.*, PEEP level adjustment, device performance monitoring, automatic control systems for leakage compensation, oxygen delivery, pressure support on top of PEEP, *etc.*) but non-critical in emergency, out-of-hospital scenarios, where the device will be used temporarily as a bridge to advanced hospital-based intervention. Specifically, priority was given to design requirements including miniaturization, ergonomic design, operational simplicity and readiness to use, and ensuring both therapeutic efficacy and patient safety. We expect that this design strategy might also enable a significant reduction in manufacturing and production costs with respect to current CPAP systems, as the device utilizes simple—yet very effective—components (*e.g.*, mechanical PEEP valves) that are available at very low costs on the medical device market.

Our design solution overcome limitations of other portable CPAP systems when applied to the pre-hospital setting. One distinctive characteristic of our device is that, unlike other portable CPAP system, it does not require connection to an oxygen line. This characteristic enables earlier use, as it can be deployed in virtually any setting by lay bystanders even before the arrival of the ambulance. Furthermore, with our device, no configuration settings or manual procedures are required to get the target PEEP level, as the desired PEEP is immediately achieved upon powering the device. In this regard, we believe that our device offers greater ease of use and intuitiveness compared to other systems that require manual adjustment of the desired PEEP or other setting configuration to initiate the therapy. Even the need for a few configuration steps could indeed "intimidate" an untrained bystander, who might thereby decide not to initiate the therapy or, in the worst-case scenario, to apply settings that may be harmful. The easiness-of-use of our device appears even more evident when compared to systems that require adjustment of oxygen flow to achieve the desired level of PEEP, an operation that can evidently be performed only by trained/qualified personnel.

The selection of a fixed PEEP level of 5 cmH_2O reflects a carefully considered trade-off between therapeutic benefit and patient safety, considering that the device is intended for use not only by healthcare professionals (*e.g.*, emergency medical services) but also by laypersons, across a wide range of respiratory failure scenarios, often in the absence of a clear diagnosis. Given the lack of prior experience with this type of application, a PEEP of 5 cmH_2O was indeed deemed the most appropriate setting, as, physiologically, it provides a degree of lung recruitment and ventilatory support while minimizing the risk of barotrauma or excessive lung distension.

To preclinically validate our new device, at the end of the design process we conducted a comprehensive experimental study aimed at gathering critical data on device functionality and performance under simulated real-world scenarios. These tests were essential to assess actual effectiveness and safety of the proposed system.

Our results clearly show that the performance of device well aligns with the anticipated pathophysiology of the respiratory systems in the different simulated scenarios (Fig. 4) and indicate that the device consistently maintained PEEP at the target value of 5 cmH_2O (Fig. 5). Accordingly, our results suggest that efficacy and safety of the device are ensured, as the recorded PEEP invariably remained below potentially harmful values.

This underscores the desired device capability to deliver adequate respiratory support under a broad spectrum of patients' profiles. Variability in experimental tests was significantly low (Figs. 5,6). This is consistent with the standardized configuration of the experimental model. The controlled and reproducible conditions inherent to the model minimize external sources of variation, leading to consistent and stable measurements. Low experimental variability also demonstrates that the design solutions we adopted are robust, ensuring highly repeatable device behavior. System robustness was also validated: we indeed recorded minimal deviations in PEEP values against variations of the device operating conditions ($\pm$10% of the fan power; W_{set} *vs.* W_{low} *vs.* W_{high}, Fig. 6), which always reached the target value and remained far from potential unsafe values. Collectively, these findings highlight the system technical validity and physiological reliability.

We then performed usability tests aimed at collecting user experience feedback from various operators, and possibly identifying potential challenges in our design solutions that might inform design improvements required to ensure safe and efficient use in real emergency situations. Our results further support the device efficacy and safety profile, with very low inter-operator variability (Fig. 7). This reinforces the consideration that the device does not rely on operator-specific skills or prior experience and instead delivers reproducible outcomes across users, even when the operator lacks technical documentation, specific instructions or training, or previous expertise on rescue maneuvers or respiratory assistance. Of note, the operator with the poorest performance (O15, Fig. 7) still applied a PEEP between 2 and 3, which, although below the defined target value, would still ensure partial patency of the alveoli of a patient receiving the treatment. The PEEP value approached potentially harmful values in none of the 15 operators' tests.

Usability tests involved the execution of repeated experimental tests by each operator, with the two-fold aim of: (i) evaluating the learning curve required for the proper utilization of the device and (ii) determining whether fatigue occurs after prolonged use of the device. The operators' feedback confirmed that the device is intuitive and promptly applicable with minimum effort required. The vast majority of the operators did not find the application physically demanding, and those who experienced mild fatigue considered it tolerable. This is further confirmed by data showing stable performance (*i.e.*, consistency of PEEP values) even upon repeated use

by the same individual (T1 and T2). Indeed, the operators' performance did not decline in the second cycle, whereas a deterioration would be expected if fatigue was present.

The intuitiveness of the device was also confirmed by the fact that, despite receiving only minimal instructions, also non-expert operators were able to successfully apply it, already at the first attempt (T1), indicating a very short learning curve.

Notably, all operators indicated they would be willing to use the device in a real emergency, thereby confirming our hypothesis of a tangible and widely perceived need for a respiratory support device tailored for emergency settings. An additional potential use case of our device could be out-of-hospital cardiac arrest, where previous studies demonstrated the effectiveness of using portable CPAP devices to provide ventilatory support during cardiopulmonary resuscitation (CPR) maneuvers [19].

A real-world validation study is ongoing, which includes direct comparison of the effectiveness of respiratory support between our device and available systems employed in patients receiving CPAP therapy (ClinicalTrials.gov identifier: NCT06716502).

4.1 Limitations

The experimental tests were conducted in preclinical settings using artificial lung simulators and did not include human subjects receiving PEEP. While useful for evaluating the device functionalities and safety under controlled laboratory conditions, the experimental platform and test protocols, including the use of pre-defined values for respiratory parameters retrieved from the software simulation libraries, cannot fully replicate the complexity of the human respiratory pathophysiology. Likely, they do not account for the variability and unpredictability of actual emergency environments, including variable ambient conditions, or human factors such as patient tolerance and willingness to receive the treatment, or patient interface seal and leakage from the mask. Furthermore, usability tests were conducted with only 15 operators from a single institution, which may limit the generalizability of our findings and introduce potential selection bias. Moreover, only short-term metrics were evaluated, as the tests conducted were of limited duration.

4.2 Future development

The results obtained in this preclinical validation study provide the basis for future possible technical enhancements of our device:

- The extension of the current battery pack autonomy (45 minutes) will be evaluated to ensure reliable operation of the device also in scenarios involving prolonged emergency response times or extended patient transport to the hospital;

- The reports of mild hand fatigue by some operators during usability tests warrant further investigation: additional testing will be conducted to better understand the underlying causes and to guide potential ergonomic optimization aimed at improving user comfort, especially during prolonged use;

- As in all clinical contexts where CPAP is applied, the optimal PEEP level remains uncertain and frequently requires individualization. This aspect could be explored in more depth in future research efforts;

- Given the lack of an automatic leak compensation system from the present prototype configuration, targeted testing will be performed involving the controlled application of different degrees of mask leaks. This will enable accurate evaluation of the effective PEEP levels delivered by our device under specified leakage conditions.

5. Conclusions

We described the development and preclinical validation of a new portable device for non-invasive respiratory support in patients with ARF, whose design solutions were specifically tailored for rapid and easy deployment in out-of-hospital emergency scenarios. In pre-clinical simulation-based validation tests, the device showed effective and safe in delivering therapeutic PEEP values in different simulated respiratory conditions relevant to ARF. Feedback by the operators who applied the device suggest that it is easy and intuitive to use and does not require previous expertise in emergency care and rescue therapy or technical background in the management of medical devices. Accordingly, the device holds the potential for effective translation into real-world emergency scenarios, serving as a bridge to in-hospital respiratory care of ARF. Its ease of use and immediate applicability could effectively promote large-scale implementation of early out-hospital application of CPAP therapy to ARF patients, helping to reduce critical delay between onset of ARF symptoms and the initiation of in-hospital treatment, ultimately improving patient outcomes. A real-world validation study in human subjects is ongoing.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of this study are available from the corresponding author upon reasonable request. However, some information cannot be disclosed due to intellectual property rights and pending patent protection.

AUTHOR CONTRIBUTIONS

FC and GL—designed the research study. ES, FCN, GM, GBF, and FC—performed the experiments. TS, GB, LC, KD, GS, and AR—provided help and advice to conduct the research. ES, FCN, GBF and FC—wrote the manuscript. All authors contributed to the review and editing of the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Giovanni Landoni is serving as Editor-in-Chief of Signa Vitae. Giacomo Monti is serving as one of the Editorial Board members of this journal. We declare that Giovanni Landoni and Giacomo Monti had no involvement in the peer review of this article and have no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to OK.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1993237236244463616/attachment/Supplementary%20material.docx.

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