

# Feasibility of Noninvasive Positive Pressure Ventilation in the Treatment of Oxygen-Dependent COVID-19 Patients in Peru

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**Abstract.** Intensive care is expensive, and availability is limited. Low- and middle-income countries in particular have struggled to cope with the large influx of critically ill patients during the COVID-19 pandemic. Noninvasive respiratory support devices delivering continuous positive airways pressure (CPAP) require less resource and staff expertise compared with invasive mechanical ventilators and can be routinely used outside of intensive care units. This study assessed the use of the UCL-Ventura Wayrachi CPAP device in hospitalized patients with COVID-19 in Peru. A secondary analysis of data collected for a feasibility study commissioned by the Peruvian Ministry of Health was conducted. Data were collected from three hospitals, including patient demographics, clinical data, and outcomes. Forty-five patients were enrolled from July 16 to September 1, 2020. Eight patients (18%) were intolerant of the CPAP mask. Of the remainder, 18 (48.7%) improved and were discharged from hospital after 6 days. Eight (21.6%) died while on CPAP and 11 (29.7%) were eventually intubated, of whom two died. In total, 27 (60%) survived to hospital discharge. Participating physicians noted the device was easy to use and provided patient benefit, though voiced concerns about the strain on hospital oxygen supplies. In conclusion, the UCL Ventura Wayrachi CPAP device proved feasible in COVID-19 patients in Peru, and offered a bridging therapy for patients who required a ventilator when none were available.

## INTRODUCTION

The first case of COVID-19 illness in Peru was reported on March 6, 2020.<sup>1</sup> Despite a national lockdown being declared on March 15,<sup>2</sup> the country has been one of the most affected by the pandemic, reaching the highest mortality per capita of any country by August 2020.<sup>3</sup>

An observational study conducted at a national hospital in Peru found that 80% of patients required high flow, high concentration oxygen support with a median oxyhemoglobin saturation of 87%. However, 90% of these patients did not get admitted to intensive care, mainly due to lack of bed capacity.<sup>4</sup> In addition, the necessary ventilators, infusion pumps, sedative and paralyzing drugs, consumables, and human resources required to intubate and mechanically ventilate a patient safely and effectively were also in short supply. Continuous positive airway pressure (CPAP) devices provide noninvasive ventilatory support to hypoxemic patients when high concentration oxygen is inadequate and intensive care unit (ICU) beds or ventilators unavailable. Continuous positive airway pressure requires less resources and can be routinely administered outside the ICU. Less staff expertise is necessary, and less time is required of medical personnel since patients remain awake and often cooperative.<sup>8</sup> Despite initial concerns regarding the risk of barotrauma and aerosol generation,<sup>9</sup> CPAP is now routinely and safely used around the world for respiratory support of COVID-19 patients outside the ICU.<sup>10</sup> Continuous positive airway pressure is also often used as a bridge therapy to intubation or as an alternative ceiling of care for patients in whom invasive mechanical ventilation is deemed inappropriate, with favorable outcomes.<sup>11,12</sup> A

downside is that commercially available CPAP devices are costly and thus scarce in low- and middle-income countries (LMIC). Additionally, CPAPs require a pressurized oxygen supply and the oxygen flow rate demands may be higher compared with mechanical ventilators.

In response to the urgent need for CPAP devices to treat COVID-19 patients in the United Kingdom in early 2020, engineers and intensivists from University College London (UCL), University College London Hospital (UCLH), and Mercedes AMG High Performance Powertrains (HPP) reverse engineered the Phillips Respironics WhisperFlow, an out-of-patent, previously CE-marked, and purely mechanical CPAP device that can connect directly to a pressurized oxygen supply. Given unprecedented demands on hospital oxygen supplies, the team implemented design changes to the CPAP and breathing circuits, reducing oxygen utilization by 70%. They rapidly prototyped and bench-tested a low-cost device, the UCL Ventura, conducted healthy volunteer and patient evaluations, secured approval from the United Kingdom Medicines and Healthcare Products Regulatory Agency, and distributed 10,000 devices to the United Kingdom National Health Services within a month of idea conception.<sup>13</sup> This device generates a high-flow oxygen-air mix by entraining environmental air into a pressurized oxygen supply. It has two manual valves that permit adjustment of air flow and the percentage of administered oxygen. It has no moving or electronic parts and does not require an electricity supply. The only required additional parts are inexpensive consumables (mask, tubing, filters, and positive end-expiratory pressure [PEEP] valves), which can be either single used or could be sterilized for patient reuse, and a reusable in-circuit oxygen concentration analyzer. University College London and Mercedes HPP released open-source designs and manufacturing data under free license to bona fide organizations to support the global COVID-19 response, allowing a group of Peruvian engineers to build a local version, named

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the “Wayrachi,” which means “wind” in Quechua. However, Peruvian national guidelines for COVID-19 disease only endorsed the use of noninvasive ventilation in individual negative pressure rooms,<sup>14</sup> which are not available in most public hospitals, and not as initial management<sup>15</sup> despite the scarcity of ICU beds nationally.<sup>16</sup>

The Peruvian Ministry of Health received a donation of Wayrachi devices and disposable patient circuits including masks, tubing, filters, and PEEP valves to test its use, and to determine whether they should be incorporated into national guidelines. This study thus assessed the feasibility of use of these CPAP devices in hypoxemic hospitalized patients with COVID-19 in Peru.

## MATERIALS AND METHODS

This is a secondary analysis of data collected for a feasibility study commissioned by the Peruvian Ministry of Health. A total of 20 CPAP devices and 40 disposable circuits were distributed to three institutions: Cayetano Heredia Hospital (Lima), Ate Vitarte Emergency Hospital (Lima), and the Naval Medical Center (Callao). Three physicians from participating institutions took part in a day-long virtual training session with experts from UCL and UCLH. At study end, they were invited to a virtual debriefing session regarding the use of the device and issues faced with its implementation.

The following data were collected: patient demographics (sex, age, body mass index), pre-CPAP physiology (respiratory rate and arterial blood gas parameters), inspired oxygen requirement and devices used, complications and tolerance of CPAP, days on CPAP, requirement for mechanical ventilation, and hospital outcome. The device was deployed on hospitalized patients in dedicated non-ICU wards.

All statistical analyses were performed in Stata version 16 (Stata Corp., College Station, TX). Frequencies and percentages are presented for categorical variables. For quantitative variables, means and SDs are provided for normally distributed data, and medians and interquartile ranges otherwise.

This study was approved by the Cayetano Heredia University Institutional Ethics Review Board with inscription code 204291. Data were anonymized prior to statistical analysis.

## RESULTS

A total of 45 patients were enrolled from July 16 to September 1, 2020. Demographics and clinical characteristics are described in Table 1. Most patients were male (66.7%), between 50 and 59 years (40%) and overweight or obese (80%). Six patients were aged  $\geq 70$  years. Thirty-eight (84.4%) patients were previously receiving high-concentration oxygen via a reservoir mask (15 L/min) and required additional respiratory support and intensive care admission, which were not available. Patients were tachypneic (median rate 38 breaths per minutes), hypoxemic (median oxygen saturation 85%), and 88.9% of patients had thoracic retractions on inspiration.

Eight (18%) patients did not tolerate the device after minutes of use due to discomfort/pressure (3), feeling of asphyxiation (4), and exhaustion (1). Of the remaining 37, 18 (48.7%) improved and were discharged after an average of 6 days and a median duration of CPAP treatment of 5 days (interquartile range [IQR]: 4–7). Eight (21.6%) patients died on CPAP

TABLE 1  
Demographic and clinical characteristics of participants prior to starting CPAP (N = 45)

Demographic characteristics	Frequency	%
Sex		
Female	15	33.3
Male	30	66.7
Age		
20–39 years	8	17.8
40–49 years	5	11.1
50–59 years	18	40.0
60–69 years	8	17.8
70–79 years	6	13.3
Body mass index category		
Normal	9	20.0
Overweight	21	46.7
Obese (I)	8	17.8
Obese (II)	7	15.6
Clinical characteristics		
Respiratory rate, median (IQR)	38 (28–44)	
Days on CPAP, median (IQR)	4 (2–6)	
Arterial blood gases		
pH, mean (standard deviation)	7.42 (0.05)	
pCO <sub>2</sub> , median (IQR)	33.5 (30.1–43)	
pO <sub>2</sub> , median (IQR)	65.6 (50–77.9)	

CPAP = continuous positive airways pressure; IQR = interquartile range.

therapy, whereas 11 (29.7%) were eventually intubated and mechanically ventilated after a median duration of CPAP treatment of 2 days (IQR: 1–6), when a ventilator became available. Two of these 11 patients died. Twenty-seven (60%) of the 45 patients started on CPAP survived and were eventually discharged from hospital.

**Physician debriefing session.** Three physicians participated in the debriefing sessions. They noted the device was easy to use, and no further training was required beyond the initial training session. Use of the CPAP device required a dedicated multipatient ward; one participating institution had negative-pressure rooms, whereas the others only used well-ventilated areas. The required personal protective equipment was similar to what would be required in the ICU during the pandemic, including N95 or KN95 masks, goggles, and coveralls.

In addition to the face mask, tubing, filters, and valves required to use the flow generator, a nipple and clamp were required to ensure a tight fit of the device to the oxygen supply outlets, which was promptly implemented. Locally sourced masks and tubing were initially procured for use with the CPAP device but physicians noted they did not seal properly and increased oxygen utilization. Consequently, they continued to use the recommended consumables, which were sourced from the United Kingdom through the Peruvian Embassy in London, with no further issues. One site sterilized the disposable elements of the system with ethylene gas and noted this did not initially damage the circuit. However, after about five sterilizations, the PEEP valve and mask start deteriorating.

Following removal of the CPAP device to allow patients to eat, drink, or receive nebulization for airway humidification, physicians noted that patients did not tolerate the device as well, and their oxygen saturation did not rise as previously. Thus, physicians opted to maintain patients on the CPAP device semipermanently with use of in-line humidifying filters, with better results. At one site, patients were fed enterally through nasogastric tubes, though this sometimes affected

the mask seal. At another site, patients were briefly taken off the device to drink formula.

There was widespread concern about the amount of oxygen required for the CPAP devices to function properly, and the strain placed on the already overloaded hospital oxygen infrastructure.

All participating physicians agreed that patients started on CPAP later during their hospitalization did not respond as well as those started earlier.

## DISCUSSION

In our feasibility study, the use of CPAP in hypoxemic COVID-19 patients not coping with oxygen therapy alone enabled 40% to survive without invasive ventilation and provided bridge therapy in a further 30% until ICU beds or ventilators became available. Sixty percent were discharged alive. Similar data have been reported from Italy<sup>12</sup> and the United Kingdom.<sup>13</sup>

Continuous positive airway pressure therapy proved to be a viable alternative for Peru and for patients not suitable for intubation and mechanical ventilation, as evidenced by the six patients aged 70 and above who would not have been routinely offered ICU admission and mechanical ventilation due to resource limitation, long waiting lists for ICU beds, and poor prognosis, despite the lack of standardized national guidelines for ICU prioritization in Peru. Such usage in COVID-19 patients deemed unsuitable for treatment escalation has also been previously described.<sup>17</sup> This category includes patients who either do not want or are ineligible for invasive ventilation, usually because of comorbidities, frailty, and/or disease severity. In such cases, though the intervention may not always be lifesaving, it can also be an important palliative measure.

Implementing more CPAP devices could greatly increase hospital capacity to care for severely hypoxemic patients, particularly in the context of massive influxes of patients. A French study noted that 40% of patients requiring ICU care at their institution had to be transferred due to unavailability of ICU beds and ventilators.<sup>18</sup> They reported initiating CPAP in hypoxemic patients that were unable to secure a ventilator, with 38% recovering with CPAP alone and 62% being eventually intubated. A retrospective study from a United Kingdom hospital reported that 64% of patients who received CPAP avoided intubation altogether, and they were able to avoid exceeding their maximum ICU occupancy.<sup>19</sup> Another United Kingdom group reported that 13 (58%) of their cohort of 24 patients avoided mechanical ventilation altogether, with eventual 79% hospital survival, thereby saving ICU beds and ventilators for even more needy patients.<sup>12</sup>

Peruvian physicians pointed out their concerns about the oxygen demands of high-flow CPAP. The device draws high flows of oxygen<sup>20</sup> with an estimated requirement between 21 and 47 L/min for a hyperventilating, tachypneic COVID-19 patient receiving 60–90% oxygen, as mimicked by healthy volunteers.<sup>21</sup> Circuit leaks caused by an ill-fitting mask will allow oxygen to escape and thus increase oxygen flow requirements. By comparison, a typical mechanical ventilator uses up to 15 L/min oxygen though automatic leak compensation can increase oxygen use in some devices to over 200 L/min.<sup>22</sup> The configuration of the breathing circuit also significantly influences oxygen flow rates. For example, using a

single port instead of a twin port mask may increase oxygen flows by 40%. The high demand of oxygen and loss through leaks are important issues to take into consideration and could become important limitations. Outbreaks of COVID-19 have resulted in widespread shortages of oxygen in Peru and many other LMICs.<sup>23,24</sup> It is imperative that oxygen supplies be verified and secured, that the patient circuit and mask should be fitted properly, and the device turned off when not in use. Additionally, oxygen stewardship protocols should be clearly defined and implemented in hospital wards, and oxygen use should be monitored in real time.

The incompatibility of locally sourced masks and tubing could also pose a challenge. Sterilizing disposable consumables, as was done in one of the participating sites, could be a useful alternative to deal with shortages of supplies. Whether a medical device can be sterilized or not depends on both manufacturer advice and regulatory approvals. Ethylene gas provides an effective way of sterilizing irregularly shaped devices and does not damage most medical grade materials. However, this requires long processing and aerating times as ethylene oxide is toxic, carcinogenic, and flammable, and may pose an environmental risk if not correctly processed within a catalytic cell.<sup>25</sup> In addition, as mentioned previously, PEEP valves and masks are prone to deterioration after a few cycles of sterilization. Governments and local health agencies should seek to establish protocols for safe sterilization or ensure adequate supplies of disposables.

Our physicians noted that patients commenced on CPAP later during their hospitalization did not respond as well as those started early. A United Kingdom study found CPAP was associated with a significantly lower risk of death but only in patients with hospital stays of 7 days or less.<sup>26</sup> Several studies have tried to identify clear parameters to determine when intubation is indicated. Described predictors of intubation in COVID-19 patients managed with CPAP include age, elevated lactate dehydrogenase, low-level improvement in the PaO<sub>2</sub>/FiO<sub>2</sub> ratio after starting CPAP,<sup>27</sup> decreased oxygenation (SpO<sub>2</sub>/FiO<sub>2</sub> or PaO<sub>2</sub>/FiO<sub>2</sub>) on hospital admission, elevated neutrophil/lymphocyte ratio and an elevated respiratory rate.<sup>28</sup> None of these risk factors are however absolute. Other forms of noninvasive advanced respiratory support such as BiPAP or high-flow nasal cannula oxygenation might provide similar benefits to hypoxemic patients; however, they are expensive and rarely available in the country. In addition, high-flow nasal cannulas require more oxygen than CPAP (around 40–60 L/min of oxygen), so they might not be a good option in the setting of oxygen shortages. The UCL Ventura is relatively inexpensive and is manufactured locally (as the Wayrachi), which makes it more easily accessible.

Despite the limitations of this small observational study, there is a clear body of evidence that highlights the benefits that CPAP may bring. A simple device such as the UCL Ventura (or Wayrachi in Peru) is less costly and less complex for the nonspecialist to manage than other existing CPAP devices, with no discernible sacrifice in effectiveness. Provided the oxygen supply bottleneck can be overcome, this makes the UCL Ventura a feasible option for countries with limited access to CPAP devices, inadequate ventilator capacity, and/or lack of financial or human resources to access existing CPAP machines. Other countries can easily build their own local version, as was done with the Wayrachi in Peru. This

device has now obtained approval from the Peruvian Ministry of Health.

In conclusion, use of the UCL Ventura Wayrachi flow generator device in COVID-19 patients in Peru was not only feasible but appears to reduce the need for mechanical ventilation, to offer a bridge therapy while awaiting ventilator availability, and to offer an alternative ceiling of care above standard oxygen therapy for patients in whom mechanical ventilation is not considered appropriate. Issues such as consumables (masks, tubing) and hospital oxygen availability have to be considered to assure effectiveness. Further studies are needed to better identify predictors of CPAP failure in a variety of settings, including LMICs.

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