Vital signs of severe COVID-19 patients during inter-hospital helicopter transfer

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Abstract

Background: During the COVID-19 pandemic in The Netherlands, critically ill ventilated COVID-19 patients were not only transferred between hospitals by ambulance, but also by the Helicopter Emergency Medical Service (HEMS). To date, little is known about the impact of helicopter transport on critically ill patients, and COVID-19 patients in particular. This study was conducted to explore the impact of inter-hospital helicopter transfer on vital signs of mechanically ventilated severe COVID-19 intensive care patients, with special focus on take-off, midflight, and landing.

Methods: All ventilated critically ill COVID-19 patients who were transported between April 2020 and June 2021 by the Dutch 'Lifeline 5' HEMS team and who were fully monitored including non-invasive cardiac output, were included in this study. Three 10 minute timeframes (take-off, midflight and landing) were defined for analysis. Continuous data of vital parameters heartrate, peripheral oxygen saturation, arterial blood pressure, end-tidal CO₂ and non-invasive cardiac output using electrical cardiometry were collected and stored at a 1 minute interval. Data were analysed for differences over time within the timeframes using 1-way analysis of variance. Significant differences were checked for clinical relevance.

Results: Ninety-eight patients were included in the analysis. During take-off an increase was noticed in cardiac output (from 6.7 to 8.1 Lmin⁻¹; $P < 0.0001$) which was determined by a decrease in systemic vascular resistance (from 1068 to 750 dyne·s·cm⁻⁵, $P < 0.0001$) accompanied by an increase in stroke volume (from 92.0 to 110.2 ml, $P < 0.0001$). Other parameters were unchanged during take-off and mid-flight. During the landing cardiac output and stroke volume slightly decreased (from 7.9 to 7.1 Lmin⁻¹, $P < 0.0001$ and from 108.3 to 100.6 ml, $P < 0.0001$ respectively) and total systemic vascular resistance increased ($P < 0.0001$). Though statistically significant, the found changes were small and not clinically relevant to the medical status of the patients as judged by the attending physicians.

Conclusions: Interhospital helicopter transfer of ventilated intensive care patients with COVID-19 can be performed safely and does not result in clinically relevant changes in vital signs. This study this has been assessed by the medical ethical committee Arnhem-Nijmegen, the Netherlands (identifier 2021-7313). The committee waived the need for informed consent. The study was registered at www.trialregister.nl (identifier NL9307).

Background

During peak coronavirus -2 (SARS-CoV-2) spread, health care systems around the world were overwhelmed with patients suffering from respiratory failure, many of which needed hospitalization for ventilatory support. Distinctive of the COVID-19 outbreak were the emergence of regional hotspots with large numbers of patients requiring intensive care (IC) due to acute respiratory failure [1]. Severe COVID-19 presents with progressive dyspnea and often with hypoxemia [2,3]. The COVID-19 lung disease resembles ARDS and may rapidly progress to multiorgan failure [4]. About 5% of severe COVID-19 patients require intubation and ventilation [5].

Before the COVID-19 pandemic, inter-hospital ICU transfer was performed with Mobile Intensive Care Units (MICU); specialized ambulances equipped as an ICU. When locally an IC bed capacity problem arose it was resolved by transferring patients regionally. Unfortunately, during the pandemic the regional ICU capacity was insufficient at several hotspots in the Netherlands. Anticipating an increase in long distance transfers, the team of Helicopter Emergency Medical Service (HEMS) Lifeliner 3 of the Radboud University Medical Center received permission by the Ministry of Health, Wellbeing and Sports to organize and operate the first ICU-equipped helicopter (Lifeline 5) for transferring and redistributing critically ill COVID-19 patients in the Netherlands. This operation was initiated in cooperation with the Medical Air Assistance subdivision of the Royal Dutch Touring Club. It has been described in literature that helicopter transport of ICU patients is feasible and safe for patients and personnel [6].

However, it has been acknowledged that (long distance) transfers of ICU patients (inter, intra and pre hospital) bear the risk of complications. Most of the (severe) complications are thought to be reflected by changes in vital signs [7-10]. With regard to helicopter transportation specific concerns have been raised with regard to the effects of barometric pressure variations and acceleration/deceleration during take-off and landing [11]. Therefore, the goal of this study was to analyze the impact of inter-hospital helicopter transfer on vital signs of mechanically ventilated severe COVID-19 ICU patients with special attention to differences between take off, mid-flight, and landing.

Methods

This prospective observational study was performed during the COVID-19 outbursts in the Netherlands. In this prospective observational study, mechanically ventilated COVID-19 ICU patients who were monitored, including non-invasive cardiac output (CO), were included from the end of the first outburst in April 2020 throughout the end of the second outburst June 2021. This study has been assessed by the medical ethical committee Arnhem-Nijmegen, the Netherlands (identifier 2021-7313). This study will be carried out in accordance with the applicable legislation and policy rules. The committee waived the need for informed consent. The study was registered at www.trialregister.nl (identifier NL9307).

Data collection

Before monitoring started, monitoring devices were synchronized with the helicopter set-time and date. Three 10 minute timeframes were defined for analysis. The first timeframe started with the actual take-off. The second timeframe represented midflight and the third timeframe ended with the landing (touching of the ground). Data were extracted from the documented flight reports in the Operational Registration and Crew Administration data system. Continuous vital parameter data; heartrate (HR), peripheral oxygen saturation (SpO₂), arterial blood pressure (IAP); systolic, diastolic and mean arterial blood pressure (SBP, DBP and MAP), end tidal CO₂ (et-CO₂) was collected for every patient during the helicopter transfer using Corpuls 3 monitor (Corpuls® Benelux, Hellevoetsluis, The Netherlands).

Non-invasive cardiac output measurement by electrical cardiometry

As cardiac involvement of SARS-CoV-2 was suggested during the first COVID-19 outbreak [12], we have expanded our standard monitoring in the second outbreak with non-invasive cardiac output measurement using electrical cardiometry (EC). Doctors and nurses were trained in the use of the non-invasive CO monitoring device (ICON[®] monitor, Osypka Medical GmbH, Germany). The EC device was connected to the patient according manufacturer instructions using 4 skin sensors. These allowed continuous measurement of changes in thoracic electrical conductivity in response to a low amplitude, high frequency electrical current. Filtering techniques isolate changes in conductivity created by the circulatory system which is mainly determined by blood in the aorta and its change in conductivity when subjected to pulsatile blood flow before and after aortic valve opening. This is used to derive the peak aortic acceleration (ACC) and left ventricle ejection time (LVET). Stroke volume (SV) is calculated using patient characteristics (gender, age, length, body weight), ACC and LVET [13,14]. Further details of the device are described by Bernstein and colleagues [13,15]. As central venous pressure was not recorded, total systemic vascular resistance (TSVR) was calculated using the formula $MAP/CO \times 80$ ($\text{dyne} \cdot \text{s} \cdot \text{cm}^{-5}$) as described in literature [16]. Vital signs including non-invasive CO data were recorded on a 1-minute interval.

Adverse events

Major adverse events during inter-hospital transfer were defined as cardiac or respiratory arrest, pneumothorax or seizure. Minor adverse events were defined as *new* undesirable changes in vital signs. Standard target values of hemodynamics for patients in the ICU are well defined, however, cut-off values for vital signs that are considered to be causing harm are less well defined. In this study cut-off values are defined according to available literature, taking into account that this study includes critically ill patients. We defined the following thresholds: MAP < 60 and < 65 or > 120 mmHg; SpO₂ <88 and 90 %; et-CO₂ <25 or >55 mmHg; HR <50 and >100 bpm requiring treatment [17-21].

Statistical analysis

For the analyses and comparison of vital parameters, the aforementioned 10-minute window of patient data at take-off, mid-flight and landing were used. The resolution for vital sign data was set at 1 minute. In case of missing data, only timeframes with ≥ 6 data points were found eligible for analysis. Missing data were interpolated with mean of previous and next data points or extrapolated with last observation carried forward. Data were assessed for normal distribution using the Kolmogorov-Smirnov test and presented accordingly (normally distributed data with mean $\pm$ standard deviation and not normally distributed data with median [interquartile range]). For every vital parameter, differences over time within the group were analysed using 1-way analysis of variance (ANOVA) and Dunnett's multiple comparison test for posthoc analysis. Not normally distributed data were $\log_{10}(x)$ transformed before analysis with 1-way ANOVA. A P-value < 0.05 was considered statistically significant. All statistical significant differences were checked for clinical relevance [16-20]. Data were analysed using the appropriate tests in GraphPad Prism version 5.03 (GraphPad software, San Diego, USA).

Results

Patient characteristics

Ninety-eight patients are included in this analysis. Patient characteristics are shown in table 1.

Table 1. **Patient characteristics**

Gender M/F	69 / 29
Age (yr)	62.3 ± 11.5
Weight (kg)	91.6 ± 16.7
Height (cm)	175 ± 9.4
Body Mass Index (kg*m ⁻²)	30.3 ± 6.0
Ventilation mode	PCV 80 (82%)
	PEEP (cmH ₂ O) 12.4 ± 2.2
	PC (cmH ₂ O) 14.3 ± 2.7
	VCV 10 (10 %)
	PEEP (cmH ₂ O) 12.3 ± 2.6
	TV (ml) 407 ± 42
	PSV 8 (8%)
	PEEP (cmH ₂ O) 10.7 ± 2.3
	PS (cmH ₂ O) 8.7 ± 3.6
Trachea cannula	4 (4)
Inspired oxygen (%)	52 ± 12
Flight time (min)	56 ± 16
Range (min)	35-149

Total flight time (min)		5497
Flight distance (km)		156 ± 46
Range (km)		71-272
Total distance (km)		15314
Sedation	Midazolam	26 (27%)
	Propofol	24 (25%)
	Midazolam + Propofol	48 (49%)
	Opioids	91 (93%)
	Rocuronium	45 (46%)
Bolus number		
	Sedation	70
	Opioids	20
	Rocuronium	45
	Vasoactive	14
Nor epinephrine		82 (84%)
Mean dose ± SD (µg/kg/minute)		0.07 ± 0.05

Most patients were deep sedated, receiving one or two (49%) sedatives (midazolam and propofol) opioids 93% and rocuronium 46%. Bolus medication (midazolam, opioid, propofol, ketamine, nor-epinephrine or phenylephrine) was given in 70 patients to facilitate safe transportation, reduce oxygen consumption and carbon dioxide production. Eighty-four patients received continuous norepinephrine to support hemodynamics.

Data

All continuous parameters were recorded at a 1- minute interval during all timeframes. Technical monitoring problems led to loss of 281 data points (1.6% of total). For CO, SV and TSVR a total of 522 timeframes were available for analysis (59.1% of total).

No profound changes in vital parameters during take-off, midflight and landing

Overall, no profound clinical relevant changes were observed in vital signs during inter-hospital helicopter transfer of ventilated COVID-19 patients (Figure 1, Figure 2, Suppl. Figure 3, Table 2). Although there were several statistical significant changes within the timeframes (Table 2) these were not deemed clinically relevant as most values were within normal ranges. [17-21].

Table 2. **Difference in vitals during take-off, midflight and landing**

	1way ANOVA on log transformed data		
	Take-off	Midflight	Landing
SpO ₂	0.58	<0.0001	0.84
HR	0.62	0.52	0.57
SVR	<0.0001	0.53	<0.0001
CO	<0.0001	0.32	<0.0001
SV	<0.0001	0.40	<0.0001
MAP	0.50	0.77	<0.0001
SBP	0.90	0.96	<0.0001
DBP	0.58	0.27	0.25
CO ₂	0.56	0.46	<0.0001

SpO₂ = peripheral venous saturation; HR = heart rate; SVR = systemic vascular resistance; CO = cardiac output; SV = stroke volume; MAP = Mean arterial pressure; SBP = systolic blood pressure; DBP = Diastolic blood pressure; CO₂ = end tidal carbon dioxide.* P < 0.05 measured using 1-way ANOVA.

During take-off there were no significant changes in key vital signs such as HR, CO₂, SpO₂ and IAP. As expected, mid-flight showed to be the most stable part, with respect to vital signs, only for SpO₂ a difference over time was seen. During take-off an increase in stroke volume (from 92.0 to 110.2 ml, P<0.0001) was found. This led to an increase in cardiac output (from 6.7 to 8.1 Lmin⁻¹; P<0.0001). With minimal changes in MAP, this led to a decrease in systemic vascular resistance (from 1068 to 750 dyne·s·cm⁻⁵, P<0.0001. In the last 1 minute MAP and et-CO₂ show significant change during landing.

Adverse events

No major adverse events took place during the transfers. Minor adverse events are depicted in Table 3. The most frequently observed adverse event was a MAP <65 mmHg, only 2 events lasted longer than 5 min. None of the MAP< 60 mmHg events lasted longer than 5 min.

Table 3. **Minor adverse events**

	Take-off	Midflight	Landing	Total
MAP < 65 mmHg	11	9	9	29
< 60 mmHg	3	1	3	7
>120 mmHg	4	2	-	6
SpO ₂ <90 %	3	-	2	5
<88%	1	1	2	4
Et-CO ₂ < 25 mmHg	-	1	-	1
>55 mmHg	1	2	1	4
HR* <50 bpm	-	-	-	-
>100 bpm	-	-	-	-
Total	23	16	17	56

SpO₂ = peripheral venous saturation; HR* = heart rate requiring treatment; MAP = Mean arterial pressure; et-CO₂ = end tidal carbon dioxide

Discussion

The current observational study, showed that inter-hospital helicopter transport of mechanically ventilated COVID-19 patients can be performed safely. No clinically relevant changes in regular heartrate, oxygen saturation, blood pressure and et-CO₂ were observed during takeoff, mid-flight and landing.

Several studies have described the organization and quality of intensive care transport [22-24], however most data is obtained from road transfers using MICUs and data about COVID-19 transports is limited [20,25,26]. In the early days, Waddell and colleagues describe the impact of ambulance transport on the vital signs of critically ill patients [27]. They documented considerable variation in haemodynamic responses to transport between patients. An increased mortality was found in individuals who developed hyper- or hypotension compared to patients with no change or a delayed hypotension. Other authors did not find an increased mortality after interhospital transfer by ambulance or MICU [10,28].

Malagon et al. have investigated noninvasive cardiac output during fixed wing air ambulance repatriating using suprasternal Doppler [29]. Six medical crew members and 7 patients were assessed on the ground, during take-off, in the air and during decent. They found a statistical significant increase in CO and SV during take-off. A possible explanation was the combination of G-forces and the occurrence of mild hypoxia releasing NO mediators. However, similar to our findings, their changes were without clinical relevance. Our patients were on mechanical ventilation and thus receiving supplemental oxygen. The cruising altitude of our the IC-helicopter was between 800-1200 feet. Taken together, relative hypoxia was

not a contributing factor during our transports. Gravitational forces are limited during medical helicopter transports. During take-off and landing acceleration/deceleration occurs in a 1-2 minute window after take-off and before landing. During the entire flight, vibration of the helicopter could induce pooling of venous blood, hereby changing cardiac preload and influencing SV and CO. During the first minute of actual lift off; the patient is positioned in a head up position, hereafter the patient is positioned in a slight head down position during the entire flight. This position might be responsible for the observed increase in SV and CO, as venous return is known to improve in Trendelenburg position [21].

Although noninvasive CO measurements have been performed before in the prehospital HEMS setting [30,31], limited data are available on CO measurements during IC-helicopter transports let alone COVID-19 transfers [30,31]. Our study is the first to attempt CO measurements during interhospital helicopter transfer in ventilated IC patients with COVID-19. In all of the 98 patients noninvasive CO measurements were performed. However 59.6% of the timeframes were available for analysis due to missing data. As the ICON measures changes of electrical conductivity within the thorax in response to a low amplitude, high frequency electrical current the signal could plausible be influenced by vibrations or movement generated during the flight [14,15,31]. In previous work, ICON hemodynamic monitoring in the prehospital emergency medical setting showed that 23.6% of all measurements were lost due to interference with the signal. In that study, five out of 50 patients were transferred by helicopter all having good measurements [31].

With only 1.65% missing data of the conventional vital sign parameters, a robust data set was created to evaluate the impact of interhospital helicopter transport. Although there is no consensus for strict target parameters, Alhazzani et al. provided guidelines for the general management of critically ill adults suffering from COVID-19 [17]. They suggest an $SpO_2 \geq 90\%$ in patients with acute hypoxemic respiratory failure. A target MAP of 60-65 mmHg is suggested often requiring vasopressor support due to high ventilation pressures needed to optimize ventilation and to counteract deeply sedated patients [3,17]. In accordance, 84% of our patients needed vasopressor therapy to support the circulation. Extra sedation was given to optimize ventilation, reduce oxygen consumption, decrease carbon dioxide production and reduce the stresses of flight which could have had an impact on the measured vital signs. No major adverse events occurred and only limited minor adverse events were recorded in our study in which we flew more than 15000 km with COVID-19 patients.

This study has some limitations. We conducted research in a relatively new patient population, in a single centre study. Therefore, extrapolation of these results to other intensive care patients may be limited. The loss of 40.4% of the non-invasive hemodynamic data may be due to signal interferes of the electrical cardiometry device by the helicopter.

Conclusion

Inter hospital helicopter transport of ventilated intensive care COVID-19 patients can be performed safely. Although some significant changes in vital signs during take-off, mid-flight and landing were found, these

seem not clinical relevant. Vital signs are merely within the normal ranges of vital signs seen during intensive care treatment.

List Of Abbreviations

ACC	aortic acceleration
CO	cardiac output
DBP	diastolic blood pressure
EC	electrical cardiometry
et-CO ₂	end tidal CO ₂
HEMS	Helicopter Emergency Medical Service
HR	heartrate
IAP	arterial blood pressure
IC	intensive care
ICU	intensive care unit
LVET	left ventricle ejection time
MAP	mean arterial blood pressure
MICU	Mobile Intensive Care Units
SBP	systolic blood pressure
SpO ₂	peripheral oxygen saturation
SV	stroke volume
TSVR	total systemic vascular resistance

Declarations

Ethics approval and consent to participate

This study this has been assessed by the medical ethical committee Arnhem-Nijmegen, the Netherlands (identifier 2021-7313) by Prof. dr. P.N.R. Dekhuijzen, Chairman 18-02-2021. This study will be carried out

in accordance with the applicable legislation and policy rules. The committee waived the need for informed consent.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Author's contributions

CS participated in the literature search, study design, data collection and analysis, interpretation, writing and approved the final version. ES participated in the study design, data collection, interpretation, writing and approved the final version. SS participated study design, data analysis, interpretation, writing and approved the final version, MT participated in the data collection, interpretation, writing and approved the final version. GL participated in the data collection, interpretation, writing and approved the final version. MF participated in the data collection, interpretation, writing and approved the final version. GJvG participated in the study design, data collection, interpretation, writing and approved the final version, LvE participated in the study design and analysis, interpretation, writing and approved the final version.

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Figures

Figure 1

Vital signs during takeoff, midflight and landing. Data are expressed as median and interquartile range. Bpm = beats per minute. * $P < 0.05$ measured using Dunnett's multiple comparison test. Consecutive measurements in each timeframe are compared to the first measurement in that timeframe.

Figure 2

Noninvasive cardiac output data during take-off, midflight and landing. Data are expressed as median and interquartile range. L/min= liter per minute; mL = milliliter. * P < 0.05 measured using Dunnett's multiple comparison test. Consecutive measurements in each timeframe are compared to the first measurement in that timeframe.

Figure 3

Systolic and Diastolic blood pressure during take-off, midflight and landing. Data are expressed as median and interquartile range. * $P < 0.05$ measured using Dunnett's multiple comparison test. Consecutive measurements in each timeframe are compared to the first measurement in that timeframe.