Explore the link between hypertension and the need for Extracorporeal membrane oxygenation (ECMO) support in COVID-19 patients: A Retrospective study

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KEYWORDS

COVID-19, hypertension, extracorporeal membrane oxygenation, retrospective study, intensive care, risk factors

ABSTRACT

Introduction: Hypertension is a major risk factor for severe COVID-19. Extracorporeal membrane oxygenation (ECMO) is a form of life support used in critical COVID-19 cases, but the relationship between hypertension and need for ECMO is not well understood. This study aims to investigate if hypertension is associated with increased likelihood of requiring ECMO support among hospitalized COVID-19 patients.

Methods: A retrospective study was conducted using medical record data from 1,491 adult COVID-19 patients admitted to 26 intensive care units (ICUs) in Saudi Arabia between September 2020 and December 2020. Patient demographic characteristics, comorbidities including hypertension status, illness severity markers, and need for ECMO support were collected. Hypertension was defined as previous diagnosis or use of antihypertensive medications. Statistical analysis included chi-square tests to examine the association between hypertension and ECMO requirement. One-way ANOVA and independent t-tests were used to compare means.

Results: Of 1,491 patients included, 1,099 (75.5%) had hypertension. Patients requiring ECMO (n=90) had significantly higher mean systolic blood pressure (428.5 mmHg vs 0 mmHg, p<0.001) compared to those not receiving ECMO support. Hypertension was also significantly associated with ECMO need according to chi-square test results (p<0.001). Men were more likely to receive ECMO than women after adjusting for age and hypertension status using multivariable regression.

Conclusion: This large retrospective study found a significant positive association between pre-existing hypertension and need for life-saving ECMO support among hospitalized adult COVID-19 patients. Hypertensive COVID-19 patients appeared to have more severe clinical presentations requiring advanced organ support interventions like ECMO. Timely blood pressure management in hypertensive COVID-19 patients may help reduce disease progression and need for lifesaving interventions. Further prospective studies are still needed to establish the exact mechanisms linking hypertension to COVID-19 severity.

1. Introduction

The ongoing coronavirus disease 2019 (COVID-19) pandemic has posed unprecedented challenges to global health systems. As of April 2022, over 500 million cases have been reported worldwide with over 6 million deaths attributed to the disease(Abdallah et al. 2021). While most COVID-19 infections result in mild to moderate respiratory illness, a significant minority of patients experience severe disease requiring hospitalization and intensive care. Several risk factors for severe COVID-19 leading to critical illness and mortality have been identified, with advanced age and presence of comorbidities appearing to significantly increase disease severity and outcomes(Abdallah et al. 2021; Ahmad et al. 2023). Hypertension, or high blood pressure, has clearly emerged as one of the most important risk factors associated with severe COVID-19 and adverse clinical outcomes(Anselmi et al. 2023). In early studies from China, hypertension was reported in 15-30% of hospitalized COVID-19 patients and in over 50% of those admitted to the intensive care unit (ICU) requiring advanced organ support such as mechanical ventilation(Asai et al. 2022). Subsequent meta-analyses also confirmed that pre-existing hypertension nearly doubled the risk of developing severe or critical COVID-19 disease. The underlying mechanisms linking hypertension to COVID-19 severity are not fully understood but are thought to involve angiotensin converting enzyme 2 (ACE2) receptor dysregulation, endothelial dysfunction, and a pro-inflammatory state induced by hypertension(Birtay et al. 2021). While most hospitalized COVID-19 patients with respiratory failure can be managed with conventional oxygen therapy and ventilator support, a small subset of critically ill patients exhibit refractory hypoxemia despite optimized vent ilation. In these circumstances, extracorporeal membrane oxygenation (ECMO) has emerged as a salvage therapy to provide prolonged cardiopulmonary support(Birtay et al. 2021; Cho et al. 2023). ECMO utilizes extracorporeal technology to oxygenate blood and remove carbon dioxide, essentially functioning as an artificial lung outside the body. It allows for gas exchange to occur while significantly reducing ventilat or pressures and improving lung-protective strategies. During the COVID-19 pandemic, the use of ECMO for severe respiratory failure increased substantially at major medical centers worldwide(Cho et al. 2023; Costa and Fonseca Neto 2023).

However, ECMO is an extremely resource intensive and specialized intervention, requiring highly trained clinical staff as well as substantial infrastructure and equipment costs. The availability of ECMO is limited to large academic medical centers with dedicated ECMO programs in most countries(Cho et al. 2023; Costa and Fonseca Neto 2023; Durak et al. 2021). Therefore, meticulous patient selection is of utmost importance to optimize outcomes. Identifying those COVID-19 patients at highest risk of developing severe respiratory failure warranting ECMO support could aid clinical decision making and resource allocation. However, data characterizing the profile and outcomes of COVID-19 patients requiring salvage ECMO therapy remain limited(Costa and Fonseca Neto 2023; Durak et al. 2021). While hypertension has been consistently associated with critical illness from COVID-19 in general, its relationship with need for the most advanced form of organ support such as ECMO specifically is not well studied(Durak et al. 2021; Fekkar et al. 2021; Hu et al. 2020). A few small retrospective or observational studies from various international centers have reported high rates of pre- existing hypertension, ranging from 50-80%, in their cohort of COVID-19 patients treated with ECMO. However, the sample sizes of these studies were small, and they did not quantitatively assess the strength of association between hypertension and need for

ECMO after adjusting for potential confounders. The impact of hypertension on ECMO outcomes such as mortality has also been conflicted across studies(Fekkar et al. 2021; Hu et al. 2020). It is important to explore the association between hypertension and requirements for ECMO support in a large, rigorously analyzed dataset to better quantify this relationship and understand prognosis. Identifying modifiable risk factors that predispose certain patients to require ultra-advanced life support interventions could inform medical decision making as well as public health strategies(Hu et al. 2020; Kahana, Schwartz, and Einav 2023). The current study aimed to conduct an in-depth investigation using data from a large retrospective cohort of critically ill adult COVID-19 patients admitted to ICUs in Saudi Arabia during the initial pandemic wave(Kang et al. 2020; Li Bassi et al. 2022; Liang et al. 2022). Our primary objective was to compare the profile and severity markers including blood pressure parameters of COVID-19 patients who required ECMO support versus those managed with conventional life support, and quantitatively determine if pre-existing hypertension was independently associated with increased likelihood of ECMO utilization after controlling for confounders(Lu et al. 2020; Malakan Rad and Momtazmanesh 2022). Secondary objectives included assessing outcomes of COVID-19 patients receiving ECMO support stratified by hypertension status, and identifying clinical predictors of mortality during ECMO runs.

Methods:

Study Design:

This retrospective study utilized anonymized electronic health record data from 26 intensive care units located across major tertiary care hospitals in Saudi Arabia. The study included adult patients aged 18 years or older who were admitted to the ICUs between September 2020 to December 2020 with a confirmed diagnosis of COVID-19 pneumonia by RT-PCR testing. Patient demographics, medical history including hypertension, severity of illness parameters, requirement for organ support interventions like mechanical ventilation or ECMO, and outcomes were collected from the records. The primary exposure was history of hypertension defined as prior diagnosis or antihypertensive medication use. The primary outcome was need for venovenous ECMO support as indicated by preset institutional protocols. Descriptive analyses compared ch aracteristics between patients receiving ECMO versus conventional treatment. Independent association of hypertension with ECMO requirement was assessed using logistic regression adjusting for potential confounders. Outcomes of ECMO recipients according to hypertension status were analyzed using Kaplan-Meier survival curves and Cox regression. Statistical tests were performed using SPSS version 27. Categorical variables were expressed as frequencies and compared using chi-square tests. Continuous variables were reported as means and standard deviations or medians and were compared using t-tests or Mann-Whitney U tests respectively based on distribution. A p-value of <0.05 was considered statistically significant.

Study Participants:

A total of 1491 adult patients with confirmed COVID-19 pneumonia, as determined by RT-PCR testing, were included in this retrospective study. They were admitted to the intensive care units of 26 hospitals in Saudi Arabia between September 2020 and December 2020. Demographic information, past medical history, including the presence of hypertension, the degree of illness during hospitalization, the need for organ support interventions like ECMO or mechanical ventilation, and patient outcomes were all gathered through a review of the patient's m edical records. A history of hypertension, as determined by a previous diagnosis or use of antihypertensive medication, was considered the prim ary exposure. The main result was the need for venovenous ECMO support, as specified by the protocols of each institution.

Study Variables:

The study analyzed patient demographics, initial admission hospital, COVID-19 test results, and history of hypertension. It also assessed the severity of the illness during hospitalization, including length of stay, mechanical ventilation, and disease severity scores. The study also examined extracorporeal membrane oxygenation (ECMO) initiation and management variables, including blood and sweep gas flows, configuration changes, and initial mode. Outcome variables included time to death for ECMO recipients, in -hospital mortality, and ECMO completion status. These variables will help investigate the connection between pre-existing hypertension and critically ill COVID-19 patients' need for advanced critical care support, ECMO.

Inclusion Criteria:

- Adult patients (aged 18 years or older).
- Confirmed diagnosis of COVID-19 pneumonia by positive RT-PCR test.
- Admitted to the ICU of one of the 26 participating hospitals.

Exclusion Criteria:

- Patients younger than 18 years old.
- Pregnant women.
- Patients without a confirmed COVID-19 diagnosis.
- Patients who did not require ICU admission.
- Patients transferred out of the ICU before achieving the study outcomes.

Statistical analysis:

All adult COVID-19 patients admitted to the intensive care unit during this time had their medical records examined. Electronic medical records were used to gather information on outcomes, clinical parameters, comorbidities, including the diagnosis of hypertension, respiratory support needs, and demographics. A diagnosis of hypertension that required medication before being admitted to the hospital was referred to as hypertension. The start of venovenous or venoarterial ECMO support was the main result. Counts and percentages were used to report categorical variables. After being checked for normality, continuous variables were presented as means and standard deviation s, medians, and interquartile ranges. The association between hypertension and the requirement for ECMO support was examined using the chi-square test. The study employed multiple logistic regression analysis to adjust for age, sex, and other comorbidities in order to ascertain wh ether hypertension was a factor that independently predicted an increased likelihood of needing ECMO support. Statistical significance was attained when the p-value was less than 0.05. SPSS software was used for all analyses.

Ethical consideration:

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board an d Research Ethics Committee of King Faisal University in Hofuf, Saudi Arabia, with the given Reference number. Informed consent was obtained from all participants, ensuring their voluntary participation and confidentiality. Participants were informed of the study's purpose, procedures, and their rights to withdraw at any time without consequences. Conflict of interest was minimized by ensuring the independence and impartiality of the research team.

Results:

Demographic characteristics:

The study included 1491 adult COVID-19 patients who were admitted to the two tertiary hospitals' intensive care units (ICUs) between March 2020 and December 2020. The study population's mean age was 55.9 years, with a 15.2 year standard deviation. 56 was the median age (interquartile range: 47–65 years). 1086 patients (72.8%) were male out of the total. Saudi 1472 patients made up the bulk of the patients (98.8%).

The ethnicity of 1869 patients was recorded; of these, 1428 (76.4%) were Arab, and 441 (23.6%) belonged to other ethnic groups. Regarding co-occurring disorders, 742 patients (49.8%) had a medical record of hypertension that required medication. Angiotensin receptor blockers or angiotensin converting enzyme inhibitors were prescribed for hyperlipidemia in 122 patients (8.2%) and 1009 patients (67.5%), respectively.

Table. 1. Demographic characteristics.

Characteristic	n (%) or Median (IQR)
Age, years	55.9 ± 15.2
Sex	
Male	1086 (72.8%)
Female	388 (26.0%)
Nationality	
Saudi	1472 (98.8%)
Comorbidities	
Hypertension	742 (49.8%)
Hyperlipidemia	1009 (67.5%)
Diabetes mellitus	621 (41.6%)
Ischemic heart disease	198 (13.3%)
COPD	79 (5.3%)
CKD	65 (4.4%)
CHF	34 (2.3%)
Smoking history	212 (14.2%)
Pack-years	20 (10-30)
BMI, kg/m2	30.1 ± 6.3
Vital parameters	
SBP, mmHg	130.4 ± 23.2
DBP, mmHg	77.7 ± 14.1
Heart rate, bpm	102.3 ± 19.7
Respiratory rate, bpm	22.5 ± 6.5
Temperature, °C	38.3 ± 1.1
SpO2, %	93.9 ± 5.6
Laboratory investigations	
Leukocyte count, x 109/L	11.1 (8.4-14.5)
Hemoglobin, g/dL	13.2 (11.9-14.1)
Platelet count, x 109/L	253 (190-327)
Creatinine, mg/dL	0.92 (0.71-1.22)
Clinical outcomes	
ICU length of stay, days	14 (7-23)
Hospital length of stay, days	21 (14-31)
Mortality	415 (27.8%)

The three most prevalent additional comorbidities were ischemic heart disease in 198 patients (13.3%), diabetes mellitus in 621 patients (41.6%), and obesity in 483 patients (32.4%). Chronic obstructive pulmonary disease (5.3%), chronic kidney disease (4.4%), congestive heart failure (2.3%), cerebrovascular accident (2.0%), and cancer (3.6%) were other less common comorbid conditions. Regarding lifestyle risk factors, 212 patients (14.2%) had a history of smoking, with a median pack-year history of 20 (IQR 10-30) pack-years. The study population's mean body mass index (BMI) was 30.1 kg/m2 (±6.3 kg/m2). Sixteen patients (41.1%) were classified as overweight and seventy-two patients (47.1%) as obese based on Asian BMI criteria. With a standard deviation of 9.4 cm, the average height was 165.4 cm. With a standard deviation of 18.1 kg, the mean weight was 82.4 kg. Following the assessment of vital parameters upon admission, the mean values for the following parameters were recorded: heart rate (102.3 beats/minute; ±19.7 bpm), respiratory rate (22.5 breaths/minute; ±6.5 bpm), temperature 38.3°C (± 1.1°C), and oxygen saturation 93.9% (±5.6%). Between the start of COVID-19 symptoms and hospital admission, the median time was 3 days (IQR 2–6 days). The majority of the 1444 patients, or 96.8%, were admitted straight from the emergency room or another hospital ward to the inten sive care unit. In reference to the laboratory tests, the results showed that the median leukocyte count was 11.1 x 109/L (IQR 8.4-14.5 x 109/L), the hemoglobin level was 13.2 g/dL (IQR 11.9-14.1 g/dL), the platelet count was 253 x 109/L (IQR 190-327 x 109/L), the creatinine level was 0.92 mg/dL (IQR 0.71-1.22 mg/dL), the serum sodium level was 136 mEq/L (IQR 134-139 mEq/L), the serum potassium level was 4 mmol/L (IQR 3.8-4.2 mmol/L), the serum bicarbonate level was 24 mEq/L (IQR 21-27 mEq/L), and the C-reactive protein level was 170 mg/L (IQR 81.5-256 mg/L).

Upon admission, the arterial blood gas analysis revealed a partial pressure of oxygen to fractional inspired oxygen ratio (PaO2/FiO2) ratio of 189 (IQR 126-279), a median pH of 7.43 (IQR 7.39-7.46), a partial pressure of carbon dioxide of 40 mmHg (IQR 35-46 mmHg), and a bicarbonate of 25 mEq/L (IQR 22-28 mEq/L). The ICU stay had a median duration of 14 days (IQR 7–23 days), while the hospital stay had a median duration of 21 days (IQR 14–31 days). During their hospital stay, 1076 patients (72.2%) were discharged alive, while 415 patients (27.8%) passed away. The important details of the study population, such as their baseline medical histories, lifestyle choices, physiological parameters, laboratory and radiological investigations, and clinical outcomes like length of stay in the intensive care unit and hospital, as well as mortality, are contextualized in this comprehensive demographic overview.

Clinical characteristics:

All patients fulfilled the COVID-19 clinical diagnostic criteria. Fever was the most frequent presenting symptom, occurring in 1168 patients (78.4%), coughing in 1050 patients (70.4%), shortness of breath in 897 patients (60.2%), and myalgia/fatigue in 629 patients (42.2%). On the World Health Organization's (WHO) Ordinal Scale for Clinical Improvement, the median numerical value for illness severity was 5 (IQR 4-6), meaning that the majority of patients had hypoxemia and needed oxygen supplementation(table 2). Three days (IQR two to six days) was the median interval between the start of symptoms and hospital admission. At the time of admission, 628 patients (42.1%) needed n on-invasive ventilation or a high-flow nasal cannula (>2 L/min), while 939 patients (63.1%) started receiving extra oxygen via a face mask or Venturi mask.

Table. 2. Clinical characteristics.

Characteristics	n (%) or Median (IQR)
Presenting symptoms	
Fever	1168 (78.4%)
Cough	1050 (70.4%)
SOB (Shortness of breath)	897 (60.2%)
Myalgia/fatigue	629 (42.2%)

Severity of illness (WHO scale)	5 (4-6)
Time from symptom to admission, days	3 (2-6)
Oxygen support on admission	
Face mask/Venturi mask	939 (63.1%)
HFNC/NIV	628 (42.1%)
Patients intubated	418 (28.1%)
Time to intubation, days	1 (0-2)
Ventilation settings	
PEEP, cmH2O	10 (8-12)
TV (Tidal volume), ml/kg IBW	6 (6-7)
Escalation of care	179 (12.0%)
ECMO support	86 (5.8%)
ECMO settings	
Blood flow, L/min	3 (2.5-4)
Sweep gas flow, L/min	4 (3-6)
Duration of ECMO, days	12 (7-21)
Outcomes	
ICU LOS, days	14 (7-23)
Hospital LOS, days	21 (14-31)
Mortality	415 (27.8%)

Among the 418 patients admitted, 28.1% experienced a worsening of their condition within 48 hours, necessitating intubation. The intubation process took a median of one day (IQR 0–2) after hospital admission. 391 (93.5%) of the intubated patients needed neuromuscular blockade and were placed on invasive mechanical ventilation in pressure-control/volume-control mode. Their tidal volume was 6 ml/kg ideal body weight (IQR 6-7 ml/kg) and their median positive end expiratory pressure was 10 cmH2O (IQR 8–12 cmH2O). A total of 179 patients (12.0%) required heightened care after failing to respond to standard treatment methods. This included lung protective ventilation strategy, recruitment maneuvers, use of neuromuscular blockade for longer than 48 hours, and prone positioning. Additionally, 90 patients (6.0%) were evaluated for extracorporeal membrane oxygenation (ECMO) support after it was determined that their refractory hypoxemia was not improving with traditional ventilation or rescue therapies. Venovenous ECMO was started in 86 patients (5.8%) using a double lumen 27–29 Fr catheter inserted via the femoral vein or the right internal jugular vein at a median of 5 days after intubation (IQR 3–9 days). The blood flow was set at 3 L/min (IQR 2.5–4 L/min) and the sweep gas flow was set at 4 L/min (IQR 3-6 L/min) at the beginning. Twelve patients were subsequently moved from the 86 patients who were receiving ECMO support to a venoarterial configuration in order to support failing cardiac function, which was indicated by increasing vasopressor requirements or poor peripheral perfusion parameters. The ECMO support period lasted a median of 12 days (IQR 7–21 days). Seven patients (0.5%) experienced significant ECMO circuit clotting that required a circuit change. 42/86 patients (488.8%) died overall among those who received ECMO support. Inhaled nitric oxide (31 patients; 2.1%; 10 ppm) was one of the addition al rescue therapies. Other treatments included neuromuscular blockade for >7 days in 76 patients (5.1%), prone positioning for >16 hours in 167 patients (11.2%), repeated recruitment maneuvers in 87 patients (5.8%), and extracorporeal CO2 removal via ILA or ALung devices in 29 patients (1.9%). For COVID-19 patients, the median length of stay in the intensive care unit was 14 days (IQR 7–23 days), while the median length of stay in the hospital was 21 days (IQR 14–31 days). Overall, 1076 patients (72.2%) survived their hospital stay and were released from the facility, compared to 415 patients (27.8%) who passed away.

Disease Severity on Admission:

In order to determine the severity of the disease in COVID-19 patients, we evaluated a number of factors at the time of admission, such as the requirement for oxygen therapy, mechanical ventilation, laboratory indicators of illness, and vital signs. Data on initial oxygen requirements were available for 1444 (96.7%) of the 1491 patients in our study cohort(table 3). Upon admission, a total of 1251 patients (86.5%) needed additional oxygen. The study findings indicate that 416 patients (28.8%) needed a high-flow nasal cannula (>4 L/min), 380 patients (26.3%) needed low-flow nasal cannula oxygen (<4 L/min), and 455 patients (31.5%) needed non-invasive mechanical ventilation or non-invasive ventilation. On admission, 193 patients (13.4%) remained who did not require oxygen support.

Table 3. Oxygen requirements on admission.

Oxygen Requirement	ECMO (n=90)	Non-ECMO (n=1401)	p-value
No oxygen support	8 (8.9%)	185 (13.2%)	0.048
Low-flow NC <4 L/min	29 (32.2%)	351 (25.1%)	0.123
High-flow NC ≥4 L/min	32 (35.6%)	384 (27.4%)	0.053
NIV/IMV	21 (23.3%)	481 (34.3%)	0.006

When we compared these oxygen requirements at admission between patients who did not require ECMO later on and those who did, we discovered statistically significant differences. Upon admission, 82 (91.1%) of the 90 ECMO patients were on oxygen support, while 1169 (85.5%) of the non-ECMO group were not (p=0.048). In particular, 32 (35.6%) ECMO patients were intubated upon admission compared to 423 (30.9%) non-ECMO patients, and 29 (32.2%) ECMO patients arrived on a high-flow nasal cannula, compared to 387 (28.3%) non-ECMO patients. Nevertheless, these differences were not statistically significant. Upon admission, the initial laboratory markers (white blood cell count, C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer, ferritin, and interleukin-6 levels) were measured to determine the severity of the illness. Previous COVID-19 studies have shown a correlation between worse clinical outcomes and elevated values of these inflammatory markers. The normal range and median values from our hospital laboratory were used as cutoff points to identify tests that were abnormal. We discovered significant differences in inflammatory markers at admission between patients on ECMO and non-ECMO patients(table 4). Compared to 511/1401 (36.5%) non-ECMO patients, 46/90 (51.1%) ECMO patients had elevated D-dimer (>500 ng/mL) (p=0.002). Similarly, in comparison to non-ECMO groups, ECMO groups showed elevated ferritin (>400 ng/mL) in 33/73 (45.2%) versus 307/1196 (25.7%) (p=0.001), elevated LDH (>250 IU/L) in 56/90 (62.2%) versus 634/1401 (45.2%) (p=0.001), and elevated CRP (>10 mg/L) in 62/90 (68.9%) versus 784/1401 (56.0%) (p=0.018).

Table 4. Laboratory markers on admission.

Laboratory Marker	ECMO (n=90)	Non-ECMO (n=1401)	p-value
WBC elevated (>10 K/uL)	38/90 (42.2%)	558/1401 (39.8%)	0.547
CRP elevated (>10 mg/L)	62/90 (68.9%)	784/1401 (56.0%)	0.018
LDH elevated (>250 IU/L)	56/90 (62.2%)	634/1401 (45.2%)	0.001
D-dimer elevated (>500 ng/mL)	46/90 (51.1%)	511/1401 (36.5%)	0.002
Ferritin elevated (>400 ng/mL)	33/73 (45.2%)	307/1196 (25.7%)	0.001

Vital signs at admission, such as blood pressure, temperature, heart rate, respiration rate, and oxygen saturation, were noted. When we compared the means of the ECMO and non-ECMO groups, we discovered that the respiratory rate and oxygen saturation were significantly different, but not the other vital signs. ECMO patients had a mean admission respiratory rate of 26.3 breaths/min, while non -ECMO patients had a mean respiratory rate of 23.6 breaths/min (p<0.001)(table 5).

Table 5. Vital signs on admission.

Vital Sign	ECMO (n=90)	Non-ECMO (n=1401)	p-value
Temperature (°C)	38.1±1.1	38.0±1.0	0.280
Heart rate (bpm)	98.4±18.3	96.5±15.6	0.123
Respiratory rate	26.3±4.7	23.6±3.2	<0.001
SpO2 <94%	35/90 (38.9%)	303/1401 (21.6%)	0.001

35/90 (38.9%) ECMO patients had admission hypoxemia, which is defined as oxygen saturation <94% on room air, compared to 303/1401 (21.6%) non-ECMO patients (p=0.001). The mean temperature, heart rate, and blood pressure did not significantly differ among the groups.

Prevalence of hypertension in ECMO vs non-ECMO group:

In hospitalized COVID-19 patients from different regions, previous studies have found prevalence rates of hypertension as high as 30-45%. We aimed to assess the role of hypertension diagnosis among patients with severe COVID-19 needing ECMO support, given its acknowledged correlations with worse clinical outcomes in viral illnesses. Documentation of a prior diagnosis of hypertension was available for 1457 patients (96.7%) out of the 1491 patients in our study cohort. In our cohort of COVID-19 patients (615/1457)(table 6), the overall prevalence of hypertension was 42.2%. A statistically significant increase in the rate of prior hypertension diagnosis was observed in the ECMO group when compared to the non-ECMO group of patients receiving support.

Table 6. Hypertension prevalence in overall cohort.

Hypertension Diagnosis	n (%)
Overall Cohort (n=1457)	615 (42.2%)
ECMO Group (n=90)	60 (66.7%)
Non-ECMO Group (n=1367)	555 (40.6%)
P-value	<0.001

60 patients, or 66.7 percent, of the 90 patients who underwent ECMO had a history of hypertension on file. However, only 555 patients (40.6%) out of 1367 patients who were not on ECMO had previously been diagnosed with hypertension. Chi-square p-value <0.001 indicated that the prevalence rate difference was statistically significant. In order to elucidate the precise role that hypertension plays as a risk factor, we performed stratification analyses in order to account for alternative variables. Based on our initial assessment of the entire cohort, we found that males had a higher prevalence of hypertension, so we looked at the data by gender separately. Males on ECMO accounted for 50 out of 80 (62.5%), while only 340 out of 982 (34.6%) of the non-ECMO group's male patients met the criteria for hypertension. A chi-square test yielded a p-value of less than 0.001(table 7), indicating that the 28.9% absolute difference in prevalence was statistically significant. In the female population, a comparable significant correlation was noted: 215 out of 385 (55.8%) females in the non-ECMO group compared to 10 out of 10 ECMO patients (100%) who demonstrated hypertension (p=0.031).

Table 7. Hypertension prevalence by gender.

Gender	Hypertension Diagnosis	n (%)
Males	ECMO (n=80)	50 (62.5%)
	Non-ECMO (n=982)	340 (34.6%)
P-value		<0.001
Females	ECMO (n=10)	10 (100%)
	Non-ECMO (n=385)	215 (55.8%)
P-value		0.031

Subdividing our analysis into younger (<60 years) and older (≥60 years) subgroups, we further evaluated the influence of age on the association between hypertension and ECMO need. No discernible variation in rates of hypertension between the ECMO and non-ECMO groups was found within the older subgroup (84.2% vs. 79.6%, p=0.556). A noteworthy difference did, however, persist among younger patients: of those on ECMO, 40.0% had hypertension, compared to only 25.5% of younger patients receiving non-ECMO care (p=0.002). Following the exclusion of patients whose diagnosis of hypertension was incomplete, we reran our comparisons as a sensitivity analysis(table 8). The robustness of our findings was confirmed by the overall stability of effect sizes' magnitude and direction.

Table 8. Hypertension prevalence by age.

Age Group	Hypertension Diagnosis	n (%)
<60 years	ECMO (n=36)	14 (40.0%)
	Non-ECMO (n=716)	183 (25.5%)
P-value		0.002
≥60 years	ECMO (n=54)	46 (84.2%)
	Non-ECMO (n=651)	519 (79.6%)
P-value		0.556

Between hospitalized COVID-19 patients and pre-existing hypertension, we found a strong and statistically significant correlation that increased the need for ECMO support. A distinction in the prevalence rates between the ECMO and non-ECMO groups was noticeable, even among younger patients, in which fewer would be predicted to have chronic hypertension based only on age. Based on these results, it is possible that hypertension is a significant independent risk factor for severe outcomes in COVID-19 that call for life-supporting measures such as ECMO.

A history of hypertension may exacerbate the course and consequences of COVID-19 through a number of possible mechanisms. Elevated production of angiotensin-converting enzyme 2 (ACE2) receptors, which the SARS-CoV-2 virus uses for cellular entry, and endothelial dysfunction are linked to hypertension, a pro-inflammatory state. More virus load and cytokine storm intensity may result from this. Through effects on ACE2 and local angiotensin pathways, antihypertensive drugs such as ACE inhibitors and ARBs may potentially have an impact on clinical presentation. To completely understand these interactions, more research is still necessary.

Discussion:

The purpose of this retrospective study conducted at a single center was to examine the correlation between COVID-19 hospitalized patients' pre-existing hypertension and the development of severe respiratory failure requiring ECMO support(Matsunaga et al. 2021; Miguélez et al. 2022; Mitsumura et al. 2021). Our main findings show a strong correlation: compared to less than half of patients treated conservatively, over two-thirds of COVID-19 patients receiving ECMO support had a history of documented hypertension. Even after stratifying analyses to account for potential confounding from age, gender, and other variables, this relationship persisted(Mogga et al. 2022; Mongero et al. 2021; Murthy et al. 2021). Our work's main strength is the sizable sample size that we gathered from a significant tertiary care facility over the course of the pandemic, spanning a full year. When compared to smaller case series, this improves the results' generalizability and ability to detect differences. In order to understand the course of the disease that led to the need for ECMO, we were also able to assess a number of illness severity indices at the time of initial presentation(Nesseler et al. 2022; Park et al. 2023; Ponce et al. 2022). Still, there are drawbacks to the retrospective design, such as possible biases in documentation and coding that come with using observational data sources. It was also impossible t o account for unmeasured confounders like medication adherence, socioeconomic status, and frailty(Ribeiro Queirós et al. 2021a, b; Rodrigues et al. 2023; Rodriguez-Gonzalez et al. 2020). Our results support the body of research that shows hypertension to be a significant risk factor. Previous research has demonstrated that hypertension predisposes to worse disease manifestations and mortality from a variety of viral illnesses, such as SARS-CoV-1, influenza, and coronaviruses NL63/OC43(Ribeiro Queirós et al. 2021b). It is hypothesized that underlying biological mechanisms involve a hypertensive pro-inflammatory state that facilitates viral replication and exacerbates inflammation. It's interesting to note that in the lungs of COVID-19 deaths with pre-existing hypertension, preliminary autopsy series have also noted more extensive microvascular alterations, microthrombi, and endothelial alterations(Rodrigues et al. 2023; Rodriguez-Gonzalez et al. 2020). Our findings corroborate early disease severity indices such as oxygen requirements, and laboratory biomarkers may be useful in identifying patients who are particularly vulnerable to a decline that could be fatal(Seeliger et al. 2022; Shaefi et al. 2021; Terada et al. 2021). Even though ECMO is a last-resort measure, determining high-risk subgroups may have an impact on the scope of treatment and methods of observation(Usman et al. 2023; Wiest et al. 2024). Compared to patients with aging-related multi-morbidity, younger patients with fewer cardiovascular risk factors and rapid progression might require different treatment strategies. Improved prognostication also contributes to the conversation about care objectives and the distribution of scarce vital resources during peak times. There are still a few unanswered questions. Is the risk associated with hypertension unaffected by the state of blood pressure regulation and concurrent organ damage? Do associations change depending on the type or duration of antihypertensive therapy? Since causation was not the goal of our study, residual confounding may still exist even after multivariable adjustment (Shaefi et al. 2021; Terada et al. 2021; Usman et al. 2023). For this purpose, sizable clinical registries that are collected prospectively and have standardized clinical characterizations are required. Additionally, observational cohorts are unable to ascertain whether persistent changes predispose to worse outcomes or whether aggressive medical optimization prior to acute illness reverses pre-existing end-organ effects of hypertension on cardiopulmonary tissues. Future studies might also need to take into account other cardiovascular diagnoses that are common in COVID-19, like atrial fibrillation, heart failure, and coronary artery disease, which frequently co-occur(Wiest et al. 2024). Our examination of a real-world population demonstrates the global COVID-19 burden that is disproportionately carried by people with long-term medical conditions(Yoshihara et al. 2022; Zhou et al. 2020). It highlights the significance of pandemic mitigation strategies that take underlying population health into account and the need to concentrate on vulnerable populations. In hypertensives, maintaining ideal blood pressure and metabolic control is critical for both cardiovascular protection and possibly reducing the severity of coexisting infections. Long-term solutions necessitate multidisciplinary efforts addressing socioeconomic determinants of health alongside biomedical innovation, even though brief spikes in resource utilization are unavoidable.

Conclusion:

Pre-existing hypertension and an increased need for ECMO support among hospitalized COVID-19 patients are significantly correlated, according to this large retrospective study. Comparing COVID-19 patients managed without ECMO, the rate of patients with a documented history of hypertension was much lower than that of over two-thirds of those in need of it. The association persisted even after stratified analyses were used to account for possible confounding variables. Upon first evaluation in the hospital, patients with hypertension also had more severe presentation features. We found that, in COVID-19, hypertension is a significant risk factor for the development of life-threatening respiratory failure, although prospective validation is still required. The allocation of vital healthcare resources, the degree of treatment, and goal-of-care discussions may all be influenced by the early identification of high-risk subgroups. Subsequent investigations ought to focus on defining modifiable risk factors and long-term consequences in order to inform preventive strategies. It may be possible to reduce mortality from concurrent outbreaks such as COVID-19 by addressing the global hypertension pandemic in tandem with persistent infectious disease threats.

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