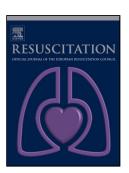# Journal Pre-proof

In-hospital cardiac arrest outcomes among patients with COVID-19 pneumonia in Wuhan, China

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2 **Wuhan, China**

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Abstract

Objective: To describe the characteristics and outcomes of patients with severe COVID-19 and in-hospital cardiac arrest (IHCA) in Wuhan, China.

Methods: The outcomes of patients with severe COVID-19 pneumonia after IHCA over a 40-day period were retrospectively evaluated. Between January 15 and February 25, 2020, data for all cardiopulmonary resuscitation (CPR) attempts for IHCA that occurred in a tertiary teaching hospital in Wuhan, China were collected according to the Utstein style. The primary outcome was restoration of spontaneous circulation (ROSC), and the secondary outcomes were 30-day survival, and neurological outcome.

Results: Data from 136 patients showed 119 (87.5 %) patients had a respiratory cause for their cardiac arrest, and 113 (83.1%) were resuscitated in a general ward. The initial rhythm was asystole in 89.7%, pulseless electrical activity (PEA) in 4.4%, and shockable in 5.9%. Most patients with IHCA were monitored (93.4%) and in most resuscitation (89%) was initiated <1 min. The average length of hospital stay was 7 days and the time from illness onset to hospital admission was 10 days. The most frequent comorbidity was hypertension (30.2%), and the most frequent symptom was shortness of breath (75%). Of the patients receiving CPR, ROSC was achieved in 18 (13.2%) patients, 4 (2.9%) patients survived for at least 30 days, and one patient achieved a favourable neurological outcome at 30 days. Cardiac arrest location and initial rhythm were associated with better outcomes.

Conclusion: Survival of patients with severe COVID-19 pneumonia who had an in-hospital cardiac arrest was poor in Wuhan.

Keywords: In-hospital cardiac arrest, Cardiopulmonary resuscitation, COVID-19, ROSC, Survival

3

Introduction

Since the outbreak of a novel coronavirus resulting in coronavirus disease 2019 (COVID-19) in Wuhan, China at the end of 2019, there have been more than 820,000 individuals in more than 170 countries with confirmed COVID-19, of whom more than 40,000 have died by April 1, 2020[1]. Several studies have already reported the clinical course and outcomes of patients with COVID-19 pneumonia[2-6]. The mortality of critically ill patients and risk factors for a poor prognosis have been assessed; however, the identification of risk factors and assessment of outcomes of patients with COVID-19 after in-hospital cardiac arrest (IHCA) remain unknown.

Therefore, in this study, we aimed to present the clinical characteristics; clinical outcomes, including return of spontaneous circulation (ROSC); and 30-day survival of patients with laboratory confirmed COVID-19 pneumonia after IHCA at Union hospital in Wuhan. We identified factors associated with improved outcomes following IHCA in patients with COVID-19.

Methods

Study design

This was a single-centred, retrospective, observational study. We identified patients who had IHCA between January 15 and February 25, 2020 in Union Hospital in Wuhan. The eligibility criteria were as follows: patients aged 14 years or older and patients with IHCA who were diagnosed with severe COVID-19 pneumonia according to the interim guidelines from the World Health Organization. All enrolled inpatients had a definite outcome after IHCA, including death, ROSC, and 30-day survival. The study was approved by the Ethics Committee Boards of Beijing Chaoyang Hospital, Capital Medical University, and Union Hospital, Tongji Medical College, and Huazhong University of Science and Technology, and the requirement

4

93   for informed consent was waived.

94

95   *Setting*

96   The west campus of Union hospital, which is a teaching tertiary hospital in Wuhan, was

97   one of the designated hospitals for patients with severe COVID-19 pneumonia. In total, 800

98   beds were modified as isolation wards and opened for admission to severe patients with

99   COVID-19 pneumonia starting from January 2020. In addition to the 800-current staff (doctors

100   nurses and others) of the hospital, over 2000 staff from 12 other provinces were employed to

101   provide medical care on the general wards and intensive care unit (ICU) of Union hospital.

102   There was a rapid response team available 24/7 to attempt resuscitation for patients with IHCA;

103   this team was also in charge of tracheal intubation and cardiopulmonary resuscitation (CPR) in

104   the general ward when needed. The team were alerted using a pager system. Resuscitation

105   followed guidelines from the American Heart Association and International Liaison Committee

106   on Resuscitation for advanced cardiac life support and post-resuscitation care. Ward staff

107   (usually nurses) started CPR and if defibrillation prior to team arrival. All staff (clinical and

108   non-clinical) working on the general ward, ICU and rapid response team donned personal

109   protective equipment (PPE) at the beginning of their shift. For all settings this included

110   protective clothing, a N95 mask and visor. Due to the exertion required of doing continuous

111   chest compressions whilst wearing PPE, the person doing compressions was changed after at

112   most one minute. A mechanical chest compression device was not available.

113

114   *Data collection*

115   We collected demographic, clinical, and outcome data of treated patients with severe

116   COVID-19 pneumonia and IHCA from an electronic medical record according Utstein style

117   guidelines during the 40 days[7].

118

5

119 Cardiac arrest was defined as the cessation of cardiac mechanical activity as confirmed by the

120 absence of signs of circulation. 'Treated IHCA' refers to a patient who experienced a cardiac

121 arrest and was treated with chest compressions and/or defibrillation. Details regarding treated

122 cases were collected by the physicians and entered into a database. We collected information

123 on age and sex of the patient; locations where IHCA occurred; witness and monitor status;

124 initial ECG rhythm such as shockable rhythm (ventricular fibrillation [VF], and pulseless VT)

125 or non-shockable rhythm (PEA and asystole); information on the response interval; and

126 presumed aetiology of the IHCA, which was categorised as cardiac, respiratory, and other.

127 Information regarding clinical symptoms, treatments, time from illness onset to hospital

128 admission, comorbidity, and length of hospital stay were also recorded.

129

130 The primary outcome was immediate survival with any ROSC, which was defined by return

131 of circulation in the absence of ongoing chest compressions (return of adequate pulse/heart rate

132 by palpation, auscultation, Doppler, arterial blood pressure waveform, or documented systolic

133 blood pressure >50 mmHg). The secondary outcome was 30-day survival and neurological

134 outcomes at 30 days recorded by cerebral performance category (CPC) score. Survival with

135 favourable neurological outcome was defined as CPC score of 1 or 2.

136

137 *Statistical methods*

138 Continuous variables are reported as means or median with interquartile ranges (IQRs) as

139 appropriate. Categorical variables are reported as numbers and percentages of patients in each

140 category. We stratified patients according to survival status. The chi-square test was used to

141 examine baseline differences in demographics and clinical characteristics across the strata of

142 resuscitation durations. A p-value <0.05 was considered statistically significant. The odds ratio

143 and 95% confidence interval were accordingly calculated. All analyses were conducted using

144 Python, version 3.6 (Python Software Foundation).

6

Results

Totally, we reviewed 761 records of patients with severe COVID-19 and identified 151

patients who had an IHCA during the study period of 40 days. After exclusions, a total of 136

patients were resuscitated and documented using the Utstein template (Fig. 1). The

characteristics of the included patients are shown in Table 1. Of these patients, 110 (80.9%)

were aged over 60 years and 46 (33.8%) were women. The most frequent comorbidity was

hypertension (30.2%), followed by diabetes (19.9%) and coronary heart disease (11.0%) (Table

1).

Of 136 patients who were resuscitated, most patients had a respiratory aetiology (119 cases),

whereas the remaining had cardiac aetiology (10 cases) and other causes (7 cases) (Table 1).

The initial cardiac arrest rhythm was VF or pulseless VT in 8 (5.9%) cases, PEA in 6 (4.4%),

and asystole in 122 (89.7%) (Table 1).

Of 136 patients resuscitated, 113 (83.1%) were in the general ward at the time of IHCA, while

23 (16.9 %) of the resuscitation efforts were initiated in the ICU (Table 1). Nearly all patients

had electrocardiogram (ECG) and pulse oximetry monitoring (93.4%) before their cardiac

arrest and in most cases resuscitation (89%) was initiated in <1 min. The length of hospital stay

was 7 (IQR, 4–11) days, and the time from illness onset to hospital admission was 10 (IQR,

7–14) days (Table 1).

The most frequent symptom was shortness of breath (75%), followed by

myalgia/arthralgia (60.3%) and cough (52.2%). Fever on admission was observed only in 52

(38.2%) cases (Table 1).

7

171   Of 136 patients who underwent resuscitation efforts, ROSC was achieved in 18 (13.2%)

172   patients, of which four patients were still alive at 30 days.

173   Resuscitation in the ICU resulted in better outcome when compared with that for the general

174   ward. Of the eight patients with an initial rhythm of VF or pulseless VT, six achieved ROSC,

175   whereas in patients with an initial rhythm of asystole, 9% achieved ROSC. The location and

176   initial rhythm between patients with different survival statuses were statistically significantly

177   different (Table 2, Supplementary Table). Only one patient achieved a favourable neurological

178   outcome at 30 days after IHCA. The overall mortality rate was 19.3% in patients with severe

179   COVID-19 pneumonia during the 40-day study period.

180

181   **Discussion**

182   To our knowledge, this is the first study to report the clinical characteristics and outcomes of

183   patients with severe COVID-19 pneumonia and IHCA using the Utstein style for reporting

184   IHCA events. In our study population, most patients with IHCA (96.3%) underwent attempted

185   resuscitation; however, there were five cases where the patients' relatives had requested no

186   resuscitation attempt be made if cardiac arrest occurred.

187   The most frequent underlying comorbidity of patients in our study was hypertension

188   followed by diabetes mellitus and coronary heart disease. This was consistent with other

189   reports in Wuhan. The common symptoms such as fever, shortness of breath,

190   myalgia/arthralgia, and cough were also similar to that of previous studies.

191   It is commonly accepted that the outcome after IHCA is more favourable when the initial

192   monitored rhythm is VF/VT rather than non-VF/VT (i.e., asystole or PEA). Most of the initial

193   monitored rhythms recorded by responders in our survey of patients who experienced an IHCA

194   were asystole (89.7 % of cases), which is more common than described in previous reports of

195   IHCA.[8-10] A shockable rhythm was recorded in only 5.9% of cases (2.7% of ward cases [3

196   patients], 22% of ICU cases [5 patients]),   but the outcome among these patients was better

8

197 than those with asystole or PEA.

198   There have been differences reported in previous studies regarding the mortality rate of

199 patients with COVID-19. A retrospective cohort study in Wuhan reported that 54 of 191

200 patients died in the hospital, and older age, higher SOFA score, and elevated d-dimer at

201 admission were risk factors for death of adults with COVID-19[2]. In another report from Wuhan,

202 the mortality rate was 62% among critically ill patients with COVID-19 and 81% among those

203 requiring mechanical ventilation[3]. Meanwhile, Washington state, USA reported a mortality rate

204 of 67%, and 24% of the patients remained critically ill and 9.5% were discharged from the

205 ICU[11]. We observed an overall mortality rate of 19.3% in patients with severe COVID-19

206 pneumonia during the study period. The difference may be due to the severity of patients

207 enrolled in the analysis, management of intensive care, and the capacity of hospitalisation for

208 patients.

209   The overall outcome of IHCA in our study was poor, with a ROSC rate of 13.2% and

210 30-day survival rate of 2.9%. The shortage of medical resources and uncertain quality of CPR

211 were key factors in the resuscitation of patients with severe COVID-19 pneumonia in Wuhan.

212 As COVID-19 spread, the number of critically ill patients exceeded the capacity of ICUs in

213 most hospitals in Wuhan. It was not rare for critically patients to stay in the general ward with

214 limited advanced life-support facilities. With an improvement in recognition and protection

215 strategies, two newly constructed hospitals and several isolation hospitals were soon brought

216 into service. As Union hospital was designated for patients with severe pneumonia, the

217 defibrillation and advanced airway interventions and mechanical ventilation could be

218 established in the general ward with the help of a 24/7 rapid response team. Although a

219 growing number of mechanical compression devices had been introduced in hospitals, there

220 was still a significant lack of intensive care resources. In addition, few patients had

221 do-not-attempt CPR (DNACPR) decision. The patients were cared for in isolation wards, and

222 visiting by relatives was very limited. Only five patients who had a cardiac arrest had a

9

223 DNACPR decision. We did not make any DNACPR decisions without discussion with a
224 relative.

225   According to recent international CPR guidelines, post-resuscitation care has been added
226 to the 'chain of survival', and its importance to the outcome of cardiac arrests has been
227 emphasized[12,13]. Although the World Health Organization and National Health Commission of
228 China have issued preliminary guidance on infection control, screening, and diagnosis in the
229 general population, in addition to the guidelines issued by the Surviving Sepsis Campaign
230 COVID-19 panel who provided recommendations to support hospital clinicians managing
231 critically ill adults with COVID-19, there is still limited guidance based on clinical research on
232 the acute management of critically ill patients with COVID-19[14,15]. Supportive care is the
233 mainstay of treatment among patients with severe COVID-19 pneumonia. In our study, there
234 were numerous patients with severe pneumonia who were resuscitated in the general ward,
235 resulting in a poor outcome when compared with those who received intensive care in the ICU.
236 The difficulties in managing rapid deterioration, acute respiratory failure and acute respiratory
237 distress syndrome in a general ward setting may have also contributed to the poor outcomes.

238   Based on our observations, chest compressions with PPE require considerable effort, and
239 the person doing compressions should change every minute. In addition, the PPE clothing
240 should be loose fitting to enable compressions and movement. The use of a mechanical chest
241 compression device should be considered if prolonged compressions are required.

242   This study had some limitations. First, many data points in the resuscitation process were
243 not documented, such as duration of resuscitation efforts, time to first defibrillation, and
244 time to first epinephrine. Second, we do not know the precise interventions that patients had
245 prior to cardiac arrest. Third, this study involved only one centre and the results may not be
246 generalisable to other settings and healthcare systems. The relatively few cases and survivors
247 means that our confidence in our estimates of outcome is low. To explore the risk factors for
248 outcome, univariable and multivariable logistic regression models were applied, but no

<div align="center">10</div>

249 significant difference were found. More studies are needed to better understand the incidence

250 and outcomes of acute respiratory distress syndrome and critical illnesses caused by

251 COVID-19, which will be important for critical care management and resource planning.

252 Finally, a lack of data regarding CPR quality is also a limitation. It was also difficult to identify

253 the differences between general wards that were managed by staff from different hospitals.

254 These variations in resuscitation efforts and post-arrest care could also affect the survival

255 outcomes and results. Finally, although we did not study this formally, we are not aware of any

256 clinical staff involved in a resuscitation attempt becoming infected with COVID-19 as a result

257 of their involvement.

258

259 **Conclusions**

260 The overall ROSC and 30-day survival rates of IHCA patients with severe COVID-19

261 pneumonia in Wuhan were poor. Factors associated with ROSC and 30-day survival were

262 initial rhythm and location of arrest. Providing care for patients at risk of cardiac arrest in an

263 intensive care setting, should be considered to improve the outcome of IHCA patients with

264 severe COVID-19 pneumonia.

11

265 **Conflicts of interest**

266 None.

267 **Acknowledgements**

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Table 1. Characteristics of patients with severe COVID-19 pneumonia and in-hospital

cardiac arrest in Wuhan

Variables	Overall (N = 136)
Sex	
Female (%)	46 (33.8)
Male (%)	90 (66.2)
Age, years	
Mean	69
Range, IQR	61-77
Age group, years, n (%)	
14-18	1 (0.7)
19-29	2 (1.5)
30-39	2(1.5)
40-49	3 (2.2)
50-59	18 (13.2)
60-69	46 (33.8)
70-79	39 (28.7)
>=80	25 (18.4)
Aetiology, n (%)	
Cardiac	10（7.4）
Respiratory	119 (87.5)
Others	7 (5.1)
Location, n (%)	
ICU	23 (16.9)
General ward	113 (83.1)
Initial rhythm, n (%)	
VF/VT	8 (5.9)
PEA	6 (4.4)
Asystole	122 (89.7)
Time to initiation of CPR, n (%)	

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≤1 min	121 (89.0)
2-4 min	12 (8.8)
≥5 min	3 (2.2)

Witnessed, n (%)

Yes	132（97.1）
No	4（2.9）

Monitored, n (%)

Yes	127 (93.4)
No	9 (6.6)

Comorbidity, n (%)

Hypertension	41 (30.2)
Diabetes	27 (19.9)
Coronary heart disease	15 (11.0)
Cancer	10 (7.4)
COPD	6 (4.4)
Cerebrovascular disease	5 (3.7)
Chronic renal disease	3 (2.2)
Others	5 (3.7)

Length of hospital stay, median, days (IQR)

7 (4-11)

Time from illness onset to hospital admission, median days (IQR)

10 (7-14)

Symptom, n (%)

Fever on admission	52 (38.2)
Shortness of breath	102 (75.0)
Myalgia/arthralgia	82 (60.3)
Cough	71 (52.2)
Fatigue	66 (48.5)
Sputum	48 (35.3)
Abnormality of mentality	45 (33.1)
Diarrhoea	27 (19.9)

16

Nausea/vomiting	14 (10.3)
Headache/dizziness	9 (6.6)
Abdominal pain	8 (5.9)

326 IQR, interquartile range; ROSC, return of spontaneous circulation; ICU, intensive care unit;

327 CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; VF, ventricular

328 fibrillation; VT, ventricular tachycardia; COPD, chronic obstructive pulmonary disease.

329

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Table 2. Outcomes of patients with severe COVID-19 pneumonia and in-hospital cardiac

331　**arrest in Wuhan**

Group	N	ROSC			30-day survival		
		n (%)	*p*-Value	OR (95% CI)	n (%)	*p*-Value	OR (95% CI)
Age, years			0.08			0.19	
>60	105	11 (10.5)		1.00	2(1.9)		1.00
≤60	31	7 (22.6)		0.40(0.13-1.37)	2(6.5)		0.28(0.02-4.09)
Sex			0.12			0.15	
Female	46	9 (19.6)		1.00	0 (0)		1.00
Male	90	9 (10)		0.46 (0.17-1.25)	4 (4.4)		4.28 (0.22-82.71)
Location			<0.01			<0.01	
General ward	113	8 (7.1)		1.00	1(1)		1.00
ICU	23	10 (43.5)		10.10 (3.38-30.14)	3 (13)		16.80 (1.663-169.70)
Witnessed			0.43			0.72	
No	4	0 (0)		1.000	0 (0)		1.00
Yes	132	18 (13.6)		1.26 (0.06-24.91)	4 (3)		0.25 (0.01-5.57)
Aetiology			0.48			0.36	
Cardiac	10	2 (20)		1.000	1(10)		1.00
Respiratory	119	16 (13.4)		0.62 (0.12-3.19)	3 (2.5)		0.23 (0.02-2.47)
Others	7	0 (0)		0.29 (0.01-7.45)	0 (0)		0.64 (0.02-22.06)
Initial rhythm			<0.01			<0.01	
VF/VT	8	6 (75.0)		1.000	3 (37.5)		1.00
PEA	6	1 (16.7)		0.07 (0.01-0.97)	0 (0)		0.14 (0.01-3.48)
Asystole	122	11 (9)		0.03 (0.01-0.18)	1 (0.8)		0.01 (0.00-0.16)

332　ROSC, return of spontaneous circulation; OR, odds ratio; CI, confidence interval; ICU,

333　Intensive Care Unit; PEA, pulseless electrical activity; VF, ventricular fibrillation; VT,

334　pulseless ventricular tachycardia.

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18

338 **Figure legend**

339 **Figure 1. Flow diagram illustrating the number of patients during the study with respect**

340 **to the location of cardiac arrests.** ROSC, return of spontaneous circulation; ICU, intensive

341 care unit; DNAR, do-not-attempt-resuscitation.

342

19

*Conflict of Interest Statement
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Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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