

1 **Clinical features and outcomes of 2019 novel coronavirus–infected patients with**
2 **cardiac injury**

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20 *Word Count:* : 3115

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1 **Abstract**

2 **Aims**

3 To explore the epidemiological and clinical features of 2019 novel
4 coronavirus(2019-nCoV)-infected patients with cardiac injury .

5 **Methods and results**

6 Data were collected from patients' medical records, and we defined cardiac injury
7 according to cardiac biomarker troponin I level > 0.03 µg/L. Among the 291 patients,
8 15 (5.2%) showed evidence of cardiac injury. Of 15 hospitalized patients with cardiac
9 injury, the median age was 65 years, and 11/15 (73.3%) were men. Underlying
10 cardiovascular diseases in some patients were hypertension (n=7, 46.7%), coronary
11 heart disease (n=3, 20%) and diabetes (n=3, 20%). The most common symptoms at
12 illness onset in patients with cardiac injury were fever (n=11, 73.3%), cough (n=7,
13 46.7%), headache or fatigue (n=5, 33.3%) and dyspnea (n=4, 26.7%). These patients
14 had higher systolic pressures, white blood cell count , neutrophil count , troponin I ,
15 brain natriuretic peptide , D-dimer and lower lymphocyte count , and platelet count,
16 compared with patients without cardiac injury, respectively. Bilateral infiltrates on
17 chest X-ray and elevated C-reactive protein occurred in all patients with cardiac injury.
18 Compared with patients without cardiac injury, patients with cardiac injury were more
19 likely to develop acute respiratory distress syndrome, and receive mechanical
20 ventilation, continuous renal replacement therapy, extracorporeal membrane
21 oxygenation and vasopressor therapy and be admitted to the intensive care unit.

22 **Conclusion**

1 Cardiac injury is a common condition among patients infected with
2 2019-nCoV. Compared with patients without cardiac injury, the clinical outcomes of
3 patients with cardiac injury are relatively worse.

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5 **Keywords:** coronavirus, cardiac injury, clinical features, outcomes

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1 **Introduction**

2 The 2019 novel coronavirus (2019-nCoV), a new fatal virus that emerged at the end
3 of 2019, remains prevalent worldwide, especially in mainland China. As of March 11,
4 2020, at least 80969 cases have been diagnosed across mainland China, and 3162
5 people have died secondary to infection with this virus¹. Because there is no specific
6 drug therapy, the virus has caused public panic and great concerns globally. Although
7 we know that infection with 2019-nCoV can lead to pneumonia, acute renal injury,
8 acute respiratory distress syndrome (ARDS), and shock, we still know little about
9 cardiac injury after infection with 2019-nCoV².

10 Some viral infections are associated with cardiac injury³. Previous studies have
11 indicated that cardiac damage by coronavirus is relatively mild, even with the most
12 fatal coronaviruses, middle east respiratory syndrome and sudden acute respiratory
13 syndrome^{4, 5}. However, as a new coronavirus, we do not know if 2019-nCoV is
14 harmful to the heart; the results from current studies are inconsistent. Chinese
15 scientists have found no obvious damage to heart tissue caused by 2019-nCoV,
16 according to autopsy results⁶; however, other studies have reported that patients
17 infected with 2019-nCoV often suffered cardiac injury^{7 8 9}. The relationship between
18 cardiac injury and the risk of death among people infected with 2019-nCoV has not
19 been clarified. Research is urgently needed to explore the clinical features and
20 outcomes of 2019-nCoV-infected patients with cardiac injury.

21 Our study summarized the clinical characteristics of 2019-nCoV-infected patients
22 with cardiac injury to provide insight into the prevention and treatment of heart

1 disease, in these patients.

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3 **Material and methods**

4 We performed a retrospective study of the clinical characteristics of confirmed corona
5 virus disease 2019(COVID-19)cases from 10 January 2020 to 24 February 2020. We
6 identified 291 patients with confirmed 2019-nCoV infections according to laboratory
7 testing after admission to hospital. The definitions of confirmed human infection with
8 2019-nCoV are based on the World Health Organization interim guidelines¹⁰. Only
9 patients with a laboratory-confirmed infection were included in the present analysis.
10 This study complies with the Declaration of Helsinki and was approved by the ethics
11 commissions of the Guangzhou Eighth people's hospital, with a waiver of informed
12 consent.

13 The research team of the Department of Cardiology, Guangzhou Eighth People's
14 Hospital analysed patients' medical records. Epidemiological, clinical, laboratory and
15 radiological characteristics and treatment, and outcomes data were extracted from
16 patients' electronic medical records. The data were reviewed by a trained team of
17 doctors in the hospital who recorded patients' demographic data, laboratory findings,
18 exposure history, comorbidities, symptoms and treatment measures.

19 Throat swab specimens were collected from all patients at admission, and
20 2019-nCoV ribonucleic acid was detected by real-time polymerase chain reaction
21 within 3 hours, as in a previous study. Virus detection was repeated twice every 24
22 hours for 3 days.

23 Cardiac injury was diagnosed if the serum levels of troponin I (TNI) were above

1 the 99th percentile of the upper reference limit ($> 0.03 \mu\text{g/L}$) using the Access
2 AccuTnI+3 test (Beckman Coulter Inc., Brea, CA, USA). The highest level of TNI
3 was used to evaluate the degree of myocardial injury. Unless otherwise specified, all
4 values are the first data after admission, and if the index was measured more than
5 twice, we chose the highest value for analysis. Symptoms, ARDS and intensive care
6 unit (ICU) admission were recorded, and we defined ARDS severity according to the
7 international guidelines for community-acquired pneumonia¹¹. Preexisting cardiac
8 conditions were defined as congestive heart failure, diabetes, arrhythmia or ischemic
9 heart disease and hypertension.

10 **Statistical Analysis**

11 Continuous variables were expressed as mean \pm standard deviation for normally
12 distributed data or as median (interquartile range, IQR) for skewed distributions.
13 Frequency data were presented as proportions. We compared continuous variables
14 using Student's t test or the Mann-Whitney U test when appropriate, whereas
15 differences in categorical variables were assessed using the Chi-square test or Fisher's
16 exact test.

17 All analyses were performed using SPSS 25.0 (IBM Corp. Armonk, NY, USA).
18 Statistical charts were created using GraphPad Prism 7 software (GraphPad, San
19 Diego, CA, USA), and a two-tailed p -value < 0.05 was considered statistically
20 significant.

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22 **Results**

1 **1. Epidemiological features of 2019-nCoV- infected patients with cardiac**

2 **Injury**

3 A total of 291 patients from Guangzhou Eighth People's Hospital were included in the
4 final analysis, and 15/219 patients (5.2%) had cardiac injury. Patients with cardiac
5 injury had a higher mean age than these without cardiac injury. The median age was
6 65 years (interquartile range, 55–72), and 11/15 (73.3%) were men. Patients with
7 cardiac injury had a higher proportion of preexisting cardiac conditions such as
8 hypertension (46.6%) and coronary heart disease (20%). The epidemiological
9 characteristics of the study participants are presented in Table 1.

10 **2. Clinical features and laboratory findings of 2019-nCoV-infected patients with** 11 **cardiac injury**

12 2019-nCoV-infected patients with or without cardiac injury had similar symptoms.
13 The most common symptoms at illness onset were fever (n = 11, 73.3%), cough (n =
14 7, 46.7%), headache or fatigue (n = 5, 33.3%) and dyspnea (n = 4, 26.6%). No
15 patients with cardiac injury complained of chest pain and palpitation, and the values
16 for most of the laboratory results were within the normal ranges. However, patients
17 with cardiac injury had higher systolic blood pressure (132 mmHg vs 124 mmHg),
18 White blood cell count ($5.6 \times 10^9/L$ vs $5.2 \times 10^9/L$), neutrophil count ($4.1 \times 10^9/L$ vs
19 $3.0 \times 10^9/L$), troponin I (0.07 ug/L vs 0.003 ug/L), brain natriuretic peptide (245.5
20 pg/mL vs 18.5 pg/mL), D-dimer (2430 mg/L vs 1090 mg/L) and lower
21 lymphocyte counts ($1.1 \times 10^9/L$ vs $1.6 \times 10^9/L$) and platelet counts ($165 \times 10^9/L$ vs
22 $208 \times 10^9/L$) vs patients without cardiac injury, respectively. However, in all patients

1 with cardiac injury, C-reactive protein levels were elevated, and patients had bilateral
2 infiltrates on chest X-ray. The clinical features and selected laboratory findings of the
3 study participants are presented in Table 2.

4 **3.Treatments and outcomes of 2019-nCoV-infected patients with cardiac Injury**

5 Complications included ARDS (20%) and severe pneumonia (73.3%), and these were
6 common in patients with cardiac injury. A greater proportion of patients with cardiac
7 injury required tracheal cannula (46.7% vs 0.4% , $P<0.0001$) , invasive mechanical
8 ventilation (53.3% vs 8.3%; $p < 0.0001$), continuous renal replacement therapy
9 (33.3% vs 0%; $p < 0.0001$), extracorporeal membrane oxygenation (26.7% vs 0%; $p <$
10 0.0001), vasopressor therapy (20% vs 0.4%; $p < 0.0001$) and admission to the ICU
11 (73.3% vs 5.4%; $p < 0.0001$) compared with patients without cardiac injury,
12 respectively. One patient with cardiac injury died during the study. Treatments and
13 outcomes of 2019-nCoV-infected patients with cardiac injury are shown in Table 3.

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15 **Discussion**

16 To our knowledge, this is one of largest studies to systematically investigate cardiac
17 injury in hospitalized patients with 2019-nCoV infection. In this retrospective
18 single-centre study, a small proportion (5.2%) of patients with 2019-nCoV infection
19 were diagnosed with cardiac injury. Our results showed that 2019-nCoV-infected
20 patients with cardiac injury had worse clinical outcomes compared with patients
21 without cardiac injury.

22 Cardiac injury is common with infections caused by influenza virus, Coxsackie

1 virus and other viruses, although viral-induced cardiac damage is relatively mild ³.
2 Even the fatal coronaviruses that caused middle east respiratory syndrome and sudden
3 acute respiratory syndrome resulted in minimal heart damage ^{4,5}. 2019-nCoV is a
4 new coronavirus, and it is unclear whether it causes serious heart damage. Recent
5 studies have yielded inconsistent results. Xu et al found that there was no obvious
6 heart damage in autopsy examinations of patients with 2019-nCoV-induced
7 pneumonia⁶. However, other studies found that patients with 2019-nCoV-induced
8 pneumonia also developed cardiac injury ^{7 8 9}. To ensure the accuracy of our cardiac
9 injury evaluation, we chose TNI as the only evaluation index. As a gold standard to
10 evaluate cardiac injury, TNI is more accurate than creatine kinase-MB and
11 electrocardiography. Our study found that a small proportion of 2019-nCoV-infected
12 patients (5.2%) developed cardiac injury, which is a lower rate than in previous
13 studies ⁹. This result may be related to using TNI as the only evaluation index in this
14 study. 2019-nCoV-infected patients with cardiac injury in our study were usually older
15 (median age: 62 y) and often had pre-existing heart disease (hypertension, coronary
16 heart disease). Furthermore, older patients with chronic disease are more likely to be
17 critically ill ⁹. Our results showed that patients with a history of heart disease are at
18 increased risk of serious illness or death if they are infected with 2019-nCoV.

19 The mechanism of cardiac injury in patients infected with 2019-nCoV is unclear.
20 In a recent study, autopsy examinations failed to detect 2019-nCoV in heart tissue,
21 and the authors found no other substantial damage to the heart tissue ⁶. However,
22 increased numbers of studies have indicated an association between 2019-nCoV

1 infection and cardiac injury¹². To explain these inconsistencies, severe infection,
2 hypoxia and mechanical ventilation settings may be associated with cardiac injury,
3 and these common conditions in patients infected with 2019-nCoV may partly explain
4 the heart damage. It is also very possible that the viral invasion of 2019-nCoV to the
5 heart does not occur directly, but indirectly, via the inflammatory response. Severe
6 2019-nCoV infection may trigger an exaggerated immune response. This finding was
7 confirmed by autopsy results⁶, which showed that overactivation of T cells accounts,
8 in part, for the severe immune injury. Another study showed that 2019-nCoV-infected
9 patients admitted to the ICU have higher cytokine levels (interleukin 2, interleukin 7
10 and other cytokines) compared with patients not admitted to the ICU¹³. According to
11 these findings, we hypothesize that 2019-nCoV may promote cardiac injury by an
12 inflammatory reaction, but this hypothesis must be explored further.

13 Our study showed that during COVID-19 epidemics, cardiac injury was
14 associated with clinical outcomes for 2019-nCoV -infected patients. The proportion of
15 patients requiring non-invasive ventilator support and extracorporeal membrane
16 oxygen, admission to ICU and developing ARDS was significantly higher in patients
17 with cardiac injury compared with patients without cardiac injury. Cardiac injury is a
18 potential indicator of risk stratification for 2019-nCoV-infected patients.

19 **Limitations**

20 There are several limitations in our study. First, this study was a single-centre study
21 involving a small number of patients, and evaluating more medical records is needed
22 to support our conclusions. Second, because our patients were from Guangzhou City,

1 only, different clinical features of patients with heart injury from other geographic
2 areas may be found in future studies. Third, of the 291 patients, some were still
3 hospitalized at submission of this manuscript. Therefore, it is difficult to assess
4 patients' long-term prognosis, and it is necessary to continue to observe the natural
5 history of the disease.

6 **Conclusions**

7 Cardiac injury is a common condition among patients infected with
8 2019-nCoV. Compared with patients without cardiac injury, the clinical outcomes of
9 patients with cardiac injury are relatively worse. Cardiac injury is a potential
10 prognostic risk indicator for patients infected with 2019-nCoV.

11

12 **Acknowledgements**

13 The authors had full access to all of the data in the study and take responsibility for
14 the integrity of the data and the accuracy of the data analysis. Study concept and
15 design: Youbin Liu, Zhongwei Hu, Zhihui Qin and Jinglong Li. Acquisition of data:
16 Dehui Liu, Huafeng Song, Chunlin Chen, Mingfang Lv, Xing Pei, Jinglong
17 Li. Analysis and interpretation of data: Dehui Liu, Huafeng Song, Chunlin Chen,
18 Mingfang Lv, Xing Pei, Jinglong Li. Drafting of the manuscript: Youbin Liu and
19 Jinglong Li. Critical revision of the manuscript for important intellectual content:
20 Youbin Liu, Dehui Liu, and Jinglong Li. Statistical analysis: Youbin Liu and Jinglong
21 Li. Administrative, technical, or material support: Dehui Liu, Huafeng Song, Chunlin
22 Chen, Mingfang Lv, Xing Pei, Jinglong Li. Supervision: Youbin Liu, Zhongwei

1 Hu ,Zhihui Qin and Jinglong Li.

2 **Conflict of Interest**

3 None declared

4 **Fundings**

5 None

6 **References**

- 7 1. <https://www.who.int> Wmw. (accessed March 11, 2020).
- 8 2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu
9 T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang
10 R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel
11 coronavirus in Wuhan, China. *Lancet* 2020;**395**(10223):497-506.
- 12 3. Pawlak A, Gil KE, Gil RJ. Viral heart disease. *Kardiol Pol* 2016;**74**(4):307-13.
- 13 4. Alsaad , Hajeer AHAB, M , Al Moaiqel, M , Al Oudah, N , Al Ajlan, A. Histopathology of
14 Middle East respiratory syndrome coronavirus (MERS-CoV) infection - clinicopathological and
15 ultrastructural study. *Histopathology* 2018;**72**(3):516-524.
- 16 5. Ding Y, Wang H, Shen H, Li Z, Geng J, Han H, Cai J, Li X, Kang W, Weng D, Lu Y, Wu D,
17 He L, Yao K. The clinical pathology of severe acute respiratory syndrome (SARS): a report
18 from China. *J Pathol* 2003;**200**(3):282-9.
- 19 6. Zhe Xu LS, Yijin Wang,Jiyuan Zhang,Lei Huang,Chao Zhang. Pathological findings of
20 COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med* 2020.
- 21 7. Huayan Xu KH, Hong Xu, Zhenlin Li, Huizhu Chen, Na Zhang. Acute Myocardial Injury of
22 Patients with Coronavirus Disease 2019. medRxiv preprint doi:

1 <https://doi.org/10.1101/2020.02.06.20020974> 2020.

2 8. Chaomin Wu XH, Jianxin Song, Chunling Du, Jie Xu, Dong Yang. Heart injury signs are
3 associated with higher and earlier mortality in coronavirus disease 2019 (COVID-19). medRxiv
4 preprint doi: <https://doi.org/10.1101/2020.02.06.20020974> 2020.

5 9. Xiaobo Yang YY, Jiqian Xu, Huaqing Shu, Jia'an Xia, Hong Liu, Yongran Wu. Clinical
6 course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a
7 single-centered, retrospective, observational study. 2020.

8 10. WHO. Clinical management of severe acute respiratory infection when Novel coronavirus
9 (nCoV) infection is suspected: interim guidance.
10 [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infect](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected)
11 [ion-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected). 2020.

12 11. Ranieri VM RG, Thompson BT, et al;. ARDS Definition Task Force. Acute respiratory
13 distress syndrome: the Berlin definition. JAMA 2012;**307**(23).

14 12. He WGZNYHWLCOJ. Clinical characteristics of 2019 novel coronavirus infection in
15 China. medRxiv preprint doi: <https://doi.org/10.1101/2020.02.06.20020974> 2020.

16 13. Suxin Wan QY, Shibing Fan, Jinglong Lv, Xianxiang Zhang, Lian Guo. Characteristics of
17 lymphocyte subsets and cytokines in peripheral blood of 123 hospitalized 2 patients with 2019
18 novel coronavirus pneumonia (NCP). medRxiv preprint doi:
19 <https://doi.org/10.1101/2020.02.10.20021832> 2020.

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1 Table 1. Epidemiological features of 2019-nCoV-infected patients with cardiac
 2 injury.

Variables	All patients (n=291)	With cardiac injury(n=15)	Without cardiac injury(n=276)	P
Age (Y),	48.1 (34-62)	65(55-72)	47(33-61)	0.001*
Male, N (%)	133(45.7)	11 (73.3)	122 (44.2)	0.03*
Exposure history in Wuhan	149(51.2)	8(53.3)	141(51.1)	1
Preexisting condition, N (%)				
Diabetes	22(7.6)	3(20)	19(6.9)	0.09
Hypertesion	54(18.5)	7(46.7)	47(17)	0.01*
CHD	12(4.1)	3(20)	9(3.3)	0.02*
Heart failure	1(0.3)	1(6.7)	0(0)	0.051
Arrhythmia	2(0.7)	1(6.7)	1(0.4)	1.006

3 CHD :coronary heart disease.Values are numbers (percentages) unless stated otherwise

4 *P<0.05

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1 Table 2. Clinical features and laboratory findings of 2019-nCoV-infected patients with
2 cardiac injury.

Variables	Normal	All patients	With cardiac	Without cardiac	P
	range	(n=291)	injury(n=15)	injury(n=276)	
Cough, N (%)	-	164(56.4)	7(46.7)	157(56.9)	0.44
Fever, N (%)	-	193(66.3)	11(73.3)	182(65.9)	0.78
Headache/Fatigue, N (%)	-	53(18.2)	5(33.3)	48(17.4)	0.16
Dyspnea, N (%)	-	33(11.3)	4(26.7)	29(11)	0.08
Chest pain, N (%)	-	1(0.3)	0(0)	1(0.4)	1
palpitation, N (%)	-	3(1)	0(0)	3(1.1)	1
Heart rate (bpm)	60-100	84(78-92)	81(72-96)	84(78-92)	0.44
Highest temperature (°C)	36.3-37.3	36.9(36.6-37.5)	37.5(36.5-38.8)	36.9(36.6-37.4)	0.06
Systolic pressure(mmHg)	90-139	124(117-136)	132(125-143)	124(116-135)	0.017*
White blood cell count (10E9/L)	4-10	5.22(4.15-6.45)	5.62(5.14-11.51)	5.15(4.1-6.39)	0.023*
Neutrophil count (10E9/L)	1.8-6.3	3.03(2.2-4.0)	4.06(3.7-10.1)	2.96(2.1-3.9)	<0.001*
Lymphocytes count (10E9/L)	1.1-3.2	1.4(1.1-2.0)	0.98(0.8-1.2)	1.5(1.1-2.0)	0.001*

Hemoglobin, g/L	113-151	135(123-147)	122(111-141)	135(124-147)	0.053
Platelets count (10E9/L)	100-300	206(159-248)	165(137-188)	209(160-250)	0.022*
C reactive protein (>10 mg/L,N%)*	<10	112(38.5)	15(100)	97(35)	0.0001*
Troponin I, (ug/L)	<0.03	0.004(0.001-0.008)	0.07(0.04-0.23)	0.003(0.001-0.006)	<0.001*
Brain natriuretic peptide (pg/mL)	0-100	35.5(12.8-111.8)	245.5(42.5-475.5)	18.5(9.3-49.8)	<0.001*
Creatinine, μmol/L	59~104	61.3(49.8-76.5)	68.5(57.8-86.3)	60.8(49-75.6)	0.05
Aspartate aminotransferase (U/L)	13-35	18.6(14.9-26.6)	23.8(18.6-40.9)	18.2(14.5-25.1)	0.25
Alanine aminotransferase (U/L)	7-40	22.1(14.3-34.5)	23.4(13.2-47.8)	22.05(14.3-34.4)	0.40
Creatine kinase (U/L)	50-310	53.5(38-80.25)	51(38-114)	54(38-80)	0.63
D-dimer(mg/L)	<1000	1100(720-1700)	2430(1090-3750)	1090(700-1640)	0.002*
Blood Oxygen Saturation	>94%	98(97-98.8)	97.9(97-99.1)	98(97-98.8)	0.07
Bilateral involvement on chest radiographs, N (%)	-	242(83.1)	15(100)	227(82.2)	0.08

1 Values are numbers / medians (percentages or interquartile ranges) unless stated

2 otherwise.* $P < 0,05$

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1 Table 3. Treatments and outcomes of 2019-nCoV-infected patients with cardiac
 2 injury.

Treatments and outcomes	All patients (n=291)	With cardiac injury(n=15)	Without cardiac injury(n=276)	p
Tracheal cannula,N(%)	8(2.7)	7(46.7)	1(0.4)	<0.00*
IMV,N(%)	31(10.7)	8(53.3)	23(8.3)	<0.00*
Vasopressor therapy,N(%)	4(1.4)	3(20)	1(0.4)	<0.00*
CRRT,N(%)	5(1.7)	5(33.3)	0 (0)	<0.00*
ECMO,N(%)	4(1.4)	4(26.7)	0(0)	<0.00*
ARDS,N(%)	3(1)	3(20)	0(0)	<0.00*
Severe pneumonia,N(%)	29(9.9)	11(73.3)	18(6.5)	<0.00*
Admission to ICU,N(%)	26 (8.9)	11 (73.3)	15 (5.4)	<0.00*
Death,N(%)	1 (0.3)	1 (6.7)	0 (0)	0.05

3 CRRT :continuous renal replacement therapy: ECMO: extracorporeal membrane oxygenation.ICU: intensive care
 4 unit. ARDS : acute respiratory distress syndrome. IMV:Invasive mechanical ventilation. Values are numbers
 5 (percentages) of patients.* $P < 0.0001$