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Use of high-flow nasal cannula and noninvasive ventilation in patients with COVID-19: A multicenter observational study

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ABSTRACT

Background: The use of high-flow nasal cannula (HFNC) and noninvasive ventilation (NIV) in patients with COVID-19 is debated.
Methods: This study was performed in four hospitals of China from January to March 2020. We retrospectively enrolled 23 and 13 COVID-19 patients who used HFNC and NIV as first-line therapy, respectively.
Results: Among the 23 patients who used HFNC as first-line therapy, 10 experienced HFNC failure and used NIV as rescue therapy. Among the 13 patients who used NIV as first-line therapy, one (8%) used HFNC as rescue therapy due to NIV intolerance. The duration of HFNC + NIV (median 7.1, IQR: 3.5–12.2 vs. 7.3, IQR: 5.3–10.0 days), intubation rate (17% vs. 15%) and mortality (4% vs. 8%) did not differ between patients who used HFNC and NIV as first-line therapy. In total cohorts, 6 (17%) patients received intubation. Time from initiation of HFNC or NIV to intubation was 8.4 days (IQR: 4.4–18.5). And the time from initiation of HFNC or NIV to termination in patients without intubation was 7.1 days (IQR: 3.9–10.3). Among all the patients, C-reactive protein was independently associated with intubation (OR = 1.04, 95% CI: 1.01–1.07). In addition, no medical staff got nosocomial infection who participated in HFNC and NIV management.
Conclusions: In critically ill patients with COVID-19 who used HFNC and NIV as first-line therapy, the duration of HFNC + NIV, intubation rate and mortality did not differ between two groups. And no medical staff got nosocomial infection during this study.

1. Introduction

At the end of 2019, a new coronavirus, now named severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), was first isolated at Wuhan, China [1]. The coronavirus causes a cluster of acute respiratory illness, now named coronavirus disease 2019 (COVID-19) [2]. It has been demonstrated that the most dangerous feature of COVID-19 was person-to-person transmission [3]. With the spread of the epidemic, many countries have reported confirmed cases associated with SARS-Cov-2. On March 11, 2020, the World Health Organization (WHO) declared the outbreak of COVID-19 was a global pandemic.

In the COVID-19 population, 14% of the patients were categorized as severe cases and 5% as critical cases [4]. A systematic review and meta-analysis has pooled 31 articles involving 46,959 cases with COVID-19 and reported that the incidence of ICU admission was 29.3% [5]. At the early stage, the high-flow nasal cannula (HFNC) or noninvasive ventilation (NIV) was used in 24% of hospitalized patients [2]. And in the critical ill patients, the use of HFNC and NIV was 31% and 37%, respectively [6]. In Lombardy Region, Italy, the NIV was used in 11% of ICU patients [7]. In Seattle Region, USA, the HFNC was used in 42% of critically ill patients [8]. However, these studies failed to report how the HFNC or NIV was used. Here, we aimed to report the clinical features, settings and outcomes of HFNC and NIV in patients with COVID-19.

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2. Methods

This was a retrospective observational study performed in four hospitals of China from January to March 2020 (the public health clinical center of Chengdu, the Central Hospital of Dazhou, Yongchuan Hospital of Chongqing Medical University and Chongqing Public Health Medical Center). In the suspected patients, the real-time reverse transcription polymerase chain reaction (RT-PCR) assay was performed according to the guideline made by our National Health Commission [9]. The COVID-19 was confirmed by a positive RT-PCR. All the patients with a confirmed COVID-19 were candidates to our study. We enrolled all the patients who used HFNC or NIV as first-line therapy. Among the HFNC patients, 17 cases extracted from a previous study were secondarily analyzed [10]. This study was approved by the local ethics committee and institutional review board (the First Affiliated Hospital of Chongqing Medical University, No. 20200201). Given its observational nature, informed consent was waived.

The application of NIV and HFNC was in the negative pressure ward or intensive care unit (ICU). To protect the medical staff, the N95 respirator, eye protection (mask with a visor), disposable gown, disposable surgical gloves, and disposable shoe covers were provided. Before entering the ward, all the medical staffs had wore these devices and checked each other.

NIV was managed according to current guidelines and the experts' suggestions [11-14]. Face mask was the first choice to delivery the NIV to the patients. Optimal size of the mask was selected based on the face type in each patient. Hearted humidification was provided to improve oral or nasal dryness. The initial continuous positive airway pressure (CPAP) or positive end expiratory pressure (PEEP) was 4 cm H_2O. When the patient tolerated this pressure, it was gradually increased to improve the oxygenation. The initial inspiratory pressure was 8–10 cm H_2O. When the patient tolerated the initial pressure, it was gradually increased to relieve dyspnea. The fraction of inspired oxygen (FiO_2) was titrated to main the peripheral oxygen saturation (SpO_2) more than 93%. When the NIV intolerance occurred, HFNC could be used as a rescue therapy if the patient did not require urgent intubation.

HFNC was managed also based on current consensus and the experts' suggestions [13-15]. The temperature was set between 31 and 37 °C, the flow was set between 30 and 60 L/min, and the FiO_2 was set to maintain the SpO_2 more than 93%. When the HFNC failed to maintain the oxygenation or relieve dyspnea, the NIV as a rescue therapy was an alternative if the patient did not require urgent intubation.

When the respiratory distress was relieved and the oxygenation was improved, the intermittent use of NIV or HFNC was performed. We gradually increased the time of conventional oxygen therapy and shortened the duration of HFNC or NIV until it was totally weaned. When the respiratory distress and oxygenation progressively deteriorated, intubation for invasive mechanical ventilation was performed based on the criteria made by our Society of Critical Care Medicine [16]. However, the intubation was decided at the discretion of the attending physicians.

Before the use of HFNC or NIV, the demographics, vital signs, laboratory tests and the arterial blood gas tests were collected. The baseline PaO_2/FiO_2 was measured with the use of conventional oxygen therapy before the use of HFNC or NIV. We estimated the FiO_2 as follows: FiO_2 (%) = 21 + 4*fow (L/min) [17]. Using these data, the acute physiology and chronic health evaluation II (APACHE II) score and sequential organ failure assessment (SOFA) score were calculated.

Data were analyzed by statistical software (SPSS 17.0; IBM Corp., Armonk, NY). Student's *t*-test was used to analyze the normally distributed continuous variables and Mann–Whitney *U* test was used to analyze the non-normally distributed continuous variables. Chi-squared test or Fisher's exact test was used to analyze the categorical variables. Variables with a p value <.1 in univariate analyses were entered into logistic regression analyses to identify independent risk factors associated with intubation. The ability to predict intubation was tested by the area under the receiver operating characteristic curve (AUC). The value at maximum Youden index was selected as optimal cutoff value [18]. A p value <.05 was considered significant.

3. Results

Among all the enrolled patients, 35 cases were in the negative pressure ward and one was in the ICU. Among them, HFNC was used as first-line therapy in 23 patients and NIV in 13 patients (Fig. 1). The clinical characteristics of the HFNC and NIV patients were summarized in Table 1. The mean age was 65 ± 14 years in HFNC group and 50 ± 14 years in NIV group (p <0.01). The proportion of male was 52% in HFNC group and 92% in NIV group (p = .03). There were no differences in disease severity, the proportion of comorbidity, and the level of oxygenation between the two groups. Patients in HFNC group had higher chlorine, low alanine aminotransferase (ALT) and lower total bilirubin than that in NIV group. Others laboratory tests were no differences between the two groups.

Table 2 shows the settings of the HFNC and NIV at the initial 24 h. In HFNC group, the temperature was around 35 °C, flow was around 40 L/min, and FiO_2 was around 40%. In NIV group, four (31%) patients used continuous positive airway pressure (CPAP) at

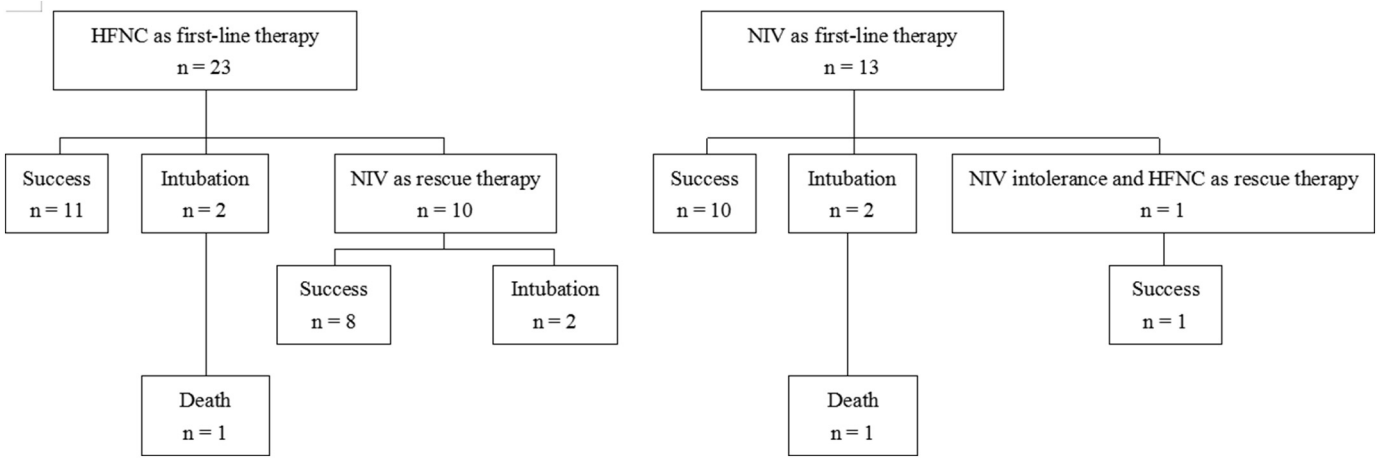

Fig. 1. The flow chart of the enrolled patients.

Table 1
Clinical characteristics of the enrolled patients at initiation of HFNC and NIV

	Total cohort	HFNC	NIV	p
	N = 36	N = 23	N = 13	
Age, years	60 ± 16	65 ± 14	50 ± 14	<0.01*
Male (%)	24 (67%)	12 (52%)	12 (92%)	0.03*
APACHE II score	9 ± 4	10 ± 5	8 ± 2	0.24
SOFA score	4 ± 1	4 ± 2	4 ± 1	0.85
The level of PaO_2/FiO_2				
>200 mmHg	12 (33%)	9 (39%)	3 (23%)	0.47
150–200 mmHg	14 (39%)	10 (44%)	4 (31%)	0.50
100–150 mmHg	10 (28%)	4 (17%)	6 (46%)	0.12
Comorbidity				
Hypertension	9 (25%)	6 (26%)	3 (23%)	>0.99
Diabetes mellitus	4 (11%)	4 (17%)	0 (0%)	0.27
Chronic heart disease	6 (17%)	6 (27%)	0 (0%)	0.07
Chronic respiratory disease	1 (3%)	1 (4%)	0 (0%)	>0.99
Laboratory tests				
White blood cell counts, $\times 10^9$/L	6.3 ± 2.6	5.8 ± 2.2	7.2 ± 3.0	0.12
Neutrophil percentage, %	78 ± 9	77 ± 9	81 ± 8	0.16
Lymphocyte count, $\times 10^9$/L	0.81 ± 0.36	0.78 ± 0.36	0.84 ± 0.37	0.63
Platelet counts, $\times 10^9$/L	187 ± 101	176 ± 95	206 ± 112	0.39
Hemoglobin, mg/dL	123 ± 19	120 ± 19	128 ± 14	0.18
Albumin, g/L	35 ± 4	35 ± 3	37 ± 4	0.08
Potassium, mmol/L	3.8 ± 0.5	3.8 ± 0.5	3.9 ± 0.6	0.56
Sodium, mmol/L	137 ± 5	138 ± 5	135 ± 4	0.14
Chlorine, mmol/L	102 ± 5	103 ± 5	100 ± 3	0.03*
Urea nitrogen, mmol/L	4.9 ± 3.4	5.2 ± 3.9	4.3 ± 2.1	0.47
Creatinine, μmol/L	66 (55–80)	62 (54–71)	77 (58–83)	0.16
ALT, U/L	32 (21–63)	29 (18–41)	55 (28–113)	0.03*
AST, U/L	37 (27–62)	35 (26–48)	39 (34–150)	0.08
Total bilirubin, μmol/L	14 ± 5	12 ± 4	17 ± 5	<0.01*
C-reactive protein, mg/L	56 ± 45	52 ± 40	62 ± 53	0.56
Procalcitonin, ng/mL	0.07 (0.04–0.10)	0.07 (0.04–0.09)	0.08 (0.04–0.19)	0.76

HFNC = high flow nasal cannula, NIV = noninvasive ventilation, APACHE II = acute physiology and chronic health evaluation II, SOFA = sequential organ failure assessment, ALT = alanine aminotransferase, AST = aspartate aminotransferase.
* $p < .05$ for comparison between HFNC and NIV.

1–2 h of NIV but one transitioned to bi-level positive pressure ventilation at 12 h of NIV. The other 9 patients (69%) used bi-level positive pressure ventilation. At 1–2 h of NIV, the inspiratory pressure was 12 cmH_2O (interquartile range [IQR]: 12–15), the positive end expiratory pressure (PEEP) or CPAP was 6 cmH_2O (IQR: 6–9), and the FiO_2 was 40% (IQR: 40–50%). The similar settings were used at 12 h and 24 h of NIV.

There were no differences in vital signs and arterial blood gas tests between HFNC and NIV groups except the respiratory rate (Table 3). At 1–2 h, 12 h and 24 h, the respiratory rate was lower in HFNC group than that in NIV group. The outcomes between the two groups were summarized in Table 4. In HFNC group, 10 (43%) patients used NIV as a rescue therapy. In NIV group, one (8%) used HFNC due to NIV intolerance. There was no difference in the duration of HFNC + NIV between the patients who used HFNC and NIV as first-line therapy (Median 7.1 days, IQR: 3.5–12.2 vs. 7.3 days, IQR: 5.3–10.0, $p = .67$). There was also no difference in intubation rate (17% vs. 15%, p >0.99) and mortality (4% vs. 8%, p >0.99) between the two groups.

Among all the patients, 6 received intubation and 30 avoided intubation (Table 5). In multivariate analyses, only C-reactive protein was independently associated with intubation (Table 6). The AUC for prediction of intubation was 0.92 (95% confidence interval [CI]: 0.77–0.98) (Fig. 2). Using C-reactive protein of 59 mg/L as cutoff value to predict intubation, the sensitivity was 100% and specificity was 79%. In addition, no medical staff got nosocomial infection in our study.

Table 3
Vital signs and arterial blood gas tests at baseline, 1–2 h, 12 h, and 24 h of intervention.

	HFNC	NIV	p
	N = 23	N = 13	
Baseline			
Respiratory rate, breaths/min	26 ± 5	27 ± 6	0.48
Heart rate, beats/min	89 ± 16	89 ± 16	0.99
Mean arterial pressure, mmHg	90 ± 12	91 ± 7	0.77
pH	7.44 ± 0.04	7.47 ± 0.07	0.19
$PaCO_2$, mmHg	35 ± 5	35 ± 5	0.74
PaO_2/FiO_2, mmHg	196 ± 46	165 ± 48	0.06
1–2 h			
Respiratory rate, breaths/min	22 ± 2	27 ± 5	<0.01*
Heart rate, beats/min	88 ± 18	85 ± 16	0.57
Mean arterial pressure, mmHg	88 ± 9	90 ± 6	0.49
pH	7.45 ± 0.04	7.48 ± 0.05	0.07
$PaCO_2$, mmHg	36 ± 5	35 ± 4	0.59
PaO_2/FiO_2, mmHg	210 ± 84	211 ± 78	0.97
12 h			
Respiratory rate, breaths/min	21 ± 2	24 ± 3	0.02*
Heart rate, beats/min	78 ± 16	81 ± 14	0.62
Mean arterial pressure, mmHg	86 ± 8	89 ± 8	0.22
pH	7.45 ± 0.05	7.47 ± 0.04	0.18
$PaCO_2$, mmHg	37 ± 5	34 ± 4	0.19
PaO_2/FiO_2, mmHg	212 ± 60	203 ± 61	0.70
24 h			
Respiratory rate, breaths/min	22 ± 2	25 ± 3	<0.01*
Heart rate, beats/min	79 ± 12	82 ± 16	0.56
Mean arterial pressure, mmHg	89 ± 9	90 ± 11	0.83
pH	7.45 ± 0.04	7.46 ± 0.05	0.72
$PaCO_2$, mmHg	36 ± 5	36 ± 5	0.91
PaO_2/FiO_2, mmHg	224 ± 92	202 ± 65	0.48

HFNC = high flow nasal cannula, NIV = noninvasive ventilation.
* $p < .05$ for comparison between HFNC and NIV.

Table 2
The settings of HFNC and NIV

	1–2 h	12 h	24 h
HFNC			
Temperature,°C	35 (34–35)	35 (34–35)	34 (34–35)
Flow, L/min	40 (33–40)	40 (36–40)	40 (40–40)
FiO_2, %	40 (40–46)	40 (40–41)	40 (35–42)
NIV			
Use of CPAP mode, %	4/13 (31%)	3/13 (23%)	3/12 (25%)
Inspiratory pressure (above zero), cmH_2O	12 (12–15)	12 (12–16)	12 (12–16)
PEEP/CPAP, cmH_2O	6 (6–9)	6 (6–9)	6 (6–10)
FiO_2, %	40 (40–50)	40 (40–48)	40 (40–49)

HFNC = high flow nasal cannula, NIV = noninvasive ventilation, CPAP = continuous positive airway pressure, PEEP = positive end expiratory pressure.

Table 4
Outcomes

	HFNC	NIV	p
	N = 23	N = 13	
Duration of HFNC, days	3.6 (1.6–8.4)	7.0#	–
Duration of NIV, days	5.1 (2.3–7.5)	6.8 (4.5–10.0)	0.26
Duration of HFNC + NIV, days	7.1 (3.5–12.2)	7.3 (5.3–10.0)	0.67
HFNC as rescue therapy, %	–	1 (8%)	–
NIV as rescue therapy, %	10 (43%)	–	–
Intubation, %	4 (17%)	2 (15%)	>0.99
Mortality, %	1 (4%)	1 (8%)	>0.99

HFNC = high flow nasal cannula, NIV = noninvasive ventilation.
#only one patient used HFNC due to NIV intolerance.

Table 5
Comparisons between patients with and without intubation

	Intubation	Without intubation	*p*
	N = 6	*N* = 30	
Age, years	72 ± 14	57 ± 15	0.03*
Male (%)	3 (50%)	21 (70%)	0.38
APACHE II score	13 ± 7	8 ± 3	<0.01*
SOFA score	5 ± 2	3 ± 1	<0.01*
From HFNC or NIV initiation to termination, days	8.4 (4.4–18.5)	7.1 (3.9–10.3)	0.52
Laboratory tests			
White blood cell counts, $\times10^9$/L	4.7 ± 2.0	6.6 ± 2.6	0.08
Neutrophil percentage, %	71 ± 9	80 ± 8	0.02*
Lymphocyte count, $\times10^9$/L	0.95 ± 0.42	0.78 ± 0.35	0.30
Platelet counts, $\times10^9$/L	106 (66–129)	159 (125–275)	<0.01*
Hemoglobin, mg/dL	120 ± 13	124 ± 19	0.62
Albumin, g/L	33 ± 3	36 ± 4	0.11
Potassium, mmol/L	3.6 ± 0.7	3.9 ± 0.5	0.22
Sodium, mmol/L	139 ± 7	136 ± 4	0.15
Chlorine, mmol/L	103 ± 5	102 ± 5	0.68
Creatinine, μmol/L	80 (52–116)	65 (56–77)	0.33
ALT, U/L	35 (16–58)	32 (22–65)	0.63
AST, U/L	62 (44–81)	35 (26–49)	0.03*
Total bilirubin, μmol/L	10 (7–15)	13 (11–18)	0.11
C-reactive protein, mg/L	113 (72–162)	35 (22–57)	<0.01*
Procalcitonin, ng/mL	0.07 (0.04–0.11)	0.07 (0.04–0.12)	>0.99
Vital signs collected at baseline			
Respiratory rate, breaths/min	30 ± 9	25 ± 4	0.06
Heart rate, beats/min	93 ± 17	88 ± 16	0.54
Mean arterial pressure, mmHg	83 ± 10	92 ± 10	0.04*
pH	7.46 ± 0.07	7.45 ± 0.06	0.87
$PaCO_2$, mmHg	36 ± 5	35 ± 5	0.48
PaO_2/FiO_2, mmHg	180 ± 47	186 ± 49	0.81
Vital signs collected at1–2 h of HFNC or NIV			
Respiratory rate, breaths/min	24 ± 6	24 ± 4	0.90
Heart rate, beats/min	91 ± 16	86 ± 18	0.52
Mean arterial pressure, mmHg	86 ± 8	89 ± 8	0.37
pH	7.45 ± 0.06	7.46 ± 0.05	0.71
$PaCO_2$, mmHg	37 ± 7	35 ± 4	0.26
PaO_2/FiO_2, mmHg	179 ± 55	217 ± 86	0.30

HFNC = high flow nasal cannula, NIV = noninvasive ventilation, APACHE II = acute physiology and chronic health evaluation II; SOFA = sequential organ failure assessment, ALT = alanine aminotransferase, AST = aspartate aminotransferase,
* $p < .05$ for comparison between patients with and without intubation.

4. Discussion

Nearly half of the patients who used HFNC as first-line therapy were transitioned to NIV as a rescue therapy. However, only fewer patients who used NIV as a first-line therapy were transitioned to HFNC. The intubation rate and mortality were relatively low. The duration of HFNC + NIV, intubation rate and mortality did not differ between the two groups. Among all the patients, C-reactive protein was independently associated with intubation. And it had high distinguishing power to predict intubation.

In China, use of HFNC ranged from 21% to 31% (pooled incidence: 26%) among the critically ill patients, and the use of NIV ranged from 14% to 37% (pooled incidence: 28%) [6,19,20]. However, the use of HFNC and NIV were largely different between China and other countries. In Lombardy Region, Italy, NIV was used in 11% of ICU patients but no patients used HFNC [7]. In Seattle Region, USA, the HFNC was used in 42% of critically ill patients but none used NIV [8]. Maybe, the availability of the HFNC and NIV, and suggestions or recommendations made by experts or consensus were various between different countries.

In China, the experts have suggested that the HFNC and NIV can be used in COVID-19 patients with $PaO_2/FiO_2 \geq 150$ mmHg, and NIV can be cautiously used in those with PaO_2/FiO_2 between 100 and 150 mmHg [13,14]. The Asian Critical Care Clinical Trials Group has suggested that the HFNC and NIV only can be used in COVID-19 patients with mild acute respiratory distress syndrome (ARDS) [21]. The Surviving Sepsis Campaign COVID-19 subcommittee (most of the experts came from European and USA) has suggested that the HFNC is superior to NIV in COVID-19 patients with acute hypoxemic respiratory failure, and the NIV can be tried with close monitoring if the HFNC is unavailable [22]. However, most of the recommendations were based on the experts' suggestion. The level of evidence is weak. To the best of our knowledge, there were no studies to focus on the use of HFNC or NIV in COVID-19 patients except our previous one paper [10]. Different with the experts' suggestions, 10 patients (17% in HFNC and 46% in NIV) with PaO_2/FiO_2 between 100 and 150 mmHg have used HFNC or NIV as a first-line therapy. And among all the patients, the duration of HFNC + NIV, intubation rate and mortality were similar between two groups. These data provide an important reference for clinical physicians to select respiratory support device on patients with COVID-19.

Among all the patients who used NIV as first-line therapy, the intubation rate was 92% in patients with Middle East respiratory syndrome, 30% in patients with severe acute respiratory syndrome, and 59% in patients with influenza pneumonia [23-25]. In hypoxemic patients whose respiratory failure caused by other reasons, the intubation rate was 36% [26]. However, in our study, the intubation rate was only 15% in COVID-19 patients who used NIV as a first-line intervention. Among the patients who used NIV as a rescue therapy, the intubation rate was 20%. And no medical staff in our study was infected by the airborne transmission. Therefore, the NIV is an alternative respiratory support for COVID-19 patients but all safety measures should be taken.

Early identification of the high-risk patients and early application of intubation decreased mortality [27]. On the contrary, delayed intubation significantly lead to mortality increase both in patients with HFNC and NIV [28,29]. In our study, we found that the C-reactive protein collected at the initiation of HFNC or NIV had high distinguishing power to predict intubation. Therefore, HFNC and NIV should be cautiously used in patients with high level of C-reactive protein. Close monitoring should be taken to avoid delayed intubation.

Table 6
Univariate and multivariate analysis for intubation

	Univariate analysis	*p*	Multivariate analysis	*p*
	OR (95%CI)		OR (95%CI)	
Age, years	1.08 (1.00–1.16)	0.05	—	—
APACHE II score	1.28 (1.03–1.59)	0.02	—	—
SOFA score	2.23 (1.10–4.52)	0.03	—	—
Neutrophil percentage, %	0.87 (0.76–1.00)	0.04	—	—
Platelet counts	0.96 (0.92–1.00)	0.04	—	—
C-reactive protein, mg/L	1.04 (1.01–1.07)	<0.01	1.04 (1.01–1.07)	<0.01
Respiratory rate at baseline, breaths/min	1.16 (0.98–1.36)	0.08	—	—
Mean arterial pressure at baseline, mmHg	0.89 (0.79–1.00)	0.05	—	—

OR = odds ratio, CI = confidence internal, APACHE II = acute physiology and chronic health evaluation II, SOFA = sequential organ failure assessment.

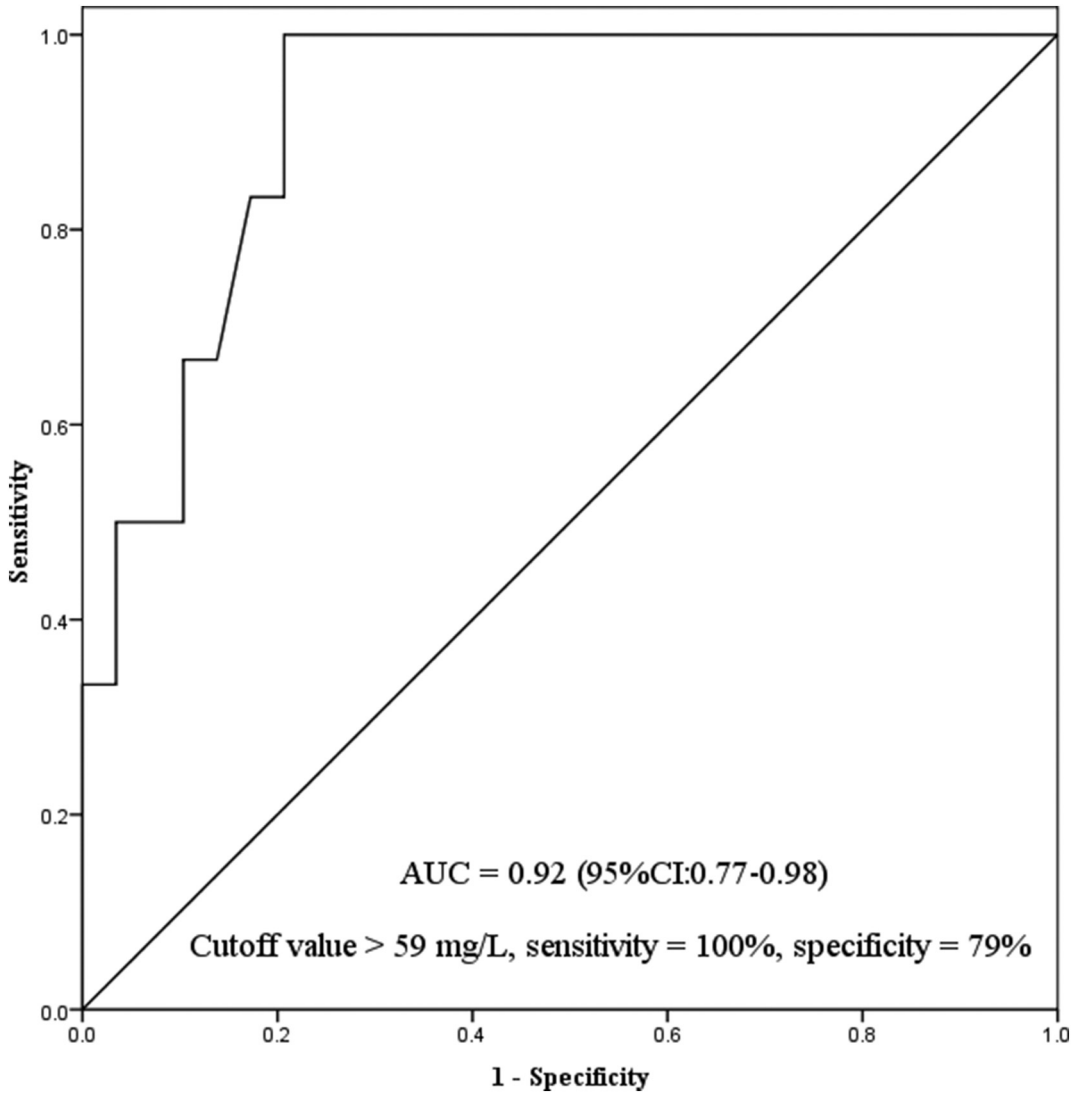

Fig. 2. Prediction of intubation tested by C-reactive protein.

Fear of aerosolized transmission was the major problem during the use of HFNC or NIV in COVID-19 patients. In theory, NIV generates more aerosols than HFNC as NIV usually generates higher pressure than HFNC [30]. In our study, use of HFNC and NIV was in the negative pressure ward or ICU, adequate protective supplies (N95 respirator, eye protector, disposable gown, disposable surgical gloves, disposable shoe covers, etc.) were provided to all the medical staffs, and strict training was applied before contact with the COVID-19 patients. Therefore, no medical staff got nosocomial infection who managed the critically ill patients in our study. Our experience provides a reference on the prevention and control of nosocomial infection when the HFNC or NIV was used in COVID-19 patients.

This study has several limitations. First, this is a retrospective study, the use of the HFNC and NIV was mainly decided based on the experts' suggestions and the physicians' experience. Second, we only enrolled 39 patients in our study. The small sample size may skew the results. Further, studies with larger sample size are required to confirm our results. Third, the median time from initiation of HFNC or NIV to intubation was 8.4 days. As intubation beyond 1–2 days after the initiation of HFNC or NIV is associated with increased mortality [27-29], delayed intubation may occur in our study. Close monitoring is needed to avoid delayed intubation.

5. Conclusions

In critically ill patients with COVID-19, the duration of HFNC + NIV, intubation rate and mortality did not differ between patients who used HFNC and NIV as a first-line therapy. Among all the patients, C-reactive protein was independently associated with intubation. And it had high distinguishing power to predict intubation. In addition, no medical staff got nosocomial infection in our study who managed the HFNC and NIV patients with COVID-19.

Authors' contributions

JD and KW conceived the study, and joined in data collection, data analysis, data interpretation and manuscript preparation, and take responsibility for the content of the manuscript. BXC, XYL, WWS, WZ, JL YSL, YLH and LFP joined in data collection, data analysis, data interpretation and manuscript preparation. All the authors revised the manuscript and approved the final revision.

Declaration of Competing Interest

We declare that we have no competing interests.

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