

The experience of high flow nasal cannula in hospitalized patients with 2019 novel coronavirus-infected pneumonia in Chongqing, China

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Abstract

Background The outbreak of a novel coronavirus (2019-nCoV)-infected pneumonia (NCIP) is currently ongoing in China. Most of the critically ill patients received high flow nasal cannula (HFNC). However, the experience of HFNC in this population is lacking.

Methods We retrospectively collected the NCIP patients who received HFNC in two hospital of Chongqing, China from January 1st to February 18th, 2020. The clinical characteristics were collected. Patients who required upgrading to noninvasive ventilation (NIV) were defined as HFNC failure.

Results We enrolled 17 patients in this study. Of them, 7 patients (41%) experienced HFNC failure (6 required upgrading to NIV, and one to NIV and further to intubation). The HFNC failure rate was 0% (0/6), 57% (4/7) and 75% (3/4) ($p = 0.03$ between 3 groups) in patients with $\text{PaO}_2/\text{FiO}_2 > 200$, 150-200, and < 150 mmHg, respectively. In the successful patients, the respiratory rate, heart rate and $\text{PaO}_2/\text{FiO}_2$ significantly improved from initiation to termination of HFNC (27 ± 3 vs. 21 ± 2 breaths/min, $p < 0.01$; 86 ± 15 vs. 76 ± 12 beats/min, $p = 0.03$; and 213 ± 49 vs. 299 ± 125 mmHg, $p = 0.04$, respectively). However, in the unsuccessful patients, the respiratory rate and $\text{PaO}_2/\text{FiO}_2$ significantly deteriorated (22 ± 3 vs. 25 ± 3 breaths/min, $p = 0.04$; and 160 ± 27 vs. 105 ± 24 mmHg, $p = 0.01$, respectively). When they upgraded to NIV, the $\text{PaO}_2/\text{FiO}_2$ improved after 1-2 h of NIV (105 ± 24 vs. 202 ± 111 mmHg, $p = 0.04$). In the total cohort, only $\text{PaO}_2/\text{FiO}_2$ at baseline was lower in unsuccessful patients than that in successful ones (213 ± 49 vs. 160 ± 27 mmHg, $p = 0.02$).

Conclusions This study firstly provides the experience of how to use HFNC in patients with NCIP. Patients with lower $\text{PaO}_2/\text{FiO}_2$ were more likely to experience HFNC failure. Among the failure patients, most of them can avoid intubation when they were ungraded to NIV.

Introduction

In December 2019, acute respiratory infection due to 2019 novel coronavirus (2019-nCoV), now known as novel coronavirus-infected pneumonia (NCIP), emerged in Wuhan, China [1, 2]. The main symptoms were fever, cough, dyspnea, myalgia, fatigue, and radiographic evidence of pneumonia [2-4]. Human-to-human transmission of NCIP has been reported, even in the incubation period [5-7]. In a hospital, 29% of health care workers and 12% of patients who were already hospitalized for other reasons have been identified as presumed hospital-related transmission and infection [4]. The NCIP has been spread worldwide and many countries have been reported the case of NCIP [8-11]. As of February 11, 2020, 44672 cases with NCIP were confirmed and 1023 cases died in China [12]. The WHO has declared the outbreak of NCIP as a Public Health Emergency of International Concern on January 30, 2020.

In the hospitalized NCIP patients, 20-29% developed acute respiratory distress syndrome (ARDS) [2, 4]. The time from disease onset to shortness of breathing was median 8 days and to development of ARDS was median 10.5 days [2]. In the hospitalized patients, the rate of development of ARDS ranged from 20-29% [2, 4]. Most of the patients received oxygen therapy. High flow nasal cannula (HFNC) is one of the oxygen therapies for critically ill patients [13]. However, to the best of our knowledge, there were no studies to report the use of HFNC in hospitalized NCIP patients. Here, we aimed to report the experience of HFNC in this population.

Methods

This was a retrospective observational study performed in two hospital of Chongqing, China. The 2019-nCoV was confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR) assay [4]. The diagnosis of NCIP was based on clinical characteristics, chest imaging and RT-PCR assay. We enrolled all the patients who received HFNC due to NCIP in two hospitals (Yongchuan Hospital of Chongqing Medical University and Chongqing

Public Health Medical Center) from January 1st to February 18th, 2020. The study protocol was approved by the local ethics committee and institutional review board (approval number 20200201). As this was a retrospective study, the informed consent was waived. The critically ill patients who received HFNC (Fisher & Paykel, Auckland, New Zealand or HUMID-BM, Respiration Medical, Shen Yang, China) were managed by their attending physicians. The temperature was set at 31 to 37°C, the flow was set at 30 to 60 L/min, and the fraction of inspired oxygen concentration (FiO_2) was set to maintain the SpO_2 more than 93%. The continuous use of HFNC was required for all the patients at the initial phase. When the respiratory failure was reversed, the intermittent use of HFNC was performed until the HFNC was totally weaned. However, if the respiratory failure progressively deteriorated, the attending physicians determined to upgrade the treatment to noninvasive ventilation or invasive mechanical ventilation. Patients who required upgrading treatment were defined as HFNC failure.

Before the use of HFNC, we collected the demographics, vital signs, laboratory tests, and the arterial blood gas tests. We also assessed the disease severity by acute physiology and chronic health evaluation II (APACHE II) score and organ failure by sequential organ failure assessment (SOFA) score. At 1-2 h and termination of HFNC, we also collected the vital signs and arterial blood gas tests. Among the patients who experienced HFNC failure and upgraded to NIV, these variables were also collected at 1-2 h and termination of NIV. Normally distributed continuous variables were reported as mean value and standard deviation. The differences between two groups were analyzed by unpaired Student's t test. Non-normally distributed continuous variables were reported as median value and interquartile range. The differences between two groups were analyzed by Mann-Whitney U test. The differences between different time points within group were analyzed by the use of paired Student's t test. Categorical variables were reported as number and

percentage, and analyzed using the Chi-squared test or Fisher's exact test. A p value < 0.05 was considered significant.

Results

We screened 291 patients with NCIP for eligibility (Fig. 1). Finally, 17 NCIP patients who used HFNC due to acute respiratory failure were enrolled. The age was 65 ± 12 years, and seven (41%) were men. The comorbidity, laboratory tests and parameters provided by HFNC were summarized in Table 1. Among the 17 NCIP patients, 7 (41%) experienced HFNC failure and were upgraded to NIV. Among the unsuccessful cases, one patient was upgraded to NIV and further to intubation.

Table 1
Clinical characteristics of the enrolled patients

	Total cohort N = 17	HFNC success N = 10	HFNC failure N = 7	p
Age, years	65 ± 12	62 ± 13	70 ± 8	0.17
Male (%)	7 (41%)	4 (40%)	3 (43%)	> 0.99
APACHE II score	8 ± 4	8 ± 4	9 ± 4	0.55
SOFA score	3 ± 1	3 ± 1	4 ± 1	0.19
Duration of HFNC, hours	74 (34-156)	84 (65-189)	26 (12-86)	0.11
Comorbidity				
Hypertension	3 (18%)	2 (20%)	1 (13%)	> 0.99
Diabetes mellitus	3 (18%)	2 (20%)	1 (13%)	> 0.99
Chronic heart disease	3 (18%)	2 (20%)	1 (13%)	> 0.99
Laboratory tests				
White blood cell counts, ×10 ⁹ /L	5.8 ± 2.3	6.8 ± 2.3	4.4 ± 1.3	0.03*
Lymphocyte count, ×10 ⁹ /L	0.74 ± 0.32	0.78 ± 0.40	0.70 ± 0.17	0.61
Platelet counts, ×10 ⁹ /L	189 ± 167	209 ± 121	160 ± 83	0.37
Hemoglobin, mg/dL	126 ± 16	124 ± 17	129 ± 16	0.53
Albumin, g/L	35 ± 4	35 ± 4	36 ± 3	0.42
Potassium, mmol/L	3.8 ± 0.5	3.7 ± 0.4	3.9 ± 0.7	0.55
Sodium, mmol/L	137 ± 3	138 ± 2	135 ± 4	0.13
Chlorine, mmol/L	101 ± 3	103 ± 2	99 ± 3	0.04*
Creatinine, μmol/L	62 ± 12	63 ± 11	61 ± 14	0.71
Total bilirubin, μmol/L	12 ± 4	12 ± 5	13 ± 2	0.84
C-reactive protein, mg/L	42 ± 28	30 ± 21	58 ± 30	0.04*
Procalcitonin, ng/mL	0.07 ± 0.04	0.06 ± 0.03	0.08 ± 0.04	0.38
Parameters provided by HFNC				
Temperature at 1-2 h, °C	34.5 ± 0.5	34.6 ± 0.5	34.4 ± 0.5	0.52
Flow at 1-2 h, L/min	39 ± 6	36 ± 6	42 ± 6	0.06
FiO ₂ at 1-2 h, %	42 ± 5	40 ± 4	44 ± 6	0.06
Temperature at termination, °C	34.6 ± 0.5	34.7 ± 0.5	34.4 ± 0.5	0.29
Flow at termination, L/min	41 ± 8	37 ± 5	46 ± 7	< 0.01*
FiO ₂ at termination, %	46 ± 17	38 ± 5	59 ± 21	< 0.01*
APACHE II = acute physiology and chronic health evaluation II; SOFA = sequential organ failure assessment, HFNC = high flow nasal cannula				
*p < 0.05 for comparison between patients with HFNC success and failure				

At baseline, the number of patients with PaO₂/FiO₂ > 200, between 150 and 200, and < 150 mmHg were 6, 7 and 4, respectively. No HFNC failure occurred in patients with PaO₂/FiO₂ > 200 mmHg (Fig. 2). However, the failure rate was 57% in patients with PaO₂/FiO₂ between 150 and 200 mmHg and it further increased to 75% in patients with PaO₂/FiO₂ < 150 mmHg.

The comparisons between patients with HFNC success and failure were summarized in

Fig. 3. At the baseline, the unsuccessful patients had lower respiratory rate than successful patients, but it was much higher at the termination of HFNC. In the unsuccessful patients, the PaO₂/FiO₂ was lower than that in successful patients at all the time points.

In the successful group, the respiratory rate was 27 ± 3 breaths/min at baseline (Table 2). After 1-2 h of HFNC, it was decreased to 23 ± 3 breaths/min (p = 0.03 for comparison with baseline), and it further decreased to 21 ± 2 breaths/min at the termination of HFNC (p < 0.01 for comparison with baseline). The heart rate also decreased from baseline to termination (86 ± 15 vs. 76 ± 12, p = 0.03). The PaO₂/FiO₂ also significantly improved from initiation to termination (213 ± 49 vs. 299 ± 125, p = 0.04).

Table 2
Vital signs and arterial blood gas tests at baseline, 1-2 h and termination of HFNC

	Baseline	1-2 h of HFNC	Termination	p ^a	p ^b
Successful patients					
RR, breaths/min	27 ± 3	23 ± 3	21 ± 2	0.03*	< 0.01*
HR, beats/min	86 ± 15	85 ± 21	76 ± 12	0.72	0.03*
SBP, mmHg	128 ± 12	120 ± 11	118 ± 7	0.06	0.05
DBP, mmHg	76 ± 8	74 ± 8	72 ± 6	0.67	0.02*
pH	7.43 ± 0.04	7.45 ± 0.04	7.45 ± 0.04	0.21	0.06
PaCO ₂ , mmHg	37 ± 4	37 ± 5	39 ± 4	0.30	0.04*
PaO ₂ /FiO ₂ , mmHg	213 ± 49	252 ± 105	299 ± 125	0.21	0.04*
FiO ₂ , %	35 ± 7	40 ± 4	38 ± 5	0.05	0.25
Unsuccessful patients					
RR, breaths/min	22 ± 3	22 ± 2	25 ± 3	0.43	0.04*
HR, beats/min	80 ± 11	86 ± 10	78 ± 12	0.24	0.51
SBP, mmHg	115 ± 16	118 ± 16	125 ± 13	0.09	0.10
DBP, mmHg	66 ± 13	70 ± 10	73 ± 6	0.12	0.19
pH	7.47 ± 0.03	7.47 ± 0.04	7.48 ± 0.02	0.28	0.39
PaCO ₂ , mmHg	34 ± 3	33 ± 3	34 ± 3	0.35	0.81
PaO ₂ /FiO ₂ , mmHg	160 ± 27	151 ± 32	105 ± 24	0.39	0.01*
FiO ₂ , %	39 ± 6	44 ± 6	60 ± 20	0.03*	0.03*
RR = respiratory rate, HR = heart rate, SBP = systolic blood pressure, DBP = diastolic blood pressure, HFNC = high flow nasal cannula					
p ^a for comparison between baseline and 1-2 h of HFNC.					
p ^b for comparison between baseline and termination of HFNC.					
*p < 0.05					

In the unsuccessful group, the clinical signs deteriorated at the termination of HFNC. The respiratory rate increased from baseline to termination (22 ± 3 vs. 25 ± 3 breaths/min, p

= 0.04). The PaO₂/FiO₂ also decreased (160 ± 27 mmHg at baseline vs. 105 ± 24 mmHg at termination, p = 0.01). There were no changes in heart rate, blood pressure, pH and PaCO₂. All the patients who experienced HFNC failure were upgraded to NIV. Only after 1-2 h of NIV, the PaO₂/FiO₂ significantly improved (105 ± 24 mmHg at HFNC failure vs. 233 ± 90 mmHg at 1-2 h of NIV) (Table 3).

Table 3

Vital signs and arterial blood gas tests at termination of HFNC, 1-2 h of upgrading to NIV and termination of NIV among patients with HFNC failure

	Termination of HFNC	1-2 h of upgrading to NIV	Termination of NIV	p ^a	p ^b
RR, breaths/min	25 ± 3	23 ± 2	22 ± 4	0.12	0.20
HR, beats/min	78 ± 12	77 ± 11	68 ± 9	0.96	0.14
SBP, mmHg	125 ± 13	121 ± 10	126 ± 9	0.34	0.78
DBP, mmHg	73 ± 6	74 ± 8	70 ± 4	0.93	0.19
pH	7.48 ± 0.02	7.49 ± 0.01	7.47 ± 0.06	0.20	0.68
PaCO ₂ , mmHg	34 ± 3	32 ± 3	37 ± 2	0.04*	0.08
PaO ₂ /FiO ₂ , mmHg	105 ± 24	202 ± 111	233 ± 90	0.04*	< 0.01*
FiO ₂ , %	60 ± 20	54 ± 16	53 ± 8	0.10	0.32
RR = respiratory rate, HR = heart rate, SBP = systolic blood pressure, DBP = diastolic blood pressure, HFNC = high flow nasal cannula, NIV = noninvasive ventilation					
p ^a for comparison between termination of HFNC and 1-2 h of upgrading to NIV					
p ^b for comparison between termination of HFNC and termination of NIV					
*p < 0.05					

Discussion

To the best of our knowledge, there were no studies to report the use of HFNC in patients with NCIP. Our study originally reported that 41% of patients required upgraded treatment from HFNC to NIV. Patients with lower PaO₂/FiO₂ were more likely to experience HFNC failure. In successful patients, the clinical signs improved after the use of HFNC. However, it deteriorated in unsuccessful patients.

In our study, we found that the number of HFNC patients were much higher than NIV patients when the HFNC or NIV was used as an initial oxygen support. It means that physicians were more likely to use HFNC among the critically ill patients caused by NCIP.

As the outbreak of NCIP in China, thousands of clinical staffs joined in the patient

management. Most of them had no experience on how to use HFNC or NIV. The current knowledge shows that 1) the HFNC is non-inferior to NIV on intubation rate in critically ill patients [14]; 2) the use of HFNC is more comfortable than NIV and the skin breakdown is less likely to occur [15, 16]; and 3) the manipulation of HFNC is much easier than NIV. Therefore, the clinical staffs were more likely to use HFNC in NCIP patients.

Person-to-person transmission of NCIP has been confirmed. In the early stages, the epidemic doubled in size every 7.4 days, and the estimated basic reproductive number was 2.2 (95% CI, 1.4 to 3.9) [5]. The virus is believed transmitted mostly via droplets or contact and possibly via aerosol [17]. People are all generally susceptible to the virus. As of February 11, 2020, 1716 clinical staffs have been infected with NCIP, and 5 of them died [12]. Therefore, a device with less production of droplets or aerosol is required. The exhaled air dispersion produced by HFNC was limited and the risk of hospital-acquired infection did not increase [18, 19]. Therefore, the use of HFNC in NCIP patients is feasible. However, the amount of condensation in the circuit increased when the ambient temperature decreased [20]. The condensed water became an important source of infection for NCIP. So, avoidance or reduction of condensation was very important when the HFNC was used.

A previous study reported that 38% of HFNC patients required intubation [13]. In this study, 13% of patients experienced HFNC failure and upgraded to NIV. Among the NIV patients who experienced HFNC failure, the intubation rate was 64%. However, in our study, 41% of patients experienced HFNC failure. Among the unsuccessful patients, all of them directly switched to NIV (no one directly switched to intubation). It means that the physicians who managed the NCIP patients were more likely to use NIV than intubation when the HFNC was unable to maintain the oxygenation. We speculated that the process of intubation made the physicians at high risk of infection because of close encounter and

irritable cough. However, among the patients with HFNC failure in our study, only 14% received intubation. It indicates that the successful rate is high after transition to NIV. Our study has several limitations. This is a retrospective observational study. We did not predefine how to manage the HFNC. The transition to NIV or intubation was decided by the attending physicians. Different physician has different opinions on the point to switch to NIV or intubation. However, this study can reflect how the HFNC has been used in the real world among the NCIP patients. In addition, we only enrolled 17 patients in this study as the enrollment period is short. To our knowledge, there were no studies to report how the HFNC was used in NCIP patients. The rapid publication is very important for public health. It also can provide an important reference for clinical physicians when the used HFNC in NCIP patients.

Conclusions

This study firstly reports the experience of how to use HFNC in patients with NCIP. Patients with lower $\text{PaO}_2/\text{FiO}_2$ were more likely to experience HFNC failure. Among the failure patients, most of them can avoid intubation when they were switched to NIV.

Key Message

The proportion of use of high flow nasal cannula as an initial oxygen support was much higher than noninvasive ventilation among the patients with a novel coronavirus (2019-nCoV)-infected pneumonia. Nearly 40% of patients with high flow nasal cannula required transition to noninvasive ventilation. Among the patients who transition to noninvasive ventilation, the intubation rate was low. Patients with lower $\text{PaO}_2/\text{FiO}_2$ were more likely to experience HFNC failure.

Abbreviations

NCIP

novel coronavirus (2019-nCoV)-infected pneumonia

HFNC

high flow nasal cannula

NIV

noninvasive ventilation

ARDS

acute respiratory distress syndrome

APACHE II

acute physiology and chronic health evaluation II

SOFA

sequential organ failure assessment

RR

respiratory rate

HR

heart rate

SBP

systolic blood pressure

DBP

diastolic blood pressure

Declarations

Consent for publication

All authors have reviewed and approved the manuscript for publication.

Availability of data and material

The datasets analyzed during the current study available from the corresponding author on reasonable request.

Ethical approval and consent to participate

The Institutional Review Board of the First Affiliated Hospital of Chongqing Medical University approved the study. Informed consent was waived as the observational nature.

Competing interests

We declare that we have no competing interests.

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Authors' contributions

JD conceived the study, joined in study design, study management, data analysis and manuscript preparation. KW, WZ and WWS participated in study design, study management, data collection and revised the manuscript. JL participated in study design and data collection, and revised the manuscript. All authors read and approved the final version.

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Figures

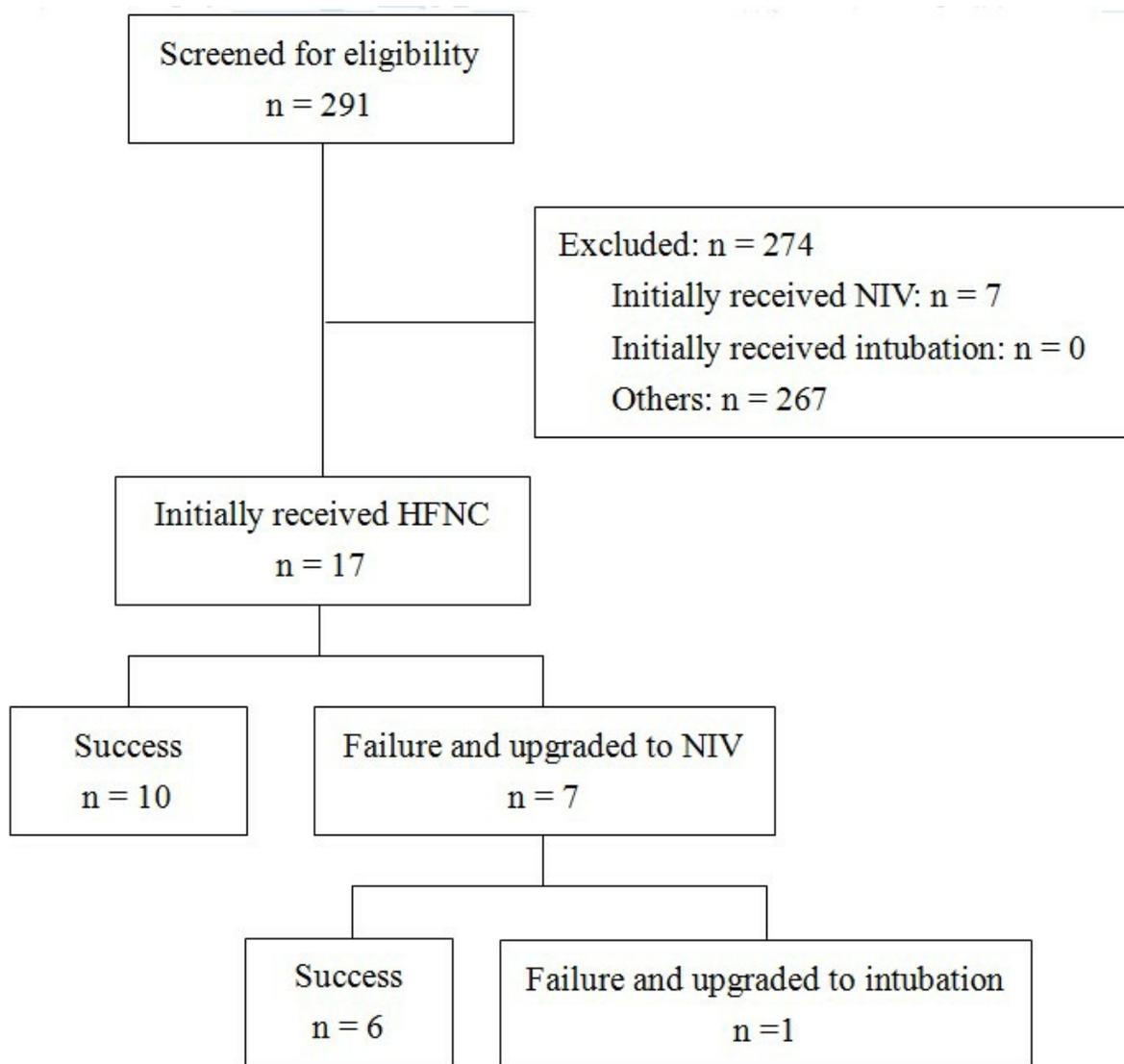


Figure 1

Flow of patient screening and enrollment.

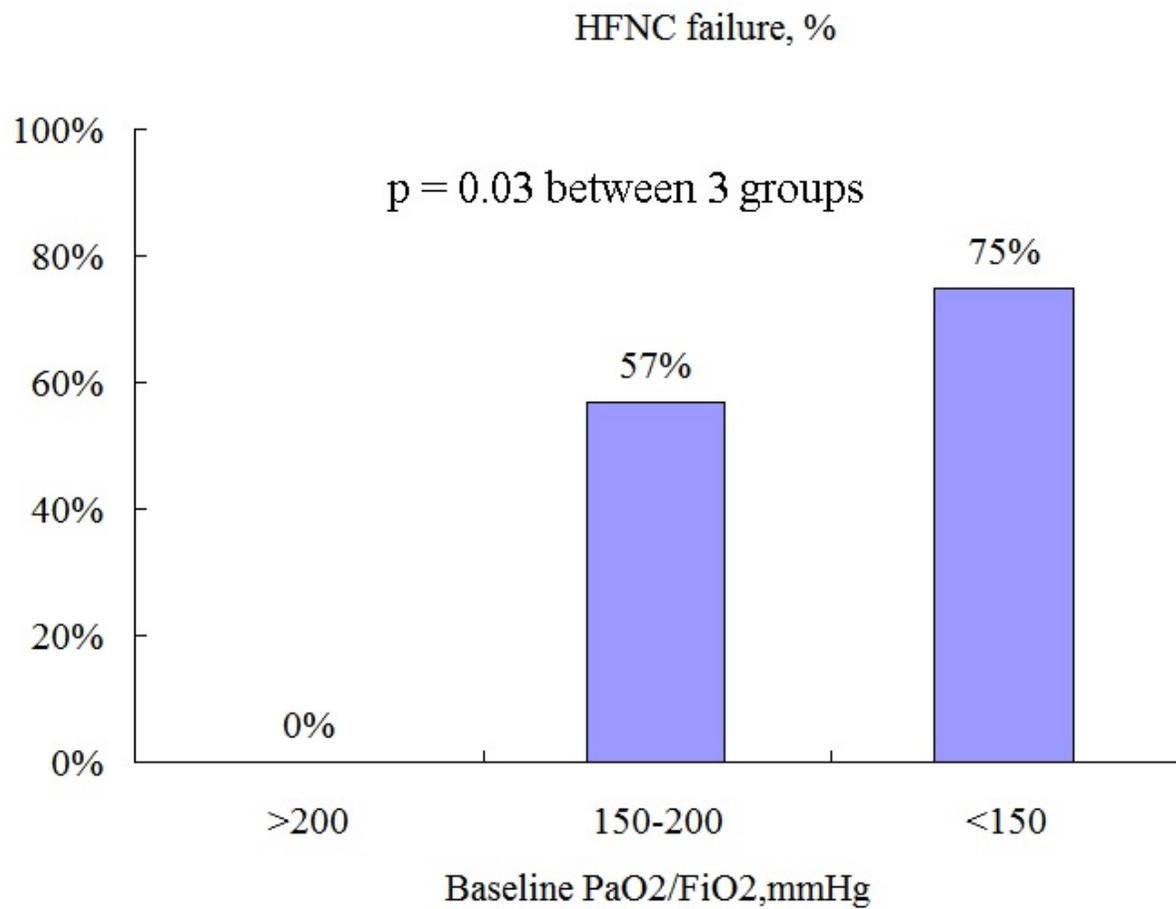


Figure 2

Flow of patient screening and enrollment.

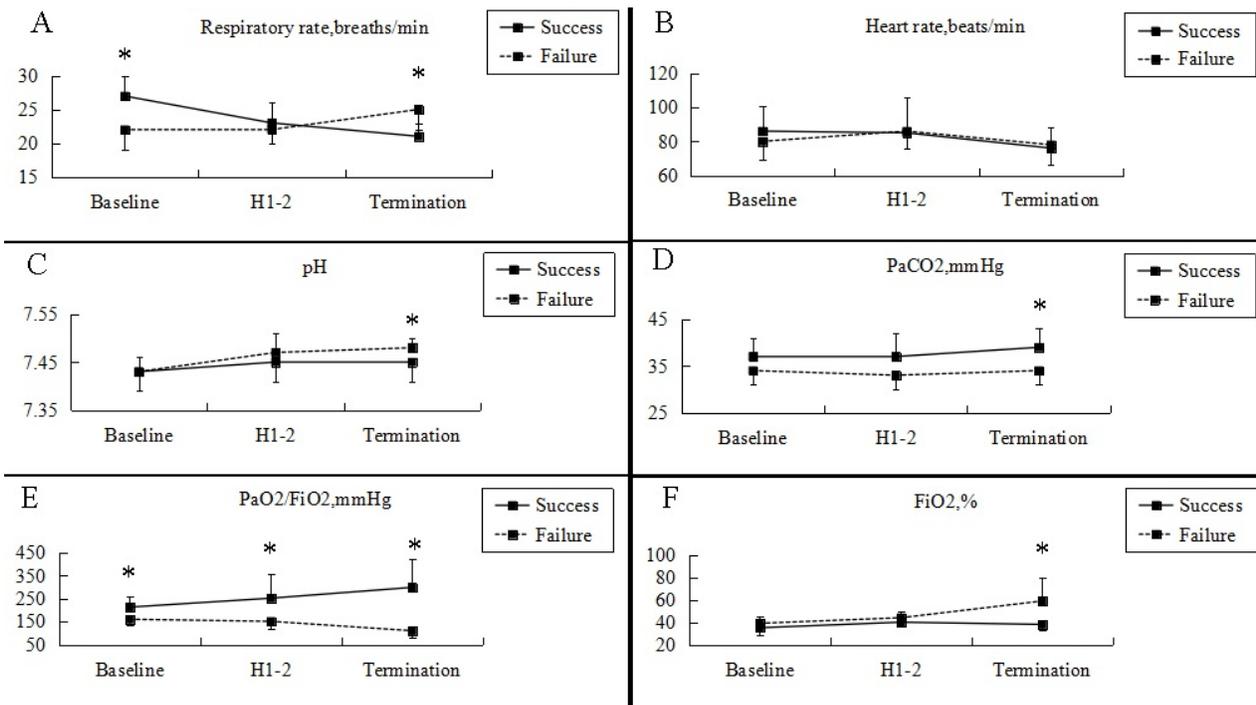


Figure 3

Vital signs and arterial blood gas tests at baseline, 1-2 h and termination of

HFNC. * $p < 0.05$ for comparisons between two groups