ORIGINAL RESEARCH



Prediction of high-flow nasal cannula failure in patients with acute respiratory failure by measuring the cross-sectional area of the diaphragmatic crus and ROX index

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Abstract

The delayed prediction of high-flow nasal cannula (HFNC) failure is associated with poor prognosis in patients with acute respiratory failure (ARF) treated with HFNCs. This study aimed to identify the early predictors for requiring mechanical ventilation (MV) in ARF patients treated with HFNCs. This was a single-center retrospective observational study based on ARF patients older than 18 years, treated with HFNC, and had chest computed tomography (CT) scans performed in the emergency department (ED) of a tertiary hospital between July 2018 and June 2020. The demographic and laboratory data were collected, and the cross-sectional area (CSA) of the diaphragmatic crus was measured on the chest CT scan. Two hundred and twenty-nine patients with ARF (92 females and 137 males) were treated with HFNCs during the study period and included in this study. Twenty-five female patients (27.17%) and 32 male patients (23.36%) required subsequent intubation and MV and were categorized as HFNC failures. Their respiratory rate-oxygenation (ROX) indexes were acquired at two hours, and the average CSA of the diaphragmatic crura was integrated to analyze the predictive power, which showed good predictive accuracy in both gender groups (area under the receiver operating characteristic curves (AUROC) for females, 0.778, and males, 0.782). The optimal ROC curve cutoff point for the average CSA of the diaphragmatic crus was estimated to be 1.48 cm² in female patients and 1.64 cm² in male patients. Altogether, these results indicated that the CSA measurement of the diaphragmatic crus on CT in ARF patients might help predict the risk of HFNC failure.

Keywords

Respiratory failure; Emergency departments; Respiratory muscles; Computed tomography; x-ray

1. Introduction

Dyspnea is defined as the subjective experience of various intensities of breathing discomfort with qualitatively distinctive sensations [1]. It has been observed in various diseases and is often associated with heart and respiratory diseases. Dyspnea is also one of the most common and major complaints of patients who visit the emergency department (ED) [2].

Acute respiratory failure (ARF) is the occurrence of hypoxia, with or without hypercapnia, due to the acute impairment of gas exchange between the lungs and blood. Rapid oxygenation is essential for maintaining adequate oxygenation in tissues during ARF. The conventional methods of oxygen delivery include nasal prongs and face masks. However, oxygen delivered via these conventional methods might often be insufficient for ARF patients [3].

The heated humidified high-flow nasal cannula therapy

(HFNC) is a safe and useful treatment recently developed for ARF patients [4]. HFNC can continuously provide a high flow rate of fresh gas breathing mixture to generate expiratory resistance. Due to high flows that meet patients' needs, oxygen dilution is decreased, giving an accurate fraction, reducing the respiratory dead space, and creating a positive airway pressure. The fraction of inspired oxygen (FiO₂) can be adjusted by changing the oxygen fraction in the driving gas [5-9].

However, one of the most difficult decisions in ARF patient care is deciding when to switch from spontaneous respiratory oxygen therapy to invasive mechanical ventilation (MV) [10]. A recent study reported that rapid intubation within 48 hours of HFNC treatment failure was associated with reduced overall intensive care unit (ICU) mortality [11]. Therefore, it is particularly important to quickly predict the need for MV

application in patients with ARF.

The respiratory rate-oxygenation (ROX) index can predict HFNC failure based on the ratio of $\text{SpO}_2/\text{FiO}_2$ to respiratory rate (RR). RR is used as the denominator because it has an inverse association with HFNC success [4]. Thus, a faster RR is correlated to a higher probability of HFNC treatment failure. However, it should also be noted that excessive breathing effort could deplete the strength and endurance of the respiratory muscles and causes fatigue and respiratory failure [12].

Previously, researchers have tried to identify ways to measure the function of the respiratory muscles. In this regard, measuring the sniff nasal inspiratory pressure (SNIP) and maximum inspiratory pressure (MIP) were proposed and are commonly used because they can effectively recognize a decrease in respiratory muscle function [13]. However, these tools are not suitable for the ED. Comparatively, computed tomography (CT) is suitable for the ED as it allows cross-sectional area (CSA) measurements and can be used to objectively perform quantitative evaluations. The diaphragm is the main muscle of inspiration and performs the essential functions required to maintain adequate ventilation, especially in elevated respiratory loads [14]. Therefore, in this study, the diaphragm was set as the target for measuring the CSA of the diaphragmatic crura for predicting HFNC failure.

2. Materials and Methods

2.1 Study Design

This was a single-center retrospective observational study of patients with ARF admitted to the ED of a tertiary university hospital between July 2018 and June 2020.

2.2 Study Settings and Population

All ARF patients who had undergone a CT scan and were treated with HFNC in the ED were included in this study. ARF was defined by any one of the following: $PaO_2 <60$ mmHg or SpO₂ <91% when breathing room air, $PaCO_2 >50$ mmHg and pH <7.35, $PaO_2/FiO_2 <300$, or PaO_2 decrease or $PaCO_2$ increase of more than 10 mmHg from baseline [15]. The exclusion criteria were age younger than 18 years, altered mental status, indication for immediate MV, those with do not resuscitate (DNR) orders, electively intubated for diagnostic or therapeutic procedures, could not hold their breath while performing a CT scan due to being tachypneic or had altered mental status, and those with an RR >20/min or decreased consciousness indicated by Glasgow Coma Scale scores of <15 upon ED admission. All included patients were followed until death or hospital discharge.

The patients' demographic variables, laboratory data and severity scores were collected by chart review of the electronic medical records. The Acute Physiology and Chronic Health Evaluation (APACHE) II score was calculated within the first 24 hours of admission [16]. The ROX index value was recorded two hours after the initiation of HFNC therapy [4]. We also recorded the use of vasopressors and MV in the ED, the length of HFNC therapy, ICU and hospital stay, and survival rate. HFNC failure was defined as the need for invasive MV or expiration within 48 hours.

In our hospital, ARF patients received oxygen therapy via an HFNC device (OptiflowTM, Fisher & Paykel Healthcare, Auckland, New Zealand) initiated with a minimum flow of 30 L/min and a FiO_2 of 1. The FiO_2 was then set to maintain a pulse oximetry value greater than 92%, and the flow rate was set according to the physician's judgment. Non-invasive ventilation (NIV) was not available due to the lack of NIV in the institution. The parameters used to assess the level of respiratory support were FiO₂ and the total flow delivered, adjusted to the individual patient's needs. The parameters for assessing respiratory failure were RR, SpO₂/FiO₂ ratio, and arterial carbon dioxide (PaCO₂) values. The criteria for intubation and MV were a decreased level of consciousness (Glasgow Coma Scale score <12), cardiac arrest, new onset of arrhythmia with hemodynamic instability, severe hemodynamic instability (norepinephrine $>0.1 \,\mu g/kg$ per minute), and persistent or worsening respiratory conditions defined by at least two of the following criteria: failure to achieve correct oxygenation (PaO $_2$ <60 mmHg despite an HFNC flow of \geq 30 L/min, and a FiO₂ of 1), respiratory acidosis (PaCO₂ >50 mmHg with pH <7.25), an RR >30 beats per minute, or the inability to clear secretions [4, 17, 18].

2.3 Measurements

A 320-channel, 64-channel, or 16-channel multi-detector CT scan was performed using various scanners (Aquilion ONE, Toshiba, Otawara, Japan; SOMATOM Definition and Sensation 16, Siemens Medical Systems, Forchheim, Germany; Optima CT 660, GE Medical Systems, Milwaukee, WI, USA). Contrast chest CT scans were performed using the following scan parameters: 0.6–1.2 collimation, 120 kVp, 100–250 mA under automatic exposure control, and 0.5–0.75 seconds rotation time. CT scans were reconstructed at section widths of 2.5 mm. The patients were routinely instructed to breathe to their functional residual capacity and hold their breath while the chest CT scan was obtained.

We used the diaphragmatic crura to directly measure the crus in the retrocaval area at the level of the origin of the celiac trunk on the axial scan [19]. A region of interest was drawn around the outermost border of each crus, where the muscle was welldelineated by using Deja-view PACS (Dongeun Information Technology, Bucheon, Korea) (Fig. 1).

All images were assessed by two different readers to account for interobserver variability. One of the readers was an emergency physician, the other was a radiologist, and both had more than seven years of experience. They were blinded to the patients' clinical data and the results for a period of two months to determine intraobserver variability. The CSA measurement took less than 30 seconds. Lastly, the data from three readers were averaged for statistical analysis.

2.4 Data Analysis

The quantitative variables are expressed as mean \pm SD or median and interquartile range if normality criteria were not met according to the Kolmogorov-Smirnov test. Categorical variables are expressed as frequencies and percentages. Continuous variables were compared using the Student *t*-test or the Mann-Whitney U test. Differences in the categorical variables



FIGURE 1. CT scan for measuring the cross-sectional area of the diaphragmatic crus. DC: diaphragmatic crus. The cross-sectional area of the DC (white triangle) was measured at the level of the origin of the celiac trunk (white arrow).

were assessed by the χ^2 or Fisher's exact test. A *p*-value < 0.05 was considered statistically significant. Males and females were analyzed separately because of gender-related differences in muscle mass.

The interobserver and intraobserver variability for measuring the diaphragmatic crura area was evaluated using intraclass correlation coefficients (ICC) with a two-way mixed absolute model.

To assess the correlation between outcomes and variables, odds ratios (OR) were estimated by univariate logistic regression analysis using the stepwise forward selection methods with a *p*-value < 0.05. Multivariate logistic regression analysis was performed to assess the stepwise correlation between outcomes and variables. A *p*-value < 0.05 with a 95% confidence interval was considered statistically significant. Receiver operating characteristic (ROC) curves were generated, and the area under the curves was calculated (AUROC) to assess the accuracy of different variables for correctly classifying patients who would succeed or fail on HFNC. The optimal threshold for continuous variables was chosen to maximize sensitivity and specificity.

3. Results

Three hundred ninety-six ARF patients (156 females and 240 males) were treated with HFNCs in the ED after receiving conventional oxygen therapy. Among them, 51 with altered mental status and 115 with an RR of >20/min were excluded. Thus, 229 ARF patients (92 females and 137 males) were eligible for this study. The baseline characteristics of the investigated population are presented in Table 1. Twenty-five females (27.71%) and 32 males (23.36%) patients were categorized as HFNC failures. The results showed that sex or age did not significantly affect HFNC success or failure. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), PaO₂, PaCO₂, PaO₂/FiO₂ ratio (P/F ratio), vasopressor use in the ED, and ROX index values at two hours were significantly different between the success and failure groups.

The CSAs of the diaphragmatic crura are presented in Table 2. The cases were divided into a success and a failure group to compare the treatment results according to the CSA of the diaphragmatic crus. Significant differences in the CSA measurement of the right and average crus were found between patients in the HFNC success and failure groups in both genders (p < 0.05). Additionally, the success group had a generally larger CSA than the failure group. The CSAs

| | Total (229) | | <i>p</i> -value* |
|-----------------------------|------------------------|------------------------|------------------|
| | Success (172) | Failure (57) | |
| Sex | | | |
| Female (92) | 67 (72.83%) | 25 (27.17%) | 0.618 |
| Male (137) | 105 (76.64%) | 32 (23.36%) | |
| Age | 75 (66~82) | 77 (67~81) | 0.664 |
| Systolic BP (mmHg) | 140 (110~160) | 120 (110~140) | 0.030 |
| Diastolic BP (mmHg) | 80 (60~90) | 70 (60~80) | 0.013 |
| MAP (mmHg) | 98.15 ± 21.57 | 89.47 ± 17.92 | 0.003 |
| Heart rate (/min) | 101.76 ± 23.83 | 99.49 ± 24.06 | 0.535 |
| Respiratory rate (/min) | 18 (18~20) | 19 (18~20) | 0.936 |
| Body temperature (°C) | 36.9 (36.4~37.5) | 36.8 (36.3~37.4) | 0.335 |
| pH | 7.4 (7.34~7.45) | 7.4 (7.34~7.46) | 0.534 |
| PaO ₂ (mmHg) | 66 (64.67~66.67) | 65.33 (64~66.67) | 0.025 |
| PaCO ₂ (mmHg) | 48 (37~57) | 37 (30~54) | 0.004 |
| White blood cell $(10^9/L)$ | 11.29 (8.03~16.23) | 10.99 (7.16~14.95) | 0.314 |
| Hematocrit (%) | 36.19 ± 6.57 | 35.17 ± 7.77 | 0.335 |
| Sodium (mg/dL) | 139 (136~141) | 138 (135~141) | 0.714 |
| Potassium (mg/dL) | 4.2 (3.9~4.8) | 4.1 (3.8~4.8) | 0.445 |
| Creatinine (mg/dL) | 0.93 (0.72~1.50) | 0.87 (0.61~1.45) | 0.223 |
| Apache II | 15.22 ± 4.93 | 14.95 ± 4.45 | 0.716 |
| PaO_2/FiO_2 | 166.67 (129.33~209.44) | 132.00 (107.78~166.67) | < 0.001 |
| ROX index an 2 hour | 13.09 (10.18~16.25) | 9.90 (8.33~13.89) | 0.001 |

TABLE 1. Baseline characteristics of the study population at emergency department.

BP: blood pressure; MAP: mean arterial pressure; ROX: respiratory rate-oxygenation.

Continuous variables are presented as mean \pm SD, if not met normality criteria, presented as median (interquartile range). Categorical variables are presents as number (proportion, %).

*Statistical comparisons of the data were performed using the Student t test or Wilcoxon Rank-Sum test for continuous variables, Chi-square tests or Cochran-Mantel-Haenszel test for categorical variables.

TABLE 2. CT Measurement of cross sectional area of diaphragm crus.

| | HF | NC | <i>p</i> -value* |
|--------------------------------|------------------|------------------|------------------|
| | Success | Failure | |
| CSA of Crus (cm ²) | | | |
| Female | | | |
| Rt. Crus | 2.16 (1.83~2.66) | 1.88 (1.64~2.16) | 0.029 |
| Lt. Crus | 1.07 (0.81~1.24) | 0.89 (0.68~1.20) | 0.122 |
| Average of Crus | 1.60 (1.35~1.92) | 1.40 (1.21~1.62) | 0.029 |
| Male | | | |
| Rt. Crus | 2.60 (2.14~3.21) | 2.15 (1.65~2.71) | 0.002 |
| Lt. Crus | 1.16 (0.93~1.46) | 0.97 (0.73~1.33) | 0.012 |
| Average of Crus | 1.90 (1.59~2.30) | 1.53 (1.34~1.96) | 0.001 |

*Statistical comparisons of the data were performed using the Student t test or Wilcoxon.

HFNC: High-flow nasal cannula; CSA, Cross sectional area.

Continuous variables are presented as median (interquartile range). Rank-Sum test.

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| Univariate Logistic Regression | | | | | |
|--|--------|---------------------|------------------|--|--|
| | ß | Odd ratio (95% CI) | <i>p</i> -value* | | |
| Age | -0.013 | 0.987 (0.951~1.025) | 0.502 | | |
| Systolic BP (mmHg) | -0.005 | 0.995 (0.980~1.009) | 0.471 | | |
| Diastolic BP (mmHg) | -0.019 | 0.981 (0.952~1.011) | 0.214 | | |
| Heart rate (/min) | 0.010 | 1.010 (0.992~1.029) | 0.266 | | |
| Respiratory rate (/min) | -0.295 | 0.744 (0.513~1.079) | 0.119 | | |
| Body temperature (°C) | -0.072 | 0.930 (0.520~1.674) | 0.810 | | |
| рН | 1.275 | 3.577 (021~10.592) | 0.627 | | |
| PaO ₂ (mmHg) | -0.350 | 0.705 (0.521~0.955) | 0.024 | | |
| PaCO ₂ (mmHg) | -0.032 | 0.969 (0.937~1.001) | 0.059 | | |
| White blood cell $(10^9/L)$ | 0.000 | 1.000 (0.999~1.000) | 0.964 | | |
| Hematocrit (%) | 0.033 | 1.033 (0.962~1.110) | 0.371 | | |
| Sodium (mg/dL) | -0.021 | 0.979 (0.899~1.067) | 0.628 | | |
| Potassium (mg/dL) | -0.283 | 0.753 (0.394~1.442) | 0.393 | | |
| Creatinine (mg/dL) | -0.622 | 0.537 (0.242~1.194) | 0.127 | | |
| Apache II | -0.028 | 0.972 (0.872~1.084) | 0.610 | | |
| ROX at 2 hour | -0.220 | 0.802 (0.691~0.931) | 0.004 | | |
| Average of Crus (cm ²) | -1.351 | 0.259 (0.073~0.922) | 0.037 | | |
| Multivariate logistic regression—Stepwise variable selection | | | | | |
| | ß | Odd ratio (95% CI) | <i>p</i> -value* | | |
| ROX at 2 hour | -0.359 | 0.699 (0.575~0.850) | < 0.001 | | |
| Average of Crus (cm ²) | -2.187 | 0.112 (0.025~0.501) | 0.004 | | |
| Respiratory rate (/min) | -0.789 | 0.454 (0.259~0.798) | 0.006 | | |
| Sodium (mg/dL) | -0.121 | 0.886 (0.795~0.987) | 0.028 | | |
| Hematocrit (%) | 0.101 | 1.106 (0.998~1.226) | 0.055 | | |

 TABLE 3. Analysis of variables associated with HFNC failure using logistic regression—female.

HFNC: High-flow nasal cannula; CI: Confidence interval; BP: blood pressure; ROX: respiratory rate-oxygenation. *Statistical comparisons of the data were performed using bimodal logistic regression analysis.

of the left crus in females were not significantly different. These data were measured twice by the two observers, and the ICC of the interobserver and intraobserver of each data was determined. The results showed that the interobserver ICC of the first measurement was 0.894 on the right, 0.917 on the left and 0.912 on average, and the interobserver ICC of the second measurement was 0.903 on the right, 0.924 on the left and 0.912 on average. The intraobserver ICC of the first observer was 0.905 on the right, 0.949 on the left and 0.916 on average, and the intraobserver ICC of the second observer was 0.921 on the right, 0.928 on the left and 0.923 on average.

Next, we performed logistic regression analysis to assess the relationship between patient variables and treatment outcomes (Tables 3 and 4). In addition, we also investigated whether the statistically significant factors in simple logistic regression would be significant in stepwise multivariate logistic regression. Our results showed that in the female group, the factors significantly related to treatment outcomes were ROX index values at two hours (OR, 0.699), average CSA of the crus (OR, 0.112), respiratory rate (OR, 0.454) and serum sodium levels (OR, 0.886). In the male group, the ROX index at two

hours (OR, 0.784), the average CSA of the crus (OR, 0.208), white blood cell count (OR, 0.999) and vasopressor use in the ED (OR, 3.563) were factors significantly related to treatment outcomes. Therefore, the factors significantly associated with treatment outcomes in both genders were ROX index values and the average CSA of the crus.

In both gender groups, the ROX index value at two hours demonstrated good predictive accuracy (AUROC for females = 0.718, males = 0.707). However, when the ROX index at two hours and the average CSA of the crus were integrated to analyze predictive power, a better predictive accuracy was observed for both gender groups (AUROC for females = 0.778, males = 0.782). Using the ROC curve, the best cutoff point for the average CSA of the crus was estimated to be 1.48 cm² in female patients and 1.64 cm² in male patients (Fig. 2). Additionally, in both gender groups, the predictive power of integrating the ROX index value at two hours and the average CSA of the crus was higher than the predictive power of individual factors.

| Univariate logistic regression | | | | | |
|--|--------|----------------------|------------------|--|--|
| | ß | Odd ratio (95% CI) | <i>p</i> -value* | | |
| Age | 0.017 | 1.017 (0.983~1.053) | 0.331 | | |
| Systolic BP (mmHg) | -0.016 | 0.984 (0.971~0.997) | 0.016 | | |
| Diastolic BP (mmHg) | -0.034 | 0.966 (0.941~0.992) | 0.011 | | |
| Heart rate (/min) | -0.017 | 0.984 (0.964~1.001) | 0.061 | | |
| Respiratory rate (/min) | 0.196 | 1.216 (0.848~1.745) | 0.288 | | |
| Body temperature (°C) | -0.375 | 0.688 (0.420~1.124) | 0.135 | | |
| pН | 0.890 | 2.436 (0.020~12.729) | 0.715 | | |
| PaO ₂ (mmHg) | -0.208 | 0.812 (0.648~1.019) | 0.072 | | |
| $PaCO_2 (mmHg)^b$ | -0.023 | 0.977 (0.950~1.005) | 0.104 | | |
| White blood cell $(10^9/L)$ | 0.000 | 0.999 (0.999~1.000) | 0.080 | | |
| Hematocrit (%) | -0.052 | 0.949 (0.896~1.005) | 0.075 | | |
| Sodium (mg/dL) | 0.016 | 1.016 (0.942~1.097) | 0.677 | | |
| Potassium (mg/dL) | -0.102 | 0.901 (0.515~1.584) | 0.722 | | |
| Creatinine (mg/dL) | 0.012 | 1.012 (0.799~1.283) | 0.919 | | |
| Apache II | -0.005 | 0.995 (0.921~1.075) | 0.906 | | |
| ROX at 2 hour | -0.216 | 0.806 (0.712~0.912) | < 0.001 | | |
| Average of Crus (cm ²) | -1.542 | 0.214 (0.080~0.572) | 0.002 | | |
| Multivariate logistic regression—Stepwise variable selection | | | | | |
| | ß | Odd ratio (95% CI) | <i>p</i> -value* | | |
| ROX at 2 hour | -0.244 | 0.784 (0.684~0.897) | < 0.001 | | |
| Average of Crus (cm ²) | -1.568 | 0.208 (0.074~0.584) | 0.003 | | |
| White blood cell $(10^9/L)$ | 0.000 | 0.999 (0.999~1.000) | 0.022 | | |
| Diastolic BP (mmHg) | -0.028 | 0.973 (0.942~1.004) | 0.086 | | |
| | | | | | |

TABLE 4. Analysis of variable associated with HFNC failure using logistic regression—male.

*HFNC: High-flow nasal cannula; CI: Confidence interval; BP: blood pressure; ROX: respiratory rate-oxygenation. *Statistical comparisons of the data were performed using bimodal logistic regression analysis.*

4. Discussion

This study aimed to investigate the significance of CSA measurement of the diaphragmatic crus as a predictive factor in HFNC failure. Multivariate logistic regression analysis showed that the CSA of the diaphragmatic crus was significantly correlated with HFNC failure in both gender groups. On the other hand, the OR of respiratory rate per minute was found to be <1 in the female group. We hypothesize that this result might be due to excluding patients with respiratory rates exceeding 20 per minute from the study group. Analysis of the ROC curve showed that when combined with the ROX index 2 hours after the ED visit, the predictive power of HFNC failure was stronger than when the CSA of the diaphragmatic crus was analyzed alone.

In recent studies, HFNC was found to reduce the intubation rate, lower ICU mortality and reduce the rate of invasive MV in patients with severe respiratory failure [20, 21]. Therefore, HFNC has resulted in better comfort and oxygenation than conventional oxygen delivery methods in patients with acute respiratory failure [21–24]. Despite the advantages of HFNC, its inappropriate use might be hazardous to some patients.

HFNC failure is defined as the need for endotracheal intubation despite HFNC application [11]. The failure of HFNC may delay intubation and increase mortality, similar to NIV [25]. A poor prognosis of HFNC failure might be caused by long-term intubation delays in patients with uncontrolled diseases, leading to respiratory muscle fatigue and bad clinical outcomes [11]. Except for our study, none of the existing studies predicted the failure of HFNC by measuring the CSA of respiratory muscles. Rapid prediction can be achieved by measuring the CSA of the crus to reduce fatal HFNC failures.

Similar to previous studies, our results showed that the ROX index could be useful for predicting HFNC failure. The ROX index had the best predictive accuracy after 12 hours, and its AUROC was 0.74 [4]. When combined with the CSA of the crus in this study, it had similar predictive accuracy after two hours. Previous indicators, such as the ROX index, are time-consuming to determine, but in our study, we showed that it could be quickly evaluated for predicting HFNC failure using CT scan.

CT is a radiologic modality commonly performed in EDs for the differential diagnosis of respiratory diseases. Here, we found that it could easily measure the CSA of respiratory mus-

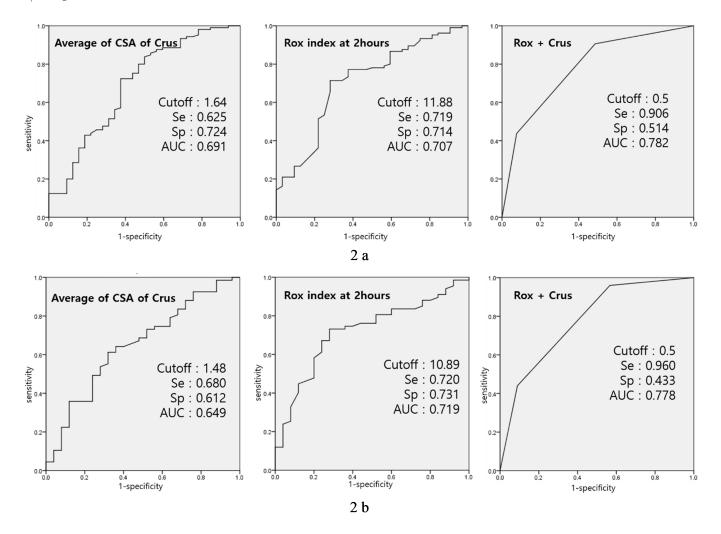


FIGURE 2. Receiver operating characteristic curves for predicting the cross-sectional area of the crus and ROX index value for high-flow nasal cannula treatment failure. Female patients (2-a); Male patients (2-b). CSA: cross-sectional area; Se: sensitivity; Sp: specificity; AUC: area under the curve.

cles. As a result, the CSA measurement value of the diaphragmatic crus had a sufficiently reliable ICC value. In patients with respiratory disease, CSA of the erector spinae muscle at the 12th thoracic vertebral region and the pectoralis muscle at the superior aspect of the aortic arch are usually selected as targets because the assessment of these muscles does not require additional radiation exposure [26–29]. Although they have other main roles, the erector spinae and pectoralis muscles also act as respiratory muscles. Therefore, the diaphragmatic crus was selected as the measurement subject of this study because the main function of the diaphragm is respiration, and CSA measurement does not require additional radiation exposure when assessed on chest CT scans.

CT is a useful test in EDs, but it has some limitations. It can be difficult to perform on critically ill patients, and the radiation delivered can be hazardous. Comparatively, ultrasonography is a good alternative in EDs. However, ultrasonography has a limited field of view and cannot easily capture the maximal CSA of muscles [30]. CT could be the preferred modality for measuring the CSA of the crus in EDs, but its limitations make it difficult to implement in all ARF patients. Thus, future studies are required to determine which ARF patients undergoing HFNC should receive CT scans.

This present study had several limitations. First, as this was a retrospectively designed study, some variables were either specified or implied. In particular, there was no data on the comorbidity, cause of ARF and timing of HFNC failure within 48 hours after HFNC therapy, which might have affected the obtained results. Second, this was a single-center study, and the criteria and threshold for applying HFNC might vary from institution to institution. Also, the results cannot be generalized to all ARF patients due to the small sample size in this study. Third, while the CSA of the diaphragmatic crus was analyzed, no analyses on the attenuation of the diaphragmatic crus were performed, indicating the need for further studies to determine whether measuring one area of a respiratory muscle in the course of a dynamic disease could be used as a predictive factor. Fourth, no direct quantitative comparisons were made between pulmonary function tests and the CSA of the diaphragmatic crus. Despite these limitations, our findings might help predict the risk of HFNC failure in ARF patients who have already undergone CT scans.

5. Conclusions

When combined with the ROX index, CSA measurement of the diaphragmatic crus of ARF patients on CT scan might help predict the risk of HFNC failure within 2 hours. It could predict HFNC failure in a shorter time than previously identified predictive factors. Additionally, patients with a small CSA of the diaphragmatic crus might need close monitoring for the accurate and rapid application of MV. Due to the inherent limitations of this study, additional well-planned studies are needed to validate these conclusions.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

HJK and JJ—contributed equally to this work as the 1st author. HJK, JJ and DL—contributed to the concept and design of the study. HJM, HJL, DJ, TYS and JAH—contributed to the collection, analysis and interpretation of data. HJK, JJ and DL—contributed to the drafting of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the Soonchunhyang University Institutional Review Board (IRB No. 2020-10-005). The IRB approved a request to waive the documentation of informed consent.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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