



Non-invasive positive pressure ventilation can reduce perioperative mortality in acute aortic dissection patients with hypoxemia

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Background: Hypoxemia is a common critical respiratory complication in patients with acute aortic dissection (AAD) before operation and results in adverse outcomes. This study aimed to identify the optimal oxygenation treatment for AAD patients with hypoxemia in the emergency department (ED).

Methods: This was a retrospective, observational, cohort study. We retrospectively collected data from 187 adult patients with AAD and hypoxemia who had been admitted to our ED. All patients were divided into nasal cannula group (n=91), Venturi mask group (n=60), and non-invasive positive pressure ventilation (NIPPV) group (n=36). The primary outcome was overall mortality in ED; the secondary outcomes were preoperative intubation rate and postoperative mortality, length of intensive care unit (ICU) stay, length of hospital stay, and length of intubation.

Results: Among all patients, those who received NIPPV treatment showed the lowest ED intubation rate (2.78%, $P=0.004$), shortest postoperative length of ICU stay (median 2.31, $P<0.001$), postoperative length of intubation (median 25.10, $P<0.001$), and post-operative length of hospital stay (median 21.00, $P<0.001$). Kaplan-Meier analysis showed the highest 3-day survival (log-rank 7.387, $P=0.03$) and 5-day survival (log-rank 14.710, $P=0.001$) in the NIPPV group. After adjustment, NIPPV therapy was independently associated with the reduced 3-day [adjusted hazard ratio (HR) 0.102, 95% confidence interval (CI): 0.013–0.791, $P=0.03$] and 5-day (adjusted HR 0.057, 95% CI: 0.008–0.427, $P=0.005$) mortality in ED.

Conclusions: Early utilization of NIPPV in AAD patients with hypoxemia in the ED can effectively decrease pre-operative intubation rate and perioperative mortality, and improve postoperative outcomes.

Keywords: Aortic dissection; hypoxemia; noninvasive ventilation; perioperative; mortality

Submitted Jan 27, 2024. Accepted for publication Jul 12, 2024. Published online Sep 19, 2024.

doi: 10.21037/jtd-24-163

View this article at: <https://dx.doi.org/10.21037/jtd-24-163>

Introduction

Acute aortic dissection (AAD) is a deadly cardiovascular disease, which might complicate some organ damage before surgery. Preoperative hypoxemia has been reported to occur in 32.2–53.8% of AAD patients (1–4) and is usually associated with poor clinical outcomes, including longer intensive care unit (ICU) and in-hospital length of stay, postoperative ventilation time, and higher mortality (5). In addition, patients with respiratory infection or preoperative hypoxemia are highly likely to have a poor prognosis after surgery and less likely to survive the surgery (6). Considering these adverse outcomes, surgeons usually postpone the operation timing or prefer conservative therapy for these patients until the hypoxemia improves. Therefore, the management of hypoxemia in these patients is of utmost importance during emergency department (ED) stay.

Supplemental oxygen therapy is not only an essential supportive treatment to correct hypoxemia and alleviate breathlessness (7), but also an effective way to reduce heart rate (8,9). Moreover, oxygen supplementation could evoke vasoconstriction (10) and abolish daytime increase in blood

pressure (11).

Although oxygen supplementation is part of first-line treatment for patients with acute cardiovascular diseases, the consensus of routine use of supplemental oxygen therapy has been challenged by recent studies (12,13). The optimal oxygen supplementary strategy for patients with cardiovascular diseases in the ED remains debatable. In a large, multicenter, crossover trial involving patients with suspected acute coronary syndrome, investigators found that high flow oxygen (6–8 L/min) by face mask, irrespective of peripheral oxygen saturation (SpO_2), when compared with low oxygen (that only supplies oxygen when $SpO_2 < 90\%$, with a target $SpO_2 < 95\%$), had no association with an increase or decrease in 30-day mortality (14). Furthermore, in another nationwide randomized clinical trial (RCT) involving patients with suspected myocardial infarction, high-flow oxygen treatment did not reduce 1-year mortality (15). The DETO2X-AMI study further revealed that supplementary oxygen therapy did not significantly ameliorate outcomes in patients with either low-normal baseline SpO_2 or hypoxia (16). To the best of our knowledge, there has been little research concerning the optimal oxygen delivery therapy in AAD patients with preoperative hypoxemia.

We therefore conducted a retrospective, observational, cohort study to evaluate the effect of different methods of oxygen delivery on short-term mortality among AAD patients with hypoxemia in the ED. We present this article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-163/rc>).

Methods

Study design

The determination of the optimal method of oxygen delivery for AAD patients with hypoxemia in the emergency room was investigated in a retrospective, observational study, in which three oxygenation methods were compared in the treatment of patients with AAD who had hypoxemia at baseline.

Patient selection

Consecutive patients who were referred to the ED and were diagnosed with acute Stanford type A aortic dissection between 1 January 2021, and 31 December 2022 were evaluated for eligibility. Eligible patients met all of the

Highlight box

Key findings

- This study revealed early utilization of non-invasive positive pressure ventilation (NIPPV) in acute aortic dissection (AAD) patients with hypoxemia in the emergency department (ED) can effectively decrease pre-operative intubation rate, and 3- and 5-day mortality in ED. Additionally, for patients who underwent surgery, preoperative utilization of NIPPV may improve postoperative outcomes.

What is known and what is new?

- Supplemental oxygen therapy is not only an essential supportive treatment to correct hypoxemia, but also an effective way to reduce heart rate. The optimal oxygen supplementary strategy for patients with cardiovascular diseases in the ED remains debatable.
- This study evaluates the effect of different methods of oxygen delivery on perioperative outcomes in AAD patients with hypoxemia in the ED. The benefit of NIPPV was observed in preoperative mortality, intubation rate, and postoperative outcomes, indicating that NIPPV could be the optimal oxygen strategy for AAD patients with hypoxemia.

What is the implication, and what should change now?

- The use of NIPPV could reduce preoperative mortality and preoperative intubation rate, and improve postoperative outcomes.
- Larger sample size and randomized controlled studies should be conducted in the future.

following criteria: age ≥ 18 years; oxygenation index [ratio of the fraction of inspired oxygen to the partial pressure of oxygen in the arterial blood ($\text{PaO}_2/\text{FiO}_2$)] between 150–300 mmHg while the patient was breathing ambient air and an absence of clinical history of underlying chronic respiratory failure. The main exclusion criteria were exacerbation of chronic lung diseases, chronic liver and renal diseases, severe neutropenia, cardiogenic pulmonary edema, severe nervous system abnormalities affecting breath, hemodynamic instability, a Glasgow Coma Scale score of 12 points or less, contraindications to non-invasive ventilation (NIV), urgent need for endotracheal intubation, or a do-not intubate order. According to the form of oxygen delivery, patients were divided into three groups: nasal cannula group, Venturi mask group, and non-invasive positive pressure ventilation (NIPPV) group. The severity of hypoxemia was defined according to $\text{PaO}_2/\text{FiO}_2$: $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$ for mild hypoxemia, $150 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}$ for moderate hypoxemia.

Data collection

Patient were obtained from the clinical record database system at Guangdong Provincial People's Hospital. The following parameters were retrospectively assessed using medical records: age, sex, body mass index (BMI), comorbidities including pre-existing lung diseases, chronic kidney disease, diabetes, hypertension, and cardiovascular disease, laboratory results, ultrasound findings, arterial blood gases, and laboratory tests including white blood cell (WBC), platelet, creatinine, lactate, C-reactive protein (CRP), D-dimer, and N-terminal pro-brain natriuretic peptide (NT-proBNP) level at ED admission. Patient outcomes, including pre-operative intubation, pre-operative mortality, in-hospital mortality, and length of stay in ICU were collected.

Ethical approval

The study was conducted in accordance with Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (No. KY-Z-2021-444-02) and informed consent was provided by all the patients.

Outcomes

The primary outcome was short-term mortality in ED.

The secondary outcomes were preoperative intubation rate and postoperative mortality, length of ICU stay, length of hospital stay, and length of intubation. The following prespecified criteria for endotracheal intubation were used: hemodynamic instability, a deterioration of neurologic status, or signs of persisting or worsening respiratory failure as defined by at least two of the following criteria: a respiratory rate of more than 40 breaths per minute, a lack of improvement in signs of high respiratory-muscle workload, the development of copious tracheal secretions, acidosis with a pH of less than 7.35, an SpO_2 of less than 90% for more than 5 minutes without technical dysfunction, or a poor response to oxygenation techniques.

Statistical analysis

Continuous variables were expressed as mean [standard deviation (SD)] or median [interquartile range (IQR)], depending on the normality of distribution; the Kolmogorov-Smirnov test was used to test the normality of distribution for continuous variables. Categorical variables and continuous variables are analyzed with Chi-squared and *t*-test, respectively. Comparisons between groups were analyzed by an independent *t*-test or the Mann-Whitney test. Differences in categorical variables were assessed using the χ^2 or Fisher's exact test. Survival was estimated using the Kaplan-Meier curve (and compared using the log-rank test) and Cox regression multivariable analysis was adopted to determine the association between different oxygenation therapies and patient survival. Cox regression multivariable analysis was performed for mortality including variables with *P* value < 0.1 in univariate analysis. Thresholds for categorization of continuous variables subsets were prespecified utilizing clinical and laboratory accepted criteria or by categorizing variables into an upper quartile versus the lower three quartiles. For all analyses, a *P* value < 0.05 was considered statistically significant. The software SPSS 20.0 (IBM Corp., Armonk, NY, USA) was adopted to perform the analysis.

Results

Participant characteristics

Between January 2021 and December 2022, 248 patients with aortic dissection and hypoxemia were retrospectively scrutinized. Among them, 187 patients were included in our study; 61 patients were excluded due to missing arterial

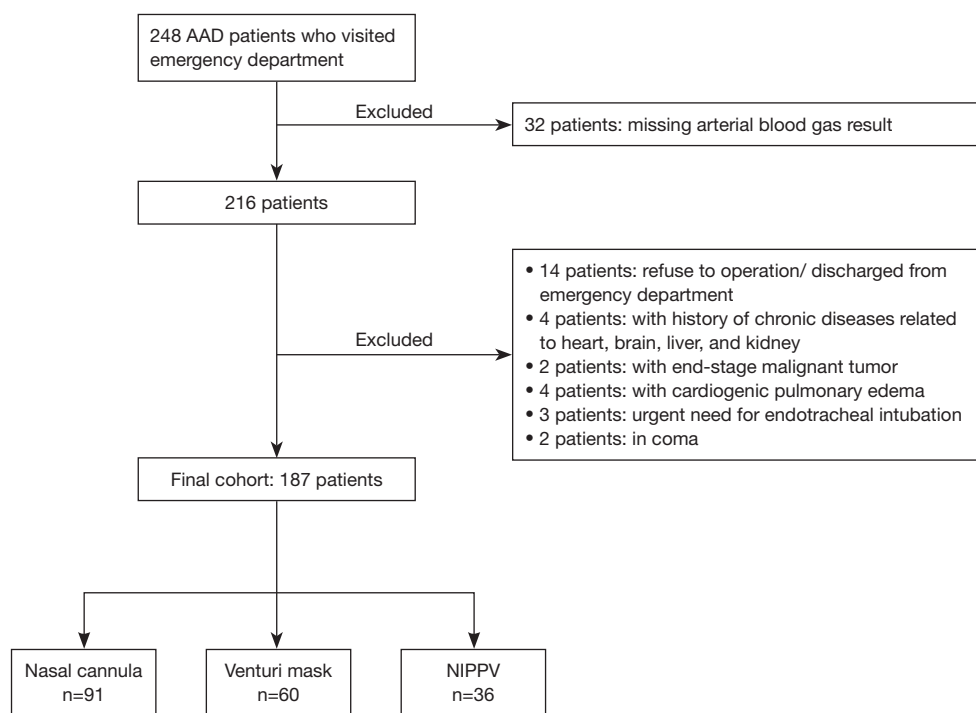


Figure 1 CONSORT diagram summarizing inclusion and exclusion criteria for developing the data set. AAD, acute aortic dissection; NIPPV, non-invasive positive pressure ventilation.

blood gas results, with a history of chronic diseases related to the heart, brain, liver, and kidneys, end-stage malignant tumor, cardiogenic pulmonary edema, an urgent need for endotracheal intubation, or coma. Oxygenation therapy via nasal cannula, Venturi mask, and NIPPV was applied to 91/187 (48.67%), 60/187 (32.09%), and 36/187 (19.25%) patients, respectively (*Figure 1*).

As shown in *Table 1*, 124/187 (66.31%) patients had mild hypoxia and 63/187 (33.69%) had moderate hypoxia, when they arrived at the ED. Around 55% of patients with hypoxia then underwent surgery. The groups were similar concerning vitals, the severity of hypoxemia, comorbidities, WBC, platelet, CRP, D-dimer, NT-proBNP level, and left ventricular ejection fraction (LVEF). The onset of AAD was significantly shorter in the nasal cannula group ($P<0.001$).

Outcomes

Primary outcome

NIPPV improved the primary outcome in ED. The overall ED mortality rate was 25.67%. The ED mortality rate was significantly lower in those who received NIV therapy

(8.33%, $P=0.002$). Kaplan-Meier analysis showed that both overall 3-day (log-rank 7.387, $P=0.03$) and 5-day survival (log-rank 14.710, $P=0.001$) were improved in patients treated with NIPPV (*Figure 2*). When stratified with the severity of hypoxemia, patients with mild hypoxemia who were treated with either a Venturi mask or NIPPV showed better 3-day (log-rank 10.274, $P=0.006$) and 5-day survival (log-rank 12.723, $P=0.002$) than those who were treated with a nasal cannula. However, in patients with moderate hypoxemia, the beneficial effect on 3- and 5-day survival in Venturi mask treatment diminished, only 5-day (log-rank 7.160, $P=0.03$) survival was improved in patients who were treated with NIPPV.

In Cox regression, univariate analysis for preoperative mortality in the ED, age, onset of symptoms, form of oxygen delivery, hypoxemia severity, and NT-proBNP were related to preoperative mortality in the ED (*Table S1*). In Cox regression analysis for 3- and 5-day mortality in the ED, NIPPV was related to a significantly low 3-day [unadjusted hazard ratio (HR) 0.189, 95% confidence interval (CI): 0.045–0.804, $P=0.02$] and 5-day (unadjusted HR 0.128, 95% CI: 0.031–0.538, $P=0.005$) mortality risk; when adjusted for hypoxemia severity and

Table 1 Baseline characteristics of patients between groups

Characteristics	Overall (n=187)	Nasal cannula (n=91)	Venturi mask (n=60)	NIPPV (n=36)	P value
Age (years)	53.24±12.66	53.76±13.3	52.35±11.38	53.42±13.25	0.80
Male	141 (75.40)	72 (79.12)	44 (73.33)	25 (69.44)	0.47
Body mass index (kg/m ²)	24.8 (23.46, 26.89)	25.1 (23.53, 26.89)	24.49 (23.47, 26.64)	24.46 (21.78, 28.17)	0.36
Smoking	105 (56.15)	52 (57.14)	36 (60.00)	17 (47.22)	0.46
Comorbidity					
Hypertension	123 (65.78)	58 (63.74)	38 (63.33)	27 (75.00)	0.46
Diabetes	8 (4.28)	2 (2.20)	3 (5.00)	3 (8.33)	0.29
Onset of AAD (h)	49.00 (20.00, 99.00)	24.00 (12, 72)	77.5 (50.5, 99.75)	75.52 (30, 138)	<0.001
Severity of hypoxemia (mild)	124 (66.31)	65 (71.43)	40 (66.67)	19 (52.78)	0.13
Underwent surgery	103 (55.08)	49 (53.85)	35 (58.33)	19 (52.78)	0.39
Vital signs					
Heart rate (bpm)	99 (90, 108)	98 (90, 107)	101 (92, 109)	98 (88, 109)	0.49
MAP (mmHg)	101 (87, 123)	100 (89, 123)	99 (82, 116)	107 (87, 138)	0.49
Laboratory tests					
Lactate (mmol/L)	1.1 (0.8, 2.0)	1.1 (0.8, 2.0)	1.1 (0.8, 2.0)	1.0 (0.73, 1.56)	0.36
WBC (×10 ⁹ /L)	12.83 (9.40, 15.39)	13.17 (9.79, 16.36)	13 (9.4, 15.19)	11.5 (7.5, 13.9)	0.13
PLT (×10 ⁹ /L)	199 (151, 255)	190 (135, 245)	210 (165.5, 256)	197.5 (145, 264.25)	0.29
NT-proBNP (pg/mL)	420 (185, 1,118)	412 (185, 1,118)	388.5 (188.25, 1,002.75)	509 (111, 2,216)	0.65
CRP (mmol/L)	91.00 (27.77, 166.00)	88.00 (22.90, 155.00)	110.80 (30.52, 167.35)	91.60 (36.00, 177.00)	0.48
Creatinine (mmol/L)	96.00 (79.00, 135.00)	98.50 (80.65, 137.25)	89.00 (77.00, 121.00)	89.52 (69.50, 166.60)	0.25
D-dimer (ng/mL)	7,920 (3,230, 17,215.00)	8,860 (3,942.50, 18,055.00)	5,580 (2,227.5, 1,4227.0)	10,190 (2,700.00, 20,000.00)	0.16
LVEF (%)	62.87±7.88	62.52±8.53	62.97±7.85	63.63±6.13	0.78

Values are mean ± standard deviation, n (%), or median (interquartile range). NIPPV, non-invasive positive pressure ventilation; AAD, acute aortic dissection; MAP, mean arterial pressure; WBC, white blood cell; PLT, platelet; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; LVEF, left ventricular ejection fraction.

the onset of AAD in Model 1, the low 3-day (adjusted HR 0.098, 95% CI: 0.013–0.761, P=0.03) and 5-day (adjusted HR 0.059, 95% CI: 0.008–0.449, P=0.006) mortality risk remained significant. Then, when we further adjusted age and gender in Model 2, the relationship between NIPPV and low 3-day (adjusted HR 0.102, 95% CI: 0.013–0.791, P=0.03) and 5-day (adjusted HR 0.057, 95% CI: 0.008–0.427, P=0.005) mortality risk remained significant, when nasal cannula group was adopted as reference group (Table 2).

Secondary outcomes

Among patients with hypoxemia, around 50% finally received surgery, and the prevalence was similar between

groups. The prevalence of intubation rate in the ED was significantly different between groups (P=0.004), which was 27.47% in the nasal cannula group, 15% in the Venturi mask group, and 2.78% in the NIPPV group. Among patients who received surgery, the post-surgery length of intubation and the length of ICU stay were the lowest in the NIPPV group (Table 3).

Discussion

Our study found that NIPPV was a useful mode of oxygenation therapy in AAD patients with hypoxemia. The use of NIPPV was associated with lower ED mortality. Of

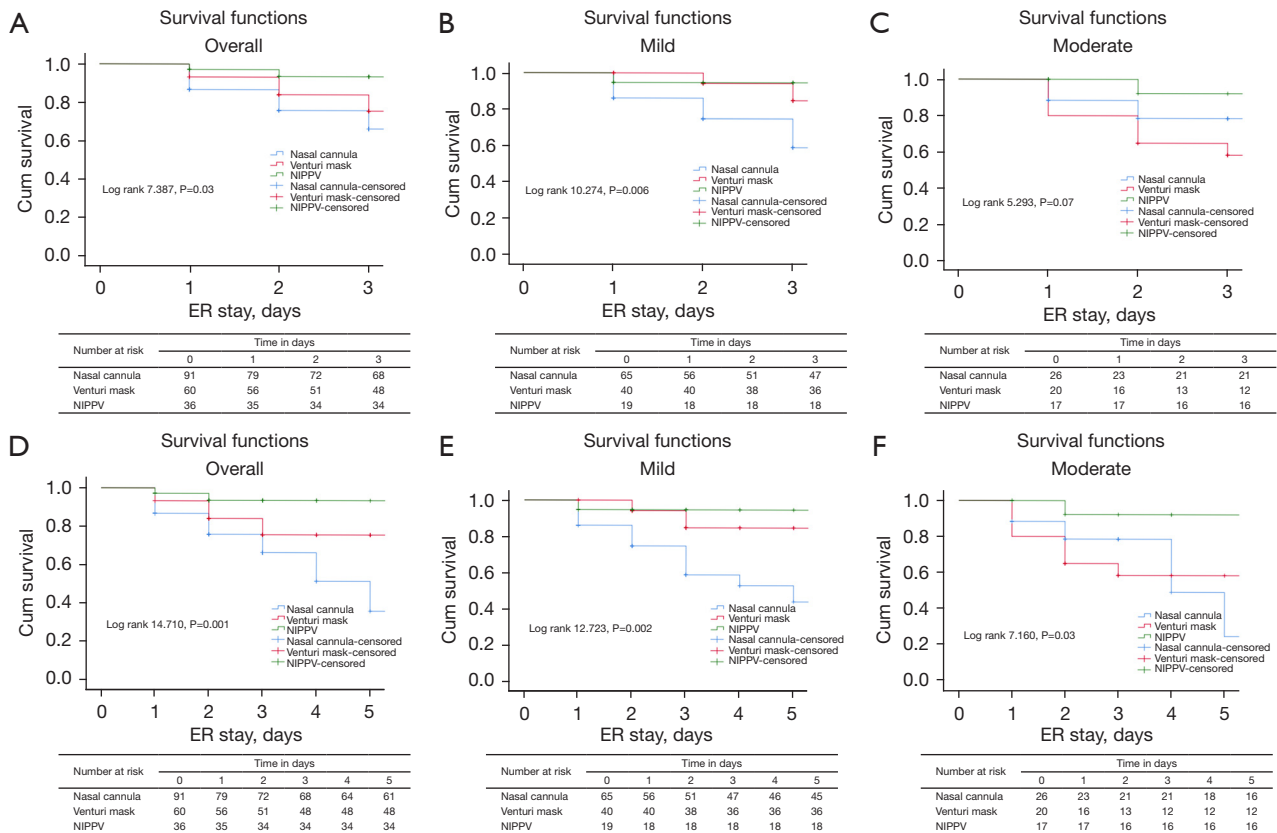


Figure 2 Effect of different oxygenation therapy on overall 3-day survival [(A) in overall patients; (B) in patients with mild hypoxemia; (C) in patients with moderate hypoxemia] and 5-day survival [(D) in overall patients; (E) in patients with mild hypoxemia; (F) in patients with moderate hypoxemia] in AAD patients with hypoxemia in the ED. ER, emergency room; NIPPV, non-invasive positive pressure ventilation; AAD, acute aortic dissection; ED, emergency department.

those who received NIPPV, only 2.78% required intubation in the ED. Among patients who underwent surgery, patients with NIPPV therapy had a shorter length of ICU stay, length of post-surgery intubation, and length of hospital stay.

NIV has long been considered a first-line therapy for acute-on-chronic conditions, such as chronic obstructive pulmonary disease (COPD) and cardiogenic pulmonary edema; however, its use is recommended beyond the two conditions mentioned above. Post-extubation in patients at high risk and immunocompromised patients could also benefit from NIV therapy (17). The beneficial effects on mortality were still less clear in non-COPD patients (18). AAD patients with hypoxemia had pathologic changes similar to acute respiratory distress syndrome (ARDS). Excessive systematic inflammation has been considered to predominately contribute to oxygen impairment in AAD and resulted in detrimental consequences (3,5).

Inflammatory mediators can amplify lung injury and epithelial permeability (19). Damage to the alveolar-capillary membrane has been shown to lead to the accumulation of protein-rich fluid in the pulmonary parenchymal interstitium, inactivation of surfactant, atelectasis, and impaired gas exchange and cause refractory hypoxemia (20). Studies on the use of a noninvasive oxygenation strategy in ARDS with diverse pathologies have shown controversial results (21,22). In the current study, NIPPV was shown to effectively reduce ED mortality in AAD patients with hypoxemia; both 3- and 5-day mortality were significantly lower in the NIPPV group, after adjustment for age, gender, brain natriuretic peptide (BNP), onset of AAD, and ARDS severity.

The noninvasive oxygenation strategy has been shown to be capable of preventing endotracheal intubation in patients with mild and mild-to-moderate hypoxemia (23) and reducing the tracheal reintubation rate in patients with hypoxemic respiratory failure after abdominal

Table 2 Cox regression analysis of risk factors for short-term mortality in AAD patients with hypoxemia

Covariates	Unadjusted model		Adjusted model 1		Adjusted model 2	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
3-day mortality						
Nasal cannula	Ref					
Venturi mask	0.659 (0.327, 1.326)	0.24	0.982 (0.426, 2.263)	0.97	1.184 (0.489, 2.865)	0.71
NIPPV	0.189 (0.045, 0.804)	0.02	0.098 (0.013, 0.761)	0.03	0.102 (0.013, 0.791)	0.03
NT-proBNP (pg/mL)						
<185	Ref					
185–1,118	0.82 (0.303, 2.218)	0.70	0.756 (0.278, 2.057)	0.58	0.657 (0.235, 1.842)	0.43
>1,118	2.184 (0.839, 5.684)	0.11	2.692 (1.011, 7.172)	0.048	2.433 (0.876, 6.758)	0.09
Age (years)						
<44	Ref					
44–61	2.262 (0.776, 6.951)	0.14	2.171 (0.741, 6.359)	0.16	2.137 (0.730, 6.529)	0.17
>61	2.840 (0.916, 8.809)	0.07	2.743 (0.879, 8.564)	0.08	2.782 (0.891, 8.691)	0.08
Gender						
Male	Ref					
Female	0.667 (0.293, 1.519)	0.34				
Hypoxemia severity						
Mild	Ref					
Moderate	1.095 (0.563, 2.13)	0.79				
Onset of AAD (h)						
<20	Ref					
20–99	0.524 (0.258, 1.064)	0.07	0.641 (0.265, 1.549)	0.32	0.663 (0.27, 1.628)	0.66
>99	0.407 (0.156, 1.059)	0.07	0.434 (0.129, 1.459)	0.18	0.439 (0.132, 1.46)	0.18
5-day mortality						
Nasal cannula	Ref					
Venturi mask	0.485 (0.248, 0.949)	0.04	0.68 (0.311, 1.486)	0.33	0.582 (0.285, 1.192)	0.14
NIPPV	0.128 (0.031, 0.538)	0.005	0.059 (0.008, 0.449)	0.006	0.057 (0.008, 0.427)	0.005
NT-proBNP (pg/mL)						
<185	Ref					
185–1,118	1.006 (0.404, 2.503)	0.99	0.981 (0.389, 2.475)	0.97	0.914 (0.353, 2.365)	0.85
>1,118	2.234 (0.918, 5.434)	0.08	2.916 (1.146, 7.416)	0.03	2.758 (1.050, 7.242)	0.04
Age (years)						
<44	Ref					
44–61	1.804 (0.737, 4.418)	0.20				
>61	2.217 (0.852, 5.772)	0.10				

Table 2 (continued)

Table 2 (continued)

Covariates	Unadjusted model		Adjusted model 1		Adjusted model 2	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Gender						
Male	Ref					
Female	0.867 (0.428, 1.755)	0.69				
Hypoxemia severity						
Mild	Ref					
Moderate	1.243 (0.681, 2.267)	0.48				
Onset of AAD (h)						
<20	Ref					
20–99	0.525 (0.272, 1.014)	0.055	0.658 (0.292, 1.486)	0.31	0.650 (0.282, 1.497)	0.31
>99	0.462 (0.198, 1.08)	0.08	0.611 (0.221, 1.683)	0.34	0.603 (0.219, 1.664)	0.33

Model 1 adjusted for hypoxemia severity and onset of AAD; Model 2 further adjusted for age and gender based on the previous model. AAD, acute aortic dissection; CI, confidence interval; NIPPV, non-invasive positive pressure ventilation; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Table 3 Perioperative clinical outcomes

Outcomes	Overall (n=187)	Nasal cannula (n=91)	Venturi mask (n=60)	NIPPV (n=36)	P value
Length of ED stay (d)	2.0 (1, 3)	2.0 (1, 3)	2.5 (2, 4)	2.5 (1.25, 4)	0.33
ED intubation rate	35 (18.72)	25 (27.47)	9 (15.00)	1 (2.78)	0.004
Underwent surgery	102 (54.55)	49 (53.85)	35 (58.33)	18 (50.00)	0.72
Death					
Pre-surgery	48 (25.67)	33 (36.26)	12 (20.00)	3 (8.33)	0.002
Post-surgery	16/102 (15.69)	11/49 (22.45)	5/35 (14.29)	0/18 (0.00)	0.08
Length of ICU stay (d)	8.54 (4.23, 283.28)	11.20 (9.75, 12.5)	4.40 (3.9, 5.1)	2.31 (2.08, 5.44)	<0.001
Length of post-surgery intubation (h)	116.50 (39.30, 159.50)	151.69 (132.43, 175.95)	40.00 (37.78, 46.38)	25.10 (20.75, 76.25)	<0.001
Length of hospital stay (d)	21.35 (12.40, 28)	28.00 (20, 35)	30.00 (19, 37.5)	21.00 (17.75, 25.75)	<0.001

Values are n (%), n/N (%), or median (interquartile range). NIPPV, non-invasive positive pressure ventilation; ED, emergency department; ICU, intensive care unit.

surgery (24). The effectiveness of NIV on improving clinical outcomes and avoiding endotracheal invasive ventilation in acute hypoxemic respiratory failure has been validated (25–27). Oranger *et al.* showed that patients with ARDS can benefit from NIV by avoiding intubation at 7 and 14 days (28). Recently, a study revealed that patients who received thoracoabdominal aortic surgery could benefit from noninvasive ventilation (29). An important finding of our study was that NIPPV could

be a useful approach for avoiding preoperative intubation in AAD patients with hypoxemia. The NIPPV group had a significantly lower preoperative intubation rate when compared with nasal cannula and Venturi mask, regardless of the severity of hypoxemia. Moreover, we found that early application of NIPPV effectively reduced the length of postoperative intubation in AAD patients with hypoxemia.

NIV is able to open de-recruited alveoli, keep them open, and decrease the patient's dyspnea through a

reduction of the work of breathing and respiratory rate, therefore NIV can theoretically benefit patients with hypoxemia (30). Since the late 1980s, NIV has become the first-line intervention for acute respiratory failure. However, NIV is still underused in certain parts of the world because of a lack of experience and inadequate training and economic resources (31). The utilization rate of NIV varies between hospitals and departments in acute settings. It has been reported that patients with acute-on-chronic lung disease and acute pulmonary edema are most often initiated on NIV in the ED, whereas patients with *de novo* acute respiratory failure are most often in the ICU (32). Although the NIV application in acute *de novo* respiratory failure was between 37.8% and 41%, the success rate was uniformly higher than 60% regardless of different primary clinical outcomes and age group (33). Practice surveys of NIV use in the ED reported less usage of NIV in other etiologies except for acute cardiogenic pulmonary oedema and COPD (34). In the current study, the utilization rate of NIPPV was only 19.25%; comparable findings have been observed in a prospective observational cohort study conducted in Australia, wherein 12% of patients with acute respiratory failure received NIPPV in the ED (35), reflecting the undertreatment status for hypoxemia in AAD patients due to the overcrowding status in ED and lack of awareness of NIV utilization in ED physicians.

Critical care delivery is commonly seen in the ED. In a study, among patients who were admitted in the ICU, 15% received critical care therapy in the ED (36). The treatment in the ED has a significant impact on ICU outcomes in critically ill patients. Earlier applications in the ED of intensive therapies such as goal-directed therapy and NIV may reduce ICU costs by decreasing the length of stay and need for admission (37). In the current study, we did not observe the difference in surgery rate between groups but observed a positive impact of NIPPV on postoperative outcomes in AAD patients. Among patients who received surgery, the NIPPV group has the lowest in-hospital mortality, the shortest length of ICU stays, the length of intubation, and the length of hospital stay, which supported patients with hypoxemia and could benefit from early application of NIPPV.

Limitations of our study include its retrospective observational design and small sample size. In addition, the data were collected from a single hospital in a region of China and may not be generalizable to other centers elsewhere. Furthermore, although the number of patients enrolled is larger than in most of the prior studies, we were limited by

the small number of cases in NIV groups. Also, although we found that the levels of lactate, creatinine, and mean arterial pressure (MAP) at admission were similar between groups at baseline and were not risk factors of preoperative mortality, the prevalence of malperfusion and dynamic monitoring data on malperfusion due to the progress of the disease should have been considered in the analysis. Interoperative data were not included in this study; we cannot eliminate the effect of surgery on postoperative outcomes. These limitations might have compromised our results.

Conclusions

Utilization of NIPPV in AAD patients with hypoxemia in the ED can effectively decrease preoperative intubation rate and preoperative mortality and improve postoperative outcomes. A multicenter RCT on the effect of NIPPV use on outcomes is needed.

Acknowledgments

The authors thank all the patients who participated in this study.

Funding: The research was supported by the Ministry of Science and Technology of the People's Republic of China (No. 2020AAA0109605 to X.L.); NSFC Incubation Program of GDPH (No. KY012021167 to Y.H.); Guangdong Medical Science and Technology Research Fund Project (No. A2021067 to W.L.); the National Natural Science Grant of China (No. 82072139 to B.H.); the Fund for Distinguished Young Scholar of GDPH (No. KJ012021184 to B.H.); and the High-level Hospital Construction Project of Guangdong Provincial People's Hospital (No. KJ0122019448 to B.H.).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-163/rc>

Data Sharing Statement: Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-163/dss>

Peer Review File: Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-163/prf>

Conflicts of Interest: All authors have completed the

ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-163/coif>). Y.H. is supported by NSFC Incubation Program of GDPH (No. KY012021167). B.H. is supported by the National Natural Science Grant of China (No. 82072139), the Fund for Distinguished Young Scholar of GDPH (No. KJ012021184), and the High-level Hospital Construction Project of Guangdong Provincial People's Hospital (No. KJ0122019448). W.L. is supported by Guangdong Medical Science and Technology Research Fund Project (No. A2021067). X.L. is supported by the Ministry of Science and Technology of the People's Republic of China (No. 2020AAA0109605). The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Guangdong Provincial People's Hospital (No. KY-Z-2021-444-02) and informed consent was provided by all the patients.

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- (English Language Editor: J. Jones)

Cite this article as: Liu B, Ye G, Wang R, Song F, Hong Y, Huang X, Hu B, Li W, Li X. Non-invasive positive pressure ventilation can reduce perioperative mortality in acute aortic dissection patients with hypoxemia. *J Thorac Dis* 2024;16(9):5835-5845. doi: 10.21037/jtd-24-163