

Effect of Sequential Noninvasive Ventilation on Early Extubation After Acute Type A Aortic Dissection

Kai Liu, Guang-Wei Hao, Ji-Li Zheng, Jing-Chao Luo, Ying Su, Jun-Yi Hou, Guo-Guang Ma, Shen-Ji Yu, Jun Li, Yong-Xin Sun, Hao Lai, Chun-Sheng Wang, Zhe Luo, and Guo-Wei Tu

BACKGROUND: Acute type A aortic dissection (aTAAD) is associated with a high incidence of prolonged postoperative invasive mechanical ventilation. We aimed to assess whether sequential noninvasive ventilation (NIV) could facilitate early extubation postoperatively after a spontaneous breathing trial (SBT) failure among aTAAD patients. **METHODS:** Beginning in December 2016, we transitioned our weaning strategy from repeated SBT until success (phase 1) to extubation concomitant with sequential NIV (phase 2) for subjects who failed their first SBT. The primary outcomes were re-intubation rate, duration of invasive ventilation, and total duration of ventilation. **RESULTS:** During the study period, 78 subjects with aTAAD failed their first postoperative SBT (38 subjects in phase 1 and 40 subjects in phase 2). Subjects extubated with sequential NIV had shorter median (interquartile range [IQR]) duration of invasive ventilation of 39.5 (30.8–57.8) h vs 89.5 (64–112) h ($P < .001$) and median (IQR) length of ICU stay of 6 (4.0–7.8) d vs 7.5 (5.8–9.0) d ($P = .030$). There were no significant differences between the 2 phases with regard to rates of re-intubation (7.5% vs 7.89%, $P = .95$), tracheostomy (2.5% vs 5.26%, $P = .53$), and in-hospital mortality (2.5% vs 2.63%, $P = .97$). **CONCLUSIONS:** Early extubation followed by sequential NIV significantly reduced duration of invasive ventilation and length of ICU stay without increasing re-intubation rate in postoperative subjects with aTAAD who failed their first SBT. *Key words:* noninvasive ventilation; extubation; acute aortic dissection. [Respir Care 2020;65(8):1160–1167. © 2020 Daedalus Enterprises]

Introduction

Surgical repair of acute type A aortic dissection (aTAAD) is a complicated cardiovascular procedure with high mortality and morbidity.^{1,2} In particular, the occurrence of prolonged mechanical ventilation after surgery is

approximately 30%,^{3–5} resulting in longer ICU length of stay (LOS), higher in-hospital mortality, and poorer long-term clinical outcomes.^{6–8} Furthermore, ventilator-associated pneumonia (VAP) is common in patients who receive prolonged mechanical ventilation after cardiac surgery and is associated with worse outcomes.^{9,10} Therefore, early liberation from invasive mechanical ventilation is an important therapeutic goal for patients with aTAAD. Our previous

Mr Liu, Mr Hao, Mr Luo, Mr Su, Mr Hau, Mr Ma, Mr Yu, Mr Tu, and Dr Luo are affiliated with the Department of Critical Care Medicine, Zhongshan Hospital, Fudan University, Shanghai, China. Mr Zheng is affiliated with the Department of Nursing, Zhongshan Hospital, Fudan University, Shanghai, China. Mr Li, Mr Sun, Mr Lai, and Mr Wang are affiliated with the Department of Cardiovascular Surgery, Zhongshan Hospital, Fudan University, Shanghai, China. Dr Luo is affiliated with the Department of Critical Care Med, Zhongshan Hospital, Fudan University, Xiamen, China.

Kai Liu, Guang-wei Hao, Ji-li Zheng contributed equally to this work.

This work was supported in part by grants from the Research Funds of Zhongshan Hospital (2019ZSYXQN34, 2019ZSQN13, 2018ZSQN53,

and XYYX201922) and the Research Fund of Shanghai Municipal Health Commission (2019ZB0105). The authors have disclosed no conflicts of interest.

Correspondence: Zhe Luo MD, Department of Critical Care Medicine, Zhongshan Hospital, Fudan University, Shanghai 200032, China. E-mail: luo.zhe@zs-hospital.sh.cn; Guo-Wei Tu MD, Department of Critical Care Medicine, Zhongshan Hospital, Fudan University, No. 180 Fenglin Road, Xuhui District, Shanghai 200032, China. E-mail: tu.guowei@zs-hospital.sh.cn.

DOI: 10.4187/respcare.07522

study showed that early extubation was feasible in cardiac surgical patients without increasing the risk of extubation failure.¹¹ However, to date, the optimal weaning strategy in patients with aTAAD has not been well demonstrated.

Noninvasive ventilation (NIV) as a weaning strategy for patients with cardiorespiratory decompensation was first reported in 1992.¹² By means of partial ventilatory support, NIV may improve arterial oxygenation, augment tidal volume, and decrease the work of breathing in patients with spontaneous breathing.^{13,14} Studies have shown that early extubation followed by immediate NIV is feasible among certain patients with mechanical ventilation.¹⁵⁻²⁰ We aimed to assess whether sequential NIV could facilitate early extubation after a spontaneous breathing trial (SBT) failure among postoperative subjects with aTAAD.

Methods

Study Design

This single-center, retrospective, historical-control study was performed in a 39-bed cardiac surgical ICU at the Zhongshan Hospital of Fudan University from November 2015 to February 2018. This is an academic teaching hospital with > 140 aTAAD surgeries performed per year. The care delivery of cardiac surgical patients in this hospital has been directed by intensivists at all times since August 2015.¹¹

To facilitate progress such as fast-track cardiac surgery, clinicians have paid more attention to early extubation. The mean duration of mechanical ventilation after general cardiac surgery has been reduced to < 24 h in our center. However, postoperative prolonged mechanical ventilation was common in subjects with aTAAD, which influences clinical efficacy. This encouraged us to make efforts to facilitate early liberation from mechanical ventilation. Since December 2016, early extubation and sequential NIV has been implemented in patients with aTAAD in our center. A before-and-after interventional study was conducted to compare clinical outcomes after implementation of this measure.

This study was approved by the Ethical Committee of the Zhongshan Hospital affiliated with Fudan University (No. B2018-011). Informed consent forms were not required because this retrospective study did not modify existing diagnostic or therapeutic strategies.

Population

We collected clinical data of subjects who underwent surgical treatment after aTAAD and who failed their first SBT between September 2015 and February 2018. Exclusion criteria were as follows: patients who died within 72 h of surgery; patients who were not suitable for NIV, such as those who had experienced stroke or spinal cord injury; and pregnancy.

QUICK LOOK

Current knowledge

Early liberation from invasive mechanical ventilation is an important therapeutic goal for patients with acute type A aortic dissection (aTAAD). To date, the optimal weaning strategy in aTAAD patients has not been well demonstrated.

What this paper contributes to our knowledge

In this retrospective, single-center study, early extubation followed by sequential noninvasive ventilation significantly reduced duration of mechanical ventilation and ICU length of stay without increasing re-intubation rate in postoperative subjects with aTAAD who failed the first spontaneous breathing trial.

There is a 2-step algorithm for the weaning procedure. First, readiness to wean is assessed by experienced intensivists who followed consistent criteria^{19,20}: clear consciousness, stable hemodynamics, adequate ventilation and oxygenation (PEEP + pressure support \leq 20 cm H₂O with PEEP of 5–8 cm H₂O; $P_{aO_2}/F_{IO_2} \geq$ 150 mm Hg), and absence of obvious abnormality on chest radiography or echocardiography. Second, the SBT was carried out using pressure support at 5 cm H₂O and PEEP at 5 cm H₂O, which continued for 30–60 min. Criteria for SBT failure included breathing frequency > 30 breaths/min or rapid shallow breathing index (breathing frequency/tidal volume) > 105 breaths/min/L; $S_{PO_2} < 90\%$; 20% increase or decrease from the baseline heart rate or blood pressure; use of accessory muscles; abdominal paradoxical movement; and substantial agitation, anxiety, or diaphoresis.²¹

Phase 1

Phase 1 extended from September 2015 to November 2016. Each subject was continued on mechanical ventilation under the previous model and settings after the first SBT failure. The intensivists tried to differentiate the reason for wean failure. This cycle was repeated daily until either the subject was extubated after a successful SBT or tracheostomy was performed.

Phase 2

Phase 2 extended from December 2016 to February 2018. After failure to succeed in the first SBT, the level of pressure support was adjusted to make the subject comfortable and to achieve a breathing frequency < 30 breaths/min. If parameters met the readiness weaning criteria (ie, PEEP + pressure support \leq 20 cm H₂O with PEEP of 5–8 cm H₂O),

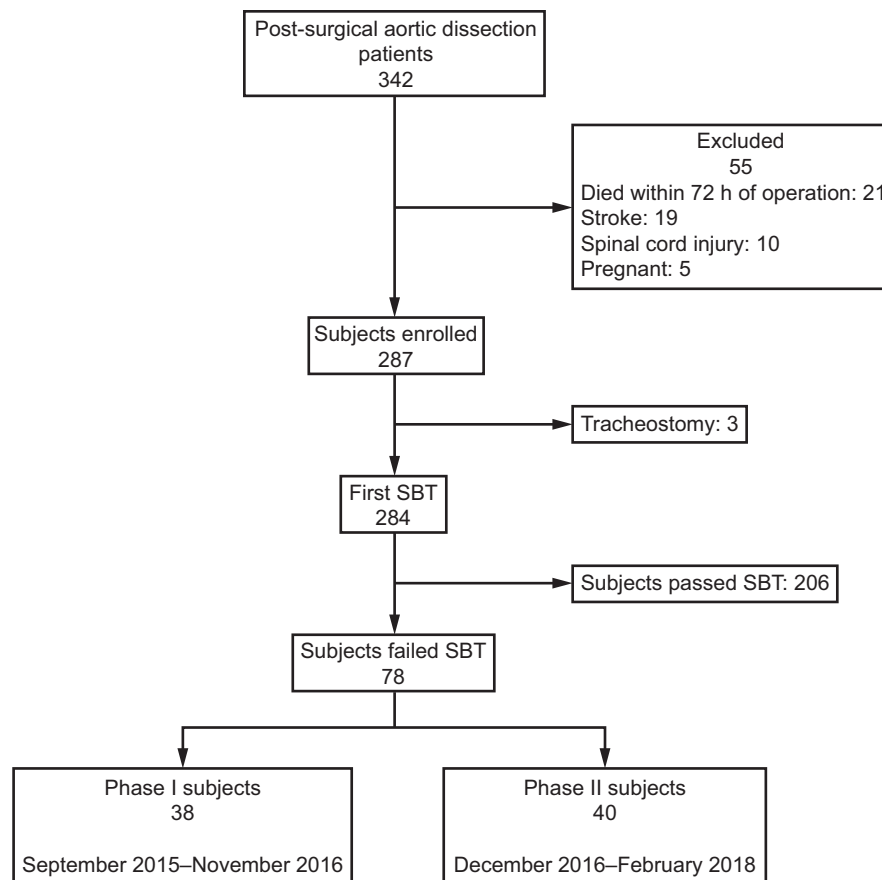


Fig. 1. Flow chart. SBT = spontaneous breathing trial.

the subject was extubated and subsequently supported with NIV. All subjects used a face mask (ZS-MZ-A, Shanghai Zhongshan Medical Technology, Shanghai, China) during NIV delivered via ICU ventilator with a heated humidifier. NIV settings were pressure support ventilation at 5–15 cm H₂O; PEEP 4–5 cm H₂O, up to 8–10 cm H₂O; inspiratory trigger sensitivity was as high as possible without auto-triggering; expiratory trigger was 25–30%; F_{IO₂} was the lowest that maintained the S_{PO₂} target. NIV targets were tidal volume 6–8 mL/kg predicted body weight, breathing frequency ≤ 30 breaths/min, and S_{PO₂} 95–98%. Intermittent or continuous NIV was decided by the physicians. This process was continued until either the subject tolerated 48 h of unsupported spontaneous breathing, was re-intubated, or required tracheostomy.

In both groups, nurses routinely used critical care pain observation tool scores to assess pain in our ICU, and analgesia drugs were used as needed to achieve a target level of 0–2. We used a VAP bundle (ie, head-up position, oral decontamination, daily awake, and peptic ulcer prophylaxis) and recommended tracheostomy after 7 d of mechanical ventilation. The decision for fiber bronchoscopy examination, lung recruitment maneuver, re-intubation, or initiation of antibiotic therapy and other treatments was made by the attending physicians. A flow chart of subject enrollment is

summarized in Figure 1, and the weaning protocols used in phase 1 and phase 2 are shown in Figure 2.

Data Collection

A paper recording system and an electronic charting system were both used in our hospital. The following data were collected: baseline demographic data (age, gender, body mass index); subjects' degree of disease severity (Acute Physiology and Chronic Health Evaluation II [APACHE II] score and European system for cardiac operative risk evaluation score [EuroScore]; comorbidities (hypertension, diabetes mellitus, and COPD); preoperative laboratory examination (creatinine and hemoglobin, left ventricular ejection fraction, N-terminal pro-brain natriuretic peptide [NT-proBNP], alanine aminotransferase, and aspartate transaminase); surgical parameters (surgery, cardiopulmonary bypass, aortic clamp, and deep hypothermic circulatory arrest duration); postoperative characteristics (left ventricular ejection fraction, NT-proBNP, pleural effusion, pneumothorax, alanine aminotransferase, aspartate transaminase, and acute renal failure, defined as requiring renal replacement therapy); hemodynamic variables (heart rate, mean artery pressure, and central venous pressure) and blood gas analysis (pH, P_aCO₂,

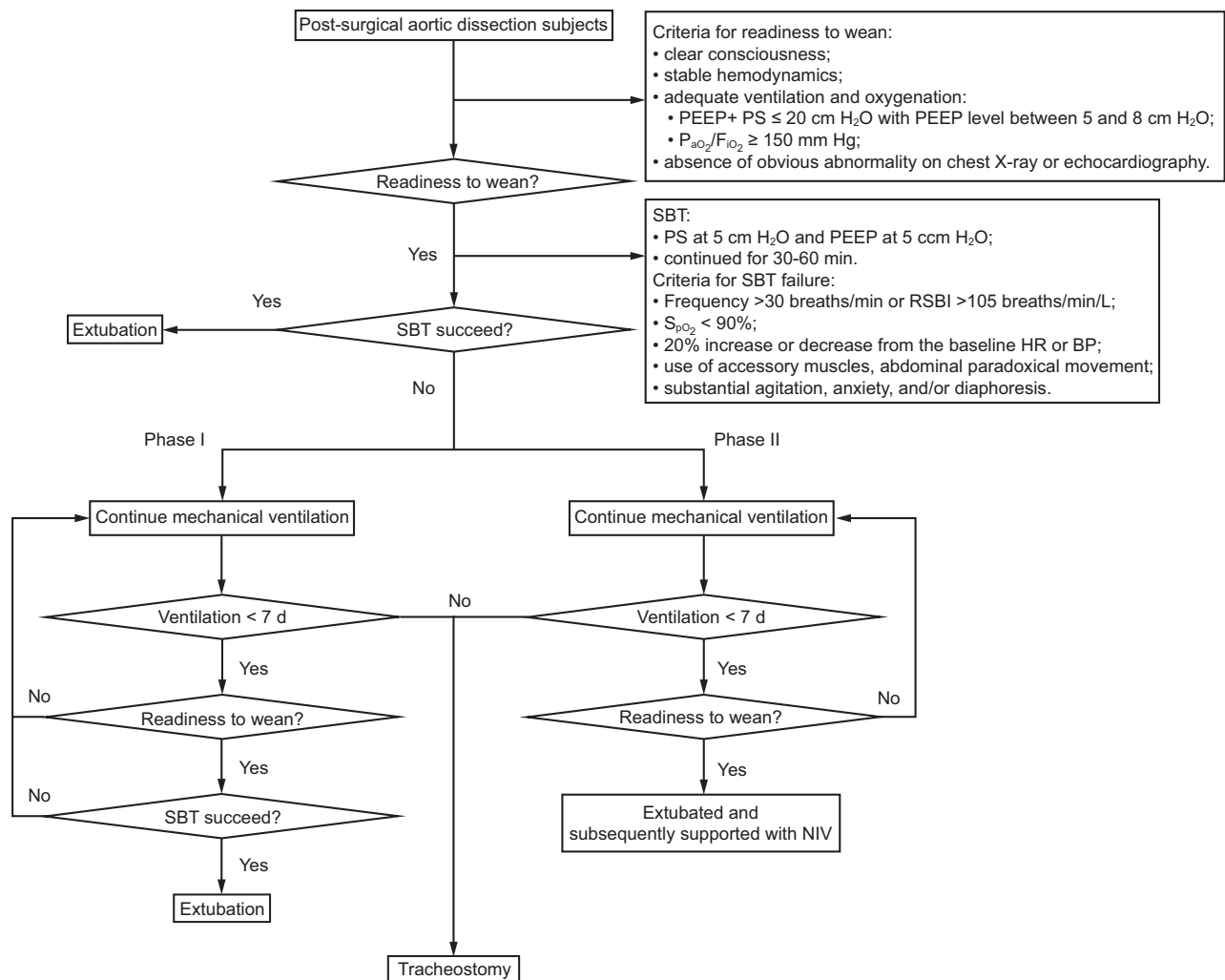


Fig. 2. Weaning protocol in phase 1 and phase 2. SBT = spontaneous breathing trial; NIV = noninvasive ventilation; RSBI = rapid shallow breathing index.

HCO_3^- , P_{aO_2}/F_{IO_2} , and lactate) of subjects before and after the first SBT; and outcomes (duration of mechanical ventilation, total duration of all mechanical ventilation, VAP, ICU LOS, hospital LOS, VAP occurrence, re-intubation, tracheostomy, and in-hospital mortality).

Clinical Outcomes

The primary outcomes of this study were mechanical ventilation duration, total duration of mechanical ventilation, and rates of re-intubation. Secondary outcomes were tracheostomy rates, ICU LOS, hospital LOS, and in-hospital mortality.

Statistical Analysis

Continuous variables were reported as the mean \pm SD or median (interquartile range [IQR]), and categorical variables were presented as adjusted proportions. Continuous data

were compared using the Student *t* test or the Mann-Whitney *U* test as appropriate, whereas differences between categorical variables were compared using the chi-square test. Kaplan-Meier curves depicting the 2 phases for mechanical ventilation duration and total duration of mechanical ventilation were determined and compared using the log-rank test. A *P* value $< .05$ was considered statistically significant. Statistical analyses were performed using Stata 13.0 (StataCorp, College Station, Texas), GraphPad Prism 5.0 (GraphPad Software, San Diego, California), and SPSS 22.0 software (IBM, Armonk, New York).

Results

Characteristics of Enrolled Subjects

Subject demographic and clinical characteristics are shown in Figure 1. A total of 342 postoperative aTAAD

Table 1. Clinical Characteristics of the Patients Enrolled

Variables	Phase 1	Phase 2	P
Preoperative characteristics			
Age, y	51 ± 12	49 ± 11	.43
Male	25 (65.8)	32 (80)	.16
Body mass index, kg/m ²	25.91 ± 2.97	26.59 ± 3.15	.34
EuroScore	7 ± 2	6 ± 2	.28
APACHE II	9 ± 3	10 ± 4	.13
Hypertension	17 (44.7)	18 (45.0)	.98
Diabetes mellitus	1 (2.6)	2 (5.0)	.59
COPD	1 (2.6)	0 (0)	.30
Creatine, μmol/L	88 ± 32	96 ± 40	.31
Hemoglobin, g/L	130 ± 15	127 ± 11	.35
Left-ventricular ejection fraction, %	62 ± 5	64 ± 4	.20
NT-proBNP, pg/mL	446 ± 353	353 ± 345	.25
ALT, U/L	24 ± 16	22 ± 19	.61
AST, U/L	22 ± 7	20 ± 7	.39
Operative characteristics			
Surgery duration, h	6.88 ± 0.62	6.72 ± 0.58	.23
CPB duration, min	199 ± 33	191 ± 20	.17
Aortic-clamp duration, min	116 ± 28	109 ± 23	.24
DHCA duration, min	28 ± 7	27 ± 5	.46
Postoperative characteristics			
Left-ventricular ejection fraction, %	61 ± 7	63 ± 4	.14
NT-proBNP, pg/mL	709 ± 491	632 ± 549	.52
Pleural effusion	6 (15.8)	9 (22.5)	.45
Pneumothorax	0 (0.0)	1 (2.5)	.33
ALT, U/L	34 ± 25	37 ± 26	.58
AST, U/L	55 ± 37	61 ± 26	.39
Acute renal failure	5 (13.2)	6 (15.0)	.82

Data are presented as mean ± SD or n (%). Phase 1: n = 38; Phase 2: n = 40.
EuroScore = European System for Cardiac Operative Risk Evaluation score
APACHE II = Acute Physiology and Chronic Health Evaluation II score
NT-pro BNP = N-terminal pro-brain natriuretic peptide
ALT = alanine aminotransferase
AST = aspartate transaminase
CPB = cardiopulmonary bypass
DHCA = deep hypothermic circulatory arrest

patients from September 2015 to February 2016 were analyzed. Fifty-five patients were excluded because of stroke, spinal cord injury, pregnancy, or death within 72 h after surgery. A total of 284 subjects were considered ready to undergo SBT, and 78 subjects failed the first SBT (ie, 38 in the phase 1 group and 40 in the phase 2 group). A total of 206 subjects who passed the first SBT were analyzed retrospectively. Median (IQR) invasive mechanical ventilation time was 30.2 (22.6–46.8) h, and fluid balance was 450 ± 220 mL before SBT. Eighteen subjects received NIV after extubation, of whom 4 were re-intubated and received tracheostomy.

Perioperative characteristics of the 78 subjects are shown in Table 1. In this study, half of the subjects had hypertension as a complication, and only 1 subject had COPD. All subjects had a normal left ventricular ejection fraction before the surgery. Overall baseline demographic

characteristics, severity of disease, preoperative comorbidities and laboratory tests, surgical parameters, and postoperative characteristics were comparable between groups. Fluid balance in subjects between the 2 phases before SBT was 485 ± 210 mL versus 476 ± 198 mL ($P = .85$). No significant differences between groups were found in hemodynamic variables and blood gas analysis during SBT. Compared with pre-SBT parameters, however, a significant increase in post-SBT heart rate, mean arterial pressure, and breathing frequency were found in both phase 1 and phase 2 subject groups (Table 2).

Outcomes

The outcomes of the enrolled subjects are shown in Table 3. Compared with the phase 1 group, subjects in the phase 2 group had a shorter median mechanical ventilation duration (39.5 vs 89.0 h, $P < .001$) and ICU LOS (6 vs 7.5 d, $P = .030$), while the median total duration of mechanical ventilation (4 vs 4 d, $P = .18$), hospital LOS (14 vs 16 d, $P = .36$), and VAP incidence (2 vs 1, $P = .53$) were similar between the 2 phases. In phase 1, 6 subjects received NIV after extubation, after which 3 subjects were re-intubated. Two subjects underwent tracheostomy after re-intubation. In phase 2, 39 subjects received sequential NIV immediately after extubation, after which 3 subjects failed NIV and were re-intubated at 8 h, 28 h, and 51 h after extubation. One patient underwent tracheostomy due to the failure to meet readiness criteria of SBT within 7 d post-surgery. There were no significant differences between the 2 phases in rates of re-intubation (7.5% vs 7.89%, $P = .95$), tracheostomy (2.5% vs 5.26%, $P = .53$), and in-hospital mortality (2.5% vs 2.63%, $P = .97$).

Kaplan-Meier Analysis

Kaplan-Meier curves indicating mechanical ventilation and total duration of mechanical ventilation are depicted in Figure 3 and Figure 4, respectively. The median (IQR) duration of mechanical ventilation was 39.5 (35.3–42.7) h in the phase 2 group and 89 (73.9–104.1) h in the phase 1 group (log-rank $P < .001$). The median total duration of mechanical ventilation was 4 (3.5–4.5) d in the phase 2 group and 4 (3.3–4.7) d in the phase 1 group (log-rank $P = .22$).

Discussion

When comparing 2 mechanical ventilation weaning strategies from after surgical treatment of subjects with aTAAD who failed their first SBT, we found significant improvement in mechanical ventilation duration and ICU LOS after early extubation followed by sequential NIV. Other important clinical outcomes, such as total mechanical ventilation

duration, re-intubation rate, proportion of VAP, and in-hospital mortality, were similar between both phases. To our knowledge, this is the first study to evaluate the safety and effectiveness of sequential NIV as a weaning strategy from

mechanical ventilation in subjects with aTAAD who failed their first SBT.

Although untested, most critical care physicians believe that patients who fail SBT are critical and not suitable to be extubated. Managing such patients is one of the greatest challenges facing ICU physicians, with duration of the weaning phase exceeding 40–50% of the overall ventilation period.^{22,23} Vitacca et al²⁴ reported that pressure support ventilation, delivered during invasive ventilation (before extubation) and during NIV (after extubation), produced the same effects in terms of gas exchange, diaphragmatic effort, and respiratory mechanics. A meta-analysis indicated that a weaning strategy including NIV may reduce rates of mortality, re-intubation, and VAP, and it may decrease the duration of mechanical ventilation and ICU LOS.²⁵ Furthermore, NIV is the only respiratory support suggested for facilitative care after extubation in patients with COPD or with hypercapnia.^{15–17,26} In highly selected subjects with nonhypercapnic respiratory failure, similar results have been shown.^{18–20} NIV after extubation has been used in patients after surgery, but the evidence for early extubation is limited.

Liu et al²⁷ reported the rate of NIV failure after cardiac surgery to be 38.4%, with the predictors of NIV failure including multiple organ dysfunction, pneumonia, and hemodynamic instability before NIV, whereas a body mass index ≥ 25 kg/m² predicted NIV success. In this study, patients with stroke or spinal cord injury were excluded because these patients were not suitable for NIV and were susceptible to multiple organ dysfunction, longer ICU LOS, and higher rate of mortality and tracheostomy.²⁸ In addition, all subjects enrolled were hemodynamically stable. The mean body mass index in the phase 2 group was 26.59 kg/m². Therefore, it was considered that subjects enrolled in this study were suitable for sequential NIV after early extubation. It should be mentioned that all subjects enrolled in phase 2 who received sequential NIV had been

Table 2. Main Clinical Characteristics Before and After First SBT

Variables	Phase 1	Phase 2
Heart rate, beats/min		
Pre-SBT	83 \pm 10	81 \pm 7
Post-SBT	92 \pm 11*	93 \pm 12*
Mean arterial pressure, mm Hg		
Pre-SBT	75 \pm 10	73 \pm 5
Post-SBT	84 \pm 10*	86 \pm 11*
Central venous pressure, mm Hg		
Pre-SBT	10 \pm 2	10 \pm 3
Post-SBT	10 \pm 3	10 \pm 3
pH		
Pre-SBT	7.39 \pm 0.05	7.40 \pm 0.04
Post-SBT	7.40 \pm 0.04	7.39 \pm 0.05
P _a CO ₂ , mm Hg		
Pre-SBT	40.56 \pm 5.91	40.26 \pm 5.12
Post-SBT	41.29 \pm 5.05*	41.36 \pm 5.53*
P _a O ₂ /F _{IO} ₂ , mm Hg		
Pre-SBT	201.46 \pm 43.72	204.38 \pm 35.65
Post-SBT	182.33 \pm 32.74	187.53 \pm 34.55
HCO ₃ ⁻ , mmol/L		
Pre-SBT	24.24 \pm 3.08	24.43 \pm 3.42
Post-SBT	25.18 \pm 3.13	24.72 \pm 3.06
Lactate, mmol/L		
Pre-SBT	1.64 \pm 0.48	1.81 \pm 0.63
Post-SBT	1.71 \pm 0.51	1.76 \pm 0.59
Breathing frequency, breaths/min		
Pre-SBT	15 \pm 2	15 \pm 3
Post-SBT	33 \pm 2*	32 \pm 2*

Data are presented as mean \pm SD.

* $P < .05$ pre-SBT versus post-SBT.

SBT = spontaneous breathing trial

Table 3. Outcome of Who Failed the First SBT

Variables	Phase 1	Phase 2	<i>P</i>
Duration to first SBT	38 (28.8–58.3)	39.5 (30.8–57.8)	.82
Duration of mechanical ventilation, h	89.5 (64–112)	39.5 (30.8–57.8)	< .001
Duration of total mechanical ventilation, h	89.5 (64–113.3)	77.5 (56.3–105.8)	.17
Noninvasive ventilation	6 (15.8)	39 (97.5)	< .001
Ventilator-associated pneumonia	2 (5.3)	1 (2.50)	.53
Re-intubation	3 (7.9)	3 (7.50)	.95
Tracheostomy	2 (5.3)	1 (2.5)	.53
ICU length of stay, d	7.5 (5.8–9.0)	6 (4.0–7.8)	.030
Hospital length of stay, d	16 (12–18)	14 (12–18)	.36
In-hospital mortality	1 (2.6)	1 (2.5)	.97

Data are presented as median (interquartile range) or *n* (%).

SBT = spontaneous breathing trial

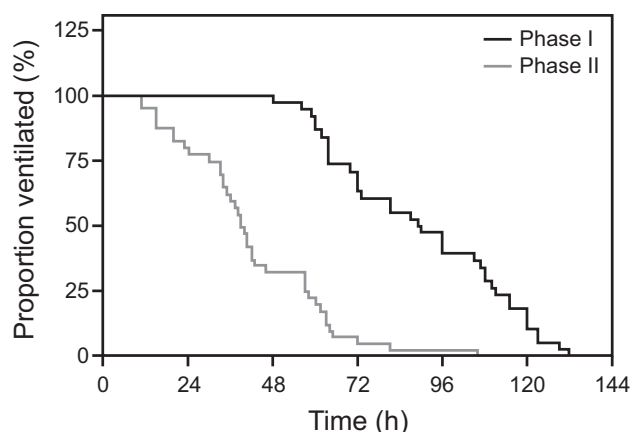


Fig. 3. Kaplan-Meier curve of percentage of subjects receiving mechanical ventilation.

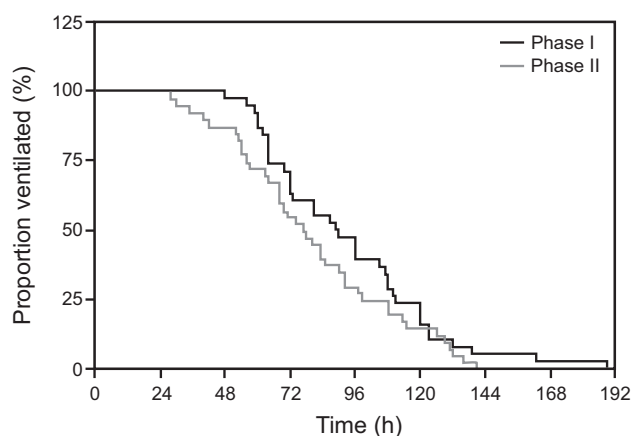


Fig. 4. Kaplan-Meier curve of percentage of subjects receiving mechanical ventilation or noninvasive ventilation.

under critical assessment of the readiness criteria for SBT to ensure the safety of early extubation.

Although re-intubation rates, tracheostomy rates, hospital LOS, and in-hospital mortality were comparable between both phases, a downward trend was seen in total mechanical ventilation duration, as was a reduction of ICU LOS. Subjects in this study received a complicated procedure including ascending aortic and hemi- or total-arch replacement concomitant with or without surgical treatment of the aortic root as well as a stent elephant trunk. Such a complicated surgery would definitely affect pulmonary function as well as diaphragmatic function.^{29,30} NIV might serve as a bridge to successful extubation by reducing the work of breathing. Patients undergoing mechanical ventilation are often unable to speak and may be under significant duress, both physically and psychologically.^{31,32} An earlier shift from mechanical ventilation to NIV for patients with aTAAD may provide more comfort and facilitate early mobilization. Although we could not provide an accurate amount of sedative use in the 2 phases in this controlled study, sedation was

believed to be less demanding in NIV than in mechanical ventilation.³³⁻³⁷ This would reduce both the cost to patients and the burden on the health care system.³⁸

There were several limitations to this study. First, this was a retrospective study, so important clinical data, such as excursion of the diaphragm and tidal volume at the end of the first SBT, were not included. Second, aTAAD is a relatively infrequent occurrence at most institutions. The small number of subjects diminished the strength of the evidence in this study. Further prospective, multi-center studies are necessary to confirm the results of this study.

Conclusions

Early extubation followed by sequential NIV significantly reduced duration of mechanical ventilation and ICU LOS, without increasing re-intubation rate, tracheostomy, or in-hospital mortality, in postoperative patients with aTAAD who failed the first SBT. Further prospective randomized studies with a larger sample size are required to validate our findings.

ACKNOWLEDGEMENTS

Six of the authors (K Liu, JL Zheng, Y Su, GG Ma, Z Luo, and GW Tu) fought against the COVID-19 epidemic in Wuhan for nearly two months. We thank them for their brave efforts.

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