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Decreasing re-intubation using prophylactic noninvasive ventilation in elderly patients: A propensity-matched study

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ABSTRACT

Purpose: Prophylactic noninvasive ventilation (NIV) reduces re-intubation in high-risk patients. However, its effects in elderly patients remain unclear. Here, we investigated the efficacy of prophylactic NIV in elderly patients after a planned extubation.

Materials and methods: From January 2011 to December 2017, patients aged ≥65 years old were enrolled after completing an SBT. After extubation, patients who immediately received NIV were classified as the prophylactic NIV group, and those who did not were classified as the control group. *Re*-intubation was recorded at postextubation 72 h.

Results: We enrolled 171 and 120 patients in the NIV and control groups, respectively. Patients in the NIV group had a lower re-intubation rate (6.4% vs. 23.3%, $p < 0.01$) and lower hospital mortality (22.2% vs. 35.8%, $p = 0.01$) than controls. In addition, prophylactic NIV was an independent protective factor for re-intubation (OR = 0.15, 95% CI: 0.07–0.34, $p < 0.01$ for all patients; OR = 0.16, 95% CI: 0.05–0.52, $p < 0.01$ for AECOPD patients, and OR = 0.17, 95% CI: 0.05–0.62, p < 0.01 for pneumonia/ARDS patients). After completing propensity-matched analyses, prophylactic NIV also reduced re-intubation and hospital mortality.

Conclusions: Elderly patients received benefits from prophylactic NIV after a planned extubation.

1. Introduction

The re-intubation rate within 72 h after extubation is 10–20% in all planned extubation patients [1]. Older age is associated with increased re-intubation [2,3]. In patients aged ≥65 years old, the rate of re-intubation is 29% [4], and it is associated with an eight-fold increase in nosocomial pneumonia, a two-fold increase in ICU and hospital stay, and a five-fold increase in death [5-7]. Therefore, it is necessary to identify effective methods to reduce re-intubation.

Noninvasive ventilation (NIV) is widely used to wean patients from mechanical ventilation [8,9]. In patients at high risk for extubation failure, NIV reduces re-intubation when it is used preventively after successful spontaneous breathing trials (SBTs) [10-12]. To the best of our knowledge, among studies that have investigated the benefits of prophylactic NIV, only two have considered age ≥65 years to be a risk factor for re-intubation [12,13]. However, those studies enrolled elderly patients as well as patients younger than 65 years old and had other confounding factors that caused them to fail to directly demonstrate the effects of prophylactic NIV on elderly patients.

We investigated the efficacy of prophylactic NIV in elderly patients with a large sample size, and herein report the benefits of this treatment (avoidance of re-intubation at postextubation 72 h).

2. Methods

2.1. General management

This was a retrospective, observational study performed in a respiratory intensive care unit. It was approved by our ethics committee and the institutional review board. No additional interventions were performed in this study beyond routine medical care, so informed consent was waived. We collected data on patients admitted to our department from January 2011 to December 2017. Those whose endotracheal tube was removed after a successful spontaneous breathing trial were candidates for this study. Patients aged ≥65 years old were enrolled. However, patients who underwent invasive mechanical ventilation for durations of <24 h were excluded. In addition, data on some patients extracted from a previous study were secondarily analyzed [14].

All patients receiving invasive mechanical ventilation were managed by our hospital protocol. Suction was performed by nurses. Secretions were collected in a suction trap, and volumes were recorded. Patients with weaning potential were screened every

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morning according to the following guidelines: adequate oxygenation (PaO_2/FiO_2 ≥ 150, PEEP ≤5 cmH_2O), temperature ≤ 38 °C, respiratory rate ≤ 30 breaths/min, heart rate ≤ 120 beats/min, and hemodynamic stability [15,16]. If a patient passed screening (all the items should be passed), an SBT was initiated to judge spontaneous breathing ability. If this failed, invasive mechanical ventilation continued until death, withdrawal of therapy, or transfer to another hospital. The SBT was performed for 120 min on 6 to 8 cmH_2O of pressure support ventilation [17]. It was terminated if the patient developed any of the following: rapid shallow breathing index >105, SpO_2 < 90% at FiO_2 ≥ 0.5, heart rate ≥ 140 or ≤ 50 beats/min, systolic blood pressure ≥ 180 or ≤ 90 mmHg, diminishing consciousness or diaphoresis, or clinical signs indicating respiratory muscle fatigue, labored breathing, or both. If the SBT failed, patients received comfortable ventilation, and screening was continued the following day.

As this was a retrospective study, the attending physicians determined whether a patient would receive prophylactic NIV (immediate use) or conventional oxygen treatment (control group) after a successful SBT. Before extubation, the following parameters were collected: Glasgow coma score (GCS), respiratory rate, heart rate, tidal volume, minute ventilation, rapid shallow breathing index, intubation periods, cough peak flow, and secretions collected over the course of the preceding 24 h. A spirometer (Chestgraph HI-101, Chest MI, Tokyo, Japan) was used to measure cough peak flow. Patients were positioned at 30° to 45° and instructed to cough through an endotracheal tube spirometer. The best of three attempts was recorded as the cough peak flow [18]. In addition, arterial blood gas tests, routine blood tests, electrolyte tests, and kidney function tests were also collected. *Re*-intubation was recorded at postextubation 72 h.

2.2. NIV management

Patients receiving prophylactic NIV (BiPAP Vision or Respironics V60) were managed as follows. The oronasal mask was the first choice. The size of the mask was selected according to the patient's facial type. If there were no contraindications, the patient was kept at 30° to 45°, to avoid aspiration. To guarantee maximal efficacy, the NIV was kept in continuous use for the initial periods, but it was intermittently disconnected from the ventilator for drinking, eating, and clearing secretions.

The expiratory positive airway pressure was set at 4–6 cmH_2O, and the inspiratory positive airway pressure was initially set at 8 cmH_2O, and adjusted by increments of 1–2 cmH_2O to obtain a tidal volume of >6 mL/kg or to the maximum tolerated level for each patient. FiO_2 was set to maintain SpO_2 at around 95%. If the patient felt at all uncomfortable during NIV, the parameters, circuit, humidification, air leaks, and straps were checked by a physician, respiratory therapist, or nurse to ensure maximal comfort for each patient. Weaning from NIV was considered 24 h later, according to hospital protocol [19].

2.3. Criteria for re-intubation

Re-intubation was determined by the attending physicians, based on the following indicators (one major criterion or at least two minor criteria). Major criteria were: (1) respiratory arrest, (2) loss of consciousness, (3) inability to correct dyspnea, (4) development of conditions necessitating intubation to protect the airway (coma or seizure disorders) or copious tracheal secretions requiring management, and (5) PaO_2/FiO_2 below 100 mmHg. Minor criteria were: (1) respiratory rate >35 breaths/min, (2) blood pH <7.35 for hypoxemic patients and 7.30 for hypercapnic patients, (3) persistent tachycardia, (4) persistent activation of accessory respiratory muscles, and (5) PaO_2/FiO_2 below 150 mmHg.

2.4. Statistical analysis

Normally distributed continuous variables are reported as mean values and standard deviations. The differences between the two groups were analyzed using the unpaired Student's *t*-test. Non-normally distributed continuous variables are reported as median values and interquartile ranges. The differences between the two groups were analyzed using the Mann–Whitney *U* test. For grouped data, the chi-square and/or Fisher's exact test were used to compare differences in proportions between groups and to derive *p* values. Multivariable logistic regression analyses were used to identify independent risk factors for re-intubation at postextubation 72 h. Values of $p < 0.05$ were taken to indicate statistical significance.

Propensity scores were estimated using multiple logistic regression analyses, with adjustments for age, sex, diagnosis, intubation periods, volume of secretions, APACHE II score at extubation, number of SBTs, cough peak flow, hemoglobin, GCS, pH, $PaCO_2$, PaO_2/FiO_2, respiratory rate, rapid shallow breathing index, and heart rate. After calculating propensity scores, we matched patients in the NIV and control groups with similar propensity scores at a 1:1 ratio, using the nearest-neighbor method, no replacement, and a 0.2 caliper width.

3. Results

We enrolled 171 patients in the prophylactic NIV group and 120 patients in the control group. After propensity matching, 88 patients were enrolled in each group. The NIV group had a higher proportion of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and a lower proportion of patients with pneumonia or acute respiratory distress syndrome (ARDS) than the control group (Table 1). In the propensity-matched cohort, only the heart rate collected at extubation was higher in the NIV group than in controls.

We entered age, sex, diagnosis, disease severity, intubation periods, volume of secretions, cough strength, number of SBTs, hemoglobin, GCS, pH, $PaCO_2$, PaO_2/FiO_2, respiratory rate, rapid shallow breathing index, and heart rate into a multivariable logistic regression analysis and found that prophylactic NIV was a protective factor for re-intubation at postextubation 72 h (odds ratio [OR] = 0.15, 95% confidence interval [CI]: 0.07–0.34, $p < 0.01$ for all patients; OR = 0.16, 95% CI: 0.05–0.52, p < 0.01 for AECOPD patients, and OR = 0.17, 95% CI: 0.05–0.62, p < 0.01 for pneumonia/ARDS patients). These results were also confirmed in the propensity-matched cohort (Table 3).

The outcomes of the two groups are summarized in Table 2. Prophylactic NIV was associated with lower rates of re-intubation within 72 h after extubation (6.4% vs. 23.3%, $p < 0.01$) and hospital mortality (22.2% vs. 35.8%, $p = 0.01$) compared with controls. These results were confirmed in the propensity-matched cohort. In subgroup analyses, prophylactic NIV was also associated with a lower rate of re-intubation in the AECOPD (5.0% vs. 24.4%, p < 0.01 for all patients, and 4.4% vs. 24.4%, p = 0.01 for propensity-matched patients) and pneumonia/ARDS (10.9% vs. 28.3%, $p = 0.03$ for all patients, and 12.8% vs. 33.3%, $p = 0.04$ for propensity-matched patients) populations compared with controls (Figs. 1 and 2). The NIV group also had a higher 90-day survival than the control group (Table 2 and Fig. 3).

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Table 1
Baseline data for each group.

	Overall cohort		*p*	Propensity-matched cohort		*p*
	NIV N = 171	Control N = 120		NIV N = 88	Control N = 88	
Age, years	76.6 ± 7.3	76.4 ± 7.4	0.78	76.7 ± 7.9	77.6 ± 7.6	0.49
Female/male	42/129	36/84	0.35	27/61	23/65	0.62
Causes for intubation						
AECOPD	121	45	<0.01	45	45	0.39
Pneumonia/ARDS	46	60		39	42	
Others	4	15		4	1	
Intubation periods before extubation, days	Median 5.9 IQR: 4.0–9.1	Median 5.6 IQR: 3.0–7.7	0.03	Median 5.9 IQR: 3.3–9.0	Median 5.9 IQR: 3.2–7.9	0.68
Secretions, mL/24 h before extubation	70 ± 44	77 ± 50	0.22	68 ± 45	80 ± 48	0.10
APACHE II score at extubation	13 ± 3	13 ± 3	0.62	13 ± 3	13 ± 3	0.77
Number of SBTs	Median 1 IQR: 1–2	Median 1 IQR: 1–2	0.64	Median 1 IQR: 1–2	Median 1 IQR: 1–2	0.84
Cough peak flow, L/min	62 ± 26	69 ± 35	0.04	62 ± 27	62 ± 32	0.88
Hemoglobin, g/dL	10.8 ± 2.3	10.7 ± 2.1	0.72	10.6 ± 2.3	10.9 ± 2.2	0.45
GCS	14.7 ± 1.1	14.6 ± 1.4	0.29	14.8 ± 0.8	14.5 ± 1.5	0.14
Physiologic parameters before extubation						
pH	7.42 ± 0.06	7.44 ± 0.05	0.03	7.43 ± 0.06	7.43 ± 0.05	0.49
$PaCO_2$, mmHg	51 ± 13	43 ± 11	<0.01	47 ± 11	45 ± 12	0.10
PaO_2/FiO_2	223 ± 71	260 ± 84	<0.01	238 ± 82	251 ± 75	0.26
Respiratory rate, breaths/min	22 ± 6	22 ± 5	0.79	23 ± 6	23 ± 4	0.44
Rapid shallow breathing index	56 ± 23	57 ± 23	0.64	57 ± 23	61 ± 22	0.22
Heart rate, beats/min	98 ± 15	93 ± 16	<0.01	100 ± 15	94 ± 16	0.01
Physiologic parameters at 72 h after extubation[a]						
pH	7.43 ± 0.06	7.44 ± 0.5	0.39	7.43 ± 0.06	7.43 ± 0.05	0.95
$PaCO_2$, mmHg	51 ± 13	45 ± 12	<0.01	49 ± 14	46 ± 12	0.20
PaO_2/FiO_2	237 ± 81	264 ± 91	0.02	240 ± 87	265 ± 91	0.10
Respiratory rate, breaths/min	23 ± 4	23 ± 3	0.67	23 ± 4	23 ± 4	0.92
Heart rate, beats/min	92 ± 16	91 ± 15	0.74	91 ± 15	92 ± 16	0.86

NIV = noninvasive ventilation, AECOPD = acute exacerbation of chronic obstructive pulmonary disease, ARDS = acute respiratory distress syndrome, IQR = interquartile range, SBT = spontaneous breathing trial, GCS = Glasgow coma score.

[a] The parameters in 25 patients who died or were discharged from the hospital within 72 h after extubation were unavailable. Among patients who stayed in the hospital longer than 72 h after extubation, arterial blood gas tests, respiratory rate, and heart rate were missed in 32, 40, and 37 patients, respectively.

4. Discussion

Our study, with a large sample size, demonstrated the benefits of prophylactic NIV in patients aged ≥65 years old. Prophylactic NIV reduced re-intubation at 72 h after extubation. This benefit was also confirmed in patients with AECOPD or pneumonia/ARDS.

The association between increased age and increased re-intubation is not surprising. Several previous studies have confirmed this point [2-4]. In one such study, the re-intubation rate was 29% in patients ≥65 years old [4]. In our study, it was 23.3% in the conventional oxygen-treatment group. This rate is much higher than the average value (15%) in the general population [20]. Thus, it is necessary to identify the appropriate means to avoid re-intubation. In our study, we preventively used NIV in elderly patients and found that re-intubation and hospital mortality decreased in this population. This indicates that the use of NIV immediately after extubation can benefit elderly patients.

To the best of our knowledge, of all studies that have investigated the efficacy of NIV in the postextubation period, only two counted patient age ≥ 65 years as a risk factor for re-intubation [12,13]. However, those studies enrolled patients younger than 65 years old along with elderly patients, and also did not perform subgroup analyses focusing on elderly patients. In contrast, we only enrolled patients ≥65 years old (171 cases in the NIV group and 120 cases in the control group). Furthermore, owing to our large sample size, we were able to confirm the benefits of prophylactic NIV in elderly patients. Moreover, we were also able to confirm these benefits in patients with AECOPD or pneumonia/ARDS.

Table 2
Outcomes of each group.

	Overall cohort		*p*	Propensity-matched cohort		*p*
	NIV N = 171	Control N = 120		NIV N = 88	Control N = 88	
ICU stay, days	Median 14 IQR: 9–19	Median 12 IQR: 7–21	0.09	Median 13 IQR: 9–21	Median 12 IQR: 8–24	0.87
Hospital stay, days	Median 21 IQR: 14–30	Median 24 IQR: 14–43	0.20	Median 23 IQR: 13–32	Median 24 IQR: 14–45	0.35
Postextubation ICU stay, days	Median 7 IQR: 3–10	Median 5 IQR: 2–11	0.14	Median 7 IQR: 4–11	Median 6 IQR: 3–14	0.81
Postextubation hospital stay, days	Median 11 IQR: 7–18	Median 14 IQR: 6–22	0.24	Median 11 IQR: 7–18	Median 13 IQR: 6–23	0.23
Re-intubation at 72 h	11 (6.4%)	28 (23.3%)	<0.01	7 (8.0%)	25 (28.4%)	<0.01
Hospital mortality	38 (22.2%)	43 (35.8%)	0.01	23 (26.1%)	37 (42.0%)	0.04
90-day survival after extubation	119 (68.6%)	68 (56.7%)	0.02	59 (67.0%)	45 (51.1%)	0.05
Nosocomial pneumonia after extubation	27 (15.8%)	28 (23.3%)	0.13	18 (20.5%)	24 (27.3%)	0.38

NIV = noninvasive ventilation, IQR = interquartile range.

Table 3
Multivariate logistic regression analyses identifying risk factors for re-intubation at postextubation 72 h.

	Overall cohort OR (95% CI)	p	Propensity-matched cohort OR (95% CI)	p
All patients				
Prophylactic NIV	0.15 (0.07–0.34)	<0.01	0.16 (0.058–0.43)	<0.01
Age, per year	1.10 (1.04–1.16)	<0.01	1.12 (1.06–1.19)	<0.01
Heart rate at extubation, per beat/min	1.03 (1.01–1.06)	0.02	1.04 (1.01–1.07)	0.02
Cough peak flow, per L/min	0.97 (0.96–0.99)	<0.01	NA	NA
AECOPD patients				
Prophylactic NIV	0.16 (0.05–0.52)	<0.01	0.13 (0.02–0.70)	0.02
pH at extubation	0.00 (0.00–0.08)	0.02	0.00 (0.00–0.04)	0.02
Cough peak flow, per L/min	0.95 (0.92–0.98)	<0.01	0.96 (0.92–0.99)	0.01
Pneumonia/ARDS patients				
Prophylactic NIV	0.17 (0.05–0.62)	0.01	0.17 (0.04–0.67)	0.01
Age, per year	1.14 (1.06–1.23)	<0.01	1.15 (1.059–1.25)	<0.01
Heart rate at extubation, per beat/min	1.05 (1.01–1.09)	0.02	1.05 (1.01–1.10)	0.03

NIV = noninvasive ventilation, OR = odds ratio, CI = confidence interval, AECOPD = acute exacerbation of chronic obstructive pulmonary disease, ARDS = acute respiratory distress syndrome.

NIV has been used after extubation for decades [10-12,21-25]. However, not all patients experience benefits from it. Two randomized controlled trials reported that NIV is used when respiratory distress occurs after a planned extubation, and the studies concluded that NIV does not reduce re-intubation or mortality [23,24]. In another randomized controlled trial, NIV was immediately used after a planned extubation in the general population but outcomes did not differ in terms of re-intubation or mortality [25]. This clarifies that NIV cannot reduce re-intubation when it is used in response to postextubation respiratory distress or preventively used in the general population. However, in three other randomized controlled trials, re-intubation was reduced when NIV was preventively used in patients at risk for extubation failure [10-12]. Thus, early use of NIV in at-risk patients after a planned extubation is recommended. Our study further confirms the benefits of prophylactic NIV in planned extubation patients ≥65 years old, suggesting a promising treatment for clinical practitioners.

The preventive use of NIV in patients with chronic respiratory disorders such as COPD has been widely investigated [10,26]. However, no studies have focused on the pneumonia/ARDS population. To the best of our knowledge, we are the first to report the preventive use of NIV in elderly patients whose respiratory failure was caused by pneumonia/ARDS and to find that NIV benefits this population. This is useful insight for clinical practitioners managing this population.

Previous studies on this topic did not report cough strength [10-12]. However, cough strength is associated with diaphragmatic function [27]. A weak cough indicates diaphragmatic dysfunction. In the general population, the average cough strength is 79.9 L/min of cough peak flow [18]. This value is much higher than what we reported because we only focused on elderly patients. In our study, most patients may have had diaphragmatic dysfunction. As NIV reduces the work of breathing, it may have compensated for insufficient diaphragmatic function in our study and thus reduced the rate of re-intubation.

This study had several limitations. Patient data at 72 h after extubation, which were retrospectively collected, were unavailable for some patients. This may have biased our results. Another weakness was the incongruent demographic data between the two groups. However, we performed a propensity-matched analysis to make the demographics comparable, used multivariable logistic regression analyses to adjust for confounders, and still found that prophylactic NIV was a protective factor for re-intubation in elderly patients. In subgroup analyses, we confirmed that prophylactic NIV reduced re-intubation in AECOPD and pneumonia/ARDS patients. However, the sample size may have been inadequate, which would diminish the strength of the evidence. Further studies should employ a larger sample size to confirm our results.

5. Conclusion

Preventive use of NIV after a planned extubation benefits patients ≥65 years old. It allows re-intubation to be avoided and reduces hospital mortality, making it a promising treatment for elderly patients.

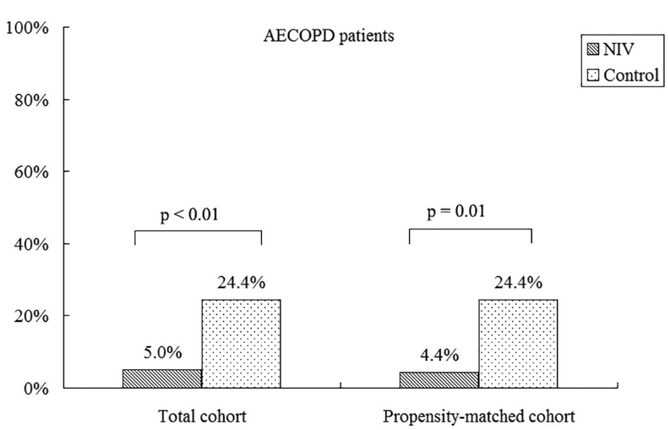

Fig. 1. *Re*-intubation rate in AECOPD patients.

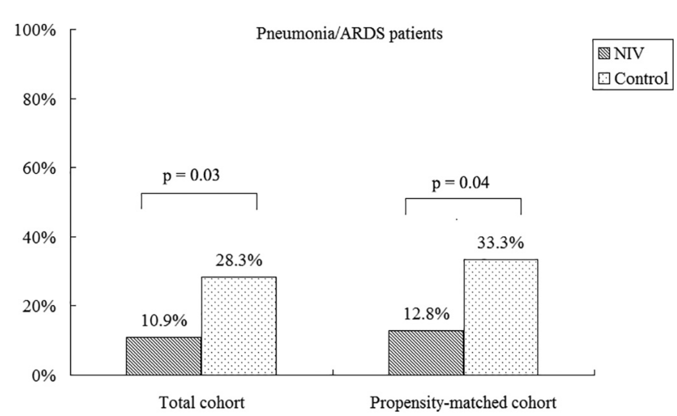

Fig. 2. Re-intubation rate in pneumonia/ARDS patients.

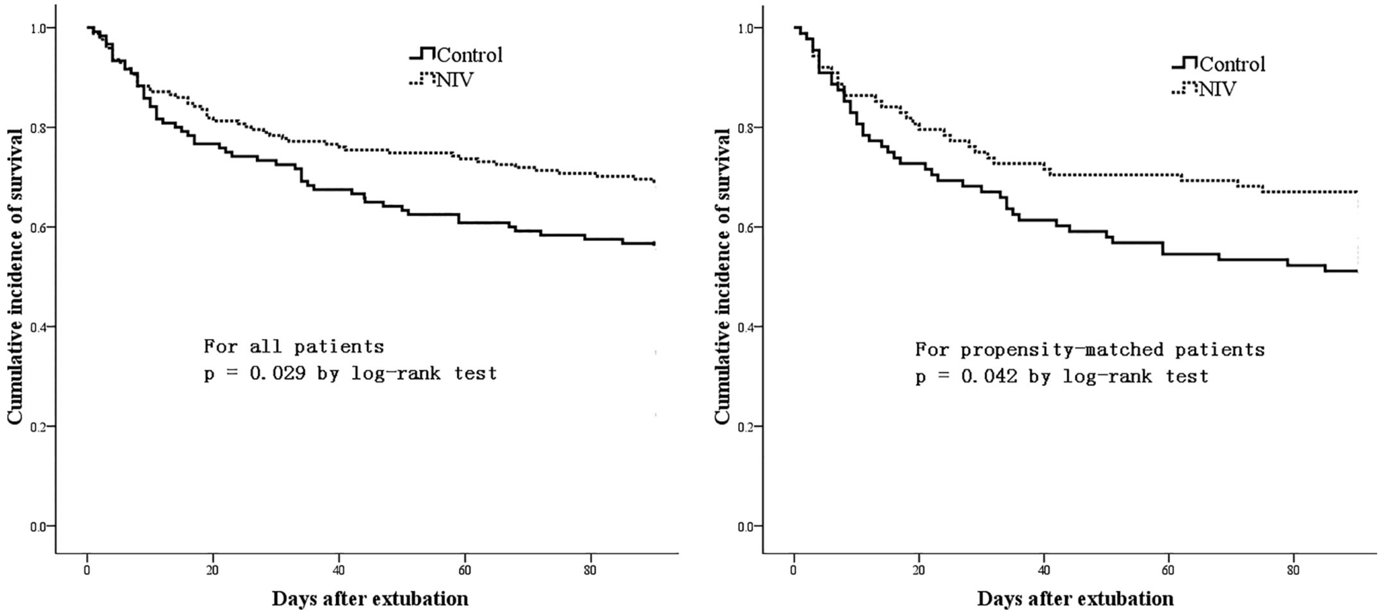

Fig. 3. Kaplan–Meier curves for 90-day survival.

Disclosures

We declare that there are no conflicts of interest in this study.

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