Noninvasive Ventilation to Treat Respiratory Failure After Cardiac Surgery: Predictors of Application and Outcome

Fotini Ampatzidou, Afroditi K Boutou, Lampros Karagounis, Nandor Marczin, Apostolos Gogakos, and George Drossos

BACKGROUND: Respiratory complications remain a major cause of morbidity in cardiac surgery patients. This study aimed to determine the prognostic parameters associated with the application of noninvasive ventilation (NIV) for the treatment of acute respiratory failure, along with the possible predictors associated with NIV failure, among the subjects who underwent cardiac surgery. **METHODS:** This was a retrospective cohort study. Data on all adult patients who underwent cardiac surgery in a single center between May 2012 and December 2016 were analyzed. Multivariate regression analysis with bootstrapping was used to identify which baseline and intraoperative parameters were associated with the application of NIV to treat acute postoperative respiratory failure. A univariate analysis was also applied to identify potential variables associated with NIV failure. $P < .05$ was considered significant. **RESULTS:** A total of 1,657 subjects (mean $\pm$ SD age 65.2 ± 10.7 y; 21.7% females) constituted the study population, 145 (8.8%) of whom were treated with NIV due to acute postoperative respiratory failure. Body mass index adjusted odds ratio 1.02, bias-corrected 95% CI 1.01–1.04, EuroSCORE (European System for Cardiac Operative Risk Evaluation) II (adjusted odds ratio 1.11, bias-corrected 95% CI 1.02–1.32), COPD (adjusted odds ratio 4.004, bias-corrected 95% CI 2.53–8.93), and preoperative estimated glomerular filtration rate (adjusted odds ratio 0.99, bias-corrected 95% CI 0.98–0.99) independently predicted NIV application. NIV treatment failed in 16 of the 145 subjects (11%) and age, EuroSCORE II, COPD, heart failure, renal replacement therapy, and postoperative stroke were all univariately associated with the outcome. **CONCLUSIONS:** NIV successfully treated acute respiratory failure in the vast majority of cardiac surgery subjects and COPD, EuroSCORE II, body mass index, and preoperative renal function were independently associated with its application. *Key words:* noninvasive ventilation; cardiac surgery; respiratory failure. [Respir Care 2019;64(9):1123–1131. © 2019 Daedalus Enterprises]

Introduction

Respiratory complications after cardiac surgery are not uncommon and contribute to increased postoperative mor-

bidity and mortality. General anesthesia effects, cardiopulmonary bypass (during which lungs are not ventilated), sternotomy, thoracotomy, postoperative pain, possible damage of the phrenic nerve, open pleural cavities, increased pulmonary capillary permeability, volume overload, systemic inflammatory responses, massive blood

Dr Ampatzidou is affiliated with the Cardiothoracic Intensive Care Unit, Cardiac Surgery Department, “G. Papanikolaou” General Hospital, Thessaloniki, Greece. Dr Boutou is affiliated with the Department of Respiratory Medicine, “G. Papanikolaou” General Hospital, Thessaloniki, Greece. Dr Karagounis is affiliated with the Cardiac Catheterization and Interventional Cardiology Department, Interbalkan Medical Centre, Thessaloniki, Greece. Dr Marczin is affiliated with the Cardiac Surgery Department, Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom. Dr Gogakos and Drossos are affiliated with the Department of Cardiothoracic Surgery, “G. Papanikolaou” General Hospital, Thessaloniki, Greece.

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Correspondence: Fotini Ampatzidou MD, Cardiothoracic Intensive Care Unit, Cardiac Surgery Department, “G. Papanikolaou” General Hospital, Exohi 57010 Thessaloniki, Greece. E-mail: fampatzidou@gmail.com.

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transfusions, and the patient's pre-existing comorbidities contribute to the postoperative risk of pulmonary complications.¹⁻⁸ The establishment of this respiratory derangement could be of variable severity, which ranges from atelectasis and lung volume reduction to acute lung injury and respiratory failure.⁹

Noninvasive ventilation (NIV), including both CPAP and noninvasive positive airway pressure modalities, is a technique used to deliver mechanical ventilation while avoiding the complications of endotracheal intubation.^{1,9} A reduced hospital infection rate, no need of sedation, and better patient tolerance, which allow for eating, drinking, coughing, and communication, are some of the many benefits of NIV.^{10,11} In cases of respiratory failure, the application of NIV has proven to reduce the reintubation rate and its associated complications, in-hospital mortality, and hospital length of stay, both among non-surgery patients, such as those with exacerbations of COPD, as well as among postoperative patients after major abdominal or thoracoabdominal surgery. Thus, the benefits of this technique are generally known.¹²⁻¹⁴ Among cardiac surgery subjects, NIV has previously been evaluated as an option to prevent or treat acute hypoxemic respiratory failure; however, results vary widely,^{1,15-17} and no specific indicators associated with the application of NIV or the outcome of this treatment have yet been identified.

Against this background, we conducted a cohort study that aimed to identify (a) the patient-specific and the operation-specific factors independently associated with NIV application as treatment modality for acute respiratory failure, and (b) the prognostic factors associated with NIV treatment success or failure in a cohort of postoperative subjects who had undergone a variety of cardiac surgery operations.

Methods

Study Population

This was a retrospective cohort study. Data on all adult subjects who underwent an elective, urgent, or emergency cardiac surgery (coronary artery bypass grafting, aortic dissection repair, thoracic aortic aneurysm repair, aortic or mitral valve repair or replacement, atrial septal defect closure, or any combination of these procedures) in the Department of Cardiothoracic Surgery, Papanikolaou Hospital, Thessaloniki, Greece, between May 2012 and December 2016, were prospectively collected into a clinical database. Data were then extracted and analyzed for all subjects who were extubated in the operating room or the ICU within 24 h, with the exception of patients who received NIV before surgery for any cause, patients who underwent off-pump surgery, patients who died during surgery or in the ICU without previous extubation, and

QUICK LOOK

Current knowledge

Acute respiratory failure after cardiac surgery is a common complication. Noninvasive ventilation (NIV) has previously been used for treatment; however, the results vary widely. No specific indicators associated with NIV application or outcomes have yet been identified.

What this paper contributes to our knowledge

NIV could successfully treat acute early postoperative respiratory failure in the majority of cardiac surgery patients. The presence of COPD, low preoperative renal function, higher body mass index, and high EuroSCORE II were independent characteristics of subjects who may need NIV for postoperative respiratory failure.

patients who were reintubated without previous application of NIV. All the participants gave informed consent for their participation in a clinical registry that collected baseline, in-hospital, and follow-up data after the cardiac operation. The construction of this clinical database had received ethical approval from the relevant institutional ethics committee, as previously described.¹⁸

Data Collection and Definitions

The baseline data, which were recorded for each subject on admission, included age; sex; body mass index (BMI); EuroSCORE (European System for Cardiac Operative Risk Evaluation) II; preoperative estimated glomerular filtration rate; left ventricle ejection fraction (evaluated by preoperative transthoracic Doppler echocardiogram); smoking habits (current or ever smoker); and a detailed medical history, which emphasized the presence of diabetes mellitus, dyslipidemia, arterial hypertension, stroke, peripheral vascular disease, COPD, heart failure according to the New York Heart Association classes I–IV, chronic atrial fibrillation, and history of previous cardiac surgery. The intraoperative data that were recorded included cardiopulmonary bypass time, type of operation (coronary artery bypass grafting or other), and complexity of operation (combined or noncombined). Also, several early postoperative complications, such as postoperative stroke, postoperative myocardial infarction, low cardiac output syndrome, and renal failure that required postoperative dialysis, were also documented for each subject.

The Modification of Diet in Renal Disease study equation was used for the estimated glomerular filtration rate.¹⁹ We defined as a current smoker subjects who had smoked at least 10 cigarettes within a month before admission. A

diagnosis of arterial hypertension, dyslipidemia, and diabetes mellitus was considered based on subject's regular medication and/or recent laboratory examinations. A diagnosis of peripheral vascular disease included lower extremity artery disease, abdominal aortic aneurysms, renal artery disease, and disease of mesenteric artery, extracranial carotid artery or vertebral artery.²⁰ The COPD diagnosis was based on spirometric evaluation, with a post-bronchodilation FEV₁:FVC of <70.²¹ PMI (post operation myocardial infarction) was identified with troponin elevation (>10 times the upper normal values), a) either new pathological Q waves or new left bundle branch block on echocardiogram, or b) new regional wall motion abnormality diagnosed by echocardiography.²² Low cardiac output syndrome was based on the Society of Thoracic Surgeons definition²³, which consists of the following criteria: the need for postoperative intra-aortic balloon pump or inotropic support for >30 min in the ICU to obtain a cardiac index value of >2.2 L/min/m² and systolic blood pressure of >90 mm Hg²³. Initiation of renal replacement treatment was based on one or more of the following criteria: azotemia > 250 mg/dL, hyperkalemia, fluid overload, and metabolic acidosis.²⁴

Study Outcomes

The use of NIV to treat postoperative acute respiratory failure, which developed among cardiac surgery patients who were extubated within 24 h after surgery, was the primary outcome of interest. We used 2-level positive ventilation in all the subjects of the study group. NIV was delivered by either ICU ventilators (bilevel pressure support mode) or by portable NIV devices. An initial inspiratory pressure of 10–12 cm H₂O was applied with a PEEP of 4–5 cm H₂O, with a gradual increase of inspiratory pressure and/or PEEP during the first 2 h of application, according to the subject's clinical condition and arterial blood gases, aiming for arterial oxygen partial pressure of >60 mm Hg without respiratory acidosis. NIV was initially applied for at least 16 h per 24-h period, which aimed for a gradual increase, both in the duration of application and the pressure level during the following days of hospitalization, according to subject's clinical condition.

Acute respiratory failure in postoperative cardiac surgery patients was defined by the presence of hypoxemia ($S_{pO_2} < 90\%$) under the use of supplement oxygen and/or hypercapnia ($P_{aCO_2} > 45$ mm Hg), high breathing frequency (>25 breaths/min), and dyspnea with or without abnormal radiographic signs, such as atelectasis or pulmonary infiltration. All patients who presented with shock, severe arrhythmias, impaired level of consciousness, copious secretions, inability to cough or to cooperate, delirium, gastric distention, gastrointestinal bleeding, multiple

organ dysfunction syndrome, or cardiac arrest were reintubated without any initial use of NIV. The need of reintubation within 72 h from the initial extubation of the subjects who were treated with NIV was defined as NIV failure and was the secondary outcome of the study.

Statistical Analysis

Statistical analysis was performed by using the Predictive Analytics Software v. 18 (SPSS, Chicago, Illinois). The normality of distribution of quantitative variables was tested by using the Shapiro-Wilk test. Continuous variables were summarized as mean $\pm$ SD or as median (range) according to the normality of the distribution, whereas categorical variables were presented as frequencies (*n*) and percentages (%). All pre-, intra-, and postoperative parameters were compared between the group that received NIV and the group that did not receive NIV, and between the group in which NIV was successful and the group in which NIV failed. These initial comparisons were conducted by using the chi-square test or the Fisher exact test for qualitative variables and the Student *t* test or the Mann-Whitney test for quantitative variables. Moreover, univariate binary logistic regression analysis was performed to investigate the independent associations among the following: (a) baseline values, intraoperative parameters, and NIV treatment in the total study population; and (b) baseline values, intraoperative parameters, postoperative parameters, and NIV failure in the study subpopulation who received NIV treatment. For the primary outcome, all univariate variables were then entered into a binary logistic multivariate model when the level of *P* in the univariate analysis was <0.1. Bootstrapping with 1,000 samples was used both in uni- and multivariate logistic regression analyses, and odds ratios (OR) were reported with corresponding bias-corrected and accelerated 95% CIs. *P* < .05 (2-tailed) was considered significant for all analyses.

Results

Study Population

A total of 1,657 post-cardiac surgery subjects with a mean $\pm$ SD EuroSCORE II of 1.9 ± 2.0 fulfilled the inclusion criteria and constituted the study population. The mean $\pm$ SD age was 65.2 ± 10.7 y, with 360 female subjects (21.7%). A total of 145 subjects (8.8%) were treated with NIV because of acute postoperative respiratory failure (NIV group), whereas the rest of the cohort constituted the no-NIV group. The demographic characteristics and perioperative variables of the total population and of the 2 study groups are presented in Table 1. The subjects in the NIV group versus the no-NIV group were older (mean $\pm$ SD 68 ± 3 y vs

NIV AFTER CARDIAC SURGERY

Table 1. Baseline and Intraoperative Characteristics for the Total Study Population and the Two Study Groups (NIV Group and No-NIV Group)

Variable	Total Population (N = 1,657)	NIV Group (n = 145)	No-NIV Group (n = 1,512)	P
Sex				
Males	1,297 (78.3)	106 (67.1)	1,210 (78.9)	.002
Females	360 (21.7)	52 (32.9)	324 (21.1)	
Age, y	65.2 ± 10.7	68 ± 3	64.9 ± 10.7	<.001
BMI, kg/m ²	29 ± 8.2	31.2 ± 5.2	28.7 ± 8.3	<.001
EuroSCORE II	1.9 ± 2	3.1 ± 2.8	1.9 ± 2.7	<.001
Estimated glomerular filtration rate, mL/min/1.73 m ²	75.5 ± 23.4	65.4 ± 20.5	76.4 ± 23.5	<.001
Smoking status	460 (27.8)	33 (22.8)	427 (28.2)	.07
Hypertension	1176 (71)	131 (82.9)	1072 (69.9)	.001
Chronic atrial fibrillation	170 (10.3)	24 (15.2)	150 (9.8)	.02
Diabetes mellitus	543 (32.8)	64 (40.5)	485 (31.6)	.004
Dyslipidemia	986 (59.5)	105 (66.5)	902 (58.8)	.02
Stroke	143 (8.9)	11 (8.9)	136 (7)	.64
COPD	116 (7)	36 (22.8)	85 (5.5)	<.001
Peripheral vascular disease	208 (12.6)	24 (15.2)	187 (12.2)	.13
Previous cardiac surgery	34 (2.1)	4 (2.8)	30 (2)	.53
NYHA classification				
No heart failure	27 (1.6)	6 (4.1)	21 (1.4)	
Class I	655 (39.5)	44 (30.3)	611 (40.4)	<.001
Class II	919 (55.5)	85 (58.6)	834 (55.2)	
Class III	55 (3.3)	9 (6.2)	46 (3)	
Class IV	1 (0.1)	1 (0.7)	0	
Left ventricle ejection fraction	55.8 ± 11.9	54.7 ± 11.3	55.9 ± 12	.23
Cardiopulmonary bypass time min	103.7 ± 44.3	114.2 ± 53.6	94 ± 43.9	.09
Type of operation				
Coronary artery bypass grafting	1178 (71.1)	98 (71.4)	1080 (67.6)	.33
Other	479 (28.9)			
Complexity of operation				
Noncombined	1477 (89.1)	15 (10.3)	165 (10.9)	.83
Combined	180 (10.9)			

Data are shown as either n (%) or mean ± SD.
 BMI = body mass index
 EuroSCORE = European System for Cardiac Operative Risk Evaluation
 NYHA = New York Heart Association

64.9 ± 10.7 y, $P < .001$), more often female, and had a higher EuroSCORE II score, higher BMI, and lower preoperative estimated glomerular filtration rate. Moreover, they had higher burden of comorbidities because they presented more often with arterial hypertension, chronic atrial fibrillation, dyslipidemia, diabetes mellitus, and COPD compared with the ones in the no-NIV group. Perioperative variables, such as cardiopulmonary bypass time, type of operation, and complexity of operation, were similar between the groups.

Predictors of NIV Application

Female sex, age, BMI, EuroSCORE II, preoperative estimated glomerular filtration rate, arterial hypertension,

chronic atrial fibrillation, diabetes mellitus, COPD, and dyslipidemia were all univariately associated with postoperative NIV application (Table 2). All these univariate predictors entered the multivariate regression analysis model, along with cardiopulmonary bypass time, which was associated with NIV application with a level of significance of <0.1 ($P = .058$) as defined. In the final model, BMI (adjusted OR 1.02, 95% CI 1.001–1.04; $P = .004$), EuroSCORE II (adjusted OR 1.11, 95% CI 1.02–1.32; $P = .02$), and COPD (adjusted OR 4.004, 95% CI 2.53–8.93; $P = .001$) were all positive independent predictors of NIV application, whereas preoperative estimated glomerular filtration rate was a negative predictor (adjusted OR 0.99, 95% CI 0.98–0.99; $P = .001$) (Table 2). The presence of COPD was the strongest pre-

Table 2. Univariate and Multivariate Predictors of NIV Application for Acute Respiratory Failure After Extubation

Variable	Univariate Analysis		Multivariate Analysis	
	Adjusted OR (95% CI)*	P	Adjusted OR (95% CI)*	P
Sex				
Males	0.56 (0.38–0.87)	.004	0.66 (0.38–1.12)	.052
Females	Reference group			
Age, y	1.04 (1.02–1.06)	.001	1.02 (1–1.04)	.18
BMI	1.02 (1.01–1.16)	.008	1.02 (1.01–1.04)	.004
EuroSCORE II	1.20 (1.13–1.27)	.001	1.11 (1.02–1.32)	.02
Estimated glomerular filtration rate	0.98 (0.97–0.99)	.001	0.99 (0.98–0.99)	.001
Smoking status				
Current smoker	1.10 (0.77–1.55)	.62	NA	
Ex-smoker or never smoker	Reference group			
Hypertension	2.07 (1.33–3.23)	.003	1.24 (0.75–2.03)	.40
Chronic atrial fibrillation	1.75 (1.03–2.72)	.02	1.19 (0.70–2.02)	.57
Diabetes mellitus	1.65 (1.16–2.31)	.004	1.23 (0.84–1.79)	.32
Dyslipidemia	1.52 (1.09–2.20)	.01	1.28 (0.85–1.94)	.26
Stroke	0.86 (0.45–1.63)	.64	NA	
COPD	4.81 (2.97–7.12)	.001	4 (2.53–8.93)	.001
Peripheral vascular disease	1.43 (0.90–2.28)	.14	NA	
Previous cardiac surgery	1.40 (0.49–4.04)	.53	NA	
Heart failure (NYHA $\geq$ 2)	1.25 (0.88–1.76)	.21	NA	
Left ventricle ejection fraction	0.99 (0.98–1.01)	.21	NA	
Cardiopulmonary bypass time, min	1.003 (1–1.01)	.058	1 (1–1.01)	.56
Type of operation				
Coronary artery bypass grafting	1.20 (0.83–1.73)	.33	NA	
Other	Reference group			
Complexity of operation				
Combined	1.06 (0.61–1.86)	.82	NA	
Noncombined	Reference group			

* Reported as bias corrected and accelerated 95% CIs

OR = odds ratio

BMI = body mass index

EuroSCORE = European System for Cardiac Operative Risk Evaluation

NA = not applicable (not entering the model)

NYHA = New York Heart Association

dicator of all, increasing the possibility of NIV application for postoperative respiratory failure by ~ 4 times. Moreover, there was a trend of an independent, negative association between male sex and NIV application, but it did not reach statistical significance ($P = .052$) (Table 2).

NIV Outcome and Predictors of NIV Failure

Among the 145 subjects who received NIV, the treatment was successful in 129 (89%), whereas only 16 subjects were reintubated within 72 h after NIV application (11%). The differences in baseline characteristics, perioperative variables, and postoperative complications between the group with successful NIV application and the group with NIV failure are presented in Table 3. The subjects who were successfully treated with NIV were younger, with a higher BMI, and with a lower burden of comor-

bilities; the incidence of chronic atrial fibrillation (13.2% vs 37.5%), COPD (18.6% vs 50%), and heart failure (55% vs 81.3%) among them was significantly lower compared with the group with NIV failure. Moreover, during NIV application, the frequency of postoperative complications, that is, myocardial infarction, postoperative stroke, and renal failure with the need for renal replacement treatment, was significantly higher among the subjects who presented with NIV failure compared with those with successful NIV application (Table 3).

Due to the small number of subjects in whom NIV failed, only the univariate analysis of the potential predictors of NIV failure was conducted. Older age (adjusted OR 1.09, 95% CI 1.01–1.17; $P = .03$), higher EuroSCORE II (adjusted OR 1.20, 95% CI 1.03–1.39; $P = .02$), the presence of COPD (adjusted OR 4.38, 95% CI 1.49–12.83; $P = .004$), presence of heart failure (adjusted OR 3.54,

Table 3. Baseline Characteristics, Perioperative Variables, and Postoperative Complications of Subjects Who Underwent NIV Treatment, Categorized According to NIV Success or Failure

Variable	Successful NIV (n = 129)	NIV Failure (n = 16)	P
Sex, n (%)			
Males	87 (67.4)	12 (75)	.54
Females	42 (32.6)	4 (25)	
Age, y	69 (13)	75.5 (9)	.02
BMI, m/kg ²	31.2 (7.5)	26.4 (5.9)	.032
EuroSCORE II	2 (2.2)	2.6 (5.8)	.19
Estimated glomerular filtration rate, mean ± mL/min/1.73 m ²	64.1 ± 19.8	70.9 ± 28.6	.29
Smoking status, n (%)	29 (22.5)	2 (12.5)	.36
Hypertension, n (%)	106 (82.2)	14 (87.5)	.60
Chronic atrial fibrillation	17 (13.2)	6 (37.5)	.01
Diabetes mellitus, n (%)	55 (42.6)	8 (50)	.58
Dislipidemia, n (%)	90 (69.8)	9 (56.3)	.27
Stroke, n (%)	9 (7)	2 (12.5)	.43
COPD, n (%)	24 (18.6)	8 (50)	.004
Pulmonary hypertension, n (%)	30 (23.3)	7 (18.9)	.08
Peripheral vascular disease, n (%)	22 (17.1)	2 (12.5)	.644
Previous cardiac surgery, n (%)	1 (0.8)	3 (18.8)	<.001
Heart failure (NYHA ≥ 2), n (%)	71 (55)	13 (81.3)	.045
Left ventricle ejection fraction, %	55 (13)	50 (18)	.10
Cardiopulmonary bypass time, min	96 (52)	96.5 (74)	.50
Type of operation, n (%)			
Coronary artery bypass grafting	89 (69)	9 (56.3)	.30
Other	40 (31)	7 (43.8)	
Complexity of operation, n (%)			
Noncombined	115 (89.1)	15 (93.8)	.57
Combined	14 (10.9)	1 (6.3)	
Postoperative complications, n (%)			
Low cardiac output syndrome	8 (6.2)	2 (12.5)	.35
Myocardial infarction	0	1 (6.3)	.004
Postoperative stroke	3 (2.3)	3 (18.8)	.002
Renal replacement therapy	1 (0.8)	8 (50)	<.001

BMI = body mass index

EuroSCORE = European System for Cardiac Operative Risk Evaluation

NYHA = New York Heart Association

95% CI 1.01–13.02; *P* = .039), presence of chronic atrial fibrillation (adjusted OR 3.95, 95% CI 1.27–12.28; *P* = .02), postoperative renal replacement therapy (adjusted OR 8.8, 95% CI 1.03–23.06; *P* = .001), and postoperative stroke (adjusted OR 3.69, 95% CI 1.77–13.01; *P* = .002) were all univariately associated with NIV failure in our cohort (Table 4).

Discussion

This retrospective cohort study aimed to investigate the predictors of NIV application to treat acute respiratory

Table 4. Univariate Predictors of NIV Failure

Variable	Univariate Analysis Adjusted OR (95% CI)*	P
Sex		
Males	1.45 (0.44–4.76)	.54
Females	Reference group	
Age, y	1.09 (1.01–1.17)	.03
BMI	0.90 (0.80–1.02)	.09
EuroSCORE II	1.20 (1.03–1.39)	.02
Estimated glomerular filtration rate	1.02 (0.99–1.04)	.36
Smoking status		
Current smoker	0.49 (0.11–2.29)	.37
Ex-smoker or never smoker	Reference group	
Hypertension	1.52 (0.32–7.15)	.60
Chronic atrial fibrillation	3.95 (1.27–12.28)	.02
Diabetes mellitus	1.35 (0.48–3.81)	.58
Dyslipidemia	0.56 (0.19–1.60)	.28
Stroke	1.91 (0.37–9.71)	.44
COPD	4.38 (1.49–12.83)	.004
Peripheral vascular disease	0.70 (0.15–3.28)	.65
Heart failure (NYHA ≥ 2)	3.54 (1.01–13.02)	.04
Left ventricle ejection fraction	0.96 (0.92–1.01)	.11
Cardiopulmonary bypass time	1.00 (0.99–1.01)	.70
Type of operation		
Coronary artery bypass grafting	1.73 (0.60–4.97)	.31
Other	Reference group	
Complexity of operation		
Combined	1.82 (0.22–14.90)	.57
Noncombined	Reference group	
Postoperative complications		
Low cardiac output syndrome	2.16 (0.42–11.20)	.25
Postoperative stroke	3.69 (1.77–13.01)	.002
Renal replacement therapy	8.80 (1.03–23.06)	<.001

* Reported as bias corrected and accelerated 95% CIs.

OR = odds ratio

BMI = body mass index

EuroSCORE = European System for Cardiac Operative Risk Evaluation

NYHA = New York Heart Association

failure after cardiac surgery and the outcome of this treatment. The presence of COPD was the strongest independent predictor of NIV application; BMI and EuroSCORE II were also positive predictors, whereas preoperative estimated glomerular filtration rate was a negative predictor. This mode of treatment was successful in the majority of subjects (89%) in whom it was applied, with treatment failure being univariately associated with older age, higher EuroSCORE II, higher burden of comorbidities, and more-frequent postoperative complications.

The data in the literature on the efficacy of NIV application for the treatment of postoperative acute respiratory failure among cardiac surgery patients vary. In the first studies in the field, a high success rate, up to 90%, was noted, especially among the subjects with mild-to-moderate hypoxemic respiratory failure.^{25–27} These data were in

agreement with our study, in which the majority of the subjects with acute respiratory failure were successfully treated with NIV. However, recent studies have failed to confirm this finding, with NIV failure rates ranging from 21.9% to 52%.^{16,28-30} A partial explanation for these discrepancies includes the application of NIV with 2 different modalities (either nasal CPAP or NIV)¹⁶; the late application of NIV (after 24 h from extubation)²⁹; different study cohort characteristics, with a significant proportion of subjects who underwent urgent surgery and operations other than coronary artery bypass grafting²⁹; and the application of NIV by using broader criteria as a method either to prevent or treat respiratory failure.³⁰

The successful treatment of postoperative acute respiratory failure with the application of NIV is due to the induction of several favorable effects on both cardiac and respiratory function. Positive-pressure ventilation during NIV induces lung volume and intrathoracic pressure changes, which can affect preload, afterload, heart rate, and myocardial contractility, whereas, with the application of PEEP, these pressures remain above the atmospheric throughout the respiratory cycle, which eventually results in lower left ventricle afterload, improving hemodynamics, and increasing cardiac output.^{9,31} Moreover, NIV restores lung volumes by opening atelectatic areas; increases alveolar requirement with more-efficient gas exchange; and reduces the work of breathing, which partially compensates for affected respiratory function.^{32,33}

In our study, the presence of COPD was the strongest independent predictor of NIV application for acute respiratory failure, which increased by ~4 times the odds of receiving this treatment. Moreover, the presence of COPD was also associated with treatment failure, although this was a univariate association. A history of COPD represents a major risk factor for postoperative pulmonary complications in non-cardiothoracic operations.³⁴ Cardiac surgery procedures, especially when performed under the use of cardiopulmonary bypass, provoke significant alterations in lung mechanics, which results in notable reductions of ~40–50% of FVC and FEV₁ during the early postoperative period. In a previous matched cohort analysis of cardiac surgery subjects, the presence of COPD was associated with the occurrence of postoperative respiratory failure, 4 times more often than in the non-COPD group, whereas it also increased mortality and overall length of hospitalization, which confirms our findings.³⁵

EuroSCORE II and BMI were 2 other independent predictors positively associated with NIV application, whereas the preoperative estimated glomerular filtration rate was a negative predictor. To our knowledge, no previous study has yet investigated the predictive value of these parameters on the application of NIV after cardiac surgery. EuroSCORE II, an index that reflects presurgery health and severity of illness, has previously been associated with

several postsurgery outcomes; cardiac surgery subjects with a higher EuroSCORE or EuroSCORE II had longer hospital and ICU stays, a higher percentage of postoperative complications, and higher mortality.^{36,37} BMI has also been associated with unfavorable outcomes after cardiac surgery; patients with a very high BMI are prone to atelectasis, prolonged mechanical ventilation, reintubation, and pneumonia,³⁸ whereas obstructive sleep apnea syndrome is often misdiagnosed in surgery patients who are obese.³⁹ Nevertheless, adverse outcomes are evident mostly among patients who are extremely obese, with BMI ≥ 40 kg/m²,³⁸ which was not true for either of the 2 groups of patients in our study, so this result was quite unexpected. Likewise, impaired preoperative estimated glomerular filtration rate has been associated with complications during the intra- and postoperative course among cardiac surgery subjects,⁴⁰ although no data exist yet regarding its potential association with NIV application due to acute respiratory failure.

The results are strengthened by the large number of participants and because all data were prospectively added to the database, so recall bias was minimized. The study was single-center, so all decisions regarding initial NIV application were made by the same team of physicians, as were follow-up assessments of NIV failure or success, which thus minimized variability of applied criteria. A limitation of the study was that the exact cause of acute respiratory failure, such as pneumonia, atelectasis, or pulmonary edema, was not recorded, so the possibility that prognostic factors could be different for each cause of respiratory failure could not be investigated. Another limitation was that details regarding NIV application, such as the exact level of positive-pressure ventilation, the average breathing frequency, and the total duration of its application, were also not systematically recorded. Nevertheless, criteria of NIV application were specific and universally applied, so technical details of the treatment could have provided the article with more descriptive information, but it is unlikely that these would have changed the final results.

Conclusions

In this large cohort study, NIV successfully treated acute respiratory failure in the vast majority of cardiac surgery subjects in whom it was applied. The presence of COPD, EuroSCORE II, BMI, and preoperative renal function were independently associated with the application of this treatment modality. Large, prospective clinical trials are needed to investigate the predictors of successful NIV application for treating acute respiratory failure of various etiologies, with the aim to further increase its efficacy among subjects after cardiac surgery.

REFERENCES

- Cabrini L, Plumari VP, Nobile L, Olper L, Pasin L, Bocchino S, et al. Non-invasive ventilation in cardiac surgery: a concise review. *Heart Lung Vessel* 2013;5(3):137-141.
- Ng CS, Wan S, Yim AP, Arifi AA. Pulmonary dysfunction after cardiac surgery. *Chest* 2002;121(4):1269-1277.
- Wynne R, Botti M. Postoperative pulmonary dysfunction in adults after cardiac surgery with cardiopulmonary bypass: clinical significance and implications for practice. *Am J Crit Care* 2004;13(5):384-393.
- Taggart DP, el-Fiky M, Carter R, Bowman A, Wheatley DJ. Respiratory dysfunction after uncomplicated cardiopulmonary bypass. *Ann Thorac Surg* 1993;56(5):1123-1128.
- Canet J, Mazo V. Postoperative pulmonary complications. *Minerva Anesthesiol* 2010;76(2):138-143.
- Kavanagh BP. Perioperative atelectasis. *Minerva Anesthesiol* 2008;74(6):285-287.
- Groeneveld AB, Jansen EK, Verheij J. Mechanisms of pulmonary dysfunction after on-pump and off-pump cardiac surgery: a prospective cohort study. *J Cardiothorac Surg* 2007;2:11.
- Wynne R, Botti M. Postoperative pulmonary dysfunction in adults after cardiac surgery with cardiopulmonary bypass: clinical significance and implications for practice. *Am J Crit Care* 2004;13(5):384-393.
- Guarracino F, Ambrosino N. Non-invasive ventilation in cardio-surgical patients. *Minerva Anesthesiol* 2011;77(7):734-741.
- Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet* 2009;374(9685):250-259.
- Evans TW. International Consensus Conference in Intensive Care Medicine: non-invasive positive pressure ventilation in acute respiratory failure. Organised jointly by the American Thoracic Society, the European Respiratory Society, the European Society of Intensive Care Medicine, and the Société de Réanimation de Langue Française, and approved by the ATS Board of Directors, Dec 2000. *Intensive Care Med* 2001;27(1):166-178.
- Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;333(13):817-822.
- Kindgen-Milles D, Müller E, Buhl R, Böhner H, Ritter D, Sandmann W, Tarnow J. Nasal continuous positive airway pressure reduces pulmonary morbidity and length of stay following thoracoabdominal aortic surgery. *Chest* 2005;128(2):821-828.
- Jaber S, Lescot T, Futier E, Paugam-Burtz C, Seguin P, Ferrandiere M, et al.; NIVAS Study Group. Effect of noninvasive ventilation on tracheal reintubation among patients with hypoxemic respiratory failure following abdominal surgery: A randomized clinical trial. *JAMA* 2016;315(13):1345-1353.
- García-Delgado M, Navarrete I, García-Palma MJ, Colmenero M. Postoperative respiratory failure after cardiac surgery: use of noninvasive ventilation. *J Cardiothorac Vasc Anesth* 2012;26(3):443-447.
- Boeken U, Schurr P, Kurt M, Feindt P, Lichtenberg A. Early reintubation after cardiac operations: impact of nasal continuous positive airway pressure (nCPAP) and noninvasive positive pressure ventilation (NPPV). *Thorac Cardiovasc Surg* 2010;58(7):398-402.
- Landoni G, Zangrillo A, Cabrini L. Noninvasive ventilation after cardiac and thoracic surgery in adult patients: a review. *J Cardiothorac Vasc Anesth* 2012;26(5):917-922.
- Drosos G, Ampatzidou F, Sarafidis P, Karaikos T, Madesis A, Boutou AK. Serum creatinine and Chronic Kidney Disease-Epidemiology Estimated Glomerular Filtration Rate: independent predictors of renal replacement therapy following cardiac surgery. *Am J Nephrol* 2018;48(2):108-117.
- Brosius FC III, Hostetter TH, Kelepouris E, Mitsnefes MM, Moe SM, Moore MA, et al.; American Heart Association Kidney and Cardiovascular Disease Council, Council on High Blood Pressure Research, Council on Cardiovascular Disease in the Young, Council on Epidemiology and Prevention, Quality of Care and Outcomes Research Interdisciplinary Working Groups. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease. *Circulation* 2006;114(10):1083-1087.
- A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Data Standards (Writing Committee to Develop Clinical Data Standards for Peripheral Atherosclerotic Vascular Disease). Data elements and definitions for peripheral atherosclerotic vascular disease. *Circulation* 2012;125(10): 395-467.
- Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report. GOLD Executive Summary. *Am J Respir Crit Care Med* 2017;195(5): 557-582.
- Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al.; Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third universal definition of myocardial infarction. *Circulation* 2012;126(16):2020-2035.
- Lomivorotov VV, Efremov SM, Kirov MY, Fominskiy EV, Karas-kov AM. Low-cardiac-output syndrome after cardiac surgery. *J Cardiothorac Vasc Anesth* 2017;31(1):291-308.
- Lameire N, Van Biesen W, Vanholder R. Acute renal failure. *Lancet* 2005;365(9457):417-430.
- Ishikawa S, Ohtaki A, Takahashi T, Koyano T, Hasegawa Y, Ohki S, et al. Availability of nasal mask BiPAP systems for the treatment of respiratory failure after cardiovascular surgery. *J Cardiovasc Surg (Torino)* 1997;38(6):611-613.
- Eremenko AA, Chaus NI, Levikov DI, Kolomiets IVa. [Noninvasive mask ventilation of the lungs in the treatment of acute respiratory insufficiency in heart surgery patients in the postoperative period]. *Anesteziol Reanimatol* 1997;(5):36-38.
- Eremenko AA, Levikov DI, Egorov VM, Zorin DE, Kolomiets VIa. [Using non-invasive mask lung ventilation in cardiosurgical patients with acute respiratory distress syndrome]. *Anesteziol Reanimatol* 2004;(5):14-17.
- Kilger E, Möhnle P, Nassau K, Beiras-Fernandez A, Lamm P, Frey L, et al. Noninvasive mechanical ventilation in patients with acute respiratory failure after cardiac surgery. *Heart Surg Forum* 2010;13(2):E91-E95.
- García-Delgado M, Navarrete I, García-Palma MJ, Colmenero M. Postoperative respiratory failure after cardiac surgery: use of noninvasive ventilation. *J Cardiothorac Vasc Anesth* 2012;26(3):443-447.
- Stéphan F, Barrucand B, Petit P, Rézaiguia-Delclaux S, Médard A, Delannoy B, et al.; BiPOP Study Group. High-flow nasal oxygen vs noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery: a randomized clinical trial. *JAMA* 2015;313(23):2331-2339.
- Guarracino F, Cabrini L, Baldassarri R, Cariello C, Covello RD, Landoni G, et al. Non-invasive ventilation-aided transoesophageal echocardiography in high-risk patients: a pilot study. *Eur J Echocardiogr* 2010;11(6):554-556.
- Guarracino F, Cabrini L, Baldassarri R, Petronio S, De Carlo M, Covello RD, et al. Noninvasive ventilation for awake percutaneous aortic valve implantation in high-risk respiratory patients: a case series. *J Cardiothorac Vasc Anesth* 2011;25(6):1109-1112.
- Guarracino F, Covello RD, Landoni G, Baldassarri R, Stefani M, Cariello C, et al. Anesthetic management of transcatheter aortic valve implantation with transaxillary approach. *J Cardiothorac Vasc Anesth* 2011;25(3):437-443.
- Smetana GW, Lawrence VA, Cornell JE; American College of Physicians. Preoperative pulmonary risk stratification for noncardiotho-

- racic surgery: systematic review for the American College of Physicians. *Ann Intern Med* 2006;144(8):581-595.
35. Ried M, Unger P, Puehler T, Haneya A, Schmid C, Diez C. Mild-to-moderate COPD as a risk factor for increased 30-day mortality in cardiac surgery. *Thorac Cardiovasc Surg* 2010;58(7):387-391.
36. Fernandez-Zamora MD, Gordillo-Brenes A, Banderas-Bravo E, Arbolada-Sánchez JA, Hinojosa-Pérez R, Aguilar-Alonso E, et al.; ARIAM Andalucía Group. Prolonged mechanical ventilation as a predictor of mortality after cardiac surgery. *Respir Care* 2018;63(5):550-557.
37. Kovacs J, Moraru L, Antal K, Cioc A, Voidazan S, Szabo A. Are frailty scales better than anesthesia or surgical scales to determine risk in cardiac surgery? *Korean J Anesthesiol* 2017;70(2):157-162.
38. Gao M, Sun J, Young N, Boyd D, Atkins Z, Li Z, et al. Impact of body mass index on outcomes in cardiac surgery. *J Cardiothorac Vasc Anesth* 2016;30(5):1308-1316.
39. Singh M, Liao P, Kobah S, Wijeyesundera DN, Shapiro C, Chung F. Proportion of surgical patients with undiagnosed obstructive sleep apnoea. *Br J Anaesth* 2013;110(4):629-636.
40. GoŹdzik AT, Jakubaszko J, Grzebieniak T, Kustrzycki W, GoŹdzik W. Does the stage of chronic kidney failure influence the outcome in cardiac surgery? *Adv Clin Exp Med* 2015;24(5):845-850.