Effectiveness and safety of noninvasive positive-pressure ventilation in hypercapnia respiratory failure secondary to acute exacerbation of chronic obstructive pulmonary disease

Ali O. Abdel Aziz, Islam M. Abdel El Bary, Mohammad T. Abdel Fattah, Mohamad A. Magdy, Ashraf M. Osman

Introduction
Noninvasive positive-pressure ventilation (NIPPV) represents a significant advancement in the management of acute respiratory failure (ARF) in patients with severe chronic obstructive pulmonary disease (COPD) [1]. It is claimed to be safe and effective and helps in preventing endotracheal intubation in ARF secondary to COPD as compared with causes [2,3]. Several randomized controlled trials show a success rate of 80–85% [4]. It has been shown that NIPPV in addition to conventional treatment of COPD exacerbation significantly reduces mortality and complications as compared with standard medical therapy alone [5]. It can be effectively used both inside and outside the ICU. Ventilators used in NIPPV range from ICU ventilators with full monitoring and alarm systems, to light-weight, freestanding devices with limited alarm systems specifically designed for this purpose [6]. Although NIPPV is well tolerated by most patients, it is not entirely free from serious adverse effects and complications. The safety of NIPPV can be enhanced by a greater awareness of factors predictive of complications and early management of such complications [7].

This prospective study was conducted to assess intubation and mortality in patients with acute hypercapnia respiratory failure (AHRF) secondary to acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and in whom NIPPV was applied, to detect differences, if any, in the clinical variables at admission in the success and failure groups of patients, and compare our results with those from other studies.

Patients and methods
The present study was conducted in the general ward and the ICU of our department from January 2014 to

Keywords: acute exacerbation of chronic obstructive pulmonary disease, noninvasive positive-pressure ventilation, respiratory failure

Departments of, "Chest Diseases, "Clinical Pathology, Faculty of Medicine, Minia University, Minia, Egypt

Correspondence to Ali O. Abdel Aziz, MD, Department of Chest Diseases, Faculty of Medicine, Minia University, Minia, 61519, Egypt; Tel: 086-2333196; fax: +20 (86) 234 2601; e-mail: info@minia.edu.eg

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Background
Patients with acute respiratory acidosis caused by an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) constitute the group that benefits most from noninvasive positive-pressure ventilation (NIPPV). However, there are some patients who do not respond to NIPPV. Studies from the west report variable failure rates. Delays in recognizing nonresponders can increase hospital morbidity and mortality.

Objective
The aim of this study was to assess the effectiveness and safety of NIPPV in patients with acute hypercapnia respiratory failure (AHRF) secondary to AECOPD.

Patients and methods
This was a prospective observational study of 119 consecutive chronic obstructive pulmonary disease patients who were admitted with a diagnosis of AHRF and in whom NIPPV was applied.

Results
The overall success rate of NIPPV in the studied group was 94%. Mortality and duration of hospitalization were significantly higher in the failure group (P=0.0001 and 0.002, respectively). The most encountered complications were air leak (29%) and mask discomfort (24%). Comparison between the success and the failure group at the time of hospital admission revealed that the failure group was associated with old age (P=0.043), low hemoglobin (Hb) (P=0.037), low albumin (0.17), lower Glasgow Coma Scale (GCS) score (P=0.0001), higher Acute Physiology and Chronic Health Evaluation II (APACHE II) score (P=0.001), higher heart rate (P=0.002), lower systolic blood pressure (SBP) (P=0.013), lower diastolic blood pressure (DBP) (P=0.034), and higher white blood cells (WBCs) (P=0.0001). Multiple regression analysis identified age more than 65 years, respiratory rate 35 or more, pH less than 7.26, and WBCs more than or equal to 20 000 or less than 4000 as significant independent predictors of NIPPV failure in our patients.

Conclusion
NIPPV is an effective and safe modality for treating patients with AHRF secondary to AECOPD. Widespread availability and training of medical staff in the use of NIPPV is recommended.

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July 2016. It included 119 consecutive patients admitted to the department for AHRF secondary to AECOPD and in whom NIPPV was applied. Thirty-five patients were managed in the ward and the remaining 84 were managed in the ICU. The randomization of the patients was not intended. It was done just before the full establishment of our ICU, when patients were managed in the ward.

The study was approved by the scientific committee of our institution.

Diagnosis of COPD was based on the Global Initiative for Chronic Obstructive Lung Disease strategy [4].

Patients were considered for NIPPV if despite the standard medical treatment (controlled oxygen therapy, nebulized salbutamol and ipratropium bromide, systemic corticosteroids, and antibiotics when indicated) they still fulfilled the criteria for NIPPV [4]: namely, pH less than 7.35 or PaCO₂ more than 45 mmHg; PaO₂ less than 60 dyspnea at rest with respiratory rate (RR) more than 25 breaths/min; and use of accessory respiratory muscles or paradoxical abdominal breathing. Exclusion criteria were refusal of NIPPV, facial deformity affecting mask fitting, severe encephalopathy unrelated to hypoxaemia and/or hypercapnia, overt gastrointestinal bleeding, upper airway obstruction, acute ischemic heart disease, and need for urgent intubation due to cardiac or respiratory arrest, prolonged respiratory pauses and psychomotor agitation requiring sedation.

NIPPV was administered by the use of standard critical care ventilators. It was delivered to patients in bed at an angle of 30–45°. An oronasal or full face mask was used. NIPPV was applied for most of the time over 24 h. Patients were instituted on NIPPV through Bilevel Positive Airway Pressure (BIPAP) mode. The setting of the machine was as follows: at the outset the patient was started on an inspiratory positive airway pressure (IPAP) of 8 and Expiratory positive airway pressure (EPAP) of 4 cmH₂O, which was gradually adjusted as tolerated on the basis of alleviation of the patient’s dyspnea, decrease in RR, and continuous pulse oximeter readings. Expiratory pressure was increased by 1–2 cmH₂O to achieve an PaO₂ of more than or equal to 60 mmHg or a SaO₂ of 90% or more. Inspiratory pressure was increased at increments of 2–3 cmH₂O (≤20 cmH₂O) to obtain a tidal volume of 6–8 ml/kg and RR of up to 30. FiO₂ was set to achieve an SaO₂ of at least 90%. Once the patient became clinically stable with satisfactory arterial blood gases (ABG), the pressure support was decreased by 2 cmH₂O every 4 h with good tolerance and with close monitoring for any change in oxygen saturation and RR. As soon as we could reduce the IPAP and EPAP levels to 8 and 4 cmH₂O, respectively, with a satisfactory ABG of pH at least 7.35, SaO₂ of at least 90%, FiO₂ up to 40%, and RR less than 30/min, the patients were allowed to breathe spontaneously. The need for intubation was established by the attending physician depending on his clinical judgment.

The following variables were recorded at admission:

Age and sex, smoking status and index, associated comorbidities, primary cause of admission, BMI, vital signs, GCS, APACHE II score, chest radiograph, computed tomography pulmonary angiography when there is high probability for pulmonary embolism according to Wells score [8], ECG, echocardiography, ABGs analysis at admission, NIPPV initiation and whenever required thereafter, laboratory data [complete blood count, liver function tests, renal function tests, serum C-reactive protein (CRP) concentration, and serum tumor necrosis factor α], duration of NIPPV, condition at ICU discharge, duration of hospitalization, and any complication developing from the use of NIPPV.

Statistical analysis

Numerical data were expressed as mean and SD. Categorical data were expressed as number and percentage. Analyses were carried out with IBM SPSS statistics (version 17; SPSS for Windows; SPPS Inc., Chicago, Illinois, USA).

Statistical significance was set at a P-value less than 0.05. Univariate and multivariate analysis and odds ratio were estimated with logistic regression for identifying the risk factors associated with noninvasive ventilation (NIV) outcome, using the clinical variables illustrated in the Patients and methods section.

Results

Patient characteristics

The present study included 119 patients who had a diagnosis of AHRF secondary to AECOPD and who needed NIPPV. The main baseline patient characteristics and underlying conditions are listed in Tables 1 and 2.

Male patients constituted 69.7% of COPD patients and the mean age was 62.2±9.64 years. About 46% of the patients were current smokers, about 30% were lifelong nonsmokers, and the remaining were ex-smokers. The most common presentation was AECOPD (76.5% of...
patients), followed by heart failure (18.5%). The most frequent comorbidities associated with COPD were heart problems (68% of patients), followed by anemia (22.7%).

The overall failure percentage (patients needed intubation) was 5.9%.

### Prognostic factors

The overall failure was 5.9% among the studied patients. Failure for patients who were managed in the ward and those who were managed in the ICU was 5.8 and 5.9%, respectively ($P=0.8$).

The failure group had a higher mean age ($P=0.043$), longer hospital stay ($P=0.002$), and higher mortality ($P=0.0001$). They also had higher mean APACHE II score ($P=0.001$) and lower mean GCS ($P=0.0001$) (Tables 3 and 4) as well as higher mean urea ($P=0.0001$), higher mean creatinine ($P=0.001$), and higher mean WBCs ($P=0.0001$). They also had lower mean albumin ($P=0.017$) and lower mean Hb ($P=0.037$). They also had higher mean heart rate ($P=0.002$), higher mean RR ($P=0.04$), lower mean SBP ($P=0.013$), and lower mean DBP ($P=0.034$). Other parameters listed in Tables 5 and 6 are not significant.

Univariate analysis for NIPPV failure showed that failure rate was higher for patients older than 65 years ($P=0.004$), those with pH less than 7.26 at baseline ($P=0.015$), those with RR at least 35 ($P=0.004$), those with total leukocyte count 20,000 or more or less than 3,000 ($P=0.04$), and those with total leukocyte count 20,000 or more or less than 3,000 ($P=0.04$).

### Table 1 Patient characteristics and underlying conditions

| Patients | 119 |
|----------|-----|
| Sex (male) | 83 (69.7) |
| Age (years) | 62.2±9.64 |
| BMI (kg/m²) | 27.4±5.6 |
| Smoking index (packs/year) | 11.2±15.8 |

Number of comorbidities

| Comorbidities | Patients |
|---------------|---------|
| One | 19 (16) |
| Two | 43 (36) |
| Three or more | 57 (48) |

Other comorbidities include pneumothorax (2 patients), interstitial lung disease (1 patient), leukemia (1 patient), kyphoscoliosis (1 patient), dementia (1 patient), parkinsonism (1 patient), hemiplegia (1 patient), old pulmonary tuberculosis, and fibrothorax (1 patient). AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CHF, congestive heart failure; DM, diabetes mellitus; OSA, obstructive sleep apnea; PE, pulmonary embolism.

### Table 2 Patient characteristics

Laboratory data

| Parameter | Result |
|-----------|--------|
| Total leukocyte count ($\times 10^9/l$) | 11.9±5.2 |
| Hemoglobin (g/dl) | 12.7±2.2 |
| Platelets ($\times 10^9/l$) | 242.6±72.1 |
| Albumin (g/dl) | 3.5±0.6 |
| Serum urea (mg/dl) | 58.9±29.5 |
| Serum creatinine (mg/dl) | 1.1±0.4 |

Vital signs at admission

| Parameter | Result |
|-----------|--------|
| Respiratory rate/min | 29.03±9.06 |
| Heart rate (beats/min) | 93.1±17.9 |
| Systolic blood pressure (mmHg) | 117.06±22.05 |
| Diastolic blood pressure (mmHg) | 76.5±13.8 |
| Temperature (°C) | 37.1±0.99 |

Prognostic scores

| Score | Result |
|-------|--------|
| GCS | 14.8±0.9 |
| APACHE II score | 7.9±2.6 |
| Length of hospital stay (days) | 13.9±11.3 |
| Duration of NIPPV (days) | 4.5±3.2 |

Overall failure rate (need for intubation) | 7 (5.9)

Data are presented as $n$ (%) or mean±SD. Other comorbidities include pneumothorax (2 patients), interstitial lung disease (1 patient), leukemia (1 patient), kyphoscoliosis (1 patient), dementia (1 patient), parkinsonism (1 patient), hemiplegia (1 patient), old pulmonary tuberculosis, and fibrothorax (1 patient). AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CHF, congestive heart failure; DM, diabetes mellitus; OSA, obstructive sleep apnea; PE, pulmonary embolism.

### Table 3 Comparisons between the success and failure groups regarding the demographic characteristics and severity scores

| Success (n=112) | Intubated patients (n=7) | P |
|----------------|-------------------------|---|
| Age (years) | 61.7±8.5 | 69.3±20.3 | 0.043 |
| Male sex [n (%)] | 79 (70.5) | 4 (57.1) | 0.357 |
| Mortality [n (%)] | 0 (0) | 6 (85.7) | 0.0001 |
| Smoking index (packs/year) | 10.8±16.8 | 18.3±14.9 | 0.706 |
| BMI (kg/m²) | 27.7±5.7 | 25.0±3.8 | 0.216 |
| GCS | 14.9±0.6 | 12.9±2.1 | 0.0001 |
| APACHE II score | 7.7±2.5 | 11.1±2.7 | 0.001 |
| Duration of NIPPV (days) | 4.5±2.8 | 4.8±7.6 | 0.841 |
| Duration before NIPPV (days) | 0.9±1.9 | 2.1±5.7 | 0.167 |
| Duration of hospitalization (days) | 13.4±7.0 | 24.0±22.1 | 0.002 |

The success group was significantly younger, have shorter hospital stay, reduced mortality, and lower APACHE II score. APACHE II, Acute Physiology and Chronic Health Evaluation II; GCS, Glasgow Coma Scale; NIPPV, noninvasive positive-pressure ventilation.
No significant differences exist in the associated comorbidities in the success and failure groups except for the presence of chronic liver and renal disease, which was higher in the failure group. CHF, the success and failure groups except for the presence of chronic liver and renal disease, which was higher in the failure group.

| Comorbidities                  | Success (n=112) | Failure (n=7) | P     |
|-------------------------------|-----------------|---------------|-------|
| Bronchiectasis                | 13 (10.9)       | 1 (14.3)      | 0.565 |
| OSA                           | 20 (16.8)       | 0 (0)         | 0.266 |
| Pneumonia                     | 3 (2.5)         | 0 (0)         | 0.832 |
| ILD                           | 1 (0.8)         | 0 (0)         | 0.941 |
| PE                            | 3 (2.5)         | 1 (14)        | 0.941 |
| CHF                           | 22 (18.5)       | 2 (28.6)      | 0.383 |
| Cor pulmonale                 | 59 (49.6)       | 4 (57.1)      | 0.301 |
| Peptic ulcer                  | 5 (4.2)         | 0 (0)         | 0.735 |
| DM                            | 21 (17.6)       | 1 (14.3)      | 0.617 |
| renal disease                 | 4 (3.4)         | 2 (28.6)      | 0.017 |
| liver disease                 | 14 (11.8)       | 3 (42.9)      | 0.035 |
| Leukemia                      | 1 (0.8)         | 0 (0)         | 0.941 |
| Kyphoscoliosis                 | 1 (0.8)         | 0 (0)         | 0.941 |

Table 5 Differences between the success and failure groups regarding the laboratory data

| Laboratory Data                  | Success (n=112) | Intubated patients (n=7) | P     |
|----------------------------------|-----------------|--------------------------|-------|
| RBS (mg/dl)                      | 176.7±70.9      | 141.0±43.1               | 0.192 |
| AST (U/l)                        | 39.4±133.7      | 51.6±40.5                | 0.811 |
| ALT (U/l)                        | 50.4±183.5      | 82.0±82.2                | 0.653 |
| Albumin (g/dl)                   | 3.7±0.5         | 3.2±0.8                  | 0.017 |
| Total bilirubin (U/l)            | 0.9±0.5         | 1.1±0.5                  | 0.442 |
| Direct bilirubin (U/l)           | 0.4±0.3         | 0.5±0.2                  | 0.406 |
| Urea (mg/dl)                     | 55.9±29.5       | 90.0±51.1                | 0.0001|
| Creatinine (mg/dl)               | 0.9±0.4         | 1.5±0.7                  | 0.001 |
| RBCs (×10^12/l)                  | 5.3±0.8         | 5.0±0.3                  | 0.261 |
| WBCs (×10^9/l)                   | 10.9±5.2        | 21.8±7.7                 | 0.0001|
| Platelets (×10^9/l)              | 244.8±72.1      | 206.0±86.4               | 0.177 |
| Hb (g/dl)                        | 13.3±2.2        | 11.6±2.2                 | 0.037 |
| HCT                              | 47.9±6.6        | 45.1±6.9                 | 0.286 |
| TNFα                             | 20.3±10.4       | 17.9±10.7                | 0.300 |
| CRP positive (%)                 | 42.9            | 50.9                     | 0.500 |

Table 6 Comorbidities in the success and failure groups

No significant differences exist in the associated comorbidities in the success and failure groups except for the presence of chronic liver and renal disease, which was higher in the failure group. CHF.

Discussion

In the present study, we prospectively determined the characteristics, effectiveness, safety, and complications associated with the use of NIPPV in patients with AHRF secondary to AECOPD.

The success rate in the present study was about 94%, which is comparable to that reported in two previous studies [9,10] and higher than the rates (50–80%) reported by some other studies [11–15]. Even in a group of COPD patients with severe respiratory acidosis with a mean arterial pH of 7.22, Carrillo et al. [16] found that NIPPV was highly effective, with a success rate of 89%.

The variability in the success rate among different studies could be attributed in part to the differences in patient characteristics and severity of illness. Table 10 shows the comparison of the main points in our study with some of these previous studies.

In the present study, we prospectively determined the characteristics, effectiveness, safety, and complications associated with the use of NIPPV in patients with AHRF secondary to AECOPD.

The present study found that NIPPV is associated with lower mortality (P=0.0001) and significantly shorter hospital stay (P=0.002). These results are in agreement with those of previous studies [2,3,10,16]. The mortality in the failure group in our study was significantly high (85.7%). The high mortality can be attributed to the more severe nature of the disease in this group, as evidenced by the higher RR, lower blood pressure, and higher WBCs, which could denote sepsis. However, it is worth mentioning that this group of patients was managed first by NIPPV and hence whether the high mortality in this group is related to the severity of the underlying disease or to the delay in the initiation of invasive ventilation must be considered.

The main cause of acute deterioration and hence hospital admission in our patients was AECOPD,
which was present in 76.5%, followed by cardiac failure, in 18.5%. This finding is in agreement with reports from other studies \[10,16,19\].

The mean age of COPD patients treated with NIPPV varies across studies. The mean age of our patients was 61.3±14.5 years. The failure group was older compared with the success group (\(P=0.043\)). Multivariate analysis demonstrated that age more than 65 years was an independent factor for NIPPV failure. These results are in agreement with previous studies \[14,20,21\].

Table 6 Comparisons between the success and failure groups regarding baseline vital signs and arterial blood gas

| Baseline data            | Total (\(n=119\)) | Success (\(n=112\)) | Intubated patients (\(n=7\)) | \(P\) |
|--------------------------|-------------------|----------------------|-----------------------------|------|
| RR/min                   | 29.0±3±9.06       | 27.6±9.1             | 37.1±7.0                    | 0.04 |
| HR/min                   | 93.1±17.9         | 91.9±17.6            | 112.9±12.6                  | 0.002|
| SBP (mmHg)               | 117.0±6±22.05     | 118.4±21.1           | 97.1±29.3                   | 0.013|
| DBP (mmHg)               | 76.5±13.8         | 77.2±13.3            | 65.7±20.7                   | 0.034|
| Temperature (°C)         | 37.1±0.99         | 37.1±1.0             | 36.6±0.4                    | 0.200|
| pH                       | 7.3±0.05          | 7.3±0.1              | 7.3±0.1                     | 0.225|
| PaCO\(_2\) (mmHg)        | 67.7±12.4         | 67.1±12.4            | 68.4±14.2                   | 0.712|
| PaO\(_2\) (mmHg)         | 55.7±11.2         | 56.1±11.3            | 53±9.6                      | 0.167|
| HCO\(_3\) (mmol/l)       | 30.5±4.5          | 30.6±4.9             | 29.1±2.5                    | 0.451|
| PaO\(_2\)/FiO\(_2\)      | 185.7±38.2        | 186.8±39.1           | 168.1±16.4                  | 0.214|

Heart rate and respiratory rate were significantly higher, whereas SBP and DBP were significantly lower in the failure group. DBP, diastolic blood pressure; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure.

Table 7 Univariate analysis of the different parameters in the success and failure groups

| Parameter                  | Success (\(n=112\)) | Failure (\(n=7\)) | Relative risk | 95% CI       | \(P\)-value |
|----------------------------|----------------------|-------------------|---------------|--------------|-------------|
| Age >65 years              | 31 (27.7)            | 6 (85.7)          | 1.7           | 1.8–1.5      | 0.004       |
| Male sex                   | 79 (70.5)            | 4 (57.1)          | 0.6           | 0.1–2.6      | 0.357       |
| Current Smoking            | 34 (30.4)            | 2 (28.6)          | 0.9           | 0.2–4.9      | 0.643       |
| Mortality                  | 0 (0)                | 6 (85.7)          | 0.9           | 0.2–4.9      | 0.0001      |
| pH <7.26 at baseline       | 27 (24.1)            | 5 (71.4)          | 0.36          | 0.12–1.21    | 0.015       |
| PaCO\(_2\) >50 at baseline| 110 (98.2)           | 7 (100)           | 1.1           | 1.0–1.1      | 0.885       |
| PaO\(_2\)/FiO\(_2\) <146 baseline | 20 (17.9) | 0 (0)              | 0.9           | 0.9–0.9      | 0.296       |
| RR >35 baseline            | 19 (17)              | 5 (71.4)          | 12.34         | 2.2–6.8      | 0.004       |
| TLC \(>20\) 000 and \(<4000\) | 9 (8.03)           | 5 (71.4)          | 0.28          | 0.07–1.07    | 0.0001      |
| LTOT                       | 59 (52.7)            | 5 (71.4)          | 0.45          | 0.34–0.61    | 0.287       |
| Duration of MV <10 days    | 9 (8.03)             | 2 (28.6)          | 0.32          | 0.11–0.98    | 0.126       |
| Frequent exacerbation >2   | 94 (83.9)            | 6 (85.7)          | 0.39          | 0.14–1.14    | 0.690       |
| Liver disease              | 12 (10.7)            | 2 (28.6)          | 2.5           | 0.86–7.56    | 0.06        |
| Renal disease              | 2 (1.8)              | 2 (28.6)          | 0.95          | 0.25–3.75    | 0.017       |
| Serum albumin <11          | 9 (8.03)             | 2 (28.6)          | 4.5           | 0.78–27.0    | 0.13        |
| Hemoglobin <11             | 4 (3.6)              | 2 (28.6)          | 10.8          | 1.5–73.6     | 0.04        |

CI, confidence interval; LTOT, long term oxygen therapy; MV, mechanical ventilation; RR, respiratory rate; TLC, total leucocyte count.

Table 8 Multivariate analysis of the different parameters in the success and failure groups

| Parameter                               | Success (\(n=112\)) | Failure (\(n=7\)) | Relative risk | 95% CI       | \(P\)-value |
|-----------------------------------------|----------------------|-------------------|---------------|--------------|-------------|
| Age >65 years                            | 31 (27.7)            | 6 (85.7)          | 0.29          | 0.09–0.89    | 0.01        |
| pH <7.26 basal                           | 27 (24.1)            | 5 (71.4)          | 0.36          | 0.12–1.21    | 0.022       |
| RR >35 basal                             | 19 (17)              | 5 (71.4)          | 0.34          | 0.11–1.07    | 0.007       |
| TLC >20 000 and <4000×10\(^6\) basal     | 9 (8.03)             | 5 (71.4)          | 0.28          | 0.07–1.07    | 0.001       |
| Liver disease                           | 12 (10.7)            | 2 (28.6)          | 2.5           | 0.86–7.56    | 0.06        |
| Renal disease                           | 2 (1.8)              | 2 (28.6)          | 0.95          | 0.25–3.75    | 0.053       |

CI, confidence interval; RR, respiratory rate; TLC, total leukocyte count.

Table 9 Complications of NIMV in the studied group

| Complications              | Incidence \([\text{n/N (\%)}]\) |
|---------------------------|-------------------------------|
| Air leak                  | 35/119 (29)                   |
| Mask-related discomfort    | 29/119 (24)                   |
| Mask-related ulcer        | 11/119 (9.2)                  |
| NIPPV failure             | 7/119 (5.9)                   |
| Abdominal distension      | 4 (3.4)                       |
| Mask intolerance          | 3 (2.5)                       |
| Pneumonia                 | 1/119 (0.8)                   |

The most common complications encountered in our patient group were air leak, followed by mask-related discomfort and mask-related ulcer. NIPPV, noninvasive positive-pressure ventilation.
On the other hand, Soo Hoo et al. [11] found that there were no differences in age in those patients successfully treated and those patients who failed NIPPV.

The prevalence of comorbidities in our patient cohort is strikingly high, with 100% of our patients having at least one comorbidity, 84% having two or more disorders, and 48% having three or more disorders. Our data are in line with recent studies focusing on the prevalence of comorbidities in COPD [22–24].

The present study found that the presence of one or more comorbidities had no significant effect on the effectiveness of NIPPV. This result is in agreement with that reported in some previous studies [25,26]. However, some other studies found a significant impact of the number of comorbidities on failure of NIPPV and mortality [13,27].

COPD can progressively affect the functions of other organs (e.g., heart, vasculature, muscles, kidney, liver, gastrointestinal apparatus, and brain); it is frequently associated with various disorders [28].

In the present study, as well as in most of the previous studies [24,29], cardiovascular problems were the most commonly associated comorbidities (68%). At the individual level, comorbid ischemic cardiovascular disease among stable COPD patients is associated with a poorer health-related quality of life and more severe dyspnea [30].

In the present study, anemia was present in 22.7% of the patients, which is higher than the reported frequency of anemia in patients with COPD in previous studies [31]. The higher prevalence of anemia in our group can be explained by the fact that our patients were in a very...
severe stage of COPD. Blood Hb was significantly lower in the failure group \( (P=0.037) \), and Hb level less than 11 g/dl was associated with failure of NIPPV on univariate analysis \( (P=0.04) \). Cohort studies suggest that the survival rate in COPD patients with anemia is lower than that in those with a normal level or who had polycythemia [32].

Diabetes mellitus was present in 17.6% of our patient group. This result is in agreement with the reported higher prevalence of diabetes among patients with COPD than that in the general population [33].

In our study, about 17% of our patients had either proved obstructive sleep apnea (OSA) or symptoms that gave a suspicion of a concomitant OSA, based on the Berlin Questionnaire [34]. This is higher than the reported frequency (8–14%) in population-based studies [35]. However, it is worth noting that all our patients had a very severe COPD, which may be reflected in the higher prevalence of associated comorbidities including OSA. Also, the high prevalence of the associated comorbidity, especially cardiac problems, could be the cause for the higher prevalence of OSA in our patient cohort [36].

The present study found that the failure group had significantly higher mean baseline GCS score \( (P=0.0001) \). Although a similar result was reported by a previous study [37], another study [38] reported no significant difference in GCS score between the success and failure groups. It is important to mention that there is a risk for interobserver variation when measuring the score [39].

The present study found that APACHE II scores were significantly higher in the failure group \( (P=0.001) \), which was unsurprising as this index incorporates several variables that independently predicted outcome. Previous studies reported that APACHE II score was an independent predictor of NIPPV failure [1].

The present study found that BMI had no significant effect on the effectiveness of NIPPV. This result is in agreement with that reported in previous studies [40]. However, some other studies found a significant impact of higher BMI on NIPPV failure and mortality [13,26]. Interestingly, on the other hand Carrillo et al. [16] reported that obesity in patients with COPD was associated with less occurrence of late NIV failure and hospital readmission at 1 year.

In the present study, serum albumin was significantly lower in the failure group \( (P=0.017) \). This matches with other studies, which showed a negative predictive value of low serum albumin in COPD patients with severe exacerbation [26,41].

In the present study, WBC \( (P=0.0001) \), urea \( (P=0.0001) \), and creatinine \( (P=0.001) \) were statistically higher in the failure group. Multivariate analysis demonstrated that WBC at least 20 000 and less than 4000×10⁹ were independent factors for NIPPV failure \( (P=0.001) \). These results are in agreement with those of previous studies [20,21].

In our study when comparing the success and the failure group no significant statistical difference was found in the levels of inflammatory markers. In contrast to our result Bastiansen [38] reported that NIPPV failure was associated with higher levels of CRP. However, it is to be noted that in our study CRP was measured by the conventional method, which is less sensitive than measuring high-sensitive CRP.

The present study found that the failure group had significantly higher mean baseline RR \( (P=0.04) \). Multivariate analysis demonstrated that baseline RR 35 or more was an independent factor related to NIPPV failure \( (P=0.004) \), which is in accordance with other studies [1,13].

In our study, heart rate was significantly higher in the failure group \( (P=0.002) \) and both SBP and DBP were significantly lower \( (P=0.013 \text{ and } 0.034, \text{ respectively}) \). In agreement with this Moretti et al. [21] found that hemodynamic variables are one of the predictors of failure of NIPPV.

Although NIPPV is generally perceived as being more comfortable for patients compared with intermittent mandatory ventilation (IMV), intolerance may affect as many as 30–50% of patients, and despite the best efforts of skilled caregivers, discomfort remains responsible for 12–33% of NIV failures [42].

The present study found that air leak was the most frequent complication (seen in 29% of patients), followed by mask-related discomfort (24%) and mask-related ulcer (9.2%). Most of these were due to ill-fitting masks, and with the use of appropriately sized mask it was minimized. Also, the machine used was able to compensate for the leaks. Similar results were reported by other studies [16,19].

Severe complications occur less frequently, including failure of NIPPV (5.9%) and pneumonia (0.8%). The reported incidence of aspiration pneumonia is less than 5% [7,16].
This study is limited by the lack of a control arm without the intervention (NIPPV). We felt that withholding NIPPV would be inappropriate, given the evidence of benefit in other studies. The small number of patients in the failure group could affect the reliability of the statistical significance and the lack of local guidelines for when we should consider NIPPV and intubate.

Conclusion
The success rate of NIPPV in patients with AHRF secondary to AECOPD was high, as reported by most of the other studies. The safety of NIPPV in those patients was good as the majority of complications in our as well as other studies are minor complications and mostly manageable. Thus, widespread availability and training of medical staff on its proper use is recommended.

The comparable success percentage in patients who were managed in the ward and those who were managed in the ICU in our as well as in other studies makes it of particular interest in countries like Egypt with limited health resources and shortage of nursing staff. This will help save a lot of resources as well as create space in the ICU for more critical cases.

In our study as well as in other studies the nonresponders had higher mortality and morbidity. This could be in part related to the delay in the initiation of invasive ventilation. Thus, to optimize outcomes, it is essential to identify patients who are less likely to respond and establish when appropriate early invasive ventilation should be instituted for those patients.

In our study, old age and disease severity at presentation, evidenced by RR at least 35 and pH less than 7.26, and markedly elevated or low WBCs were significant independent factors for failure of NIPPV. However, because of the small number of patients in the failure group these factors need to be validated in larger multicenter studies.

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Our department had been in a latent phase since its establishment in the late 1980s, until 2010. Since 2010, thanks to the willingness of good people in the department, marked progress has been achieved. Our ICU has been established, bronchoscopy units have been introduced, and last but not the least the sleep study laboratory has been established.

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Conflicts of interest
There are no conflicts of interest.

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