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Comparative study between bilevel non-invasive ventilation versus conventional oxygen therapy in management of acute cardiogenic pulmonary edema.

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Abstract.
Background:
Non-invasive ventilation (NIV) seems to be of benefit in the immediate management of cases with acute cardiogenic pulmonary edema (ACPE). There is no obvious data about parameters that forecast the use of non-invasive mechanical ventilation from the start among these cases. This study aimed to assess the safety and efficiency of Bi-level NPPV compared with the standard oxygen therapy among adult cases with ACPE, moreover to recognize the factors that favor NIV use from the start.
Methods:
A prospective randomized study includin 100 cases diagnosed with acute cardiogenic pulmonary edema (ACPE). Patients were randomized into two groups. Group I: Fifty patients received bi-level ventilation or transferred from O2 to NIV plus anti-failure measures. Group II: Fifty patients received standard face mask oxygen therapy plus anti-failure measures.
Results:
We identified several factors to predict the use of BiPAP in the study population such as APACHE II score >20, LVEF ≤50, PASP>48, PH ≤7.18, SO2 ≤ 82%, PO2 ≤ 55, HCO3 ≤13, and hospital stay >12days. APATCHE II score at a cutoff value >20, had the highest sensitivity and Specificity (95,100% respectively) with the AUC (0.97).
Conclusion:
APACHE II score > 20, Left ventricular ejection fraction, pulmonary artery systolic pressure, and ABG were the most factors that forecast the need for use of BiPAP from the start in management of ACPE.
Key words: APACHE score, Bi-level NPPV, ACPE, Oxygen therapy

1Introduction.

Acute cardiogenic pulmonary edema (ACPE) is a frequent, precious, and fatal dilemma with related decease rates of 10-20% (**Nieminen et al, 2018).** Excessive interstitial and alveoli fluid resulting in a considerable reduction of gas exchange reduction and respiratory failure. ACPE is a stressful scenario with progressive RF that may lead to cardio-respiratory collapse within minutes or hours, unless therapeutic action is taken **(Masip et al, 2018).**

Cases with pulmonary edema are vulnerable to progressive acute respiratory failure or even decease. So, ventilation choice is essential. There are two types of ventilation , either conventional invasive ventilation with endotracheal tube insertion which has several obstacles such as anxiety, airway injury and hazard of nosocomial contagion, or non-invasive ventilation which is a ventilatory support to lungs by either nasal or full face mask without use of endotracheal tube aiming to decrease the complications of intubation, resulting in increased hospital morbidity and diminish the duration of hospital stay (**Carvalho et al,2016**).

There is no obvious data about parameters that forecast the use of non-invasive mechanical ventilation from the start among these cases. This study aimed to assess the safety and efficiency of Bi-level NPPV compared with the standard oxygen therapy among adult cases with ACPE, moreover to recognize the factors that favor NIV use from the start.

2Methods.

A prospective randomized study including 100 cases diagnosed with ACPE recruited from emergency department resuscitation rooms in Aswan University Hospital during the period from

December 2019 to November 2020. Patients with impaired consciousness, dementia, those with acute renal shut down or respiratory distress due to chest problems were excluded from the study.

Study classification

Patients were randomized into two groups:

Group I: Fifty patients received bi-level ventilation or transferred from O2 to NIV plus anti-failure measures.

Group II: Fifty patients received standard face mask oxygen therapy plus anti-failure measures. The decision to commence oxygen, or BiPAP was taken by the attending physicians

For BiPAP Vision (**Elisa, federal republic Germany**) bi-level positive airway pressure system had been utilized, initiating the inspiratory positive airway pressure (IPAP) at the level (from 10 to 15 cmH2O) and Expiratory positive airway pressure (EPAP) had been established at a lower-most of 5 cmH2O in the initial hour, Augmentation of EPAP in additions of 1–2 cm H2O (extreme levels were IPAP 20 and EPAP 10 cmH2O) and as patient endure with improvement **(Mehta & Hill, 2001).** All cases had be managed within the resuscitation room of the emergency department, in the two groups, the objective had been to sustain the arterial oxygen saturation over 90% by varying the oxygen flow rates as essential.

All patients were subjected to:

The following data were recorded:

(1) Demographic data including age, sex, smoking, and BMI.

(2) Complete clinical examination including cardiovascular examination

(2) Arterial blood gases: withdrawn at baseline, one hour and two hours

(3) Full laboratory assessment.

(4) Hemodynamic data, including mean arterial blood pressure, calculated as diastolic pressure+1/3 pulse pressure, respiratory rate (RR), heart rate, and temperature.

(5) **Acute Physiology and Chronic Health Evaluation (APACHE) II score**:

Was calculated on the day of ICU entrance, APACHE II score consisting of twelve variables including, vital signs (heart rate, mean arterial blood pressure, RR, temperature, and Glasgow coma score), variables derived from routine venous blood tests (hematocrit, white blood cell count, serum potassium, serum sodium, and serum creatinine), and two variables derived from arterial blood gas tests (serum pH and PaO2) **(Knaus et al, 1985).**

(6)Electrocardiography:12 leads ECG was done to all patients and recorded at baseline, 1 hour and 2 hours to monitor for the development of acute myocardial infarction & to detect the presence of ischemic heart disease or cardiac Arrhythmia.

(7) Echocardiography: was performed in all the patients once the clinical condition allowed to Identify the cause of acute pulmonary edema.

(8) Chest X-Ray

Ethical consideration

The study was approved by the Institutional Ethics Committee Faculty of Medicine, Aswan University. Moreover, a written consent was given by the surrogate decision maker.

Statistical analysis

Statistical analysis was done by SPSS, version 21 (IBM Inc., Armonk, New York, USA). Non-parametric tests were utilized in the current study. P≤ 0.05 deliberated statistically important.

3Results:

The study included 100 adult patients. The demographic data of the patients included in the study was shown in Table (1) where there was considerable variance between both groups regarding age (P < 0.001), and the presence of co-morbidities including DM, HTN, IHD, and PAD (P < 0.0001 each respectively).

Cases with decompansated heart failure, ischemic and valvular heart diseases have ominously higher distribution of using BIPAP (86.4, 95, and 94.1% respectively) in comparison to COT (13.6, 5,and 5.9% respectively) (P<0.05). Conversely, hypertensive cases have considerably higher distribution of using COT (97.9%) in comparison to BIPAP (2.1%) (P< 0.05) (Table 2).

Regarding the echo findings, Cases with RWMA, AR, MS, AS, prosthetic valve, moderate, severe mitral regurgitation, diastolic dysfunction grade 2 and 3 in Echo have ominously higher distribution of using BIPAP (P< 0.05). Moreover, the mean PASP was ominously higher in cases using BIPAP, while the mean EF is considerably lower in cases using BiPAP in comparison to cases using COT (P< 0.05). On the other hand, the cases with diastolic dysfunction grade 1 have ominously higher distribution of using COT (85.2%) in comparison to BIPAP (14.8%) (P < 0.05) (Table 3).

The mean APACHE score is ominously higher in cases using BiPAP (P< 0.05). Regarding ABG findings, there was considerable higher mean value of PCO2, in cases using BiPAP, while mean PH, SO2, PO2 and HCO3 levels were considerably higher in cases using COT in comparison to cases using BiPAP (P< 0.05). Furthermore, cases using BiPAP had considerable longer hospital stay (P< 0.05) (Table 4).

Diagnostic performance tests of each clinical parameter used to predict BIPAP need including ABG, APACHE II score and Echo findings were summarized in (Table 5). APACHE II score at a cutoff value >20, had the highest sensitivity and Specificity (95,100% respectively) with the AUC (0.97).

4Discussion

In the immediate management of cases with ACPE, NIV use appears to be beneficial. This study aimed to evaluate the safety and efficacy of NIV (Bi-level NPPV) compared with the standard oxygen therapy for adults patients with ACPE and to identify the factors that favor use of NIV from the start.

Regarding the demographic data, we found that BiPAP group included older patients compared to the other group (72.14 vs. 50.76). However, the gender distribution was similar between both groups (p value= 0.550). In contrast to our study, **Çiftci et al.** evaluated the age as a hazard factor for clinical efficacy of NIV and found that there was no substantial variance between the diverse age groups regarding the success rates of NIV (**Çiftci et al. 2017**). There were a higher proportion of obese patients among BiPAP group patients compared to oxygen therapy group (62.1 vs. 37.9). This was in harmony with a retrospective analysis that summarized that patients with the most severe obesity were more likely to receive long-term NIV after initial management of acute respiratory failure in the ICU (**Bry et al. 2018**).

We found that in BiPAP group, there was a higher prevalence of chronic diseases compared to other group including; DM, HTN, IHD, Stroke and chest diseases (P value < 0.0001 each respectively). On contrast to our study, a large multi-center study summarized that both oxygen therapy and BiPAP groups had virtually equivalent distribution of chronic diseases including COPD, DM, chronic kidney disease, HTN, AF, CHF, IHD, and valvulopaty **(Aliberti et al. 2018).**

As regard the etiology of pulmonary edema as a determining factor for the need of NIV successful NIV. We found that BiPAP group had higher cases of decompensated HF (86.4% vs. 13.6%), IHD (95% vs. 5%) and valvular heart disease (94.1% vs. 5.9%) while conventional oxygen therapy group had higher cases due to HTN (97.9% vs. 2.1%). A previous study done on cases with chronic congestive heart failure patients studied the effects of NIV on echo-cardiographic parameters in addition to the clinical criteria, predicting considerable stroke volume, ejection fraction, and oxygenation improvement **(Acosta et al, 2000).**

Baseline pH was found to be a predictor for NIV success, In our study, BiPAP group were associated with worsen ABG parameters compared to conventional group. **Aliberti et al, (2018)** summarized that high respiratory rate; lower pH and higher level of PaCO2 are indications for NIV from the start. Acosta et al. Investigated BiPAP use in cases of ACPE and found improvement in the oxygenation rates, though there was no variation in the admittance rate and intubation rate between with BIPAP treated cases and those were not **(Acosta et al, 2000).**

In terms of length of hospital stay, we found BiPAP group were associated with longer hospital stay compared to conventional group (13.60 vs. 9.74). On the contrary, **Masip et al.** randomized 40 cases into conventional oxygen therapy or NIV and summarized that despite lower rates of endotracheal intubation in NIV group and substantial improvement concerning several clinical parameters, there was no dis-similarity in hospital length of stay or decease between both groups (**Masip et al. 2000**). Moreover, recently there was no ideal proof about whether NIV increases the duration of hospital stay or not (**Berbenetz et al. 2019).**

We evaluated the diagnostic performance tests of each clinical parameter used to predict BIPAP need including ABG, APACHE II score and Echo findings and we summarized that APACHE II score at a cutoff value >20, had the highest sensitivity and specificity (95,100% respectively) with the AUC (0.97). However, **Okazaki et al,** (**2014),** found that the APACHE II scoring system cannot be utilized to sufficiently forecast the prognosis of cases with AHF.

Our findings are consistent with many recent guidelines. Several studies estimated that ACPE is currently the 2 nd most frequent NIV indication **(Burns et al, 2005)** (**Ponikowski et al, 2016)** (**Vagnarelli et al, 2017) (Rochwerg et al, 2017).** NIV was considered a class IIa reference in cases with AHF and tachypnea with respiratory rate over 25 breaths/ min and SpO2 below 90**% (McMurray et al, 2012**) (**Ponikowski et al, 2016).**The NICE guidelines recommended NIV in cases with ACPE

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with severe shortness of breath and acidotic PH (**National Institute for Health and Care Excellence, 2014**). Recently, **Masip et al, (2018)** advocate that NIV should be utilized in patients with ACPE, in order to improve RF faster, avoid EI and, with lower proof, potentially decrease mortality in high risk cases.

5Study limitations

There are a number of limitations of this study. First, larger study population are required to confirm the predictive role of echo-cardiographic parameters as mean PASP, EF and ABG value for using bi-level ventilation in patients with ACPE. Second, other markers for using bi-level ventilation need to be evaluated. Third, our study was conceived to categorize the selection criteria for NIV candidates in ACPE cases from the start not for the NIV failure risk factors. Furthermore, unlike recent studies, a third limb receiving CPAP therapy was not deliberated.

6Conclusions

We found that BiPAP therapy in the management of ACPE allied with older age, obesity, concomitant chronic diseases and worsening ECG, echocardiography and ABG findings. Furthermore, APACHE II score > 20, Left ventricular ejection fraction, PASP, and ABG were the most considerable factors that forecast the need for use of BiPAP from the s **Acknowledgments**

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Disclosure

There were no conflicts of interest in this work.

7References.

- **Acosta B, DiBenedetto R, Rahimi A, Acosta MF, Cuadra O, Van Nguyen A, Morrow L.** Hemodynamic effects of noninvasive bilevel positive airway pressure on patients with chronic congestive heart failure with systolic dysfunction. Chest. 2000 Oct 1; 118(4):1004-9

- **Aliberti et al . 2018.** "A Real Life Evaluation of Non Invasive Ventilation in Acute Cardiogenic Pulmonary Edema: A Multicenter, Perspective, and Observational Study for the ACPE SIMEU Study Group." BMC Emergency Medicine.

-**Berbenetz, Nicolas, Yongjun Wang, James Brown, Charlotte Godfrey, Mahmood Ahmad, 2019**. "Non-Invasive Positive Pressure Ventilation (CPAP or Bilevel NPPV) for Cardiogenic Pulmonary Oedema."Cochrane Database of Systematic Reviews.

-**Bhattacharyya, D., S. M. Prasad, P. S. Tampi, and R. Ramprasad. 2011.** "Early Predictors of Success of Non-Invasive Positive Pressure Ventilation in Hypercapnic Respiratory Failure." Medical Journal Armed Forces India.

- **Burns KE, Sinuff T, Adhikari NK, Meade MO, Heels-Ansdell D, Martin CM, Cook DJ.** Bilevel noninvasive positive pressure ventilation for acute respiratory failure: survey of Ontario practice. Critical care medicine. 2005 Jul 1;33(7):1477-83

- **Bry, Charlotte, Sandrine Jaffré, BéatriceGuyomarc'h, FrédéricCorne, SylvaineChollet, Antoine Magnan, and François Xavier Blanc. 2018.** "Noninvasive Ventilation in Obese Subjects after Acute Respiratory Failure." Respiratory Care.

- **Carvalho L, Carneiro R, Freire E and Pinheiro P (2010):** Non-invasive ventilation in cardiogenic pulmonary edema in the emergency department. Rev Port Cardiol ; 27(2):191-8.

-**Çiftci, Fatma, AydınÇiledağ, SerhatErol, and Akın Kaya. 2017**. "Non-Invasive Ventilation for Acute Hypercapnic Respiratory Failure in Older Patients." Wiener KlinischeWochenschrift.

- **Di Angelantonio E, BhupathirajuShN; et al. (2016-08-20).**"Body-mass index and all-cause mortality: Lancet. 388 (776–86): 776–786. Doi: 10.1016/S0140-6736(16)30175-1. (World Health Organization. Retrieved 5 February 2019).

- fadaizadeh L, Tamadon R, Saeedfar K, Jamaati HR. Performance assessment of Acute Physiology and Chronic Health Evaluation II and Simplified Acute Physiology Score II in a referral respiratory intensive care unit in Iran. ActaAnaesthesiol Taiwan.2012;50:59–62. 10.1016/j.aat.2012.05.004.

- **Knaus WA, Draper EA, Wagner DP. APACHE II**: a severity of disease classification system. Crit Care Med. 1985;13(10):818-29. PMID 3928249.

- **Masip et al. (2000)**. "Non-Invasive Pressure Support Ventilation versus Conventional Oxygen Therapy in Acute Cardiogenic Pulmonary Oedema: A Randomised Trial." Lancet.

- **McMurray JJ et al.** ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2012 Jul; 33(14):1787-847.
- **Nieminen MS, Brutsaert D and Dickstein K (2008):** Euro Heart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. Eur Heart J; 27:2725-36.
- **Okazaki H et al.** New scoring system (APACHE-HF) for predicting adverse outcomes in patients with acute heart failure: evaluation of the APACHE II and Modified APACHE II scoring systems. Journal of cardiology. 2014 Dec 1; 64(6):441-9.
- **Ponikowski P, Voors AA, Ander SD, et al., ESC Scientific Document Group**.(2016) The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC).Eur Heart J; 37:2129–2200.
- **RialpCervera, G., A. Del Castillo Blanco, O. Pérez Aizcorreta, and L. Parra Morais. 2014**. "Noninvasive Mechanical Ventilation in Chronic Obstructive Pulmonary Disease and in Acute Cardiogenic Pulmonary Edema." MedicinaIntensiva.
- **Rochwerg B, et al. Official ERS/ATS clinical practice guidelines**: noninvasive ventilation for acute respiratory failure. European Respiratory Journal. 2017 Aug 1;50(2).
-**Tallman et al. 2008. "**Noninvasive Ventilation Outcomes in 2,430 Acute Decompensated Heart Failure Patients: An ADHERE Registry Analysis." Academic Emergency Medicine.
- **Vagnarelli, Fabio, Marco Marini, Giorgio Caretta, FabianaLucà, Emilia Biscottini, Alberto Lavorgna, 2017.** "NonInvasive Ventilation: General Characters, Signs and Literature Review."
- **Yamamoto et al. 2012.** "Noninvasive Ventilation in Pulmonary Edema Complicating Acute Myocardial Infarction." Circulation Journal.iornaleItaliano Di Cardiologia.

		Group 1 BiPAP (n=50)	**Group 2 COT (n=50)**	**P value**
Age (years)	Mean ±SD	72.14 ± 6.47	0.76 ±7.23	< 0.001*
Gender Males Females	 N (%) N (%	 27 (54) 23 (46)	 24 (48) 26 (52)	 0.5504
BMI Normal Overweight Obesity	 N (%) N (%) N (%)	 15 (46.9%) 17 (43.6%) 18 (62.1%	 17 (53.1) 22 (56.4) 11 (37.9)	 0.2929
Co-morbidities DM	 N (%)	 47 (85.5)	 8 (14.5)	 < 0.0001*
HTN	N (%)	48 (65.8)	25 (34.2)	< 0.0001*
IHD	N (%)	44 (91.7)	4 (8.3)	< 0.0001*
Stroke	N (%)	21 (91.3)	2 (8.7)	< 0.0001*
PAD	N (%)	28 (82.4)	6 (17.6)	< 0.0001*
Chest diseases	N (%)	50 (74.6)	17 (25.4)	< 0.0001*

Table 1: Demographic data among the study population (n=100)
BiPAP: Bilevel Positive Airway Pressure, COT: Conventional oxygen therapy, PAD: Peripheral arterial diseases. *P < 0.05 is considered significant

Table 2: Comparison between two groups regarding etiology of APO (n=100)

Etiology of APO	**Group 1 BiPAP (n=50)**		**Group 2 COT (n=50)**	
	N	**(%)**	**N**	**(%)**
Decompensated HF	19	86.4	3	13.6
Hypertension	1	2.1	46	97.9
Ischemic HD	19	95	1	5
Valvular HD MS Prosthetic valve	 9 7	 100 87.5	 0 1	 0 12.5

Chi-squared	101.832
P value	< 0.0001*

PO: Acute pulmonary oedema, *P < 0.05 is considered significant

		Group 1 BiPAP (n=50)	Group 2 COT (n=50)	P value
RWMA	N (%)	46 (86.8)	7 (13.2)	< 0.0001*
AR	N (%)	15 (88.2)	2 (11.8)	0.0006*
MS	N (%)	9 (100)	0 (0)	0.0018*
Prosthetic valve	N (%)	7 (87.5)	1 (12.5)	0.0278*
AS	N (%)	10 (100)	0 (0)	0.0009*
MR				
Moderate MR	N (%)	12 (100)	0 (0)	< 0.001*
Severe MR		11 (100)	0 (0)	
PASP (mmHg)	Mean±SD	56.02±10.33	41.62±5.96	< 0.001*
EF (%)	Mean±SD	40.68±10.06	58.42±8.44	< 0.001*
Diastolic dysfunction				
Grade 1		4(14.8)	23 (85.2%)	
Grade 2	N (%)	31(56.4)	24 (43.6%)	< 0.0001*
Grade 3		15(83.8)	3 (16.7%)	

Table 3: Echo-cardiographic findings among the studied groups.

RWMA: Regional wall motion abnormalities, PASP: pulmonary artey systolic pressure, EF: ejection fraction, MR: MR: mitral regurgitation, AS: aortic stenosis, AR: aortic regurgitation, P < 0.05 is considered significant.

Table 4: Comparing between the two groups regarding APACHE II score, ABG and hospital stay.

		Group I		Group II		P value
		mean	SD	mean	SD	
APACHE II score		45.42	5.23	13.74	3.27	<0.001*
ABG	PH	7.20	0.166	7.30	0.087	< .001*
	PCO2	46.42	16.77	40.9	9.60	0.046
	SAO2	78.74	5.07	86.10	2.45	< .001*
	PO2	55.46	8.20	60.22	5.45	< .001*
	HCO3	13.92	3.66	15.78	1.83	0.002
Length of hospital stay		13.60	3.38	9.74	2.29	< .001*

P <0.05 is considered significant, ABG = arterial blood gas.

		BIPAP need				
			Cut off value	Sensitivity	Specificity	AUC
ABG	**PH**		≤7.18	60	0.789	0.789
	PCO2		>54	40	0.598	0.598
	SAO2		≤82	78	0.918	0.918
	PO2		≤55	58	0.686	0.686
	HCO3		≤13	56	0.671	0.671
APACHEII			>20	95	100	0.97
ECHO findings						
EF %			≤50	88	88	0.929
PASP (mmHg)			>48	78	86	0.882

Table (5): Diagnostic test performance of each clinical parameter used to predict BIPAP need.

P < 0.05 is considered significant, ABG = arterial blood gas.