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Hyperacute Hemodynamic Effects of BiPAP Noninvasive Ventilation in Patients With Acute Heart Failure and Left Ventricular Systolic Dysfunction in Emergency Department

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Abstract

Background: Acute heart failure (AHF) is one of the leading causes of admission to emergency department (ED); severe hypoxemic AHF may be treated with noninvasive ventilation (NIV). Despite the demonstrated clinical efficacy of NIV in relieving symptoms of AHF, less is known about the hyperacute effects of bilevel positive airway pressure (BiPAP) ventilation on hemodynamics of patients admitted to ED for AHF. We therefore aimed to assess the effect of BiPAP ventilation on principal hemodynamic, respiratory, pulse oximetry, and microcirculation indexes in patients admitted to ED for AHF, needing NIV. **Methods:** Twenty consecutive patients admitted to ED for AHF and left ventricular systolic dysfunction, needing NIV, were enrolled in the study; all patients were treated with NIV in BiPAP mode. The following parameters were measured at admission to ED (T_0, baseline before treatment), 3 hours after admission and initiation of BiPAP NIV (T_1), and after 6 hours (T_2): arterial blood oxygenation (pH, partial pressure of oxygen in the alveoli/fraction of inspired oxygen ratio, $Pa{CO_2}$, lactate concentration, HCO_{3-}), hemodynamics (tricuspid annular plane systolic excursion, transpulmonary gradient, transaortic gradient, inferior vena cava diameter, brain natriuretic peptide [BNP] levels), microcirculation perfusion (end-tidal CO_2 [$ETCO_2$], peripheral venous oxygen saturation [$SpvO_2$]). **Results:** All evaluated indexes significantly improved over time (analysis of variance, $P < .001$ in quite all cases.). **Conclusions:** The BiPAP NIV may rapidly ameliorate several hemodynamic, arterial blood gas, and microcirculation indexes in patients with AHF and left ventricular systolic dysfunction.

Keywords

acute heart failure, noninvasive ventilation, hemodynamics, BiPAP

Introduction

Acute heart failure (AHF) is one of the leading causes of admission to emergency department (ED),[1] with a reported inhospital mortality ranging from 3% to 16%.[2] Severe AHF may be treated with assisted ventilation[3]; in meta-analysis studies, noninvasive ventilation (NIV) may represent an efficient option for patients with AHF.[4]

Despite the demonstrated clinical efficacy of NIV in relieving symptoms of AHF,[3,5] less is known on hyperacute effects of bilevel positive airway pressure (BiPAP) ventilation on hemodynamics of patients admitted to ED for AHF.

We therefore aimed to assess the effect of BiPAP ventilation on principal hemodynamic, respiratory, pulse oximetry, and microcirculation indexes in patients admitted to ED for AHF needing NIV. Hemodynamic monitoring was achieved primarily by echocardiographic assessment, so as to enable real-time acute bedside analysis.

Methods

This is an observational, monocentric, prospective study. After a preliminary screening of 100 patients to identify those with AHF and left ventricular systolic dysfunction by echocardiography, 20 consecutive patients (13 males, 7 females) admitted

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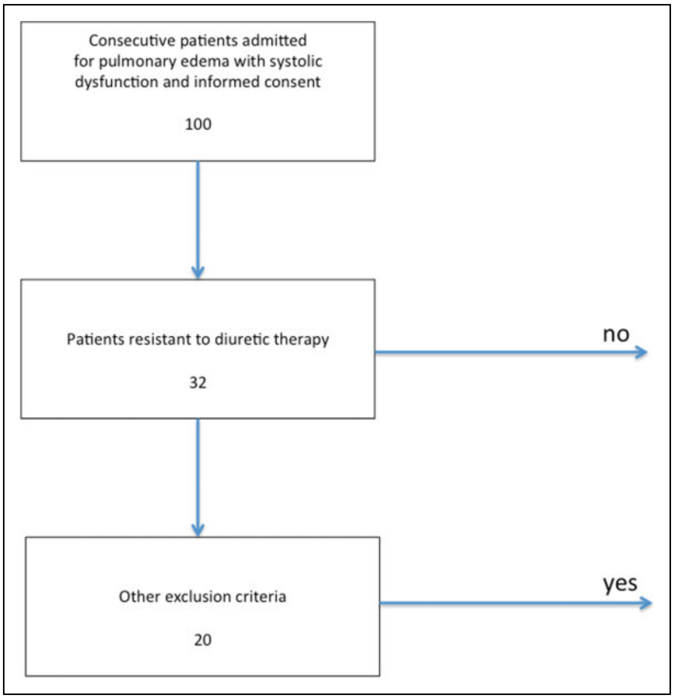

Figure 1. Flowchart showing patients' selection.

to ED of the Ospedali Riuniti University Hospital from January to May 2016 for AHF needing NIV were enrolled in the study (Figure 1). The ED of Ospedali Riuniti University Hospital is a tertiary care facility with an intensive care unit and rapid access to echocardiography and NIV.

Inclusion criteria were severe dyspnea, accessory muscle activation, thoracic abdominal dyskinesia, Glasgow coma scale >12, respiratory rate >24/min, partial pressure of oxygen in the alveoli/fraction of inspired oxygen (PaO_2/FiO_2) <300, left ventricular systolic dysfunction (left ventricular ejection fraction <35%).

Exclusion criteria were age <18 years, pregnancy, respiratory rate <12/min, Glasgow coma scale <12, severe hemodynamic instability (systolic blood pressure <90 mm Hg), hypertensive emergencies (arterial blood pressure >180/120 mm Hg), angina, valvular heart disease, abnormal troponin levels (>0.5 ng/mL; troponin assay, Beckman Coulter, Brea, California), ST-elevation at electrocardiogram, malignant arrhythmias (ventricular tachycardia, ventricular fibrillation), pneumothorax, NIV mask intolerance, intubation, and use of catecholamines, nitrates, or morphine.

All patients were treated with NIV in BiPAP mode with a V60 polyfunctional-assisted, pressure-controlled ventilation device (Philips, Eindhoven, the Netherlands). The levels of inspiratory positive airway pressure and expiratory positive airway pressure were set so as to obtain a tidal volume of 6 to 8 mL/kg, a lower respiratory rate of 20 breaths/min, no use of accessory respiratory muscles, and an arterial oxygen saturation >90%. In case of respiratory rate <12/min, a controlled ventilation modality was activated with an inspiratory/expiratory rate of 0.35. Ventilation was performed in a level 2 care unit within the ED until weaning or hospitalization. All patients were treated with diuretics.

The NIV and clinical care were managed by the ED medical team (emergency medicine specialists), with simple research team observation; researchers were not included in clinical management of the patients. Echocardiograph examinations were performed by skilled emergency medicine specialists with an additional training in echocardiography. All 3 consecutive echocardiographic assessments were held by the same operator; however, echo images were double checked by researchers involved in the study. In all cases, the quality of echo images was deemed adequate for data analysis. In the case of disagreement, a final decision was taken by the study coordinator (V.P.).

Electrocardiogram, hemodynamics (heart rhythm and rate, systolic and diastolic blood pressure, urine output), and respiratory function (pulse oximetry and respiratory rate, capnography by nasal sidestream capnography) were continuously monitored.

The following parameters were measured at admission to ED (T_0, baseline, arrival, immediately before treatment with NIV), 3 hours after admission and initiation of BiPAP NIV (T_1), and after 6 hours (T_2): arterial blood oxygenation (pH, PaO_2/FiO_2 ratio, $PaCO_2$, lactate concentration, HCO_{3-}), hemodynamics (tricuspid annular plane systolic excursion [TAPSE], transpulmonary gradient, transaortic gradient, inferior vena cava diameter, BNP levels), microcirculation perfusion (end-tidal CO_2 [$ETCO_2$], $SpvO_2$, assessed by venous blood gas analysis).

The study was held according to Helsinki principles and Declaration. All participants gave written informed consent. The study was approved by the local ethical committee.

Statistical Analysis

Continuous variables were expressed as mean (standard deviation) and compared with Student *t* test or Mann-Whitney *U* test as required, categorical variables as percentages and compared with χ^2 or Fisher test as required.

Multiple comparisons were made with analysis of variance (ANOVA) for repeated measures. The Kolmogorov-Smirnov test was used to identify variables with normal distribution. Linear correlations were determined by measuring the Pearson correlation coefficient. Multivariable linear regression analysis was used for correcting bias of principal confounders (age, gender, and systolic function). A $P < .05$ was considered as statistically significant.

Results

Of 20 patients (13 male and 7 female) enrolled, 2 had hypoxemic respiratory failure and the remaining 18 had hypoxemic–hypercapnic respiratory acidosis. Mean age was 78 (8) years. No case of NIV treatment failure requiring invasive ventilation was observed; from the ED, 10 patients were shifted to cardiology ward patients and 10 to internal medicine ward.

All parameters considered significant changed over time as shown in Figures 2 and 3. Tricuspid annular plane systolic excursion values increased from 14.3 (3.9) mm at T_0, to 18.2 (3.6) mm

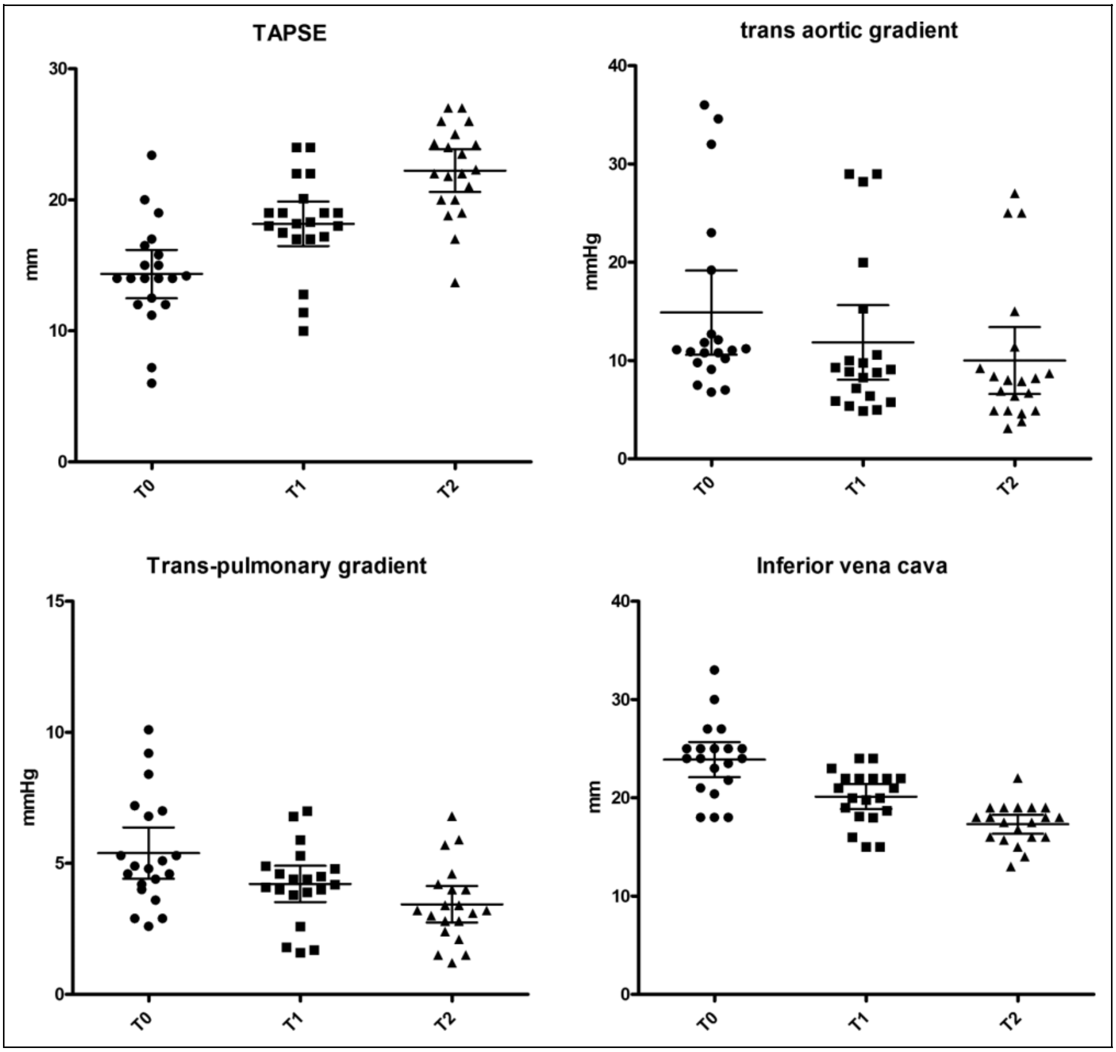

Figure 2. Changes in hemodynamic indexes with bilevel positive airway pressure noninvasive ventilation over time (admission [T_0], after 3 hours [T_1], and after 6 hours, [T_2]). Changes were statistically significant in all cases.

at T_1, up to 22.2 (3.5) mm at T_2 (ANOVA $P < .001$). Transaortic gradient values decreased from 14.9 (9.1) mm Hg at T_0 to 11.8 (8.1) mm Hg at T_1, down to 10.0 (7.3) mm Hg at T_2 (ANOVA $P < .001$). Transpulmonary gradient values decreased from 5.4 (2.1) mm Hg at T_0 to 4.2 (1.5) mm Hg at T_1, down to 3.4 (1.5) mm Hg at T_2 (ANOVA $P < .001$). The diameter of inferior vena cava decreased from 23.9 (3.8) mm at T_0 to 20.1 (2.7) mm at T_1, down to 17.3 (2.1) mm Hg at T_2 (ANOVA $P < .001$).

Pao_2/Fio_2 ratio values increased from 184.4 (51.3) at T_0 to 264.1 (39.5) mm at T_1, up to 302.6 (36.3) mm Hg at T_2 (ANOVA $P < .001$). $Paco_2$ values decreased from 67.4 (17.9) mm Hg at T_0 to 59.9 (14.1) mm Hg at T_1, down to 51.7 (10.8) mm Hg at T_2 (ANOVA $P < .001$).

The $ETCO_2$ values increased from 19.0 (6.8) mm Hg at T_0 to 28.6 (6.6) mm Hg at T_1, up to 35.4 (7.1) mm Hg at T_2 (ANOVA $P < .001$). The arteriovenous saturation values increased from 61.9 (11.9) mm Hg at T_0 to 70.6 (8.6) mm Hg at T_1, up to 78.0 (4.9) mm Hg at T_2 (ANOVA $P < .001$). The BNP values decreased from 7612.5 (8163.4) ng/mL at T_0 to 6808.9 (7572.2) mm Hg at T_1, down to 5737.7 (6999.0) mm Hg at T_2 (ANOVA $P < .001$).

The pH values increased from 7.30 (0.08) at T_0, to 7.35 (0.07) at T_1, up to 7.39 (0.03) at T_2 (ANOVA $P < .001$). The HCO_{3-} values increased from 20.8 (6.9) mmol/L at T_0 to 31.5 (6.4) mmol/L at T_1, up to 32.1 (6.7) mm Hg at T_2 (ANOVA $P < .01$). Lactate values decreased from 2.32 (1.09) mmol/L at T_0 to 1.75 (0.9) mmol/L at T_1, down to 1.51 (0.8) mmol/L at T_2 (ANOVA $P < .001$). All differences remained statistically significant after correction for age and gender at multivariable analysis.

Discussion

To the best of our knowledge, this is the first study showing the early effect of NIV in ED patients with respiratory failure. In the present study, NIV treatment was associated with a significant improvement in all indexes assessed.

The study remains original in its obtaining of real-time serial echo data in the acute phase of AHF. Our study therefore

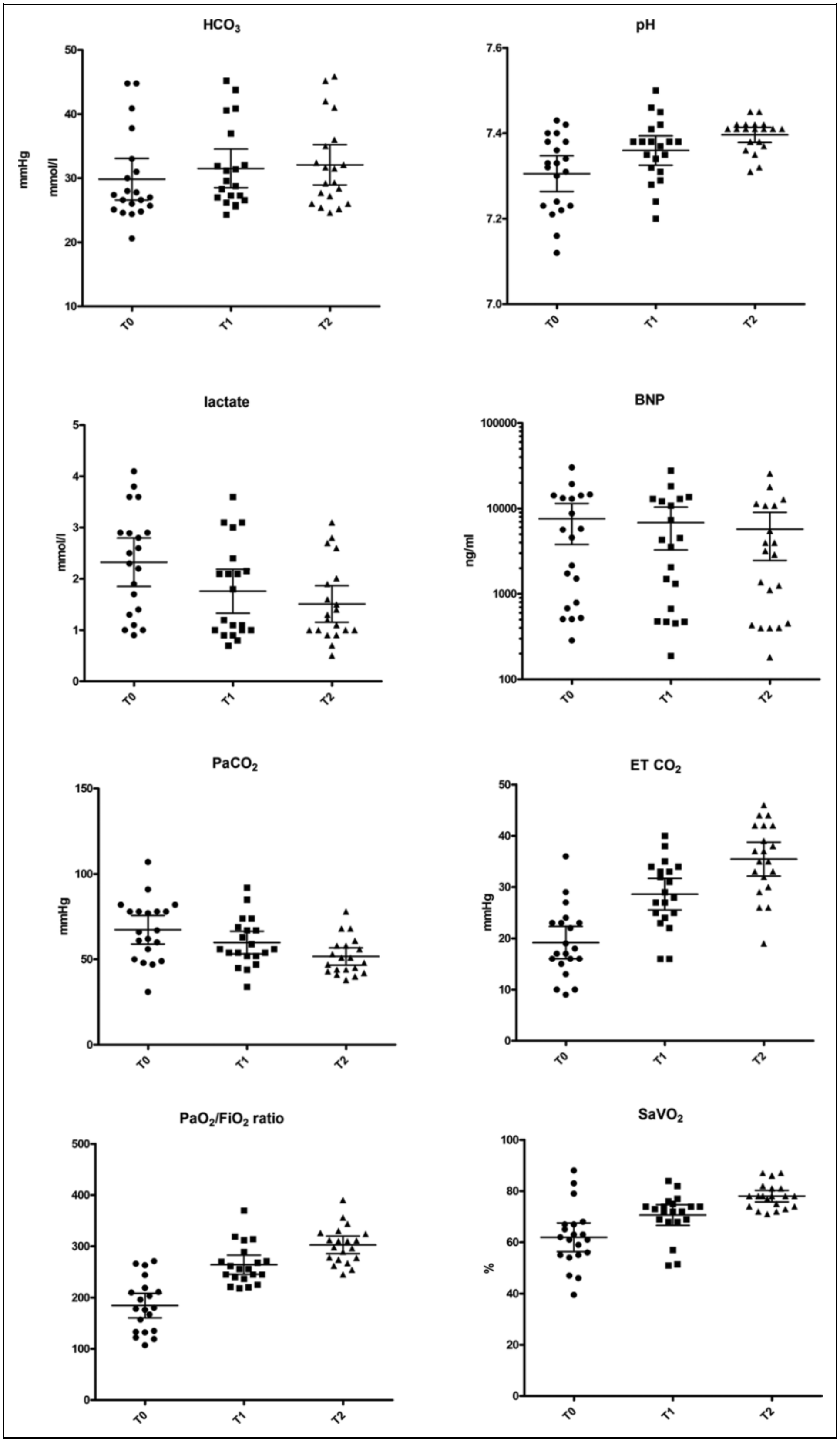

Figure 3. Changes in arterial blood gas analysis and microcirculation indexes with bilevel positive airway pressure noninvasive ventilation over time (admission [T_0], after 3 hours [T_1], and after 6 hours, [T_2]). Changes were statistically significant in all cases.

appears to be the first dedicated echocardiographic, multiparameter hemodynamic evaluation of NIV and systolic AHF in the ED environment, even though not the first ever acute hemodynamic/circulation evaluation of NIV in the emergency arena. Most previous studies were focused on improving pH and pulse oximetry in ED bilevel patients,[6] improvement confirmed in our study.

Noninvasive ventilation has been shown to be effective in acute respiratory failure of various etiologies and in different ward settings. The largest body of evidence on the use of NIV comes from patients with chronic obstructive pulmonary disease (COPD) having exacerbation and respiratory failure.[7] Also short period of treatment (6 hours) may be effective in improving symptoms.[8]

Several studies also evaluated the efficacy of NIV in patients with cardiogenic pulmonary edema. Compared to continuous positive airway pressure (CPAP) to treat cardiogenic pulmonary edema, BiPAP more rapidly improves oxygenation and dyspnea scores and reduces the need for intensive care admission[9,10]; furthermore, BiPAP does not increase myocardial infarction rates compared to CPAP. Noninvasive ventilation is effective in improving gas exchanges in cardiogenic pulmonary edema.[11] As compared to standard oxygen therapy, NIV was associated with greater mean improvements at 1 hour after the beginning of treatment in patient-reported dyspnea, heart rate, acidosis, and hypercapnia.[6]

Noninvasive ventilation support delivered by either CPAP or non-invasive positive pressure ventilation safely provides early improvement and resolution of breathlessness, respiratory distress, and metabolic abnormality in pulmonary edema.[12] After 1 hour of ventilation and at the end of the ventilation period, clinical parameters of respiratory distress and blood gas exchange significantly improve with NIV.[13]

Less is known, however, on very early effects of NIV on hemodynamics and other nonhemodynamic indexes in patients with cardiogenic respiratory failure. In prior studies, NIV significantly reduced transmural mean right atrial pressure and transmural pulmonary arterial occlusion pressure.[14] In several other studies, however, NIV did not change cardiac output.[15]

Continuous positive airway pressure ventilation, even in the absence of a significant increase in stroke volume and cardiac output, may modulate ventricular filling pressure,[16] by reducing pre- and afterload.[17] Other studies showed a better clinical outcome in patients poorly responsive to CPAP, when treated with BiPAP.[18]

In 2002, Summers et al found that in patients with COPD and AHF, BiPAP improved hemodynamics, heart rate, both systolic and diastolic pressure, cardiac index, ejection time, diastolic time, and systemic resistances; these effects were not inducible in healthy controls.[19] Kasai et al in 2005[20] and Dohi et al[21] in 2008 further showed that patients with central sleep apnea and heart failure not responsive to CPAP had less episodes of Cheyne-Stokes breathing after BiPAP treatment.

As shown by Brochard et al, CPAP may also reduce ventricular pre- and afterload by increasing intrathoracic pressure,[8] while BiPAP may further restore ventilator synchronism, moderate adrenergic hypertone, and improve pulmonary circulation.[22]

Originally, we describe a wide range of positive effects of NIV in patients with AHF, thus further supporting the clinical efficacy of such treatment in patients not responsive to drug therapy. A better understanding of mechanism of action of BiPAP and CPAP in heart failure may allow us to target particular subgroups that may or may not do well with NIV. This pilot study may further support the use of serial hemodynamic echo evaluation at the bedside in the ED.

Conclusions

The BiPAP NIV may rapidly ameliorate several hemodynamic, arterial blood gas, and microcirculation indexes in patients with AHF and systolic dysfunction.

Limitations

These are preliminary data coming from a very small cohort of patients, hence needing to be confirmed in larger populations. Results of this did not involve a control group.

This is a small pilot study unable to perform subgroup or multivariable analyses based on several potential confounders, which must be acknowledged. There were no data on the presence of COPD, sleep apnea, asthma, obesity, diastolic dysfunction, and hypertension. Presence of coronary artery disease was not ascertained in patients enrolled in the study, thus possibly biasing the results obtained.

The study is prospective, observational, and monocentric. A male predominance in the study cohort might have a potential effect. The number and background of the echocardiographers may be a limitation.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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