

Hemodynamic Effects of Noninvasive Ventilation in Patients with Venocapillary Pulmonary Hypertension

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Abstract

Background: The hemodynamic effects of noninvasive ventilation with positive pressure in patients with pulmonary hypertension without left ventricular dysfunction are not clearly established.

Objectives: Analyze the impact of increasing airway pressure with continuous positive airway pressure on hemodynamic parameters and, in particular, on cardiac output in patients with variable degrees of pulmonary hypertension.

Methods: The study included 38 patients with pulmonary hypertension caused by mitral stenosis without left ventricular dysfunction or other significant valvulopathy. The hemodynamic state of these patients was analyzed in three conditions: baseline, after continuous positive pressure of 7 cmH₂O and, finally, after pressure of 14 cmH₂O.

Results: The population was composed of predominantly young and female individuals with significant elevation in pulmonary arterial pressure (mean systolic pressure of 57 mmHg). Of all variables analyzed, only the right atrial pressure changed across the analyzed moments (from the baseline condition to the pressure of 14 cmH₂O there was a change from 8 ± 4 mmHg to 11 ± 3 mmHg, respectively, $p = 0.031$). Even though there was no variation in mean cardiac output, increased values in pulmonary artery pressure were associated with increased cardiac output. There was no harmful effect or other clinical instability associated with use application of airway pressure.

Conclusion: In patients with venocapillary pulmonary hypertension without left ventricular dysfunction, cardiac output response was directly associated with the degree of pulmonary hypertension. The application of noninvasive ventilation did not cause complications directly related to the ventilation systems. (Arq Bras Cardiol. 2014; 103(5):410-417)

Keywords: Hypertension, Pulmonary; Heart Failure; Noninvasive Ventilation; Hemodynamics.

Introduction

Noninvasive positive pressure ventilation (CPAP) is a mode of ventilation commonly applied to a large spectrum of clinical situations. Its use has already been described both in patients in critical conditions such as acute pulmonary congestion, acute respiratory failure in patients with chronic pulmonary disease and during recovery from cardiac and non-cardiac surgeries, and in chronic patients with obstructive sleep apnea.

It is known that, in general, application of airway pressure may benefit the hemodynamic condition of patients with pulmonary congestion and left ventricular systolic dysfunction primarily by increasing cardiac output¹⁻³. This effect has been attributed mainly to an elevation in intrathoracic pressure and

consequent reduction in left ventricular afterload, improving the systolic function of this chamber^{2,4}. The ultimate impact from use of CPAP in the cardiac performance of patients with previous systolic dysfunction is of a complex nature and reflects the interaction between the compromised heart and the intrathoracic vasculature. In fact, this intricate relationship can be even more complex in the presence of venocongestive pulmonary hypertension.

In contrast, in the presence of pulmonary hypertension, invasive mechanical ventilation has been associated with unfavorable hemodynamic effects⁵. Therefore, patients with pulmonary hypertension due to pulmonary venocapillary congestion may be subject to unpredictable hemodynamic effects during application of airway pressure.

Still today, the hemodynamic effects of CPAP in patients without left ventricular dysfunction have not been entirely described. Particularly in patients with pulmonary hypertension, a subclass of patients often encountered in daily clinical practice, the impact of CPAP has been poorly characterized. Even though its use is widely accepted as beneficial in patients with sleep apnea and some elevation in pulmonary pressure, its effects have not yet been completely described in a population with marked pulmonary hypertension^{6,7}.

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The aim of this study, therefore, is to analyse the impact of increasing airway pressure with CPAP on hemodynamic parameters in patients with variable degrees of pulmonary hypertension. In particular, the primary aim is to evaluate the effects of CPAP on the cardiac output of patients with chronic pulmonary hypertension.

Methods

Studied cohort

This study included a total of 38 patients with pulmonary hypertension (resting systolic pulmonary arterial pressure equal to or higher than 30 mmHg) confirmed by cardiac catheterization. In order to homogenize the cohort, the analysis included only patients with pulmonary hypertension caused by mitral stenosis who were selected to undergo balloon catheter mitral valvuloplasty (BCMV). The selection was conducted according to medical history, physical examination and echocardiogram with two-dimensional color Doppler. This last was conducted in all patients up to 3 months before the invasive evaluation. Patients with left ventricular dysfunction, any greater than mild valvular heart disease, and left atrial thrombus were excluded. The consent term was obtained from all patients and the study was approved by the Ethics Committee of our institution.

Protocol

Patients were evaluated in the catheterization laboratory immediately before BCMV. Analgesia was only performed with local lidocaine infiltration on the puncture site and sedative medications were avoided. Hemodynamic parameters were obtained in the supine position on three moments: 1) at baseline, in ambient air; 2) 5 minutes after CPAP set at 7 cmH₂O; and 3) 5 minutes after CPAP set at 14 cmH₂O. Noninvasive ventilation was delivered with a CPAP equipment (Solo LX Deluxe, Respironics Inc, USA) and oronasal mask (model Comfortfull, Respironics Inc, USA).

In each of the three conditions, heart rate and rhythm, as well as digital oximetry were measured continuously with a multiparameter monitor. Right atrial pressure, pulmonary arterial pressure and pulmonary capillary pressure were measured with a 7-Fr Swan-Ganz catheter (Edwards Laboratories, Santa Ana, USA), inserted via the right femoral vein. Systemic arterial and left ventricular pressures were measured with a 5-Fr pigtail catheter inserted via the left femoral artery. All measurements were performed at the end of expiration and the pressure transducers were zeroed at the level of the mid-axillary line.

Cardiac output was calculated by thermodilution as a mean of three measurements obtained after injection of 10 mL of 5% dextrose solution randomly performed during the respiratory cycle. If one of the measurements differed in more than 10% of the mean, two other cardiac output measurements were determined and the highest and lowest values were discarded for calculation of the mean. Samples of arterial and venous blood gases were collected from the aorta and the pulmonary artery, respectively. The derived hemodynamic and oxymetric variables were calculated from standard formulas.

Statistical analysis

Categorical variables were shown in tables with absolute (n) and relative (%) frequencies, whereas quantitative variables were presented as mean and standard deviation.

Quantitative variables, measured on each of the three conditions (baseline, CPAP 7 cmH₂O and CPAP 14 cmH₂O), were presented in tables as means and standard deviations and were evaluated with analysis of variance with repeated measurements. When significant, contrasts of maximum likelihood were conducted to discriminate the differences.

Correlation coefficients were calculated to evaluate the variation in cardiac output with echocardiographic and hemodynamic parameters.

P values < 0.05 were considered statistically significant.

Sample size was calculated using the software G Power 3.1 with the formula for calculation of samples of repeated measures. A statistical power of 80%, significance level of 5%, and an effect (f) size of 0.25 were stipulated. This way, the minimum number of individuals was defined as 33.

Results

Thirty-eight patients with mitral stenosis and pulmonary hypertension followed as outpatients were recruited for this research. The population was composed of individuals predominantly young, females and with significant elevation in pulmonary arterial pressure, with a mean pulmonary arterial pressure of 57 mmHg. Table 1 presents the clinical and echocardiographic characteristics of the cohort, whereas Table 2 presents hemodynamic and blood gases data (Tables 1 and 2).

Variation in cardiac output

Table 2 also shows the stability of the mean value of the variables that represent left ventricular systolic capacity, cardiac output, cardiac index and systolic volume. Even though the mean cardiac output values of the cohort showed no variation across all three conditions, there was a significant variation among the patients. It was not possible, therefore, to identify the factors that modulated its variation during different moments of the study. The interactions between baseline characteristics and the effect of CPAP on the cardiac output are presented in Table 3. In the analysis of the use of CPAP set at 7 cmH₂O, it was not possible to identify at baseline variables associated with the variation in cardiac output. However, in the analysis of the use of CPAP set at 14 cmH₂O, the pressures in the pulmonary system and the oxygen saturation were associated with changes in cardiac output. The pressures in the pulmonary system were the main determinants of the changes in cardiac output, with increase in cardiac output in those with increased levels of pulmonary hypertension (Graphs 1 to 3). The arterial oxygen saturation of hemoglobin was also associated with changes in cardiac output across the studied conditions (Graph 4).

There was no association between the variation in cardiac output and the nonparametric variables functional class (p = 0.07 for CPAP 7 cmH₂O and p = 0.14 for CPAP 14 cmH₂O) and presence of atrial fibrillation (p = 0.77 for CPAP 7cmH₂O and p = 0.52 for CPAP 14 cmH₂O).

Table 1 – Demographic and echocardiographic features

Age, years	38.9 ± 11.8
Female gender	33 (87%)
NYHA class II	24 (63%)
NYHA class III or IV	14 (37%)
Chronic atrial fibrillation	4 (10%)
Systemic arterial hypertension	3 (8%)
Mitral valve area, cm ²	0.9 ± 0.2
Ejection fraction, %	69 ± 6
Left ventricular end-diastolic diameter, mm	47 ± 4
Left atrial diameter, mm	48 ± 4

Variation in hemodynamic parameters across the conditions

As for hemodynamic modifications during the different moments of the study, only right atrial pressure showed variation. From baseline to CPAP 14 cmH₂O, there was an increase from 8 ± 4 mmHg to 11 ± 3 mmHg, respectively (p = 0.031). In contrast, compared with baseline, the increase with CPAP 7 cmH₂O was not significant (p = 0.993). Despite a trend towards an increase, there was no expressive variation in values of systemic arterial and pulmonary arterial pressures. Other clinically relevant parameters, such as heart rate and oxygen saturation, also did not show modifications along the study.

It is important to highlight that no harmful effect was observed. There was no occurrence of clinical instability associated with use of CPAP. In addition, all patients, after

Table 2 – Hemodynamic and blood gases data before and after CPAP

	Baseline	CPAP 7 cmH ₂ O	CPAP 14 cmH ₂ O	p
Heart rate, beats/min	86 ± 16	85 ± 16	83 ± 16	0.686
Systolic systemic pressure, mmHg	117 ± 15	119 ± 14	120 ± 16	0.710
Diastolic systemic pressure, mmHg	73 ± 10	75 ± 11	76 ± 11	0.542
Systolic pulmonary pressure, mmHg	57 ± 24	58 ± 24	58 ± 24	0.957
Diastolic pulmonary pressure, mmHg	30 ± 14	31 ± 13	32 ± 13	0.883
Pulmonary capillary pressure, mmHg	27 ± 10	27 ± 9	27 ± 9	0.961
Right atrial pressure, mmHg	8 ± 4	9 ± 4	11 ± 3	0.035 *
Cardiac output, l/min	4.6 ± 1.2	4.6 ± 1.1	4.5 ± 1.2	0.877
Cardiac index, l/min/m ²	2.7 ± 0.7	2.7 ± 0.6	2.6 ± 0.7	0.838
Indexed systolic volume, ml/beat/m ²	32.3 ± 8.1	32.4 ± 8.0	32.1 ± 7.0	0.987
Arterial oxygen saturation, %	95.2 ± 2.9	95.6 ± 2.1	96.0 ± 2.1	0.330
Mixed venous oxygen saturation, %	69.6 ± 7.5	69.6 ± 7.0	69.2 ± 7.2	0.950

* Significant variation only in the comparison between baseline and CPAP set at 14 cmH₂O.

Table 3 – Correlation between baseline characteristics and effect of CPAP on cardiac output variation

Baseline parameters	CPAP 7 cmH ₂ O		CPAP 14 cmH ₂ O	
	Correlation of Pearson	p	Correlation of Pearson	p
Mitral valve area, cm ²	-0.257	0.12	-0.250	0.13
Left ventricular ejection fraction, %	0.000	0.99	0.300	0.07
Left ventricular diastolic diameter, mm	0.200	0.22	0.094	0.83
Left atrial diameter, mm	0.074	0.66	-0.073	0.66
Heart rate, beats/min	0.920	0.58	0.304	0.06
Systolic systemic pressure, mmHg	0.019	0.91	0.279	0.09
Diastolic systemic pressure, mmHg	0.027	0.87	0.192	0.25
Systolic pulmonary pressure, mmHg	0.210	0.20	0.516	0.001
Diastolic pulmonary pressure, mmHg	0.209	0.21	0.509	0.001
Pulmonary capillary pressure, mmHg	0.245	0.14	0.528	0.001
Right atrial pressure, mmHg	0.115	0.49	0.088	0.60
Arterial oxygen saturation, %	-0.244	0.14	-0.387	0.02
Mixed venous oxygen saturation, %	-0.276	0.09	-0.310	0.06

a brief explanation about the use of CPAP, tolerated its application satisfactorily during the study.

Discussion

The main result of this study was the association of the pressures in the pulmonary system as the main determinants of the variation in cardiac output with CPAP use in a population of patients with pulmonary hypertension. As expected, the hemodynamic changes were more evident with application of higher levels of airway pressure. In the analysis during CPAP set at 7 cmH₂O, none of the variables correlated with changes in cardiac output. Following that, the evaluation during CPAP set at 14 cmH₂O showed the importance of the pulmonary hypertension in cardiac output response. Higher values of systolic, diastolic and occlusion pulmonary arterial pressures were associated with increased cardiac output.

The association between higher values of pulmonary artery occlusion pressure (PAOP) and positive response to use of CPAP has been previously documented by other authors in a population with a very distinct hemodynamic profile. Baratz et al¹, during a study with patients with idiopathic myocardial pathology after use of CPAP set at 5 cmH₂O, identified two groups of patients. The first group, with PAOP equal to or higher than 12 mmHg, responded with an increase of 17% in cardiac output. The second group of patients with PAOP below 12 mmHg, presented a reduction of 8% in cardiac output. Bradley et al³ confirmed this concept, observing that the use of CPAP set at 5 to 10 cmH₂O caused an elevation in cardiac output proportional to the level of pressure offered in patients with cardiac failure and elevated PAOP. These studies have in common with the present study the association between higher PAOP values and positive response to use of CPAP. However, only patients with left ventricular dysfunction were included, which was a condition excluded in the current study. It is known that the reduction in left ventricular afterload imposed by CPAP may be particularly advantageous in the presence of systolic dysfunction. In contrast, in patients with pulmonary hypertension and respiratory failure, it is known that mechanical ventilation with positive pressure can impose negative hemodynamic effects. The increase in pulmonary volume and decrease in functional residual capacity can increase the pulmonary vascular resistance and, consequently, the right ventricular output impedance, mainly in patients with pre-existent right ventricular failure⁵. The acute effects of noninvasive ventilation in patients with extreme pulmonary hypertension are not well described. Even though the use of CPAP has been extensively studied in patients with sleep apnea syndrome, this condition is usually associated with a more mild pulmonary hypertension than that observed in the current study^{6,7}. In a study that included 20 patients without cardiac or pulmonary pathologies, only five of these patients fulfilled the criteria of pulmonary hypertension. In this study, the mean pulmonary artery pressure of the group was 16.8 mmHg⁶. In 40 patients with obstructive sleep apnea and pulmonary hypertension studied by Laks et al⁸, the pulmonary artery systolic pressure estimated by echocardiogram ranged from 20 to 52 mmHg and the mean was only 29 mmHg⁸. A study with only nine

patients with respiratory failure due to decompensation of chronic obstructive pulmonary disease were studied with hemodynamic monitoring during application of noninvasive ventilation with pressure support and positive end-expiratory pressure (PEEP)⁹. There was a significant decrease in cardiac output associated with use of PEEP set at 5 cmH₂O. However, even though all patients presented at least moderate pulmonary hypertension, the mean pulmonary artery pressure was 27 mmHg, which was much below the value found in our study.

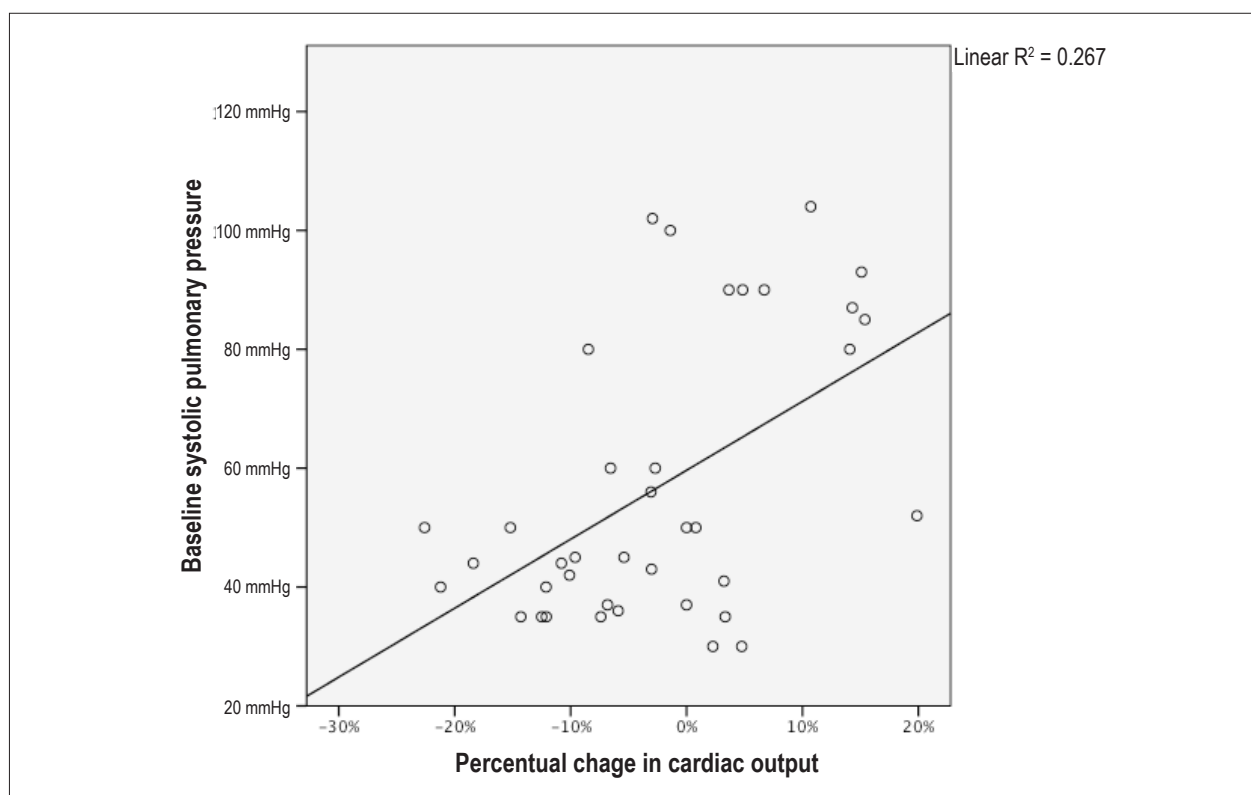
Up to where an extensive review of the literature allows us to consider, the evaluation of the acute hemodynamic effects of noninvasive ventilation in patients with such marked pulmonary hypertension had not yet been conducted. Although our sample, composed of patients with severe mitral stenosis, may represent a profile of patients with preserved left ventricular systolic performance associated with venocapillary pulmonary hypertension, it is not possible to determine whether other etiologies of pulmonary hypertension without left ventricular dysfunction would respond similarly to use of CPAP.

Another important result of this study was that use of CPAP was safe in the conditions applied in the current study, similarly to what has been described by other authors. Only right atrial pressure presented a significant variation during application of airway pressure. In the conditions evaluated in this study, there were no significant variations in relevant clinical parameters, such as heart rate, systemic arterial pressure, cardiac output, pulmonary arterial pressure and arterial oxygen saturation. After the researchers explained the procedures to the patients, including details of aspects related to noninvasive ventilation, use of CPAP was well tolerated, even at a pressure of 14 cmH₂O. There were no cases in which noninvasive ventilation had to be removed by request from the patient. It should also be highlighted that there was no register of complication related directly to the use of pressurized ventilation systems.

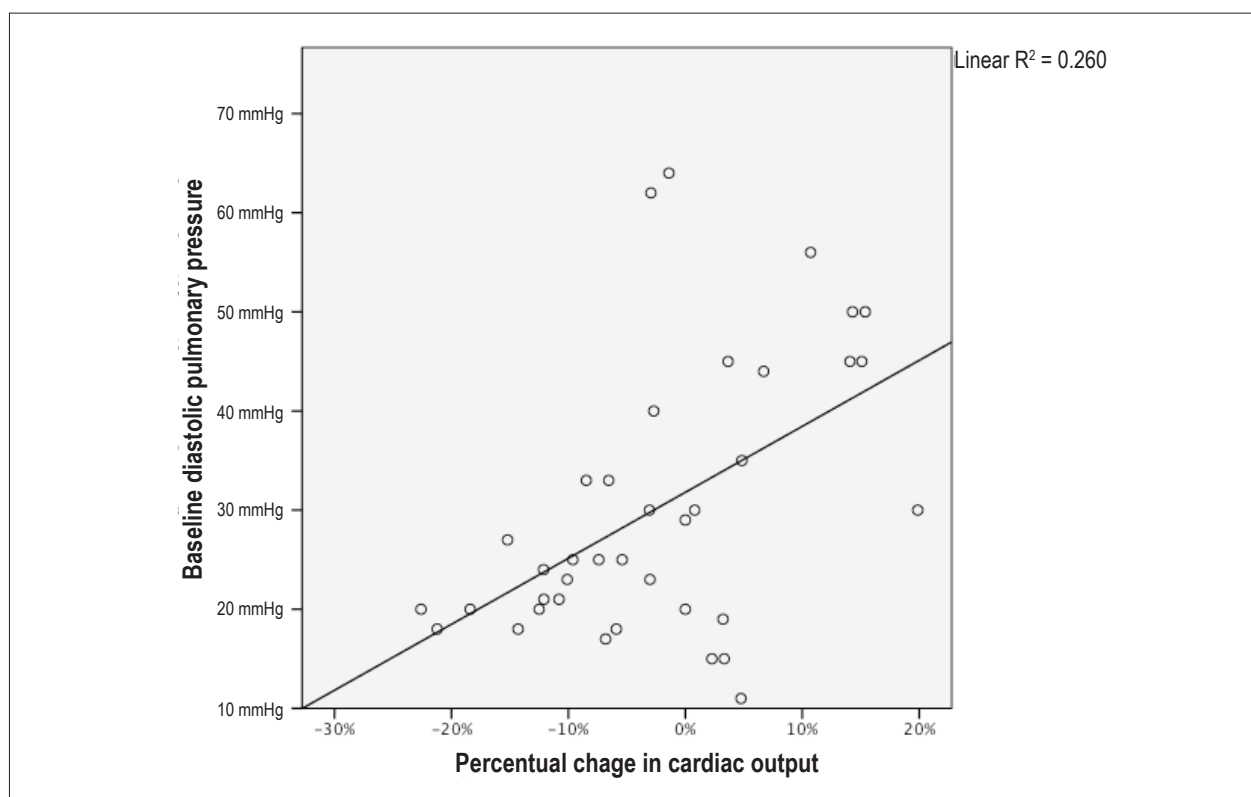
The use of noninvasive ventilation has been shown capable to reduce the need for intubation, length of stay and ICU mortality in patients with hypoxemic acute respiratory failure. This is due to its effects on the hemodynamic status and pulmonary mechanics. With respect to the respiratory system, its application has as main physiological benefits the decrease in respiratory work, in addition to an improve in oxygenation. As for the clinical applicability of the current study, considering that the respiratory benefits of CPAP would be maintained, the small variation in relevant hemodynamic parameters favors use of CPAP in patients with hypoxemic respiratory failure and hemodynamic profile similar to that in this study.

Study limitations

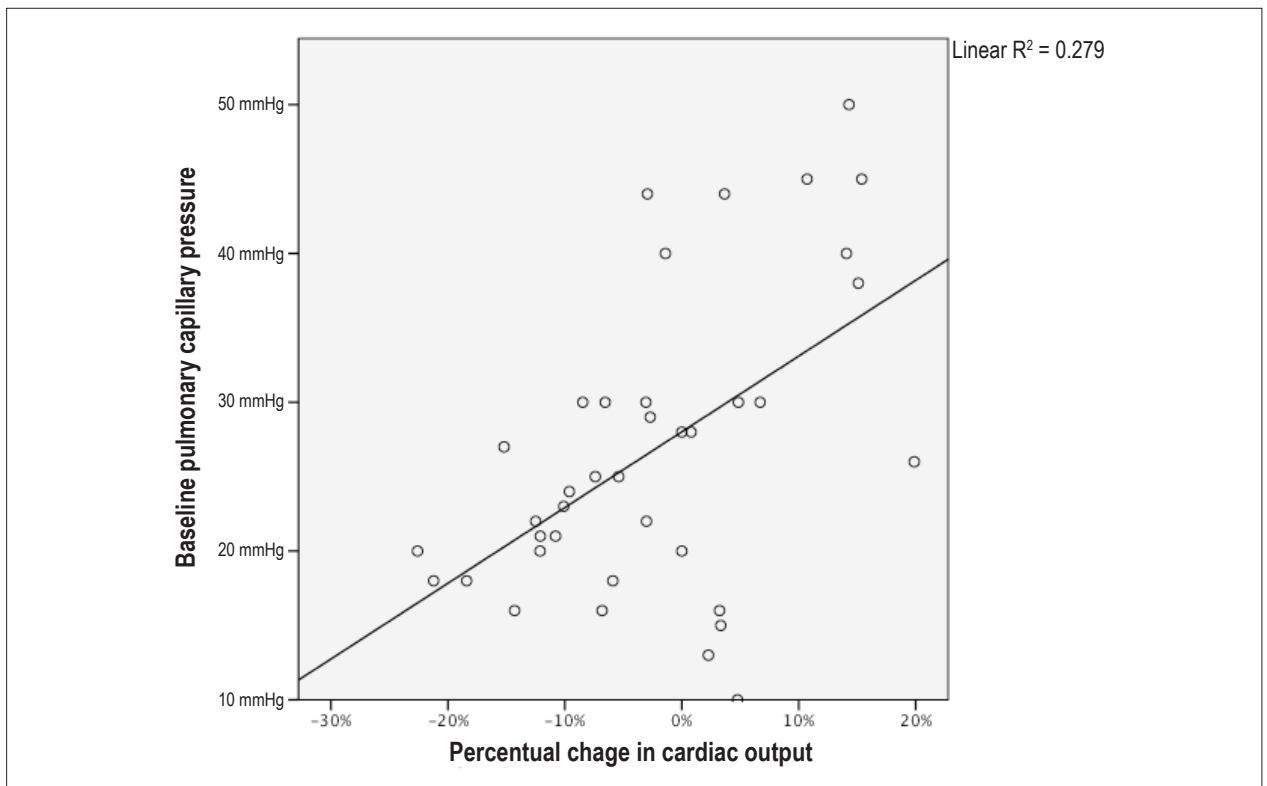
The main limitation of the study was the fact that the patients were clinically stable during the study procedures. Usually, the application of noninvasive ventilation is indicated in patients with respiratory failure. Therefore, with regard to the best scientific methodology, the ideal would be to evaluate the hemodynamic conditions of patients with pulmonary congestion before any treatment and during noninvasive ventilation. However, this approach



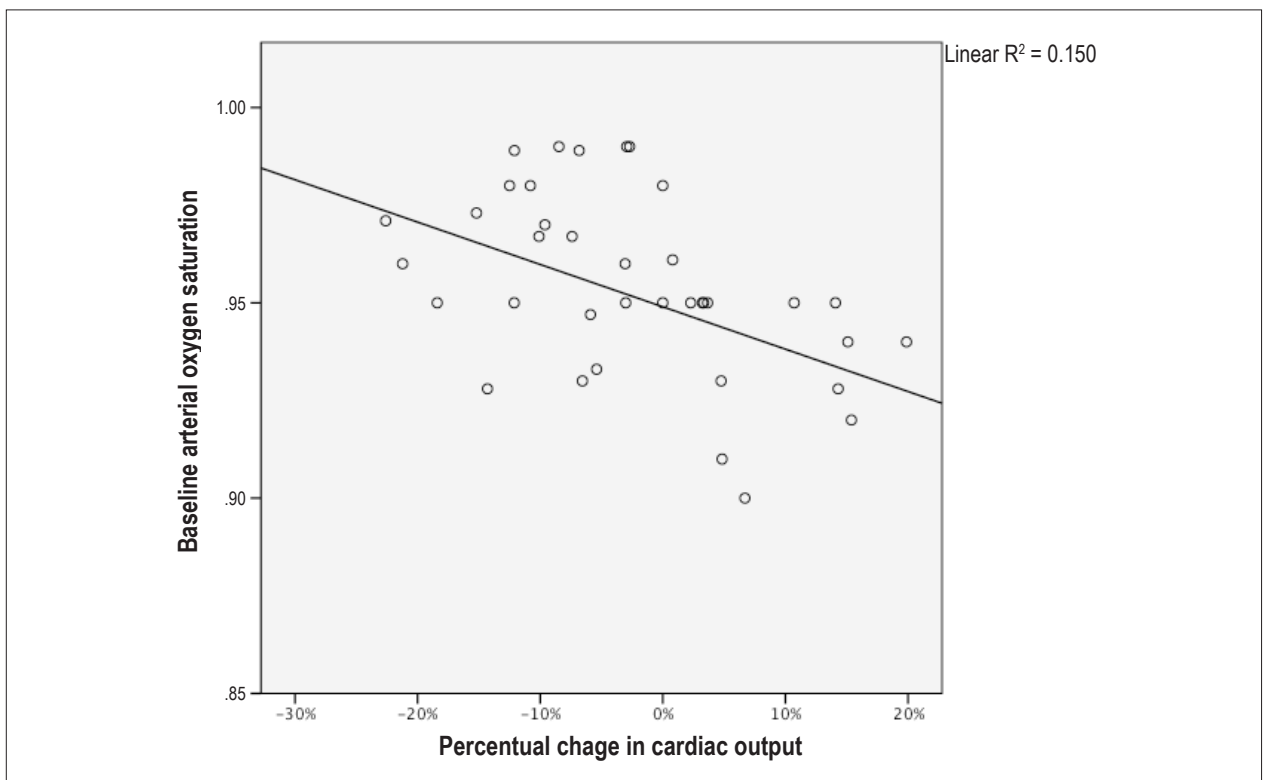
Graph 1 – Percentage change in cardiac output from baseline to CPAP set at 14 cmH₂O according to baseline systolic pulmonary pressure.



Graph 2 – Percentage change in cardiac output from baseline to CPAP set at 14 cmH₂O according to baseline diastolic pulmonary pressure.



Graph 3 – Percentage change in cardiac output from baseline to CPAP set at 14 cmH₂O according to baseline pulmonary capillary pressure.



Graph 4 – Percentage change in cardiac output from baseline to CPAP set at 14 cmH₂O according to baseline arterial oxygen saturation.

was not possible due to a series of factors. First, it would be risky to keep a patients with pulmonary congestion without adequate treatment while invasive monitoring is provided. Second, the great majority of the patients with pulmonary congestion and/or acute pulmonary edema do not require invasive monitoring as part of the therapy. Monitoring is related to a number of complications that would increase the risk to the patient and would, therefore, imply in a questionable ethical judgment. Finally, this strategy would limit substantially the number of selectable patients, jeopardizing the viability of the study. It is also worth mentioning that even though the study was not performed in patients with clinical instability, nothing prevents its value to be extended to this situation.

Conclusion

In patients with mitral stenosis, venocapillary pulmonary hypertension and without left ventricular dysfunction, the cardiac output response to use of CPAP was directly associated with the degree of pulmonary hypertension. The application of CPAP did not incur in complications directly related to the ventilation systems.

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Author contributions

Conception and design of the research: Bento AM, Cardoso LF, Tarasoutchi F, Sampaio RO, Kajita LJ; Acquisition of data: Bento AM, Cardoso LF, Sampaio RO, Kajita LJ; Analysis and interpretation of the data and Statistical analysis: Bento AM, Cardoso LF, Lemos Neto PA; Writing of the manuscript: Bento AM, Cardoso LF; Critical revision of the manuscript for intellectual content: Bento AM, Tarasoutchi F, Sampaio RO, Lemos Neto PA.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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