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Literature review

Effects of continuous positive pressure and of two levels on the airline in acute cardiogenic lung edema: a systematic review

Efeitos da pressão positiva contínua e de dois níveis na via aérea em edema agudo de pulmão cardiogênico: uma revisão sistemática

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RESUMO | INTRODUÇÃO: O edema agudo de pulmão cardiogênico (EAPC) representa uma importante causa de insuficiência respiratória aguda podendo ser atenuada com a instalação de ventilação mecânica não-invasiva (VNI). **OBJETIVO:** Comparar pressão positiva contínua (CPAP) e pressão positiva de dois níveis (BIPAP) na via aérea em pacientes adultos com EAPC, quanto à função pulmonar, ao tempo de permanência, suas complicações e a dispneia através de uma revisão sistemática. **METODOLOGIA:** Ensaios clínicos controlados e randomizados (ECR), revisados por dois revisores independentes, conforme recomendações PRISMA, nas bases de dados PubMed e Biblioteca Cochrane. Incluídos estudos originais que utilizaram a CPAP e a BIPAP em pacientes com EAPC publicados na língua inglesa. A Escala PEDro foi utilizada para analisar a qualidade metodológica dos estudos e a Cochrane Collaboration para análise de risco de viés. **RESULTADOS:** Foram incluídos 13 artigos, publicados entre os anos 1997 e 2014. Os níveis de CPAP variaram entre 5 e 20 cmH_2O nos estudos, e BIPAP apresentou-se com pressão inspiratória positiva (IPAP) entre 8 e 20 cmH_2O e pressão expiratória positiva (PEEP) entre 3 e 10 cmH_2O. Os estudos apresentaram CPAP e BIPAP sem diferença estatisticamente significante para a melhora da função pulmonar (FR, PaO_2 e $PaCO_2$), tempo de internamento, taxas de mortalidade, entubação e infarto agudo do miocárdio (IAM); mostrando-se como modalidades igualmente eficazes. **CONCLUSÃO:** CPAP e a BIPAP garantem os mesmos efeitos para melhora da função pulmonar, não mantém relação com a permanência da internação e complicações, e melhoram o quadro de dispneia.

PALAVRAS-CHAVE: Ventilação não invasiva. Ventilação com pressão positiva. Ventilação positiva em dois níveis. Edema pulmonar cardiogênico agudo. Insuficiência cardíaca congestiva.

ABSTRACT | INTRODUCTION: Acute cardiogenic lung edema (EAPC) represents an important cause of acute respiratory failure and can be attenuated with the installation of non-invasive mechanical ventilation (NIV). **OBJECTIVE:** To compare the use of continuous positive pressure (CPAP) and two-way positive airway pressure (BIPAP) in adult patients with acute pulmonary edema of pulmonary function, length of stay and complications, and dyspnea through a systematic review. **METHODOLOGY:** Systematic review of randomized controlled trials (RCTs) performed by two independent reviewers, as recommended by the PRISMA platform, in the PubMed and Cochrane Library databases. Original studies using CPAP and BIPAP were used in patients with acute cardiogenic lung edema published in English. The PEDro Scale was used to analyze the methodological quality of the studies and Cochrane Collaboration. **RESULTS:** We included 13 articles, published between 1997 and 2014. CPAP levels ranged from 5 to 20 cmH_2O in the studies, and BIPAP presented positive inspiratory pressure (IPAP) between 8 and 20 cmH_2O and positive expiratory pressure (EPAP) between 3 and 10 cmH_2O. The studies presented CPAP and BIPAP without statistically significant difference for the improvement of the pulmonary function (FR, PaO_2 and $PaCO_2$), permanence of hospitalization, mortality rates, intubation and acute myocardial infarction (AMI); as equally effective modalities. **CONCLUSION:** CPAP and BIPAP guarantee the same effects to improve pulmonary function, does not maintain relation with the permanence of hospitalization and complications, namely: mortality, intubation and AMI, and improve dyspnea.

KEYWORDS: Non-invasive ventilation. Positive pressure ventilation. Bilevel positive airway pressure. Acute cardiogenic pulmonary edema. Congestive heart failure.

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Introduction

Acute cardiogenic lung edema (EAPC) represents an important cause of acute respiratory insufficiency[1], refers to the clinical condition in which the respiratory system is unable to maintain adequate blood pressure values for oxygen and carbon dioxide[23]. The presence of pulmonary congestion also causes changes in gas exchange and pulmonary mechanics. The increased impedance of the respiratory system determines the increase in respiratory work and a greater variation of intrathoracic pressures during inspiration. This variation, in turn, leads to a sequence of hemodynamic changes that can be attenuated with the installation of non-invasive mechanical ventilation (NIV)[1].

Over the last two decades, positive pressure NIV has emerged as an important tool in the treatment of acute respiratory failure, with strong evidence supporting the use of this technique to treat CPSC[17]. However, there is evidence in the literature about the advantages of the use of positive airway mask for the treatment of this patient profile, there are still doubts as to the best ventilatory modality[3].

Management of this clinical condition generates a dilemma in the attending professionals, especially in relation to the prompt intubation or the attempt to institute NIV, which has been considered an effective alternative, especially for reducing the need for intubation and the risks related to it. The application of NIV is then a more frequent and safe procedure[24.25].

The physiological effects of NIV include increased cardiac output and oxygen delivery, improving residual capacity and functional respiratory and ensuring reduced respiration effort in[2]. The application of positive pressure per mask has been suggested as an effective therapeutic modality in the treatment of EAPC, which should be associated with conventional drug treatment, since it provides a faster recovery of vital and gasometric data, when compared to the conventional oxygen treatment administered by mask[3]. Moreover, the increased interest in using such a method is the prevention of complications of invasive ventilation and aspiration of gastric contents, oropharyngeal trauma, ventilator - associated pneumonia, tracheal stenosis[26] and pneumothorax. There are multiple mechanisms involved in improving respiratory distress in patients with PADS using positive pressure, such as improvement in hypoxemia, reduction of preload and post-load in the left ventricle, and increased pulmonary compliance due to recruitment of the units alveolar collars[3].

It is known that the use of continuous positive airway pressure (CPAP) leads to a decrease in the elastic and resistive components of respiratory work, as well as attenuates the inspiratory variations of intrathoracic pressures in patients with pulmonary congestion. The technique is simple and can be performed with a flow generator connected to an oxygen source and mask with expiratory valve to keep intrathoracic positive pressure constant[1].

On the other hand, two-level positive airway pressure (BIPAP) requires a ventilator to ensure two levels of positive airway pressure: inspiratory pressure (IPAP) and expiratory pressure (PEEP). The use of BIPAP in the EAPC is based on physiological foundations and is supported by the fact that BIPAP presents similar benefits to CPAP and further decreases respiratory work due to the existence of supportive pressure during the inspiratory phase of the cycle. Despite this, studies using BIPAP in the treatment of EAPC are scarce and do not provide consistent evidence. They range from greater myocardial ischemia rate to a reduced need for intubation and, especially in patients hypercapnics[1].

Therefore, the objective of this study was to compare the use of CPAP and BIPAP in the airways in adult patients with EAPC regarding air pulmonary function, hospitalization time, rates of intubation, mortality and acute myocardial infarction (AMI), and dyspnea through a systematic review.

Methods

The present systematic review was elaborated according to the methodological recommendations Preferred reporting items for systematic reviews and meta-analyzes (PRISMA)[4].

Sources of information and search strategy

The search for articles to obtain the clinical outcome of CPAP and BIPAP in patients with EAPC was performed in the databases Public Medline (PubMed), Cochrane Library and PEDro. The articles were obtained from the English language by means of combinations, with the boolean operators "AND" and "OR", of the following descriptors and their correlates: " Non- invasive ventilation", "Positive pressure ventilation", "Bilevel positive airway pressure", "Acute cardiogenic pulmonary edema", "Congestive heart failure". The search strategy for the PubMed databases is shown in Chart 1.

Chart 1. Research strategy in the PubMed data library and Cochrane Library respectively

#1 (((((((Acute cardiogenic pulmonary edema) OR Cardiogenic pulmonary edema) OR congestive heart failure) OR heart failure) OR pulmonary edema) OR lung edema)) AND ((((((((((((((non-invasive ventilation) OR positive pressure ventilation) OR noninvasive ventilation) OR NIPPV) OR CPAP) OR BIPAP) OR Bilevel positive pressure) OR NPPV) OR Intermittent positive-pressure ventilation) OR positive pressure respiration) OR intermittent positive-pressure breathing) OR Noninvasive positive pressure ventilation) OR Noninvasive positive-pressure ventilation) OR Noninvasive continuous positive airway pressure) OR Continuous positive airway pressure) Filter: Clinical Trial
#2 Non-invasive ventilation OR Positive pressure ventilation OR Bilevel positive airway pressure OR Acute cardiogenic pulmonar edema OR Congestive heart failure

The selection of articles was conducted from April 2017 to November 2018 by two (2) independent reviewers. The articles were selected by checking the consistency between the title and the objective of each study, followed by the reading of the abstracts. In case of divergence in the selection of articles, the participation of a third reviewer was considered. After this step, a critical summary was prepared summarizing the information provided by the articles that were included in the review.

Eligibility criteria

Were considered for this review the randomized controlled trials (RCTs) used as a treatment therapy CPAP and BiPAP in patients with EAPC. Articles that included only one of two modalities of Noninvasive Ventilation (NIV) were excluded.

Methodological quality

The quality of the included articles was evaluated using the PEDro scale. This evaluates the tests by means of 11 pre-established items. The first item is an additional criterion and represents the external validity (or "generalization potential" or "applicability" of the clinical study), not being included in the full scale score. The other items analyze two aspects of article quality: internal validation (items 2 to 9) and if the article contains sufficient statistical information so that the results can be interpreted (items 10 and 11). These items qualify as "applicable" or "not applicable", generating a total score ranging from 0 to 10 points[5].

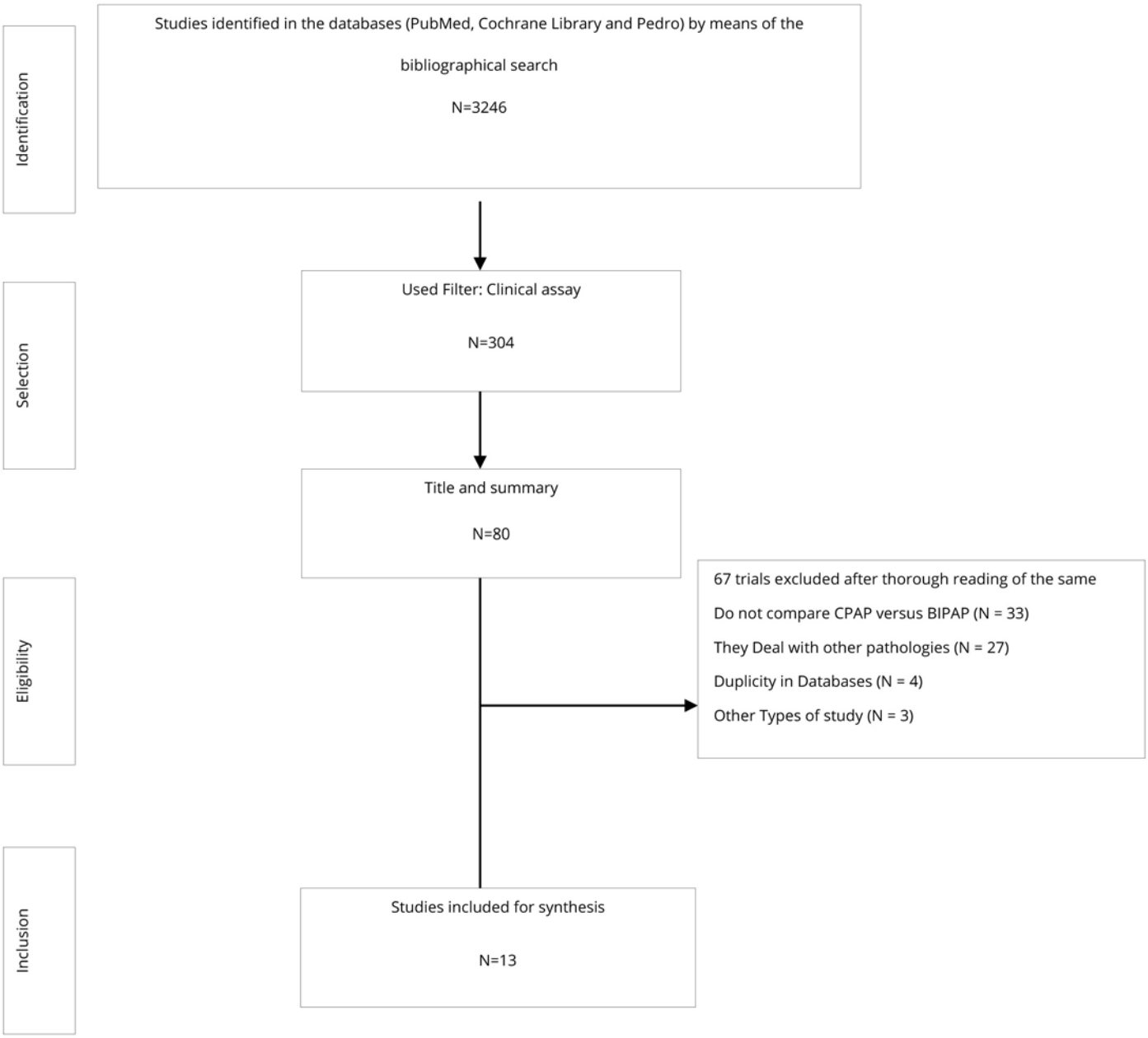
In order to search for a rigor in the methodological quality of the selected articles, they were analyzed and classified as "high quality" when they reached score ≥4 points on the PEDro scale, or as "low quality" when they obtained a score <4 on the referred scale[6]. It should be noted that PEDro's score was not used as a criterion for inclusion or exclusion of articles, but rather as an indicator of the scientific evidence of the studies.

Results

In the search conducted in PubMed databases and Cochrane Library, started in the period of April 2017 by 2 researchers, a total of 3246 articles were identified, reducing to 304 when applied the "filter": clinical trial. Of these, 224 were excluded due to

inadequacy after reading titles and abstracts. 80 articles were analyzed in full text, 13 these were included in this systematic review, according to the eligibility criteria. Figure 1 shows the process of selecting the articles through the flowchart of the PRISMA[4] platform.

Figure 1. Search and selection of studies for inclusion in the systematic review according to the PRISMA methodology



Regarding the methodological quality of the included articles (Table 1), only one of the studies was not considered "high quality", since the others reached a score equal to or higher than 4 in the PEDro Scale , were classified according to criteria Van Peppen et al6. As can be seen, all the studies presented eligibility criteria and distributed the subjects randomly in the groups. No study performed "blinds" of therapists, two performed "blinding" of the subjects and only one performed "blinds" of evaluators.

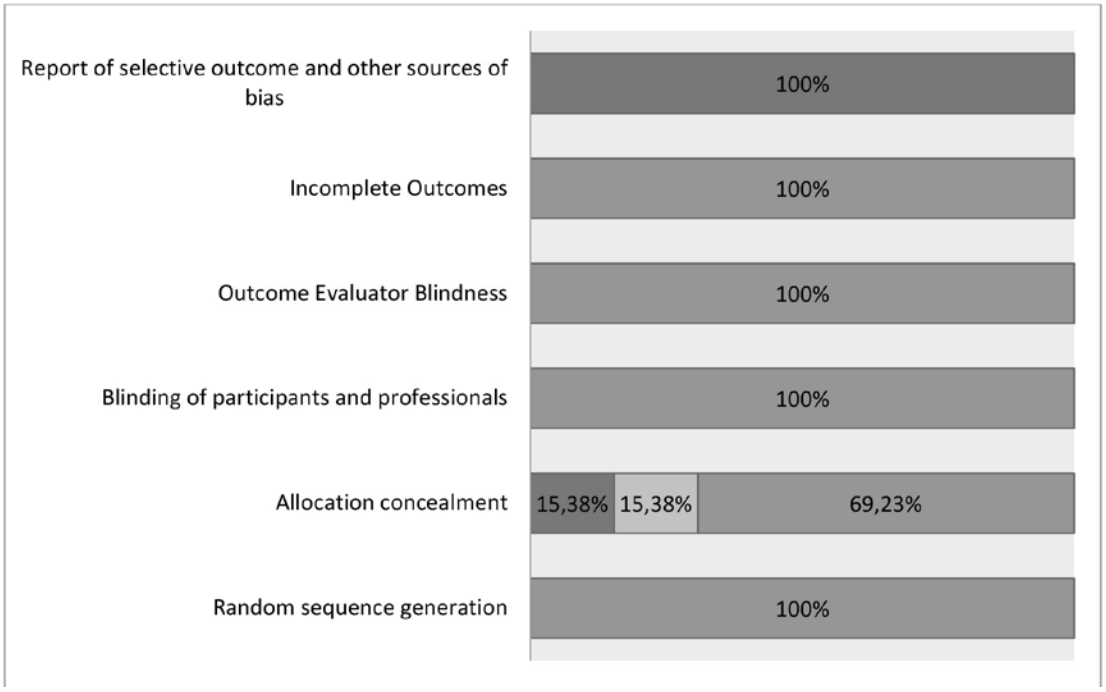
Table 1. Methodological quality of the studies by the PEDro Scale of included studies (1997 to 2017)

AUTHOR	1	2	3	4	5	6	7	8	9	10	11	TOTAL
Mehta *et al*, 1997[7]	X	X		X	X					X	X	5
Park *et al.*, 2001[3]	X	X								X		2
Cross *et al*, 2003[8]	X	X		X				X	X	X	X	5
Bellone *et al*, 2004[9]	X	X	X	X				X		X	X	6
Crane *et al*, 2004[10]	X	X	X	X					X	X	X	6
Park *et al*, 2004[11]	X	X	X					X	X	X	X	7
Bellone *et al*, 2005[12]	X	X		X				X	X	X	X	6
Ferrari *et al*, 2007[13]	X	X	X	X				X		X	X	7
Moritz *et al*, 2007[14]	X	X	X					X	X	X	X	6
Gray *et al*, 2008[15]	X	X	X	X			X	X	X	X	X	8
Ferrari *et al*, 2010[16]	X	X	X	X				X	X		X	6
Nouira *et al*, 2011[17]	X	X	X	X				X	X	X	X	7
Liesching *et al*, 2014[18]	X	X	X	X	X				X	X	X	7

Legend: 1) specification of inclusion criteria (item not punctuated); 2) random allocation; 3) secrecy in the allocation; 4) similarity of the groups in the initial or basal phase; 5) masking of subjects; 6) masking the therapist; 7) masking the evaluator; 8) measurement of at least one primary outcome in 85% of subjects allocated; 9) analysis of intention to treat; 10) comparison between groups of at least one primary endpoint and 11) reporting of measures of variability and estimation of the parameters of at least one primary variable.

To assess the risk of bias, the Cochrane Collaboration was used, which was developed between 2005 and 2007 by a group of methodologists, editors and authors of systematic review, and is domains based, with a critical evaluation done separately for different aspects of risk of bias of the type of study in question[27]. Of the seven items that are described in the Cochrane Collaboration, the 13 studies included in this review were mostly classified as low risk of bias, Figure 2.

Figure 2. Risk of bias established by the Cochrane Collaboration of included studies (1997 to 2017)



The articles included in this systematic review had year of publication between 1997 and 2014. The sample size ranged from 36 to 1069 adult subjects, randomized to the CPAP or BIPAP group. The 10 cmH2O level for CPAP was used in 8 studies[7,9,10-12,14,17,18], the level of 12 cmH2O[3,13,16] in 3 studies and the other two remaining studies used 5 to 20 cmH2O[8] and 5 to 15 cmH2O[15] respectively; in relation to the levels used for BIPAP, the 15 cmH2O level was found for inspiratory pressure in 6 studies[7,9,10-13] and the 7 studies[3,8,14-18] the others used levels ranging from 8 to 20 cmH2O and for the final expiratory pressure 8 studies[7-10,12,14,16,17] used the value of 5 cmH2O and the other 5 studies[3,11,13,15,18] levels ranging from 3 to 10 cmH2O. The duration of intervention for CPAP varied from 1h to 8,46h between studies and for BIPAP from 1h to 7h. Table 2 presents objective, sample characterization, methodology, results and conclusion of each study included in the qualitative synthesis.

From the results found in the 13 studies, they were divided into 3 major groups of outcomes: Pulmonary function (RR, PaO2 and PaCO2); Length of hospitalization and complications (hospital stays and intensive care unit (ICU), mortality, intubation and AMI); and dyspnea, as the third group.

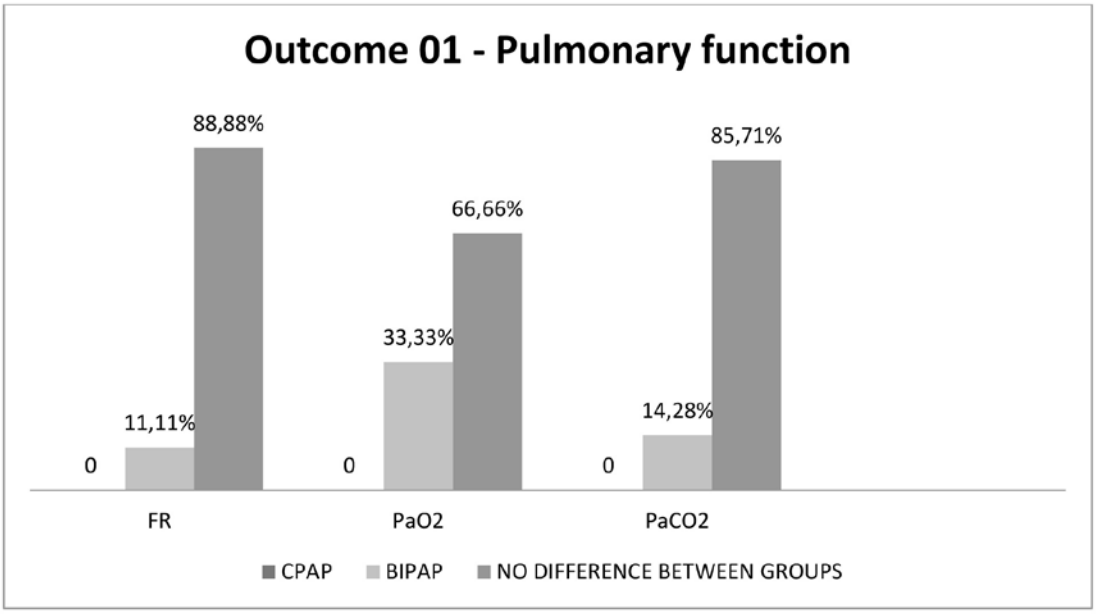
Pulmonary function

The general analysis of pulmonary function in the outcomes is descript al percent u in Figure 2. In detail, 13 studies, 3[8,10,17] did not present any results for pulmonary function, in the FR question . The improvement of the FR is described as having no significant difference between the CPAP and BIPAP groups by 8 authors: (32 ± 4 to 28 ± 5 versus 32 ± 4 to 26 ± 5 ipm) (p <0.05)[7] , (21, 2 ± 6.5 versus 20.9 ± 4.7) (p <0.01)[9], (improvement in both groups at 10', 30' and 60 'intervention)[11], (21.3 ± 5, 1 versus 21.2 ± 4.6)[12] , with no difference between groups (OR = 4.0) (95% CI: 0.0 to 1.9)[14], (7.3 vs. 7.1 ipm) p = 0.82)[15], (p <0.001)16 and (p> 0.05)[18], however, 1 author3 presented difference at 10' intervention with FR improvement only for the BIPAP group (34 ± 5 versus 28 ± 6) (p <0.05).

With respect to PaO2, 2 authors[12,15] presented the two groups without difference, as opposed to a third[3] that demonstrates a significant difference for the BIPAP group at the 10' intervention.

Finally, regarding PaCO2 , the authors[9,13,15,16,18] (41.3 ± 6.3 vs. 43.3 ± 5.4) (p <0.01), (44.2 ± 4.5 vs. 48.4 ± 20.2) (p <0.05) (1.5 versus 1,4kPa) (p = 0.67) (p <0.01) and (p <0.05) showed no differences in both groups as well as an article[11], demonstrates that variations of PaCO2 were similar between groups. However, 1 author7 (p = 0.057) presented improvement for the BIPAP group.

Figure 3. Percentage of Studies regarding the outcome 01 - pulmonary function (FR, PaO2 and PaCO2), of the studies included (1997 to 2017)



Length of hospitalization and complications

The general analysis of time outcomes and complications and hospitalization STA percential described in Figure 3. Detail hospital stay is regarded as no difference between the groups are CPAP and BiPAP to park[11] (11 ± 8 vs 10 ± 7 days) (p = 0.854), Moritz[14] (interquartile range - IQR 8.5 vs. 10.0 days),15 Gray (11.3 versus 11.5) (p = 0 , 81), Ferrari 16 (10.5 ± 15.41 days vs. 10.06 ± 8.13 days) (p = 0.706), Liesching[18] (6.64 versus 6.50 days) (p = 0.623), and Ferrari Mehta[7 13] (12.9 ± 9.9 versus 23.7 ± 7.4 days) (p = 0.529) and for the latter two also showed no difference in ICU stay (Ferrari[16] presented 4.0 ± 2.5 days versus 4.1 ± 3.2 days) (p = 0.437).

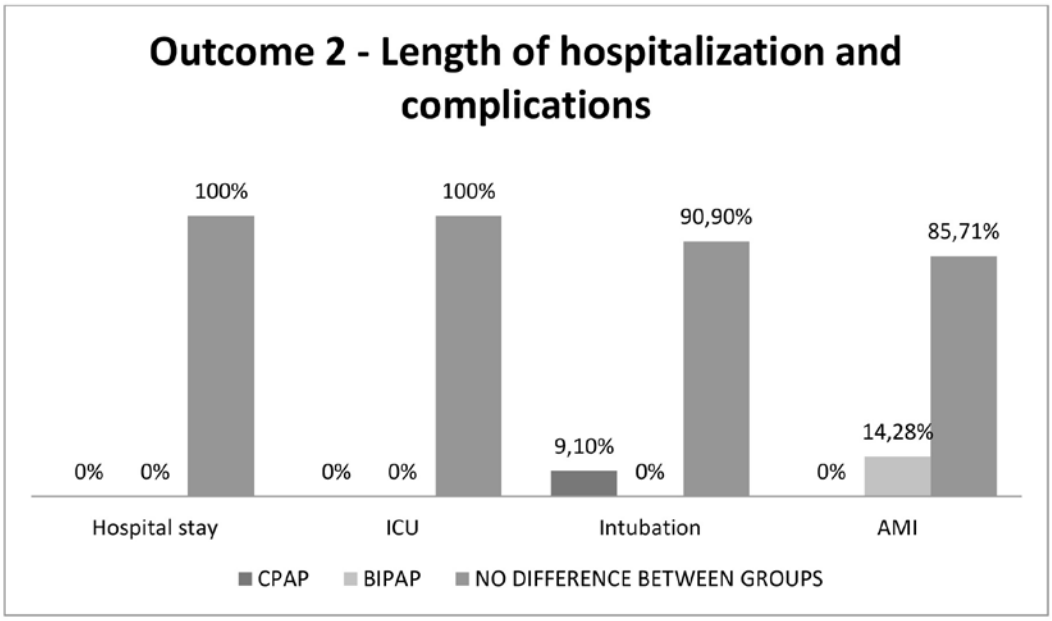
With RELAC will mortality rate, Mehta[7,8] Cross (5 patients versus 3 patients) (p = 0.710),[11] Park (patient 1 vs. 2 patients) (p = 0.061), Bellone[12] (1 patient versus No patient) (p 0 = 0.5), Ferrari[13] (3 patients vs. 2 patients) (p = 0.662), Moritz[14] (8 patients versus 4 patients) (OR = 1.8) (95% CI: 0, 4 to 8.8), Gray[15] - (9.6% versus 9.4%) (p = 0.91) and (15.4% versus 15.1%) (p = 0.92) presented rates within 7 and 30 days respectively, Ferrari[16] (2 patients versus 7 patients) (p = 0.154), Nouira[17] (3 patients versus 5 patients) (p = 0.56) and Liesching[18] (14.28% versus 7.69%) (p = 0.084) presented the same without difference between the two groups.

The intubation rate for Mehta[7], Crane[10] (1 patient 1 vs. patient),[11] Park (2 patients vs. 2 patients), Bellone[12] (patient 1 vs. 2 patients) (p = 0.5), Ferrari[13] (p = 0.481), Moritz[14] (1 versus 2 patients) (OR = 0.4) (95% CI: 0.0 to 8.4), Ferrari[16] (3 patients versus no patient) (p = 0.241),[17] Nouira (4 patients versus 6 patients) (p = 0.46),[18] Liesching (1 patient versus no patient) and Cross[8] (4 patients versus 1 patient) showed no difference between the two groups, being greater in just CPAP Park[3] (3 patients versus no patient) (p <0.05).

Regarding the rate of AMI was considered similar between the CPAP and BIPAP groups for Crane[10] (3 patients versus 9 patients) (p = 0.117), Ferrari[13] (26.9% versus 16%) (p = 0.224), Moritz[14] (6% versus 3%) (R O = 0.5) (95% CI: 0.0 to 3.4),[5] Gray[1] (49.1% versus 54.7%) (P = 0.14), Nouira[17] (2 patients versus

4 patients), and Liesching[18] (no patient 1 versus patient) (p = 0.97), however, only to Mehta[7] (71% versus 31%) (p = 0.05) in myocardial infarction rate was considered to be higher in BiPAP group.

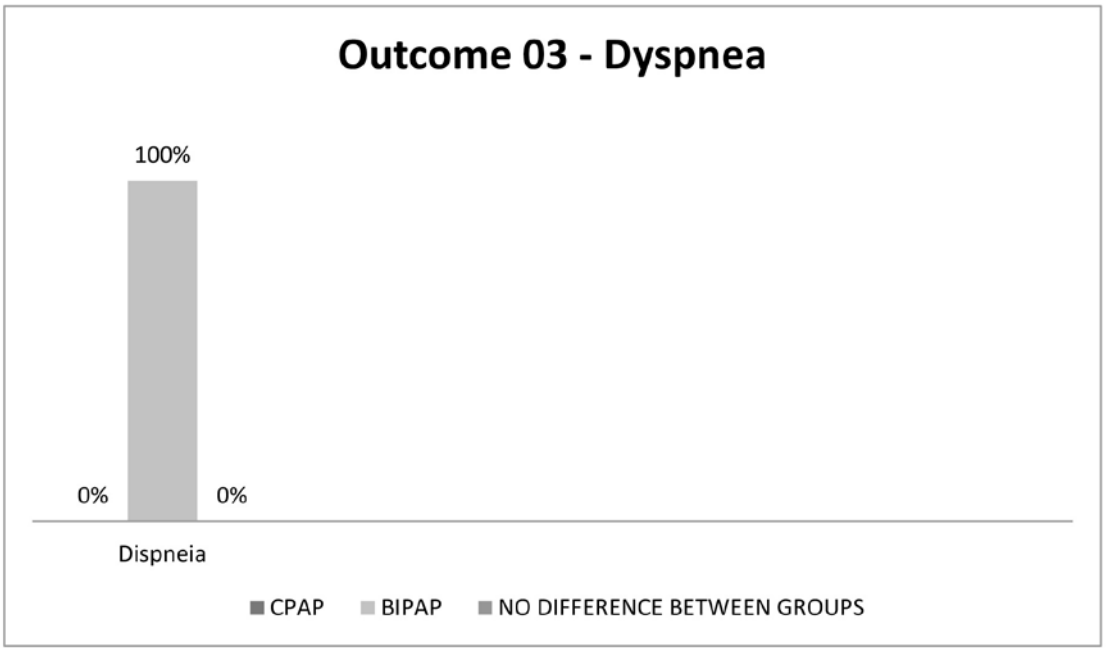
Figure 4. Percentage of studies regarding the outcome 02-hospitalization time and complications (hospital Stay, ICU stay, orotracheal intubation rate and AMI rate, of the studies included (1997 to 2017)



Dyspnea

With regard to dyspnea (Figure 4), only 4 studies were devoted to the analysis of the data, and all of them evidenced improvement of the symptom in the BIPAP group compared to the CPAP group: Mehta[7] presented improvement in the DYSPNEA scores (P < 0.05), PARK[11] reported Decrease in dyspnea at 60 ' of intervention (p < 0.01) and Liesching[18] reported a decrease in the dyspnea score at 30 ' of intervention (P = 0.05). GRAY[15] also evidenced a reduction in the visual analogue scale score for dyspnea, but this reduction was considered similar between the groups (4.5 vs 4.7 points) (P = 0.52).

Figure 5. Percentage of studies in relation to outcome 03-dyspnea, of the studies included (1997 to 2017)



Discussion

Over the last two decades, positive pressure NIV has emerged as an important tool in the treatment of acute respiratory failure, with strong evidence supporting the use of this technique to treat CPSC[17]. However, there is evidence in the literature about the advantages of the use of positive airway mask for the treatment of this patient profile, there are still doubts as to the best ventilatory modality[3]. This systematic review aimed to investigate the effects of CPAP and BIPAP on lung function, length of hospital stay and complications, and dyspnea. Overall, this study has identified that positive pressure NIV, whether applied by CPAP or BIPAP, is effective for the population with EAPC. This finding is in agreement with the literature[19,20] since NIV is a modality considered as the first option for this patient profile, and that there are no significant differences in clinical results when comparing CPAP and BIPAP.

The results on pulmonary function and dyspnea can be considered as strengths of this review because it is known that a long time, NIV may result in important physiological improvements, mainly characterized by the reduction of RF, improvements in PaO2 and PaCO2 , present similar benefits and equivalent efficacy between the two modalities , for analysis d these parameters. As for dyspnea, BIPAP is superior because it provides inspiratory assistance and allows the reduction of respiratory muscle work[21]. This additional benefit is also verified in this study, since most of the included trials that analyzed this data demonstrated the relevance of BIPAP for improvement of dyspnea.

Regarding hospitalization time, both in the hospital and in the ICU, no study of this review showed a difference between positive pressure NIV modalities. Up to the present moment, there is no evidence among the articles already published in the literature that proves the relation of the stay rates with the superiority of either technique.

Some studies affirm BIPAP's potential ability to decrease or delay EOT (intubation orotracheal), consequently impacting on mortality, and increasing the patient's chance of presenting AMI[1,7,21]. However, all studies in this review showed similarities between the CPAP and BIPAP groups for mortality, intubation and AMI. The results in this case are s were characterized as weak points of this review by presenting low impact reduction; however, they are supported by the Brazilian Recommendations of Mechanical Ventilation[22] that recommend the use of NIV both applied by CPAP and by BIPAP for EAPC, stating that both are equally effective and that aim to reduce the need or prevent intubation and reduce mortality. In the same way as either modality, it does not maintain correlation with the rates of AMI.

The limitations of this study were mainly regarding the presentation of measures of variability and estimation of the parameters of some variables, since some studies presented standard and median deviations, and others only interquartile range or confidence interval, resulting in incongruent data when compared. In addition, the sample size of the studies varied considerably, which also contributes as a limitation, since it is known that the more representative and significant the population sample, the greater the external validity.

Chart 2. Characterization of the sample, methodology, result and conclusion of the included studies (1997 to 2017) of the qualitative synthesis

AUTHOR	KIND OF STUDY	GOAL	SAMPLE	INTERVENTION	RESULTS	CONCLUSION
Mehta[7]	Randomized, prospective, randomized, controlled, double-blind study.	Evaluating whether BIPAP compared to CPAP improves ventilation,acidemia, and dyspnea more rapidly.	**GC:** 13 **GB:** 14	**GC:** 10 cmH_2O **GB:** IPAP: 15 cmH_2O/ PEEP: 5 cmH_2O **TI:** 5,8h GC/ 7,1h GB	Both groups had a significant improvement in RF. GB had a higher rate of AMI (71% and GC 31%) and a significant improvement in PaCO2 ($p = 0.057$) and dyspnea ($p < 0.05$). The ICU and hospital stay, the rate of intubation and mortality were similar between the two groups.	GB improves ventilation and vital signs faster than GC. Further studies to clarify the hemodynamic effects of BIPAP and the rate of AMI, in addition to determining optimal pressure configurations.
Park[3]	Prospective randomized clinical trial.	Compare oxygen therapy, CPAP and BIPAP in relation to intubation.	**GC:** 9 **GB:** 7	**GC:** 12 cmH_2O **GB:** IPAP: 8: cmH_2O/ PEEP: 3 cmH_2O **TI:** 60'	GB showed a significant improvement in RR and PaO2 ($p < 0.05$) at the 10' intervention. GC presented higher intubation rate (3 patients and none in GB).	GB was effective in the treatment of EAPC, as it accelerated the recovery of vital signs and gasometric data, and avoided EOT.
Cross[8]	Randomized prospective study.	To determine if there is a difference in the duration of treatment between CPAP and BIPAP in patients with acute pulmonary edema.	**GC:** 36 **GB:** 35	**GC:** 5 a 20 cmH_2O **GB:** IPAP: 10 a 25 cmH_2O/ PEEP: 5 cmH_2O **TI:** 123' GC/ 132' GB	GC presented higher rate of intubation (11%) and mortality (14%) and GB longer hospital stay.	There was no significant difference in duration of treatment between GC and GB, nor was there any difference in the other points analyzed.
Bellone[9]	Randomized, prospective and controlled study.	Investigate whether the use of BIPAP increases the rate of AMI compared to the use of CPAP.	**GC:** 22 **GB:** 24	**GC:** 10 cmH_2O **GB:** IPAP: 15 cmH2O PEEP: 5 cmH_2O **TI:** 103'±25' GC/ 98'±39' GB	GB had a higher rate of intubation (8.3%) and a decrease in RR after 1h (17.1ipm). GC had a higher mortality rate (9%). Rate of AMI with no significant difference, and similar PaCO2 decrease.	It demonstrated that GC was as effective as GB for EAPC and that there was no difference in the occurrence in the two treatment modalities.
Crane[10]	Prospective, randomized, controlled study.	Investigate whether CPAP or BIPAP promotes recovery faster than oxygen therapy.	**GC:** 20 **GB:** 20	**GC:** 10 cmH_2O **GB:** IPAP: 15 cmH_2O/ PEEP: 5 cmH_2O **TI:** 2h	GC had a higher survival rate at hospital discharge (100%). AMI and intubation without significant difference between the groups. There was no difference between the groups of any physiological or gasometric parameters.	GC patients more likely to survive hospital discharge. Survival rates were similar to other studies, despite the low rate of intubation (one occurrence in each group).
Park[11]	Randomized and controlled trial.	Compare oxygen therapy, CPAP and BIPAP in relation to intubation.	**GC:** 27 **GB:** 29 (27)	**GC:** 10 cmH_2O **GB:** IPAP: 15 cmH_2O/ PEEP: 10 cmH_2O **TI:** 102'±41'GC/ 124'±62'GB	The GC and GB groups showed similar improvement regarding RF and the same rate of intubation. GB presented higher mortality rate (7%), lower dyspnea score at 60 ', lower average PaCO2, and shorter hospital stay.	NIV applied by GC or GB had similar effects and was effective in endotracheal intubation in patients with respiratory difficulty of cardiac origin. This positive intrathoracic pressure is seen as a non-pharmacological form of treatment for EAPC and not as a supportive measure.

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Chart 2. Characterization of the sample, methodology, result and conclusion of the included studies (1997 to 2017) of the qualitative synthesis

AUTHOR	KIND OF STUDY	GOAL	SAMPLE	INTERVENTION	RESULTS	CONCLUSION
Bellone[12]	Prospective, randomized study.	Compare BIPAP and CPAP in relation to resolution time.	**GC:** 18 **GB:** 18	**GC:** 10 cmH_2O **GB:** IPAP: 15 cmH_2O/ PEEP: 5 cmH_2O **TI:**220'±82' GC/ 205'±68'GB	There was no statistical difference between the groups for the rates of intubation, mortality, PaO2 and RF and time of resolution of the clinical picture.	It has been shown that GB is as effective as GC in the treatment of EAPC and that the two modalities of NIV lead to similar benefits.
Ferrari[13]	Randomized clinical trial.	Evaluate whether BIPAP compared to CPAP increases the rate of AMI; in addition to comparing them in relation to intubation, death, duration of ventilation, and duration of hospitalization.	**GC:** 27 **GB:** 25	**GC:** 12 cmH_2O **GB:** IPAP: 15 ± 3,1 cmH_2O/ PEEP: 7 ± 1,2 cmH_2O **TI:** 8,1±8,3h GC/ 6,0±4,7h GB	There was no significant difference in relation to hospital and ICU stay, the rate of intubation, AMI, mortality and PaCO2 between the 2 groups.	The study indicates that GC and GB are equally effective for the treatment of patients with severe acute respiratory failure secondary to EAPC, and that the AMI rate did not differ between the two techniques. However, because of the ease and the lower cost of use, it is suggested that CPAP be used as a first-line ventilatory treatment.
Moritz[14]	Randomized, prospective, multicenter study.	To compare the efficacy of CPAP and BIPAP in relation to intubation, AMI and death within 24 hours of initiation of ventilation.	**GC:** 60 (59) **GB:** 60 (50)	**GC:** 10 cmH_2O **GB:** PEEP 5 cmH_2O para obter volume corrente 8-10ml/kg **TI:** 2,3h GC/ 2,8h GB	There was no statistical difference between the two groups for RF, hospital stay, and mortality rates, AMI and intubation.	Both GC and GB were effective in rapidly improving respiratory distress.
Gray[15]	Randomized, controlled clinical trial, prospective and multicenter study.	To determine if NIV reduces mortality and if there are important differences in the outcome associated with the treatment method.	**GC:** 346 **GB:** 356	**GC:** 5 a 15 cmH_2O **GB:** IPAP: 8 a 20 cmH_2O/ PEEP: 4 a 10 cmH_2O **TI:** 2,2±1,5h GC/ 2,0±1,5h GB	GB presented lower rates in absolute values for dyspnea, RR, PaO2 and PaCO2 and higher rates in absolute value for mortality within 30 days, AMI and hospital stay. However, compared to CG the results for these variables are similar and without significant difference.	The NIV delivered to the CG or GB presents improvement and earlier resolution of dyspnoea and respiratory distress compared to standard therapy. However, these effects do not result in improved survival rates.
Ferrari[16]	Randomized, prospective, multicenter clinical trial.	To compare the rate of intubation using CPAP and BIPAP, and to evaluate mortality, improvement in gas exchange, duration of ventilation and length of hospital stay.	**GC:** 40 **GB:** 40	GC: 12 cmH2O GB: Initial pressure support 10 cmH2O increased by 2 cmH2O to obtain 6-8 ml / kg; Initial PEEP 5 cmH2O TI: 8.46 ± 7.14h GC / 5.91 ± 4.01h GB	GB presented higher absolute number mortality, however, both groups were similar, as they resulted in a rapid improvement in vital signs and gasometric data. There was no significant difference between GC and GB regarding the rates of intubation, mortality, hospital stay, PaO2, PaCO2 and FR.	Both CG and GB were effective for the treatment of patients with PADS, improving gas exchange with no significant difference in the rates of intubation, mortality or length of hospital stay. Because of the lower cost and ease of use, CPAP should be considered as first-line intervention for these patients.

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Chart 2. Characterization of the sample, methodology, result and conclusion of the included studies (1997 to 2017) of the qualitative synthesis

AUTHOR	KIND OF STUDY	GOAL	SAMPLE	INTERVENTION	RESULTS	CONCLUSION
Nouira[17]	Randomized, prospective clinical trial.	To evaluate the benefit and adverse effects of BIPAP and CPAP.	**GC:** 101 (95) **GB:** 99 (97)	**GC:** 10 cmH_2O **GB:** IPAP: 13,5 ± 3,6 cmH_2O/ PEEP: 5,1 ± 1,2 cmH_2O **TI:** 210'±73' GC/ 159'±54' GB	There was no significant difference between the two groups for mortality, intubation and AMI, although GB presented higher rates in absolute value. GB also showed significantly shorter resolution time compared to GC.	Further evidence that GC and GB have the same effect on mortality and intubation rates in patients with PADS, in addition to the fact that GB is associated with a rapid improvement in respiratory failure.
Liesching[18]	Randomized clinical trial.	Evaluating whether BIPAP compared to CPAP improves dyspnea and ventilation faster, without increasing the rate of AMI.	**GC:** 17 (14) **GB:** 19 (13)	**GC:** 10 cmH_2O **GB:** IPAP: 12 cmH_2O e PEEP: 4 cmH_2O **TI:** 2,13h GC/ 2,65h GB	No significant difference was found between the groups for the rates of AMI, intubation, hospital stay, mortality, PaCO2 and RF. GB presented a shorter stay in the ICU compared to CG and rapidly improved the dyspnea score (p = 0.05) and oxygenation, which may be associated with a smaller number of patients needing to be admitted to the ICU (38% vs. 92 % GC).	GB compared to GC improves oxygenation more rapidly, dyspnea scores and reduce the need for ICU admission. In addition, GB did not increase the rate of AMI compared to GC.

CPAP - Positive Continuous Pressure; BIPAP - Two Level Positive Pressure; EOT – Intubation Orotraqueal; GC - Group that used CPAP as therapy; GB - Group that used BIPAP as therapy; IPAP – Positive pressure Inspiratory; PEEP – Final Positive Expiratory Pressure; TI - Intervention time in hours or minutes; AMI - Acute Myocardial Infarction; EAPC – Acute Cardiogenic Lung Edema; NIV - Non-Invasive Mechanical Ventilation; ICU - Intensive Care Unit; FR - Respiratory frequency; $PaCO_2$ - Partial Carbon Gas Pressure; PaO_2 - Partial Oxygen Pressure.

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Conclusion

According to all available data from this review, there is no evidence to support the superiority of CPAP or BIPAP for patients with EAPC. It can be concluded that both modalities guarantee the same effects promoting improvement of lung function and dyspnea, without significantly changing the permanence of hospitalization and complications such as mortality, intubation and AMI.

Contributions author

Brito FCS c ontribuiu in search of items for systematic review en the data collection of these items . Martinez BP has contributed in the design and writing of the article and in the search for articles . Gomes Neto M contributed in the analysis of the data of the articles for the preparation of the results . Saquetto MB c ontribuiu the final draft of the article. Conception CS c ontribuiu n to search for articles , in the qualifying examination of the articles and the r end edação . Silva CMS c contributed to the design and writing of the article .

Conflicts of interest

No financial, legal, or political conflict involving third parties (government, business and private foundations, etc.) was declared for any aspect of the work submitted (including but not limited to grants and funding, participation in advisory council, study design, preparation manuscript, statistical analysis, etc.).

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