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Non-invasive ventilation in acute respiratory failure after esophagectomy in patients with esophageal cancer: an integrative review

Ventilação não invasiva na insuficiência respiratória aguda no pós-operatório de esofagectomia em pacientes com câncer de esôfago: uma revisão integrativa

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Abstract

Introduction: Respiratory complications may occur after esophagectomy despite advances in postoperative management. One of the strategies used to minimize these complications is non-invasive ventilation (NIV). **Objective:** To review evidence on the use of NIV in acute respiratory failure/acute respiratory distress syndrome (ARF/ARDS) in the postoperative period of esophagectomy in patients with esophageal cancer. **Materials and Methods:** This study was conducted using the PUBMED, Virtual Health Library (BVS), LILACS, and SCIELO databases from August 2021 to October 2021. **Results:** Two of the 20 selected studies were included in this review. One study showed that the application of non-invasive ventilation in ARF in the postoperative period of esophagectomy was associated with a lower rate of reintubation, lower frequency of ARDS, reduced ICU stay, and improved gas exchange. The other study looked at non-invasive ventilation applied as a first-line intervention for ARDS after esophagectomy for esophageal cancer and showed that it avoided intubation in 48.4% of patients. The differences in PaO_2/FiO_2 after 24 h of NIV and the presence of surgery-related complications were highly significant. **Conclusion:** NIV is a potential treatment for ARF/ARDS during the postoperative period of upper abdominal surgery. However, for the postoperative period of esophagectomy, it is necessary to expand the studies in this area so that NIV is used more safely and effectively, benefitting the early recovery of patients, and minimizing postoperative pulmonary complications.

Keywords: non-invasive ventilation, postoperative care, esophagectomy, acute respiratory failure; acute respiratory distress syndrome

Resumo

Introdução: Apesar dos avanços no manejo pós-operatório, complicações respiratórias podem ocorrer após a esofagectomia. Uma das estratégias utilizadas para minimizar essas complicações é a Ventilação Não Invasiva (VNI). **Objetivo:** reunir as evidências sobre o uso da VNI na insuficiência respiratória aguda/ síndrome do desconforto respiratório agudo no pós-operatório de esofagectomia em pacientes com câncer de esôfago. **Materiais e Métodos:** pesquisa realizada nas bases eletrônicas PUBMED, Biblioteca Virtual em Saúde (BVS), LILACS, SCIELO no período de agosto a outubro de 2021. **Resultados:** Dos 20 estudos selecionados, dois foram incluídos na revisão. Um estudo mostrou que a aplicação da ventilação não invasiva na Insuficiência Respiratória Aguda (IRA) no pós-operatório de

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esofagectomia foi associada a uma menor taxa de reintubação, menor frequência de síndrome do desconforto respiratório agudo e uma redução na permanência na UTI. Também houve melhora nas trocas gasosas. O outro estudo analisou a ventilação não invasiva aplicada como intervenção de primeira linha para Síndrome do Desconforto Respiratório Agudo (SDRA) após esofagectomia para câncer de esôfago e mostrou que evitou intubação em 48,4% dos pacientes. As diferenças na PaO2 / FiO2 após 24h de VNI e a presença de complicações relacionadas à cirurgia foram altamente significativas. **Conclusão:** A VNI parece ser benéfica no tratamento da IRA/SDRA em pós-operatórios de cirurgias abdominais altas. No entanto, para pós-operatórios de esofagectomia, se faz necessário ampliar os estudos nessa área, para que a VNI seja utilizada com mais segurança e eficácia, trazendo benefícios para a recuperação precoce dos pacientes, minimizando as complicações pulmonares pós-operatórias.
Palavras-chave: ventilação não invasiva; cuidados pós-operatório; esofagectomia; insuficiência respiratória aguda; síndrome do desconforto respiratório agudo.

Introduction

Esophageal cancer is the eighth most frequent type of cancer and the sixth leading cause of cancer-related deaths worldwide, occurring twice as often in men than in women[1]. The number of cases of esophageal cancer estimated for Brazil, for each year of the triennium 2020–2022, is 8,690 cases in men and 2,700 in women. These values correspond to an estimated risk of 8.32 new cases per 100,000 men and 2.49 per 100,000 women[2]. The incidence also increases with age, and the most common factors are gastroesophageal reflux disease, smoking, alcohol consumption, and risk of obesity[3].

Esophagectomy is a surgery that removes and treats esophageal cancer, and it can be performed through an open or minimally invasive incision. When performed through an open incision, it is considered a complex and major surgery and is associated with a significant risk of perioperative morbidities[4]. The most common postoperative complications are pulmonary, which could progress to acute respiratory failure (ARF)[5]. Its occurrence can increase the length of hospital stay, morbidity and mortality rates, and healthcare costs[6].

In addition to ARF, anastomotic leakage is one of the most common postoperative complications of this type of surgery[7], and gastric conduit ischemia and impaired oxygen supply are predisposing factors for this negative outcome[8].

Thoracic surgery is also associated with acute respiratory distress syndrome (ARDS), a clinical complex characterized mainly by alveolar capillary injury and several extra- and intrapulmonary contributing factors. It is a type of severe acute lung injury that is clinically characterized by increased respiratory rate, respiratory distress, progressive hypoxemia, and diffuse pulmonary infiltrate[9].

The treatment of ARDS is challenging, and intubation and invasive mechanical ventilation are often required. However, non-invasive ventilation (NIV) can be an effective technique for improving gas exchange and avoiding endotracheal intubation in selected patients with ARF due to ARDS[10].

The maintenance of adequate oxygenation in the postoperative period of these patients is of great clinical relevance, especially when pulmonary complications such as ARF occur[11]. The most commonly applied strategies to prevent postoperative complications include adequate analgesia, supplemental oxygen, early mobilization, bronchial hygiene, and use of NIV[12,13].

NIV is a mode of mechanical ventilation that does not require an artificial airway (orotracheal tube or tracheostomy). Compared to invasive ventilation, NIV does not require sedation, promotes greater patient comfort, and reduces the incidence

of ventilator-associated pneumonia[14]. In addition, NIV is as safe and efficient as invasive mechanical ventilation in patients with various ARF patterns[14,15]. Recent results support the safe use of NIV in patients with ARF after upper abdominal surgery[16,17].

In the esophagectomy scenario, the balance between the potential benefits of NIV and its disadvantages remains unclear, and studies on this population are scarce. Therefore, this study aimed to review the evidence on the use of NIV for pulmonary complications in the postoperative period of esophagectomy in patients with esophageal cancer.

Materials and methods

Type of study and research design

This study consists of an integrative review, with a synthesis of scientific articles identified through research carried out in the PUBMED, Virtual Health Library (BVS), LILACS, and SCIELO databases from August 2021 to October 2021. The study was structured and organized according to Population, Intervention, Comparison, Outcomes, and Study (PICOS). Population of interest (P) corresponds to patients in the postoperative period of esophagectomy for esophageal cancer; intervention (I) refers to the use of NIV; comparison (C) corresponds to patients who did not use NIV; outcomes (O) refer to the effect of NIV on ARF/ARDS; and study (S) corresponds to the controlled clinical trials, cross-sectional study, observational study, case-control studies, and case reports.

The following descriptors were used to search the databases: “non-invasive ventilation”, “postoperative period”, “esophagectomy”, “acute respiratory failure”, “acute respiratory distress syndrome”, and their respective Portuguese counterparts, associated with the Boolean operators AND and OR. No publication year or language restrictions were applied.

Inclusion and Exclusion Criteria

The selected studies met the following inclusion criteria: 1) studies with adult patients (age > 18 years) diagnosed with esophageal cancer who underwent esophagectomy; 2) studies that reported the use of NIV in ARF/ARDS in the postoperative period of esophagectomy; and 3) articles available in full. Abstracts and articles from event proceedings, theses, dissertations, monographs, or protocols were excluded.

Procedures

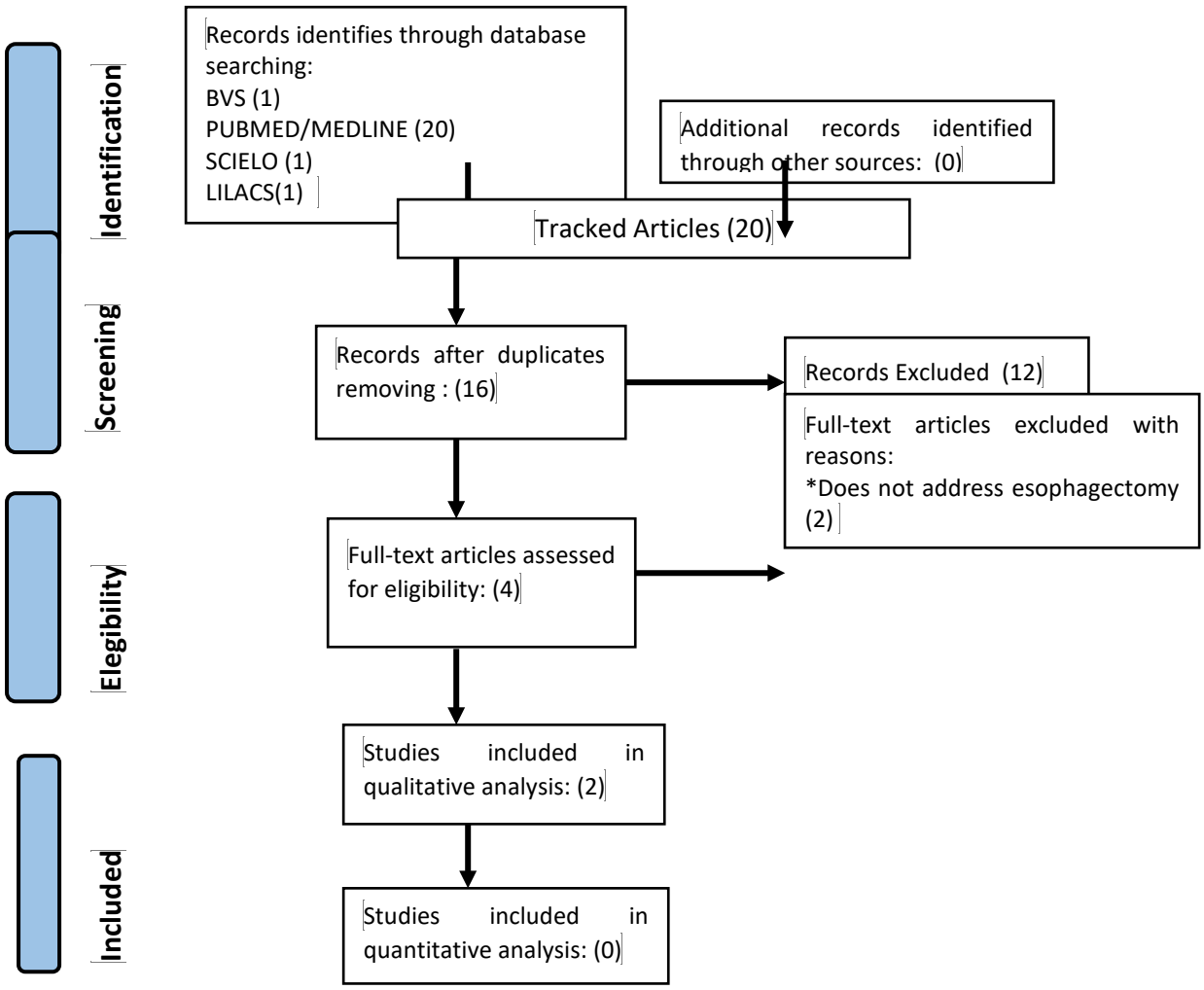
Initially, geographically separated researchers screened the articles by reading the titles and abstracts. Studies that met the eligibility criteria or were relevant were included in the full-text reading stage. In case of doubts regarding the inclusion of any article, a third reviewer was consulted.

Complete articles were independently reviewed, and data were extracted regarding publication year, author, country, sample, age, sex, study objective, study design, intervention protocol (NIV parameters used), main outcomes, and the results obtained. The data are summarized in tables and are described qualitatively.

Results

From the reference search, 23 scientific articles were identified in the selected databases, of which seven articles were excluded due to duplicity, resulting in 16 references. After analyzing the titles and abstracts, 12 references were excluded, and four studies were selected for full reading. After reading the full articles, two studies were excluded and two references were included in our review (Figure 1).

Figure 1: Flowchart of selection and inclusion of studies.



After selecting the studies, two articles focused on the researched topic were included[8,18], a case-control study and a retrospective cohort referring to the years 2009 and 2013, respectively. The samples from these studies included 136 patients, with 68 patients undergoing NIV in the postoperative period of esophagectomy. Table 1 presents the characteristics of these studies.

Table 1. Characteristics of the studies included in the review

Author, year	Country	Type of study	Sample(n), Sex	Middle Age (SD)	Study Purpose
Michelet, P et al, 2009[8]	France	Case control	36 (30 women,6 men)	62 (8)	To compare the effectiveness of NIV with conventional treatment in patients who developed acute respiratory failure after esophagectomy.
Yu, K. et al, 2013[18]	China	Retrospective cohort	32 (31 men e 1 women)	61,1(7,2)	To evaluate the effectiveness of NIV in the treatment of ARDS in the

					postoperative period of esophagectomy for esophageal cancer.

n: number of patients; SD: standard deviation; NIV: non-invasive ventilation ARDS: acute respiratory distress syndrome.

The results found in the selected articles are described in Table 2.

Table 2. Results of studies that evaluated NIV as a post-esophagectomy intervention in patients with esophageal cancer

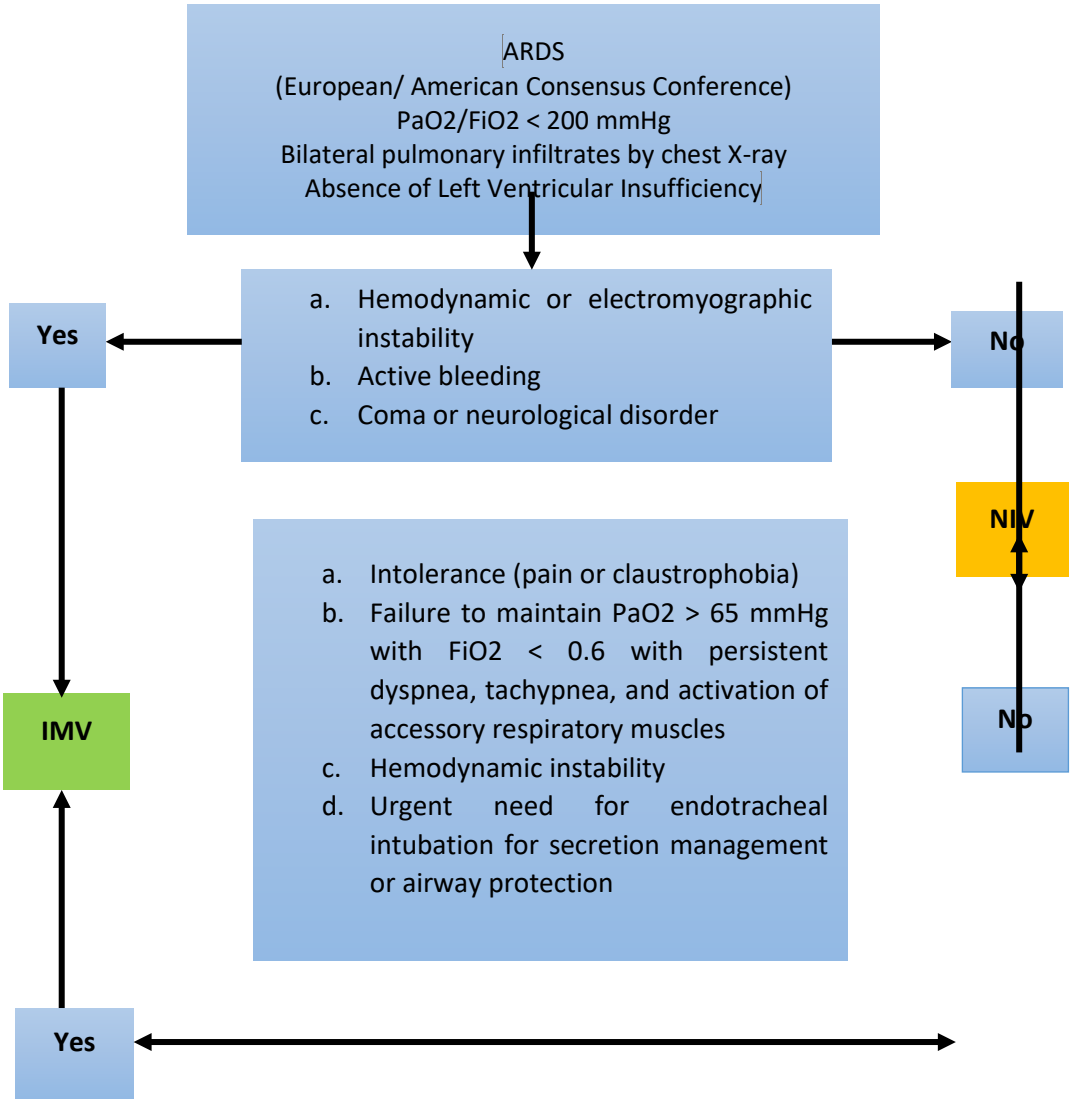
Author, year	**Intervention**		**Protocol**	**Results**			
	VNIG	**GC**		**Outcomes**	**VNIG**	**GC**	**p**
Michelet, P et al, 2009[8]	PSi: 8cmH2O VCexp: 6-8ml/Kg) PEEPi:4cm H2O PEEPf: 8cmH2O (p/ SpO2> 90%) Max pins: < 25 cm H2O	Res. Physio. (30 min, 2X/day), Inc. Spiro., Deamb. Early and O2 per mask for SpO2>90%.	**First 24h:** NIV: 45 to 60 min Using O2 by mask. **After 24 hours:** Weaning from NIV with longer periods of oxygen therapy, if clinical improvement. **NIV suspension:** PaO2/FiO2 > 200 mmHg and period longer than 24 hours without NIV.	Pneumonia infectious aspiration SAPS II* post-op. reintubation ARDS Septic shock Leak. Anastomosis ICU Intern (days) Inter.Hosp.(days) Post-op death.	 13 23 27(5) 9 8 7 2 14(13) 34 (19) 4	 12 24 28(7) 23 19 16 10 22(18) 40(21) 7	1.000ŧ 0.517ŧ 0.008ŧ 0.015ŧ 0.043ŧ 0.027§ 0.034ŧ 0.208ŧ 0.512§
	VNIG	**IMVG**		**Outcomes**	**VNIG**	**IMVG**	
Yu, K. et al, 2013[18]	Patients selected by the clinical flowchart shown in **figure 2.**		The PaO2/FiO2 ratio was evaluated at the beginning of the application of NIV and IMV, 2h and 24h later. SOFA and APACHE II were evaluated at the beginning and 24 hours after the interventions	PaO_2/FiO_2 (h_0)mmHg PaO_2/FiO_2 (h_2)mmHg PaO_2/FiO_2 (h_{24})mmHg SOFA(h_0) SOFA(h_{24}) APACHE-II(h_0) APACHE-II(h_{24}) Post-op complications	126(+31.9) 182(+29.8) 207(+35.5) 4.3(+0.63) 4.2(+0.61) 21.3(+3.58) 22.1(+3.66) 1.25(+0.58)	121(+23.4) 165(+25.5)** 174(+28.5)* 4.4(+0.71) 4.5(+0.82) 20.9(+4.21) 23.6(+3.2) 2.13(+0.81)**	

NIVG: non-invasive ventilation group; IMVG: invasive mechanical ventilation group; CG: control group; PSi: initial support pressure; PEEP: end-expiratory pressure; PEEPi: end-expiratory pressure at initial expiration; PEEPf: end-expiratory pressure at end-expiratory; VCexp: expiratory tidal volume; Max pins: maximum inspiratory pressure; Resp Physio: respiratory physiotherapy; min: minute; Inc. spiro: incentive spirometry; Deamb: ambulation; O2: oxygen; PaO2: arterial oxygen pressure; FiO2: fraction of inspired oxygen; SAPS II*: Simplified Acute Physiology Score II; ARDS: Acute Respiratory Distress Syndrome; intern ICU: admission to the Intensive Care Unit; Inter Hospital: Hospitalization; post-op: postoperative; IMV: invasive mechanical ventilation; NIV: non-invasive ventilation; *p<0.05; **p<0.01; SOFA: assessment of sequential organ failure; APACHE-II: Classification II system of acute physiology and chronic diseases; h0: ι: Pearson's chi-square test; ŧ: Student's t test; §: Fisher's exact test.

In one of the selected studies[8], of the 84 patients with postoperative ARF who met the inclusion criteria, 36 were treated with NIV and were correctly matched with 36 control patients. Infectious pneumonia was confirmed in 13 patients in the NIV group and 12 patients in the control group, with no difference in microbiological isolates. The likelihood of avoiding reintubation was significantly higher in patients treated with NIV than in those treated with conventional care (p=0.003). No complications of NIV such as significant gastric distention or skin necrosis were observed. The use of NIV was associated with a lower rate of septic shock and anastomotic leakage, as well as a shorter length of stay in the ICU. There was no difference between the groups in terms of the overall hospital stay or hospital mortality.

The other study included 64 patients (59 men and 5 women; age range, 49–83 years; mean age, 61.1±7.2 years) with ARDS after esophagectomy for esophageal cancer[18]. The patients were classified into two groups according to the modality of mechanical ventilation: those treated with NIV (NIVG) and those who required invasive mechanical ventilation (IMVG). The treatment of all the patients followed the clinical flowchart shown in Figure 2.

Figure 2: Flow for patient selection in the implementation of Non-Invasive Ventilation or fraction of inspired oxygen (oxygenation index); NIV: non-invasive ventilation; IMV: invasive mechanical ventilation



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Thirty patients avoided intubation after the application of NIV, and the mean length of stay in the ICU in patients with NIV was 11.5 days. Sixteen patients failed NIV and were converted to IMV. Predetermined criteria for endotracheal intubation after starting NIV included the following: failure to maintain PaO_2 > 65 mmHg with $FiO_2 \leq 0.6$ and persistent dyspnea, tachypnea, and accessory respiratory muscle activation; need for urgent endotracheal intubation to control tracheal secretions or protect the airway in case of coma or neurological disorders; NIV intolerance due to pain, discomfort or claustrophobia; and hemodynamic instability. The mean time of conversion to IMV was 3.82±7.23 days.

There were no significant differences in PaO_2/FiO_2 (NIV, 126±31.9 vs. IMV, 121±23.4), sequential assessment of organ failure (SOFA) (NIV, 4.3±0.63 vs. IMV, 4.4 ±0.71), or acute and chronic physiology health assessment, APACHE-II (NIV, 21.3±3.58 vs. IMV, 20.9±4.21), at baseline between the two groups ($p>0.05$), nor were there significant differences in SOFA (NIV, 4.2±0.61 vs. IMV, 4.5±0.82) or APACHE-II scores (NIV, 22.1±3.66 vs. IMV, 23.6 ±3.21) between the two groups at 24 h after treatment ($p>0.05$). However, there were significant differences in PaO_2/FiO_2 at 2 h (NIV, 182±29.8 vs. IMV, 165±25.5, $p<0.01$) and 24 h (NIV, 207±35.5 vs. IMV, 174±28.5, $p<0.05$) after treatment between the two groups. There were no significant differences in the 28-day fatality or PaO_2/FiO_2 at baseline, and no significant differences in SOFA or APACHE II scores at 2 h and 24 h after treatment ($p>0.05$).

Discussion

This study aimed to review the evidence on the use of NIV in ARF and ARDS during the postoperative period of esophagectomy for esophageal cancer. After applying the eligibility criteria, only two studies were included in this review, demonstrating that this topic has been explored less in scientific publications, as it is a specific and controversial topic from a surgical perspective. Among the studies included, it was observed that NIV in this context was associated with a reduction in the rate of reintubation, a decrease in ARDS cases and days of hospital stay in the ICU, and a reduction in cases of anastomotic leakage and septic shock.

In the esophagectomy setting, the balance between the benefits of NIV and its disadvantages, especially in relation to the construction of the gastric tube, remains unclear[17], possibly causing the limited studies related to the use of NIV in the treatment of ARF/ARDS in the postoperative period of esophagectomy.

For several years, NIV has been used in the postoperative period[19]. When applied in the early postoperative period, it seems to prevent atelectasis and postoperative complications after major abdominal surgery[20]. While most studies used continuous positive airway pressure (CPAP)[21], another mode, bilevel positive airway pressure (BIPAP), is increasingly being used[20]. There is little evidence of superiority of one mode over the other, although it is debated that BIPAP may be more appropriate given the risk of diaphragmatic dysfunction and respiratory pump failure after upper abdominal surgery[22].

In this scenario, some authors suggest two potential goals for the use of NIV in the postoperative period: to prevent and treat ARF and to avoid reintubation[21,23]. Tracheal reintubation for ARF is associated with higher mortality and greater use of health services, with longer lengths of stay in the ICU and hospital unit[24]. The reasons for increased mortality include complications during the reintubation period and healthcare-associated infections such as pneumonia[25,26]. This suggests that

postoperative outcomes can be improved by strategies aimed at avoiding reintubation and invasive mechanical ventilation[12]. A multicenter randomized clinical trial showed that NIV reduced the need for reintubation compared to standard oxygen therapy in patients with hypoxemic ARF after abdominal surgery[17].

One of the studies selected for this review was a case-control study[8]. Patients in the NIV group showed an improvement in oxygenation and a reduction in ICU length of stay, in addition to the safety and efficacy of NIV in avoiding endotracheal intubation in patients who developed post-esophagectomy ARF. A decrease in the incidence of endotracheal intubation and other serious complications has also been reported in patients with hypoxemia after esophagectomy using CPAP[27].

It was also shown in a selected study that the use of NIV was not associated with an increase in anastomotic leakage[8]. Another study used NIV during the postoperative period of bariatric surgery in morbidly obese patients[28]. In this study, NIV was performed with two pressure levels: positive inspiratory pressure (IPAP) set at 12 cm H_2O and positive expiratory pressure (EPAP) set at 8 cm H_2O, with improved oxygenation and no increase in the incidence of fistulas or anastomotic dehiscence. These results are consistent with those of previous clinical studies that have demonstrated the safety of CPAP after major abdominal surgery[27,29]. Nasogastric drainage was performed postoperatively. This suggests that CPAP or NIV in patients with postoperative hypoxemia favors the protective effect of improved oxygenation over the hypothetical risk of anastomotic leakage[29].

In this review, a study[18] retrospectively analyzed the effectiveness of NIV in the treatment of ARDS in post-esophagectomy patients[18]. ARDS is a clinical complex characterized mainly by alveolar capillary injury and several extra- and intrapulmonary contributing factors[10]. The treatment of ARDS is a clinical challenge in thoracic surgery, but NIV can be an effective technique for improving gas exchange and avoiding endotracheal intubation in patients with ARF due to ARDS[11].

Another study included in this review[8] refers to a case-control design that evaluated the effects of NIV in the treatment of ARDS in a post-esophagectomy patient, as well as the factors related to NIV failure, to better define its indications in the treatment of NIV. According to this study, NIV is not suitable for patients with increased secretion, decreased ability to self-clean the airways, or a recent history of esophageal surgery[8].

However, a retrospective meta-analysis of NIV trials for the treatment of ARDS between 1995 and 2009 showed that the success rate was approximately 50%, suggesting that NIV could be safely applied in appropriate cases under close supervision[30], corroborating our results. NIV is not an absolute contraindication in the postoperative period of esophagectomy, and it is a good treatment option in appropriate cases[18].

Studies have shown that there was no significant difference in PaO_2/FiO_2 between the NIV success groups and early-stage NIV failure groups[31,32]. However, as PaO_2/FiO_2 improved continuously after treatment in the NIV success group, it was considered an independent factor for predicting NIV failure in the treatment of acute lung injury [32]. Other authors have also proposed that $PaO_2/FiO_2 \leq 175$ at 1 h after NIV was an independent factor for predicting NIV failure in the treatment of APL[31]. Similarly, the study included in this review found no significant difference in PaO_2/FiO_2 between the IMV and NIV groups at baseline, but found significant differences at 2 h ($p<0.01$) and 24 h ($p<0.05$) between the two groups, indicating that PaO_2/FiO_2 can be a predictor of success or failure of NIV treatment[18].

In that same study, in the group that underwent NIV, 24 h PaO_2/FiO_2 improved significantly compared to the group that underwent IMV, and the mean number of surgery-related complications was significantly lower. After excluding patients with two or more complications, there were no significant differences in the actual deaths between the two groups. Thus, IMV may be the first choice for patients with ARDS with two or more complications, including acute renal failure and cardiac arrest related to postoperative esophageal surgery, hemodynamic instability, active bleeding, persistent dyspnea, tachypnea, or respiratory muscle activation. accessory. In such cases, early oral intubation or tracheostomy is necessary.

A limitation of the present review is the inadequate methodological design of the included studies, as well as the low number of publications included, which reinforces the need for new studies to better establish the effects and contraindications of NIV in patients with gastroesophageal cancer. Although the conclusions of the studies are encouraging, for better quality of evidence, it is recommended to conduct pragmatic randomized clinical trials following the international methodological and prescribing guidelines for NIV. In addition to the inadequate type of study, the lack of power calculation and sample size, retrospective design, and inclusion of participants with different stages of the disease also stand out as limitations of the studies.

Conclusion

NIV appears to be beneficial for the treatment of ARF/ARDS in the postoperative period of upper abdominal surgery as long as patients are well selected and ventilation is applied by experienced professionals using safe parameters. For a good selection of patients, it is necessary to observe the following parameters: absence of neurological disorders, coma, or convulsion; absence of cardiogenic or septic shock; leakage or anastomotic dehiscence, and tolerance to the use of NIV. However, the use of NIV in the postoperative period of esophagectomy for esophageal cancer remains controversial. Few existing studies have an inadequate methodological design, limiting the generalization of evidence and the applicability of the resource in clinical practice. It is necessary to expand studies in this area so that NIV is used more safely in clinical practice. This can be done by producing better evidence on efficacy and clinical benefits in reducing the rate of reintubation, reduction of ARDS cases and days of hospital admission in the ICU, and reduction in cases of anastomotic leakage and septic shock.

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