Elevated Extravascular Lung Water Index (ELWI) as a Predictor of Failure of Continuous Positive Airway Pressure Via Helmet (Helmet-CPAP) in Patients With Acute Respiratory Failure After Major Surgery

Francisco Javier Redondo Calvo, Natalia Bejarano Ramirez, Rafael Uña Orejon, Ruben Villazala Garcia, Ana Sofia Yuste Peña, Francisco Javier Belda

Aim: The objective of this study was to ascertain if EVLW index and PVPl index may predict failure (intubation) or success (non-intubation) in patients developing acute respiratory failure (ARF) in the postoperative period following major abdominal surgery, where the first line of treatment was non-invasive continuous positive airway pressure via a helmet.

Methods: Hemodynamic variables, EVLWI and PVPl, were monitored with a transpulmonary thermodilution hemodynamic monitor device (PICCO™) before and after the application of CPAP.

Results: Avoidance of intubation was observed in 66% of patients with Helmet-CPAP. In these patients after the first hour of application of CPAP and PaO2/FiO2 ratio significantly increased (303.33±65.2 vs 141.6±14.6, P<.01). Before starting, Helmet-CPAP values of EVLWI and PVPl were significantly lower in non-intubated patients (EVLWI 8.6±1.08 vs 11.8±0.99 ml/kg IBW, P<.01 and PVPl 1.7±0.56 vs 3.0±0.88, P<.01). An optimal cut-off value for EVLWI was established at 9.5, and at 2.45 for PVPl (sensitivity of 0.7; specificity of 0.9, P<.01).

Conclusion: In this type of patient the physiological parameters that predict the failure of Helmet-CPAP with the greatest accuracy were the value of the EVLWI and PVPl before Helmet-CPAP institution and the PaO2/FiO2 ratio and the respiratory rate after 1 h of CPAP.

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La elevación del índice de agua pulmonar extravascular como factor predictivo del fracaso de la presión continua en la vía aérea con casco (CPAP-Helmet) en pacientes con insuficiencia respiratoria aguda tras intervención quirúrgica mayor

RESUMEN

Introducción: La ventilación no invasiva (VNI) se utiliza cada vez más para la prevención y el tratamiento de las complicaciones y la insuficiencia respiratorias. Algunos pacientes ingresan en las unidades de reanimación postanestésica portando monitores hemodinámicos avanzados que permiten cuantificar el agua pulmonar extravascular (EVWL) mediante la técnica de termodilución transpulmonar y la permeabilidad vascular pulmonar (PVP), parámetros que permiten obtener información sobre el edema pulmonar.

Objetivo: El objetivo de este estudio fue determinar si el índice de EVWL y el índice de la PVP pueden pronosticar el fracaso (intubación) o el éxito (no intubación) en pacientes que desarrollan insuficiencia respiratoria aguda (IRA) durante el período postoperatorio de una intervención quirúrgica mayor abdominal y cuyo tratamiento de primera línea es la presión positiva continua en la vía aérea (CPAP) administrada mediante casco (CPAP-Helmet).

Métodos: Se monitorizaron las variables hemodinámicas, el índice de agua pulmonar extravascular (EVWL) y el índice de permeabilidad vascular pulmonar (PVP) mediante un dispositivo de monitoreo hemodinámico de termodilución transpulmonar (PiCCO®), antes y después de la aplicación de la CPAP.

Resultados: En un 66% de los pacientes con CPAP-Helmet se evitó la intubación. En dichos pacientes, el cociente PaO₂/FIO₂ aumentó de forma significativa (303,33 ± 65,2 vs. 141,6 ± 14,6, p < 0,01) tras la primera hora de aplicación de la CPAP. Antes de iniciar la CPAP-Helmet los valores de EVWL y PVP eran significativamente inferiores en los pacientes no intubados (EVWL 8,6 ± 11,8 vs. 11,8 ± 0,99 ml/kG de peso corporal ideal (PCi), p < 0,01 y PVP 1,7 ± 0,56 vs. 3,0 ± 0,88, p < 0,01). Se establecieron unos valores de corte óptimos de 9,5 para el EVWL y de 2,45 para el PVP (sensibilidad de 0,7; especificidad de 0,9, p < 0,01).

Conclusión: En este tipo de pacientes, los parámetros fisiológicos que pronosticaron el fracaso de la CPAP-Helmet con mayor precisión fueron el EVWL y el PVP previos al inicio de la CPAP-Helmet, el cociente PaO₂/FIO₂ y la frecuencia respiratoria tras una hora de CPAP.

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Palabras clave: Monitorización hemodinámica
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Agua pulmonar extravascular
Índice de permeabilidad vascular pulmonar
Insuficiencia respiratoria postoperatoria

Introduction

Non-invasive positive pressure ventilation (NPPV) has improved the management of respiratory failure, particularly in patients with heart failure. Patients receiving NPPV demonstrate both clinical and blood gas improvements. In the majority of cases, NPPV also eliminates the need for intubation and invasive mechanical ventilation.

Continuous positive airway pressure may stimulate clearance of pulmonary edema through various mechanisms. The most obvious mechanism would be an increase in functional residual capacity, thus enlarging the surface area for alveolar-capillary exchange, which would contribute to the reabsorption capacity of edema fluid in the lungs.

In patients admitted to post-anesthesia care units after major surgery, NPPV is increasingly used for prevention and treatment of respiratory complications and failure. Randomized studies have shown that continuous positive airway pressure reduces atelectasis and prevents pneumonia more effectively than standard therapy after upper abdominal surgery, and that non-invasive ventilation (NIV) significantly improves gas exchange and pulmonary function abnormalities after procedures such as thoracic, cardiac, vascular surgeries and liver resection. These studies support the use of continuous positive airway pressure or NIV in the postoperative setting, but more studies are required before specific recommendations can be made.

High-risk surgical patients are managed intra- and postoperatively with advanced hemodynamic monitoring. Several studies have shown that goal-directed hemodynamic therapy (GDIT) and fluid optimization may result in improved outcomes. These advanced monitoring systems guide postoperative therapy in patients admitted to the post-anesthesia care unit.

The PiCCO® device (Pulsion, Medical Systems, Munich, Germany) quantifies extravascular lung water index (EVLIW) by transpulmonary thermodilution (TPTD), which provides information on the magnitude of the edema as well as tracking its evolution. Another parameter is the pulmonary vascular permeability index (PVP) which determines the cause of pulmonary edema: high PVP indicates increased lung permeability (as in ARDS or sepsis), while normal values are present in hydrostatic pulmonary edema (heart failure and volume overload). However EVLW and PVP values have not been related to the onset and evolution of postoperative respiratory failure. We hypothesized that pre-NPPV EVLWI values could be related to the failure (intubation) or success (non-intubation) of NPPV in this setting. Using data from a previous study, we analyzed the evolution of EVLW and PVP values in 30 patients with ARF following major abdominal surgery, where the first line of treatment was continuous positive airway pressure applied via a helmet (helmet continuous positive airway pressure).

Materials and Methods

Data for the present analysis were extracted from a previous retrospective study of 99 patients admitted to the post-anesthesia care unit after major surgery. All these patients developed clinical signs of multi-etiologic acute respiratory distress, and were treated with helmet continuous positive airway pressure.

The original study was approved by the Clinical Research Ethics Committee of the Hospital General Universitario de Ciudad Real, Spain (Chairperson Dr. Teresa Rodriguez Cano) (Ethics Committee No. PI-207/01) on 11 September 2007. Clinical data were obtained from the standard medical records of patients treated in the post-anesthesia care unit.

Indications for continuous positive airway pressure included hypoxemia (PaO₂/FIO₂ ratio of less than 200 mmHg while spontaneous breathing with supplemental oxygen by facemask),
respiratory acidosis (PaCO$_2$ >45 mmHg and pH <7.35), respiratory rate>24 breaths/min, and presence of severe dyspnea and contraction of the accessory inspiratory muscles or paradoxical abdominal motion.

From this population, only those who were monitored with the PiCCO$^\text{TM}$ device via transpulmonary thermiodulation were included for the analysis (Fig. 1).

**NPPV Technique**

Continuous positive airway pressure was administered via a helmet (CaStar, Starmed, Italy)$^{14}$ using different levels of pressure (cmH$_2$O) according to the degree of dyspnea and hypoxemia. Pressure was generated using a flow generator with adjustable inspiratory oxygen fraction, and delivered through a latex-free polyvinyl chloride transparent helmet at different pressure readings. A flow meter allowed high flows to be administered, with mixtures of O$_2$ and air.

The fraction of inspired oxygen (FiO$_2$) was adjusted to obtain an oxygen saturation of SpO$_2$ >92%. A heat-moisture exchanger filter was placed at the outlet to reduce dryness and to diminish the noise inside the helmet.

Helmet continuous positive airway pressure success was defined as the avoidance of endotracheal intubation and invasive mechanical ventilation after 24 h. NPPV failure was defined as the requirement for endotracheal intubation. The decision to perform endotracheal intubation was made by the attending physician according to the usual criteria used in the unit, i.e., the inability to maintain a PaO$_2$/FiO$_2$ ratio >100 for 1 h of NPPV, cardiac arrest, respiratory arrest, respiratory pauses with loss of consciousness, severe encephalopathy, agitation not controlled by sedation, shock, intolerance of continuous positive airway pressure (discomfort or claustrophobia), or deterioration in gas exchange.$^{15}$

**Data Collection**

The following data were collected from the records: demographic data, simplified acute physiology score (SAPS) II, sepsis-related organ failure assessment (SOFA), associated co-morbidities (cardiovascular, respiratory), surgery time, hemoglobin and body temperature. The type of surgery (head and neck, esophagectomy+gastrectomy, morbid obesity, lower abdomen, thoracic surgery, aortobifemoral bypass, and trauma surgery) and the cause of the acute respiratory failure (ARDS, acute cardiogenic pulmonary, pneumonia, atelectasis, exacerbations of COPD and pleural effusion) are shown in the previous study.$^6$

Respiratory and hemodynamic data were collected before and immediately after start of Helmet-CPAP, and at 1, 3, 6, 12, 24 and 48 h and at intermediate intervals if noted in the records.

Respiratory data included arterial blood gases (PaO$_2$, PaCO$_2$, HCO$_3^-$, pH), PaO$_2$/FiO$_2$ ratio and respiratory rate.

Hemodynamic parameters included heart rate, systolic, diastolic and mean arterial pressure, cardiac index (CI), intrathoracic blood volume (ITBV), EVLWI indexed to the ideal body weight, PVPI, systemic vascular resistance index (SVRI) and the surrogate for left ventricular contractility (dP$_{\text{max}}$). All were recorded from data displayed on the PiCCO$^\text{TM}$ monitor.

Quantification of EVLWI measured via transpulmonary thermiodulation (TTPD) on the PiCCO$^\text{TM}$ device indicates the magnitude of the edema and monitors its evolution. Another parameter shown by this device is the pulmonary vascular permeability index (PVPI), which is measured as the ratio of EVLWI to pulmonary blood volume. It has been used to determine the cause of pulmonary edema: high PVPI indicates increased lung permeability due to an inflammatory process (such as ARDS), while normal values are present in hydrostatic pulmonary edema (heart failure and volume overload).$^{11,12}$

**Statistics**

Nominal variables were expressed as mean±SD (standard deviation) and processed as continuous variables. Qualitative variables between two groups were compared using Fisher’s exact test or the χ² test. For quantitative variables, comparisons were performed using the Mann Whitney U test. Analysis was made with a non-parametric paired Wilcoxon test to compare data obtained before and after NPPV for each patient. A P value of <.01 was considered statistically significant. Receiver operating characteristic (ROC) curves were used to analyze the best predictor for postoperative respiratory failure. All statistical analyses were performed using SPSS 11.0.1 statistical software.

**Results**

Of the 99 patients managed with helmet-NPPV for postoperative ARF included in the previous study,$^6$ 30 had been monitored with PiCCO$^\text{TM}$ and were therefore included in this study. The characteristics of these patients on admission to the post-anesthesia care unit are shown in Table 1. There were no statistically significant differences in the characteristics of patients who were subsequently intubated (intubated patients) and those that were not (non-intubated patients).

Changes in physiological parameters (heart rate, respiratory rate and mean arterial pressure) and arterial blood gases obtained before and after NPPV are shown in Table 2. After 1 h of NPPV, respiratory frequency decreased significantly only in the non-intubated

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Fig. 1. Study flow diagram.
group (26.33±2.5 vs 17.48±5.8, P<0.01). After NPPV, the intubated group had a significantly lower PaO2/FiO2 ratio (141.6±14.6 vs 303.3±65.2, P<0.01).

Analysis of the ROC curve showed a very good predictive capacity for respiratory frequency and PaO2/FiO2 ratio, with an area under the curve of 0.91 (95 CI, 0.80–1.01, P<0.01) and 0.85 (95% CI, 0.72–0.99, P<0.01) respectively (Fig. 2). A higher level of CPAP cmH2O (10.42±1.03 vs 13.96±1.7, P<0.01) and higher FiO2 (0.42±0.04 vs 0.49±0.06, P<0.01) was applied in the intubated group vs the non-intubated group.

The hemodynamic parameters from the PiCCO™ monitor obtained before and 1 h after NPPV are shown in Table 3. The non-intubated group had significantly lower pre-NPPV EVLWI than the intubated group (8.6±1.08 vs 11.8±0.99, P<0.01). However, after 1 h of NPPV, EVLWI only decreased significantly in the non-intubated group (8.6±1.08 vs 6.2±0.96, P<0.01) accompanied by a significantly lower PVPI (1.7±0.56 vs 3.0±0.88, P<0.01). After NPPV, this difference was maintained in both groups (1.68±0.46 vs 3±0.76, P<0.01).

When the EVLWI and PVPI were included in ROC curve analysis (Fig. 3), both variables showed very good predictive capacity, with an area under the curve of 0.8 and 0.9, respectively. An optimal cut-off value for EVLWI was established at 9.5 (sensitivity 0.78; specificity 0.8, P<0.01), and at 2.45 for PVPI (sensitivity 0.7; specificity 0.9, P<0.01).
Several patients were analyzed in this study, with 562 patients presenting an accuracy of 0.99, 0.96, and 0.92 for NPPV, BiPAP, and CPAP, respectively. The ROC curve for PVPI showed a sensitivity of 0.88, with a specificity of 0.76, indicating a high diagnostic accuracy.

**Discussion**

In our study, the application of NPPV with continuous positive airway pressure in patients with postoperative ARF was associated with an improvement in gas exchange, and avoided the need for intubation in 66.6% of the patients. We found for the first time that pre-NPPV EVLWI and PVPI values predicted the failure of NPPV with an accuracy similar to changes in PaO2/FiO2 ratio and respiratory frequency after 1 h of NPPV. An EVLWI value of 9.5 ml/kg and a PVPI of 2.45 predicted the need for intubation with high sensitivity and specificity.

Various studies have shown that application of continuous positive airway pressure in postoperative ARF improves gas exchange, increases functional residual capacity, and minimizes the formation of atelectasis. The use of NPPV relieves work of breathing, reduces pulmonary extravascular water, and enlarges pulmonary volume by re-expanding areas of atelectasis. The role of NPPV in the management of ARF is gaining ground in the literature. Indeed, our success rate and gas exchange improvements were similar to those described in patients with postoperative ARF following abdominal surgery.

If we compare the intubated group with the non-intubated group, we observed that the post-NPPV PaO2/FiO2 ratio in the non-intubated group presented a statistically significant improvement. This could indicate a reversal in areas of atelectasis, which did not occur in the intubated group (303.33±65.2 vs 171.03±71.6).

The helmet has been shown to be an effective interface for the application of NPPV; however, it can increase patient ventilator asynchrony and CO2 rebreathing when compared to the facemask. The helmet, however, is better tolerated, and can thus be used for longer periods. In this study, PaCO2 increased non-significantly in the non-intubated group (42.5±7.9 vs 43.8±8.2) compared to the intubated group (43.7±7.7 vs 44.1±7.4) 1 h after start of NPPV; however, the changes were clinically insignificant (Table 2).

Extravascular lung water is a valuable tool for measuring pulmonary edema before it is clinically evident, and for guiding therapy with electrolyte solutions and vasoconstrictors in the critically ill patient. In the future, it may be included in the definition of acute lung injury (ALI) and ARDS. Several studies have demonstrated that EVLWI is an independent predictor of mortality in septic patients with or without ARDS.

PVPI has been shown to be useful in differentiating hydrostatic edema due to left ventricular failure (normal values of PVPI <3) from high permeability edema due to ARDS (higher PVPI values >3). Increased PVPI values indicate possible changes in the permeability of the alveolar-capillary membrane as a consequence of an inflammatory process and lung injury, while high EVLWI would indicate edema. In these cases, the probability of NPPV failure is higher when compared to patients with lower (normal) PVPI and EVLWI without lung injury.

In our study, pre-NPPV EVLWI and PVPI values (1.7±0.56 vs 3±0.88, P<.01) were significantly higher in the intubated group (8.6±1.08 vs 11.8±0.99, P<.01). In the non-intubated group, EVLWI decreased (8.6±1.08 vs 6.2±0.96, P<.01) after start of NPPV, but values remained within normal range. The intubated group, however, had higher initial values that did not change after NPPV (11.8±0.99 vs 11.7±1.1, NS). The same was observed in the case of PVPI (3.0±0.88 vs 3±0.76, NS).

Gust et al. analyzed the effects of NPPV in patients after coronary bypass surgery. They found that EVLWI was significantly lower in patients on CPAP or BiPAP compared to the group that remained on O2 alone. Nevertheless, other studies indicate that EVLWI does not diminish or can even increase after the application of positive pressure.

Results from other series cannot be interpreted without knowledge of PVPI values. However, we hypothesize that in patients with normal permeability, EVLWI may be reduced when alveolar surface area is increased with continuous positive airway pressure. In ARDS with high permeability edema, meanwhile, positive pressure would not affect PVPI or EVLWI.

The ROC curve shows that the model has prognostic value (greater EVLWI and PVPI predict a greater incidence of intubation after PNNV). For EVLWI, the optimal cut-off point to predict need for intubation was 9.5. For PVPI, this value was 2.45. Based on these results, early intubation and immediate mechanical ventilation would be indicated in the presence of these EVLWI and PVPI values. This is because the increase in extravascular lung water is not due to increased hydrostatic pressure, but rather to altered vascular permeability with a possible inflammatory origin that will only resolve over time.

Our study has some limitations. First of all, it is a sub-analysis of a retrospective observational study with no control group. Therefore, we are unable to conclude that the results seen in these subjects were modified by the use of NPPV. However, our study explores the possible causal relationship of high EVLWI and the failure of non-invasive management of the patients. Our descriptive study could provide the basis for a wider prospective randomized clinical trial to confirm our preliminary findings. Another limitation is our small sample size, which restricts the accuracy of PVPI and EVLWI cut-off values, sensibility and specificity. Finally, the study is limited to patients with access to a PiCCO; most patients on NPPV are monitored with non-invasive or less invasive techniques that do not measure EVLWI and PVPI index.
Conclusions

In patients with postoperative ARF, the physiological parameters that predict the failure of NPPV with the greatest accuracy are PaO2/FiO2 ratio and respiratory frequency. However, in this small pilot study, we have seen a good predictive value for pre-NPPV EVLWI and PVPI. High EVLWI and PVPI values indicate an alteration in the alveolar-capillary membrane and could suggest when NPPV could be avoided in favor of early intubation. A prospective randomized clinical trial would be necessary to confirm these results.

Conflicts of Interest

FJB is a member of the Medical Advisory Board of Pulsion Medical Systems, Munich, Germany.

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References