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# CLINICAL EXPERIENCE WITH THE ILA MEMBRANE VENTILATOR IN INTENSIVE CARE UNIT TIMISOARA

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*Through this retrospective study we aim to evaluate the usefulness of ILA depending on the different existing pathologies and their degree of severity. The data from 18 intensive care unit patients were analysed in the period between March 2013 and July 2015. We presented some established principles, the responsive pathology and not least the problems we faced. The ILA systems may be indicated in severe refractory and predominantly hypoxemic lung failure ($PaO_2/FiO_2$<100 mmHg or even lower), or refractory respiratory acidosis ($pCO_2$>80 or low pH). Improving gas exchange and a reduction of ventilator-induced lung injury due to a more protective ventilation can be achieved. Through our experience we obtained survival rates of more than 58%. Severe complications (in connection with the vascular approach during the whole period) can occur with all of the modalities of extracorporeal support and have to be rapidly recognized and controlled. We prove that modern extracorporeal lung support devices represent an important therapeutic method of the critically ill patients with severe respiratory dysfunctions. Because of potentially severe complications the use should be restricted to specialized centres*.

*Keywords:* ARDS, Asthma, COPD, ILA Membrane Ventilator, protective ventilation

## INTRODUCTION

The emergence of a new therapeutic extracorporeal minimal invasive method to increase the tissue oxygenation and to remove the carbon dioxide, captured the interest of many intensive care unit specialists concerned with the severe respiratory dysfunction present in patients with ARDS (Acute Respiratory Distress Syndrome), especially during the epidemic flu with $H_1N_1$ 2009, COPD (Chronic Obstructive Pulmonary Disorder), bronchopneumonia and asthma, for whom the therapeutic resources of mechanical ventilation were insufficient or inadequate. Through this retrospective study we aim to evaluate the usefulness depending on the different existing pathologies and their degree of severity, the time point of implementation and the potential problems that may occur during the treatment with this method.

Part of the patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) did not benefit from the beginning by this extracorporeal method of gas exchange and they

had no recovery during the first week, this has been termed as late-phase ARDS[1]. In this period we noticed that compliance and other respiratory parameters have worsened. Factors responsible for this are collagen remodelling and increased permeability for water in the lung (ELWI and PVPI were higher)[2]. The consequence was: low tidal volume ventilation with lung hyperdistension and high inspiratory airway plateau pressures[3]. Biologically and clinically it features hypercapnia and hypoxemia which needs an increased inspiratory flows and tidal volumes, and decreased breath-to-breath variability in tidal volumes. Those complications in patient ventilator interaction prolonged the weaning from mechanical ventilation[4,5]. In fact, severe hypercapnia, hypoxia and possible patient distress are reasons why low tidal volume ventilation strategies are steel not universally implemented in ALI/ARDS patients[6,7].

It is clearer that microvascular lung injury and pulmonary edema during mechanical ventilation are not consequence of "barotrauma", but rather of "volutrauma"[8]. The main determinant of volutrauma seems to be end-inspiratory volume (the overall distension) rather than tidal volume or FRC (which is dependent on level of PEEP)[9]. It is more obvious that ventilation has effects on previously injured lungs, and the distribution of this aggression is not the same in the whole lung. There are islands of health in the lung: "baby lung" that must to be protected by the alveolar changes in response to high airway pressure[10].

## MATERIAL AND METHODS

The data from 18 intensive care unit patients were analysed in the period between March 2013 and July 2015. These patients had a severe respiratory pathology with hypoxemic or hypercapnic disturbances or both. They were treated for this pathology once in a while with mechanical ventilation in a protective mode, trying to decrease the extravascular lung water (with PEEP, albumins and diuretics), and low tidal volumes, taking care to pulmonary compliance and resistance. We assessed the impact of ILA on airway pressures, the tidal volumes, the $PaCO_2$ levels, the $PaO_2$ levels and the breathing pattern. Upon transfer from outside of our hospitals most patients were ventilated in a pressure-controlled mode or volume controlled mode with tidal volume less than 6 ml/kg predicted body weight (PBW). Patients received standardized treatment including permissive hypercapnia and PEEP adjusted to oxygenation. The triggers for putting patients on the ILA device were inspiratory plateau pressures higher than 30 cm $H_2O$, $PaO_2/FiO_2$<80 or $pCO_2$ more 80mmHg with severe acidosis (pH<7,2). Using this extracorporeal help, we tried to reduce the ventilator settings according to the clinical and biological statement of the patient. For the same blood gas analysis we were able to use lower parameters for mechanical ventilation: lower tidal volumes, lower frequency and $FiO_2$.
We collected data about the patients in this period and an interactive online national registry was created, where these data were included and could be updated and evaluated (Figure 1).

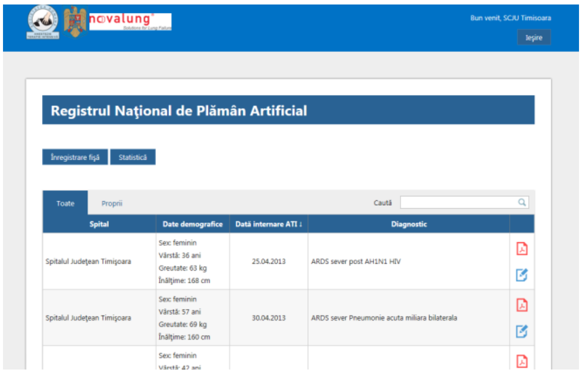


**Figure 1** Online registry for Interventional Lung Assist

Data were about gender, age, APACHE II score, pathology, anticoagulation, length of stay on mechanical ventilation, length of stay on extra-corporeal ventilation, length of stay in ICU, complications, types of canullas for ILA and place of insertion (Table 1). Besides there are clear evidence that veno-venous catheters are more efficient[11], for some patients with hypoxic or mixed respiratory insufficiency we used twin cannulas and arterio-venous without pump with low flow <1,5L/min.

| | Age | Gender | APACHE II | CPIS | ILA* | MV* | ICU* | death |
|---|---|---|---|---|---|---|---|---|
| 1 | 33 | F | 24 | 6 | 5 | 5 | 16 | NO |
| 2 | 65 | M | 10 | 6 | 16 | 45 | 45 | Y |
| 3 | 47 | M | 12 | 5 | 7 | 6 | 10 | NO |
| 4 | 60 | M | 24 | 8 | 8 | 11 | 17 | NO |
| 5 | 62 | F | 29 | 9 | 3 | 4 | 4 | Y |
| 6 | 54 | M | 23 | 7 | 12 | 22 | 26 | Y |
| 7 | 20 | M | 15 | 4 | 4 | 4 | 5 | NO |
| 8 | 27 | F | 17 | 5 | 10 | 1 | 11 | NO |
| 9 | 29 | F | 15 | 6 | 16 | 28 | 42 | NO |
| 10 | 36 | F | 16 | 6 | 17 | 1 | 22 | NO |
| 11 | 57 | F | 19 | 7 | 4 | 4 | 4 | NO |
| 12 | 42 | F | 21 | 7 | 7 | 9 | 9 | Y |
| 13 | 32 | M | 12 | 4 | 7 | 10 | 13 | NO |
| 14 | 53 | F | 20 | 6 | 5 | 16 | 16 | Y |
| 15 | 78 | M | 20 | 5 | 7 | 6 | 14 | Y |
| 16 | 67 | F | 22 | 8 | 8 | 7 | 11 | Y |
| 17 | 55 | F | 27 | 7 | 21 | 36 | 48 | Y |
| 18 | 41 | F | 13 | 4 | 3 | 2 | 7 | NO |

ILA/MV/ICU days describe the length of stay for patient on extracorporeal device (ILA), on mechanical ventilation (MV) and length of stay in ICU (ICU).

**Table 1.** Clinical and demographic characteristics of patients.

The period for using ILA device was between 3 and 21 days (Figure 2). Only 2 treatments were stopped due to the problems faced to the circuit.

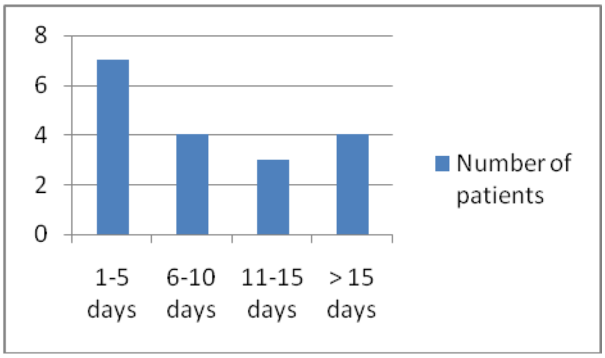


**Figure 2** Time of treatment

Most of the patients were young, (mean 45.8 years). There was no child included in this study. Pathological profiles were different. We tried this device for patients with different severe respiratory diseases: ARDS due to viral infections with AH1N1 or other subspecies, ARDS due to ventilator associated pneumonia, acute severe tuberculosis, COPD in late stages and asthma. We did not use a clear recommendation for these cases and unfortunately, for some patients, interventional lung assist was the last disparate solution. Decisions regarding the type of cannula or using the pump to get high flow in the extrapulmonary circuit was connected to products that we had available at that time. We used cannulas with different sizes between 15 and 23 Fr. 7 patients benefited by the circuit with pump, especially those with predominant hypoxemic respiratory insufficiency. To protect the circuit from clotting we used heparin, fractionated heparin +/- acetylsalicylic acid to keep the partial thromb oplastin time activated between 45-75.

| | Diagnostics | Resp. Insuff. | Cannula |
|---|---|---|---|
| 1 | ARDS drowning CRA | Hypoxemic | twin |
| 2 | ARDS VAP cerebral aneurism | Mixt | A-V |
| 3 | ARDS AH1N1 VAP | Mixt | F-J |
| 4 | COPD septic shock | Mixt | Twin |
| 5 | ARDS AH1N9septic shock | Hypoxemic | F-F |
| 6 | COPD VAP | Mixt | Twin |
| 7 | ARDS Traheobronhial aspiration sindrom | Mixt | F-J |
| 8 | ARDS AH1N1 | Hypoxemic | Twin |
| 9 | ARDS AH1N1 | Hypoxemic | F-J |
| 10 | ARDS AH1N1 | Hypoxemic | F-J |
| 11 | ARDS AH1N1 | mixt | A-V |
| 12 | ARDS tuberculosis | Mixt | Twin |
| 13 | Asthma | Hypercapnic | A-V |
| 14 | ARDS | Mixt | Twin |
| 15 | ARDS VAP | Mixt | Twin |
| 16 | VAP - stroke | Hypoxemic | F-J |
| 17 | COPD | Hypercapnic | A-V |
| 18 | ASTHMA | Mixt | F-J |

**Table2.** Diagnostics of patients

## RESULTS AND DISCUSSIONS

The ILA systems may be indicated in severe, refractory and predominantly hypoxemic lung failure ($PaO_2/FiO_2$<100 mmHg or even lower) or refractory respiratory acidosis ($pCO_2$>80 or low pH). Improving gas exchange and a reduction of ventilator-induced lung injury due to a more protective ventilation can be achieved. Through our experience we obtained survival rates of more than 55%.

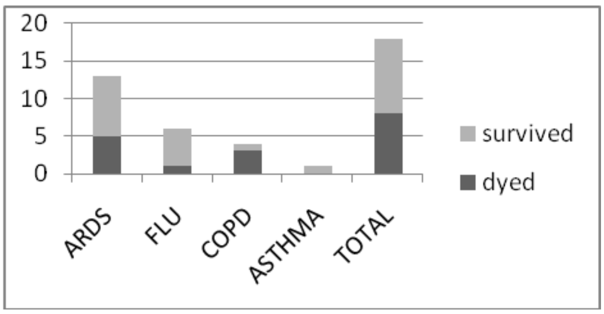
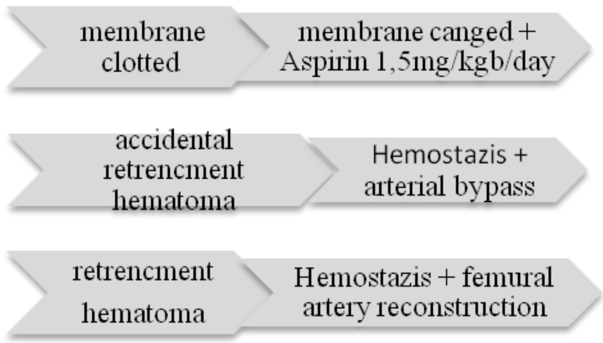


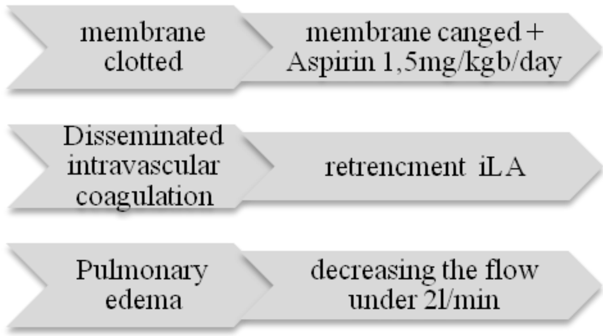

**Figure 3** Evolution depending of pathology

Most of the patients, 13/18 had moderate or severe ARDS, 8/13 (61%) and 4/5 patients (80%) with flu and ARDS were treated successfully. One of the 4 patients with acute COPD who fell into the above criteria was introduced on extracorporeal ventilation and it did survive. One patient with severe asthma benefited successfully from this procedure. As the diagnosis of progression to ARDS is made faster, early protective ventilation can be a favourable prognostic factor in the medium term. Severe complications (some of them in connection with the vascular approach) during the whole period can occur with all the modalities of extracorporeal support and have to be rapidly recognized and controlled. There is a risk for leg amputation because of femoral artery rupture: "leg for life".

Complications with "passive" ILA




Complications with "active" ILA (with pump).




We noticed 4 complications connected with the vascular approach: 2 haemorrhagic incidents at cannulation, 2 incidents at retrenchment. Twice the circuit clotted (in one case anticoagulation was made only with acetylsalicylic acid), and a hemodynamic complication (acute pulmonary edema) in the moment of increased flow over 4 L/min in the pump.

The current study is the first to systematically investigate the efficacy of ILA onoxygen transfer capacity and carbon dioxide removal in a small human study population with severe ARDS. It provides detailed information regarding the factors that influence ILA, the performance and supports the use of ILA as a highly effective method in severe lung injury with hypoxia, hypercapnia and respiratory acidosis. For active ILA the flow is related to the pump speed and to the size of the cannulas, for passive ILA, blood flow through the ILA depends on both total inherent resistance of the device and on the pressure difference across the system. Thus the flow resistance of the cannulas is the predominant factor of total resistance of the device. According to the Hagen – Poiseuille equation blood flow ismost strongly influenced by the diameter of the cannula: blood flow = $\pi$

Δp r4/(8 l η), (Δp = pressure difference, l = length of cannula, η = viscosity, r = radius of cannula).

The second important factor for blood flow through the device is the difference of pressure before (mean arterial pressure, MAP) and after the system (central venous pressure, CVP).Cardiac output (CO) per se is for blood flow through the ILA is not so important. Blood flow amounted to 20 % of CO with 15 Fr cannulas and up to 25 % of CO with 19 Fr cannulas on average. More important seems to be the size of cannulas. In most patients a significant increase of CO after start of ILA was observed. This can be explained by two mechanisms: firstly bycreating an artificial low resistance arterio–venous shunt and secondly by rapid correction of acidosis resulting in improved vasotonus and possibly cardiac pump function. The oxygen transfer capacity of the ILA is mainly limited by the fact that arterial blood, already well oxygenated, is fed into the device, and therefore only a small additional amount of oxygen can be bound to haemoglobin[12].

## CONCLUSIONS

There is now wide spread consensus on the need to ease the stress on diseased lungs during mechanical ventilation. We showed that modern extracorporeal lung support devices allow an effective extracorporeal gas exchange. They represent an important therapeutic method of the critically ill patients with severe respiratory dysfunctions. Because of potentially severe complications the use should be restricted to specialized centres, where departments of vascular surgery, of infectious or lung diseases exist and work in a multidisciplinary team.

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