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Extracorporeal Membrane Oxygenation for Acute Interstitial Pneumonia

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Aos meus pais

Ao meu irmão

Ao Rafael

Extracorporeal Membrane Oxygenation for Acute Interstitial Pneumonia

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Conflicts of interest

There are no conflicts of interest.

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ABSTRACT

INTRODUCTION: Acute Interstitial Pneumonia (AIP) is a rare form of interstitial lung disease, with a non-specific clinical and radiologic presentation, which frequently mimics acute respiratory distress syndrome (ARDS). The diagnosis is one of exclusion. No proven effective treatment exists and the use of glucocorticoids remains controversial. Venovenous Extracorporeal membrane oxygenation (VV-ECMO), referring to an extracorporeal circuit that directly oxygenates and removes carbon dioxide from the blood, may be considered in refractory cases of severe acute respiratory failure, as a bridge to a diagnosis, treatment and eventually recovery. We present 3 cases of patients with AIP supported with VV-ECMO.

METHODS: One male and two female patients are described. After excluding known causes of ARDS, AIP was diagnosed after a lung biopsy and immunosuppressive treatment was initiated.

RESULTS: Despite the usual care for severe acute respiratory failure, patients were not improving and VV-ECMO was started and used as a bridge to diagnosis. Two patients survived (duration of ECMO support: 15 days in both patients) and one died as a result of lung biopsy complication (ECMO support: 73 days).

CONCLUSIONS: Our report highlights the potential role of VV-ECMO in the diagnosis and management of refractory severe acute respiratory failure associated to AIP.

KEYWORDS: Acute Interstitial Pneumonia; Extracorporeal Membrane Oxygenation, Acute Respiratory Distress Syndrome.

INTRODUCTION

Acute Interstitial Pneumonia (AIP) is a rare form of interstitial lung disease of unknown etiology, first described in 1965 by Hamman and Rich.[1] AIP has a poor prognosis with a mortality >50 % in the first two months after the onset of the disease.[2] It mostly occurs in previously healthy individuals without pre-existing lung disease, has no gender predominance nor association with smoke and can manifest at any age with a mean age of occurrence of 50 years.[3] AIP has an acute onset and is generally preceded by upper respiratory infection symptoms or by a flu-like disease, followed by rapidly progressive hypoxemic respiratory failure frequently requiring invasive mechanical ventilatory support.[4]

The clinical and radiologic presentation of AIP is non-specific and frequently mimics acute respiratory distress syndrome.[5] There are no specific laboratory findings but patients may present with nonspecific leukocytosis with neutrophilia.[6] Chest x-ray display bilateral, diffuse air-space opacities sparing the costophrenic angles.[3] High

resolution computed tomography reveals bilateral ground glass opacities, frequently with consolidation of the dependent lung regions.[7] Bronchoalveolar lavage (BAL) shows increased total cell number including red blood cells, neutrophils and occasionally lymphocytes; atypical reactive pneumocytes as well as hyaline membrane fragments can also be seen[3].

The diagnosis of AIP requires the presence of a diffuse alveolar damage (DAD) histologic pattern in lung biopsy, which is also frequently observed in patients with ARDS. Therefore, known causes of DAD such as infection, acute exacerbation of idiopathic pulmonary fibrosis, acute hypersensitivity pneumonitis, connective tissue disorders, drug toxicity, aspiration, inhalants toxins and pancreatitis need to be excluded in order to establish a diagnosis of AIP[6]. The DAD characteristic histologic pattern in the initial phases of the disease consists of edema, acute interstitial inflammation and hyaline membrane formation, with absorption of these membranes as the progression of disease occurs, as well as migration of fibroblasts to the alveolar septa. In more advanced phases, an interstitial thickening caused by fibroblasts can be seen as a loose organizing fibrosis.[3]

There is no proven effective treatment for AIP.[3] In patients requiring invasive mechanical ventilation a lung-protective approach consisting in tidal volumes of 6 ml/kg

predicted body weight and a plateau pressure below 30 cmH_2O is recommended in order to minimize ventilator-induced lung injury, as in ARDS.[8] Regarding the pharmacological treatment, the use of glucocorticoids remains controversial.[3] The use of high dose glucocorticoids in the treatment of AIP is based on a lower mortality described in lupus pneumonitis [9] and ARDS[6], with such therapy, claiming that the same can occur with AIP. However, some authors have not found benefits of glucocorticoid therapy neither for AIP [4] nor for ARDS.[10]

Extracorporeal membrane oxygenation (ECMO), referring to an extracorporeal circuit that directly oxygenates and removes carbon dioxide from the blood, may be considered in refractory severe acute respiratory failure when positive-pressure ventilation alone is insufficient to maintain adequate gas exchange, or when adherence to lung-protective ventilation strategies, neuromuscular block, prone position and conservative strategy of fluid management results in unacceptable levels of hypoxemia, hypercapnia and acidemia.[11] In most cases of ECMO for severe acute respiratory failure, venovenous (VV) ECMO is utilized, in which blood is withdrawn from and returned to a central vein.[12] Recently, there has been increasing interest in ECMO as a result of advances in extracorporeal technology, with more efficient oxygenators and lower rates of complications, along with several reports of improved survival with

ECMO for severe ARDS.[13] In the Conventional ventilation or ECMO for Severe Adult Respiratory failure (CESAR) trial, transferring of adult patients with severe but potentially reversible respiratory failure to an ECMO Center significantly improved survival without severe disability at 6 months, when compared with the conventional management group.[14]

Centro Hospitalar São João is a 1100-bed tertiary university hospital and the sole ECMO referral center of the north of Portugal, a region with approximately 4 million inhabitants. It has a case volume of 40 to 50 patients per year, being an Extracorporeal Life Support Organisation (ELSO) member (Center 227).

In the present study we describe 3 cases of refractory severe acute respiratory failure of unclear etiology rescued with VV-ECMO.

METHODS

Case 1

A 27-years-old woman with a past medical history of obesity and on oral contraceptives began with odynophagia and fever (Table 1), that persisted despite antibiotic therapy. Five days later purulent cough developed and levofloxacin was started. She evolved with prostration, asthenia, worsening dyspnea and she went to the emergency department of a secondary hospital. On admission she had a

respiratory rate of 32 breaths pm, peripheral saturation of 56% on air, crackles in the right hemithorax, blood pressure 110/60 mmHg, heartbeat of 110 pm, Glasgow Score of 15 and a tympanic temperature of 39.5ºC. Arterial blood gas analysis on air showed severe respiratory insufficiency (P_{O2} 17 mmHg, pH 7.50, CO_2 32mmHg, HCO_3 26mEq/L). Lactate was 2.3mmol/L. Blood tests revealed an elevated C reactive protein (128.7 mg/dL), normal white blood count and no renal, hepatic and hematological dysfunction. Chest X-ray showed consolidation of the right pulmonary base. A provisional diagnosis of severe community-acquired pneumonia (CAP) was made, treatment started with meropenem, oseltamivir, fluids, invasive mechanical ventilation and transfer to our hospital for ICU care. Reassessment on mechanical ventilation revealed severe acute respiratory insufficiency (P_{O2} 46 mmHg with a PEEP of 15 and F_{IO2} of 100%, with normal P_{CO2}, HCO_3 and lactate values) and hemodynamic stability. Chest X-ray showed consolidation of the right and of the inferior two thirds of the left lungs. (Figure 1) Neuromuscular blockade was initiated and antibiotics changed to piperacillin/tazobactam, azithromycin plus oseltamivir. Cultural and non-cultural microbiological results from BAL were negative, including for virus and atypical agents. Oseltamivir was stopped and the antibiotics were kept for 8 and 5 days, respectively. The clinical status continued to worse over the next days and a chest CT scan was

performed, showing diffuse bilateral ground glass pattern and inferior lobar consolidation. Refractory hypoxemia with aggressive ventilation (plateau pressure (Pplat) 30 cm H_2O, PEEP 15, F_{IO2} 100%) was still needed by day 6 of mechanical ventilation (Table 2), when ECMO was initiated (23Fr aspiration cannula in the femoral vein and a 17Fr arterialize cannula in internal jugular vein) (Table 3). A surgical lung biopsy was performed on the 2nd day of ECMO and a diffuse alveolar damage pattern in organizing phase was observed (Figure 2), with negative microbiological and cancer search (Table 4). Immunosuppressive therapy was started with methylprednisolone (1g a day during 5 days and then 2mg/kg/d) and intravenous cyclophosphamide (2g/month), on the 3rd day of ECMO. Right hemopneumothorax developed as a consequence of the lung biopsy and was managed with chest tubes (two) and hematologic support according with the needs. Minor vaginal bleeding responded to estradiol. After 15 days of progressive improvement on ECMO, decannulation was safely performed and the patient weaned from mechanical ventilation in the next 5 days. She was transferred to a level II-ICU in the 28th inpatient day, where she stayed for 11 days, recovering from critical illness myopathy and residual respiratory failure, treating a recurrent pneumothorax and *Proteus mirabilis* acute pyelonephritis (5 days meropenem). Later she was transferred to the pulmonology ward where respiratory

failure fully resolved, completing 51 days of global hospital stay. Currently she remains without respiratory symptoms and without any immunosuppressive therapy, after a two years azathioprine course.

Case 2

A 59-year-old man with a past medical history of ulcerative colitis managed with mesalazine and prednisolone, came to our emergency department with a 3-day history of progressive worsening dyspnea, asthenia and dry cough. On admission, he had a respiratory rate of 32 breath pm, peripheral saturation of 70% on air and diminished breath sounds and crackles in both lung bases on auscultation. He was hemodynamically stable, with a Glasgow Score of 15 and a tympanic temperature of 38.4ºC. The arterial blood analysis on air showed a severe type I respiratory failure (P_{O2} 35mmmHg). Blood tests revealed hemoglobin 12g/dL, leucopenia (WBC 3000/mm^3), elevated C reactive protein (91mg/dL) and no renal, hepatic or hematologic dysfunction. Chest X-ray showed heterogeneous infiltrates in both inferior halves of the lungs. (Figure 3) A provisional diagnosis of CAP was made and treatment with ceftriaxone, azithromycin and oseltamivir started, together with ICU admission for non-invasive mechanical ventilation support. Due to negative non-cultural microbiological results and confirmation of recent exposure to prednisolone, antibiotics were changed

to piperacillin/tazobactam plus azithromycin. Cultural results (endotracheal aspirate and blood cultures) were also negative. The patient evolved with worsening respiratory failure despite invasive mechanical ventilation, curarization, prone positioning, negative fluid balance and an attempt of protective ventilator strategy with permissive hypercapnia. On the 5th ICU day, ECMO was started (19Fr cannula in the right internal jugular vein and 25Fr cannula in the right femoral vein). A flexible bronchoscopy showed no signs of typical and atypical infections (bacteriologic, acid-fast, mycological, virological study as well as PCR for *Aspergillus*, *Chlamydia*, CMV, *Legionella*, Influenza A and *Coxiella* were all negative) or of lung cancer. The bronchalveolar lavage fluid had a neutrophil predominance with mild eosinophilia (11%) and no lymphocytosis. A right pneumothorax subsequent to bronchoscopy led to pleural drain insertion. A CT scan performed on the 3rd ECMO day showed right pneumothorax with well-placed drain, minor bilateral pleural effusion, inferior and superior lobes consolidation with a ground glass pattern in the remaining parenchyma. A surgical lung biopsy was performed on the 9th ECMO day and it showed pulmonary parenchyma with diffuse alveolar damage pattern in organizing phase (Figure 4), with negative microbiological and cancer search. Methylprednisolone was started (2mg/kg/d) and the patient evolved favorably in the next days, being successfully decannulated on the 15th ECMO day. He

stayed for more 16 days in the ICU due to difficult mechanical ventilation weaning associated with a bronchopleural fistula (post bronchoscopy and biopsy) and myopathy secondary to corticosteroids and critical illness. He was transferred to a level II-ICU on the 37th inpatient day, where he stayed for 22 days and was transferred to an internal medicine ward on the 59th inpatient day, and 7 days later to a rehabilitation center. Currently he remains on hospital follow-up as a rheumatology and gastroenterology outpatient, without respiratory symptoms.

Case 3

A 56-year-old woman with a past medical history of unilateral renal agenesis and major depressive disorder treated with quetiapine, sertraline, clomipramine and lorazepam, went to the emergency department with a 3-day history of fever, dry cough, dizziness and respiratory difficulty. On admission she had a respiratory rate of 36 breaths pm, peripheral saturation of 81% with a nonrebreathing face mask with reservoir (F_{IO2} 85%), severe dyspnea, crackles on the right hemithorax, hemodynamic stability and a Glasgow Score of 15. The arterial blood gas showed severe hypoxemia (pH 7.41, P_{CO2} 41mmHg, P_{O2} 48mmHg, HCO_3 26.0mEq/L). Lactate was 1.1 mmol/L. Blood tests revealed normal white blood count (with neutrophilia), elevated C reactive protein (350mg/dL), myoglobin and D-dimers, with no renal, hepatic and hematological

dysfunction. Chest X-ray showed diffuse bilateral infiltration. A provisional diagnosis of severe CAP was made and ceftriaxone, hydrocortisone, enoxaparin and invasive mechanical ventilation initiated. During the ICU stay azithromycin was added to ceftriaxone. Blood cultures and urinary antigens for Pneumococcus and *Legionella* were negative (no influenza virus testing was made). She evolved in the next days with persistent hypoxemia refractory to prone position, curarization, recruitment maneuvers, negative fluid balance and aggressive ventilation (tidal volume 470cc, PEEP 16, F_{IO2} 100% Inspiration: Expiration 1:1, Pplat 30 cmH_20). Shock and persistent inflammatory syndrome was also present, despite antibiotics switch to piperacillin plus tazobactam (initiated after a thoracic angio-CT scan, a flexible bronchoscopy with bronchalveolar lavage and new blood cultures). ECMO was started *in loco* on the 7th ICU day (25Fr cannula in the femoral vein and a 19Fr cannula in internal jugular vein), followed by transport to our hospital (Figure 5). Rest ventilation was initiated and antibiotic sustained for a total of 8 days, according to negative microbiological results in the reference hospital. She persisted on ECMO with multiorgan dysfunction and with an increasing inflammatory syndrome. Vesicles and ulcers develop on the oral mucosa and acyclovir initiated after a blood positive molecular result to herpes simplex type 1 infection. The patient showed no signs of improvement and a thoracic and abdominal

CT scan showed extended areas of consolidation and ground glass pattern more exuberant in the inferior pulmonary lobes. A surgical lung biopsy (access by minithoracotomy, with chest tube insertion under direct visualization) was held, revealing a morphologic picture of diffuse alveolar damage in organizing phase (Figure 6), without evidence of infection or cancer. Methylprednisolone (1g/day in the first 5 days, then 2 mg/kg/day) was started. The patient developed signs of intubation associated pulmonary infection and imipenem plus vancomycin were initiated. An *Acinetobacter baumannii* only susceptible to imipenem and aminoglycosides was isolated in a bronchial lavage, and combined therapy with meropenem plus sulbactam initiated. A bronchopleural fistula with a persistent pneumothorax developed as a consequence of the lung biopsy, despite the placement of multiple chest tubes. A massive hemothorax emerged and the patient was disconnected from the ventilator during 3 days, remaining on ECMO, in a conservative attempt to solve the hemopneumothorax, but without success. A surgery (access by right lateral thoracotomy) was tried for closure of the fistula and clots removal, but during the procedure tissues were very friable and marked blood loss was seen, forcing massive blood transfusion. After the surgery the patient was readmitted in the ICU very

unstable, evolving to refractory shock and death a few hours after the end of surgery (on the 73rd day of ECMO).

DISCUSSION

In the present report, three AIP cases with refractory severe acute respiratory failure rescued with VV-ECMO are described. Extracorporeal gas exchange allowed minimization of further ventilator-induced lung injury and the prosecution of a diagnostic work-up that included a surgical lung biopsy, bridging the patient to definite treatment and eventual recovery.

All of the patients had no previous lung disease, did not smoke and had an acute onset of disease, although with shorter median times for dyspnea development than those usually depicted in the literature.[3] The evaluation on hospital admission highlights severe type 1 respiratory failure with an accompanying inflammatory syndrome, without hemodynamic instability or other concomitant major organ dysfunction. The chest x-rays showed alterations consistent with pneumonia, and this diagnosis was erroneously made, leading to an inadvertent use of antibiotics, without any benefits for the patients and delaying the correct diagnosis. The diagnostic work–up for AIP is very laborious, requiring the exclusion of other diseases and ending with a lung biopsy – “idiopathic ARDS”.[6] ECMO played a major role as a supportive measure

initiated to “buy time” until the final diagnosis was made, the lung inflammatory process controlled, the native lung functions re-established and simultaneously avoiding the additional lung injury of the aggressive mechanical ventilation needed to support the respiratory failure.

Controversies exist regarding the need and safety of lung biopsy in ICU patients, in an era of better laboratory expertise and techniques that can contribute to a more accurate diagnosis in the majority of pulmonary diseases. Regarding this evidence, lung biopsies are still highlighted in some papers as the only way to perform the correct diagnosis in some patients, namely those with persistent ARDS with negative blood and BAL results, with potential impact on treatment decisions and on outcome.[15] The best lung biopsy technic for ICU patients seems to be the surgical one, with direct visualization of the lung for better representativeness of the tissue specimen. The best timing for its execution, seems to be the early phase of the disease, namely the first week of mechanical ventilation, a time where the initiation of new treatments can have impact on survival and morbidity.[15, 16] The biopsy can be safely done at patient bedside, being the pneumothorax, low-grade air leak and hemothorax the most frequent complications, with the potential of being life-

threatening.[15] In our case-series a trend to late biopsies was seen, all with associated complications, one of them with serious consequences leading to death.

The best treatment for AIP is still undefined, being steroids and other immunomodulatory treatments not free from criticism.[5] According to some guidelines, early diagnosis and early treatment is highly desirable. Although no controlled data on this issue exists, the use of pulsed intravenous methylprednisolone as the first line therapy for rapidly progressive interstitial lung diseases is recommended, with the possibility of adding a second immunosuppressive agent, such as cyclophosphamide, in severe cases.[17] As corticosteroids inhibit the production of a number of proinflammatory mediators, which are involved in the pathogeneses of AIP and can inhibit the fibrotic response, some authors advocate that corticosteroids effectiveness depends on the extent and ratio of inflammation to fibrosis at the time of diagnosis.[9] Maybe that is why some papers show lower mortality rates associated with early corticosteroids use.[9] Reflecting these controversies in this case series, we have used three different immunosuppressive regimens.

Less controversial is the need to support the acute respiratory failure with all the specific “weapons” of critical care medicine, namely ECMO, which, when correctly and safely performed by experienced teams, can be of great value to some patients.

Despite the experience of our ECMO Center, some unfavorable outcomes can still be seen, as it was the case of one of our patients, in a very complex situation of persistent severe respiratory failure requiring ECMO, shock, multiorgan dysfunction, ECMO induced coagulopathy, post operative care of emergent thoracic surgery requiring massive blood transfusion and all the other usual complexity typical of this patients, that make so challenging our work.

CONCLUSION

Our report highlights the potential role of VV-ECMO in the diagnosis and management of refractory severe acute respiratory failure associated to AIP. Effective extracorporeal gas exchange allows the minimization of further ventilator-induced lung injury, the establishment of AIP diagnosis, bridging the patient to diagnosis, definite treatment and eventual recovery.

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Current Knowledge

Acute Interstitial Pneumonia is a rare form of interstitial lung disease of unknown etiology with high mortality rate (>50%). The diagnostic work–up is very laborious, requiring the exclusion of other diseases, which ends with a lung biopsy – “idiopathic ARDS”. There is no proven effective treatment for AIP.

What this paper contributes to our knowledge

With Extracorporeal Membrane Oxygenation, minimization of ventilator-induced lung injury is possible. This permits establishment of difficult diagnosis and bridges patients to definite treatment and/or recovery.

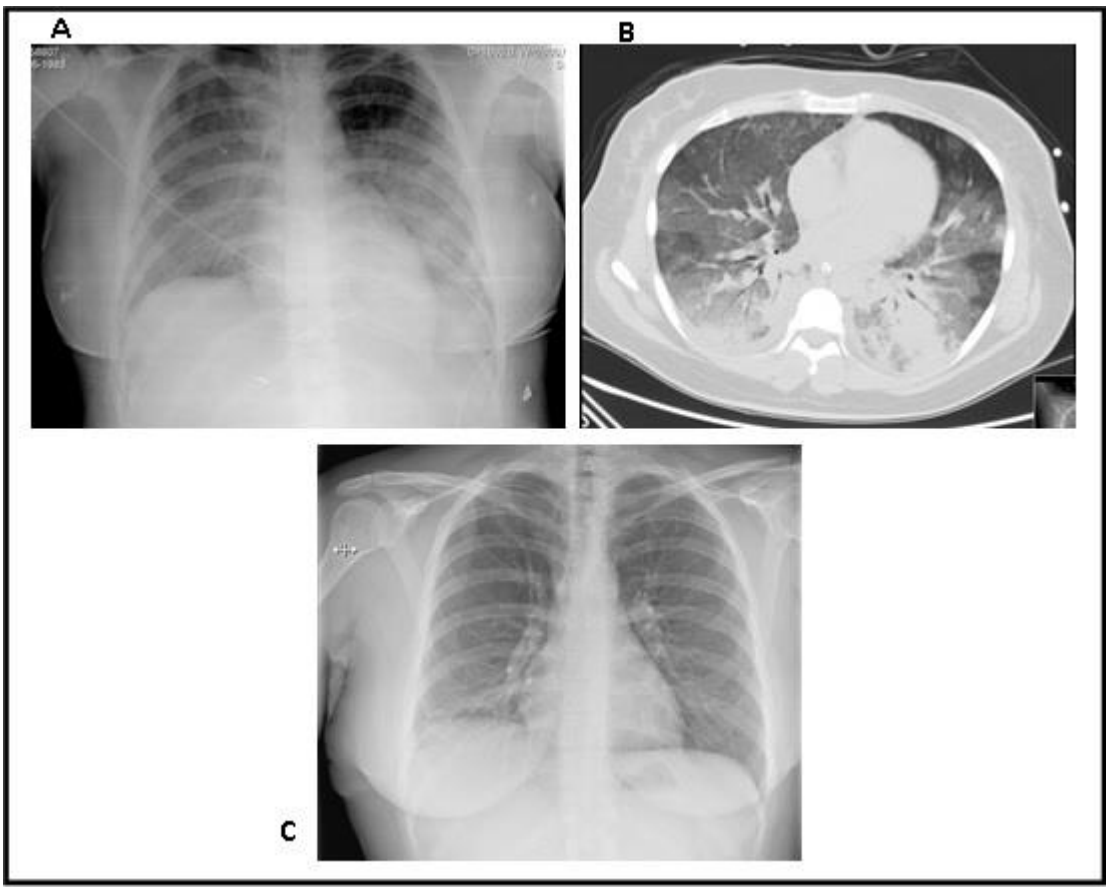

Figure 1 Chest X-ray (A) and Thoracic computed tomography (B) at admission and Chest X-ray of the last pulmonology consultation of patient 1. A. consolidation of the right and of the inferior two thirds of the left lungs. **B**. diffuse bilateral ground glass pattern and inferior lobar consolidation. **C**. Complete resolution of bilateral infiltrates.

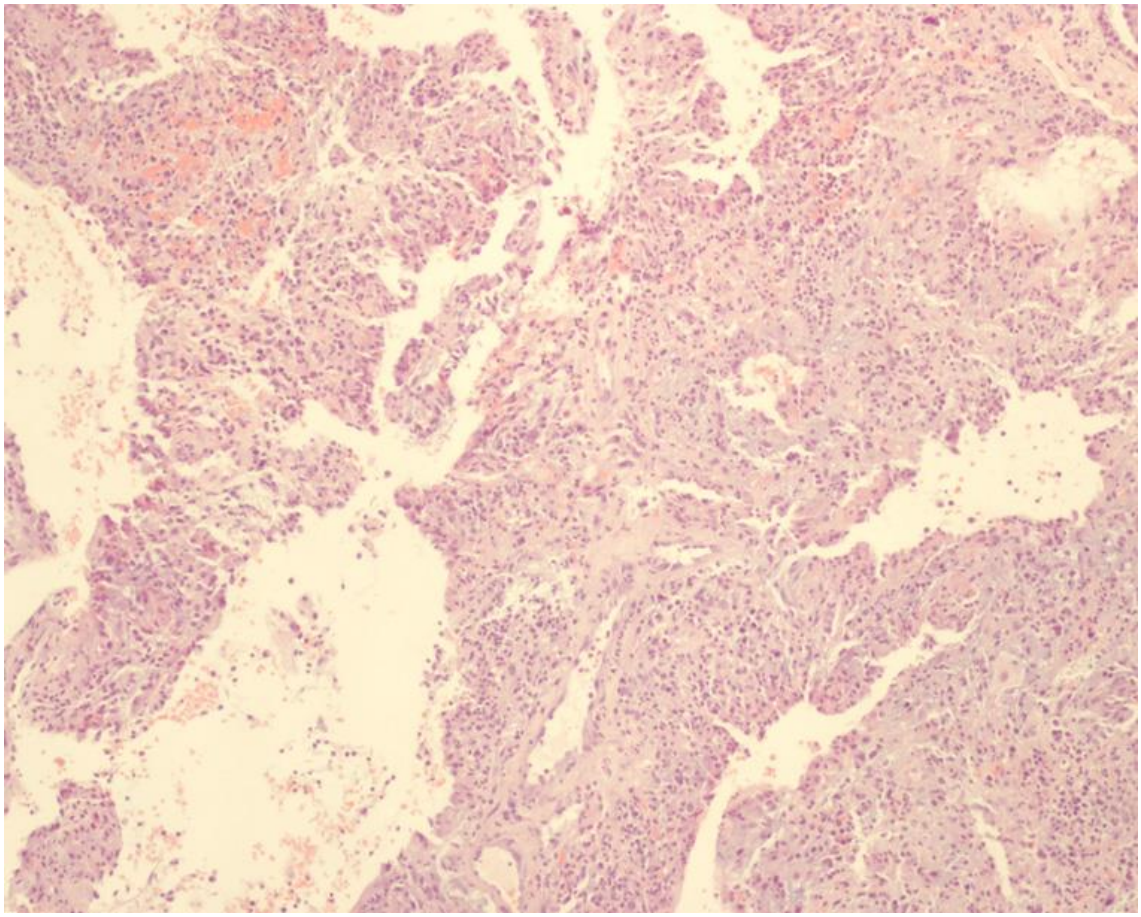

Figure 2 Lung biopsy of patient 1: Diffuse alveolar damage with uniform-appearing widning of alveolar septa by fibrosis and pneumocytes hyperplasia (hematoxylin and eosin-stained section; x100).

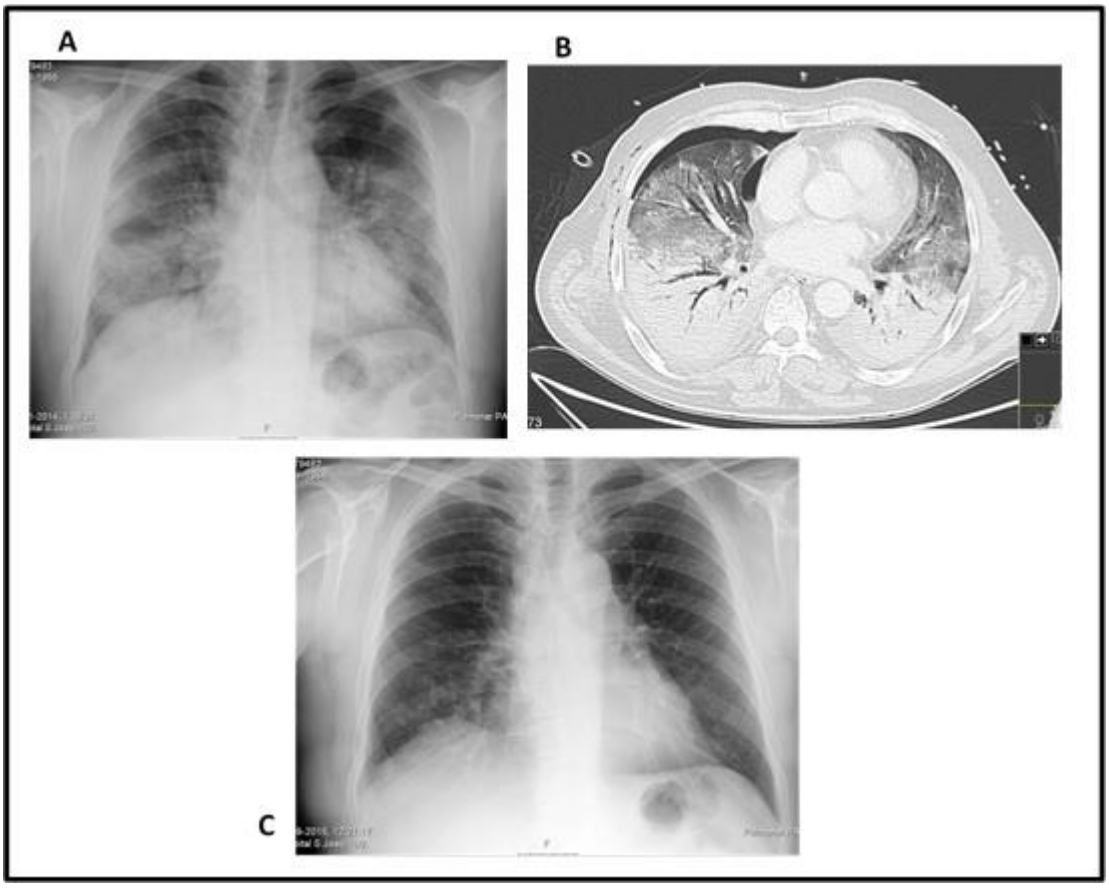

Figure 3 Chest X-ray (A) at admission at the Emergency room, Thoracic computed tomography (B) pre-ECMO and Chest X-ray of the last rheumatology consultation of patient 2. A. heterogeneous infiltrates in both inferior halves of the lungs. **B**. diffuse bilateral ground glass pattern with lobar consolidation and right pneumothorax. **C**. Complete resolution of bilateral infiltrates.

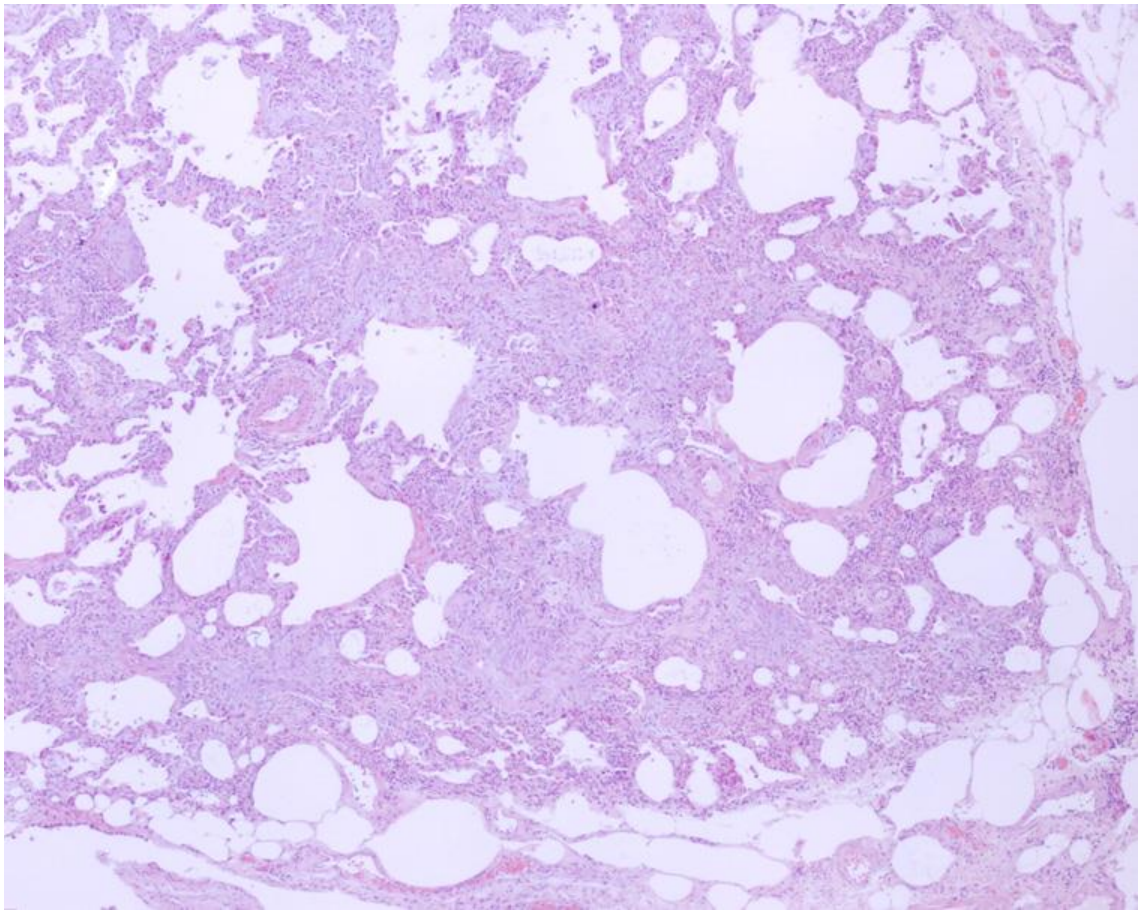

Figure 4 Lung biopsy of patient 2: Diffuse alveolar damage with alveolar collapse with interstitial fibroblast proliferation (hematoxylin and eosin-stained section; x40).

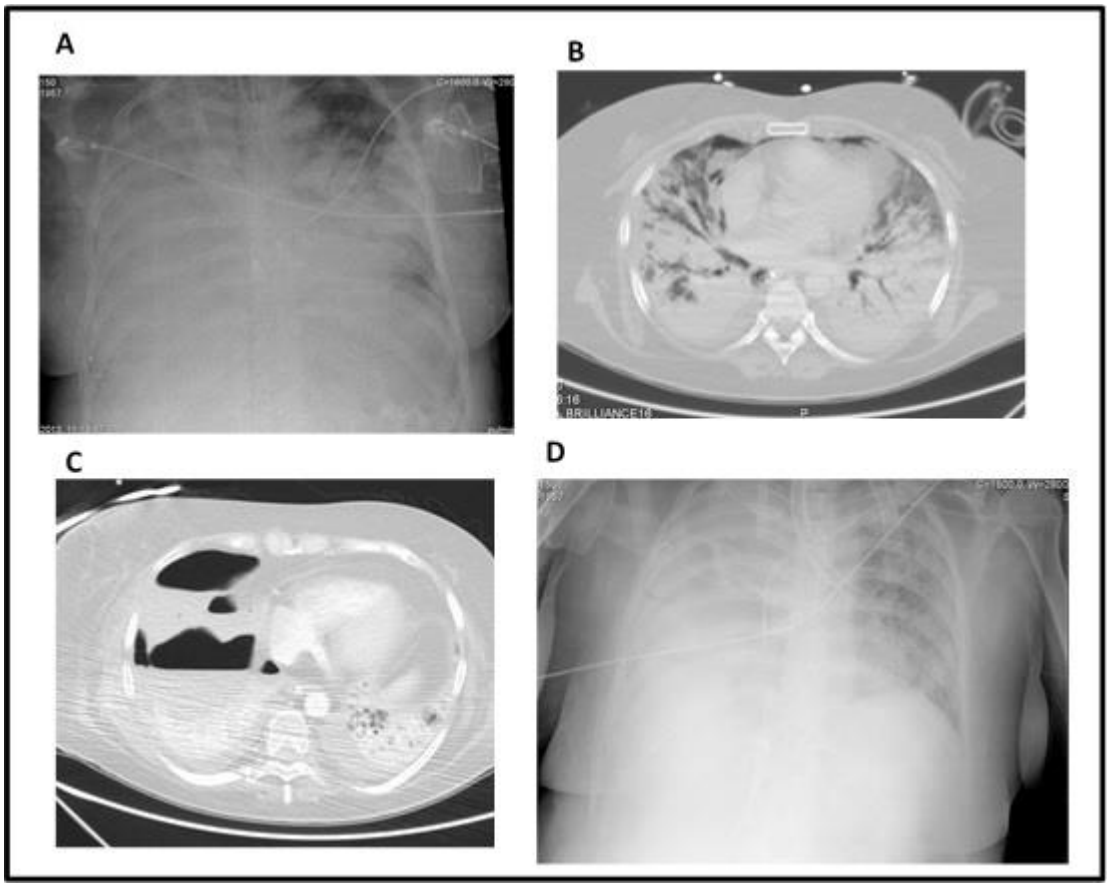

Figure 5 Chest X-ray (A) at Centro Hospitalar São João admission, 1st (B) and 4th (C) Thoracic computed tomography and last Chest X-ray of patient 3. A. diffuse bilateral infiltration. **B**. extended areas of consolidation and ground glass pattern more exuberant in the in the inferior pulmonary lobes. **C.** Persistent pneumothorax with hemothorax and persistent consolidation. **D**. diffuse bilateral infiltration

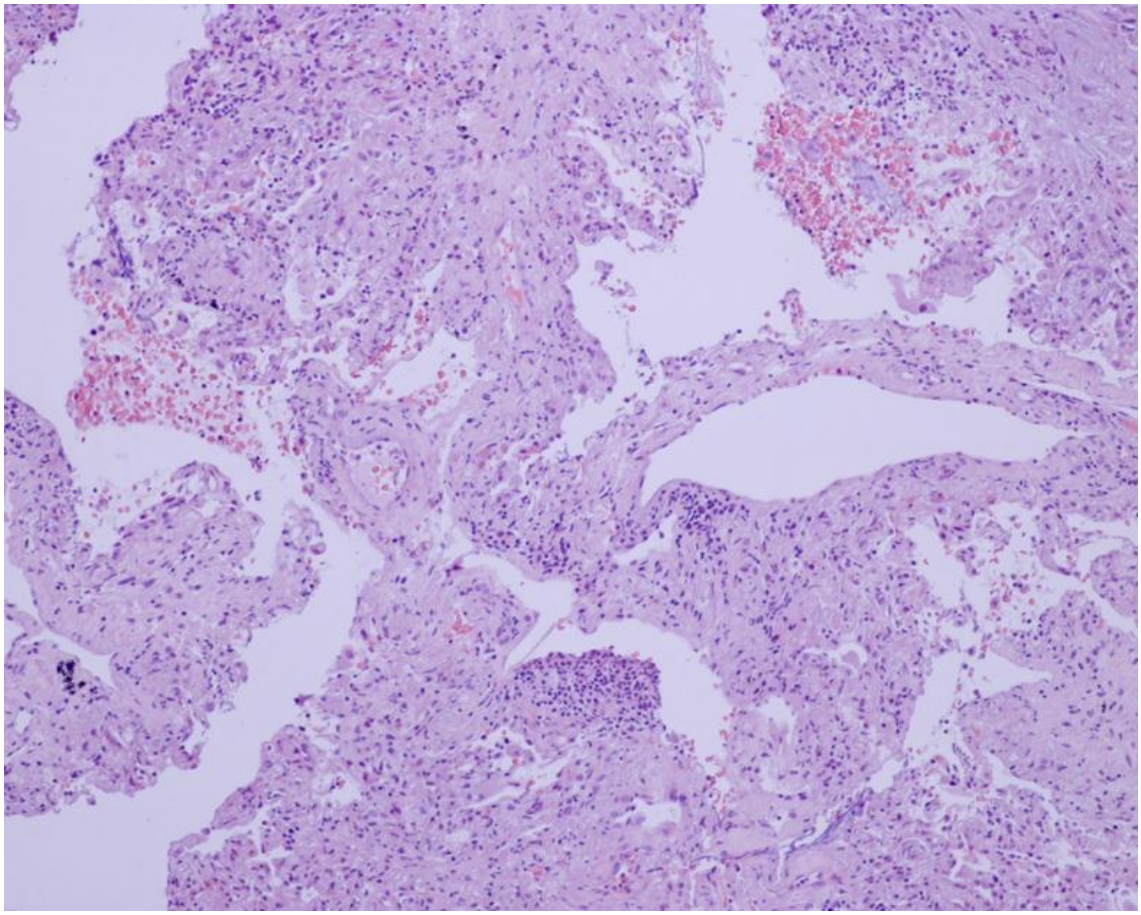

Figure 6 Lung biopsy of patient 3: Diffuse alveolar damage with extensive interstitial fibroblast proliferation along with alveolar collapse and scant inflammatory cells (hematoxylin and eosin-stained section; x100).

Table 1 - Characteristics of patients with AIP

Case	**1**	**2**	**3**
Gender	Female	Male	Female
Age	27	59	56
Comorbidities	Obesity	Ulcerative colitis	Unilateral renal agenesis, depressive disorder
Smoking	No	No	No
Hospital admission:			
Fever	Yes	Yes	Yes
Resp Rate	32	32	36
P/F	80	166	56
Rx	Consolidation	Consolidation	Consolidation
Initial diagnosis	Severe CAP	Severe CAP	Severe CAP
Surgical lung biopsy (SLB)	Yes	Yes	Yes
ICU to SLB (days)	8	14	25
ECMO to SLB (days)	2	9	25

Complications	Hemopneumothorax	Pneumothorax Bronchopleural fistula	Hemopneumothorax Bronchopleural fistula
Immunosuppression	Methylprednisolone + cyclophosphamide	Methylprednisolone	Methylprednisolone
Outcome	Alive	Alive	Dead

Table 2 - Characteristics of patients requiring ECMO

Case	1	2	3
Clinical deterioration (days)			
Symptoms to Hospital Admission	10	3	3
Hospital to ICU admission	0	0	0
ICU admission to ECMO	6	4	7
IMV to ECMO	6	3	7
SAPS II*	26	28	46†
SOFA Score*	9	10	12
Before ECMO			
Prone Positioning	No	Yes	Yes
Neuromuscular blockade	Yes	Yes	Yes
Tidal volume 6 ml/kg (predicted body weight)	Yes	Yes	Yes
Plateau pressure < 30	Yes	Yes	Yes
Permissive hypercapnia	Yes	Yes	Yes
Negative fluid balance	Yes	Yes	Yes
Acute circulatory dysfunction	No	No	Yes

Renal replacement therapy	No	No	No
Murray Score	3.5	3	3.25
During ECMO			
Prone Positioning	No	No	No
Renal replacement therapy	No	Yes	No
Rest ventilation	Yes	Yes	Yes
Acute circulatory dysfunction	No	No	Yes
Renal replacement therapy	No	Yes	No
Mechanical Ventilation (days)	26	35	73
ECMO (days)	15	15	73
ICU LOS (days)	28	37	73
ICU survival	Survivor	Survivor	Non-Survivor
Hospital Survival	Survivor	Survivor	Non-Survivor

IMV – Invasive Mechanical Ventilation; SAPS II – Simplified Acute Physiology Score II; SOFA Score – Sequential Organ Failure Assessment Score; LOS – Length Of Stay; *First day of ICU; †24 at 1st UCI

Table 3- ECMO characteristics

Case	**1**	**2**	**3**
Cannulas	RIJV - 17 Fr RFV - 23 Fr	RIJV - 19 Fr RFV - 25 Fr	RIJV - 19 Fr RFV - 25 Fr
ECMO Circuit	Rotaflow Maquet	Cardiohelp Maquet	Cardiohelp Maquet
Total number of oxygenators	1	2	3
Decannulation complications	None	None	Not applicable

RIJV - Right Internal Jugular Vein; RFV - Right Femoral Vein; Fr - French

Table 4 - Diagnostic work-up

All the patients had the following diagnostic work-up with negative our normal results
• Nasal swab for influenza and MRSA, blood cultures, sputum cultures, legionella and pneumococcal urinary antigen test, urine culture
• Serology's for CMV, EBV, herpes simplex 1 and 2, mycoplasma pneumonia, parvovirus B19, HIV, Hepatitis B and C
• Polymerase chain reaction (PCR) in blood for EBV, CMV, Influenza A e B, Herpes, Mycoplasma e Parvovirus B19
• BAL bacteriological, pneumocystis (immunofluorescence), tuberculosis, mycological, virological (sincicial respiratory virus, adenovirus, influenza A e B, parainfluenza 1, 2 and 3; CMV e Herpes Simplex).
• PCR in BAL for legionella, mycoplasma, chlamydia, coxiela, influenza A e B, CMV, Aspergilus
• Immunophenotyping of BAL with predominance of neutrophils or lymphocytes
• Normal determination of immunoglobulin's, complement, antinuclear antibodies, antibodies double stranded DNA, anti neutrophil antibodies, anti glomerular basement membrane antibodies

- PCR Influenza, Herpes Simplex, Clamydia, Micobacterium Tb, Mycoplasma, CMV, pneumocystis, legionella in lung biopsy
- Bacteriological and mycological studies in lung biopsy and pleural fluid
- Neoplastic cells, granulomatous lesions, vasculitis, CMV, Herpes simplex, study's by histochemical methods PAS, PAS-E, Grocott and Gram, in lung tissue
- Normal Brain Natriuretic Peptide
- Preserved left ventricular systolic function on transthoracic echocardiography

AGRADECIMENTOS

Ao Dr. Nuno Príncipe, pela excelente pessoa e orientador que foi comigo. Foi um prazer fazer este trabalho consigo, sempre em boa disposição. Obrigada pelas oportunidades que me deu "extra-tese" de "ser inglesa" e ver o que é e como funciona uma UCI. "O bichinho ficou cá dentro".

Ao doutor Roberto Roncon agradecer a disponibilidade sempre bem-disposta em ajudar e rever o trabalho, além da oportunidade de o acompanhar a uma sessão de esclarecimento sobre ECMO à minha tão querida cidade.

Ao Dr. Nuno Cortesão agradeço a indicação do Dr. Nuno Príncipe como orientador. Não poderia ter sido melhor a sugestão!

Aos meus pais, obrigada é pouco! Obrigada por serem quem são, mas acima de tudo por me permitirem e ensinarem a ser quem sou.

Ao meu irmão, obrigada por apoiares a "irmã chata".

Ao meu Rafael do coração, as palavras não chegam… por estares sempre lá, pela palavra certa na hora certa… por tudo… muito obrigada!

À minha Amiga Laura agradecer o constante apoio e paciência... a tua presença ativa em todas as fases foi importante para chegar a bom porto.

À minha Amiga Daniela, pelo apoio e conselhos sábios de quem por lá já passou... Obrigada!

"Aqueles que passam por nós, não vão sós, não nos deixam sós. Deixam um pouco de si, levam um pouco de nós."

Obrigada a todos!

ANEXOS

RESPIRATORY CARE

RESPIRATORY CARE welcomes original manuscripts related to the science of respiratory care. The Journal is published in both print and electronic formats and appears online at www.rcjournal.com.

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Registration of Clinical Studies

Ethics of Investigation

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APPENDICES

1. Preferred Pulmonary Terms and Symbols
2. Preferred Ventilator Mode Nomenclature

GENERAL GUIDELINES

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Manuscripts must conform to the International Committee for Medical Journal Editors' (ICMJE) Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals and to these instructions.

All authors must:

- Give consent to submission and publication of the work
- Have participated in the research and in the shaping of the manuscript
- Have read and approved the manuscript
- Be able to publicly discuss and defend the manuscript's content

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The contributions of each author must be listed on the Title Page (literature search, data collection, study design, data analysis, manuscript preparation, manuscript review).

Any editorial contributions made by outside organizations, persons, funding bodies, or persons employed by funding sources must be acknowledged on the Title Page.

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The conflict of interest policy of RESPIRATORY CARE is consistent with that of JAMA,[1] ICMJE,[2] CSE,[3] and WAME.[4] Disclosures must be made at the time of submission and must be indicated on the title page. The Editor will decide whether the presence of conflicts of interest affects the suitability of the manuscript for publication.

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- Being an employee of a company that designs, manufactures, or sells respiratory care equipment
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Disclosure of relationships will not necessarily affect the decision to publish a manuscript. Having such relationships is not considered unethical. However, not disclosing such relationships *is* unethical.

1. Flanagin A, Fontanarosa PB, DeAngelis CD. Update on JAMA's conflict of interest policy. JAMA 2006;296(2):220-221. doi: 10.1001/jama.296.2.220
2. International Committee of Medical Journal editors. Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals. *Updated December 2014. Accessed January 27, 2015*

3. Council of Science Editors. Editorial policy statements approved by the CSE Board of Directors. http://www.councilscienceeditors.org/i4a/pages/index.cfm?pageid=3332 *Accessed January 27, 2015*
4. World Association of Medical Editors. Recommendations on publication ethics policies for medical journals. http://www.wame.org/about/recommendations-on-publication-ethics-policie *Accessed January 27, 2015*

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Individuals who provided paid contributions to the paper (including writers, statisticians, epidemiologists, and any others involved with data management and analyses) may meet the criteria for authorship. If they do not, they should be listed in the Acknowledgment section.

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For additional information related to relationships between authors and industry, refer to: Fontanarosa PB, Flanagin A, DeAngelis CD. Reporting conflicts of interest, financial aspects of research, and role of sponsors in funded studies. JAMA 2005;294(1):110-111 doi:10.1001/jama.294.1.110.

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Authors must comply with the Health Insurance Portability and Accountability Act (HIPAA). This applies to any information (eg, text, photo, or radiograph) that could potentially identify a patient or subject. Authors must provide written consent from the individual, next of kin, or guardian.

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A report of an original investigation. Must include: Title Page, Structured Abstract, Key Words, Introduction, Methods, Results, Discussion, Conclusions, References, and Quick Look. May also include Tables, Figures, and Acknowledgments. Supplementary Material, such as a survey instrument or details related to the methods, may be provided for online publication only. Authors of randomized clinical trials must follow the CONSORT guidelines.

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A comprehensive review of the literature. Must include: Title Page, Outline, Narrative Abstract, Key Words, Introduction, Review of the Literature, Summary, and References. May also include Tables, Figures, Acknowledgments, and Supplementary Material for online publication only. Review articles are generally written by persons with established expertise in the subject area. Narrative reviews are acceptable, but systematic reviews are preferred. A systematic review and meta-analysis may be prepared as an original research paper.

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Indicate the specific contributions of each author to the paper:

- Literature search
- Data collection
- Study design
- Analysis of data
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- Review of manuscript

Title Page must also include:

- Name and location of the institution where the study was performed
- Name, date, and location of any meeting or forum where research data were previously presented, and who presented
- Sources of financial support
- Conflict of interest statement. If no potential conflicts of interest exist, a statement to this effect must be included

Identify corresponding author and provide contact information

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Structured Abstracts include these sections: Introduction, Methods (how the study was performed, including the number of subjects), Results (brief summary of the data), and Conclusions. Abstracts must not contain any facts or conclusions that do not also appear in the text.

Narrative Abstracts are written as a narrative paragraph and fewer than 300 words.

Include the Abstract in the main manuscript text file.

Key Words

List 6–10 key words or phrases that reflect the content of your manuscript. Key words may be selected from the Medical Subject Headings (MeSH terms) used by MEDLINE.

Text

Double-space all text (including Tables and References). Number the pages. Center and bold 1st level headings; flush-left and bold 2nd level headings; indent and bold 3rd level headings.

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EndNote contains the style for RESPIRATORY CARE:
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Journal Article
Article. List the first 6 authors, then "et al". Exception – in a paper with 7 total authors, list all 7:

Wallet F, Delannoy B, Haquin A, Debord S, Leray V, Bourdin G, et al. Evaluation of recruited lung volume at inspiratory plateau pressure with PEEP using bedside digital chest x-ray in patients with acute lung injury/ARDS. Respir Care 2013;58(3):416-423.

Corporate authors:
Chang SY, Dabbagh O, Gajic O, Patrawalla A, Elie MC, Talmor DS, et al; on behalf of the United States Critical Illness and Injury Trials Group: Lung Injury Prevention Study Investigators (USCIITG-LIPS). Contemporary ventilator management in patients with and at risk of ALI/ARDS. Respir Care 2013;58(4):578-588.

Article in a supplement:
del Giudice MM, Leonardi S, Ciprandi G, Galdo F, Gubitosi A, La Rosa M, et al. Probiotics in childhood: allergic illness and respiratory infections. J Clin Gastroenterol 2012;46(Suppl):S69-S72.

Corrected article:
Mireles-Cabodevila E, Hatipoğlu U, Chatburn RL. A rational framework for selecting modes of ventilation. Respir Care 2013;58(2):348-366. Erratum in: Respir Care 2013;58(4):e51.

Articles e-published online ahead of print:
Nozoe M, Mase K, Murakami S, Okada M, Ogino T, Matsushita K, et al. The relationship between spontaneous expiratory flow-volume curve configuration and airflow obstruction in elderly COPD patients. Respir Care 2013 [Epub ahead of print] doi: 10.4187/respcare.02296

Abstract. Citing abstracts is highly discouraged. Those more than 3 years old should not be used:

Blakeman TC, Rodriquez D, Branson RD. Evaluation of five chemical oxygen generators (abstract). Respir Care 2012;57(10):1751.

Editorial:
Rouby JJ, Arbelot C, Brisson H, Lu Q, Bouhemad B. Measurement of alveolar recruitment at the bedside: the beginning of a new era in respiratory monitoring? (editorial). Respir Care 2013;58(3):539-542.

Editorial, no author given:
Asthma: not just for kids (editorial). Johns Hopkins Med Lett Health After 50 2012;24(8):6.

Letter:
Haynes JM. Expiratory reserve volume maneuver may be the preferred method for some patients during spirometry testing (letter). Respir Care 2013;58(2):e14-e15. author response: e15.

Books
Book. Corresponding pages should be cited whenever reference is made to specific statements or content:

Wilkins RL, Stoller JK, Kacmarek RM. Egan's fundamentals of respiratory care, 9th edition. St Louis: Mosby|Elsevier; 2009:400-404, 917.

Corporate authors:
Panel on Understanding Cross-National Health Differences Among High-Income Countries; Committee on Population Division of Behavioral and Social Sciences and Education; Board on Population Health and Public Health Practice; National Research Council; Institute of Medicine of the National Academies. U.S. health in international perspective: shorter lives, poorer health. Washington, DC: National Academies Press; 2013.

Chapter:
Heffner JE. Chronic obstructive pulmonary disease. In: Hess DR, MacIntyre NR, Mishoe SC, Galvin WF, Adams AB. Respiratory care principles and practice, 2nd edition. Sudbury, MA: Jones & Bartlett; 2012:735-764.

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Static material must be listed in the References and include the digital object identifier (DOI). Use a DOI for content published online only. Because these items are static, there is no need to include an access date:

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News sources:
Productivity at work improved for sleep apnea patients using CPAP. Medical News Today: April 15, 2013. http://www.medicalnewstoday.com/releases/259016.php *Accessed January 27, 2015.*

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Manuscript accepted but not yet published. A copy of cited unpublished manuscripts should be uploaded:

Strickland SL. Year in review: airway clearance. Respir Care 2015 (in press).

Research not yet accepted for publication should be cited in the text as personal communication. You must obtain written permission from the authors to cite unpublished data.

"Recently, Smith et al found this treatment effective in 45 of 83 patients (Smith R, personal communication, 2015)."

Your own unpublished work that has not been accepted for publication should be mentioned in the text: "We found this type of aerosol is no more effective than placebo (unpublished data)."

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Write 2–4 declarative sentences summarizing current understanding of the topic being studied. Think of it as defining the state of the art or establishing equipoise.

DO – State the current evidence on the subject
DO – Provide clear declarative statements

DO NOT – Ask a question
DO NOT – State what is not known or that a topic "requires further study" or "remains to be elucidated"

What This Paper Contributes To Our Knowledge

Write 2–4 declarative sentences summarizing the take-home message of the study. Use past tense. Provide only information supported by the data. Do not overstate the importance of your results and do not suggest further research; this section is about the paper at hand.

DO – Describe the main take-home points and findings
DO – Describe the environment (eg, if a lung model was used)
DO – Write statements that can be understood without re-stating the data

DO NOT – Allude to further work that needs to be accomplished
DO NOT – Overstate the importance of the findings or speculate. (eg, The use of APRV improved oxygenation [data from the study]. Due to improved oxygenation, APRV might reduce mortality in ARDS [speculation]).
DO NOT – Include statistics or numerical data

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Example Quick Look

Current knowledge
The endotracheal tube cuff allows positive pressure ventilation and protects the airway from aspiration. Standard cuff pressures of 20–30 cm H_2O are typically used to prevent leakage of fluid around the cuff and to prevent mucosal injury. In recent years, laboratory evaluations of cuffs in glass models have demonstrated reduced fluid leakage, but clinical studies have not confirmed these findings in vitro.

What this paper contributes to our knowledge
In a realistic viscoelastic model of the trachea, endotracheal tube cuffs of different designs provided an adequate seal at a pressure of 12 cm H_2O. With increased PEEP, higher cuff pressures were required. Tubes with a subglottic suction channel performed best in the lateral position.

Figures

Use of Figures is encouraged. Include only Figures that clarify and augment the text. All Figures must be called-out in the text. Number consecutively as Figure 1, Figure 2, etc.

The first Figure in the report of a clinical trial must be a flow diagram showing phases of the trial (ie, enrollment, subject allocation, follow-up, and analysis). See CONSORT.

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Minimum 1200 dpi required for line art (graphs or drawings), 600 dpi required for images with labeling, and 300 required dpi for images (color or black and white) without labeling.

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Any identifiable image must be accompanied with written consent (see Ethics of Investigation).

Identify stains and magnifications for all photomicrographs.

Arrows, numbers, letters, lines and other markers used to identify parts of a Figure must be defined in the Figure Legend.

Figures are redrawn for stylistic consistency. Contact the Editorial Office if you would like assistance in creating an original Figure.

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Every Figure must have a legend explaining every component of the Figure. The legend should be self-sufficient and allow the reader to understand the figure without referring to the text.

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Equations

Write equations as normal text. Do not use the equation function in Microsoft Word or other mathematics software.

Statistical Analysis

For original research papers, the Editor recommends working with a biostatistician to assure appropriate analysis. The Editor may request a letter from your biostatistician assuring that the analysis is correct.

In the Methods section, identify the statistical tests used to analyze the data. Indicate the *P*-value that was taken to indicate significance. State whether tests were one-tailed or two-tailed; justify the use of one-tailed tests. Identify post-hoc analyses. Cite references to support your choice of tests and identify any statistical analysis software used. Indicate how the power analysis was conducted to determine appropriate sample size.

Report measurements with an appropriate degree of precision. Report both numerators and denominators for percentages.

For continuous data, description statistics should be expressed as mean and standard deviation (not standard error). For ordinal data, median and interquartile range should be reported.

For ratios (odds ratio, relative risk, etc.), provide 95% confidence interval.

Report actual *P* values rather than thresholds. Example: write "$P = .18$", not "$P > .05$" or "P = NS." Note that *P* cannot equal 0 or 1.

P values should be expressed to 2 digits for $P \geq .01$. $P < .001$, rather than $P < .0001$ or $P = .00001$. If $P > .99$, $P = .999$ for example, it should be expressed as $P > .99$.

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Use the Preferred Pulmonary Terms and Symbols (Appendix 1). Use abbreviations sparingly. Do NOT invent new abbreviations for terms with long-held standard abbreviations. Use an abbreviation only if the term occurs 4 or more times in the manuscript.

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Appendix 1. Preferred Terms and Symbols

Primary Symbols	
S	Saturation
C	content
F	Fractional concentration
T	Temperature
P	Pressure
V	Volume
Qualifying symbols are denoted by subscripted character; uppercase for values in the lungs and lowercase for values in the blood	
A	Alveolar
I	Inspired
B	Barometric
L	Lung
D	Dead space
T	Tidal
E	Expired
$\overline{E}$	Mixed expired
a	Arterial
b	Blood
c	Capillary
v	Venous
c'	Pulmonary end-capillary
$\bar{v}$	Mixed venous
t	Time
Pulmonary Function testing	
D/V_A	
DLCOsb	Lung diffusing capacity determined by the single-breath technique
ERV	Expiratory reserve volume
$FEF_{25-75\%}$	Forced expiratory flow over the middle half of the FVC
FEV_1	Forced expiratory volume in the first second

FEV_t	Forced expiratory volume in the first *t* seconds
FRC	Functional residual capacity
FVC	Forced vital capacity
IC	Inspiratory capacity
IRV	Inspiratory reserve volume
IVC	Inspiratory vital capacity
MVV	Maximal voluntary ventilation
PEF	Peak expiratory flow
RV	Residual volume
RV/TLC%	Residual volume expressed as percent of TLC
TGV	thoracic gas volume
TLC	Total lung capacity
V_A	Alveolar gas volume
VC	Vital capacity
Ventilation	
f	Breathing frequency
V_T	Tidal volume
$\dot{V}_A$	Alveolar ventilation
$\dot{V}_D$	Dead space ventilation
$\dot{V}_{CO_2}$	Carbon dioxide production
$\dot{V}_{O_2}$	Oxygen consumption
V/Q	ventilation-perfusion ratio
Pulmonary mechanics	
C	Compliance
E	Elastance
Gaw	Airway conductance
$P_{0.1}$	Airway occlusion pressure at 0.1 s
P_A	Alveolar pressure
Paw	Pressure in the airway
$\bar{P}aw$	Mean pressure
PE_{max}	Maximal expiratory pressure
P_{es}	Esophageal pressure
PI_{max}	Maximal inspiratory pressure
PIP	Peak inspiratory pressure
P_L	Transpulmonary pressure
P_{pl}	Intrapleural pressure
Pplat	Plateau pressure
R	Resistance
Raw	Airway resistance
R_E	Expiratory resistance
R_I	Inspiratory resistance
sGaw	Specific airway conductance
WOB	Work of breathing

Blood gases	
$\bar{P}$	Mean pressure
P_{O_2}	Partial pressure of oxygen
P_{aO_2}	Arterial partial pressure of oxygen
P_{AO_2}	Alveolar partial pressure of oxygen
P_{aCO_2}	Arterial partial pressure of carbon dioxide
P_{ACO_2}	Alveolar partial pressure of carbon dioxide
P_{ETCO_2}	End-tidal partial pressure of carbon dioxide
$P_{\bar{E}CO_2}$	Mixed exhaled partial pressure of carbon dioxide
$P_{\bar{v}CO_2}$	Mixed venous partial pressure of oxygen
P_{tcO_2}	tcPO2 transcutaneous partial pressure of oxygen
P_{tcCO_2}	tcPO2 transcutaneous partial pressure of carbon dioxide
$P(A\text{-}a)O_2$	Alveolar-arterial PO_2 difference
$P(a/A)O_2$	Arterial to alveolar PO_2 ratio
C_{aO_2}	Arterial oxygen content
$C_{\bar{v}CO_2}$	Mixed venous oxygen content
$C_{c'O_2}$	Pulmonary capillary oxygen content
S_{aO_2}	Arterial oxygen saturation
S_{pO_2}	Oxygen saturation as measured by pulse oximetry
$S_{\bar{v}CO_2}$	Mixed venous oxygen saturation
$C(a - \bar{v})O_2$	Arterial-venous oxygen content difference
pH	
$\dot{Q}$	Blood flow
$\dot{Q}_T$	Cardiac output
Q	Blood volume
$\dot{Q}_S/\dot{Q}_T$	Shunt fraction
R	Respiratory quotient
Ventilator Nomenclature	
APRV	Airway pressure release ventilation
AVAPS	Average volume assured pressure support
CMV	Continuous mandatory ventilation (rather than assist-control)
CPAP	Continuous positive airway pressure
EPAP	Expiratory positive airway pressure
F_{IO_2}	Fraction of inspired oxygen (expressed as a fraction, not percent)
HFJV	High frequency jet ventilation
HFOV	High frequency oscillatory ventilation
I:E	Inspiratory time to expiratory time ratio
IPAP	Inspiratory positive airway pressure
NAVA	Neurally adjusted ventilatory assist
NIV	Noninvasive ventilation (rather than NPPV)

PAV	Proportional assist ventilation
PC-CMV	Pressure-control continuous mandatory ventilation (rather than pressure assist-control)
PC-IMV	Pressure-control intermittent mandatory ventilation
PCIRV	Pressure control inverse ration ventilation
PEEP	Positive end-expiratory pressure
PRVC	Pressure regulated volume control
PSV	Pressure support ventilation
T_E	Expiratory time
T_I	Inspiratory time
VC-CMV	Volume-control continuous mandatory ventilation (preferred rather than volume assist-control)
VC-IMV	Volume-control intermittent mandatory ventilation
VDR	Volumetric diffusion respiration
VS	Volume support
Other preferred terms	
6MWD	Six-minute walk distance
6MWT	Six-minute walk test
AARC	American Association for Respiratory Care
ABG	Arterial blood gas
ALS	Amyotrophic lateral sclerosis
ARDS	Acute respiratory distress syndrome
ARF	Acute respiratory failure
ATPS	Ambient temperature and pressure saturated
BMI	Body mass index
BPAP	Bilevel positive airway pressure (rather than BiPAP)
BTPS	Body temperature and pressure saturated
CCI	Chronic critical illness
CDC	Centers for Disease and Prevention
CF	Cystic fibrosis
CI	Confidence interval
CMS	Centers for Medicare and Medicaid services
CO	Carbon monoxide
COPD	Chronic obstructive pulmonary disease
CPR	Cardiopulmonary resuscitation
CPT	Chest physical therapy
CT	Computed tomography
DNR	Do not resuscitate
DPI	Dry powder inhaler
EAdi	Electrical activity of the diaphragm
EBUS	Endobronchial ultrasound
ECLS	Extracorporeal life support
ECMO	Extracorporeal membrane oxygenation
EIB	Exercise-induced bronchospasm

FDA	US Food and Drug Administration
HFNC	High flow nasal cannula
HME	Heat and moisture exchanger
HMEF	Heat and moisture exchanging filter
HRCT	High resolution computed tomography
Hz	Hertz
IBW	Ideal body weight
IBW	Ideal body weight
ICP	Intracranial pressure
ICU	Intensive care unit
ICU	Intensive care unit
ILD	Interstitial lung disease
IQR	Interquartile range
MDI	Metered dose inhaler
MRI	Magnetic resonance imaging
NG	Nasogastric (tube)
NIH	National Institutes of Health
NO	Nitric oxide
OSA	Obstructive sleep apnea
PAP	Positive airway pressure
PEP	Positive expiratory pressure
PFT	Pulmonary function test or testing
PMV	Prolonged mechanical ventilation
PSG	Polysomnography
r	Correlation coefficient
RSBI	Rapid shallow breathing index
RT	Respiratory therapist
SBT	Spontaneous breathing trial
SD	Standard deviation
SE	Standard error
STPD	Standard temperature and pressure dry
TBLB	Transbronchial lung biopsy
TBNA	Transbronchial needle aspiration
VA	Veterans Administration
VAE	Ventilator-associated event
VAC	Ventilator-associated condition
VAP	Ventilator-associated pneumonia
VILI	Ventilator induced lung injury

Appendix 2. Preferred Ventilator Mode Nomenclature

Preferred Term	**Preferred Symbol**	**Intended Meaning**	**Similar Terms to be Avoided**
Volume Control Continuous Mandatory Ventilation	VC-CMV	Mechanical ventilation with preset tidal volume and inspiratory flow. Every breath is mandatory (ie, inspiration is patient or machine trigged and machine cycled).	Assist/Control, A/C, CMV, Volume Assist/Control, Volume Control, Volume Limited Ventilation, Volume Control Ventilation, Controlled Ventilation, Volume Targeted Ventilation
Volume Control Intermittent Mandatory Ventilation	VC-IMV	Mechanical ventilation with preset tidal volume and inspiratory flow. Spontaneous breaths (ie, inspiration is patient triggered and patient cycled) can exist between mandatory breaths.	Synchronized Intermittent Mandatory Ventilation, SIMV
Pressure Control Continuous Mandatory Ventilation	PC-CMV	Mechanical ventilation with preset inspiratory pressure and inspiratory time. Every breath is mandatory (ie, patient or machine trigged and machine cycled).	Assist/Control, A/C, CMV, Pressure Assist/Control, Pressure Control, Pressure Limited Ventilation, Pressure Control Ventilation, Pressure Targeted Ventilation

Pressure Control Intermittent Mandatory Ventilation	PC-IMV	Mechanical ventilation with preset inspiratory pressure and inspiratory time. Spontaneous breaths (ie, inspiration is patient triggered and patient cycled) can exist between mandatory breaths.	Synchronized Intermittent Mandatory Ventilation, SIMV
Continuous Spontaneous Ventilation	CSV	Any mode of mechanical ventilation where every breath is spontaneous (ie, patient triggered and patient cycled)	Spont
Mandatory Breath	None	A breath type during mechanical ventilation for which inspiration is machine triggered and/or machine cycled.	Machine breath, mechanical breath
Spontaneous Breath	None	A breath type for which inspiration is both patient-triggered and patient cycled. Applies to assisted or unassisted breathing.	N/A
Assisted Ventilation or Breath	None	Ventilation or breath for which a machine provides some or all of the work of breathing.	Patient triggered ventilation or breath

Patient Triggered Breath	None	A breath that is initiated by the patient, independent of ventilator settings for frequency.	Patient assisted breath, assisted breath
Auto-triggering	None	Unintended initiation of breath delivery by the ventilator, eg, by an external disturbance such as movement of the breathing tube or an inappropriate trigger sensitivity setting.	Auto-cycling