Early View

Invited review

ERS International Congress 2023: highlights from the Respiratory Intensive Care Assembly

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Title:
ERS International Congress 2023: highlights from the Respiratory Intensive Care Assembly

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Abstract:

Early Career Members of Assembly 2 (Respiratory Intensive Care) attended the 2023 European Respiratory Society Annual Congress in Milan. The conference covered acute and chronic respiratory failure. Sessions of interest to our Assembly members and to those interested in respiratory critical care are summarized in this article.

Summary of the take home messages:

Latest updates in respiratory intensive care, in particular ARDS and mechanical ventilation, presented at the 2023 European Respiratory Society Annual Congress in Milan and summarized by the Early Career Members of Assembly 2 (Respiratory Intensive Care).

Introduction

Respiratory failure is the principal cause of intensive care admission and leads to chronic impairment. This report by the early career members of Assembly 2 of the European Respiratory Society summarizes the latest updates in respiratory intensive care that have been presented by international experts at the European Respiratory Society International Congress in Milano in 2023.
This work completes and updates the information provided during the European Respiratory Society Annual Congress 2022 (1) and from the Respiratory Failure and Mechanical Ventilation 2022 Conference (2).

The sessions covered advances in mechanical ventilation, addressing the place of non-invasive mechanical ventilation, high-flow nasal cannula (HFNC) and positive airway pressure both in acute and chronic respiratory care; and also updates from the Global Consensus Conference on acute respiratory distress syndrome (ARDS), summary of COVID-19 recommendations on management of complex pleural diseases and factors linked to the quality of survival after intensive care unit (ICU) admissions for ARDS.

**Acute respiratory distress syndrome: Update and future treatment**

Lorraine Ware (Nashville, United States of America) presented the new proposed global definition of ARDS, focussing on different criteria and limitations on Berlin Definition (3) adding some minor modifications: The new definition of ARDS includes patients that require high flow nasal oxygen at >30 L/min and the SpO\textsubscript{2}/FiO\textsubscript{2} as a non-invasive alternative to PaO\textsubscript{2}/FiO\textsubscript{2} for the oxygenation criteria. (4,5). The global expert committee recommended the use of ultrasound as an alternative of radiographic imaging for diagnosing alveolar infiltrates. (6)

Christian Karagiannidis (Cologne, Germany) presented the new guidelines by European Society of Intensive Care Medicine guidelines for ARDS and focused on the non-pharmaceutical treatments of ARDS (figure 1). Future randomized trials are needed to assess whether non-invasive respiratory support techniques (i.e. HFNC, CPAP or NIV) reduces mortality or intubation rate (7). NIV should be carefully applied in ARDS patients as it might lead to patient self-inflicted lung injury (8). High-pressure lung recruitment manoeuvres are currently not recommended in ARDS patients. (9–12).

Danny McAuley (Belfast, United Kingdom) highlighted the importance of identifying the two main phenotypes in ARDS: 1) hyper-inflammatory (high IL-6, IL-8, sTNFR1) and 2) hypo-inflammatory (low bicarbonate, protein C, systolic blood pressure), in order to personalize medical treatments in critical care. (13,14) According to a retrospective analysis hyper-inflammatory phenotypes may benefit from simvastatin administration (15).

Leo Heunks (Amsterdam, Netherlands) concluded the session by presenting the WEAN-SAFE study. The 90-day mortality rate was nearly 30% in patients who received mechanical ventilation for at least two days. The modifiable factors for weaning success were the level of sedation and the delay of weaning initiation (16).
Take home messages:

- The Global Consensus Conference on ARDS recommended an update of the Berlin definition criteria by adding ultrasound, $S_pO_2/FiO_2$ ratio and the use of high flow nasal oxygen in the diagnosis of ARDS patients.
- Future studies focusing on sub-phenotypes among ARDS patients are needed to develop individuals-targeted treatments.
- Weaning success rates may be improved by optimizing the sedation levels and avoiding weaning delay.

**Non-invasive and invasive mechanical ventilation in acute respiratory diseases**

Martin Witzenrath (Berlin, Germany) discussed therapeutic targets for endothelial dysfunction in ventilator induced lung injury. Adrenomedullin reduced endothelial permeability in mice models (17) and adrenomedullin-targeting antibody (Adrecizumab) has been tested in Phase IIa trials. (18) New therapies targeting C5a and Vilobelimab reduced endothelial dysfunction in mice models and improved outcomes in ventilated COVID-19 patients respectively. (19) The role of Tie-2 (20), TRPV4 (21) and B-MAL (22) in developing ventilator induced lung injury have been explored in-vivo and are future potential therapeutic targets.

Lise Piquilloud (Lausanne, Switzerland) provided an evidence-based medicine update for ARDS. New recommendations by expert consensus suggested broadening the ARDS diagnostic criteria to include non-intubated patients, lung ultrasound findings and modified criteria for resource variable settings. (4) The updated European Society of Intensive Care Medicine guidelines recommended the use of controlled tidal volumes (4-8ml/kg) and prone positioning but recommended against routine use of neuromuscular blockers. (7)

Christian Karagiannidis (Cologne, Germany) specified that extracorporeal membrane oxygenation (ECMO) should be managed in experienced centers using the EOLIA trial method and criteria (10) for an acceptable outcome. (23) Prone positioning should be applied in ECMO patients (24) whereas use of extracorporeal CO$_2$ removal is not recommended (11) and the use of corticosteroid is of uncertain usefulness and should be studied further. (25)

Leo Heunks (Rotterdam, Netherlands) set out the steps to optimize weaning from mechanical ventilation. Firstly, it is necessary to quantify effort to limit the adverse effects of high or low drive using the occlusion pressure ($P_{occ}$). (26) When weaning eligibility criteria is obtained, zero assist spontaneous breathing test (t-tube trial) (27) should be perform with the
lowest possible level of sedation and without delay. (16) But more importantly underlying cause of weaning failure must be identified and treated accordingly.

Take home message:

Controlled tidal volumes and prone positioning are recommended for patients with severe ARDS whereas use of neuromuscular blockers and extracorporeal CO2 removal are not recommended.

Hot topics: non-invasive high-flow nasal therapy or positive pressure ventilation in acute and chronic respiratory care

Lara Pisani (Italy, Bologna) emphasized that HFNC therapy is widely employed in acute respiratory failure. This therapy increases expiratory airway resistance, thus extending respiratory cycles (28), additionally it decreases CO2 re-breathing by dead-space washout and applies positive nasopharyngeal pressure (29), which collectively yield improved clinical outcomes. Physiological studies have revealed that a greater prong/nare area ratio of the cannula and maintaining mouth closure during therapy can enhance nasopharyngeal pressure (30–32).

Claudia Crimi (Italy, Catania) elucidated the various physiological and clinical benefits of CPAP and NIV in the treatment of acute respiratory failure (33,34). Emerging evidence suggests that NIV strategies, compared to standard oxygen therapy, are significantly associated with a reduced risk of death in de novo acute hypoxemic respiratory failure (35). A thorough physical examination (assessing respiratory effort) and vigilant monitoring are crucial for optimizing treatment, mitigating the risk of treatment failure and patient self-inflicted lung injury, and avoiding delays in intubation (36,37).

Rebecca D’Cruz (London, UK) discussed flow treatment in chronic respiratory care. High-flow treatment has long been studied in patient with airways disease (38), reducing PaCO2 in patients with chronic hypercapnia (39). Furthermore, in patients with chronic obstructive pulmonary disease (COPD), treatment with eight hours/day HFNC demonstrated a reduction in exacerbation frequency and symptoms (40–42). Emerging evidence suggests palliative HFNC treatment may be of use for refractory breathlessness (43) as it is well tolerated in end-of-life patients (44).
Wolfram Windisch (Witten, Germany) summarized pressure treatment in chronic respiratory disease. Long-term high-intensity NIV confers improvements in lung function, gas exchange, and symptoms and is better tolerated than standard NIV (45,46). Further studies have shown that long-term NIV improves survival and quality of life in patients with COPD (47–49). Current ERS guidance recommends long-term NIV for patients with stable hypercapnia, suggesting pressures be titrated to normalize PaCO2 (50).

Take home message:
Flow and pressure treatment have proven beneficial in the acute and chronic setting. Further clinical trials are required to elucidate which modality is optimal for selected patients.

**Hot topics in intensive care medicine**

Adrian Ceccato (Barcelona, Spain) (51) showed from a multicenter national cohort using k-prototype algorithm that clustering ARDS patients in two groups impacts their prognosis (cluster 1 having less organ failure and higher PaO2/FiO2 ratio compared to cluster 2). (52) Israel Duarte Herrera (Spain) presented the results of transcriptomic profiling of ARDS survivors in a prospective cohort: latent class analysis identified a persistent weakness group with 22 genes differentially expressed at admission. (53) Phruet Soipetkasem (Bangkok, Thailand) showed in a prospective cohort of 80 patients intubated for acute respiratory failure that a predicted Δ transpulmonary pressure ≤20 cmH2O was independently associated with longer ventilator free days. (54) Clemens Wiest (Regensburg, Germany) showed that pulmonary superinfections were more frequent and with more aspergillosis in patients treated with veno-venous ECMO for COVID-19 than for influenza. (55) Endry H.T Lim (Amsterdam, Netherlands) presented the results of a worldwide randomized controlled trial of vilobemalib showing a significant reduction of 28 days all-cause mortality in intubated ARDS COVID-19 patients. (19) Dilip Jayasimhan (Auckland, New Zealand) discussed the influence of an elevated dead-space and ventilatory ratio as independent predictors of mortality in patients with ARDS, based on a systematic review and meta-analysis of 21 studies. (56) Jessica González (Lleida, Spain) showed the evolution of pulmonary sequelae, symptoms, and quality of life throughout the two years after a critical COVID-19, highlighting a long-term negative impact of invasive mechanical ventilation. (57) Renaud Prével (Bordeaux, France) illustrated the different compositions of both bacteriobiota and lung mycobiota among patients with influenza, COVID-19 and bacteria-related ARDS by analysing endotracheal aspirates of 28 patients. (58)
Marie Gaffier (Paris, France) shared the data of a monocentric retrospective study evaluating nebulized tranexamic acid in patients requiring ICU for hemoptysis without immediate arterioembolization, showing no reduction of bleeding recurrence. (59)

Take home message: Exploring the heterogeneity of patients with ARDS using clustering, transcriptomic and bacteriobiota are promising new tools for future research.

**Mini Symposium: Rise of the Machines: Advances in Home Mechanical Ventilation**

Wolfram Windisch (Cologne, Germany) highlighted that the severe respiratory insufficiency questionnaire is a valuable tool for assessing the quality of life in COPD patients receiving NIV (60). Exacerbation history, presence of anemia, autonomy level and participating in rehabilitation programs impacts quality of life scores. (61,62) HFNC is an interesting treatment option in patients with chronic respiratory failure (CRF) due to its respiratory physiologic effects, but more trials are needed to recommend it as a first line treatment specially in hypercapnic patients due to the absence of significant reduction in hypercapnia. (63)

Patrick Murphy (London, United Kingdom) focused his presentation on the description of auto-titrating NIV and the use of these algorithms and devices in the management of patients with chronic respiratory failure. He raised the question of whether there might be more effective modes than the spontaneous-timed mode, that might not always be able to meet the respiratory demands during the different sleep cycles. He introduced auto-EPAP and auto-IPAP modes, which can sense and respond to obstructive events in the upper airway and hypoventilation, respectively. Theses modes improve quality of sleep, gas exchange and compliance. (40,64–66) NIV can be an adjunct to respiratory rehabilitation and physical activity particularly during as it improves endurance exercise capacity and recovery after physical activity. (67) Small portable devices are a good option for this indication.

Marieke Duiverman (Groningen, Netherlands) highlighted the challenges and evidence of telemonitoring in patients on home mechanical ventilation. Telemonitoring may not necessarily prevent acute COPD exacerbations but could potentially shorten their duration (68). The challenges associated with telemonitoring are the increased time required by nursing staff in the management around telemonitoring and trying to assure its cost-effectiveness by saving hospitalization days. (69,70) Nevertheless, telemonitoring increases patient empowerment, enables patient and family centered care, and facilitates knowledge sharing between healthcare providers and across healthcare systems. (71–73) Home initiation of NIV with
telemonitoring is feasible and non-inferior regarding efficiency in comparison to in-hospital initiation. (74)

Take-home messages

- Long-term NIV for chronic hypercapnic COPD patients is standard of care, improves long-term survival and improves quality of life.
- High-flow nasal cannula improves respiratory mechanics but has a small effect on $P_aCO_2$ reduction; it’s role in chronic respiratory diseases still needs to be defined.
- Auto-NIV modes enhances physiological control of sleep-disordered breathing and improves NIV tolerance and compliance.
- Home initiation of NIV with telemonitoring is feasible and non-inferior regarding efficiency in comparison to in-hospital initiation.

Quality of survival

Sabrina Eggmann (Bern, Switzerland) discussed the best strategy for rehabilitation in ICU, presenting data from the TEAM trial. High intensity rehabilitation did not reduce mortality nor hospital stay and had more adverse events than the usual intensity group. (75) Importantly, no rehabilitation is not an option. The optimal strategy is resumed in figure 2 and should include close monitoring of patients, a stepwise increment in intensity using individualised, short, and frequent sessions, prioritising out of bed and functional exercises (76).

Daniel Langer (Leuven, Belgium) demonstrated how inspiratory muscle training facilitates weaning from mechanical ventilation. In the only randomised trial with a sham arm, inspiratory muscle training improved weaning rates from 47% to 71% (77). Presenting unpublished data from the IMTCO study (78), high intensity inspiratory muscle training did not improve weaning above lower intensity. In both groups, muscle activation was similar, suggesting pre-existing low respiratory compliance can be sufficient to generate enough workload. (79)

Michele Vitacca (Pavia, Italy) explored the multiple dimensions of post-ICU disability (80–83), Post Intensive Care Syndrome, which leads to long-term impairments (84), and the high level of disability in weaning centre patients. The need to evaluate patients in these centres with a variety of tools was stressed (85,86) as well as the importance of multidimensional (65) and volitional assessments (87) (such as spirometry and muscle strength) and preventive actions (88).

Carolyn Rochester (New Haven, USA) discussed implications (89) and prevention (90) of Post Intensive Care Syndrome. Evidence supporting improvement of outcomes with rehabilitation programmes is scarce (91) even though several programs have been tested. To optimize
rehabilitation, at-risk patients (92) and patients’ rehabilitation needs (92) must be identified, in association with optimized early post-hospital care. (93) A multidisciplinary team is necessary to implement these post-ICU rehabilitation programs. (94,95)

**Take-home messages**

- Post-ICU disability has multiple dimensions, which must be evaluated using several tools and assessments to improve rehabilitation outcomes.
- Rehabilitation from critical illness should be individualized to patients’ needs as the workload intensity that may lead to overload without adding extra benefit varies between patients.
- Inspiratory muscle training improves weaning from mechanical ventilation although the optimal regimen is not established.

**Covid 19 diagnosis and treatment summary**

Respiratory related mortality remains up to 30% higher than pre-pandemic levels in Spain, as evidenced by Joan Soriano (Madrid, Spain) (96,97). Vaccination strategy could be impacted by the findings of Guy Hazan (Beer Sheva, Israel) who demonstrated improved immune response and reduced infection risk with mid-morning COVID-19 vaccination in a trial of 1.5 million patients (98).

Novel ambulatory diagnosis of COVID-19 was proposed by Stanislas Grassin Delyle (Montigny le Bretonneux, France) using real-time mass spectrometry breath analysis. Volatile organic compound signatures alongside clinical data accurately identified COVID-19 cases with 98% sensitivity and 74% specificity (99). Anna Semenova (Munich, Germany) presented liquid chromatography of matched serum and broncho alveolar liquid to create disease specific signatures to differentiate COVID-19 from other causes of pneumonia, also showing unique protein profiles on the first day of intubation, that were sustained for 45 days after intubation (100).

Erik Duijvelaar (Amsterdam, Netherlands) demonstrated disruption of protein expression in COVID-19 infection; this more accurately predicted critical illness progression than clinical data. Imatinib reversed dysregulated protein pathways in COVID-19 induced critical illness (101).

Caroline Lindö (Lund, Sweden) identified decreased IL-33 concentrations and elevated plasma levels of soluble ST2 receptor in lung tissue of COVID-19 fatalities vs controls, particularly prominent changes were found in areas of diffuse alveolar damage (102).
A novel prophylactic treatment of influenza infection including a TLR2/6 agonist nasal spray was presented by Francesca Mercuri (Melbourne, Australia) inducing increased expression of antiviral immune genes and a reduced infection duration (103). Stefan-Marian Frent (Timisoara, Romania) showed in a small trial that vagal nerve stimulation resulted in less ICU admissions and low mortality in COVID-19 patients, hypothesizing an anti-inflammatory response reducing critical illness (104).

Omer Elneima (Leicester, UK) presented PHOSP-COVID trial outcomes showing more than 60% of patients hospitalized with COVID-19 have ongoing symptoms and physical impairment at 1 year (105). This correlates with the findings presented by Tamara Cruz (Barcelona, Spain) showing T cell exhaustion, and altered cytokine profiles in patients with persisting respiratory symptoms, and objective decline in DLCO <80%, at 1 year after infection (106).

Take home messages:

- Proteomics may hold the key to developments in COVID-19 diagnosis and treatment targets.
- There is objective evidence of immune dysfunction in long-covid patients.

Mini symposium: Complex pleural disease: management in the critically ill patient

Marco Nardini (London, United Kingdom) discussed pneumothorax in critically ill patients. Pneumothorax in these patients is most commonly a result of a surgical or intensive care procedure. (107) Chest computerised tomography is the most sensitive imaging method for pneumothorax detection. (108) Thoracic ultrasound also has a very important role in detecting pneumothorax in the critically ill, because it can be performed at the bedside. (109) Treatment options include watchful waiting, tube thoracostomy and surgery. Furthermore, the role of endobronchial valves as a treatment option for patients with persistent air leaks was highlighted. (110) Finally, the question regarding the need for dedicated guidelines for management of pneumothorax in critically ill patients was raised.

David Sanchez (Barcelona, Spain) discussed the management of complex pleural effusion in critically ill patients. He highlighted the rising incidence of pleural infection. He further addressed the role of thoracic ultrasound, which is superior to chest x-ray or CT for diagnosis of complex pleural effusion. (111) Furthermore, management strategies, which are based on early antibiotic administration and early complex pleural effusion evacuation were discussed.
Additionally, the role of intrapleural fibrinolytic therapy was highlighted, as well as surgical modalities and alternative options for those not fit for surgery.

Mario Nosotti (Milan, Italy) discussed chylothorax and bronchopleural fistula. Chylothorax is a condition with a high morbidity. Traumatic chylothorax is mainly caused by surgery (90%), whereas non-traumatic causes include malignancy and non-malignant diseases. (112) Conservative management should be first line. Interventional management includes surgical ligation and embolization. (113,114)

Bronchopleural fistula can occur post lobectomy/pneumonectomy and post lung transplant. Other causes include chemotherapy, radiation therapy and chest trauma. Symptoms can be acute of tension pneumothorax or subacute symptoms of empyema. A computed tomography scanner and/or bronchoscopy is necessary for diagnosis. Chest drain is generally required for management. Other options include surgery and stenting or occluder devices, depending on patient suitability, the size and timing post operatively. (115)

Take home message: There are many complex pleural diseases which can be encountered in critically unwell patients and a multidisciplinary approach is necessary in the management to achieve the most optimal outcome.

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Conflict of interest disclosure

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Figures legends:

Figure 1:
Figure summarizing the changes in the European Society of Intensive Care Medicine recommendations concerning the clinical definition and therapeutic management of Acute Respiratory Distress Syndrome (ARDS). The left-hand column shows the 2017 recommendations and the right-
hand column the changes established or not
in 2023, with the additions concerning the management of COVID 19 patients. HFNC: high
flow nasal cannula; PEEP: positive end-expiratory pressure; ECMO: extracorporeal
membrane oxygenation; ECCO2R: extracorporeal carbon dioxide removal.

Figure 2:
Recommendations for rehabilitation during post-critical care admission regarding frequency,
intensity, duration and type of sessions of rehabilitation.
**ARDS clinic**

<table>
<thead>
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<th>Definition</th>
<th>Berlin definition</th>
<th>HPNC use</th>
<th>SpO2/PrO2 use</th>
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<tr>
<td>Phenotypes</td>
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<td>+</td>
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Impact on short term mortality different between sub-phenotypes (Systemic inflammatory response, radiographic morphology, recruitable, clinical features, longitudinal changes)

**ARDS management**

<table>
<thead>
<tr>
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<th>2017</th>
<th>2023</th>
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<tr>
<td>HFNC</td>
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<td>Low tidal volume</td>
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<td>High PEEP</td>
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<td>Recruitment maneuvers</td>
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Covid 19

Figure 1
Figure 2

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