

# **Respiratory failure and mechanical ventilation**

## **000017 - Neurally adjusted ventilatory assist versus pressure support ventilation in patients weaning from mechanical ventilation**

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### **Introduction**

Difficult weaning is a common problem of patients and result in prolonged weaning duration and poor outcome. Neurally adjusted ventilatory assist (NAVA) is a partial support ventilatory mode which triggers and tailors the level of assistance delivered by the ventilator to the electrical activity of the diaphragm.

### **Objectives**

The present study was designed to compare NAVA and PSV on weaning outcome in difficult-to-wean patients. The primary outcomes is to determine the difference in duration of weaning between NAVA and PSV. We hypothesize that in patients with difficult weaning NAVA reduces duration of weaning compared to PSV.

### **Methods**

A total of 99 difficult-to-wean patients who were able to sustained PSV in the critical care medicine unit (ICU) of the Zhongda Hospital, Southeast University were enrolled in the study. Patients were classified according to the reason for weaning failure and were randomly assigned to receive NAVA or PSV during weaning. The primary outcome was the duration of weaning, which was defined as time from study enrollment to extubation or disconnection of the ventilator continuously for 12 hours or more in patients tracheotomized. Secondary outcomes included the proportion of

successful weaning, ventilation free days within 28 days after enrollment, patient-ventilator asynchrony, length of stay in ICU and hospital, ICU and hospital mortality.

## Results

There were 17% (8/47) and 33% (17/52) patients in the PSV and in the NAVA group never weaned from mechanical ventilation ( $P = 0.073$ ). The duration of weaning was significantly shorter in the NAVA group [2.4 (1.1-5.3) days], than in that in the PSV group [4.1(1.1-7.7) days] ( $P = 0.041$ ). The proportion of patients with successful weaning was 70% (n=33/47) in NAVA group which was much higher than that in PSV group (48%, n=25/52) (RR for NAVA, 1.74 [95 % CI, 1.04–2.91],  $P = 0.040$ ). Compared with PSV, NAVA improved the rate of successful weaning in patients with single reason (74% vs. 49%,  $P = 0.019$ ) but not in patients with multiple reasons for difficult weaning (50% vs. 45%,  $P = 0.656$ ). NAVA decreased ineffective efforts and improved the trigger and cycling-off delays when compared with PSV. The number of invasive ventilator-free days [25 (20-27) vs. 21 (0-26),  $P = 0.002$ ] and ventilator-free days [24 (20-26) vs. 21 (0-26),  $P = 0.002$ ] were lower in the NAVA group on day 28. Mortality and length of stay in ICU and in hospital, were similar in the two groups.

## Conclusion

In patients who were difficult to wean, NAVA decreased duration of weaning and increased the probability of successful weaning. NAVA which improved patient-ventilator asynchrony, is safe, feasible and effective over a prolonged period of time during weaning.

# 000040 - Risk factors that influenced hospital mortality in patients under various rescue therapies for acute respiratory distress syndrome

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## Introduction

Rescue treatment for acute respiratory distress syndrome (ARDS) has been studied, such as systemic steroids, prone positioning, extracorporeal membrane oxygenation (ECMO), including lung protective ventilator strategy. We elucidated the trends of rescue therapies of ARDS and risk factors of mortality based on the real-world treatment data under various rescue therapies.

## Methods

We performed a single center, retrospective cohort study of patients who admitted to intensive care unit (ICU) from Mar, 2013 to Feb, 2018 and diagnosed as ARDS by the Berlin definition. The baseline characteristics and different methods of rescue therapies were collected. Additionally, the parameters of mechanical ventilator while applying the paralysis agent were analyzed.

## Results

Total 181 of ARDS patients who treated in ICU with MV were enrolled. Most of patients were male (72%), the mean age 72, and the mean APACHE II score 31.6. The duration of mechanical ventilator was 14.8 days, and ICU stay 19.0. 96 (51.6%) were died in ICU and 105 (56.5%) in hospital. Prone positioning increased from the 2014 to 2015, whereas the application of ECMO decreased from 2014 to 2017. Regardless of various rescue therapies, the appropriate dynamic driving pressure reduced the mortality of ARDS patients in multivariate logistic regression analysis [odds ratio (OR) 0.31, 95% CI 0.12-0.77, P = 0.0117].

## Conclusion

Dynamic driving pressure was the most important risk factor of hospital mortality in patients with ARDS regardless of various rescue therapies.

# **000046 - High-flow oxygen therapy improved mortality in more severe immunocompromised patients with acute respiratory failure: A systematic review and meta-analysis**

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## Introduction

High-flow nasal-cannula (HFNC) may be an oxygen modality useful for preventing invasive mechanical ventilation and mortality. However, its role in immunocompromised patients with acute respiratory failure (ARF) is still not clearly defined.

## Objectives

To evaluate the effect of HFNC on outcomes for this patient population compared with other alternative noninvasive oxygen therapies.

## Methods

We systematically searched Cochrane library, Embase, PubMed databases and Web of Science before 19. Nov, 2018 for eligible articles which reporting the use of HFNC in immunocompromised subjects and evaluated its impact on mortality and invasive mechanical ventilation. A meta-analysis was performed for measuring short-term mortality (defined as intensive care unit (ICU), hospital or 28-days mortality) and intubation rate as the primary outcomes, and length of stay in ICU as the secondary outcome. To compare HFNC with every separate oxygen therapy, network analysis and Bayesian analysis were also used in our study in mortality and intubation rate.

## Results

Upon review of 491 articles, nine studies involving 2328 patients were included in our meta-analysis. There was no difference between HFNC group and control group in short-term mortality and stay in ICU (RR 0.82, 95% CI, 0.66 to 1.01,  $p = 0.07$ ,  $I^2 = 51\%$ ; MD -0.26 days, 95%CI, -2.34 to 1.83,  $p = 0.81$ ;  $I^2 = 67\%$ ). Use of HFNC only was significantly association with a reduction in intubation rate (RR 0.84, 95% CI, 0.71 to 0.99;  $p = 0.03$ ,  $I^2 = 40\%$ ). For patients whose SAPS II score was higher than 40, HFNC use decreased mortality significantly (RR 0.66, 95% CI, 0.48 to 0.90;  $p = 0.009$ ,  $I^2 = 28\%$ ) when compared with control group. No significant benefits were shown in any single oxygen therapy (HFNC, COT, NIV or HFNC+NIV) when compared with others in mortality or intubation rate. In the mortality and intubation rate rank probability graphs, the probabilities of HFNC regimen were 1% and 0% respectively, which were lower than any other oxygen therapy.

## Conclusion

The results of current meta-analysis suggested that use of HFNC didn't improve short-term mortality of acute respiratory failure in immunocompromised patients. But for those more severe patients, HFNC improved mortality significantly. HFNC also reduced intubation rate in immunocompromised patients. Owing to the quality of the included studies, further adequately powered randomized controlled trials (RCTs) are needed to confirm our results.

# 000062 - Safety of high-flow oxygen via nasal cannulae compared to non-invasive ventilation in acute respiratory failure

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## Introduction

The use of humidified oxygen via high flow nasal cannula (HFNC) to treat acute respiratory failure (ARF) is increasing, there for is important to evaluate the efficacy and safety of HFNC in this patients.

## Objectives

Should HFNC be a safe first line therapy in ARF, as an alternative to non-invasive ventilation (NIV)?

## Methods

Retrospective study of patients, aged 18 years or more, admitted in the Intensive Care Department with ARF diagnosis and submitted to HFNC or NIV, from January 2017 to November 2018. Patients received HFNC or NIV therapy according to the attending physician's criteria.

Exclusion criteria: hypercapnia ( $\text{paCO}_2 > 45 \text{ mmHg}$ ) on admission, pulmonary fibrosis, immunosuppressed patients and the use as a therapeutic limitation in neoplastic patients.

The aim of this study is to compare the influence of HFNC and NIV in ARF patients on respiratory rate, pH and  $\text{paCO}_2$ . The 4, 12 and 24 hours after the treatment began were assessed, and the need for intubation.

Statistics: Mann-Whitney U, Pearson's chi-squared test and the T-Student test.

## Results

A total of 88 patients were admitted with ARF diagnosis. Sixty-four patients meet the exclusion criteria. Twenty-four patients were enrolled, 13 in the HFNC group and 11 in the NIV group. The HFNC group had an average age of  $61.62 \pm 17.70$  and 69.2% were men. In the NIV group, the median age was higher,  $73.18 \pm 9.16$ , 27.3%, with 72.7% of male gender.

There was a difference in decreasing PaCO<sub>2</sub> and increasing pH in the HFNC group, that was significative at the 4 hours after treatment ( $p=0,04$ ) ( $p=0,03$ ).

There was no evidence for a significative difference in the reduction on respiratory rate in patients receiving HFNC vs. NIV. The NIV group had higher progression to intubation (27,3%) than the HFNC group (15,4%) ( $p=0,48$ ).

## Conclusion

HFNC vs NIV didn't increased the risk of respiratory acidosis or had higher rate of intubation in ARF patients. This therapy is feasible and safe.

# 000063 - Non invasive ventilation in end of life patients: Rethinking clinical targets

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## Introduction

The main role of non-invasive ventilation (NIV) in end of life care is symptomatic relief. Nevertheless, impairment of consciousness is a frequent finding in this context, and difficulties evaluation of success in palliative treatment with NIV. Incidence of this scenario is still unknown. Evaluation of Minute Ventilation (MV) could be a better way to assess success in palliative NIV, although the effect on MV once NIV is initiated is unknown.

## Objectives

Characterize a cohort of patients with acute respiratory failure (ARF) and palliative NIV. Report the incidence of consciousness impairment that does not allow patients to refer symptomatic relief. Describe MV during first hours since incitation of NIV.

## Methods

Single-center, prospective and observational study. For two years, we recovered data from adult patients with ARF that required palliative treatment with NIV. We registered etiology of ARF, demographic and clinical parameters (including MV, arterial blood gases, state of consciousness and inability to refer symptomatic relief) at baseline and after 6 hours of initiating NIV, the need of use of sedation and early (<6hours) and in hospital mortality. We considered as “responders” patients who decreased MV more than 10% after NIV initiation.

## Results

Thirty-nine patients were included, of which 14 were women (35,6%), age 70 years old ( $\pm 12,7$ ). Main etiology of ARF was hypoxemic failure in 19/39 (48,7%). Early and in hospital mortality was 8/39 (20,5%) and 26/39 (66,7%) respectively. The need of use of coadjuvant sedation was registered in 10/39 patients (25,6%). Twenty-seven patients (69,2%) were unable to refer symptomatic relief.

After 6 hours of NIV, 31 patients (79,5%) were still alive, of which 17/31 (54,8%) decreased MV and were considered as responders, without significant changes in PaCO<sub>2</sub> nor oxygenation, while non-responders had a significant increase in MV (Table 1).

Table 1. Respiratory variables and use of sedation.

	RESPONDERS (n=17)		NON RESPONDERS (n=14)	
	Baseline	6hrs	Baseline	6hrs
MV(l/m)	16,7 ( $\pm 5,14$ )**	12,6 ( $\pm 4,9$ )*	12,9 ( $\pm 4,1$ )**	14,3 ( $\pm 4,3$ )*
PaCO <sub>2</sub> (mmHg)	33,1 ( $\pm 12,2$ )	29 ( $\pm 7,1$ )	35,7 ( $\pm 15,1$ )	34,7 ( $\pm 13$ )
PaO <sub>2</sub> /FiO <sub>2</sub>	299 ( $\pm 160,4$ )	308,9 ( $\pm 131,3$ )	237,5 ( $\pm 106$ )	251,6 ( $\pm 96$ )
Sedation(n)		5 (29,5%)		4 (24%)

MV: Minute Ventilation. \* p<0,05 vs baseline. \*\*p<0,05

## Conclusion

While symptomatic relief is one of the main “theoretical” targets when using NIV in patients with ARF which are at end of life care process, in daily practice it would not be a good indicator of success, due to the frequent inability of referring relief from patients undergoing impairment of consciousness. On the other hand, using the ventilatory drive allows to an early identification two different patterns of response:

one group in which it decreases respiratory work (responders) and one group it does not.

# **000064 - The impact of interruptions of active weaning process on the outcomes of patients with prolonged mechanical ventilation: a retrospective analysis at a dedicated weaning unit of a medical center in Taiwan**

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## **Introduction**

Interruptions during the process of weaning from mechanical ventilation (MV) for patients with prolonged weaning course are common, with the reason ranging from acute clinical deterioration and unplanned medical interventions. Different from failed weaning attempts with the hallmarks of worsened gas change, development of respiratory muscle fatigue or severe distress, interrupted weaning trials might not be associated with signs of failure. However, the impact of these interruptions on weaning outcome has remained uncertain.

## **Objectives**

To investigate the occurrence and patterns of interruptions during ventilator weaning and their impact on outcomes of tracheostomized patients.

## **Methods**

In this retrospective study, we included tracheostomized patients with prolonged MV treated at the Respiratory Care Center (RCC) of a university-affiliated medical center in Taiwan between July 2014 and December 2018. Since 2014, this RCC has implemented a protocolled weaning process for admitted patients, who will receive



unassisted breathing trials (UBT) such as direct liberation, stepwise weaning or slow weaning trial as decided by the care team. Interruption of weaning is defined as premature termination or postponing of the UBT session when the clinical condition does not fulfill the criteria of failed weaning attempt. We collected the clinical, physiological, and outcome data to compare the patients with and without interruption of UBT in RCC patients who received active weaning management.

## Results

A total of 1,162 patients were included; 986 (84.9%) had attempts at active weaning, and 657 (66.6%) were successfully weaned at RCC discharge. Of these patients under weaning process, 168 (17.0%) had at least one episode of documented interruption, contributing to 1,506 (8.2%) of the 18,418 patient-days at the RCC, with a mean of 9.0 [range, 1-40] patient-days. In 73 (43.5%) patients, interruption occurred during the sessions of UBT, while fever/infection (n=23) accounted for 13.7% of the interruption. Patients who failed to wean at RCC discharge had more proportion of tracheostomized before RCC admission ( $p<0.001$ ), and more proportion with any type of interruption ( $p<0.001$ ), interruption due to respiratory condition ( $p<0.001$ ), and interruption after failed weaning attempt ( $p<0.001$ ). Multivariate logistic regression analysis showed age (OR=1.018, 95%CI=1.008-1.028,  $p<0.001$ ), tracheostomized on admission to RCC (OR=1.744, 95%CI=1.274-2.386,  $p=0.001$ ), and interruption after failed weaning attempt, most due respiratory manifestations (OR=4.929, 95%CI=1.890-12.854,  $p=0.001$ ), were associated with weaning outcome at RCC discharge. Cox-proportional hazard analysis showed that age (OR=0.989, 95%CI=0.985-0.993,  $p<0.001$ ), and interruption due to respiratory condition (OR=0.667, 95%CI=0.451-0.985,  $p<0.042$ ) were associated with time-dependent successful weaning. In both multivariate models, interruptions due to fever/infection were not associated with weaning outcomes of the patients receiving active weaning at the RCC ( $p=0.831$  and  $0.131$ , respectively).

## Conclusion

Interruptions occurring during the active weaning process for tracheostomized patients, mostly due to respiratory reasons but not infection-related ones, are a poor prognosis factor for liberation from prolonged mechanical ventilation.

# **000074 - Change of Flow Rate and Peak Airway Pressure Depending on Diameter of Endotracheal Tube During Chest Compression: a Manikin Study**

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## Introduction

Adequate air way management plays an important role in high-quality cardiopulmonary resuscitation (CPR). Airway management during in-hospital CPR is usually performed by using an endotracheal tube (ETT).

## Objectives

However, there is little research regarding the changes in flow rate and airway pressure depending on the size of ETT used during CPR.

## Methods

We were divided into two groups depending on whether chest compression was performed. We measured flow rate (FR), peak airway pressure (P<sub>peak</sub>), mean airway pressure (P<sub>mean</sub>), and tidal volume (TV) for ETTs of different sizes (diameter 6.0 to 8.0 mm). TV (500 mL) was supplied at a rate of 10 times per minute using a ventilator. Chest compression was maintained at a constant compression depth and speed using an automatic chest compression device.

## Results

Several respiratory physiological parameters during chest compression were found to be significantly different according to the diameter of each ETT [group B, 6.0 mm vs. 8.0 mm, median (inter-quartile range, IQR)]; FR (L/min) 3.21 (3.05-3.53) vs. 2.89 (2.75-3.08),  $p < 0.001$ ; P<sub>peak</sub> (cmH<sub>2</sub>O) 48.84 (27.46-52.11) vs 27.45 (22.53 - 52.57),  $p = 0.007$ ; P<sub>mean</sub> (cmH<sub>2</sub>O) 18.34 (14.61-21.66) vs. 13.66 (8.41-19.24),  $p < 0.001$ ; TV (ml) 502 (487-507) vs 504 (464-512),  $p = 1.0$ .

## Conclusion

Significant differences were observed in FR, P<sub>peak</sub>, and P<sub>mean</sub> according to ETT size. As the ETT size increased, FR, P<sub>peak</sub>, and P<sub>mean</sub> decreased and showed a larger change during chest compression.

## 000085 - Correlation between muscle specific micro RNA in plasma and

# diaphragmatic dysfunction in patients undergoing mechanical ventilation

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## Introduction

Mechanical ventilation can cause diaphragm dysfunction. It is important to explore possible predictors of VIDD in MV patients , and to take a practical and feasible method to prevent and treat them.

## Objectives

To investigate the effect of MV on diaphragmatic function in patients undergoing cardiothoracic surgery and figure out the relationship between plasma miRNA and diaphragmatic function in mechanical ventilation patients.

## Methods

1. Patient inclusion: patients admitted to Department of Critical Care Medicine, Zhongda Hospital from June to December 2017, aged between 18 and 75 years old, underwent elective cardiac surgery. Peripheral blood sample were collected on the 1 day before operation, before the extubation and the third days after operation, respectively. 2, Bedside ultrasound and NAVA evaluation of diaphragm function. 3, Bedside ultrasound assessed the thickness of skeletal muscle of four limbs. 4. Plasma miRNA test: fluorescence quantitative PCR was used to detect the circulating threshold of muscle tissue specific miRNA in plasma.

## Results

1. A total of 40 patients were analyzed. Average APACHE II score was  $13.9 \pm 5.2$ , total MV time was  $26.1 \pm 2.3$ h. 2. Effect of MV on diaphragm function: diaphragmatic activity and thickening fraction decreased significantly before extubation and the third days after the operation compared with 1 day before operation ( $P < 0.05$ ), but there were no difference between before extubation and the third days after the operation, while diaphragm thickening fraction improved on the third days after the operation. Thickness of diaphragmatic muscle was significantly higher than the other time points ( $P < 0.05$ ), but there was no difference between 1 days before operation and third days after operation ( $P > 0.05$ ). Before extubation, NVE was  $62.2 \pm 22.5$  ml/Edi and NME was  $1.9 \pm 0.9$  cmH<sub>2</sub>O/Edi. 4. Effect of MV on thickness of skeletal muscle of extremities: there was no significant change in the thickness of biceps brachii and the thickness of the four head rectus femoris ( $P > 0.05$ ) at 3 time points in the perioperative period. 5. Effect of MV on plasma MyomiR: level of plasma miR-1 and miR-206 in patients after cardiac surgery was significantly lower before extubation

than 1 days before operation and third days after operation ( $3.6\pm 3.7$  vs.  $5.4\pm 4.1$  vs.  $6.0\pm 3.8$ ,  $P=0.037$ ;  $4.8\pm 2.8$  vs.  $8\pm 4$  vs.  $7.2\pm 4.2$ ,  $P=0.001$ ), but there was no obvious change between 1 day before operation and third days after operation. The other 5 miRNA levels did not change significantly during the perioperative period ( $P>0.05$ ). 6. Correlation of MyomiR and diaphragm function: Ratio of miR-206 and diaphragm thickening fraction on before extubation and third days after preoperative have correlation ( $r_{\text{left}}=0.427$ ,  $P_{\text{left}}=0.042$ ;  $r_{\text{right}}=0.640$ ,  $P_{\text{right}}=0.000$ ). There was no significant correlation between the other 6 MyomiR and diaphragm function indexes ( $P>0.05$ ).

## Conclusion

Short time mechanical ventilation can lead to the decrease of diaphragmatic function in patients with cardiac surgery, and the expression level of miR-1 and miR-206 also decreases, but it is still not recovered to the preoperative level on the third day after operation. The decrease of plasma miR-206 level is positively correlated with the decrease of diaphragm function in mechanically ventilated patients.

# 000103 - Mesenchymal stem cell paracrine hepatocyte growth factor induces dendritic cells immune tolerance via AKT pathway to alleviate acute lung injury

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## Introduction

Acute respiratory distress syndrome (ARDS) is a life-threatening form of respiratory failure characterized by acute, diffuse, and inflammatory lung injury. Mesenchymal stem cells (MSCs) are multipotent cells have been shown to alleviate acute lung injury via paracrine hepatocyte growth factor (HGF). Recent reports suggested that MSC and HGF also inhibit the maturation and function of dendritic cells (DCs), further inhibiting T cell activation and proliferation. However, it remains unclear whether MSCs alleviate acute lung injury from dendritic cell immune tolerance via paracrine HGF and its specific mechanisms.

## Methods

In the current study, MSCs with low or high expression of HGF gene, were co-cultured with DCs derived from mouse bone marrow using Transwell culture plates in vitro conditions for 3 days, or were used to treat LPS-induced ALI C57BL/6 mice for 24 hours. Flow cytometry was performed to measure phagocytosis, accumulation and maturation of DCs, as well as activation and proliferation of T cells in vivo or in vitro experiments. IL-12, TGF- $\beta$ , IL-10 were quantified to evaluate lung inflammation. Lung injury was estimated by lung wet weight/body weight ratio (LWW/BW) and histopathological analysis. To investigate the novel mechanism by which the mammalian c-met/AKT signaling pathway mediates HGF-induced immune-tolerant DCs to attenuate ARDS lung injury, we used recombinant mouse HGF in mDCs. In addition, we used AKT inhibitor MK-2206 to inhibit the AKT pathway.

## Results

Results demonstrate that MSC induced mDC immune tolerance by paracrine HGF and reduced its ability to stimulate T cell activation and proliferation to alleviate lung injury. Furthermore, c-met/Akt was activated by HGF and appears to increase c-met and AKT phosphorylated proteins, inducing mDC immune tolerance. Reversely, MK-2206 inhibited AKT activation and weakened DC immunosuppression in vitro, and attenuated MSC's protection against lung injury in LPS-ALI mice and immunomodulatory effects on dendritic cells in the lung.

## Conclusion

our findings may provide a novel explanation for the alleviation of lung injury by MSC-secreted HGF from inducing mDC immune regulation, and highlight that the activation of the c-met/Akt pathway is an important mechanism for its protection of LPS-ALI.

# 000105 - The homing and protective effects of mesenchymal stem cells overexpressing CXCR7 in LPS-induced acute respiratory distress syndrome mice

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## Introduction

Stromal cell-derived factor 1 (SDF-1), also known as CXCL12 is expressed by a variety of tissues including the bone marrow, heart, liver, lung, lymph nodes, brain, kidney, and pituitary. It was revealed to bind a second chemokine receptor CXCR7 with has an even 10-fold higher affinity compared with CXCR4. In the previous study , we constructed long-term and stable mMSCs lines overexpressing CXCR7 modifications with lentiviral vectors and we found that CXCR7 gene overexpression promoted mMSCs proliferation and migration in vitro. Therefore, we hypothesized that a treatment with MSC overexpressing CXCR7 would improve the engraftment of MSCs and achieve better therapeutic effect in ARDS mice.

## Objectives

To evaluate the increasing restoration of MSC overexpressing CXCR7 in the injured lung, attenuation of inflammatory response and lung protective effect in LPS-induced ARDS mice.

## Methods

90 C57BL/6 mice were randomly divided into Control group (NS+PBS), ALI group (LPS+PBS), MSC group (LPS+MSC), MSC-GFP group (LPS+MSC-GFP) and CXCR7 group (LPS + MSC-CXCR7). Murine model of ARDS was generated by intratracheal instillation of 5mg/kg lipopolysaccharide (LPS) and cell suspension/PBS was injected into the tail vein according to subgroup 4h later. After different treatment the specimens were harvested at 30min, 24h and 72h to perform: (1) Evaluation of the severity of injured lung in ARDS mice after MSC overexpressing CXCR7 treatment: obtaining lung specimens and observing the degree of lung injury generally were achieved after the mice were sacrificed. Lung edema was estimated by lung wet weight/body weight ratio (LWW/BW), what's more, histopathological analysis of lung tissues were performed by H&E staining and quantified by using Smith lung injury scores.(2) Observation the homing of MSC overexpressing CXCR7 in the injured lung: near-infrared (NIR) fluorescence imaging of the ex vivo organs, fluorescence microscopy of the lung tissue and examination of adhesion factor VCAM-1 and COL-1 by ELISA.(3) evaluation of the effect of MSC overexpressing CXCR7 homing on inflammation in ARDS injured lung: the levels of anti-inflammatory factor IL-10 and pro-inflammatory factor TNF- $\alpha$  in lung homogenates were measured by ELISA .

## Results

MSC-CXCR7 treatment could significantly improve lung histopathology involving decreasing hemorrhage, infiltration of inflammatory cells and formation of hyaline membrane. Moreover it reduced LWW/BW and lung injury score. NIR fluorescence imaging of organs ex vivo showed that the MSC-GFP predominantly peaked at 24h

compared with Control group, and then decreased at 72 h; MSC-CXCR7 treatment could increase the accumulation of MSC in the lungs than MSC-GFP group. What's more fluorescence microscopy of the lung tissue validated the results at the cellular level. MSC-CXCR7 treatment could decrease inflammatory factor secretion in the lungs after injection

## **Conclusion**

MSC modified with the CXCR7 gene homing to the LPS-induced injured lung was markedly increased and provided an additional attenuation of lung inflammatory response compared with MSC alone, which was much favorable for promoting the protective effect of MSC on ARDS injured lung.

# **000124 - Long-term mechanical ventilation-dependent patients in ICU and Home Mechanical Ventilation Units (HMVU). The solution ?**

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## **Introduction**

A Home mechanical Ventilation Unit (HMVU) provides the ability to transfer stable and long-term mechanical ventilation dependent patients from an intensive care unit to an specific unit to continue with the weaning process.

## **Methods**

Observational retrospectively study of all patients who underwent mechanical ventilation (MV) therapy in our intensive care unit of 20 beds and became ventilatory dependent and were transferred to our HMVU, situated in a different hospital in the same city, in a 23 year period (1995-2018). Variables analyzed: age, sex, cause for prolonged MV, type of IMV dependency (full-time, parcial), NIMV, if they were still mechanically dependent at the time of discharge from HMVU, ICU and HMVU length of stay, overall survival.

## **Results**

In 23 years of study, 46 patients ventilatory dependent were transferred from ICU to our HMVU as a long term weaning process. 27 were male (58.69%), mean age 52 year, and 19 female (41.31%), mean age 53 years. Cause for prolonged MV: 27 (58.69%) neuromuscular disease, 9 (19.56%) chronic pulmonary disease, 7 (15.22%) complicated surgery, 3 (6.52%) neurovascular disease. ICU length of stay of 75 days (6-322) At the time to transfer to HMVU: 40 (86.96%) patients with IVM, from these, 26 (56.52%) were full-time ventilated and 15 (32.6%) only partially ventilated (12 hours at night). 5 (10.87%) patients with NIMV. At the time of discharged from the HMVU and thus the length of stay was, depending of the type of ventilation: 9 months (93-144) in full-time IMV, 134 days (3-2880) in partially IMV and 15 days (10-22) in NIMV. Overall survival: 36 (78.3%) of the patients outlive more than 2 years and 21 (45.6%) of them outlive 5 years (2-16). 14 (30.4%) of the patients still alive today, with a mean time of 4.6 years.

## **Conclusion**

The HMVU has become part of the process for treating mechanical ventilation dependent patients and thus offloads intensive care unit longterm patients. From the ICU income until discharge from the HMVU it takes from 15 days in patients with NIMV to 134 days in those depending of IMV partially and extends until the 9 months in the ones totally dependent. 78% of the patients survive more tan 2 years, and more than half of them outlive 5 years

# **000049 - Determinants of symptom burden in old patients with chronic obstructive pulmonary disease**

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## **Introduction**

Symptom burden is common and has a negative impact on rehabilitation and survival. However, its pathogenesis and contributing factors remain unclear.

## **Objectives**

The purpose of this study was to identify factors influencing the occurrence of symptom burden and described the symptom frequency, severity and distress in old patients with COPD.

## **Methods**



We were enrolled patients at the lung function laboratory, respiratory clinic and respiratory ward in Henan, China. Data were collected in face-to-face interviews using validated questionnaires and through reviews of medical records. Symptom burden using the Memorial Symptom Assessment Scale(MSAS). Multivariate linear regression was used to examine symptom burden in relation to socio-demographic, lifestyle, clinical characteristics, self-efficacy, hospital anxiety and depression

## Results

The mean number of symptoms in the total sample was 11.1(SD=3.6). Highly prevalent symptoms were shortness of breath (97.5%), lack of energy (95.4%), worrying (82.1%), cough (80.4%), difficulty sleeping (72.1%), pain(68.8%), feel sad (64.6%), I don't look like myself (53.3%). Correlation was found between the symptom experience and self-care behavior( $r=-0.233, P< 0.01$ ), self-efficacy( $r=-0.226, P< 0.01$ ). Correlation with anxiety and depression  $r(r=0.496, P< 0.01)$ . Multiple linear regression analysis results showed that the influence factors affecting the symptom experience of the older adults with COPD were staging of disease, work before disease, the way of treatment cost and HADS total score

## Conclusion

In order to improved their quality of life and satisfy their diversified service needs, the particularity of their influence should be considered, enhance their self-care behavior, self-efficacy and reduce anxiety and depression more important.

# 000108 - Prior Use of Antipsychotics and Risk of Mortality in Patients with Sepsis - A Population-Based Cohort Study Using High Dimensional Propensity Score Analysis

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# Introduction

Antipsychotics have been used to treat a wide range of psychiatric issues, including off-label indications such as delirium symptoms in critically-ill patients. The adverse effects of antipsychotics raised concerns recently. Several studies have also correlated the use of antipsychotics with increased in the number of total ventilator days, ICU length of stay and mortality in critically-ill patients. However, the association between chronic antipsychotics use and sepsis outcome is still unclear.

## Objectives

To determine whether the use of antipsychotic medications before sepsis development may increase the risk of mortality.

## Methods

We conducted a population-based cohort study using the National Health Insurance Research Database of Taiwan from 2000 to 2012. Hospitalized sepsis patients were identified by ICD-9 codes compatible with the sepsis-3 definition. Current use of antipsychotic medications was defined as a filled antipsychotic prescription within 90 days before the index date of sepsis. The primary outcome is 30-day all-cause mortality, and the secondary outcome is lower respiratory tract infections (LRTI). We determined the association between the use of antipsychotic medications and the outcome by Cox proportional hazard model. To account for the potentially unmeasured confounders, a high-dimensional propensity score (hdPS) algorithm was used to adjust for the potential unknown confounders associated with a claims database research.

## Results

Our study identified 49,336 sepsis patients, of which, 3025 were prescribed first-generation antipsychotics (FGAs) 1015 prescribed second-generation antipsychotics (SGAs). Both FGAs and SGAs users were associated with an increased 30-day all-cause mortality (FGAs 21.26%, SGAs 20.39%) and higher LRTI prevalence (FGAs 59.51%, SGAs 62.30%), compared with nonusers. After hdPS adjustment, the use of FGAs was associated with a 23% increase in the odds risk of 30-day mortality (HR 1.23, 95% CI: 1.02, 1.48), but was not associated with an increased risk of LRTI (HR 1.17, 95%CI: 0.97, 1.40). Use of SGAs, however, was not associated with an increased risk of 30-day mortality (HR 1.17, 95%CI: 0.97, 1.40), but was associated with an increased risk of LRTI (HR 1.19, 95%CI: 1.06, 1.33). Subgroup analyses showed a higher risk of mortality in younger or with lower burden of comorbidities patients prescribed with antipsychotics.

## Conclusion

Use of FGA was found to associate with increased risk of death in patients with sepsis. Findings of our work do not support the off-label use of FGA in sepsis patients with delirium symptoms or in demented patients with psychotic symptoms.

# 000114 - The ability of conditioned media from stem cells to improve lung injury in rats with sepsis

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## Introduction

How to reduce sepsis mortality in all the critical care units around the world is a long-standing question. After decades of research, and numerous pre-clinical and clinical trials, sepsis remains without a specific and effective pharmacotherapy. In the last few years, cell therapies gained potential as a therapeutic treatment for various diseases. However, there are still many problems that limit the therapeutic use of stem cells, including immunological rejection phenomena and unwanted cells differentiation. In recent years, researchers have found that therapeutic activity of stem cells may be mediated by a paracrine effect.

## Objectives

In this study, we investigated the potential protective effects of iPSCs-conditioned media (iPSCs-CM) on E.coli-induced lung injury in rats and LPS/IFN-g-induced inflammatory responses in murine macrophage RAW 264.7 cells, and identified the mechanisms underlying these effects.

## Methods

Rats underwent intraperitoneal inoculation with 10<sup>9</sup> CFU of Escherichia coli isolated from patient. Animals were randomized to receive (i) co-administration of conditioned medium from iPSCs in combination with ceftriaxone (ii) IV administration of conditioned medium from iPSCs following 4 hr of infection in combination with ceftriaxone; (iii) IV administration of ceftriaxone (30mg/kg) following 8 hr of infection; and (iv) IV instillation of PBS vehicle. Raw 264.7 cells were pretreated with iPSCs-CM for 2 hr prior to LPS/INF-g stimulation or were treated with iPSCs-CM after 1 hr of LPS/TNF-g treatment. Lethality; lung injury scores, including protein leakage and

inflammatory cell infiltration; cell count in bronchoalveolar lavage (BAL) fluid; and chemokines and cytokines concentrations in serum were determined to evaluate the effects of iPSCs-conditioned media on sepsis-induced lung injury.

## Results

Administration of iPSCs-CM in combination with ceftriaxone (iPSCs-CM/ceftriaxone) has a higher survival rate than ceftriaxone treatment alone. iPSCs-CM/ceftriaxone treatment also significantly decreased the cell counts in BAL fluid in comparison to ceftriaxone treatment alone. Histological examination of lung tissue showed that the iPSCs-CM/ceftriaxone group was less than the ceftriaxone group in macrophage infiltration and MMP-9 expression. Serum levels of CXCL2, IL-1b, and IL-6 also showed decreased in E.coli-induced lung injury rat model, as well as in cells treated with LPS/INF-g. Further, expression of NLRP3, ASC, HMGB1, IL1b, IL-6, and CXCL2 mRNA was significantly decreased in iPSCs-CM/ceftriaxone group compared with no treatment. Similar effects of iPSCs-CM on LPS/INF-g-stimulated raw 264.7 cells.

## Conclusion

Our results revealed that treatment of iPSCs-CM ameliorates lung inflammatory responses through inhibiting NLRP3 inflammasome activation, which attenuates lung injury and improves the survival rate. These data suggested that iPSCs-CM may be important in sepsis and shed light on therapeutic strategies.

# 000145 - Carboxyhemoglobin and Methemoglobin Formation As Early Detectors of Hemolysis In Patients On ECMO: Report of Three Cases

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## Introduction

Increasing evidence suggests that hemolysis has been a major complication of Extracorporeal membrane oxygenation (ECMO) and related with increased mortality. Because death is inevitable, early recognition and management is of crucial importance. However, plasma free hemoglobin (pfHb) measurement, which is the gold standard diagnostic test, requires time and may not be widely available.

## Objectives

With this case series report we suggest that production of carboxyhemoglobin(COHB) and methemoglobin(MetHb) on ECMO is a consequence of hemolysis and can allow a rapid bedside detection by use of point-of-care oximetry.

## Methods

**Case 1:** A 22 year-old woman, with severe acute respiratory distress syndrome(ARDS) related with Influenza A infection on day 8 of hospitalisation,

**Case 2:** A 57 year-old man, who has a history of immunosuppressive therapy for renal transplantation, with bacterial pneumonia and severe ARDS on day 3 of hospitalisation,

**Case 3:** A 59 year-old man, with viral pneumonia and severe ARDS on day 5 of hospitalisation,

All of 3 cases continued to deteriorate despite management with medical therapy, mechanical ventilation, recruitment and prone positioning and Venovenous ECMO (VV ECMO) was employed. High flow rates were achieved according to the cardiac output measurements by the first days of management. Accidentally, oxymetric analyses showed gradual increases in COHb and MetHb levels as soon as the ECMO flow starts. No clinical signs of hemolysis were detected through the patients. Laboratory tests including indirect bilirubin, lactate dehydrogenase, and haptoglobin were all compatible with hemolysis and serial measurements showed gradual increase in levels of pfHb. As the flow rates of ECMO were decreased analyses showed that levels of CO-Hb and MetHb tended to decrease concomitant with levels of pfHb.

## Results

Case 1			Case 2			Case 3		
	COHb(%) fHb(mg/dL)	MetHb(%)	p	COHb(%) Hb(mg/dL)	MetHb(%) pf	COHb(%) pfHb(mg/dL)	MetHb(%)	
<b>D1</b>	2 1.9	5		0.6 12.5	2	0.8 14	1.8	
<b>D2</b>	5 12.6	3.9		1.2 24.6	3.5	2.9 51	4.5	
<b>D3</b>	5.5 31	5.2		3.6 44.2	5.6	6.2 95	6.8	

## Conclusion

Hemolysis is an increasing complication in patients on ECMO and cause catastrophic results if not detected rapidly. COHb and MetHb measurement by point-of-care co-oximetry would be useful for early detection and management of hemolysis.

# **000146 - Role of Dexamethasone for post extubation stridor and extubation failure in critically ill adult patients**

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## **Introduction**

Laryngeal edema (LE) is a frequent complication of intubation and is caused by trauma to the larynx.

The edema results in a decreased size of the laryngeal lumen, which may present as stridor or respiratory distress (or both) following extubation.

Reintubation may result in increased morbidity and mortality.

## **Objectives**

To evaluate whether dexamethasone started 2 hours prior to planned tracheal extubation and up to 24 hours after extubation, can prevent post extubation stridor and extubation failure in critically ill adults.

## **Methods**

The two centers, prospective, randomized controlled trial were performed among 84 patients, aged >18 who met weaning criteria after being intubated for more than 48

hours, with cuff leak volume (CLV) of less than 110ml. Patients were randomly allocated to two groups: receive either intravenous dexamethasone 8mg or identical volume of intravenous placebo (normal saline) before 2 hours of planned extubation and continued eight hourly up to 3 doses (total 24 mg) after extubation. Cuff leak volume was measured before at the time first injection and one hour after first injection. Patients were extubated after two hours of first injection dexamethasone or identical volume of intravenous placebo. Occurrence of stridor and extubation failure was noted within 48 hours of extubation.

## **Results**

Compared with placebo, dexamethasone given before planned extubation increased CLV significantly ( $P=0.001$ ). Post extubation stridor significantly lowered (51.6% lower in the dexamethasone group than in placebo group).

## **Conclusion**

The administration of Dexamethasone before a planned extubation, substantially reduced the incidence of post- extubation stridor and extubation failure in critically ill adults at high risk for post- extubation laryngeal oedema, identified by cuff leak test.

# **000179 - Home Mechanical Ventilation Units support for Intensive Care Units**

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## **Introduction**

Chronic mechanical ventilation dependency is not infrequent in intensive care units (ICUs). These patients should have an alternative plan rather than stay all the time in our intensive care units. Ideally, at the end and if their personal situation allows, is to try a follow-up at home discharge, thus it is necessary the support of a Home Mechanical Ventilation Unit (HMVU) where these patients can rehabilitate and adapt their family and personal needs for being home-ventilated. The HMVU created in the beginning for neuromuscular patients also allows the transfer of other kind of patients.

## **Methods**

Retrospectively five-year study (1/1/2014 to 12/31/2018) from our own data base. Variables analysed: sex, age, etiology of ICU admission, etiology of prolonged mechanical ventilation, ordinary hospital, hours on mechanical ventilation (MV) dependency at admission and discharge in the HMVU, ICU length of stay, HMVU length of stay, evolution of the process and destination at discharge.

## Results

We registered 16 patients. 10 (62.5%) were male. Average age:  $57.7 \pm 8.4$  years. 9 patients (56.2%) were postoperative cardiac/vascular or general surgery and 7 (43.8%) reactivated chronic respiratory failure. Etiology of prolonged mechanical ventilation (more than three tests of spontaneous breathing and/or the process lengthens more than 7 days): 5 tetraparesis (31.2%), 7 multifactorial (weakness, COPD, obesity...) (43.7%), 3 bilateral diaphragmatic paralysis (18.7%), severe kyphoscoliosis 1 (8.4%). Ordinary hospital: H. San Cecilio 5 (41.7%), H. Virgen de las Nieves 6 (50%), H. Santa Ana Motril 1 (6.2%). Hours of MV dependency on admission at HMVU: 12 hours at night: 7 (43.8%) and 24 hours a day: 9 (56.2%). Length of stay in ICU: 89.3 (range 57-253). Length of stay in HMVU: 167 (range 58-397). Evolution of the process: decanulation 9 (56.2%), nocturnal VM dependency 4 (25%) and 24 hours dependency in 3 (18.7%), it was impossible the weaning of VM patients with bilateral diaphragmatic paralysis and severe kyphoscoliosis. Destination at discharge: home 13 (81.3%) and exitus 3 (18.7%) due to cardiac arrest not recovered. ICU bed-occupancy of the 16 patients: 1359 days, with an average length of stay:  $104.3 \pm 51.7$  days.

## Conclusion

There is a short subgroup of patients who after aggressive surgeries remain chronically dependent on MV, resulting in prolonged ICU stay. With the support of HMVU more than half of these patients were discharged without Mechanical

Ventilation. Also with these HMVU we reduced ICU length of stay and occupation rates.