Critical Rounds
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Critical Rounds Newsletter
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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"Critical Rounds Newsletter"** which contain latest and interesting news in the field of Critical Care.

This issue contains:

1. Investigation of the association between protein intake and outcomes in ventilated critically ill patients

2. Risk factors for mortality in patients with pneumonia caused by Stenotrophomonas maltophilia in the critical care unit

3. A retrospective study on the long-term outcomes of new-onset refractory status epilepticus

4. Case report on Extracorporeal life support as a successful bridge to recovery in pulmonary arterial hypertension

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Medical Team, Micro Labs Limited

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Investigation of the association between protein intake and outcomes in ventilated critically ill patients

Introduction

A daily protein intake of 0.8-1.2 g/kg, but not above this amount, was linked to decreased mortality rates.

Mechanical ventilation (MV) is the most crucial life-saving technique for severely ill patients with respiratory insufficiency. While most patients recover from their initial acute illness and may readily wean off the ventilator, 30% require prolonged weaning and extubation. Nutrition therapy is no longer a support approach for critically ill patients, but rather a crucial therapeutic measure.[1] Currently, there is debate about whether medical nutrition treatment may reduce the length of mechanical ventilation (MV) or potentially increase the death rate of patients who need MV. A number of earlier observational studies revealed a strong correlation between increased protein consumption and improved results. According to the Nutrition en Réanimation (NUTRIREA-3) study, increasing daily protein intake from 0.2 to 0.9 g/kg during the first week following ICU admission might considerably delay weaning. The EFFORT Protein experiment found that increasing protein intake up to 1.6 g/kg/d did not enhance the length of MV, but may have prolonged the time to discharge alive in high-risk ventilated patients. There is debate concerning the relationship between the consumption of proteins and the requirement for mechanical ventilation (MV).[2] The purpose of this study was to evaluate at the relationships between outcomes and protein consumption in critically ill ventilated patients.

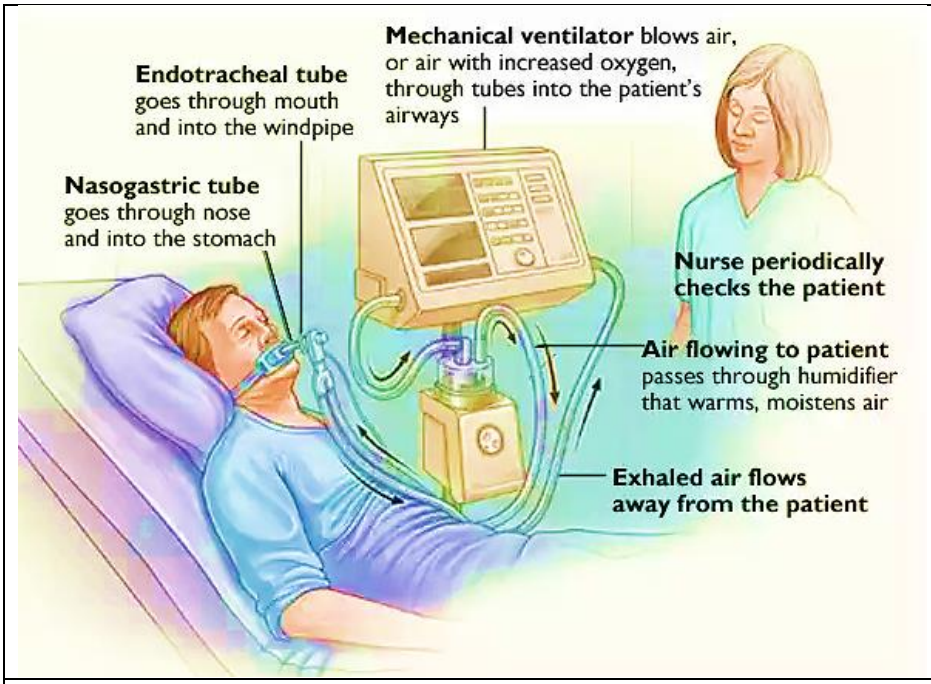

Figure 1. Weaning A Patient From Mechanical Ventilation

Methods

An analysis of a subgroup of a large worldwide point prevalence survey on nutritional habits in intensive care units. A total of 12,930 patients were admitted to the ICU for at least 96 hours and required mechanical ventilation by the fourth day. Daily protein intake was monitored from

the first day of ICU admission to 11 days later. Patients requiring MV were monitored for up to 60 days. This study examined the relationship between the adjusted hazard rate (aHR) of mortality in patients needing MV, effective weaning (competing hazards), and three types of protein intake (low: < 0.8g/kg/d, standard: 0.8-1.2g/kg/d, high: > 1.2g/kg/d). Visualization, data analysis, and model estimates were performed using the statistical programming environment R.

Results

The analysis included 121,853 diet records, with an average of 9.4 days per patient. This study examined five hypothetical protein diets: strictly low protein consumption, standard protein intake provided early (days 1-4) or late (days 5-11) following ICU admission, and early or late high protein intake. Protein consumption did not correlate with time to weaning. Standard protein consumption was shown to be related with a decreased risk of death in MV, with an aHR of 0.60 (95% CI, 0.45-0.80), compared to a low protein diet. Early high consumption was associated with a greater risk of mortality in patients requiring MV, with a maximal aHR of 1.35 (95% CI, 0.99–1.85) compared to a standard diet (Figure 2).

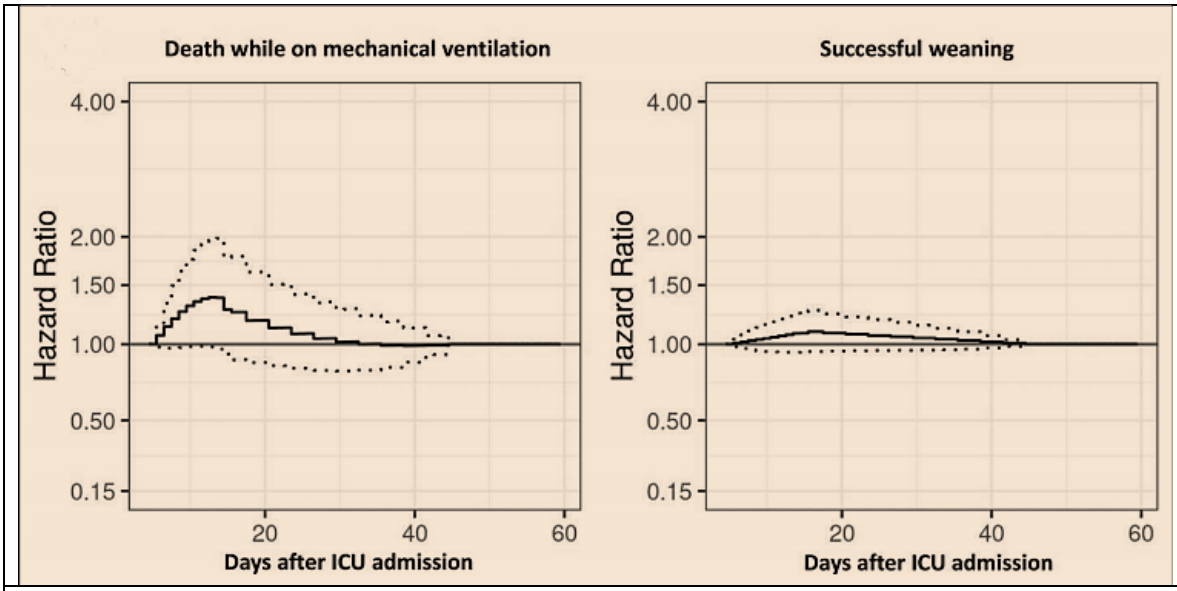

Figure 2: A comparison of early vs late standard protein intakes. The graph demonstrating the relationship between different meals and the rate of mortality in patients requiring mechanical ventilator or effective weaning over time. Solid lines represent cause-specific adjusted hazard ratios (aHR), whereas dotted lines represent 95% confidence intervals.

Discussion

This study demonstrated that increasing daily protein intake from 0.7 to 1.0 g/kg/d did not affect the duration of MV, either in absolute days or VFDs over a 28-day period.[2] In contrast to this findings, the NUTRIREA-3 study by Reignier J et al. found that increasing protein consumption from 0.2 to 0.9 g/kg/d resulted in a one-day longer duration of MV.[3]

Conclusion

Protein consumption does not affect the length of MV. However, a regular protein intake may improve mortality in patients undergoing MV.

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Risk factors for mortality in patients with pneumonia caused by Stenotrophomonas maltophilia in the critical care unit

Introduction

Stenotrophomonas maltophilia is a gram-negative, glucose, non-fermenting bacteria that was commonly found in medical settings. In recent decades, it has been identified as an important pathogen causing hospital-acquired infections in extremely ill or immunocompromised persons. It typically leads to pneumonia and bacteremia, but can also cause infections in the urinary tract, intra-abdominal organs, and wounds. *S. maltophilia* infections are challenging to treat because they are resistant to multiple antibiotic classes. [1] There is a substantial risk of ICU mortality from ICU-acquired *S. maltophilia* pneumonia, which has been linked to frequent factors seen in patients hospitalized to the intensive care unit (ICU), including severe illness, invasive procedures, and exposure to broad-spectrum antibiotics. According to previous studies, the incidence of *S. maltophilia* pneumonia in intensive care units appears to rise with time. Furthermore, there has been a rise in the rates of resistance to medications that have historically demonstrated excellent susceptibility. Despite its growing clinical significance, *S. maltophilia* has received far less research attention than other Gram-negative bacteria, and there is a lack of information on clinical cases of *S. maltophilia* pneumonia in intensive care units.[2] The purpose of this study was to retrospectively examine *S. maltophilia* pneumonia patients who were in the intensive care

ICU patients with *S. maltophilia* pneumonia had a significant mortality rate. In-hospital mortality was shown to be greater with older age, higher Sequential Organ Failure Assessment (SOFA) score, and corticosteroid usage, while lower with polymicrobial infection.

unit (ICU) in order to characterize their clinical characteristics and investigate antibiotic therapy, associated with mortality.

Methods

A retrospective analysis was performed on patients with *S. maltophilia* pneumonia who were hospitalized to two tertiary referral institutions' ICUs. Electronic medical records were used to collect baseline information about patients, such as demographics, co-morbidities, and laboratory test results. Variables indicative of severity at the time of ICU admission, such as scores from the Sequential Organ Failure Assessment (SOFA) and the Acute Physiological and Chronic Health Evaluation (APACHE) II, were assessed and the possibility of prior antibiotic exposure within the previous 90 days was examined. Vasopressor usage before *S. maltophilia* infection was documented. Multivariable logistic regression studies were carried out to evaluate risk variables related to in-hospital mortality.

Results

The data from 117 individuals with *S. maltophilia* were examined. The study population's median age was 71 years. Prior to the initial identification of *S. maltophilia*, the median length of ICU hospitalization was 15 days, and 76.1% of cases had ventilator-associated pneumonia. The overall in-hospital mortality rate was 82.1%. Factors independently associated with mortality included age (odds ratio [OR], 1.05; 95% confidence interval [CI], 1.00-1.09; P=0.046), SOFA score (OR, 1.21; 95% CI, 1.02-1.43; P=0.025), corticosteroid use (OR, 4.19; 95% CI, 1.26-13.91; P=0.019), and polymicrobial infection (OR, 95% CI 0.07-0.69) (Table 1). Appropriate antibiotic treatment did not significantly reduce mortality. In a sample of 58 patients who received proper antibiotic therapy, there was no significant connection between antibiotic treatment mode (combination or empirical therapy) and survival.

Variable	Univariate analysis			Multivariable analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age (yr)	1.04	1.00–1.09	0.043	1.05	1.00–1.09	0.046
APACHE II score	1.04	0.97–1.12	0.300			
Vasopressor use	1.17	0.25–4.14	0.800			
SOFA score on the day of index culture collection	1.13	0.99–1.30	0.082	1.21	1.02–1.43	0.025
Polymicrobial infection	0.20	0.07–0.54	0.002	0.22	0.07–0.69	0.009
Corticosteroid use	3.48	1.25–11.3	0.024	4.19	1.26–13.91	0.019
Appropriate antibiotic therapy	1.10	0.43–2.87	0.800			

Table 1. Variables related with in-hospital death evaluated using multivariable logistic regression analysis. (OR: odds ratio; CI: confidence interval; APACHE: Acute Physiological and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment.)

Discussion

In this study of 117 critically sick patients with *S. maltophilia* pneumonia, the in-hospital death rate was approximately 82%. Age, SOFA score, corticosteroid usage, and polymicrobial infection all had an independent association with in-hospital mortality.

Appropriate antibiotic treatment, including empiric or combination therapy, did not significantly impact mortality rates.[2] Puech B et al. on critically sick patients with *S. maltophilia* pneumonia showed a hospital or ICU death rate of around 50% [3], which was less than the present study.

Conclusion

Patients in ICU with *S. maltophilia* pneumonia had a significant mortality rate. Older age, higher SOFA score, and corticosteroid usage were linked to higher in-hospital mortality, but polymicrobial infection was related with decreased mortality. Appropriate antimicrobial medication did not significantly impact prognosis.

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A retrospective study on the long-term outcomes of new-onset refractory status epilepticus

Introduction

The results of this study suggested that the long-term prognosis for NORSE survivors may still be quite good, even during a lengthy and complicated ICU stay.

New onset refractory status epilepticus (NORSE) is a neurological emergency that occurs in people who do not have a history of epilepsy or a clear etiology.[1] NORSE is uncommon and generally affects healthy young adults and school-aged children. The adult series had more female subjects, whereas children had more male individuals. The disorder rarely affects older persons over 60 years old. The average stay in intensive care was 15 days for adults and 20-40 days for children. Patients with cryptogenic NORSE experience prolonged status epilepticus.[2] Despite comprehensive diagnostics, at least half of NORSE patients remain cryptogenic. Patients with severe NORSE often require sedation and invasive therapies, leading to admission to the Intensive Care Unit (ICU). The ICU stay can be lengthy, lasting weeks to months. There are no established predictive tools to assist physicians and families in deciding between the benefits and the risks.[1] The purpose of this study was to investigate ICU treatments, short- and long-term outcomes, and ethical judgments in Norse patients.

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Methods

This retrospective analysis examined people (≥18 years old) hospitalized with SE to the Neurocritical Care Unit (NCCU). The data was collected retrospectively from the included patients' medical records. The research collected demographic, clinical, diagnostic, treatment, and outcome data from medical records. Outcome data (modified Rankin scale (mRS)) were evaluated at discharge, 12 months, and final available follow-up for survivors. Descriptive statistics were used.

Results

Out of 283 SE patients admitted to the ICU, 25 satisfied the NORSE criteria and were included in the research. The majority of patients were female (68%), previously healthy (Charlson comorbidity score 1 [0-4]), and relatively young (54±17 years). Super-refractory SE was present in 96% of cases. Despite comprehensive testing, 68% of cases remained cryptogenic. The majority of patients had a long and complicated ICU stay. In-hospital mortality was 36% (n = 9). Thirty months following ICU admission, the average mortality was 56% (n=14) at the final follow-up that was available. Withholding or stopping therapy was the reason for 89% (n=8) of the patients' in-hospital mortality. The end-of-life (EOL) decision was made 29 [12-51] days following ICU admission (Table 1). The functional result of 13/16 (81%) hospital survivors improved with time (median mRS at hospital discharge = 4 [3.75-5] vs. median mRS at final available follow-up = 2 [1.75-3], p<0.001).

In hospital death, *n* (%)	9 (36)
Death at last available follow-up, *n* (%)	14 (56)
Limitation of treatment in deceased patients (data available for 12/14 pts), *n* (%)	10 (77)
Presence of written advance directives in deceased patients, (data available for 12/14 pts), *n* (%)	3 (25)
Trigger of EOL decision, data for patients who died in hospital *n* = 9	
Medical staff, *n* (%)	8 (89)
Relatives, *n* (%)	1
Time of EOL decision from ICU admission, days (*n* = 10)	29 [12–51]
Time from EOL decision to death, days, (*n* = 10)	6 [1–8.5]
mRS at hospital discharge (*n* = 25, median and range)	5 [4-6]
mRS at hospital discharge for survivors (*n* = 16)	4 [3.75–5]
mRS at 12 months for survivors (data available for 14/16 patients)	2 [1.25–2.75]
mRS at last available follow-up for survivors (*n* = 16; median and range)	2 [1.75–3]
Favorable mRS (0–2) at last available follow-up for hospital survivors (*n* = 16) *n* (%)	10 (62.5)
Timing of last available follow-up for hospital survivors (*n* = 16) from admission date (days, median and IQR)	728 [521–997]

Table 1: Outcome and end of life process. (EOL, End of life; mRS, modified Rankin scale; ICU, intensive care unit; Data were presented as counts/percentages, or as median including the interquartile range (IQR), as appropriate)

Discussion

NORSE is an uncommon, relatively new disorder. The research group experienced prolonged ICU and hospital stays, requiring invasive therapies and resulting in many complications. In-hospital mortality reached 36%.[1] In previous research on new-onset refractory status epilepticus by James J. Gugger et al. found that 35% died in the hospital or within six months of discharge.[3]

Conclusion

This study finding indicate that even after a long and complex ICU stay, the long-term prognosis for NORSE survivors may still be excellent. To avoid self-fulfilling prophecy, clinicians should be caution while making end-of-life choices. This study encourages doctors to continue therapy, even in instances that are initially refractory.

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Case report on Extracorporeal life support as a successful bridge to recovery in pulmonary arterial hypertension

Introduction

Pulmonary arterial hypertension (PAH) is characterized by increasing pulmonary vascular resistance (PVR) caused by minor pulmonary artery remodeling. Acute right ventricular failure might exacerbate the condition and lead to 30-40% mortality in the intensive care unit (ICU). Patent foramen ovale (PFO) causes a right-to-left (RL) shunt, lowering RV stress but resulting to hypoxemia.[1] PAH is diagnosed after ruling out cardiac, pulmonary, or thrombo-embolic causes of elevated pulmonary artery pressure (PAP). A right heart catheterization revealed a mean pulmonary arterial pressure (mPAP) of >20 mmHg, a wedged PAP (PAWP) of ⩽15 mmHg, and a PVR of ⩾3 Wood units.[2] To manage advanced RV dysfunction, it was important to address potential triggering factors, optimize hemodynamics by fluid volume control and pharmacological support, and use PAH medications to reduce RV afterload. Extracorporeal life support (ECLS) should be considered for patients with extensive RV failure or severe hypoxemia. The goal was to restore patients to their baseline clinical condition before or after lung transplantation, or to facilitate pharmaceutical optimization of PAH. There were few reports of using ECLS as a bridge to initiate PAH medications in patients with acute RV failure or severe hypoxemia.[1] This case report described a patient with undiagnosed PAH experienced severe hypoxemia and effectively recovered with PAH medication following ECLS implementation.

In a case of heritable PAH with refractory hypoxemia, VA-ECMO can be employed as a "bridge-to-recovery" method to initiate triple treatment and improve hemodynamics and clinical outcomes.

Case Presentation

A 30-year-old woman with no medical history was hospitalized after experiencing increased shortness of breath with exercise over a month. Her shortness of breath worsened even at rest, causing her to seek emergency care. The patient had a temperature of 37.5°C, blood pressure of 104/82 mm Hg, heart rate of 112 beats per minute, respiratory rate of 17 breaths per minute, and pulse oxygen saturation of 92% while breathing via a high-flow nasal cannula (HFNC) with a fraction of inspired oxygen (FiO2). Physical examination revealed pulsing jugular veins, regular tachycardia, elevated second heart sound, and normal pulmonary auscultation. The patient experienced significant shortness of breath. A blood check showed a white cell count of 14,200 cells/mm^3 (56.2% lymphocytes, 37.2% neutrophils, 5% monocytes, 0.8% eosinophils, and 0.8% basophils), a hemoglobin level of 14.2 g/dL, and a platelet count of 254,000 cells/mm^3.The N-terminal prohormone brain natriuretic peptide (NT-pro BNP) level was 1,328 pg/mL. The arterial blood gas (ABG) under HFNC at FiO2 1 indicated a pH of 7.45, PaCO2 of 25 mm Hg, PaO2 of 66 mm Hg,

HCO3- of 19 mmol/L, SaO2 of 92%, and lactate of 0.7mmol/L^{-1}. Chest radiography revealed an elevated cardiothoracic index and a protrusion in the left middle arch (Figure 1). CT angiography of the chest showed no parenchymal abnormalities or pulmonary embolism, however the pulmonary artery trunk was 35 mm dilated with a ratio of 1.1 between pulmonary artery diameter and aortic diameter. The ECG revealed sinus tachycardia with right-axis deviation and high P-waves in leads II, III, and V3-V5. A transthoracic echocardiography (TTE) revealed a normal left ventricular shape and 55% ejection fraction. The RV was severely dilated with impaired systolic function. The tricuspid annular plane had a systolic excursion of 16 mm and the RV S-wave was 10 cm/s. The estimated pulmonary artery pressure was 93 mm Hg. Early positive contrast was seen on transthoracic contrast echocardiography, which confirmed PFO (Figure 2). The patient was admitted to the ICU for treatment of acute hypoxemia. A right heart catheterization in the ICU revealed severe pre-capillary pulmonary hypertension, with mPAP of 65 mm Hg, RAP of 15 mm Hg, PAWP of 14 mm Hg, cardiac index of 1.7 L/min/m2, and PVR of 18 Woods units. When faced with hypoxemic respiratory failure, mechanical ventilation (MV) was administered. MV was modified by adjusting FiO2 and PEEP levels, alveolar opening pressure, and individualized tidal volume in volume control mode. High dosages of diuretics were started with adaptive monitoring. Despite this, the patient remained significantly hypoxemic. ECLS was established to prevent tissue hypoxia. The mechanical alternative chosen was peripheral femoro-femoral venoarterial extracorporeal membrane oxygen (VA-ECMO), implanted percutaneously with a 15 Fr arterial cannula and 19 Fr venous cannula. The ECMO flow was set to 3.5 L/min, the sweep at 2.0 L/min, and the membrane oxygen percentage at 0.45. Following VA-ECMO implantation, lung-protective ventilator techniques were implemented. The absence of evidence for chronic respiratory illness or chronic thromboembolic pulmonary hypertension on medical history and chest CT angiography led to the diagnosis of PAH as the cause of severe pre-capillary hypertension. As a result, a combination of PAH medicines was immediately started. A combination of oral therapies (bosentan and tadalafil) and a continuous intravenous epoprostenol infusion (starting at 4 ng/kg/min and subsequently increasing to 10 ng/kg/min every 12 hours) were administered. PAH medications resulted in a significant improvement, allowing for decannulation 7 days after therapy began. The patient was discharged from ICU and sent to a hospital ward. After 29 days, the patient was discharged from the hospital on epoprostenol (16 ng/kg/min, progressively increasing), bosentan, and tadalafil. After 2 years of follow-up, clinical, biochemical, and hemodynamic data show minimal risk.

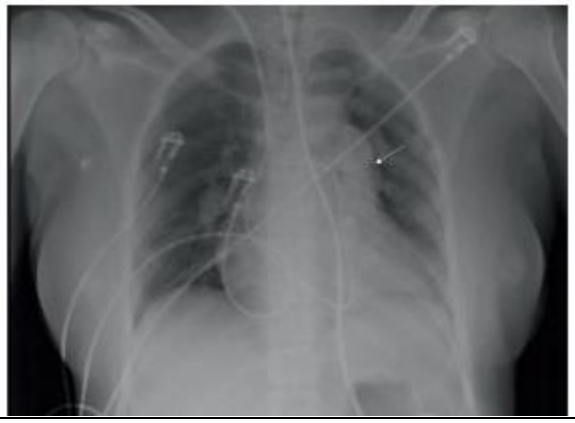

Figure 1: Chest radiography following ICU admission. The image shows a big left central pulmonary artery with an obliterated aortopulmonary window (white arrow).

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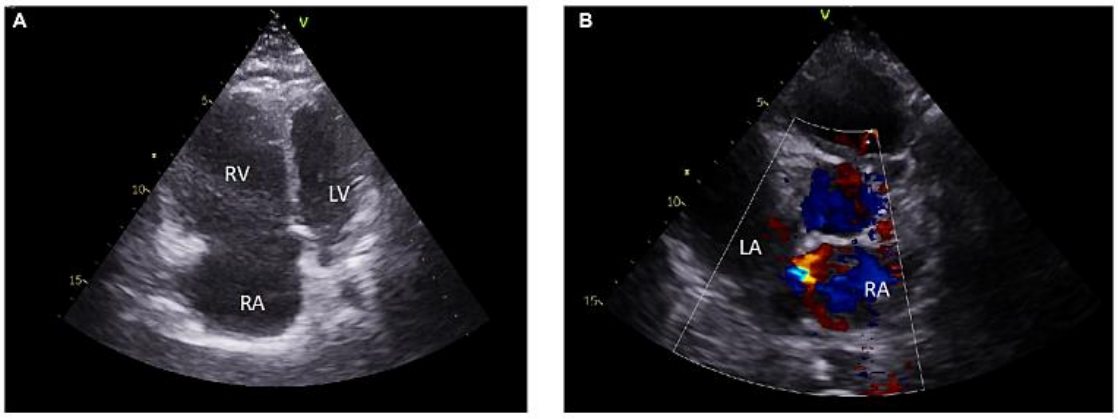

Figure 2: Initial transthoracic echocardiography. Echocardiograms revealed an enlarged right ventricular cavity, dilated right atrial cavity, and smaller left ventricular cavity with flattening of the interventricular septum (A). There was indications of a patent foramen ovale. RA refers to the right atrium, RV to the right ventricle, and LV to the left ventricle.

Discussion

This case report demonstrated a heritable PAH patient with acute hypoxemic respiratory failure caused by a massive PFO. Treatment with PAH medications and ECLS resulted in significant hemodynamic and clinical improvements. ECLS has been shown to effectively treat patients with WHO Group 1 pulmonary hypertension and acute RV failure or refractory hypoxemia under the "bridge-to-transplantation" approach.[1] Tyler Pitre et al. found that, for treatment of pulmonary arterial hypertension combination treatment with endothelin receptor antagonists (ERA) with phosphodiesterase-5 inhibitors (PDE5i) decreased clinical deterioration and was superior to either ERA or PDE5i alone, both of which reduced clinical worsening, as did riociguat monotherapy.[3] In the present case, a combination of oral therapies (bosentan and tadalafil) and continuous intravenous epoprostenol infusion (starting at 4ng/kg/min and subsequently increasing to 10ng/kg/min every 12 hours) were used.[1]

Conclusion

This case with heritable PAH with refractory hypoxemia highlighted the effectiveness of VA-ECMO as a "bridge-to-recovery" method, leading to rapid beginning of triple treatment and significant hemodynamic and clinical improvements.

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