Critical Rounds Newsletter
VOL 5 | Issue 50 | 2024

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. Association between timing of mechanical ventilation and the clinical outcomes in patients with sepsis ventilated in intensive care unit

2. Characteristics and outcomes of acute respiratory distress syndrome in hematological malignancies patients

3. Incidence of hypothermia and the predictive factors for developing hypothermia during continuous renal replacement therapy

4. Case report on acute pancreatitis caused by hypertriglyceridemia treated with therapeutic plasma exchange

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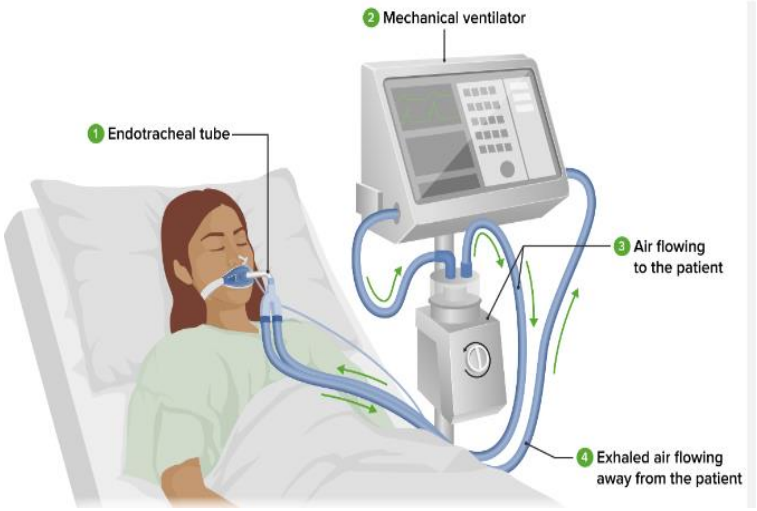
Best Regards,
Medical Team, Micro Labs Limited

Association between timing of mechanical ventilation and the clinical outcomes in patients with sepsis ventilated in intensive care unit

Introduction

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. Extending the duration of mechanical ventilation was linked to a higher risk of complications, chronic dysfunction, and mortality, and may result in serious consequences.[1] However, MV increases gas exchange, lowers the work of breathing, and minimizes the risk of patient self-inficted lung injury and lowers the venous return and reduces the left ventricular afterload. Together, these effects can help stabilize hemodynamics and alleviate acid-base abnormalities in sepsis patients. There was conflicting evidence in the literature regarding when to intubate sepsis patients. While some studies has indicated positive effects of early MV, other investigations have not found any significant benefits.[2] The purpose of this study was to investigate the relationship between the timing of MV and the clinical outcomes of sepsis patients in the intensive care unit (ICU).

Early Mechanical ventilation (MV) initiation may be associated with a lower mortality rate in sepsis patients ventilated in the intensive care unit.



Invasive Mechanical Ventilation

Methods:

This prospective multicenter cohort study collected data of adult patients with sepsis and comprised patients who received MV and were hospitalized to the intensive care unit. Patients were divided into 'early MV' and 'delayed MV' groups based on whether they were on MV on the first day of ICU admission or later. To reduce bias between the groups, propensity score matching was used and patients in the two groups were compared 1:1. Results were compared for ICU mortality, hospital mortality, length of stay in the ICU and hospital, and organ failure at ICU discharge.

Results

A total of 2440 patients on mechanical ventilation during their ICU stay were examined; 2119 cases were classified as "early MV" and 321 as "delayed MV." The median respiratory rate for the "early MV" group was lower than that of the "delayed MV" group (22 [18–27] vs. 25 [21–31] breaths/min, p <0.01). The "early MV" group had a higher initial SOFA score (8 [5–10] vs. 7 [4–9], p < 0.01) than the "delayed MV" group. Propensity score matching identified 295 patients with comparable baseline characteristics in each group. ICU mortality was reduced in the early MV group compared to the delayed MV group (36.3% vs. 46.4%; odds ratio, 0.66; 95% confidence range, 0.47-0.93; p=0.015). Better results were seen in ICU mortality (38.4% vs. 45.2%, p=0.025), in-hospital mortality (47.7% vs. 54.8%, p=0.020), hospital duration (19 [8–37] days vs. 24 [12–50] days, p <0.001), and duration of ICU stay (7 [3–15] days vs. 12 [6–20] days, p <0.001) when the "early MV" group was compared to the "delayed MV" group (Table 1).

	(A) Unmatched cohort			(B) Propensity score-matched cohort			
	Early MV n = 2119	Delayed MV n = 321	*p* value	Early MV n = 295	Delayed MV n = 295	OR (95% CI)	*p* value
ICU mortality	814 (38.4)	145 (45.2)	0.025	107 (36.3)	137 (46.4)	0.66 (0.47–0.93)	0.015
In-hospital mortality	1010 (47.7)	176 (54.8)	0.020	132 (44.7)	165 (55.9)	0.64 (0.46–0.89)	0.008
Hospital duration (days)	19 [8, 37]	24 [12, 50]	< 0.001	18 [8, 35.5]	23 [12, 48.5]		0.001
ICU duration (days)	7 [3, 15]	12 [6, 20]	< 0.001	7 [3, 14]	12 [6, 20]		< 0.001
MV duration (days)	5 [2, 12]	6 [2, 14]	0.249	4 [2, 10.5]	6 [2, 13.5]		0.060
During ICU stay							
ARDS	150 (7.1)	26 (8.1)	0.587	13 (4.4)	25 (8.5)	0.50 (0.23–1.04)	0.065
Renal replacement therapy	566 (26.7)	58 (18.1)	0.001	83 (28.1)	55 (18.6)	1.71 (1.14–2.57)	0.009
At ICU discharge							
Oxygen requirement	737 (56.5)	93 (52.8)	0.406	104 (55.3)	83 (52.5)	1.12 (0.72–1.75)	0.682
MV	186 (14.3)	22 (12.5)	0.608	22 (11.7)	19 (12.0)	0.97 (0.48–1.98)	1.000
HFNC	175 (13.4)	27 (15.3)	0.559	23 (12.2)	26 (16.5)	0.71 (0.37–1.36)	0.333
Tracheostomized	290 (22.2)	53 (30.1)	0.025	31 (16.5)	49 (31.0)	0.44 (0.25–0.75)	0.002
Renal replacement therapy	93 (7.1)	24 (13.6)	0.004	16 (8.5)	22 (13.9)	0.58 (0.27–1.20)	0.152

Table 1. Outcomes of the study population

Discussion

This study demonstrated that "early MV" initiation by the first day of ICU admission was linked with a shortened length of ICU stay and lower mortality (both ICU mortality and in-hospital mortality) in sepsis patients ventilated in the ICU.[2] Retrospective investigation of 358 patients with septic shock revealed that intubation within 24 hours after the start of sepsis was linked to fewer days without hospitalization through 28 days.[3] A study of 735 septic shock patients found no significant differences in hospital mortality or length of stay between the early and delayed MV groups.[4]

Conclusion

Early MV initiation (first day of ICU admission) may be linked to a decreased mortality rate in patients with sepsis ventilated in the ICU.

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Characteristics and outcomes of acute respiratory distress syndrome in hematological malignancies patients

Introduction

Acute respiratory distress syndrome (ARDS) is characterized by extensive lung inflammation and edema, leading to acute respiratory failure (ARF). In 2016, ARDS was found in 10.4% of patients admitted to the intensive care unit.[1] The number of patients with hematological malignancies (HM) admitted to critical care units (ICUs) has increased. ARDS was reported in around 40% of HM patients admitted for ARF. HM is an uncommon disease which makes interpreting the relationship between ARDS and a particular kind of HM very challenging.[2] The purpose of this study was to characterize the features and outcomes of ARDS in HM patients who were hospitalized in intensive care units (ICUs) over a year.

In the patients with hematological malignancies (HM), mortality was predicted by a diagnosis of lymphoma or acute leukemia, age, a high modified SAPS II score, renal replacement therapy, invasive fungal infection, and septic shock.

Methods

This was a retrospective nationwide cohort study that included all patients (18 years or older) admitted to ICUs and with a diagnosis of ARDS. Three groups were compared based on the existence of an HM, solid cancer, or no cancer. The characteristics and outcomes of ARDS patients with HM were compared to those with no cancer or solid cancer. The primary outcome was 90-day mortality. The explanation of ICU management, the causes of ARDS, and the risk factors for mortality were secondary outcomes.

Results

A total of 12,846 patients with ARDS were included. Among them, 990 had HM, whereas 2744 had solid cancer. The three most common cancers were multiple myeloma (19.7%), acute myeloid leukemia (20.4%), and non-Hodgkin lymphoma (NHL, 28.5%). Patients with HM had a higher day-90 death rate than those without cancer (64.4% vs. 46.6%, p=0.01), but remained similar to those with solid cancer (64.4% vs. 61.4%, p=0.09) (Table 1). Compared to both groups, patients with HM had a decreased intubation rate (87.7% vs. 90.4% p=0.02 for patients with solid cancer and 87.7% vs. 91.3%; p<0.01 for patients without cancer). A diagnosis of lymphoma or acute leukemia, age, a high modified SAPS II score, renal replacement treatment, an invasive fungal infection, and septic shock were independent predictors of mortality for patients with HM. Protective factors were bacterial pneumonia, extrapulmonary infections, and non-invasive ventilation.

	Hematological Malignancies (*n* = 990)	Solid cancer (*n* = 2744)	No cancer (*n* = 9112)	HM vs. no cancer comparison		HM vs. solid cancer comparison	
				p value	Standardized difference	*p* value	Standardized difference
Outcomes							
ICU mortality	595 (60.10%)	1570 (57.22%)	4046 (44.40%)	< 0.0001	**0.3182**	0.1149	0.0586
In-hospital mortality	627 (63.33%)	1661 (60.53%)	4273 (46.89%)	< 0.0001	**0.3351**	0.1209	0.0577
90-day mortality	638 (64.44%)	1685 (61.41%)	4249 (46.63%)	< 0.0001	**0.3644**	0.0910	0.0629
Duration of stay							
Duration of ICU stay, median (IQR), days	11.00 [3.00–20.00]	11.00 [5.00–22.00]	13.00 [5.00–26.00]	< 0.0001	**0.2100**	0.0395	0.0739
Duration of hospital stay, median (IQR), days	25.00 [11.00–44.00]	23.00 [11.00–42.00]	23.00 [10.00–43.00]	0.7121	0.0114	0.1970	0.0473

HM: hematological malignancies ICU: intensive care unit IQR: interquartile range

Table 1. Outcomes

Discussion

This study characterized the patients diagnosed with HM and admitted to the ICU for ARDS. The three primary cancers were MM, AML, and NHL. Predictors of mortality in this population were a diagnosis of lymphoma or acute leukemia, age, a high modified SAPS II score, renal replacement treatment, invasive fungal infection, and septic shock.[2] A previous study found that the presence of carbapenem-resistant gram-negative bacteria, the amount of blood product transfusion, severe ARDS, and progressing or refractory disease were the variables that were independently linked to a greater ICU mortality.[3]

Conclusion

Patients with HM in ICU with ARDS have a higher mortality rate compared to those without cancer. Predictors of mortality in this population were a diagnosis of lymphoma or acute leukemia, age, a high modified SAPS II score, renal replacement treatment, invasive fungal infection, and septic shock.

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Incidence of hypothermia and the predictive factors for developing hypothermia during continuous renal replacement therapy

Introduction

Hypothermia during Continuous renal replacement therapy (CRRT) is prevalent and can occur within 24 hours. Increased temperature variability was linked to higher ICU mortality.

Continuous renal replacement therapy (CRRT) is a type of dialysis used for extremely ill patients who cannot tolerate hemodialysis. Renal replacement therapy (RRT) replaces certain functions of underperforming kidneys. The physician's assessment of a patient's medical history, vital signs, laboratory findings, and medications plays a significant role in deciding whether to initiate CRRT. Unfortunately, almost 50% of people on CRRT do not survive.[1] Hypothermia is a common consequence of extracorporeal blood purification. Hypothermia can cause cardiac arrhythmia, increased oxygen demand, hemodynamic instability, coagulopathy, and mask fever or infection, leading to poor results. CRRT-related hypothermia may worsen with greater doses or usage of unheated dialysate and replacement fluid. Lowering blood temperature can improve hemodynamic stability while maintaining hepatosplanchnic oxygen concentration and energy balance. The standard guidelines and present recommendations do not address this issue, causing confusion to persist.[2] So, this study determined the prevalence of hypothermia in critically ill patients with acute kidney injury (AKI) requiring CRRT, as well as the factors related to hypothermia. This study also investigated how temperature manipulation during CRRT affects patient outcomes.

Methods

This was a retrospective cohort study conducted in five intensive care units (ICUs) to assess the prevalence and risk factors for hypothermia during CRRT. This study included all critically ill patients with severe AKI receiving CRRT. Hypothermia was defined as a time-weighted average temperature of <36°C. The primary outcome of this study was the prevalence of hypothermia in the first 24 hours of CRRT. Secondary outcomes included variables related to hypothermia among patients starting CRRT.

Results

This study included 300 patients. Within the first 24 hours of CRRT commencement, 23.7% experienced hypothermia. Hypothermic patients were older, had lower body weight, experienced greater acidemia, and had higher ICU and 30-day mortality rates than non-hypothermic patients. In the multivariate analysis, hypothermia was significantly linked with age >70 years (odds ratio [OR], 2.59; 95% CI, 1.38-4.98; P=0.004), positive fluid balance on the day before CRRT (OR, 1.11; 95% CI, 1.02-1.22; P=0.02), and CRRT dosage (OR, 1.003; 95% CI, 1.00-1.01; P=0.04). A higher body weight was related to a lower incidence of

hypothermia (OR, 0.89; 95% CI, 0.81-0.97; P=0.01) (Table 1). A higher coefficient of variance of temperature was linked to higher ICU mortality (OR, 1.41; 95% CI, 1.13-1.78; P=0.003).

Variable	Univariable model		Multivariable model[a]	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Age (yr)	1.02 (1.00–1.03)	0.005	1.02 (1.00–1.04)	0.05
Age >70 yr	2.04 (1.19–3.54)	0.01	2.59 (1.38–4.98)	0.004
Body weight (kg)	0.97 (0.95–0.99)	0.01	0.89 (0.81–0.97)	0.01
Metabolic acidosis[b]	2.19 (1.28–3.84)	0.005	1.56 (0.80–3.08)	0.20
Fluid balance on the day before CRRT (L)	1.12 (1.03–1.23)	0.01	1.11 (1.02–1.22)	0.02
Fluid balance on the day of CRRT (L)	1.10 (1.03–1.17)	0.007	1.10 (1.00–1.21)	0.05
Dose of CRRT (ml/kg/hr)	1.04 (1.01–1.06)	0.01	1.003 (1.00–1.01)	0.04
Temperature of CRRT (°C)	1.12 (0.91–1.37)	0.27	-	-

CRRT: continuous renal replacement therapy.
a) Multivariable models were performed by significant factors on univariable models; b) Defined as blood pH less than 7.3.

Table 1. Univariable and multivariable models for time-weighted average temperatures of less than 36°C

Discussion

This study assessed the prevalence and risk factors for hypothermia during the first 24 hours of CRRT. This study found that older age, positive cumulative fluid balance, and larger CRRT dose were independently linked with hypothermia. Conversely, higher body weight was associated with a reduced risk of hypothermia.[2] A previous study showed that low body weight, continuous venovenous hemodiafiltration, drowsiness, immobility, and infection are risk factors for CRRT-related hypothermia.[3]

Conclusion

Hypothermia during CRRT was prevalent and can occur within 24 hours. Risk factors include older age, lower body weight, positive fluid balance on the day before CRRT, and higher CRRT dose. Increased temperature variability was linked to higher ICU mortality.

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Case report on acute pancreatitis caused by hypertriglyceridemia treated with therapeutic plasma exchange

Introduction

Acute pancreatitis is an inflammatory of the exocrine pancreas that results in severe abdominal discomfort and organ dysfunction. It can lead to pancreatic necrosis and prolonged organ failure, with a mortality rate of 1-5%. Acute pancreatitis causes significant short and long-term morbidity.[1] The key clinical difficulty is identifying patients at risk of deterioration and admitting them to the intensive care unit (ICU) early on. Treatment for AP is primarily supportive, except for specific triggering causes such as biliary obstruction or cholangitis, which require urgent endoscopic retrograde cholangiopancreatography, and high triglyceride levels (TG). Lowering TG levels can help reduce inflammation.[2] This case report discusses an emergency therapeutic plasma exchange (TPE) for a patient with AP caused by elevated TG levels.

Therapeutic plasma exchange (TPE) may be used in conjunction with other blood purifying techniques to reduce HTG and inflammatory mediators.

Case Presentation

A 49-year-old woman was admitted to the intensive care unit (ICU) for hypotension, dyspnea, severe abdominal pain, and vomiting. She had no relevant clinical history. The symptoms started 6 hours ago and quickly intensified, along with breathlessness. The patient was overweight (BMI = 29), with a mean arterial pressure (MAP) of 55 mmHg, a heart rate of 125 bpm, and a respiratory rate of 28 with a SpO2 of 92% and a FiO2 of 50%. She also had oliguria and an intra-abdominal pressure (IAP) of 12 mmHg, which remained stable throughout the clinical course. A CT scan of the abdomen revealed an edematous pancreas with significant ascites. Intravenous administration of 3000 ml of crystalloids resulted in better MAP, HR, and urinary output, with milky urine. Blood samples had to be resent twice due to an analyzer congestion that prevented processing. Blood tests revealed that the patient had significant HTG and hypercholesterolemia. To lessen lipid burden, an emergency filter-based TPE was used to replace 1.5 times the total plasma volume (TPV). This variable was calculated using the formula.

$$TPV = Total\ Blood\ Volume(TBV) * (1 - Hematocrit)$$

After removing 3000 ml of plasma and replacing it with 5% albumin, the TG and cholesterol levels reduced significantly (94% and 77%, respectively), and the plasma no longer appeared lipemic. In the following days, TG and cholesterol levels remained elevated (Figure 1), but amylase levels decreased. However, CRP levels were increased, indicating an ongoing inflammatory process. Following 48 hours, enteral feeding with Omega-3 fatty acids was begun. Six days following ICU admission, the patient was shifted to the surgery ward. After a CT scan two weeks later, the pancreas was almost totally replaced by a huge pseudocyst. Despite this, the patient was asymptomatic and went home a few days later to be monitored on an outpatient basis.

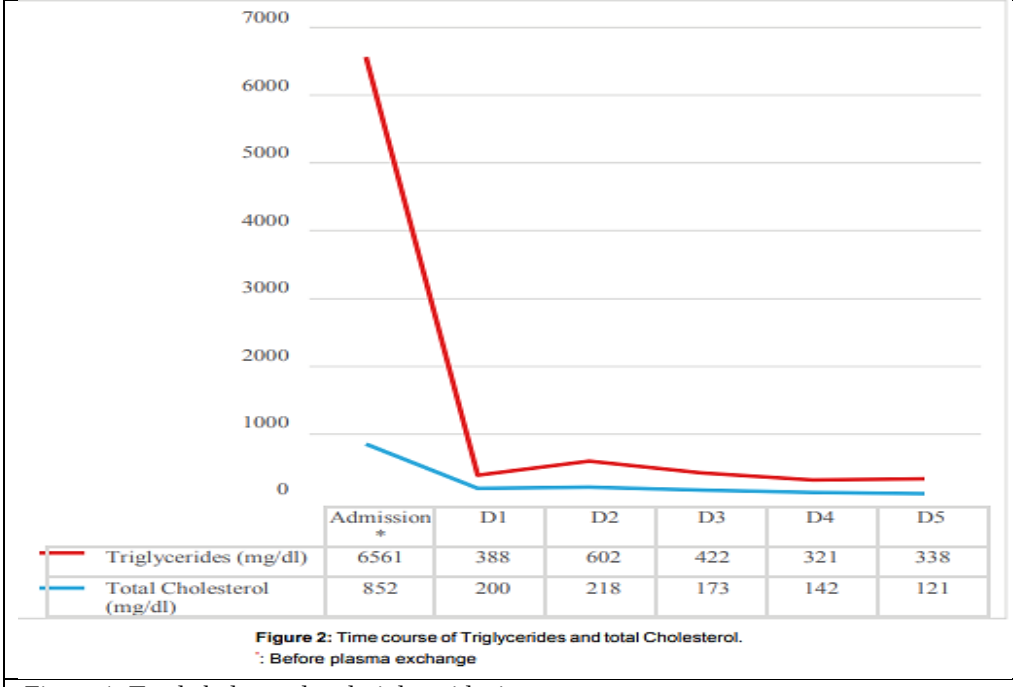

Figure 1: Total cholesterol and triglyceride time courses.

Discussion

Severe AP treatment includes fluid resuscitation, vasopressor medication, organ support, and nutrition supplements through the enteral route.[2] A previous study showed that disease-specific treatment is currently unclear and supportive care, including nutrition intervention, is critical. Nutritional treatment not only prevents malnutrition, but also plays an important role in reducing systemic inflammation, complications, and mortality. Some nutritional supplements, such as intravenous glutamine in patients with complete parenteral nutrition (PN), can result in good results.[3]

Conclusion

HTG-associated AP is a rare and life-threatening condition that requires rapid diagnosis and treatment. TPE may be used in conjunction with other blood-purifying techniques to reduce HTG and inflammatory mediators.

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