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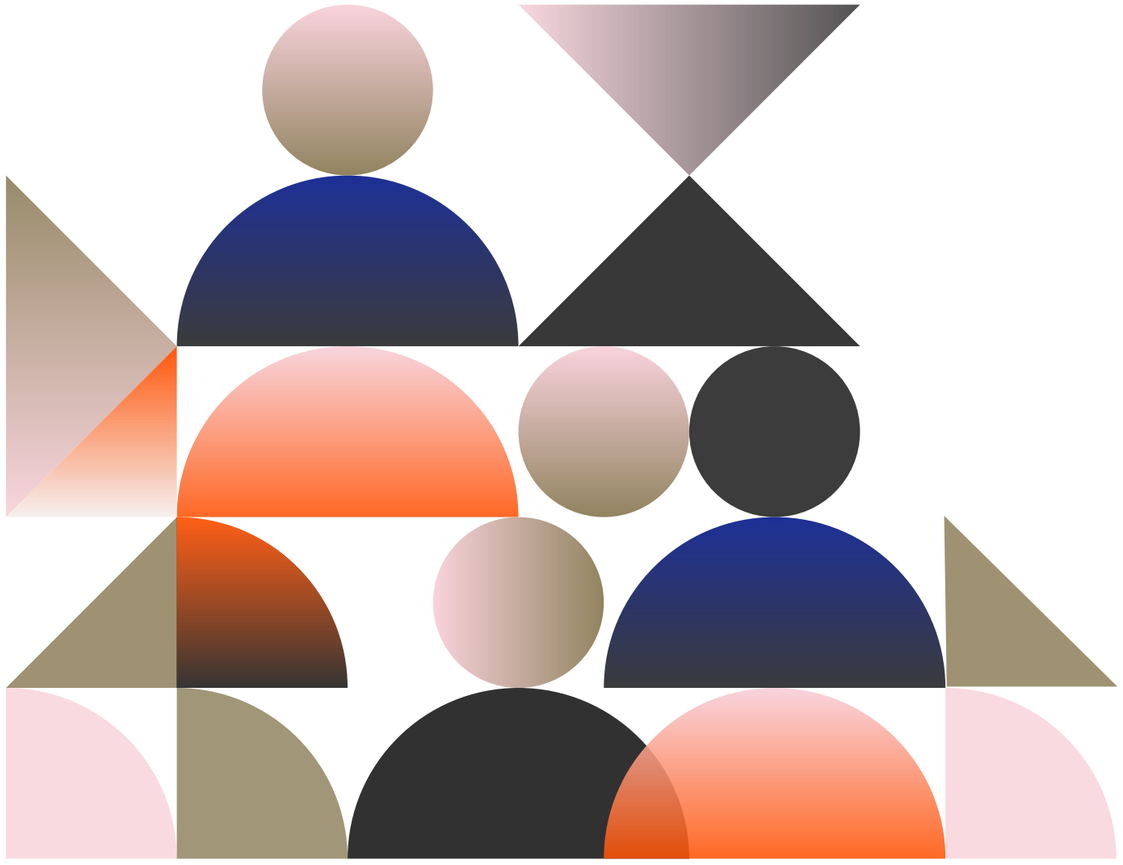

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Aims and Scope

Archives of Pediatric Critical Care (abbreviated as Arch Pediatr Crit Care, APCC) is the official journal of Korean Society of Pediatric Critical Care Medicine. This is a peer-reviewed scientific journal that considers articles on all aspects of pediatric intensive and critical care medicine. It publishes current clinical and research works and ideas in these fields. The journal aims to accumulate evidence and rapid dissemination of recently updated knowledge from clinical and experimental results through the prompt publication to inform all pediatricians, pediatric intensivists, pediatric critical care nurses, and other healthcare professionals, researchers, and policy makers related to pediatric critical care to improve the field of pediatric critical care. Additionally, it will initiate dynamic, international, and academic discussions concerning the major topics related to pediatric critical care. The journal is published biannually on the last day of June and December. It publishes editorial, original articles, review articles, case reports, and letters to the editor in the field of pediatric intensive and critical care medicine.
Its regional focus is mainly Korea, but it welcomes submissions from researchers all over the world.

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The importance of nutritional support in critically ill pediatric patients: a focus on refeeding syndrome

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Normally, our body copes with a critical illness in a protective manner, aiming to minimize the insult by activating multiple immunological, metabolic, and hormonal responses. During this acute phase, energy delivery is primarily targeted to vital organs for lifesaving purposes. However, when adequate energy delivery and utilization are impaired, the body shifts into an intense catabolic state, which includes muscle breakdown, insulin resistance, stress hyperglycemia, and negative protein balance [1,2]. These significant metabolic disturbances can progress to a profound state of malnutrition if proper nutritional support is not initiated and provided in a timely manner [3,4].

Adequate nutritional support is a fundamental and critical component for the early recovery and improvement of clinical outcomes in critically ill pediatric patients. Despite its importance, it has often received relatively little attention and has been a low priority in intensive care settings. However, recommendations and guidelines developed over the past several decades have emphasized the importance of timely and appropriate nutritional support for these patients, achieving consensus among intensive care healthcare providers [2,5,6]. The primary goal is to minimize catabolism and muscle wasting through early enteral nutrition support. Conversely, it is also acknowledged that excessive delivery of energy and protein through overfeeding can have detrimental effects. There is a growing recognition of the importance of the rate of delivery and the gradual increase of energy and nutrients, which can be equally critical. Just as the shift to a catabolic state during the acute phase of critical illness can lead to significant metabolic disturbances, the transition from a catabolic to an anabolic state can also cause substantial metabolic disruptions. Sudden changes may result in various electrolyte imbalances, which, in turn, can lead to organ damage, including musculoskeletal weakness, encephalopathy, and cardiorespiratory failure. In some cases, these imbalances can be fatal unless they are properly corrected with established supplementation.

In the intensive care setting, patients with underlying critical illnesses face numerous risks for undernutrition and malnutrition, which can be exacerbated by various therapeutic interventions and procedures. Despite its significance, this issue has often been overlooked. However, there is growing evidence and understanding of the acute metabolic disturbance known as refeeding syndrome, which can occur upon the reintroduction of nutrition after a period of prolonged fasting or a state of undernourishment [7]. In response to this issue, the American Society for Parenteral and Enteral Nutrition (ASPEN) developed consensus recommendations in 2020 for identifying patients at risk of refeeding syndrome, including undernourished children [8].

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Kim [9] reviewed refeeding syndrome in critically ill children, focusing on its understanding, prevention, and management. It is important to increase awareness among intensive care healthcare providers about refeeding syndrome, which, although not rare, can sometimes lead to fatal outcomes if not recognized and managed appropriately [10]. The most important point is to remain vigilant about the possibility and risks of refeeding syndrome during the course of intensive care. Moreover, it should be emphasized that nutritional support is fundamental and critical in intensive care, alongside the support and management of specific vital organs, including hemodynamic and neurologic status.

CONFLICT OF INTEREST

Won Kyoung Jhang is an Editor-in-Chief of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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Review Article

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초보자를 위한 소아 기계환기 초기 설정과 모니터링

김경원

연세대학교 의과대학 세브란스병원 소아과학교실

Easy steps for the initial settings and early monitoring of mechanical ventilation in children

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Invasive mechanical ventilation is a crucial strategy for saving the lives of patients with acute or chronic respiratory failure, even in children. Physicians should be capable of establishing the initial settings for mechanical ventilation when faced with a patient in need. This review paper offers practical guidance on the initial settings of pediatric mechanical ventilation, covering indications for mechanical ventilation; initial settings such as basic modes, peak inspiratory pressure or tidal volume, respiratory rate, inspiratory time or ratio, fraction of inspired oxygen, positive end-expiratory pressure, and trigger; and the early monitoring strategy after the initial settings. This information is expected to be beneficial for physicians, particularly residents and early-career pediatric practitioners.

Keywords: Mechanical ventilators; Pediatric intensive care units; Respiratory insufficiency

서론

기계환기(mechanical ventilation) 방법은 크게 비침습적(noninvasive) 방법과 침습적(invasive) 방법으로 나눌 수 있다. 호흡부전(respiratory failure) 환자에서 비침습적 방법을 시도 후 적절하게 유지되지 않는 경우에 침습적 기계환기를 단계적으로 적용하는 경우도 있고, 환자의 호흡부전이 급격하게 진행되는 경우에는 침습적 기계환기를 즉시 적용하는 것이 필요한 경우도 있다. 침습적 기계환기는 호흡부전 환자들의 생명을 구하는 중재술이다. 그러나 기계환기 적용으로 부작용이 발생할 수 있다는 점을 기억하고 부작용을 최소화하는 전략으로 사용해야 한다.

소아는 키와 몸무게를 포함한 몸의 크기의 환자 간 차이가 크고, 폐의 성숙도 차이도 상당하다. 더욱이 급성 또는 만성 질환 유무에 따라 침습적 기계환기의 적용 전략이 다를 수 있어 임상적인 근거 마련도

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어려움이 있다[1]. 본 종설에서는 입문자를 위한 소아 침습적 기계환기의 실제 초기 적용에 대해 다루고자 한다. 기계환기 원리, 모드(mode), 모니터링(monitoring) 및 이탈(weaning)을 포함한 전반적인 내용에 대해서는 다른 문헌을 참고하기 바란다[2-4].

기계환기의 적응증

기계환기는 양압환기(positive pressure) 방법으로 이루어지며 자발호흡을 완전히 또는 부분적으로 대체하는 방법이다. 침습적 기계환기는 기관삽관 후 적용하게 되는데, (1) 산소화 또는 (2) 환기가 부적절하거나, (3) 기도가 안전하게 확보되지 않는 경우에 적용한다[5]. 부적절한 산소화에 해당하는 경우는 비침습적 기계환기에도 불구하고 저산소증(hypoxemia)이 지속되는 경우, 폐부종(pulmonary edema) 또는 폐출혈(pulmonary hemorrhage) 등으로 호기말양압(positive end-expiratory pressure [PEEP])이 필요한 경우와 과도한 호흡 부담을 보이는 경우 등이 있다. 부적절한 환기는 호흡근의 기능 부전, 호흡 의지의 감소, 기도 저항의 증가 또는 기도 폐쇄 등으로 야기될 수 있다.

기계환기의 초기 세팅

기계환기의 초기 세팅이 환자의 기저질환과 호흡부전의 원인 및 질병 상태에 맞는 최적의 세팅이면 좋겠지만, 환자의 상황에 따라서 응급상황에서 설정하다 보면 처음부터 가장 적절하게 세팅하는 것이 어려울 수 있다. 호흡부전으로 인한 악화를 막는 지체 없는 세팅으로 시작하고 환자에 맞는 최적의 세팅으로 빠르게 조절하는 것이 적절한 경우도 있다. 연령에 따른 기계환기의 초기 세팅을 Table 1에 정리하였다.

기계환기 모드(mode)

압력조절환기(pressure-controlled ventilation)는 환기 압력을 일정하게 공급하고, 용적조절환기(volume-controlled ventilation)는 용적과 유속(flow rate)을 일정하게 공급하는 모드이다. 즉, 압력조절환기는 정해진 시간 동안 일정한 압력을 공급하므로 환자의 상태에 따라 용적과 유속이 변할 수 있고, 용적조절환기는 일정한 유속으로 정해진 용적을 공급하는 방식으로 환자의 상태에 따라 압력이 달라진다(Fig. 1). 압력조절환기가 어린 소아에서 일반적으로 우선적으로 적용되는 경향이 있지만 용적조절환기와 비교하여 우월하다는 근거는 없다[4,6]. 초기부터 환자의 호흡 부전의 원인과 상태에 따라 선택하면 좋겠지만 익숙한 모드로 시작하고 모니터링하면서 최적화하는 것도 가능하다.

최고흡기압(peak inspiratory pressure) 및 일회호흡량(tidal volume)

압력조절환기 모드로 선택한 경우 최고흡기압을 정해야 한다. 최고흡기압은 16–25 cm H_2O로 시작한다. 폐질환이 없는 경우 16 cm H_2O으로, 폐질환이 있는 경우 25 cm H_2O로 시작한다. 호흡기에 따라 최고흡기압으로 세팅하는 경우도 있고, 최고흡기압과 호기말양압의 차이(above PEEP, delta pressure)로 세팅해야 하는 경우도 있으므로 주의해야 한다. 세팅한 최고흡기압에서 적절한 일회호흡량이 확보되고 있는지 모니터링해야 한다. 폐의 유순도가 낮아지면 동일한 최고흡기압을 유지해도 일회호흡량이 줄어들기 때문에, 일회호흡량 확보를 위하여 최고흡기압을 높이는 것이 필요할 수 있다.

용적조절환기 모드로 선택한 경우 일회호흡량을 정해야 한다. 일반적으로 일회호흡량은 5–8 mL/kg로 시작한다[7]. 이때 환자의 몸무게는 실제 몸무게가 아닌 예측 몸무게를 기준으로 하지만[8], 약 152 cm 보다 키가 작은 소아 환자들에게 적용하기는 어려워서 실제 몸무게로 적용하는 경우가 많다. 환자의 질환을 고려하여 설정하도록 하며, 고원압력(plateau pressure) (Fig. 1)이 30 cm H_2O 미만으로 유지하는 것을 권고한다[9]. 폐의 유순도가 낮아지면 동일한 일회호흡량을 유지해도 최고흡기압이 높아지기 때문에, 최고흡기압 모니터링이 필요하다[7].

분당 호흡수(respiratory rate), 흡기 시간(inspiratory time) 및 흡기 대 호기 비율

분당 호흡수 및 흡기시간은 연령에 따른 정상범위를 고려하여 설정한

Table 1. Initial settings for mechanical ventilation in children according to age group

Variable	Age group		
	<1 yr	1–12 yr	>12 yr
PIP for pressure-controlled ventilation (cm H_2O)		16–25	
TV for volume-controlled ventilation (mL/kg)		5–8	
Respiratory rate (breaths/min)	20–40	15–25	12–20
Inspiratory time (sec)	0.4–0.6	0.7–0.9	0.9–1.2
FiO_2 (%)		Start with 1.0, rapidly wean to ≤0.6	
PEEP (cm H_2O)		3–8	
Flow trigger (L/min)	0.25–0.5	0.8–2.0	

Values are presented as range.
PIP, peak inspiratory pressure; TV, tidal volume; FiO_2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure.

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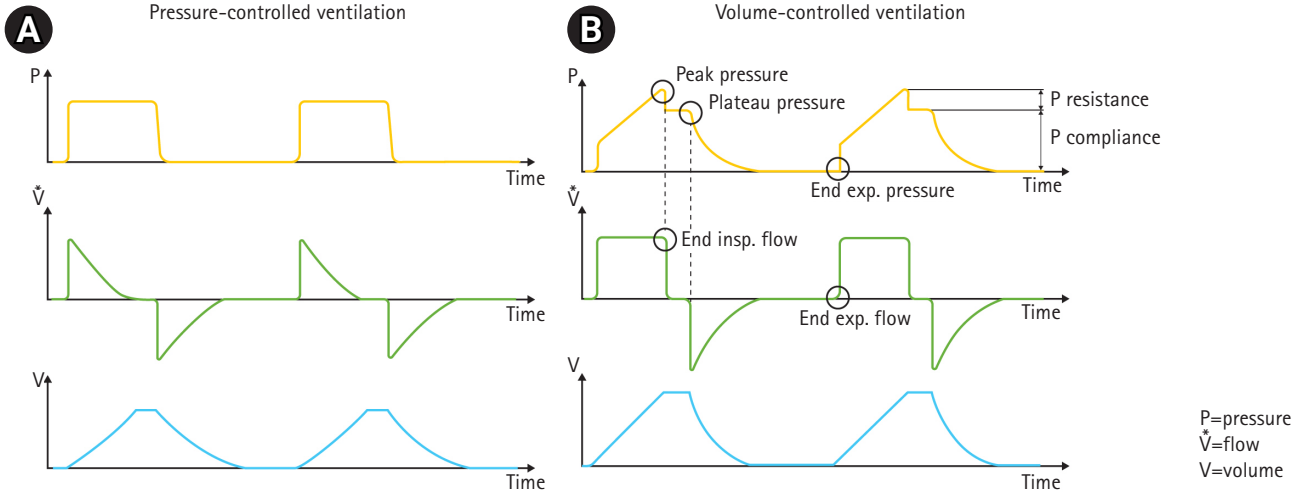

Fig. 1. Pressure, flow, and volume waveforms for pressure-controlled (A) and volume-controlled ventilation (B). Pressure-controlled ventilation requires the physician to set the peak inspiratory pressure, whereas volume-controlled ventilation requires the physician to set the tidal volume and peak inspiratory flow rate, which affect the inspiratory time or ratio. exp, expiratory; insp, inspiratory.

다[10]. 흡기 대 호기 비율의 정상범위는 1:2 또는 1:3 정도이다. 분당 호흡수는 1세 미만 영아에서 20–40회, 2세 이상 12세 이하 소아에서 15–25회, 13세 이상 청소년에서 12–20회 범위에서 설정하는 것이 일반적이다. 흡기시간은 1세 미만 영아에서 0.5초 전후, 2세 이상 12세 이하 소아에서 0.8초 전후, 13세 이상 청소년에서 1초 전후로 한다. 부적절하게 분당 호흡수가 높아지면 자가 호기말양압(auto-PEEP)이 생길 수 있어서 주의가 필요하다. 용적조절환기에서 흡기시간을 조절하면 유속에 영향을 준다는 것도 기억해야 한다.

흡기 산소 분압(fraction of inspired oxygen [FiO_2])

기계환기 시작 전의 환자의 산소 요구량에 따라 결정한다. 1.0에서 시작하여 PaO_2를 모니터링하면서 0.5–0.6 수준으로 빠르게 줄이는 전략을 사용한다.

호기말양압(PEEP)

호기말양압은 기도 폐쇄와 폐포 허탈을 예방하여 산소화를 호전시킨다[7]. 초기 세팅으로 5–6 cm H_2O에서 시작하는 경우가 많다. 급성호흡부전증후군(acute respiratory distress syndrome)에서 높은 호기말양압을 적용하는 경우가 있는데 적절하게 호기말양압과 FiO_2의 균형을 맞춰서 조정하도록 한다[7]. 예를 들어, FiO_2를 0.6 이하 수준으로 줄일 수 없는 경우에는 호기말양압을 10 이상으로 올리는 것을 고려해야 한다.

트리거(trigger)

트리거는 기계가 호흡보조를 시작하게 하는 기전에 따라 다르다. 기류의 변화를 감지하여 호흡보조가 시작되는 경우(flow trigger) 보통 영아 0.4–1.0 L/min에서 청소년 0.8–2.0 L/min 정도로 트리거 역치(trigger threshold)를 세팅하면 적절하다[11]. 즉, 환자가 자발호흡이 있을 때, 자발호흡으로 인한 기류의 변화가 세팅 되어있는 역치를 넘어서면 환자의 자발호흡의 시작으로 인식되어 호흡보조가 시작되는 것이다(assisted ventilation). 압력의 변화를 감지하여 호흡보조가 시작되는 경우(pressure trigger)에는 소아의 경우 –1 cm H_2O 로 트리거 역치를 세팅하면 된다[12].

기계환기 초기 세팅의 고려 사항

기계환기는 기계환기로 인한 이차적인 폐손상을 최소화하는 가능한 한 낮은 압력에서 환자의 대사 요구량을 충족시키는 충분한 분당 호흡량(minute ventilation)과 산소를 전달해야 한다[4,6]. 또한 기계환기는 환자의 호흡 부담을 줄이고 호흡이 편안하도록 최적화해야 한다. 이를 위하여 환자가 필요로 하는 흡기 유량에 맞추어 유속을 세팅하는 것이 필요할 수 있다. FiO_2은 산소 독성 위험을 줄이기 위하여 적절한 선에서 가능한 한 빠르게 줄여야 한다. 호기말양압은 환자에게 혈역학적 부담을 주지 않는 선에서 폐포 허탈을 예방하고 산소화를 호전시킬 수 있도록 최적화해야 한다.

기계환기 적용 후 초기 모니터링

기계환기의 초기 세팅이 완료되면 초기 모니터링이 필수적이다. 기계환기의 목적에 따라 적절하게 산소화 및 환기 여부를 관찰해야 하며, 기계환기의 세팅이 부적절해서 생기는 2차 폐손상 여부 및 혈역학적 변화를 관찰해야 한다[4]. 적절한 산소화 여부는 동맥혈 가스 결과로

판단할 수 있고, 목표 범주는 pH 7.35–7.45, $PaCO_2$ 35–45 mm Hg, PaO_2 80–100 mm Hg, HCO_2 22–26 mEq/L, BE-ECF −2 to 2이다. 만약, 기계환기 중에 급격하게 산소포화도가 떨어진다면 다음의 사항을 확인해야 한다. 기관 내 삽관된 관의 위치(Displacement of tracheal tube) 및 폐쇄(Obstruction of tracheal tube) 여부 확인, 기흉(Pneumothorax) 등의 공기 누출 확인, 기계 작동 이상(Equipment failure) 확인이 필요하며, 이를 약자로 DOPE이라고 부르며 기억하기도 한다.

기계환기를 적용하는 목적 중 중요한 한 가지가 호흡부전 환자의 호흡을 편안하게 보조하는 것인데, 환기기계와 환자의 요구도가 잘 맞지 않으면 환자의 호흡부담은 줄어들지 않고, 불필요한 진정을 유지해야 하는 경우도 발생할 수 있다[13,14]. 환자의 호흡 노력이 줄어들지 않는다면, 환기기계의 트리거 역치의 설정이 적절한지, 적절한 유속으로 알맞은 유량이 공급되고 있는지를 확인하고, 호흡 주기와 호기말양압 등을 조절해 주면서 기계 세팅을 다시 한번 살펴볼 필요가 있다. 또한 환자의 질환 경과에 맞추어 통증 조절과 적절한 진정으로 호흡 노력과 구동을 맞추는 등의 환자 측면의 요소도 살펴야 한다.

결론

기계환기의 적용은 실제 경험이 중요하다. 경험하지 못한 지식은 특히 기계환기를 다루는데 오히려 상당한 장애물이 될 수도 있다. 실제로 기계환기를 적용하고 있는 환자들에게 가서 기계를 만져보고 모니터를 보면서 실제적인 지식과 경험을 쌓는 것이 중요하다. 또한 본 종설의 내용을 시작으로 기계환기의 원리를 포함한 심화 교육이 필수적이다.

CONFLICT OF INTEREST

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Refeeding syndrome in critically ill children: understanding, prevention, and management

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Refeeding syndrome, a critical condition in undernourished patients, is characterized by metabolic and electrolyte imbalances that occur upon reintroducing nutrition after a period of prolonged fasting. This syndrome, which includes hypophosphatemia, hypokalemia, hypomagnesemia, and thiamine deficiency, frequently affects critically ill pediatric patients who are often at risk of undernutrition due to various chronic or acute conditions. Despite its potential lethality, awareness and recognition of refeeding syndrome in this population remain low. This review addresses the clinical importance of refeeding syndrome in critically ill children and underscores the need for prevention and management strategies. Essential actions involve identifying patients at risk, reintroducing nutrition gradually, consistently monitoring serum electrolytes—especially phosphorus, potassium, and magnesium—and ensuring adequate supplementation, including thiamine. These recommendations are in line with the 2020 consensus guidelines from the American Society for Parenteral and Enteral Nutrition. The review calls attention to the frequently underestimated severity of refeeding syndrome in critically ill pediatric patients and urges the prompt development of comprehensive, evidence-based clinical protocols and educational strategies to enhance patient outcomes.

Keywords: Refeeding syndrome; Critical illness; Pediatrics; Child; Nutrition therapy

INTRODUCTION

Refeeding syndrome was first identified as a significant medical issue during World War II, when it affected severely malnourished individuals such as concentration camp detainees and prisoners of war [1]. This condition arises when individuals who have experienced prolonged periods of undernutrition are reintroduced to regular nutrition, which can lead to a sharp increase in morbidity and mortality rates following their release and the resumption of a normal diet. It is characterized by metabolic disturbances and electrolyte imbalances that can lead to severe complications, including death [2-4].

The occurrence of refeeding syndrome is well-documented in conditions such as anorexia nervosa [3,5]. However, its prevalence among critically ill pediatric patients remains unclear. These patients often suffer from undernutrition due to chronic

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illnesses, various congenital and acquired diseases, malabsorption, or child abuse [6]. There is an increasing awareness of the unexpectedly high prevalence of undernutrition and refeeding syndrome in this population. Studies indicate that between 13% and 20% of patients admitted to pediatric critical care units are undernourished [7-10]. Furthermore, a study involving 1,261 children in a French pediatric intensive care unit (PICU) found that 7.4% developed refeeding syndrome. Notably, among the 15.8% of patients who were undernourished, the incidence of refeeding syndrome was much higher at 46.7%, and 58.1% of these patients experienced severe forms of refeeding syndrome [9].

The early initiation of enteral nutrition is often recommended for its overall benefits in critically ill children [11,12]. However, it may inadvertently increase the risk of refeeding syndrome. The difficulty in managing this patient population stems from the frequent occurrence of electrolyte imbalances and the nonspecific nature of the syndrome's symptoms, which complicates diagnosis and treatment. Furthermore, the syndrome is likely underreported in the clinical setting due to a lack of awareness. A study revealed that only 14% of 281 surveyed physicians and medical students could accurately identify refeeding syndrome [13]. Consequently, it is imperative to enhance awareness of the potential complications associated with nutrition therapy, especially in undernourished critically ill children. This review aims to highlight these challenges and advocate for heightened awareness and proactive management strategies to better the outcomes for these high-risk pediatric patients.

PATHOPHYSIOLOGY AND CLINICAL FEATURES

Glucose is the body's primary energy source, metabolized to provide immediate energy. Any excess glucose is stored as glycogen in the liver and muscles, or it is converted into fat for long-term storage. Additionally, fat constitutes an essential long-term energy reserve. It undergoes lipolysis to produce fatty acids and glycerol when needed. Fatty acids are an important energy source for muscles, while glycerol can be converted back into glucose. During prolonged fasting, the body efficiently prioritizes its energy sources. Initially, it depletes glycogen stores before shifting to the metabolism of proteins and fats. This metabolic shift leads to increased ketogenesis, which helps to mitigate muscle and protein breakdown. However, this adaptive response to limited energy resources can only sustain life for a limited time. Extended periods of starvation eventually result in the depletion of stored energy, along with a critical reduction in micronutrients and electrolytes, particularly phosphate, potassium, and magnesium [14].

Upon refeeding, there is an immediate transition from a catabolic to an anabolic state, marked by a rapid increase in caloric intake and a subsequent rise in insulin secretion. This increase in insulin enhances glycolysis—the process of breaking down glucose for energy. The resulting spike in insulin levels can lead to hypoglycemia and promote the transfer of electrolytes from the extracellular to the intracellular space [3,15]. This movement can significantly reduce extracellular concentrations of potassium, phosphate, magnesium, and thiamine, which acts as a coenzyme. Given the pre-existing deficiencies in these electrolytes and micronutrients due to prolonged starvation, their levels can quickly fall as they are consumed during the metabolic response to refeeding. This abrupt change can precipitate severe complications associated with refeeding syndrome, which stem from imbalances and deficiencies in electrolyte and micronutrient levels [2-4].

The clinical presentations of refeeding syndrome, which typically manifest in the initial days of nutritional reintroduction, include disturbances in fluid balance, hypoglycemia, hypophosphatemia, hypomagnesemia, hypokalemia, and thiamine deficiency. This syndrome can lead to a range of symptoms that affect the neurological, cardiac, hematological, and gastrointestinal systems, primarily due to electrolyte imbalances. Despite the variety of symptoms, refeeding syndrome often goes undetected because its clinical manifestations are nonspecific [2-4,16].

Phosphorus plays a critical role in synthesizing adenosine triphosphate (ATP), a crucial molecule for energy storage. Moreover, during refeeding, the production of ATP can cause a marked decrease in phosphorus levels [14]. This phenomenon was exemplified in the case of a 28-year-old woman with chronic diarrhea and malabsorption. When she resumed nutritional intake, she developed severe hypophosphatemia, with her serum phosphorus level dropping to 0.4 mg/dL. This led to arrhythmia, hypotension, respiratory failure, and ultimately resulted in her death [17].

Potassium is essential for maintaining the sodium-potassium membrane gradient, and its deficiency, known as hypokalemia, disrupts the electrochemical balance and impairs the transmission of electrical impulses in the body. Magnesium, which is as crucial as potassium, serves as a cofactor in ATP phosphorylation and is vital for neuromuscular and enzymatic functions [14]. Deficiencies in either electrolyte can result in neuromuscular disorders, arrhythmias, and gastrointestinal symptoms [18,19].

Thiamine, an essential cofactor in glucose-dependent metabolic pathways, sees a significant increase in demand during the transition from starvation to refeeding [20]. A deficiency in thiamine can result in neurological abnormalities, including enceph-

alopathy, delirium, and coma [21,22]. Furthermore, thiamine plays a critical role in converting lactate to pyruvate, and its deficiency can cause lactic acidosis [23,24]. Thiamine deficiency may also lead to decreased ATP production in the myocardium, potentially resulting in congestive heart failure [24].

DEFINITIONS

A universally agreed-upon definition of refeeding syndrome was lacking until 2020, when the American Society for Parenteral and Enteral Nutrition (ASPEN) committee and clinical practice task force introduced diagnostic criteria [16]. The ASPEN consensus definitions for refeeding syndrome represent a significant shift from previous descriptions by broadening the scope of assessment to include three critical electrolytes: phosphorus, potassium, and magnesium. The diagnostic criteria and severity stratification are as follows. (1) Any decline in serum phosphorus, potassium, and/or magnesium levels: mild refeeding syndrome—a decrease ranging from 10% to 20%; moderate refeeding syndrome—a reduction between 20% and 30%; severe refeeding syndrome—a decrease of over 30% or the emergence of organ dysfunction due to these electrolyte imbalances or thiamine deficiency. (2) These alterations typically manifest within 5 days of reintroducing or substantially augmenting energy intake.

ASSESSING RISK FACTORS FOR REFEEDING SYNDROME

Refeeding syndrome, which often presents with nonspecific symptoms, may be overlooked because these signs are subtle and not overtly associated with nutritional issues, potentially delaying appropriate treatment. Identifying high-risk factors for refeeding syndrome is crucial in managing the nutritional needs of critically ill children. Table 1 lists conditions that are associated with an increased risk of this syndrome. The ASPEN consensus recommendations categorize the risk into three levels: mild, moderate, and significant, as shown in Table 2 [16]. These categories are determined based on multiple factors, including body mass index (BMI)-for-age z-scores (or weight-for-length z-scores for children under 2 years), history of weight loss, duration of inadequate energy intake, serum electrolyte levels, and the presence of comorbidities.

Endorsed by the Society of Critical Care Medicine (SCCM) and ASPEN in 2017 [11], and subsequently by the European Society of Pediatric and Neonatal Intensive Care (ESPNIC) in 2020 [12], these nutritional support guidelines for critically ill children underscore the importance of assessing nutritional status through z-scores of anthropometric measurements upon admission to the PICU. The BMI-for-age z-score, in particular, is a quick and effective method for evaluating the nutritional status of these patients. For instance, a child presenting with a BMI-for-age z-score of −3 or lower is considered to be at high risk for refeeding syndrome based on this criterion alone.

PREVENTION AND MANAGEMENT OF REFEEDING SYNDROME

To prevent and manage refeeding syndrome in at-risk patients, a gradual and cautious reintroduction of nutrition is advised. The cornerstone of reintroducing nutrition is to incrementally increase caloric intake over a period of several days. It is crucial to monitor serum electrolytes, particularly phosphorus, potassium, and magnesium, and provide supplementation as necessary. The shifts in these electrolytes during refeeding are closely associated

Table 1. Conditions that place critically ill children at high risk for refeeding syndrome [3,6,16]

Clinical conditions
Chronic critical illness (e.g., congenital heart disease)
Advanced neurologic impairment
Eating disorders (e.g., anorexia nervosa)
Dysphagia
Gastrointestinal dysmotility
Malabsorption (e.g., short bowel syndrome, inflammatory bowel disease, chronic pancreatitis, cystic fibrosis)
Malignancy
Child abuse
Significant vomiting and diarrhea
Unintentional weight loss of >5%–10% of body weight in 1–6 months
Prolonged fasting >7–10 days
Inadequate nutritional intake for >10 days

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Table 2. Identification of pediatric patients at risk for refeeding syndrome, adapted from the ASPEN Consensus Recommendations on Refeeding Syndrome [16]

Indicators	Mild risk: 3 risk criteria needed	Moderate risk: 2 risk criteria needed	Significant risk: 1 risk criterion needed
Weight-for-length z-score (1–24 months) or BMI-for-age z-score (2–20 years)	z-score of –1 to –1.9 that is a change from baseline	z-score of –2 to –2.9 that is a change from baseline	z-score of ≤–3 that is a change from baseline
Weight loss	<75% Of norm for expected weight gain	<50% Of norm for expected weight gain	<25% Of norm for expected weight gain
Energy intake	3–5 Consecutive days of protein or energy intake <75% of estimated need	5–7 Consecutive days of protein or energy intake <75% of estimated need	>7 Consecutive days of protein or energy intake <75% of estimated need
Abnormal pre-feeding serum potassium, phosphorus, or magnesium concentrations	Mildly abnormal or decreased to 25% below the lower limit of normal	Moderately/significantly abnormal or decreased to 25%–50% below the lower limit of normal	-
Higher-risk comorbidities	Mild disease	Moderate disease	Severe disease
Loss of subcutaneous fat	Evidence of mild loss or mid-upper arm circumference z-score of –1 to –1.9 z-score	Evidence of moderate loss or mid-upper arm circumference z-score of –2 to –2.9	Evidence of severe loss or mid-upper arm circumference z-score of –3 or greater
Loss of muscle mass	-	Evidence of mild or moderate loss or mid-upper arm circumference z-score of –2 to –2.9	Evidence of severe loss or mid-upper arm circumference z-score of –3 or greater

ASPEN, American Society for Parenteral and Enteral Nutrition; BMI, body mass index.

with the patient's tolerance to the increased caloric load, underscoring the importance of their management. If patients exhibit signs of intolerance to the calories despite these precautions, it is advisable to temporarily reduce or maintain the caloric intake at its current level. Once the patient's condition has stabilized, a careful and gradual increase in caloric intake may be continued. Additionally, thiamine supplementation is important due to its essential role in carbohydrate metabolism [2-4,16]. The information that follows, as well as that in Table 3, is derived from the ASPEN 2020 consensus recommendations on refeeding syndrome.

Energy Intake

In pediatric patients at risk for refeeding syndrome, the ASPEN guidelines suggest starting critically ill pediatric patients at 40%–50% of their energy goal, or with a glucose infusion rate of 4–6 mg/kg/min (equivalent to 23–35 kcal/kg/day), and then increasing the rate by 1–2 mg/kg/min each day. This recommendation applies to both enteral and parenteral glucose administration. If difficulties in correcting electrolyte levels occur, or if there is a sharp decline in electrolyte levels at the onset of nutritional therapy, it may be necessary to reduce the caloric intake or dextrose content by 50%. Subsequently, the dextrose or caloric intake should be gradually increased by approximately 33% of the target every 1–2 days, guided by the patient's clinical response [16].

The ASPEN guidelines notably do not advocate for a specific, universal energy target for nutritional support. Additionally, the SCCM/ASPEN and ESPNIC nutrition guidelines for critically ill pediatric patients advise that nutritional intake, especially during the acute phase of catabolism, should be limited to the patient's resting energy expenditure (REE) and should not exceed it [11,12]. This approach is particularly prudent for critically ill children who are at an increased risk of developing refeeding syndrome. While indirect calorimetry is recognized as the most accurate method for determining REE [25], its lack of practicality often leads to the recommendation of the Schofield equation as an alternative. This equation provides an estimate of nutritional needs based on a patient's weight and height [12,26].

The guidelines [11,12] recommend initiating enteral nutrition within the first 24 hours of hospitalization [12], unless contraindicated. Reaching up to two-thirds of the nutritional goal during the first week of critical illness is associated with improved clinical outcomes [11]. For critically ill children, enteral nutrition is the preferred method over parenteral nutrition when feasible [11,12]. This approach includes active feeding methods such as oral, nasogastric tube, or trans-pyloric feeding techniques.

Ultimately, for critically ill children at risk of refeeding syndrome, the recommendation is to initiate early enteral nutrition. A suggested strategy involves starting with an initial energy intake that is lower than what the ASPEN guidelines recommend, such as 20%–30% of the target based on the REE. This should be gradually increased over the course of a week, with close moni-

Table 3. Prevention and management of refeeding syndrome in at-risk pediatric patients, modified from the ASPEN Consensus Recommendations on Refeeding Syndrome [16]

Aspect of care	ASPEN Consensus Recommendations
Identification of patients at risk	• Consider higher-risk comorbidities • Obtain a careful history of weight loss and energy intake • Measure anthropometrics: weight, length • Calculate the weight-for-length z-score for ages 1–24 months, or BMI-for-age z-score for ages 2–20 years • Conduct examinations for subcutaneous fat and muscle mass
Energy intake	• Initiate nutrition at a maximum of 40%–50% of the goal • Start the glucose infusion rate at approximately 4–6 mg/kg/min, increasing it by 1–2 mg/kg/min daily, up to a maximum of 14–18 mg/kg/min • In cases of uncontrolled electrolyte drops, decrease calories/g of dextrose by 50%, and then advance by approximately 33% of the goal every 1–2 days • Note on energy goal for critically ill children: measure resting energy expenditure via indirect calorimetry or calculate it using the Schofield equation[a] [11,12]
Electrolytes (phosphorus, potassium, magnesium)	• Check serum electrolytes before initiation of nutrition • Monitor every 12 hours for the first 3 days in high-risk patients • Replete low electrolytes as needed
Thiamine	• Administer thiamine at a dose of 2 mg/kg, up to a maximum of 100–200 mg/day, before initiating nutrition • Continue thiamine supplementation for 5–7 days or longer in patients at high risk for deficiency
Multivitamins	• For parenteral nutrition: add a daily injectable multivitamin • For enteral nutrition: administer a multivitamin once daily for at least 10 days
Monitoring and long-term care	• Vital signs every 4 hours in the first 24 hours after initiation of calories in patients at risk • Daily weights with monitored intake and output • Daily assessment of short-term and long-term nutritional goals during the initial days until the patient stabilizes • Patient stabilization is indicated by no requirement for electrolyte supplementation over 2 days

ASPEN, American Society for Parenteral and Enteral Nutrition; BMI, body mass index.
[a]The ASPEN consensus recommendations on refeeding syndrome does not include a specific recommendation for energy goals.

toring of electrolytes.

Electrolytes

Before starting nutrition, serum levels of potassium, magnesium, and phosphorus should be checked. In high-risk patients, these electrolytes should be monitored every 12 hours during the first 3 days [16], with more frequent monitoring as required. Any deficiencies identified should be corrected in accordance with established standards of care. The use of prophylactic electrolyte supplementation is still a matter of debate when pre-feeding levels are within the normal range [16].

Thiamine and Multivitamins

Administering thiamine before refeeding is crucial, particularly in high-risk patients. The recommended dosage is 2 mg/kg, with a maximum of 100–200 mg per day, to be given before nutrition is reintroduced. It is advised to continue supplementation for at least 5–7 days, or longer, in patients at high risk of deficiency. Patients on parenteral nutrition should receive a daily multivitamin infusion. For those on enteral nutrition, a daily multivitamin is recommended for at least 10 days, depending on the patient's clinical status [16].

Monitoring and Long-term Care

For patients at risk, it is recommended to monitor vital signs every 4 hours during the first 24 hours after initiation. For unstable patients or those with severe deficiencies, cardiorespiratory monitoring should be performed in accordance with established standards of care. It is advisable to assess weight daily and to carefully monitor fluid intake and output. For patients on oral feeding, energy requirements should be estimated as needed. Additionally, short- and long-term nutrition care goals should be evaluated daily during the initial days until the patient stabilizes, which is indicated by the absence of a need for electrolyte supplementation for two consecutive days. Subsequent evaluations should be carried out in accordance with institutional standards of care [16].

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Acute Care Concerns

Recent case reports highlight the effectiveness of extracorporeal life support (ECLS) in treating severe left ventricular dysfunction and heart failure resulting from refeeding syndrome in adults [27,28]. These examples suggest that ECLS could be a viable treatment option for life-threatening cardiac complications related to refeeding syndrome in critically ill children.

CONCLUSION

The review focuses on refeeding syndrome in critically ill children, a severe and potentially lethal condition that is frequently overlooked in clinical practice. Establishing comprehensive, evidence-based clinical protocols and educational initiatives is essential for improving care and reducing the morbidity and mortality related to refeeding syndrome.

CONFLICT OF INTEREST

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Review Article

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Evaluation of disseminated intravascular coagulation in critically ill pediatric patients

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Disseminated intravascular coagulation (DIC) is characterized by the extensive activation of the coagulation system, which leads to fibrin deposition within the microcirculation and the consumption of coagulation factors. The pathophysiology of DIC involves three primary pathways: activation of coagulation, suppression of inhibitory systems, and inhibition of fibrinolysis. These pathways can lead to extensive thrombosis and/or bleeding, ultimately resulting in poor clinical outcomes. Therefore, early detection of DIC is of crucial importance. However, no gold standard currently exists for the diagnosis of DIC in critically ill children. While several diagnostic criteria have been established for adults, incorporating coagulation-related laboratory data and associated clinical conditions, they have limitations and their applicability and accuracy in the pediatric population are not well established. Thus, it is necessary to validate the diagnostic criteria previously used in adults through large-scale multicenter studies of pediatric populations and develop an evidence-based, appropriate diagnostic tool for the accurate and early detection of DIC in these patients.

Keywords: Pediatrics; Critical care; Disseminated intravascular coagulation; Multiple organ dysfunction; Mortality

INTRODUCTION

In critically ill pediatric patients, a range of disorders—including severe infections, inflammatory conditions, solid tumors, and hematologic malignancies—can initiate coagulation activation. This activation, coupled with the suppression of natural anticoagulant pathways and fibrinolysis, may result in intravascular fibrin formation and the depletion of platelets and coagulation factors. The most extreme outcome of this dysregulation is disseminated intravascular coagulation (DIC), which carries a high risk of serious complications and poor clinical prognosis [1-4]. This paper aims to provide a review of the pathophysiology and clinical significance of DIC, as well as the currently available diagnostic criteria.

PATHOPHYSIOLOGY

DIC is defined as an acquired disorder characterized by abnormalities in both the coagulation and anticoagulation systems. The pathophysiology of DIC can be explained by three main pro-

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cesses: the activation of coagulation, the suppression of physiological inhibitory anticoagulant pathways, and impaired fibrinolysis (Fig. 1) [5,6]. Activation of coagulation and increased thrombin generation are primarily mediated by the extrinsic pathway (factor VIIa), which is triggered by tissue factors. These tissue factors are initially released into the circulation from damaged vascular endothelial cells. Through the extrinsic pathway, thrombin and fibrin are produced, leading to the formation of diffuse microthrombi.

Depressed antithrombin levels and diminished activity in the protein C pathway are often a consequence of activated inflammatory responses and a deficiency in tissue factor pathway inhibitors. This suppression of the body's natural anticoagulant mechanisms contributes to the enhanced production of thrombin and fibrin. Furthermore, damaged vascular endothelial cells release tissue plasminogen activator (tPA), initiating the fibrinolytic pathway. Both tPA and plasminogen bind to fibrin polymers, with plasmin subsequently breaking down fibrin into D-dimers and other fibrin degradation products. However, this fibrinolytic process is hindered by elevated levels of plasminogen activator inhibitor type 1, which acts to inhibit fibrinolysis.

CLINICAL IMPORTANCE

As DIC can arise from a broad spectrum of clinical scenarios, its impact on morbidity and mortality risk is likely influenced by the underlying disease status (Table 1) [6-8]. Depending on the clinical context and the extent of platelet and/or coagulation factor consumption, DIC may predominantly lead to widespread thrombosis and/or substantial bleeding.

The formation of microthrombi can lead to disturbances in the microcirculation, impairing organ perfusion and resulting in tissue ischemia. This, in turn, contributes to the development of multiple organ dysfunction syndrome [9]. Recent studies have highlighted the significant prognostic value of DIC in critically ill patients, emphasizing its association with poor clinical outcomes [10-16]. Therefore, the early detection and aggressive management of DIC are of paramount importance [5,17].

DIAGNOSIS

Despite the clinical significance of DIC, no single diagnostic test can definitively confirm or rule out its presence. DIC is typically

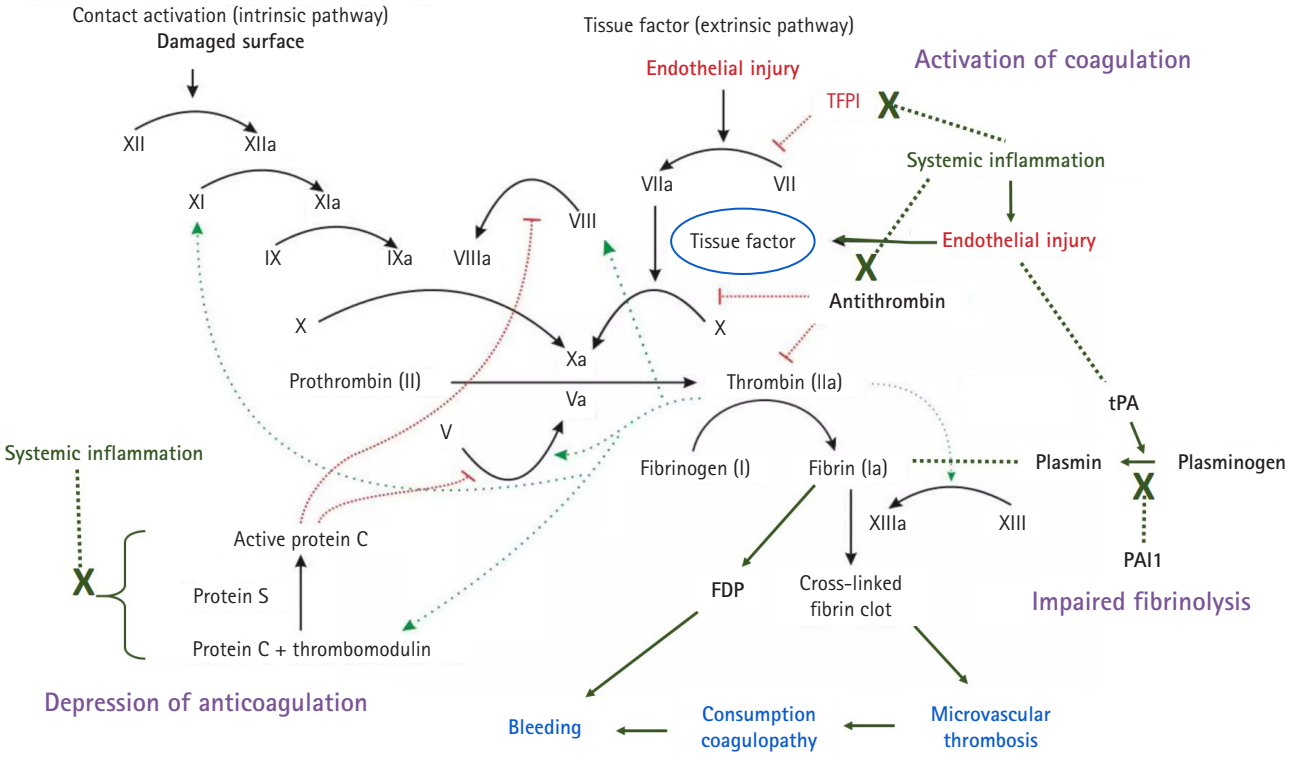

Fig. 1. Pathophysiology of disseminated intravascular coagulation. TFPI, tissue factor pathway inhibitor; tPA, tissue plasminogen activator; PAI, plasminogen activator inhibitor, FDP, fibrinogen degradation product.

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diagnosed through a combination of coagulation-related laboratory tests and clinical findings [7]. However, since the Japanese Ministry of Health, Labor and Welfare proposed diagnostic criteria for DIC, numerous research studies and trials have aimed to establish more accurate definitions and diagnostic approaches for this condition [18-26]. Consequently, several diagnostic scoring systems have emerged, primarily integrating coagulation-related factors such as platelet count, fibrinogen level, prothrombin time, and fibrin degradation products. These factors are used either individually or in conjunction with clinical parameters (Table 2). Additionally, these criteria have been adapted to suit specific clinical scenarios, and validation studies have been conducted [11,12,27-31].

These scoring systems offer certain advantages as they are relatively straightforward and can be easily calculated at the bedside. They provide quantified guidance for the diagnosis of DIC, which can aid in its detection, management, and prognostic evaluation. However, there are certain limitations to consider. The

Table 1. Common clinical conditions associated with disseminated intravascular coagulation in critically ill pediatric patients

Clinical conditions
Infectious diseases
Sepsis
Oncologic disorders
Leukemia
Solid tumors
Vascular disorders
Giant hemangioma (Kasabach-Merritt syndrome)
Vascular aneurysm
Microangiopathic hemolytic anemia
Immunologic disorders
Severe allergic reaction
Hemolytic transfusion reaction
Transplant rejection
Reactions to toxins
Severe trauma
Burns
Anaphylaxis
Acute pancreatitis

Table 2. Comparison of various DIC scoring systems

Parameter	Score	ISTH overt	JAAM	JMHW	KSTH	SIC
Platelets ($\times 10^3/\mu L$)	0	>100	≥120	≥120	>100	>150
	1	≥50 to ≤100	≥80 to <120 or 30% decrease within 24 hr	≥80 to <120	≤100	≥100 to ≤150
	2	<50		>50 to <80		<100
	3		<80 or 50% decrease within 24 hr	≤50		
PT (sec)	0	<3	<1.2 (PT ratio)	<1.25 (PT ratio)	<3	<1.2
	1	≥3 to <6		≥1.25 to <1.67	≥3 (or aPTT ≥5 sec)	≥1.2 to ≤ 1.4
	2	≥6		≥1.67		>1.4
	3		≥1.2			
Fibrin-related marker (mg/L)	0	D-dimer <1.0	FDP <10	FDP <10	D-dimer <1.0	
	1		≥10 to <25	≥10 to <20	≥1.0	
	2	≥1 to ≤ 5		≥20 to <40		
	3	>5	≥25	≥40		
Fibrinogen (g/L)	0	>1.0	>3.5	>1.5	>1.5	
	1	≤1.0	≤3.5	>1.0 to <1.5	≤1.5	
	2			≤1.0		
SIRS score	0		0–2			
	1		≥3			
SOFA score	0					
	1					1
	2					≥2
Underlying disease			Present	Present		
Bleeding				Present		
Organ failure				Present		
Overt DIC		≥5	≥5	≥7	≥3	≥4

DIC, disseminated intravascular coagulation; ISTH, International Society on Thrombosis and Haemostasis; JAAM, Japanese Association for Acute Medicine; JMHW, Japanese Ministry of Health and Welfare; KSTH, Korean Society on Thrombosis and Hemostasis; SIC, sepsis-induced coagulopathy; PT, prothrombin time; aPTT, activated partial thromboplastic time; FDP, fibrin/fibrinogen degradation product; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

transition from an activated hemostatic system to a clearly defined overt state of DIC may not always be distinct, and the borderline between normal and abnormal values can be challenging to discern. Additionally, these laboratory parameters can be influenced by various clinical conditions, such as hematologic malignancies, severe hepatic dysfunction, or acute inflammatory states. Furthermore, although a few reports have applied and validated these scoring systems in critically ill children, the limited number and heterogeneity of the study populations necessitate further large-scale multicenter validation studies and the establishment of evidence-based diagnostic criteria for DIC in critically ill pediatric patients [32-36].

CONCLUSIONS

DIC is a complex and potentially life-threatening condition characterized by the dysregulation of coagulation and fibrinolysis. In critically ill pediatric patients, DIC can have serious implications and lead to poor clinical outcomes. Although diagnostic criteria exist for DIC in adults, their applicability to pediatric patients remains uncertain. Future research should concentrate on creating evidence-based diagnostic tools tailored to critically ill children. This would facilitate the early and accurate detection of DIC, thereby improving patient outcomes.

CONFLICT OF INTEREST

Won Kyoung Jhang is an Editor-in-Chief of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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Archives of Pediatric Critical Care

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Table of contents

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Similarity Check is used to screen submitted manuscripts for possible plagiarism or duplicate publication upon arrival. If plagiarism or duplicate publication is detected, the manuscript will be rejected, the authors will be announced in the journal, and their institutions will be informed. There will also be penalties for the authors.

If the author(s) wishes to obtain a duplicate or secondary publication for various other reasons, such as for readers of a different language, he/she should obtain approval from the editors-in-chief of both the first and second journals.

3.6. Secondary Publication

It is possible to republish a manuscript if it satisfies the condition of secondary publication of the ICMJE Recommendations, available from: https://www.icmje.org/ as follows:

(1) Certain types of articles, such as guidelines produced by governmental agencies and professional organizations, may need to reach the widest possible audience. In such instances, editors sometimes deliberately publish material that is also published in other journals with the agreement of the authors and the editors of those journals.

(2) Secondary publication for various other reasons, in the same or another language, especially in other countries, is justifiable and can be beneficial provided that the following conditions are met. The authors have received approval from the editors of both journals (the editor concerned with secondary publication must have a photocopy, reprint, or manuscript of the primary version). The priority of the primary publication is respected by a publication interval of at least one week (unless specifically negotiated otherwise by both editors).

(3) The paper for secondary publication is intended for a different group of readers; therefore, an abbreviated version could be sufficient. The secondary version faithfully reflects the data and interpretations of the primary version. The footnote on the title page of the secondary version informs readers, peers, and documenting agencies that the paper has been published in whole or in part and states the primary reference. A suitable footnote might read: "This article is based on a study first reported in the [title of a journal, with full reference]."

3.7. Management of Research and Publication Misconduct

When the Journal faces suspected cases of research and publication misconduct such as redundant (duplicate) publication, plagiarism, fraudulent or fabricated data, changes in authorship, undisclosed conflicts of interest, ethical problems with a submitted manuscript, a reviewer who has appropriated an author's idea or data, or complaints against editors, the resolution process will follow the flowchart provided by the COPE (https://publicationethics.org/resources/flowcharts). Discussions and decisions on suspected cases are conducted by the Editorial Board.

3.8. Editorial Responsibilities

The Editorial Board will continuously work to monitor and safeguard publication ethics: guidelines for retracting articles; maintenance of the integrity of the academic record; preclusion of business needs from compromising intellectual and ethical standards; publishing corrections, clarifications, retractions, and apologies when needed; and ensuring that there is no plagiarism and no fraudulent data in publications. Editors maintain the following responsibilities: the responsibility and authority to reject and accept articles; no conflicts of interest with respect to articles they reject or accept; the acceptance of a paper when reasonably certain; promoting the publication of corrections or retractions when errors are found; and the preservation of the anonymity of reviewers.

4. EDITORIAL POLICY

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Authors must declare that the submitted work is their own and that copyright has not been breached in seeking its publication. The copyrights of all published materials are owned by Korean Society of Pediatric Critical Care Medicine. Every author should sign the authorship responsibility and copyright transfer agreement form, attesting that he or she fulfills the authorship criteria. The corresponding author is responsible for submitting the Copyright Transfer Form during the submission process. In addition, it is the authors' responsibility to obtain written permission to reproduce (in all media, including electronic) any material that has appeared previously in another publication. Authors should provide copies of permission letters for any material reproduced from copyrighted publications. Submitted material will not be returned to the author unless specifically requested.

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open-access journal, permission must be obtained from Korean Society of Pediatric Critical Care Medicine (email: kspccm@kspccm.org).

4.3. Article Sharing (Author Self-Archiving) Policy

APCC is an open-access journal, and authors who submit manuscripts to APCC can share their research in several ways, including on preprint servers, social media platforms, at conferences, and in educational materials, in accordance with our open-access policy. However, it should be noted that submitting the same manuscript to multiple journals is strictly prohibited.

4.4. Registration of Clinical Trial Research

Any research that deals with a clinical trial should be registered with a primary national clinical trial registration site such as https://cris.nih.go.kr/cris/index.jsp, or other primary national registry sites accredited by the World Health Organization (http://www.who.int/ictrp/network/primary/en/) or clinicaltrial.gov (http://clinicaltrials.gov/), a service of the United States National Institutes of Health.

4.5. Data Sharing Policy

APCC encourages data sharing wherever possible unless this is prevented by ethical, privacy, or confidentiality matters. Authors wishing to do so may deposit their data in a publicly accessible repository and include a link to the digital object identifier (DOI) within the text of the manuscript. APCC accepts the ICMJE Recommendations for data sharing statement policy (http://www.icmje.org/recommendations/). Authors may refer to the editorial, "Data Sharing Statements for Clinical Trials: A Requirement of the International Committee of Medical Journal Editors," in J Korean Med Sci 2017;32:1051-3 (https://doi.org/10.3346/jkms.2017.32.7.1051).

4.6. Archiving

In accordance with the Korean Library Act, the full-text of the APCC can be archived in the National Library of Korea (NLK; https://seoji.nl.go.kr/archive). APCC provides an electronic backup and preservation of access to the journal content in the event the journal is no longer published by archiving in NLK and the National Library of Korea can permanently preserve submitted APCC papers.

4.7. Preprint Policy

A preprint can be defined as a version of a scholarly paper that precedes formal peer review and publication in a peer-reviewed scholarly journal. APCC allows authors to submit preprints to the journal. It is not treated as duplicate submission or duplicate publication. APCC recommends that authors disclose the existence of a preprint with its DOI in the letter to the Editor during the submission process. Otherwise, a plagiarism check program—Similarity Check (Crosscheck) or Copy Killer—may flag the results as containing excessive duplication. A preprint submission will be processed through the same peer-review process as a usual submission. If a preprint is accepted for publication, the authors are recommended to update the information on the preprint site with a link to the published article in APCC, including the DOI at APCC. It is strongly recommended that authors cite the article in APCC instead of the preprint in their next submission to journals.

4.8. Peer Review Policy

All papers, including those invited by the editor, are subject to peer review. APCC has adopted a double-blind peer review policy, where the author identities remain anonymous to the reviewers, and vice versa and the identities of the reviewers and authors are visible to (decision-making) the editor throughout the peer review process. The Editorial Board selects reviewers based on expertise, publication history, and past reviews. During the peer review process, reviewers can interact directly or exchange information (e.g., via submission systems or email) with only an editor, which is known as "independent review." An initial decision will normally be made within 2 weeks after the reviewers agree to review a manuscript. No information about the review process or editorial decision process is published on the article page.

All manuscripts from editors, employees, or members of the editorial board are processed in the same way as other unsolicited manuscripts. During the review process, submitters will not engage in the selection of reviewers or the decision process. Editors will not handle their manuscripts even if the manuscripts are commissioned. The conflict of interest declaration should be added as follows.

Conflicts of Interest: OOO has been an editorial board member of *Archives of Pediatric Critical Care* since OOO but has no role in the decision to publish this article. No other potential conflicts of interest relevant to this article were reported.

5. MANUSCRIPT PREPARATION

5.1. General Principles

- The manuscript must be written in English or Korean. When the manuscript is written in Korean, medical terminology should be translated according to the medical terminology most recently published by the Korean Medical Association. In the case of a Korean manuscript, title, an abstract, tables, and figures should be all provided in English. Manuscripts should be submitted in the file format of Microsoft Word (DOC). The text of the manuscript, including tables and their footnotes and figure legends,

must be double-spaced and in standard 12-point font on A4 paper size with left and right margin spaces of 2 cm and top and bottom margins of 3 cm.

- Abbreviations are strongly discouraged except for units of measurement. Do not use abbreviations in the title. The full term for which the abbreviation stands should be used at its first occurrence in the text.
- The use of international standardized units is encouraged. Measurement of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) and laboratory values should be displayed in International System of Units (SI). These are available at https://www.nist.gov/pml/owm/metric-si/si-units.
- Statistical methods must be described and the program used for data analysis, and its source, should be stated. Standard deviation and standard error should be described in the format of mean ± SD and mean ± SE, respectively. *p*-values should be described as $p < 0.05$ or $p = 0.003$. It is recommended that the *p*-value be written with up to 3 decimal places unless there are special cases.

5.2. Categories of Manuscripts

APCC publishes editorials, original articles, review articles, case reports, and letters to the editor.

- **Editorials:** Editorials are commentaries on current topics or manuscripts related to materials within the current issue. they raise challenging questions or explore controversies. The editor solicits such opinion pieces. Editorials are invited by the Editors. The order of the submitted manuscript includes a title page, integrated discussion, and references. The text should be limited to 1,500 words and 10 references. A maximum of 2 figures or tables may be included.
- **Original articles:** Original articles are papers containing the results of clinical or laboratory investigations in areas relevant to pediatric critical care medicine, which are sufficiently well documented to be acceptable to critical readers. The basic structure of manuscripts reporting original articles should include the following: abstract (structured abstract of no more than 300 words); maximum length: 4,000 words in English and 8,000 characters in Korean (not including abstract, tables, figures, acknowledgments, references); no more than a total of 6 tables and/or figures; no more than 50 references.
- **Review articles:** Reviews on clinical topics provide an up-to-date review for clinicians on a topic of general common interest from the perspective of internationally recognized experts in the pediatric critical care field. The focus of review articles will be an update on the current understanding of the physiology of the disease or condition, diagnostic consideration, and treatment. The basic structure of manuscripts reporting review articles should include the following: Abstract (unstructured abstract of no more than 300 words); maximum length: 5,000 words in English and 10,000 characters in Korean (not including abstract, tables, figures, acknowledgments, references); no more than a total of 6 tables and/or figures; no more than 100 references.
- **Case reports:** Case reports describe unique and instructive cases that make an important teaching point or scientific observation, novel techniques, use of new equipment, or new information on diseases that are of importance to the pediatric critical care field. The basic structure of manuscripts reporting case reports should include the following: abstract (unstructured abstract of no more than 250 words); section headings in the main text (introduction, case report, discussion); maximum length: 2,000 words in English and 4,000 characters in Korean of text (not including abstract, tables, figures, acknowledgments, references); no more than a total of 5 tables and/or figures; no more than 20 references.
- **Letters to the editor:** Letters to the Editor should include brief constructive comments that concern a published article; a short, free-standing opinion; or a short, interesting case. Letters discussing a recent article in this journal should be submitted within 6 months of the publication of the article in print. Letters should not exceed 1,000 words in English and 2,000 characters in Korean of text and 10 references, 1 of which should be to the recent article. No abstract is required.

Table 1. Recommended maximums[a] for articles submitted to ACPP

Type	Abstract/ keyword	Text (English & Korean)[b]	Figure & table	Reference
Editorials	-	1,500 Words & 3,000 characters	2	10
Original articles	300 Words/6	4,000 Words & 8,000 characters	6	50
Review articles	300 Words/6	5,000 Words & 10,000 characters	6	100
Case reports	250 Words/6	2,000 Words & 4,000 characters	5	20
Letters to the editor	-	1,000 Words & 2,000 characters	-	10

[a]The requirements for the number of references and length of the main text can be consulted with the Editorial Office; [b]Not including an abstract, tables, figures, acknowledgments, and references.

5.3. Reporting Guidelines for Specific Study Designs

For the specific study design, it is recommended that authors follow the reporting guidelines, such as CONSORT (http://www.consort-statement.org) for randomized controlled trials, STROBE (http://www.strobe-statement.org) for observational studies, PRIS-

MA (http://www.prisma-statement.org) for systematic reviews and meta-analyses, and CARE (https://www.care-statement.org) for case reports. A good source for reporting guidelines is the EQUATOR Network (https://www.equator-network.org/) and the United States National Institutes of Health/National Library of Medicine (https://www.nlm.nih.gov/services/research_report_guide.html).

5.4. Format of Manuscript

(1) Title page

All contents on the title page should be written in English. For manuscripts written in Korean, the title and authors' names must also be written in both Korean and English.

- Title: The title should be concise and precise. Only the first letter of title must be capitalized.
- Running title: A running head of no more than 50 characters including letters and spaces should be included in English.
- Author list and affiliations: Full names of authors and institutional affiliation(s) should be included for each author. If several authors and institutions are listed, it should be made clear with which department and institution each author is affiliated. For a multicenter study, indicate each individual's affiliation using a superscript Arabic number (e.g., [1,2,3]).
- Corresponding author: The corresponding author's name, postal code, address, and email should be included.
- ORCID (Open Researcher and Contributor ID): ORCIDs of all authors are recommended to be provided. They can obtain ORCIDs at the website (http://orcid.org/).
- Author contributions: The contributions of all authors must be described using the Contributor Roles Taxonomy (CRediT; https://credit.niso.org/).
- Conflict of interest: If there are any conflicts of interest, authors should disclose them in the manuscript. Disclosures allow editors, reviewers, and readers to approach the manuscript with an understanding of the situation and background of the completed research. If there are no conflicts of interest, authors should include the following sentence: "No potential conflict of interest relevant to this article was reported."
- Funding statement: Describe the sources of funding that have supported the work. Please include relevant grant numbers and the URL of any funder's website. Also, describe the role of any sponsors or funders.
- Acknowledgments: Any persons that contributed to the study or the manuscript, but not meeting the requirements of authorship could be placed here. If you do not have anyone to acknowledge, please write "Not applicable" in this section.

(2) Abstract and keywords: The abstract of original article should be concise (less than 300 words) and describe concisely the Background, Methods, Results, and Conclusion, in a structured format. In principle, acronyms and informal abbreviations should be avoided, but they, if needed, can be kept to an absolute minimum with proper identifications. The abstracts of review articles and case reports should be in an unstructured format and limited to 300 and 250 words, respectively.

A maximum of 6 keywords should be listed at the end of the abstract to be used as index terms. For the selection of keywords, refer to Medical Subject Headings (MeSH) in Index Medicus, or http://www.nlm.nih.gov/mesh/MBrowser.html.

(3) Introduction: A brief background, references to the most pertinent papers general enough to inform readers, and the relevant findings of others should be included. It is recommended that the introduction includes general and specific background, a debating issue, and the specific purpose of this study.

(4) Methods: When reporting experiments with human or animal subjects, the authors should indicate whether they received approval from the relevant committees for the study. The materials and study design should be presented in detail. The sources of special chemicals or preparations should be given (name of company). The method of statistical analysis and the criteria for determining significance levels should be described.

Clearly describe the selection of observational or experimental participants (healthy individuals or patients, including controls), including eligibility and exclusion criteria and a description of the source population. Ensure correct use of the terms sex (when reporting biological factors) and gender (identity, psychosocial or cultural factors), and unless inappropriate, report the sex and/or gender of study participants, the sex of animals or cells, and describe the methods used to determine sex and gender. If the study was done involving an exclusive population, for example in only one sex, authors should justify why, except in obvious cases (e.g., prostate cancer). Authors should define how they determined race or ethnicity and justify their relevance.

(5) Results: This section should be presented logically using text, tables, and illustrations. Excessive repetition of table or figure contents should be avoided. Results should not be presented in duplicate as table and figure.

(6) Discussion: The discussion should focus on the interpretation and significance of the findings and include the objective comments that describe their relation to other work in the area as well as new and important aspects of the study. The data should be interpreted concisely without repeating materials already presented in the results

section. A summary or conclusion should be included at the end of this section.

(7) References

- References should be listed in the sequence cited in the paper, and sequential numbers should be attached in the middle or at the end of the corresponding sentences in the body of the text.
- References should be identified in the text with full-size Arabic numerals on the line and in square brackets. e.g., In the study by Song et al. [23]...
- All authors up to 6 can be listed. If author number is more than 6, the names of all authors after the first 6 authors should be abbreviated to "et al".

- **Examples of reference style**

Journal article

1. Scumpia PO, Sarcia PJ, Kelly KM, DeMarco VG, Skimming JW. Hypothermia induces anti-inflammatory cytokines and inhibits nitric oxide and myeloperoxidase-mediated damage in the hearts of endotoxemic rats. Chest 2004;125:1483-91.
2. Chakdour S, Vaidya PC, Angurana SK, Muralidharan J, Singh M, Singhi SC. Pulmonary Functions in Children Ventilated for Acute Hypoxemic Respiratory Failure. Pediatr Crit Care Med 2018;19:e464-71.
3. Nam KH, Kang HK, Lee SS, Park SH, Kang SW, Hwang JJ, et al. Effects of high-flow nasal cannula in patients with mild to moderate hypercapnia: a prospective observational study. Acute Crit Care 2021;36:249-55.
4. Ghorbanzadeh K, Ebadi A, Hosseini M, Madah SS, Khankeh H. Challenges of the patient transition process from the intensive care unit: a qualitative study. Acute Crit Care 2021 Jan 28 [Epub]. https://doi.org/10.4266/acc.2020.00626

Book and book chapter

5. Shaffner DH, Nichols DG. Rogers' textbook of pediatric intensive care. 5th ed. Wolters Kluwer; 2016.
6. Ventre KM, Arnold JH. Acute lung injury and acute respiratory distress syndrome. In: Shaffner DH, Nichols DG, editors. Rogers' textbook of pediatric intensive care. 5th ed. Wolters Kluwer; 2016. p.766-93.

Website

7. Extracorporeal Life Support Organization. ECLS registry report & international summary of statistics [Internet]. Extracorporeal Life Support Organization; 2019 [cited on 2021 Dec 15]. Available from: https://www.elso.org/registry/internationalsummaryandreports.aspx

(8) Tables

- Tables should be referenced in the main text in sequential order and uploaded separately with the main text. Each table should be inserted on a separate page, with the table number and table title above the table.
- Titles of tables should be concise using a phrase or a clause. The first character should be capitalized. Table footnotes should be indicated with superscript small letters (e.g., $^{a), b), c)}$) in alphabetical order.
- All symbols and abbreviations should be described below the table. All units of measurements and concentrations should be designated. Unnecessary longitudinal lines should not be drawn.
- If a table has been previously published should be accompanied by the written consent of the copyright holder and the footnote must acknowledge the original source.

(9) Figures and figure legends

- Figure numbers, in Arabic numerals, should appear in the figure legends. Arabic numerals should be used in the order in which the figures are referred to in the main text. In cases where more than two photographs are used with the same number, alphabet characters should be used next to the Arabic numeral (e.g., Fig. 1A, Fig. 1B).
- All pictures and photographs should be described in the legend with complete sentences rather than incomplete phrases or a clause. All symbols and abbreviations should be described below the figure. The description of footnotes below the figure should follow the order of that of acronyms and then symbols. Symbols should be marked with small alphabet letters in the order of their usage such as $^{a), b), c)}$.
- Figures should be submitted separately from the text of the manuscript. APCC publishes in full color and encourages authors to use color to increase the clarity of figures. All pictures and photographs should be of excellent quality and supplied as TIFF, JPEG, GIF, or PPT files with a resolution of more than 300 dpi. Except for particularly complicated drawings that show large amounts of data, all figures are published at one page or one column width. All kinds of figures may be reduced, enlarged, or trimmed for publication by the editor.
- A previously published figure should be accompanied by a footnote acknowledging the original source and the consent of the copyright holder.

(10) Supplemental data

Nonessential tables and figures may accompany articles as online-only supplemental files. All online-only supplementary files

should be combined in one document file (whenever possible) and uploaded separately during the submission process. These files must be referenced in the main text of the manuscript at least once (e.g., Supplementary Table 1). All online-only supplemental files are subject to review, but such files will not be copyedited or proofread by production staff. As such, authors are encouraged to review their supplemental files carefully before submitting them.

6. MANUSCRIPT SUBMISSION AND PEER REVIEW PROCESS

6.1. Online Submission

All manuscripts should be submitted online via the online submission system available at: https://submit.apccjournal.org/. Under this online system, only corresponding authors can submit manuscripts. The process of reviewing and editing will be conducted entirely through this system. Once you have logged into your account, the online system will lead you through the submission process in a step-by-step orderly process. Submission instructions are available on the website. In case of any trouble, please contact the editorial office (Email: kspccm@kspccm.org).

6.2. Screening after Submission

Screening process will be conducted after submission. If the manuscript does not fit the aims and scope of the Journal or does not adhere to the Instructions to authors, it may be returned to the author immediately after receipt and without a review. Before reviewing, all submitted manuscripts are inspected by "Similarity Check powered by iThenticate (https://www.crossref.org/services/similarity-check/), a plagiarism-screening tool. If a too high a degree of similarity score is found, the Editorial Board will do a more profound content screening. The criterion for similarity rate for further screening is usually 15%; however, the excess amount of similarity in specific sentences may be also checked in every manuscript. The settings for Similarity Check screening are as follows: It excludes quotes, a bibliography, small matches of 6 words, small sources of 1%, and the Methods section.

6.3. Peer Review Process

Submitted manuscripts will be reviewed by two or more experts in the corresponding field. The Editorial Board may request authors to revise the manuscripts according to the reviewer's opinion. After revising the manuscript, the author should upload the revised files with a reply to each item of the reviewer's opinion. The revised part should be marked in red font with an underline.

The author's revisions should be completed within 30 days after the request. If it is not received by the due date, the Editorial Board will not consider it for publication again. The manuscript review process can be finished with the second review. If further revision is requested, the Editorial Board may consider it. Editorial Board will make a final decision on the approval of the submitted manuscript for publication and can request any further corrections, revisions, and deletions of the article text if necessary. Statistical editing is also performed if the data requires professional statistical review by a statistician.

6.4. Appeals of Decisions

Any appeal against an editorial decision must be made within 2 weeks of the date of the decision letter. Authors who wish to appeal against a decision should contact the editor-in-chief, explaining in detail the reasons for the appeal. All appeals will be discussed with at least one other associate editor. If consensus cannot be reached thereby, an appeal will be discussed at a full editorial meeting. The process of handling complaints and appeals follows the guidelines of COPE available from (https://publicationethics.org/appeals). APCC does not consider second appeals.

7. MANUSCRIPT PROCESSING AFTER ACCEPTANCE

7.1. Final Version

After a paper has been accepted for publication, the author(s) should submit the final version of the manuscript. The names and affiliations of authors should be double-checked, and if the originally submitted image files were of poor resolution, higher-resolution image files should be submitted at this time. TIFF and PDF formats are preferred for the submission of digital files of photographic images. Files containing figures must be named according to the figure number (ex: Fig. 1. tiff). Symbols (e.g., circles, triangles, squares), letters (e.g., words, abbreviations), and numbers should be large enough to be legible on reduction to the journal's column widths. All symbols must be defined in the figure caption. If references, tables, or figures are moved, added, or deleted during the revision process, they should be renumbered to reflect such changes so that all tables, references, and figures are cited in numeric order.

7.2. Manuscript Corrections

Before publication, the manuscript editor will correct the manuscript such that it meets the standard publication format. The author(s) must respond within 2 working days when the manuscript editor contacts the author for revisions. If the response is delayed, the manuscript's publication may be postponed to the next issue.

7.3. Galley Proof

After corrections have been made, an accepted manuscript will be sent to the publisher for printing. The proof may be revised more than once by the corresponding author, if needed. The author should double-check for corrections in the content, title, affiliation, capitalization, locations of figures, and references. Corresponding authors are responsible for further corrections made after printing.

7.4. Post-publication Discussions

Post-publication discussions can be held through letters to the editor. If any readers have concerns about any articles published, they can submit a letter to the editor related to the articles. If any errors or mistakes are found in an article, they can be corrected through an erratum, corrigendum, or retraction.

8. AUTHOR'S CHECKLIST

- All manuscripts are typed in 12-point font size, double-spaced, and saved as an MS Word file.
- All pages are numbered consecutively starting from the abstract page.
- The order of the manuscript is a title page, abstract, main body, references, and table and legend of figures.
- Figures are inserted into the separated files in the order of citation.
- The title page includes the article title, running title (no more than 50 characters), authors' full name(s) and affiliation, address for correspondence (including address and e-mail), ORCID (all authors), conflict of interest, funding statement, and footnotes, if any.
- The title page states that the manuscript has not been published previously and will not be submitted for publication elsewhere. It discloses conflicts of interest of all listed authors if any.
- The abstract for an original article/review should be less than 300 words, and the abstract for a case report should be less than 250 words.
- The format of an original article is Background, Methods, Results, and Conclusion, and each component should be on the next line.
- A maximum of 6 keywords should be listed at the end of the abstract to be used as index terms. For the selection of keywords, refer to Medical Subject Headings (MeSH) in Index Medicus.
- The order of the main text is Abstract with Keywords, Introduction, Methods, Results, Discussion, References, and Table and Figure legends.
- All pages are numbered consecutively starting from the abstract page.
- Change the author information (Name, Institute) to "OOO".
- The reference items are listed in the correct format and all references listed in the references section are cited in the text.
- Manuscript for original articles should be limited strictly up to 50 references. For reviews, case reports, and editorials and letters to the editor should be limited strictly to 100, 20, and 10 references).
- Tables are provided in English and an Arabic figure. It should be placed at the end of the manuscript.
- All figures are submitted as a separate file in TIFF, JPEG, GIF, or PPT formats higher than 300 dpi.
- All authors must read the manuscript and agree with the submission.

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Author's checklist

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Confirm the checklist before submitting the manuscript. Checking on every point is needed to proceed.

1. Manuscript Form

☐ All manuscripts are typed in 12-point font size, double-spaced, and saved as an MS Word file.
☐ All pages are numbered consecutively starting from the abstract page.
☐ The order of the manuscript is a title page, abstract, main body, references, and table and legend of figures.
☐ Figures are inserted into the separated files in the order of citation.

2. Title Page

☐ The title page includes the article title, running title (no more than 50 characters), authors' full name(s) and affiliation, address for correspondence (including address and e-mail), ORCID (all authors), conflict of interest, funding statement, and footnotes, if any.
☐ The title page states that the manuscript has not been published previously and will not be submitted for publication elsewhere. It discloses conflicts of interest of all listed authors if any.

3. Abstract

☐ The abstract for an original article/review should be less than 300 words, and the abstract for a case report should be less than 250 words.
☐ The format of an original article is Background, Methods, Results, and Conclusion.
☐ A maximum of 6 keywords should be listed at the end of the abstract to be used as index terms. For the selection of keywords, refer to Medical Subject Headings (MeSH) in Index Medicus.

4. Main Body

☐ The order of the main text is Abstract with Keywords, Introduction, Methods, Results, Discussion, References, and Table and Figure legends.
☐ All pages are numbered consecutively starting from the abstract page.
☐ Change the author information (Name, Institute) to "OOO".

5. References

☐ The reference items are listed in the correct format and all references listed in the references section are cited in the text.
☐ Manuscript for original articles should be limited strictly up to 50 references. For reviews, case reports, and editorials and letters to the editor should be limited strictly to 100, 20, and 10 references).

6. Tables and Figures

☐ Tables are provided in English and an Arabic figure. It should be placed at the end of the manuscript.
☐ All figures are submitted as a separate file in TIFF, JPEG, GIF, or PPT formats higher than 300 dpi.

☐ **All authors must read the manuscript and agree with the submission.**

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Archives of Pediatric Critical Care

☐ Editorial ☐ Original article ☐ Review ☐ Case report ☐ Letter to the editor

Title : _____

Each author must read and sign the following statements. Completed statements should be send to the Editorial Office through the online manuscript submission system or e-mail (apcc@apccjournal.org).

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