



# Awakening ECMO During Pediatric Extracorporeal Membrane Oxygenation: A Single-center Experience

## Pediyatrik Ekstrakorporeal Membran Oksijenasyonu Sırasında Uyanık ECMO: Tek Merkez Deneyimi

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### Abstract

**Introduction:** Recently, some centers have used extubation during extracorporeal membrane oxygenation (ECMO) to eliminate barotrauma and volutrauma as a lung rest strategy. This study aims to demonstrate the use of extubation during ECMO in children.

**Methods:** This retrospective study was conducted from January 1, 2015, to April 1, 2023, in our pediatric intensive care unit.

**Results:** In this study, we presented six cases that were extubated during ECMO support. In addition, we followed 130 pediatric patients on ECMO in the same period. Two patients were primarily diagnosed with cardiomyopathy, one with myocarditis, two with congenital heart defect, and one with necrotizing pneumonia. The median age of patients was 99 (interquartile range 25-75) (16.5-192) months, and all were male. Venoaerterial ECMO was connected to 4 patients, and venovenous ECMO was connected to 2 patients. Six patients were extubated during ECMO on the 5<sup>th</sup>, 12<sup>th</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, 3<sup>rd</sup> and 14<sup>th</sup> days of their treatment, respectively. While the patients were extubated, three of them were supported by biphasic positive airway pressure, one was supported by nasal continuous positive airway pressure, and two were provided with supplementary oxygen. Three patients were extubated under ECMO and discharged.

**Conclusion:** The risk of mechanical ventilation related complications such as volutrauma and barotrauma could be minimized in patients extubated under ECMO. In addition, sedatives, analgesics, and

### Öz

**Giriş:** Son zamanlarda, bazı merkezler ekstrakorporeal membran oksijenasyonu (ECMO) sırasında hastaları ekstübe ederek akciğer dinlenme stratejisi olarak barotravma ve volütravmayı ortadan kaldırmayı planlamışlardır. Bu çalışmada, ECMO desteği sırasında ekstübe edilen çocuk hastaların klinik sonuçlarını göstermeyi planladık.

**Yöntemler:** Bu geriye dönük çalışma, 1 Ocak 2015 ile 1 Nisan 2023 tarihleri arasında çocuk yoğun bakım ünitemizde gerçekleştirilmiştir.

**Bulgular:** Bu çalışmada, ECMO desteği sırasında ekstübe izlenen altı çocuk hasta sunulmuştur. Aynı zaman aralığında merkezimizde 130 çocuk hasta ECMO'da izlendi. ECMO'da uyanık takip edilen hastalardan ikisi kardiyomiyopati, ikisi doğuştan kalp hastalığı, biri miyokardit ve biri nekrotizan pnömoni tanısına sahipti. Hastaların median yaşı 99 (çeyrekler arası aralık 25-75) (16,5-192) aydı ve hastaların hepsi erkekti. Dört hasta venoaerteriyel ECMO, 2 hastaya venovenöz ECMO'ya bağlandı. Altı hasta ECMO'ya bağlandıktan sonra sırasıyla 5., 12., 3., 4., 3. ve 14. günlerinde ekstübe edildi. Hastalar ekstübe edildikten sonra üç hastaya Bifazik pozitif hava yolu basıncı, bir hastaya nazal sürekli pozitif hava yolu basıncı non-invaziv solunum desteği verildi. ECMO altında ekstübe edilen üç hasta taburcu edildi.

**Sonuç:** ECMO desteği sırasında ekstübe edilen hastalarda volutrauma ve barotravma gibi mekanik ventilasyonla ilişkili komplikasyon riski en aza indirilebilir. Ayrıca, sedatifler, analjezikler ve kas gevşeticilerle

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## Abstract

muscle relaxant related complications such as delirium, muscle weakness, or prolonged ventilation could reduced via awake ECMO.

**Keywords:** Extracorporeal membrane oxygenation, extubation, mechanical ventilation, child

## Öz

ilişkili komplikasyonlar olan deliryum, kas zayıflığı veya uzun süreli ventilasyon, uyanık ECMO ile azaltılabilir.

**Anahtar Kelimeler:** Ekstrakorporeal membran oksijenasyonu, ekstübasyon, mekanik ventilasyon, çocuk

## Introduction

Extracorporeal membrane oxygenation (ECMO) is a widely used life-saving intervention for children with circulatory and respiratory failure that is refractory to standard therapies.<sup>1</sup> Due to advances in extracorporeal life support (i.e., technical devices, cannulation technique, specialized ECMO teams), ECMO has become a safe tool in pediatric intensive care.<sup>2</sup> These developments in ECMO may be used for pediatric and adult patients for weeks for recovery and bridge therapy to left ventricular assist device implantation or transplantation.<sup>2</sup> ECMO performs this by regulating cellular respiration, improving tissue oxygenation, and allowing CO<sub>2</sub> removal.<sup>3</sup> It is, however, an invasive treatment method and can cause potential serious complications. ECMO has been considered the last treatment option to be used only when traditional treatments do not respond and only for a sufficient duration until the patient may be returned to more "standard" support modalities (mechanical ventilation, inotropic support, and cardiopulmonary resuscitation).<sup>3</sup>

During ECMO, patients are often prescribed a lot of sedatives-analgesics and invasive mechanical ventilation (MV) to avoid fatal decannulation and facilitate ECMO performance. Sedation also reduces oxygen consumption, thereby improving arterial oxygen transport and organ perfusion. Nevertheless, both sedation and MV may cause complications.<sup>4</sup> Long-term sedation and neuromuscular blockade therapy may cause muscle weakness, disability, tolerance, delirium, or prolonged recovery time. Possible invasive MV-related complications include tracheal irritation due to the intubation tube, discomfort, and the need for more sedation. In addition, it might cause ventilator-related complications, such as ventilator-associated pneumonia, pneumothorax, or respiratory muscle weakness.<sup>3</sup> There is a growing interest in reducing exposure to narcotics, sedatives, and neuromuscular blocking agents and keeping ECMO patients awake and mobile to maintain muscle strength and shorten recovery times. Recently, a method of extubation from MV under ECMO, especially for patients with respiratory failure and as a bridge therapy to lung transplantation, has emerged.<sup>5-8</sup> However, extubation practices and management options during ECMO in pediatric intensive care units have not been adequately reported. This study presents the clinical findings of six children who were

electively extubated during ECMO, along with an expanded discussion of two representative cases.

## Materials and Methods

### Patients

This retrospective study was conducted from 2015 to 2023 in our pediatric intensive care unit. We present six cases of extubation during ECMO support. In addition, we followed up 130 pediatric patients on ECMO during the same period. Patient demographic data and clinical and laboratory data were obtained from medical records.

In our clinic, 130 pediatric patients have been connected to ECMO so far, and 6 of them have been extubated during ECMO. Based on the extubation protocol in our clinic;

1. The patient's FiO<sub>2</sub><40% and SpO<sub>2</sub>>92% in IMV,
2. No respiratory effort at low pressures and minimal settings in the IMV,
3. The patient becomes conscious after discontinuing sedation,
4. After monitoring the IMV in continuous positive airway pressure (CPAP)/pressure support ventilation (PSV) mode (PSV 6, positive end-expiratory pressure 6 FiO<sub>2</sub> 40%) for 1-2 hours, there is no respiratory effort, and the patient is extubated if there is no acidosis or hypercarbia in the blood gas.

### Ethical Considerations

Voluntary consent was obtained from the families of the patients included in the study. The study was approved by the Institutional Review Board of the Ankara University Faculty of Medicine (approval number: İ06-384-23, 2023/06).

### Statistical Analysis

Statistical analyses were performed using SPSSv26.0 (Statistical Package for Social Sciences for MacOS, Inc., USA). Descriptive variables are presented as frequencies and proportions (%). Continuous variables are presented as median (lower-upper limit) values.

## Results

Six children were extubated during ECMO support. The median age of patients was 99 [interquartile range (IQR) 25-75] (16.5-

192) months, and all were male. Two patients were primarily diagnosed with cardiomyopathy, one with myocarditis, two with congenital heart defects, and one with necrotizing pneumonia. Venoarterial (VA) ECMO was connected to 4 patients, and venovenous-venoarteriovenous (VV) ECMO were connected to 2 patients. The peripheral ECMO was connected in five patients, whereas the central ECMO was connected in one patient. One patient who was connected to VV ECMO subsequently underwent venoarteriovenous (VAV) ECMO due to cardiogenic shock. Five patients were connected to ECMO for cardiac failure, and one patient was connected to respiratory failure.

Six patients were extubated during ECMO on the 5<sup>th</sup>, 12<sup>th</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, 3<sup>rd</sup> and 14<sup>th</sup> days of treatment, respectively. The median number of days extubated during ECMO was 4.5 (IQR3-12.5) days. The durations of remaining extubation while on ECMO were 8, 9, 3, 6, 13, and 3 days for six patients, respectively. The median day of extubation duration under ECMO was 7(IQR 3-10) days. While the patients were extubated, three received biphasic positive airway pressure (BIPAP), one received nasal-CPAP (N-CPAP), and two were provided with supplementary oxygen. Five patients were reintubate during ECMO. Four patients were intubated due to increased respiratory distress, and one patient was intubated after decannulation. ECMO complications were observed in 4 patients, including bleeding in 4 cases, limb ischemia in 1 case, and circuit clotting in 3 cases. Three patients who were extubated under ECMO survived. Two patients were discharged with no neurological sequel.

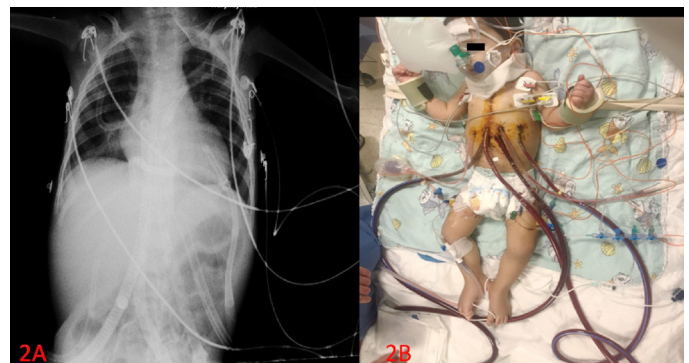
### Case 1

A 3-year-old male patient was transferred to our pediatric intensive care unit (PICU) following video-assisted thoracoscopic surgery (VATS) for necrotizing pneumonia and



**Figure 1.** (A) Chest X-ray of patient 1 on the first day of PICU admission, showing poor pleural effusion and lung parenchyma. (B) Awake ECMO and supported by non-invasive mechanical ventilation via full face interface. (C) Lung parenchyma was better on chest X-ray when the child was discharged to the infectious ward  
 PICU: Pediatric intensive care unit, ECMO: Extracorporeal membrane oxygenation

empyema. When the patient was admitted to intensive care, chest tubes were placed in both hemithorax. The chest X-ray taken in another center revealed pleural effusion, and the fluid was exudated via thoracentesis (Figure 1A). It was reported that the patient had cavitory lesions and consolidation areas that were evaluated in favor of bilateral necrotizing pneumonia and bilateral pleural effusion on CT thorax. The patient had respiratory distress and desaturation, requiring intubation. VATS was performed on the 2<sup>nd</sup> day of hospitalization. The patient was diagnosed with necrotizing pneumonia and metapneumovirus and was intubated following video-assisted thoracoscopic surgery (VATS). Oseltamivir was administered after the pleural fluid sample tested positive for influenza A (H1N1) and bocavirus via polymerase chain reaction (PCR). In addition, meropenem, vancomycin, and levofloxacin were initiated. On the 7<sup>th</sup> day of PICU admission, the patient was admitted to venovenous (VV) ECMO because of severe hypoxemia and respiratory acidosis in a high ventilator setting. The ECMO settings were an RPM of 4500/min and LPM of 1200 mL/min. Cardiac arrest occurred twice, and cardiopulmonary (CPR) resuscitation was performed within 5 and 12 min, respectively. The patient was extubated on the 12<sup>th</sup> day of ECMO, and BIPAP was subsequently applied at the full-face interface (Figure 1B, C). He was decannulate on



**Figure 2.** (2A) Patient 2' chest X-ray and (2B) appearance during mechanical biventricular support; he is extubated and only given oxygen support



**Figure 3.** Patient 3 was extubated despite femoral ECMO, and a non-rebreathing mask was applied  
 ECMO: Extracorporeal membrane oxygenation

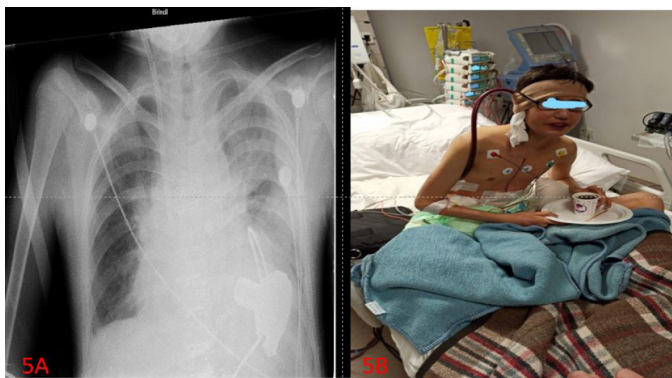
the 22<sup>nd</sup> day of ECMO, but BIPAP was continued until two days after ECMO removal. The patient was subsequently transferred to the pediatric infection disease unit on the 38<sup>th</sup> day of PICU admission with normal vital signs. He was discharged on the 44<sup>th</sup> day of hospitalization.

## Case 2

A 17-month-old male patient was admitted to our PICU after the establishment of central VA ECMO due to fulminant myocarditis. The patient's cardiac function was poor, with an ejection fraction of the left ventricular of 15%, and there was severe metabolic acidosis and recurrent ventricular tachycardia. ECMO was connected for these reasons. When the patient was admitted to the PICU, the ECMO settings were RPM 5200/min and LPM 1100/min. On the 2<sup>nd</sup> day of



**Figure 4.** Image of Patient 4 during ECMO extubation. He could communicate and be fed at the same time  
ECMO: Extracorporeal membrane oxygenation



**Figure 5.** (A) Patient 5' chest X-ray during extubation while under VV ECMO and LVAD implantation. (B) Patient 5 could speak easily and eat breakfast during awake  
ECMOLVAD: Left ventricular assist device, ECMO: Extracorporeal membrane oxygenation, VV: Venoarteriovenous

PICU admission, we changed to a central ECMO cannulation site as VA-ECMO was set biventricular separately (for left ventricular, from apex of the left ventricle to ascending aorta; for right ventricle, from right atrium to pulmonary artery). Via a levitronix support device. The patient was started on lidocaine and amiodarone because of ventricular tachycardia attacks. Influenza A was identified as the cause of myocarditis based on respiratory viral PCR panel analysis. On the 3<sup>rd</sup> day of PICU admission, the ECMO circuit was changed because of a thrombus.

We decided to extubate him due to the clinical state of the lung, and neurologic findings were good despite biventricular dysfunction in the heart. The patient was extubated on the 10<sup>th</sup> day of ECMO, and subsequently, a non-rebreathing mask was applied (Figure 2A). On the 15<sup>th</sup> day, the right ventricular support device was removed, and the patient was reintubated before surgery. On the 22<sup>nd</sup> day after left support device placement, the patient was extubated again (Figure 2B). The left support device was removed on day 26, but the patient was not intubated. On the 34<sup>th</sup> day of admission, the patient was transferred to the cardiology department with intermittent ventricular tachycardia and a good neurological state.



**Figure 6.** Patient 6 was supported by N-CPAP during awake ECMO  
ECMO: Extracorporeal membrane oxygenation, N-CPAP: Nasal-continuous positive airway pressure

**Table 1. Patients' demographic, diagnoses and clinical features**

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (y)	3,5	1,5	16	16	13	1
Gender	Male	Male	Male	Male	Male	Male
Weight (kg)	18	11	40	54	50	7.5
Height (cm)	95	80	145	170	170	67
BSA (m2)	0.73	0.50	1.28	1.54	1.47	0.38
Primary disease	Necrotizing pneumonia	Myocarditis	Epstein anomaly	Dilated cardiomyopathy-implanted LVAD Heart transplanted	Discordant criss-cross heart	Ventricular septal defect, patent ductus arteriosus
ECMO indication	Respiratory	Cardiac	Cardiac	Cardiac	Cardiac	Cardiac
ECMO type	VV	VA	VA	VA	VV, VA-V	VA
Venous cannula insertion site	RIJV	Right atrium-left atrium (BVAD)	LFV	RFV	RFV, RIJV	RIJV
Artery cannula insertion site	N	Pulmonary artery-Ascending aorta (BVAD)	LFA	RFA	RFA	Ascendin aorta
Duration of ECMO (days)	23	28	6 (47)	46	28	16
Complications during ECMO	Bleeding	Clotting in circuit	Limb ischemia	Bleeding, clotting in circuit	Bleeding, Clotting in circuit	Bleeding
Sedation type during ECMO	Midazolam, fentanyl	Midazolam, fentanyl	Midazolam	Midazolam	Midazolam, fentanyl	Midazolam, fentanyl
Sedation used during post extubation on ECMO	Fentanyl	Fentanyl	N	N	N	N
Duration of extubation (days)	8	5 (under BVAD), 4 (under LVAD)	3	6	13	3
Extubation day under ECMO	5.	12.	3.	4.	3.	3.
Respiratory support while extubated under ECMO	BIPAP	Oxygen mask	BIPAP	BIPAP	Oxygen mask	N-CPAP, BIPAP
Reintubation during ECMO	Y	Y	Y	Y	Y	N
Reintubation indication	Respiratory distress	when removing the cannula RVAD	Respiratory distress and hypotension	Respiratory distress and hypotension	Respiratory distress and hypotension	
On the day after decannulation, it was extubated	Yes	Yes	N	N	N	Y
Length of duration between decannulation and discharge (days)	8	8	N	N	N	95
Neurological sequel	None	None				
Outcome	Survived	Survived	Non-survived	Non-survived	Non-survived	Survived

BSA: Body surface area, VA: Venoarterial, VV: Venovenous, VA-V: Venoarterio-venous, Y: Yes, N: No, RIJV: Right internal jugular vein, RFA: Right femoral arteria, LFA: Left femoral arteria, LFV: Left femoral vein, BVAD: Biventricular assist device model, BIPAP: Bilevel positive airway pressure, N-CPAP: Nasal-continuous positive airway pressure

The demographic characteristics, diagnoses, and clinical features of the patients are presented in Table 1. Image of the other patients during awake ECMO are shown in Figures 3-6 respectively.

## Discussion

Patients are often subjected to severe sedation and invasive MV to avoid fatal decannulation during ECMO running.<sup>4,8</sup> Some centers use extubation during ECMO to completely

eliminate barotrauma and volutrauma as a lung rest strategy in adults.<sup>9</sup> Sedation reduces oxygen consumption, thereby improving arterial oxygen transport and organ perfusion, and decreases the irritative effect of the endotracheal tube.<sup>4,8</sup> However, complications such as sedation habits, dose increase, delirium, or neuromuscular decompression may occur due to sedation. In addition, clinical conditions such as stroke may be masked in patients under sedation.<sup>3,4,10</sup> Benefits include reduced sedation need, increased mobility, and enhanced

interaction with the environment. However, the adoption of this application requires careful planning. Patients who are extubated can be reintubated again.<sup>11</sup> In our study on sedation therapy under ECMO, two patients were treated with midazolam and four were treated with midazolam and fentanyl. After extubation while still connected to the ECMO, the dose of sedation treatment was reduced and then stopped.

In addition, awake ECMO is important to assess the clinical and neurological status before transplantation in patients who are candidates for lung transplantation followed by on ECMO.<sup>12</sup> The practice of awake ECMO may strengthen the transplant candidacy by improving the neuromuscular condition of these patients through physiotherapy and advanced nutrition.<sup>12</sup>

A study on awake ECMO in adults was beneficial for pulmonary transplant candidates.<sup>13</sup> In this study, patients intubated during ECMO required longer invasive respiratory support after transplantation and longer intensive care unit stays compared with the awake ECMO group.<sup>13</sup> The 6-month survival rate was higher in the awake ECMO group in this study.<sup>13</sup>

Pediatric awake ECMO was first reported by Anton-Martin et al.<sup>3</sup>. This study was conducted between 1996 and 2013 with 16 pediatric patients who were extubated while receiving ECMO support. There were 511 patients connected to ECMO. Fourteen of them were connected to ECMO due to respiratory failure and 2 patients for cardiac reasons. Eleven patients had VV ECMO, and 5 patients had VA ECMO. Three patients were reintubated due to arrhythmia and intracranial bleeding. During ECMO, the extubation time was reported as an average of 6 days. Eleven patients who were extubated during ECMO survived.<sup>3</sup> In our study, we reported 6 cases with awake ECMO and followed up 130 pediatric patients who were connected to an ECMO for the same period of time in our PICU.

Similarly, in a study conducted by Schmidt et al.<sup>2</sup> 6 pediatric patients were extubated under ECMO. Six patients were connected to VA ECMO support for cardiac reasons. The number of days extubated under ECMO was 9.5 days, and the mean time to extubation was 78% of the total ECMO time in these patients. The mean duration of ECMO was 17.4 days. One patient was lost during follow-up.<sup>2</sup>

In this study, we presented 6 cases that were extubated while under ECMO. Four of the patients were connected to VA ECMO, and two of them were connected to VV ECMO. Patient 2 was connected to central ECMO, while the others were connected to peripheral ECMO. The durations of our patients' stays at ECMO were 23, 28, 47, 46, 28, and 16 days, respectively. The patients were extubated while still

connected to ECMO on the 5<sup>th</sup>, 12<sup>th</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, 3<sup>rd</sup>, and 14<sup>th</sup> days, respectively. Extubation under ECMO was performed on the 8<sup>th</sup>, 9<sup>th</sup> (5 days when the right support device was removed, 4 days when the left support device was removed), 3<sup>rd</sup>, 6<sup>th</sup>, 13<sup>th</sup>, and 3<sup>rd</sup> days, respectively.

During ECMO, an average extubation time was reported as an average of 7-8 days. Two patients who underwent VV ECMO had the longest extubation time. During awake ECMO, three patients were supported by BIPAP, one patient was supported by N-CPAP, and two patients were given only oxygen supplement. Except for patients 1 and 6, four patients were reintubated for various reasons during ECMO support. Patients 3, 4, and 5 were intubated during decannulation. These patients were reconnected to ECMO because of their worsening status on the same day after decannulation, and three patients were lost despite all interventions during follow-up. Patient 2 was intubated during decannulation, and then patient 2 was extubated. Patient 6 was intubated 29 days after ECMO decannulation. Three patients were extubated during ECMO support and survived.

In our study, ECMO-related complications were observed. ECMO complications are common, including bleeding, stroke, limb ischemia, thrombosis, and infection.<sup>14</sup> Although the most common complications are bleeding (30-40%) and infection (31%), it has been reported that there is at least one major complication in more than half of ECMO patients.<sup>14</sup> In our study, bleeding was observed in four of the patients as an ECMO complication. The ECMO set was changed in 3 patients due to thrombus (changed twice in one patient). None of the patients underwent incidental ECMO decannulation. All patients were treated with heparin during ECMO. The heparin dose was evaluated using activated clotting time and activated partial thromboplastin time tests. CRRT treatment was administered to patients 3, 4, and 5 due to the fluid load under ECMO.

The implementation of awake ECMO requires meticulous team planning and a thorough evaluation of the potential benefits and risks to the patient. To avoid the risks of decannulation, under the supervision of the patient's parents, nurses, and physicians, the patient's cannula was also fixed with a coban bandage, and a mesh cap was placed in the exit of the cannula.

Before performing extubation during ECMO, the benefits of extubation should be determined on a patient-based basis. Before this procedure, the expected time to ECMO, possibility of accidental decannulation of the ECMO circuit during extubation, and possibility of emergency reintubation should be considered. This important decision should be made by a multidisciplinary team, and the patient's family should be informed about this issue.

## Conclusion

As a result, the risk of mechanical ventilation-related complications, such as volutrauma and barotrauma, is minimized in patients extubated under ECMO. In addition, sedatives, analgesics, and muscle relax-related complications, such as delirium, muscle weakness, and prolonged ventilation, are reduced via awake ECMO. In patients whose sedation needs are reduced, communication with the environment increases, and clinical conditions such as stroke may be noticed more easily.

## Ethics

**Ethics Committee Approval:** The study was approved by the Institutional Review Board of the Ankara University Faculty of Medicine (approval number: İ06-384-23, 2023/06).

**Informed Consent:** Voluntary consent was obtained from the families of the patients included in the study.

## Footnotes

### Authorship Contributions

Concept: E.G., T.K., Design: E.G., E.B., F.K., M.C.S., A.G., T.K., Data Collection or Processing: E.G., E.B., F.K., M.C.S., A.G., T.K., Analysis or Interpretation: E.G., E.B., M.C.S., A.G., T.U., Ö.S.C., E.Ç., M.Ç., Z.E., A.R.A., T.K., Literature Search: E.G., T.U., Ö.S.C., E.Ç., M.Ç., Z.E., A.R.A., T.K., Writing: E.G., T.K.

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