REVISTA BIO CIENCIAS
http://revistabiociencias.uan.edu.mx
https://doi.org/10.15741/revbio.12.e1805
ISSN 2007-3380

Artículo original / Original article

Monitoring of anticoagulation during Extracorporeal Membrane Oxygenation and outcomes in pediatric post cardiac surgery

Monitorización de la anticoagulación durante la oxigenación por membrana extracorpórea y resultados en el postoperatorio pediátrico de cirugía cardiaca

Vargas Camacho, G.[1], *Contreras Cepeda, V.*[1], *Gómez Gutiérrez, R.*[1], *Quezada Valenzuela, G.*[1], *Quiroz Herrera, F.Y.*[2], *Zardain-Medlich-Ducoulombier, O.*[2], *Patrón Romero, L.*[3], *Almanza Reyes, H.*[3*], *González Salazar, F.*[2,4*]

[1] *Unidad de Cuidados Intensivos Pediátricos. Hospital Christus Muguerza, Monterrey, Nuevo León, México.*
[2] *Departamento de Ciencias Básicas, Universidad de Monterrey, San Pedro Garza García, Nuevo León, México.*
[3] *Facultad de Medicina y Psicología, Universidad Autónoma de Baja California, Tijuana, Baja California, México.*
[4] *Centro de Investigación Biomédica del Noreste, Instituto Mexicano del Seguro Social, Monterrey, Nuevo León, México.*

Please cite this article as/Como citar este artículo: Vargas-Camacho, G., Contreras-Cepeda, V., Gómez-Gutiérrez, R., Quezada-Valenzuela, G., Quiroz-Herrera, F.Y., Zardain-Medlich-Ducoulombier, O., Patrón-Romero, L., Almanza-Reyes, H., González-Salazar, F. (2025). Monitoring of anticoagulation during Extracorporeal Membrane Oxygenation and outcomes in pediatric post cardiac surgery. *Revista Bio Ciencias*, 12, e1805. https://doi.org/10.15741/revbio.12.e1805

Article Info/Información del artículo
Received/Recibido: October 23th 2024.
Accepted/Aceptado: August 11h 2025.
Available on line/Publicado: August 21th 2025.

ABSTRACT

The use of extracorporeal membrane oxygenation (ECMO) in the cardiac complications treatment is growing. Anticoagulation control in pediatrics is one of the most complicated aspects in post-cardiac surgery patients. This study aimed to determine whether an anticoagulation monitoring protocol in pediatric post-cardiac surgery patients treated with venoarterial ECMO (VA) results in fewer complications and improves morbidity. This is a quasi-experimental before-and-after study, with a retrospective, observational, descriptive design, conducted at the Christus Muguerza Hospital in Monterrey, Mexico. The variables were activated clotting time (ACT), activated partial thromboplastin time (aPTT), anti-Factor Xa (anti-Xa) activity, and antithrombin III (AT III) parameters. Test results were correlated with the unfractionated Heparin (UFH) infusion rate (IU/kg/h) at the sampling time. The mean heparin dose was 21.09 IU/kg/hr. ACT got 188.6 seconds, and ACT-based therapeutic anticoagulation got in 180–220 seconds. The aPTT in this study was 62.15 seconds. The anti-Xa level was 0.27 UL/mL, and the AT III level was 47.52 IU. We got a survival rate of 60 %. The main hemorrhagic complications were severe bleeding at 10 % and systemic thrombosis at 10 %. The major complications were sepsis, renal failure, and severe bleeding. More prospective trials are required to delineate the dose change with UFH and prevent adverse clinical outcomes in different pediatric cardiac surgery conditions.

KEY WORDS: Extracorporeal Life Support, Extracorporeal Membrane Oxygenation, Anticoagulants, Heparin, Factor Xa Inhibitors, Pediatrics.

***Corresponding Author:**

Horacio Almanza-Reyes. Facultad de Medicina y Psicología, Universidad Autónoma de Baja California. Universidad, 14418, Parque Internacional Industrial Tijuana, C.P. 22390, Tijuana, Baja California, México. Teléfono: +52 (664) 979 7576.

E-mail: almanzareyes@hotmail.com | **Francisco González-Salazar**. Departamento de Ciencias Básicas, Universidad de Monterrey. Av. Ignacio Morones Prieto 4500, Zona Valle Poniente, C.P. 66238, San Pedro Garza García, Monterrey, Nuevo León, México. Teléfono: +52 (81) 8215-1000. Centro de Investigación Biomédica del Noreste, Instituto Mexicano del Seguro Social, Calle 2 de abril núm. 501 esq. con San Luis Potosí, Col. Independencia C.P. 64720, Monterrey, Nuevo León, México. Teléfono: +52 (81) 8190 4036.

E-mail: francisco.gonzalez@udem.edu

Revista Bio ciencias
ISSN 2007-3380

RESUMEN

El uso de la oxigenación por membrana extracorpórea (ECMO) en el tratamiento de las complicaciones cardíacas es cada vez mayor. El control de la anticoagulación en pediatría es uno de los aspectos más complicados en los pacientes postcirugía cardiaca. Esta investigación tuvo como objetivo determinar si un protocolo de monitorización de la anticoagulación en pacientes pediátricos postcirugía cardíaca tratados con ECMO venoarterial (VA) resulta en menos complicaciones y mejorar la morbilidad. Se trata de un estudio cuasiexperimental de tipo antes y después, con un diseño retrospectivo y observacional, descriptivo, realizado en el Hospital Christus Muguerza de Monterrey, México. Las variables fueron el tiempo de coagulación activado (ACT), el tiempo de tromboplastina parcial activada (aPTT), la actividad anti-Factor Xa (anti-Xa) y los parámetros antitrombina III (AT III). Los resultados de las pruebas se correlacionaron con la tasa de infusión de heparina no fraccionada (UFH) (UI/kg/h) en el momento de la toma de muestras. La dosis media de heparina fue de 21.09 UI/kg/h. La ACT fue de 188.6 segundos y la anticoagulación terapéutica basada en ACT de 180 a 220 segundos. El aPTT obtenido en este estudio fue de 62.15 segundos. El nivel de anti-Xa fue de 0.27 UL/mL y el de AT III de 47.52 UI. Obtuvimos una tasa de supervivencia del 60 %. Las principales complicaciones hemorrágicas fueron sangrado grave al 10 % y trombosis sistémica al 10 %. Las principales complicaciones fueron sepsis, insuficiencia renal y hemorragia grave. Se necesitan más ensayos prospectivos para delinear el cambio de dosis con la UFH y prevenir resultados clínicos adversos en diferentes afecciones de cirugía cardíaca pediátrica.

PALABRAS CLAVE: Soporte vital extracorpóreo, Oxigenación por Membrana Extracorpórea, Anticoagulantes, Heparina, Inhibidores del factor Xa, Pediatría.

Introduction

Extracorporeal membrane oxygenation (ECMO) is a life support procedure that has been used globally since the 1960s (Soares *et al.,* 2021). Its use is often indicated in severe respiratory or cardio-respiratory insufficiency (Bembea *et al.,* 2013). ECMO is a procedure in which an extension of blood circulation is created. During the process, the blood is oxygenated, warmed to a suitable temperature, and pumped back into the patient (Lequier *et al.,* 2013). While blood is pumped in the extracorporeal circuit, the risk of activation of the natural coagulation process, hemostasis, and thrombosis is very high (Mosier *et al.,* 2015). Blood clot formation is activated when the blood comes in contact with any non-endothelial surface, regularly at the site of vascular injury or in the extracorporeal circuits. The disrupted vascular endothelium or non-endothelial

Revista Bio ciencias
ISSN 2007-3380

surface releases von Willebrand factor and tissue factor, which exert procoagulant properties and help in platelet plug formation (Chegondi *et al.,* 2022). The cell surface glycoprotein receptors help platelet adhesion to the endothelial cells and the extracellular matrix. Following adhesion, platelets get activated through their secreted substances and intracellular signaling mechanisms (McMichael *et al.,* 2022). The extrinsic coagulation pathway starts when the tissue factor binds to factor VII, which further activates factor X with the help of platelet-derived phospholipids and calcium. Activated factor X interacts with factor V, phospholipid, and calcium and converts prothrombin to thrombin (factor IIa). Using a positive feedback loop, thrombin activates the intrinsic pathway coagulation factors V, VIII, XI, and XIII, and further produces thrombin. Prothrombin to thrombin conversion represents the initial step in the common pathway. Thrombin further activates fibrinogen to form fibrin strands. Then factor XIII converts the fibrin strands into fibrin mesh, which ultimately stabilizes the platelet plug (Ozment *et al.,* 2020).

Then, it is necessary to use anticoagulation therapy to avoid thrombosis in ECMO-treated patients. Although there are some conditions in which ECMO is run without anticoagulant for a few hours, cardiac surgery has active bleeding as a complication with prolonged Activated Partial Thromboplastin Time (aPTT) (Davenport, 1997). Consensus on the optimal tests for assessing anticoagulation during ECMO has yet to be established. For the success of ECMO, anticoagulation is a very important factor among others such as vascular access and cannula position (Barton *et al.,* 2019). There is no ideal anticoagulant, however, the most widely used in all centers in the world is unfractionated heparin (UFH), it is the known one. Among the most widely used anticoagulants for ECMO, UFH is the first choice because of its advantages, such as ease of monitoring, low cost, availability, intravenous administration, and reversibility (Levy *et al.,* 2022). Heparin is a naturally occurring glycosaminoglycan that normally adheres to the endothelium, but it can also be secreted into the bloodstream (ELSO, 2014; MacLaren & Monagle, 2014).

Generally, in most centers, if the patient does not have active bleeding and their PTTs are adequate, a heparin bolus of 50-100 IU/kg is started at the time of cannulation. Each case should be preferred, especially in the postoperative period. In cardiac surgery if heparin with protamine has not been reversed, we must wait, and take an activated clotting time at the bedside Activated Clotting Time (ACT), if the ACT drops to 300 seconds or less, the heparin infusion should be started at 10-20 IU/Kg/hour as long as there is no active bleeding, or in the case of postoperative cardiac surgery in children that the cost of the tubes is less than 50 mL/hour (ELSO, 2014). According to ELSO recommendations (ELSO, 2014) the protocol drives to maintain ACT 180-220 with a heparin infusion regimen between 20-50 IU/kg/hour, considering that the use of diuretics and renal replacement therapy increases heparin clearance and the possibility of needing more doses. Coagulation monitoring during support is carried out by ACT times a day, depending on the patient. With this, we evaluate the activation of the intrinsic and the common coagulation pathway during ECMO support., it is about doubling the aPTT to maintain it for 70–80 seconds. Anti-factor X is the gold standard test for the measurement of heparin action. This evidence relies on the ability of heparin to catalyze antithrombin inhibition of factor Xa. The range goes from 0.2 to 0.5 U/mL to consider a good anticoagulant activity (Chlebowski *et al.,* 2020). To date, no consensus on a standardized method of administering and monitoring anticoagulation during ECMO has been reached (Chlebowski *et al.,* 2020).

Revista Bio ciencias
ISSN 2007-3380

Since the first use of ECMO in a newborn, performed by Bartlett *et al.* (1976), over 40,000 newborns have been treated with this therapy worldwide (Van Ommen *et al.,* 2018). Despite technological advances and increased clinical experience, hemostatic complications, including hemorrhage and thrombosis, continue to be significant problems in infants undergoing ECMO globally (Perez Ortiz *et al.,* 2021). Hemorrhagic complications, including intracranial hemorrhage, have been reported in up to 29.1 % of neonatal patients and 28.5 % of pediatric patients treated with ECMO. Likewise, thrombotic complications, such as circuit thrombosis and cerebral infarction, have been documented in up to 16.7 % of neonates and 12.4 % of pediatric patients, representing a critical factor of morbidity and mortality in these populations (Drop *et al.,* 2020; Perez Ortiz *et al.,* 2021). In Mexico, the implementation of ECMO is relatively recent, and only initial findings of the ECMO program have been reported by the Neonatology Department of the Hospital Christus Muguerza in Monterrey, Mexico (Vargas-Camacho *et al.,* 2020). Thus, this study aimed to describe the anticoagulation procedures, tests, and outcomes in post-cardiac surgery neonates and children treated with ECMO at Christus Muguerza Hospital in Monterrey, Mexico.

Material and Methods

Design

This is a quasi-experimental before-and-after study, with a retrospective and observational, descriptive design, conducted at the Christus Muguerza Hospital in Monterrey, Mexico.

Objective

Whether an anticoagulation monitoring protocol in pediatric post-cardiac surgery patients treated with venoarterial (VA) ECMO (VA-ECMO) results in fewer complications and improved morbidity.

Population

In this study, the postoperative records of all neonates and children who underwent congenital heart disease and were treated with VA-ECMO in the Pediatric Intensive Care Unit of Christus Muguerza Hospital in Monterrey, Mexico, from 2013 to 2018 were reviewed. This hospital is a private third-level hospital, and has 6 beds in intensive care therapy, as ECMO treatment has given relatively high treatment costs, only a few children in postoperative cardiac surgery are eligible to use this procedure. The ECMO in the Pediatric Intensive Care Unit of Christus Muguerza Hospital in Monterrey, Mexico, has almost eleven years of experience treating pediatric patients (2013 to date). The data of the patients were separated into 2 groups: neonates, when they were from patients operated on at the month of birth, and children when they were operated on after one month of life.

Revista Bio ciencias
ISSN 2007-3380

Selection criteria

Inclusion criteria

The criteria of inclusion were all records of postoperative neonates and children with congenital heart disease, regardless of age, gender, or reason for cardiovascular surgery. This will include complications because of sepsis, multiorgan dysfunction syndrome, complications because of acute renal failure, multiorgan dysfunction syndrome, and hemorrhagic complications, including intracranial hemorrhage (ICH), pulmonary hemorrhage, gastrointestinal bleeding, bleeding at the cannulation site, mediastinal or thoracic hemorrhage, bleeding in other organs and tissues.

Exclusion criteria

Patients with chromosomal abnormalities or congenital coagulation disorders.

Elimination criteria

Files with illegible or incomplete data.

Procedures

In the Christus Muguerza Hospital in Monterrey, all patients operated on for congenital heart disease are cannulated. The cannulation was central, leaving the thorax open and covered with sterile plastic. During cardiac surgery, this patient's extracorporeal circulation is not ECMO. After surgery, some patients may need cardiac and pulmonary support with ECMO. If clinical and economic conditions are met these patients, enter an ECMO treatment protocol. During these procedures, all patients use a VA Ma quet© ECMO circuit with Bioline cover and Quadrox© pediatric oxygenating membrane (Maquet Cardiopulmonary AG, Hirrlingen, Germany) with Rotaflow system (Maquet Cardiovascular, Wayne, NJ, USA). The patients underwent ultrasound evaluation before the procedure to rule out cerebral hemorrhage. In the mentioned period, 25 patients were found, and all of them met the requirements to be included in this study.

Sample

A census-ratio method was carried out to identify all patients who meet the selection criteria. Demographic, clinical, laboratory, imaging, and survival data were prospectively collected for each enrolled subject.

Blood sampling and analysis

Venous blood samples (5 mL in 3.2 % sodium citrate) were collected at 3 h, 6 h, 24 h, and daily after ECMO initiation until discontinuation. ACT was monitored every 3 hours; prothrombin time (PT), aPTT, and platelets every 6 hours; and anti-factor Xa and antithrombin III (AT III) every 24 hours, and homeostasis was maintained according to ELSO guidelines 11.

Revista Bio ciencias
ISSN 2007-3380

Survival to decannulation and hospital discharge

The primary outcomes of interest were complications up to decannulation and hospital discharge. Procedures performed in the pediatric intensive care unit in patients treated with ECMO include monitoring of vital signs, fluid balance, diuresis, and with near-infrared tissue spectroscopy. All patients were managed with analgesia and sedation, and 54.5 % underwent hemofiltration or hemodiafiltration. A pediatric cardiologist performed echocardiography every 24 hours to measure ejection fraction, ventricular function, and changes in the targets of anticoagulation in response to decreased flow. Weaning criteria were applied by consensus according to the clinical and echocardiographic data of each patient. SvO2, hematocrit, and continuous post-membrane saturation were also monitored. All patients were managed during the procedure with heparin anticoagulation until they had an ACT <300 seconds and aPTT <80 seconds. ACT was monitored every 3 hours; PT, aPTT, and platelets every 6 hours; and anti-factor Xa and AT III every 24 hours, and homeostasis was maintained according to ELSO (ELSO, 2014) guidelines. Blood flows were maintained between 100 and 150 mL/kg/h with resting pulmonary flows and volume-controlled ventilation.

Statistical Analysis

Data were obtained from the files by direct observation and then compiled in a database using Microsoft Office® Excel® (Microsoft Corp., Redmond, WA/USA). The data recorded included sociodemographic information, ECMO times, kind of circuit, blood flow parameters, anticoagulation drugs used, and coagulation parameters during ECMO. Data are presented as the median of each variable after longitudinally calculating the variables for each patient. The Independent Variables (IV) included in the study were the main intervention as a study factor, where we included the anticoagulation monitoring protocol in VA-ECMO, and heparin dose adjustments based on ELSO guidelines. As well as the clinical and demographic characteristics of the patients, such as age (neonates ≤30 days vs. infants >30 days), sex (male/female), and the different primary diagnoses of heart disease. The IVs also included those related to VA-ECMO support (in days), the dose of heparin administered (U/kg/h), the type of ECMO circuit used, the anticoagulation parameters monitored (ACT, PT, aPTT, Anti-Xa, AT III), and the use of hemofiltration or hemodiafiltration. The Dependent Variables (DV) included in the study were the different bleeding complications, thrombotic complications, systemic complications, and clinical outcomes.

Results and Discussion

Of the 25 patients reviewed, 52.0 % were neonates, and 48 % were children. Of which 52 % were female and 48 % male. The percentage of newborns (10 days) was 52 %, and the percentage of infants (≤30 days) was 48 %. The most common postoperative diagnoses (Table 1) were transposition of the great vessels (20.0 %), tetralogy of Fallot (16.0 %), hypoplastic left heart (16.0 %), pulmonary atresia (12.0 %), pulmonary stenosis (12.0 %), Interventricular communication (IVC) (12.0 %), and two other heart diseases (8.0%). In this case, all participants

Revista Bio ciencias
ISSN 2007-3380

underwent VA-ECMO. The most relevant outcomes were, the mean dose of heparin determined in this study was 21.09 U/kg/h, while the average ACT was 188.6 seconds, and finally, the mean levels of Xa were 0.27 UI/mL. All the averages of the anticoagulation parameters monitored during the procedure are shown in Table 2. During weaning, treatment modifications were made based on changes in blood flow determined by the procedures established by the ECMO management protocol described by the ELSO. Survival was 12/20 patients (60.0 %), and the average length of stay on ECMO was 5.5 days. The main bleeding complications were severe bleeding (defined as +6-7 mL x Kg/hr) in 2/20 patients (10 %) and systemic thrombosis in 2/20 patients (10 %). The main causes of mortality were sepsis, acute renal failure, and multiple organ failure syndrome (Table 3).

The recommended dose of heparin to start anticoagulation therapy in pediatric patients on ECMO (McMichael *et al.,* 2022) is 10–20 UI/kg/h, which can be increased up to 20–50 U/kg/h according to ACT. In this study, we maintain a level of heparin according to ELSO recommendations (ELSO, 2014). Sulkowski *et al.* (2014), reported heparin doses of 28.5 U/kg/h in 26 neonates treated with ECMO. Likewise, Bembea *et al.* (2013), used heparin at 34 U/kg/h in their study in 34 pediatric patients treated with ECMO. In both studies, they used higher doses of heparin in similar samples of patients. ACT results can be affected by factors other than UFH, including anemia, hypofibrinogenemia, thrombocytopenia, and other coagulation factor deficiencies, which may accurately reflect a patient's overall anticoagulation state. Therapeutic anticoagulation has been classically defined as an ACT range of 180–220 seconds (ELSO, 2014). The average ACT obtained in this study was 188.6 seconds, considering that Sulkowski *et al*. (2014), described an average ACT level of 196 seconds in 27 neonates treated with ECMO. In this study, PT reported was at 21.85 seconds, whereas Bembea *et al.* (2013), reported 11.9 seconds. This represents 1.8 times more elevated. We did not find a statistically significant difference between elevated PT and liver damage or increased risk of bleeding in our patients. However, it may be necessary to increase the sample to be able to determine these differences. The aPTT is a plasma-based test that uses an activator (silica, ellagic acid), calcium, and phospholipids to measure the time to fibrin formation in the absence of cellular components. Each center's laboratory should establish a therapeutic range for aPTT results to compensate for the variable response of aPTT reagents to UFH (ELSO, 2014). Bembea *et al.* (2013), reported that aPTT levels averaged 91.5 seconds in 34 patients, with a range of 66.4-128.3 seconds. The aPTT level recorded in this study was 62.15 seconds, whereas Bingham *et al.* (2018), reported 83 seconds in a study of 35 pediatric patients. Measuring *ex vivo* UFH concentrations by protamine titration is both reliable and reproducible, but is not as readily available or easy to automate. Most ELSO centers that use the anti-Xa assay as part of their anticoagulation protocol aim for 0.3–0.7 IU/mL. However, anti-Xa assays can also vary in their responsiveness to UFH and are subject to significant problems in assay standardization (ELSO, 2014).

A study involving 20 patients in the pediatric cardiac intensive care unit at the University of Alabama used an anti-Xa assay to monitor ECMO patients for a median of 88 hours. Their results correlated well with UFH status. Additional advantages of the assays include a reduced need for blood sampling, fewer blood product transfusions, and fewer thrombotic/hemorrhagic complications (Cho *et al.,* 2017; Sulkowski *et al.,* 2014). Our protocol supports these results, at

Revista Bio ciencias
ISSN 2007-3380

a mean sampling time of 3.9 days versus 88 hours (3.6 days), an even lower population of 20 patients, and a survival rate of 50 %. As shown by different research groups, there is a weak or no correlation between ACT and concurrent heparin dose during ECMO, while anti-Xa demonstrates a stronger correlation with heparin dosing (Liveris *et al.,* 2014; Sulkowski *et al.,* 2014). This is because heparin functions to inhibit coagulation by binding to and accelerating antithrombin activity. The active form of heparin in the blood is the heparin/antithrombin complex. The anti-Xa measures the activity of the heparin/antithrombin complex and is sensitive to changes in heparin and antithrombin levels in the sample (Saifee *et al.,* 2020). Rama *et al.* (2021), reported better outcomes in anticoagulation with anti-Xa levels in the range of 0.3–0.7 UI/mL. Our results are comparable with those described by Rama *et al.* (2021), as they match (0.27 ± 0.12 IU/mL) within the reported threshold in the mean of the reported samples from our 25 patients. Henderson *et al.* (2018), reported that an anti-Xa level above 0.25 IU/mL was optimal for preventing circuit thrombosis in 26 pediatric patients receiving VA-ECMO and reported a 61 % survival. Likewise, obtained results are very similar to those reported by Henderson *et al.* (2018), where observed that a mean heparin anti-Xa level of at least 0.25 IU/mL reduced circuit thrombosis, with survival results very similar to those of our study (60 % / 61 %) in a very similar number of pediatric patients (25 / 26) receiving VA-ECMO.

AT III is often produced by the liver and is a natural inhibitor of all serine proteases (except for factor VIIa and protein C). Most of its anticoagulant effects result from the inhibition of thrombin and factor Xa. The optimal AT III activity for any patient receiving UFH anticoagulation during an ECMO procedure is unknown. Low AT III activity (normal in infants) produces a reduction in the effect of heparin (Moynihan *et al.,* 2017). The AT III level determined in this study was 47.52 UL, whereas Nelson *et al.* (2017), reported that a group of pediatric VA-ECMO patients given recombinant AT III got significantly higher AT III activity levels, with activity levels defined as >80 %, compared to 28 % in historical patients. Longer time within the ACT target range was achieved with a lower heparin dose, no increase in hemostatic complications, and trends toward fewer heparin changes and less use of blood products. Suggesting that continuous infusion of AT III during ECMO may define changes in practice that could improve patient safety.

Sepsis is a highly relevant complication in pediatric patients undergoing VA-ECMO. Several studies have documented a high incidence of infections in this population, highlighting the importance of strict surveillance and effective preventive strategies. A retrospective study by Santiago-Lozano *et al.* (2018), which included 100 children treated with ECMO, reported that 60.4 % of patients developed infections during extracorporeal support. Although this high rate of infections did not show a statistically significant association with increased mortality, a trend toward longer length of stay in the pediatric intensive care unit (PICU) was clear in infected patients. In addition, this same study identified duration of ECMO support as a key risk factor for the infection development. It was observed that patients with an ECMO duration longer than seven days had a higher incidence of infections, suggesting that prolonged extracorporeal support may predispose to infectious complications (Santiago-Lozano *et al.,* 2018). Another critical aspect of reducing the risk of infections is the experience of the personnel in the cannulation technique. It has been shown that peripheral cannulation is a viable option in patients with pediatric septic shock, especially when the procedure is performed in centers with a high volume of ECMO and

Revista Bio ciencias
ISSN 2007-3380

with experience in the sepsis management (Melnikov *et al.,* 2022). Adequate training of the health care team in the insertion and maintenance of vascular access is essential to minimize the risk of infections associated with extracorporeal support.

Acute kidney injury (AKI) is a frequent and severe complication in pediatric patients undergoing VA-ECMO. The AKI incidence in this population varies widely, with reports ranging from 26 % to 85 %, depending on the primary diagnosis of heart disease, the severity of renal involvement, the management by the multidisciplinary team, and the hospital setting. This variability underscores the complexity in the identification, prevention, and treatment of AKI in patients on VA-ECMO (Ostermann & Lumlertgul, 2021). Patients on VA-ECMO have a higher incidence of AKI compared to those on ECMO-venous (VV-ECMO), with reported rates of 61 % and 46 %, respectively. This difference may be attributed to the greater severity of cardiac disease in patients requiring VA-ECMO, as well as to the hemodynamic alterations inherent to this type of support, which include renal hypoperfusion, fluctuations in arterial pressure, and ventricular dysfunction. The etiology of AKI in pediatric patients undergoing VA-ECMO is multifactorial. The most frequent causes include renal hypoperfusion secondary to hemodynamic instability, systemic inflammation generated by activation of the immune response, the use of nephrotoxic agents such as aminoglycoside antibiotics or loop diuretics, sepsis that compromises perfusion and renal function, and different factors intrinsic to ECMO, such as hemolysis, activation of the inflammatory cascade and alterations in renal autoregulation (Rodríguez-Durán *et al.,* 2022). The presence of AKI in pediatric patients on VA-ECMO is associated with a significant increase in morbidity and mortality. Several studies have shown that in-hospital mortality in patients on VA-ECMO ranges from 40 % to 60 %, with AKI being a contributing factor to this adverse outcome. In addition, the need for renal replacement therapy (RRT) is common in this population, with a reported incidence of up to 45 %, which emphasizes the importance of prevention and treatment strategies aimed at optimizing renal function in these patients (Ostermann & Lumlertgul, 2021; Rodríguez-Durán *et al.,* 2022).

Anticoagulation in pediatric patients undergoing VA-ECMO represents a significant clinical challenge due to the delicate balance between the risk of thrombosis and bleeding, both associated with high mortality and morbidity (Dalton *et al.,* 2015, 2017). The marked interindividual variability in response to UFH, influenced by factors such as age, weight, liver, and renal function, as well as the presence of underlying coagulopathies, highlights the need to implement personalized anticoagulation protocols in this population (Cunningham *et al.,* 2016). Traditionally, anticoagulation monitoring during ECMO has been based on conventional tests, such as ACT and aPTT. However, measurement of anti-factor Xa (anti-Xa) activity has emerged as a more accurate alternative to assess the anticoagulant effect of UFH. Unlike ACT and aPTT, the anti-Xa assay is specific for heparin activity and is not affected by factors such as coagulopathies, thrombocytopenia, or hemodilution. Additionally, advanced tools such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM) allow a comprehensive assessment of hemostasis, providing detailed information on clot formation and stability, which is crucial in the context of ECMO (Fuentes *et al.,* 2019). Another key factor in the efficacy of UFH is AT III, whose acquired deficiency is frequent in critical pediatric patients and can generate resistance to heparin, requiring higher doses to achieve an adequate anticoagulant effect. In this sense, monitoring and supplementation

Revista Bio ciencias
ISSN 2007-3380

of AT III when necessary is a fundamental pillar in personalized anticoagulation protocols (Fuentes *et al.,* 2019). The implementation of individualized anticoagulation protocols, which integrate the combined monitoring of anti-Xa, TEG/ROTEM, and AT III levels, can significantly improve clinical outcomes in pediatric patients undergoing VA-ECMO. These protocols allow precise adjustments in UFH dosing, reducing the risk of thrombotic and hemorrhagic complications. In addition, training of medical and nursing staff in the interpretation of these advanced tests is essential to ensure correct application and optimization of anticoagulation therapy in this vulnerable population (Fuentes *et al.,* 2019).

Our study shows that specific coagulation outcomes for heparin anticoagulation in pediatric postsurgical cardiac patients treated with VA-ECMO depend on different factors, both patient and heparin infusion rate, as it should be tailored to the individual according to cardiac pathology, the situation in the institution, an assessment of heparin effect, and global assessments of overall hemostatic function. However, the choice of dose and dosing regimen of UFH remains a challenge for medical staff for several reasons. UFH has a narrow therapeutic window and wide variability in the dose-response relationship (Derbalah *et al.,* 2019). It's pharmacodynamic (PD) properties are difficult to characterize due to complex mechanisms of interaction with the hemostatic system. The complex, heterogeneous chemical composition of UFH prevents accurate characterization of its pharmacokinetic (PK) properties (Derbalah *et al.,* 2019). Despite the challenges presented by heparin, it is the standard systemic anticoagulant in ECMO worldwide. Its advantages include its low cost, rapid onset of action, short half-life, reversibility, and familiarity of use. Other advantages of UFH are its non-anticoagulant effects, anti-inflammatory properties, inhibition of reactive oxygen species generation, tissue repair and protection properties, and cardiovascular protective effects. Despite its widespread use, dose titration remains controversial, with a low correlation between anti-Xa, ACT, and aPTT, and expected results during this protocol (Baird *et al.,* 2007; Cashen *et al.,* 2019; Cassinelli & Naggi, 2016). Our results of UFH dose response in different pediatric cardiac pathologies were remarkably similar between patients, suggesting that individualized therapy could be an alternative in absolute values. There is an urgent need for population-based studies to standardize pharmacokinetic/pharmacodynamic models of infusion dose response to heparin (Moynihan *et al.,* 2017). Since the pharmacokinetics and pharmacodynamics of heparin differ with age, blood product administration, and renal replacement therapy (Moynihan *et al.,* 2017).

The results suggest that the type of cardiac surgery in pediatric ECMO patients may explain some variability in UFH dose. However, these results should be interpreted with caution, since there are no previous research studies with response to UFH treatment in our population, where different pathologies with pediatric complications of cardiac surgery were included with a small sample of patients, as were included in this study. More multicenter clinical trials are needed to better explain our results and improve dose prediction with UFH and improve anticoagulation complications in pediatric surgeries.

Revista Bio ciencias
ISSN 2007-3380

Table 1. Characteristics of the study population.

Variable	Scale	Cases (n)	Percentage (%)
Gender	Male	12	48
	Female	13	52
Age (Stage)	Newborn (≤30 days)	13	52
	Lactant (>30 days)	12	48
Diagnosis	Transposition of the great vessels (GVT)	5	20.0
	Tetralogy of Fallot	4	16.0
	Hypoplastic left heart	4	16.0
	Pulmonary atresia	3	12.0
	Pulmonary stenosis	3	12.0
	Interventricular communication (CIV)	3	12.0
	Others	2	8.0
ECMO mode	VA-ECMO	25	100
	VV-ECMO	0	0
	VV- to VA-ECMO	0	0

ECMO: Extracorporeal Membrane Oxygenation; VA: venoarterial; VV: veno-venous; n: numbers of participants; %: Percentage.

Table 2. Mean extracorporeal membrane oxygenation (ECMO) times and anticoagulant parameters used during ECMO therapy*.

Variable	Mean	Standard Deviation
ECMO time	5.5 days	2.3 days
Heparin (dose)	21.09 U/kg	8.5 U/kg
ACT	188.6 s	34.7 s
PT	21.85 s	4.3 s
aPTT	62.15 s	9.4 s
Anti-Xa	0.27 UI/mL	0.12 UI/mL
Antithrombin III	47.52 UI	12.3 UI

ECMO: Extracorporeal Membrane Oxygenation; ACT: Activated Coagulation Time; PT: Prothrombin Time; aPTT: Activated Partial Thromboplastin Time; Seconds: s. *Data are presented as median for each variable after longitudinally calculating the variables for each patient.

Revista Bio ciencias
ISSN 2007-3380

Table 3. Main complications observed during extracorporeal membrane oxygenation therapy in pediatric patients.

Complications	Cases (n)	Percentage (%)
Sepsis	3	30
Acute renal injury	3	30
Multi-organ dysfunction syndrome	2	20
Cerebral hemorrhage	2	20

The numbers of the complications are n; Percentages are %.

Study strengths

This study presents important strengths that position it as a valuable contribution to research on postsurgical pediatric patients treated with VA-ECMO. First, the sample size of our study is comparable to previous research conducted in different countries (Bembea *et al.,* 2013; Cho *et al.,* 2017; Henderson *et al.,* 2018; Rama *et al.,* 2021; Sulkowski *et al.,* 2014).The use of standardized sampling and data collection methodologies ensures homogeneity in outcome assessment and allows comparability with international studies, strengthening the external validity of our findings. Secondly, the multidisciplinary approach of the research represented an added value in the interpretation and analysis of the data. The integration of a steering committee composed of academic researchers, intensivists, cardiovascular surgeons, specialized nurses, and ECMO experts ensured a rigorously designed study protocol and an interpretation of the results based on clinical and scientific experience. Another relevant strength was the use of multiple biomarkers and coagulation tests to assess the hemostatic status of patients. Indicators such as Heparin, ACT, PT, aPTT, Anti-Xa, and AT III allowed an accurate and detailed assessment of the anticoagulation profile in patients treated with VA-ECMO. The use of these objective parameters reduced the possibility of variability in the results and facilitated the identification of interindividual differences according to the different postsurgical diagnoses. Finally, the study design was performed in a high-specialty referral hospital in Mexico, with access to advanced technologies and state-of-the-art medical services in VA-ECMO. This reinforces the feasibility and replicability of the study in other institutions with similar infrastructure within the country. However, it also provides a methodological basis that can be used as a reference in centers with fewer resources, favoring the adaptation and optimization of anticoagulation strategies in VA-ECMO in different hospital contexts.

Study limitations

This study has certain methodological and contextual limitations that should be considered when interpreting its findings. First, the cross-sectional and observational nature of the study precludes establishing causal relationships between anticoagulation monitoring and clinical outcomes in postsurgical pediatric patients treated with VA-ECMO. The associations identified

Revista Bio ciencias
ISSN 2007-3380

reflect correlations but cannot be considered direct determinants of outcomes. Second, the sample size is limited due to the high complexity and cost of ECMO treatment in Mexico, which restricts access to this therapy in the pediatric population. This may affect the statistical power of the study and limit the generalizability of the results to other clinical settings with different resources and hospital capabilities. Another limitation is the exclusion of certain patients due to the paucity of clinical and laboratory data, which prevented a more comprehensive analysis of hemostatic variables and long-term outcomes. In this regard, follow-up data on long-term survival and possible clinical sequelae in this population are not yet available.

Furthermore, the study focused exclusively on patients undergoing VA-ECMO, without including cases of VV-ECMO. Given that VV-ECMO has different indications and physiological dynamics, the results of this study cannot be extrapolated to this modality, suggesting the need for further investigations in patients treated with VV-ECMO. In addition, a control group was not included due to the low prevalence of pediatric ECMO patients in the region, making direct comparison with populations not exposed to the intervention difficult. The limited availability of patients with sufficient economic coverage to access treatment is a determining factor in the reduction of the sample size. It has been documented that hospital costs for ECMO support can range from $42,554 to $537,554 USD, which restricts access and the possibility of larger studies (Aiello & Loomba, 2017; Moynihan *et al.,* 2017). On the other hand, there is high heterogeneity in the underlying diagnoses, as the cohort included seven distinct types of congenital heart disease in which VA-ECMO was used (Table 1). This diversity in the population studied may have influenced the variability of the results, which represents a limitation in terms of clinical homogeneity and comparison of outcomes between the different subgroups. Despite these limitations, this study provides valuable information that allows us to compare our results with international literature and to recognize areas of opportunity to optimize the management of anticoagulation in VA-ECMO. Furthermore, the findings obtained may serve as a reference for other institutions with limited experience in ECMO, contributing to the improvement of therapeutic and monitoring strategies in clinical settings with limited resources.

Future research

First, large-scale multicenter studies are needed in several Mexican cities to optimize the monitoring of anticoagulation in pediatric post-surgical patients undergoing VA-ECMO. These investigations would allow assessment of variability in the response to anticoagulation and facilitate the design of personalized therapeutic strategies according to the specific cardiac diagnosis. Secondly, the implementation of educational programs aimed at health professionals in public and private hospitals where VA-ECMO is not currently used is required. Training on its indication, management, and follow-up would help to expand its availability and improve the care of pediatric patients with acute heart failure. Thirdly, it is crucial to develop sex- and age-differentiated interventions aimed at pediatric populations with greater susceptibility to cardiovascular disease early in life. The identification of these high-risk subgroups would allow the design of more effective preventive and therapeutic strategies. Fourth, future research should address the impact of socioeconomic and sociocultural factors on the prevalence, access to treatment, and clinical outcomes of pediatric heart disease in Mexico. Analyzing these variables will allow a better

Revista Bio ciencias
ISSN 2007-3380

understanding of health inequalities and will favor the implementation of public policies aimed at improving equity in access to VA-ECMO and other advanced cardiovascular treatments.

Conclusions

A slightly lower mean value of anti-Xa (0.27 ± 0.12 IU/mL) was obtained following the anticoagulation guidelines described by ELSO in ECMO patients; with these results, we obtained a survival rate of 60 %. The main hemorrhagic complications were severe bleeding in 10 % and systemic thrombosis in 10 %. The mortality rate was 40 % of them, and 20 % were caused by coagulation disorders. The main complications were sepsis, renal failure, and severe bleeding. The high prevalence of sepsis in children undergoing VA-ECMO highlights the need for comprehensive strategies that include prevention, early detection, and adequate treatment of infections. Implementation of strict infection control protocols and optimization of cannulation techniques are essential to improve clinical outcomes in this vulnerable population. It is essential to implement strategies for early monitoring and management of renal function in pediatric patients undergoing VA-ECMO. Early identification of risk factors, hemodynamic optimization, minimization of the use of nephrotoxic agents, and continuous monitoring of renal function can contribute to reducing the incidence and severity of AKI in this vulnerable population. The variability in the response to anticoagulation in pediatric patients undergoing VA-ECMO justifies the need for personalized protocols. The adoption of more specific monitoring tools and consideration of individual factors may lead to safer and more effective management of anticoagulation in this vulnerable population. Pharmacokinetic/pharmacodynamic modeling of the pediatric population is required, as well as a greater number of prospective trials to delineate the dose adjustment with UFH and prevent adverse clinical outcomes in different pediatric cardiac surgery conditions.

Authors´ contribution

Work conceptualization, VCG, CCV, GGR, QVG. Methodology development, VCG, CCV, QVG. Software management, ZMDO, GSF. Experimental validation: ZMDO, GSF. Analysis of results, GSF, ARH, QHFY, PRL. Data management, GSF, ARH, QHFY, PRL. Manuscript writing and preparation, GSF, ARH, QHFY, PRL. Writing, revising, and editing, GSF, ARH, QHFY, PRL; project manager, ARH.

All the authors of this manuscript have read and accepted the published version of the manuscript.

Financing

This research did not receive external funding.

Revista Bio ciencias
ISSN 2007-3380

Ethical statements

Ethical approval for this study was obtained from the Medical Research Committee of the University of Monterrey (Ref: 02052019 CI). The Medical Research Committee of the University of Monterrey gives us a waiver about the informed consent. This waiver says informed consent was not necessary because data were obtained from patient records, and all personal information was managed confidentially.

Statement of Informed Consent

Not applicable.

Acknowledgments

To the staff of the Intensive Care Unit of the Christus Muguerza Hospital, Monterrey for the facilities provided for this research.

References

Aiello, S., & Loomba, R. S. (2017). Factors associated with the need for, and the impact of, extracorporeal membrane oxygenation in children with congenital heart disease during admissions for cardiac surgery. *Children*, *4*(11). https://doi.org/10.3390/children4110101

Baird, C. W., Zurakowski, D., Robinson, B., Gandhi, S., Burdis-Koch, L., Tamblyn, J., Munoz, R., Fortich, K., & Pigula, F. A. (2007). Anticoagulation and Pediatric Extracorporeal Membrane Oxygenation: Impact of Activated Clotting Time and Heparin Dose on Survival. *Annals of Thoracic Surgery*, *83*(3), 912–920. https://doi.org/10.1016/j.athoracsur.2006.09.054

Bartlett, R. H., Gazzaniga, A. B., Jefferies, M. R., Huxtable, R. F., Haiduc, N. J., & Fong, S. W. (1976). EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) CARDIOPULMONARY SUPPORT IN INFANCY. *ASAIO Journal*, *22*(1). https://journals.lww.com/asaiojournal/fulltext/1976/04000/extracorporeal_membrane_oxygenation__ecmo_.25.aspx

Barton, R., Ignjatovic, V., & Monagle, P. (2019). Anticoagulation during ECMO in neonatal and paediatric patients. *Thrombosis Research*, *173*, 172–177. https://doi.org/10.1016/j.thromres.2018.05.009

Bembea, M. M., Schwartz, J. M., Shah, N., Colantuoni, E., Lehmann, C. U., Kickler, T., Pronovost, P., & Strouse, J. J. (2013). Anticoagulation monitoring during pediatric extracorporeal membrane oxygenation. *ASAIO Journal*, *59*(1), 63–68. https://doi.org/10.1097/MAT.0b013e318279854a

Bingham, K. R., Riley, J. B., & Schears, G. J. (2018). Anticoagulation Management during First Five Days of Infant-Pediatric Extracorporeal Life Support. In *The Journal of ExtraCorporeal Technology Colorado* (Vol. 50). PMCID: PMC5848082, PMID: 29559752

Cashen, K., Meert, K., & Dalton, H. (2019). Anticoagulation in Neonatal ECMO: An Enigma Despite a Lot of Effort! *Frontiers in Pediatrics*, *7*. https://doi.org/10.3389/fped.2019.00366

Cassinelli, G., & Naggi, A. (2016). Old and new applications of non-anticoagulant heparin. *International Journal of Cardiology*, *212*, S14–S21. https://doi.org/10.1016/S0167-5273(16)12004-2

Revista Bio ciencias
ISSN 2007-3380

Chegondi, M., Vijayakumar, N., & Totapally, B. R. (2022). Management of Anticoagulation during Extracorporeal Membrane Oxygenation in Children. In *Pediatric Reports* (Vol. 14, Issue 3, pp. 320–332). MDPI. https://doi.org/10.3390/pediatric14030039

Chlebowski, M. M., Baltagi, S., Carlson, M., Levy, J. H., & Spinella, P. C. (2020). Clinical controversies in anticoagulation monitoring and antithrombin supplementation for ECMO. In *Critical Care* (Vol. 24, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s13054-020-2726-9

Cho, H. J., Kim, D. W., Kim, G. S., & Jeong, I. S. (2017). Anticoagulation Therapy during Extracorporeal Membrane Oxygenator Support in Pediatric Patients. *Chonnam Medical Journal*, *53*(2), 110. https://doi.org/10.4068/cmj.2017.53.2.110

Cunningham, D., Besser, M. W., Giraud, K., Gerrard, C., & Vuylsteke, A. (2016). Agreement between ACT and aPTT during extracorporeal membrane oxygenation shows intra- and inter-individual variation. *Perfusion (United Kingdom)*, *31*(6), 503–507. https://doi.org/10.1177/0267659116637420

Dalton, H. J., Garcia-Filion, P., Holubkov, R., Moler, F. W., Shanley, T., Heidemann, S., Meert, K., Berg, R. A., Berger, J., Carcillo, J., Newth, C., Harrison, R., Doctor, A., Rycus, P., Dean, J. M., Jenkins, T., & Nicholson, C. (2015). Association of bleeding and thrombosis with outcome in extracorporeal life support. *Pediatric Critical Care Medicine*, *16*(2), 167–174. https://doi.org/10.1097/PCC.0000000000000317

Dalton, H. J., Reeder, R., Garcia-Filion, P., Holubkov, R., Berg, R. A., Zuppa, A., Moler, F. W., Shanley, T., Pollack, M., Newth, C., Berger, J., Wessel, D., Carcillo, J., Bell, M., Heidemann, S., Meert, K. L., Harrison, R., Doctor, A., Tamburro, R. F., … Nicholson, C. (2017). Factors associated with bleeding and thrombosis in children receiving extracorporeal membrane oxygenation. *American Journal of Respiratory and Critical Care Medicine*, *196*(6), 762–771. https://doi.org/10.1164/rccm.201609-1945OC

Davenport, A. (1997). The Coagulation System in the Critically Ill Patient With Acute Renal Failure and the Effect of an Extracorporeal Circuit. *American Journal of Kidney Diseases: The Official Journal of the National Kidney Foundation*, *30*(5), S20–S27. https://doi.org/https://doi.org/10.1016/s0272-6386(97)90538-2

Derbalah, A., Duffull, S., Newall, F., Moynihan, K., & Al-Sallami, H. (2019). Revisiting the Pharmacology of Unfractionated Heparin. In *Clinical Pharmacokinetics* (Vol. 58, Issue 8, pp. 1015–1028). Springer International Publishing. https://doi.org/10.1007/s40262-019-00751-7

Drop, J. G. F., Wildschut, E. D., Gunput, S. T. G., de Hoog, M., & van Ommen, C. H. (2020). Challenges in Maintaining the Hemostatic Balance in Children Undergoing Extracorporeal Membrane Oxygenation: A Systematic Literature Review. In *Frontiers in Pediatrics* (Vol. 8). Frontiers Media S.A. https://doi.org/10.3389/fped.2020.612467

Extracorporeal Life Support Organization [*ELSO*.] (2014). *ELSO Anticoagulation Guideline*. https://ima-contentfiles.s3.amazonaws.com/ELSOResp.pdf

Fuentes, A. E., Sánchez, C. J. C., Anguiano, A. M., Benítez, R. G., Clavijo, D. S., & Gómez, B. R. (2019). *Protocolo de anticoagulación para ECMO infantil Anticoagulation management in neonatal and pediatric ECMO*. https://www.aep.es/revista-articulo/70/67_4.pdf

Henderson, N., Sullivan, J. E., Myers, J., Wells, T., Calhoun, A., Berkenbosch, J., & Todd Tzanetos, D. (2018). Use of Thromboelastography to Predict Thrombotic Complications in Pediatric and Neonatal Extracorporeal Membranous Oxygenation. In *The Journal of ExtraCorporeal Technology* (Vol. 50). PMCID: PMC6146278, PMID: 30250340

Lequier, L., Horton, S. B., McMullan, D. M., & Bartlett, R. H. (2013). Extracorporeal membrane oxygenation circuitry. *Pediatric Critical Care Medicine*, *14*(5 SUPPL). https://doi.org/10.1097/

PCC.0b013e318292dd10

Levy, J. H., Staudinger, T., & Steiner, M. E. (2022). How to manage anticoagulation during extracorporeal membrane oxygenation. *Intensive Care Medicine*, *48*(8), 1076–1079. https://doi.org/10.1007/s00134-022-06723-z

Liveris, A., Bello, R. A., Friedmann, P., Duffy, M. A., Manwani, D., Killinger, J. S., Rodriquez, D., & Weinstein, S. (2014). Anti-factor Xa assay is a superior correlate of heparin dose than activated partial thromboplastin time or activated clotting time in pediatric extracorporeal membrane oxygenation. *Pediatric Critical Care Medicine*, *15*(2). https://doi.org/10.1097/PCC.0000000000000028

MacLaren, G., & Monagle, P. (2014). Endogenous glycosaminoglycan anticoagulation in extracorporeal membrane oxygenation. In *Critical Care* (Vol. 18, Issue 6). BioMed Central Ltd. https://doi.org/10.1186/s13054-014-0636-4

McMichael, A. B. V., Ryerson, L. M., Ratano, D., Fan, E., Faraoni, D., & Annich, G. M. (2022). 2021 ELSO Adult and Pediatric Anticoagulation Guidelines. *ASAIO Journal*, *68*(3), 303–310. https://doi.org/10.1097/MAT.0000000000001652

Melnikov, G., Grabowski, S., & Broman, L. M. (2022). Extracorporeal Membrane Oxygenation for Septic Shock in Children. *ASAIO Journal*, *68*(2), 262–267. https://doi.org/10.1097/MAT.0000000000001464

Mosier, J. M., Kelsey, M., Raz, Y., Gunnerson, K. J., Meyer, R., Hypes, C. D., Malo, J., Whitmore, S. P., & Spaite, D. W. (2015). Extracorporeal membrane oxygenation (ECMO) for critically ill adults in the emergency department: History, current applications, and future directions. In *Critical Care* (Vol. 19, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s13054-015-1155-7

Moynihan, K., Johnson, K., Straney, L., Stocker, C., Anderson, B., Venugopal, P., & Roy, J. (2017). Coagulation monitoring correlation with heparin dose in pediatric extracorporeal life support. *Perfusion (United Kingdom)*, *32*(8), 675–685. https://doi.org/10.1177/0267659117720494

Nelson, K. M., Hansen, L. A., Steiner, M. E., Fischer, G. A., Dehnel, J., & Gupta, S. (2017). Continuous antithrombin III administration in pediatric veno-arterial extracorporeal membrane oxygenation. *Journal of Pediatric Pharmacology and Therapeutics*, *22*(4), 266–271. https://doi.org/10.5863/1551-6776-22.4.266

Ostermann, M., & Lumlertgul, N. (2021). Acute kidney injury in ECMO patients. In *Critical Care* (Vol. 25, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s13054-021-03676-5

Ozment, C. P., Scott, B. L., Bembea, M. M., & Spinella, P. C. (2020). Anticoagulation and transfusion management during neonatal and pediatric extracorporeal membrane oxygenation: a survey of medical directors in the United States. *Pediatric Critical Care Medicine*, *22*(6), 530–541. https://doi.org/10.1097/PCC.0000000000002696

Perez Ortiz, A., Dempfle, C. E., Jung, T., Doniga, T., Weiß, C., Hetjens, S., Schaible, T., & Rafat, N. (2021). Assessing Anticoagulation in Neonates With Congenital Diaphragmatic Hernia During Extracorporeal Membrane Oxygenation: Does Anti-Factor Xa or Thromboelastometry Provide Additional Benefit? *Frontiers in Pediatrics*, *9*. https://doi.org/10.3389/fped.2021.685906

Rama, G., Middlesworth, W., Neunert, C., Streltsova, S., & Cheung, E. W. (2021). Antifactor Xa Monitoring and Hematologic Complications of Pediatric Extracorporeal Membrane Oxygenation. *ASAIO Journal*, *67*(1), 91–95. https://doi.org/10.1097/MAT.0000000000001195

Rodríguez-Durán, A., Martínez-Urbano, J., Laguna-Castro, M., & Crespo-Montero, R. (2022).

Revista Bio ciencias
ISSN 2007-3380

Acute kidney injury in the paediatric patient: An integrative review. *Enfermeria Nefrologica*, *25*(1), 11–27. https://doi.org/10.37551/S2254-28842022002

Saifee, N. H., Brogan, T. V., McMullan, D. M., Yalon, L., Matthews, D. C., Burke, C. R., & Chandler, W. L. (2020). Monitoring Hemostasis during Extracorporeal Life Support. *ASAIO Journal*, *66*(2), 230–237. https://doi.org/10.1097/MAT.0000000000000993

Santiago-Lozano, M. J., Barquín-Conde, M. L., Fuentes-Moreno, L., León-Vela, R. M., Madrid-Vázquez, L., Sánchez-Galindo, A., & López-Herce Cid, J. (2018). Infectious complications in paediatric patients treated with extracorporeal membrane oxygenation. *Enfermedades Infecciosas y Microbiologia Clinica*, *36*(9), 563–567. https://doi.org/10.1016/j.eimc.2017.10.025

Soares, T., Nunes Salvado, A. C., Raupp Nunes, C., Larini Rimolo, M., & Concatto, R. C. (2021). Cuidado ao paciente em ecmo (extracorporeal membrane oxygenation): um desafio para a enfermagem neonatal. *Revista Nursing*, *24*, 6923–6928. https://pesquisa.bvsalud.org/portal/resource/pt/biblio-1371964

Sulkowski, J. P., Preston, T. J., Cooper, J. N., Duffy, V. L., Deans, K. J., Chicoine, L. G., & Minneci, P. C. (2014). Comparison of Routine Laboratory Measures of Heparin Anticoagulation for Neonates on Extracorporeal Membrane Oxygenation. *The Journal of Extra-Corporeal Technology*, *46*(1), 69–75. https://doi.org/https://doi.org/10.1051/ject/201446069

Van Ommen, C. H., Neunert, C. E., & Chitlur, M. B. (2018). Neonatal ECMO. In *Frontiers in Medicine* (Vol. 5, Issue OCT). Frontiers Media S.A. https://doi.org/10.3389/fmed.2018.00289

Vargas-Camacho, G., Contreras-Cepeda, V., Gómez-Gutierrez, R., Quezada-Valenzuela, G., Nieto-Sanjuanero, A., Santos-Guzmán, J., & González-Salazar, F. (2020). Venoarterial extracorporeal membrane oxygenation in heart surgery post-operative pediatric patients: A retrospective study at Christus Muguerza Hospital, Monterrey, Mexico. *SAGE Open Medicine*, *8*, 205031212091035. https://doi.org/10.1177/2050312120910353