Supplementary material 1. Search strategy

Search strategy

Used on 11-12-2020

Sources: Embase.com, Medline ALL via Ovid, Web of Science Core Collection (Science Citation Index Expanded; Social Sciences Citation Index; Arts & Humanities Citation Index; Conference Proceedings Citation Index- Science; Conference Proceedings Citation Index- Social Science & Humanities and Emerging Sources Citation Index) and the Cochrane Central Register of Controlled Trials via Wiley, Google Scholar (top 200)

Embase.com

(‘bleeding'/exp OR 'thrombosis'/exp OR 'blood clotting'/exp OR 'anticoagulation'/de OR (Bleed* OR Hemorrhag* OR haemorrhag* OR Blood-clot* OR clotting OR Thromb* OR anticoagul* OR coagula*):ab,ti,kw) AND (‘incidence'/exp OR 'thromboelastograph'/de OR 'thromboelastography'/de OR 'thromboelastometry'/de OR 'bleeding time'/exp OR 'blood clotting time'/de OR 'partial thromboplastin time'/exp OR 'prothrombin time'/de OR 'thrombin time'/de OR 'thromboplastin time'/de OR (incidence* OR Thromboelastograph* OR Thromboelastomet* OR ROTTEN OR TEG OR ((bleeding* OR clotting* OR coagulation* OR prothrombin* OR thrombin* OR thromboplastin*) NEXT/3 (time)) OR international-normali*-ratio OR INR OR ACT OR APTT OR PT OR PTT):ab,ti,kw) AND (‘extracorporeal oxygenation'/de OR 'extracorporeal circulation'/de OR 'extracorporeal membrane oxygenation device'/de OR 'membrane oxygenator'/de OR 'mechanical circulatory support'/de OR (ECMO OR ECLS OR ((Extracorporeal* OR membrane* OR sheet*) NEAR/6 (oxygen* OR life-support* OR circulat* OR treat* OR therap*))) AND (child/exp OR adolescent/exp OR adolescence/exp OR 'child behavior'/de OR 'child parent relation'/de OR 'childhood'/de OR 'child nutrition'/de OR 'infant nutrition'/exp OR 'child welfare'/de OR 'child abuse'/de OR 'child advocacy'/de OR 'child development'/de OR 'child growth'/de OR 'child health'/de OR 'child health care'/exp OR 'child care'/exp OR 'childhood disease'/exp OR 'child death'/de OR 'child psychiatry'/de OR 'child psychology'/de OR 'pediatric ward'/de OR 'pediatric hospital'/de OR 'pediatric anesthesi'/de OR 'pediatric intensive care unit'/de OR (adolescen* OR preadolescen* OR infan* OR newborn* OR (new NEXT/1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under NEXT/1 (age* OR aging)) OR juvenil* OR youth* OR kindergar* OR puberty OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool* OR suckling* OR PICU OR NICU OR PICUs OR NICUs):ab,ti,kw)

Medline (Ovid)

(exp Hemorrhage/ OR exp Thrombosis/ OR exp Blood Coagulation/ OR (Bleed* OR Hemorrhag* OR haemorrhag* OR Blood-clot* OR clotting OR Thromb* OR anticoagul* OR coagula*).ab,ti,kf.) AND (Incidence/ OR thromboelastograph/ OR thromboelastography/ OR thromboelastometry/ OR Bleeding
Time/ OR Whole Blood Coagulation Time/ OR Partial Thromboplastin Time/ OR Prothrombin Time/ OR Thrombin Time/ OR (incidence* OR Thromboelastograph* OR Thromboelastomet* OR ROTEM* OR TEG OR ((bleeding* OR clotting* OR coagulation* OR prothrombin* OR thrombin* OR thromboplastin*)) ADJ3 (time)) OR international-normali*-ratio OR INR OR ACT OR APTT OR PT OR PTT).ab,ti,kf.) AND (extracorporeal therapy/ OR extracorporeal membrane oxygenation device/ OR membrane oxygenator/ OR (ECMO OR ECLS OR ((Extracorporeal* OR membrane* OR sheet*) ADJ6 (oxygen* OR life-support* OR circulat* OR treat* OR therap*)) OR mechanic*-circul*-support*).ab,ti,kf.) AND (exp Child/ OR exp Infant/ OR exp Adolescent/ OR exp "Child Behavior"/ OR exp "Parent Child Relations"/ OR exp "Pediatrics"/ OR "Child Nutrition Sciences"/ OR "Infant nutritional physiological phenomena"/ OR exp "Child Welfare"/ OR "Child Development"/ OR exp "Child Health Services"/ OR exp "Child Care"/ OR "Child Rearing"/ OR "Child development Disorders, Pervasive"/ OR "Child Psychiatry"/ OR "Child Psychology"/ OR "Hospitals, Pediatric"/ OR exp "Intensive Care Units, Pediatric"/ OR (adolescen* OR infan* OR newborn* OR (new ADJ born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under ADJ 1 (age* OR aging)) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool* OR suckling* OR PICU OR NICU OR PICUs OR NICUs).ab,ti,kf.)

Web of Science

TS=(((Bleed* OR Hemorrhag* OR haemorrhag* OR Blood-clot* OR clotting OR Thromb* OR anticoagul* OR coagula*)) AND (incidence* OR Thromboelastograph* OR Thromboelastomet* OR ROTEM* OR TEG OR ((bleeding* OR clotting* OR coagulation* OR prothrombin* OR thrombin* OR thromboplastin*)) NEAR/2 (time)) OR international-normali*-ratio OR INR OR ACT OR APTT OR PT OR PTT)) AND ((ECMO OR ECLS OR ((Extracorporeal* OR membrane* OR sheet*) ADJ6 (oxygen* OR life-support* OR circulat* OR treat* OR therap*)) OR mechanic*-circul*-support*) ADJ6 (oxygen* OR life-support* OR circulat* OR treat* OR therap*) OR mechanic*-circul*-support*).ab,ti,kf.)

Cochrane CENTRAL

((Bleed* OR Hemorrhag* OR haemorrhag* OR (Blood NEXT/1 clot*)) OR clotting OR Thromb* OR anticoagul* OR coagula*):ab,ti) AND (incidence* OR Thromboelastograph* OR Thromboelastomet* OR ROTEM* OR TEG OR ((bleeding* OR clotting* OR coagulation* OR prothrombin* OR thrombin* OR thromboplastin*) NEXT/3 (time)) OR (international NEXT/1 normali*-ratio OR INR OR ACT OR APTT OR PT OR PTT):ab,ti) AND ((ECMO OR ECLS OR (Extracorporeal* OR membrane* OR sheet*) NEAR/6 (oxygen* OR "life-support**" OR circulat* OR treat* OR therap*)) OR mechanic*-circul*-support*)) ab,ti) AND ((adolescen* OR paedolescen* OR infan* OR newborn* OR (new NEAR/1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under NEAR/1 (age* OR aging)) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool* OR suckling* OR PICU OR NICU OR PICUs OR NICUs).ab,ti,kf.)
puber* OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool* OR suckling* OR PICU OR NICU OR PICUs OR NICUs:ab,ti)

Google Scholar Top 100 relevant references

bleeding|hemorrhage|haemorrhage|clotting|thrombus|thrombosis|coagulation|incidence|thromboelastograph|ROTEM|TEG ECMO|ECLS|"extracorporeal|extra-corporeal oxygenation"
child|children|baby|babies|kid|kids|boy|girl|boys|girls|pediatric|paediatric|PICU|NICU|PICUs|NICUs
Supplementary material 3. Included studies

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### Supplementary material 4. Summaries of included studies.

| Author, year | Study design | Sample size | Study population                                                                                                                                                                                                                                                                                                                                 | Main objective                                                                                                                                                                                                 | NOS score |
|--------------|--------------|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| Gupta, 2012  | Retrospective | *n = 22*    | ECMO runs (>28d) from children <18 years old supported with prolonged ECMO for refractory cardiac or pulmonary failure between January 1991 and September 2011 at the Arkansas Children’s Hospital.                                                                                                                                  | To evaluate the morbidity and mortality associated with prolonged ECMO therapy (>28 days).                                                                                                                                                                                                 | 5         |
| Wilson, 2002 | Retrospective | *n = 42*    | Neonatal and pediatric patients transported on ECMO by the WHMC ECMO transport team until 2001.                                                                                                                                                                                                                                                                                                                 | To characterize the patient population referred for ECMO transport and to determine survival to discharge or transfer in the various diagnostic groups of transported patients (neonatal respiratory, pediatric respiratory, cardiac). | 6         |
| Snyder, 2020 | Retrospective | *n = 42*    | Neonates (≤28 days) with CDH treated with ECMO and single-agent bivalirudin anticoagulation at a single institution between June 2016 and November 2018. Patients who underwent ECMO cannulation or repair at another institution were excluded.                                                                                                                                                                        | To describe an initial experience with a perioperative bivalirudin protocol in neonates with CDH and evaluate the relationship of bivalirudin dose to activated partial thrombin time and TEG reaction time monitoring assays. | 6         |
| Kubicki, 2019| Prospective   | *n = 18*    | Children on ECMO support aged 1 day–19 years undergoing mechanical circulatory support for a cardiac and/or pulmonary indication between 2008 and 2017. Children without data or with a bleeding disorder were excluded.                                                                                                                                                                                     | To determine VWF parameters in a paediatric cohort undergoing temporary ECLS, ECMO or long-term VAD support.                                                                                                                                                               | 6         |
| Maul, 2012   | Retrospective | *n = 172*   | Neonatal and pediatric patients placed on ECMO for respiratory and/or cardiac distress at Children’s Hospital of                                                                                                                                                                                                                                                                                        | To determine whether activated partial thromboplastin times are a better heparin management tool than                                                                                                                                                                  | 6         |
Pittsburgh during 2007–2010 were reviewed. activated clotting times in pediatric extracorporeal membrane oxygenation.

| Study | Design | n | Description | Goals |
|-------|--------|---|-------------|-------|
| Ryerson, 2016 (6) | Retrospective | 36 | Infants and children on ECLS who received ATC as part of clinical management between July 2008 and May 2011 at Stollery Children’s Hospital, Edmonton, Canada. Data were collected on all infants (>37 weeks gestation) and children weighing 20 kg or less who received ATC were prescribed UFH. | To review clinical experience giving 1,000 units (U) of ATC to patients on ECLS and UFH anticoagulation. |
| Nasr, 2016 (7) | Retrospective | 132 | Neonates and children with PAH were identified using International Classification of Diseases. Children with congenital heart disease were excluded from the analysis. | To assess mortality and outcomes in neonates and children with PAH supported with ECMO |
| Okochi, 2018 (8) | Retrospective | 96 | Pediatric patients cannulated for ECMO between January 2014 and June 2016 at Morgan-Stanley Children’s Hospital of New York-Presbyterian. Patients with a previous ECMO run, who were supported for less than 24 hours, or lacked complete medical records, were excluded. | To analyze predictive variables associated with hemolysis and determine its influence on outcomes of pediatric ECMO patients. |
| Baird, 2007 (9) | Retrospective | 604 | Pediatric ECMO patients at Children’s Hospital of Pittsburgh from 1980 to 2001. | To determine the relationships between heparin dose, ACT, and survival in pediatric ECMO patients. |
| Author(s)          | Study Design | Sample Size | Population Description                                                                 | Study Objective                                                                                                                                                                                                 | Page |
|-------------------|--------------|-------------|----------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|
| Bingham, 2018     | Retrospective| n = 35      | Infant-pediatric patients who were supported more than 3 days on ECLS between January 2013 and February 2016. | To compare the relationships between the anticoagulation variables of aPTT, ACT, INR, blood loss, thrombus formation in the circuit, alpha angle, and kaolin TEG reaction time, vs. the variables of heparin dose rates, AT, anti-Xa, bivalirudin dose rate, argatroban dose rate, circuit interventions, and transfusions. | 5    |
| Bembea, 2013      | Prospective  | n = 34      | Patients less than 18 years who required ECMO between April 2008 and September 2010 for any indication were included in this study. Exclusion criteria were history of heparin-induced thrombocytopenia and use of direct thrombin inhibitors for anticoagulation during ECMO and no consent within the 6-h window. | To compare global (ACT, aPTT) and specific (anti-factor Xa activity) measures of anticoagulation used in clinical practice and determine the agreement among them and potential confounding by low antithrombin or high factor VIII activity. | 6    |
| Liveris, 2014     | Retrospective| n = 17      | Pediatric patients managed on ECMO with at least three sets of simultaneous measurements for all tests being studied. Second ECMO runs were excluded. All patients were managed by a single surgeon between March 2010 and August 2012 at The Children’s Hospital at Montefiore (Bronx, NY). | To determine the correlation of ACT, aPTT, and anti-Xa to an administered unfractionated heparin dose in pediatric ECMO patients.                                                                                   | 6    |
| Author, Year | Study Type | n | Description | Purpose |
|-------------|------------|---|-------------|---------|
| Byrnes, 2014 (13) | Retrospective | 21 | ECMO patients with ATIII supplementation aged 0–18 years with a cardiac indication for ECMO between January 1, 2007, and December 31, 2008. Patients who were supported with ECMO for <72 hours were excluded from the study. | To determine the effect of routine ATIII supplementation for activity <70% on 1) heparin dose immediately after ATIII treatment, 2) effective circuit life in ATIII supplemented versus nonsupplemented deployments, 3) unfractionated anti-Xa levels the day after supplementation, and 4) coincident blood product administration. |
| O'Meara, 2015 (14) | Retrospective | 22 | ECMO cases in the pediatric cardiac intensive care unit (ICU) were reviewed between January 2013 and June 2014 after introduction of an ECMO anticoagulation protocol featuring heparin therapy managed with anti-Xa levels. In addition, a limited dataset from 10 consecutive cases who had heparin managed with ACT just before the new protocol from January 2012 to December 2012 was reviewed. All patients had congenital or acquired cardiac disease. | The purpose of the study was to report the results of this QI project, describing our experience with an anti-Xa-based protocol and its impact on blood sampling, heparin management, and frequency of ECMO oxygenator/circuit change-outs. As a secondary objective, we sought to describe the effects of antithrombin III (ATIII) replacement and heparin-free ECMO after cardiac surgery—two other key elements of our anticoagulation protocol. |
| Nankervis, 2007 (15) | Retrospective | 12 | Patients placed on venoarterial ECMO in the Columbus Children’s Hospital neonatal intensive care unit during 2004 and 2005. Children without anti Xa data were excluded. | Tested the hypothesis that the ACT levels will be positively correlated with heparin dose and therefore would correlate with the anti-factor Xa activity. |
| Dalton, 2015 (16) | Retrospective | 2036 | Pediatric patients (less than 19 years) in the ELSO registry who underwent ECLS at any of the eight current CPCCRN | Analyzed the bleeding and thrombosis complication rate and the association of such complications with survival. |
centers during a seven-year period (2005–2011).

| Study | Design | n | Description | Objective |
|-------|--------|---|-------------|-----------|
| Barrett, 2017 (17) | Retrospective | 3069 | Patients ≤18 year old discharged from a participating Children’s Hospital from January 1, 2003 to June 30, 2014 with an International Classification of Diseases, Ninth Revision, Clinical Modification procedure code or CTC code for cardiac surgery and those undergoing cardiac transplantation. | To examine the association between center ECMO volume, surgical volume and mortality in pediatric cardiac surgical patients that required ECMO support. |
| Nagle, 2013 (18) | Retrospective | 12 | Patients who received bivalirudin at any point between May 2006 and February 2011 during their extracorporeal life support course. Patients older than 18 years old were excluded. | This analysis describes the dosing and monitoring of bivalirudin as an alternative to heparin in pediatric extracorporeal life support patients who developed heparin-induced thrombocytopenia, heparin resistance, or significant thrombosis while on heparin. |
| Machado, 2020 (19) | Retrospective | 35 | Patients treated with ECMO <18 years of age at time of ECMO cannulation admitted to the PCICU. | To analyze the differences between the two methods of anticoagulation regarding blood product utilization, bleeding, thrombosis and safety during invasive procedures. |
| Citation     | Study Design | n   | Description                                                                 | Objective                                                                 | Page |
|--------------|--------------|-----|-----------------------------------------------------------------------------|---------------------------------------------------------------------------|------|
| Ranucci, 2011 (20) | Retrospective | 21  | Postcardiotomy ECMO patients from a single institution from 1 January 2008 through 30 April 2011. | To analyze a conventional heparin-based anticoagulation (from January 2008 through May 2009) versus the bivalirudin-based anticoagulation (from June 2009 through April 2011) with a specific respect for blood loss, thromboembolic complications, allogeneic blood product use, and costs associated with postcardiotomy ECMO. | 8    |
| Raets, 2013 (21)   | Retrospective | 677 | Neonates who received ECMO treatment in either of the two ECMO centers in The Netherlands (Erasmus MC-Sophia Children's Hospital, Rotterdam, and University Medical Center St Radboud, Nijmegen) between September 1989 and October 2010. | To review the types of brain injury seen in all neonates receiving neonatal ECMO in The Netherlands. | 7    |
| Pinto, 2017 (22)   | Retrospective | 828 | Pediatric patients between January 2000 and July 2015, who were >28 days and <18 years of age at the time of ECMO cannulation that survived ECMO to successful decannulation with a complete diagnostic brain MRI performed at any point after ECMO cannulation were included. | To describe and analyze the post-ECMO MRI findings of pediatric patients, outside the neonatal period. | 6    |
| Cengiz, 2005 (23)  | Retrospective | 4942| Pediatric patients 1 month to 18 yrs of age listed in the ELSO registry between June 1981 and August 2002. The analysis was limited to patients who underwent only a single run of ECLS, to avoid the potential increased risk of thromboembolic effect associated with a second run of ECLS. | To identify risk factors CNS complications by reviewing ELSO registry. | 8    |
| Author            | Year   | Study Type   | n   | Description                                                                                                                                                                                                 | Objective                                                                                                                                                                                                 | Page |
|-------------------|--------|--------------|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|
| Behr, 2020 (24)   |        | Retrospective| 573 | Patients from the Limited Data Set between 1989 through 2017. We queried the registry for all pediatric patients (<18 years), with International Classification of Disease codes corresponding to traumatic injury. | To characterize the indications, technical aspects, clinical parameters, complications, and outcomes of children placed on ECMO secondary to a traumatic insult and to determine the overall appropriateness of ECMO in the setting of pediatric trauma. | 7    |
| Stephens, 2020 (25) |        | Retrospective| 40  | Single ventricle patients less than 18 years old who underwent venoarterial ECMO support at our institution from January 2010 to December 2017. Exclusion criteria included SV patients who required ECMO after orthotopic heart transplantation (OHT). | To describe an institutional experience of SV patients on ECMO.                                                                                                                                          | 7    |
| Jackson, 2014 (26) |        | Retrospective| 189 | Pediatric patients managed at two large pediatric ECMO centers between March, 1997 and June, 2012.                                                                                                          | To define the outcome of chest tube placement in pediatric patients managed with ECMO.                                                                                                                  | 7    |
| Zhao, 2008 (27)    |        | Retrospective| 20  | Pediatric patients from December 2004 to October 2006 in Fuwai Cardiovascular Hospital.                                                                                                                        | To report the summarized clinical findings from 20 consecutive pediatric extracorporeal membrane oxygenation (ECMO) patients and to investigate the factors associated with mortality. | 6    |
| Moynihan, 2017 (28)|        | Retrospective| 31  | Patients (<18 years) receiving ECLS with anticoagulation monitoring undertaken including Thromboelastogram®6s (TEG®6s) over a 12-month period from July 2015 were eligible.                                                | To determine the strength of the correlation between hemostatic test results evaluating heparin effect and heparin infusion dose in pediatric ECLS.                                                      | 8    |
| Study Authors | Study Type | n | Study Details | Research Objective | Page |
|---------------|------------|---|---------------|-------------------|------|
| Anton-Martin, 2017 (29) | Retrospective | 241 | Neonates and children (1 day to 18 years of age) supported on ECMO between January 2009 and December 2014, cases of intracranial hemorrhage and infarct were identified along with matched control subjects. Patients with prior neurologic injury, syndrome or chromosomal abnormalities were excluded, as well as patients with incomplete laboratory or imaging data. | To study whether the traditional coagulation profile would predict an intracranial hemorrhage or infarct in pediatric ECMO patients. | 7 |
| Sulkowski, 2014 (30) | Retrospective | 26 | Neonates placed on ECMO between March 2008 and February 2013. | To evaluate how well ACT and aPTT levels reflect heparin anticoagulation as determined by antifactor Xa levels for neonatal patients on ECMO. | 6 |
| Nelson, 2017 (31) | Retrospective | 14 | 14 ECMO patients who received recombinant ATIII from August 2013 to July 2014 were included. Patients were excluded if they remained on ECMO <24 hours, did not receive anticoagulation, or did not receive heparin per institutional guidelines. | To assess the effectiveness of an ECMO continuous ATIII infusion protocol as compared to intermittent dosing of ATIII in regards to outcomes of anticoagulation. | 7 |
| Figueroa Villalba, 2020 (32) | Retrospective | 145 | Pediatric ECMO patients during 2015–2018. Runs <24 hours, without anticoagulant, anticoagulant other than heparin or circuit change due to mechanical failure were excluded. | To describe the transition from ACT to anti-Xa heparin monitoring and the associated clinical changes that occurred. | 6 |
| McMichael, 2019 (33) | Retrospective | 69 | Neonatal and pediatric patients treated with ECMO at a single institution between 0 days to less than 18 years of age at the time of ECMO cannulation and received ECMO in our pediatric intensive care unit or pediatric cardiac intensive care unit between September 2012 and December 2014. | To examine the correlation among antifactor Xa level, aPTT, and UFH dose to help define the most effective anticoagulation monitoring strategy for neonatal and pediatric ECMO patients. | 6 |
| Authors          | Study Type                  | N      | Description                                                                                                                                                                                                 | Objective                                                                                                                                                                                                 | Reference |
|------------------|-----------------------------|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| Alexander, 2010  | Retrospective               | 27     | Children receiving temporary ECLS between December 2006 and April 2008, in whom TEG was performed at least once. 171 pairs (342 tracings in total) met the necessary criteria for inclusion in this audit. | To explore the correlation between TEG and APTT, ACT, and platelet count.                                                                                                                                 | 9         |
| Chao, 2020       | Retrospective               | 109    | Neonates born between January 2015 and December 2017 with TGA or SVP in our center were included in the study. Participants were excluded for a gestational age less than 35 weeks old or a confirmed genetic syndrome. | To identify the spectrum of brain abnormalities associated with ECMO in infants with two prevalent forms of critical CHD, d-transposition of the great arteries (TGAs), and single ventricle physiology (SVP) | 8         |
| Campbell, 2020   | Retrospective chart review  | 34     | Pediatric patients less than 18 years of age receiving bivalirudin for ECMO/VAD anticoagulation from March 2014 to September 2018. Patients were excluded if they received bivalirudin for an indication other than ECMO/VAD anticoagulation or if they received less than 24 hours of bivalirudin. | To characterize the overall usage, dosage, and safety profile of bivalirudin in both ECMO and VAD patients.                                                                                           | 6         |
| Baily, 2019      | Prospective                 | 514    | First ECMO run data from subjects birth to less than 19 years old enrolled at the eight pediatric hospitals affiliated with the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network between December 2012 and September 2014 from the BATE dataset | To develop a prognostic model for predicting mortality at time of extracorporeal membrane oxygenation initiation for children which is important for determining center-specific risk adjusted outcomes. | 8         |
| Sivarajan, 2011  | Retrospective | n = 116 | Children with cardiac disease who required ECMO from November 1990 to April 2006. We excluded all patients placed on veno-venous ECMO, patients on ECMO for primary respiratory or septic indications and all patients with congenital diaphragmatic hernia. For patients requiring multiple ECMO episodes during a single hospital admission, only the initial ECMO episode was analysed with respect to the outcomes of interest. | To review the outcomes of all children with cardiac disease who required veno-arterial (VA) ECMO support at a single institution. | 9 |
| Cook, 2020      | Retrospective | n = 170 | Children who received ECMO from the Michigan Medicine Pediatric Neuro-Critical Care Registry between November 2015 and September 2018. Exclusion criteria included receipt of initial pediatric neurology consultation after decannulation from ECMO, lack of reconsultation in established consults after cannulation onto ECMO, death during ECMO cannulation, and lack of cEEG monitoring. For children who underwent multiple ECMO runs, the first ECMO run during which the neurology service was consulted was included for this study, and later runs were excluded. | To determine the prevalence of seizures and brain injury, identify associated risk factors, and better understand current neuromonitoring practice patterns in the ECMO population at a tertiary/quaternary care children’s hospital. | 7 |
| Author(s) | Year and Reference Number | Study Design | n | Study Description                                                                                                                                                                                                                                                                                                                                 | Objective(s) | Page |
|-----------|---------------------------|--------------|---|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|------|
| Karam, 2020 (40) | Retrospective | 514 | Consecutive patients under 19 years old treated with ECMO initiated in a PICU, cardiac ICU (CICU), or neonatal ICU (NICU) of eight Eunice Kennedy Shriver National Institute of Child Health and Human Development’s Collaborative Pediatric Critical Care Research Network institutions between December 2012 and September 2014. The study was limited only to the initial ECMO course for patients who might have required multiple runs of ECMO support. | To describe the epidemiology of hemostatic transfusions in children supported by ECMO. The secondary objective was to identify risk factors associated with the receipt of hemostatic transfusions. | 8 |
| Werho, 2015 (41) | Retrospective | 3517 | Cardiac surgical patients requiring ECMO postoperatively from the ELSO registry during a hospitalization from all children (<18 years at ECMO onset) who underwent cannulation for venoarterial ECMO for cardiac support between January 1, 2002, and April 30, 2013. Records with missing, implausible, or out-of-range values were also excluded. | To investigate whether cannulation techniques, thromboses in the ECMO circuit, and pump flows are associated with risk of stroke. | 7 |
| Khaja, 2010 (42) | Retrospective | 21 | Neonates on ECMO in the neonatal intensive care unit patients at the Texas Children’s Hospital, Houston, from 2006 to 2008. Patients with incomplete coagulation records were excluded. | To identify the usefulness of the anti-Xa assay vs PTT or ACT. and to attempt to find correlations among these coagulation values. | 7 |
| Speggiorn, 2015 (43) | Retrospective | 72 | Patients who, within the first 30 days of life, were cannulated with an Avalon® double-lumen veno-venous (DLVV) cannula for ECMO due to refractory respiratory failure | To report an institutional experience with the use of Avalon® cannula in neonatal respiratory ECMO. | 5 |
| Author(s) | Year | Study Design | n | Sample Description | Research Objectives | Citation |
|-----------|------|--------------|---|--------------------|---------------------|----------|
| Bailly, 2020 | Retrospective | 514 | ECLS runs from subjects <19 years between December 2012 and September 2014. ELSO subjects without a recorded pH, with unknown survival status, or unknown timing of infection were excluded. | To externally validate the PEP model using data retrospectively collected from the ELSO registry. | (44) |
| Shakoor, 2019 | Retrospective | 71 | Patients younger than 21 years who underwent ECPR between January 2010 and November 2017. | To review an institutional experience with ECPR and evaluate factors that affect survival. | (45) |
| Guo, 2019 | Retrospective | 31 | Children with congenital heart disease who required ECMO support postoperatively at Shanghai Children’s Medical Center. | To analyze ECPR cases after pediatric congenital heart surgery in our center in 2017. | (46) |
| Almond, 2011 | Retrospective | 773 | The OPTN database and ELSO Registry were used to identify children <18 years of age who were supported with venoarterial ECMO and listed for orthotopic heart transplantation in the United States between January 1, 1994, and February 20, 2009. | To describe the safety and efficacy profile of ECMO as a bridge to heart transplantation in children, to develop objective performance goals for ECMO as a bridge to transplantation, and to determine whether ECMO duration is associated with in-hospital mortality. | (47) |
| Aharon, 2001 | Retrospective | 50 | Patients at the Vanderbilt University Medical Center who required ECMO for cardiopulmonary support after cardiac operation between May of 1997 and October of 2000. | To determine predictors of successful salvage of children requiring postcardiotomy mechanical assistance. | (48) |
| Thiagarajan, 2007 | Retrospective | 682 | Patients with ECPR during the years of the study (1992–2005) <18 years of age | To describe the type of pediatric patients treated with ECPR and to report trends in the use of and survival after ECPR | (49) |
| Author                  | Year       | Study Type | n     | Description                                                                                                                                                                                                 | Objective                                                                 | Page |
|------------------------|------------|------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|------|
| Dalton                 | 2017       | Prospective| 514   | Consecutive patients under 19 years of age treated with ECMO initiated in a pediatric, cardiac, or neonatal intensive care unit of eight CPCCRN institutions between December 2012 and September 2014. The study was limited to the initial ECMO course for patients who required multiple episodes of ECMO. | To report the results of this prospective study.                         | 6    |
| Melvan                 | 2020       | Retrospective| 184   | Patients who required ECPR at Children Healthcare of Atlanta Egleston Hospital between 2002 and 2017.                                                                                                              | To report our large single-institution experience and to study factors associated with hospital survival. | 8    |
| Mehta                  | 2010       | Retrospective| 58    | Patients who received ECMO at our institution from January 1, 1999, to October 31, 2008, and selected those above the age of 30 days, who received ECMO for respiratory failure and/or hemodynamic instability. Children requiring ECMO support for primary cardiac failure, congenital heart disease, or congenital diaphragmatic hernia were excluded. | To examine outcomes of ECMO therapy in the pediatric population with the aim to identify pre-ECMO and on ECMO characteristics that are associated with survival. | 7    |
| Balasubramanian        | 2007       | Retrospective| 53    | From April 1990 to December 2003, patients who required VA ECMO following the surgical correction of congenital cardiac defects in our institution, Glenfield Hospital U.K.                                                   | To study the long-term outcome of children who had circulatory support with VA-ECMO following repair of congenital heart defects in our institution. | 7    |
| Jenks                  | 2019       | Retrospective| 240   | Pediatric patients between 0 and 18 years of age, placed on ECMO during 2009 to 2014. The only exclusionary criterion was ECMO support for less than 24 hours.                                                              | To determine whether a higher Hb level is associated with an increase in hemolysis. | 9    |
| Author          | Year | Study Type | n     | Description                                                                                                                                                                                                                                                                                                                                 | Objective                                                                                                                                                                                                 |
|-----------------|------|------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Rozmiarek       | 2004 | Retrospective | n = 14305 | All patients less than 30 days old in the ELSO registry (14305) between 1991 and 2002 were divided into those less than 2 kg (663) and more than 2 kg (13642). Patients with cardiac anomalies were excluded. | To determine if ECMO is both effective and safe in babies less than 2.0 kg and to determine the lowest effective birth weight at which ECMO could be used safely.                                                                                           |
| Von Stumm       | 2020 | Retrospective | n = 15  | Neonatal patients who were placed on ECMO after congenital heart surgery during a period of 3 years (2015-2017) from our institutional database.                                                                                                                                                                                          | To report benefits and risks of delayed systemic heparinization regarding thrombosis, bleeding, requirement of blood products, and survival in these patients.                                                                                         |
| Saini           | 2015 | Retrospective | n = 24 | Children <18 years of age who received ECMO support from 9/1/2011 to 12/31/2012 at St. Louis Children’s Hospital in the neonatal (NICU), cardiac (CICU), and pediatric intensive care units (PICU). All the patients on whom TEG®–PM was performed during ECMO support were included in the study cohort. | To determine the frequency and magnitude of platelet dysfunction according to TEG®–PM.                                                                                                                       |
| Hardart         | 2004 | Retrospective | n = 1524 | Patients with gestational age (GA) <37 weeks who received ECMO in the years 1992 through 2000 and were reported to the ELSO Registry. Patients previously treated with ECMO, those with ICH before ECMO, and those who were treated with ECMO. | To determine the relationship between patient age and ICH development.                                                                                                                                       |
older than 28 days at ECMO initiation were excluded from the analysis.

| Author          | Design     | n   | Study Details                                                                                                                                                                                                                                                                                                                                 | Objective                                                                                                                                                                                                 |
|-----------------|------------|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| De Mol, 2008    | Retrospective | 24  | Newborns who developed an ICH during VA-ECMO treatment could be matched with 1 or 2 control patients from September 1989 through November 2005, treated with VA-ECMO at the Radboud University Nijmegen Medical Centre. Newborns were excluded from the study when there were congenital abnormalities other than congenital diaphragmatic hernia; a second ECMO treatment, ICH before the initiation of ECMO; or coagulation disorders as screened for by the determination of prothrombin time, activated partial thromboplastin time, and platelet count. | To investigate whether there is a relationship between intravascular volume administration and the occurrence of ICH in the neonate during treatment with VA-ECMO. |
| Cashen, 2018    | Prospective | 267 | Neonatal patients (<30 days of age) were included. Only the initial ECMO course was included for patients who received ECMO more than once.                                                                                                                                                                                                  | To further investigate the relationship between the use of therapeutic hypothermia during neonatal ECMO and complications, mortality and functional status among survivors.                                           |
| Reed, 2010      | Retrospective | 29  | Patients at Seattle Children’s Hospital who were on ECMO prior to death and underwent autopsy between January 2004 and December 2008 were identified by review of autopsy records and included in the study.                                                                                                                                                                         | To assess the current incidence of thrombosis and hemorrhage in pediatric patients who die after ECMO therapy.                                                                                              |
| Ning, 2013      | Retrospective | 5   | 5 children with acute fulminant myocarditis admitted to the pediatric intensive care unit (PICU) of the Affiliated Children’s Hospital, Zhejiang                                                                                                                                         | To summarize the clinical application of ECMO in five children with acute fulminant myocarditis and discusses its effects.                                                                                 |
| Study                           | Design     | n  | Description                                                                 | Objective                                                                 | Page |
|--------------------------------|------------|----|-----------------------------------------------------------------------------|---------------------------------------------------------------------------|------|
| Fenton, 2003 (64)              | Retrospective | 20 | Patients supported with ECMO early or late after transplantation from February 1982 through October 2002; these patients form the study population. | To determine whether ECMO would provide time for recovery of cardiac function early and late after transplantation and allow long-term survival. | 7    |
| Fleming, 2007 (65)             | Retrospective | 80 | 20 and 60 samples were recorded for the Hemochron 401 and Response machines, respectively from the University of Michigan ECMO database was queried for all consecutive patients on ECMO at our institution from June 2003 through May 2005. | To evaluate for and establish differences between the results obtained with each model of ACT machine. | 7    |
| McMullan, 2011 (66)            | Retrospective | 25 | ECMO patients who required postoperative ECLS within 24 h of surgery between November 2002 and April 2007. | To compare postoperative bleeding between patients supported with standard extracorporeal membrane oxygenation (ECMO) or centrifugal pump system initiated within 24 h of surgical repair. | 7    |
| Teruya, 2017 (67)              | Retrospective | 18 | Pediatric patients treated with bivalirudin infusion while being supported with VAD or ECMO at a large tertiary care pediatric hospital (Texas Children's Hospital, Houston, USA). | To report a comparison study between parameters of ROTEM and conventional plasma based coagulation assays in the setting of bivalirudin therapy in children on ECLS. | 7    |
| Karimova, 2009 (68)            | Retrospective | 718 | Neonates treated with ECMO for AHRF in the UK between January 1993 and December 2005. Neonates with congenital heart disease were excluded. | To describe and evaluate the use of ECMO for neonatal AHRF in the UK since the service was set up in 1993. | 8    |
| Reference                        | Study Type | n   | Description                                                                                                                                                                                                 | Conclusion                                                                                                                                                                                                 |
|---------------------------------|------------|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Polito, 2015 (69)               | Retrospective | 1898| Patients less than 30 days of age at the time of ECMO deployment and a diagnosis of CHD during the calendar years 2005–2010.                                                                                | To ascertain the incidence of neurologic injury in neonates with CHD and supported with ECMO and to evaluate patient demographic, pre ECMO, and ECMO support-related variables associated with acute neurologic injury in these patients.          |
| Hervey-Jumper, 2011 (70)       | Retrospective | 26,529| 26,529 children and 1170 adults treated during the period between January 1, 1990, and August 1, 2009. Patients undergoing ECMO for extracorporeal cardiopulmonary resuscitation and vascular cannulation technique were excluded from analysis. | To more precisely identify the incidence of ICH, stroke, and seizures associated with ECMO according to age classification and the indications for ECMO.                                                                   |
| Barrett, 2009 (71)             | Retrospective | 682 | 682 ECPR patients <18 years of age from the ELSO registry between 1992–2005.                                                                                                                                   | To determine the incidence of acute neurologic injury as well as to evaluate patient demographic, pre-ECMO and ECMO support-related variables associated with neurologic injury in children undergoing E-CPR.                                |
| Meehan, 2002 (72)              | Retrospective | 205 | Neonates who required multiple ECMO courses listed in the ELSO registry from its inception to January 2000.                                                                                                        | To assess the efficacy of recannulation and to better understand the potential complications.                                                                                                               |
| Zamora, 2014 (73)              | Retrospective | 1323| The ELSO registry was queried for all children between 31 days and 18 years of age treated with venovenous ECMO between January 1, 1998 and December 31, 2011 using either VVDL or VVMS cannulation techniques. | To investigate the national trends in the use of VVDL cannulation in the pediatric population, to evaluate complication and survival rates associated with these cannulas, and compare these outcomes to those associated with |
| Authors          | Study Type   | Subjects | Description                                                                                                                                                                                                 | Goals                                                                                      | Page |
|------------------|--------------|----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|------|
| Stansfield       | Retrospective| n = 162  | Subjects included neonates receiving ECMO support for primary respiratory failure in the neonatal intensive care unit at Children's Hospital of Georgia between January 2002 and December 2014. Patients who were supported with ECMO for less than 24 hours or for which primary cardiac support was the indication for ECMO were excluded. | To determine the effect of routine AT3 replacement on circuit/component lifespan, thrombotic and hemorrhagic complications, blood product utilization, and heparin utilization. | 7    |
| Yang             | Retrospective| n = 56   | Patients receiving a VA-ECMO for refractory cardiogenic shock from July 2007 to May 2018.                                                                                                                     | To describe a single institution’s 11-year experience with pediatric VA-ECMO for RCS, addressing the characteristics of our patient population, the analysis of clinical outcomes including mortality and complications of support, and the identification of risk factors associated with 30-day mortality. | 8    |
| Maue             | Retrospective| n = 38   | Patients receiving ECMO support in the pediatric critical care unit at a large quaternary care pediatric hospital from 2011 to 2016. Patients in the cardiovascular intensive care unit (ICU) and neonatal ICU were excluded. | To compare the outcomes of the oncology and HCT population to the general pediatric intensive care unit (PICU) population who have received ECMO support in a single institution. | 7    |
| LaRovere         | Retrospective| n = 179  | Patients who were treated with venoarterial (VA) and venovenous (VV) ECMO in the intensive care units at Boston Children’s Hospital between the years 2009 and 2013 were reviewed. 82/179 of children underwent 113 portable CT scans. | To describe the type and distribution of abnormalities detected on head CT during the course of ECMO in children. Additionally to compare clinical factors, including the occurrence of seizures detected on electroencephalography (EEG) and outcomes, between those with CT abnormalities and those without imaging abnormalities. | 7    |
| Study | Type       | n  | Description                                                                                                                                                                                                 | Objective                                                                                                                                                                                                 | Page |
|-------|------------|----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|
| Barrett, 2013 (78) | Retrospective | 2611 | Patients ≤ 18 years of age undergoing venoarterial (VA) ECMO support from January 1, 2007, to December 31, 2009. Patients were excluded if documentation of pump type was missing. The propensity score matching identified 548 patients (centrifugal = 274, roller = 274); | To compare survival to hospital discharge in pediatric ECMO patients supported with centrifugal versus roller pumps. The secondary aim was to compare ECMO-related complications between pump types. | 8    |
| Chow, 2004 (79)    | Retrospective | 90  | Children who received ECLS for cardiac indications between January 1990 and June 2000.                                                                                                                      | To determine the incidence and risk factors for adverse neurological outcomes and death in children receiving extracorporeal life support (ECLS) for cardiac indications.                               | 7    |
| Tiruvoipati, 2007 (80) | Retrospective | 52  | Patients with CDH during the 13-year study period were included.                                                                                                                                           | To identify pre ECMO and ECMO variables that could predict mortality in patients with CDH requiring ECMO.                                                                                                  | 7    |
| Anton-Martin, 2017 (81) | Retrospective | 175 | Pediatric patients 1 day to 18 years of age supported on ECMO in the pediatric ICU between January 2009 and December 2014 were included in the study. Exclusion criteria included patients with lack of coagulation laboratory data within the 24-hour period prior to ECMO cannulation. | To determine the incidence of coagulopathy before ECMO cannulation and its association with hemorrhage occurrence during extracorporeal support.                                                       | 7    |
| Ryerson, 2020 (82) | Prospective   | 18  | Neonatal and pediatric ECMO patients (age < 17 yr) receiving bivalirudin                                                                                                                               | To determine if bivalirudin resulted in less circuit interventions than unfractionated heparin.                                                                                                         | 7    |
| Study | Study Type | n | Description | Purpose |
|-------|------------|---|-------------|---------|
| Yu, 2017 (83) | Prospective | 32 | Neonatal and pediatric ECLS patients (age < 18 yr) at University of Michigan from May 2014 to September 2015 and 56 patients at University of Alberta from May 2013 to May 2015 were included. Patients with disseminated intravascular coagulation preexisting coagulopathy or thrombotic disorder, anticoagulated with an agent other than heparin or who received no anticoagulation, had an ECLS run less than 24 hours, or where the majority of the ECLS run occurred at another site were excluded from the study. | To compare extracorporeal life support complications and outcomes between two large-volume pediatric extracorporeal life support centers that use different anticoagulation strategies. |
| Church, 2017 (84) | Retrospective | 755 | Neonates of EGA ≤ 34 weeks were identified in the Extracorporeal Life Support Organization (ELSO) Registry (1976–2008). The registry includes cases from all international institutions that utilize ECLS. | To characterize outcomes of ECLS use in this population, comparing neonates born at earlier gestational ages to those at the currently accepted cutoff of 34 weeks. |
| Kane, 2010 (85) | Retrospective | 172 | Pediatric ECMO patients from the Children’s Hospital Boston ECMO database during 1995 to 2008 with cardiac disease (congenital and acquired) supported with ECMO for CA after failed conventional CPR therapies. | To report on the survival to hospital discharge after ECPR used to support children with cardiac disease at Children’s Hospital Boston. |
| Doymaz, 2015 (86) | Retrospective | 32 | Infants between 1997 and 2010 with PPHN diagnoses who required ECMO support. | To investigate the occurrence of ICH and to identify risk factors in neonates with PPHN. |
| Reference | Type            | n  | Description                                                                 | Objectives                                                                                                                                                                                                 |
|-----------|-----------------|----|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nardell,  | Retrospective   | 145| Patients between January 1998 and June 2007, (<18 years of age) were identified from the Extracorporeal Life Support Organization Registry with congenital heart disease requiring ECLS following cardiotomy. | To detail a recent experience with bleeding complications in post-cardiotomy pediatric patients on ECLS, with a specific aim to identify relevant risk factors for bleeding and potential treatment strategies. |
| 2009 (87) |                 |    |                                                                             |                                                                                                                                                                                                       |
| Melbourne,| Retrospective study | 81 | Newborns treated with ECMO at a single-center level IV neonatal intensive care unit in a freestanding academic children’s hospital with MRI data between July 2005 and February 2015 were included in this retrospective study. | To determine which clinical risk factors correlate with severe intracranial injury seen on MRI imaging post-ECMO in a contemporary cohort of neonatal ECMO patients.                                                                 |
| 2020 (88) |                 |    |                                                                             |                                                                                                                                                                                                       |
| Morris,   | Retrospective   | 137| Patients treated with ECMO in the pediatric cardiac intensive care unit between January 1, 1995, and June 30, 2001.                   | To describe and compare mortality rates following cardiac ECMO in the two major subsets of children studied here.                                                                                      |
| 2004 (89) |                 |    |                                                                             |                                                                                                                                                                                                       |
| Kasniya,  | Retrospective   | 7  | Pediatric ECMO patients aged 1 month to 15 years received rFVIIa at the University of Michigan C.S. Mott Children’s Hospital from 2004 to 2009. | To add to the retrospective data on the use of rFVIIa in the pediatric patient on ECMO with severe, refractory hemorrhage.                                                                               |
| 2016 (90) |                 |    |                                                                             |                                                                                                                                                                                                       |
| Flóres,   | Retrospective   | 104| Children supported with ECMO between 2007 and 2013                          | To review a model of ECMO care including the staffing, training, circuit, and daily care of these patients as well as the associated costs.                                                                     |
| 2015 (91) |                 |    |                                                                             |                                                                                                                                                                                                       |
| Chrysotomo | Retrospective   | 95 | Children undergoing ECMO support in the cardiac intensive care unit of Children’s Hospital of Pittsburgh, a tertiary academic center | To describe the Children’s Hospital of Pittsburgh approach to the management of cardiac patients requiring E-CPR, OR-ECMO, and LCOECMO.                                                                  |
| u, 2013   |                 |    |                                                                             |                                                                                                                                                                                                       |
| Hastings, | Prospective     | 50 | ECMO circuits were collected after separation from patients at              | To characterize clot formation and location within the circuit, to                                                                                                                                                                                                   |
| 2017 (93) |                 |    |                                                                             |                                                                                                                                                                                                       |
| Study | Study Design  | n   | Population | Study Objectives                                                                                     | Reference |
|-------|---------------|-----|------------|---------------------------------------------------------------------------------------------------|-----------|
| Shuhaiber, 2011 (94) | Retrospective | 20 | Pediatric ECMO patients 18 years of age or younger with cardiac disease supported by more than one ECMO run after congenital cardiac surgery between January 1995 through December 2008 from our cardiac ECMO database. | To evaluate an experience with use of multiple ECMO runs for cardiorespiratory dysfunction during a single hospital admission after congenital heart surgery. |
| Muensterer, 2011 (95) | Retrospective | 164 | Pediatric ECMO patients between 2000 and 2008. Exclusion criteria were incomplete patient data and previously known congenital coagulation disorders. | To investigate the impact of the bleeding protocol on the survival time of the ECMO circuit. |
| Kessel, 2017 (96) | Retrospective | 18 | Patients who were placed on ECMO between January 2004 and March 2013 in the Pediatric Intensive Care Unit at Cohen Children’s Medical Center of New York | To determine if the new protocol would improve the amount of time that the ACT and aPTT are within range and whether the mean heparin infusion dose during both time periods would remain unchanged. |
| Derbalah, 2020 (97) | Retrospective | 31 | Paediatric patients who received UFH infusion for prevention of thrombosis during ECMO support | To explore the effect of developmental haemostasis on the dose–response relationship of UFH in paediatric patients receiving UFH therapy during extracorporeal membrane oxygenation (ECMO) support. |
| Author(s) | Type | n | Study Description | Findings |
|-----------|------|---|-------------------|----------|
| Northrop, 2015 (98) | Retrospective | n = 366 | ECMO runs at a single institution from January 1, 2007, through September 30, 2013. To determine whether incorporating a comprehensive ECMO anticoagulation laboratory protocol that follows anti Xa levels, antithrombin would lead to fewer hemorrhagic complications, a decrease in blood product usage, and an increase in circuit life. | 7 |
| Tzanetos, 2017 (99) | Retrospective | n = 81 | Patients less than 18 years of age requiring ECMO at a freestanding tertiary children’s hospital over a 2 year period. To evaluate the relationship between ATIII levels and subsequent replacement of low levels with clinical events of thrombosis and bleeding in 7 pediatric and neonatal ECMO patients. | 8 |
| Kawai, 2015 (100) | Retrospective | n = 14 | Patients aged 4 months to 16 years of age from gestational age 37 weeks up to age 17 years who received TPE while on ECLS admitted to C.S. Mott Children’s Hospital from January 2005 through January 2013. To report a single center accumulated experience with TPE use for children who require ECLS for sepsis-induced MODS. | 7 |
| Phillips, 2020 (101) | Retrospective | n = 46 | CDH patients supported by ECMO between January 2008 and December 2018 at Children’s Hospital Colorado, a quaternary pediatric referral hospital with a dedicated fetal care center during the 10 year study period. To determine whether the standardization of coagulation management, including the implementation of our TEG-guided blood product replacement protocol will result in a reduction in bleeding and thrombotic complications. | 8 |
| Hastings, 2016 (102) | Prospective | n = 16 | ECMO circuits with centrifugal pumps were collected from Children’s Healthcare of Atlanta, Emory University (Atlanta, GA, USA). To examine neonatal (<= 30 days old) and pediatric (>30 days old, <18 years old) ECMO circuits after patient use and offer an in vitro recreation of a centrifugal pump circuit, validated by similarity to clinical results. | 5 |
| Study | Type | $n$ | Description | Purpose |
|-------|------|-----|-------------|---------|
| Irby, 2014 (103) | Retrospective | $n = 62$ | Patients supported with ECMO from January 2009-March 2011. Inclusion criteria were children (1) supported with ECMO at Arkansas Children's Hospital, (2) between the ages of 0-21 years, and (3) who had daily measurement of anti-Factor Xa levels. Fifty patients were excluded from initial data analysis based on predetermined exclusion criteria. | To investigate whether sub-therapeutic anti-Factor Xa levels are associated with an increased need for ECMO circuit/membrane oxygenator changes in children during ECMO support. |
| Agati, 2006 (104) | Prospective | $n = 11$ | Patients who required ECMO for postcardiotomy cardiorespiratory failure from November 2004 through February 2006 | To describe a novel anticoagulation strategy with continuous intravenous antithrombin III infusion and intermittent heparin infusion in order to reduce bleeding and hemorrhagic complication during the early stages of pediatric ECMO. |
| Henderson, 2018 (105) | Retrospective | $n = 30$ | Pediatric and neonatal patients who received ECMO over a 2-year period in a large tertiary care center was conducted. Patients less than the age of 18 years, more than 2 kg, and requiring ECMO from July 2013 through July 2015 were included in the study. Patients with known underlying coagulation disorders or heparin-induced thrombocytopenia, patients requiring the use of a direct thrombin inhibitor rather than UFH while on ECMO, and pregnant females were excluded from this study. | To examine the performance of anticoagulation targets for predicting a significant bleed and/or a significant thrombotic event, to identify a target anti-Xa activity and TEG R time which could minimize both bleeding and thrombotic complications, and to evaluate the correlation between TEG parameters and traditional measures of coagulation in pediatric and neonatal ECMO patients. |
| Study | Type     | n   | Patients | Study Objective |
|-------|----------|-----|----------|-----------------|
| Carpenter, 2018 (106) | Retrospective | 160 | Patients cannulated for ECMO by pediatric general surgeons at a tertiary children’s hospital from 2005 to 2016. Patients that were cannulated for primary congenital heart disease were excluded from the study. | To present the evolution of VV ECMO, including management trends and outcomes, over a 10-year time period in a tertiary neonatal and pediatric ECMO program. |
| Pasala, 2014 (107) | Prospective | 6 | 6 patients between the ages 0 to 18 years requiring ECMO support at a single institution between December 2010 and April 2011 were enrolled. Exclusion criteria for the study were 1) patients transferred from an outside institution on ECMO support, 2) lack of timely informed consent, and 3) patients requiring cardiopulmonary bypass before going on ECMO support. | To investigate whether changes in HMW vWF multimers occur over time after the initiation of ECMO in children. |

Abbreviations: ACT, activated clotting time; AHRF, acute hypoxemic respiratory failure; APTT, activated partial thromboplastin time; ATC, antithrombin concentrate; ATIII, antithrombin; BATE, bleeding and thrombosis during ECMO; CA, cardiac arrest; CDH, congenital diaphragmatic hernia; cEEG, continuous electroencephalography; CHD, congenital heart disease; CNS, central nervous system; CPCCRN, Collaborative Pediatric Critical Care Research Network; CT, computed tomography; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; EGA, estimated gestational age; ELSO, extracorporeal life support organization; Hb, hemoglobin; HCT, hematopoietic cell transplant; HMW, high molecular weight multimer; ICH, intracranial hemorrhage; INR, international normalized ratio; LCOS, low cardiac output syndrome; MODS, multiple organ dysfunction syndrome; MRI, magnetic resonance imaging; NOS, Newcastle-Ottawa Scale; OPTN, organ procurement and transplantation network; OR, operating room; PAH, pulmonary arterial hypertension; PCICU, pediatric cardiac intensive care unit; PEP, pediatric extracorporeal membrane oxygenation prediction; PPHN, persistent pulmonary hypertension; PTT, partial thromboplastin time; QI, quality improvement; RCS, refractory cardiogenic shock; rFVIIa, recombinant activated factor VII; SV, single ventricle; SVP, single ventricle physiology; TEG, thromboelastography; TGA, transposition of the greater arteries; TPE, Therapeutic plasma exchange; UFH, unfractionated heparin; VA, veno arterial; VAD, ventricular assist device; VV, veno venous; VVDL, veno venous double lumen; VVMS, veno venous multisite; VWF, von willebrand factor.
Supplemental material 5. Factors and frequency of neurological complication definitions.

| Parameter                                              | Frequency, n (%) |
|--------------------------------------------------------|------------------|
| Cerebral hemorrhage                                    | 17 (81)          |
| Stroke                                                 | 20 (95)          |
| Abnormalities on ultrasound or computed tomography 14  | (67)             |
| Brain death                                            | 7 (33)           |
| Clinical neurologic abnormalities                      | 2 (10)           |
| Clinical seizures                                      | 9 (43)           |
| Seizure activity on EEG                                 | 7 (33)           |
Supplementary material 6. Frequency of description of transfusion parameters in 107 studies.

| Parameter                                | Frequency |
|------------------------------------------|-----------|
| Platelet transfusion threshold           | 28 (26)   |
| Fibrinogen transfusion threshold         | 21 (20)   |
| Erythrocyte transfusion threshold        | 19 (18)   |
| Antithrombin suppletion                  | 9 (8)     |
| Frequency of antithrombin testing        | 8 (7)     |
| Target range antithrombin               | 14 (13)   |