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Eliminate Unnecessary Laboratory Work to Mitigate Iatrogenic Anemia and Reduce Cost for Patients on Extracorporeal Membrane Oxygenation

Maureen Welty, DNP;* Beth Nachtsheim Bolick, DNP†

**Pediatric Critical Care, Children's Hospital of Illinois at OSF HealthCare Saint Francis Medical Center, Peoria, Illinois; and †Acute Care Pediatric Nurse Practitioner Program, Department of Women, Children, and Family Nursing, Rush University College of Nursing, Chicago, Illinois*

Abstract: Laboratory testing is a helpful tool for clinicians, but can be costly and harmful to patients. A quality improvement project was initiated to reduce laboratory testing for patients receiving extracorporeal membrane oxygenation (ECMO) in a pediatric intensive care unit (PICU) at a tertiary care center. Preliminary data was gathered to demonstrate preimplementation practice, cost, and patient need for packed red blood cell (pRBC) transfusions. A new protocol was created by an interprofessional team based on best practice and benchmarking with high-performing organizations. The project was evaluated using two comparison groups, pre- and postimplementation for anyone receiving ECMO therapy in the PICU. The average laboratory tests per ECMO day decreased by 52% (128.4 vs. 61.1), cost per case decreased by 14.7%, pRBC transfusions decreased from 100% to 85%, length of stay (LOS) decreased by 8 days, and mortality rates decreased by 9.5%. The revised pediatric ECMO laboratory testing guidelines were successfully implemented and reduced laboratory cost without adverse effects on mortality rates or LOS. **Keywords:** pediatric ECMO, pediatric ECLS, iatrogenic anemia, pediatric critical care, laboratory testing. *J Extra Corpor Technol. 2022;54:123–7*

Extracorporeal life support (ECLS) and extracorporeal membrane oxygenation (ECMO) are interchangeable terms for a machine that sustains hemodynamic function and provides gas exchange to support the cardiovascular and/or pulmonary systems (1). ECMO is a complex therapy managed at the patient's bedside. Two common types of ECMO: venoarterial (VA) assists heart and lung function, whereas venovenous (VV) supports lung function (2). Morbidities of ECMO therapy are iatrogenic anemia, bleeding, thrombosis, coagulopathy, air embolism, circuit failure or rupture, and infection (2). Iatrogenic anemia is defined as anemia caused by the volume of blood removed from the patient by medical professionals.

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Address correspondence to: Maureen Welty, DNP, Nurse Practitioner, Children' s Hospital of Illinois at OSF HealthCare Saint Francis Medical Center, 530 NE Glen Oak Ave, Peoria, IL 61637. E-mail: maureen.e.welty@osfhealthcare.org
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In 2015, 2016, and 2017, our children's hospital was identified as among the best ECMO programs in the state for patient outcomes; however, it was failing to meet certain quality metrics. The average number of laboratory tests per ECMO day and direct cost per case increased over this 3-year time frame. Five high-performing organizations were contacted to share their laboratory testing guidelines. There was no standardized testing schedule across the different organizations.

Laboratory testing provides information to validate clinical assessments and for early identification of adverse events, response to ECMO, and complications of therapy. Common tests include coagulation profiles, hemoglobin, hematocrit, platelet count, blood gases, lactic acid, metabolic panels, and electrolytes. Testing requires accessing central catheters located in major veins and arteries with inherent risk for central line-associated blood stream infection (CLABSI) and iatrogenic anemia requiring packed red blood cell (pRBC) transfusion (3). Laboratory testing is accomplished via one of two formats: point-of-care testing (POCT) or in-house laboratory. The advantages of

POCT are speed of results and smaller blood volumes for testing; however, its ease of use subjects POCT to overuse and does this at a higher cost than in-house laboratory testing. The cost differences between POCT and in-house testing averages 1.5–1. Regardless of laboratory location, more testing does not correlate with improved clinical outcomes (3–5).

Reducing the number of laboratory tests/blood volume, known as blood conservation, decreases the necessity for pRBC transfusions to treat iatrogenic anemia (6,7). Transfusion-related adverse effects include infection, acute lung injury, electrolyte disturbance, circulatory overload, hemolysis, and immune system deficiency (3,8,9). The number of transfusions a patient receives while undergoing ECMO therapy correlates with increased morbidity and mortality (10).

Coagulation status during ECMO therapy requires routine monitoring; a fine balance exists with frequency of monitoring—too much testing increases risk of iatrogenic anemia and cost of care, whereas too little testing increases risk of hemorrhage and thrombosis (11). There is no standardized approach to routine anticoagulation monitoring and the Extracorporeal Life Support Organization (ELSO) recommends each center use the method in which they are most comfortable.

To prevent thrombotic events, anticoagulation therapy must be implemented. The most common tests for anticoagulation monitoring are the anti-factor Xa activity level (anti-Xa), activated partial thromboplastin time (aPTT), and activated clotting time (ACT) POCT. The anti-Xa is a better correlation of heparin level and is not skewed by coagulopathy; however, the data about its use are limited and the test is more expensive than the others listed. An aPTT test represents the patient's response to heparin and is used more than anti-Xa in the pediatric population. An aPTT test better correlates to unfractionated heparin doses when compared to ACT POCT (11). An ACT is a low-cost whole blood test, but is prolonged by hemodilution, thrombocytopenia, and decreased coagulation factor levels. These altered states could overestimate the heparin effect (12). The use of ACT to monitor anticoagulation is associated with larger total volume of pRBC transfusions (11).

The Institute for Healthcare Improvement's (IHI) framework for quality improvement was chosen because its Plan-Do-Study-Act (PDSA) cycle tests changes made on a small scale in a real work setting (13). The assumption was made that revising laboratory guidelines for pediatric ECMO would increase the quality of care and decrease its cost, meeting or exceeding national benchmarks in the DRG 3 category (14). The purpose of this project was to revise the pediatric ECMO laboratory monitoring guidelines.

METHODS

The project took place at a 132-bed children's hospital within a larger nonprofit healthcare system. There are 16 beds in the PICU with a population of cardiovascular, medical, surgical, trauma, and neurological patients. The unit services an average of 775 patients per year. The pediatric ECMO program is an ELSO designated Gold Center of Excellence and cares for an average of 13 ECMO patients per year: neonatal, pediatric, and adult patients (with congenital heart problems).

Interventions

The most frequent laboratory tests performed for patients on ECMO were identified by the in-house data analysis team and reviewed for diagnostic reasoning value and frequency. The laboratory testing guidelines were modified to align with current evidence, best practices of other high-performing organizations, and national benchmarks identified using iVantage Healthcare Analytics (Table 1). iVantage is a tool used by our healthcare system during the time of this quality improvement project to deliver statistical support, report information, and benchmark cost of care with other PICUs and patient populations across the nation (14).

The practice changes were categorized into three groups: 1) hematology, 2) electrolytes, and 3) gas exchange and when to use POCT vs. in-house laboratory. The new guidelines for laboratory testing were trialed for 3 months. All stable pediatric and adult patients receiving ECMO therapy in the PICU were included. Patients with hemorrhage or sub/supra therapeutic anticoagulation were opted out of the new guidelines until stable. For example, in the face of hemorrhage, additional hematology studies were drawn. Once bleeding was controlled, the new laboratory guidelines were followed. Data were collected every shift on all PICU ECMO patients regardless of level of stability. The laboratory test, volume of blood drawn, and POCT vs. in-house laboratory were recorded. The practice in this acute care setting is to draw the absolute minimum volume of blood per test as defined by our in-house laboratory. The previous guidelines called for a minimum of almost 25 mL per day compared to the new guidelines of 16 mL per day.

Hematology

Hematologic laboratory testing was the main target of guideline revision because of the high risk of hemorrhage and thrombosis while on the circuit. The ECMO program used continuous unfractionated heparin and continuous and bolus antithrombin for circuit anticoagulation. Point-of-care ACT was obtained every 1–4 hours and the aPTT tests as needed per ECMO specialist preference. The new guidelines reduced the number of ACT

Table 1. Previous vs. revised ECMO laboratory testing guidelines.

Time	Previous Guidelines	Revised Guidelines
01:00	–	–
02:00	ACT	–
03:00	–	–
04:00	Sr. Free Hgb, TEG, Coagulation profile, CMP, CBC with differential, AT III activity, Triglyceride, Phosphorous, Magnesium, ACT Recalibrate ECMO circuit: SvO_2, ABG	ACT, Coagulation profile, CMP, CBC with differential, Triglyceride, Phosphorus, Magnesium, AT III activity* (Sr. Free Hgb†) (TEG‡) Recalibrate ECMO circuit: SvO_2, ABG
05:00	–	–
06:00	ACT	–
07:00	–	–
08:00	ACT	–
09:00	–	–
10:00	ACT	aPTT
11:00	–	–
12:00	ACT, aPTT, H&H with platelets	–
13:00	–	–
14:00	ACT Recalibrate ECMO circuit: SvO_2, ABG	–
15:00	–	–
16:00	ACT	ACT, aPTT, H&H with platelets Recalibrate ECMO circuit: SvO_2, ABG
17:00	–	–
18:00	ACT, aPTT, AT III, H&H with platelets, BMP, iMg	–
19:00	–	–
20:00	ACT	–
21:00	–	–
22:00	ACT Recalibrate ECMO circuit: SvO_2, ABG	aPTT
23:00	–	–
24:00	ACT, aPTT, H&H with platelets	–
	Total scheduled labs: 36	Total scheduled labs: 19
	Minimal blood volume: 24.5 mL	Minimal blood volume: 16 mL

*AT III is every 12 hours × 4 and then daily.

†Sr. Free Hgb to be drawn after extended time on pump and if hemoglobin is repeatedly low.

‡TEG available upon request.

ABG, arterial blood gas; ACT, activated clotting time; aPTT, activated partial thromboplastin time; AT III, antithrombin III activity; BMP, basic metabolic panel; CBC, complete blood count; CMP, complete metabolic panel; ECMO, extracorporeal membrane oxygenation; H&H with platelets, hemoglobin and hematocrit with platelets; iMg, ionized magnesium; Sr. Free Hgb, serum free hemoglobin; SvO_2, mixed venous oxygen saturation; TEG, thromboelastography.

tests to twice daily and aPTT testing to every 4 hours until anticoagulation stabilized, then routinely every 6 hours. A full coagulation panel was scheduled every morning and antithrombin III activity testing every 12 hours for 2 days and then daily. The new guidelines replaced the afternoon complete blood count test with a focused hemoglobin, hematocrit, and platelet count. The thromboelastography (TEG) test was removed from routine ordering and used when specified from the hematology attending.

Electrolytes

A practice review reduced electrolyte measurements to once per day and as needed.

Gas exchange

Providers were encouraged to use clinical indicators to evaluate gas exchange function (i.e., arterial blood gases) and the organization added a POCT blood gas cartridge that used the same volume of blood but at a lower cost.

The pertinent institutional review boards determined this project did not meet the definition of human subject research and it proceeded as a quality improvement project. The preimplementation and postimplementation population demographics are presented in Table 2. Retrospective preimplementation data were obtained for the PICU ECMO population October 1, 2016 through September 30, 2017. These data were compared for quality improvement with postimplementation data. All stable patients regardless of age or size undergoing ECMO therapy in the PICU from October 1, 2017 through September 30, 2018 were included in the postimplementation group. Each group had one patient who had undergone two ECMO "runs" and both "runs" are included in the data.

RESULTS

The quality metrics are listed in Table 3. Key findings were the following: total length of hospital stay (TLOS) decreased by 8 days, mortality rates decreased by 9.5%,

Table 2. Patient demographics.

	Preimplementation	Postimplementation
Number of ECMO cases	15	20
Number of patients	14	19
Ethnicity		
White	10	11
African American	2	2
Hispanic	0	5
Asian	1	0
Other		1
Age (average in months)	20.13	3.83
Sex		
Female	4	2
Male	10	17
Type of ECMO		
VA	14	16
VV	1	4
Post CV surgery (CPB)	2	7
ECPR	4	3
Cardiogenic shock/ Hemodynamic instability	8	12
Respiratory failure	3	5

CPB, cardiopulmonary bypass; CV, cardiovascular; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; VA, venoarterial ECMO; VV, venovenous ECMO.

CLABSI rates were unchanged, pRBC transfusions while on ECMO decreased from 100% to 85%, average laboratory tests per ECMO day decreased by 52% (128.4 vs. 61.1) even with an increase in ECMO hours and days per case, and direct cost per case decreased by 14.7%.

DISCUSSION

Patients on ECMO require laboratory testing to evaluate therapeutic progress and adverse effects of therapy.

Table 3. Pediatric ECMO quality improvement project summary.

Metrics	Preimplementation	Postimplementation
Cases	15	20
Patients	14	19
Average TLOS	86.1	78.1
Average ECMO hours per case	143.8	165.5
Average ECMO days per case	7.2	8.1
Mortality rate	20%	10.5%
CLABSI	0	0
Cases receiving pRBC transfusion	15	17
Average lab test per ECMO day	128.4	61.1

CLABSI, central line-associated blood stream infection; ECMO, extracorporeal membrane oxygenation; pRBC, packed red blood cell; TLOS, total length of stay.

This quality improvement (QI) project safely reduced the number of laboratory tests, costs, and iatrogenic anemia in this specialized patient population. The majority of patients in both groups received ECMO therapy for cardiogenic shock/hemodynamic instability (8 vs. 12), other reasons for support included emergent placement with cardiopulmonary resuscitation (CPR) (4 vs. 3), and respiratory failure (3 vs. 5). Secondary findings of this study included a decrease in mortality rates (20% vs. 10.5%) and reduced TLOS (86.1 vs. 78.1 days). It is important to address these specific metrics to show that reducing lab tests did not negatively impact mortality or TLOS at our institution. Rates for CLABSI while on ECMO remained zero in both groups; however, there was a concurrent QI project for CLABSI reduction.

Historically, the unit performs more VA than VV ECMO. Hemolysis is more common in VA-ECMO and these patients traditionally consume more blood products when compared with VV-ECMO (15). Considering this, usually VA-ECMO therapy resulted in more laboratory testing; yet this project was able to reduce laboratory testing and pRBC transfusions for both types of ECMO therapy. The postimplementation group decreased the number of laboratory tests and volume of blood drawn even though more patients received VA than VV-ECMO (16 vs. 4) and patients were younger (20.13 months vs. 3.83 months). The practice in our PICU is to draw the absolute minimum volume of blood per test as deemed by our laboratory. The previous guidelines required a minimum of almost 25 mL per day compared to the new guidelines of 16 mL per day. Every patient in the preimplementation group received a blood product transfusion while on ECMO. Three patients did not receive additional blood products while on ECMO, two of these patients were on VV ECMO and one on VA ECMO. This finding is important because of the risks associated with blood product transfusion (8). Reducing the volume of blood drawn decreases the risk for iatrogenic anemia and the need for blood product transfusions.

In the postimplementation group, six patients had hemorrhage requiring $\geq$100 mL/kg of blood product transfusion. At the time of this project, a potential treatment option with aminocaproic acid was not possible because of a national shortage.

One patient in the preimplementation group required ECMO therapy twice, separated by 8 days, both times for hemodynamic instability. One patient in the postimplementation group required ECMO therapy twice, separated by 9 days. For both of these patients, their first ECMO therapy followed congenital heart surgery. The patient in the postimplementation group required ECMO the second time for respiratory failure.

Laboratory tests are essential diagnostic tools for managing critically ill patients receiving ECMO therapy and

there is no national standard regarding their use. It is important to recognize the laboratory guidelines outlined in Table 2 worked best for our organization and style of practice. Using EBP, national benchmarking against high-performing centers, and interprofessional collaboration our goal to improve care while decreasing cost was realized. Following this project, the organization became the benchmark institution within iVantage for fiscal year 2018.

CONCLUSIONS

This project took place at one organization with a small sample size. Replication in a large-volume ECMO center is recommended to determine whether these results are reproducible. The revised ECMO lab draw guidelines were successfully implemented and reduced cost and decreased blood transfusions without adverse effects on TLOS or mortality rates. Recommendations for future projects include more quality improvement initiatives targeted at patients undergoing ECMO therapy.

At our institution, a set of structured guidelines combining planned laboratory testing with clinical assessment improved the organization's use of resources, and improved the patient experience for those undergoing ECMO therapy.

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