

Case Reports

Long-term Extracorporeal Circulation Management: The Role of Low- and High-range Heparin ACT Tests

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Abstract: Modern management of extracorporeal circulation, especially during long-term support of post-cardiac surgical patients, remains challenging and requires optimal care of the patient's fluid balance and coagulation hemostasis for its successful outcome. The activated clotting time assay is one of the tests used to manage extracorporeal circulation and is available in a low- and high-range level. The question of which assay is more appropriate for procedures that require low to moderate heparin

dosing is still unclear. We report our experience with a neonate diagnosed with hypoplastic left heart syndrome who needed emergent extracorporeal membrane oxygenation support for 13 days after Norwood stage I palliation using a Sano shunt. Although successful, bleeding complications prompted us to review our strategy for management of coagulation hemostasis. **Key-words:** extracorporeal, membrane, oxygenation, heparin, clotting, thrombelastograph. *JECT. 2008;40:271–274*

Management of post-cardiac surgical patients on extracorporeal membrane oxygenation (ECMO) remains a challenge because bleeding complications and hemodynamic instability remain formidable barriers to its successful outcome. Moreover, the complexities in understanding and treating deficiencies in coagulation are compounded by many factors, causes, and effects of the ECMO system itself. This reality underscores the importance of the rapid bedside testing needed to direct therapies that promote and maintain hemostasis during these critical life-saving procedures. Heparin therapy for anticoagulation management may be divided into high-, moderate-, and low-dose regimens depending on the level of anticoagulation required. Different activated clotting time (ACT) tests have therefore been developed to improve test sensitivity for varying circulating heparin concentrations. High-range ACT assays with lower sensitivity to heparin are intended for use during procedures needing moderate to high heparin levels, whereas low-range ACT assays have a higher sensitivity to heparin and more accurately monitor the

response of low to moderate heparin concentrations. We report herein a neonate with hypoplastic left heart syndrome (HLHS) that needed emergent ECMO support for 13 days after Norwood stage I palliation using a Sano shunt. Although successful, bleeding complications prompted us to review our strategy for management of coagulation hemostasis.

CASE REPORT

A 2.7-kg 10-day-old girl diagnosed with HLHS and aortic atresia underwent a modified Norwood stage I procedure with right ventricle to pulmonary artery conduit (Sano modification). After three failed attempts to wean from cardiopulmonary bypass (CPB), the patient was placed on emergent ECMO consisting of a BP50 centrifugal pump, carmeda-coated tubing pack, AVECOR 800 membrane oxygenator (Medtronic, Minneapolis, MN), DHF 0.2 hemoconcentrator (Dideco, Mirandola, Italy), TWINFUSE syringe pump (Sims Graseby, Watford Herts, UK), Hemochron Jr ACT monitor (International Technidyne, Edison, NJ), and a thrombelastograph (TEG) analyzer model 5000 (Haemoscope, Niles, IL). Full flow of .55 L/min was based on a cardiac index of 3.0 L/min/m². Pressure ventilation with a rate of 25 breaths/min and 40% oxygen was used to maintain pulmonary

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insufflations. Initial ACT values after CPB were >600 seconds. ACT tests were performed every 20 minutes for the first 6 hours using high-range cartridges. A heparin infusion of 30 units/kg/h was started 6 hours after the initiation of ECMO and over the following 24 hours would reach 120 units/kg/h to maintain our target ACT range of 180–200 seconds. ACT testing continued with high-range cartridges each hour after the first 6 hours or as needed during platelet administration and periods of increased urine output. TEG studies were performed every 24 hours and used to guide component therapies with the following trigger points: platelet transfusions for a maximum amplitude (MA) <51 mm, cryoprecipitate transfusions for a alpha angle (α) <55°, and fresh frozen plasma transfusions for a reaction time (R) >8 minutes. All vital signs and ECMO system parameters were monitored every hour with hematology and biochemistry workups done every 4 hours. Blood product transfusions were given any time: platelet counts <100,000 $\times 10^9/\mu\text{L}$, hemoglobin <12 g/dL, and fibrinogen <1.5 mg/dL. Fluid balance was calculated every hour and chest x-rays performed daily. Oxygen transfer and extraction values were calculated routinely to assess oxygenator function. On day 13, the patient was successfully weaned from ECMO support with intact neurologic function.

Postoperative blood loss of >8 L during the ECMO period required 115 blood product transfusions to promote hemostasis and volume replacement. On day 8, as ACT heparin requirements exceeded 200 units/kg/h and blood loss continued to increase, high-range ACT cartridges were replaced with low-range cartridges to rule out over heparinization and inadequate test sensitivity. The effects of this change can be seen graphically in Figure 1. A new target ACT of 220 seconds was also instituted to avoid possible complications of inadequate anticoagulation while using a more heparin sensitive low-range ACT assay.

Ultrasound examination of the head on days 7 and 10 showed multiple small (2–4 mm) petechial hemorrhages in both cerebral hemispheres with no ventricular bleeds or dilation. Despite adequate urine output, a hemoconcentrator was started on day 8 to address a worsening generalized edema. Over the following 5 days, >1400 mL were removed resulting in a progressive improvement in the patients fluid balance as shown in Figure 2. A syringe pump attached to the hemoconcentrator's effluent line was used to precisely control the amount of clear fluid removed from the ECMO system. Native kidney function was maintained with a Lasix infusion during hemofiltration, which lasted until weaning was completed on day 13.

Mechanical failure of the ECMO system was low with only the centrifugal pump head requiring replacement on days 6 and 10 because of the presence of hematuria, while membrane oxygenator performance remained adequate

throughout the ECMO run with no perceived changes after modification to our anticoagulation management.

DISCUSSION

ECMO may be one of the greatest challenges in the post-cardiac surgical patient and anticoagulation with appropriate volume replacement forms the cornerstone of its management. Inadequate anticoagulation may precipitate a consumptive coagulopathy causing further blood loss or possible clot formation and premature oxygenator failure. Conversely, bleeding caused by overheparinization may limit ECMO pump flow and tissue oxygenation and exposes the patient to increased risk of blood product transfusions and further derangements in fluid and electrolyte balance. The ability to make rapid bedside decisions for therapies directed at controlling this delicate poise is crucial in achieving hemostasis.

Bedside management of heparin therapy with ACT testing alone is difficult and can be deceiving. ACT results are used as a valuable guide to heparin response but can easily be influenced by factors other than the effects of heparin (1). Moreover, poor platelet function, low platelet counts, and depleted coagulation proteins with elevated fibrin split products can all affect ACT results (2,3). When platelet function and circulating concentrations of coagulation proteins are low, final clot formation may be weak, giving a prolonged endpoint ACT value. This scenario may elicit a false sense of security, whereas heightened activation and continued consumption of coagulation proteins exists.

Under these circumstances, the TEG may be used to see more clearly the bigger picture of coagulation management (4,5). In our experience, the TEG has proven to be a useful bedside test that together with ACT monitoring greatly simplifies hemostasis management during cardiac ECMO. TEG studies can rapidly detect specific causes of bleeding and aid in the implementation of their related blood component therapies. The TEG model 5000 is a dual channel analyzer that allows the user to run two kaolin-activated tests simultaneously to evaluate clot mechanics. Heparinase is used in one channel to compare test results with and without the effects of heparin. The thrombelastograph is capable of monitoring both enzymatic activation and platelet function separately and can help differentiate between surgical bleeding, Von Willebrand's factor deficiency, general clotting factor deficiencies, low fibrinogen levels, poor platelet function, coagulation disturbances caused by hypothermia, and a host of hypercoagulable and hyperfibrinolytic states.

The ECMO setting, however, may be further complicated by the constant fluctuation of circulating blood heparin levels. Different ACT tests are designed to perform

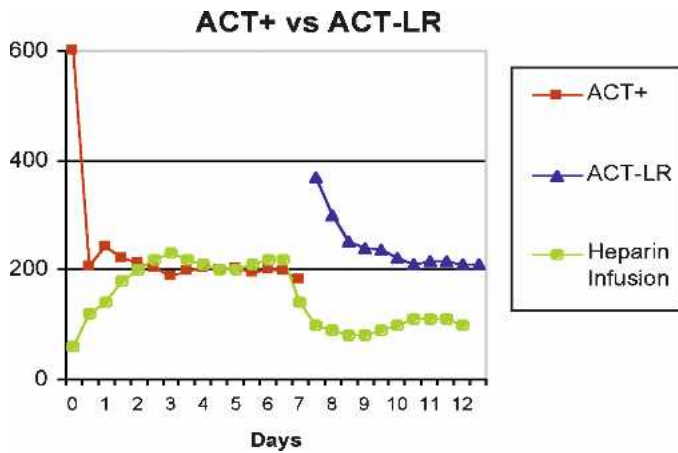


Figure 1. Heparin infusion rates at 12-hour intervals for ACT+ and ACT-LR tests. ACT+, activated clotting time test (high range) in seconds; ACT-LR, activated clotting time test (low range) in seconds; Heparin Infusion, heparin infusion rate in units/kg/h.

with sensitivity to specific ranges of circulating heparin. The manufacturer recommends the Hemocron Jr ACT+ test be use for heparin levels between 1 and 6 units/mL of blood and the Hemocron Jr ACT-LR test for levels up to 2.5 units/mL of blood. Because circulating heparin level requirements for cardiac ECMO commonly fall within the overlap in functional ranges between the two ACT assays, the decision as to which test to use is often left to the individual clinician. Furthermore, the patient’s constantly evolving coagulation profile, fluid balance, metabolic rate, and urine output will all have an effect on blood heparin levels and resulting ACT values.

Patients needing ECMO support after failure to wean from CPB will have a higher circulating heparin concentration at the start of ECMO compared with several hours after its initiation and after high-range ACT values have been allowed to drift down toward 200 seconds. This raises the question of whether changes in ACT test sensitivity are appropriate for the changes in circulating heparin levels invariably seen in the post-surgical ECMO patient. We changed our ACT monitoring to low-range tests on day 8

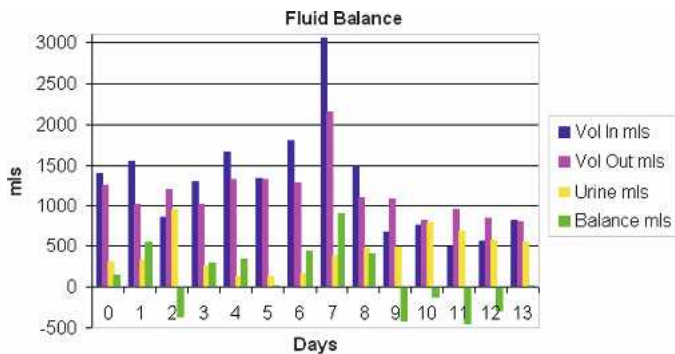


Figure 2. Volume intake and output vs. net daily fluid balance. Vol In mLs, volume intake in milliliters; Vol Out mLs, volume output in milliliters; Urine mLs, urine production in milliliters; Balance mLs, net daily fluid balance in milliliters.

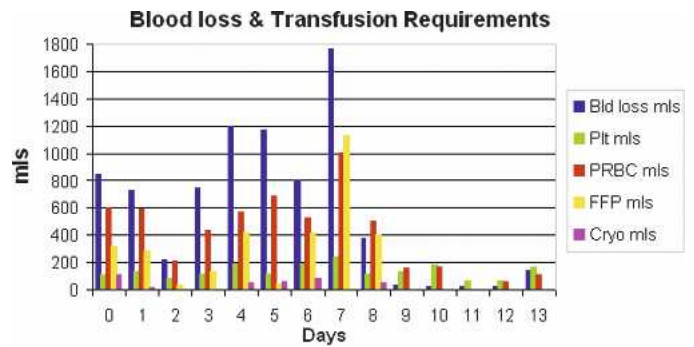


Figure 3. Blood loss vs. blood product transfusion at 24-hour intervals. Bld loss mLs, daily blood loss in milliliters; Plt mLs, daily platelet transfusion in milliliters; PRBC mLs, daily pack red blood cell transfusion in milliliters; FFP mLs, daily fresh frozen plasma transfusion in milliliters; Cryo mLs, daily cryoprecipitate transfusion in milliliters.

and confirmed a decrease in heparin requirements needed to maintain a target ACT value of 220 seconds. The decreased heparin infusion rate was quickly paralleled by a dramatic drop in blood loss as shown in Figure 3, suggesting overheparinization may have played a role in transfusion requirements seen before day 8. Normalization in TEG values, specifically reaction time (R time), was also achieved after the change in ACT monitoring as shown in Figure 4.

Heparin assay testing may also be used in this instance to determine circulating heparin levels and to guide the transition to a more appropriate ACT test if needed (6,7). Monitoring heparin levels may have helped detect an exaggerated heparin requirement earlier and could have saved this patient from numerous blood product transfusions. Although not used here, this case highlights the need for its consideration in the future.

Although the question of which ACT test is more appropriate for this patient population is still unclear, Figures 1–4 support the logic that a more sensitive low-range ACT test may be better suited in managing the lower circulating heparin levels commonly used during cardiac ECMO procedures.

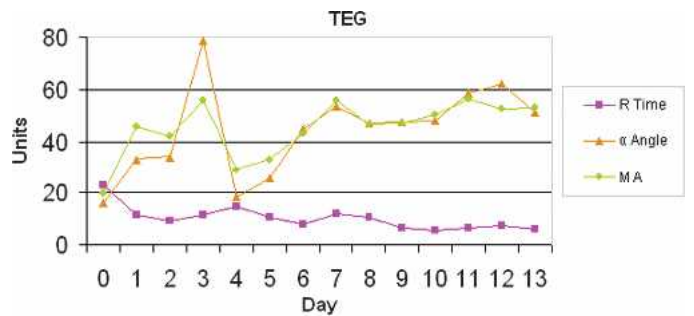


Figure 4. Heparinase TEG results at 24-hour intervals. R Time, reaction time in minutes (normal range, 4–8 minutes); α Angle, alpha angle in degrees (normal range, 47–74 degrees); MA, maximum amplitude in millimeters (normal range, 55–73 mm).

CONCLUSION

This case highlights the complexities of monitoring anticoagulation and shows the importance of using multiple strategies to manage heparin therapy during cardiac ECMO. The high circulating heparin concentrations typically seen when converting from CPB to ECMO necessitates the use of high-range ACT test cartridges. The question remains: should it continue to be used throughout the ECMO procedure as circulating heparin concentrations decrease?

We routinely use TEG studies in conjunction with high-range ACT testing to monitor heparin therapy during ECMO. This case report has helped us further in recognizing the potential advantages of also monitoring circulating heparin levels and the possible need for a more heparin-sensitive ACT test during extracorporeal procedures requiring low to moderate heparin dosing.

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