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CLINICAL PRACTICE

Point-of-care coagulation testing and transfusion algorithms

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Patients with cardiovascular disease have an array of haemostasis disorders that predispose to the development of thrombotic and embolic disease states. These patients are often maintained on anti-thrombotic medication to prevent adverse cardiovascular events. Patients undergoing cardiac surgery also have haemostatic disorders that include their intrinsic disease state, adjunctive medication, and the coagulation disturbances induced by cardiopulmonary bypass. The following review introduces the monitors that are available for monitoring perioperative coagulation, with an emphasis on cardiovascular surgery. Heparin monitors, platelet function monitors for use in transfusion algorithms, and monitoring anti-platelet drugs will be discussed.

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Patients undergoing coronary artery bypass grafting (CABG) account for ~10% of the estimated 3.2 million annual recipients of red blood cell transfusions.[41] The haemostatic management of patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) necessitates an important and delicate balance between anticoagulation during CPB and proper haemostasis after CPB. These patients are at risk for excessive perioperative blood loss often requiring transfusion of blood products. In the past, clinicians administered blood products empirically due to long turnaround times of laboratory-based coagulation tests. This practice exposes patients to inappropriate blood therapy resulting in increased morbidity and mortality and hospital costs.[3 10 65] Today, point-of-care (POC) devices are available providing rapid bedside monitoring to aid the clinician in directing appropriate targeted therapy.[59 62] The majority of POC devices used today can perform multiple coagulation tests. The use of transfusion algorithms in conjunction with POC testing has been shown to reduce both transfusion requirements and blood loss in cardiac surgery.[1 9 15 17 25 27 29 56 66 69] This review discusses current and pertinent perioperative POC monitors for coagulation, platelet function, and anti-platelet drug therapy and their respective roles in transfusion-guided algorithms.

Platelet dysfunction in cardiac surgery

Patients who present for cardiac surgery often have pre-existing platelet defects that can be acquired or drug-induced. Many patients are prescribed anti-thrombotic medication for disease states such as peripheral vascular disease and cerebrovascular disease, and thus can present for surgery with pharmacologically impaired coagulation and/or platelet function.[28] Platelet number can also be reduced in patients who have been exposed to heparin. The potential for relative thrombocytopenia and platelet dysfunction makes platelet function very vulnerable. CPB itself also has many anti-platelet adverse effects.[36] The literature supports that CPB down-regulates glycoprotein (GP)Ib and GPIIbIIIa receptors and decreases platelet responsiveness to thrombin and adenosine diphosphate (ADP).[23 44 55 70 76] After cardiac surgery utilizing CPB, platelet function is compromised for at least 24 h. Couple this dysfunction with pre-existing anti-platelet effects from medication, and it becomes evident why it is so important to monitor platelet function in cardiac surgery.[26 67] POC platelet analysers provide rapid assessment of platelet function and can measure the effects of anti-platelet therapy.

Platelet function is a complex series of interactions of the endothelium with whole blood that provides platelets and coagulation factors for haemostasis. The gold standard measure of platelet function is platelet aggregometry using platelet-rich plasma. This laboratory technique is labour-intensive and time-consuming and thus is not applicable for the surgical patient. POC tests of platelet function have become more prevalent in monitoring both surgical and medical patients. Because these tests assay whole blood, are portable, and are user-friendly, they are more easily

adaptable for use at the bedside. All platelet function tests are not alike; the aetiology of the platelet dysfunction dictates that the type of test can be used to monitor platelet function. Platelet inhibition in patients treated with anti-thrombotic drugs can be tested using a variety of tests as discussed below. After CPB, the platelet defect is quite profound and is best monitored with visco-elastic whole-blood tests such as thromboelastography without modification.

Platelet function can be assessed in the static phase, dynamic phase, and as a response to an agonist. Static measures of platelet function, such as the measure of β-thromboglobulin release or mean platelet volume, are not very valuable measures of platelet function, as they capture function at a single point in time. Dynamic tests, such as the visco-elastic tests and the response to a platelet agonist, are more reflective of platelet function over time. The specific agonist used can be thrombin or collagen which test the platelet response to endothelial injury and thus its ability to mediate haemostasis *in vivo*. These agonists are commonly used for platelet function tests as utilized in transfusion algorithms for bleeding patients. Other agonists can be used to assess platelet responsiveness in patients taking anti-thrombotic drugs. The commonly used tests use ADP or arachidonic acid in order to test the efficacy of clopidogrel or aspirin, respectively, in inhibiting platelet function.

POC platelet function tests using a platelet agonist

Platelet Function Analyzer (PFA-100®)

The Platelet Function Analyzer (PFA-100) (Siemens, Deerfield, IL, USA) monitor conducts a modified quantitative *in vitro* bleeding time under artificially created high-shear conditions. Whole blood is placed on a test cartridge and a vacuum perfuses the blood across a collagen-coated membrane. An aperture is created in the membrane by a 'punch' in the presence of either epinephrine or ADP as agonist. The shear force of whole blood being drawn through a vacuum activates platelets and promotes platelet adherence and aggregation. The time it takes for a clot to form inside the glass tube and prevent further blood flow is measured as closure time.[38] Measurements of closure time depend on functional platelet GPIb and GPIIbIIIa, von Willebrand factor, platelet count, and haematocrit.[39] The response to epinephrine can detect aspirin-induced platelet dysfunction.[51] Clopidogrel effect could not be measured by the ADP channel in testing of cardiology patients.[52] Both channels, ADP and epinephrine, accurately detect platelet dysfunction in von Willebrand's disease and in uraemia. In cardiac surgical patients, Slaughter and colleagues[63] demonstrated that the PFA-100 closure time has only a high negative predictive value and thus might help in identifying patients who are unlikely to need platelet transfusions to reduce bleeding. Its positive predictive value is low and thus it is not very useful in transfusion algorithms to direct transfusion therapy as many 'false-positive' patients would be transfused.[16 21 63 75] Positive predictive value has been difficult to attain with many POC tests of platelet function.[16] Cammerer and colleagues have prospectively studied a group of cardiac surgical patients using observational measurement of platelet function to predict bleeding. They reported that thromboelastography (discussed later) was a better predictor of bleeding than the PFA-100, however if the PFA-100 ADP test was used in addition to thromboelastography, the predictive accuracy was enhanced.[5]

VerifyNow®

The VerifyNow system (Accumetrics, San Diego, CA, USA) is a POC turbidimetric-based optical detection system that measures agonist-induced agglutination of whole blood. A mixing chamber contains the platelet agonist [thrombin receptor-activating peptide (TRAP), arachidonic acid, or ADP, and fibrinogen-coated beads]. After anticoagulated whole blood is added to the mixing chamber, platelets are activated if they are responsive to the agonist. The activated GPIIb/IIIa receptors on the platelets bind to adjacent platelets via the fibrinogen on the beads and cause agglutination of the blood and the beads. Light transmittance through the chamber is measured and increases as agglutination increases, much like standard aggregometry. Anti-thrombotic drug effects reduce agglutination (measured by light transmittance) and thus the degree of platelet inhibition can be quantified. Direct pharmacological block of GPIIb/IIIa receptors with a GPIIb/IIIa antagonist is detected with a very high accuracy using this device and the TRAP agonist. More recent cartridges using arachidonic acid as the agonist have been developed that can accurately assess aspirin-induced platelet dysfunction. Through inhibition of arachidonic acid, indirect prevention of GPIIb/IIIa expression is accomplished. The anti-platelet effects of clopidogrel can also be measured using a VerifyNow cartridge that incorporates ADP as the agonist.[43 52] Each of these drug effects can be measured using the appropriate cartridge of the VerifyNow device.[74]

Platelet Works®

Platelet Works (Helena Laboratories, Beaumont, TX, USA) is a whole-blood assay that uses the principle of the platelet count ratio to assess platelet reactivity. The instrument is a Coulter counter that compares platelet counts in a standard ethylenediaminetetraacetic acid tube with platelet counts in a citrate tube after aggregation with either ADP or collagen. When blood is added to these agonist tubes, platelets activate, adhere to the tube, and are effectively eliminated from the platelet count. The ratio of the

activated platelet count to the non-activated platelet count is a function of reactivity of the platelets. Early investigation indicates that this assay correlates well with standard platelet aggregometry and is capable of measuring the platelet dysfunction induced by GPIIb/IIIa receptor inhibitors and clopidogrel.[8 40] Although the disadvantage of Platelet Works is that it is not well studied, investigations show that it is capable of measuring the platelet dysfunction that accompanies CPB.[49]

The real value in testing the platelet response to a specific agonist is derived from the measure of specific platelet defects that accompany anti-thrombotic drug therapy. Many of these tests utilize small doses of agonists that are sensitive to drug therapy but are not sufficient to challenge platelet function that is more severely compromised. When platelet function is overtly deranged, such as after CPB, a potent agonist is necessary to determine whether the platelet can respond. This potent agonist is usually thrombin and is the 'natural' platelet agonist that is used in the visco-elastic tests of clot formation. Thus, the visco-elastic tests, thromboelastography and thromboelastometry, have been most frequently used in transfusion algorithms for bleeding patients as described below.

Visco-elastic tests of clot formation

Sonoclot

The Sonoclot Analyzer (Sienco Inc., Wheat Ridge, CO, USA) is a test of the visco-elastic properties of blood that provides accurate information on the entire haemostasis process including coagulation factors, fibrin gel formation, clot retraction (platelet function), and fibrinolysis. This device consists of a tubular probe that oscillates up and down within a blood sample. The viscous force of the blood creates impedance to the ultrasonic vibrating probe as it clots, which is converted to an output signal. This electronic signal is processed by a microcomputer and is reported as the Clot Signal. The Sonoclot Analyzer reports these properties by graphically recording the dynamics of clot formation as a Sonoclot Signature and also yields quantitative results. The Sonoclot Signature is the plotted values of the Clot Signal value *vs* time. The quantitative results include a lag period (SonACT) that corresponds to activated clotting time (ACT) and a wave that occurs as a result of cross-linkage of fibrin (Clot RATE). Other parameters in the tracing indicate platelet–fibrin binding, fibrin formation, and clot retraction. Clot retraction is a measure of platelet activity and its quantitative parameter is the time to peak. Haemostasis abnormalities including platelet dysfunction, factor deficiencies, anticoagulant effects, hyperfibrinolysis, and hypercoagulable states can be detected using the Sonoclot. In addition, Sonoclot analysis has been successfully used for diagnosing and treating platelet dysfunction and bleeding disorders after CPB.[20 46 51]

Thromboelastograph

The thromboelastograph (TEG), invented in 1948, is another test of the visco-elastic properties of blood that examines the time of initiation through acceleration, control, and eventual lysis. Initially used for coagulation monitoring during liver transplantation, the TEG has found applications in cardiovascular surgery, obstetric anaesthesia, and trauma anaesthesia.[5 22 34 35 77] A small amount of blood (0.36 ml) is placed in an oscillating cuvette and a piston is lowered into the blood sample. The cuvette oscillates at an arc angle of 4° 45 min. As the blood begins to clot, the elastic force exerted on the piston is translated to a signature tracing (thromboelastogram; Fig. 1) that reveals information about fibrin formation, platelet–fibrin interactions, platelet clot strength, and fibrinolysis. With the current disposables, an activator is needed because the onset to coagulation varies, and the time to clot formation can conveniently be accelerated so that the test is useful in POC settings. Celite, kaolin, or tissue factor have all been used to activate the TEG.[30 72]

There are five parameters to the TEG tracing that measure different stages of clot development: *R*, *K*, α angle, maximum amplitude (MA), and MA60 (Fig. 2). In addition, clot lysis indices are measured at 30 and 60 min after MA (LY30 and LY60). Normal values vary depending on the type of activator used. The *R* value is a

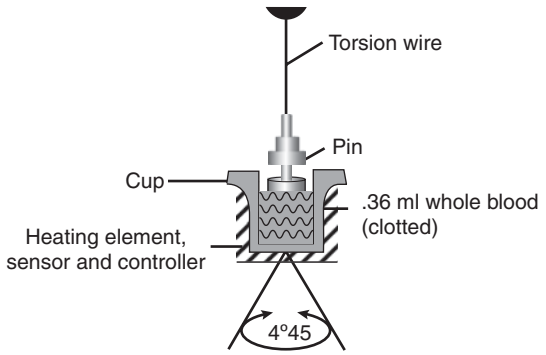

Fig 1 The thromboelastograph uses whole blood in an oscillating cuvette into which a piston is lowered. The movement of the cuvette is translated to an oscillograph tracing as the blood thickens and exerts a force on the piston. This generates the signature thromboelastographic tracing.

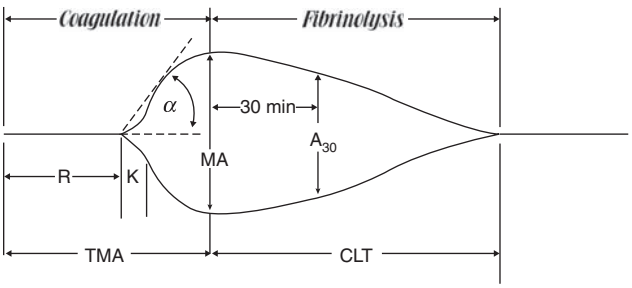

Fig 2 The signature thromboelastograph tracing is shown here with parameters labelled. See text for further details.

measure of clotting time (CT) which is the period of time from the start of the test to the initial fibrin formation. The *K* value is the clot kinetics measurement of the speed to reach a specific level of clot strength: the time from beginning of clot formation (the end of *R* time) until the amplitude reaches 20 mm. The α angle is the angle between the horizontal line in the middle of the TEG tracing and the line tangential to the developing 'body' of the TEG tracing at 2 mm amplitude. The α angle represents the acceleration (kinetics) of fibrin build up and cross-linking (clot strengthening). The MA reflects the ultimate strength of the clot which depends on the number and function of platelets and their interaction with fibrin. The MA is the parameter most frequently measured because it correlates with platelet dysfunction in cardiac surgery. The MA is used as a marker for platelet function and has thus been incorporated into transfusion algorithms used to reduce platelet and other transfusions given to patients after CPB. LY30, or the lysis index at 30 min after MA, is increased with fibrinolysis.

A limitation of the TEG is its inability to detect impairment in platelet function induced by anti-platelet agents. The development of the Platelet Mapping Assay® has overcome this shortfall.

TEG can be used to predict bleeding in cardiac surgery.[12 14 37 71] In large retrospective and prospective studies, incorporation of the TEG into clinical decision-making has resulted in decreased blood loss and transfusions.[3 58 61 68] Spiess and colleagues analysed 1079 patients before and after the introduction of TEG as part of an overall transfusion management strategy. They found significantly less use of all blood and blood components except cryoprecipitate. There was also a significant decrease in the re-exploration rate. However, this study may have been biased by the Hawthorne effect (an improvement in results that may be found just by monitoring a process).[66] In a prospective randomized controlled study, Shore-Lesserson and colleagues[61] compared transfusion requirements with 'TEG-based' and 'traditional' protocols in the management of postoperative bleeding. Patients in both groups received the antifibrinolytic epsilon aminocaproic acid (EACA). Although the study showed no significant difference in mediastinal tube drainage between the groups, blood and blood component therapy were significantly less in the 'TEG' than in the 'traditional group'. Royston and von Kier[58] studied 60 patients who had undergone complex surgery comparing their actual blood and blood product use to predicted usage derived from a TEG-based algorithm. They utilized the TEG *R* value to determine the quantity of fresh frozen plasma needed to reverse the coagulation defect in the post-cardiac surgical patient (Table 1). Though TEG is the best-studied POC device for use in cardiac surgery, further studies are required to recommend TEG as the standard of care for postoperative transfusion management.[13 32]

Table 1 TEG-based transfusion algorithm (from Royston and von Kier[58])

TEG variable	Implication	Therapy
R>14 and <21 mm	↓clotting factors	One fresh frozen plasma
R>21 and <28 mm	↓↓clotting factors	Two fresh frozen plasma
R>28 mm	↓↓↓clotting factors	Four fresh frozen plasma
MA <48 mm	↓↓platelet number/function	One pooled platelets
MA <40 mm	↓↓↓platelet number/function	Two pooled platelets
Lys30 >7.5%	Increased lysis	Aprotinin

TEG modifications

Platelet Mapping Assay®

The development of the Platelet Mapping Assay overcomes some of the shortcomings of the TEG, in that it allows for the thromboelastographic measurement of platelet function in patients on anti-platelet medication. Platelet mapping uses three cuvettes. One incorporates thrombin to activate platelets and overrides the inhibition of other activation pathways such as arachidonic acid, ADP, and GPIIb/IIIa. A second cuvette contains reptilase plus factor XIII to create a fibrinogen clot or a 'thrombin-less' clot. This clot strength will be smaller and will not have the contribution of thrombin-activated platelets. The third cuvette incorporates the fibrinogen clot and adds back ADP or arachidonic acid to stimulate the platelets. The ability of the MA to increase in response to ADP (clopidogrel) or arachidonic acid (aspirin) is a measure of drug-induced platelet inhibition via that particular pathway.[7] This POC test correlates well with the gold standard optical aggregometry.[8]

Rotational thromboelastometry

Rotational thromboelastometry (ROTEM) (Pentapharm, Munich, Germany) provides a visco-elastic measurement of clot strength in whole blood. A small amount of whole blood (0.3 ml) and coagulation activators are added to a disposable cuvette that is placed in a heated holder. A disposable pin (sensor) fixed on the tip of a rotating shaft is lowered into the blood sample. The loss of elasticity upon clotting affects rotation of the shaft that is detected by the reflection of light on a small mirror attached to the shaft. A detector records the axis rotation over time and this rotation is translated into a graph or thromboelastogram.[64 73]

The main descriptive parameters derived by ROTEM are: CT, corresponding to the time (s) from the beginning of the reaction to a 2 mm increase in amplitude. This represents the initiation of clotting, thrombin formation, and the start of clot polymerization. Clot formation time, the time (s) between an increase in amplitude from 2 to 20 mm. This identifies the fibrin polymerization and stabilization of the clot with platelets and factor XIII. Maximum clot firmness (MCF), the MA (mm) reached in the tracing, which correlates with platelet count, platelet function, and the

concentration of fibrinogen. Alpha (α) angle, the tangent to the clotting curve through the 2 mm point. Maximum lysis, the ratio of the lowest amplitude after MCF to the MCF. Maximum velocity (maxVel), the maximum of the first derivative of the clot curve. Time to maximum velocity (t-maxVel), the time from the start of the reaction until maxVel is reached. The area under curve, defined as the area under the velocity curve, that is, the area under the curve ending at a time point that corresponds to MCF.

ROTEM is approved for use in coagulation monitoring in Europe and its use and familiarity are highest there. In a recent study by Spalding and colleagues[64] comparing transfusion rates before and after implementation of a ROTEM-based transfusion algorithm, ROTEM®-guided coagulation management was useful in the choice of the appropriate therapeutic option in the bleeding patient. This reduced costs by avoiding administration of fresh frozen plasma, cryoprecipitate, and platelet concentrates.[64] Its use in cardiac surgery and in transfusion algorithms is likely to be similar to that of TEG. ROTEM is currently under consideration as a coagulation monitoring device by the US Food and Drug Administration.

Impact Cone and Plate(let) Analyzer

In the Impact Cone and Plate(let) Analyzer (CPA; DiaMed Cressier, Switzerland), whole blood is exposed to uniform shear by the spinning of a cone in a standardized cup. This allows for platelet function testing under conditions that mimic physiological blood flow, thus achieving the most accurate and authentic pattern of platelet function. After automated staining, platelet adhesion to the cup is evaluated by image analysis software. The success of the CPA in screening for congenital primary haemostasis abnormalities and in testing platelet response to GPIIb/IIIa antagonists, aspirin, and clopidogrel has been demonstrated.[60] Recent studies suggest that the CPA is a useful tool for testing perioperative platelet function and might help predict postoperative blood loss.[24] Experience with this instrument is limited as it has just become commercially available.

POC testing of heparin effect

Heparin and anticoagulation for CPB

CPB perturbs multiple aspects of haemostatic function. Contact between blood and the artificial circuit surface can activate coagulation. Optimal anticoagulation during CPB is necessary to prevent platelet activation and antagonize coagulation to prevent microvascular clots. The most common anticoagulant in clinical use is heparin because it is easy to dose, administer, measure, and reverse.[4] Heparin works by activating antithrombin III (ATIII). Therefore, appropriate levels of ATIII are necessary for heparin to be effective. Activated ATIII inactivates thrombin and other proteases involved in blood clotting, most notably factor Xa.[31] For decades, most cardiac surgery programmes utilized empiric heparin dosing starting with a bolus based on a patient's weight (300 U kg^{-1}) and subsequent interval dosing. Empiric dosing has since been replaced by the monitored use of heparin.

Heparin monitoring

Activated clotting time

The ACT is the most commonly used functional POC test to measure heparin anticoagulation. The ACT is an automated variation of the Lee-White CT that uses an activator such as celite or kaolin to activate clotting in a test tube. Early tests used whole blood placed in a warmed test tube with diatomaceous earth as an activator. The tubes were tilted back and forth manually until evidence of clot appeared. Currently, the two most commonly used ACT devices are the Hemochron (International Technidyne Inc., Edison, NJ, USA) and the Hemotec (Medtronic Hemotec, Parker, CO, USA). The Hemochron system consists of a precision aligned magnet within a test tube and a magnet detector located within the well. Whole blood is added to a test tube containing an activator (celite, kaolin, glass beads, or a combination of these) and placed in the well. As clot begins to form, the magnet is lifted within the tube displacing the magnet from the magnet detector. The CT is the time the clot takes to displace the magnet at a given distance. The Hemotec device uses a two-chamber cartridge containing kaolin as an activator. Blood (0.4 ml) is placed into each chamber and a daisy-shaped plunger increases and decreases in the chamber. The formation of clot slows the rate of descent of the plunger, and the decrease in velocity of the plunger is detected by a photo-optical system that signals the end of the test. Each ACT analyser is consistent in its ability to reproducibly measure the CT using its specific methodology. There are intrinsic biases built into some of the measurement devices, but repeatability within a given device is high.[2]

ACT monitoring of heparinization has been criticized because of its high variability.[42 47 50 54] The main limiting factor is that it correlates poorly with anti-Xa measures of heparin activity, or with heparin concentration during CPB as a result of hypothermia and haemodilution. This is especially true of paediatric patients whose consumption of heparin is increased.[45] Other factors altering ACT include thrombocytopenia, the presence of platelet inhibitors, platelet membrane receptor antagonists, and the use of the antifibrinolytic aprotinin (celite only). Blood loss and transfusion requirements in patients undergoing CPB can be reduced with more accurate control of heparin anticoagulation and its reversal.

Cascade POC System

A completely different technology for measuring the effect of heparin is used by the Cascade POC System (Helena). This system uses disposable cards with celite

activator to measure heparin activity. This variant of the ACT is called the heparin management test (HMT). This card contains paramagnetic iron oxide particles that move in response to an oscillating magnetic field. When clot formation occurs, movement of the iron oxide particles is decreased. This system is capable of measuring prothrombin time (PT) and activated partial thromboplastin time (aPTT), which will be discussed below. The suitability of this platform for monitoring of ACT during cardiac surgery has been demonstrated in a variety of clinical studies.[53 57] HMT correlates well with anti-Xa heparin activity in CPB and is less variable than standard ACT. In a comparison with ACT, the coefficients of variation were similar between the tests at baseline but were three times higher for the ACT during heparinization. This degree of agreement with plasma anti-Xa measurements has not been demonstrated universally in patients undergoing CPB.[19]

Individual heparin dosing

In vitro techniques have been introduced to measure patient dose–response to heparin. These assays measure the sensitivity to a known quantity of heparin and generate a dose–response curve that enables calculation of the heparin dose required to attain the target anticoagulation. Blood loss and transfusion requirements in cardiac surgical patients can be reduced with more accurate control of heparin anticoagulation and its reversal.[27 32] Similarly, a protamine dose–response curve can be generated using an *in vitro* sample with a known quantity of protamine, thus enabling protamine dosing to be based only upon the level of circulating heparin. The Hemochron RxDX (International Technidyne Corp.) system is an ACT-based heparin dose–response (HDR) assay. Heparin requirement is measured by the heparin response test, and the required protamine dose is measured by the protamine response test.[33] A separate test, the protamine dose assay measures residual-free heparin in the blood. Using this system, other investigators have been able to significantly lower protamine doses, and some have reported significantly reduced transfusions and chest tube drainage in the group that received individualized dosing with RxDx. Another *in vitro* heparinized dose–response assay is the Hepcon (Medtronic) HDR, which constructs a three-point HDR curve using the baseline, 1.5, and 2.5 IU ml^{-1} heparin. From this curve, extrapolation to the desired ACT or heparin concentration yields the indicated dose of heparin. These dose–response assays are used less frequently than weight-based heparin dosing since the latter technique is faster, less expensive, and extremely safe when monitored. It is not clear that individualized heparin dosing alone, in the absence of individualized protamine dosing, affects perioperative blood loss and transfusions in cardiac surgery.

POC monitoring of coagulation status

Current transfusion guidelines for blood-component therapy strongly recommend results of PT and aPTT to guide administration of fresh frozen plasma and cryoprecipitate. Because of the lag time in obtaining results from a central laboratory, many decisions regarding transfusion of blood products are based on clinical judgement.[23] Several POC coagulation analysers are currently available. The former Thrombolytic Assessment System (Pharmaetics Inc., Raleigh, NC, USA), now the Cascade POC (Helena), which was previously discussed for its ability to measure heparin by the HMT, also measures PT and aPTT. The sample is added to a cartridge containing paramagnetic iron oxide particles that oscillate in a magnetic field as described. Specific activating reagents are used for each assay, including rabbit brain thromboplastin for the PT, aluminium magnesium silicate for aPTT, and celite for HMT. The blood moves by capillary action and mixes with paramagnetic iron oxide particles and reagent within the testing chamber. The decreased movement of the particles is detected optically as the sample clots and the result is displayed as time (s) and as international normalized ratio (INR) for PT. The CoaguChekProDM monitor (Roche Diagnostics, Manheim, Germany) uses a whole-blood sample added to a test cartridge that contains a soybean activator and phospholipids. As the sample clots, a laser optically monitors the decrease in blood flow, and the resultant CT is displayed in seconds for PT and aPTT, and as a ratio for INR. This device has been studied in cardiac surgical patients, and the PT result compared favourably with laboratory plasma-based assays at most perioperative time points. The aPTT result also correlated with plasma-based samples but was slightly less accurate and had a significant bias.[48] These same authors used a previous version of this monitor to define normal *vs* abnormal aPTT and PT values after CPB to predict which patients were more likely to have bleeding. A very important application of this POC device has been its use in transfusion algorithms to direct transfusion of fresh frozen plasma and platelets after cardiac surgery.[18] Despotis and colleagues[9] randomly assigned patients with microvascular bleeding to a transfusion algorithm using only the platelet count and the POC PT/aPTT device. The control group received transfusion therapy using standard laboratory testing. In their algorithm, bleeding patients with abnormal coagulation tests were transfused fresh frozen plasma, and bleeding patients with near normal coagulation tests were given platelet pharmacological enhancers or platelet concentrates. Overall, the patients who were treated using the POC transfusion algorithm received significantly fewer allogeneic transfusions than the control group.[9 10]

Conclusions

The benefits of POC testing in surgical patients include rapid turnaround times and specific measurements of haemostasis defects that can direct therapy. The use of specific tests that can be used at the bedside has enabled

Table 2 POC transfusion algorithm outcome studies

Author	Surgery type	Study type	Patients	Outcome
Despotis and colleagues[11]	Cardiac	Prospective	362	Algorithm decreased transfusion and bleeding
Avidan and colleagues[3]	Cardiac	Prospective	102	Two algorithms decreased transfusion
Spiess and colleagues[66]	Cardiac	Retrospective	1079	TEG use decreased transfusion
Shore-Lesserson and colleagues[61]	Cardiac	Prospective	102	TEG algorithm decreased transfusion
Nuttall and colleagues[48]	Cardiac	Prospective	836	Algorithm decreased transfusion and bleeding
Capraro and colleagues[6]	Cardiac	Prospective	1412	Algorithm increased platelet transfusion, no difference in bleeding
Royston and von Kier[58]	Cardiac and heart transplant	Prospective	60	TEG algorithm decreased transfusion

the incorporation of these tests into transfusion algorithms that more directly address the haemostatic problem and allow treatment using fewer allogeneic blood products (Table 2). The tests reviewed here are those that have been studied in the laboratory, in patients, or both and have proven accurate in monitoring haemostatic function. Many have been used in algorithms to treat bleeding patients. There is a major need for anti-platelet drug testing in surgical patients. The ability to detect preoperative platelet inhibition due to clopidogrel or other anti-thrombotic agents will allow stratification and rational management of surgical patients. The use of platelet function monitoring in transfusion algorithms for bleeding patients will increase as we continue to perform more complex surgeries in cardiovascular patients.

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