



NATIONAL BLOOD AUTHORITY
AUSTRALIA

POINT OF CARE COAGULATION TESTING

CASE STUDY
The Prince Charles
Hospital Brisbane

Guidance for Australian Health Providers

November 2014





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Patient Blood Management

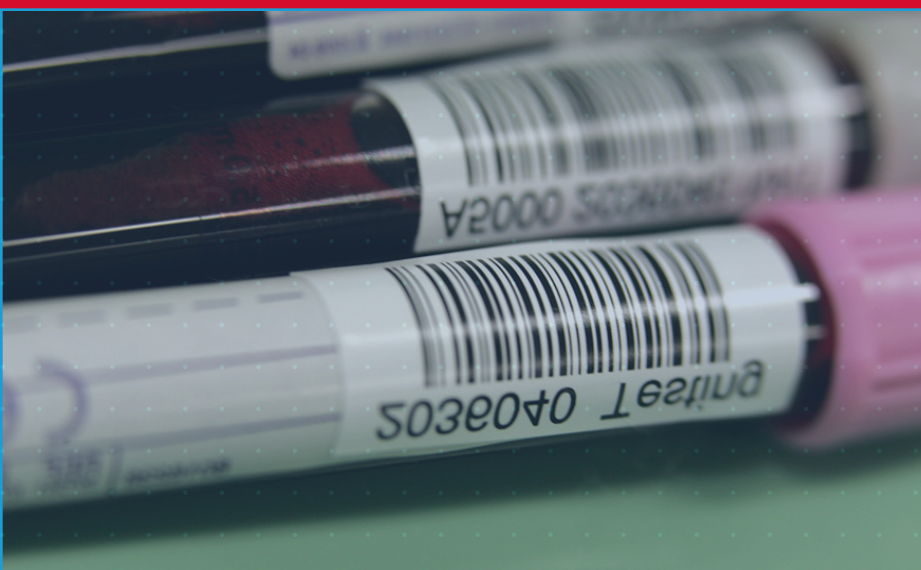
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POINT OF CARE COAGULATION TESTING



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Summary

This case study illustrates efforts undertaken by clinical staff at The Prince Charles Hospital in detecting, managing and monitoring critical bleeding in cardiac surgery patients through the use of Point of Care Coagulation Testing.

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Bleeding Management supported by Point of Care Coagulation Testing



1. Patient Blood Management

Patient Blood Management (PBM) improves patient outcomes through the application of evidence based medical and surgical strategies that optimise and conserve the patient's own blood. The PBM approach requires identification of critical opportunities in the continuum of patient care where communication and coordination between different disciplines can reduce the likelihood that a patient will require an allogeneic blood transfusion.

The clinical practice described in this document primarily focuses on the point of care coagulation testing (POCCT) component of a bleeding management treatment protocol implemented at The Prince Charles Hospital. The use of POCCT and other components in the protocol are underpinned by recommendations in the Patient Blood Management Guidelines: Module 2 Perioperative

R1

GRADE C

Health-care services should establish a multidisciplinary, multimodal perioperative patient blood management program (Grade C). This should include preoperative optimisation of red cell mass and coagulation status; minimisation of perioperative blood loss, including meticulous attention to surgical haemostasis; and tolerance of postoperative anaemia.

R15

GRADE C

In adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, intraoperative cell salvage is recommended (Grade C).

R16

GRADE C

In adult patients undergoing cardiac surgery, the use of TEG should be considered (Grade C).

R17

GRADE A

In adult patients undergoing cardiac surgery, the use of intravenous tranexamic acid is recommended (Grade A).

R21

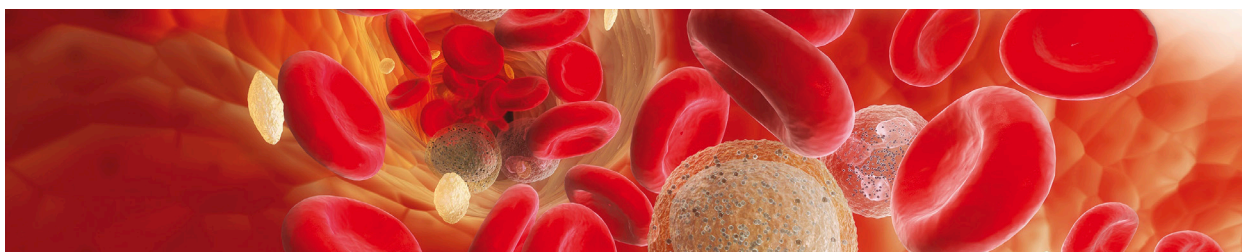
GRADE B

The prophylactic use of FFP in cardiac surgery is not recommended (Grade B).

R22

The prophylactic or routine therapeutic use of rFVIIa is not recommended because concerns remain about its safety profile, particularly in relation to thrombotic adverse events (Grade C).

The following case study illustrates an example of a hospital that has implemented a Bleeding Management Protocol supported by Point of Care Coagulation Testing to detect, manage and monitor critical bleeding in cardiac surgery patients. It demonstrates the systems and tools used to assist with implementation within the cardiac surgery population based on available evidence, developing local expertise and resources.



2. Background The Prince Charles Hospital Experience

The Prince Charles Hospital (TPCH) is a 630 bed major tertiary referral hospital located in the Metro North Hospital and Health Service District in Brisbane, Queensland.

TPCH at a glance

- ◆ 30772 total occupied bed days from July 2013 until June 2014
- ◆ 4969 total separations for surgery from July 2013 until June 2014
 - Orthopaedic surgery: 1758 separations and 10022 occupied bed days
 - General surgery: 1761 separations and 5225 occupied bed days
 - Cardiothoracic surgery: 1450 separations and 15525 occupied bed days

The high volume of blood products required at TPCH was a driver to introduce a comprehensive patient blood management (PBM) program supported by 3 Clinical Nurse Consultants

- ◆ PBM CNC - Anaemia Management: optimisation of iron stores, haemoglobin and red cell mass (0.8 FTE)
- ◆ PBM CNC – Haemostasis Management: optimisation of haemostasis, minimising bleeding & blood loss (0.6 FTE)
- ◆ PBM CNC – Blood Component Therapy & Haemovigilance: optimisation of blood product management and minimisation of transfusion associated risks (0.8 FTE)

Haemostasis Management in Cardiac Surgery

Some bleeding and blood loss is an unavoidable consequence of cardiac surgery. However, excessive and uncontrolled bleeding is a complication which may have a negative impact on patient outcomes. Treatment of bleeding complications invariably includes the transfusion of allogeneic blood products but there is accumulating data this may independently compound complications and mortality. Therefore timely, accurate diagnosis of the cause of bleeding, combined with appropriate management is key to improving outcomes in these situations.

The clinical team at TPCH became aware that a change in culture was needed to shift the focus from 'transfusion practice' to one of 'patient blood management'. After consideration, the team chose to focus initially on intra-operative management of critical bleeding and blood loss. In 2011, Clinical Nurse Consultant Bronwyn Pearse was successful with an application for a 'Metro North SEED Innovation Grant' to initiate implementation of a

bleeding management protocol. The project was also supported financially by 'QLD Health Clinical Access and Redesign' and TPCH. Implementation commenced in July 2012 and ran for a period of 12 months. Implementation involved process mapping across the intra operative and intensive care environment, to identify what current processes were in place and how a bleeding management supported by POCCT could fit in or align with current work practices.

In our centre prior to the introduction of the bleeding management protocol:

- ◆ standard coagulation test results were not practically utilised as results were generated in approximately 50 minutes, rendering them impractical to support active haemostasis management;
- ◆ decisions regarding treatment of bleeding varied widely amongst clinicians and was often pre-emptive.

Empiric and/or pre-emptive bleeding management may result in treatment over and above that which is actually required. Treating the cause of bleeding prophylactically may also lead to dilutional coagulopathy and anaemia.

POCCT in TPCH's bleeding management protocol provided an evidenced based rationale for haemostatic therapy with the following advantages:

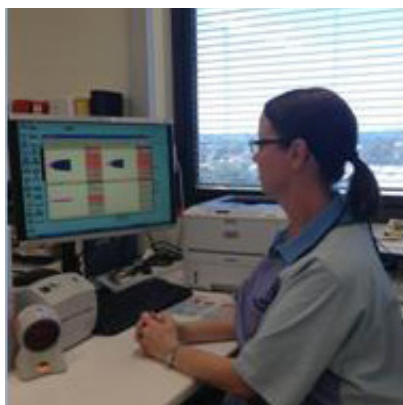
- ◆ rapid generation of results (results available for analysis in 10 minutes) supported prompt diagnosis and timely and appropriate individualised haemostatic interventions.
- ◆ rapid turnaround time was supported by locating the POCCT instruments in a laboratory adjacent to the cardiac operating theatres (OT) and intensive care unit (ICU).
- ◆ subsequent POCCT can be used to track response of treatment.

Results could be streamed live into the appropriate OT or ICU and blood bank permitting concurrent surgical/anaesthesiology/ICU contribution to decision making.

Streaming into OT



Streaming into Blood Bank



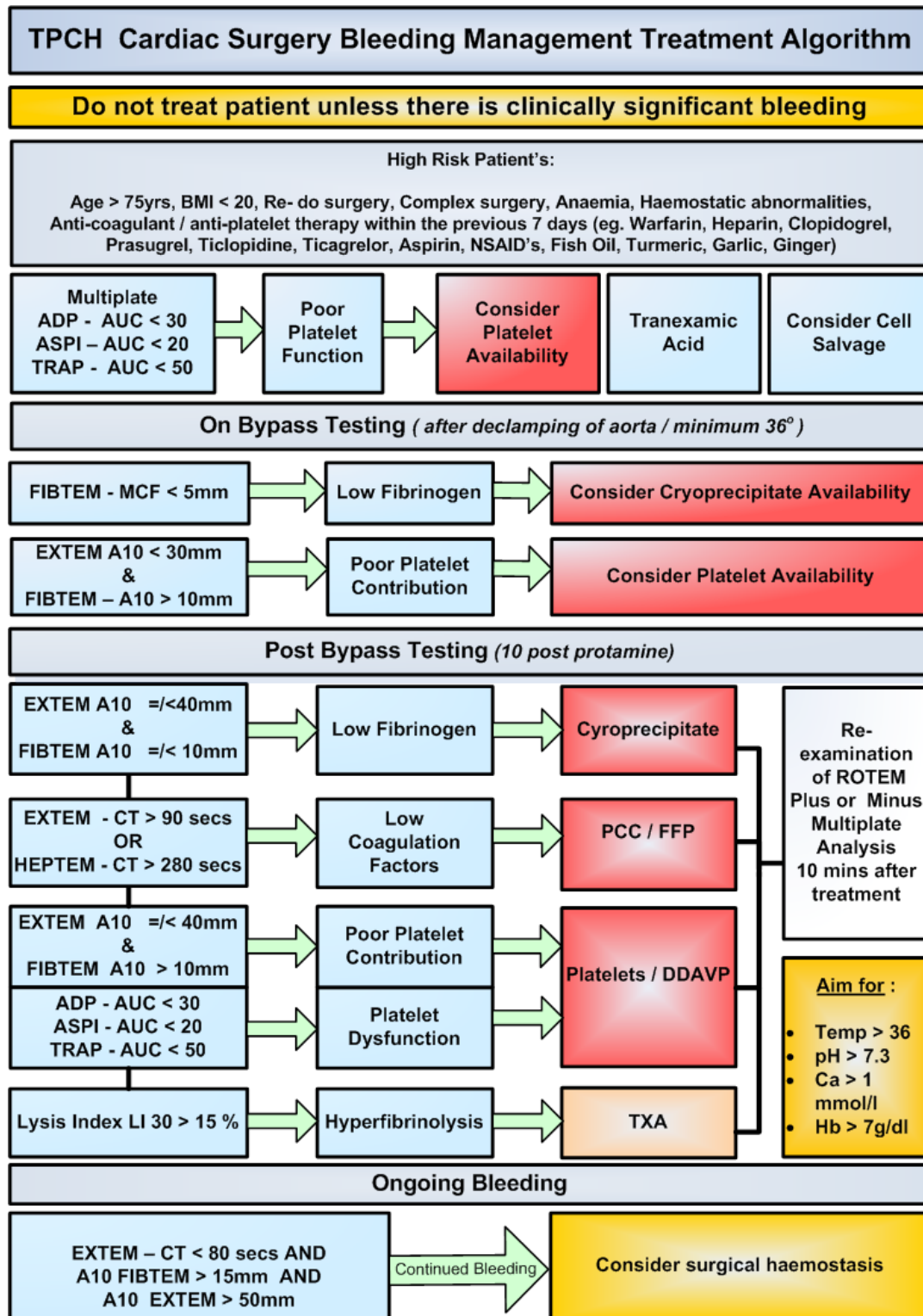
Streaming into ICU



3. Bleeding Management supported by POCCT

Bleeding Management Treatment Algorithm

A bleeding management treatment algorithm was developed to formalise and standardise practice regarding bleeding risk, diagnostic testing and treatment options. The protocol supports the use of Tranexamic Acid (TXA) and cell salvage for patients who are identified as high risk of bleeding. The protocol is supported by the use of the POCCTs Rotational Thromboelastometry (ROTEM®; Tem International GmbH, Munich, Germany) and Impedance Platelet Aggregometry (Multiplate®; Roche Diagnostics, Switzerland).



Rotational Thromboelastometry (ROTEM)

ROTEM® delta is a POCCT instrument that can measure the viscoelastic properties on multiple aspects of coagulation from a sample of citrated whole blood. The system can run four independent measurements to provide information on extrinsic and intrinsic clotting times, the contribution of platelets and fibrinogen to clot quality and the degree of fibrinolysis.

ROTEM results can provide a global picture of the patient's haemostatic capacity in 12-15 minutes from the start of the measurement. The assay requires 1 x citrate tube. ROTEM tests are started by re-calcification and accelerated by the addition of an activator, with differential diagnostic options enabled by adding specific system reagents. Assay options include:

INTEM	Intrinsic activation by ellagic acid to determine intrinsically activated clotting time, the contribution of platelets and fibrinogen to clot quality, as well as the stability of the clot over time. The INTEM assay is able to detect the presence of heparin in the sample.
HEPTEM	Coagulation is activated in the same way as the INTEM assay, however the HEPTEM assay contains heparinase (to eliminate any heparin effect). Comparison of the INTEM result with the HEPTEM will reveal the influence of heparin.
EXTEM	Extrinsic activation by tissue factor to monitor the coagulation process via the extrinsic pathway including the clotting time, the contribution of platelets and fibrinogen to clot quality, as well as the stability of the clot over time. Not sensitive to heparin up to 5U/ml unfractionated heparin (UFH) in blood.
FIBTEM	Coagulation is activated in the same way as the EXTEM (extrinsically activated) assay. The FIBTEM assay supports the assessment of isolated fibrinogen contribution to clot quality, where any contribution of platelets to clot firmness is inhibited by cytochalasin D. Consequently, the resulting clot is only dependent on fibrin formation and fibrin polymerisation. The FIBTEM is used in a comparative analysis with the EXTEM assay.
APTEM	Coagulation is activated in the same way (extrinsically activated) as the EXTEM assay. The APTEM assay contains the antifibrinolytic drug aprotinin. Comparison of this result with EXTEM enables verification of hyperfibrinolysis.

Limitations

Impaired primary haemostasis due to von Willebrand disease or the effect of antiplatelet drugs (e.g. aspirin, clopidogrel, prasugrel, ticagrelor etc.) cannot be detected by ROTEM alone; a combination of ROTEM and platelet function analysis (Multiplate Analyser) is useful.

Impedance Platelet Aggregometry

The Multiplate instrument measures platelet function using whole blood impedance aggregometry. This instrument allows the simultaneous measurement of whole blood samples with five channels. The Multiplate assay requires 1 x Hirudin Tube. Platelet function is affected by antiplatelet drugs including aspirin, non-steroidal anti-inflammatory drugs, platelet P2Y12 receptor antagonists, glycoprotein IIb/ IIIa receptor antagonists, and potentially by cardiopulmonary bypass. Several test reagents are available to allow triggering of different receptors / signal transduction pathways of the platelet in order to detect its function, or drug effects. Assay options include:

ADPtest	In ADPtest platelets are activated by ADP, which triggers several receptors on the platelet surface. Clopidogrel and related drugs block the P2Y12 ADP receptor, which is believed to be the most important receptor for ADP on the platelet surface.
ASPItest	In the ASPItest platelets are activated by arachidonic acid, which is converted by the platelet cyclooxygenase (COX) to the potent platelet agonist Thromboxane A2. Arachidonic acid alone is not a platelet agonist. Therefore the platelet activation in ASPItest allows a very sensitive and specific detection of Aspirin action. Arachidonic acid is the physiological substrate of the platelet COX.
TRAPtest	TRAPtest platelets are activated by TRAP-6, a peptide that mimics the activation of platelets by the action of thrombin. TRAPtest allows detection of platelets blocked by GpIIb/IIIa antagonists. Its action is not blocked by Aspirin® or clopidogrel.

The area under the curve (AUC) is expressed in AU min, or arbitrary unit's per minute and is used as the main variable for assessing platelet function. Utilising the Multiplate in conjunction with ROTEM aids the diagnostic ability of the clinician to appreciate the patients' full haemostatic potential. Multiplate results are available within 12 minutes from the start of the measurement. These results do not stream live.

Stat Lab

Situated off the corridor between the operating theatres and the intensive care unit
Blood gas machines and blood fridge are also located in the stat lab.





4. Collaborative Implementation Strategy

The project strategy was to apply a collaborative inter-departmental approach:

- to engage a working group of relevant stakeholders
- to identify where we had the opportunity to improve (process mapping)
- define clinical requirements and expectations
- identify instrument operators/result interpreters
- outline governance arrangements/reporting structure
- define and develop quality control process
- monitor and analyse outcomes
- embed as sustainable practice

Partnerships were formed with Anaesthetists, Cardiac Surgeons, Intensive Care Consultants, Nurses, Anaesthetic Technicians, Perfusionists, Haematologists, Blood Bank, Haematology Scientists and Data Management.



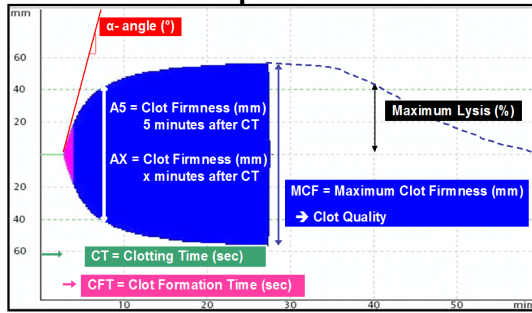
5. Education to Embed Bleeding Management and PBM as Standard Care

Implementation of a bleeding management protocol at TPCH required engagement across all clinical groups with targeted information sessions to a wide range of staff, both formally and informally, utilising every avenue available to increase awareness and education. Tools were developed to support clinical staff:

- ◆ bleeding management treatment algorithm
- ◆ educational tools and competencies to support POCCT operators
- ◆ various local tools to support daily operation of instruments
- ◆ educational tools for interpreters of POCCT's
- ◆ POCCT work unit guidelines and POCCT procedure
- ◆ massive transfusion protocol inclusive of POCCT



ROTEM® parameters



CT (clotting time): time from start of measurement until initiation of clotting
 => initiation of clotting, thrombin formation, start of clot polymerisation

CFT (clot formation time): time from initiation of clotting until a clot firmness of 20mm is detected
 => fibrin polymerisation, stabilisation of the clot with thrombocytes and F XIII

MCF (maximum clot firmness): firmness of the clot
 => increasing stabilisation of the clot by the polymerised fibrin, thrombocytes as well as F XIII

ML (maximum lysis): reduction of the clot firmness after MCF in relation to MCF
 => stability of the clot (ML < 15%) or fibrinolysis (ML > 15% within 1h)

EXTEM Extrinsic pathway screening test

- CT not sensitive for heparin (up to 5 U/ml UFH in blood)
- CT sensitive for factor deficiency (factor deficiency is only detected when approximately = <30% factors are left)
- Amplitude (A) & CFT influenced by fibrinogen & platelets

INTEM Intrinsic pathway screening test

- CT sensitive for heparin (UFH)
- CT prolongation from > 0.15 U/ml UFH in blood
- CT sensitive for factor deficiency (factor deficiency is only detected when approximately = <30% factors are left)
- Amplitude (A) and CFT influenced by fibrinogen & platelets

FIBTEM

- identifies isolated fibrinogen contribution to clot firmness
- EXTEM activation with platelet inhibition reagent added
- Amplitude influenced by fibrinogen concentration & function

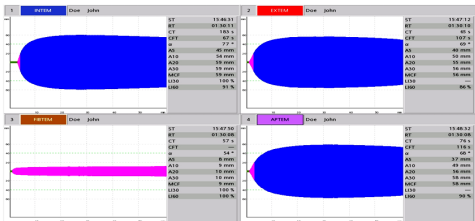
HEPTEM

- identifies heparin effect when CT compared with INTEM CT
- INTEM activation & heparin inhibition with heparinase

APTEM

- confirms presence of hyperfibrinolysis
- compare EXTEM ML / LI% with APTEM ML / LI%
- EXTEM activation & fibrinolysis inhibition with aprotinin

Normal ROTEM Results



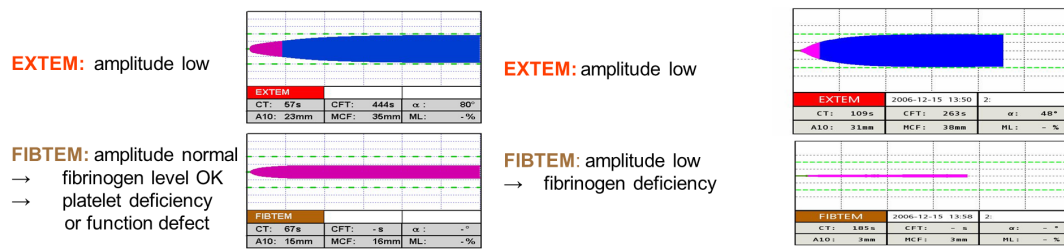
Normal Clotting Time (CT)
 → Clotting Factors Sufficient

Normal Amplitudes (A)
 → Platelet Contribution Sufficient
 → Fibrinogen Level Sufficient

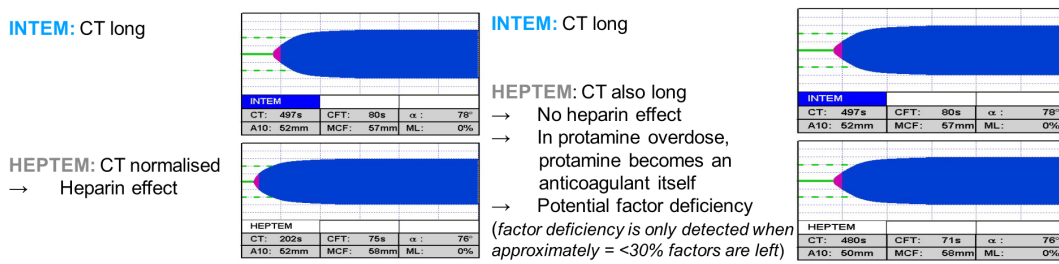
No evidence of hyperfibrinolysis (ML < 15%)

No evidence of Heparin effect

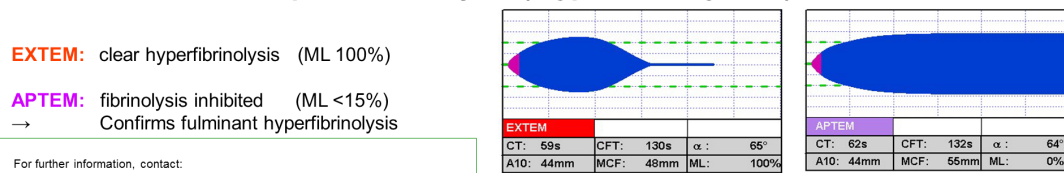
EXTEM / FIBTEM Comparative Analysis (Platelets or Fibrinogen?)



INTEM / HEPTEM Comparative Analysis (Heparin Effect?)



EXTEM / APTEM Comparative Analysis (Hyperfibrinolysis?)



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The Clinical Nurse Consultants for Patient Blood Management, 20 Anaesthetic technicians and 28 ICU nurses (28) are trained, competent operators. All surgeons, anaesthetists and intensive care consultants and registrars are interpreters. Quality control is performed as per instrument and product guidelines.



6. Governance Reporting, Quality Assurance

Progress reporting was instrumental in the uptake of the bleeding management initiative at TPCH. As part of the project planning phase, parameters were identified to accurately measure and evaluate outcome performance against project expectations. Some of the parameters that were included in reporting were:

- ◆ Percentage of patients receiving transfusion of packed red blood cells, fresh frozen plasma (FFP), platelets and cryoprecipitate
- ◆ No of units transfused of packed red blood cells, FFP, platelets and cryoprecipitate
- ◆ Percentage of patients receiving prothrombin complex concentrate, rFVIIa and tranexamic acid
- ◆ Re-operation for bleeding
- ◆ Length of stay from operation date to discharge
- ◆ In-hospital mortality
- ◆ Infection (deep sternal, superficial chest and leg wound infection)
- ◆ New atrial fibrillation
- ◆ New renal replacement therapy
- ◆ Thrombotic complications
- ◆ Neurological complications

Monitoring and reporting against key parameters ensured that any effects of the change in practice were appropriate, safe, efficient and cost effective. Results were communicated to key stakeholders, involved clinicians and the Patient Blood Management Steering Committee.

7. Benefits

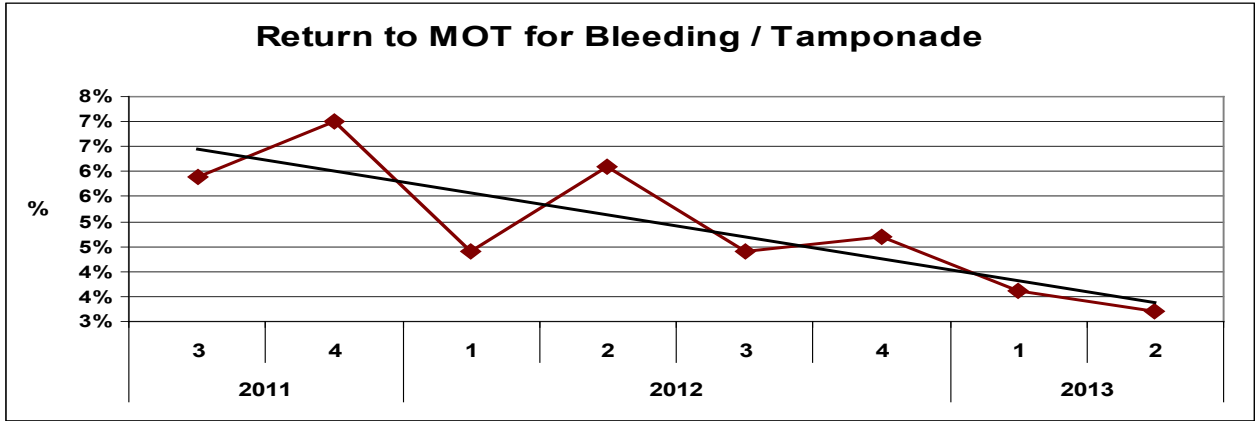
Improved patient outcomes were the core objective of implementing bleeding management supported by POCCT as part of TPCH's wider PBM program. Patient Blood Management improves patient outcomes by improving the patient's medical and surgical management in ways that boost and conserve the patient's own blood. As a consequence of better management, patients usually require fewer transfusions of donated blood components thus avoiding transfusion-associated complications. Using a structured bleeding management protocol supported by POCCT demonstrated fewer patients required transfusions of donated blood components thus avoiding transfusion associated complications.

Percentage Patients (no. of pts) Receiving Blood Products Pre and Post Bleeding Management Supported by POCCT			
Blood Products	(n=1120) 12 Months Prior POCT	(n=1056) 12 Months Post POCT	% Relative Change
PRBC's	47 % (524)	35 % (370)	- 26 %
Platelets	34 % (380)	14.5 % (153)	- 57 %
FFP	26 % (291)	9.4 % (99)	- 64 %
Cryo	10 % (112)	9.6 % (101)	- 0.04 %

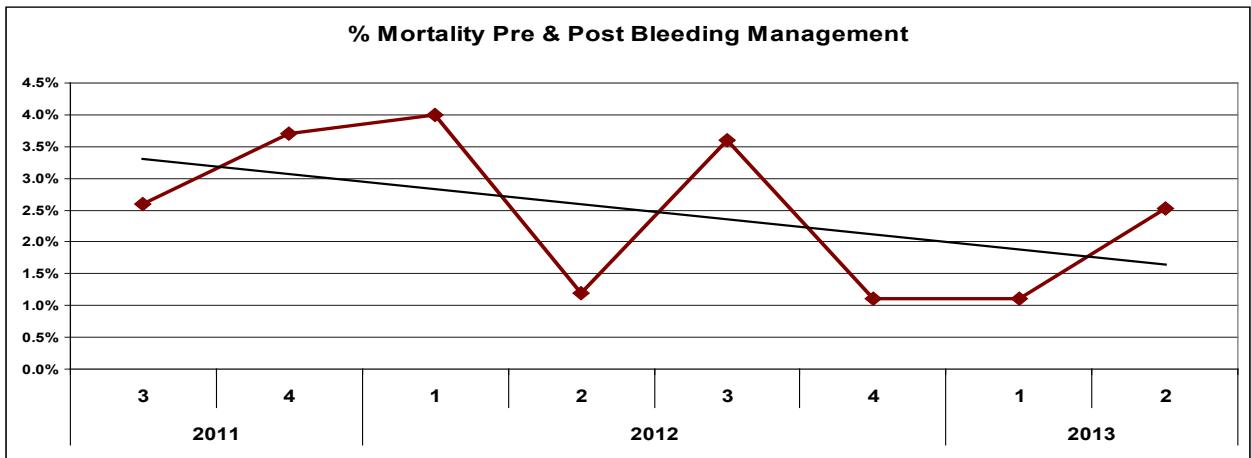
Table 1. Percentage of patients and number of patients receiving packed red blood cells (PRBCs), Platelets, fresh frozen plasma (FFP), Cryoprecipitate (Cryo), Pre (01/07/2011-30/06/2012) & Post (01/07/2011-30/06/2012) bleeding management supported by POCCT

No. Of Units Of Allogeneic Blood Products Transfused Pre & Post Bleeding Management Supported by POCCT				
Blood Product	(n=1120) Pre POCCT	(n=1056) Post POCCT	Difference	% Relative Change
PRBC's	2840	1859	- 981	- 35.5%
Platelets	966	359	- 607	- 62.8%
FFP	1531	400	- 1131	- 73.9%
Cryo	980	1225	+ 245	+ 25.0%
TOTAL	6317	3843	- 2474	

Table 2. No. of units transfused of packed red blood cells (PRBCs), Platelets, fresh frozen plasma (FFP), Cryoprecipitate (Cryo), Pre (01/07/2011-30/06/2012) & Post (01/07/2011-30/06/2012) bleeding management supported by POCCT



Graph 1. Re-exploration for bleeding pre (n=1120) & post (n=1056) bleeding management



Graph 2. Mortality pre (n=1120) & post (n=1056) bleeding management supported by POCCT

We also demonstrated decreases in superficial chest and leg wound infection and length of stay from operation to discharge. There was no change in deep sternal wound infection, thrombotic complications, new renal replacement therapy, new atrial fibrillation or neurological complications.

Although improved patient outcomes were the key objectives for implementing bleeding management guided by POCCT, TPCH demonstrated significant savings in the acquisition cost of blood products during the 12 month implementation phase.

Blood Product Cost Savings over 12 months*
Pre and Post Bleeding Management with POCCT

	Pre POCCT	Post POCCT	Saving	\$ per Unit
Red Blood Cells	\$979,800	\$641,355	\$338,445	\$345
Platelets	\$430,836	\$160,114	\$270,722	\$446**
Fresh Frozen Plasma	\$453,176	\$118,400	\$334,776	\$296
Cryoprecipitate	\$59,780	\$74,725	-\$14,945	\$61
TOTAL	\$1,923,592	\$994,594	\$928,998	
Total Percentage Reduction in Blood Product Cost: 48.3%				
*Savings based on total yearly blood use				
** Costing based on average cost of pooled/ apheresis platelets				

Graph 3. Acquisition cost of transfused packed red blood cells (PRBCs), Platelets, fresh frozen plasma (FFP), Cryoprecipitate (Cryo), Pre (01/07/2011-30/06/2012) & Post (01/07/2011-30/06/2012) bleeding management supported by POCCT



8. Outcomes

The implementation of ROTEM at TPCH has led to a variety of successes including:

- ◆ Increased awareness of the need for a comprehensive Patient Blood Management program
- ◆ Improved patient outcomes
- ◆ Decreased cost
- ◆ Adoption of bleeding management supported by POCCT into orthopaedic surgery, general surgery and general ICU
- ◆ Implementation of anaemia management for all surgery patients



> 9. Hurdles for Implementing Patient Blood Management

- ◆ Reluctance to acknowledge PBM guidelines
- ◆ Lack of enthusiasm to change practice – this is often based on the principle that current practice isn't harmful
- ◆ Economic and logistical issues surrounding implementing change in practice
- ◆ Translating evidence into practice – potentially one of the biggest hurdles as this requires dedicated drivers to implement evidenced based guidelines



