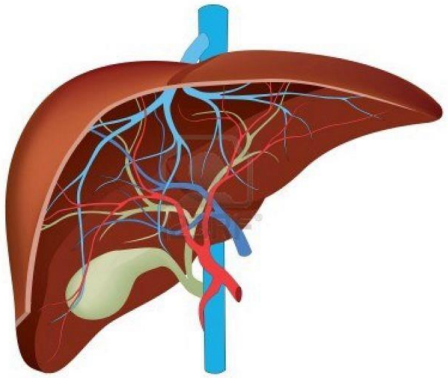
Point of care monitoring in liver transplantation

Dr Ciara Donohue
Consultant Anaesthetist
Royal Free Hospital
RTC
9th May 2017

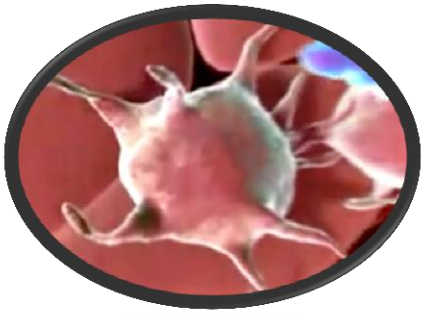
Overview

- Coagulation changes in
  - liver disease
  - liver transplantation
- Why conventional lab tests are of limited value
- What global viscoelastic tests (VETs) can tell us
- How we use VETs in liver transplantation – treating TEG parameters
- Impact on transfusion and outcome

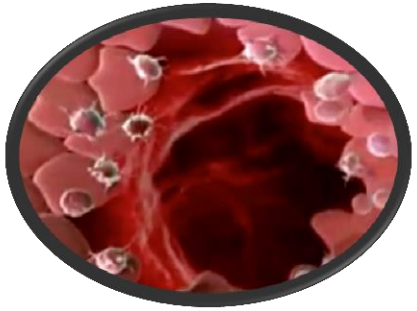


COAGULATION CHANGES IN LIVER DISEASE AND TRANSPLANTATION

Cell based model of coagulation

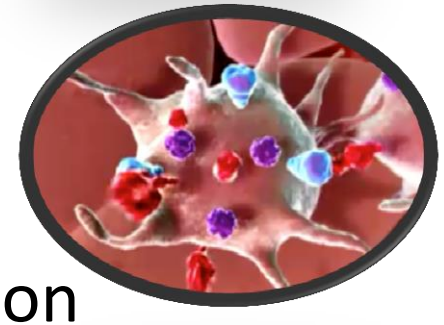


Primary haemostasis

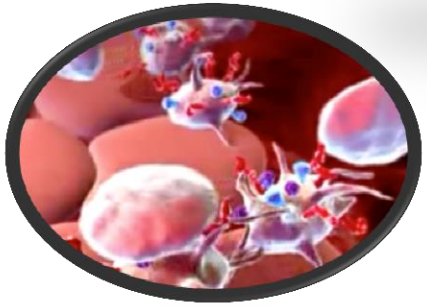


Initiation

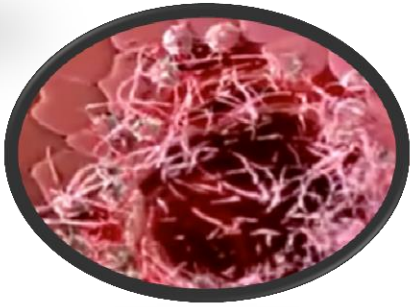
Amplification



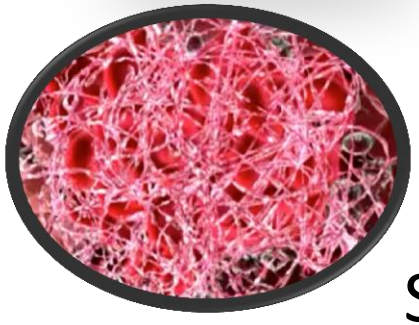
Propagation

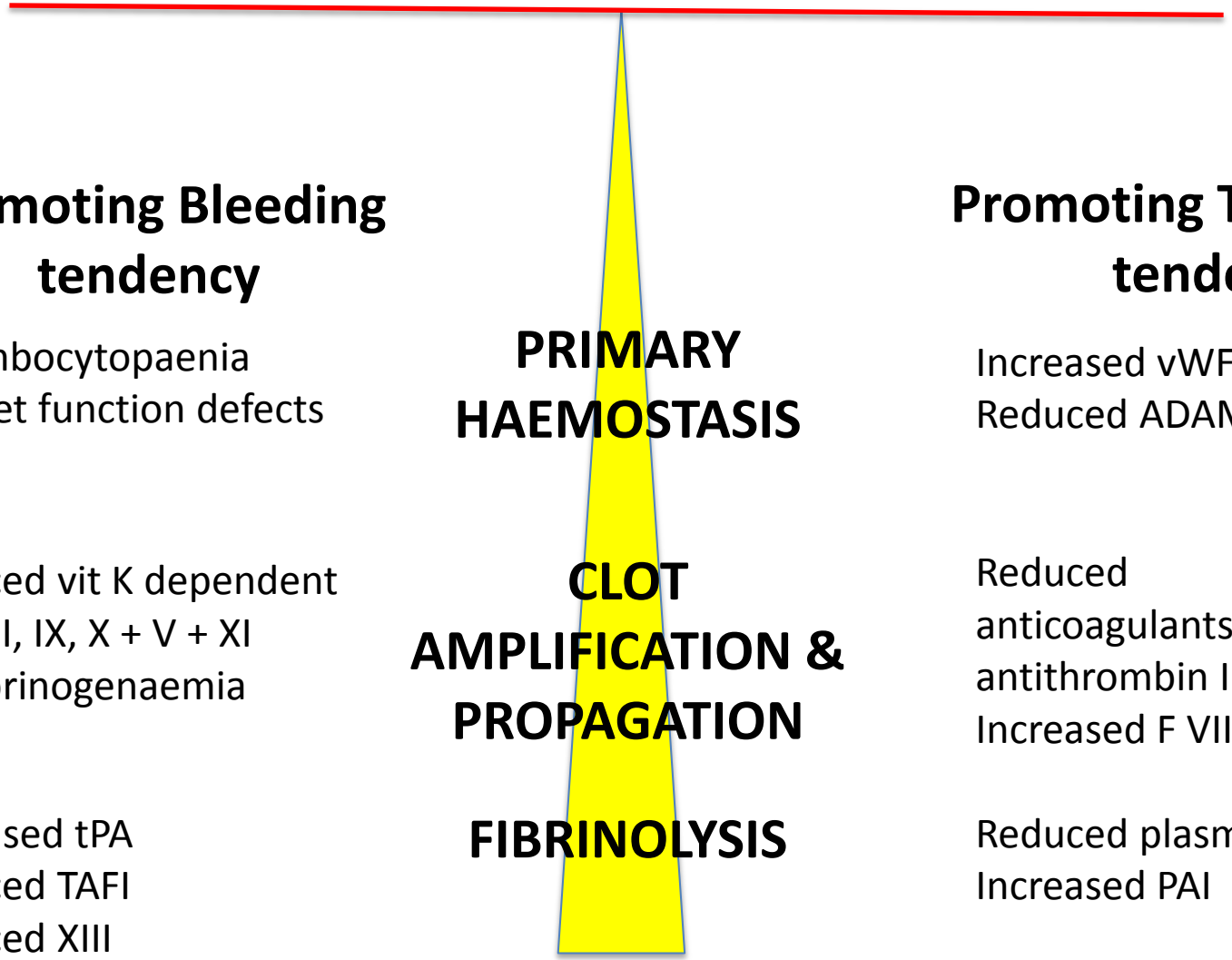


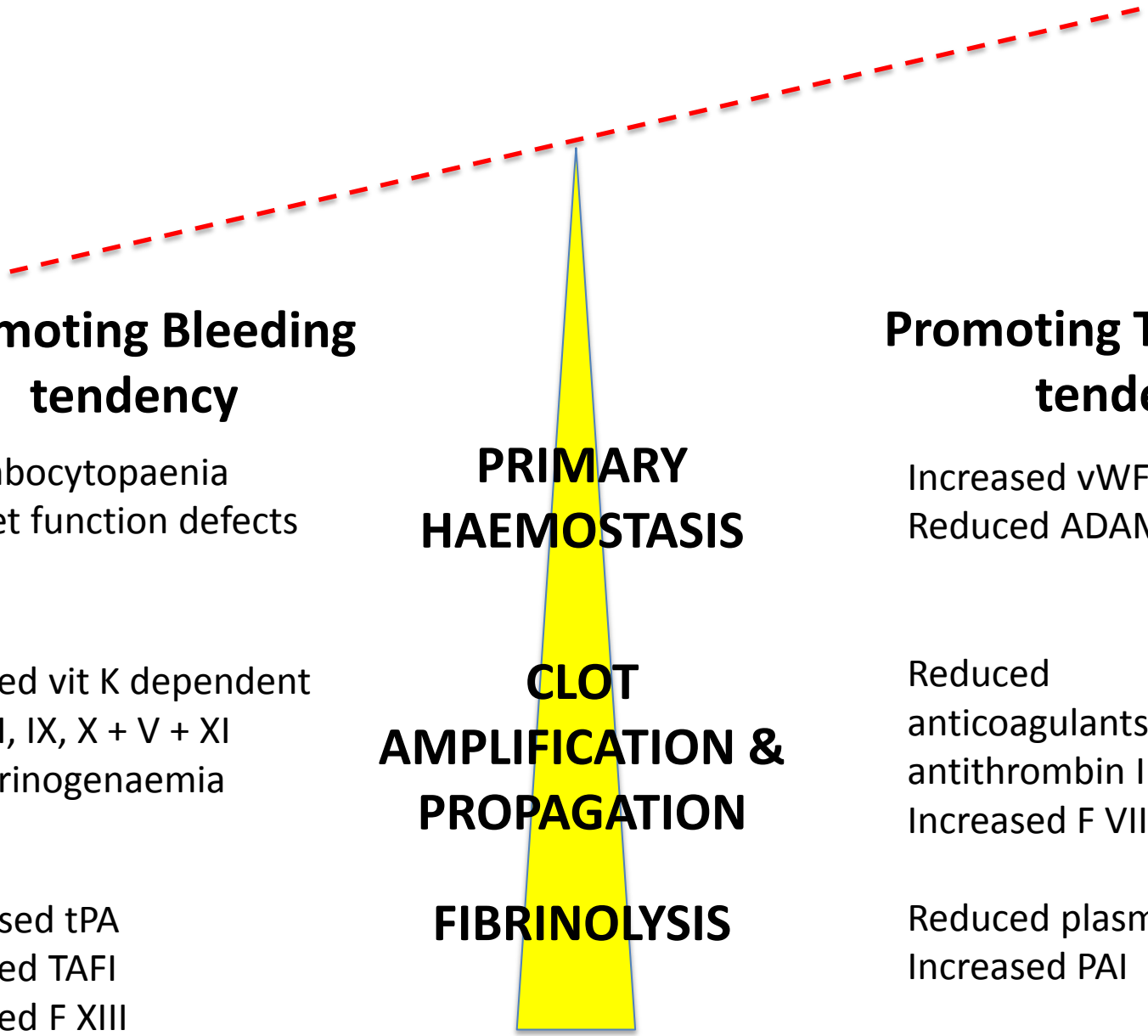
Stabilisation



Lysis




Promoting Bleeding tendency
Thrombocytopaenia
Platelet function defects
Reduced vit K dependent
F II, VII, IX, X + V + XI
Dysfibrinogenaemia
Increased tPA
Reduced TAFI
Reduced XIII
PRIMARY HAEMOSTASIS
CLOT AMPLIFICATION & PROPAGATION
FIBRINOLYSIS
Promoting Thrombotic tendency
Increased vWF
Reduced ADAMTS-!3
Reduced anticoagulants C, S, antithrombin III,
Increased F VIII
Reduced plasminogen
Increased PAI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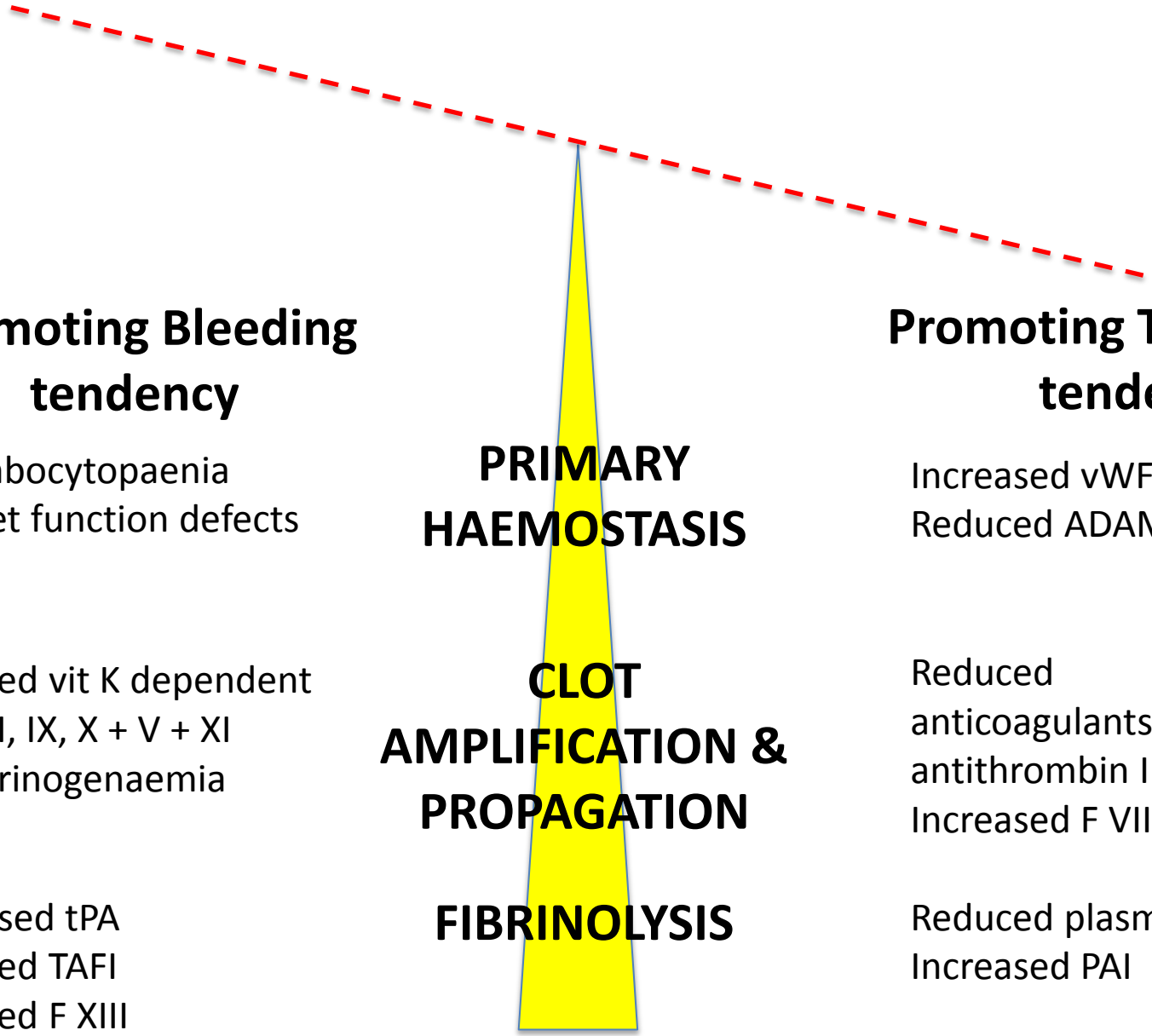
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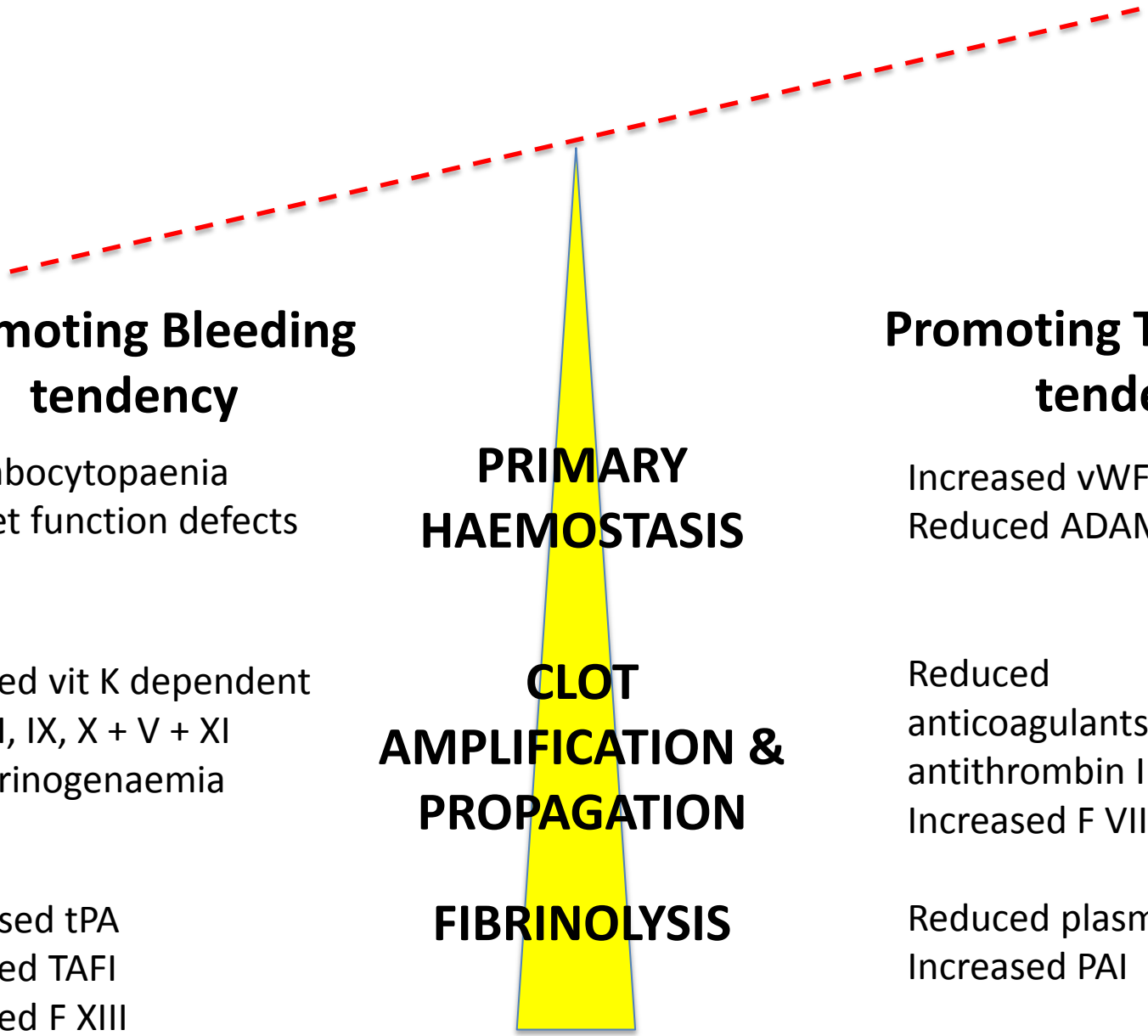
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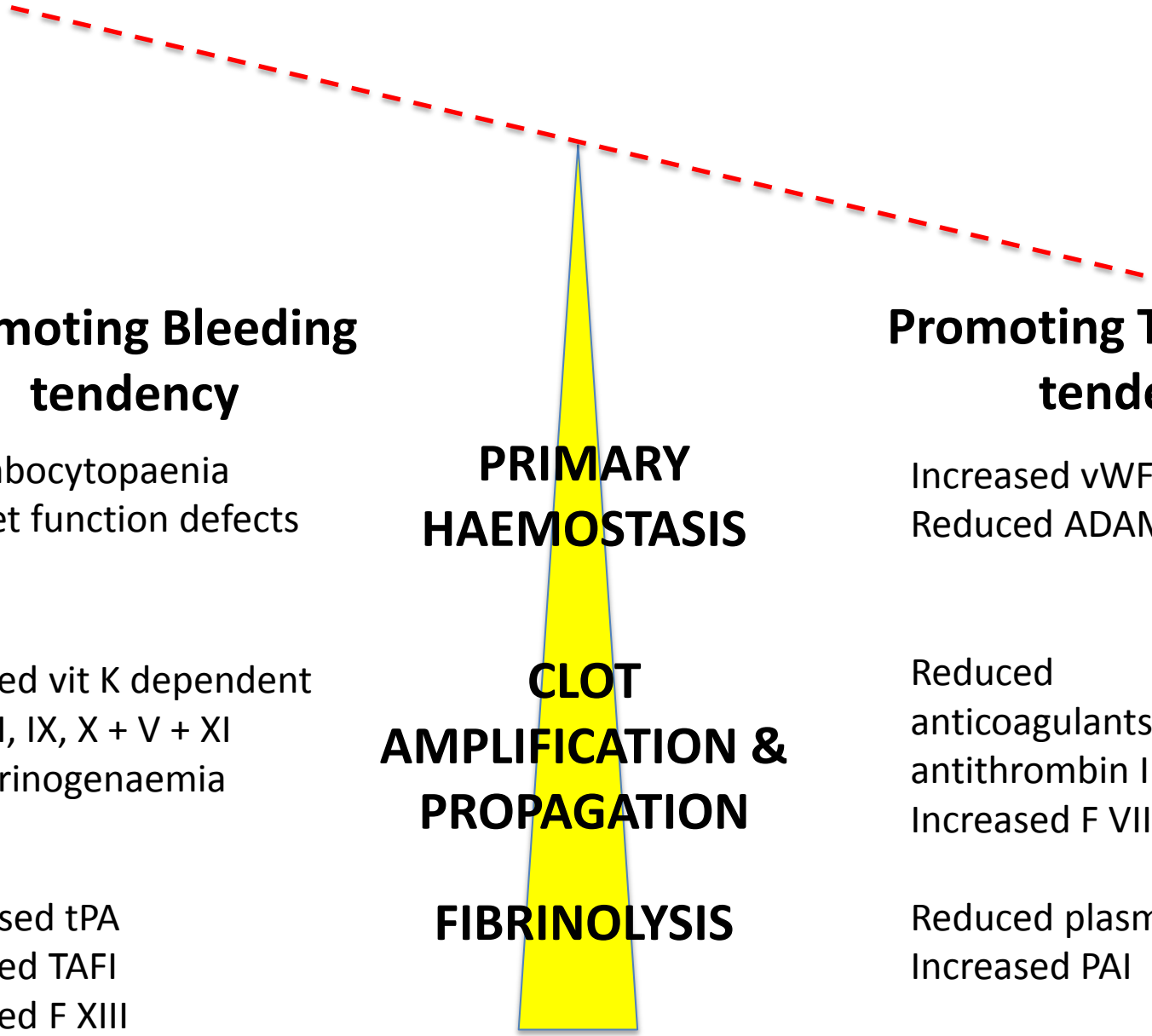
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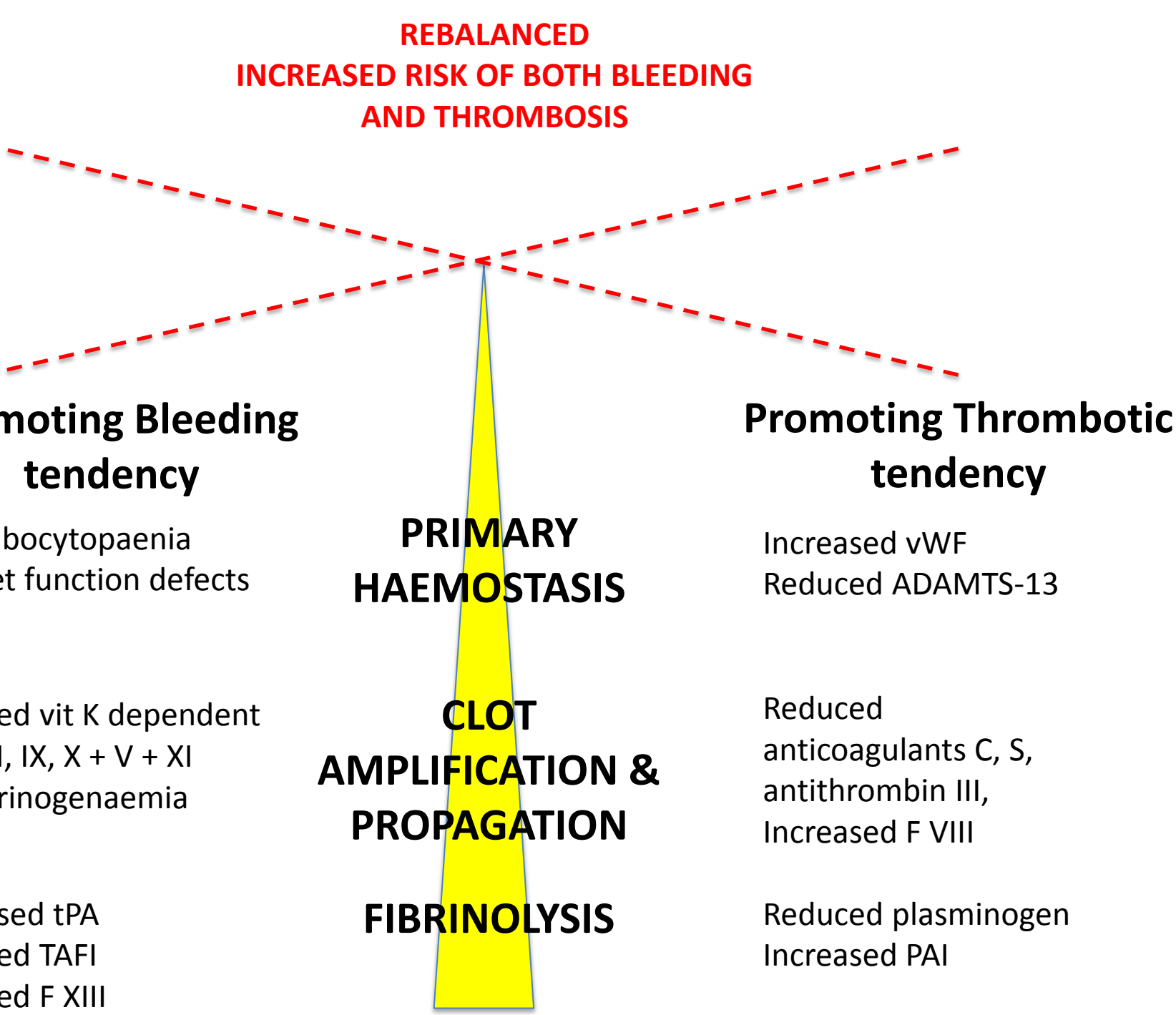
REBALANCED
INCREASED RISK OF BOTH BLEEDING
AND THROMBOSIS
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Promoting Thrombotic tendency
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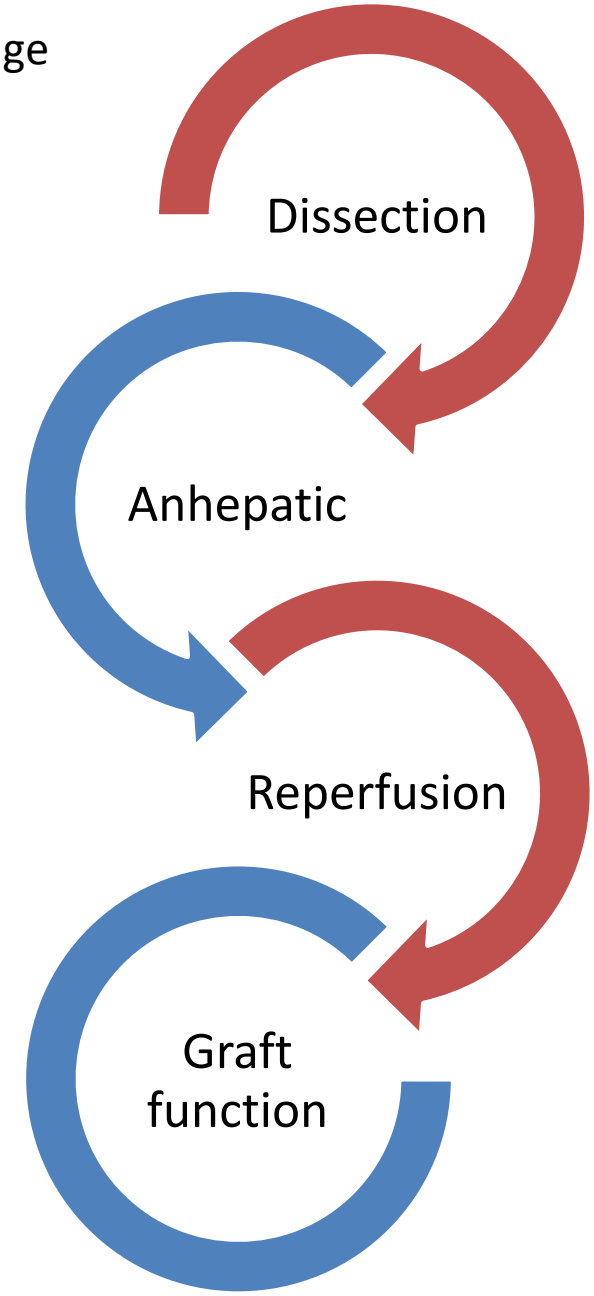
Liver disease does NOT cause an autoanticoagulated state

- DVT and PE occur in cirrhotics
- PVT 8-26% of cirrhotics
- Hypercoagulable viscoelastic parameters frequently seen (esp in cholestatic liver diseases + ALF with SIRS)
- Prophylactic FFP to treat INR is inappropriate and may lead to excess morbidity
- Transfusion free transplants increasingly common

From this complex ‘rebalanced’ baseline….

The intraoperative minefield of transplantation…

Unpredictable haemorrhage
Portal HTN
Collateral vessels



Fluid management
Dilutional coagulopathy

Global loss of factors
Increased Fibrinolysis

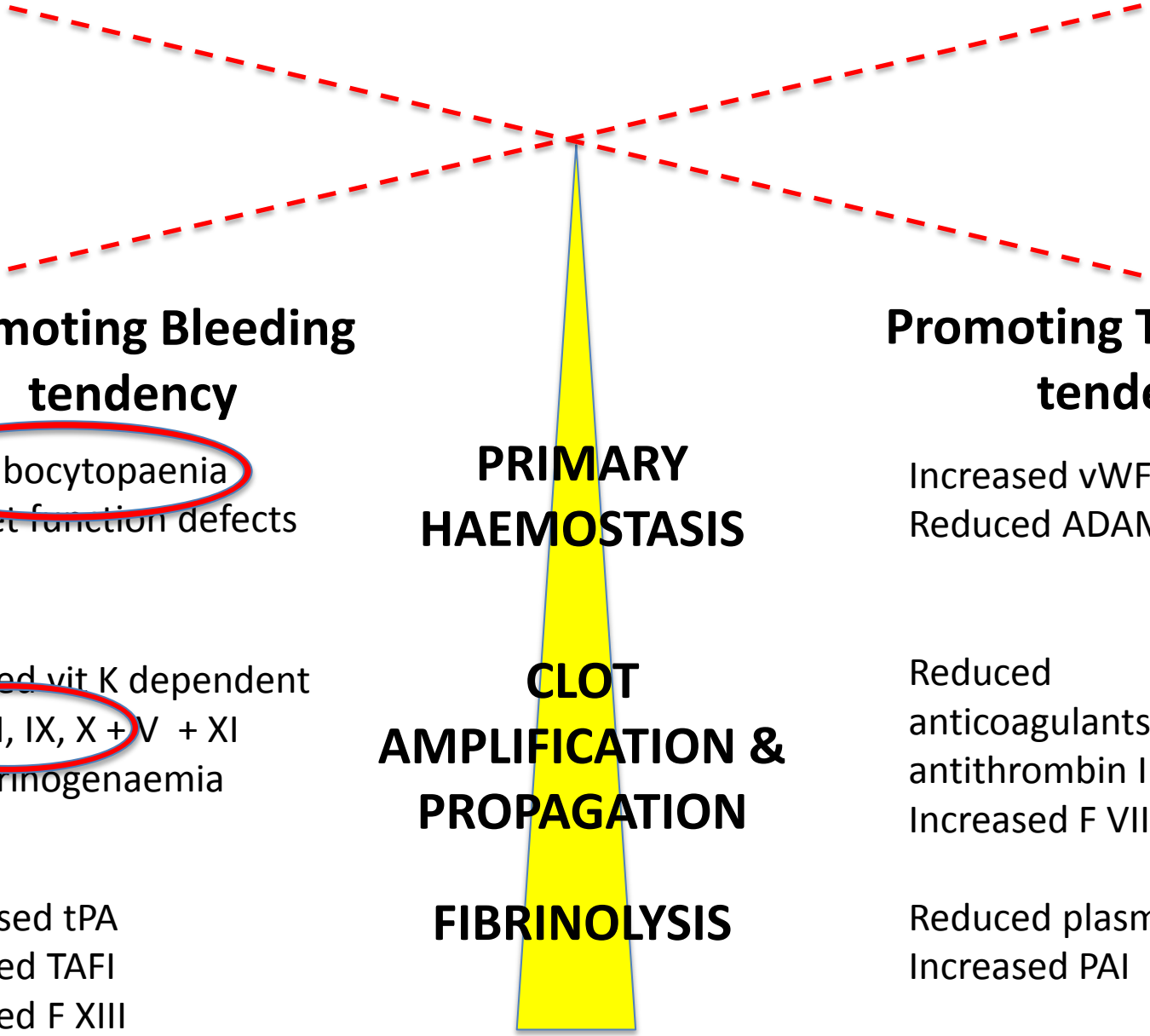
Global reduction of factors
Hyperfibrinolysis
Platelet entrapment
Endogenous heparin release

Marginal graft
Delayed/non-function
Sustained/worsening coagulopathy

Tip towards
Prothrombotic state
Arterial/venous
Thrombotic complications

LIMITATIONS OF CONVENTIONAL LABORATORY TESTS

REBALANCED
INCREASED RISK OF BOTH BLEEDING AND THROMBOSIS



Promoting Bleeding tendency		Promoting Thrombotic tendency
Thrombocytopaenia Platelet function defects	**PRIMARY HAEMOSTASIS**	Increased vWF Reduced ADAMTS-13
Reduced vit K dependent F II, VII, IX, X + V + XI Dysfibrinogenaemia	**CLOT AMPLIFICATION & PROPAGATION**	Reduced anticoagulants C, S, antithrombin III, Increased F VIII
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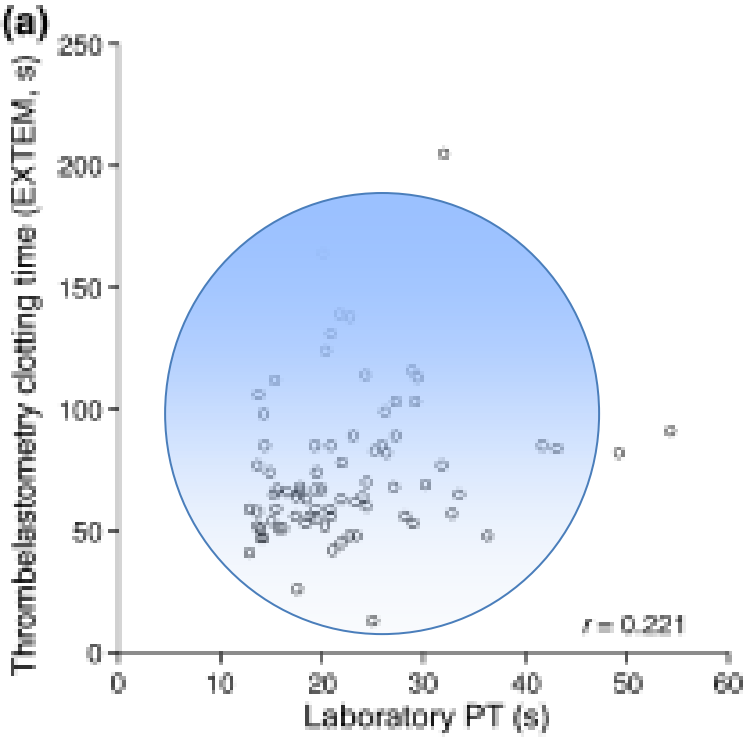
Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland
Anaesthesia, 2010, **65**, pages 44–49 doi:10.1111/j.1365-2044.2009.06159.x

ORIGINAL ARTICLE

Monitoring of haemostasis in liver transplantation: comparison of laboratory based and point of care tests

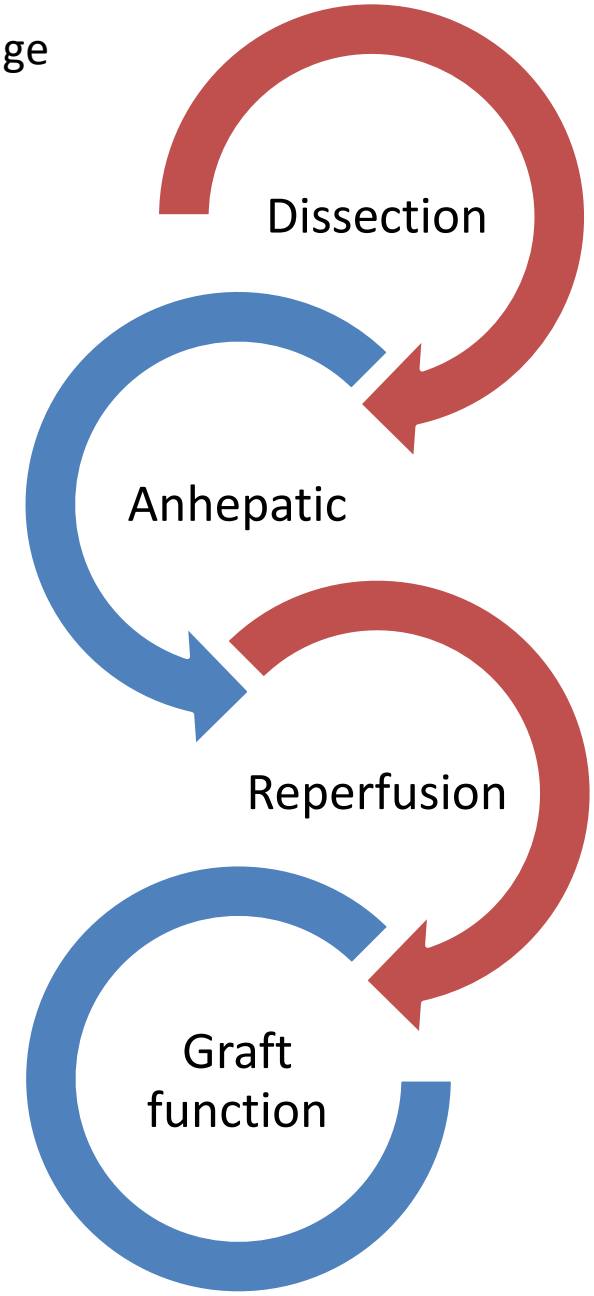
F. Herbstreit,[1] E. M. Winter,[2] J. Peters[3] and M. Hartmann[4]

1 Staff Anaesthetist, 2 Resident, 3 Professor of Anaesthesiology and Intensive Care Medicine, and Chairman, 4 Privatdozent, Klinik für An



No correlation between PT/INR and Clotting time on VET

Unpredictable haemorrhage
Portal HTN
Collateral vessels



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Marginal graft
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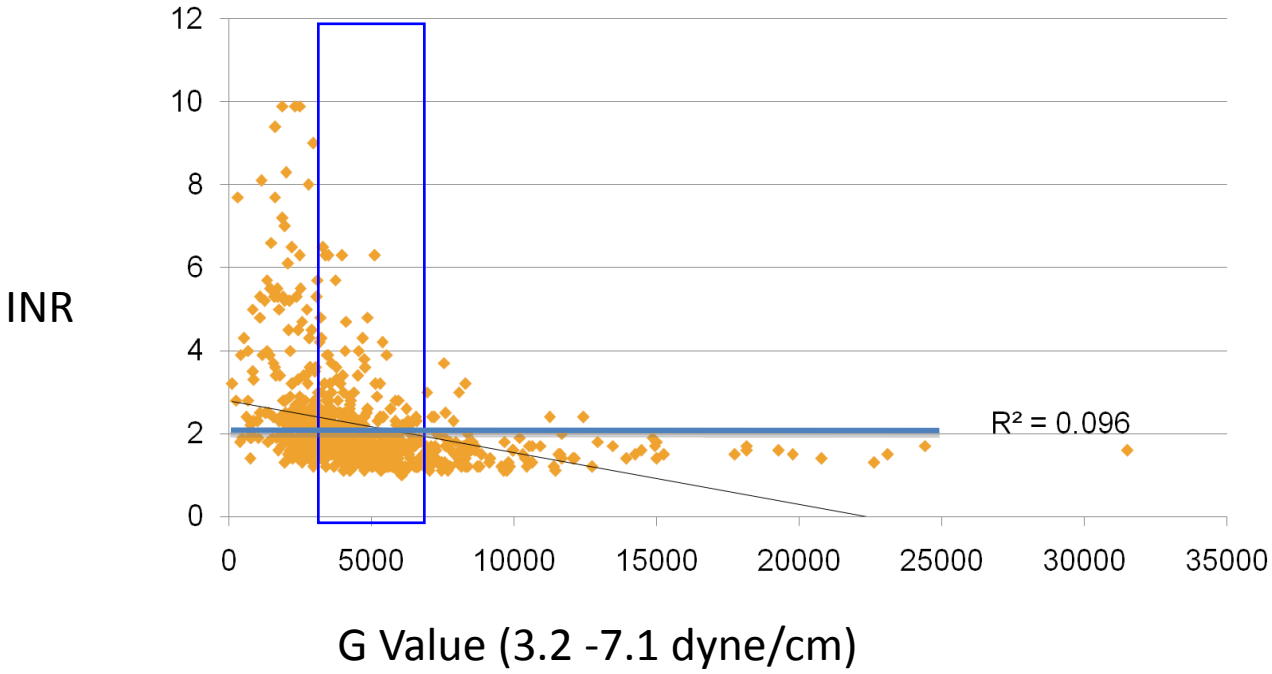
Tip towards
Prothrombotic state
Arterial/venous
Thrombotic complications

LIVER TRANSPLANTATION 19:852-861, 2013

ORIGINAL ARTICLE

Intraoperative Hypercoagulability During Liver Transplantation as Demonstrated by Thromboelastography

Dominik Krzanicki, Anita Sugavanam, and Susan Mallett
Department of Anaesthesia, Royal Free Hospital, London, United Kingdom

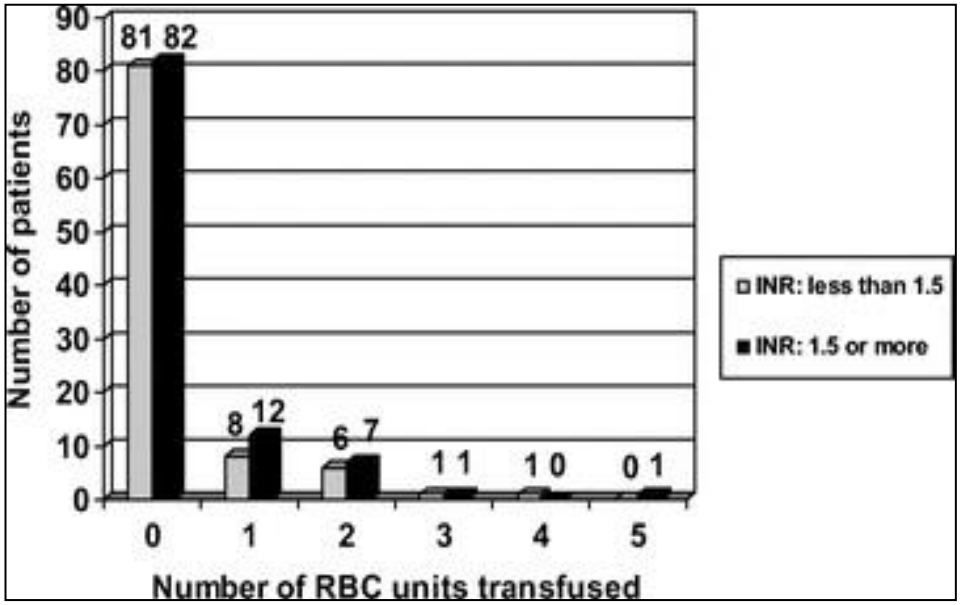


No relationship between INR and presence of TEG hypercoagulability

Transplantation. 2008 Apr 15;85(7):956-62. doi: 10.1097/TP.0b013e318168fcd4.

Coagulation defects do not predict blood product requirements during liver transplantation.

Massicotte L[1], Beaulieu D, Thibeault L, Roy JD, Marleau D, Lapointe R, Roy A.



Classical Notions of Coagulation Revisited in Relation with Blood Losses, Transfusion Rate for 700 Consecutive Liver Transplantations

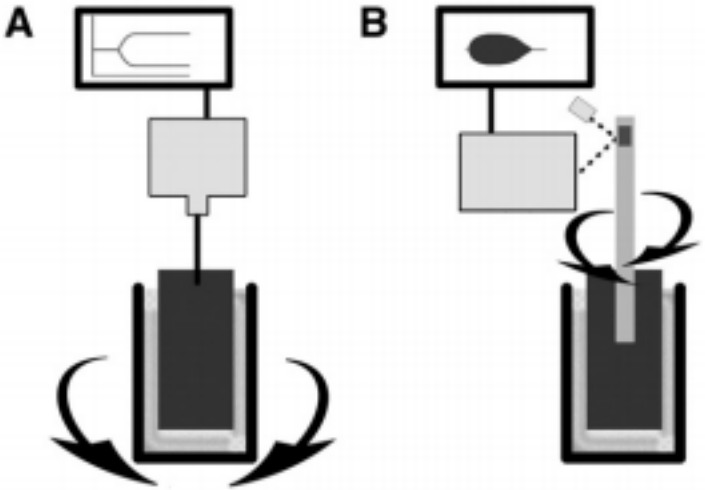
Luc Massicotte, MD[1] Lynda Thibeault, MD, MSc[2] André Roy, MD[3]

Demographic and health characteristics for the patients who did not receive transfusion (542 patients) and the ones who received blood products (158 patients)

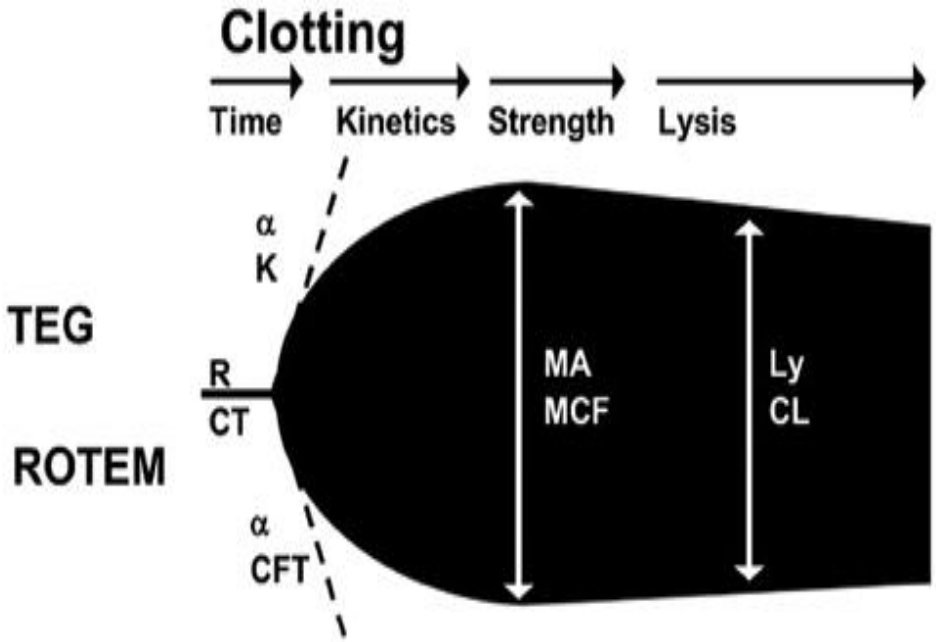
Characteristics	Without blood product 542 patients	With transfusions 158 patients	*p*-Value
Starting Hb value (g/L)	111 ± 25	90 ± 25	< 0.0001
Starting INR value	1.9 ± 1.1	2.1 ± 1.6	NS
Starting platelet count (10^9 pl/L	102 ± 80	88 ± 54	NS
Starting fibrinogen value (g/L)	2.3 ± 1.2	1.6 ± 1.6	NS
CTP high score	9.7 ± 2.8	10.4 ± 2.8	NS
MELD score	22 ± 9	21 ± 9	NS
Starting creatinine value (µmol/L)	99 ± 84	128 ± 63	NS
Starting bilirubin value (µmol/L)	90 ± 112	112 ± 111	NS

GLOBAL VISCOELASTIC ASSAYS

TEG


A
B

ROTEM


Clotting
Time
Kinetics
Strength
Lysis
α
K
TEG
R
CT
ROTEM
α
CFT
MA
MCF
Ly
CL

Next generation TEG 6s

Utilises novel **resonance frequency** viscoelasticity measurements & microfluidic **cartridge** technology

- ✓Multiple assays from small sample
- ✓Minimises pipetting
- ✓Reduced sensitivity to vibrations
- ✓Increased reliability/reduced variability
- ✓Reduced training
- ✓Increased accessibility

What global viscoelastic assays can tell us

1. Is clot forming and how rapidly?

   Pro and anti-coagulant activity

2. How strong is the clot?

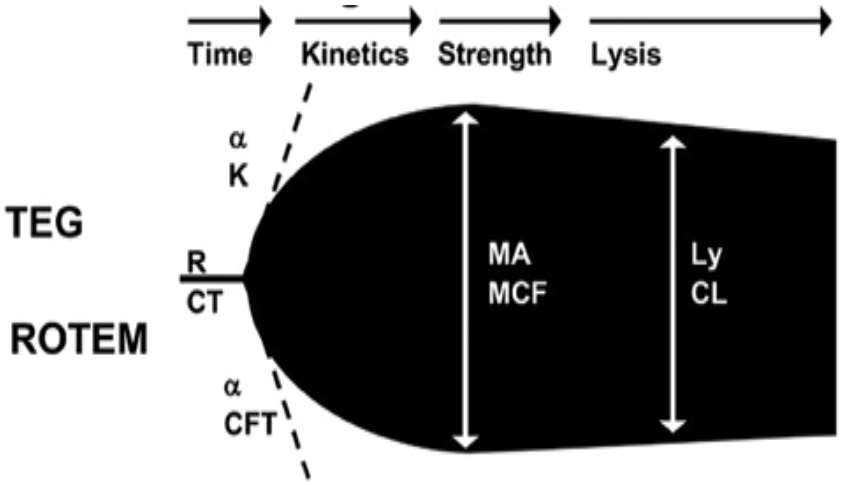
   Platelets and fibrinogen

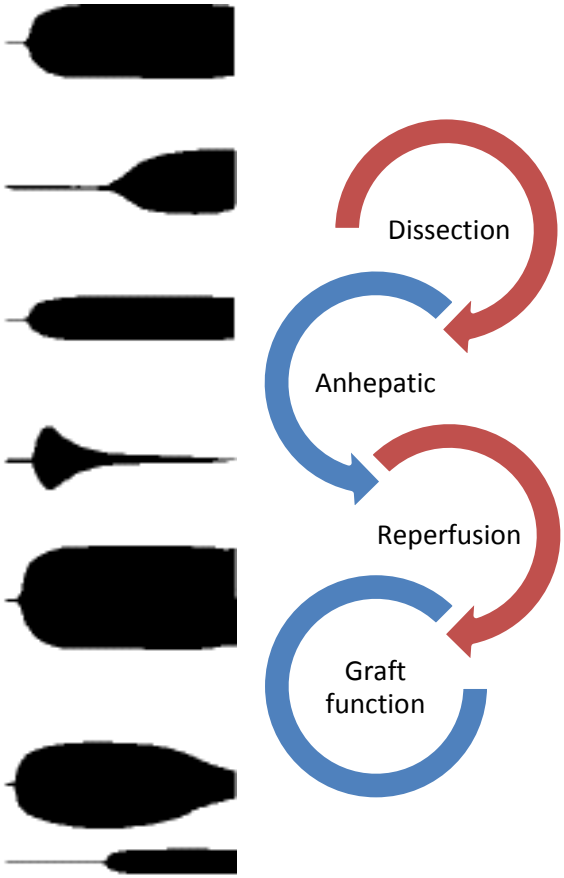
3. Is the clot stable?

   Fibrinolysis and FXIII

✓Bedside

✓Real time





USE OF GLOBAL VISCOELASTIC ASSAYS AND TREATING TEG PARAMETERS IN LIVER TRANSPLANTATION

How we use POC tests in liver transplantation

POC Laboratory next to Liver Theatre, Royal Free

Routine serial analysis of TEG, FBC, INR and ABG at:

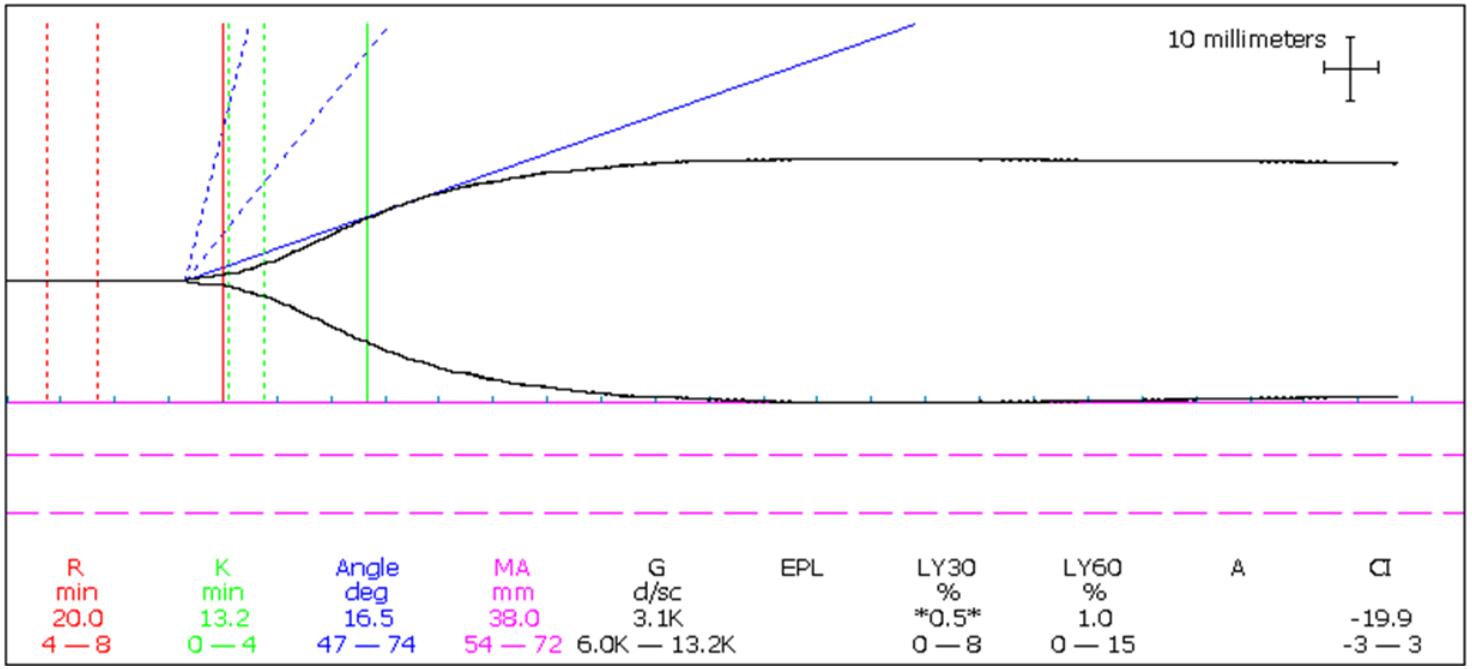
1: Baseline
2: Dissection: hourly
3: Anhepatic
4: 5 mins post reperfusion
5: 30 mins post reperfusion
6: End of case

Increased frequency of analysis if active bleeding

Local availability of factor conc

Hypocoagulable

Prolonged R time
Reduced α angle
Reduced MA

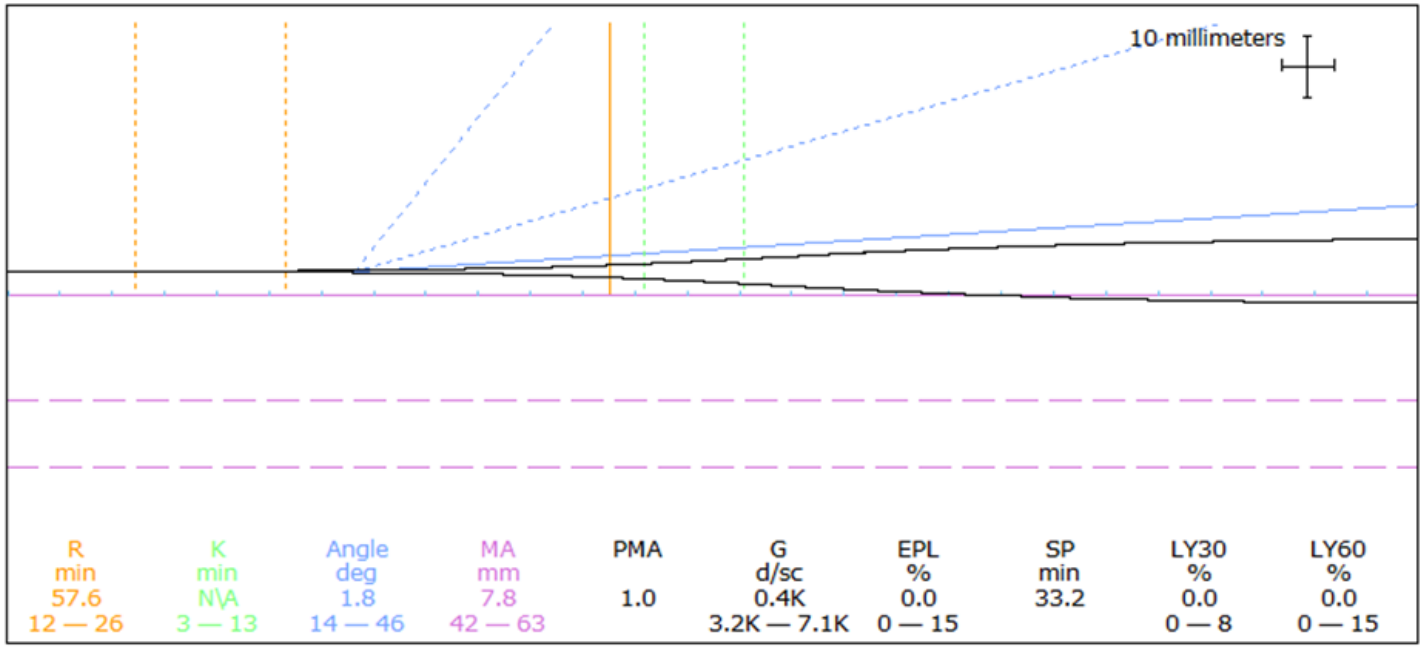


Management?

- Check surgical field
- Dry – do nothing
- Wet – clotting factors FFP

Dilutional coagulopathy

‘ARROWHEAD’ TRACE
Loss of thrombin generation

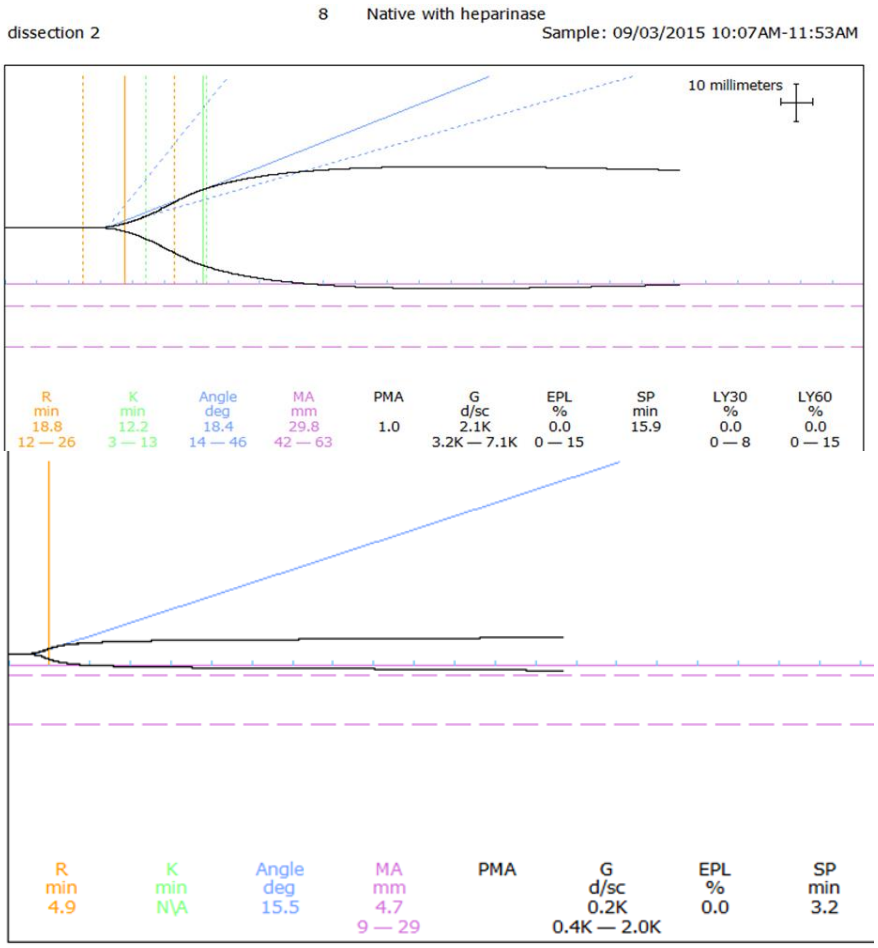


Management?

- Support Thrombin generation
- Avoid further dilution with volume
- Prothrombin Complex Conc
- Fibrinogen Conc
- Platelets

Low Fibrinogen

Low MA



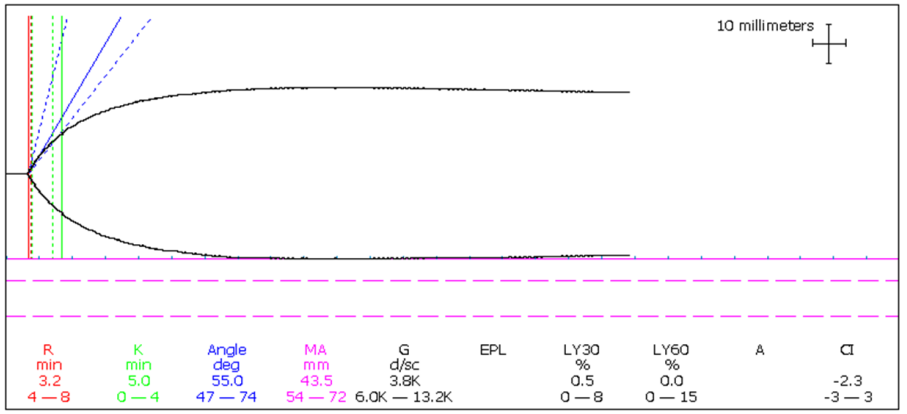
Low fibrin MA

Management?

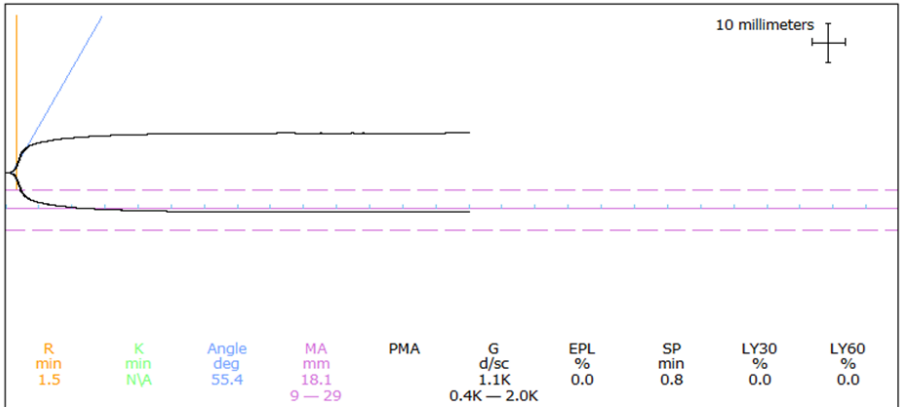
- Assess field
- Supplement fibrinogen
- Cryo or fibrinogen conc

Low Platelets/dysfunction

Low MA



High normal fibrin MA

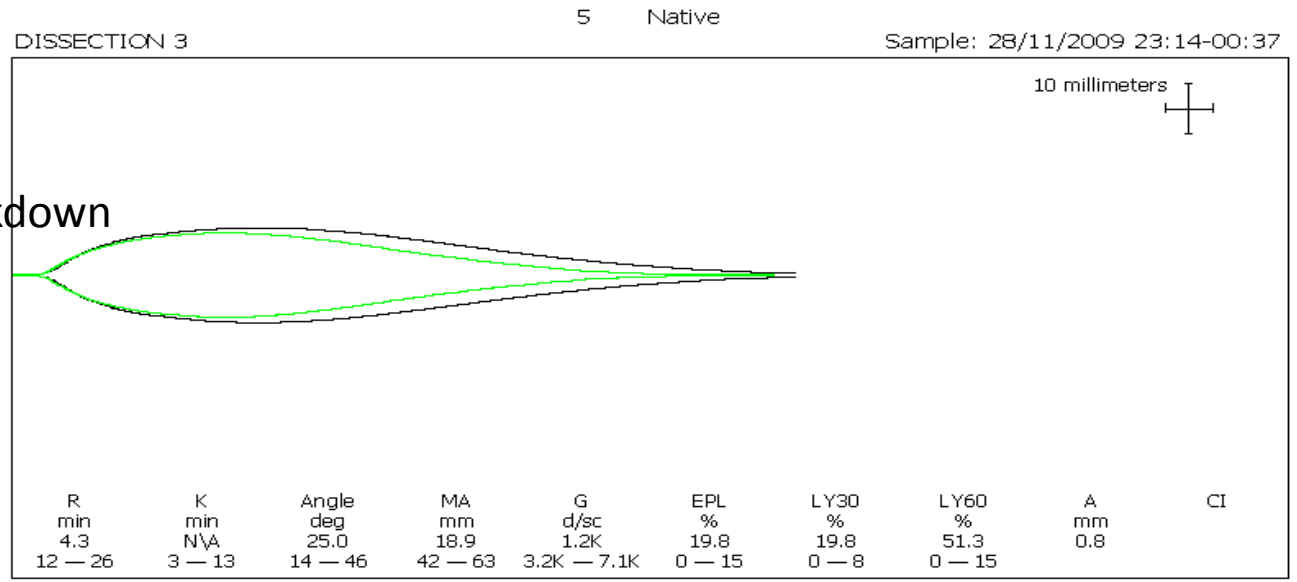


Management?

- Assess field
- Dry field – do nothing
- Wet field – Platelets

Hyperfibrinolysis

Accelerated clot breakdown
Clot instability



Management?

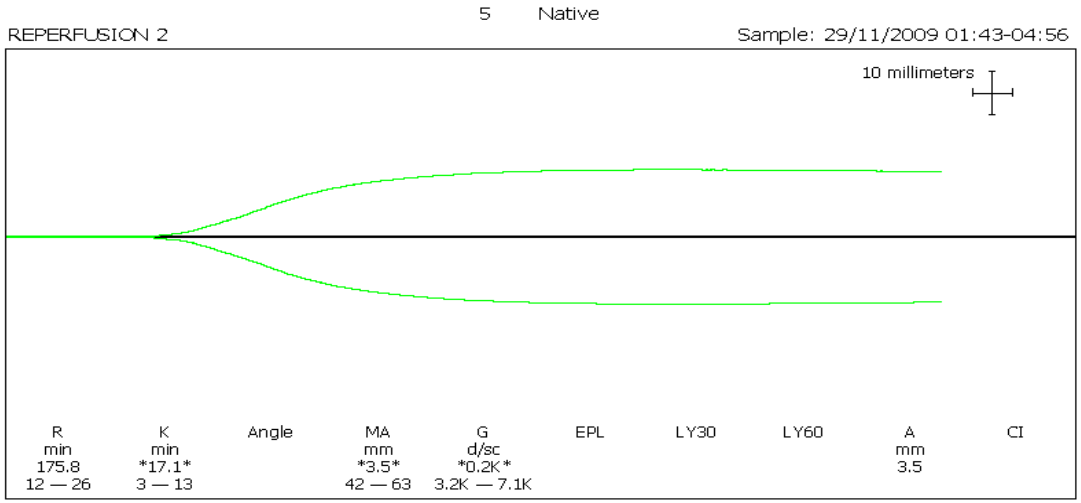
- What stage are you at?
- Is there visible clot dissolution?

- Dissection/Anhepatic: TXA 1g +
- Post reperfusion: expected and not usually clinically significant – may not require treatment

Detection of Heparin (or HLE)

Native TEG – no clot initation due to presence of heparin (endogenous – endothelial glycocalyx)

With heparinase cup – reveals underlying clotting potential

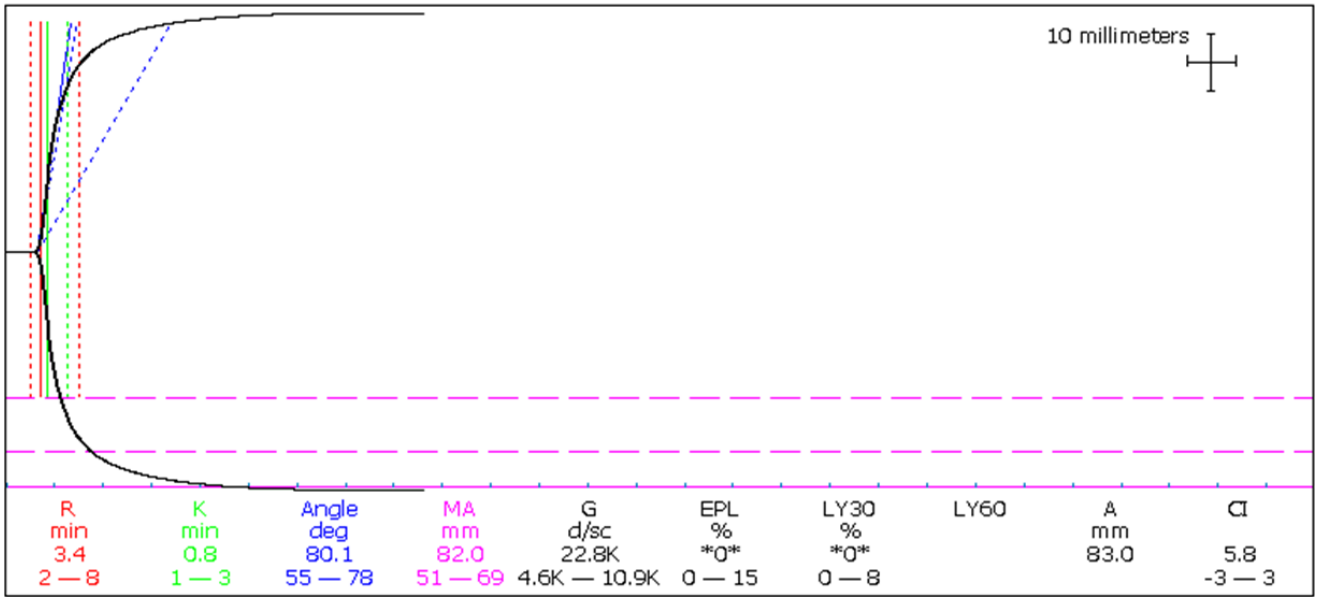


Management?

- What stage are you at?
- Is there clinically significant bleeding?
- Common post reperfusion – rarely clinically significant
- If bleeding – consider low dose protamine

Hypercoagulability

Short R time
Increased α angle
Massive thrombin generating potential
Increased MA
G value

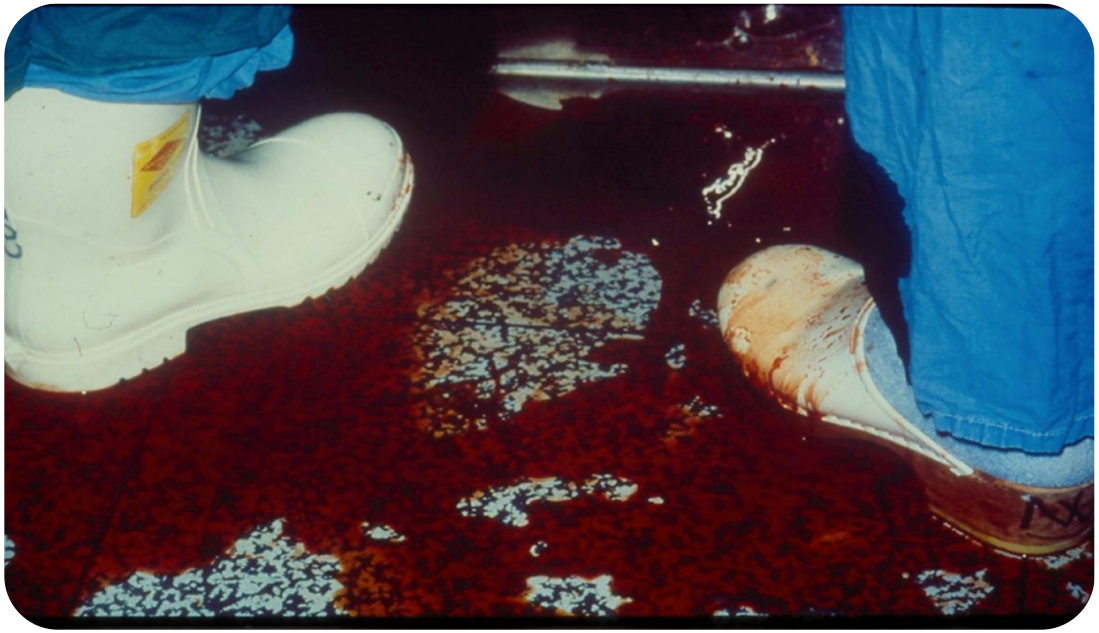


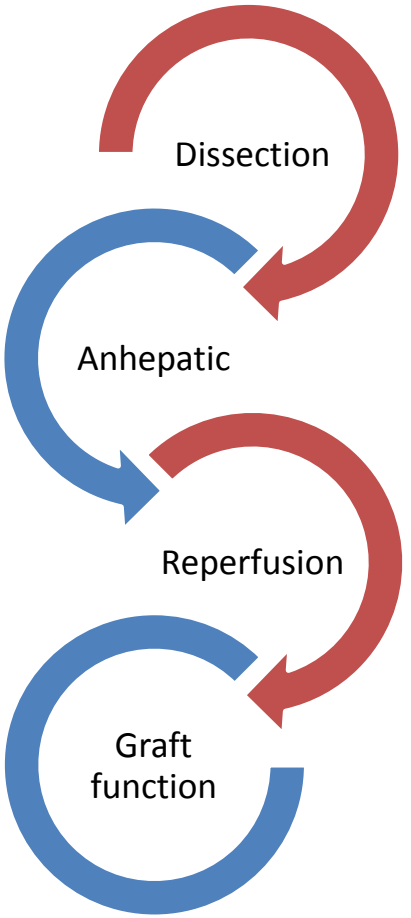
Management?

- Risk of thromboembolic complications eg hepatic artery thrombosis
- Early prophylaxis
- Heparin anticoagulation

CONTEXT is everything…

Always assess operative field: dry or wet?





Where in the transplant are you?

IMPACT ON OUTCOMES

Thromboelastography-Guided Transfusion Decreases Intraoperative Blood Transfusion During Orthotopic Liver Transplantation: Randomized Clinical Trial

S.-C. Wang, J.-F. Shieh, K.-Y. Chang, Y.-C. Chu, C.-S. Liu, C.-C. Loong, K.-H. Chan, S. Mandell, and M.-Y. Tsou

Transplantation Proceedings, 42, 2590–2593 (2010)

Table 3. Perioperative Data*

Variable	Control Group	TEG Group
Intake		
Blood product		
Total transfusion, mL	6587.1 (3254.6)	4937.1 (2038.2)
Fresh-frozen plasma, U	21.5 (12.7)	12.8 (7.0)†
Cryoprecipitate, U	15.6 (9.5)	13.0 (10.3)
Platelet concentrates, U	30.1 (18.5)	27.3 (13.9)
Whole blood, U	1.4 (2.5)	0.3 (1.1)
Packed RBCs, U	16.7 (12.8)	14.2 (7.1)
IV fluid		
Fluid total, mL	10053.8 (4966.8)	9198.0 (4546.9)
HAES, mL	214.3 (544.7)	150.0 (231.2)
Albumin, mL	664.3 (474.9)	829.2 (588.7)
Output		
Blood loss, mL	6348.0 (3704.1)	4775.7 (4264.7)
Urine output, mL	2139.3 (1208.0)	2312.9 (1491.5)

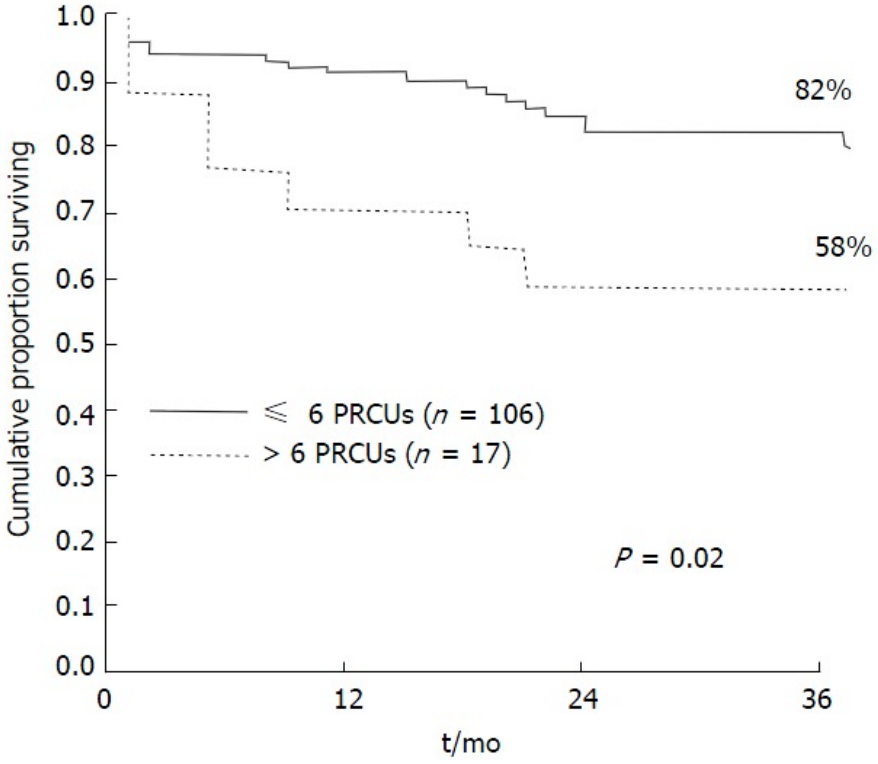
Point-of-care haemostasis monitoring during liver transplantation reduces transfusion requirements and improves patient outcome

Antonio Leon-Justel [a,*], Jose A. Noval-Padillo [b], Ana I. Alvarez-Rios [b], Patricia Mellado [c],

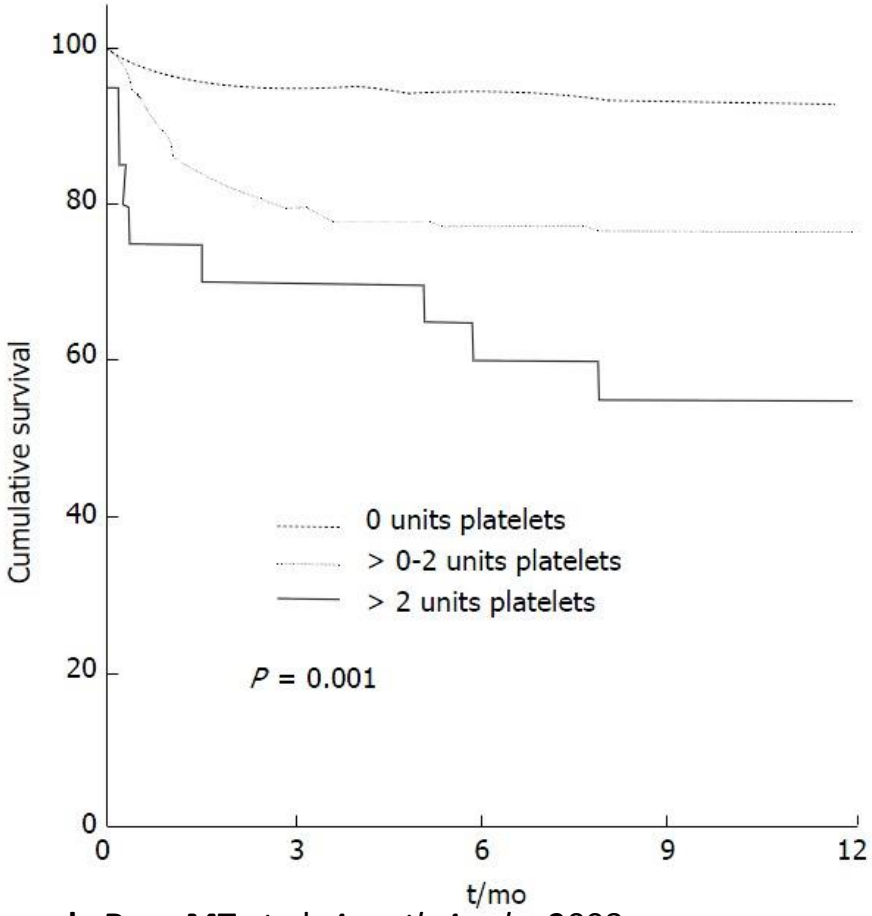
Clinica Chimica Acta 446 (2015) 277–283

	Standard-care group	POC group	p-Value
Number	100	100	
Intraoperative variables			
Venous ischemia, min	392 ± 110	388 ± 97	0.783
Arterial ischemia, min	423 ± 116	418 ± 101	0.740
Surgical haemorrhage	14	6	0.099
Transfusion avoidance	5	24	<0.001
Massive transfusion (>10U RBCs)	13	2	0.005†
RBC, units/patient	5 [2–8]	3 [0–5]	<0.001
Plasma, units/patient	2 [0–4]	0 [0–0]	<0.001
Platelets, units/patient	1 [0–4]	0 [0–1]	<0.001
Tranexamic acid	1	4	0.369†
Fibrinogen concentrate, g/patient	0.48 ± 1.28	1.13 ± 1.44	0.001

Why avoiding transfusion of blood products is desirable



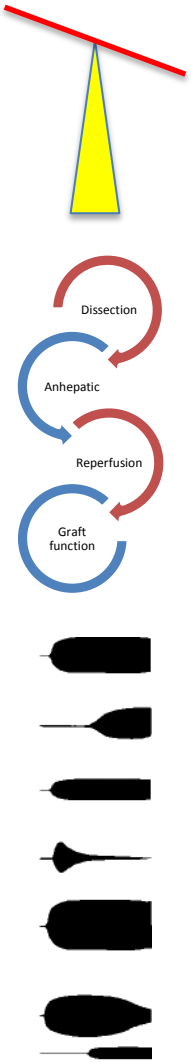
Ramos E et al. *Liver Transpl*. 2003
Intraoperative red blood cell transfusion in liver transplantation: influence on patient outcome, prediction of requirements, and measures to reduce them.



de Boer MT et al. *Anesth Analg*. 2008
The impact of intraoperative transfusion of platelets and red blood cells on survival after liver transplantation.

Summary

- Rebalanced coagulation in liver disease
- Dynamic predictable and unpredictable haemostatic changes during transplantation
- Limitations of conventional lab tests to describe and detect
- Comprehensive and clinically relevant information from viscoelastic tests
- Reduction in transfusion with VETs and why this is desirable



Clinical Utility of Viscoelastic Tests of Coagulation (TEG/ROTEM) in Patients with Liver Disease and during Liver Transplantation

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Point-of-Care Testing in Liver Disease and Liver Surgery

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REVIEW

Reducing transfusion requirements in liver transplantation

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