Revista Mexicana de Anestesiología

CONFERENCIAS MAGISTRALES
Vol. 37. Supl. 1 Abril-Junio 2014
pp S307-S311

Perioperative monitoring of coagulation

Alexandru Gottlieb, M.D. FACA*

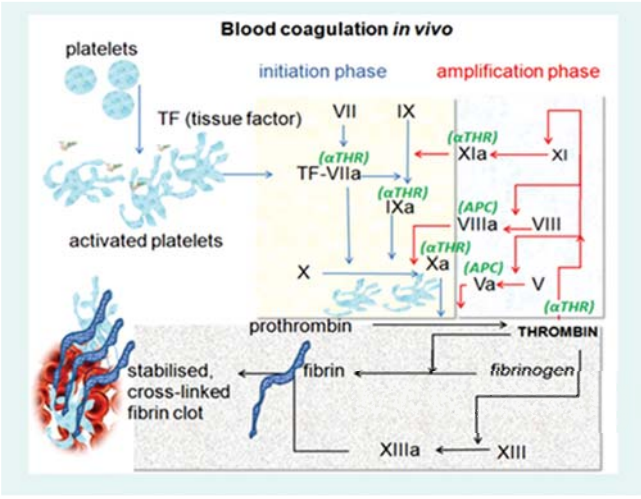
* Associate Professor of Anesthesia, Cleveland Clinic Lerner College of Medicine, Case Western Reserve University, Cleveland Clinic, Cleveland Ohio, USA.

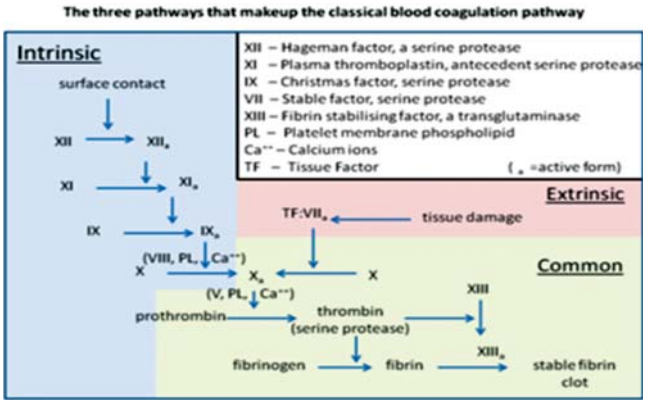
I. OUTLINE OBJECTIVES

The lecture will address the normal primary, secondary and tertiary stages of Hemostasis, elaborate on the effect of communally perioperative use of antiplatelet and anticoagulants on this hemostasis and review the perioperative monitoring of these effects including bedside testing of whole blood.

II. THE HEMOSTATIC FUNCTION

The aim of the hemostatic mechanism is to keep the blood flowing through intact vessels. Arteries have rapid high pressured flow. Any injury to arterial bed requires an immediate plug. And rapid, localized, controlled seal but preserving the Integrity of the blood flow. Veins system has a slower, intermittent flow





Antiplatelets and coronary stent

PCI	Length of RX	Drugs
Angioplasty	4-6 wks	Plavix®
BMS	3mo	Plavix®
DES: Sirulimus	3mo? 12mo*	Plavix®, ASA
Paclitaxel	6mo? 12 mo*	Plavix®, ASA

PCI = percutan coronary intervention, BMS = bare-metal stents, DES = drug-eluting stents, * lifetime.

Table I. Clinical signs/cause-Bleeding

Primary hemostatic disorder	
• Platelet Function Number • VWD	Immediate bleeding, bruising, petechia, epistaxis,
Secondary hemostatic disorder	
• Clotting factor Dysfunction Deficiency Inhibition • Fibrin deficiency	delayed bleeding, soft tissue hematoma ecchymosis
Tertiary hemostatic disorder	
• Failure to crosslink fibrin • Excessive fibrinolysis	general bleeding following clot
Why we need to monitor coagulation?	
1. Differentiate bleeding 2. Administer specific blood products 3. Identify & correct hypo/hypercoagulability 4. Monitor anticoagulation/antiplatelet RX 5. Identify thrombosis/fibrinolysis	

which makes them prone for intravascular thrombosis. The hemostatic mechanism developed systemic anticoagulants and clot dissolving systems to keep the vein patent.

Any interference in integrity of blood vessel starts the hemostasis mechanism that is made of 3 stages: 1) Primary hemostasis - platelets adhesion and aggregation. 2) Secondary hemostasis - Plasma factors cascade leading to Fibrin formation. 3) Tertiary hemostasis - fibrin crosslink and lysis of clot (Figure 1 and Table I).

The normal **plasma factor cascade** is demonstrated in PIC-2. It is comprised of Intrinsic, extrinsic and common pathways:

Intrinsic pathway - surface contact, factors; XII, XI, IX, VIII
Extrinsic pathway - tissue factor, VII
Common pathway - factors; X, V, II, I.

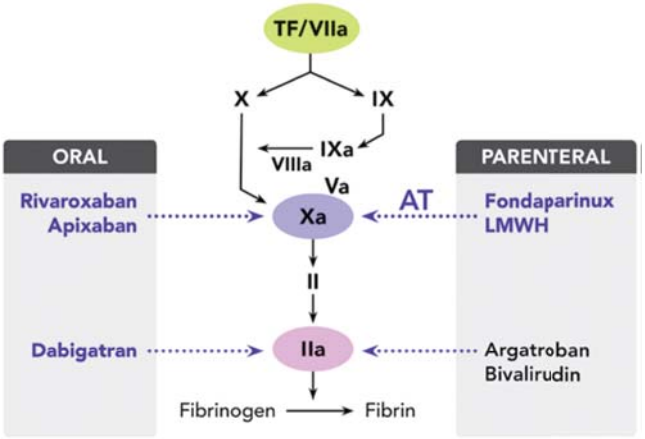
THE NEWER ORAL ANTICOAGULANTS

Direct thrombin inhibitor

Dabigatran etexilate (Pradaxa®)

Direct factor Xa inhibitors

Rivaroxaban (Xarelto),
Apixaban (Eliquis),



Advantages of these new agents- 1) rapid onset. 2) predictable anticoagulant effect. 3) routine coagulation monitoring is not required.

However, laboratory monitoring may be relevant and assessment of the anticoagulation status is needed in medical conditions such as; postoperative bleeding, overdose, trauma, and elective or emergent surgical procedures.

III. Monitoring of coagulation is done by clinical signs, by Tests of Clotting Factors (PT/PTT/INR, ACT, Factor assays) Platelet tests (Platelet count, Platelet aggregation) and by bedside whole blood functional tests [Bleeding time, Thrombelastography (TEG), SonoClot (SNC)].

a. Prothrombin time (PT) - is a functional test, of extrinsic & common pathway the will vary according to the type and batches of tissue factor (III). This is why the International normalized ratio (INR) was devised to standardize the results: Each manufacturer assigns an ISI value (International Sensitivity Index) for any tissue factor. And INR is then calculated by

$$INR = \left(\frac{PT_{test}}{PT_{normal}} \right)^{IST}$$

b. Partial thromboplastin time (PTT) - is a functional test of Intrinsic & common Pathway.
c. Thrombin time (TT) - measure the time to fibrin formation.
d. TECHNOCLOT® DTI (direct thrombin inhibitors)

IV. Point of care testing (near patient, bedside testing)

It was proven that bedside testing improved disease management and outcome in the 5Ds: **D**isease, **D**isability,

Perioperative used anticoagulants - drug effects

Drug	Mechanism of Action	Use	1/2-life, hour
Heparin (UH)	(+)Antithrombin-III Anti-IIa, IXa, Xa, XIa, XIIa	DVT	1.5
Warfarin (VKA)	Anti-VII, IX, X, and II	DVT	
LMWH (FH)	Anti-Xa, IIa (+) Antithrombin-III	DVT, ACS	4.5
Airxtra	(+) Antithrombin-III Anti-Xa	DVT	21
Hirudin	Antithrombin	HIT	3
Hirulog	Antithrombin	HIT	1
Argatroban	Antithrombin	Hemodialysis, HIT, AT-III-deficiency	1
Refludan	Antithrombin	HIT, DVT	2
Bivalirudin	Antithrombin	PCI, ACS, HIT	1/2
Pradaxa	Antithrombin	DVT	17

DVT = deep vein thrombosis, HIT = heparin induced thrombocytopenia, ACS = acute coronary syndrome, PCI = percutan coronary intervention.

Perioperative used antiplatelates - drug effects

Medication	Family	Use	Comments ½ life/h (bio)	
Ticlopidine (Ticlid)	Thienopyridine	ACS, PCI	Neutropenia	30-50 (12D)
Clopidogel (Plavix)	Thienopyridin e	ACS, PCI	PO only	120 (7D)
Prasugrel (Efient)	Thienopyridine	ACS, PCI	PO, fast onset	(9D)
Ticagrelor (Brilinta)	P2Y12 receptor Inb	ACS, PCI		(5D)
Abciximab (ReoPro)	IIb IIIa receptors blk	ACS	Thrombocytopenia	(48 h)
Eptifibarid (Integriline)	IIb IIIa receptors blk	ACS		(8 h)
Tirofiban (Aggrastat)	IIb IIIa receptors blk	ACS		(24 h)
Cilostazol (Pletal)	Phosphodiesterase IIIa Inb.	ACS, claudication		17 (5D)

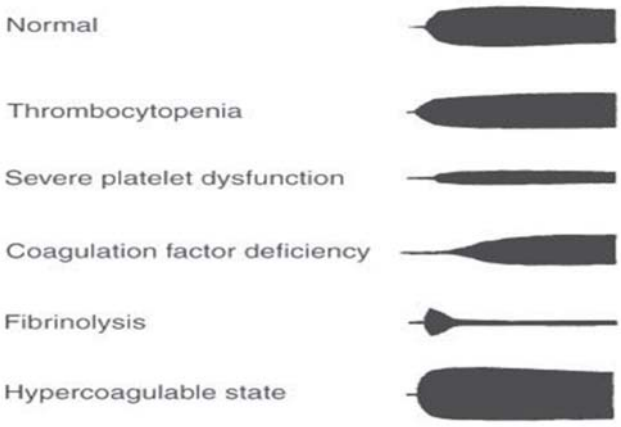
NAB (Epidural/Intrathecal) and anticoagulants

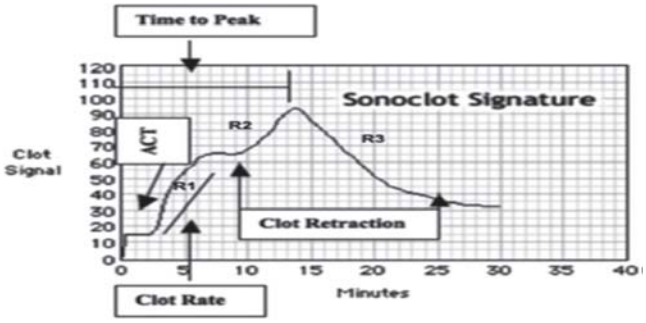
Agents	Time to NAB	Time to catheter removal	Time to antiCoag restart
Heparin Unfrac 5000Sq	No problem	No problem	No problem
7500	8 h	No	2 h
IV or 5000sq BID	aPTT< 44	No	2 h
Enoxaparin Lovenox	12 h	8-12 h	2 h
40-80 mgqd	24 h	No	2 h
1.5 mg/kg			
Fondaparinux (Arixtra) 2.5,10	2-3 D	1.5D	2 h
Rivaroxaban (Xarelto) 10,20mgpo	2D	2D, No	6 h
Dabigatran (Pradaxa)	3D	1.5 D	2 h
Warfarin (Coumadin)	INR< 1.5 , 10 D	No	no
Argatroban IV	DTI< 40, aPTT<40	No	2 h
Bivalirudin (Angiomax)	DTI< 40, aPTT<40	No	2 h
Lepirudin (Refludan)	DTI< 40, aPTT<40	No	2 h

NAB (epidural/intrathecal) and antiplatelet agents

Agents	Time to NAB	time to Catheter removal	time to antiCoag restart
Aspirin or NSAIDS	No problem	No problem	No problem
aspirin/dipyridamole (Aggrenox)	7 D	No	2 h
abciximab (Reopro)	48 h	No	2 h
eptifibatide (Integrelin)	8 h	No	2 h
clopidogrel (Plavix)	7 D	No	2 h
prasugrel (Effient)	7D	No	2 h
ticagrelor (Brilinta)	7D	No	2 h
tirofiban (Aggrastat)	8 h	No	2 h
Thrombolytic agents			
Alteplase (TPA)	No, 10 D	No	10 D

TEG





Figura

Figura

b. Platelet function Test

Monitor	Method	Uses	Comments
Ultegra, Verify Now	Light transmission	aspirin, Plavix, Gp IIbIIIa	(Disposable cartridge)
PFA-100 by Siemens	Closure time (CT)	Aspirin++ Tienopyridines +-	
The Cone, Plate (let) Analyzer (CPA)	Thrombogenic surface formation		Sensitive to Plt. count
Platelet analysis system (Hemodyne)	Platelet contraction force (PCF)		
Plateletworks by Helena Lab, Tx	Platelet aggregation By counting platelets		Uses ADP or collagen

Discomfort, **D**issatisfaction and **D**eath. In clinical outcomes surrogates studies it was shown to allow: faster decision, earlier treatment, improved compliance, reduced complications, faster optimization, reduced re-admission, and Increase patient satisfaction.

a. **Activated coagulation time (ACT):** monitor the activation of **intrinsic** pathway [Factor XII]. Done on whole blood with surface activator [celite, kaolin, glass). Technique sensitive, but demonstrates linear correlation to effects of Heparin. ACT and a PTT are not interchangeable. Normal range 100-300 seconds.
b. **Viscoelastic hemostatic tests (thrombelastogran (TEG), sonoclot (SCT):** *in vitro* whole blood hemostasis testing (see signatures below).

V. Monitoring of platelets

1. **Platelet count** - 140-400, <100 increased bleeding time, <50 can cause Surgical bleed and at <20 Spontaneous bleeding.

2. **Platelet function** - The different POC devises use the following methods (Table II): 1) Light transmittance aggregometry, 2) Impedance aggregometry, 3) Surface friction/adhesion, 4) Time for membrane occlusion, 5) Platelet contraction force, 6) Thrombogenic surface formation. All methods use an activator/facilitator such as: Arachidonic acid, Thrombin receptor, activating peptide, GP IIb/IIIa, ADP or epinephrine (Table II).

a. **Bleeding time** - Is not a predictor of risk of hemorrhage or effect of antiplatelet therapy. It is technique sensitive and poorly reproducible.
b. **Platelet function tests**

In conclusion: It is important for the Anesthesiologist to know and recognize the anti-platelet/coagulation mechanism and treatment of the patient, also to know how to monitor the coagulation perioperativelly in order to minimize the risk for thrombosis or bleeding.