Tips on Diagnosis and Management in Bleeding and Coagulopathy

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Objectives

At the end of this lecture, you will be able to:

- Apply evidence-based approach to the use of plasma and the INR value
- Evaluate hemostasis in cirrhotic patients
- Analyze and manage coagulopathic patients

Concepts related to plasma and International Normalized Ratio (INR)

- No study supports that a mild-moderate elevation of INR is predictive of bleeding
- Plasma does not correct a mild elevation in INR
- Vitamin K IV is reliably effective at reducing the INR to ~2 after 8 hours
- Adverse effects of plasma include serious or life-threatening: transfusion-related acute lung injury, transfusion-associated circulatory overload, anaphylaxis, infection
- A “normal” INR has never been redefined despite the advance of technology

Why is Plasma Transfused?

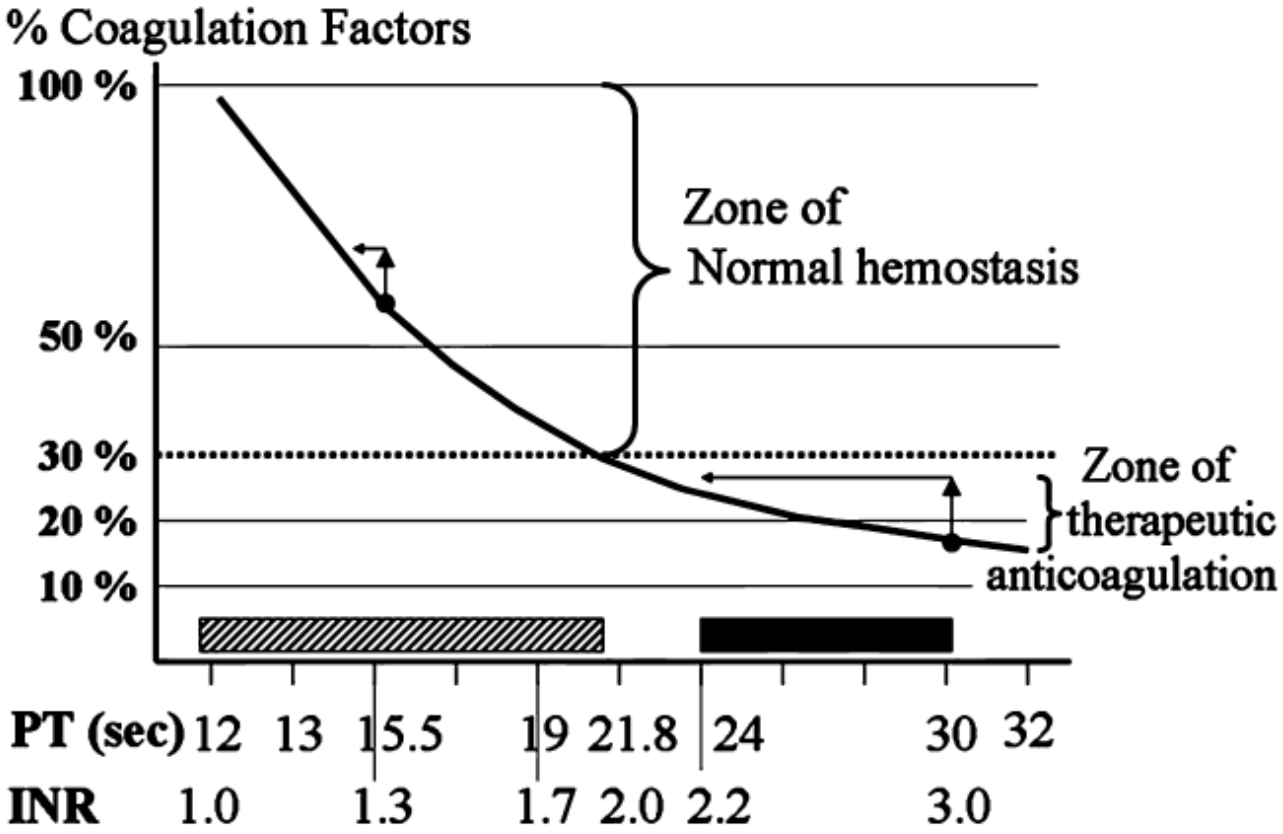
- Prophylactically
  - To reduce or prevent bleeding in patients with a coagulopathy prior to an invasive diagnostic or therapeutic procedure
    - The prothrombin time and its derivative, the INR, appears the most common test used to gauge hemostatic risk
- Therapeutically
  - Therapeutic plasma exchange when plasma is required as the replacement fluid rather than albumin
  - As clotting factor replacement in patients with active bleeding who have a known (e.g. patient on warfarin) or suspected coagulopathy (e.g. massive transfusion)
- Historical precedent (“we’ve always done it this way”)
- Eminence-based medicine
  - Opinion of a highly regarded authority figure
  - Consensus conference composed of experts in which there is insufficient evidence for a firm conclusion

Prothombin time and the International Normalized Ratio (INR)

- The PT/INR is an artificial reconstruction of the clotting system which attempts to mimic in vivo thrombin generation:
  - End-point is clot formation which occurs after about 4% of prothrombin is converted to thrombin

- Usefulness depends on the context:
  - PT/INR useful to measure the effect of vitamin K antagonists
  - Extreme prolongations ***may be*** (though not necessarily) indicative of a hemostatic risk
  - Are mild (INR 1.2 – 2.0) or moderate (INR 2 –3) prolongations of use in predicting clinical bleeding?

Relationship between PT/INR and percentage of clotting factors in blood



The hatched horizontal bar represents INR values that correspond to the zone of adequate factor levels. The dark horizontal bar represents INR values of anticoagulation. Arrows depict the effect of 1 to 2 units of FFP.

Redefining “normal” INR

- Laboratory reagent sensitivity has improved in recent years
- There has been no corresponding re-evaluation of normal coagulation parameters
- Only 5-30% of normal clotting factor activity levels are required for normal hemostasis
- Thus factor levels that prolong the PT/INR with modern, sensitive reagents do NOT correlate to factor levels that cause hemorrhage

Evidence **against** plasma transfusion

Paper	n	PATIENTS	DESIGN	RESULT
Spector, NEJM, 1966	13	Liver disease, prolonged PT, not bleeding, no procedure	Vol. plasma needed to shorten PT to within 3 secs normal	600-1200 mL plasma needed; correction failed in 5/13; correction only lasted 2-4 hrs
Ewe, Dig Dis Sci, 1981	200	Liver biopsy at time of laparoscopy	Measure PT prebiopsy and liver bleeding time	No correlation between liver bleeding time and PT
Ragni, Alcohol Clin Exp Res, 1982	30	Alcoholic cirrhosis	Measure PT, aPTT, TT, reptilase time and observe for hemorrhage	21/31 had bleeding; no correlation between bleeding and any tests
Friedmann, Clin Lab Haemat, 1989	39	Liver disease with prolonged PT 15-29 sec and invasive procedure (thoracentesis, LP, CVC, paracentesis)	71 procedures: 57/71 in 30 pts did not get plasma; 14/71 in 12 pts got plasma	3/71 procedures associated with bleeding: 2/12 pts (same patient) who got plasma 1/57 procedures without plasma
McVay, Transfusion, 1991	395	Patients getting thoracentesis or paracentesis	Measured bleeding by Δ 2g pre Hgb – post Hgb and clinical assessment	Bleeding 3.1%, transfusion 0.2%, no increased bleeding in mild coagulopathy (PT >2x norm (INR <3.8) or plt >50K)

Evidence **against** plasma transfusion

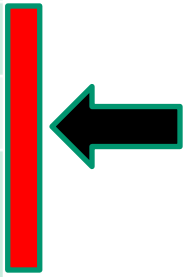
Paper	n	PATIENTS	DESIGN	RESULT
Zins, Radiology, 1992	72	78 US-guided percutaneous liver biopsies (with gelatin/thrombin plugging of needle track in 72)	Patients grouped by severity of coagulopathy (1=normal, 4=most severe)	2/72 bled (both were in group 4, which had a total of 30 patients) • One of these had plt 28K • One had aPTT ratio >2.2 with significant tumor burden
Foster, Arch Surg, 1992	40	Liver transplant: 259 CVC placements (149 internal jugular, 110 subclavian)	202/259: abn PT, aPTT, or plt • None got plasma or plts	Only one bleeding event (in patient where inadvertent cannulation of subclavian artery occurred)
Caturelli, Liver, 1993	85	Hepatic cirrhosis: 229 US-guided fine needle liver biopsies	All had plt <50K or PT<50% control; none got plasma or plts	No bleeding
Kozak, Chest, 1994	274	Fiber-optic bronchoscopy	28/274 had abnormal PT	35 bleeding events: 3/28 with abnormal PT and 32/246 with normal PT
Inabnet, Amer Surgeon, 1995	22	58 laparoscopic liver biopsies in patients with coagulopathy, portal hypertension, ascites	Coagulopathy = inc PT, bleed time, or plt <100 5 patients got plasma or plts	One patient bled and that patient had received plasma pre-procedure

Evidence **against** plasma transfusion

Paper	n	PATIENTS	DESIGN	RESULT
Delougherty, Transfusion, 1996	490	ICU patients getting 938 invasive line placements	388 had hemostatic defects (144/388 got plasma)	16 bleeding events, two life-threatening, 15/16 had coag abnormality; no single test predictive of bleeding • Score based on PT/aPTT, plt count, and creatinine correlated with bleeding risk • Operator experience of line placement most predictive
Gilmore, Gut, 1995	1500	Percutaneous liver biopsies	Overall bleeding rate=1.7% INR 1.3-1.5 3.3% bled INR >1.5 7.7% bled	No mention of plasma, cannot conclude that plasma attenuates bleeding Cannot be discerned whether patients with suspected malignancy (37%) had higher INR, therefore cannot conclude that INR is independent variable associated with bleeding
Seeff, Clin Gastro Hepatol	2740	HCV, liver biopsies "HALT-C" study	16/2740 bleeding events	All bleeding events occurred at INR <1.5

Bleeding risk with liver biopsy

	UK Study	HALT-C Study	Roger Williams Study
# Biopsies	1500	2740	491
Overall Risk	26/1500 (1.7%)	16/2740 (0.58%)	0/491 (0%)
Unknown			0/322 (0%)
INR < 1.0		6/1517 (0.3%)	0/10 (0%)
INR 1.1		3/743 (0.4%)	0/95 (0%)
INR 1.2		3/279 (1.1%)	0/57 (0%)
INR > 1.3	(1/30) 3.3%	3/123 (2.4%)	0/6 (0%)
INR >1.5	(1/14) 7.7%	0/8 (0%)	0/1 (0%)



The INR of thawed plasma varies between 1.14 and 1.4

Summary of data

- The preponderance of data from observational studies shows that the PT/INR does not show any correlation with clinical bleeding in association with invasive procedures unless very abnormal.
- The evidence that prophylactic plasma attenuates bleeding risk in patients with a prolonged PT/INR undergoing an invasive diagnostic procedure can best be summarized as :

NONE

Risks of Transfusion

- Greatest risk of transfusion is NOT viral.
  - HIV 1:2,000,000
  - Hepatitis C 1:1,390,000
  - Hepatitis B 1:280,000
- Noninfectious complications of blood transfusion statistically are of greatest risk to the patient.
  - Fever 1:100
  - Allergic 1:100
  - TACO 1:100
  - TRALI 1:10,000

TACO=transfusion associated circulatory overload

- Transfusion-related acute lung injury (TRALI) and hemolytic transfusion reactions (HTR) are two of the three most reported causes of transfusion-related mortality causally linked to a reaction.
- Noninfectious complications of blood transfusion are under-recognized and under-reported.

Geisinger Plasma Transfusion Guidelines

- Warfarin reversal ONLY IF vitamin K and/or 4-factor prothrombinase complex concentrate are not available
- Thrombotic thrombocytopenic purpura if plasmapheresis is not available
- INR >1.7 and need for invasive procedure
- Post massive transfusion protocol to prevent development of coagulopathy
- Single factor deficiency where commercial concentrates are not available (factor V, factor XI)
- Treatment or prophylaxis of thromboembolism in antithrombin, protein C or protein S deficiency

Plasma transfusion contraindications

- Normalizing INR <1.7 in the absence of bleeding
- Increasing blood volume or albumin concentration
- Coagulopathy that can be corrected with vitamin K administration
- Factor VII deficiency
- Single factor deficiency where commercial concentrates are available

4-Factor Prothrombinase Complex Concentrate (PCC)

- **Nonactivated** lyophilized concentrates of vitamin K-dependent coagulation factors (VKDC) II, VII, IX, X, plus antithrombotic proteins C and S and heparin
  - PCC concentration of VKDC is 25x higher than plasma
  - One dose of PCC = 2000 mL plasma in terms of VDKC concentration
  - Contains antithrombotic agents to combat the risk of thrombosis
- Trade name Kcentra in US
- FDA approved and effective for urgent vitamin K antagonist reversal during acute major bleeding or a need for urgent surgery
- Off-label use of 4-factor PCC for major hemorrhage has shown some efficacy in observational studies
- Carries the risk of fatal and non-fatal arterial and venous thromboembolic complications and has not been studied in patients with recent (3 month) history of thromboembolic events, MI, DIC, CVA, TIA, UA, or severe PVD.

Geisinger Best Practice Guidelines for the Utilization of 4-Factor PCC

- **URGENT WARFARIN REVERSAL (FDA approved)**
  - In patients with acute major or life-threatening bleeding, including intracranial hemorrhage or in need for an URGENT (<12 hours) surgery/invasive procedure
  - In conjunction with IV vitamin K (phytonadione)
  - Patients that do not require urgent reversal should have their coagulopathy corrected with vitamin K without KCentra.

- **URGENT Xa INHIBITOR REVERSAL*: rivaroxoban, edoxaban, apixaban, fondaparinux**
  - Severe or life threatening bleeding, emergent surgery or invasive procedure in patients who are thought to have acquired coagulopathy from Xa inhibitors.

- **Use for coagulopathy not caused by warfarin or Xa inhibitors such as for patients with cirrhosis* or post-operative bleeding* requires approval from the coagulation pathologist on-call**

*Off-label

Chronic Liver Disease and Hemostasis

- Chronic liver disease often results in multiple defects in routine coagulation laboratory studies
  - PT and INR are linked to prognosis and progression of liver disease, and mortality risk scores for cirrhosis have key components related to PT or INR
  - Platelet count is commonly regarded as an indirect measure of portal hypertension related to splenic sequestration and loss of hepatic production of thrombopoietin
- There is growing evidence that these patients are effectively “rebalanced” with regard to procoagulant and anticoagulant activity and that most patients remain in a tenuous but **balanced** state of hemostasis

Chronic Liver Disease and Hemostasis

- No established laboratory tests accurately reflect the changes in both the procoagulant and anticoagulant systems, making routine laboratory testing misleading to the clinician and may prompt inappropriate or risky therapies with little real benefit to the patient
  - e.g. INR: linked to prognosis and severity of protein synthetic dysfunction in acute and chronic liver disease but a very poor marker for bleeding risk and should not be used in isolation for this purpose
- Yet cirrhotic patients often present with hemorrhage and/or in need of invasive intervention

➢ *What is a clinician to do?*

- Suggested approach:
- PT/INR, aPTT, platelet count, fibrinogen
  - Add TEG up front if urgent
  - Await results of above if not urgent

Diagnostic Tests of Coagulation in Liver Disease

Test	System analyzed	Strengths	Weaknesses
INR and PT	Classic procoagulant extrinsic pathway only	• Widely available • Inexpensive • Quick • Good correlation with severity of liver disease	• High interlaboratory variability • Narrow measure of procoagulant system only • Not predictive of bleeding
Activated partial thromboplastin time	Classic procoagulant intrinsic pathway only	• Widely available • Inexpensive • Quick • Can detect congenital factor deficiencies	• Usually does not reflect hepatic dysfunction • Narrow measure of procoagulant system only • Usually normal or nearly normal in liver disease
Platelet count	Platelet	• Widely available • Inexpensive • Quick • Reproducible and has some clinical correlate with bleeding at low levels	• Does not reflect platelet function • Is not useful in predicting bleeding at higher levels
Platelet function assays	Platelets and primary hemostasis	• Can give some evidence of generalized platelet function compared with normal	• Most assays assume normal platelet counts and are not calibrated for thrombocytopenia • Not universally available • Not studied extensively in liver disease

Diagnostic Tests of Coagulation in Liver Disease (continued)

Test	System analyzed	Strengths	Weaknesses
Fibrinogen	Fibrinolysis	• Low levels suggestive of hyperfibrinolysis • Levels >100 mg/dL suggest adequate fibrinogen for initiation of coagulation	• Acute phase reactant • Low levels are common in stable nonbleeding cirrhosis patients • Not predictive of disseminated intravascular coagulation in cirrhosis
Factor levels	Procoagulant and anticoagulant pathways	• Can give a relative sense for factor deficiencies on either procoagulant or anticoagulant system	• Significant laboratory variation • Factor levels are affected by acute clotting and other disease processes • No clear relationship to bleeding or clotting risks
Thromboelasto-graphy	Universal hemostasis	• Used for decades for intraoperative transfusion guidance • Can show defects in multiple components of hemostasis to guide therapies	• Whole blood test requiring near immediate turnaround • No standardization of most parameters • Requires experience to interpret tracings • Not validated in predicting bleeding or clotting in nonsurgical patients • May be insensitive in the hypercoagulation population

Thromboelastography parameters

Thromboelastography parameter	Correlations with physiologic phase of hemostasis	Correlations with standard hemostatic laboratory tests
Reaction time (min)	Time from initiation of coagulation cascade to initial formation fibrin	INR, aPTT, procoagulant factor levels
Kinetic time (min)	Time from initial formation of fibrin to specific clot firmness (20 mm)	Fibrinogen, platelet count
α-angle (degrees)	Rate of fibrin formation and crosslinking	Fibrinogen, platelet count
Maximum amplitude (mm)	Maximum clot strength	Fibrinogen, platelet count
Lysis-30 (%)	Fibrinolysis 30 minutes after maximum amplitude	Fibrin degradation products

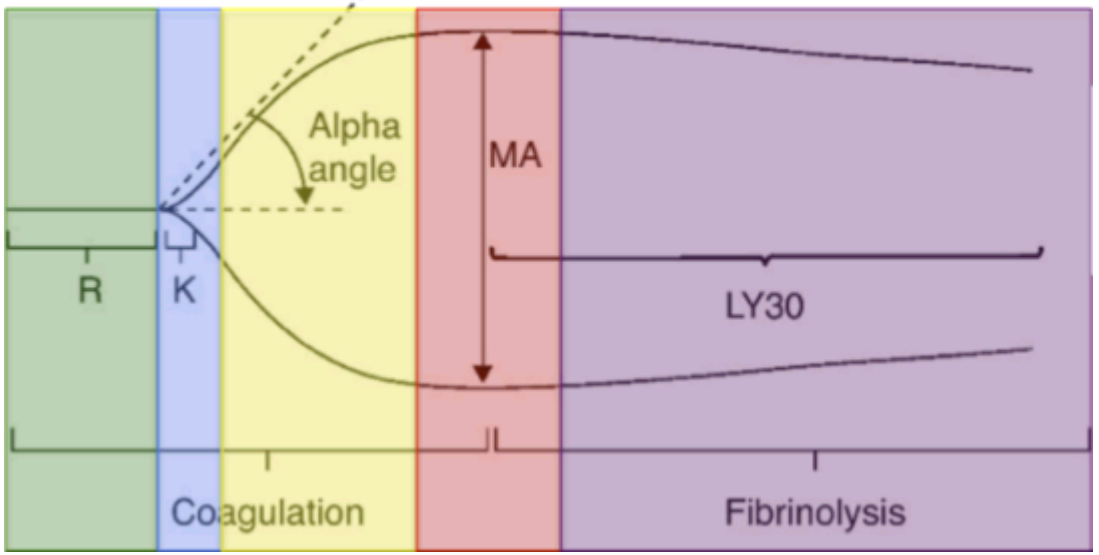


Photo credit rebelem.com

Common TEG tracings

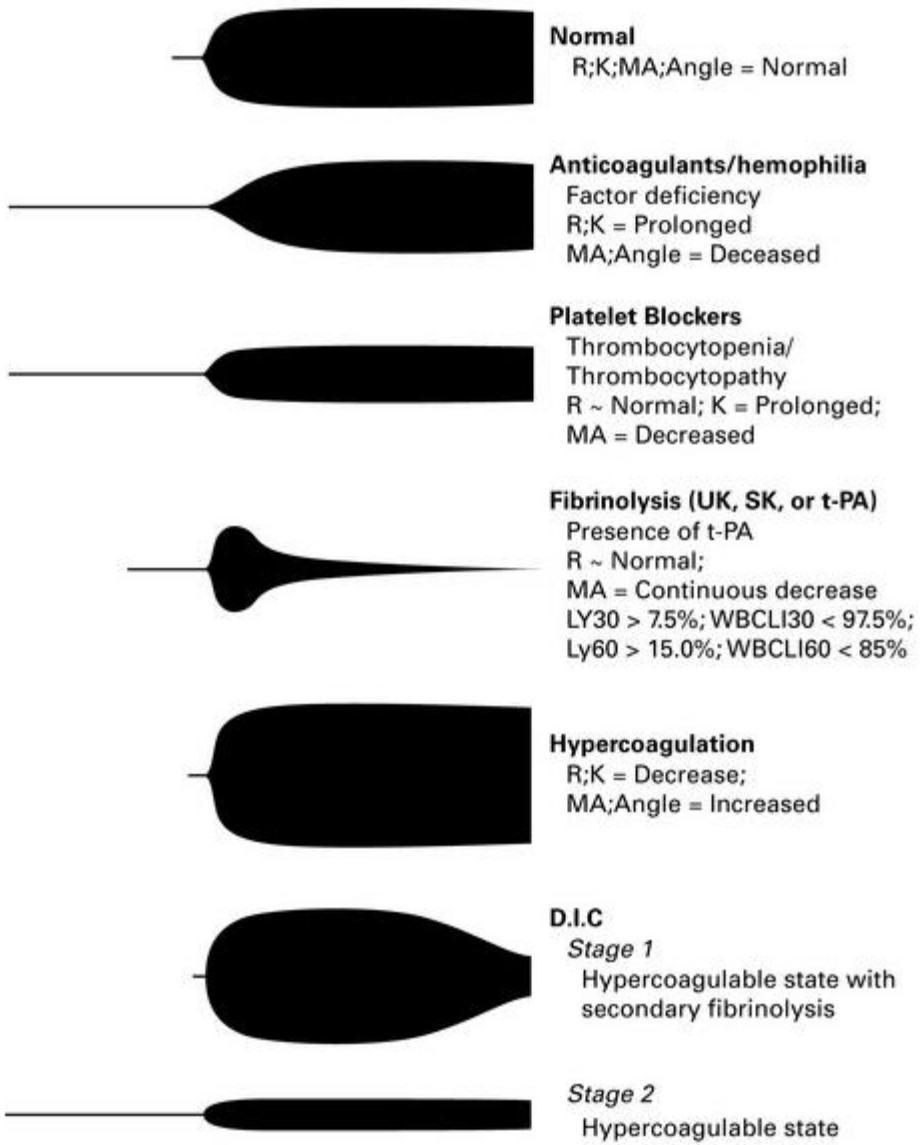


Photo credit
http://clinicalgate.com/general/

Approach to bleeding evaluation

- Considerations include vascular integrity, platelet number and function, coagulation factors, and fibrinolysis
- Medications
- CBC, PT/INR, PTT, fibrinogen, soluble fibrin monomer, TEG

General tips when managing bleeding with transfusion

- Be aware of volume, risk of circulatory overload
- Red out does not mean only red in
  - 4 units RBC in 4 hours
  - 6 units RBC in 24 hours
- Laboratory-guided versus balanced resuscitation

PT and PTT results

- PT, PTT both prolonged: may be a decrease in final common pathway factors (prothrombin, fibrinogen, V, X) or combined intrinsic and extrinsic factors decreased
  - often warfarin or liver disease
- PT prolonged, PTT not: factor VII decreased
  - there is no factor VII in plasma due to its significantly short t(1/2) so do not give plasma in this instance
- PT not, PTT prolonged: extrinsic factors decreased (VIII, IX, XI, XII)
  - possible lupus anticoagulant or factor inhibitor

One approach from UK Trauma

Laboratory Value	Interpretation	Blood Product Transfusion
R less than 4 min	Enzymatic Hypercoagulability	No treatment if bleeding
R between 11-14 min	Low clotting factors	Plasma and RBC's
R greater than 14 min	Very low clotting factors	Plasma and RBC's
a-angle<45 degrees	Low fibrinogen level	Cryoprecipitate/ Fibrinogen /Platelets
MA between 46-54 mm	Low platelet function	Platelets / Cryoprecipitate/ Fibrinogen
MA between 41-45 mm	Very low platelet function	Platelets / Cryoprecipitate/ Fibrinogen
MA at 40 mm or less	Extremely very low platelet function	Platelets / Cryoprecipitate/ Fibrinogen
MA greater than 73 mm	Platelet Hypercoagulability	No treatment if bleeding
LY30 greater than 3% , CI less than 1.0	Primary fibrinolysis	**Tranexamic acid** 1g IV over 10 minutes followed by 1g in 250cc NS infused over 8 hours

Credit: uktraumaprotocol.blogspot.com

Oral anticoagulants

- Vitamin K antagonist versus direct oral anticoagulants (DOACs)

	Pros	Cons
Warfarin	Extensive clinical experience; well-known antidotes available	Narrow therapeutic range; drug and food interactions; need for laboratory monitoring
DOACs	Well-described efficacy, safety, predictable effect	Reversal not well characterized in setting of bleeding, trauma, surgery

- Among patients with atrial fibrillation on DOACs, annualized major bleeding rate 2.1-3.5% (associated with increased risk of death)
- If urgent surgical procedures required, DOAC patients higher risk of life-threatening bleeding

Antiplatelet Agents

Four groups:

- COX-1 inhibitors (*aspirin, nonsteroidal anti-inflammatory drugs*)
- ADP receptor inhibitors (*clopidogrel, prasugrel, ticlopidine, ticagrelor*)
- GPIIb/IIIa (fibrinogen receptor) inhibitors (*abciximab, eptifibatide, tirofiban*)
- Miscellaneous (*dipyridamole, cilostazol, anagrelide, vorapaxar*)

…as well as fish oil and herbs like gingko biloba and ginseng

	ASA	Clopidogrel	Prasugrel	Dipyridamole	Eptifibatide	Tirofiban
Half-life (hr)	0.5	7-8	7	13.5	2.5	1.4-1.8
Bleed risk	+	+++	++++	+	+++	+++
Elective surgery	No wait	7 days	7 days	No wait	8 hours	8 hours

Platelet Function Test	Description
Platelet function screen (with collagen/epinephrine reagents) (AKA PFA 100)	• Whole blood flows at high shear rate through aperture in collagen-coated membrane. One cartridge coated with ADP and one coated with epi; these agonists activate platelets and platelet plug gradually closes aperture, measured by time (in secs) • Used to screen for intrinsic platelet defects, von Willebrand disease (VWD), or exposure to platelet inhibiting agents (ASA). • May reflex to confirm with ADP/collagen reagent if indicated.
Verify Now (ASA)	• Whole blood added to cartridge where platelets are activated by arachidonic acid; agglutination of fibrinogen-coated beads is recorded optically as the endpoint. • Used to detect drug effect; often used for guiding anti-platelet drug therapy if there is a poor response to an APA. • The effect of aspirin lasts while the platelets are in circulation.
Verify Now (P2Y12)	• Whole blood added to cartridge where platelets are activated by ADP; agglutination of fibrinogen-coated beads is recorded optically as the endpoint. • Used to detect drug effect; often used for guiding anti-platelet drug therapy if there is a poor response to an APA. • Resistance is seen in 20-30% of patients.
Thromboelastograph	• Whole blood viscoelastometry (assesses viscosity and elasticity of clotted whole blood). • Platelets increase both the dynamic viscosity and elasticity of clotted whole blood in a dose-dependent manner; ~70% of the elasticity of the clot is directly proportional to platelet count in the sample, with the remaining due to fibrinogen concentration. • Test is dependent on platelet activation by thrombin and is therefore **insensitive to platelet inhibition by aspirin, NSAIDs, and thienopyridines**, as well as VWD. The test is **sensitive to GPIIb/IIIa antagonists**.

Vitamin K Antagonist

- INR between 4.5 and 9 with NO evidence of bleeding.
  - Hold warfarin
  - Optional: Vitamin K 2.5mg oral once
- INR greater than 9 with NO evidence of bleeding.
  - Hold warfarin
  - Vitamin K 2.5 mg oral once

Expect response in 24 hours from PO vitamin K

- Reversal of INR needed for urgent procedure (in GREATER than 12 hours).
  - Vitamin K 5 mg IV, once STAT

Expect response in 6 hours from IV vitamin K

- Severe or life threatening bleeding with ANY INR elevation or for emergency procedure (WITHIN 12 hours):
  - Hold warfarin
  - Vitamin K 5 mg IV, once STAT
  - IF INR <4
    - Prothrombin Complex Concentrate (Kcentra) 25 units/kg, IV, once STAT, Max dose 2500 units
  - IF INR 4 – 6
    - Prothrombin Complex Concentrate (Kcentra) 35 units/kg, IV, once STAT, Max dose 3500 units
  - IF INR > 6
    - Prothrombin Complex Concentrate (Kcentra) 50 units/kg, IV, once STAT, Max dose 5000 units
  - If INR unavailable
    - Prothrombin Complex Concentrate (Kcentra) 25 units/kg, IV, once STAT, Max dose 2500 units

Factor Xa inhibitors

- Reversal of Rivaroxaban (XARELTO), Apixaban (ELIQUIS), Fondaparinux (ARIXTRA), and Edoxaban for severe or life threatening bleeding or for emergency procedure (WITHIN 12 hours):
  - Prothrombin Complex Concentrate* (Kcentra) 25 units/kg, IV, once STAT

- For intracranial hemorrhage specifically
  - Prothrombin Complex Concentrate* (Kcentra) 50 units/kg, IV, once STAT
- If ingestion of rivaroxaban or apixaban within past two hours:
  - Charcoal activated oral liquid 100 g, once STAT

- For emergency procedures, need to determine when the last dose was taken, half-life of the medication, and patient's renal function
- INR is NOT an accurate marker of anticoagulation for these agents and may be falsely elevated.

*Off-label

Direct Thrombin Inhibitor

- Reversal of Dabigatran (PRADAXA) for severe or life threatening bleeding or for emergency procedure (WITHIN 12 hours):
  - Idarucizumab (Praxbind) 2.5gm IV, q15min x 2 doses
- Repeat CBC and PTT (at 1 hour and 24 hours after completion of Idarucizumab)
  - If bleeding recurs within 24 hours after having been controlled by Idarucizumab AND repeat aPTT elevated:
    - Repeat Idarucizumab 2.5gm IV, q15min x 2 doses
- If ingestion of dabigatran within past two hours:
  - Charcoal activated oral liquid 100 g, oral, once STAT

- For emergency procedures, need to determine when the last dose was taken, half-life of the medication, and patient's renal function.
- INR is NOT an accurate marker of anticoagulation and may be falsely elevated.
- At normal concentrations, the aPTT will be 2x normal between 1-6 hours after ingestion and 1.5x normal 12 hours after ingestion.
- At overdose concentrations, PTT will be unmeasurable > 120 seconds

Guideline for Evaluation and Management of Coagulopathy in Cirrhosis for GI Procedures

Component	Recommendation
Platelet transfusions for low risk procedures*	Transfuse if platelet count <30K/uL
Platelet transfusions for high risk procedures**	Platelets may be warranted during procedures if platelet count ≤30 K/uL (for percutaneous liver biopsy target ≥50 K/uL)
Clotting factor support	INR ≤ 2.5, no clotting factor support needed If INR ≥2.6 and procedure not emergent: give 5 mg IV vitamin K; if IV vitamin K does not correct INR to acceptable level after 6-8 hours: order a TEG and get a Laboratory Medicine consult if assistance needed in interpretation If INR ≥2.6 and procedure emergent: give 5 mg IV vitamin K and order a TEG and get a Laboratory Medicine consult if assistance needed in interpretation
Cryoprecipitate	Give one 5-pool of cryoprecipitate if fibrinogen < 100 mg/dL
RBC transfusion in hemodynamically stable patients without cardiovascular disease	Transfuse one unit if hemoglobin <7 g/dL; target hemoglobin not to exceed 8 g/dL

* Low-risk procedures include the following: diagnostic endoscopy with or without biopsy, esophageal dilation, endoscopic interventions for gastrointestinal bleeding such as clip placement, cauterization or epinephrine injection, elective variceal banding, and routine screening colonoscopy (polyps up to 1 cm in size can be biopsied or removed with cold snare).

** High-risk procedures involving significant disruption of mucosa such as snare polypectomy (for polyps >1 cm in size), PEG, endoscopic ultrasound with fine-needle aspiration or biopsy, endoscopic mucosal resection, endoscopic retrograde cholangiopancreatography with sphincterotomy.

Adapted from Yates S, Gavva C, Agrawal D, Sarode R. How do we transfuse blood components in cirrhotic patients undergoing gastrointestinal procedures? Transfusion 2016;56;791–798.

Guideline for Evaluation and Management of Coagulopathy prior to IR procedures

- Procedures with low-risk of bleeding: INR<2, Plt>25, heparin off at 1 hour
- Procedures with moderate- or high-risk of bleeding: INR<1.5, Plt>50, heparin off at 2 hours

Low

Vascular
Dialysis access interventions (AV fistulas, access-Non-tunneled)
Non-tunneled Venous access
Tunneled CVC exchange
Venography
Central line removal
IVC filter placement
PICC placement
Non-vascular
Drainage catheter exchange
Thoracentesis/paracentesis
Superficial aspiration/biopsy, thyroid/Lymph Node, neck Mass
Superficial abscess drainage
Biliary and Nephrostomy catheter exchange

Moderate

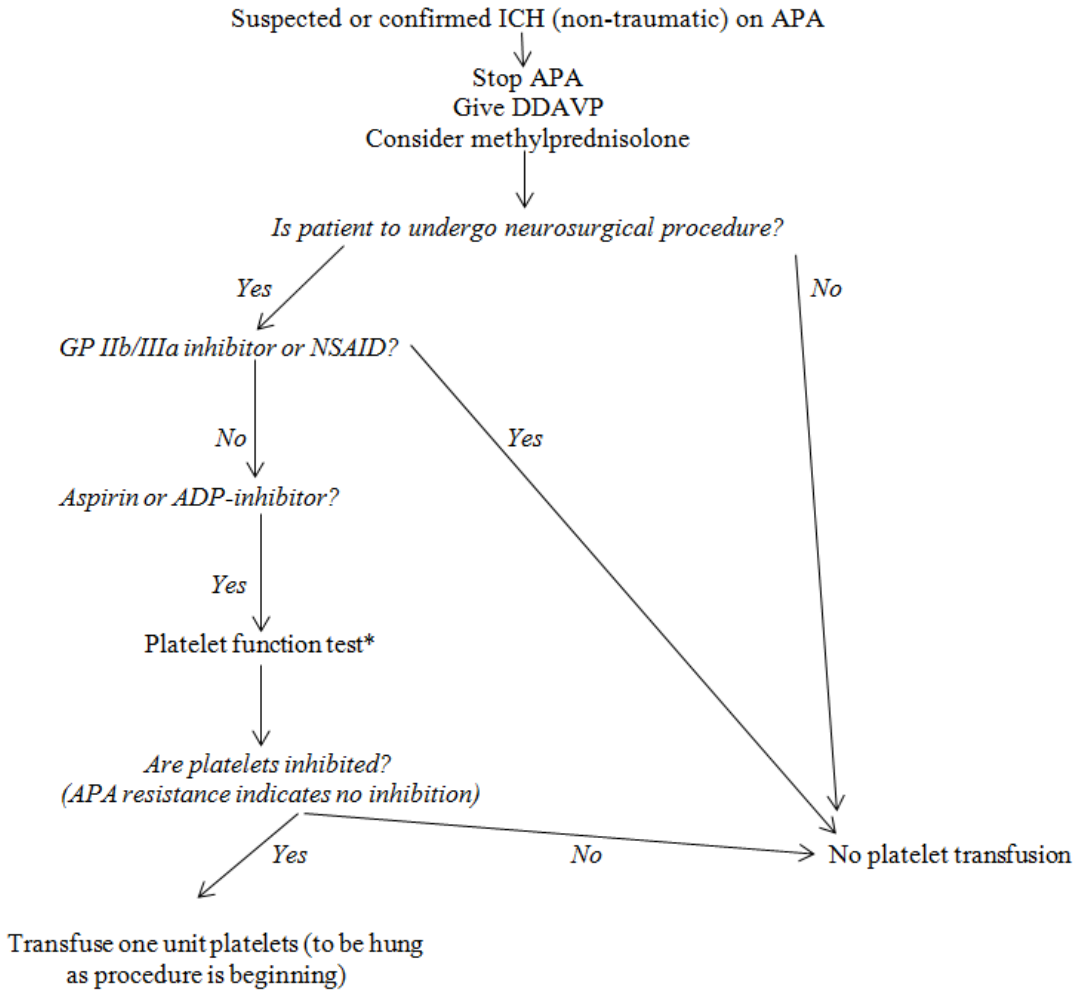
Vascular
Angiography, arterial interventions
Venous interventions
Chemoembolization
Uterine Artery Embolization
Transjugular liver biopsy
Tunneled CVC
Port
Non-Vascular
Intra-abdominal chest wall of RP abscess or biopsy
Lung Biopsy
Percutaneous liver bx/cholecystostomy
G tube – initial placement
Ablation: straightforward
Spine procedures (Kyphoplasty, LP)

High

Vascular
TIPS
Non-vascular
Renal Biopsy
Biliary Interventions (new tract)
Nephrostomy tube placement
Ablation - complex

- Coagulation Profile and Platelets work-up NOT required for following procedures: Non-Tunneled Catheter removal, Gastrostomy Change, and G J tube change

Guideline for Evaluation and Management of Platelet Dysfunction related to Antiplatelet Agents in Non-Traumatic Intracerebral Hemorrhage Patients



* At discretion of attending physician based on stability of patient and ability to await test results

Plasma and INR Conclusions

- When the INR is 2.0 or less
  - The % coagulation factors present correlates to zone of normal hemostasis
  - Small doses (or even larger doses) of plasma will not make any meaningful change in the INR
- In vivo defect in thrombin generation (if any) in liver disease is poorly reflected in the INR
  - Thus the prophylactic use of plasma based on the INR to “normalize” in vivo thrombin generation does not have an established basis
- Use of vitamin K to reverse warfarin partially or otherwise is far more effective than plasma without a great difference in response time