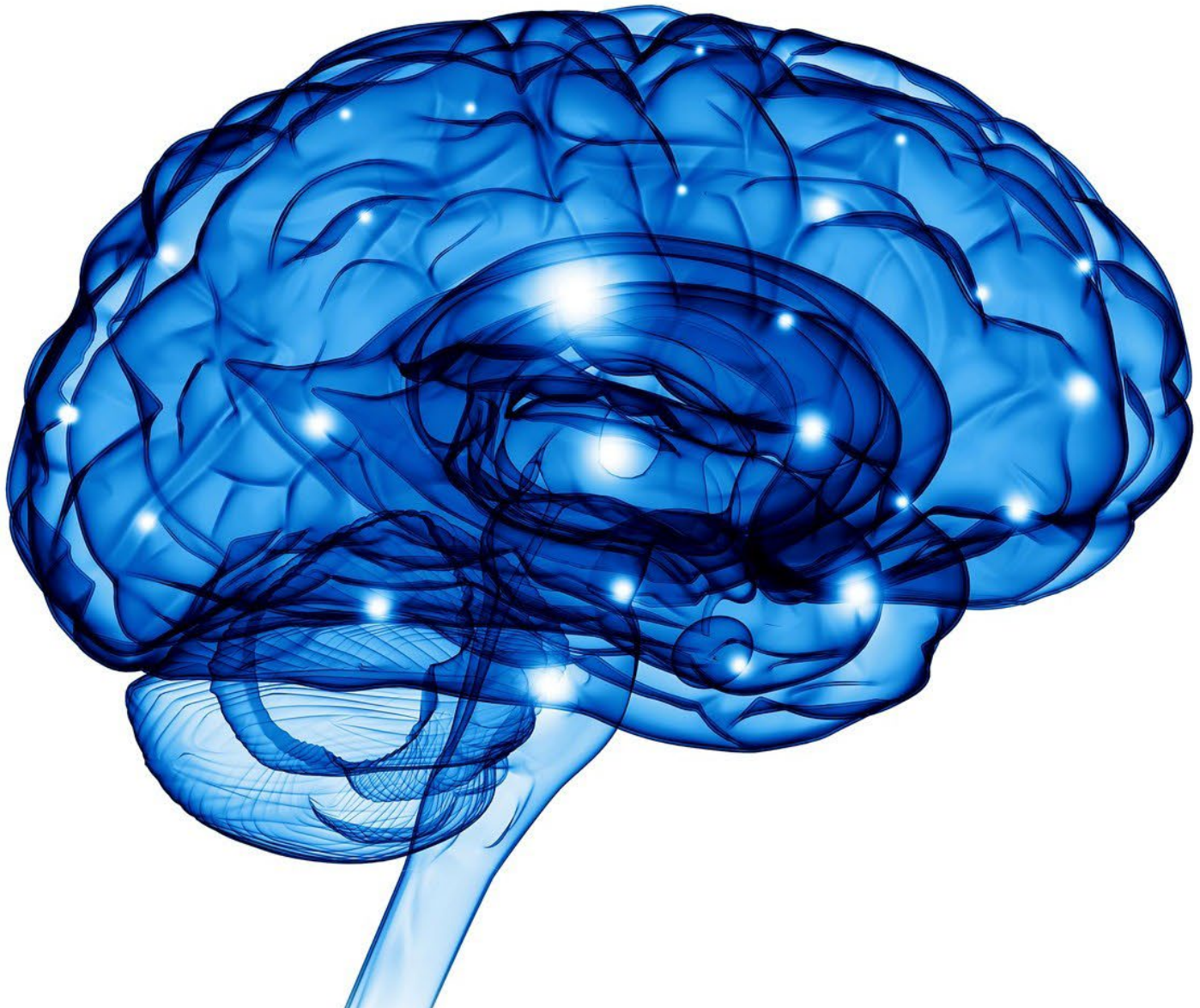


Thromboelastography for Bleeding Patients

Tiffany Chang, MD

Associate Professor, Neurosurgery and Neurology

Director, Neurocritical Care Fellowship Program

UTHealth® Neurosciences

The University of Texas Health Science Center at Houston

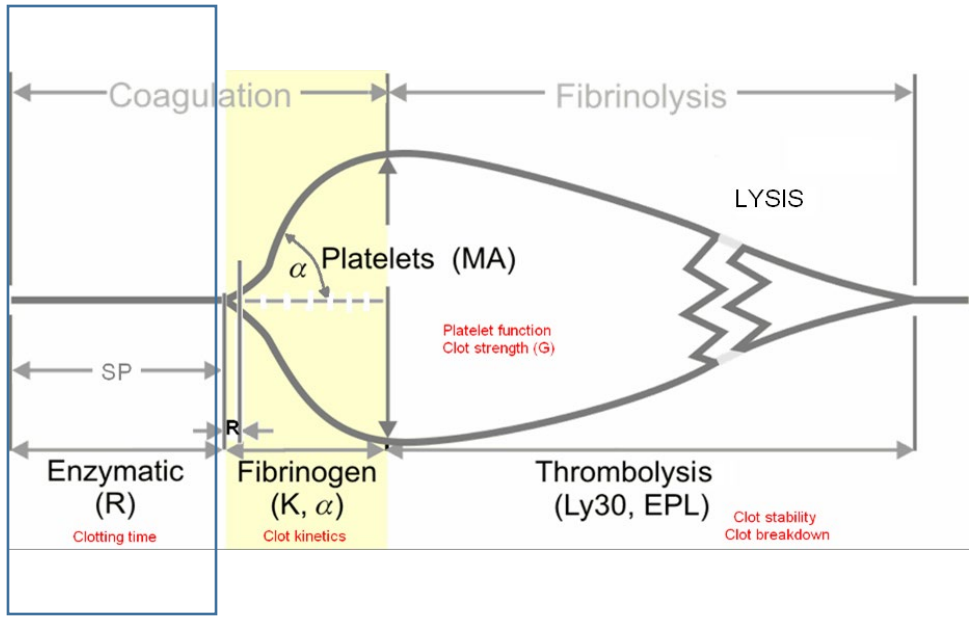
Disclosures

- I do not have relevant financial relationships with commercial interests related to the content of this presentation

Objectives

1. Define various thrombelastography (TEG) parameters
2. Explain the significance of coagulopathy in the critical care population
3. Utilize TEG to benefit Neuro ICU patients

CLOT TIME



Activity:

Thrombin generation, fibrin formation

Components:

Coagulation pathways

Hypocoag: ↑R

Hypercoag: ↓R

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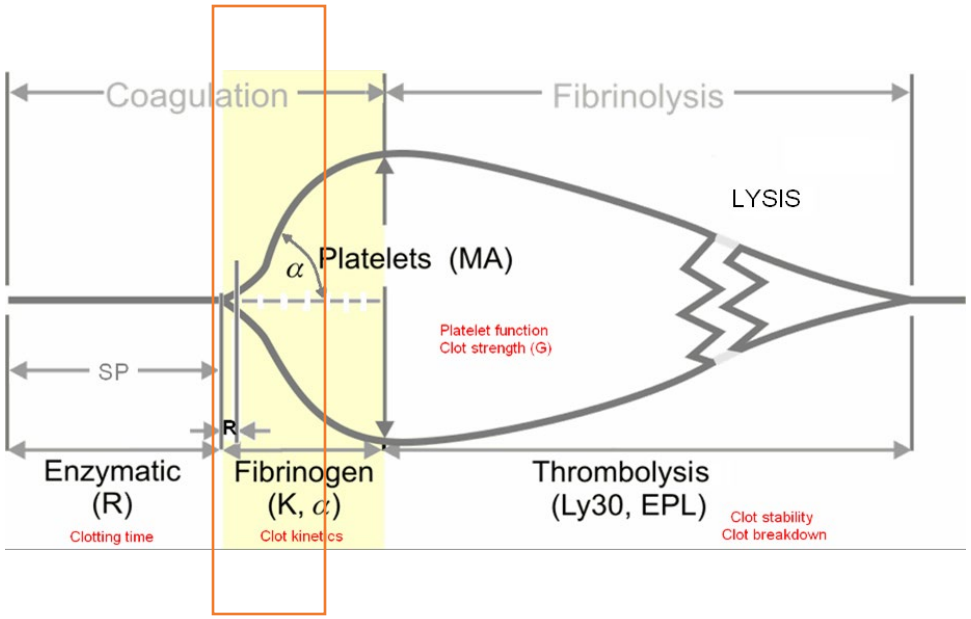
CLOT RATE



Activity:

Fibrin cross-linking, platelet interactions

Components:

Coagulation pathways, platelets

Hypocoag: ↑K, ↓α

Hypercoag: ↓K, ↑α

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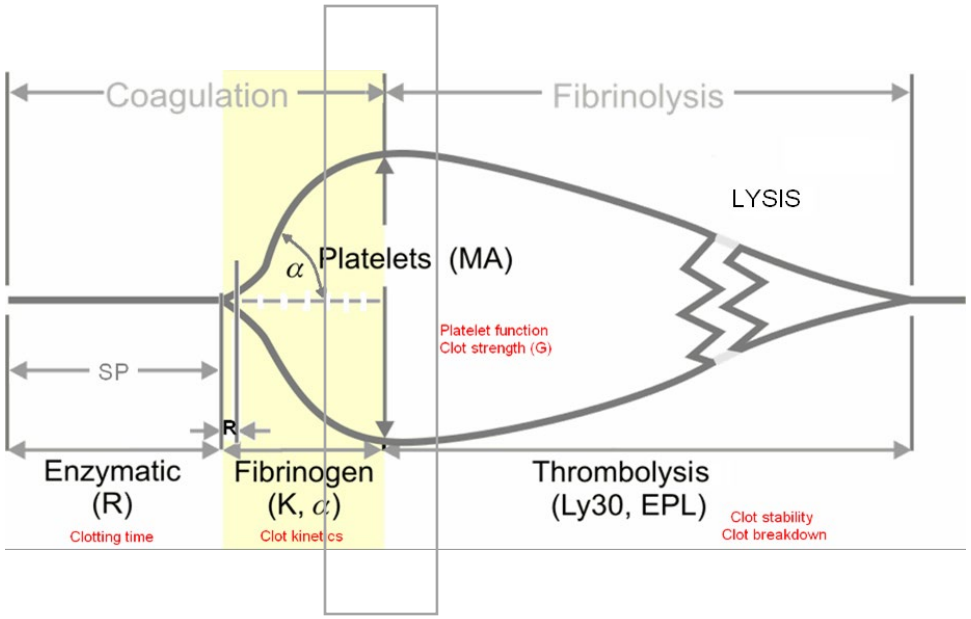
CLOT STRENGTH



Activity:

Platelet-fibrin interactions

Components:

Platelets (~80%)

Fibrin (~20%)

Hypocoag: ↓MA

Hypercoag: ↑MA

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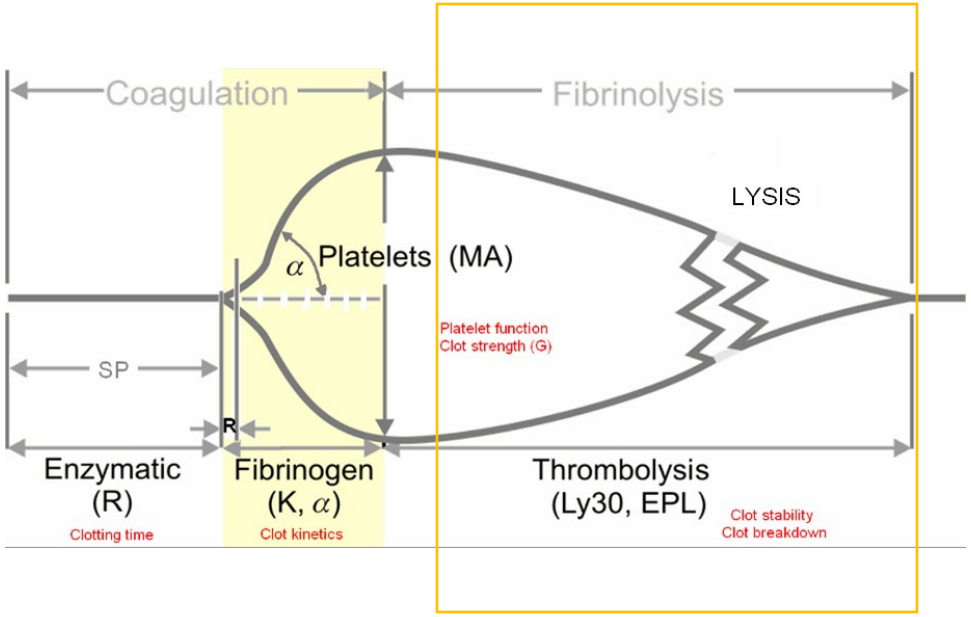
CLOT STABILITY



Activity:

Reduction in clot strength

Components:

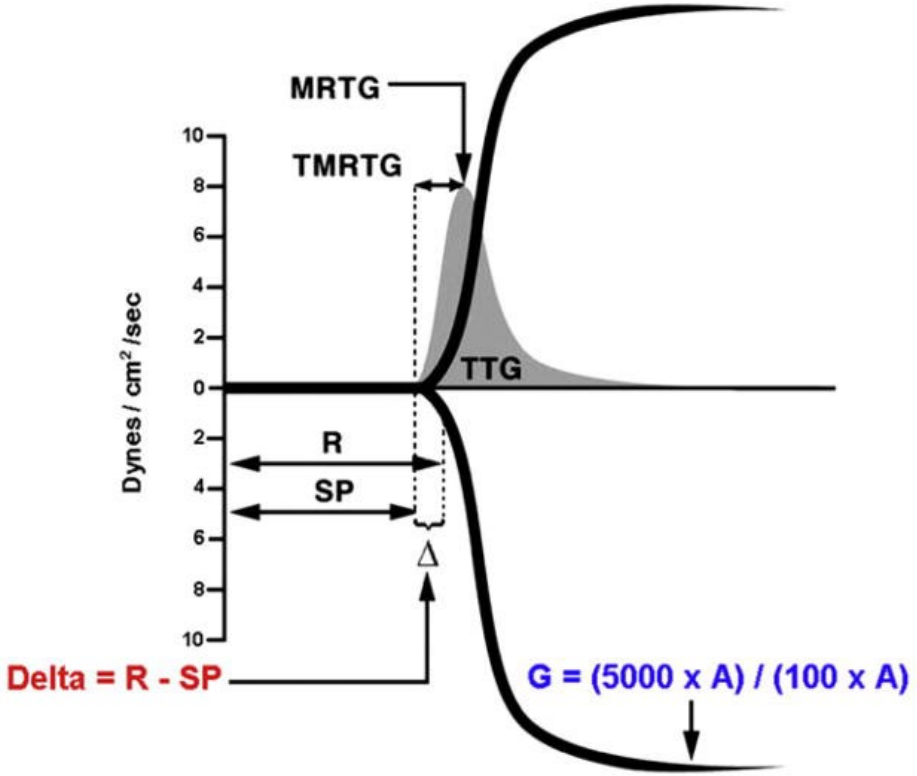
Fibrinolysis

Hyperfibrinolysis:

↑Ly30 (>8%)

Delta

- Time to maximum rate of thrombin generation



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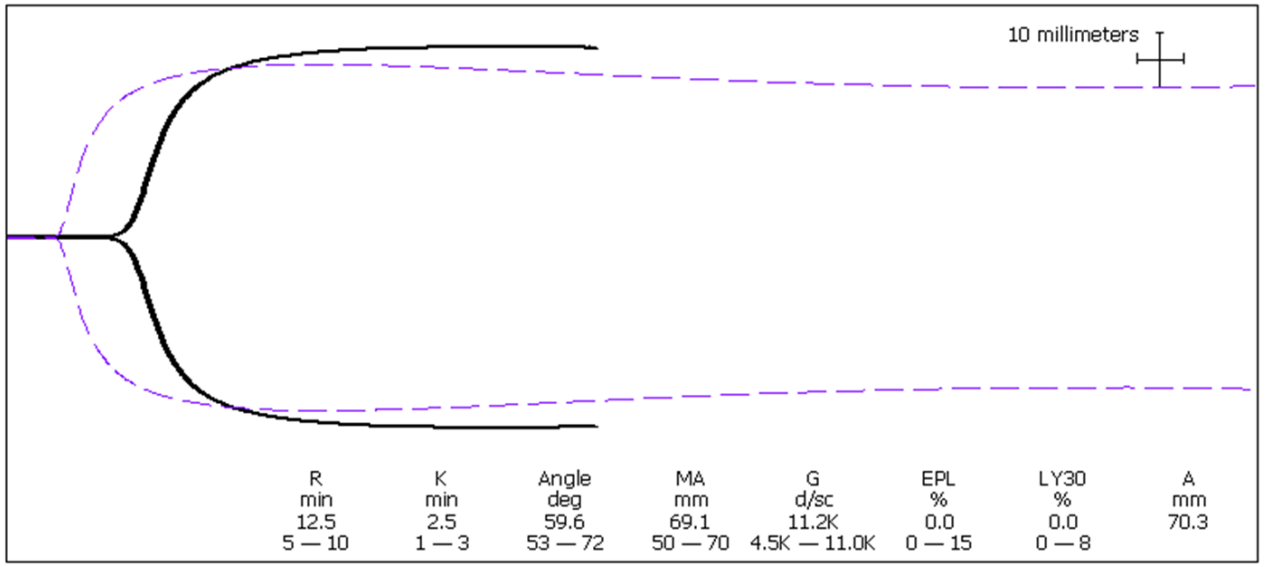
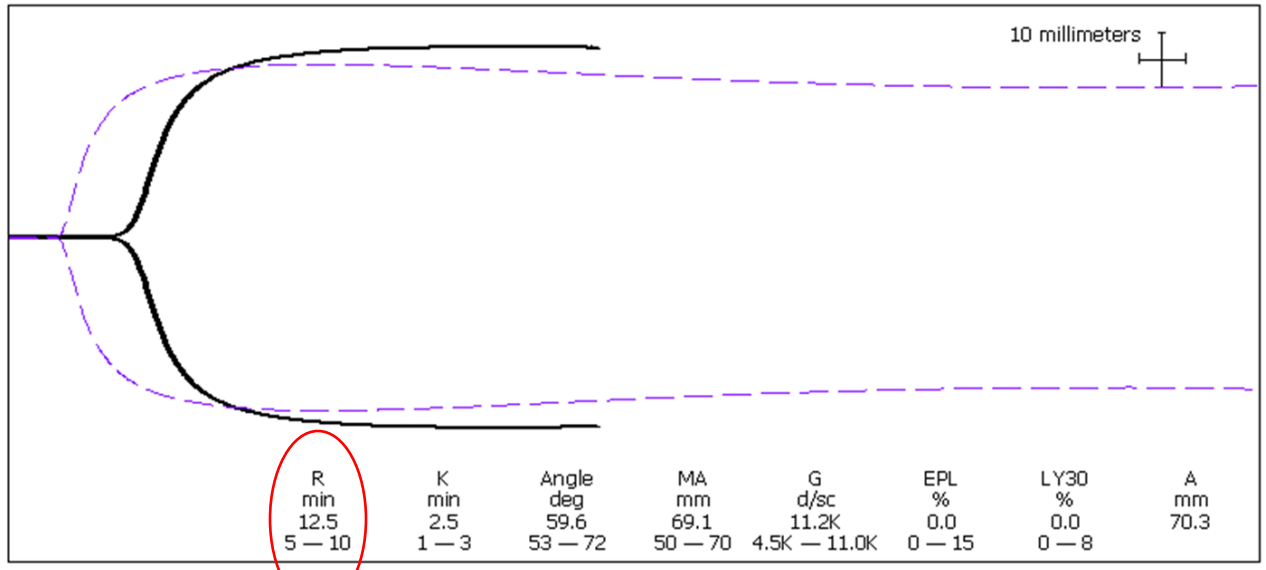
Example 1



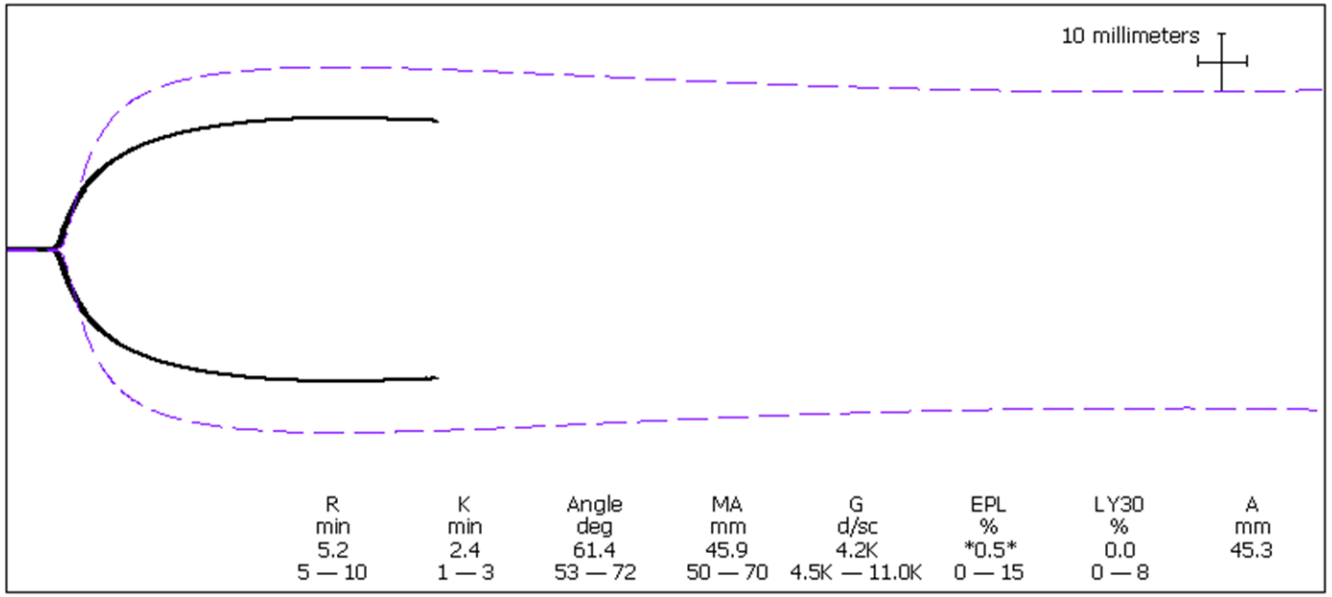
A. Thrombocytopenia
B. Anticoagulants
C. Fibrinolytics
D. Hypercoagulability

Example 1



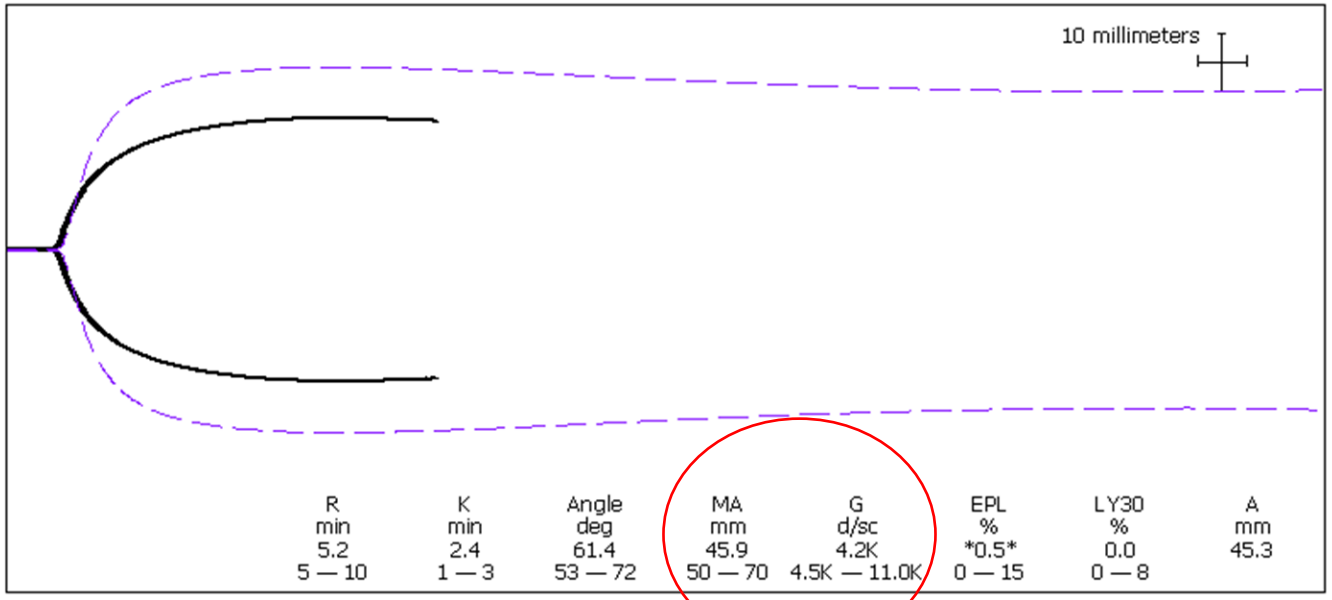
A. Thrombocytopenia
B. Anticoagulants
C. Fibrinolytics
D. Hypercoagulability

Example 2



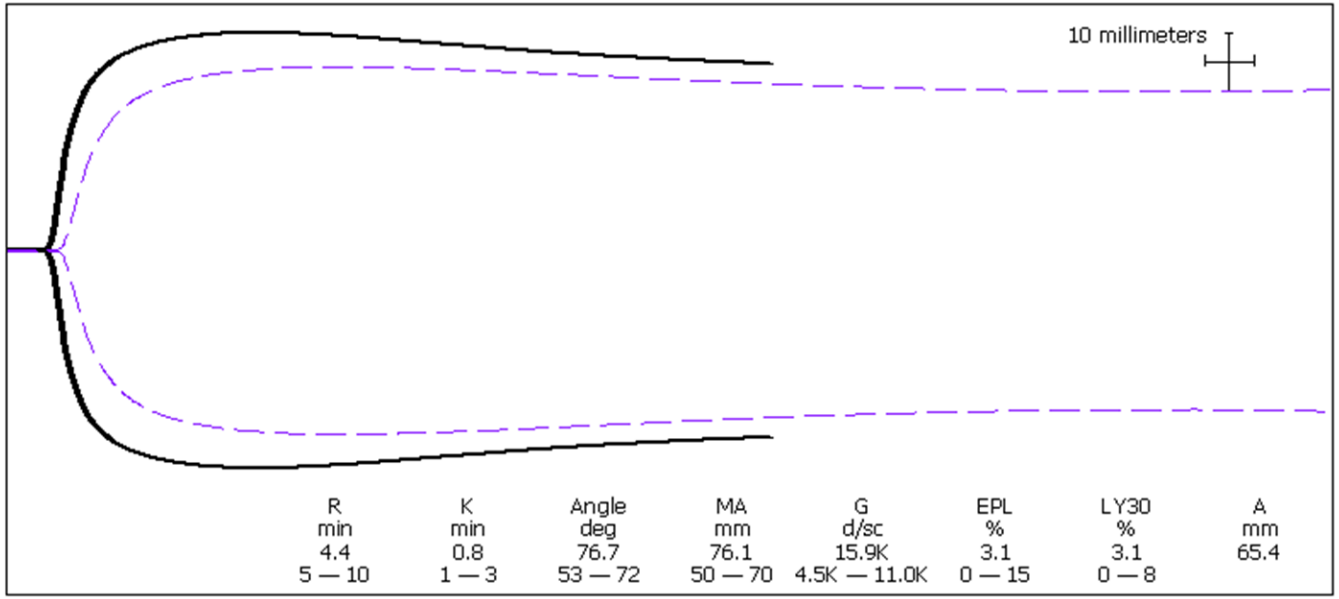
A. Thrombocytopenia
B. Anticoagulants
C. Fibrinolytics
D. Hypercoagulability

Example 2



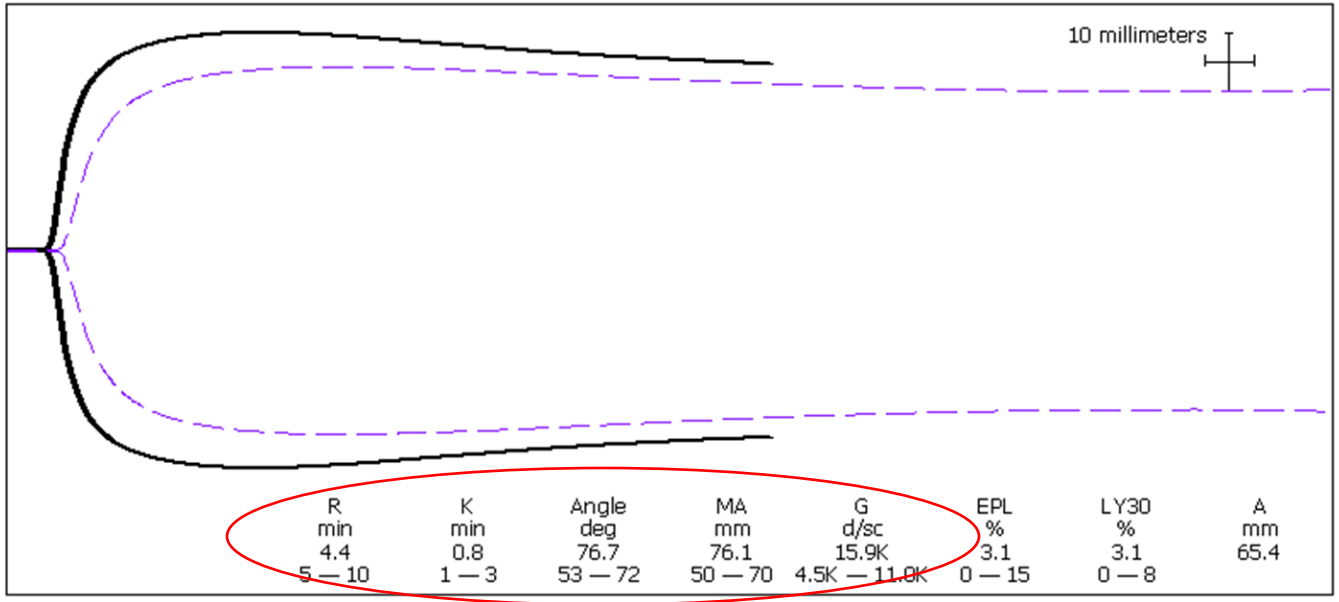
A. **Thrombocytopenia**
B. Anticoagulants
C. Fibrinolytics
D. Hypercoagulability

Example 3



A. Thrombocytopenia
B. Anticoagulants
C. Fibrinolytics
D. Hypercoagulability

Example 3



A. Thrombocytopenia
B. Anticoagulants
C. Fibrinolytics
D. **Hypercoagulability**

TEG in the Neuro ICU

Stroke
A Journal of Cerebral Circulation

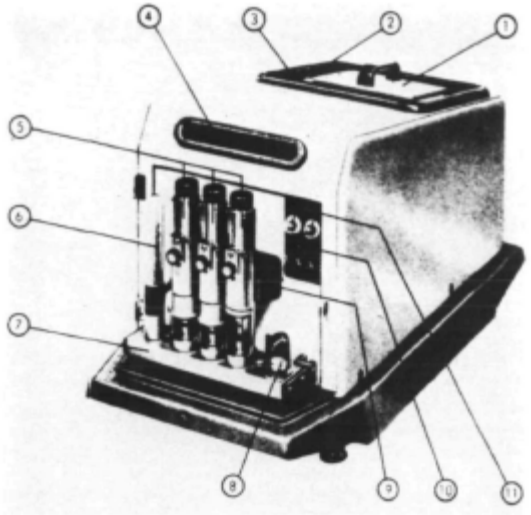
MAY-JUNE 1970
VOL. 1 NO. 3

Coagulation Abnormalities in Subarachnoid Hemorrhage

BY M. G. ETTINGER, M.D.*

Thromboelastographic Studies in Cerebral Infarction

BY MILTON G. ETTINGER, M.D.



1. *Recording camera*
2. *Counter for used paper*
3. *Control knob for camera drive and manual paper transport*
4. *Ground glass plate and scale*
5. *Measuring units*
6. *Contact thermometer*
7. *Metal thermostat*
8. *Levelling indicator*
9. *Light-proof box*
10. *Handles for cover plates*
11. *Indicator lamps*

FIGURE 1

Thromboelastogram unit demonstrating various components.

Ettinger MG. Stroke 1970.
Ettinger MG. Stroke 1974.

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AIS

Thromboelastography in patients with acute ischemic stroke

Andrea Elliott[1], Jeremy Wetzel[1], Tiffany Roper[1], Evan Pivalizza[1], James McCarthy[1], Cristina Wallace[1], Mary Jane Hess[1], Hui Peng[2], Mohammad H. Rahbar[2], Navdeep Sangha[1], and James C. Grotta[1]

- 49 AIS patients presenting within tPA window (3 hours)
- Confirmed presence of hypercoagulable state compared with controls
  - Shorter R: 4.8 vs 6 (p=0.0004)
  - Greater α: 65 vs. 61.5 (p=0.01)
  - Shorter K: 1.7 vs. 2.1 (p=0.002)

- 10 minutes post tPA
  - Significant changes in MA, G, and LY30

Elliott et al. Int J Stroke 2012.

Normal

Fibrinolysis

Thrombelastography Maximal Clot Strength Could Predict One-Year Functional Outcome in Patients with Ischemic Stroke

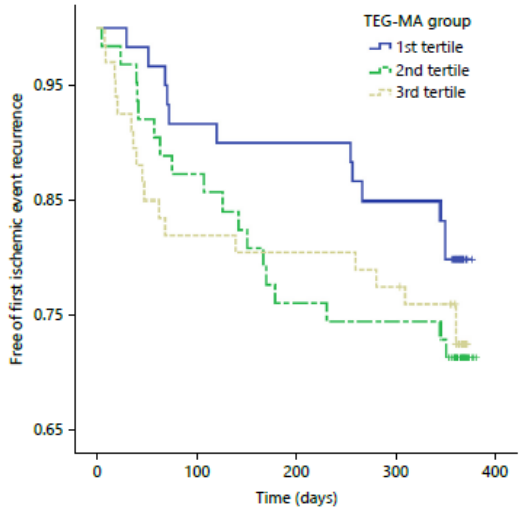
Xiaoying Yao Quan Dong Yeping Song Yanqing Wang Ye Deng Yansheng Li

Department of Neurology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Table 2. Clinical outcomes at one-year follow-up in ischemic stroke patients stratified according to admission thrombelastography (TEG) maximum amplitude (MA)

Variables	All patients (n = 211)	1st tertile TEG MA ≤62.4 (n = 70)	2nd tertile TEG MA 62.4–66 (n = 69)	3rd tertile TEG MA ≥66 (n = 72)	p value
Patients loss to one-year follow-up, n	28 (12.8%)	10 (14.3%)	12 (17.4%)	5 (6.9%)	NS
mRS 0–1 at one-year follow-up	91 (49.5%)	36 (60.0%)	31 (54.4%)	24 (35.8%)	0.017[a, b]
First recurrent ischemic event at one-year follow-up	47	12	17	18	NS
Fatal or non-fatal ischemic stroke	43	11	15	17	NS
Fatal or non-fatal MI	4	1	2	1	NS
Death from ischemic events	10	2	3	5	NS
Hemorrhagic stroke	2	0	1	1	NS

[a] $p < 0.05$: 1st tertile vs. 3rd tertile; [b] $p < 0.05$: 2nd tertile vs. 3rd tertile.



- 184 patients with 1 year follow-up
- MA independent predictor of mRS ≥2 (OR 1.192, 95% CI 1.067-1.331, p=0.002)
- Other predictors: age, DM, prior TIA/stroke, admission NIHSS

Yao et al. Cerebrovasc Dis 2014.

ICH and TEG

Thrombelastography Detects Possible Coagulation Disturbance in Patients With Intracerebral Hemorrhage With Hematoma Enlargement

Jorge Kawano-Castillo, MD; Eric Ward, BS; Andrea Elliott, MD; Jeremy Wetzel, MD; Amanda Hassler, BS; Mark McDonald, BS; Stephanie A. Parker, RN; Joancy Archeval-Lao, BS; Chad Tremont, BBS; Chunyan Cai, PhD; Evan Pivalizza, MD; Mohammad H. Rahbar, PhD; James C. Grotta, MD

- 64 patients
- ICH vs. controls
  - Baseline: shorter R, delta
  - 36h: increased MA, angle, G
- Hematoma expansion
  - Slower clot formation compared with non-expanders

Table 3. Adjusted Means and 95% CI for Baseline TEG Values by Hematoma Enlargement Status (Yes versus No) Groups After Controlling for Potential Confounding Effects

Baseline TEG Values	Adjusted Mean (95% CI) Hematoma Enlargement		*P* Values
	Yes (n=11)	No (n=38)	
R	5.7 (4.5, 6.9)	4.4 (3.5, 5.4)	0.09
Delta	0.8 (0.6, 1.0)	0.5 (0.4, 0.7)	0.02
K	3.1 (2.0, 4.1)	1.6 (0.6, 2.6)*	0.04
MA	61.7 (52.0, 71.4)	61.6 (53.5, 69.7)	0.99
Angle	58.0 (50.6, 65.4)	62.0 (55.8, 68.1)	0.39
G	9.1 (6.5, 11.6)	10.3 (8.2, 12.5)	0.42

Adjusted means are calculated based on multivariable analysis after controlling for the following potential confounders: age, clopidogrel use, baseline international normalized ratio, and baseline platelet count. CI indicates confidence intervals; and TEG, thrombelastography.

*n=36.

Kawano-Castillo et al. Stroke 2014.

Hematoma location

- Deep 154 (74%) vs lobar 53 (26%)
- Deep location associated with longer R time
- No significant differences in conventional coagulation studies

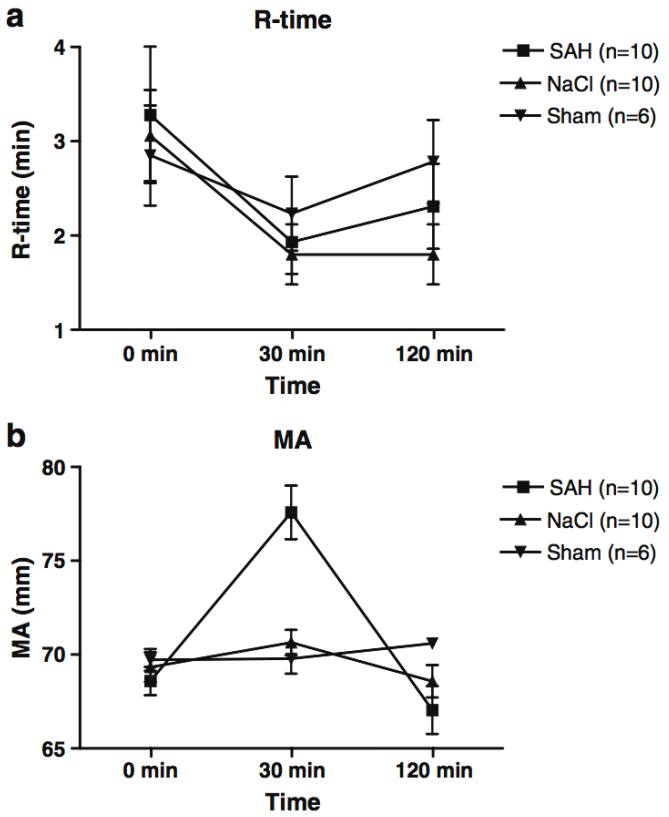
TABLE 2. Crude and Adjusted Linear Regression Assessing Association of Deep ICH Location With TEG Results

Outcome	All ICH n = 207 Mean (SD)	Deep-ICH n = 154 Mean (SD)	Lobar-ICH n = 53 Mean (SD)	Unadjusted mean difference (95% CI)	*P* value	Adjusted mean difference (95% CI)	*P* value
R time (min)	4.9 (1.6)	5.1 (1.6)	4.4 (1.3)	0.68 (0.20 to 1.16)	.006	0.57 (0.02 to 1.11)	.04
K time (min)	0.6 (0.5)	0.6 (0.5)	0.5 (0.3)	0.09 (−0.05 to 0.23)	.13	0.09 (−0.07 to 0.26)	.27
Alpha angle (degrees)	68 (8)	68 (9)	68 (6)	−0.76 (−3.32 to 1.80)	.47	0.09 (−2.82 to 2.99)	.95
MA (mm)	67 (10)	67 (10)	65 (10)	2.82 (−0.23 to 5.88)	.07	3.19 (−0.31 to 6.69)	.07
LY30 (%)[a]	0.0 (0.0-0.3)	0.0 (0.0-0.3)	0.0 (0.0-0.2)	NA	NA		

Roh et al. Neurosurgery 2020.

SAH

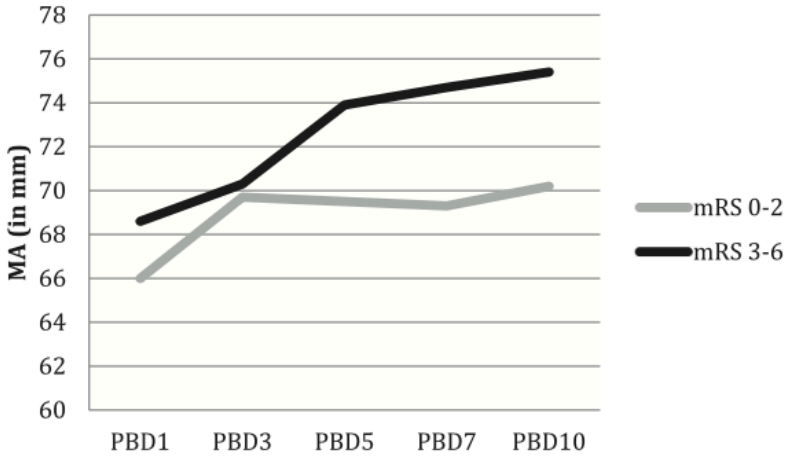
Hypercoagulability compared with controls (animals and humans)



Larsen et al. Acta Neurochir 2010.
Frontera et al. J Thromb Haemost 2012.
Ramchand et al. World Neurosurg 2016.

SAH outcomes

- High grade SAH (HH 4-5) reported to have higher MA during the acute period than low grade (HH 1-3)
- MA associated with poor mRS at discharge
- Unknown
  - Aneurysm re-rupture
  - Vasospasm/DCI



Larsen et al. Acta Neurochir 2010.
Frontera et al. J Thromb Haemost 2012.
Ramchand et al. World Neurosurg 2016.

Which TEG pattern are you most likely to find in a trauma patient?

A. Hypocoagulability
B. Hypercoagulability
C. Hyperfibrinolysis
D. Mixed coagulation disturbance
E. Normal

Which TEG pattern are you most likely to find in a trauma patient?

A. Hypocoagulability
B. Hypercoagulability
C. Hyperfibrinolysis
D. Mixed coagulation disturbance
E. Normal

Kaufmann et al. J Trauma 1997.
Schreiber et al. J Trauma 2005.

Traumatic injury:
TEG markers of severity

Hypocoagulability: 25-35%

- Elevated PT/PTT, low platelets, low fibrinogen
- TEG: abnormalities in clotting time (R), kinetics (α), and strength (MA)

Hyperfibrinolysis: 2-6%

- Elevated D-dimer, FDP
- TEG: increased Ly30

→ Increased injury severity, transfusion requirements, and mortality

Johansson et al. Scand J Trauma Resusc Emerg Med 2009.
Johansson et al. Transfusion 2013.

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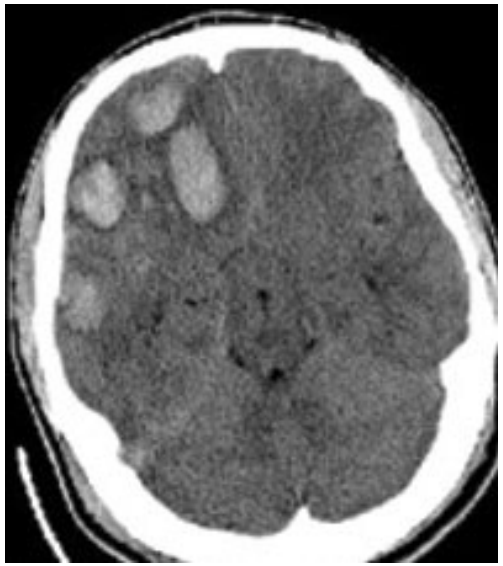
Acute traumatic coagulopathy

- Trauma stimulates tissue factor release→ activation of extrinsic pathway → consumptive coagulopathy and fibrinolysis

- Associated with severity of injury
  - Isolated TBI: up to 33% of patients
  - Severe TBI: 60%

- Strong association with worse outcomes



Harhangi et al. Acta Neurochir 2008.
Kunio et al. Am J Surg 2012.

TBI

Thrombelastography-identified coagulopathy is associated with increased morbidity and mortality after traumatic brain injury

Nicholas R. Kunio, M.D.*, Jerome A. Differding, M.P.H., Katherine M. Watson, B.A., Ryland S. Stucke, B.S., Martin A. Schreiber, M.D.

- 69 patients with TBI and ICH on admission CT
- R time > 9 min
  - Increased hospital mortality
  - Also increased ISS, admission ICH volume, and MAP
- MA < 55 mm also associated with increased mortality
  - 33% vs. 9.8% (p=0.04)

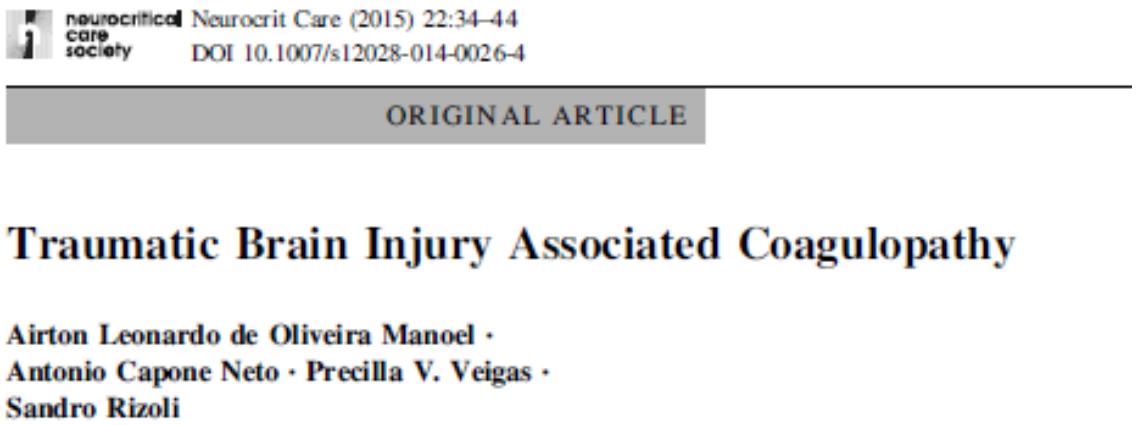
Table 3 Outcomes by coagulation status based on R time

	R time, min		
Patient outcomes	≤ 9	> 9	*P* value
Mortality, %	11.7	50.0	.04
ICU-free days*	27 (20–29)	8 (0–26)	.05
Hospital-free days*	24 (4–27)	5 (0–20)	.03
Neurosurgical intervention, %	34.9	83.3	.03

*Median (interquartile range) shown.

Kunio et al. Am J Surg 2012.

Acute traumatic coagulopathy


neurocritical care society Neurocrit Care (2015) 22:34–44
DOI 10.1007/s12028-014-0026-4

ORIGINAL ARTICLE

Traumatic Brain Injury Associated Coagulopathy

Airton Leonardo de Oliveira Manoel · Antonio Capone Neto · Precilla V. Veigas · Sandro Rizoli

- Severe TBI ± multisystem trauma
- Isolated TBI
  - Less coagulopathy (12.5% vs. 30.5%)
  - Shorter R at admission (5.57 vs. 8.17)
  - All other TEG similar
- Isolated TBI with coagulopathy: mortality 66% (vs. 16.6%)

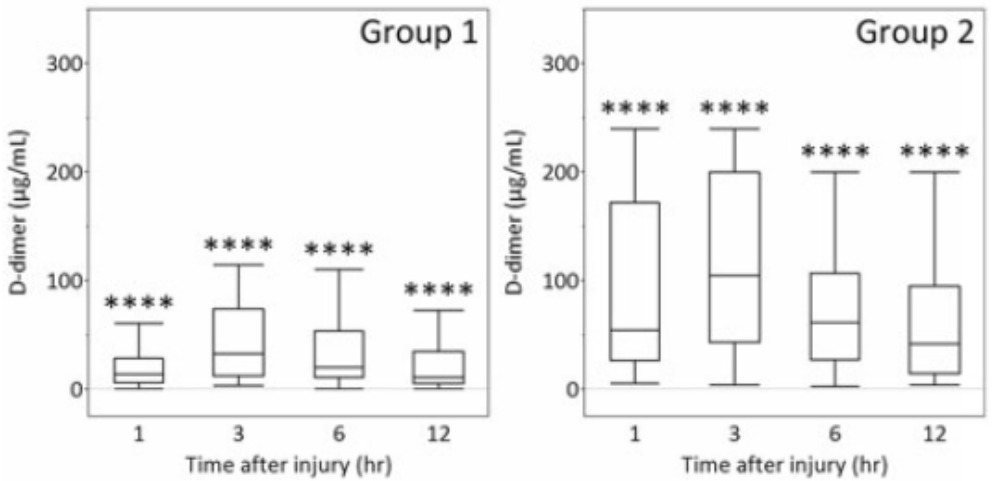
Blunt vs. penetrating TBI

- Penetrating
  - Higher incidence of coagulopathy on admission
    - Higher ACT, longer K, lower angle, lower MA, higher Ly30
  - Transfused more RBC, FFP, and platelets
  - TEG coagulopathy not detected on coags or PFA
  - Coagulopathy more common in non-survivors
- Coagulopathy by TEG independently associated with mortality in all isolated TBI
- Consider group differences

Martin et al. Neurocrit Care 2018.
Folkerson et al. Am J Emerg Med 2018

Role of hyperfibrinolysis

Good outcome



Poor outcome
Severe disability
Vegetative
Death

- D-dimer: significant negative prognostic indicator at all time points
- D-dimer at admission: independent risk factor for poor outcome (OR 1.2)

Nakae et al. J Neurotrauma 2016.

Delayed hypercoagulability

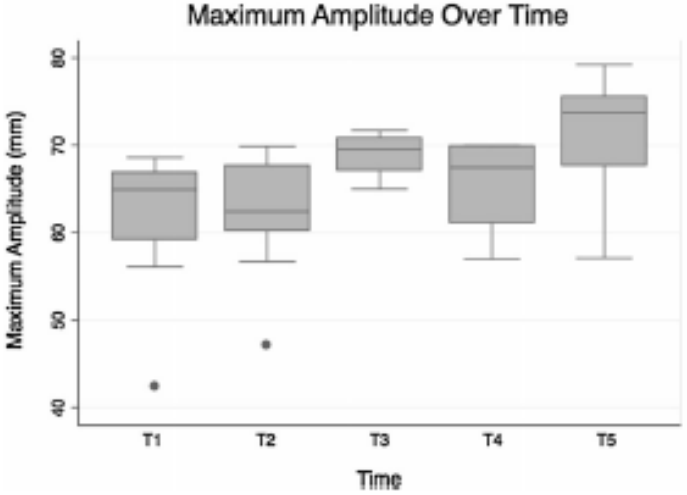


Fig. 1 Maximum amplitude (MA) over successive TEG timepoints. There was a general upward trend of MA values over the 5 study timepoints and reached significance at T5 (96–120 h) when compared to controls ($p = 0.02$)

MA increased by 2.6 mm daily

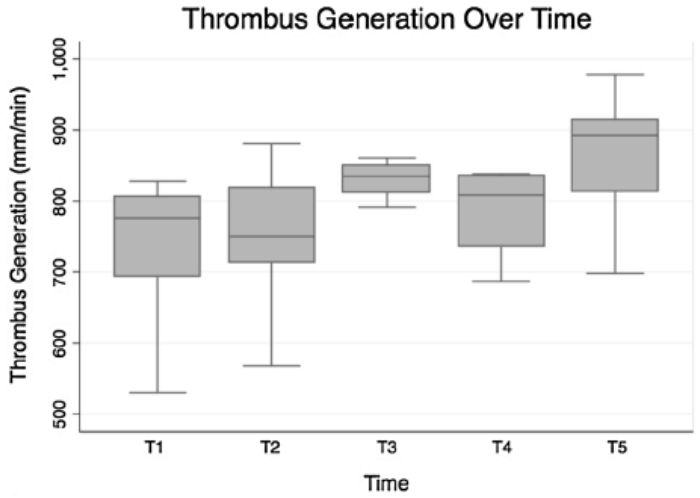


Fig. 2 Thrombus generation (TG) over successive TEG timepoints. There was a general upward trend of TG values over the 5 study timepoints and reached significance at T5 (96–120 h) when compared to controls ($p = 0.03$)

TG increased by 31.9 mm/min daily

Massaro et al. Neurocrit Care, 2015.

Why not PT/PTT?

- Plasma based
  - No interaction between clotting factors, tissue factor, and platelets
- Poor correlation with clinical bleeding and transfusion requirements
- Do not demonstrate the effect of novel anticoagulation agents or antiplatelet therapy
- No measurement of fibrinolysis

Windelov et al.

- 78 patients with ICH or isolated TBI
- Hypocoagulable by TEG=8, INR/PTT/platelets=16, both=2

Table 2 Demographics and outcome by coagulation status

	TEG			APTT/INR/Platelets		
	Hypocoaguable	Nonhypocoaguable	*P*	Hypocoaguable	Nonhypocoaguable	*P*
Number of patients	8 (10%)	70 (90%)		16 (21%)	62 (79%)	
Age	55 (47–65)	55 (44–63)	0.92	53 (44–72)	55 (45–62)	0.95
Male sex	6 (75%)	41 (59%)	0.37	13 (81%)	34 (55%)	0.05
Diagnosis						
Epidural haemorrhage	0 (0%)	11 (16%)		4 (18%)	7 (13%)	
Subdural haemorrhage	1 (13%)	14 (20%)		7 (32%)	8 (14%)	
Subarachnoid haemorrhage	4 (50%)	24 (34%)		6 (27%)	22 (39%)	
Intracerebral haemorrhage	1 (13%)	10 (14%)		2 (9%)	9 (16%)	
Traumatic brain injury	2 (25%)	11 (16%)	0.67	3 (14%)	10 (18%)	0.38
Glasgow Coma Scale Score (GCS)						
GCS at admission to NICU	6 (4–14)	8 (3–14)	0.89	7 (6–13)	9 (3–15)	0.40
GCS approximately 24 h after admission to NICU	3 (3–14)	11 (7–15)	0.14	10 (7–14)	11 (6–15)	0.34
Decline i						
Surgery						
Underwe						
Outcome						
Length o						
Decease						
30 da						
Decease						

Table 3 Variables associated with 30-day mortality

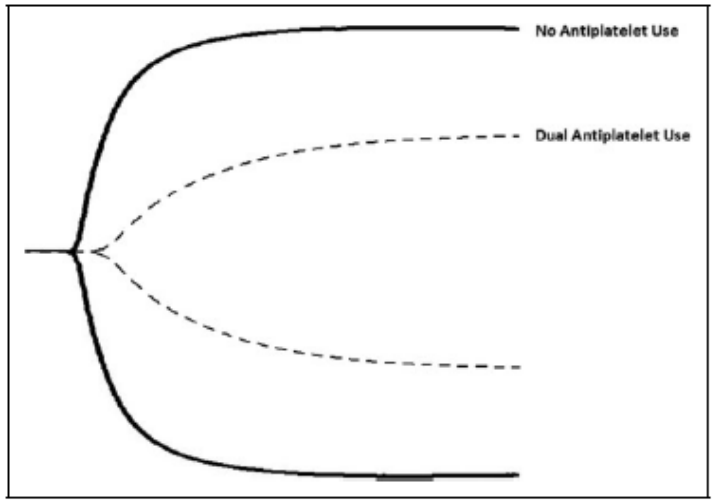
Univariable regressions	OR (95% CI)	χ^2	*P*
Age (per year)	1.0 (1.0–1.0)	0.06	0.81
GCS upon admission to the NICU (per reduced point)	1.2 (1.0–1.3)	5.7	0.03
Subarachnoid haemorrhage	2.9 (0.9–9.0)	3.5	0.06
Hypocoaguable according to INR, APTT and/or platelet count	0.5 (0.1–2.4)	0.9	0.49
Hypocoaguable according to TEG	8.9 (1.8–42.9)	7.7	0.006
Categori			
partial th			
Multivariable regression of variables with $P<0.1$	OR (95% CI)	χ^2	*P*
GCS upon admission to the NICU (per reduced point)	1.3 (1.1–1.5)	9.6	0.006
Subarachnoid haemorrhage	5.3 (1.3–22.3)	5.6	0.02
Hypocoaguable according to TEG	14.8 (2.2–100.1)	8.8	0.006

Odds ratio (OR) with 95% confidence interval (95% CI). APTT, activated partial thromboplastine time; GCS, Glasgow coma scale score; INR, international normalized ratio; NICU, neurointensive care unit; TEG, thrombelastography.

Windelov et al. Blood Coagul Fibrinolysis 2011.

Antiplatelet agents

- Dual AP therapy
  - Prolonged time to initiate clotting (↑R)
  - Slower rate of clot formation (↓α)
  - Reduced final clot strength (↓MA)
- Single AP therapy: no sig differences compared with no AP



- Platelet mapping: % inhibition
  - AA: aspirin, NSAIDs
  - ADP: clopidogrel, prasugrel

McDonald et al. J Intensive Care Med 2017.

Question

60 yo F with history of A fib, HTN, DM presents with acute onset of aphasia and R hemiparesis. She takes apixaban for A fib, but lives alone and family is unsure of when she last took the medication. What is the next appropriate step in management?

A. Check PT/PTT
B. Check TEG
C. Give FFP
D. Give PCC
E. Activated charcoal

Anticoagulation reversal

Agent	Mechanism	Half-life	Reversal
Warfarin	Reduction in vitamin K-dependent clotting factors (II, VII, IX, X)	20-60 h	Vitamin K 10 mg IV PCC 25-50 U/kg FFP 10-15 ml/kg if PCC not available
Dabigatran	Direct thrombin inhibitor	13 h 22-35 h if ClCr <30	Idarucizumab 5 mg IV x2 doses PCC if idarucizumab not available Hemodialysis
Rivaroxaban, apixaban, edoxaban	Xa inhibitor	Rivaroxaban 7-9 h Apixaban 9-14 h	PCC 50 U/kg
Heparin	Indirectly inhibits Xa and IIa via antithrombin	45-90 min	Protamine 1 mg per 100 U heparin given within past 2-3 h
Enoxaparin	Same as heparin but mainly Xa	4 h	Protamine reverses ~60% of effect <8 h: 1 mg per 1 mg enoxaparin 8-12 h: 0.5 mg per 1 mg enoxaparin

Guidelines for Reversal of Antithrombotics in Intracranial Hemorrhage. Neurocrit Care 2016.

Admission Rapid Thrombelastography Can Replace Conventional Coagulation Tests in the Emergency Department

Experience With 1974 Consecutive Trauma Patients

John B. Holcomb, MD, Kristin M. Minei, BS, Michelle L. Scerbo, BS, Zayde A. Radwan, BS, Charles E. Wade, PhD, Rosemary A. Kozar, MD, PhD, Brijesh S. Gill, MD, Rondel Albarado, MD, Michelle K. McNutt, MD, Saleem Khan, MD, Phillip R. Adams, MD, James J. McCarthy, MD, and Bryan A. Cotton, MD, MPH

- All rTEG values predictive of significant bleeding
- α angle (<56º) superior in predicting massive RBC, FFP, platelet, and cryo transfusions
- All rTEG values independent predictors of 24 hour and 30 day mortality
  - Of CCT, only aPTT predictive
- Cost similar
  - $317 rTEG vs. $286 for CCT

Correlations

ACT – INR, aPTT

K – aPTT

α angle – fibrinogen

MA – platelet count, fibrinogen

TABLE 7. Current Memorial Hermann Hospital Transfusion Recommendations Based on Abnormal r-TEG Values in Bleeding Patients

Laboratory Values	Blood Product Transfusion
ACT > 128	Plasma and RBCs
r-value > 1.1	Plasma and RBCs
k-time > 2.5	Cryoprecipitate / fibrinogen / plasma
α-angle < 56	Cryoprecipitate / fibrinogen / platelets
MA < 55	Platelets / cryoprecipitate / fibrinogen
LY30 > 3%	Tranexamic acid
PT > 18.0	Plasma
aPTT > 35	Plasma
INR >1.5	Plasma
Platelet count < 150×10^9/L	Platelets
Fibrinogen < 180 g/L	Cryoprecipitate / fibrinogen

Holcomb et al. Ann Surg 2012.

Conclusions:
TEG in Neuro ICU

- Risk stratification
  - Hematoma expansion, IVH
  - Transfusion requirements
  - Surgical intervention
  - Thrombotic complications

- Therapeutic interventions
  - Product administration
  - Antiplatelets/anticoagulants

- Mortality and outcome implications

Thank you!

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