Menagement delle emorragie cerebrali in pazienti in trattamento con vecchi e nuovi anticoagulanti orali

F. Del Gaudio

Cerebral Homeostasis

Normovolemia	**CVP 2-4 cmH_2O**
Normotension	**MAP >75 mmHg**
Normoventilation	**$PaCO_2$ 32-36 mmHg**
Normothermia (core)	**36.5-37.5 °C**
Slight hyperosmolality	**~300 mosm kg^{-1}**

Review

Clinical review: Critical care management of spontaneous intracerebral hemorrhage

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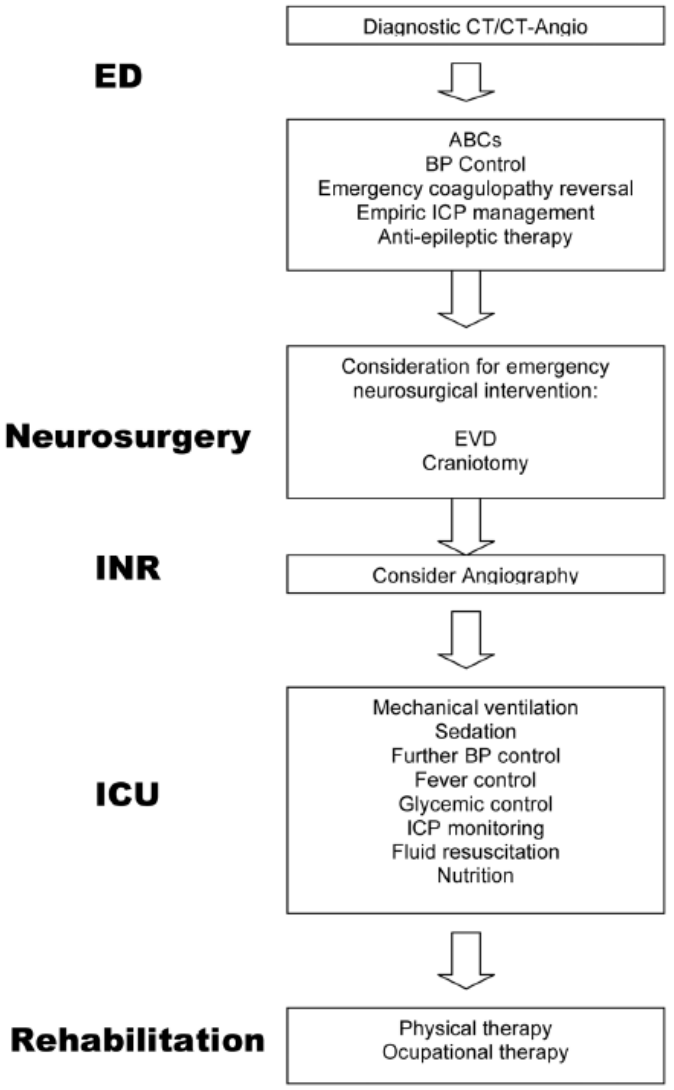
Figure 3



Approach to intracerebral hemorrhage from the emergency department to the intensive care unit.

Table 3 Anticoagulants and reversal strategies

Drug	Target	Elimination and half-life (hours)	Rate of ICH	Monitoring coagulation tests	Antidote and reversal	Possible intervention	Guidelines
Vitamin K antagonist							
Warfarin	Factors II, VII, IX, X; proteins C, S	Hepatic metabolism	0.3–1.1 % [90]	Good linear correlation PT/INR	Vitamin K	Not dialyzable	Withhold VKA + intravenous vitamin K + replace vitamin K–dependent factors (three- or four-factor PCC IV or FFP if PCCs are not available), and correct the INR (keep INR < 1.4) (Class I; Level of Evidence C) [9]
		92 % renal elimination			Vitamin K 10 mg IV associated with 4-FPCC 20 IU/kg (or FFP = 10–15 ml/kg, if PCC is not available)		PCCs might be considered over FFP (Class IIb; Level of Evidence B) [9]
		20–60			Goal: INR < 1.4 [90]		rFVIIa is not recommended for VKA reversal in ICH (Class III; Level of Evidence C) [9]
Unfractionated heparin, LMWHs, and heparinoids							
UFH	Binds and activates antithrombin (which blocks coagulation factors Xa and IIa). By inactivating thrombin, heparin prevents fibrin formation	Renal	0.1 to 0.2 % [90, 151]	Good linear correlation aPTT	Protamine sulfate 1 mg of protamine per 100 units of UFH infused over the preceding 3 hours	Not dialyzable	Protamine sulfate—1 mg for every 100 units of heparin given in the previous 2–3 hours with a maximum single dose of 50 mg (Strong recommendation, moderate quality evidence) [90]
		0.5–2.5 (dose dependent)					If aPTT is still elevated, repeat administration of protamine at a dose of 0.5 mg protamine per 100 units of UFH (Conditional recommendation, low quality of evidence) [90]
							Reversal of prophylactic SC heparin only if aPTT is significantly prolonged (Good Practice statement) [90]
Enoxaparin	LMWH Binds and activates antithrombin (which blocks coagulation factors Xa and IIa)	40 % renal	0.2–0.5 % [98] Enoxaparin 1 mg/kg BID; bridging warfarin with target INR 2–3	Anti-factor Xa	Protamine sulfate partially reverses (60 %) LMWH effect. One mg protamine for every 1 mg enoxaparin	Not dialyzable	Strong recommendation, moderate quality evidence [90]
		4.5 hours					Protamine sulfate 1 mg per 1 mg of enoxaparin (maximum single dose of 50 mg—if enoxaparin was given within 8 hours)
							Protamine sulfate 0.5 mg of protamine per 1 mg of enoxaparin (if enoxaparin was given within 8–12 hours)
							After 12 hours, protamine is not needed
Dalteparin	LMWH Binds and activates antithrombin (which blocks coagulation factors Xa and IIa)	Renal	Not established	Anti-factor Xa	Protamine sulfate partially reverses (60 %) LMWH effect. One mg protamine for every 100 anti-Xa IU dalteparin	Not dialyzable	Protamine sulfate 1 mg per 100 IU of dalteparin administered in the past 3–5 half-lives (maximum 50 mg) (Strong recommendation, moderate quality evidence) [90]
		2.5 hours					
		3.7–7.7 hours with RF					

Table 3 Anticoagulants and reversal strategies *(Continued)*

Nadroparin	LMWH Binds and activates antithrombin (which blocks coagulation factors Xa and IIa)	Renal 3.5 hours	Not established	Anti-factor Xa	Protamine sulfate partially reverses (60 %) LMWH effect. One mg protamine for every 100 anti-Xa IU nadroparin	Not dialyzable	Protamine sulfate 1 mg per 100 IU of nadroparin administered in the past 3–5 half-lives (maximum 50 mg) (Strong recommendation, moderate quality evidence) [90]
Pentasaccharides							
Fondaparinux (Aristra®)	Binds with antithrombin and potentiates inhibition of free factor Xa, preventing formation of the prothrombinase complex	50–77 % renal 17–21 hours Prolonged in older patients and in RF	Not established	Anti-factor Xa	None	Activated PCC (FEIBA 20 units/kg) Dialyzable (clearance increased by 20 %)	aPCC 20 IU/kg (Conditional recommendation, low-quality evidence) [90] rFVIIa (90 μg/kg) if aPCC is not available (Conditional recommendation, low-quality evidence) [90] Protamine sulfate is not recommended (Strong recommendation, low-quality evidence) [90]
Direct thrombin (factor IIa) inhibitors							
Argatroban (Acova®)	Competitive direct inhibition of thrombin (factor IIa) including thrombin-mediated platelet activation and aggregation	No renal excretion 0.75 hours (prolonged in hepatic dysfunction)	Not established	aPTT, ACT	None	Activated PCC (FEIBA 50–80 units/kg) Antifibrinolytic agent (e.g., tranexamic acid, epsilon-aminocaproic acid) Hemodialysis (approximately 20 % over 4 hours)	aPCC (50 units/kg) or four-factor PCC (50 units/kg) (Conditional recommendation, low-quality evidence) [90] rFVIIa or FFP are not recommended in direct thrombin inhibitor-related ICH (Strong recommendation, low-quality evidence) [90]
Bivalirudin	Reversible direct inhibition of thrombin (factor IIa) including thrombin-mediated platelet activation and aggregation	20 % renal 0.5 (prolonged in renal impairment) GFR 30–59, 34 minutes GFR 10–29, 57 minutes	0.1 % [151]	ECT (PT, aPTT, ACT has nonlinear prolongation)	None	Activated PCC (FEIBA 50–80 units/kg) Antifibrinolytic agent (e.g., tranexamic acid, epsilon-aminocaproic acid) Hemodialysis (approximately 25 % over 4 hours)	aPCC (50 units/kg) or four-factor PCC (50 units/kg) (Conditional recommendation, low-quality evidence) rFVIIa or FFP are not recommended in direct thrombin inhibitor-related ICH (Strong recommendation, low-quality evidence)
Dabigatran (Pradaxa®)	Reversible direct inhibition of thrombin (factor IIa) including	>80 % renal	0.30 % (150 mg) [98]	Modified TT/ECT/ prolongs PT linearly with	Idarucizumab or Praxbind® (humanized antibody fragment against	Activated PCC (FEIBA 50–80 units/kg)	Idarucizumab 5 g IV in two divided doses if dabigatran was administered within 3–5 half-lives and no RF (Strong

Table 3 Anticoagulants and reversal strategies *(Continued)*

	thrombin-mediated platelet activation and aggregation			increasing serum levels, while aPTT is affected in a nonlinear way	dabigatran), in two doses of 2.5 g IV 15 minutes apart		recommendation, moderate quality of evidence) or in the presence of RF leading to continued drug exposure beyond the normal 3–5 half-lives (Strong recommendation, moderate quality of evidence)
		12–17 hours 16.6 hours in mild RF 18.7 hours in moderate RF 27.5 hours in severe RF 34.1 hours in patients on hemodialysis	0.23 % (110mg) [98] ICH distribution: 46 % intraparenchymal, 45 % SDH, and 8 % SAH [90]			Activated charcoal if last dose was taken < 2 hours Hemodialysis (approximately 57 % over 4 hours) Antifibrinolytic agent (e.g., tranexamic acid, epsilon-aminocaproic acid)	Hemodialysis if idarucizumab is not available (Conditional recommendation, low-quality data)
Desirudin	Irreversible direct inhibition of thrombin (factor IIa) including thrombin-mediated platelet activation and aggregation	40–50 % renal 2 hours (12 hours with renal impairment)	Not established	aPTT	None	Dialyzable	aPCC (50 units/kg) or four-factor PCC (50 units/kg) (Conditional recommendation, low-quality evidence) [90] rFVIIa or FFP are not recommended in direct thrombin inhibitor-related ICH (Strong recommendation, low-quality evidence) [90]
Direct factor Xa inhibitors							
Apixaban (Eliquis®)	Prevents factor Xa-mediated conversion of prothrombin to thrombin	Mainly fecal 27 % renal 8–14 hours	Apixaban 5 mg twice daily 0.33 %/year [98]	Anti-factor Xa There are scant data regarding the effect of apixaban on traditional coagulation tests	Currently, there is no FDA-approved specific antidote for this class of anticoagulants Antidotes under investigation: – Aripazine (PER977—synthetic small molecule) – Andexanet (PRT064445—recombinant modified factor Xa protein)	Unactivated four-factor PCC (50 units/kg). If not available, a three-factor PCC can be used. Activated charcoal if last dose was taken < 2 hours Antifibrinolytic agent (e.g., tranexamic acid, epsilon-aminocaproic acid) Minimal removal with dialysis (decreased by 14 % over 4 hours)	Activated charcoal (50 g) within 2 hours of ingestion (Conditional recommendation, very low-quality evidence) [90] aPCC (50 units/kg) or Four-factor PCC (50 U/kg) or activated PCC (50 U/kg) if ICH happened within 3–5 half-lives of drug or if liver failure (Conditional recommendation, low-quality evidence) [90] Four-factor PCC or activated PCC over rFVIIa (Conditional recommendation, low-quality evidence) [90]
Rivaroxaban (Xarelto®)	Prevents factor Xa-mediated conversion of	66 % renal 28 % fecal	Rivaroxaban 20 mg daily	Anti-factor Xa	Currently, there is no FDA-approved specific antidote	Unactivated four-factor PCC	

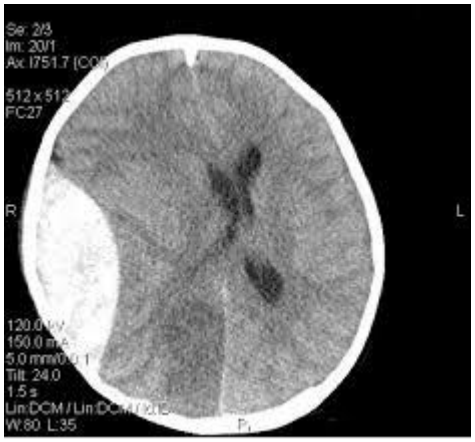
Table 3 Anticoagulants and reversal strategies *(Continued)*

	prothrombin to thrombin	7 to 11 hours	- < 0.5 % /year	Rivaroxaban levels linearly increase PT and aPTT levels	for this class of anticoagulants Antidotes under investigation: – Aripazine (PER977—synthetic small molecule) – Andexanet (PRT064445—recombinant modified factor Xa protein)	(50 units/kg). If not available, a three-factor PCC can be used. Activated charcoal if last dose was taken < 2 hours Antifibrinolytic agent (e.g., tranexamic acid, epsilon-aminocaproic acid) Not dialyzable (rivaroxaban is highly protein bound)	Activated charcoal (50 g) within 2 hours of ingestion (Conditional recommendation, very low-quality evidence) [90] Four-factor PCC (50 U/kg) or activated PCC (50 U/kg) if ICH happened within 3–5 half-lives of drug or if liver failure (Conditional recommendation, low-quality evidence) [90] Four-factor PCC or activated PCC over rFVIIa (Conditional recommendation, low-quality evidence) [90]
Edoxaban	Prevents factor Xa-mediated conversion of prothrombin to thrombin	50 % renal 10–14 hours	Edoxaban 60 mg daily compared with warfarin (HR 0.54, 95 % CI 0.38–0.77) [90]	There are scant data regarding the effect of edoxaban on traditional coagulation tests	Currently, there is no FDA-approved specific antidote for this class of anticoagulants Antidotes under investigation: – Aripazine (PER977—synthetic small molecule) – Andexanet (PRT064445—recombinant modified factor Xa protein)	Unactivated four-factor PCC (50 units/kg). If not available, a three-factor PCC can be used. Activated charcoal if last dose was taken < 2 hours Antifibrinolytic agent (e.g., tranexamic acid, epsilon-aminocaproic acid) Not dialyzable (edoxaban is highly protein bound)	Activated charcoal (50 g) within 2 hours of ingestion (Conditional recommendation, very low-quality evidence) [90] Four-factor PCC (50 U/kg) or activated PCC (50 U/kg) if ICH happened within 3–5 half-lives of drug or if liver failure (Conditional recommendation, low-quality evidence) [90] Four-factor PCC or activated PCC over rFVIIa (Conditional recommendation, low-quality evidence) [90]
Antiplatelets							
Aspirin	Irreversible COX-1 and 2 enzyme inhibitor (inhibits thromboxane A2)	5.6–35.6 % renal 0.3 hours	It is unclear if antiplatelet therapy increases the incidence of ICH	Light Transmission Platelet Aggregation with or without Secretion	None The usefulness of platelet transfusions in ICH patients with a history of antiplatelet use is uncertain	Dialyzable DDAVP 0.4 μg/kg	DDAVP 0.4 μg/kg IV (Conditional recommendation, low-quality evidence) [90] Platelet transfusion is not recommended (Conditional recommendation, low-quality evidence) [90] Platelet transfusion for patients who will undergo a neurosurgical procedure (Conditional recommendation, moderate quality of evidence) [90] DDAVP can be used in addition to platelet transfusion in patients who will undergo

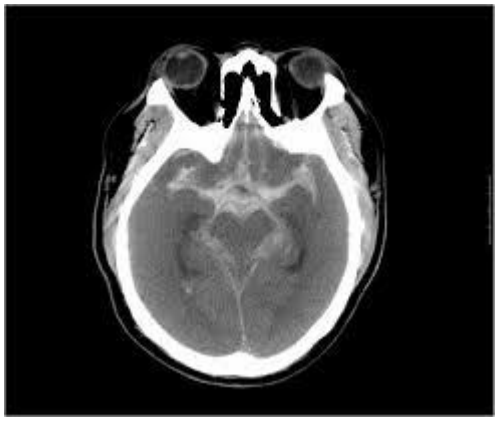
Table 3 Anticoagulants and reversal strategies *(Continued)*

							neurosurgical procedure (Conditional recommendation, low-quality evidence) [90]
Clopidogrel	Irreversible inhibition of P2Y12 ADP receptor	50 % renal 46 % fecal 6–8 hours	It is unclear if anti platelet therapy increases the incidence of ICH	Light Transmission Platelet Aggregation with or without Secretion	None The usefulness of platelet transfusions in ICH patients with a history of antiplatelet use is uncertain	Not dialyzable DDAVP 0.4 μg/kg	DDAVP 0.4 μg/kg IV (Conditional recommendation, low-quality evidence) [90] Platelet transfusion is not recommended (Conditional recommendation, low-quality evidence) [90] Platelet transfusion for patients who will undergo a neurosurgical procedure (Conditional recommendation, moderate quality of evidence) [90] DDAVP can be used in addition to platelet transfusion in patients who will undergo neurosurgical procedure (Conditional recommendation, low-quality evidence) [90]
Prasugrel	Irreversible inhibition of P2Y12 ADP receptor	68 % renal 27 % fecal 2–15 hours	It is unclear if anti platelet therapy increases the incidence of ICH	Light Transmission Platelet Aggregation with or without Secretion	None The usefulness of platelet transfusions in ICH patients with a history of antiplatelet use is uncertain	Not dialyzable DDAVP 0.4 μg/kg	DDAVP 0.4 μg/kg IV (Conditional recommendation, low-quality evidence) [90] Platelet transfusion is not recommended (Conditional recommendation, low-quality evidence) [90] Platelet transfusion for patients who will undergo a neurosurgical procedure (Conditional recommendation, moderate quality of evidence) [90] DDAVP can be used in addition to platelet transfusion in patients who will undergo neurosurgical procedure (Conditional recommendation, low-quality evidence) [90]
Ticlopidine	Irreversible inhibition of P2Y12 ADP receptor	60 % renal 23 % fecal 12 hours (increases with RF to 4–5 days after repeated doses)	It is unclear if anti platelet therapy increases the incidence of ICH	Light Transmission Platelet Aggregation with or without Secretion	None The usefulness of platelet transfusions in ICH patients with a history of antiplatelet use is uncertain	Not dialyzable DDAVP 0.4 μg/kg	DDAVP 0.4 μg/kg IV (Conditional recommendation, low-quality evidence) [90] Platelet transfusion is not recommended (Conditional recommendation, low-quality evidence) [90] Platelet transfusion for patients who will undergo a neurosurgical. procedure (Conditional recommendation, moderate quality of evidence) [90] DDAVP can be used in addition to platelet transfusion in patients who will undergo neurosurgical procedure (Conditional recommendation, low-quality evidence) [90]
Dipyridamole	Reversible adenosine reuptake inhibitor	Fecal 10 hours	It is unclear if anti platelet therapy increases the incidence of ICH	Light Transmission Platelet Aggregation with or without Secretion	None The usefulness of platelet transfusions in ICH patients with a history of antiplatelet use is uncertain	Not dialyzable DDAVP 0.4 μg/kg	DDAVP 0.4 mcg/kg IV (Conditional recommendation, low-quality evidence) [90] Platelet transfusion is not recommended (Conditional recommendation, low-quality evidence) [90] Platelet transfusion for patients who will undergo a neurosurgical procedure

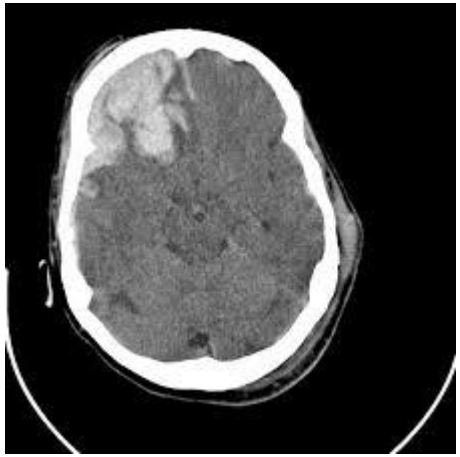
Emorragia cerebrale in paziente scoagulato: dove, quando e perché?



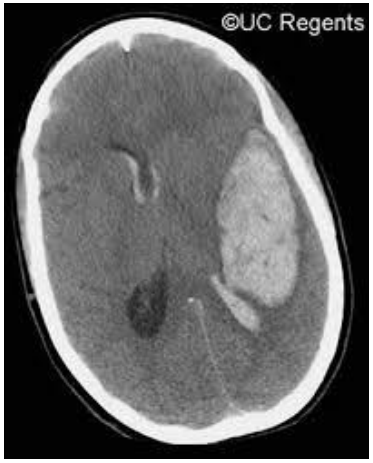
Ematoma epiurale



ESA



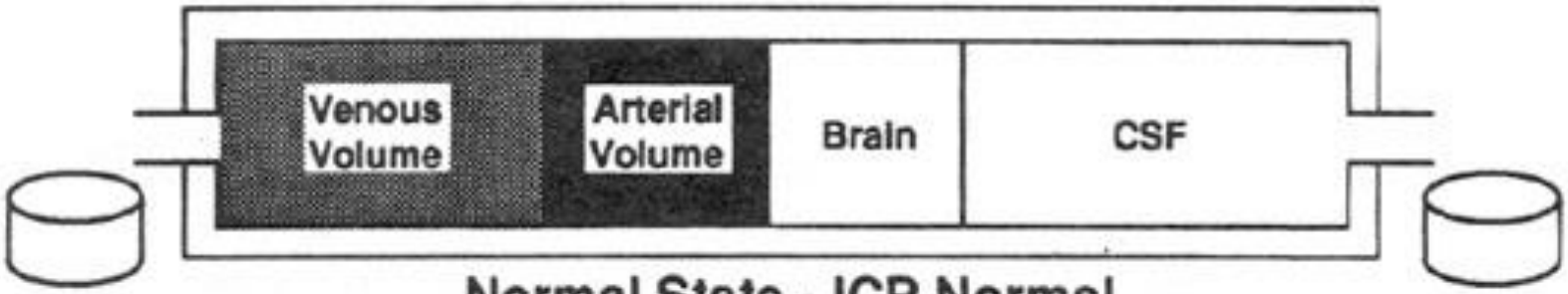
Trauma Cranico



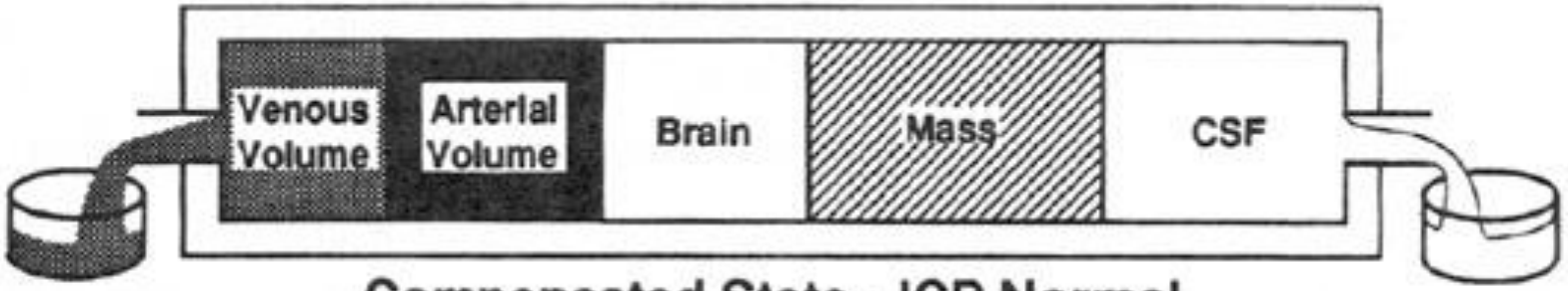
Emorragia cerebrale

FIGURE 1
MONRO-KELLIE DOCTRINE

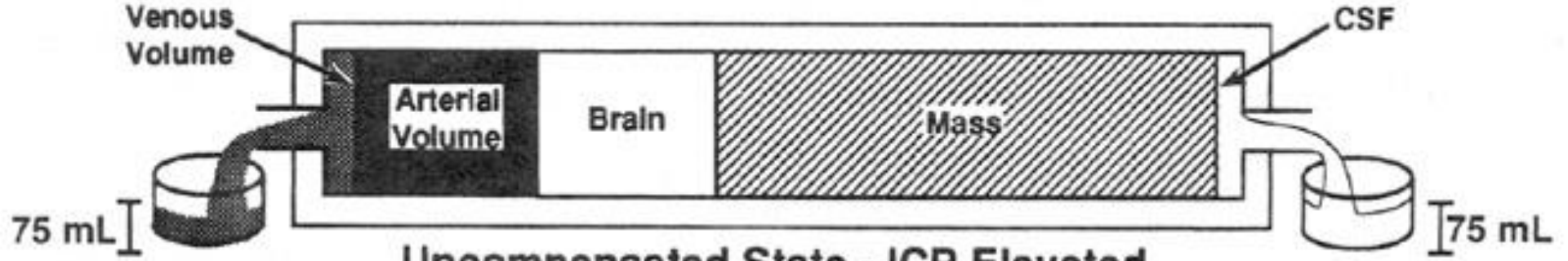
INTRACRANIAL COMPENSATION FOR EXPANDING MASS



Normal State - ICP Normal

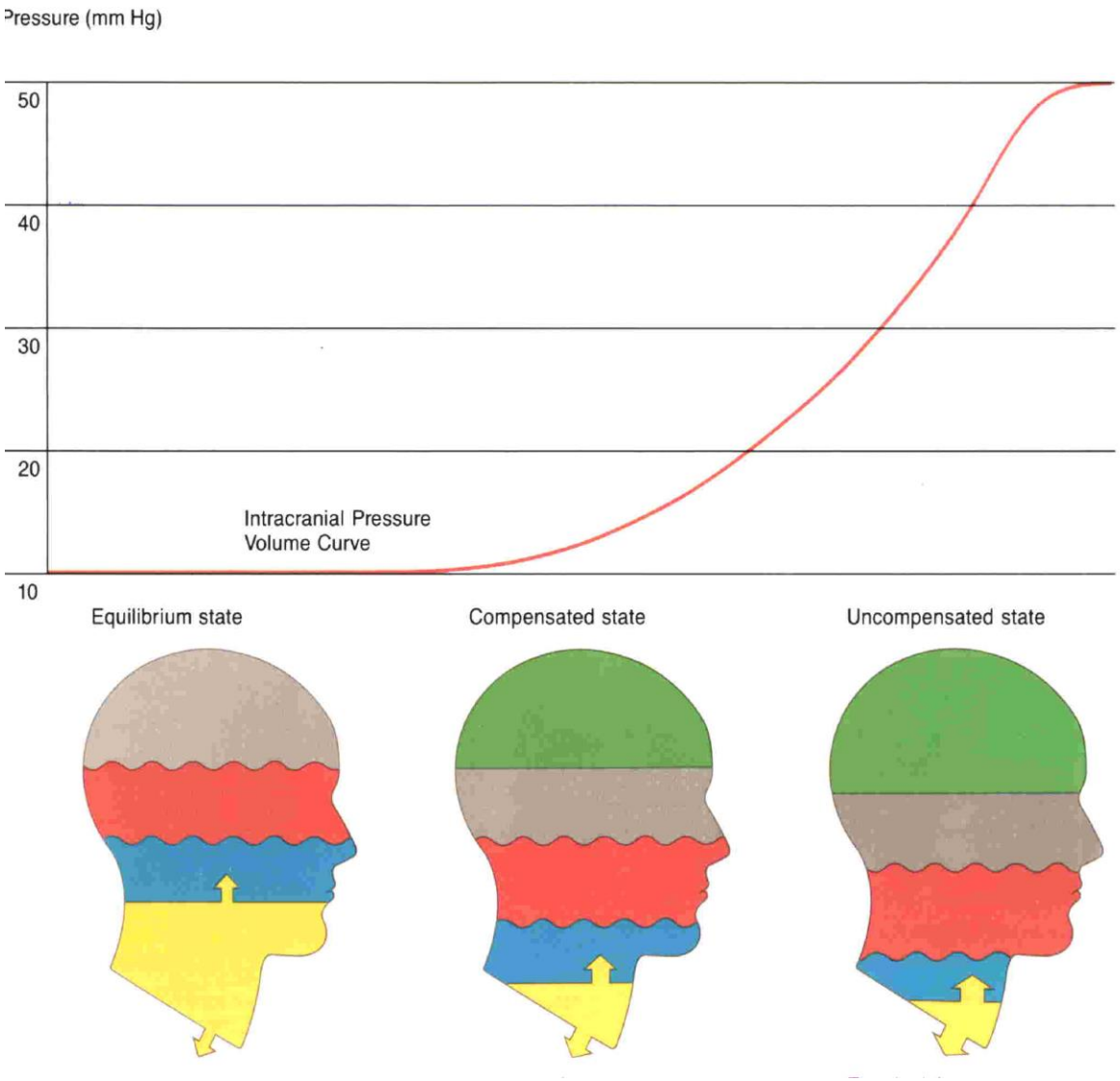


Compensated State - ICP Normal



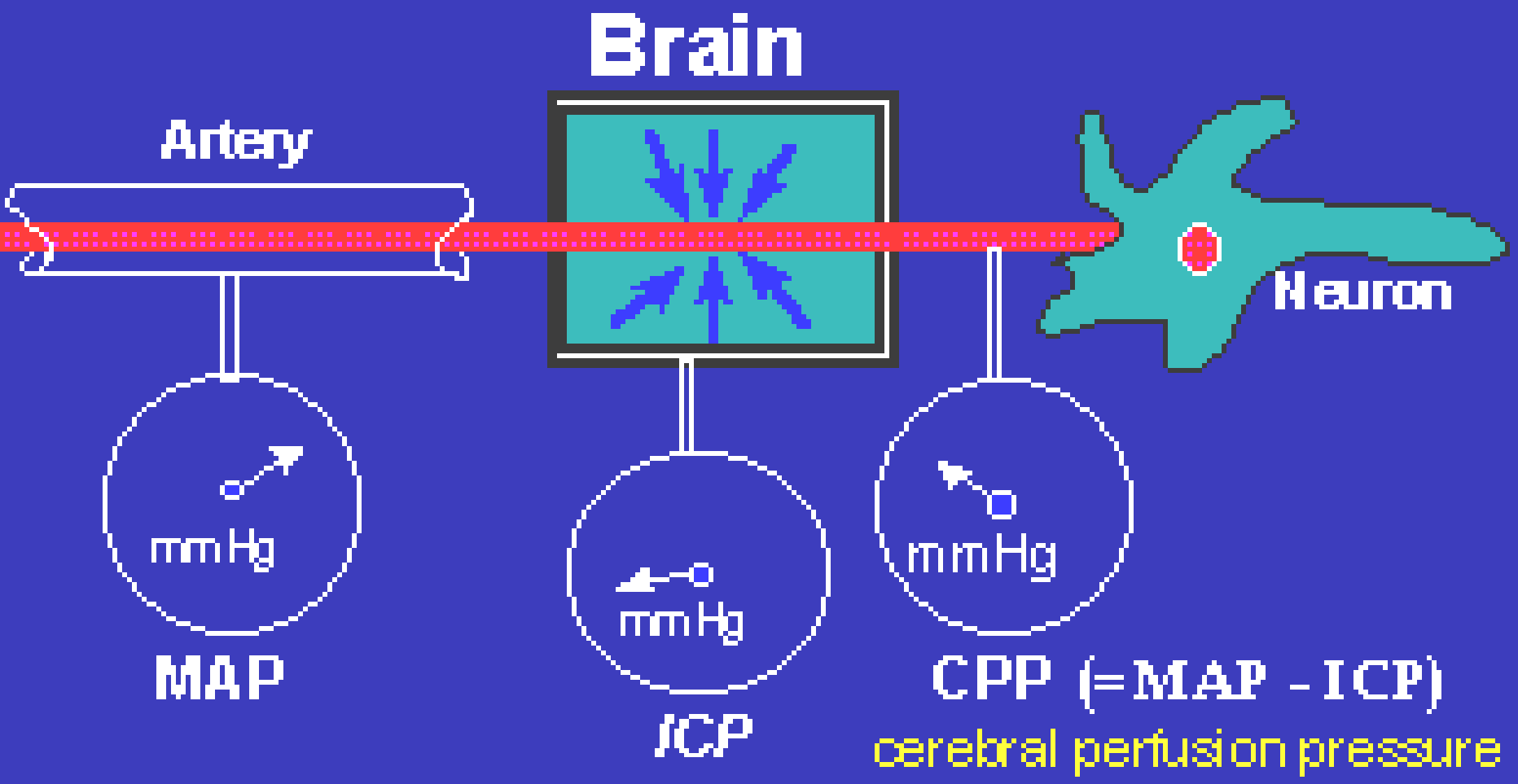
Uncompensated State - ICP Elevated

Curva pressione/volume



- Volume cerebrale
- Volume lesione
- Volume sangue arterioso
- Volume sangue venoso
- Volume LCR

O_2 → Neuron: Cerebral Perfusion Pressure



Early trauma induced coagulopathy (ETIC): Prevalence across the injury spectrum

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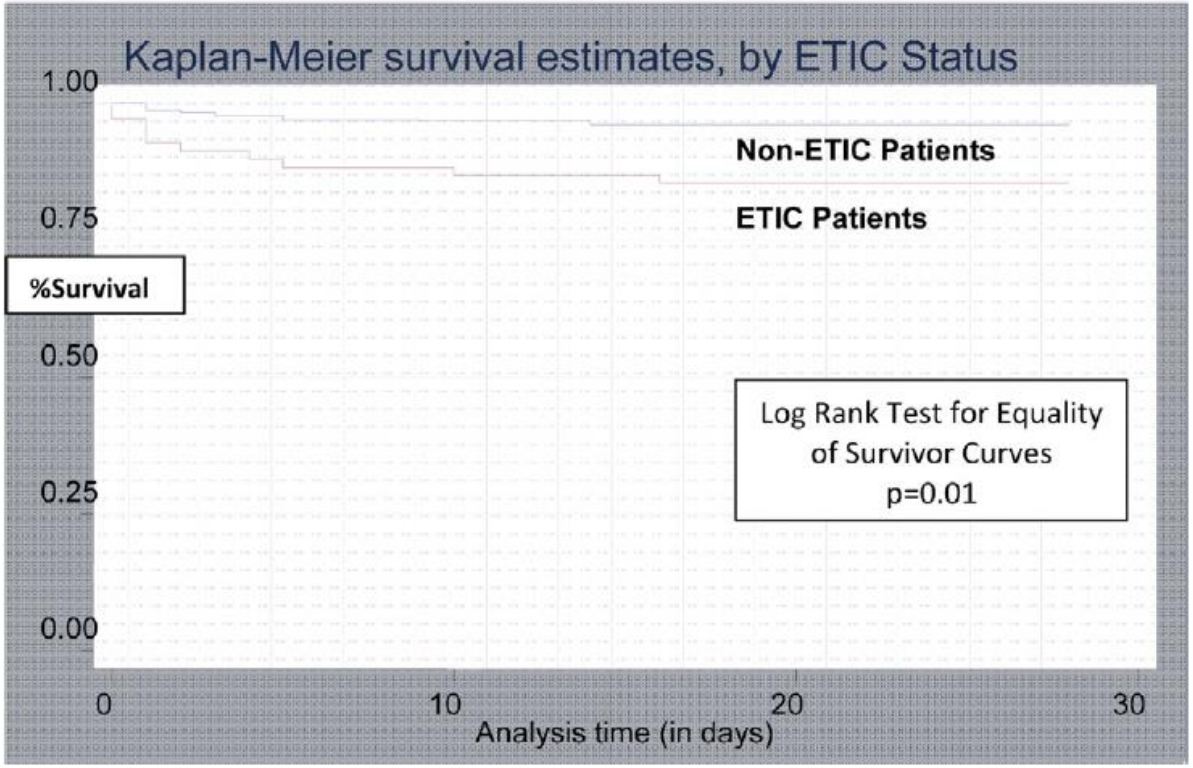

Fig. 2. The Kaplan–Meier survival estimates stratified by the patient's ETIC status.

Review Article

Coagulation disorders after traumatic brain injury

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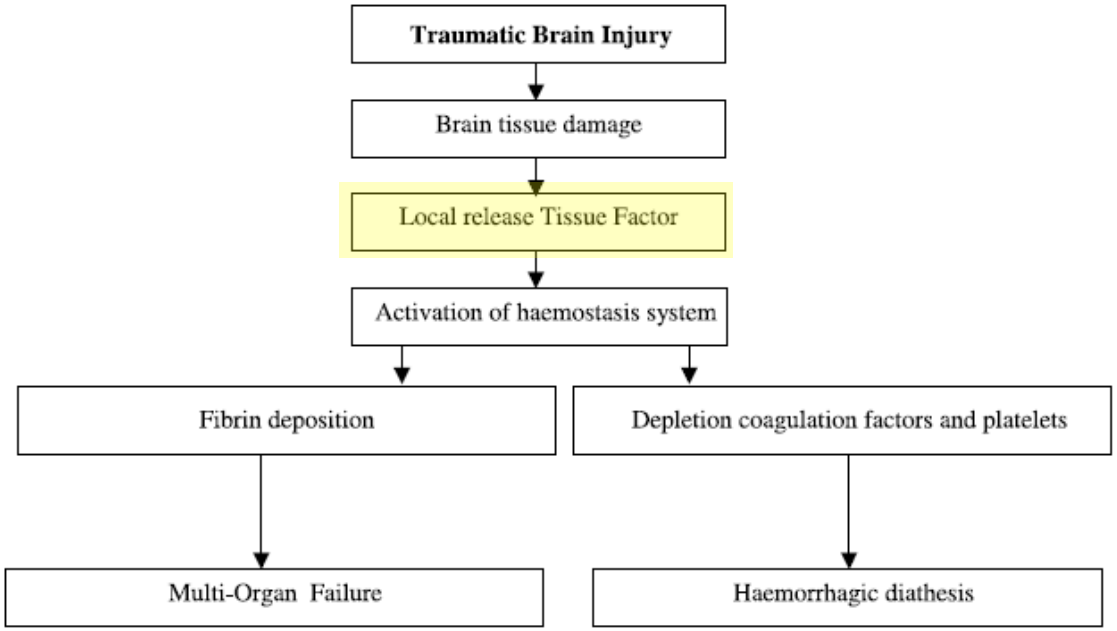
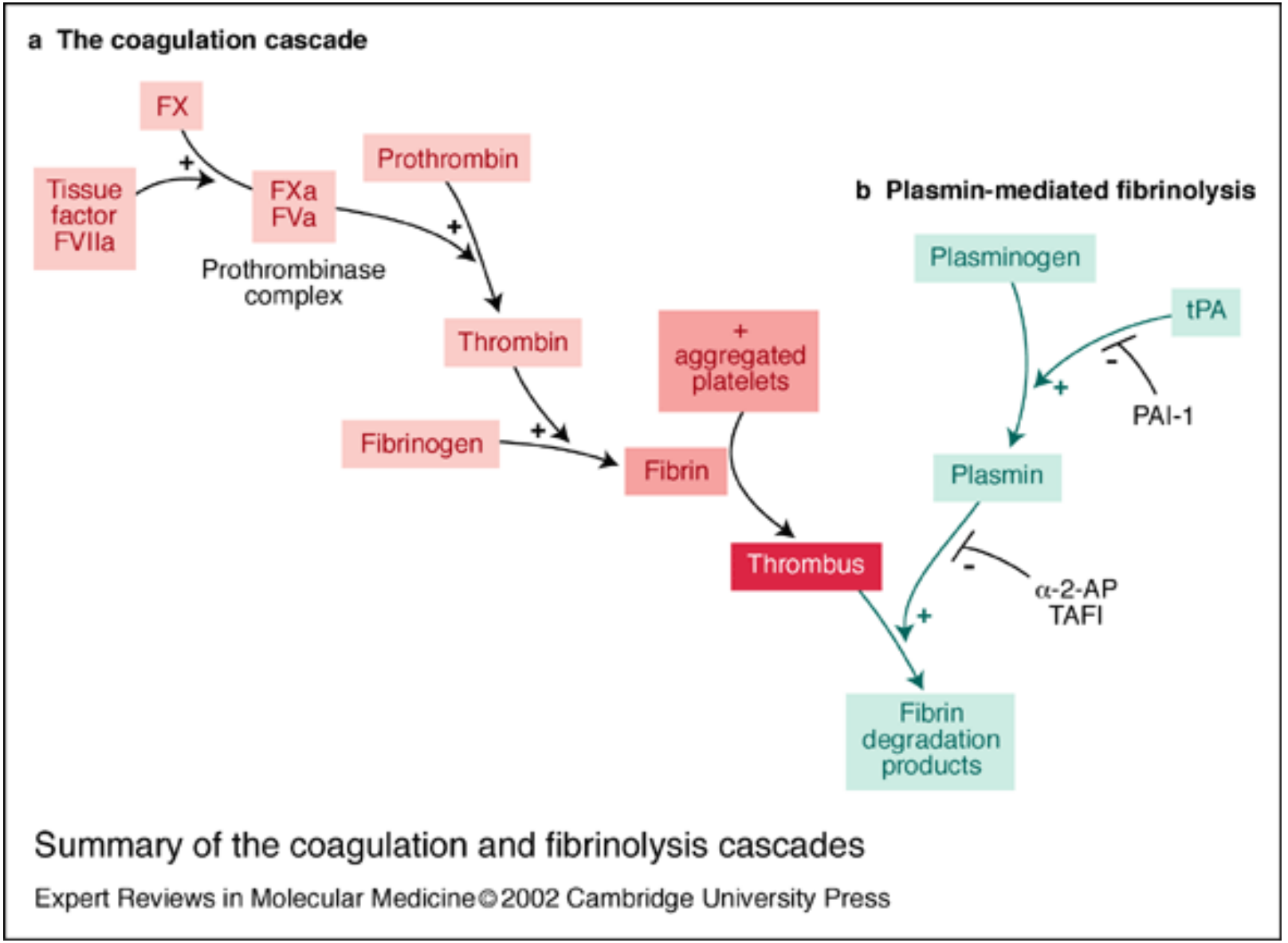


Fig. 1. Schematic diagram of traumatic brain injury and coagulopathy



Summary of the coagulation and fibrinolysis cascades

Endogenous plasminogen activators mediate progressive intracerebral hemorrhage after traumatic brain injury in mice

Nuha Hijazi,[1] Rami Abu Fanne,[1] Rinat Abramovitch,[2] Serge Yarovoi,[3] Muhamed Higazi,[1] Suhair Abdeen,[1] Maamon Basheer,[1] Emad Maraga,[1] Douglas B. Cines,[3] and Abd Al-Roof Higazi[1,3]

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Key Points

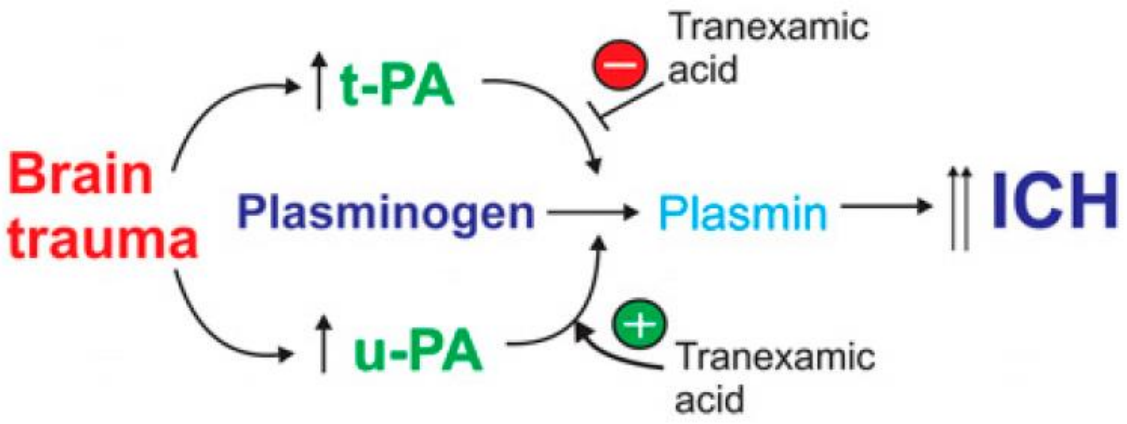
- Closed head trauma sequentially releases tPA followed by uPA from injured brain.
- Increased uPA is responsible for delayed intracerebral hemorrhage, which is prevented by a tPA variant that inhibits uPA activity.

Persistent intracerebral hemorrhage (ICH) is a major cause of death and disability after traumatic brain injury (TBI) for which no medical treatment is available. Delayed bleeding is often ascribed to consumptive coagulopathy initiated by exposed brain tissue factor. We examined an alternative hypothesis, namely, that marked release of tissue-type plasminogen activator (tPA) followed by delayed synthesis and release of urokinase plasminogen activator (uPA) from injured brain leads to posttraumatic bleeding by causing premature clot lysis. Using a murine model of severe TBI, we found that ICH is reduced in $tPA^{-/-}$ and $uPA^{-/-}$ mice but increased in $PAI\text{-}1^{-/-}$ mice compared with wild-type (WT) mice. $tPA^{-/-}$, but not $uPA^{-/-}$, mice developed a systemic coagulopathy post-TBI. Tranexamic acid inhibited ICH expansion in $uPA^{-/-}$ mice but not in $tPA^{-/-}$ mice. Catalytically inactive tPA-S^{481}A inhibited plasminogen activation by tPA and uPA, attenuated ICH, lowered plasma D-dimers, lessened thrombocytopenia, and improved neurologic outcome in WT, $tPA^{-/-}$, and $uPA^{-/-}$ mice. ICH expansion was also inhibited by tPA-S^{481}A in WT mice anticoagulated with warfarin. These data demonstrate that protracted endogenous fibrinolysis induced by TBI is primarily responsible for persistent ICH and post-TBI coagulopathy in this model and offer a novel approach to interrupt bleeding. (*Blood*. 2015;125(16):2558-2567)

Comment on Hijazi et al, page 2558

The traumatic side of fibrinolysis

Robert L. Medcalf MONASH UNIVERSITY



Following TBI, there is an increase in brain-derived tPA- and uPA-mediated fibrinolysis that promotes ICH. TXA blocks tPA-mediated fibrinolysis and ICH, but potentiates uPA-mediated plasminogen activation promoting ICH.

In this issue of *Blood*, Hijazi et al challenge the view that consumptive coagulopathy that accompanies traumatic brain injury (TBI) results in a sequence of events that lead to intracranial hemorrhage (ICH).[1]

Endogenous plasminogen activators mediate progressive intracerebral hemorrhage after traumatic brain injury in mice

Nuha Hijazi,[1] Rami Abu Fanne,[1] Rinat Abramovitch,[2] Serge Yarovoi,[3] Muhamed Higazi,[1] Suhair Abdeen,[1] Maamon Basheer,[1] Emad Maraga,[1] Douglas B. Cines,[3] and Abd Al-Roof Higazi[1,3]

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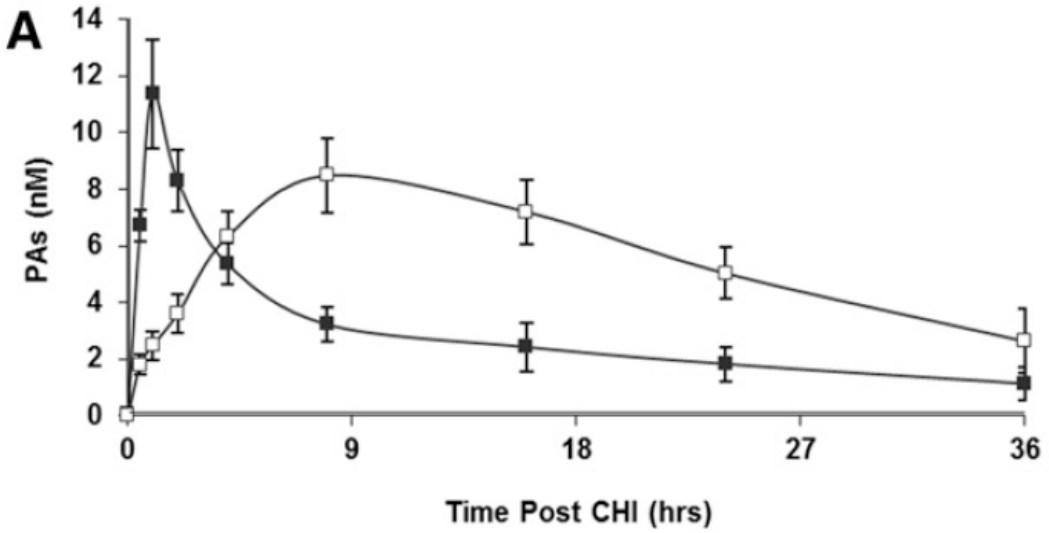

Figure 7. tPA and uPA participate in the delayed bleeding post-CHI. (A) Time course of tPA and uPA release post-CHI. The concentrations of tPA (filled squares) and uPA (empty squares) in the CSF of WT mice were measured by enzyme-linked immunosorbent assay before or at different time points after CHI. The mean ± SE of 3 experiments is shown (n = 3-7). (B) uPA mediates the delayed ICH in untreated mice. CHI was induced in WT mice. Thirty minutes or 8 hours postinjury, mice were given tPA-S^{481}A (1 mg/kg) or tranexamic acid (TA; 150 mg/kg). Twenty-four hours

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Review

Acute traumatic coagulopathy in the setting of isolated traumatic brain injury: A systematic review and meta-analysis

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[c] Department of Surgery, Monash University, Melbourne, Australia
[d] Department of Neurosurgery, The Alfred Hospital, Melbourne, Australia
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Table 2
Study size, ATC definition, reported incidence and outcomes.

Author (year)	Definition of iTBI	Definition of ATC	Proportion of ATC	Mortality among patients with ATC
Carrick (2005)	GCS < 14, extracranial AIS < 3	PT > 14.2 or PTT > 38.4 s	21%	62%
Chang (2006)	Head AIS > 3, non-penetrating, admission CT with IPH, subsequent CT within 72 h.	PT > 13.2 s or PTT > 32 s	18%	–
Chhabra (2010)	GCS < 13	Fibrinogen ≤ 200 mg/dL	7%	–
Cohen (2007)	Head abbreviated injury score [AIS] ≥ 3 and all other AIS < 3	PT and PTT**	28%	66%
Franschman (2012) (J Neurotrauma)	GCS ≤ 13, CT confirmed brain injury, extracranial AIS < 3	aPTT > 40 s or INR > 1.2 or platelet count < 120×10^9/L	34%	52%
Genet (2013)	Head abbreviated injury score [AIS] ≥ 3 and all other AIS < 3	aPTT > 35 s or INR > 1.2	13%	–
Greuters (2011)	CT confirmed isolated TBI, AIS extracranial < 3	aPTT > 40 s or INR > 1.2	54%	–
Hulka (1996)	CT evidence of brain injury	Disseminated intravascular coagulation score ≥ 5	41%	40%
Kearney (1992)	GCS ≤ 9	Modified DIC score ≥ 5	86.1%	50%
Kuo (2004)	Midline shift on CT and GCS measurement**	Modified coagulopathy score ≥ 1	78.1%	75%
Kushimoto (2001)	"Isolated head injury from blunt trauma"	Alpha-2 plasmin inhibitor deficiency less than 60% normal	83%	86%
Lustenberger (2010) (J Trauma)	Head abbreviated injury score [AIS] ≥ 3 and all other AIS < 3	Plt < 100,000 or INR > 1.2 or aPTT > 36 s	36.4%	37%
Piek (1992)	GCS ≤ 8	PLT < 50,000 or PT > 16 s or PTT > 50 s	19%	35%
Schochl (2011)	Head abbreviated injury score [AIS] ≥ 3 and all other AIS < 3	PTI > 70% or aPTT > 35 s or fibrinogen < 150 mg/DL or PLT < 100,000	15.8%	–
Selladurai (1997)	GCS ≤ 14 and parenchymal/extra-axial lesions on CT	DIC score ≥ 2	38%	17%
Stein (2008) (J Trauma)	Head AIS > 3, GCS > 8	INR ≥ 1.4	13.9%	–
Stein (1992)	GCS > 13, serial CT scans	PLT count, PT, PTT	55%	41%
Sun (2011)	Head AIS ≥ 2, exclude existing coagulopathy, acidosis, massive transfusions, hypothermia, penetrating.	DIC score ≥ 5 or PT > 13.4 s	36%	21%
Takahasi (2000)	GCS ≤ 14	DIC score > 6	35.7%	–
Talving (2009)	Head abbreviated injury score [AIS] ≥ 3 and all other AIS < 3	PLT < 100,000 or INR > 1.1 or aPTT > 36 s	34%	50%
Wafaisade (2010)	Head abbreviated injury score [AIS] ≥ 3 and all other AIS < 3	INR > 1.3 or PLT < 100,000	22.7	50.4%
Zehtabchi (2008)	AIS head > 2, brain haematoma on CT	INR > 1.3 or PTT > 34 s	17%	–

GCS, Glasgow coma scale; PTT, partial thromboplastin time; ICU, intensive care unit; AIS, abbreviated injury scale; aPTT, activated partial thromboplastin time; GOS, Glasgow outcome scale; IPH, intraparenchymal haemorrhage; INR, international normalized ratio; CT, computerised tomography; DIC, disseminated intravascular coagulation; PT, prothrombin time; Plt, platelet.

Research Article

Coagulation Parameters and Risk of Progressive Hemorrhagic Injury after Traumatic Brain Injury: A Systematic Review and Meta-Analysis

Danfeng Zhang, Shun Gong, Hai Jin, Junyu Wang, Ping Sheng, Wei Zou, Yan Dong, and Lijun Hou

Department of Neurosurgery, Changzheng Hospital, Second Military Medical University, Shanghai 200003, China

Our findings showed statistically significant positive associations between PT, D-dimer level, INR, and the risk of PHI after TBI. Higher level of PLT and Fg seemed to suggest a lower risk of PHI. Independent PTT seemed to be of no indicative value. As for dichotomous variables, the contributions to PHI were as follows: DD > INR > PT > Fg > PLT. But when examined as continuous variables, the sequence seemed to be INR > DD > Fg > PLT. Meta-analysis of continuous data was perceived to be more meaningful compared with that of dichotomous data because of less conversion steps to correlation coefficient (r).

Prehospital Resuscitation of Traumatic Hemorrhagic Shock with Hypertonic Solutions Worsens Hypocoagulation and Hyperfibrinolysis

Matthew J. Delano*, Sandro B. Rizoli‡, Shawn G. Rhind§, Joseph Cuschieri‖, Wolfgang Junger¶, Andrew J. Baker**, Michael A. Dubick††, David B. Hoyt†, and Eileen M. Bulger‖

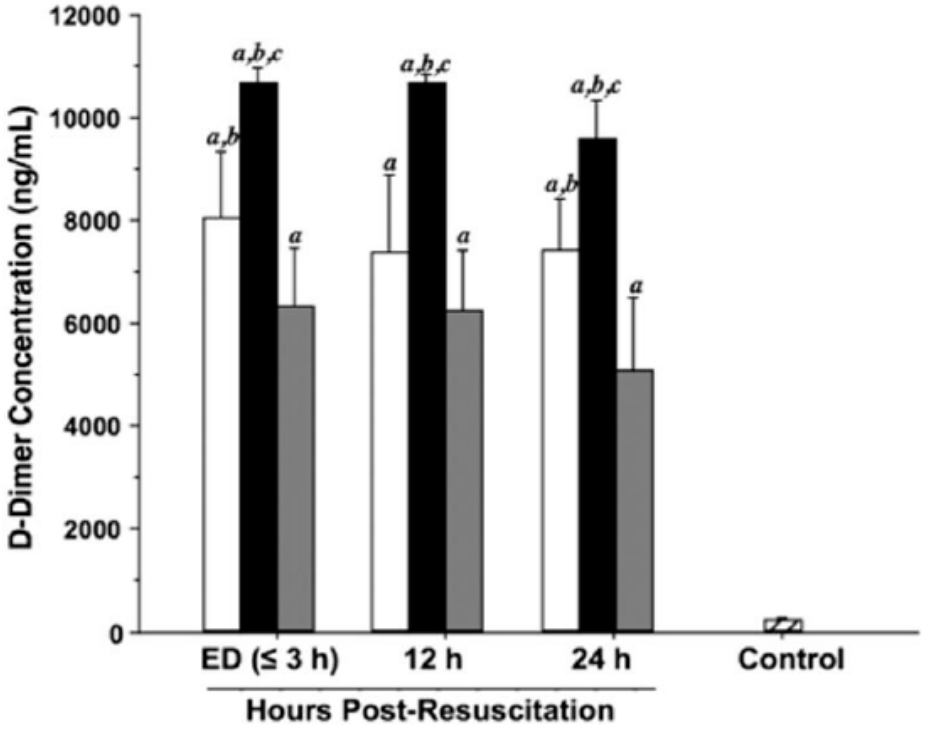
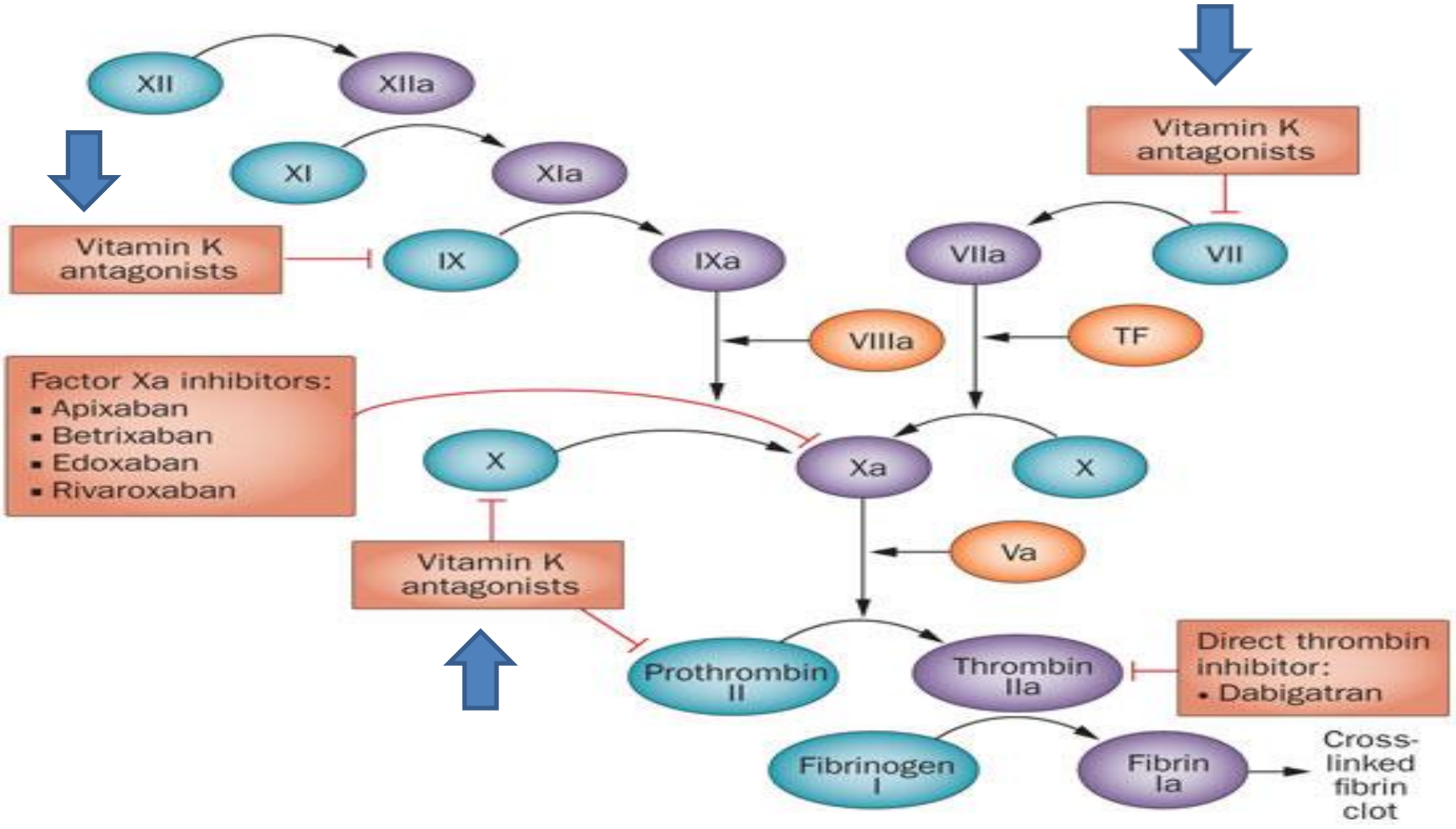


Fig. 2. Plasma D-dimer levels determined on emergency department (ED) admission (≤3 h) and at 12 and 24 h after resuscitation in trauma patients treated prehospital with HS (n = 9), HSD (n = 8), or NS (n = 17) and in healthy controls (n = 20)

Data are shown as mean ± SEM; [a]$P < 0.05$ vs. age-matched controls; [b]$P < 0.05$ vs. time-matched NS-treated patients; [c]$P < 0.05$ vs. time-matched HS-treated patients, by ANOVA.

Coagulazione e anticoagulanti vecchi e nuovi



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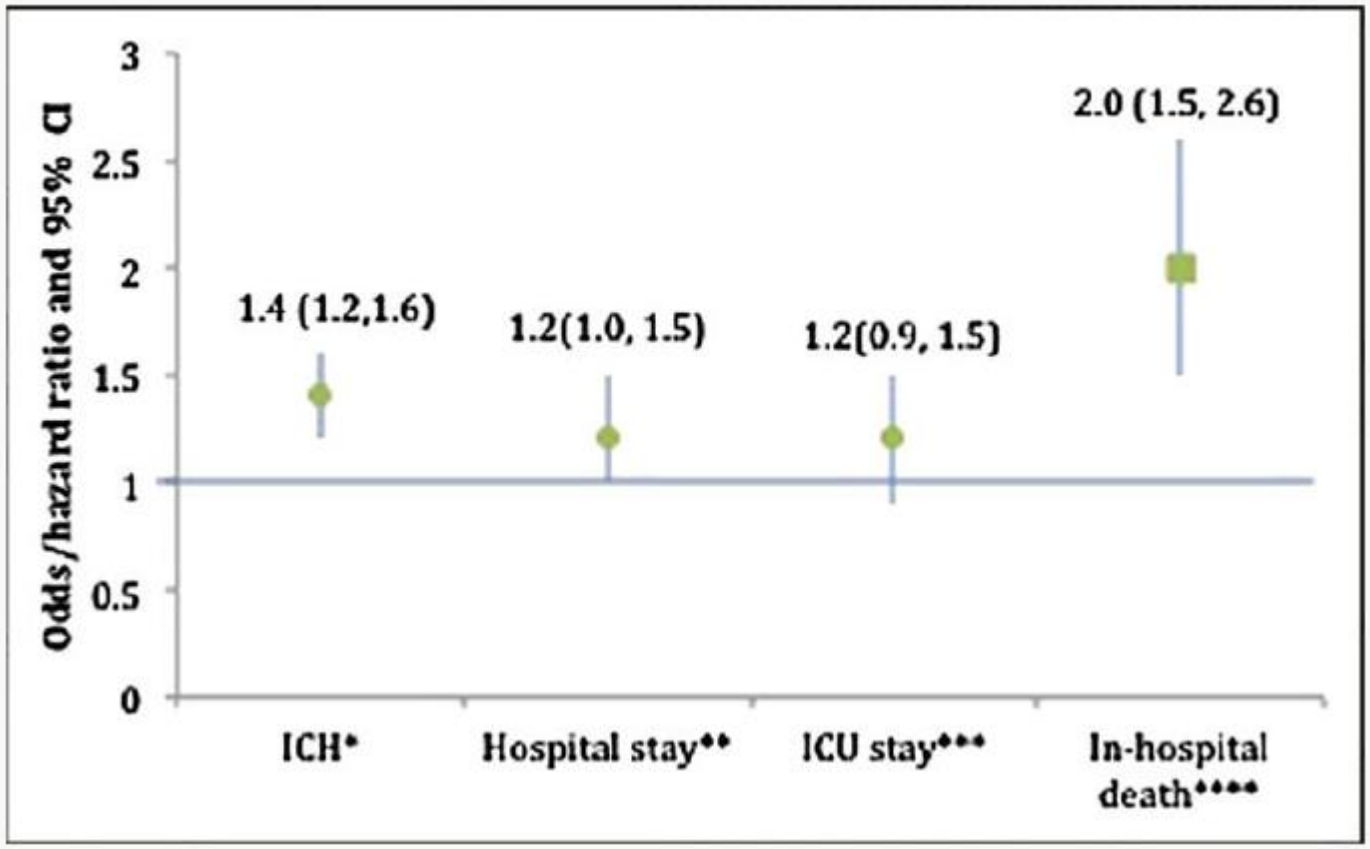
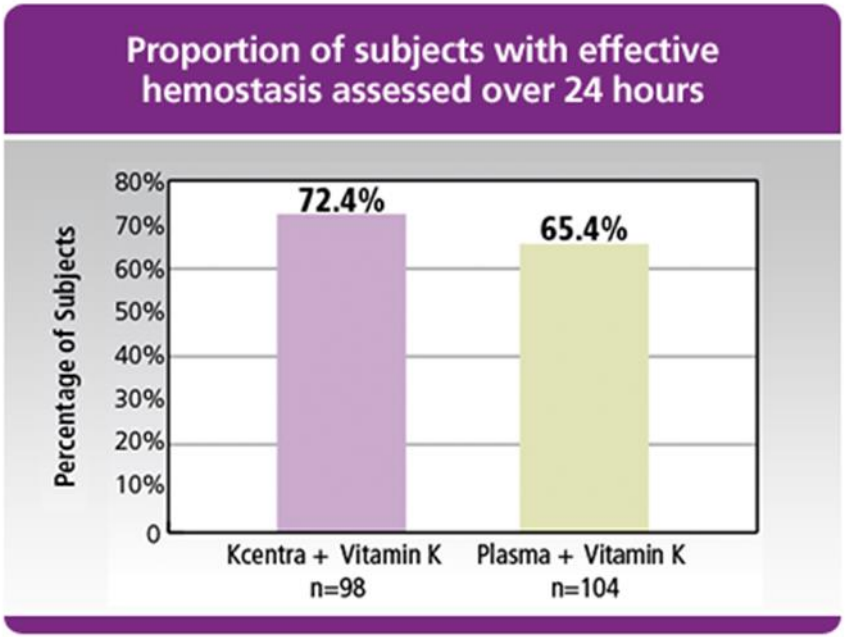
Effect of preinjury warfarin use on outcomes after head trauma in Medicare beneficiaries

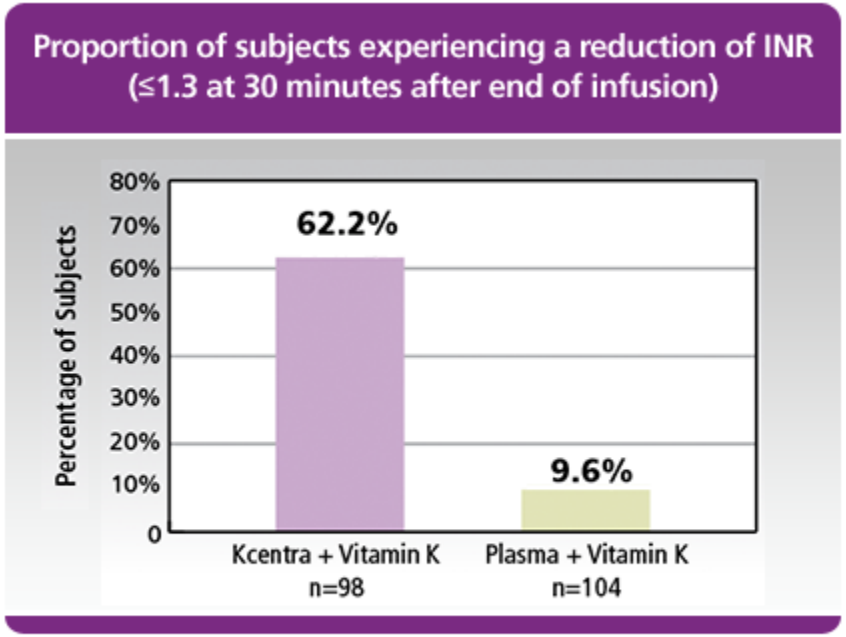
Courtney E. Collins, M.D., Elan R. Witkowski, M.D., Julie M. Flahive, M.S., Fred A. Anderson Jr, Ph.D., and **Heena P. Santry, M.D.***
Department of Surgery, University of Massachusetts Medical School, Worcester, MA, USA



Kcentra: a non-activated **4F-PCC** (Protrombin Complex Concentrate) containing vitamin K-dependent coagulation Factors II, VII, IX, and X and antithrombotic Proteins C and S



Kcentra - plasma (%) [95% CI] = 7.1 [-5.8, 19.9]
(prespecified non-inferiority margin >-10%).



Kcentra - plasma (%) [95% CI] = 52.6 [39.4, 65.9]
(prespecified superiority margin >0)

Use of Prothrombin Complex Concentrate as an Adjunct to Fresh Frozen Plasma Shortens Time to Craniotomy in Traumatic Brain Injury Patients

Division of Trauma, Emergency Surgery, Critical Care, and Burns, Department of Surgery, University of Arizona, Tucson, Arizona

Bellal Joseph, MD

Viraj Pandit, MD

TABLE 3. Blood Product Requirement and Action of Therapy[a]

	PCC + FFP (n = 74)	FFP (n = 148)	*P* Value
Time of initiation of therapy, min, mean ± SD	59 ± 35	65 ± 33	.61
International normalized ratio			
Correction of INR, n (%)	71 (96)	130 (94)	.53
Time to correction, min, mean ± SD	212 ± 108	425 ± 226	**.001**
Blood product requirement			
FFP units, mean ± SD	3.1 ± 2.5	4 ± 2.3	**.041**
PRBC units, mean ± SD	3.2 ± 2.2	3.8 ± 2.6	**.035**
Platelets units, mean ± SD	1.4 ± 1.8	1.2 ± 1.7	.2

[a]PCC, prothrombin complex concentrate; FFP, fresh frozen plasma; SD, standard deviation; INR, international normalized ratio; FFP, fresh frozen plasma; PRBC, packed red blood cells.
The bold font identifies statistically significant values.

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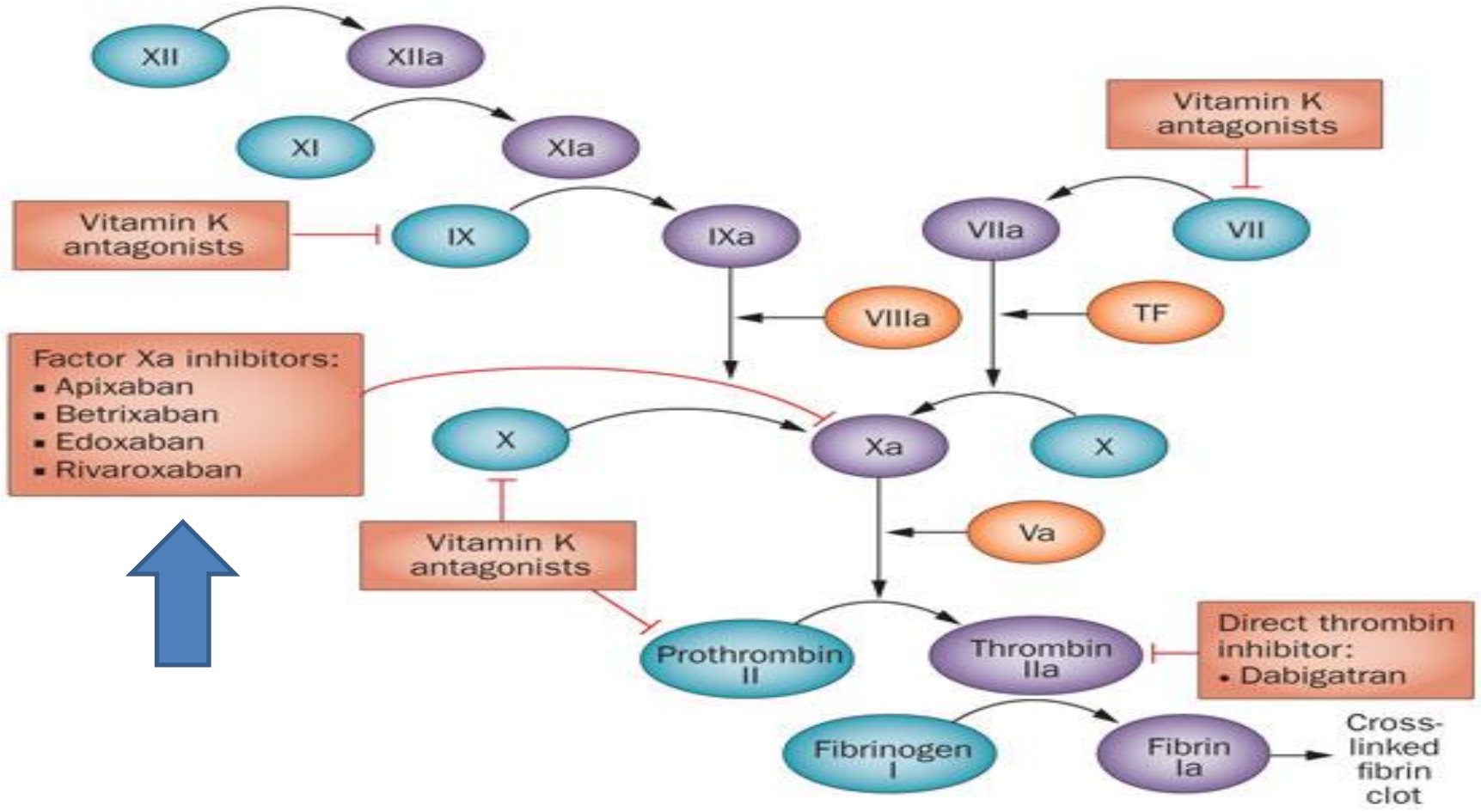
Coagulazione e anticoagulanti vecchi e nuovi



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Rivaroxaban and intracranial haemorrhage after mild traumatic brain injury: A dangerous combination?

Christopher Beynon*, Anna Potzy, Oliver W. Sakowitz, Andreas W. Unterberg

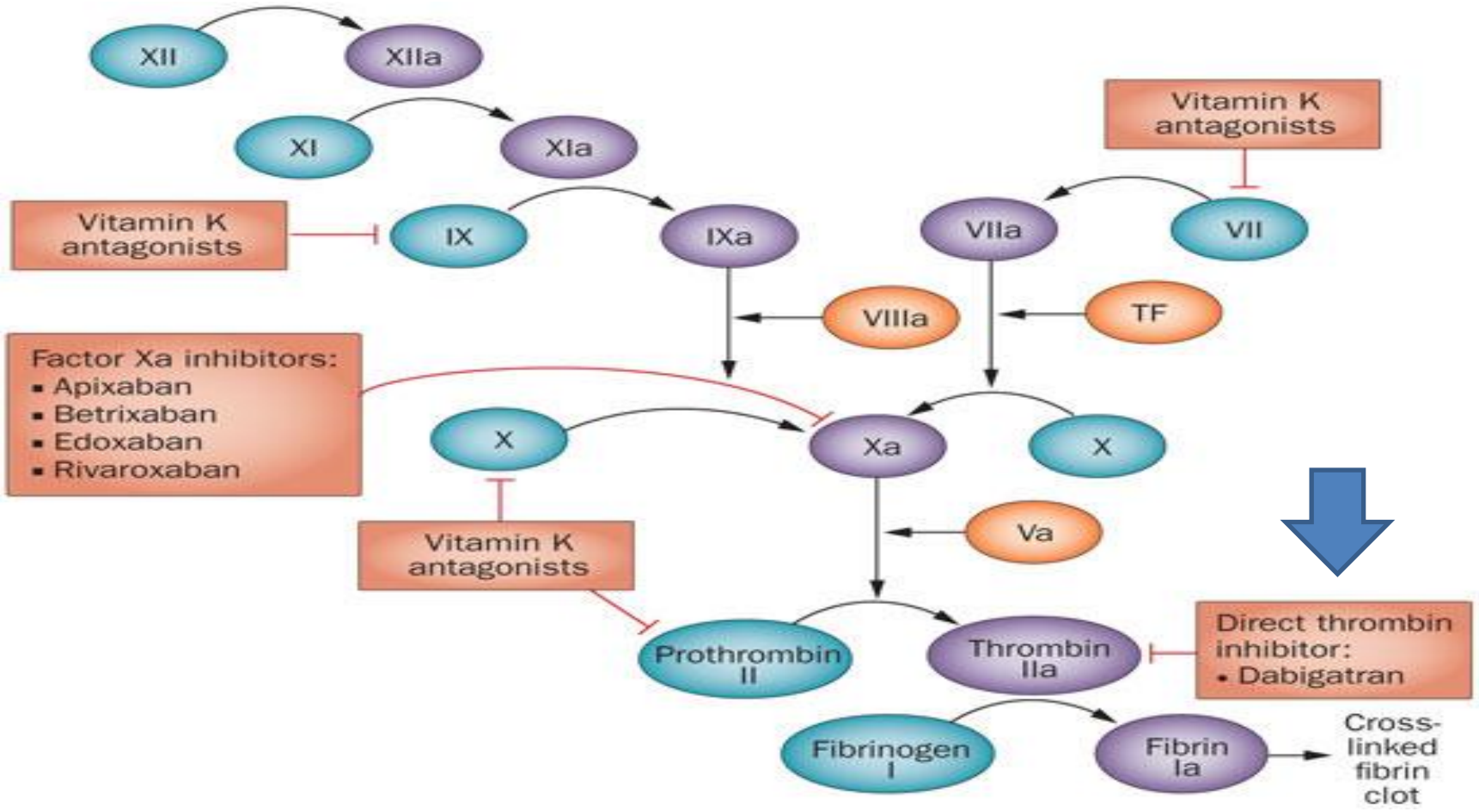
Department of Neurosurgery, Heidelberg University Hospital, Heidelberg, Germany

Table 2
Details of rivaroxaban-treated patients with posttraumatic intracranial haemorrhage.

No.	Age Gender	Trauma mechanism	Traumatic intracranial haemorrhage	Laboratory results (initial)		Serum creatinine (mg/dl)	Haemostatic measures	Laboratory results (repeated)		Neurosurgical intervention	Repeated CT (progression)	GOS at discharge
				INR	aPTT (s)			INR	aPTT (s)			
1	80 Male	Ground fall	Intracerebral haemorrhage	1.77	41.3	1.14	PCC: 3400 I.U.	1.34	34.9	None	Yes (Yes)	GOS 1
2	21 Male	Ground fall	Subarachnoid haemorrhage	1.00	24	0.75	None	–	–	None	No	GOS 5
3	84 Female	Ground fall	Intracerebral haemorrhage	1.28	32.8	0.62	None	1.21	30.7	None	No	GOS 5
4	77 Female	Ground fall	Subdural haematoma	1.45	43	0.8	PCC: 500 I.U.	1.09	26.5	Craniotomy, haematoma evacuation	Yes (Yes)	GOS 5
5	73 Male	Motorcycle accident	Intracerebral haemorrhage	1.46	38.5	1.28	PCC: 1500 I.U.	1.24	31.2	None	No	GOS 5
6	89 Male	Ground fall	Subdural haematoma	1.57	35.4	1.75	PCC: 2000 I.U. FFP: 4 units	1.15	29.0	Craniotomy, haematoma evacuation	Yes (Yes)	GOS 1

aPTT, activated partial thromboplastin time; FFP, fresh frozen plasma; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; I.U., international unit; INR, international normalized ratio; PCC, prothrombin complex concentrate.

Coagulazione e anticoagulanti vecchi e nuovi



Traumatic Intracranial Hemorrhage in Patients Taking Dabigatran: Report of 3 Cases and Review of the Literature

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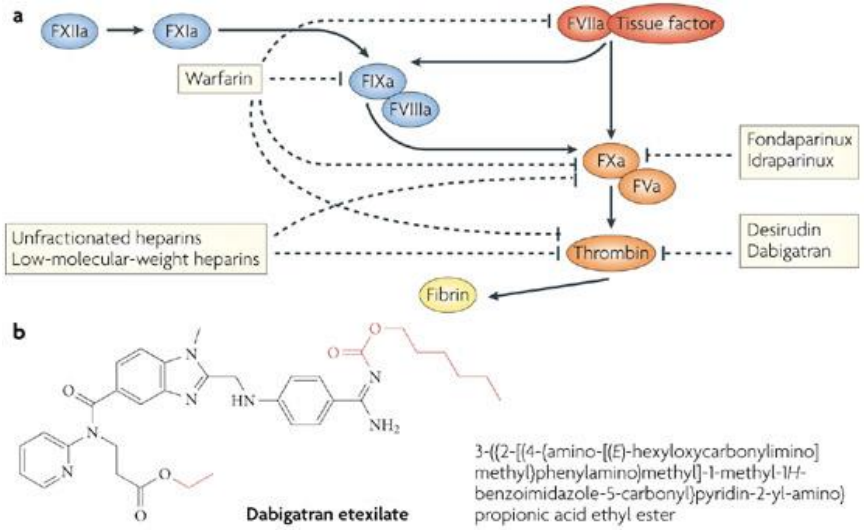

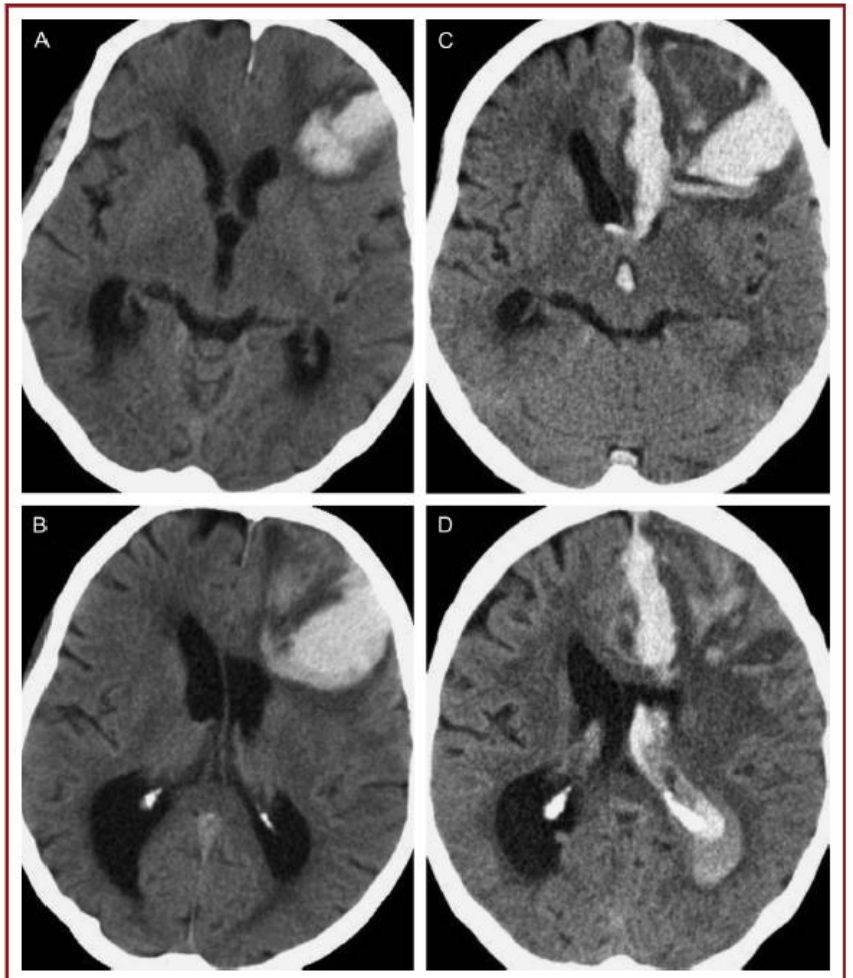

FIGURE 1. *Traumatic intraparenchymal hemorrhage in case 1.* **A** *and* **B**, *initial noncontrast head CT on admission showing large left frontal IPH.* **C** *and* **D**, *repeat head CT obtained 6 hours after the initial study. There is enlargement of the IPH with intraventricular extension. CT, computerized tomography; IPH, intraparenchymal hemorrhage.*

Traumatic Intracranial Hemorrhage in Patients Taking Dabigatran: Report of 3 Cases and Review of the Literature

Although there is currently no specific antidote for thrombin inhibitor–induced coagulopathy, several management strategies have been proposed for reversal. Because dabigatran is excreted renally, adequate diuresis should be maintained to promote renal perfusion and concomitant dabigatran clearance. Additionally, because of the renal excretion of dabigatran, body weight and renal function have some influence on dabigatran metabolism and should influence dosing accordingly.[18] Charcoal lavage may be considered if the last dabigatran ingestion was less than 2 hours from presentation. Prothrombin complex concentrates have been proposed as a rapid reversal agent for dabigatran, but more data are required to determine the clinical efficacy of these agents.[1,19] Animal

and considering hemodialysis. If surgery to manage the patient's hemorrhage can be delayed, we recommend serial monitoring of TT over the course of days to ensure that the effects of dabigatran have resolved before making an incision. Practitioners must remember that INRs are inappropriate measures of anticoagulation by dabigatran. However, aPTT may allow for the identification of anticoagulant activity of dabigatran and also for the determination of intoxication levels.

Figure 1. International normalized ratio (INR) values over time as determined in rats anticoagulated with apixaban (blue) or warfarin (green) as well as in control animals (beige).

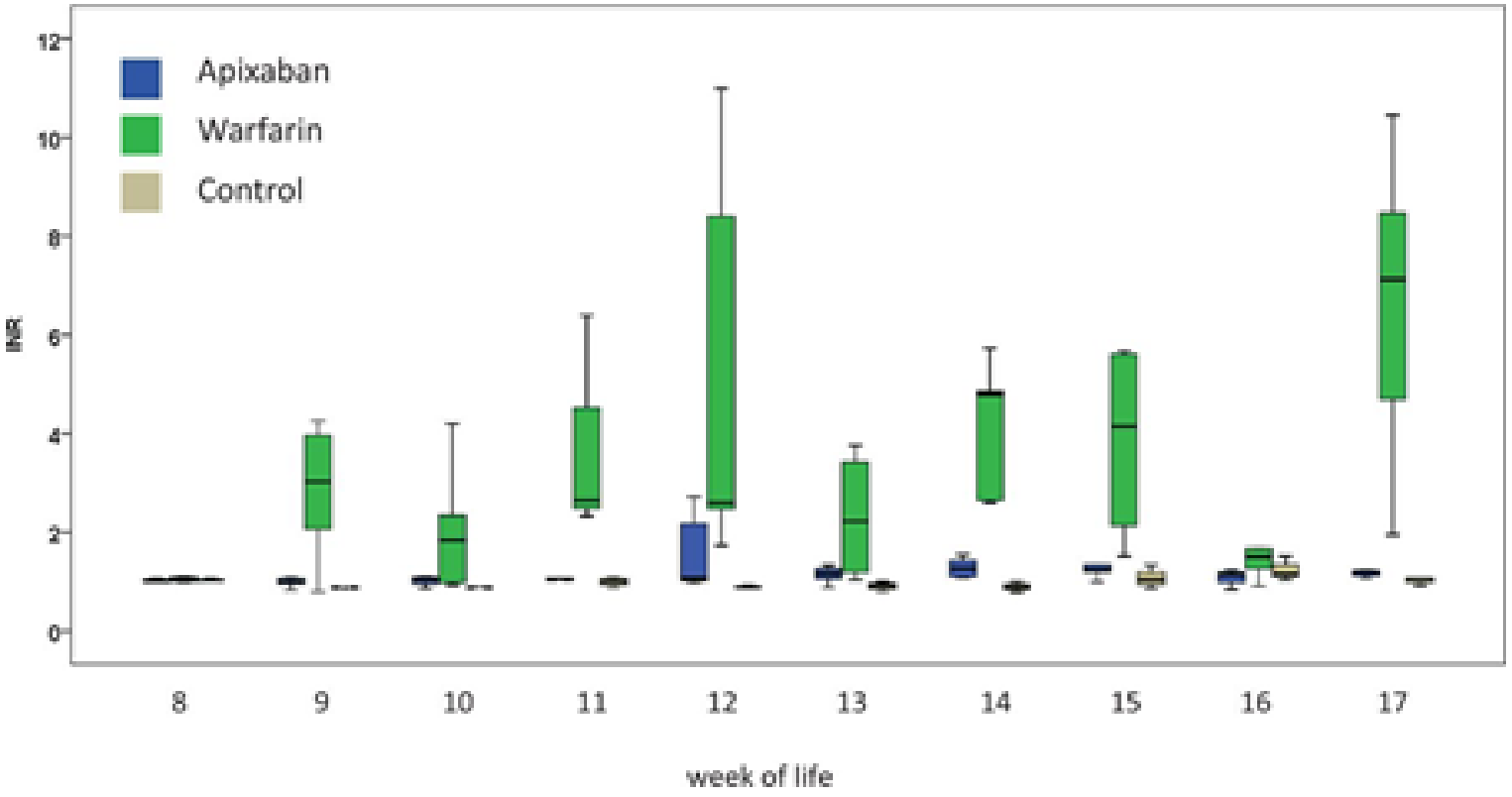

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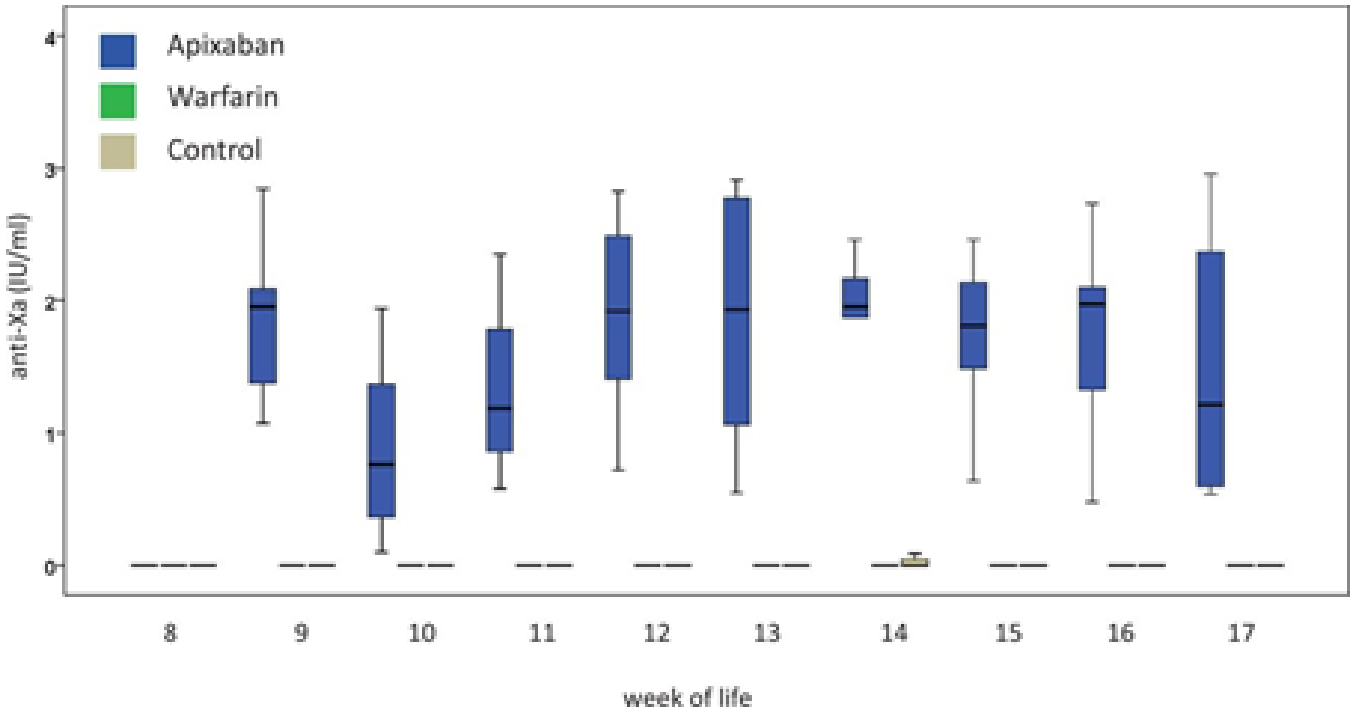
Figure 2. Anti-factor Xa levels (IU/ml) over time as determined in rats anticoagulated with apixaban (blue) or warfarin (green) as well as in control animals (beige).



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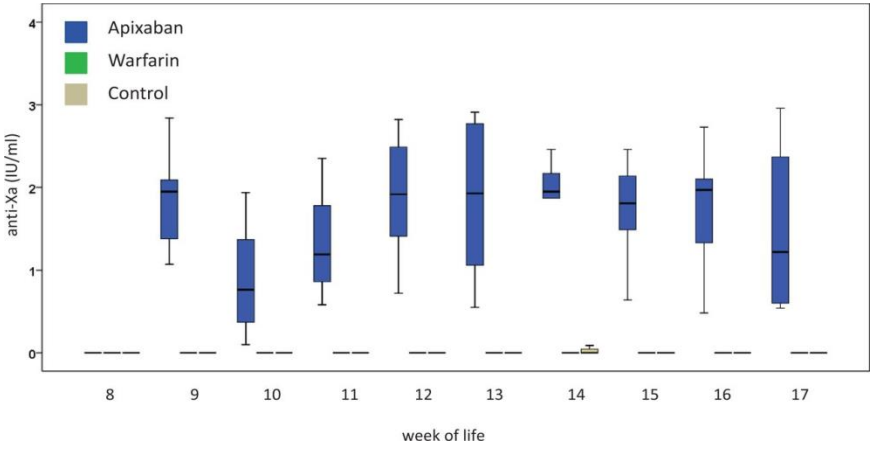
Risk of long-term anticoagulation under sustained severe arterial hypertension: A translational study comparing warfarin and the new oral anticoagulant apixaban



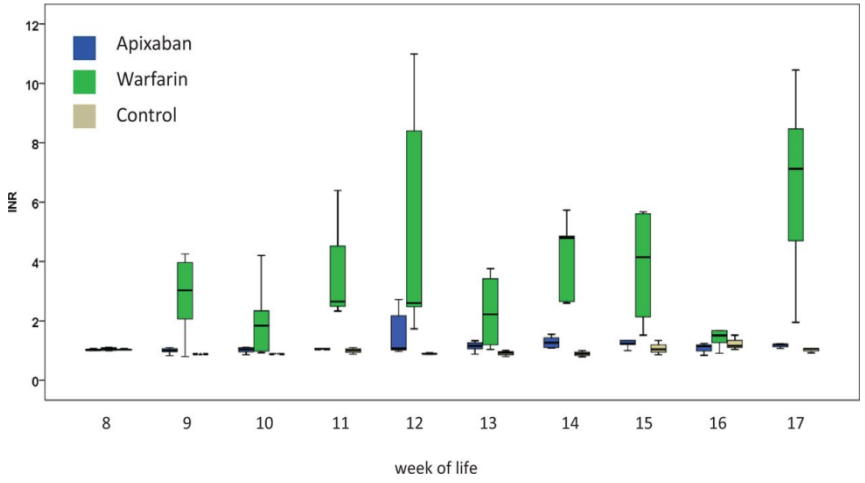
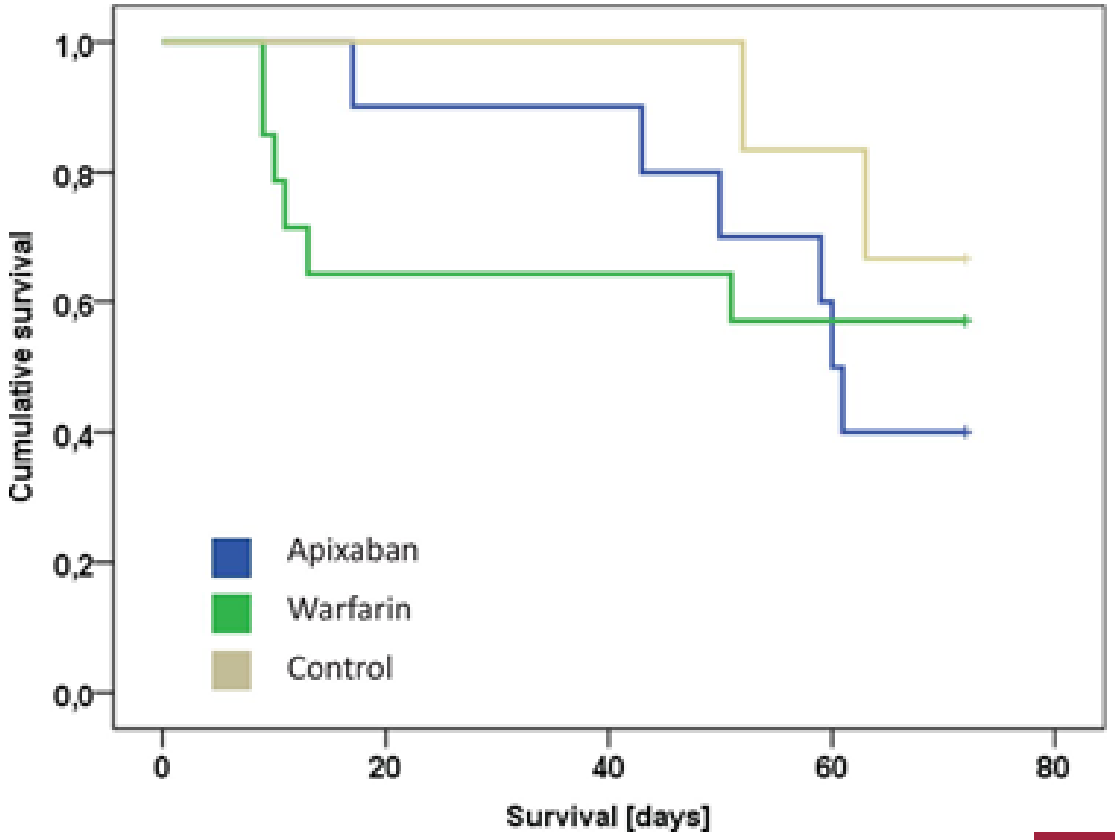


Figure 6. Kaplan–Meier curves displaying cumulative survival rates of rats anticoagulated with apixaban (blue) or warfarin (green) as well as in control animals (beige).



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ICH «SCORE»

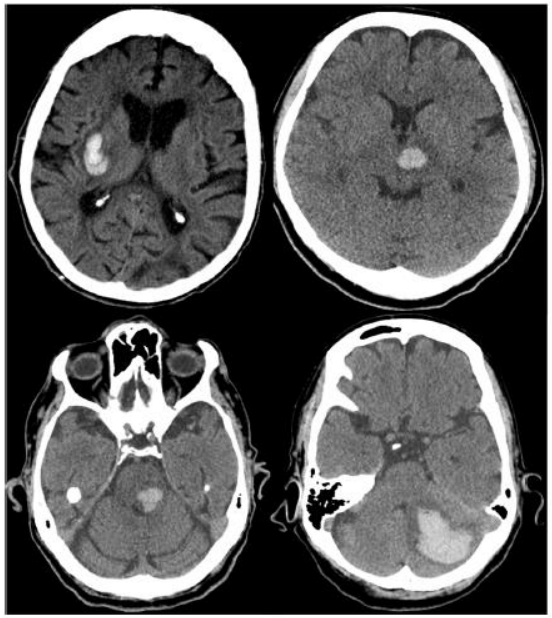


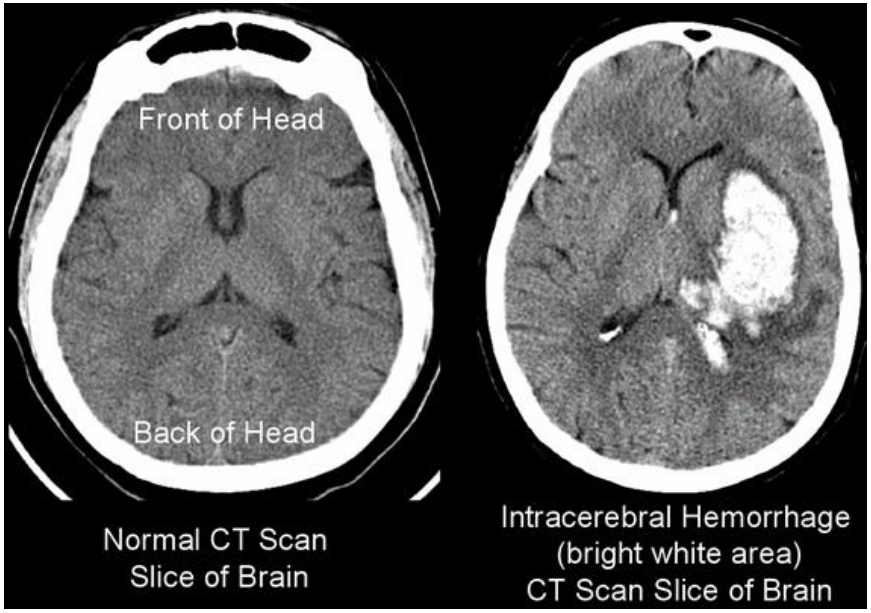
Fig. 2 Deep intracranial hemorrhage. Common locations of hypertensive hemorrhage (*clockwise*: putamen, thalamus, cerebellum, and pons)

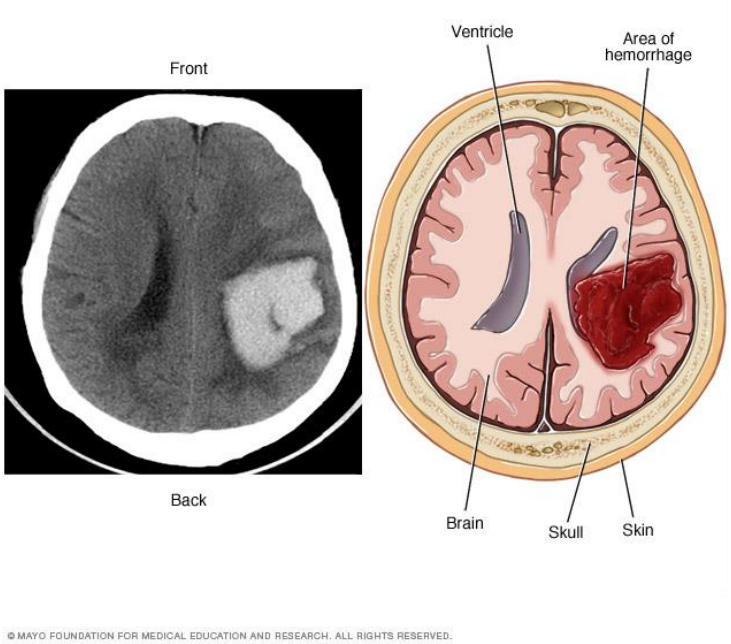
Table 1 Original ICH score and predicted 30-day mortality according to total score

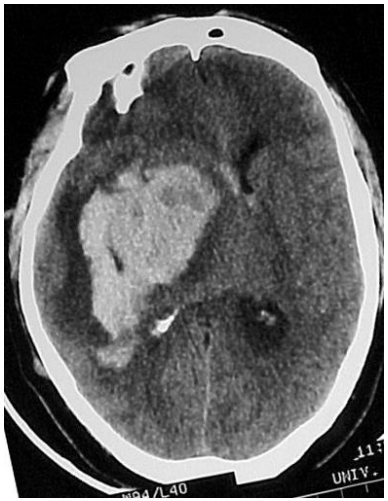
Component	Points	Total ICH score	30-day mortality (%)
Glasgow Coma Scale			
3–4	2	0	0–10
5–12	1		
13–15	0		
Age (years)			
≥80	1	1	7–13
<80	0		
ICH volume (ml)			
≥30	1	2	30–44
<30	0		
Presence of intraventricular hemorrhage			
Yes	1	3	56–78
No	0		
Infra-tentorial origin of ICH			
Yes	1	4	70–100
No	0		
Total ICH score	0–6	5–6	100

The five independent predictors of 30-day mortality according to the original ICH score are displayed in the first column (Glasgow Coma Scale, age, ICH volume, intraventricular hemorrhage, and infra-tentorial location of ICH). The total score is the sum of the five components, varying from 0 to 6 points (column 3). The higher the total score (column 3), the higher the predicted 30-day mortality (column 4)
ICH intracerebral hemorrhage

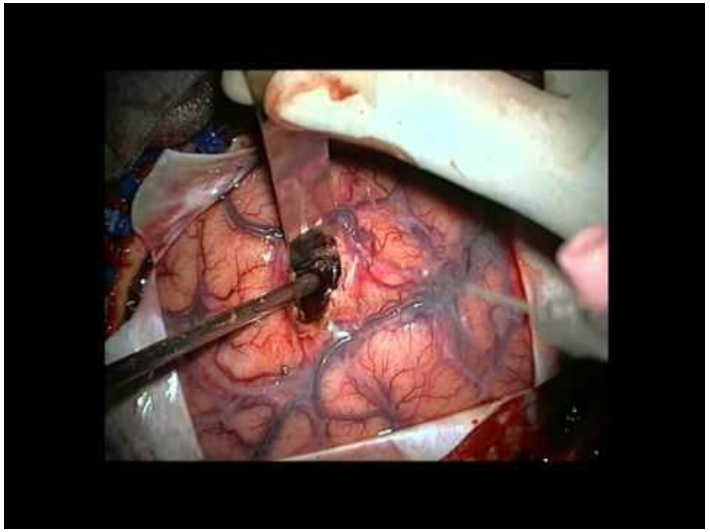
EMORRAGIA INTRAPARENCHIMALE: Come si presenta

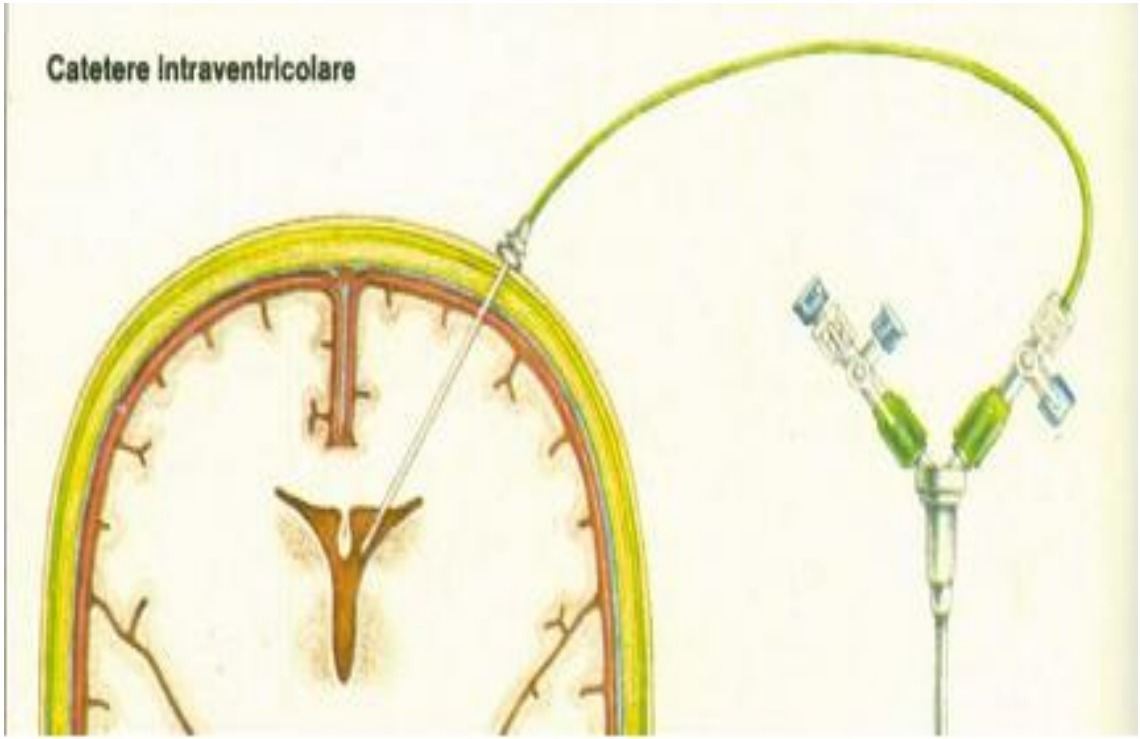






Reversal
Intervento chirurgico
DVE, Monitoraggio PIC
Monitoraggio clinico





MONITORAGGIO PIC: Catetere intraventricolare

Contrast extravasation : spot sign

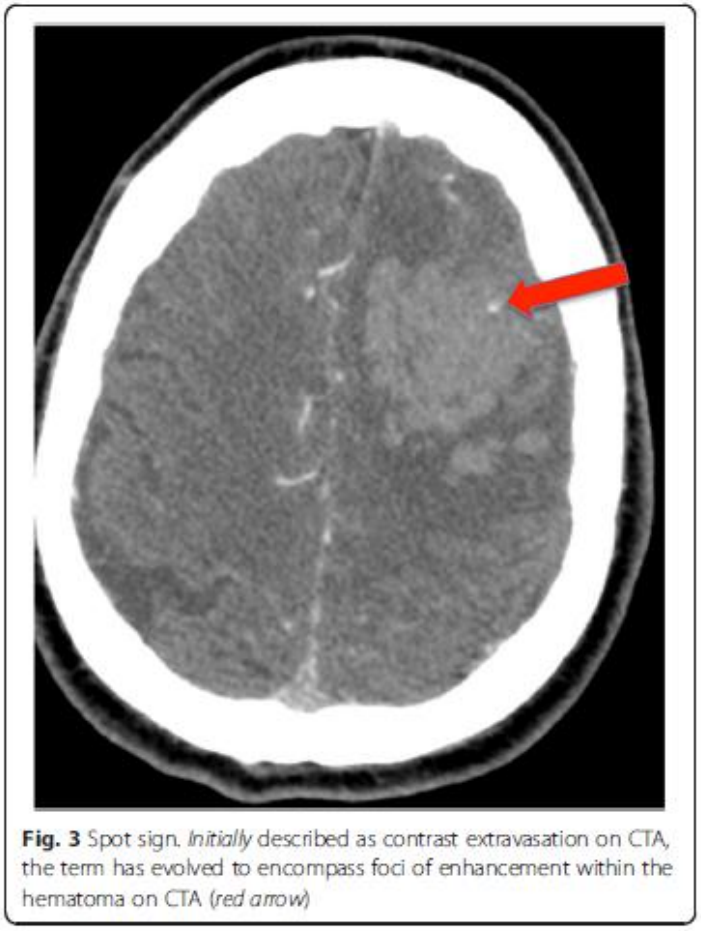


Fig. 3 Spot sign. *Initially* described as contrast extravasation on CTA, the term has evolved to encompass foci of enhancement within the hematoma on CTA (*red arrow*)

Identification of a spot sign on CT may have several clinical implications:

A. Identification of contrast extravasation and the spot sign are potent and independent predictors of hematoma expansion [60]. In the multicenter prospective "Prediction of hematoma growth and outcome in patients with ICH using the CT-angiography spot sign" (PREDICT) study [66], the presence of spot sign was associated with a relative risk of 2.3 (95 % CI 1.6–3.1) for hematoma expansion, defined as an absolute increase > 6 ml or a relative increase > 33 % from baseline ICH volume. However, identification of spot sign does not necessarily infer definite hematoma expansion. A spot sign score has been developed to help predict hematoma expansion [62]. The score includes: number of spot signs (1–2 or ≥3), maximum axial dimension (1–4 mm or ≥5 mm), and maximum attenuation in Hounsfield Units (120–179 HU or ≥180 HU). A score of 0 indicates that no spot sign was identified on CTA, and it has been associated with minimum risk of hematoma expansion (2 %). In patients with the maximum score (4 points), the risk for hematoma expansion approaches 100 % [62].

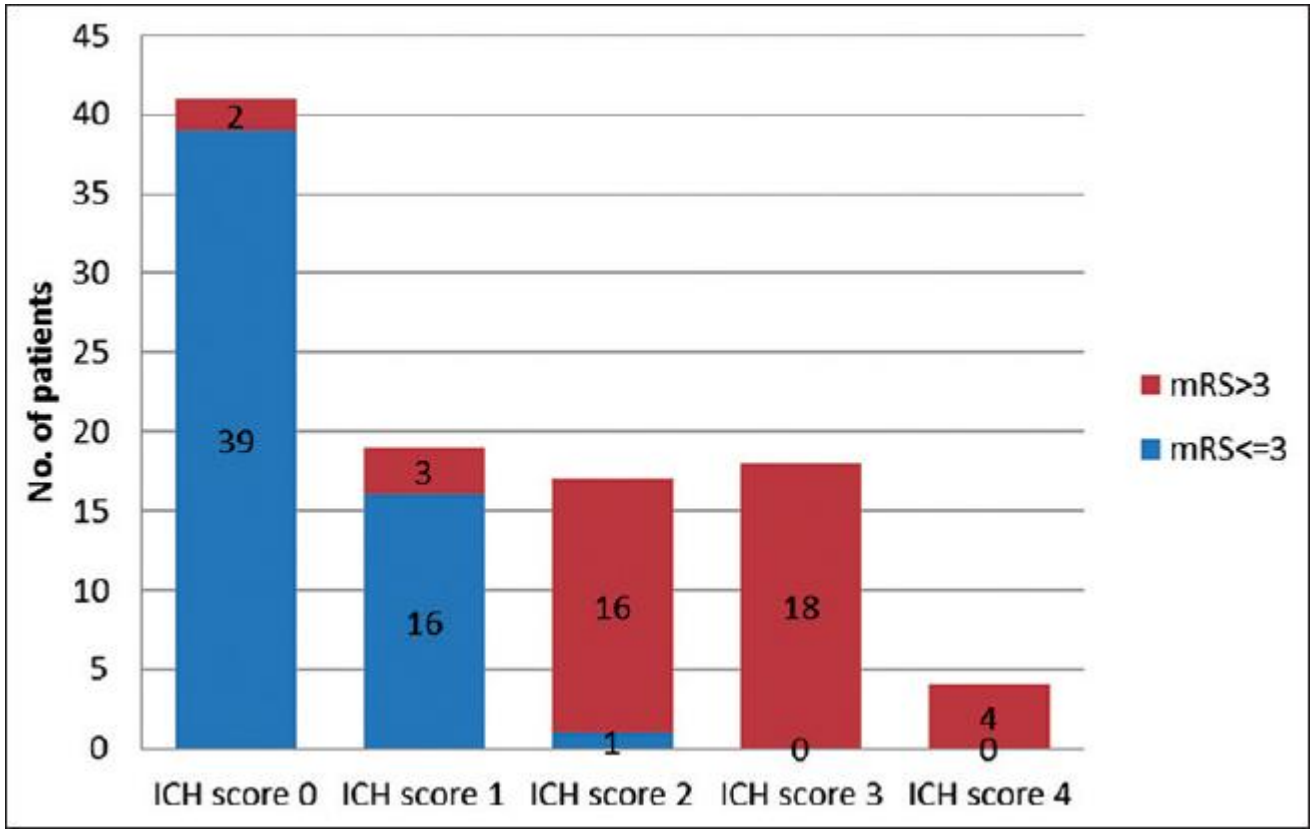
Table 2 INTERACT 2 [71] vs ATACH 2 [77] studies

	INTERACT 2 ($n = 2794$)		ATACH 2 ($n = 1000$)	
	Control	Intervention	Control	Intervention
Number of enrolled patients	1430	1399	500	500
Treatment target (SBP in mmHg)	<180	<140	140–179	110–139
Inclusion criteria	GCS > 5		ICH (volume < 60 cm^3), GCS score ≥ 5	
Primary outcome	Death or major disability (mRS = 3–6) at 3 months		Death or disability (mRS = 4–6) at 3 months	
Recruitment window	6 hours		4.5 hours	
Medications used to lower blood pressure	Urapidil: 32.5 %		Nicardipine ± labetalol	
	Nicardipine or nimodipine: 16.2 %		Intravenous diltiazem or urapidil could be used	
	Labetalol: 14.4 %			
	Nitroglycerin: 14.9 %			
	Furosemide: 12.4 %			
	Nitroprusside: 12.1 %			
	Hydralazine: 5.9 %			
Period of blood pressure intervention	7 days		24 hours	
Time goal of blood pressure lowering	1 hour		2 hours	
Mean interval between symptom onset and randomization	3.7 hours	3.7 hours	3.0 hours	3.0 hours
Systolic blood pressure at presentation (mmHg)	179 ± 17	179 ± 17	201.1 ± 26.9	200 ± 27.1
Mean systolic blood pressure achieved (mmHg)	164 within 1 hour	150 within 1 hour	141.1 ± 14.8 (2 hours)	128.9 ± 16 (2 hours)
	153 within 6 hours	139 within 6 hours		
Primary treatment failure[a] (%)	66		12.2	
Baseline hematoma volume (ml)	11	11	10.2	10.3
Asian (%)	68.0	67.7	57.0	55.4
Death or disability (%)—mRS = 3–6	55.6	52.0	56.1	56.2
Modified Rankin Scale (%)				
0	7.6	8.1	7.1	5.0
1	18.0	21.1	19.6	19.8
2	18.8	18.7	17.3	19.1
3	16.6	15.9	18.3	17.5
4	19.0	18.1	26.5	26.0
5	8.0	6.0	4.2	5.8
6	12.0	12.0	7.1	6.9

[a]Primary treatment failure was defined as target SBP < 140 mmHg not achieved within 1 hour of randomization in the intensive-treatment group in the INTERACT 2 trial or within 2 hours in the ATACH 2 trial

GCS Glasgow Coma Scale, *ICH* intracerebral hemorrhage, *mRS* modified Rankin Scale, *SBP* systolic blood pressure

Clinical outcome in relation to intracerebral hemorrhage score



Resuming anticoagulant therapy after intracerebral bleeding.

Becattini C1, Sembolini A2, Paciaroni M2.
Author information

Abstract

The clinical benefit of resuming anticoagulant treatment after an anticoagulants-associated intracranial hemorrhage (ICH) is debated. No randomized trial has been conducted on this particular clinical issue. The risk of ICH recurrence from resuming anticoagulant therapy is expected to be higher after index lobar than deep ICH and in patients with not amendable risk factors for ICH. Retrospective studies have recently shown improved survival with resumption of treatment after index anticoagulants-associated ICH. Based on these evidences and on the risk for thromboembolic events without anticoagulant treatment, resumption of anticoagulation should be considered in all patients with mechanical heart valve prosthesis and in those with amendable risk factors for anticoagulants-associated ICH. **Resumption with direct oral anticoagulants appears a reasonable option for non-valvular atrial fibrillation (NVAF) patients at moderate to high thromboembolic risk after deep ICH and for selected NVAF patients at high thromboembolic risk after lobar ICH. For VTE patients at high risk for recurrence, resumption of anticoagulation or insertion of vena cava filter should be tailored on the estimated risk for ICH recurrence.**

KEYWORDS:

Anticoagulants; Apixaban; Cerebral bleeding; Dabigatran; Intracranial hemorrhage; Rivaroxaban; Warf

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Benefits and Risks of Anticoagulation Resumption Following Traumatic Brain Injury

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Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore (Albrecht, Liu, Zuckerman); Department of Epidemiology and Public Health,

We observed an elevated risk of hemorrhagic events associated with warfarin use after TBI but a decreased risk of hemorrhagic stroke and thrombotic events. These effects did not change significantly over time, suggesting that barring strong contraindication, most patients would benefit, in terms of a reduction in the risk of stroke, from resuming warfarin therapy immediately following hospital discharge for TBI. These results are consistent with prior research conducted among patients with atrial fibrillation, suggesting that the benefits of warfarin use outweigh the risks, even among patients at high risk for falls.[32-38] Similarly, among patients who experienced an episode of warfarin-associated gastrointestinal tract bleeding, resumption of warfarin therapy has been found to decrease risk of thrombosis and death.[39]

CRITICAL CARE

REVIEW

Clinical review: Traumatic brain injury in patients receiving antiplatelet medication

Christopher Beynon*, Daniel N Hertle, Andreas W Unterberg and Oliver W Sakowitz

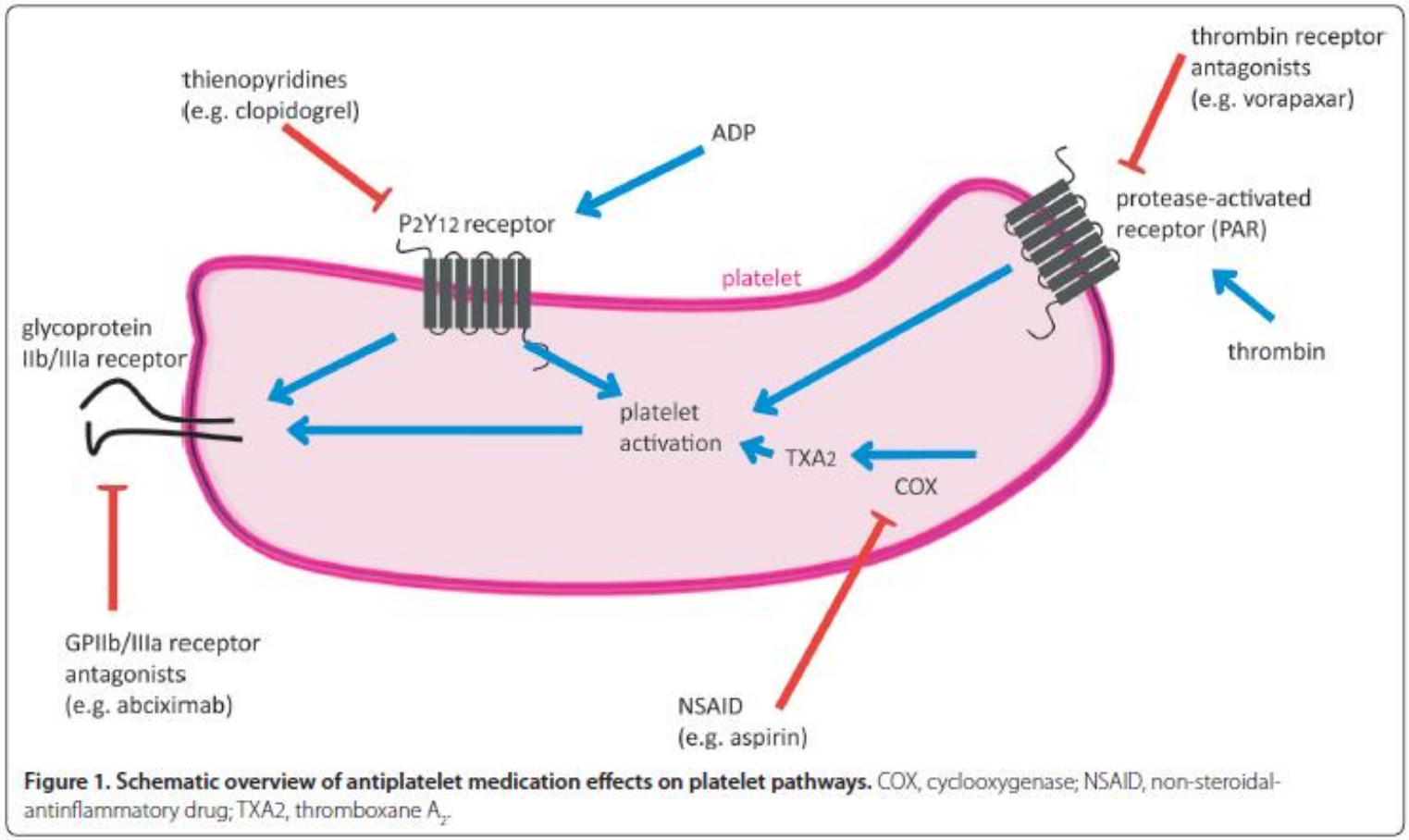

Figure 1. Schematic overview of antiplatelet medication effects on platelet pathways. COX, cyclooxygenase; NSAID, non-steroidal-antinflammatory drug; TXA2, thromboxane A_2.

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Table 1. Overview of retrospective studies on the effects of antiplatelet medication in patients with traumatic brain injury

Study	Inclusion criteria	Antiplatelet therapy	Number of subjects	Mortality rate	Major findings
Mina *et al.* 2002 [20]	Posttraumatic ICH	Aspirin	19	47% aspirin group; 8% control group	Mortality significantly increased with aspirin therapy. No difference in mortality rates between aspirin and warfarin treated patients
Spektor *et al.* 2003 [23]	Mild and moderate TBI, age >60 years	Aspirin (100 mg/day)	110	NR	Aspirin therapy had no effect on incidence of posttraumatic ICH after mild to moderate TBI
Ohm *et al.* 2005 [21]	Posttraumatic ICH	Aspirin, clopidogrel	90	23% antiplatelet group; 8% control group	Mortality threefold increased with antiplatelet therapy. GCS <12 and age >76 years risk factors for death in patients on antiplatelet therapy
Jones *et al.* 2006 [24]	All TBI, age >50 years	Clopidogrel	43	7% clopidogrel group	Clopidogrel-treated patients have higher rates of cranial surgery and episodes of rebleeds. More blood products were transfused in clopidogrel-treated patients
Wong *et al.* 2008 [25]	All TBI	Aspirin, clopidogrel	111	14% clopidogrel group; 3% aspirin group	Clopidogrel-treated patients were more likely to be discharged to long-term inpatient facilities
Major *et al.* 2009 [22]	All TBI	Aspirin, clopidogrel	287	1.4% aspirin group	Mortality rate 21% in patients on aspirin with posttraumatic ICH. Three of the four patients who died in the aspirin group deteriorated with a significant delay
Bonville *et al.* 2011 [26]	All TBI	Aspirin, clopidogrel	271	12.3% aspirin group; 9.3% clopidogrel group	Use of antiplatelet agents did not affect mortality or length of hospital stay

GCS, Glasgow Coma Scale; ICH, intracranial haemorrhage; TBI, traumatic brain injury.

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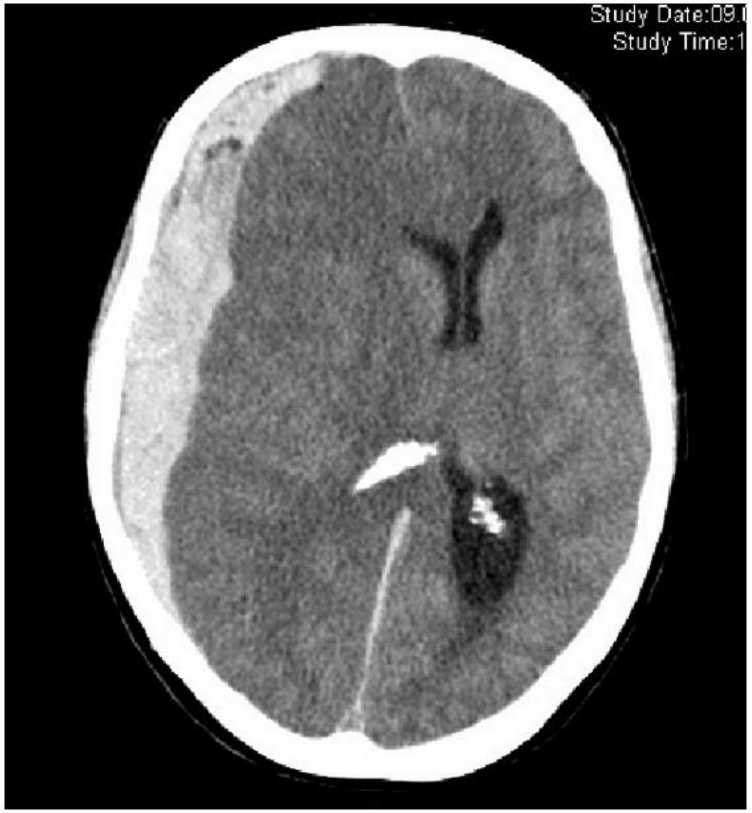
Conclusion

The use of antiplatelet agents in patients will increase as the population ages and because cardiovascular diseases have one of the highest incidence rates of all diseases in industrialized countries. TBI plays a major economic role in society since survivors often suffer serious neurologic sequelae resulting in high dependency. Available data from studies suggest that the pre-injury use of antiplatelet agents yields risks for TBI patients that may lead to an unfavourable outcome. Options to (partially) restore platelet activity include transfusion of platelets and application of haemostatic drugs such as desmopressin, TXA and FVIIa. Guidelines regarding their use are missing since these agents have not been subject to controlled trials in TBI so far. Withdrawal of antiplatelet agents may carry high risks for patients, so treatment has to consider comorbidities and an interdisciplinary approach should be chosen. Further trials are needed to characterise the impact of pre-injury antiplatelet therapy on TBI victims and to establish protocols optimizing treatment modalities for those patients.

CASO CLINICO -1



Paziente ,sesso maschile , 42 aa in trattamento con warfarin per FA cronica,
Pugile, allenamento in palestra e trauma con ematoma subdurale dx ed emorragia del tronco, anisocoria dx>sn effettua CT-encefalo, esami di laboratorio ed intervento di asportazione di ematoma subdurale muore 48 h dopo il ricovero

CASO CLINICO -1

Fondazione
CASA SOLLIEVO DELLA SOFFERENZA
Opera di San Pio da Pietrelcina
OSPEDALE
Istituto di Ricovero e Cura a Carattere Scientifico
San Giovanni Rotondo

VERBALE OPERATORIO

UNITA' OPERATIVA **RIANIMAZIONE 1 UOMINI**

SALA OPERATORIA **SALA NCH C** *NOSOGRAFICO* **2015 38210**

Cognome Nome: **DEL VECCHIO CIRO** Data di nascita: **05/12/1974**
Luogo nascita: **SAN SEVERO**

Diagnosi preoperatoria: **FALDA SOTTODURALE A DESTRA CENTIMETRICA, RIGONFIAMENTO CEREBRALE EMISFERICO DESTRO, EMORRAGIA DEL TRONCO DELL' ENCEFALICO**

SPECIALITA' CHIRURGICA **NEUROCHIRURGIA** *NR° VERBALE* **773**

Data intervento: **22/09/2015** Ora inizio anestesia: **0.01** Ora fine anestesia: **0.30**

Tipo Anestesia: **GENERALE - TIVA**

1° Anestesista: **MANUALI ALDO** 2° Anestesista:

Ora posizionamento: **0.05**

Ora inizio intervento **0.06** Ora fine intervento **0.25**

1° Operatore: **SAVARESE LUCIANO** 2° Operatore:
3° Operatore: 4° Operatore:

1° Strumentista: **PETRUCCELLI DANIELA** 2° Strumentista:
3° Strumentista:

DESCRIZIONE INTERVENTO - PROCEDURA
CRANIOSTOMIA.

DESCRIZIONE ATTO OPERATORIO
INCISIONE LINEARE PARIETALE DESTRA. DIVARICAZIONE. EMOSTASI DIFFICOLTOSA. DIVARICAZIONE. FORO DI TRAPANO. COAGULAZIONE DURALE ED INCISIONE. FUORIUSCITA DI UN FIOTTO EMATICO FRANCAMENTE IPERTESO. ENCEFALO A PARETE. SINTESI A STRATI.

Firma primo operatore
SAVARESE LUCIANO

OSPEDALE "CASA SOLLIEVO DELLA SOFFERENZA"
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO
San Giovanni Rotondo (FG)
SERVIZIO DI MEDICINA TRASFUSIONALE E DI LABORATORIO ANALISI
Direttore: dott. Lazzaro di Mauro
Segreteria - Tel. 0882410229 Fax 0882457769

Data di Produzione Referto: 22/09/2015 Ore: 11:08 Pag.: 1 / 1

Id. Paziente: 80199828 Sesso: M Routine Sig. **DEL VECCHIO CIRO**
Età: 40 Anni Data Nascita: 05/12/1974
Richiedente: 630 Rianimaz.1
Richiesta: **80803905** del **22/09/2015 08:00**

Esame	*Risultato*	*U.d.M.*	*Valori Riferimento*
PT (T.di Protrombina)			
Attivita'	**35** <	%	70 - 130
INR	**2.19** >	*Ratio*	0.80 - 1.20
PTT (T.Trombopl.Parziale)			
Tempo	**35.9**	*sec*	25.0 - 38.0
Rapporto	**1.10**	*Ratio*	0.80 - 1.20
ANTITROMBINA	**115**	*% nhp*	75 - 120
FIBRINOGENO	**355**	*mg/dl*	150 - 400
DIMERO-D	**3405.00** >	*ng/ml*	0.00 - 250.00

Motivi della richiesta:DONATORI DI ORGANI

Referto Parziale id 13714474 firmato digitalmente. ANTONIO FERNANDO SAVINO 22/09/2015 Ore: 11:35

Segreteria - Tel. 0882410229 Fax 0882457769

Data di Produzione Referto: 25/09/2015 Ore: 21:16 Pag.: 1 / 1

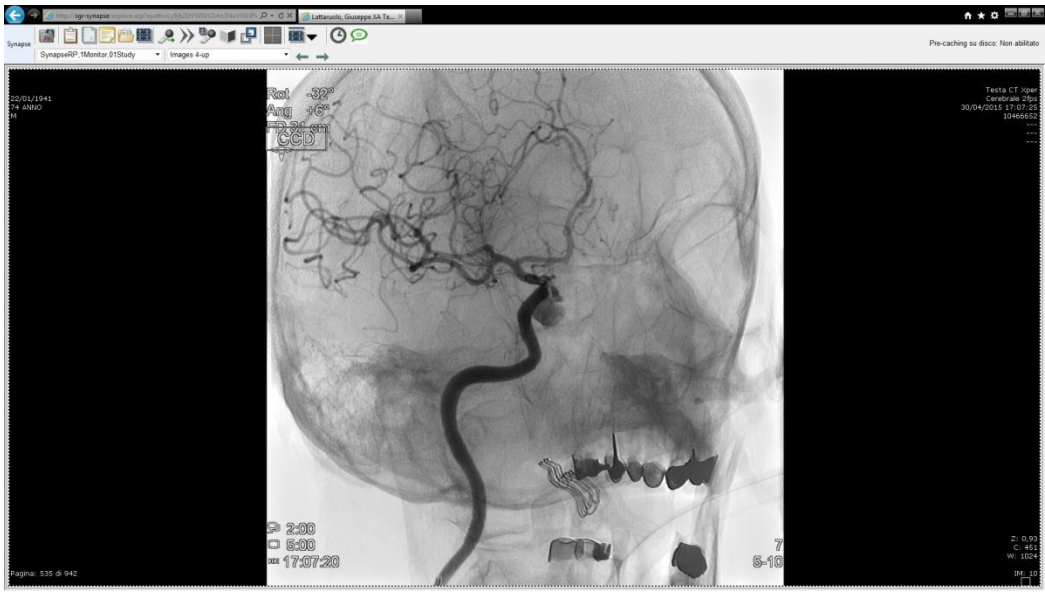
Id. Paziente: 80199828 Sesso: M Urgenza Sig. **DEL VECCHIO CIRO**
Età: 40 Anni Data Nascita: 05/12/1974
Richiedente: 630 Rianimaz.1
Richiesta: **80806423** del **25/09/2015 21:12**

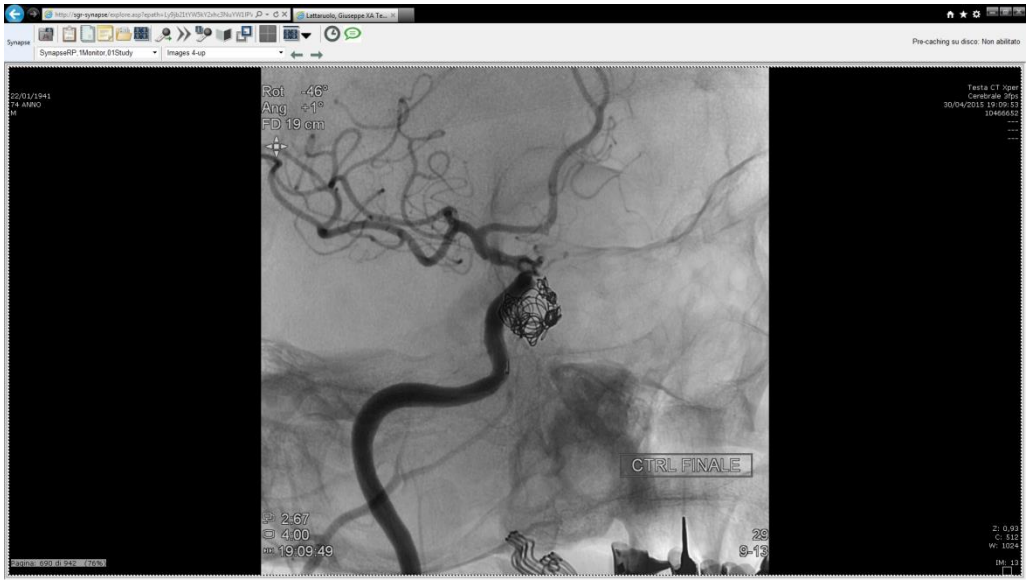
Esame	*Risultato*	*U.d.M.*	*Valori Riferimento*
DIMERO-D	**35539.00** >	*ng/ml*	0.00 - 250.00

Referto Completo id 13727964 firmato digitalmente. ANTONIO LONGO 25/09/2015 Ore: 21:20

CASO CLINICO -2

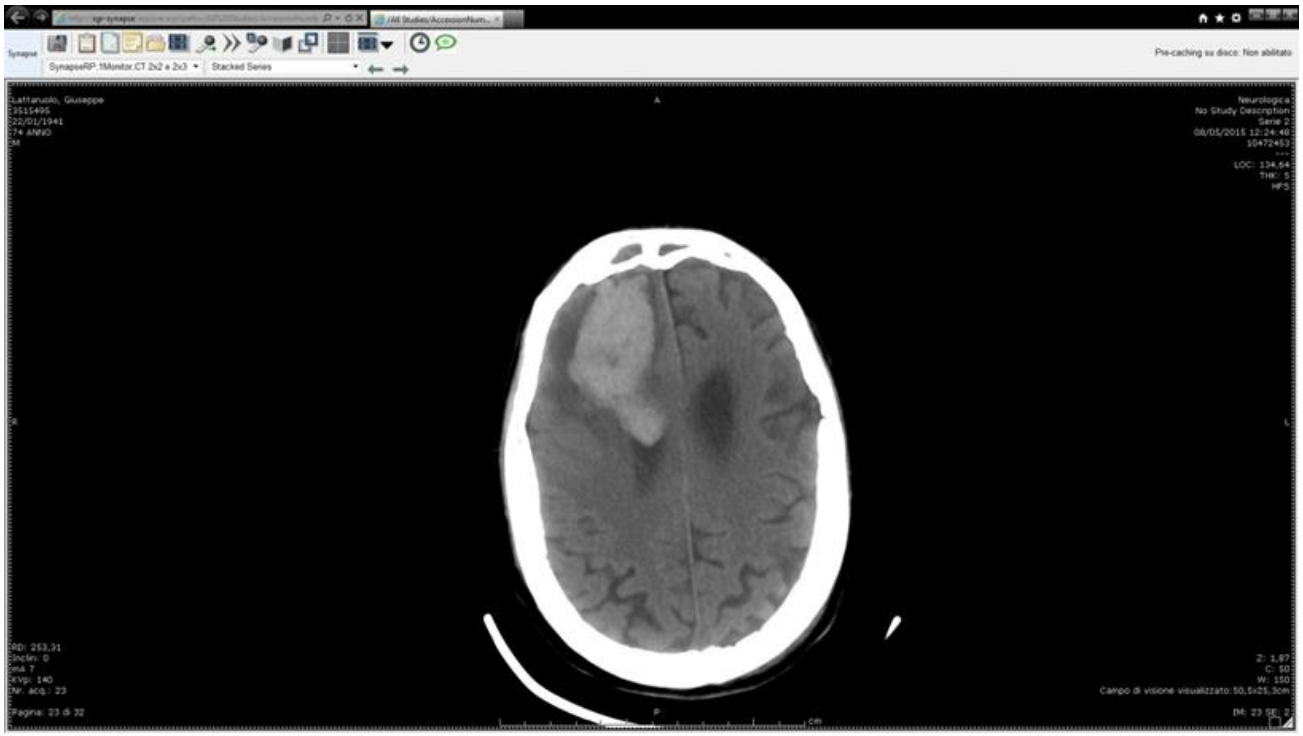
Man 74 years old diagnosis of hypophyseal adenoma, surgical treatment by nose with carotid lesion and pseudoaneurysm, treatment with coils and two stents. At the end of procedure patient in good conditions is admitted in NICU with this therapy: Clopidogel 150 mg x2 and acetylsalicylic acid 100 mg /die and herparin 0.4 sc die for two days and clopidogel 75 mg x2 and acetylsalicylic acid 100 mg/die and heparin for a long period.



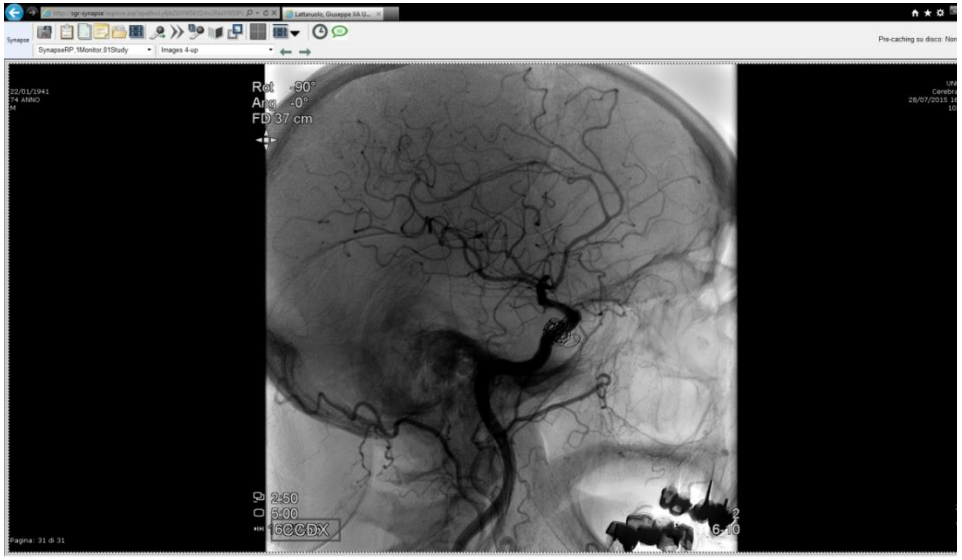


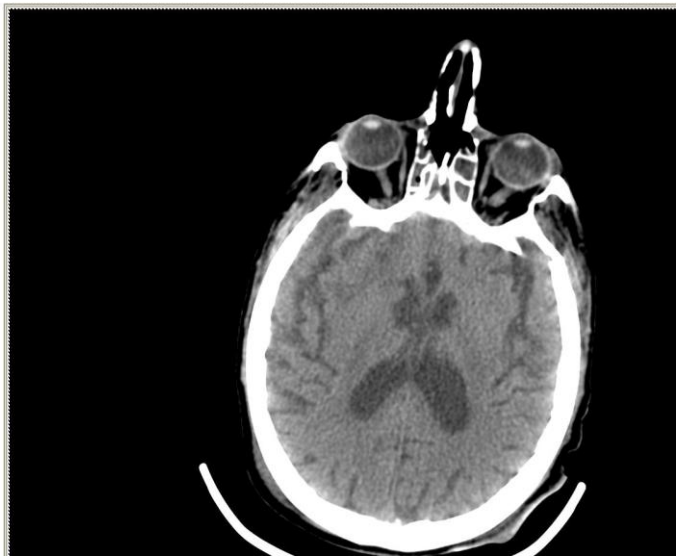
CASO CLINICO -2

Two days after this treatment important intraparenchimal haemorragya and revision of therapy and sospension of the anticoagulant therapy. After 30 days new administration of heparn one dose (0.4/die) with resolution of the clinic state



CASO CLINICO -2





These are angiography and CT-scanner at the end of july: the stents are working very well, the patient is awake without deficits

de Oliveira Manoel et al. Critical Care (2016) 20:272
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REVIEW Open Access

The critical care management of spontaneous intracranial hemorrhage: a contemporary review

Airton Leonardo de Oliveira Manoel[1,2,3*], Alberto Goffi[4,5], Fernando Godinho Zampieri[6,7], David Turkel-Parrella[1], Abhijit Duggal[8,9], Thomas R. Marotta[1], R. Loch Macdonald[10] and Simon Abrahamson[2,11]

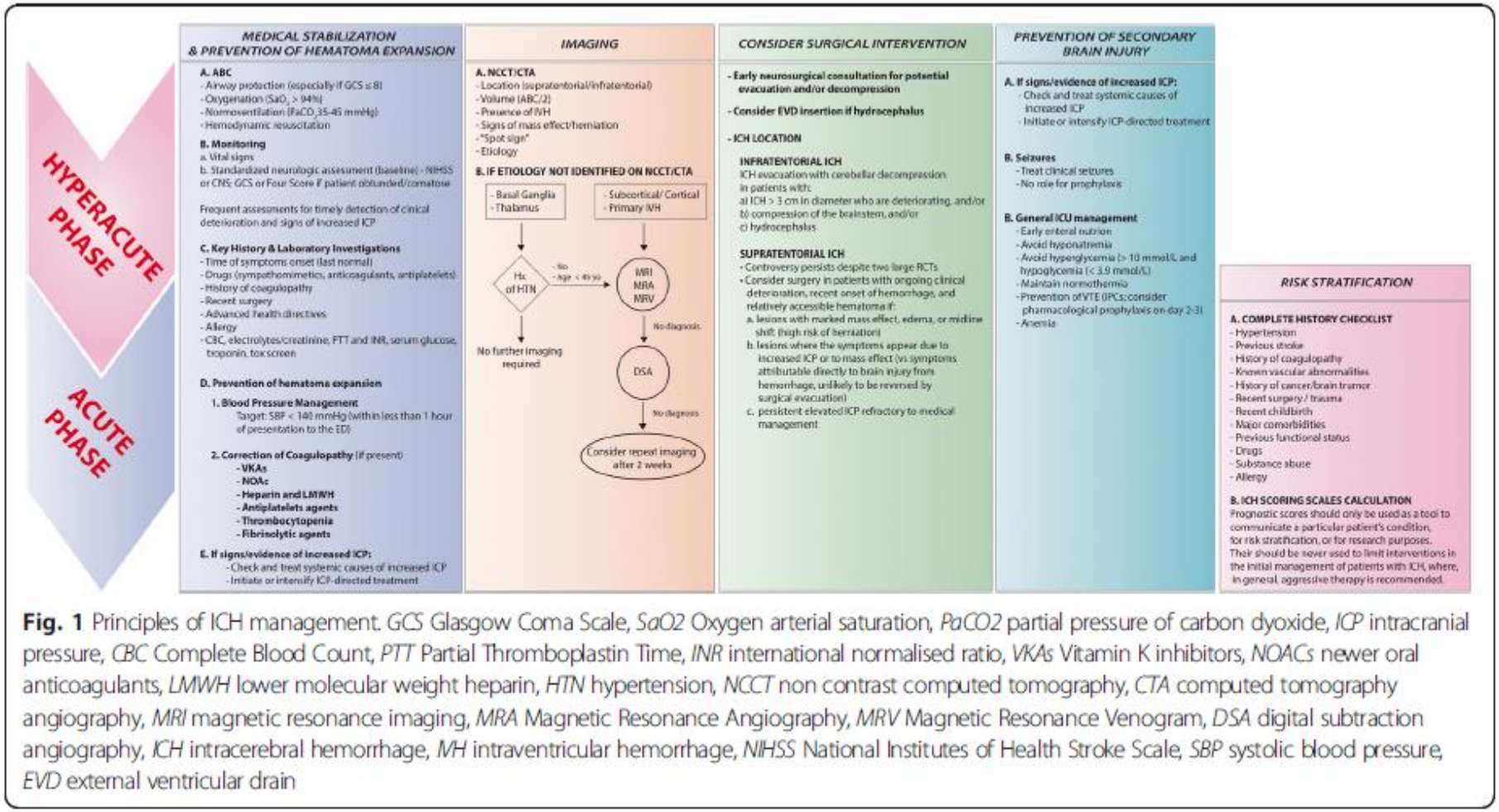
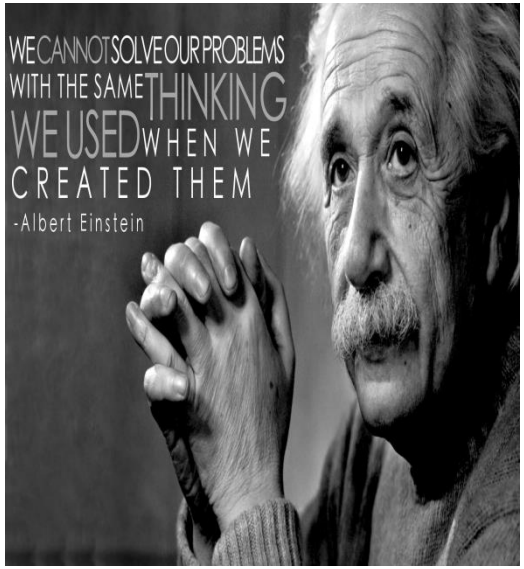


Fig. 1 Principles of ICH management. *GCS* Glasgow Coma Scale, *SaO2* Oxygen arterial saturation, *PaCO2* partial pressure of carbon dyoxide, *ICP* intracranial pressure, *CBC* Complete Blood Count, *PTT* Partial Thromboplastin Time, *INR* international normalised ratio, *VKAs* Vitamin K inhibitors, *NOACs* newer oral anticoagulants, *LMWH* lower molecular weight heparin, *HTN* hypertension, *NCCT* non contrast computed tomography, *CTA* computed tomography angiography, *MRI* magnetic resonance imaging, *MRA* Magnetic Resonance Angiography, *MRV* Magnetic Resonance Venogram, *DSA* digital subtraction angiography, *ICH* intracerebral hemorrhage, *MH* intraventricular hemorrhage, *NIHSS* National Institutes of Health Stroke Scale, *SBP* systolic blood pressure, *EVD* external ventricular drain



1. La coagulopatia traumatica acuta (ACT) di per se è una delle maggiori complicanze del trauma cranico è evidentemente più importante in pazienti scoagulati
2. Probabilmente i meccanismi che portano alla emorragia cerebrale sono legati in parte al consumo ed in parte alla fibrinolisi attivata
3. Gli indicatori biologici più efficaci della ACT sono DD>INR>PT>FG>PLT
4. L'uso delle soluzioni ipertoniche può incrementare ipocoagulabilità e iperfibrinolisi
5. L'utilizzo di anticoagulanti peggiora l'outcome del trauma cranico minore
6. L'emorragia intracerebrale nel soggetto iperteso è nettamente più frequente nei pazienti in trattamento anticoagulante
7. Gli indicatori biologici variano sulla base del tipo di farmaco utilizzato
8. La trasfusione di 4F-PCC, PFC, piastrine, desmopressina, tromboxano e Fattore VIIIa sembrano essere al momento le opzioni terapeutiche di scelta, sulla base del farmaco utilizzato
9. Secondo i più il trattamento anticoagulante va ripreso dopo la dimissione dall'ospedale in tutte le patologie cerebrali esaminate
10. La terapia va sartorializzata ogni paziente è diverso dall'altro