

Do platelet transfusions reduce neurosurgical traumatic bleeding in patients on anti-platelet agents?

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Objectives

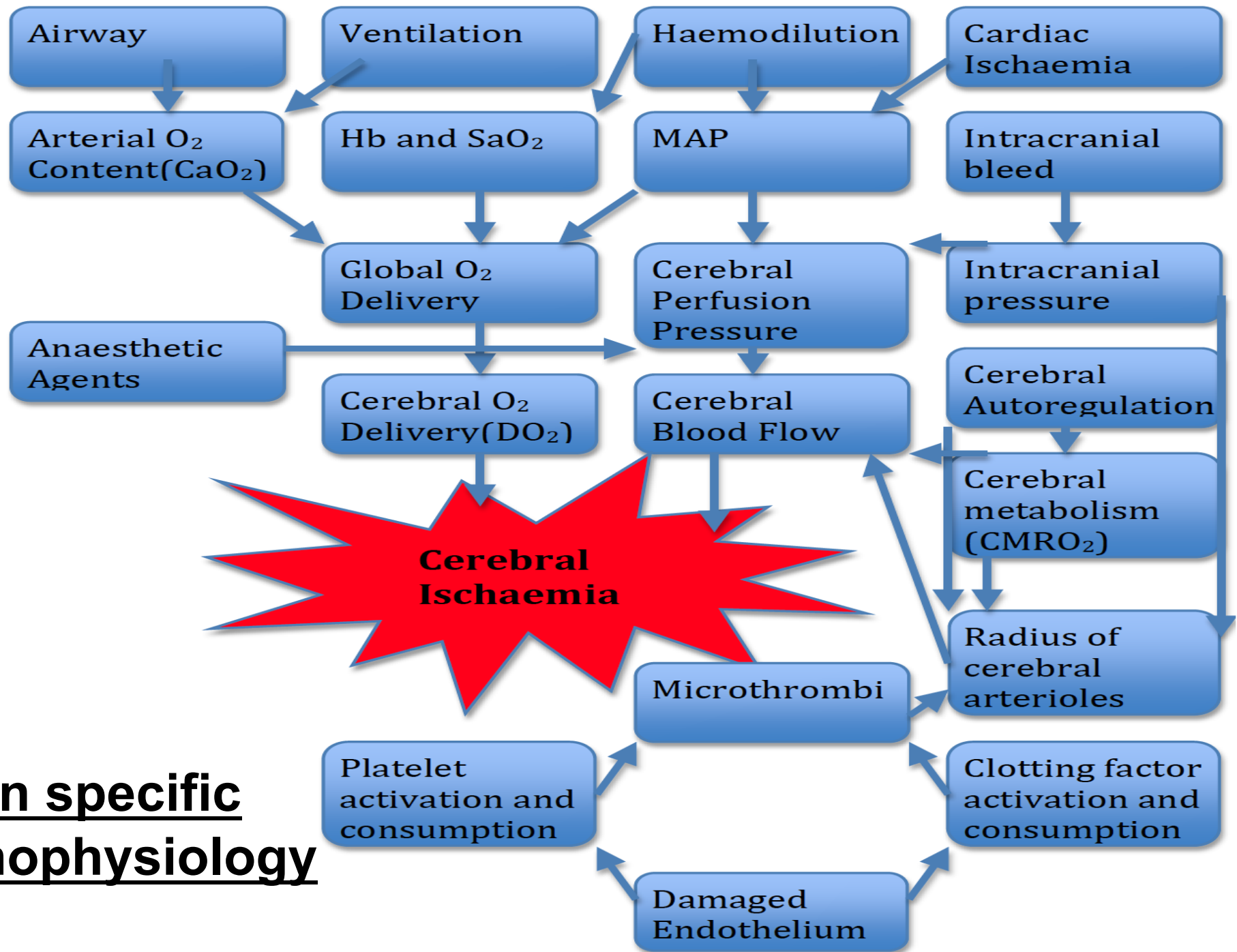
- Importance of platelets in TBI
- Who is on antiplatelets and why
- Current transfusion guidelines
- Evidence for platelet transfusion for TBI patients on antiplatelets
- Problems with the evidence
- Results of national audit of practice

Why is platelet management important in Traumatic Brain Injury?

- Leading cause of mortality < 45 year olds
- Fall trauma leading cause of mortality in >75 year olds and group most likely to be on antiplatelets
- Older age and haemorrhage expansion are individually predictors of unfavourable outcome in TBI
- More than half of TBI patients will have expansion of bleed within 24 hours

Why is platelet management important for neurosurgical trauma?

- 25% thrombocytopenic on admission
- 50% thrombocytopenic during ITU stay
- 42% of patients who could give no history had aspirin induced platelet inhibition
- Platelet count $\leq 100 \times 10^9/L$ increases adjusted risk of death 9 fold
- Blood safety profile



Antiplatelets

Who is on them?

People with a history of the following:

- Myocardial Infarction
- Coronary Heart Disease
- Non-haemorrhagic Stroke, TIAs
- Atrial Fibrillation with a CHADS2 score of 1
- Peripheral Arterial Disease

People who cannot give a history:

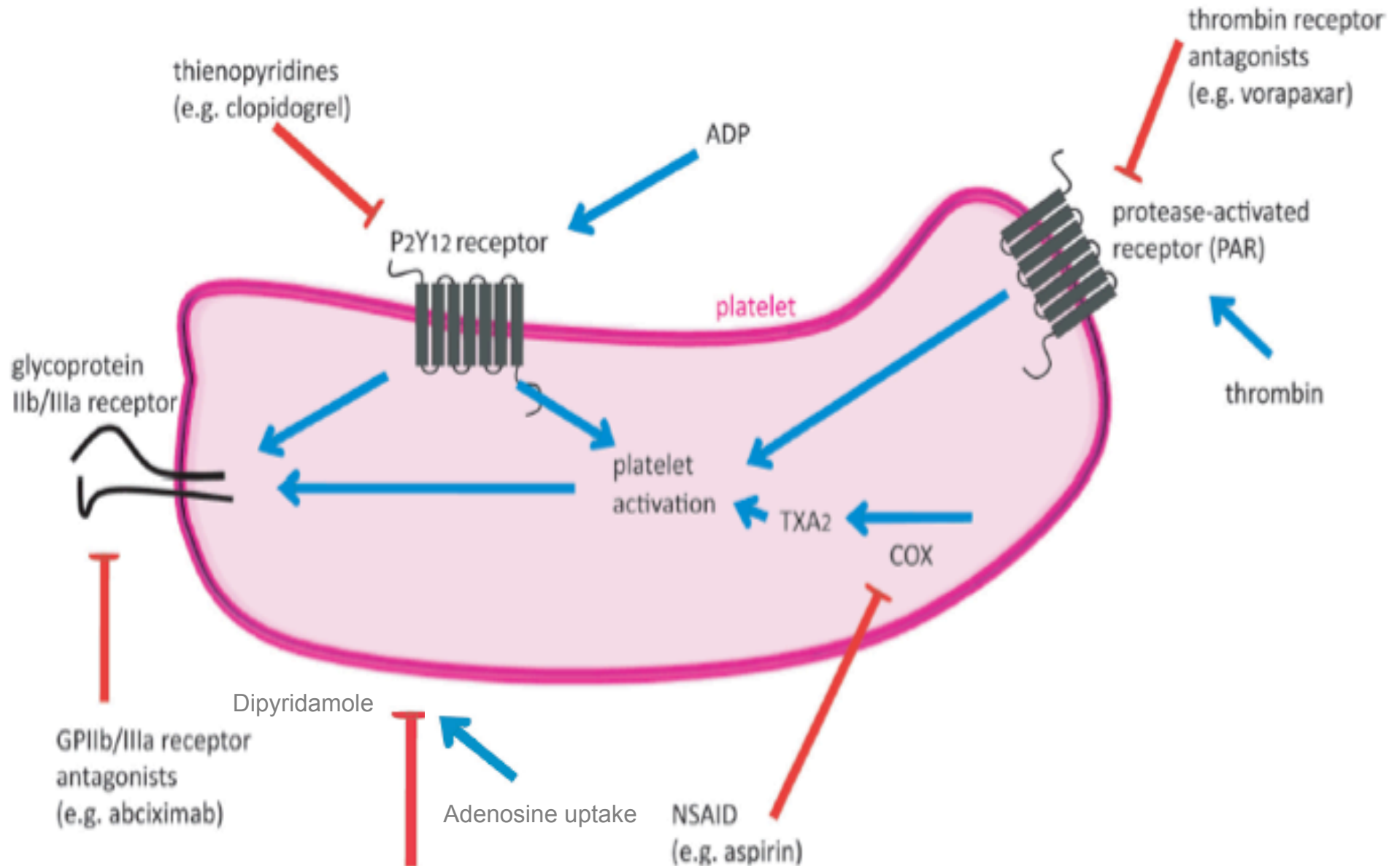
- High risk: elderly, murmur, signs of PVD, AF on ECG
- Medium risk: >40, obesity
- Low risk: <40

Antiplatelets

- Aspirin
- Thienopyridines/ P2Y₁₂ antagonists
- Dipyridamole
- Glycoprotein IIb/IIIa inhibitors
- Protease activated receptor (PAR)/ thrombin antagonists

How do they work?

Activated platelets initiate & worsen atherosclerosis



Guideline

GUIDELINES FOR THE USE OF PLATELET TRANSFUSIONS

Spahn *et al. Critical Care* 2013, 17:R76
<http://ccforum.com/content/17/2/R76>



RESEARCH

Open Access

Management of bleeding and coagulopathy following major trauma: an updated European guideline

bjh guideline

Guideline on the management of bleeding in patients on antithrombotic agents

Mike Makris,^{1,2} Joost J. Van Veen,² Campbell R. Tait,³ Andrew D. Mumford⁴ and Mike Laffan⁵ on behalf of the British Committee for Standards in Haematology

Standards and Guidelines

For platelet transfusion in TBI:

- Transfuse if $\text{Plts} \leq 100 \times 10^9/\text{L}$ (Grade 2C)
- Transfuse if $\text{Plts} > 100 \times 10^9/\text{L}$ and have had an anti-platelet (Grade 2C)
- Measure platelet function if anti-platelets have been given (Grade 2C)
- Transfuse if platelet dysfunction and continued bleeding (Grade 2C)

Standards and Guidelines

For platelet transfusion in TBI:

- Consider withdrawal of antiplatelets as MDT (Grade 1C)
- Platelet transfusion of 2-3 adult doses to reverse critical bleeding, or for emergency surgery (Grade 2C)

Evidence for platelet transfusion for TBI and antiplatelets

- Rationale: platelet transfusion delivers platelets with normal enzymatic activity to allow activation and aggregation
- 7 studies

Study	Design	No	Antiplatelets	Transfusion	Outcomes
Ohm et al, 2005	Retro, 1 centre, 4 yrs	90	50 aspirin 12 clopidogrel 20 both 6 warfarin, aspirin 2 warfarin, clopidogrel	Physician discretion	Mortality 47.6% v 20.2% p=0.013
Ivascu et al, 2008	Retro, 1 centre, 5 yrs	109	61 aspirin 17 clopidogrel 31 both	Physician discretion	Mortality 27.5% v 13% p=0.064
Fortuna et al, 2008	Retro, 1 centre, 2.5 yrs	126	91 aspirin 17 clopidogrel 18 both 29 warfarin 11 other	Physician discretion	Mortality 30.3% v 16% p=NS
Downey et al, 2009	Retro, 2 centres, 4 yrs	166	Aspirin Clopidogrel Both 89% also on warfarin	1 centre used PFA 100	Mortality 17.5 % v 16.7% p=0.85
Washington et al, 2011	Retro, 1 centre, 2 yrs	108	Aspirin Clopidogrel Both	Physician discretion	Mortality 5% v 0% p=NS
Bachelani et al, 2011	Retro, 1 centre, 2 yrs	36 or 54	Aspirin	ART Verifynow	Mortality responders v non p=NS
Joseph et al, 2013	Prosp, 1 centre	28	Aspirin	All, protocol	Mortality responders 0% v non 5% p=0.5

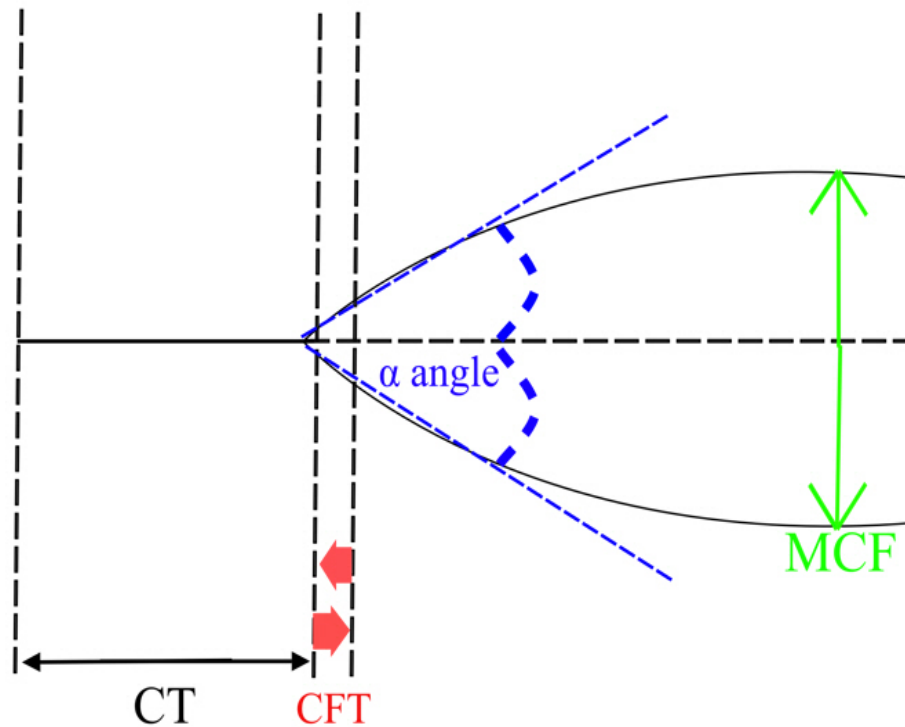
Problems with evidence

- Small, retrospective, secondary data sets
- History as measure of antiplatelet use

Point of care platelet function measurement

Problems for TEG and ROTEM:

- Dilution and thrombocytopaenia
- Platelet dysfunction



Problems with evidence

- Inclusion, or exclusion, of posterior fossa hemorrhages
- Polytrauma v Isolated Head Injury
- Lack of control for confounders (warfarin)
- Different timings of imaging
- Outcome measures of $>33\%$ *versus* any measurable volume increase
- Mortality bias, more severe TBI excluded
- Reporting of transfusion related morbidity

Measurement of TBI outcomes

Which measure is significant?

- Clinical –neurological status, haemodynamic status
- Imaging – CT, MRI – scoring systems
- Impairment of surgery
- Patient orientated rather than pathology orientated outcomes – GOS, mRS

Modified Rankin Scale	Description
0	No symptoms
1	No disability
2	Mild disability
3	Moderate-severe disability and independent with a device
4	Not independent
5	Bed bound
6	Dead

Other options

- Desmopressin reduces bleeding in healthy volunteers on aspirin
- Recombinant Factor VIIa reverses thrombin generation inhibition, but not recommended
- Tranexamic Acid – CRASH 3

What is current practice?

National Comparative Audit of the use of blood components in Neurocritical Care Units in the United Kingdom

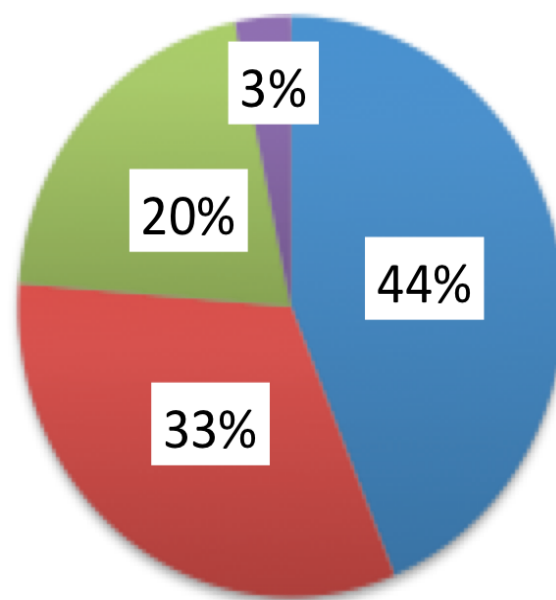
- TBI, SAH, ICH, Stroke
- All blood products
- 2013



Map of trusts that
undertook the audit

Demographics

N= 274



- TBI 120
- SAH 89
- ICH 56
- Stroke 9

Demographics	This Audit	RAIN	CRASH	CRASH2
n	120	2975	2482 (high income countries)	256
Age	Median 49 (32-62)	Median 44 (28-59)	Mean 40.6 (19.4)	Mean 37 (13.7)
% Male	70	76.1	78.9	85.4
% Extracranial Injury	66	41	22.5	
% Alcohol Intoxication	42	45		
% Unfavourable outcome	53 (end of audit)	44 (6 months)	38.5 (14 days)	
% Death	20 (at the end of audit)	18.4 (6 months)	16 (14 days)	
CT Findings				
% Traumatic SAH	68%	56%	26.4%	52%
% Obliteration of 3rd ventricle, or basal cisterns	17.5%	25.7%	9.6%	
% Midline shift >5mm	33%	31.5%	11.1%	22%
% Evacuation of haematoma	64%	34.3%	7.9%	22.3%
% Petechial haemorrhages	27%		28.7%	

TBI Demographics

Laboratory markers

	First Laboratory blood results in NCCU	Last Laboratory blood results in NCCU
Hours from event to blood results*	8.0 (4.5-13.0) hours N=222	102 (82-114) hours N=226
PT above site threshold	20% (51/249)	24% (52/215)
APTT above site threshold	6% (14/235)	14% (30/210)
Clauss Fib below site threshold	16% (16/102)	6% (5/78)
Hb below site threshold	45% (120/266)	82% (211/258)
Platelets below site threshold	17% (45/265)	27% (69/259)
WCC above site threshold	64% (168/264)	43% (112/259)

*Median (IQR) stated, WCC = White Cell Count

Antiplatelet Use

- 24 Aspirin
- 1 Dipyridamole
- 2 Aspirin, Clopidogrel
- 2 Aspirin, Dipyridamole
- 1 Aspirin, Clopidogrel, Warfarin
- Lack of history and platelet function testing

24 hours before NCCU

- 50 episodes of blood product transfusion were recorded
- Platelets given equally as often as red cells
- Big variation in ratio practice



On Neurocritical Care Units

- 88 transfusion episodes recorded
- 27% single product, platelets
- 44% for prophylaxis of bleeding

Platelet Transfusions

Pathology	Number of patients with Plts $<50 \times 10^9/L$ transfused	Number of patients with Plts $\geq 50 \times 10^9/L < 100 \times 10^9/L$ transfused	Number of patients with Plts $> 100 \times 10^9/L$ transfused
TBI	4	17	3
SAH	0	2	3
ICH	0	3	2
Stroke	0	0	1

Mortality and transfusion

- 28% (24/85) of those on antiplatelets were transfused v 20% (32/162) not on antiplatelets $p=NS$
- 21% (7/33) on antiplatelets died v 15% (12/78) not on antiplatelets $p=NS$
- 24% (10/42) of transfused died v 18% (14/78) not transfused $p=0.48$

Other Findings

- Half of the units that responded had access to ROTEM or TEG (6/12)
- Tranexamic acid was recorded as given in 16 of the 120 TBI cases
- 26% of the sample were prescribed an anticoagulant in the first 5 days of admission
- Patients not prescribed thromboprophylaxis had significantly higher % death ($p < 0.001$)

So what should we do?

Basis for clinical practice	Marker	Measuring Device	Unit of measurement
Evidence	Randomised controlled trial	Meta-analysis	Odds ratio
Eminence	Radiance of white hair	Luminometer	Optical density
Vehemence	Level of stridency	Audiometer	Decibels
Eloquence	Smoothness of tongue	Teflometer	Adhesin score
Providence	Level of religious fervour	Sextant to measure angle of genuflexion	International units of piety
Diffidence	Level of gloom	Nihilometer	Sighs
Nervousness	Litigation phobia level	Every conceivable test	Bank balance
Confidence *	Bravado	Sweat test	Sweat

Isaacs D and Fitzgerald D. Seven alternatives to evidence based medicine. BMJ 1999; 319:618.

Conclusions

- Platelet transfusion for TBI patients on antiplatelets is of uncertain value
- We are following current guidelines for platelet transfusion
- Need access to and training on POC PFA
- Need for large prospective work specific to TBI patients on antiplatelets
- Longterm outcomes

Declaration of Interests

- CSL Behring Funding for the Intensive Care Study of Coagulopathy 2 (ISOC2)

We are one profession
We stand together

