



This is a repository copy of *Survey evaluating clinical equipoise around platelet transfusion after head injury and traumatic intracranial haemorrhage (ICH) in patients on antiplatelet medications*.

White Rose Research Online URL for this paper:
<https://eprints.whiterose.ac.uk/181824/>

Version: Accepted Version

Article:

Ashton, C., Laffan, M., Hutchinson, P.J. et al. (6 more authors) (2022) Survey evaluating clinical equipoise around platelet transfusion after head injury and traumatic intracranial haemorrhage (ICH) in patients on antiplatelet medications. *Emergency Medicine Journal*, 39 (3). pp. 220-223. ISSN 1472-0205

<https://doi.org/10.1136/emered-2021-211189>

This article has been accepted for publication in *Emergency Medicine Journal*, 2021 following peer review, and the Version of Record can be accessed online at <http://dx.doi.org/10.1136/emered-2021-211189>. © Authors (or their employer(s)). Reuse of this manuscript version (excluding any databases, tables, diagrams, photographs and other images or illustrative material included where another copyright owner is identified) is permitted strictly pursuant to the terms of the Creative Commons Attribution-Non Commercial 4.0 International. (<https://creativecommons.org/licenses/by-nc/4.0/>)

Reuse

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial (CC BY-NC) licence. This licence allows you to remix, tweak, and build upon this work non-commercially, and any new works must also acknowledge the authors and be non-commercial. You don't have to license any derivative works on the same terms. More information and the full terms of the licence here:
<https://creativecommons.org/licenses/>

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



eprints@whiterose.ac.uk
<https://eprints.whiterose.ac.uk/>

Survey evaluating clinical equipoise around platelet transfusion after head injury and traumatic intracranial haemorrhage (ICH) in patients on anti-platelet medications

Authors: C Ashton¹, M Laffan², PJ Hutchinson³, F Lecky^{4,5,6}, S Ralhan¹, JE Smith^{7,8}, JP Coles⁹, S Stanworth^{10,11,12}, N Curry^{11,12}

1. Department of Geratology, Oxford University Hospitals
2. Centre for Haematology, Department of Immunology and Inflammation, Imperial College London, London, UK
3. Department of Clinical Neurosciences, University of Cambridge
4. Centre for Urgent and Emergency Care Research, University of Sheffield
5. Trauma Audit and Research Network, University of Manchester
6. Emergency Department Salford Royal Hospital
7. Emergency Department, University Hospitals Plymouth NHS Trust
8. Academic Department of Military Emergency Medicine, Royal Centre for Defence Medicine
9. Division of Anaesthesia, Department of Medicine, University of Cambridge
10. Transfusion Medicine, NHS Blood and Transplant, Oxford, United Kingdom.
11. Department of Haematology, Oxford University Hospitals NHS Foundation Trust, United Kingdom.
12. Radcliffe Department of Medicine, University of Oxford, and NIHR Oxford Biomedical Research Centre, United Kingdom

Abstract

Patients aged 60 or over account for over half of severely injured trauma patients and a traumatic brain injury is the most common injury sustained. Many of these patients are taking antiplatelet medications but there is clinical equipoise about the role of platelet transfusion in patients with traumatic intracranial haemorrhage taking prior antiplatelet medications. A pre-piloted survey designed to explore a range of issues in this patient group was sent via email to Consultants and Specialty Registrar members of a variety of relevant societies and working groups. 193 responses were received, mostly from colleagues in Emergency Medicine, Neurosurgery, Anaesthesia and Haematology. Respondents indicated that there is lack of evidence to support the use of platelet transfusion in this patient population but also lack of evidence of harm. Results also demonstrate uncertainties as to whether platelets should be given to all or some patients and doubt regarding the value of Viscoelastic (VE) testing. Our survey demonstrates equipoise in current practice with regards to platelet transfusion in patients admitted with a traumatic ICH who are taking antiplatelet medication. There is support for additional trials to investigate the effect of platelet transfusion in this rising population of frail, high risk patients, in order to provide a better evidence-base for guideline development.

What this paper adds

Older patients sustaining traumatic brain injuries account for a large proportion of trauma patients, many of whom are taking antiplatelet medications. Evidence suggests that platelet dysfunction following traumatic brain injury is associated with worse outcome. However, although platelet transfusions seems an appropriate intervention, recent evidence suggests administration of platelets may cause harm and worse neurological outcome.

Our survey explored the beliefs of clinicians when faced with this clinical question on the use of platelet transfusions. We demonstrate equipoise in current practice with regards to platelet transfusion in patients admitted with a traumatic ICH who are taking antiplatelet medication. The results support the need for additional research to investigate the effect of platelet transfusion in this patient population.

Background

Patients aged 60 and over now account for over 50% of severely injured trauma patients presenting to the Emergency Department. The most frequent mechanism of injury in this patient group is a fall from less than two metres. A traumatic brain injury is the most common injury sustained². The use of antiplatelet medication is particularly high in older patients (up to half of this patient group) and is associated with a high mortality rate³⁻⁶. Evidence suggests that platelet dysfunction following traumatic brain injury is associated with worse outcome⁷. Platelet transfusion therefore seems a suitable intervention, but the PATCH trial, which assessed the use of platelet transfusion in patients with non-traumatic intracranial haemorrhage (ICH) on prior antiplatelet therapy, reported worse neurological outcomes at three months⁸. As part of a programme of research, we undertook a national survey to explore uncertainties in practice and clinical equipoise about the role of platelet transfusion in patients with traumatic ICH taking antiplatelet medications.

Method

A pre-piloted survey was designed to explore a range of issues in patients admitted with traumatic ICH taking prior antiplatelet medications (table 1), including existing evidence for platelet transfusion, current practice and factors influencing platelet transfusions, and attitudes towards further study to address this clinical equipoise.

An invitation to complete the survey was distributed via email in July 2020. Consultants and Specialty Registrars from the following UK societies and working groups were asked to complete the survey (membership numbers of each group in brackets). The Society of British Neurological Surgeons (660), Major Trauma Centre Geriatric Medicine (27), the British Society for Haemostasis and Thrombosis (225), the Neuro Anaesthesia and Critical Care Society (402), the United Kingdom Doctors' Haemophilia Organisation (146), TARN trauma leads (253) and the Royal College Emergency Medicine study group (50).

Please tell us your grade and speciality

N=193

1. Do you think there is adequate evidence to support the use of platelet transfusions in patients who present with traumatic ICH on antiplatelet therapy?

Yes 13%, No 86%, NR 0.5%

2. Do you think there is sufficient evidence of harm to recommend against giving a platelet transfusion in this patient group?
Yes 7%, No 93%
3. If faced with a patient with a head injury known to be on aspirin or clopidogrel who has a traumatic ICH on CT/MRI, would you:
- Treat with platelet transfusions? Yes 21%
If so, how many would you give?
1 unit: Yes 37%
2 units: Yes 46%
More than 2 units: Yes 1%
Don't know: Yes 16%
 - Only treat with platelets if due for neurosurgery Yes 37%
 - Only treat with platelets if clinical deterioration (more severe cases) Yes 19%
 - Not give platelets Yes 23%
4. If you have a patient with a traumatic ICH on an anti-platelet, do you take any additional information into consideration prior to giving platelets?
- Duration from time of injury: Yes 87%
 - Presence of thrombocytopenia: Yes 93%
Transfuse if platelet count was less than 150 x10⁹/L Yes 2%
Transfuse if platelet count was less than 100 x10⁹/L Yes 49%
Transfuse if platelet count was less than 80 x10⁹/L Yes 21%
Transfuse if platelet count was less than 50 x10⁹/L Yes 28%
 - I would use additional coagulation test information which is (routinely) available?
TEG, Rapid TEG, ROTEM, VerifyNow, PFA, Multiplate, Platelet aggregation studies or other
Yes 86%
 - I would like to have additional coagulation information but these are not routinely available
Yes 2%
 - The type of anti-platelet agent the patient takes as this influences my options for platelet transfusion therapy?
Clopidogrel, aspirin or dual anti-platelet therapy
Yes 95%
5. The following statements best describe my transfusion practice
- I would give 1 unit of platelets if patient taking clopidogrel Yes 21%
 - I would give 2 (or more) units of platelets if patient taking clopidogrel Yes 24%
 - I would give 1 unit of platelets if patient taking aspirin Yes 9%
 - I would give 2 (or more) units of platelets if patient taking aspirin Yes 7%
 - I would give 1 unit of platelets if patient taking dual anti-platelets Yes 15%
 - I would give 2 (or more) units of platelets if patient taking dual anti-platelets Yes 27%
6. With patients taking anti-platelet agents with a traumatic ICH, would you be willing to randomise this group to allocation of platelet transfusion vs no platelet transfusions?
Yes 82%
7. Would you make any exclusions to study entry?
Yes 46%
- Intraparenchymal haemorrhage, intracerebral haemorrhage, intraventricular haemorrhage, subarachnoid haemorrhage, subdural haematoma, extradural haematoma, GCS 13-15, GCS 9-12, GCS 3-8, operation planned, conservative management, frail patients

Table 1: The survey distributed to establish opinions on evidence of, current practice and future studies regarding platelet transfusions to patients admitted with traumatic ICH already taking anti-platelet medication. TEG – Thromboelastography. ROTEM – Rotational Thromboelastometry. PFA – Platelet Function Assay

Results

There were 193 responses from 169 Consultants and 24 Specialty Registrars; an approximate response rate of 11% based on the membership of the aforementioned groups. The most frequent responders were colleagues in Emergency Medicine (n = 45), Neurosurgery (n = 42), Anaesthesia (n = 37) and Haematology (n = 33).

The responses to the survey indicate that in patients sustaining traumatic ICH on antiplatelets, there is inadequate evidence to support the use platelet transfusion (86% of respondents) or advise against platelet transfusion due to risk of harm (93% of respondents).

21% (n = 44) of respondents would treat those on prior antiplatelet therapy with platelet transfusion (mostly Haematologists and Anaesthetists). Conversely, 23% (n = 47) of respondents felt platelet transfusion was not indicated (mostly from Emergency Medicine). Some favoured platelet transfusion in specific circumstances, such as when neurosurgical intervention was required (37%) (favoured mostly by Neurosurgeons) or if the patient was clinically deteriorating (19%) and thus perhaps indicating a more severe head injury. A summary of the responses is in the figure below (figure 1).

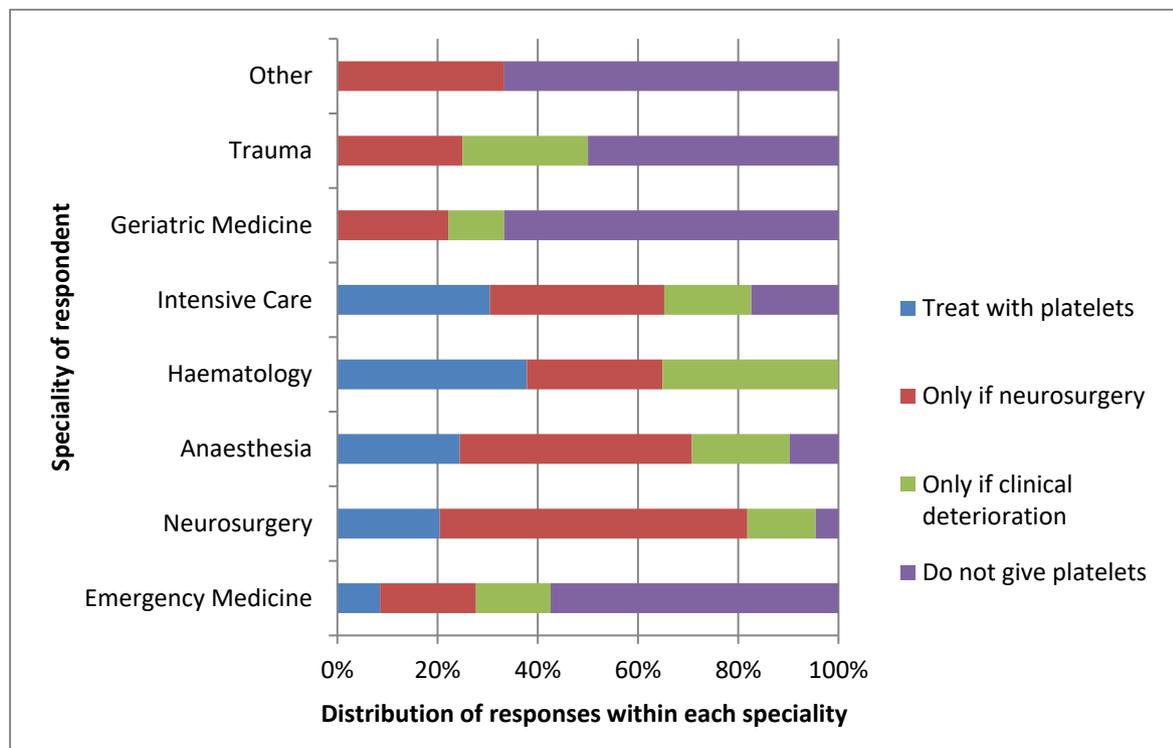


Figure 1: A graph to show responses within each speciality with regards to their current practice of platelet transfusion for patients admitted with a traumatic brain injury, already taking anti-platelet medication

The majority indicated the following factors would influence their decision about platelet transfusion; type of antiplatelet agent, duration of time from injury and if additional coagulation tests were available. In thrombocytopenic patients there was no consensus as to where the threshold for platelet transfusion should be set, but most indicated at least at a platelet count less than $100 \times 10^9/L$. Regarding coagulation studies, the favoured tests were thromboelastography (TEG) (17%) and rotational thromboelastometry (ROTEM) (12%). However, these tests do not detect any antiplatelet effect for the two most common antiplatelet agents (aspirin and clopidogrel).

Considering their current practice, most were more likely to transfuse platelets to those on clopidogrel or dual antiplatelet therapy than aspirin alone (45% and 42% vs 17% on aspirin). The majority electing to transfuse two or more units of platelets.

Responders acknowledged that further research is required for patients on clopidogrel or dual antiplatelets. Most (82%) would be willing to randomise patients to receive platelet transfusion or not, if a trial were to be conducted regarding its role in patients with a traumatic ICH, taking antiplatelet therapy beforehand. Suggested exclusion criteria would include those requiring operative management (n = 45), a lower GCS (GCS 3-8) (n = 20) and patients living with frailty (n = 20). To some extent the site of bleeding may also contribute to decisions about exclusion from such a study.

Conclusion

Key findings from this survey include:

- Respondents often indicate no evidence of harm from platelet transfusions in this patient population despite the PATCH trial
- Uncertainties in whether platelets should be given to all or some patients
- Uncertainties regarding the value of Viscoelastic (VE) testing, although many thought they would be valuable
- Willingness to support further study

The suggestion of conducting TEG and ROTEM testing from colleagues particularly in Anaesthesia and Intensive Care Medicine, in order to help decide whether or not to transfuse platelets, may reflect a desire for a sensitive and reliable test of bleeding risk in the presence of antiplatelet medications. Whilst standard TEG or TEM testing do not show effects on the commonly used antiplatelet medications, more targeted tests are available (such as platelet mapping) that can detect antiplatelet effects, however these tests are not routinely available. Platelet mapping additionally detects a trauma-induced platelet dysfunction, making interpretation of results challenging. There is no current data as to how to differentiate between the effect of trauma and antiplatelet medications in platelet mapping. Viscoelastic haemostatic assay (VHA) augmented transfusion strategy was not included in our survey but the ITACTIC trial suggests further study of its use in patients with traumatic brain injury would be of value⁹.

A limitation to our survey is that we did not explore the decision-making process relating to the responses made, such as guidelines utilised or if cross-speciality advice is sought.

In conclusion, our survey demonstrates equipoise in current practice with regards to platelet transfusion in patients admitted with a traumatic ICH who are taking antiplatelet medication. This disparity is not only across medical specialties, but also within a particular specialty. There is support for additional trials to investigate the effect of platelet transfusion in this rising population of frail, high risk patients, in order to provide a better evidence-base for guideline development.

Acknowledgements: The authors would like to thank Tom Woolley and John Grant-Casey for their help in the distribution of the survey and collation of results. PJ Hutchinson is supported by the NIHR and the Royal College of Surgeons of England.

References

1. Kehoe A, Smith JE, Edwards A, et al. The changing face of major trauma in the UK. *Emergency Medicine Journal* 2015;**32**:911-915.
2. Trauma Audit and Research Network (TARN): Major trauma in older people. 2017. Available at: <https://www.tarn.ac.uk/content/downloads/3793/Major%20Trauma%20in%20Older%20People%202017.pdf>
3. Williams CD, Chan AT, Elman MR, Kristensen AH, Miser WF, Pignone MP, Stafford RS, McGregor JC. Aspirin use among adults in the U.S.: results of a national survey. *Am J Prev Med*. 2015 May;**48**(5):501-8
4. Li L, Geraghty O, Mehta Z et al. Age-specific risks, severity, time course and outcome of bleeding on long-term antiplatelet treatment after vascular events: a population-based cohort study. *Lancet* 2017 **390**: 490-499
5. Ivascu, F, Howells G, Junn F et al: Predictors of mortality in trauma patients with intracranial haemorrhage on preinjury aspirin or clopidogrel. *Journal of Trauma: Injury, Infection, and Critical Care*, 2008, **65**(4):785-788
6. Ohm C, Mina A, Howells G et al.: Effects of antiplatelet agents on outcomes for elderly patients with traumatic intracranial haemorrhage. *Journal of Trauma: Injury, Infection, and Critical Care*, 2005, **58**(3):518-522
7. Nekludov M, Bellander BM, Blomback M, Wallen HN: Platelet dysfunction in patients with severe traumatic brain injury. *Journal of Neurotrauma* 2007, **24**(11):1699–1706
8. Baharoglu M, Cordonnier C, Al-Shahi Salamn R et al. Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral hemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial. *Lancet* 2016 **387**: 2605-2613
9. Baksaas-Aasen, K., Gall, L.S., Stensballe, J. *et al*. Viscoelastic haemostatic assay augmented protocols for major trauma haemorrhage (ITACTIC): a randomized, controlled trial. *Intensive Care Med* (2020). <https://doi.org/10.1007/s00134-020-06266-1>