

Protocol for a survey study

Platelet transfusions in the ICU - an international survey among ICU clinicians

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(Final author sequence based on number of survey replies)

Affiliations:

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Background

Thrombocytopenia is common in the intensive care unit (ICU)¹⁻³ and increases the risk of major bleeding complications.⁴ Thrombocytopenia is seen in different subpopulations, such as trauma patients⁵, cardiac ICU patients,^{6,7} patients with sepsis and in patients with cancer. Therefore, the pathogenesis behind thrombocytopenia may differ among ICU patients. Platelet transfusions are often used to try to correct thrombocytopenia in ICU patients⁸ in order to prevent or treat bleeding,^{9,10} however, evidence is still scarce within this area, and specific guidelines for ICU subpopulations are often lacking. Therefore, the decision to transfuse platelets is often left to the treating physician.

Purpose

To identify and describe ICU physicians' preferences regarding platelet transfusions and explore which variables influence their decisions.

Research questions

- a) Which specific clinical findings and variables influence ICU physicians' decision to give prophylactic platelet transfusions?
- b) Which platelet transfusion thresholds do ICU physicians find acceptable in different clinical scenarios?
- c) Do personal preferences and experience guide their practice with regard to the transfusion of platelets?
- d) If ICU physicians were to include patients in a randomised trial, which transfusion thresholds would they find acceptable?

Methods

We will conduct an international, online cross-sectional survey using the commercial secure web application onlineundersoegelse.dk. The survey will be in English. The cover letter and survey can be found in Appendix A and B. Ethical approval will be sought for the study in individual countries, if applicable. The survey will be designed using a non-response option to most close-ended questions, and all close-ended questions will be made mandatory to increase the completeness of the survey. We will include a few open-ended questions to facilitate further data interpretation; however, open-ended questions will not be mandatory.¹¹ The survey has been validated by an international panel of

intensivists and experts in qualitative research to ensure validity before distribution. We will use well-defined and proven scientific methods for improving the response rate, including assurance of confidentiality and offering the results when the survey is completed.¹² We will invite intensive care physicians through the Nine-I research network. We will inform all participants that by answering the survey online, they are providing informed consent for data publication. We will send three reminders with two weeks in between to all participants before database closure, which includes a statement that others have responded.^{13,14} No financial support will be provided. We will use the Consensus-Based Checklist for Reporting of Survey Studies (CROSS) when reporting the study.¹⁵

Statistics

Estimation of sample size: Using a theoretical estimate of a total sample size of 100.000 ICU physicians in developed countries (www.who.int/data), we would have to include approximately 400 respondents in the final analysis to achieve a margin of error of 5% and a confidence level of 95%; and 660 respondents in the final analysis to achieve a confidence level of 99%. This is based on the assumption that the doctors in the included countries can be viewed as a homogenous sample. Due to colleague-to-colleague distribution through the Nine-I network, we aim for a response rate of approximately 70%, higher than in most electronic surveys.¹⁶ We will distribute the survey to a minimum of 1000 ICU doctors in 15 European and American countries, expecting to include around 700 respondents in the final analysis. We will present the data descriptively with continuous variables as medians with interquartile ranges (IQRs) and categorical variables as numbers and percentages with 95% CIs and report the proportion of missing data.

Discussion

Surveys are the principal method used to address topics about attitudes or opinions, which cannot be assessed using other approaches.¹¹ We will therefore use the survey method to collect information on intensivists practices and beliefs on platelet transfusions in a sample that we believe is large enough to assume that the results will apply in general for intensivists in developing countries. Other surveys on platelet transfusion have been performed. The TRACE survey evaluated transfusion practices in the ICU, which included platelet transfusions, among 745 respondents world-wide.¹⁴ They found that in non-bleeding patients without a planned invasive procedure, respondents would transfuse patients at a platelet count of $20 \times 10^9/L$ (10–25), however higher transfusion triggers was used prior to invasive procedures. Another smaller survey investigated the use of platelet transfusions specifically prior

to placement of central venous catheters (CVC)¹⁷ and found current transfusion practice prior highly variable and the decision to be based mainly on clinical parameters, insertion site and technique applied. Outside the ICU setting, a recent study of haematological outpatients with severe thrombocytopenia found that prophylactic platelet transfusions are widely used in patients with acute leukemia and myelodysplastic syndroms (87%-98% of respondents). In this survey, a platelet threshold of $\leq 10 \times 10^9/L$ was found to be routinely applied; however, this changed when clinical conditions that potentially could increase bleeding risks were present. When this was the case, a wide range of thresholds between $10 \times 10^9/L$ to $50 \times 10^9/L$ were applied.

To our knowledge, no surveys have been performed that investigate which specific clinical findings and conditions that influence ICU physicians' decision to give prescribe prophylactic platelet transfusions and if these thresholds vary depending on the underlying diagnosis. We are also interested in whether personal beliefs, culture and previous experiences influence the decision-making process; therefore, this survey study will be combined with an in-depth qualitative study on how ICU physicians are making decisions on when to prescribe a platelet transfusion as well as their concerns and views in general with regards to blood transfusions. Together, these two studies will contribute to a more complete picture of transfusion practices in the ICU today.

References

1. Williamson DR, Lesur O, Tétrault J-P, Nault V, Pilon D. Thrombocytopenia in the critically ill: prevalence, incidence, risk factors, and clinical outcomes. *Can J Anaesth* 2013; 60: 641–51.
2. Crowther MA, Cook DJ, Meade MO, Griffith LE, Guyatt GH, Arnold DM, Rabbat CG, Geerts WH, Warkentin TE. Thrombocytopenia in medical-surgical critically ill patients: Prevalence, incidence, and risk factors. *J Crit Care* 2005; 20: 348–53.
3. Strauss R, Wehler M, Mehler K, Kreutzer D, Koebnick C, Hahn EG. Thrombocytopenia in patients in the medical intensive care unit: bleeding prevalence, transfusion requirements, and outcome. *Crit Care Med* 2002; 30: 1765–71.
4. Cook RJ, Sigouin CS, Heddle NM, Webert KE. The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia. *Haematologica* 2006; 91: 1530–7.
5. Hanes SD, Quarles DA, Boucher B. Incidence and risk factors of thrombocytopenia in critically ill trauma patients. *Ann Pharmacother* 1997; 3: 285–9.
6. Selleng S, Selleng K, Wollert HG, Muellejans B, Lietz T, Warkentin TE, Greinacher A. Heparin-induced thrombocytopenia in patients requiring prolonged intensive care unit treatment after cardiopulmonary bypass. *J Thromb Haemost* 2008; 6: 428–35.

7. Vonderheide RH, Thadhani R, Kuter DJ. Association of thrombocytopenia with the use of intra-aortic balloon pumps. *Am J Med* 1998; 105: 27–32.
8. Stanworth SJ, Walsh TS, Prescott RJ, Lee RJ, Watson DM, Wyncoll DLA. Thrombocytopenia and platelet transfusion in UK critical care: A multicenter observational study. *Transfusion* 2013; 53: 1050–8.
9. McIntyre L, Tinmouth AT, Fergusson D a. Blood component transfusion in critically ill patients. *Curr Opin Crit Care* 2013; 19: 326–33.
10. Wandt H, Schaefer-Eckart K, Wendelin K, Pilz B, Wilhelm M, Thalheimer M, Mahlkecht U, Ho A, Schaich M, Kramer M, Kaufmann M, Leimer L, Schwerdtfeger R, Conradi R, Dölken G, Klenner A, Hänel M, Herbst R, Junghans C, Ehninger G. Therapeutic platelet transfusion versus Routine prophylactic transfusion in patients with haematological malignancies: An open-label, multicentre, randomised study. *Lancet* 2012; 380: 1309–16.
11. Gaur PS, Zimba O, Agarwal V, Gupta L. Reporting Survey Based Studies – a Primer for Authors. *J Korean Med Sci* 2020; 35: 1–15.
12. Edwards PJ, Roberts I, Clarke MJ, DiGuseppi C, Wentz R, Kwan I, Cooper R, Felix LM, Pratap S. Methods to increase response to postal and electronic questionnaires. *Cochrane Database Syst Rev* 2009. doi: 10.1002/14651858.MR000008.pub4
13. Jones TL, Baxter M, Khanduja V. A quick guide to survey research. *Ann R Coll Surg Engl* 2013; 95: 5–7.
14. De Bruin S, Scheeren TWL, Bakker J, Van Bruggen R, Vlaar APJ. Transfusion practice in the non-bleeding critically ill: An international online survey-the TRACE survey. *Crit Care* 2019; 23: 1–8.
15. Sharma A, Minh Duc NT, Luu Lam Thang T, Nam NH, Ng SJ, Abbas KS, Huy NT, Marušić A, Paul CL, Kwok J, Karbwang J, de Waure C, Drummond FJ, Kizawa Y, Taal E, Vermeulen J, Lee GHM, Gyedu A, To KG, Verra ML, Jacqz-Aigrain ÉM, Leclercq WKG, Salminen ST, Sherbourne CD, Mintzes B, Lozano S, Tran US, Matsui M, Karamouzian M. A Consensus-Based Checklist for Reporting of Survey Studies (CROSS). *J Gen Intern Med* 2021; 36: 3179–87.
16. Fincham JE. Response rates and responsiveness for surveys, standards, and the Journal. *Am J Pharm Educ* 2008; 72: 43.
17. van de Weerd EK, Peters AL, Goudswaard EJ, Binnekade JM, van Lienden KP, Biemond BJ, Vlaar APJ. The practice of platelet transfusion prior to central venous catheterization in presence of coagulopathy: a national survey among clinicians. *Vox Sang* 2017; 112: 343–51.

APPENDIX A. COVER LETTER TO SURVEY PARTICIPANTS

Dear intensive care colleague,

We would be very grateful if you would take a few minutes to complete the attached survey about thrombocytopenia and platelet transfusions in the intensive care unit. The survey will take about 10 minutes to complete, and the data collection activities will be conducted anonymously.

The survey consists of seven parts and covers several aspects of platelet and blood transfusions. Please note that we will consider the completion of the survey link as informed consent on your part. We will send you the survey results via email once the survey is closed and the results are analysed.

Your response is extremely important. Please feel free to call or email us if you have any questions, concerns or feedback on the survey. We have provided a short rationale for the study beneath.

Thank you!

Kind regards,

On behalf of the Nine-I Research Group

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Background and rationale for the survey

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ICU patients,^{6,7} patients with sepsis and in patients with cancer. Therefore, the pathogenesis behind thrombocytopenia may differ among ICU patients. Platelet transfusions are often used to correct thrombocytopenia in ICU patients⁸ in order to prevent or treat bleeding,^{9,10} however, evidence is still scarce within this area, and specific guidelines for ICU subpopulations are often lacking. Therefore, the decision to transfuse platelets is often left to the treating physician.

We are performing this study as part of a larger platelet transfusion research program to identify and describe the preferences of ICU physicians regarding platelet transfusions and explore which variables influence their decisions.

With this survey, we aim to investigate common practices and establish whether variations exist and the extent to which they may be present. We sincerely hope that the information we will receive through this survey will help us design future research on platelet transfusions in the ICU and thereby provide the evidence that can help us improve treatment for our patients.

References

1. Williamson DR, Lesur O, Tétrault J-P, Nault V, Pilon D. Thrombocytopenia in the critically ill: prevalence, incidence, risk factors, and clinical outcomes. *Can J Anaesth* 2013; 60: 641–51.
2. Crowther MA, Cook DJ, Meade MO, Griffith LE, Guyatt GH, Arnold DM, Rabbat CG, Geerts WH, Warkentin TE. Thrombocytopenia in medical-surgical critically ill patients: Prevalence, incidence, and risk factors. *J Crit Care* 2005; 20: 348–53.
3. Strauss R, Wehler M, Mehler K, Kreutzer D, Koebnick C, Hahn EG. Thrombocytopenia in patients in the medical intensive care unit: bleeding prevalence, transfusion requirements, and outcome. *Crit Care Med* 2002; 30: 1765–71.
4. Cook RJ, Sigouin CS, Heddle NM, Webert KE. The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia. *Haematologica* 2006; 91: 1530–7.
5. Hanes SD, Quarles DA, Boucher B. Incidence and risk factors of thrombocytopenia in critically ill trauma patients. *Ann Pharmacother* 1997; 3: 285–9.
6. Selleng S, Selleng K, Wollert HG, Muellejans B, Lietz T, Warkentin TE, Greinacher A. Heparin-induced thrombocytopenia in patients requiring prolonged intensive care unit treatment after cardiopulmonary bypass. *J Thromb Haemost* 2008; 6: 428–35.
7. Vonderheide RH, Thadhani R, Kuter DJ. Association of thrombocytopenia with the use of intra-aortic balloon pumps. *Am J Med* 1998; 105: 27–32.
8. Stanworth SJ, Walsh TS, Prescott RJ, Lee RJ, Watson DM, Wyncoll DLA. Thrombocytopenia and platelet transfusion in UK critical care: A multicenter observational study. *Transfusion* 2013; 53: 1050–8.
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10. Wandt H, Schaefer-Eckart K, Wendelin K, Pilz B, Wilhelm M, Thalheimer M, Mahlknecht U, Ho A, Schaich M, Kramer M, Kaufmann M, Leimer L, Schwerdtfeger R, Conradi R, Dölken G, Klenner A, Hänel M, Herbst R, Junghans C, Ehninger G. Therapeutic platelet transfusion versus Routine prophylactic transfusion in patients with haematological malignancies: An open-label, multicentre, randomised study. *Lancet* 2012; 380: 1309–16.
11. Gaur PS, Zimba O, Agarwal V, Gupta L. Reporting Survey Based Studies – a Primer for Authors. *J Korean Med Sci* 2020; 35:

- 1–15.
12. Edwards PJ, Roberts I, Clarke MJ, DiGiuseppi C, Wentz R, Kwan I, Cooper R, Felix LM, Pratap S. Methods to increase response to postal and electronic questionnaires. *Cochrane Database Syst Rev* 2009. doi: 10.1002/14651858.MR000008.pub4
 13. Jones TL, Baxter M, Khanduja V. A quick guide to survey research. *Ann R Coll Surg Engl* 2013; 95: 5–7.
 14. De Bruin S, Scheeren TWL, Bakker J, Van Bruggen R, Vlaar APJ. Transfusion practice in the non-bleeding critically ill: An international online survey-the TRACE survey. *Crit Care* 2019; 23: 1–8.
 15. Sharma A, Minh Duc NT, Luu Lam Thang T, Nam NH, Ng SJ, Abbas KS, Huy NT, Marušić A, Paul CL, Kwok J, Karbwang J, de Waure C, Drummond FJ, Kizawa Y, Taal E, Vermeulen J, Lee GHM, Gyedu A, To KG, Verra ML, Jacqz-Aigrain ÉM, Leclercq WKG, Salminen ST, Sherbourne CD, Mintzes B, Lozano S, Tran US, Matsui M, Karamouzian M. A Consensus-Based Checklist for Reporting of Survey Studies (CROSS). *J Gen Intern Med* 2021; 36: 3179–87.
 16. Fincham JE. Response rates and responsiveness for surveys, standards, and the Journal. *Am J Pharm Educ* 2008; 72: 43.
 17. van de Weerdt EK, Peters AL, Goudswaard EJ, Binnekade JM, van Lienden KP, Biemond BJ, Vlaar APJ. The practice of platelet transfusion prior to central venous catheterization in presence of coagulopathy: a national survey among clinicians. *Vox Sang* 2017; 112: 343–51.

