Platelet transfusion threshold before central line insertion: An elusive yardstick?

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SUMMARY

This randomized study was conducted in haematology wards and intensive care units (ICUs) of 10 hospitals in the Netherlands, where patients with thrombocytopenia (platelet count of 10 000 to 50 000/cmm within 24 hours before the procedure) were randomized to either prophylactic platelet transfusion or no transfusion before CVC insertion. Patients were randomly assigned in a 1:1 ratio to each group and ultrasound-guided placement by experienced operators was mandated. The primary outcome was the occurrence of grades 2 to 4 catheter-related bleeding within 24 hours of placement. Grades 2–4 bleeding includes bleeds of all severity except minor bleeds that need less than 20 minutes of manual compression to stop.

Over a period of 6 years, a total of 393 study eligible CVC placements were done, of which 373 were finally included in the analysis. The median platelet count in both the groups was 30 000/cmm with median values of prothrombin time (PT) and activated partial thromboplastin time (aPTT) being in the normal range. Of these, nearly 56% of procedures in both arms were performed in the haematology ward and the remaining in the ICU. About 50% of CVCs were inserted into the internal jugular vein, 37% in the subclavian vein and the remaining in the femoral vein.

At the end of the trial period, grades 2 to 4 bleeding after CVC insertion was noted in 9 of 188 patients (4.8%) in the transfusion arm and 22 of 185 (11.9%) in the control arm. The risk of grades 3 and 4 bleeding was also lower in the transfusion arm (2.1% *v*. 4.9%). The transfusion arm also had a higher platelet count at one hour (median 54 000/cmm *v*. 26 000/cmm) and 24 hours (36 000/cmm *v*. 26 000/cmm) post procedure. There was no significant difference between duration of hospital stay and overall mortality between both groups. Major findings on subgroup analysis included a higher risk of bleeding in patients receiving a subclavian line and those in the haematology ward compared to the ICU. In addition, the risk of bleeding was seen to increase for patients with platelet counts less than 20 000/cmm. The final conclusion was that withholding platelet transfusions did not meet margins for non-inferiority, implying that withholding transfusions can potentially lead to inferior outcomes in this patient population.

COMMENT

In patients with haematological disorders, central line insertion is the most common procedure requiring prophylactic platelet transfusions, impacting the findings of this study.[1] Although these results may lack universal applicability and may not align with routine practice, they offer valuable insights and lessons.

Thrombocytopenia is not the sole factor contributing to bleeding risk in patients with haematological diseases or those in the ICU. Bleeding risk is determined by several factors including sepsis, liver disease, platelet dysfunction and disseminated intravascular coagulation.[2] The precise interplay and convergence of these simultaneous factors in determining the ultimate risk of bleeding remains uncertain. However, it is clear that the incidence of bleeding after CVC insertion is uniformly low in this setting, even in the presence of active sepsis and coagulopathy.[3,4] In a previous study, all CVC inserted without ultrasound guidance at a median platelet count of 14 000/cmm were not associated with any incidence of severe bleeding. Importantly, the median post-procedure count even with transfusion was 24 000/cmm, reinforcing that platelet counts may not be the sole determinant of bleeding risk during CVC insertion.[5]

Most data on this subject are available from observational studies, with no major randomized trials. Most observational studies have considered a platelet count of less than 20 000/cmm as a common threshold for transfusion.[6] This low risk of bleeding has robustly served as the basis for several published guidelines, which typically recommend a platelet count cut-off of 20 000/cmm before line insertion (Table I). Most observational studies have noted a bleeding risk even lower than that in the current trial. For instance, the recent British Society of Haematology guidelines included 19 observational studies in the review process, in which only one case of severe bleeding was identified.[7] The extremely low risk of bleeding observed in previous observational studies has established a longstanding threshold of 20 000/cmm in published guidelines for over two decades. Indeed, the only consistent predictors of bleeding in several studies have been platelet counts of less than 10 000–20 000/cmm and absence of ultrasound guidance during the procedure.[8,9]

The data presented above are consistent with the findings of the current trial. While the risk of bleeding observed in this trial is slightly increased compared to observational studies, as expected due to the prospective design, the overall level of risk remains low. A low baseline risk of bleeding in the control arm has implications for statistical interpretation. If the baseline risk is already low, a marginal absolute reduction in risk (even if statistically significant) may lack clinical significance.[10] For example, a study may find a 5% absolute risk reduction in the risk of death from a new drug may be statistically significant, but the clinical benefit may be small if the baseline risk of death is only 1%.

Reduced risk of bleeding with platelet transfusions (2.1% *v*. 4.9%) translates to an absolute risk reduction (ARR) of 2.7% and indicates a number needed to treat (NNT=1/ARR) of 37 to prevent one episode of severe bleeding. This indicates over

TABLE I. Summary of current guidelines recommending platelet count thresholds of 20×10^9/L or more before central line insertion

Study	Year of publication	Society or institution
Optimal preprocedural platelet transfusion threshold for central venous catheter insertions in patients with thrombocytopenia	2018	American Society of Clinical Oncology (ASCO)
Prophylactic platelet transfusion before central venous catheter placement in patients with thrombocytopenia: Study protocol for a randomized controlled trial	2017	Dutch Society of Clinical Haematology (NVvH)
Comparison of different platelet transfusion regimens before insertion of central lines in patients with thrombocytopenia	2016	British Committee for Standards in Haematology (BCSH)
British Society for Haematology Guidelines for the Use of Platelet Transfusions	2019	BCSH
UpToDate: Central venous access in adults: General principles	2023	UpToDate

37 patients requiring unnecessary platelet transfusions to prevent one episode of severe bleeding with CVC insertion. Considering that the majority of patients in the study experienced grade 2–3 bleeding, it may be difficult to justify platelet transfusion, given the potential risks involved.

Furthermore, the generalizability of the study findings to patients with primary haematological disorders is challenging, given that these individuals often require multiple transfusions and may experience alloimmunization due to exposure to several HLA (human leucocyte) and HPA (human platelet) antigens. There is an added risk of platelet transfusion refractoriness, which can reduce the efficacy of platelet transfusions in the future. These factors not only diminish the potential benefits of platelet transfusions but also elevate the risk of harm.[11]

Given the multifactorial and consistently low risk of bleeding associated with CVC insertion, the administration of potentially harmful platelet transfusions to a large number of patients, without clear clinical benefits, lacks a compelling justification. Instead of providing further evidence for the efficacy of platelet transfusions, this study has two crucial lessons:

1. The baseline risk of bleeding during CVC insertion is minimal, and the existing evidence regarding the need to correct thrombocytopenia for prevention of bleeding remains inconclusive.
2. The primary factor in reducing the risk of bleeding is the use of ultrasound guidance, which should be used maximally in clinical practice.[12–14]

Adopting a single platelet count threshold may not be the optimal approach for all patients. Randomized trials in this setting are limited, but a superiority trial that incorporates platelet count thresholds of 20 000/cmm or 50 000/cmm may help to better define the risk of bleeding. Such an approach would provide a more precise estimation of bleeding risk in real-world situations. In the absence of such data, it may be wiser to adhere to the older guidelines suggesting a cut-off of 20 000/cmm, particularly when ultrasound guidance is used.

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