# Chapter 2

# Clinical practice of platelet transfusions in hemato-oncology

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## Abstract

Platelets are prophylactically transfused to patients receiving myeloablative chemotherapy. The trigger can be adapted if a patient has risk factors for bleeding. We performed an international survey to quantify differences in transfusion policies. While platelet counts are most important, bleeding, fever, use of anticoagulants and invasive procedures also determine transfusion strategies. The largest variation of triggers was observed for lumbar punctures and removal of central venous catheters.

## Introduction

Patients suffering from hematological malignancies often experience thrombocytopenia. Platelets are routinely administered at a trigger of $10x10^9$/L. However, this does not prevent bleeding in all patients. Uremia, hypoalbuminea, recent bone marrow transplantation, recent bleeding, fever, and use of anticoagulation are associated with increased bleeding risk.[1-3] The precise influence of these factors is unclear and therefore guidelines are based on expert opinion and differ between countries.

The Dutch guideline (CBO) recommends to increase the trigger to $20x10^9$/L in case of fever and to $50x10^9$/L for the use of anticoagulation.[4] The British Committee for Standards in Haematology (BCSH), the American Society of Clinical Oncology (ASCO) and the American Association of Blood Banks (AABB) recommend likewise a more liberal transfusion policy in these conditions, but they don't specify triggers.[5-7] The same heterogeneity in recommendations is seen in case of invasive procedures, like lumbar punctures and insertion and removal of central venous catheters. So, the decision to transfuse is based on the opinion of the treating physician and may differ significantly. We performed an international survey to quantify these differences in order to establish in which situation the need for more knowledge is highest.



## Material and methods

A survey was conducted among participants of the symposium of the foundation of Hemato-Oncologie voor Volwassenen Nederland (HOVON – the Haemato Oncology foundation for Adults in the Netherlands), and the congress of the European Hematology Association, (EHA), held in 2014.
Recorded data included characteristics of the respondents, determinants for alternative triggers, used triggers in specific situations and use of premedication. Regarding alternative triggers we asked about adherence to a prophylactic or therapeutic transfusion policy in autologous and allogeneic stem cell transplantation and which specific determinants they take into account when deciding to transfuse platelets to patients receiving myeloablative chemotherapy. Options were albumin, fibrinogen, liver function, renal function, C-reactive protein, fever, leukocyte count, platelet count, and hematocrit. In the questionnaire used at the EHA, bleeding and use of anticoagulants were added. Additionally, they were asked to specify which trigger they use in case of fever, severe mucosal damage, use of intravenous amphotericin B or asparaginase, bleeding in the previous five days,

use of different types of anticoagulants, insertion and removal of central venous catheter, and lumbar puncture. Besides platelets, they were asked if they give red blood cells to anemic thrombocytopenic patients to decrease the bleeding risk, and if yes, at which hematocrit.

Comparative statistics were used to describe the influence of experience on transfusion triggers. Seniors were defined as ≥11 year working as medical specialist or age ≥44 years, if work experience was not known.

## Results and discussion

Respondents

Fifty-two hematologists filled in the questionnaire, 25 at the HOVON symposium and 27 at the EHA. All participated in the supportive care meeting, so they probably reflect a group of hematologists with special interest in transfusion medicine. Thirty respondents were Dutch, 15 came from nine other European countries and six from five countries outside Europe, one did not specify the country of origin. Median age of respondents was 43.5 years (range 30 to 70) with a median work experience as medical specialist of 11 years (range 0-36 years).

Risk factors

All respondents adhered to a prophylactic transfusion policy. For autologous stem cell transplantation 88% used a trigger of $10x10^9$/L and 12% of $20x10^9$/L. For allogeneic stem cell transplantation 83% used a trigger of $10x10^9$/L and 17% of $20x10^9$/L.

Platelet counts (98%), bleeding (97%) and use of anticoagulants (87%) were the most common determinants influencing transfusion decisions (Table 1). Years of experience did not influence the considered determinants, with exception of renal function which was more often taken into account by junior hematologists (30.4% versus 14.2%, 95%CI for difference -40.2 to 7.9). Thirty-eight percent of respondents additionally transfused erythrocytes to reduce the bleeding risk, using a mean hematocrit of 0.27% (range 0.21 to 0.40%). Rationale for this practice could be that erythrocytes are responsible for platelet margination to the vessel wall and the observed association between a higher hematocrit and delayed first bleed in acute myeloid leukaemia.[2]

**Table 1.** Determinants influencing the decision to transfuse

| Parameter | Total n=52 (%) | Junior n=23 (%) | Senior n=21 (%) | Risk difference (%) | 95% CI interval |
|---|---|---|---|---|---|
| Platelet count | 51 (98.1) | 22 (95.6) | 21 (100) | 4.4 | -4.0; 12.6 |
| Bleeding* (n=34) | 33 (97.0) | 15 (100) | 16 (94.1) | 5.9 | -5.3; 17.1 |
| Fever | 32 (61.5) | 14 (60.8) | 14 (66.7) | 5.8 | -22.6; 34.1 |
| Use of anticoagulants * (n=31) | 27 (87.1) | 14 (87.5) | 12 (85.7) | 1.8 | -26.3; 22.7 |
| Renal function | 13 (25.0) | 7 (30.4) | 3 (14.2) | -16.1 | -40.2; 7.9 |
| Hematocrit | 12 (23.1) | 3 (13.0) | 4 (19.0) | 6.0 | -15.7; 27.7 |
| Fibrinogen | 6 (11.5) | 1 (4.3) | 4 (19.0) | 14.7 | -4.0; 33.4 |
| Leukocyte count | 3 (5.8) | 2 (8.7) | 0 (0) | -8.7 | -20.2; 2.8 |
| CRP | 2 (3.9) | 2 (8.7) | 0 (0) | -8.7 | -20.2; 2.8 |
| Liver function | 2 (3.9) | 1 (4.3) | 1 (4.8) | 0.4 | -11.9; 12.8 |
| Albumin | 1 (1.9) | 0 (0) | 1 (4.8) | 4.8 | -4.3; 13.9 |
| Other | | | | | |
| Need for invasive procedures | 2 (3.9) | - | - | - | - |
| Splenomegaly | 1 (1.9) | - | - | - | - |
| INR | 1 (1.9) | - | - | - | - |
| ATG treatment | 1 (1.9) | - | - | - | - |

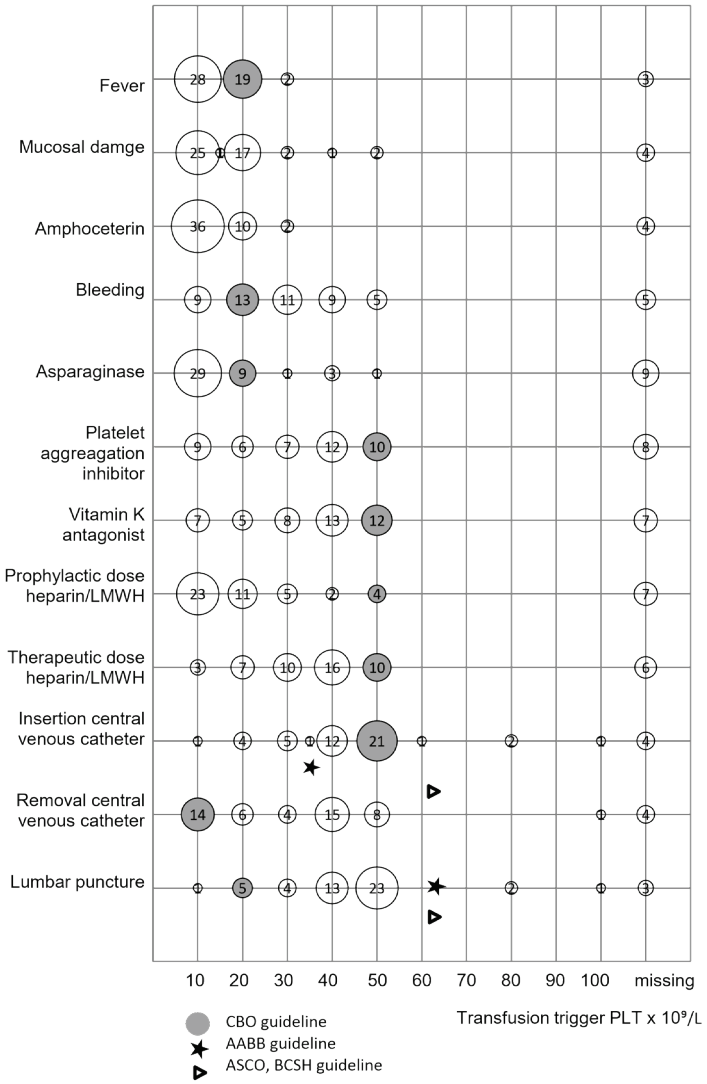
**Bleeding and use of anticoagulants were not standard items in the version used at the HOVON symposium, but mentioned in "others".*



Triggers

The triggers used in several situations are shown in figure 1. In case of fever, 54% of respondents used a trigger of $10x10^9$/L, whereas the Dutch guideline recommends a trigger of $20x10^9$/L. Although fever is associated with an increased risk of refractoriness[8], the influence on bleeding risk is less clear, which could explain this difference.[1,2] Before removal of a central venous catheter, 29% used a trigger of $10x10^9$/L, 12% of $20x10^9$/L and 59% used triggers between 30 and $100x10^9$/L, whereas the guideline advises to maintain the trigger of $10x10^9$/L.[4] Before a lumbar puncture, 47% used a trigger of $40x10^9$/L or lower, 47% a trigger of $50x10^9$/L and 6% of at least $80x10^9$/L, although the recommended trigger is $20x10^9$/L.

**Figure 1.** Used transfusion triggers




*The size of the bubbles and the numbers in the bubbles indicate the number of respondents. The recommended triggers by the CBO[4], ASCO[6], BCSH[7] and AABB[5] are marked. If no bubble is marked, the guideline does not specify a trigger for that situation.*

Premedication

Six percent of respondents gave premedication to each patient, regardless of history. After a severe allergic reaction, 98% prescribed premedication for subsequent transfusions. Fifty-three percent gave antihistamines, which is in line with the guideline,[4] 10% gave corticosteroids, 29% a combination of these and 8% the combination and additionally paracetamol. According to a Cochrane review, routine administration of premedication is not effective in preventing allergic transfusion reactions.[9] In addition, paracetamol, diphenhydramine and a combination of both failed to reduce the incidence of allergic transfusion reactions in patients who previously experienced an allergic transfusion reaction.[10]



Conclusion

This study indicates large heterogeneity in transfusion policies. Guidelines mention risk factors for bleeding, but often refrain from recommending triggers and differ in recommendations before procedures. Although the majority of participants was Dutch and the survey was not validated, this study illustrates the need for evidence which trigger should be adhered in case of risk factors or invasive procedures.

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