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ORIGINAL RESEARCH

Transfusion Practice

TRANSFUSION

Massive transfusion policy in the Netherlands, a nationwide survey

A. M. Van der Heiden[1] | **M. ter Horst**[1] | **M. R. van Bohemen**[2] | **F. Noorman**[3] | **V. M. J. Novotny**[4] | **T. R. L. Klei**[5] | **N. A. Ottenhof**[1]

[1]Department of Anesthesiology, Erasmus Medical Center, Rotterdam, The Netherlands

[2]Department of Hematology, Erasmus Medical Center, Rotterdam, The Netherlands

[3]Military Blood Bank, Central Military Hospital, Utrecht, The Netherlands

[4]Department of Transfusion Medicine, Sanquin Blood supply, Amsterdam, The Netherlands

[5]Department of Product and Process Development, Sanquin Blood supply, Amsterdam, The Netherlands

Correspondence
N. A. Ottenhof, Department of Anesthesiology, Erasmus Medical Center, Rotterdam, The Netherlands.
Email: n.ottenhof@erasmusmc.nl

Abstract

Background: Massive transfusion protocols (MTPs) guide the physician in optimizing transfusion strategies. Although international guidelines on massive transfusion exist, it is unknown whether all Dutch hospitals adhere to these guidelines. The main objective of this study was to create an overview of the massive transfusion strategies of Dutch hospitals and to evaluate if logistical factors, for example, the unavailability of thawed plasma, influence transfusion practices. Furthermore, this study was initiated to evaluate the interest in a ready-to-use plasma product.

Study Design and Methods: A questionnaire on transfusion strategy, available resources, and yearly usage/wastage of transfusion products was distributed to all hospitals in the Netherlands.

Results: Sixty-nine hospitals were approached, of which 58 responded (response rate 84%). The majority of hospitals (67%) strived for a 1:1 erythrocyte/plasma ratio. Five percent of the hospitals used an erythrocyte/plasma ratio >2:1, which did not meet (inter)national guidelines. No relation was found between the clinical strategy described in the MTP and available resources; moreover, direct plasma availability did not increase plasma wastage. Hospitals for which it takes longer to have plasma available for transfusion generally are more interested in a ready-to-use plasma product ($n = 55$, 75.0% vs. 57%).

Conclusion: This was the first nationwide survey on massive transfusion practices in the Netherlands. There is clear uniformity when it comes to using an MTP. Logistics surrounding plasma availability or plasma thawing capacity did not influence MTPs. Nevertheless, there seems to be substantial interest in a ready-to-use plasma product, especially in hospitals with limited plasma use.

Abbreviations: MTP, massive transfusion protocol; MEC, medical ethics Committee.

1 | INTRODUCTION

Acute massive blood loss is a life-threatening condition, and massive hemorrhage accounts for 30%–40% of trauma mortality.[1] The transfusion strategy for massive hemorrhage is often incorporated in massive transfusion protocols (MTPs), guiding the treating physician. Studies have shown that the use of an MTP leads to improved outcomes.[2–4] Since laboratory findings are not available in the most acute phase of trauma transfusion, balanced transfusion using a fixed ratio of transfusion products is initially advised.

In 2011, the Netherlands introduced their first national guideline on massive transfusion. These guidelines have been kept up to date in conformity with improved insights. The current (inter)national guideline advises transfusing a maximum of two units of erythrocytes for every one unit of plasma.[5] However, in recent studies, a 1:1 ratio of erythrocyte/plasma units shows potential clinical benefit, although some controversy still exists.[6] Ideally, all Dutch hospitals should adhere to the guidelines when formulating their massive transfusion strategy. However, studies show that there is some variety in how these guidelines are followed; in other words, (inter)national guidelines do not seem to translate into uniformity of MTPs.[7–9]

Although MTPs have been examined for level 1 trauma centers in the Netherlands, insight into transfusion policy in smaller hospitals is lacking.[8] To gain more understanding, a nationwide survey on massive transfusion policy in Dutch hospitals was performed. The main objective of this study was to create an overview of the current transfusion strategies used in Dutch hospitals in relation to the (inter)national guidelines.

Previous studies have shown that early plasma transfusion might result in a mortality benefit,[10,11] other investigations show that transfusion with the optimal transfusion ratio of different products is often not achieved.[12] Recently, Allen et al. concluded that thawed plasma availability allows for lower erythrocyte/plasma transfusion ratios,[13] in other words, having plasma readily available for transfusion leads to more plasma transfusion. From this, it could be deducted that logistical factors, such as plasma thawing capacity or thawed plasma availability, might influence clinical practice. It is unknown whether this is the case in Dutch hospitals. For this survey, we evaluated logistical capacity in relation to massive transfusion policy and product usage versus wastage.

Currently, in the Netherlands, there is no ready-to-use plasma product available, although surrounding countries have incorporated these products into their transfusion policy. This survey was also initiated to evaluate the possible interest in a ready-to-use plasma product.

2 | STUDY DESIGN AND METHODS

This study was reviewed by the medical ethics committee of the Erasmus Medical center under the MEC number MEC-2022-0063.

This cross-sectional questionnaire study was conducted between January and April 2022. A questionnaire was sent to all Dutch hospitals with transfusion capacity. Sanquin Blood Supply provided contact information for transfusion specialists in all hospitals. The hospitals were sent an e-mail request to fill out the online questionnaire. In the following months, two reminders were sent with a 2-week interval. Four weeks later, the nonresponding hospitals were contacted by phone to remind them of the questionnaire and answer any questions they had concerning participation.

2.1 | Survey content

The questionnaire contained a total of 24 questions divided into three sections and was written in Dutch. The questionnaire was developed by a consortium consisting of transfusion specialists from within the Erasmus Medical Center Rotterdam, the ministry of Defense, and Sanquin Blood Supply. The first section focused on general transfusion practices. The second section focused on the ratio of blood products used during massive transfusion. In the third section, hospitals were asked about the preparation of the transfusion products, how many transfusion products they use, and how many go to waste.

The online questionnaire was created using LimeSurvey (version 2.06 lts Build 160524). The usage of LimeSurvey as an application is authorized by the MEC of the Erasmus Medical Center.

2.2 | Data analysis

All responses were collected in LimeSurvey and exported to SPSS. Analysis was performed using SPSS version 28. For close-ended questions, descriptive statistics were used and are reported in numbers and percentages. Parameters were tested for differences using the Mann–Whitney U test, Student t test, or Chi-Squared test, when appropriate.

3 | RESULTS

Sixty-nine hospitals were approached. A total of 58 hospitals responded after three reminders (response rate 84%).

TABLE 1 Overview of transfusion component ratio as described in the massive transfusion protocols of hospitals in the Netherlands, erythrocyte/plasma unit ratio as described in the massive transfusion protocol of hospitals in the Netherlands.

Number of hospitals (*n*) and percentages (%)	
Transfusion ratio, erythrocytes: plasma: thrombocytes ($n = 58$)	
3:3:1	23 (40)
4:4:1	5 (9)
5:5:1	6 (10)
Other	24 (41)
Erythrocyte/plasma unit ratio ($n = 55$)	
<1	2 (4)
1	37 (67)
1–2	4 (7)
2	9 (16)
>2	3 (5)

TABLE 2 Mean erythrocyte/plasma unit ratio in relation to timing of plasma unit availability, number of hospitals with interest in a ready-to-use plasma product, number of hospitals with interest in a ready-to-use plasma product in relation to timing of plasma unit availability.

Number of hospitals (*n*) and percentages of total (%)	
Time to plasma availability	**Mean erythrocyte/plasma ratio (SD)**
Direct, $n = 8$ (15.7)	1.21 (0.40)
<15 min, $n = 5$ (9.8)	1.20 (0.45)
15–30 min, $n = 27$ (53.0)	1.46 (0.69)
>30 min, $n = 11$ (21.6)	1.07 (0.32)
Interest ready-to-use plasma product ($n = 58$)	
Yes	35 (60)
No	23 (40)
Thawed plasma available	**Interest ready-to-use plasma**
<15 min	8/14 (57)
>15 min	27/36 (75)

Sixteen surveys (28%) had missing values; these were primarily in the section of the questionnaire where the respondents were asked how many blood products are transfused on a yearly basis. These numbers were presumably not available to all respondents.

3.1 | Massive transfusion protocol

All responding hospitals used an MTP during massive transfusion (100%). In 16 hospitals (27.6%) there were different MTPs for adults and children. Although the MTP guided the caretakers in transfusion ratios, most hospitals ($n = 38$, 65.5%) used a form of point of care testing as soon as possible to achieve goal-directed transfusion.

3.2 | Transfusion ratios

Hospitals were asked to report on the transfusion products used during massive transfusion. The transfusion ratios were defined as follows: units of erythrocytes (270 mL)versus units of plasma (200 mL)versus units of thrombocytes (310 mL). Of note, standard thrombocyte transfusion in the Netherlands is available in 5-donor units. Three hospitals did not disclose the transfusion ratio. Twenty-three hospitals (40%) reported transfusing in a 3:3:1 ratio. Five hospitals (9%) used a 4:4:1 ratio, and six hospitals (10%) used a 5:5:1 ratio for transfusion. Among the remaining hospitals, transfusion ratios varied (Table 1). Most hospitals (67%, $n = 37$) transfused equal units of plasma and erythrocytes (1:1), including 11 of the 12 level 1 trauma centers. Three hospitals (5%) reported a ratio higher than the advised maximum of two units of erythrocytes for every unit of plasma. These hospitals did neither comply with the Dutch National guidelines nor with European guidelines (Table 1). All but one hospital initiated their trauma transfusion with erythrocytes; however, four hospitals claimed they would initiate transfusion with plasma if it was readily available ($n = 5$, 10%).

We hypothesized that the plasma handling capacity might influence transfusion strategy. To examine a relation between plasma availability and erythrocyte/plasma transfusion ratio, we questioned hospitals on the time it takes to have plasma available for transfusion. Eight hospitals (15.7%) reported having thawed plasma (which can be stored for 5 days at 4°C) readily available for transfusion. All these hospitals carry a level 1 status for trauma care. Five hospitals (9.8%) reported having plasma ready within 15 min, and 27 hospitals within 30 min (53.0%). For the remaining hospitals (21.6%, $n = 11$) it takes longer than 30 min to have plasma available for transfusion. We found no relation between plasma availability and the erythrocyte/plasma ratio described in the MTP (Table 2).

Thirty-five hospitals (60%) claimed to be interested in incorporating a ready-to-use plasma product into their transfusion strategy. We found that hospitals that take >15 min to have plasma available for transfusion generally were more interested in a new plasma product compared with the hospitals that have plasma ready for transfusion within 15 min ($n = 55$, 75.0% vs. 57%) (Table 2).

TABLE 3 Total number of transfusion products transfused/wasted in 2019, percentage of product wastage in relation to direct plasma unit availability, mean total number of plasma unit transfusions in 2019 per hospital in relation to direct plasma unit availability.

Transfusions in 2019		
Units of erythrocytes	Number of units	Percentage of wastage
Transfused	266,664	1.21%
Not transfused	4244	
Units of plasma		
Transfused	34,393	7.41%
Not transfused	2155	
Units of thrombocytes		
Transfused	42,930	6.55%
Not transfused	2141	
Thawed plasma directly available		**% plasma wastage (SD)**
Yes ($n = 8$)		7.44 (7.9)
No ($n = 28$)		7.30 (4.8)
Thawed plasma directly available	**Mean number of plasma transfusions (SD)**	
Yes ($n = 8$)	1929 (1325)	$p = 0.005$
No ($n = 34$)	881 (1231)	

Apart from the logistical difficulties of thawing plasma, we suspected that having thawed plasma continuously available increased plasma wastage. To gain insight into the percentage of wastage, we asked the hospitals about the total number of transfusions in 2019 (baseline before COVID) and the number of units wasted. In total, 42 hospitals responded to this section of the questionnaire, reporting in total more than 300.000 transfusions. The percentage of discarded units of erythrocytes was 1.2%. The percentage of discarded plasma units was 7.4%, that is, plasma is six times more likely to get wasted compared with erythrocytes. There was no relation between having thawed plasma readily available and the percentage of plasma wasted. There was, however, a significant relation between direct plasma availability and yearly number of transfusions, that is, the hospitals with direct plasma availability perform significantly more transfusions than the hospitals without direct plasma availability (Table 3).

4 | DISCUSSION

The main objective of this survey was to create an overview of the massive transfusion policy of all Dutch hospitals, resulting in a better understanding of the current massive transfusion strategies in the Netherlands. Moreover, the survey allowed us to examine whether uniformity exists in MTPs and if (inter)national guidelines are followed. The Netherlands only has access to a frozen plasma product; we therefore hypothesized that logistics around thawed plasma availability might influence the MTPs and that the introduction of a ready-to-use plasma product into the Dutch transfusion strategy might be valuable.

Our survey showed that 2 out of 3 hospitals transfuse with equal units of erythrocytes and plasma. This shows a relative consensus within the nation. Moreover, when comparing the hospitals that are most often presented with massive trauma transfusion, that is, the level 1 trauma centers, all but 1 strived for the 1:1 erythrocyte/plasma ratio.

Achieving a 1:1 erythrocyte/plasma ratio in a massive transfusion scenario is often difficult because of limited plasma availability.[13] Aiming for a 1:1 transfusion puts great pressure on the transfusion laboratory of a hospital. We hypothesized that the plasma thawing capacity might be related to the transfusion ratio aimed for; in other words, the protocol would have been written with the thawing capacity in mind. However, our survey showed no relation between thawing capacity and the transfusion ratio aimed for. From this, it could be concluded that the transfusion system of the Dutch hospitals is in order and clinical decisions are not guided by logistics in this case. However, since we did not evaluate actual transfusion cases, it might also be possible that, although the protocol advises it, in practice the 1:1 erythrocyte/plasma ratio is often not achieved due to logistical difficulties.

Rijnhout et al. investigated the massive transfusion policy in level 1 trauma centers in the Netherlands in 2017–2018. They concluded that there was little uniformity in transfusion practices, the ratio of transfusion products differed regularly from the 3:3:1 guideline, and nearly every level 1 trauma center had a different erythrocyte/platelet ratio disclosed within their MTP.[8] In the current study, we found uniformity in transfusion ratios for level 1 trauma centers, indicating that a 3:3:1 ratio is now more accepted. However, the international guideline of a 1:1 ratio is based on volume suppletion with 270 mL of erythrocytes ±300 mL of fresh frozen plasma. Since the Dutch system only supplies plasma units of 200 mL, the Dutch 1:1 erythrocyte/plasma ratio is based on a lower volume plasma. One could therefore argue that in this case, the 1:1 ratio is still too high in erythrocytes, and a 1:1.5 erythrocyte/plasma ratio would be more in line with the advised ratios.

This is the first survey investigating all Dutch hospitals. In the past, the smaller hospitals have been

overlooked since they do not encounter the massive transfusion scenario often. However, one could argue that the MTPs in these hospitals might be more important than in the larger level 1 hospitals since the experience with massive transfusion is limited and having a protocol for these rare situations guides the clinician through the unusual scene. Therefore, the fact that 5% of the responding hospitals did not adhere to (inter)national guidelines in their MTP, accepting erythrocyte/plasma ratios higher than 2:1, requires attention, especially when considering the transfused volumes. In the acute phase of massive transfusion, it is often difficult to obtain adequate transfusion ratio's, even if one aims to achieve the 1:1 ratio. Having an MTP which advises a erythrocyte/plasma ratio of >2:1, could result in even higher ratio's, leading to a potentially worse outcome. It is the hope that since the survey was performed, these hospitals have updated their MTPs in conformity with the guidelines.

We found that the average waste of plasma was approximately six times higher than the waste of erythrocytes. Although the Dutch national blood bank has created a reliable inflow of transfusion products and there is rarely a shortage, any unnecessary wastage should be avoided. Over 1/13 plasma units were thrown away in 2019, suggesting there is room for improvement. We hypothesized that having thawed plasma continuously available might lead to a higher percentage of wastage, but we did not find a relation between thawed plasma availability and plasma wastage. What we did find was a relation between direct plasma availability and the yearly number of transfusions; in other words, the hospitals with direct plasma availability perform more transfusions. These hospitals apparently have a successful system in place where thawed plasma is used before it expires, thereby hampering plasma wastage. Nevertheless, it is impossible to erase the massive transfusion scenario as an important factor in plasma wastage. The urgent setting leads to uncertain transfusion needs, and therefore units are often ordered but not transfused. This affects plasma more than erythrocytes because the long thawing time leads to more liberal ordering and therefore more wastage. A ready-to-use plasma product might in this case lower wastage, as the direct availability makes liberal ordering unnecessary.

We dedicated a section of our questionnaire to evaluate the interest in a ready-to-use plasma product. Currently, there are several types of dried plasma products in development, and in many countries, a freeze-dried plasma product has been introduced, but not in the Netherlands.[14,15] In 2023, a new product was approved by the EMA, and this product is expected to become available in the upcoming year.[16] When comparing freeze-dried plasma to conventional plasma products, there are some clear logistical advantages. The stability at room temperature and the rapid reconstitution (<10 min) lead to the popularity of freeze-dried plasma in the prehospital setting and during early in-hospital treatment. In vitro studies have shown that the hemostatic potential is comparable with frozen plasma products, and although currently strong evidence is lacking for a clinical benefit, several countries have incorporated a freeze-dried plasma product into their clinical practice.

We found that 60% of the respondents were interested in incorporating a ready-to-use plasma product into their transfusion strategy. Hospitals that did not have plasma available for transfusion within 15 min were more likely to be interested in the ready-to-use plasma product than the hospitals with early plasma availability. This suggests that the frozen plasma is sometimes not available in a timely fashion in these hospitals, demonstrating the logistical challenges when using a frozen plasma product. Taken together, the results from this survey show support for the introduction of a ready-to-use plasma product in the Netherlands.

This was the first nationwide survey on massive transfusion practices in the Netherlands. There is uniformity when it comes to using an MTP to guide clinical practice and the ≤2:1 erythrocyte/plasma transfusion ratios used in the MTP. Logistics surrounding plasma availability and plasma thawing capacity do not influence MTPs; moreover, direct plasma availability did not increase plasma wastage. Nevertheless, there seems to be substantial interest in a ready-to-use plasma product, especially in low-volume hospitals with limited plasma usage.

4.1 | Strength and limitations

This survey allowed us to critically analyze the current Dutch massive transfusion practice in relation to the (inter)national guidelines. Through several reminders, we managed to achieve a high response rate, ensuring that the results we gathered were a true reflection of transfusion practices in the Netherlands.

Nevertheless, this study has a few potential limitations. Data collected through questionnaires comes with a risk of bias. Misinterpretation must be considered. Another point of discussion, regarding the opinionated questions, could be whether a self-reported answer by a specialist is valid and can rightfully represent the hospital for which he/she is corresponding. Moreover, although all the contacted people were transfusion specialists, we did not confirm if they had the knowledge on the clinical situation in their hospital. It is possible that some of the information supplied was therefore biased by the respondents. Nevertheless, the questions concerning the

protocol and the number of transfusions were not a matter of opinion and are therefore not up for interpretation.

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ORCID

M. ter Horst https://orcid.org/0000-0002-4990-4620
F. Noorman https://orcid.org/0000-0002-4891-2047
N. A. Ottenhof https://orcid.org/0009-0004-3713-4747

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