The practice of platelet transfusion prior to central venous catheterization in presence of coagulopathy: a national survey among clinicians

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Background Correction of coagulopathy prior to central venous catheter (CVC) placement is advocated by guidelines, while retrospective studies support restrictive use of transfusion products.

Study Design and Methods We conducted a mixed vignette and questionnaire web survey to investigate current practice and preferences for CVC placement. Clinical vignettes were used to quantify the tendency to administer platelet concentrate. A positive β-coefficient is in favour of administering platelet concentrate.

Results Ninety-seven physicians answered the survey questions (36 critical care physicians, 14 haematologists, 20 radiologists and 27 anaesthesiologists). Eighty-six physicians subsequently completed the clinical vignettes (response rate 71%). Preferences in favour of correcting thrombocytopenia prior CVC placement were platelet counts of $10^9$ to $20^9/L$ ($β = 3.9; β = 3.2$, respectively), the subclavian insertion site ($β = 0.8$). An elevated INR (INR = 3; $β = 0.6$) and an elevated aPTT (aPTT = 60 s; $β = 0.4$) showed a positive trend towards platelet transfusion. Platelet transfusion was less likely in an emergency setting ($β = -0.4$). Reported transfusion thresholds for CVC placement varied from $<10^9/L$ to $80^9/L$ for platelet count, from 1.0 to 10.0 for INR and from 25 s to 150 s for aPTT. Implementation of ultrasound guidance as standard practice was limited.

Conclusion Current transfusion practice prior to CVC placement is highly variable. Physicians adjust the decision to correct coagulopathy prior CVC placement based on clinical parameters, insertion site and technique applied.

Key words: bleeding, central venous catheter, coagulopathy, platelets, trombocytopenia, transfusion.

Introduction

Central venous catheters (CVCs) provide vascular access, which enables blood sampling, haemodynamic monitoring, haemodialysis and the administration of medication, fluids and parenteral nutrition. Although pivotal for treatment, CVC placement may cause serious complications, including pneumothorax, incorrect position, haemothorax and catheter-related bloodstream infection [1–4]. Patient and procedural characteristics, such as catheter insertion site, insertion technique and the presence of coagulopathy influence peri-procedural complications.
The use of real-time ultrasound during CVC insertion reduces the amount of complications compared to the traditional method based on anatomical landmarks [5]. Ultrasound guidance leads to fewer complications by reducing the number of unsuccessful placements, puncture attempts, haematomas, inadvertent arterial punctures and the time to placement [5–9]. Despite this evidence supporting ultrasonography for central venous cannulation, various authors showed limited implementation of real-time ultrasonography [10–13]. This study presents the first survey among Dutch physicians.

Central veins commonly used for cannulation are the internal jugular vein, the subclavian vein and the femoral vein. Catheter site selection is based on the preference of the physician- and patient-related factors. A catheter located on the chest is more is more comfortable for ambulant patients as compared to the neck and groin region. The femoral vein is often presumed to have a higher infection rate, although the literature does not support that the amount of catheter-related bloodstream infections differs per site [14]. The internal jugular vein and femoral vein are relatively superficially located, allowing manual compression in case of a postprocedural bleeding. These factors may play a role in catheter site selection in patients with coagulopathy. We assumed that physicians adjust their preference for access site on the above-mentioned clinical parameters. If patient-related factors result in a strong preference for a specific insertion site, physicians may choose to accept possible disadvantages of that insertion site.

Patients in need for CVC frequently suffer from haemostatic disorders. In patients with coagulopathy, physicians are often hesitant to insert a CVC due to the perceived increased risk of bleeding. Based on guidelines, coagulopathy was defined as abnormal classical coagulation tests (i.e. aPTT >1.5 ULN and INR >1.5) or a reduced platelet count (platelet count <50×10^9/L) in this study [15–18].

Only limited evidence on the minimal preprocedural platelet count prior to central venous catheter placement is available. Classical coagulation tests, including PT, INR and platelet count, are poor predictors of bleeding complications after CVC placement [19–21]. The minimal platelet count in which a CVC can safely be inserted remains a matter of debate [19]. Current guidelines are based on very low-quality evidence. Different guidelines contradict and support correction of a platelet count varying from 20 to 50×10^9/L. Recent evidence suggests that ultrasound-guided CVC placement can safely be performed up to an uncorrected platelet count of 20×10^9/L [23]. Little is known about how this has influenced current practice. Data on physician’s attitude towards the correction of thrombocytopenia prior to CVC placements and preferences on CVC placement in presence of coagulopathy are lacking.

This study aimed to designate factors that influence the clinical decision to transfuse platelets prior to central venous catheter insertion. This gives insight into the current transfusion practice and factors influencing the decision to transfuse platelets prophylactically. This can provide direction for expert-based guidelines and might reveal possible targets for the reduction of the use of transfusion products.

Materials and methods

Setting

We contacted the chiefs of the departments of critical care, haematology, (interventional) radiology and anaesthesiology for participation in this study. Hospitals were included if an intensive care unit with five or more beds equipped for mechanical ventilation was present (N = 64). Chiefs were requested to indicate the physician in their department who was most experienced with central venous catheters and coagulopathy. An email invitation with a brief introduction on the aim of the study was sent to this physician. If either the chief or the designated physician did not respond, at least two reminders were sent.

The survey

The questions in the survey were assigned in a fixed order. (The complete Survey Questionnaire and Clinical vignettes are provided in Appendix S1.) The survey began with characteristics of the physician, after which questions about current practice and preference on central venous catheter placement in the various centres were asked. Subsequently, local practice for transfusion triggers and policy were surveyed. Thereafter, the sixteen vignettes were posed. Finally, respondents were asked to indicate whether they support the national guideline that advocates correction of a platelet count below 50×10^9/L prior to CVC placement. Space for a write-in was available.

To pretest the survey, an independent representative of each specialty was asked to assess the survey questions for clarity and consistency. The content of the survey was not altered after this consultation.

The questions and vignettes were hosted on Survey Monkey® (http://www.surveymonkey.com). A bar representing progress in the survey was displayed. The survey could be paused and resumed at all times. The survey was opened between November 2015 and April 2016.
Vignettes

A vignette is a brief hypothetical scenario that provides information for participants to have an understanding of the scenario being depicted, asking how they would react in the given situation. Vignette-based surveys are particularly useful in the quantitative study of attitudes and preferences [24]. This method was validated to assess physician practice variation in clinical decision-making [25]. Physicians were asked to express their tendency to administer platelet concentrate with different combinations of factors. Vignettes were used to identify clinical factors that contribute to the decision to administer prophylactic platelets prior to CVC placement.

Elements that could influence the tendency to transfuse prophylactic platelets prior to central venous catheter placement were identified through previous studies and the clinical expertise of the authors. Risk factors for bleeding were presumed to influence the clinical decision to administer prophylactic platelet transfusion. Factors were divided into laboratory-, patient-, catheter- and procedure-related risk factors. Laboratory risk factors included classical coagulation parameters, for example platelet count, aPTT and PT [20, 26–28]. Insertion site has been reported to influence bleeding complications. The femoral access site carries the largest risk of mechanical complications [29]. Subclavian catheterization is more likely to be complicated by haemothorax as compared to the internal jugular site [29]. We postulated that the absent possibility to apply manual compression on the subclavian site would improve the likelihood to transfuse prophylactic platelets, as compared to the femoral and jugular site.

To enhance feasibility, factors were reduced based on interdisciplinary consensus (Table S1. Patient and catheter related factors that were presumed to be considered before administering platelet concentrate prior to CVC placement). Six factors remained after assessment for clinical relevance by a critical care physician, a haematologist and an interventional radiologist. The levels of the determinants were based on agreement. The factors and levels implemented in the vignettes are displayed in Table 1. Two factors with three levels and four factors with two levels were embedded in the survey. A full factorial design would require 144 vignettes, which is not feasible. Therefore, the number of representative clinical vignettes was reduced to 16 using an orthogonal main effects design (SPSS Version 22, SPSS, Inc., Chicago, IL) [24, 30]. Respondents were asked to rate the extent to which they were inclined to administer prophylactic platelet concentrate. A Likert scale was used ranging from 0 (totally disagree) to 7 (totally agree) to answer the following question: “Would you administer platelet concentrate prior to central venous catheter placement?” (Appendix S1. The Survey Questionnaire and Clinical vignettes).

Statistical analysis

Parametric data were expressed as medians with ranges, nonparametric data as means with standard deviations. Categorical variables were expressed as n [%]. To test groups of continuous normally distributed variables, Student’s t-test was used or, when more than two independent groups were involved, the ANOVA analysis. Likewise, if continuous data were not normally distributed, the Mann–Whitney U-test was used or the Kruskal–Wallis test to compare three or more groups. Categorical variables were compared with the Chi-square test or Fisher’s exact tests when appropriate. A P-value of less than 0.05 was considered to be significant. To correct for multiple testing, tests were followed by Bonferroni post-test. For the Kruskal–Wallis test, the incorporated Bonferroni post-test was using SPSS software. For the Chi-square test, with 12 tests, an adjusted P-value of 0.004 was considered to be significant.

The preferences for the vignettes were expressed as utilities. To test internal consistency, Cronbach’s α was determined for the clinical vignettes. Conjoint analysis was performed to calculate the relative weights for each level of the factor levels. This resulted in a utility score (common unit) for each factor level expressed as β with 95% confidence interval. The β value represents the direction of the preference and its effect size. Higher values indicate greater preference. Negative β values indicate preferences against the positive direction of the statement, that is against the administration of prophylactic platelet concentrate. The utility for a particular factor level is determined by multiplying the β with the defined factor category, that is one times β, two times β depending on the number of levels per factor. Analyses were carried out using SPSS software (Version 22, SPSS, Inc., Chicago, IL).

Table 1 Factors and levels implemented in the vignette

| Factor                          | Level                                      |
|---------------------------------|--------------------------------------------|
| 1. Severity of thrombocytopenia | Platelet count of $10^9$, $20 	imes 10^9$ or $50 	imes 10^9$ |
| 2. INR                          | 1.5 or 3                                   |
| 3. aPTT                         | 30 s or 60 s                               |
| 4. Location                     | Jugular, femoral or subclavian vein        |
| 5. Setting                      | Emergency or elective                      |
| 6. Insertion technique          | Ultrasound-guided or landmark              |

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Results

Chiefs of 122 departments gave consent for participation in the study. Of the 122 questionnaires sent, 97 physicians completed the questionnaire (response rate 80%). The responding physicians represented the fields of critical care \((N = 36)\), anaesthesiology \((N = 27)\), radiology \((N = 20)\) and haematology \((N = 14)\). The physicians were employed in 54 hospitals. A total of 86 physicians completed the vignettes (response rate 71%). Characteristics of the responding physicians are listed in Table 2. No differences in age and years of experience per specialty were present. The responding haematologists worked more frequently in academic hospitals, compared to the respondents of other specialties.

Questionnaire

Site of insertion

The first set of questions investigated current practice and preferences for central venous catheter placement. The respondents were asked to indicate their preferences for CVC insertion site (Table 3). The jugular vein was most frequently preferred (54%), followed by the subclavian vein (37%), and the femoral vein (3%); 5% of the respondents did not have a general preference for insertion site. The preferences for insertion site per discipline are displayed in Table 4. Haematologists differed significantly from radiologists and anaesthesiologists, and preferred the subclavian and femoral site more frequently (Adjusted Residual of \(-2.7\) for jugular site, \(P < 0.05\)). The majority of respondents (92%) believed an association between catheter location and catheter-related bloodstream infections exists. Most respondents considered the femoral vein to be at most risk for infection.

Physicians adjusted their preferences based on clinical parameters. If the catheter was expected to be in place for at least 5 days, the subclavian vein was preferred over the femoral and jugular site. In case of chemotherapy, the subclavian vein was preferred more frequently. No differences were found if the indication for CVC was haemodialysis (CVVH). In patients with increased bleeding tendency, the jugular and femoral vein were chosen above the subclavian vein.

Landmark versus Ultrasound

The disciplines varied in the use of ultrasound for CVC placement. 86% of physicians performed central venous catheter placement in the previous year. All radiologists used ultrasound at all times, which differed from the other specialties (adjusted residual 5.2, \(P < 0.01\)). Only a minority of critical care physicians (39%), anaesthesiologists (26%) and haematologists (14%) used ultrasound at all times. Almost a third of haematologists (29%), 17% of critical care physicians and 11% of anaesthesiologists never used ultrasound for CVC placement. Disciplinary differences in the use of ultrasound are displayed in Fig. 1. The physicians that always used ultrasound had a preference for the jugular site (Adjusted residual 4.0, \(P < 0.01\)). Contrastingly, physicians with a preference for the subclavian site made less use of ultrasound as compared to the other preferences (Adjusted residual \(-3.5\), \(P < 0.05\)).

Correction of coagulopathy

The questionnaire revealed that interdisciplinary differences in triggers for correction of coagulopathy are present. The intensive care physicians had a more restrictive transfusion policy for platelet count and INR as compared to all other surveyed medical specialists (Kruskal Wallis

Table 2 Characteristics of responding physicians

| Medical specialty | Critical care \((n = 36)\) | Haematology \((n = 14)\) | Radiology \((n = 20)\) | Anaesthesiology \((n = 27)\) | Total \((n = 97)\) |
|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age (SD)         | 44 ± 7          | 46 ± 14         | 47 ± 19         | 47 ± 7          | 46 ± 7          |
| Years of experience % |
| 0–5              | 25              | 14              | 15              | 7               | 17              |
| 6–10             | 44              | 43              | 30              | 22              | 35              |
| 11–15            | 11              | 5               | 30              | 30              | 16              |
| 16–20            | 11              | 7               | 20              | 8               | 11              |
| >20              | 8               | 14              | 30              | 33              | 21              |
| Hospital         |                 |                 |                 |                 |                 |
| Academic         | 17              | 57*             | 20              | 15              | 28              |
| Non-academic     | 83              | 43              | 80              | 85              | 72              |

These numbers represent the lowest platelet count, maximum aPTT and maximum INR that was prior to CVC placement, without preprocedural correction of haemostasis with blood products.

*Haematologists more frequently worked in an academic centre as compared to other medical specialties, difference significant at the 0.05 level.
test, \( P = 0.047 \) and \( P = 0.045 \), respectively). Furthermore, platelet transfusion practice varied among physicians. Of the respondents, 46% indicated to correct a platelet count of \( 30–50 \times 10^9/L \). This amount increased to 64% of physicians for a platelet count between \( 10–30 \times 10^9/L \). Haematologists corrected a low platelet count more frequently compared to the other surveyed disciplines. Only a minority of physicians stated to transfuse platelet concentrate if the patient uses a single platelet inhibitor (2%). This number increased to 17% if a patient uses double platelet aggregation. If thrombocytopenia is corrected prior to CVC placement, 63% of physicians stated to administer a fixed amount of one unit pooled donor platelet concentrate, while 38% indicated to determine the amount of transfused platelets based on platelet increment. Platelet increment was measured by 51% of physicians.

### Bleeding complications

Of the surveyed physicians, 26% had seen at least one central venous catheter-related bleeding complication in the previous year, resulting in a total of 37 bleeding events (range 0–5). Two of these bleeding events occurred in patients with a platelet count below \( 50 \times 10^9/L \).

### Vignette

The relative preferences of all disciplines in favour of administering prophylactic platelet transfusion prior to central venous catheterization are shown in Fig. 2. The platelet count was the most important factor that contributed to the decision to administer platelet concentrate. A platelet count of \( 10 \times 10^9/L \) was a stronger positive preference for administering platelet concentrate (\( \beta = 3.9 \) [3.7–4.3] vs. neutral) than a platelet count of \( 20 \times 10^9/L \) (\( \beta = 3.2 \) [2.9–3.5] vs. neutral). The subclavian site had a positive preference for transfusion (\( \beta = 0.8 \) [0.5–1.1] vs neutral). In contrast, the femoral insertion site showed a negative trend for the administration of platelet concentrate (\( \beta = -0.2 \) [0.5–0.06] vs neutral). A central venous line in an emergency setting was a negative determinant for platelet transfusion as compared to an elective setting (\( \beta = -0.4 \) [0.6–0.2] vs neutral). A patient with an INR of 3.0 showed a positive trend for platelet transfusion as

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**Table 3** Laboratory thresholds for correction of haemostasis per specialty

| Medical specialty | Critical care | Haematology | Radiology | Anaesthesiology | Total |
|------------------|---------------|-------------|-----------|-----------------|-------|
| Platelet count   | 20 [10–60]*   | 40 [10–60]  | 50 [10–60]| 40 [10–80]     | 30 [10–80] |
| aPTT             | 60 [35–150]   | 40 [30–50]  | 45 [60]   | 50 [25–120]    | 50 [0–150] |
| PT (INR)         | 3 [1–10]*     | 1 5 [1–2 5]| 2 [1 5–2 5]| 2 [1 4–5]      | 2 [1–10] |

These numbers represent the lowest platelet count, maximum aPTT and maximum INR that was prior to CVC placement, without preprocedural correction of haemostasis with blood products.

*Critical care physicians had a lower platelet count threshold and higher INR threshold as compared to other medical specialties, mean difference significant at the 0.05 level.

**Table 4** Preferences for catheter insertion site

| Indicator | Subclavian vein | Internal jugular vein | Femoral vein | No preference |
|-----------|----------------|-----------------------|--------------|---------------|
| General preference (%) | 37 | 54 | 3 | 5 |
| Anaesthesiology | 26 | 70 | 0 | 4 |
| Critical Care | 50 | 47 | 0 | 3 |
| Haematology | 50 | 21* | 14 | 14 |
| Radiology | 13 | 73 | 7 | 7 |
| In increased bleeding tendency | 3 | 66 | 29 | 2* |
| Expected indwelling time >5 days | 61* | 33* | 2 | 3 |

*Haematologist had a negative preference for the IJV compared to other disciplines. \( P < 0.05 \).  
*In increased bleeding tendency, physicians less frequently had no preference \( P < 0.01 \).  
*For an expected indwelling time of >5 days, the SCV was preferred over the IJV and FV \( P < 0.05 \).  
*For chemotherapy, the SCV was preferred over the internal jugular vein \( P < 0.05 \).
compared to a patient with an INR of 1.5 (β = 0.6 [-0.2–1.4] vs neutral). Likewise, a patient with an aPTT of 60 showed a stronger positive trend for platelet concentrate than an aPTT of 30 (β = 0.4 [-0.4–1.2] vs neutral). The vignettes were reliable with a Cronbach’s α of 0.901.

**Discussion**

The main findings of this study are the following: (1) current transfusion practice prior to CVC placement is highly variable; (2) physicians adjust the decision to correct thrombocytopenia prior CVC placement based on clinical parameters, insertion site and technique applied; (3) despite proven superiority, the use of ultrasound is still not well implemented among all disciplines involved in CVC placement.

The decision to administer platelet concentrate was influenced by patient and procedural factors, such as insertion site and technique used. Physicians were more inclined to administer prophylactic platelet concentrate in patients with an elevated INR or APTT. However, it is known that plasmatic coagulation disorders are not corrected by platelet concentrate. Our results suggest that physicians take multiple risk factors into account and construct a ‘risk profile’ for bleeding. However, current guidelines set the indication for prophylactic platelet transfusion solely based on absolute platelet count. This might explain why a considerable fraction of physicians did not adhere to current guidelines on correction of coagulopathy prior to CVC placement. This is also in line with the finding that absolute platelet count is a poor predictor for
bleeding complications after central venous catheterization [19, 20].

The majority of physicians preferred the internal jugular vein as access site for CVC placement in presence of coagulopathy. However, haematologist preferred the subclavian site. An explanation for this may be that the subclavian site might give more patient comfort compared to the other sites. On the other hand, the subclavian vein cannot be manually compressed in case of bleeding and is more difficult to visualize using ultrasound, in contrast to the other access sites. In line with this, we showed that the catheter location influenced the decision to administer platelets. Consequently, physicians might adjust transfusion triggers based on the preferred catheter site and their ability to perform ultrasound-guided CVC placement. Hence, physicians may correct coagulopathy to allow catheter placement in the subclavian site.

Ultrasound guidance for CVC placement was not routinely used by all physicians, despite the proven superiority of ultrasound-guided CVC placement over the landmark technique [5–9]. We did not look into motives for the omission of ultrasound during insertion. In a previous survey among emergency physicians in the United States, insufficient training and lack of equipment were identified as top barriers for the use of ultrasound during CVC placement [31]. Other authors identified ‘no apparent need’ and limited availability of ultrasound equipment as important reasons not to use ultrasound [10, 12, 13].

It was striking to observe that the implementation of ultrasound was limited among critical care physicians, while critical care physicians were most restrictive with the use of blood products to correct coagulopathy. The restrictive policy may be explained by the increasing evidence on transfusion related morbidity in this patient population [32–34].

The vignettes showed a decreasing trend in the tendency to administer platelet concentrate if ultrasound was present during CVC placement. This is in line with retrospective studies that support a more restrictive transfusion policy, on the condition that CVC placement is performed by an experienced physician under ultrasound guidance [23, 35]. The finding that the use of ultrasound for CVC placement is lacking is important to generalize the results of such trials on the correction of coagulopathy prior to CVC placement. Currently, a randomized trial is conducted on omitting correction of severe thrombocytopenia prior to ultrasound-guided CVC placement, by well-trained physicians (PACER Trial, registered at http://www.trialregister.nl, registration number NTR5653). If this study concludes that it is safe to omit correction of coagulopathy prior to CVC placement, implementation of the routine use of ultrasound in coagulopathic patients is warranted. Before lowering transfusion thresholds prior to CVC placement, training and education on application of ultrasound is essential among disciplines involved in CVC placement.

Our study had several limitations. First, the four medical specialties treat partially distinct patient populations, with various illnesses. Age and years of experience did not differ between respondents of different specialties. However, haematologists more frequently worked in an academic hospital. This might have affected our results. Second, the questionnaire and clinical vignette used a fixed clinical scenario which may not have been representative for all disciplines which may have influenced the outcome. Our overall response rate was good, but we were not able to reach all Dutch hospitals with at least five beds equipped for mechanical ventilation. However, we believe that the high rate of respondents of all disciplines from academic hospitals, large teaching hospitals and small regional hospitals ensures that our study results are representative practice of CVC placement in the presence of coagulopathy.

In conclusion, physicians adjust the decision to correct coagulopathy prior CVC placement based on clinical parameters, insertion site and technique applied. Ultrasonographic guidance during CVC placement is not implemented as standard care for all disciplines. Current practice for preprocedural correction of haemostasis varied widely, with a trend towards a more restrictive transfusion policy. Well-designed studies are needed to determine the optimal transfusion trigger prior CVC placement in presence of coagulopathy.

Authorship
E.K.W., A.L.P., E.J.G., J.M.B., B.J.B., K.P.L. and A.P.V. designed the study. E.K.W., A.L.P., E.J.G. and A.P.J. performed the research and collected the data; E.K.W. and J.M.B. analysed the data; A.P.V. supervised the conduct of the study; E.K.W. and A.P.V. wrote the manuscript. All authors read and corrected the manuscript. All authors approved the final version of the manuscript.

Conflict of interest
The authors declare that they have no conflict of interest relevant to the manuscript submitted to Vox Sanguinis.

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Supporting information

Additional Supporting Information may be found online in the supporting information tab for this article.
Appendix S1 The Survey Questionnaire and Clinical vignettes.
Table S1 Patient and catheter related factors that were presumed to be considered before administering platelet concentrate prior to CVC placement.