Platelet Transfusion before CVC Placement in Patients with Thrombocytopenia

Key Article: *van Baarle FLF, van de Weerdt EK, van der Velden WJFM, et al. Platelet transfusion before CVC placement in patients with thrombocytopenia. N Engl J Med. 2023;388(21):1956-1965.*

Background

- Central venous catheter placement is a frequently performed procedure in critically ill patients in the ED requiring vasoactives, hypertonic solutions, hemodynamic monitoring, and occasionally for temporary renal replacement therapy.
- Thrombocytopenia along with other coagulopathies are also common, but evidence-based guidance about when to treat severe thrombocytopenia prior to central line placement is limited.
- Recommendations for platelet transfusion thresholds generally range from 20,000 – 50,000/mm^3 in current guidelines.
    - Just a reminder/clinical pearl: In general, one can expect 1 unit of apheresis platelets will generally increase the platelet count between 20-40k, so a transfusion threshold of 20k should get you to about the 50k mark
- Certainly, routine ultrasound use has decreased the rate of complications, but platelet transfusion in it of itself is not benign
    - Platelets have a very high antigen load, and transfusion can lead to a significant immune response, hypotension, infection, and acute lung injury.

Objective

- To evaluate whether the *omission of* platelet transfusion before central line placement in patients with a platelet count of 10k – 50k/mm would increase the risk of catheter-related bleeding.

Methods

- Unblinded, Randomized, controlled noninferiority trial
- Location: Hematology ward and ICUs of 10 hospitals in the Netherlands (academic and community)
- Patients
    - General Inclusion Criteria
        - Adults aged $\geq$ 18 years old
        - Thrombocytopenic with platelet count 10-50k within 24 hours of the procedure
        - Central lines were in place for > 24 hours
    - Excluded patients:
        - Receiving medical anticoagulant
        - History of congenital or acquired factor deficiency or bleeding risk
        - Spontaneous INR > 1.5, which was later increased to > 3 after 2/3 of trial events (because at an interim analysis, the trial team found evidence of safety at even at higher INR levels)

- Enrollment
  - 2 types of informed consent
    - Stable patients: traditional written informed consent
    - Critically ill patients: Deferred initially where central lines were placed emergently; After stabilization, the patient or their authorized representative was approached for approval
    - If the patient died prior to consent, they were included in the analyses
- **Procedure**: Ultrasound guided by an operator who has performed at least 50 central lines
  - **Central line was** placed 1 hour after randomization, included multiple sizes (including larger bore temporary HD catheters), at all major anatomic sites (IJ, subclavian, & femoral)
- **Intervention**: Randomized 1:1 to either no transfusion or a 1 unit prophylactic transfusion of platelet concentrate (which in general, is similar to a unit of apheresis platelets)

- **Primary outcome:** Occurrence of grade 2 or higher catheter-related bleeding within 24 hours of placement at 1 and 24 hours after the procedure was completed.

Table 1. CVC-Related Bleeding.*

Bleeding Grade	Definition
Grade 0	No bleeding
Grade 1	Oozing; hematoma; bleeding that results in <20 min of manual compression to stop
Grade 2	Bleeding that results in minor interventions to stop, such as prolonged manual compression (>20 min)
Grade 3	Bleeding that results in radiologic or elective operative intervention or red-cell transfusion without hemodynamic instability
Grade 4	Bleeding associated with severe hemodynamic instability (hypotension, defined as a decrease of >50 mm Hg or >50% in either systolic or diastolic blood pressure), with associated tachycardia (heart rate increase, >20% for 20 min) and resulting in increased red-cell transfusion or fatal bleeding

* CVC denotes central venous catheter.

- Secondary Outcomes
  - **Major bleeding:** Included grade 3 or 4 events
  - **Minor bleeding**: Grade 1 bleeding
  - Blood product transfusion within 24 hours of the procedure
  - Onset of transfusion related complications: Allergy, acute lung injury, etc.
  - Length of ICU stay, hospital stay, mortality, and costs
- Sample size:

- Power calculation: **196 patients in each group** to provide 80% power determine noninferiority of no-transfusion strategy with a one-sided alpha of 0.05

Results

- **393 patients included** of the final analysis of 411 patients enrolled
  - 3 patients withdrew consent after deferred enrollment
  - 20 patients were excluded after protocol violations, similar between groups
- Demographics were well matched between groups
  - Median age was about 58 years old
  - About 65% male
  - Median Platelet count prior to procedure was 30k
  - INR: 1.1
  - Hemoglobin > 8 g/dL
- **Location**: 60% ward patients, 40% ICU patients
- **Catheter types**: 80% CVC, 20% dialysis catheters
- **Site**: 50% Internal jugular, 40% subclavian, 10% femoral

- **There was a significant difference in the primary outcome:** Grade 2 – 4 bleeding
  - Transfusion group: 9 events in 188 patients (4.8%)
  - No-Transfusion group: 22 events in 185 patients (11.9%)
  - Transfusion group had a 7.1% lower absolute risk (90% Confidence interval of 1.3 – 17.8) which equates to a 2.45 relative risk reduction in bleeding events for the transfusion group (90% CI: 1.27 – 4.70)
- **Secondary Outcomes & subgroup analyses**
  - Risk of Grade 3 or 4 bleeding complications was lower in the transfusion group (2.1% vs. 4.9%)
  - No grade 4 bleeding complications in either group

  - ***Central Line Location*****:** appears that the subclavian vein site had the most bleeding events (2/71 v 13/70), all other sites were similar
  - Highest incidence of bleeding were in ward patients with platelet counts of 10-20k
  - **Transfusion Complications**: 3 allergic reactions and 1 acute lung injury event recorded

Limitations Identified by the Authors

- Clinical providers were not blinded to the patient randomization, but effort was taken to try and keep the operator blinded as much as possible
- Platelet response to transfusion was not checked, so can't be sure whether platelet count sufficiently rose to a specific minimum threshold

Author conclusions

- In patients with Severe Thrombocytopenia (10-50k), withholding prophylactic platelet transfusion before CVC placement was not inferior and resulted in more CVC-related bleeding.
- Decisions about platelet transfusions should still be individualized, but prophylactic transfusion should be considered in patients less thank 30k, especially floor patients.
- ICU patients may not need prophylactic platelet transfusions since they are so closely monitored

Subgroup of Bleeding Risk	Transfusion	No Transfusion	Relative Risk (90% or 95% CI)
	no. of events/total no. (%)		
Primary analysis	9/188 (4.9)	22/185 (11.9)	2.45 (1.27–4.70)
Type of catheter			
Tunneled	3/20 (15.0)	3/18 (16.7)	1.26 (0.25–6.34)
Nontunneled	6/168 (3.6)	18/167 (10.8)	3.01 (1.20–7.55)
Insertion site			
Internal jugular vein	7/93 (7.5)	6/93 (6.5)	0.93 (0.31–2.79)
Subclavian vein	2/71 (2.8)	13/70 (18.6)	6.19 (1.39–27.64)
Femoral vein	0/24	2/22 (9.1)	3.72 (0.38–36.52)
Department			
Hematology ward	6/108 (5.6)	18/104 (17.3)	2.99 (1.19–7.54)
Intensive care unit	3/80 (3.8)	4/81 (4.9)	1.36 (0.30–6.11)
Platelet count per mm^3			
10,000–19,000	7/45 (15.6)	9/41 (22.0)	1.30 (0.48–3.55)
20,000–29,000	0/46	8/51 (15.7)	7.53 (0.91–62.50)
30,000–39,000	1/59 (1.7)	3/51 (5.9)	3.90 (0.41–37.05)
40,000–50,000	1/38 (2.6)	2/42 (4.8)	1.68 (0.15–18.68)