Chapter 92
Approach to Thrombocytopenia in the ICU

92.1 Introduction

Thrombocytopenia, defined as a platelet count below 150×10^9/L, is a prevalent concern in the intensive care unit (ICU), affecting up to 41% of critically ill patients. The incidence varies significantly across different ICU settings—medical, surgical, cardiac—and among diverse patient demographics due to varying underlying conditions, interventions, and comorbidities. Thrombocytopenia is more than a laboratory anomaly; it is closely associated with adverse outcomes such as increased mortality, heightened bleeding risk, and a greater need for organ support therapies [1, 2] [Ref: Algorithm 92.1].

A systematic and nuanced approach is essential to promptly identify the etiology of thrombocytopenia, guide targeted management, and improve patient outcomes.

92.2 Confirm True Thrombocytopenia

- Rationale: Before initiating a workup, it is crucial to ensure that the thrombocytopenia is genuine and not an artifact (pseudothrombocytopenia).
- Key Considerations:
- Platelet Count Verification: Confirm that the platelet count is below 150×10^9/L.
- Exclude Pseudothrombocytopenia:
- Peripheral Smear Examination: Look for platelet clumping, giant platelets, or platelet satellitism, which may indicate laboratory artifacts.
- Repeat Testing: If clumping is observed, repeat the platelet count using a citrated or heparinized blood sample to eliminate EDTA-induced clumping.
- Management: If pseudothrombocytopenia is confirmed, no further investigation is needed.

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92.3 Evaluate Platelet Trajectory

- Rationale: Assessing the trend of platelet counts over time (platelet trajectory) provides valuable diagnostic and prognostic information.
- Key Considerations:
- Acute vs. Chronic Decline:
- Acute Drop (1–2 Days): Suggests conditions like disseminated intravascular coagulation (DIC), thrombotic microangiopathies (TMAs), or immune-mediated thrombocytopenias.
- Gradual Decline: May indicate bone marrow suppression, chronic liver disease, or sepsis.
- Predictive Value: Studies have shown that certain platelet trajectories correlate with increased mortality and morbidity. For instance, a persistent decline may predict worse outcomes.
- Action: Regular platelet count monitoring to detect significant changes and intervene promptly [3].

92.4 Explore Underlying Pathophysiological Mechanisms

- Rationale: Understanding the mechanisms leading to thrombocytopenia aids in narrowing down the differential diagnosis.
- Mechanisms Specific to ICU Patients:
- Decreased Production:
- Bone Marrow Suppression: Due to chemotherapy, radiation, severe infections, or infiltrative diseases like leukemia
- Nutritional Deficiencies: Vitamin B12 or folate deficiency impairs megakaryocyte function.
- Increased Consumption:
- DIC: Thrombin-mediated platelet activation leads to widespread microthrombi formation.
- Sepsis: Systemic inflammation accelerates platelet consumption.
- Extracellular Histones: Released during cell death, they can activate platelets and promote thrombosis.
- HELLP Syndrome (Hemolysis Elevated Liver Enzyme Low Platelet).
- Immune-Mediated Destruction:
- Heparin-Induced Thrombocytopenia (HIT): Antibodies against platelet factor 4-heparin complexes cause platelet activation and thrombosis.
- Immune Thrombocytopenic Purpura (ITP): Autoantibody-mediated platelet destruction.

- Drug-Induced Thrombocytopenia: Certain drugs can trigger immune-mediated platelet destruction.
  - Antimicrobials- Piperacillin, vancomycin, linezolid, trimethoprim/sulfamethoxazole, aztreonam.
  - Other- Phenytoin, Valproic acid, Aspirin, Ranitidine, Frusemide, Haloperidol.
- Thrombotic Microangiopathies (TMAs):
- Thrombotic Thrombocytopenic Purpura (TTP): Due to ADAMTS13 deficiency, leading to accumulation of ultra-large von Willebrand factor multimers and microthrombi.
- Hemolytic Uremic Syndrome (HUS): Often related to endothelial damage from shiga-toxin producing bacteria.
- Sequestration:
- Splenomegaly: Enlarged spleen traps platelets, reducing circulating counts.
- Portal Hypertension: Common in liver disease, leading to hypersplenism.
- Pseudothrombocytopenia:
- Laboratory Artifact: EDTA-induced platelet clumping falsely lowers automated platelet counts [4].

92.5 Detailed Etiological Framework

- Classification of Thrombocytopenia:
- Decreased Production:
- Bone Marrow Disorders: Aplastic anemia, myelodysplastic syndromes.
- Nutritional Deficiencies: B12, folate, iron.
- Increased Consumption:
- DIC, Sepsis, Massive Hemorrhage: Accelerated platelet use.
- Mechanical Devices: ECMO, intra-aortic balloon pumps causing platelet activation.
- Immune-Mediated Destruction:
- HIT, ITP, Drug-Induced Thrombocytopenia: Immune system targets platelets.
- Hemophagocytic Lymphohistiocytosis (HLH): Hyperinflammatory state causing phagocytosis of blood cells.
- Sequestration:
- Splenomegaly, Cirrhosis: Platelet pooling in an enlarged spleen.
- Pseudothrombocytopenia:
- Laboratory Artifacts: Platelet clumping in vitro.
- Rarer Causes:
- HLH: Consider in patients with persistent fever, cytopenias, organomegaly, and high ferritin levels.
- Drug-Induced Thrombocytopenia: Suspect in patients with new medications; common culprits include quinine, antibiotics, anticonvulsants.
- Other TMAs: Atypical HUS, often associated with complement pathway dysregulation.

92.6 Advanced Diagnostic Insights

- Peripheral Smear Evaluation:
- Microangiopathic Hemolysis: Presence of schistocytes indicates TMA or DIC.
- Giant Platelets: May suggest a myeloproliferative disorder or inherited platelet disorders.
- Laboratory Tests:
- Coagulation Profile: PT/INR, aPTT, fibrinogen, D-dimer for DIC assessment.
- ADAMTS13 Activity: Low levels (<10%) support TTP diagnosis.
- HIT Testing: ELISA for PF4-heparin antibodies and functional assays like serotonin release assay.
- Diagnostic Algorithms:
- DIC: Prolonged PT/INR, low fibrinogen, elevated D-dimer.
- TTP: Severe thrombocytopenia, microangiopathic hemolytic anemia, normal coagulation tests.
- HUS: Similar to TTP but often with renal failure; stool cultures may identify shiga-toxin.

92.7 Management Algorithm Enhancements

- Treat the Underlying Cause:
- Sepsis: Prompt antibiotic therapy, source control, supportive care.
- DIC: Address the trigger (e.g., infection, malignancy), replace coagulation factors cautiously.
- HIT: Discontinue heparin, initiate alternative anticoagulation (argatroban, bivalirudin).
- TTP: Urgent plasma exchange, steroids, and possibly rituximab.
- HUS: Supportive care; eculizumab for atypical HUS.
- HLH: Immunosuppressive therapy (steroids, etoposide), treat underlying infection or malignancy.
- Platelet Transfusion Guidelines:
- Prophylactic Transfusion:
- Counts $<10 \times 10^9$/L: Recommended to prevent spontaneous bleeding.
- Higher Thresholds: For patients with fever, sepsis, or coagulopathy, consider transfusion at $<20 \times 10^9$/L.
- Therapeutic Transfusion:
- Active Bleeding: Maintain platelet count $>50 \times 10^9$/L.
- Invasive Procedures:
- Major Surgery or Lumbar Puncture: Target $>50 \times 10^9$/L.
- Neurosurgery or Ophthalmic Surgery: Target $>100 \times 10^9$/L.
- Patients undergoing central line insertion: Target $>20 \times 10^9$ cells/L.
- Risks and Considerations:
- Transfusion Reactions: Allergic reactions, febrile nonhemolytic reactions.

- Alloimmunization: Reduced efficacy of future transfusions.
- Thrombosis Risk: In HIT or TTP; platelet transfusions may exacerbate thrombosis.
- Condition-Specific Management:
- Avoid Platelet Transfusion:
- HIT and TTP: Platelet transfusions are generally contraindicated unless life-threatening bleeding occurs.
- ECMO Patients:
- Anticoagulation Management: Balance between preventing circuit thrombosis and minimizing bleeding risk.
- Platelet Count Targets: Maintain platelet counts $>50 \times 10^9$/L to reduce bleeding complications [5].

92.8 Emerging Insights

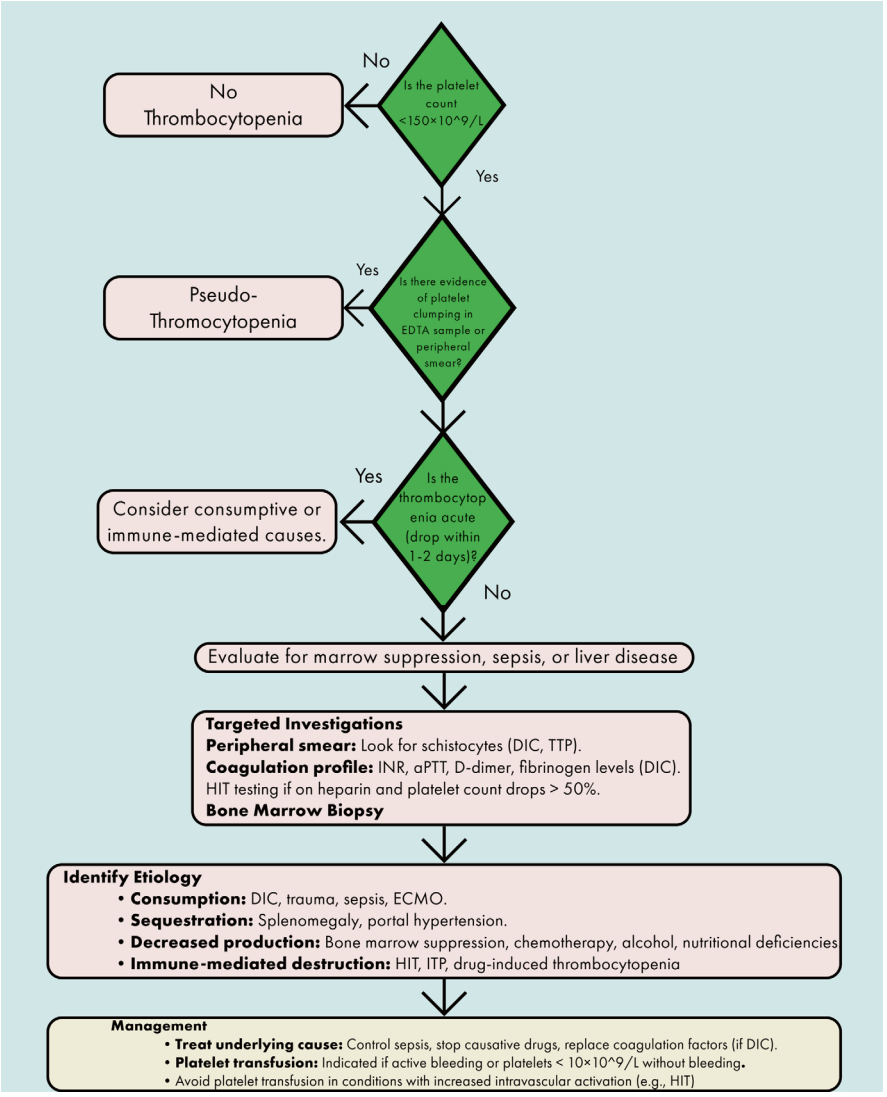
- Recent Studies:
- PLOT-ICU Study:
- Objective: Evaluated the efficacy and safety of prophylactic platelet transfusions in ICU patients.
- Findings: Restrictive transfusion strategy (transfusing at lower platelet counts) was non-inferior regarding bleeding events and reduced transfusion-related complications.
- Implications: Supports individualized transfusion strategies and reconsideration of transfusion thresholds.
- Ongoing Research:
- Novel Therapeutics: Agents targeting specific pathways like complement inhibitors in atypical HUS.
- Biomarkers: Identifying early detection and prognosis markers, such as elevated histone levels indicating endothelial damage.

92.9 Conclusion

Thrombocytopenia in the ICU represents a complex interplay of factors that can significantly impact patient outcomes. A comprehensive approach—starting from confirming true thrombocytopenia to exploring advanced diagnostic insights and understanding pathophysiological mechanisms—is essential for effective management. Incorporating recent evidence from studies like the PLOT-ICU trial and emerging therapies can refine treatment strategies.

Individualizing patient care by considering specific etiologies, severity, patient age, and comorbid conditions enhances the efficacy of interventions and minimizes risks. By staying abreast of emerging insights and maintaining a patient-centered focus, healthcare providers can improve survival rates and quality of care for critically ill patients with thrombocytopenia.

Algorithm 92.1: Approach to thrombocytopenia in the ICU



Bibliography

1. Anthon CT, Pene F, Perner A, Azoulay E, Puxty K, Van De Louw A, et al. Thrombocytopenia and platelet transfusions in ICU patients: an international inception cohort study (PLOT-ICU). Intensive Care Med. 2023;49(11):1327–38.
2. Patil KR, Patil RB. Approach to thrombocytopenia in ICU. In: Critical care hematology. Singapore: Springer; 2024. p. 75–85.
3. Vincent JL, Castro P, Hunt BJ, Jorres A, Praga M, Rojas-Suarez J, et al. Thrombocytopenia in the ICU: disseminated intravascular coagulation and thrombotic microangiopathies-what intensivists need to know. Crit Care. 2018;22(1):158.
4. Ostadi Z, Shadvar K, Sanaie S, Mahmoodpoor A, Saghaleini SH. Thrombocytopenia in the intensive care unit. Pak J Med Sci. 2019;35(1):282–7.
5. Greinacher A, Selleng S. How I evaluate and treat thrombocytopenia in the intensive care unit patient. Blood. 2016;128(26):3032–42.