Preoperative and Postoperative Consultation in Platelet Disorders

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Outlines

- **Platelet transfusion** for preparation for invasive procedures
- Before major surgery but **unable to benefit from platelet transfusion**
- **Liver disease** and thrombocytopenia
- **Inherited platelet function disorders** undergoing surgery
- Thrombocytopenia in **postoperative**
- Consultation in **thrombocytosis**

Preoperative Evaluation

- **Risk Stratification**
  - High vs. low bleeding risk procedures
  - Patient-specific risk factors (history, labs, previous bleeding events)
- **Laboratory Assessment**
- **Perioperative Management Strategies**

Platelet transfusion

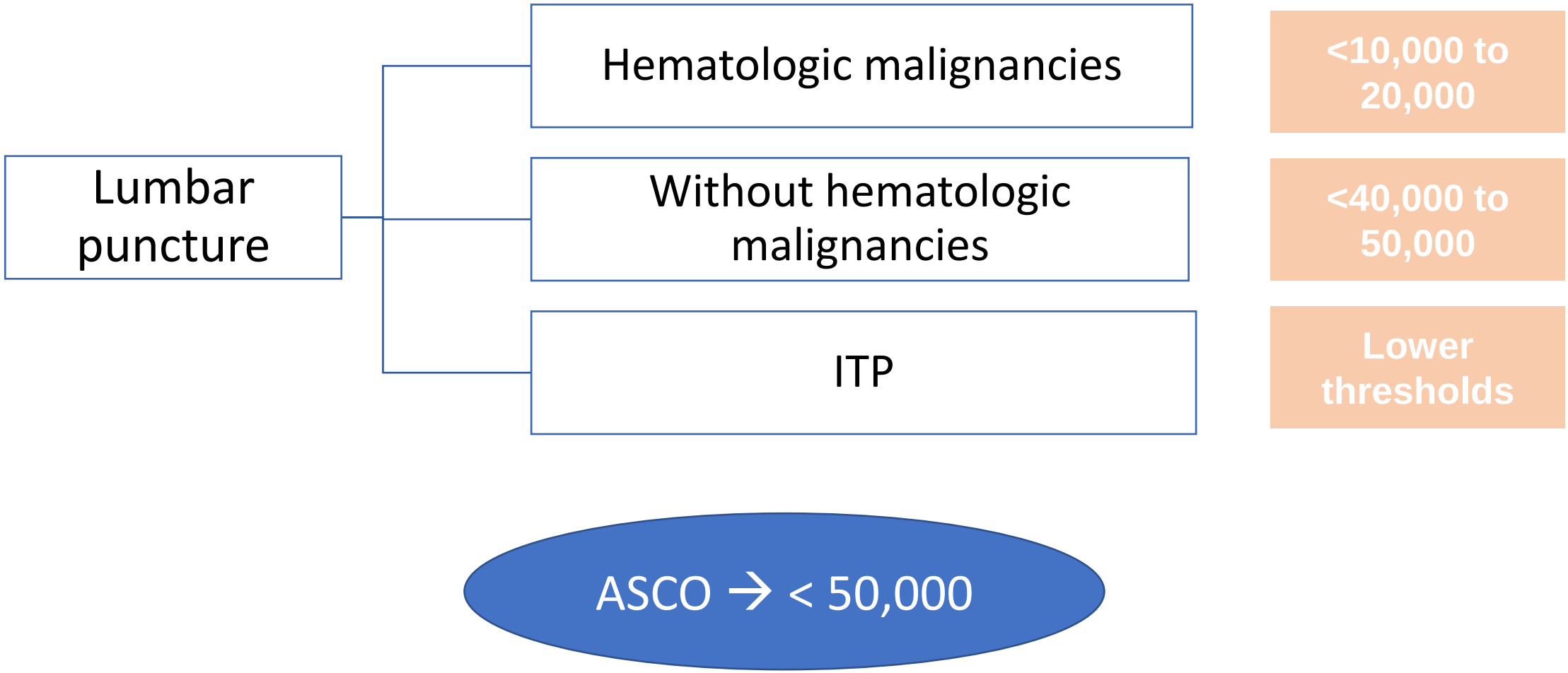
DDAVP

Antifibrinolytic

rFVIIa

TPO agonist

Procedures	Platelet threshold/microL
Neurosurgery or ocular surgery	< 100,000
Neuraxial analgesia/anesthesia	<80,000
Most other major surgery	<50,000
Endoscopic procedures (therapeutic)	<50,000
Endoscopic low risk diagnostic procedures	<20,000
Bronchoscopy with bronchoalveolar lavage (BAL)	<20,000 to 30,000
Central line placement	<20,000
BMA/BMB	<20,000


Lumbar puncture
Hematologic malignancies
Without hematologic malignancies
ITP
<10,000 to 20,000
<40,000 to 50,000
Lower thresholds
ASCO → < 50,000

What if patient is unable to benefit from platelet transfusion due to alloimmunization or religious belief

- **TPO receptor agonists** may play a role in providing adequate platelet counts

Al-Samkari H, Marshall AL, Goodarzi K, Kuter DJ. Romiplostim for the management of perioperative thrombocytopenia. Br J Haematol 2018

- ***Romiplostim*** may be appropriate for some patients with platelet counts < 50,000

- While concerns regarding the possible exacerbation of thromboembolic disease remain, especially for patients with underlying thrombophilia and/or thrombosis, few were reported

- Dosage : **2 to 3 mcg/kg** once per week from **two to four weeks** prior to surgery

Types of thrombopoietin

First-generation thrombopoietins
rHuTPO (tpiao)
PEG-rHuMGDF
Second-generation thrombopoietins
Peptide TPO receptor agonists
Romiplostim (Nplate, Romiplate, AMG 531)
Non-peptide TPO receptor agonists
Eltrombopag (Promacta, Revolade, SB497115)
Avatrombopeg (Doptelet, E5501, YM-477, AKR-501)
Lusutrombopag (Mulpleta)
Hetrombopag

1- Mechanism different from endogenous TPO, recombinant TPO, or romiplostim

2- Effect may be additive to that of TPO

3- Oral

Liver disease and thrombocytopenia

- Immune thrombocytopenia (ITP)-like process commonly related to chronic hepatitis C virus (HCV)
- Splenic pooling of platelets when portal hypertension causes splenic enlargement
- Reduced TPO production by a damaged liver

Liver disease and thrombocytopenia

- **Case Presentation:**

  - A 58-year-old man with cirrhosis due to hepatitis C presents for elective laparoscopic cholecystectomy. His platelet count is 48,000/µL.

    He has no history of bleeding but has mild esophageal varices on endoscopy

- **Risk assessment:**
  - Bleeding risk: Moderate due to thrombocytopenia, coagulopathy (low fibrinogen, prolonged INR), and portal hypertension
  - Thrombotic risk: Increased risk of PVT due to hypercoagulability in cirrhosis

- Two TPO receptor agonists (avatrombopag and lusutrombopag) have been approved by the FDA for the treatment of thrombocytopenic patients with chronic liver disease prior to elective procedures

Terrault N, Chen YC, Izumi N, et al. Avatrombopag Before Procedures Reduces Need for Platelet Transfusion in Patients With Chronic Liver Disease and Thrombocytopenia. Gastroenterology 2018

- Administration of ***eltrombopag*** to patients with advanced chronic liver disease and cirrhosis raised platelet counts and reduced the need for platelet transfusions prior to invasive procedures
- However, this was associated with an ***apparent increase in portal vein thrombosis, resulting in premature termination of the trial.***

Afdhal NH, Giannini EG, Tayyab G, et al. Eltrombopag before procedures in patients with cirrhosis and thrombocytopenia. *N Engl J Med*. 2012

How about *Romiplastim*??

Romiplostim			
Basu *et al*[38], 2012	65 patients with CLD and thrombocytopenia randomized 1:1:1 to 500 µg romiplostim: 75 mg eltrombopag: 7 units of platelet transfusion	Improved platelet count > 180 × 10^9/L in all groups	Nausea, vomiting, dry mouth, headache, insomnia, irritability, local skin rash, shortness of breath, myalgia, arthralgia, erythema
Moussa *et al*[3], 2013	35 male patients with thrombocytopenia and CLD secondary to hepatitis C infection, dosed 2 µg/kg romiplostim weekly	Improved platelet count ≥ 70 × 10^9/L	No serious AEs reported
Marshall *et al*[39], 2015	18 patients with various etiologies of thrombocytopenia, including CLD, undergoing wide range of procedures	Improved platelet counts in all patients; all patients could receive surgery without delay or cancellation	No venous thromboembolic events
Al-Samkari *et al*[9], 2018	48 patients with various etiologies of thrombocytopenia, including CLD, undergoing 51 procedures, dosed 3 µg/kg romiplostim weekly (range 1-10 µg/kg/wk)	Improved platelet counts achieved in all patients after 1, 2 or 3 doses	Bleeding and thromboembolic events within acceptable limits

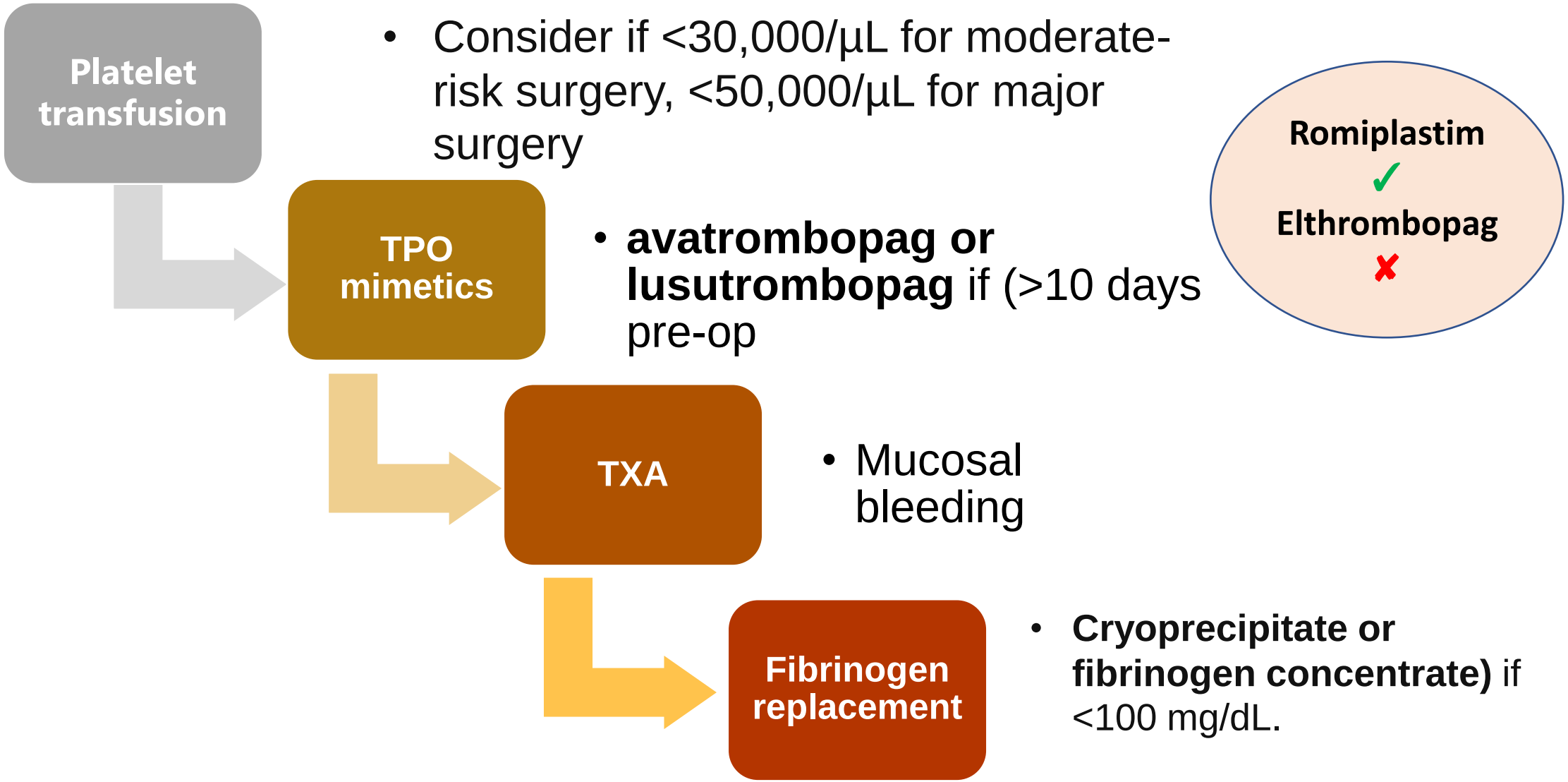
Qureshi, Kamran, and Alan Bonder. "Thrombopoietin-receptor agonists in perioperative treatment of patients with chronic liver disease." *World Journal of Meta-Analysis* 8.3 (2020)

Shorter half life (19-21 hrs)

Agent	Preferred Use	Key Advantage	Key Disadvantage
Avatrombopag	**First-line for CLD**	Oral, predictable response, no thrombosis spike	Requires at least 10 days before procedure
Lusutrombopag	**Alternative to avatrombopag**	Shorter course (7 days), predictable	Not widely available in some regions
Romiplostim	**Off-label, last resort**	Can be used in CLD if no access to oral options	Unpredictable response, thrombosis risk, not approved

Highly variable half life (1-14 days)

Management plan:



Inherited platelet function disorders undergoing surgery

Platelet transfusion

Serious bleeding
Major surgery
Scott syndrome (not routinely)

- Dose: 1 SD or 6 RD units
- Glanzmann thrombasthenia **<u>fourfold</u>**

(rFVIIa)

- Dose: 28 to 450 mcg/kg; median: 90
- One to three doses per admission

TXA

- Mucosal bleeding
- Dose: 25 mg/kg per dose q6-8h po ; 10 mg/kg q8h IV

TPO agonist

TPO agonist in IPFD:

- A thrombopoietin receptor agonist (TPO-RA; such as **eltrombopag** or **romiplostim**) may temporarily increase platelet counts
- A TPO-RA would only be expected to raise the platelet count, not to correct the underlying platelet dysfunction.

1- Zaninetti C, et al. Eltrombopag for the treatment of inherited thrombocytopenias: a phase II clinical trial. Haematologica 2020; 105:820.
2- Khoreva A, et al. Efficacy of romiplostim in treatment of thrombocytopenia in children with Wiskott-Aldrich syndrome. Br J Haematol 2021

Platelet should be irradiated if:

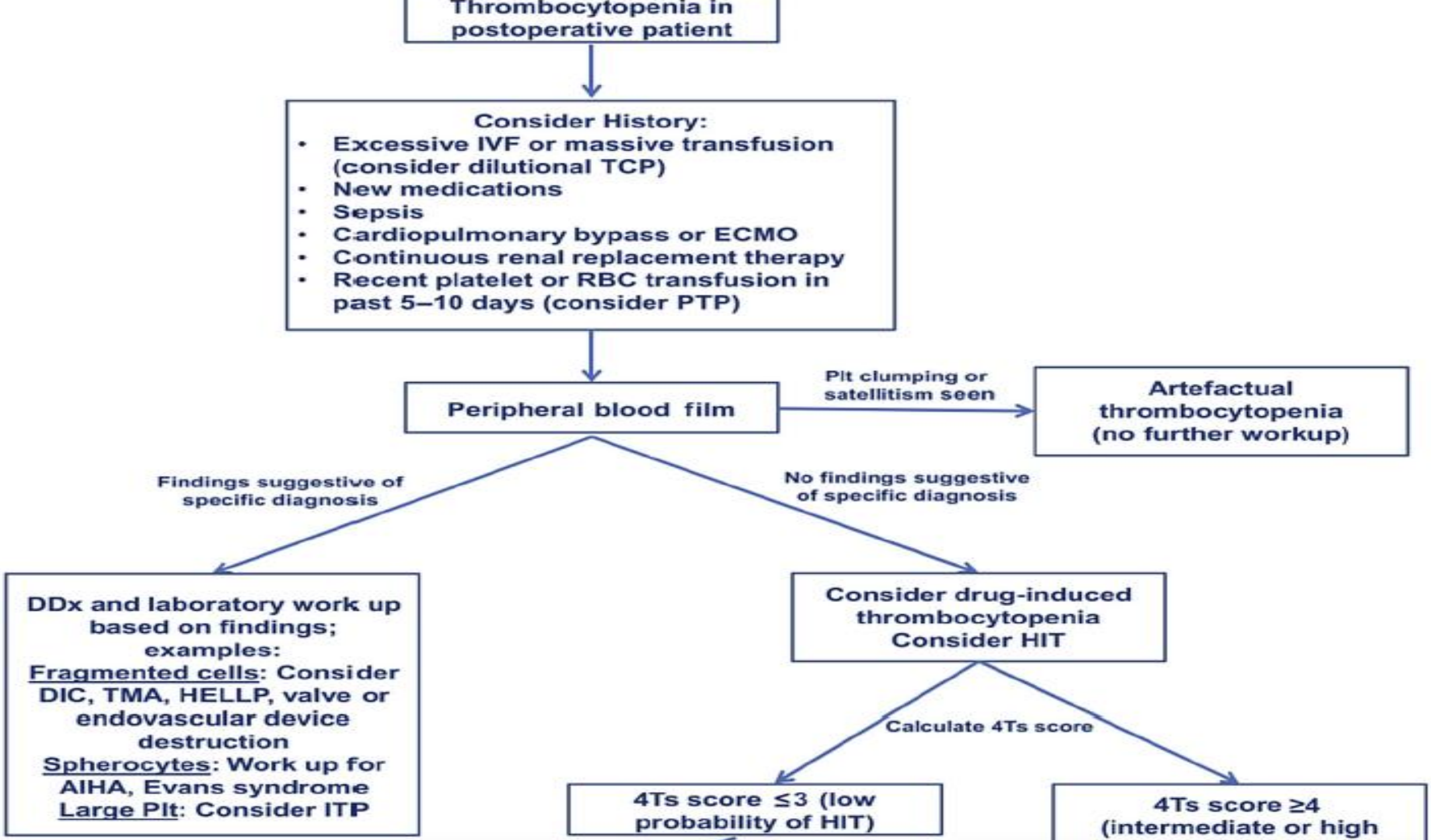
- ARPC1B deficiency
- Chediak-Higashi syndrome
- Hermansky-Pudlak syndrome
- Stormorken syndrome
- Wiskott-Aldrich syndrome/X-linked thrombocytopenia
- Wiskott-Aldrich syndrome 2

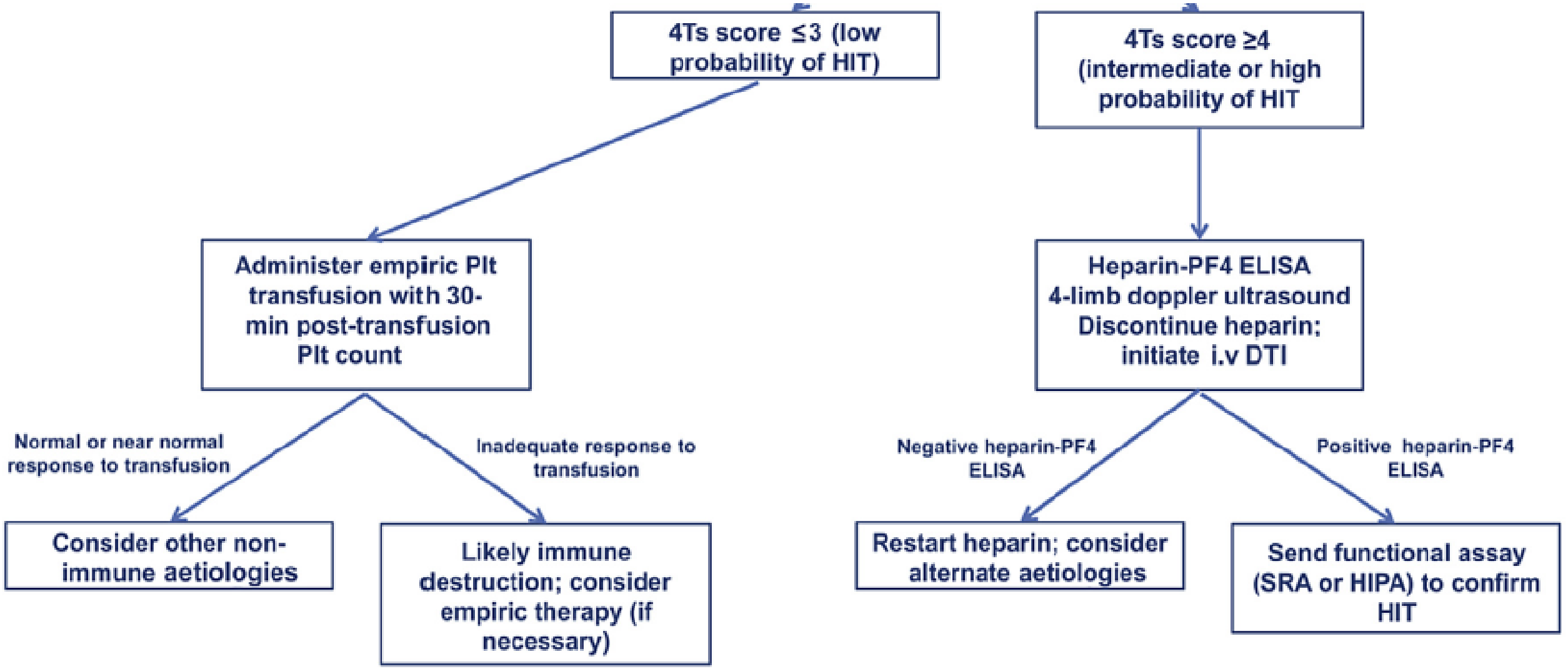
Thrombocytopenia in postoperative

Table 1 Typical aetiologies of thrombocytopenia in the postoperative patient by pathophysiologic mechanism

Decreased platelet production	Increased platelet destruction	Platelet sequestration or dilution
Drug-induced marrow suppression	Immune thrombocytopenia	Significant i.v. fluid administration
Infection	Drug-induced immune platelet destruction	Massive red blood cell transfusion
Liver disease (thrombopoietin deficiency)	Heparin-induced thrombocytopenia	Splenomegaly
	Post-transfusion purpura	
	Sepsis	
	Cardiopulmonary bypass	
	Extracorporeal membrane oxygenation (ECMO)	
	Continuous venovenous haemodialysis	
	Microangiopathy (e.g. thrombotic microangiopathy, disseminated intravascular coagulation)	
	Neonatal alloimmune thrombocytopenia (neonates only)	

Nagrebetsky, A., et al. "Perioperative thrombocytopenia: evidence, evaluation, and emerging therapies." *British journal of anaesthesia* (2019)


Thrombocytopenia in postoperative patient
Consider History:
• Excessive IVF or massive transfusion (consider dilutional TCP)
• New medications
• Sepsis
• Cardiopulmonary bypass or ECMO
• Continuous renal replacement therapy
• Recent platelet or RBC transfusion in past 5–10 days (consider PTP)
Peripheral blood film
Plt clumping or satellitism seen
Artefactual thrombocytopenia (no further workup)
Findings suggestive of specific diagnosis
No findings suggestive of specific diagnosis
DDx and laboratory work up based on findings; examples:
Fragmented cells: Consider DIC, TMA, HELLP, valve or endovascular device destruction
Spherocytes: Work up for AIHA, Evans syndrome
Large Plt: Consider ITP
Consider drug-induced thrombocytopenia Consider HIT
Calculate 4Ts score
4Ts score ≤3 (low probability of HIT)
4Ts score ≥4 (intermediate or high


4Ts score ≤3 (low probability of HIT)
4Ts score ≥4 (intermediate or high probability of HIT
Administer empiric Plt transfusion with 30-min post-transfusion Plt count
Heparin-PF4 ELISA
4-limb doppler ultrasound
Discontinue heparin; initiate i.v DTI
Normal or near normal response to transfusion
Inadequate response to transfusion
Negative heparin-PF4 ELISA
Positive heparin-PF4 ELISA
Consider other non-immune aetiologies
Likely immune destruction; consider empiric therapy (if necessary)
Restart heparin; consider alternate aetiologies
Send functional assay (SRA or HIPA) to confirm HIT

Consultation in thrombocytosis

- **Preoperative Assessment:**
    - **Confirm Diagnosis:** Repeat platelet counts after a few weeks to rule out transient elevations, especially in cases of incidental findings.
    - **Evaluate Underlying Causes:** Identify and manage potential causes of reactive thrombocytosis, such as infections…
- Secondary thrombocytosis per se does not convey a risk of thromboembolic morbidity absent confounding factors such as malignancy or major surgery

Szuber, Natasha, et al. "Perioperative outcomes in patients with myeloproliferative neoplasms: a multicentric analysis of 354 surgical procedures." *Blood Vessels, Thrombosis & Hemostasis* (2024)

- **Discontinue** agents like **aspirin 7-10 days** before major surgeries and resume postoperatively once hemostasis is assured
- For patients receiving cytoreductive therapy, **control of blood counts should be optimized** preoperatively and interruptions in therapy kept to a minimum.
- **Elective Surgeries:** Defer surgery for high-risk or symptomatic patients until platelet counts are reduced below 400,000/μL using cytoreductive therapies

- For patients not receiving treatment, temporary cytoreductive therapy may be considered on a case-by-case basis
- **Thrombocytapheresis :** can be used to prepare acutely symptomatic patients with poorly controlled severe thrombocytosis for cardiovascular surgery **(plt >1.5-2 million/ul??)**

- **Post operative:** Implement thromboprophylactic measures, including maintaining hydration, early ambulation, mechanical prophylaxis (e.g., compression devices), and cautious use of pharmacological agents.

Take home message

- **Platelet transfusion** for preparation for invasive procedures
  - neurosurgery/ocular: 100,000
  - most other srgery : 50,000
  - LP: 40-50,000
  - BAL, CV line, BMA/BMB : 20,000
- **If unable to benefit from platelet transfusion** → Romiplastim 2 to 3 mcg/kg weekly
- **Liver disease** and thrombocytopenia → avatrombopag and lusutrombopag
- **IPFD undergoing surgery** → - avoid routine plt transfusion
  - consider (rFVIIa) / TPO agonist
  - TXA for minor surgery
- **Thrombocytosis** → discontinue aspirin 7-10 days
  CBC should be optimized
  consider post surgery VTE prophylaxis


Thanks for
your attention