

Neuraxial Procedures in Obstetric Patients with Thrombocytopenia

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The Society for Obstetric Anesthesia and Perinatology Interdisciplinary Consensus Statement on Neuraxial Procedures in Obstetric Patients With Thrombocytopenia

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Outlines

- Definition and background
- Methods
- Anesthetic risks
- Laboratory considerations
- Platelet transfusion prior to neuraxial procedure
- **Recommendations**
- Aspirin therapy
- Conclusions

Definition and Background

- Thrombocytopenia in pregnancy
 - Defined during pregnancy as a platelet count $<150,000 \times 10^6/L$
 - Moderate to severe disease defines as $<100,000 \times 10^6/L$
- Occurs up to 12% of women (1% moderate to severe disease)
- Most common diagnosis
 - Gestational thrombocytopenia
 - Immune thrombocytopenia
 - Thrombocytopenia associated with hypertensive disease (preeclampsia, HELLP syndrome)

Table 1. Common Etiologies of Thrombocytopenia During Pregnancy and Postpartum

Disease	Incidence during pregnancy (%)	Diagnostic features	Laboratory findings	Clinical symptoms and physical examination	Pathophysiology
Gestational thrombocytopenia	<u>5–11</u>	Common onset during late second or third trimester, normal platelet count outside of pregnancy	Platelet count $>75,000 \times 10^6/L$	Typically normal	Unclear
ITP	<1	Onset at any trimester, thrombocytopenia outside of pregnancy possible	Platelet count $<100,000 \times 10^6/L$ \pm large platelets on PBS	Rarely may have signs of bleeding, bruising, and petechiae	Antibody induced peripheral platelet destruction and decreased bone marrow production
Preeclampsia	<u>5–8</u>	Onset in late second or third trimester (>20 wk of gestation)	≥ 300 mg urine protein in 24 h or protein/creatinine ratio of ≥ 0.3 or end-organ injury	Systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg	Systemic endothelial dysfunction Inadequate placentation
HELLP syndrome	<1	70% onset in late second or third trimester, 30% onset postpartum	MAHA elevated LFTs elevated LDH	Any or all signs of preeclampsia may be present, in 15%–20% of cases no hypertension or proteinuria is present, platelet count nadir occurs 24–48 h after delivery	Systemic endothelial dysfunction Inadequate placentation

Adapted with permission from Rajasekhar et al.¹²

Abbreviations: BP, blood pressure; HELLP, hemolysis, elevated liver enzymes, low platelet count; ITP, immune thrombocytopenia; LDH, lactate dehydrogenase; LFTs, liver function tests; MAHA, microangiopathic hemolytic anemia; PBS, peripheral blood smear.

Definition and Background

- Additional causes (rare)
 - Acute fatty liver of pregnancy
 - Thrombotic thrombocytopenic purpura
 - Inherited thrombocytopenia
 - Sepsis-induced thrombocytopenia
- Obstetric patients with thrombocytopenia are often denied neuraxial procedures due to perceived risk of **spinal epidural hematoma!!**
- However, there are significant maternal and fetal risks associated with general anesthesia during pregnancy

Definition and Background

- Multiple professional societies (obstetrics, interventional pain, and hematologic) → guidelines about platelet thresholds for safe neuraxial procedures
- The **US anesthesia** professional societies have been **silent on this topic**
- **The anesthesiologist** must make clinical decisions (often with time constraints)

Definition and Background

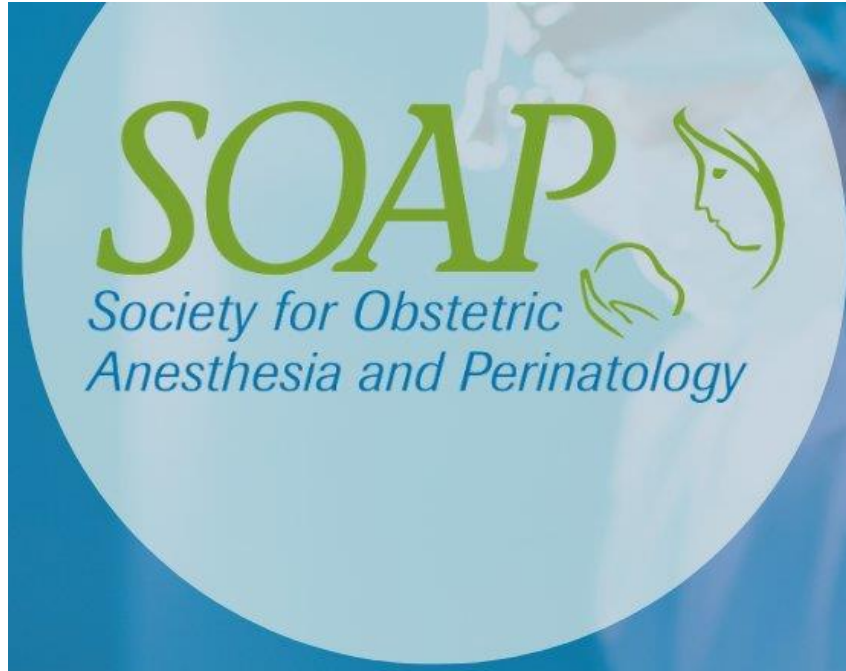
- This consensus was developed to provide the **best available evidence and a clinical decision** with patients and obstetricians engage in **effective shared decision making**

Interdisciplinary Consensus Statement on Neuraxial Procedures in Obstetric Patients with Thrombocytopenia

Mar 1, 2021

Society for Obstetric Anesthesia and Perinatology

ASRA, along with the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine, has examined and endorsed these guidelines developed by the Society of Obstetric Anesthesia and Perinatology. The guidelines have been e-published in *Anesthesia and Analgesia*.



IMPROVING PREGNANCY
RELATED OUTCOMES OF
WOMEN AND NEONATES

SOAP.ORG

How does this statement differ from existing guidelines?

- This consensus focuses on **obstetric patients with moderate to severe thrombocytopenia (platelet count < 100,000 x 10⁶ /L)**
- Whereas existing guidelines cover a range of other related topics and patient populations, primary related to lumbar puncture



Methods

- **Systematic review of the literature**
- **Modified Delphi process** between January 2018-December 2019
 - Round 1 : diverse geographic and practice settings
 - Round 2 : focused questionnaire to 5 hematology experts
- Participating specialty professional organizations
 - American society of regional anesthesia and pain medicine (ASRA)
 - American college of obstetricians and gynecologists (ACOG)
 - Society for maternal-fetal medicine (SMFM)
 - American society of hematology (ASH)

Literature and systematic review

- Previous published systematic review and meta-analysis identified all published cases of neuraxial procedure
- Performed in diverse populations of patients with **thrombocytopenia subsequent development of spinal epidural hematoma**
- The meta-analysis found ;
 - Spinal epidural hematoma for all neuraxial procedures to be low above range beginning around 70,000-75,000 x 10⁶ /L*

Lumbar neuraxial procedures in thrombocytopenic patients across populations: A systematic review and meta-analysis

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- 131 articles
- 7,476 procedures
- 33 procedures with spinal hematoma (**0.097%**, 95% CI = 0.002-0.2)
 - <25,000 x 10⁶ /L → 14
 - 26,000-50,000 x 10⁶ /L → 6
 - 51,000-75,000 x 10⁶ /L → 9
 - 76,000-99,000 x 10⁶ /L → 4

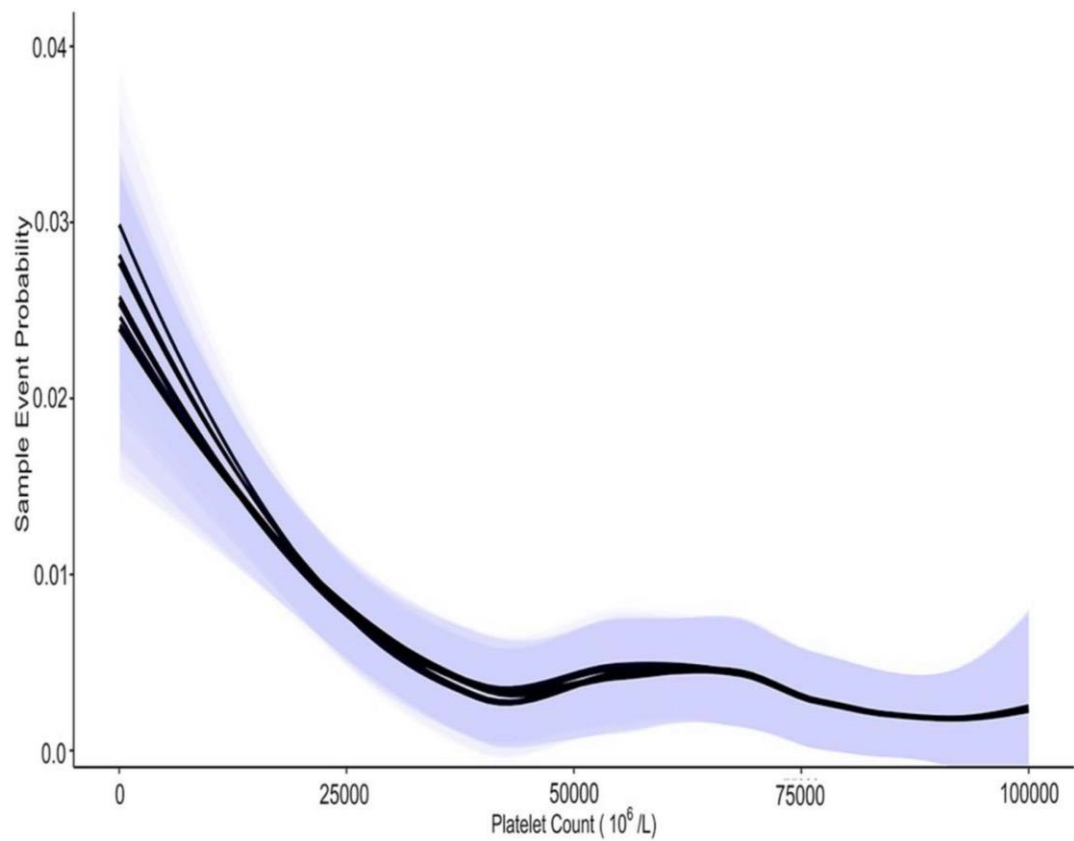


Fig. 3. Estimated event rate (black line) with 95% confidence intervals (grey).

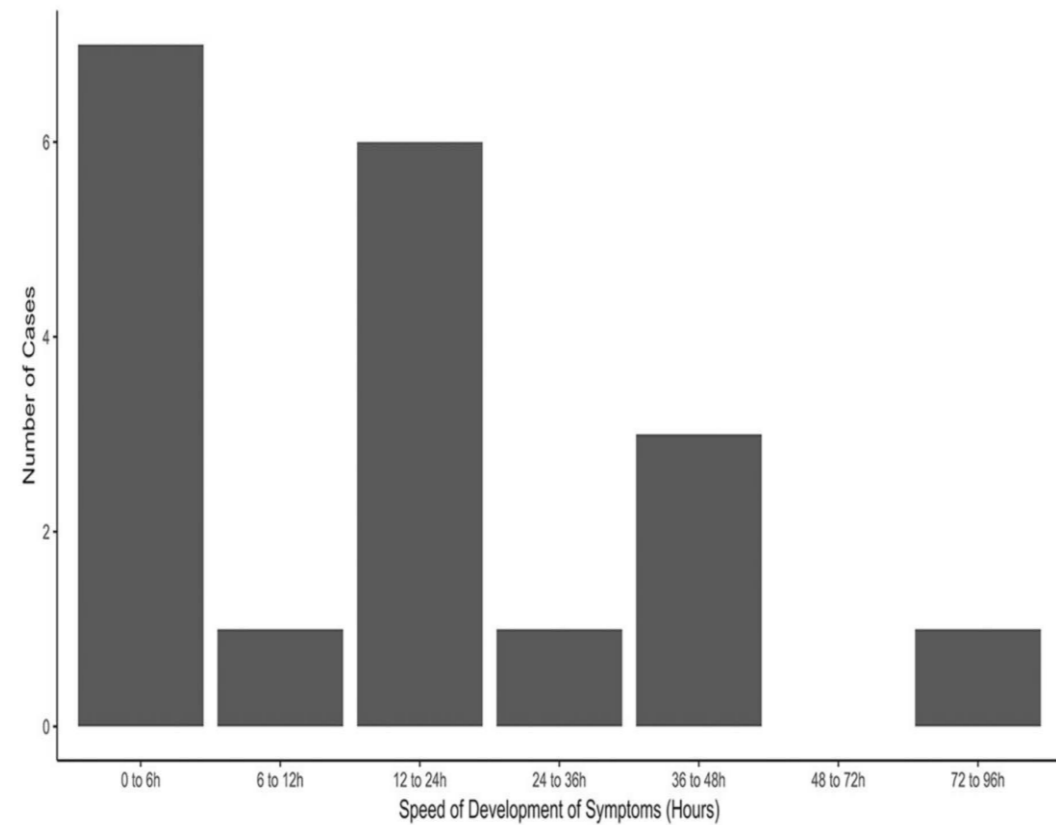


Fig. 4. Histogram of timing of symptoms of spinal epidural hematoma after procedure.

population, reports of spinal epidural hematomas are very rare [23]. In our review, there were only 5 reported obstetric cases of spinal epidural hematoma with a platelet count range of 44,000–91,000 × 10⁶/L. Two of the cases had apparent risk factors besides thrombocytopenia; one had an underlying arteriovenous malformation and the other was coagulopathic at the time of (inadvertent) epidural catheter removal. Of the 3 remaining patients, two had HELLP and one had eclampsia.

1 case → U/D AVM

1 case → Coagulopathic at the time of epidural catheter removal (inadvertent)

3 case → 2 HELLP, 1 eclampsia

Anesthetic risks

Neuraxial anesthesia: Thrombocytopenia-Related Spinal Hematoma

- Spinal hematoma is the neuraxial anesthesia complication that is associated with the **highest potential morbidity**
- Incidence
 - General obstetric population: 1:200,000 to 250,000
 - Incidence based on platelet count

70,000-100,000 x 10 ⁶ /L	0.2%
50,000-69,000 x 10 ⁶ /L	3%
<50,000 x 10 ⁶ /L	11%

Risk of Epidural Hematoma after Neuraxial Techniques in Thrombocytopenic Parturients: A Report from the Multicenter Perioperative Outcomes Group FREE

Linden O. Lee, M.D. [✉](#); Brian T. Bateman, M.D., M.Sc.; Sachin Kheterpal, M.D., M.B.A.; Thomas T. Klumpner, M.D.; Michelle Housey, M.P.H.; Michael F. Aziz, M.D.; Karen W. Hand, M.D.; Mark MacEachern, M.L.I.S.; Christopher G. Goodier, M.D.; Jeffrey Bernstein, M.D. ... [Show more](#)

[+ Author and Article Information](#)

Anesthesiology June 2017. Vol. 126. 1053–1063.

Platelet Range, mm ⁻³	Systematic Review Data			MPOG Data Combined with Systematic Review Data		
	n (%)	Frequency of Epidural Hematoma Requiring Surgical Decompression	95% CI for Risk of Epidural Hematoma, %	n (%)	Frequency of Epidural Hematoma Requiring Surgical Decompression	95% CI for Risk of Epidural Hematoma, %
0–49,000	12 (1)	0	0–25	27 (2)	0	0–11
50,000–69,000	53 (6)	0	0–6	89 (6)	0	0–3
70,000–100,000	764 (80)	0	0–0.4	1,286 (84)	0	0–0.2
Total	951 (100)	0		1,524 (100)	0	

MPOG = Multicenter Perioperative Outcomes Group.

Anesthetic risks

Symptoms

- Lower extremity motor deficit (59%), back pain, lower extremities pain and paresthesia, urinary/bowel dysfunction
- 95% present symptoms within 48 hours of procedure

Management

- Prompt imaging and neurosurgical consultation are critical
- Treatment → decompressive laminectomy within 8 hours of symptom onset

Anesthetic risks

Risks associated with General Anesthesia

- Maternal
 - Severe adverse events related to induction
 - Failed tracheal intubation
 - Severe hypertensive response to tracheal intubation
 - Uterine atony
 - Inability to provide neuraxial opioids for pain control
- Fetal
 - Respiratory depression
 - Apgar < 7 at 5 minutes
 - Limitation on immediate breastfeeding

Laboratory considerations

- CBC

- Absolute platelet count: +/- 3% coefficient of variation

- Rarely, low platelet counts due to clumping induced by EDTA
→ collect in a tube with an alternative anticoagulant (e.g., citrate) or count manually

- PTT, PT

- No utility in predicting bleeding risk in pregnant women with thrombocytopenia (except coagulation defect is known or suspected)

Laboratory Considerations

- Thromboelastography (TEG) and rotational thromboelastometry (ROTEM)
 - Dynamic point of care tests
 - Insufficient evidence to recommend routine use
- Platelet function analyzer (PFA-100)
 - Evaluates **platelet function** by stimulating in-vivo platelet plug formation
 - Insufficient evidence to recommend routine use

Table 3. Laboratory Testing Assessments

Test	Assay principle	Clinical application	Limitations
CBC	Whole blood assay based on the Coulter principle or electrical impedance that provides quantitative assessment of platelet count among other parameters	Assesses quantitative number of platelets	Cannot assess for qualitative disorders
PBS	Blood film that involves cytology of peripheral blood cells smeared on a slide	To evaluate for specific causes of thrombocytopenia with characteristic patterns on peripheral blood smear such as thrombotic microangiopathies, congenital macrothrombocytopenias, pseudothrombocytopenia (clumping)	Morphologic review by hematologists, pathologist, or expert laboratory technician required Assesses for specific causes of thrombocytopenia but does not assess bleeding risk
PT and aPTT	One-stage clot-based assay based on the time required for a fibrin clot to form after the addition of an activator to phospholipids, calcium, and platelet-poor plasma	To assess secondary hemostasis pathways including deficiencies or inhibition of coagulation factor cascade	Does not assess for qualitative or quantitative platelet disorders
PFA-100	Assess platelet plug formation by measuring the time required for citrated whole blood to occlude a membrane impregnated with either collagen and epinephrine (PFA-Epi) or collagen and adenosine 5'-diphosphate (PFA-ADP)	Screening for platelet function defects	Prolongation of both phases of the PFA-100 (PFA-Epi and PFA-ADP) may be found in patients with thrombocytopenia (PLT <100,000 × 10 ⁶ /L), anemia (Hb <10 g/dL), or a significant qualitative platelet defect Affected by anemia, thrombocytopenia, and antiplatelet medications Lack of specificity and predictive value for any particular disorder and absence of correlation with bleeding risk
Platelet aggregation study	Measures platelet agglutination and aggregation in response to different weak and strong agonists	Used in specialized centers for the evaluation of acquired and inherited platelet function defects	Affected by thrombocytopenia Limited correlation with bleeding phenotype in patients with mild platelet function disorders
Viscoelastic testing - TEG - ROTEM	Based on viscoelastic properties of a clot formed when applying a rotational force providing quantitative information on clot development, stabilization, and dissolution	Validated in guiding transfusion strategy in trauma and surgical patients	Limited correlation with clinical outcomes in patients with acquired and inherited bleeding disorders Very limited evidence for using viscoelastic testing before placing neuraxial procedures in obstetric patients with thrombocytopenia

Abbreviations: ADP, adenosine 5'-diphosphate; aPTT, activated partial thromboplastin time; CBC, complete blood count; Epi, epinephrine; Hb, hemoglobin; PBS, peripheral blood smear; PFA-100, platelet function analyzer-100; PLT, platelet; PT, prothrombin time; ROTEM, rotational thromboelastometry; TEG, thromboelastography.

Platelet transfusion before neuraxial procedure

- Risks of platelet transfusion
 - Transfusion reaction
 - Transfusion-related acute lung injury (TRALI)
 - Transfusion associated circulatory overload (TACO)
- ACOG recommends platelet transfusion in **preeclampsia with active bleeding**
- Expected increase: 30,000-50,000 $\times 10^6$ /L after apheresis-derived bag of platelets
 - Less effective in preeclampsia or consumption disorders

Platelet transfusion before neuraxial procedure

- *ACOG Platelet transfusions are recommended for
 1. Life-threatening hemorrhage
 2. In preparation for **cesarean delivery**
- **A Recent Cochrane Review** assessed the benefit of platelet transfusion prior to neuraxial anesthesia and concluded that

*“no evidence from RCTs or non-randomized studies on which to base an assessment of the **correct platelet transfusion threshold** prior to insertion of a lumbar puncture needle or epidural catheter”*

Recommendations

Recommendations

1. Recommendations from other professional **organizations**

→ Platelet thresholds for neuraxial procedures

2. Recommendations for anesthesiologists and other practitioners

Professional organizations regarding platelet thresholds for neuraxial procedures

- Lumbar puncture had the lowest recommended acceptable range **20,000-50,000 x 10⁶ /L** for diagnostic LP in patients with **leukemia or suspected meningitis** ¹
- Society recommendations for anesthetic neuraxial procedures **most common** used a limit of **80,000 x 10⁶ /L** ²
- The Scandinavian Society of Anesthesiology recommends **lower thresholds** for neuraxial procedures
 - **Lower risk** for anesthesia-related **morbidity and mortality than general anesthesia**
 - **Single-shot spinal** compared to epidural procedures

¹ridey JB, Borge D, Brunker PA, et al. Platelets. In: Friley JL, ed. A Compendium of Transfusion Practice Guidelines. American National Red Cross, 2017:156.

²Fonseca NM, Alves RR, Pontes JPI. Recomendações da SBA para segurança na anestesia regional em uso de anticoagulantes. Rev Bras Anesthesiol. 2014;64:1-15

Supplemental Table 1. Society Recommendations for Neuraxial Procedures in the Setting of Thrombocytopenia

Society Recommendations for Neuraxial Procedures in the Setting of Thrombocytopenia

Society and Year of Publication	Neuraxial Procedure Types	Indications to Assess Platelet Number Prior to Procedure	Platelet Count (x10⁶/L) Recommendations
Anesthesiology Societies			
American Society of Regional Anesthesiology and Pain Medicine (ASRA), 2018¹	Anesthesia	If unfractionated heparin administered > 4 days, check plts prior to NB/CR	NA
American Society of Anesthesiologists, 2016²	Obstetric anesthesia	Decision to check plts should be individualized and based on patient's history, physical examination, and clinical signs. Routine plts not necessary in healthy parturient.	NA
American Society of Regional Anesthesiology and Pain Medicine (ASRA), 2015³	Pain procedures	Check plts if glycoprotein IIb/IIIa receptor antagonist (abciximab, eptifibatide, tirofiban) administered	NA

Professional organizations regarding platelet thresholds for neuraxial procedures

The association of anesthetists of Great Britain and Ireland (AAGBI)

is the only society that

- Specific obstetric patients
- Recommend various platelet count thresholds for specific disease
 - Preeclampsia
 - ITP
 - Intrauterine fetal demise
 - Placental abruption

**Association of
Anaesthetists of Great
Britain and Ireland
(AAGBI),
2013⁵**

Obstetric
anesthesia

DIC: incompatible with
neuraxial anesthesia

Massive transfusion:
assessment of plt function
should occur in patients who
have been given plt transfusions
prior to NB

Liver failure: assessment of
coagulopathy including plt
number and function

Uremia: assessment of plt
number and function

Trauma: coagulopathy should
be assessed

Sepsis: coagulopathy should be
assessed

**Risk assessment for spinal
hematoma in obstetric patients:**

Normal risk

- Preeclampsia: >**100,000** within
6hrs of NB
- ITP: >**75,000** within 24hrs of NB
- IUFD: COAGS normal within 6hrs
of block

Increased risk

- Preeclampsia:**75-100,000**
- ITP: **50-75,000**
- IUFD: no clinical tests and no
COAGS available

High risk

- Preeclampsia:**75-100,000**
(decreasing) and normal COAGS
- ITP: **20-50,000**

Very high risk

- Preeclampsia: <**75,000** or
abnormal COAGS or HELLP
syndrome
- ITP: <**20,000**
- IUFD: abruption or overt sepsis

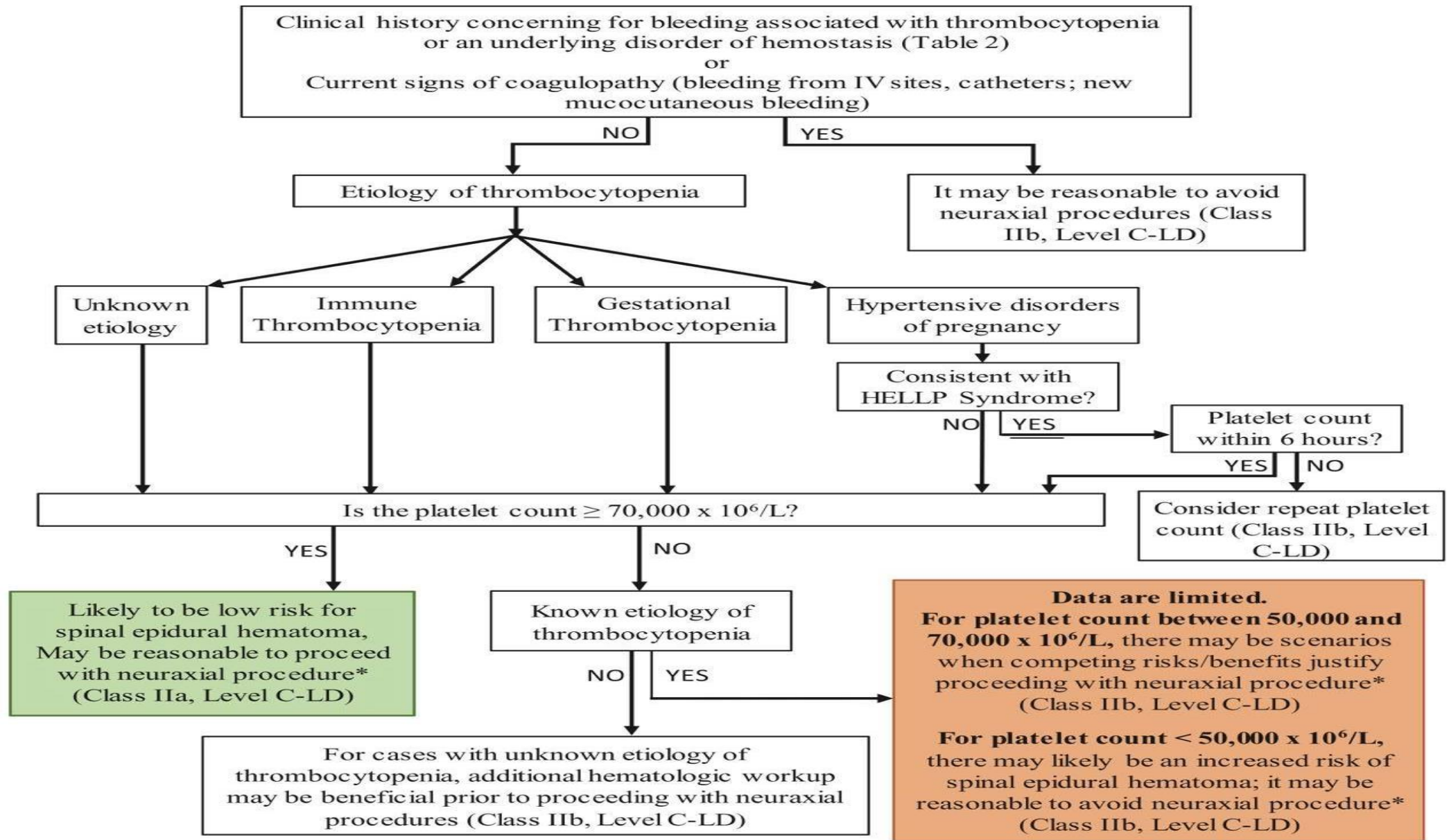
Recommendations for anesthesiologists and other practitioners

Recommendations for anesthesiologists and other practitioners

- This consensus
 - Not intended to set out a **legal standard of care**
 - Subject to periodic **revision** as additional data become available
 - In all cases, assumed that the obstetrics patients do not have additional contraindications to neuraxial anesthesia
- **The decision occurs within clinical context**

Recommendations for anesthesiologists and other practitioners

- The potentially relevant factors
 - Comorbidities
 - Obstetric risk factors
 - Airway examination and available airway equipment
 - Risk of general anesthesia
 - Patient preference
- The taskforce, with its representative from SOAP, ASRA, ASH, ACOG, and SMFM choose the **threshold platelet count for neuraxial procedures of $70,000 \times 10^6 /L$**



**Assumes patient has no additional risk factors. Clinical context and competing risks might include, but are not limited to, the presence of high-risk comorbidities or difficult airway, the need for urgent or emergent general anesthesia, or the choice of neuraxial technique (i.e. spinal versus epidural anesthetic).*

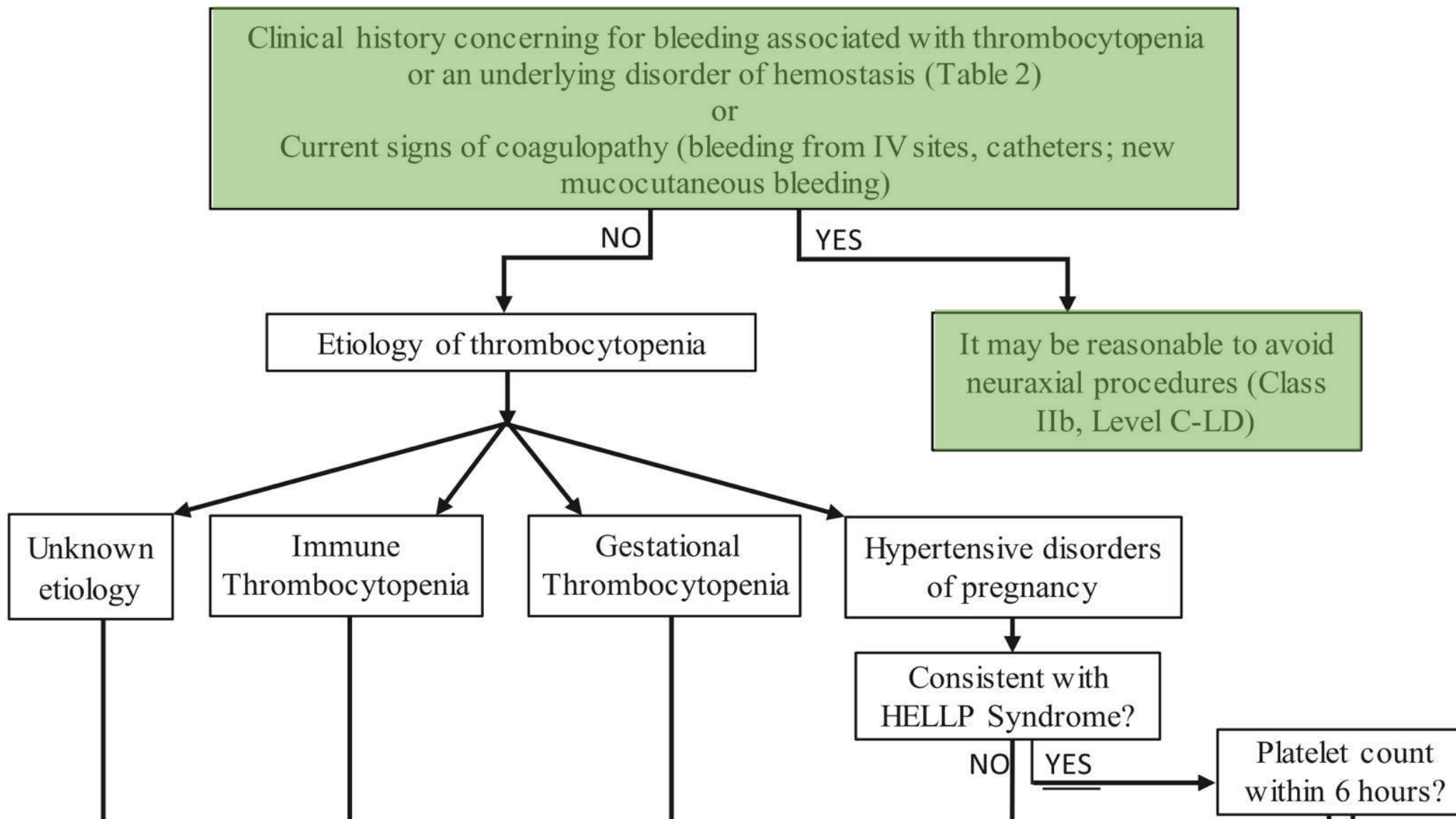
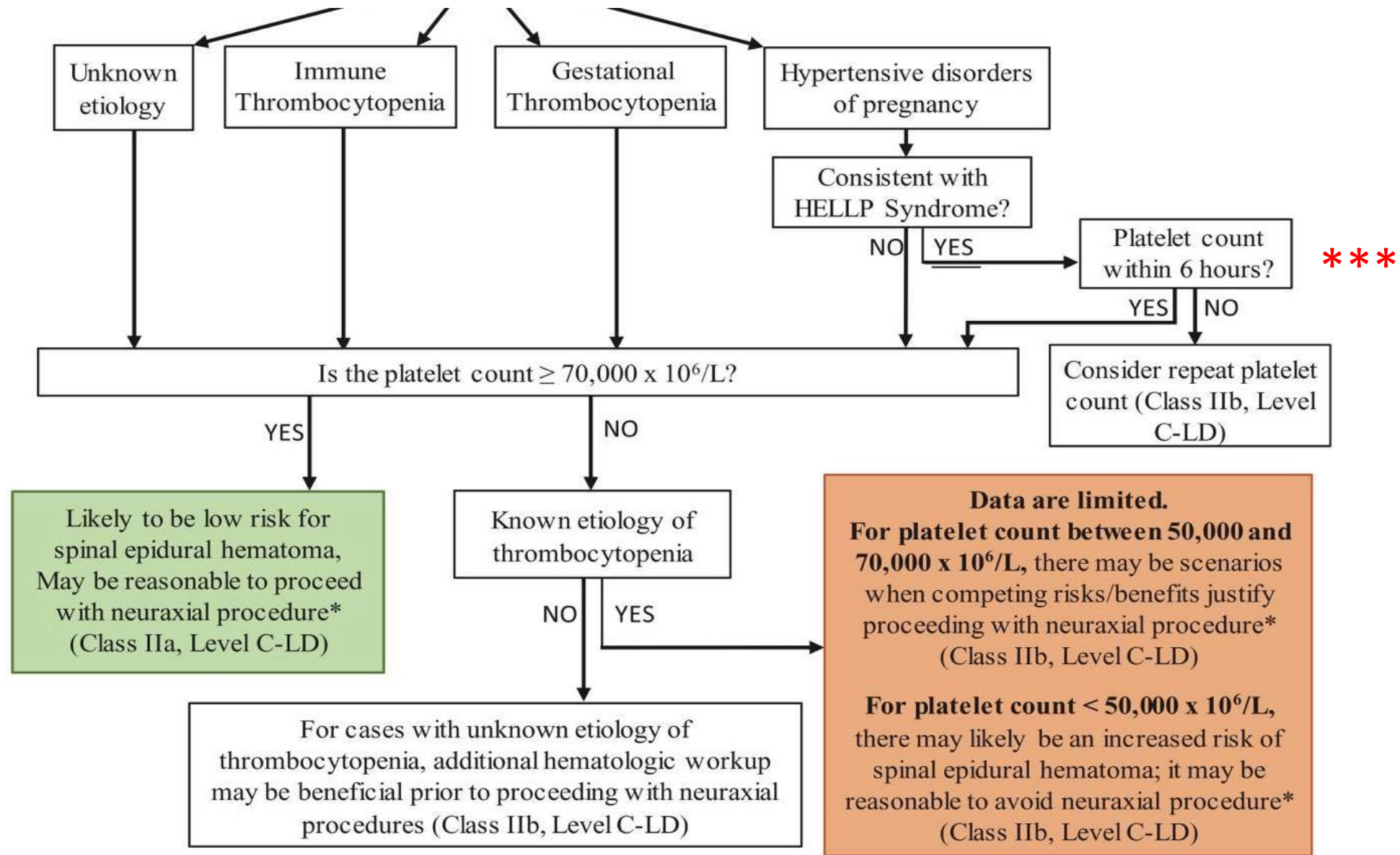


Table 2. Assessment of Bleeding History and Possible Underlying Disorder of Hemostasis in the Obstetric Patient^a

- Heavy menstrual bleeding since menarche (suggested by bleeding >7 d, soaking through a menstrual pad or tampon every 1–2 h, passing blood clots >2.5 cm)
- Hemostatic challenges not related to the procedure itself, organ, or vascular damage (one of the following)
 - Postpartum hemorrhage
 - Surgery-related bleeding
 - Bleeding associated with dental work
- Spontaneous major bleed not associated with anatomic lesion/trauma especially if requiring transfusion (one of the following)
 - Gastrointestinal bleeding
 - Intramuscular or intraarticular bleeding
 - Central nervous system bleeding
- Bleeding symptoms (2 of the following)
 - Frequent epistaxis outside of pregnancy (>5/y or >10 min)
 - Severe easy bruising
 - Prolonged bleeding after minor injury (>5/y or >5 min)
 - Family history of bleeding symptoms/disorder



**Assumes patient has no additional risk factors. Clinical context and competing risks might include, but are not limited to, the presence of high-risk comorbidities or difficult airway, the need for urgent or emergent general anesthesia, or the choice of neuraxial technique (i.e. spinal versus epidural anesthetic).*

Known etiology of Thrombocytopenia

(Gestational thrombocytopenia, ITP and hypertensive disease of pregnancy)

- Assess for history of bleeding associated thrombocytopenia and confirm no visible signs of DIC such as bleeding from IV sites, catheters, wounds, or new mucocutaneous bleeding
- The optimal frequency of laboratory testing in unknown
- Patient with HEEP syndrome most likely a rapid decline in platelet count
 - The expert panel agreed that reasonable to verify the platelet count within 6 hours of the planned neuraxial procedure or catheter removal

Known etiology of Thrombocytopenia

(Gestational thrombocytopenia, ITP and hypertensive disease of pregnancy)

-Platelets count $\geq 70,000 \times 10^6/L$

-Reasonable to proceed with neuraxial procedure

-Platelets count $50,000-70,000 \times 10^6/L$

-Risk/benefits may justify proceeding with neuraxial procedure (dependent on clinical setting)

-Platelets count $< 50,000 \times 10^6/L$
-Concern for hemostasis disorder or DIC

-Reasonable to avoid neuraxial procedures

Without known etiology of Thrombocytopenia

- ✓ Thrombocytopenic without formal diagnosis
- ✓ New thrombocytopenia
- ✓ Patient without prior platelet counts available for comparison

Without known etiology of Thrombocytopenia

-Platelets count $\geq 70,000 \times 10^6/L$ without history of/or current bleeding

-Reasonable to proceed with neuraxial procedure

-Platelets count $< 70,000 \times 10^6/L$

-Additional (hematologic) workup may be beneficial prior to proceeding with neuraxial procedure

-Concern for hemostasis disorder or DIC

-Reasonable to avoid neuraxial procedures

Other Recommendations

1. Aspirin

“There was insufficient evidence to make a recommendation in obstetric patients with thrombocytopenia taking aspirin”

2. Other laboratory testing

“There was insufficient evidence to make a recommendation about the use of additional laboratory tests (e.g., PT, aPTT, TEG, ROTEM, and PFA) to aid a decision making”

Aspirin therapy and bleeding risk

- ACOG recommends a low dose (81 mg/d) aspirin to pregnant woman at **high risk for preeclampsia**
- ASRA guidelines : do not add significant risk to develop spinal hematoma and **do not recommend to withhold** the drug to perform neuraxial anesthesia
- There is **“insufficient evidence”** regarding neuraxial procedures in pregnant and postpartum women with **thrombocytopenia who are taking aspirin**

Clinical Trial

> Lancet. 1994 Mar 12;343(8898):619-29.

CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group

- 1422 woman had epidural procedures while taking 60 mg aspirin daily
- **None of the patients developed an epidural hematoma**

*Not known the platelet count profile

OBSTETRICS

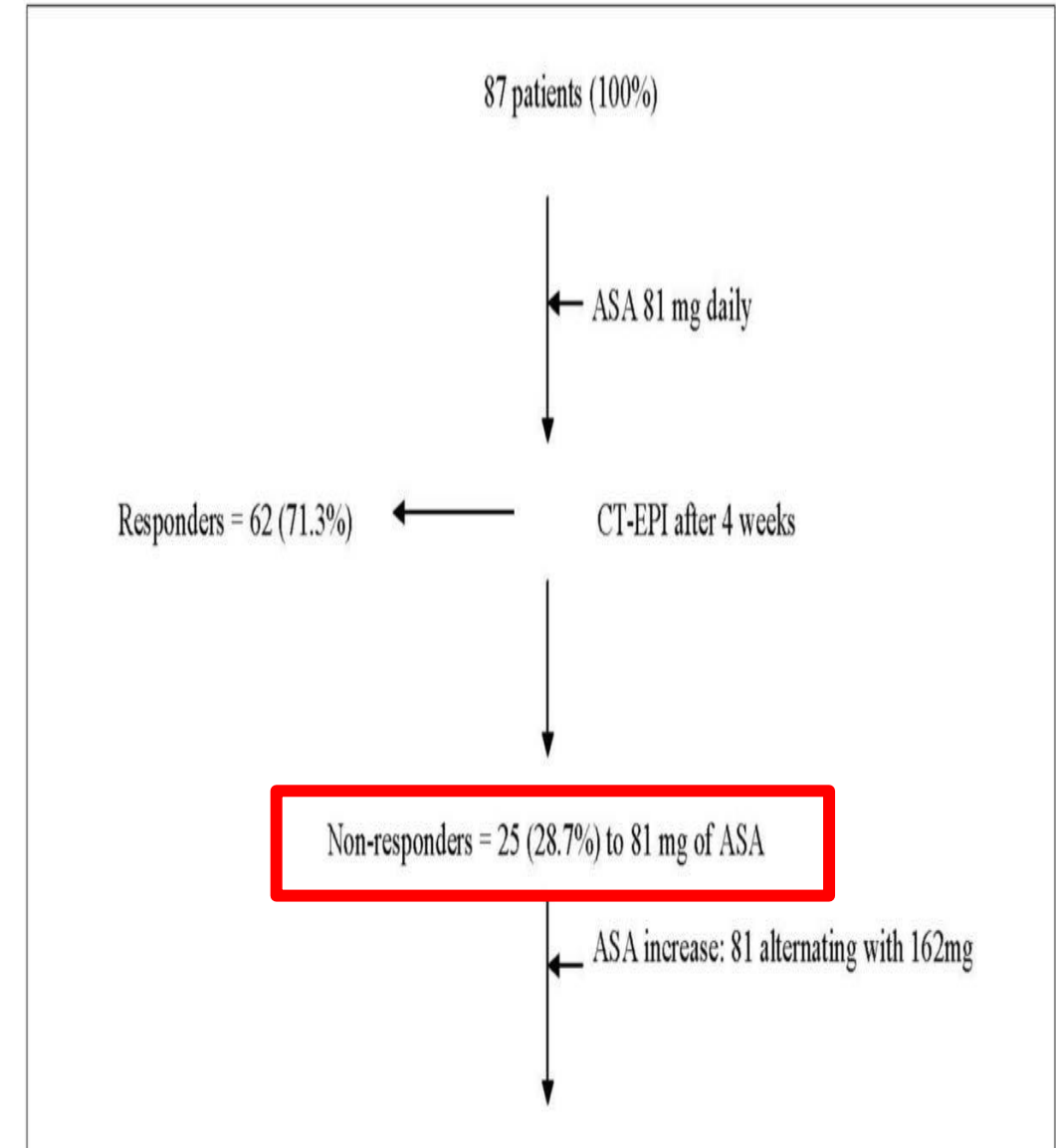
Low-dose ASA Response Using the PFA-100 in Women With High-risk Pregnancy

- The PFA-100 to **analyze platelet function**

After 4 weeks follow up

- **28.7%** did not change in the PFA-100
- “Not all woman have changes in platelet function while taking low dose aspirin”

Flow chart of intervention with increasing low-dose ASA



Aspirin therapy and bleeding risk

- Due to limited data

...clinicians and patients should engage in shared decision-making about the perceived competing risks/benefits of proceeding with or withholding neuraxial anesthesia in cases of severe thrombocytopenia and concurrent aspirin use...

Frequency of lab testing with preeclampsia

- Limited evidence for frequency of testing in women with thrombocytopenia and preeclampsia
- However, in the presence of HELLP, the panel recommends that “it may be reasonable to verify platelet **count within 6 hours of the planned neuraxial procedure**”

Quality assurance/Quality improvement

- Depend on optimal **interdisciplinary communication**

Specific recommendation include

1. Interdisciplinary **knowledge** of the
 - Etiologies of thrombocytopenia in pregnancy
 - Associated protocols related to neuraxial procedures
2. Early consultation with **anesthesiology and hematology experts**
 - Coordinate treatment plan and address patient expectations

Quality assurance/Quality improvement

3. Institutional pathways to **quickly identify patients with suspected spinal epidural hematoma**

- Urgent magnetic resonance imaging (MRI) and follow-up care

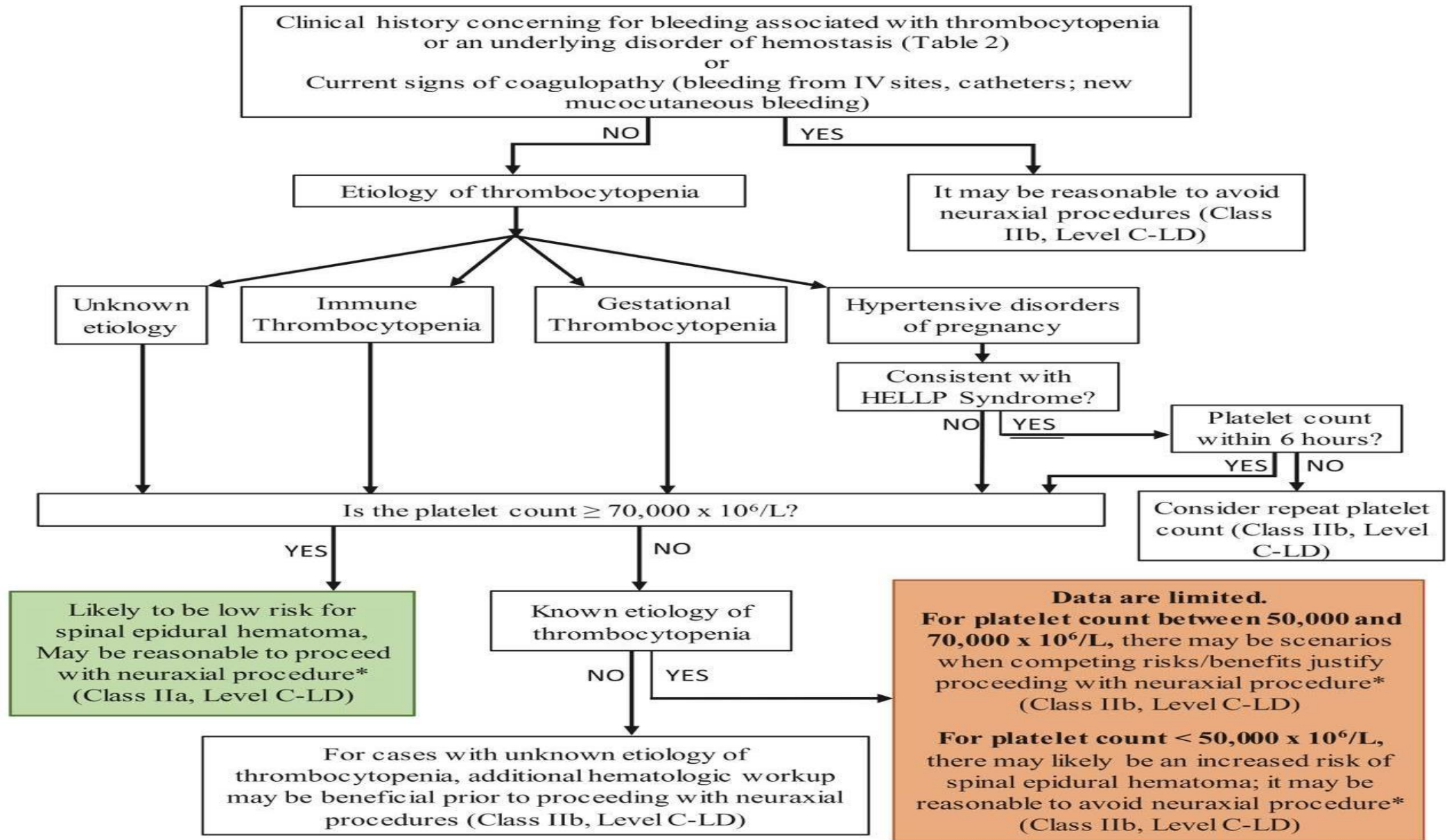
4. Population-level data

- Complications of neuraxial anesthesia in patients with thrombocytopenia, such as a national or international registry

- Incidence of spinal epidural hematomas

Conclusions

- Best available evidence is platelet count $\geq 70,000 \times 10^6 /L$
- Investigate bleeding **history and etiology** before admission for delivery
- **Multidisciplinary approach** with obstetrician and hematologist
- **Clinical context with relevant factors** include
 - Maternal comorbidities and obstetric risk factors
 - Airway examination and available airway equipment
 - Type of neuraxial procedure
 - Patient preference
- **Share decision making** with obstetric patient



**Assumes patient has no additional risk factors. Clinical context and competing risks might include, but are not limited to, the presence of high-risk comorbidities or difficult airway, the need for urgent or emergent general anesthesia, or the choice of neuraxial technique (i.e. spinal versus epidural anesthetic).*