

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

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Because up to 12% of obstetric patients meet criteria for the diagnosis of thrombocytopenia in pregnancy, it is not infrequent that the anesthesiologist must decide whether to proceed with a neuraxial procedure in an affected patient. Given the potential morbidity associated with general anesthesia for cesarean delivery, thoughtful consideration of which patients with thrombocytopenia are likely to have an increased risk of spinal epidural hematoma with neuraxial procedures, and when these risks outweigh the relative benefits is important to consider and to inform shared decision making with patients. Because there are substantial risks associated with withholding a neuraxial analgesic/anesthetic procedure in obstetric patients, every effort should be made to perform a bleeding history assessment and determine the thrombocytopenia etiology before admission for delivery. Whereas multiple other professional societies (obstetric, interventional pain, and hematologic) have published guidelines addressing platelet thresholds for safe neuraxial procedures, the US anesthesia professional societies have been silent on this topic. Despite a paucity of high-quality data, there are now meta-analyses that provide better estimations of risks. An interdisciplinary taskforce was convened to unite the relevant professional societies, synthesize the data, and provide a practical decision algorithm to help inform risk-benefit discussions and shared decision making with patients. Through a systematic review and modified Delphi process, the taskforce concluded that the best available evidence indicates the risk of spinal epidural hematoma associated with a platelet count  $\geq 70,000 \times 10^6/L$  is likely to be very low in obstetric patients with thrombocytopenia secondary to gestational thrombocytopenia, immune thrombocytopenia (ITP), and hypertensive disorders of pregnancy in the absence of other risk factors. Ultimately, the decision of whether to proceed with a neuraxial procedure in an obstetric patient with thrombocytopenia occurs within a clinical context. Potentially relevant factors include, but are not limited to, patient comorbidities, obstetric risk factors, airway examination, available airway equipment, risk of general anesthesia, and patient preference. **Endorsed by the American Society of Regional Anesthesia and Pain Medicine (ASRA), American College of Obstetricians and Gynecologists (ACOG), and the Society for Maternal-Fetal Medicine (SMFM).** (Anesth Analg XXX;XXX:00–00)

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On October 9, 2020, the American Society of Hematology (ASH) affirmed that this consensus statement has value for hematologists. The consensus panel that developed the statement included three ASH representatives, and the final statement was reviewed by the Guideline Oversight Subcommittee and Committee on Quality. ASH did not otherwise have input into the development of this consensus statement.

Reprints will not be available from the authors.

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## GLOSSARY

**95% CI** = 95% confidence interval; **AAGBI** = Association of Anaesthetists of Great Britain and Ireland; **ACC/AHA** = American College of Cardiology/American Heart Association; **ACOG** = American College of Obstetricians and Gynecologists; **ADP** = adenosine 5' diphosphate; **AFLP** = acute fatty liver of pregnancy; **ALT** = alanine aminotransferase; **aPTT** = activated partial thromboplastin time; **ASH** = American Society of Hematology; **ASRA** = American Society of Regional Anesthesia and Pain Medicine; **AST** = aspartate aminotransferase; **CBC** = complete blood count; **CLASP** = Collaborative Low-dose Aspirin Study in Pregnancy; **COR** = Class of Recommendation; **COX** = cyclooxygenase; **CSE** = combined spinal-epidural; **CT** = closure time; **DIC** = disseminated intravascular coagulation; **EDTA** = ethylenediamine tetra-acetic acid; **EO** = expert opinion; **Epi** = epinephrine; **Hb** = hemoglobin; **HELLP** = hemolysis, elevated liver enzymes, low platelet count; **ITP** = immune thrombocytopenia; **IV** = intravenous; **IVIG** = intravenous immunoglobulin; **LD** = limited data; **LDH** = lactate dehydrogenase; **LOE** = level of evidence; **MPV** = mean platelet volume; **MRI** = magnetic resonance imaging; **NR** = nonrandomized; **PBS** = peripheral blood smear; **PFA** = platelet function analyzer; **PLT** = platelet; **PT** = prothrombin time; **RCT** = randomized controlled trial; **REDCap** = Research Electronic Data Capture; **ROTEM** = rotational thromboelastometry; **SMFM** = Society for Maternal Fetal Medicine; **SOAP** = Society for Obstetric Anesthesia and Perinatology; **TEG** = thromboelastography; **TTP** = thrombotic thrombocytopenic purpura

### Why was this consensus statement developed?

This consensus statement was commissioned by the Society for Obstetric Anesthesia and Perinatology (SOAP) to address the risks and benefits of performing neuraxial procedures in obstetric patients with thrombocytopenia. Representatives were chosen to provide interdisciplinary input by the following subspecialty professional organizations: American Society of Regional Anesthesia and Pain Medicine (ASRA), American College of Obstetricians and Gynecologists (ACOG), Society for Maternal-Fetal Medicine (SMFM), and the American Society of Hematology (ASH).

### What other statements or guidelines are available on this topic?

There are multiple national subspecialty professional organizations (hematology, obstetric, and transfusion medicine) that address the performance of neuraxial procedures in patients with thrombocytopenia, but the US anesthesia professional organizations have remained silent on this topic.

### How does this statement differ from existing guidelines?

This consensus statement focuses on obstetric patients with moderate to severe thrombocytopenia (platelet count  $<100,000 \times 10^6/L$ ), whereas existing guidelines cover a range of other related topics and patient populations, primarily related to lumbar punctures.

Up to 12% of obstetric patients with pregnancy-related complications meet criteria for the diagnosis of thrombocytopenia in pregnancy, with ~1% of patients having moderate to severe disease defined as  $<100,000 \times 10^6/L$ .<sup>1</sup> Obstetric patients with thrombocytopenia are often denied neuraxial procedures due to the perceived increased risk for spinal epidural hematoma. Opting for general anesthesia rather than neuraxial anesthesia has the potential to result in maternal morbidity and fetal exposure to pharmacologic agents.<sup>2-4</sup> Despite the paucity and low quality of evidence to guide anesthetic practice, anesthesiologists must make clinical decisions (often with time constraints) about whether to proceed with neuraxial anesthesia in obstetric patients with thrombocytopenia. This consensus statement was developed to provide the best available evidence and a clinical decision aid to inform risk-benefit discussions with patients and obstetricians and to enable anesthesiologists to engage in effective shared decision making.

## METHODS

The taskforce formulated this consensus statement based on a modified Delphi process that occurred between January 2018 and December 2019 and included a systematic review of the literature, 2 anonymous questionnaires, 2 face-to-face meetings, and multiple telephone and e-mail exchanges (Supplemental Digital Content 1, Figure, <http://links.lww.com/AA/D308>). The taskforce members were designated by the 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], and American Society of Hematology [ASH]), taskforce Co-Chairs (L.L. and M.E.B.), and approved by the Society for Obstetric Anesthesia and Perinatology (SOAP) board of directors to comprise the taskforce. These designees included experts in the hematologic and obstetric implications of thrombocytopenia in pregnancy, neuraxial anesthesia, and statistical methods. Prospective members were initially contacted by

their professional organization to assess their interest (all elected to participate), and then received a standard, formal letter of invitation. The taskforce members (4 hematologists, 2 obstetricians, 9 anesthesiologists, 1 statistician, and 1 librarian scientist) came from 15 US academic institutions (Supplemental Digital Content 1, Figure, <http://links.lww.com/AA/D308>). An obstetric patient with thrombocytopenia without a background in health care was confidentially identified and invited to review the decision aid and provided feedback as well. The completed consensus statement was sent to SOAP members for public comment. The statement was also sent to ACOG, SMFM, ASRA, and ASH for endorsement.

The modified Delphi consensus process included both formal and informal methods.<sup>5</sup> An extensive risk assessment for spinal epidural hematoma was done using a Research Electronic Data Capture (REDCap) questionnaire sent to the taskforce members and 17 additional SOAP-affiliated anesthesiologists chosen by the Co-Chairs (M.E.B. and L.L.) to represent diverse geographic and practice settings (Supplemental Digital Content 1, Figure, <http://links.lww.com/AA/D308>). A second focused questionnaire was then administered to the 5 hematology experts. These results, national and international society recommendations and guidelines (Supplemental Digital Content 2, Table 1, <http://links.lww.com/AA/D309>) as well as the results of published surveys of the willingness of anesthesiologists to perform neuraxial procedures in the obstetric patient with thrombocytopenia (Supplemental Digital Content 2, Table 2, <http://links.lww.com/AA/D309>), were reviewed and incorporated into deliberations. Differences of opinion were discussed, and consensus between taskforce members was attained. All taskforce members reviewed and approved the final recommendations and decision aid.

### Literature and Systematic Review

The taskforce reviewed the relevant literature to create this consensus statement. The search strategy is available in a previously published systematic review and meta-analysis that identified all published cases of neuraxial procedures (lumbar puncture; spinal, epidural, and combined spinal epidural procedures; and epidural catheter removal) performed in diverse populations of patients with thrombocytopenia with subsequent development of spinal epidural hematoma.<sup>6</sup> The meta-analysis found the sample probability of spinal epidural hematoma for all neuraxial procedures to be low above an imprecise range beginning around  $70,000\text{--}75,000 \times 10^6/\text{L}$ , with an estimated event rate within this sample of 7476 procedures to be 0.097% (95% confidence interval [CI], 0.002-0.2). This estimate is consistent with previous upper bound risk

estimates in prior studies of obstetric patients with thrombocytopenia.<sup>7-10</sup>

### Grading of Consensus Recommendations

Recommendations are categorized by Class of Recommendation (COR) and level of evidence (LOE) based on the American College of Cardiology/American Heart Association (ACC/AHA) classification system.<sup>11</sup> COR denotes the risk-benefit ratio and strength of recommendation (class I [strong], class IIa [moderate], class IIb [weak], and class III [no benefit or harm]). LOE describes the quality of evidence (level A [high-quality evidence from >1 RCT], level B-R [randomized], level B-NR [nonrandomized], level C-LD [limited data], and level C-EO [expert opinion]). Two authors (M.E.B. and K.A.) reviewed the evidence and graded the recommendations with a third author (L.L.) engaged for discussion of any questions or disagreements that arose. All taskforce members reviewed the classes and levels of recommendations during the review process and any disagreements were reconciled.

## BACKGROUND

### Thrombocytopenia in Pregnancy and Postpartum

The more common etiologies of thrombocytopenia in pregnancy include (1) gestational thrombocytopenia, (2) immune thrombocytopenia (ITP), and (3) thrombocytopenia associated with hypertensive disorders of pregnancy (eg, preeclampsia; hemolysis, elevated liver enzymes, low platelet count [HELLP] syndrome). Rarer conditions either associated with pregnancy ([eg, acute fatty liver of pregnancy {AFLP}] or not associated with pregnancy [eg, thrombotic thrombocytopenic purpura {TTP} or inherited thrombocytopenia]), and sepsis-induced thrombocytopenia were outside the scope of these recommendations. The incidence and associated findings of each condition are presented in Table 1.

The detailed evaluation and workup of thrombocytopenia in pregnancy is outside the scope of these recommendations, but has been described elsewhere.<sup>13,14</sup> Some general components include comparison of platelet counts before and during pregnancy and a thorough evaluation of bleeding history and signs of disseminated intravascular coagulation (DIC). Knowing that 25%–46% of healthy patients without a bleeding diathesis will have at least 1 symptom normally associated with a bleeding diathesis,<sup>15</sup> it is prudent to try to determine whether further workup is needed before the patient's admission for delivery. Studies comparing general screening questions on bleeding symptoms administered to controls and patients with Von Willebrand disease are variable in sensitivity for predicting disease.<sup>15,16</sup> However, targeted questions

**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	5–11	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	5–8	Onset in late second or third trimester ( $>20$ wk of gestation)	$\geq 300$ mg urine protein in 24 h or protein/creatinine ratio of $\geq 0.3$ or end-organ injury	Systolic BP $\geq 140$ mm Hg or diastolic BP $\geq 90$ 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.<sup>12</sup>

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.

addressing family history of bleeding disorders and bleeding after surgical procedures (tonsillectomy and tooth extraction) may be useful to detect bleeding disorders.<sup>16–18</sup> For this consensus statement, specific bleeding risk assessment models were reviewed and distilled by the taskforce into a set of categories to evaluate bleeding history (Table 2).<sup>19–21</sup> These bleeding history assessments can serve as a guide to compose patient questions to aid in clinical decision making, although these tools have not been validated in pregnancy or in patients with thrombocytopenia.

### Thrombocytopenia Etiology and Bleeding Risk

The bleeding risk in the setting of a specific thrombocytopenia etiology likely results from a complex interplay of platelet number, maturity, activation, and maternal factors including comorbid hepatic and renal function and other coagulation defects. As such, it is not practical to make categorical generalizations about the risk of bleeding in patients with thrombocytopenia with ITP versus those with preeclampsia. In ITP, platelet function can either be increased or decreased compared to healthy controls.<sup>22</sup> Similarly, a recent systematic review and meta-analysis on platelet function in pregnant women highlighted an increase in mean platelet volume ([MPV] a marker of platelet activation) in women with preeclampsia compared to those without preeclampsia.<sup>23</sup> There was no significant difference in platelet aggregation in the 2 groups, and platelet adhesion was not investigated.

### Thrombocytopenia-Related Complications of Neuraxial Anesthesia: Spinal Epidural Hematoma

Spinal epidural hematoma can be associated with high morbidity. The incidence in the general obstetric population is estimated to be between 1:200,000 and 1:250,000.<sup>3,24</sup> However, the incidence of spinal epidural hematoma specifically in obstetric patients with thrombocytopenia ( $<100,000 \times 10^6/L$ ) is unknown. In a 2020 systematic review and meta-analysis of papers published between 1947 and 2018 reviewing 7509 neuraxial procedures in a cohort of heterogeneous patients with thrombocytopenia, most spinal epidural hematomas occurred in patients with lumbar punctures and platelet counts  $<50,000 \times 10^6/L$ .<sup>6</sup> Of a total 33 spinal epidural hematomas, within the platelet count ranges of  $1,000–25,000 \times 10^6/L$ ;  $26,000–50,000 \times 10^6/L$ ;  $51,000–75,000 \times 10^6/L$ ; and  $76,000–99,000 \times 10^6/L$ , there were 14, 6, 9, and 4 spinal epidural hematomas, respectively. There were only 5 reported obstetric patients with spinal epidural hematoma with platelet counts between  $44,000$  and  $91,000 \times 10^6/L$  (2 after epidural and 3 after spinal procedures). One of the patients had an underlying spinal arteriovenous malformation and a second was coagulopathic at the time of inadvertent epidural catheter removal both of which were thought to be contributory comorbidities. Of the 3 remaining patients, 2 had HELLP syndrome and 1 had eclampsia.<sup>6</sup>

In that same study, the clinical presentations summarized in the systematic review were diverse: presenting symptoms comprised lower extremity motor deficits 13 (59%), back pain 9 (41%), lower extremity

**Table 2. Assessment of Bleeding History and Possible Underlying Disorder of Hemostasis in the Obstetric Patient<sup>a</sup>**

- 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

<sup>a</sup>Patients with a history concerning for a hemostatic disorder should be considered for further evaluation, including consultation with a hematologist and focused laboratory testing. These bleeding history assessments can serve as a guide to compose patient questions to aid in clinical decision making although these tools have not been validated in pregnancy or in patients with thrombocytopenia.

pain 2 (9%), lower extremity paresthesia 5 (23%), saddle paresthesia 2 (9%), and urinary or bowel dysfunction 6 (27%). Multiple patients presented with >1 deficit. Notably, 18 (95%) were symptomatic within 48 hours of the procedure. Review of the cases highlighted the importance of urgent imaging and surgical consultation to determine best course of action to improve outcomes.

An additional study analyzing 573 obstetric patients with thrombocytopenia combined with 951 cases from the literature reported 1524 patients received neuraxial procedures without developing a spinal epidural hematoma.<sup>9</sup> Although no spinal epidural hematomas were reported, the authors were able to estimate the upper limits of the 95% CI for the risk of spinal epidural hematoma stratified by platelet count. For platelet counts between 70,000 and 100,000  $\times 10^6/L$ , 50,000 and 69,000  $\times 10^6/L$ , and <50,000  $\times 10^6/L$ , the upper limits of the 95% CI were 0.2%, 3%, and 11% respectively.<sup>9</sup> A more recent study added an additional 471 patients and further reduced the upper limits of the 95% CI to 0.19%, 2.6%, and 9%.<sup>10</sup>

### Laboratory Assessment of Bleeding Risk

The complete blood count (CBC), which provides the absolute platelet count within approximately  $\pm 3\%$  coefficient of variation, can identify which obstetric patients have thrombocytopenia.<sup>25</sup> Rarely, a patient may have a spuriously low automated platelet count due to clumping induced by ethylenediamine tetraacetic acid (EDTA). If there is a spuriously low platelet count due to clumping, once the sample has been collected in a tube with an alternative anticoagulant

(eg, citrate) or counted manually on peripheral blood smear, the platelet count will be normal.

Available coagulation tests are summarized in Table 3. Ideally, additional laboratory testing would assess the interplay between platelet number, platelet function, and other essential coagulation elements to elucidate which obstetric patients are at increased risk for major neuraxial bleeding. The activated partial thromboplastin time (aPTT) and prothrombin time (PT) assays use a phospholipid emulsion instead of platelets to activate coagulation and test for inherited or acquired factor deficiencies. Unless an inherited or acquired coagulation defect is known or suspected, the PT and aPTT have no utility in predicting bleeding risk in a pregnant woman with thrombocytopenia.

Thromboelastography (TEG) and rotational thromboelastometry (ROTEM) are dynamic tests that may be performed at the point of care to evaluate the viscoelastic properties of blood clots in whole blood subjected to rotational forces. There have been studies reporting the use of ROTEM or TEG with normal parameters before neuraxial procedures in obstetric patients with thrombocytopenia without spinal epidural hematoma formation,<sup>26,27</sup> other studies in oncologic patients with thrombocytopenia have reported no correlation between TEG and ROTEM parameters and clinical bleeding except at very low platelet counts (<50,000  $\times 10^6/L$ ).<sup>28,29</sup>

The platelet function analyzer (PFA)-100 (Siemens, Munich, Germany) tests platelet function by simulating the in vivo hemostatic mechanism of platelet plug formation. Time to formation of the platelet plug is the closure time (CT). An abnormal CT may be found in patients with thrombocytopenia (platelet <100,000  $\times 10^6/L$ ), anemia (hemoglobin <10 g/dL), or a significant qualitative platelet defect. However, this test lacks specificity and predictive value for a specific disorder and does not correlate with degree of bleeding risk.<sup>30</sup> The platelet aggregation test measures agglutination and aggregation of platelets in response to different agonists, but studies evaluating its utility in obstetric patients are lacking.

There are several studies that suggest abnormalities in hemostasis parameters such as PT, aPTT, TEG, and PFA-CT in some patients with preeclampsia.<sup>26,27,31–36</sup> Some have demonstrated that, compared to patients without preeclampsia, preeclamptic patients with normal platelet count appear to be hypercoagulable.<sup>37,38</sup> Two of these studies highlight a platelet count of 70,000–75,000  $\times 10^6/L$  as the cut-off below which TEG suggests hypocoagulability.<sup>33,34</sup> However, there is a notable degree of inconsistency correlating hemostatic laboratory parameters in these studies and lack of data showing correlation between these laboratory tests and the risk of spinal epidural hematoma. Therefore, the expert panel felt that there

<b>Table 3. Laboratory Testing Assessments</b>			
<b>Test</b>	<b>Assay principle</b>	<b>Clinical application</b>	<b>Limitations</b>
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 <sup>6</sup> /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.

was insufficient evidence to recommend the routine use of 1 or more of these laboratory tests in pregnant or postpartum women with thrombocytopenia for determination of the safety of neuraxial anesthesia.

### **Platelet Transfusion Before Neuraxial Procedures**

Some professional organizations recommend administering prophylactic platelet transfusions before lumbar puncture for platelet counts ranging from <20,000 to <50,000 × 10<sup>6</sup>/L to decrease the risk of spinal epidural hematoma (Supplemental Digital Content 2, Table 1, <http://links.lww.com/AA/D309>).<sup>39-41</sup> However, careful consideration of the associated risks and benefits is required to evaluate whether this approach is advisable. A recent Cochrane review found "no evidence from randomized controlled trials 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."<sup>42</sup> Furthermore, they suggested that to detect a decrease in the number of patients with major procedure-related bleeding from 2 of 1000 to 1 of 1000, the sample size for a randomized controlled trial comparing the outcome with and without platelet transfusion would be >47,000 patients.

Platelet transfusion also has associated risks, including transfusion reaction, transfusion-related acute lung injury, and transfusion-associated circulatory overload. In the United Kingdom, 34% of transfusion-related adverse events were due to platelet transfusion.<sup>43</sup> Although a transfused whole blood unit of platelets is expected to increase the platelet count between 5000 and 10,000 × 10<sup>6</sup>/L, and an apheresis-derived bag of platelets is expected to increase the platelet count between 30,000 and 50,000 × 10<sup>6</sup>/L, increases in platelet numbers are variable in response to transfusions. Furthermore, platelet transfusions

may be less effective in patients with preeclampsia or other disorders, likely due to platelet consumption.<sup>13,44</sup> There are a few reports of improvement in platelet count in HELLP syndrome after plasma exchange, but generally not with platelet transfusion alone.<sup>45-47</sup> ACOG recommends platelet transfusion in preeclampsia for active bleeding or to improve the platelet count to  $50,000 \times 10^6/L$  before cesarean delivery.<sup>13</sup>

For the treatment of ITP in pregnancy, platelet transfusion alone is not usually effective, but can be considered with concurrent intravenous immunoglobulin (IVIG) or corticosteroid therapy.<sup>48</sup> However, specific platelet thresholds at which pregnant patients with ITP should be treated were not identified. According to ACOG, in pregnant women with thrombocytopenia, treatment with IVIG or corticosteroids is recommended if the patient has symptomatic bleeding, for a platelet count  $<30,000 \times 10^6/L$ , and/or to increase to platelet counts considered safe for procedures (eg, neuraxial procedures and cesarean delivery).<sup>13</sup> Platelet transfusions are recommended to temporize only in cases of life-threatening hemorrhage or to prepare for urgent surgery because the response to platelet transfusion is short-lived.<sup>13</sup>

### Thrombocytopenia, Aspirin Therapy, and Bleeding Risk

ASRA guidelines state that nonsteroidal anti-inflammatory drugs (including aspirin) do not add significant risk to the development of spinal epidural hematoma and do not recommend withholding medications to perform a neuraxial procedure.<sup>49</sup> However, what is not addressed is whether aspirin in the setting of thrombocytopenia increases the risk for spinal epidural hematoma. This is a clinically relevant question because ACOG recommends a low-dose (81 mg/d) aspirin be administered to pregnant women at high risk for preeclampsia and be considered for women with 1 or more of several risk factors for preeclampsia.<sup>50</sup> Aspirin irreversibly inhibits cyclooxygenase (COX) required for thromboxane synthesis, subsequently reducing platelet aggregation for the life of the platelet. The plasma half-life of aspirin is 20 minutes and once discontinued, does not affect new platelets once they are formed.<sup>51</sup> Although the lifetime of the affected platelet can be up to 10 days, platelet activity is restored by approximately 10% each day due to platelet turnover. It may take up to 10 days for the entire platelet population to be renewed; however, normal hemostasis has been shown with as little as 20% normal platelet COX activity.<sup>52</sup>

There are limited data that can be gleaned from studies of pregnant women on aspirin regarding platelet function and/or neuraxial procedures, although these patients did not have concomitant thrombocytopenia. In the Collaborative Low-dose Aspirin Study in Pregnancy (CLASP), 1422 women had epidural

procedures while taking 60 mg aspirin daily.<sup>53</sup> None of the patients developed an epidural hematoma. In a separate study, the PFA-100 was used to analyze platelet function in pregnant women taking aspirin (81 mg).<sup>54</sup> After 4 weeks, 25 of 87 women (28.7%) did not have changes in the PFA-100 testing suggesting that not all women have changes in platelet function while taking low-dose aspirin. Similarly, a TEG study of platelet function did not show any measurable changes in 12 pregnant and 8 nonpregnant volunteers 6 hours after ingesting high-dose aspirin 600 mg.<sup>55</sup>

In summary, considering the paucity of evidence to guide practice in obstetric patients with thrombocytopenia and concomitant aspirin use, 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.

### Recommendations From Other Professional Organizations Regarding Platelet Thresholds for Neuraxial Procedures

Obstetric, hematologic, oncologic, radiologic, transfusion medicine, and neurological societies have made recommendations regarding platelet thresholds for neuraxial procedures (Supplemental Digital Content 2, Table 1, <http://links.lww.com/AA/D309>). Lumbar punctures had the lowest recommended acceptable range ( $20,000-50,000 \times 10^6/L$ ) to perform diagnostic lumbar puncture in patients with leukemia or suspected meningitis.<sup>40,41,56,57</sup> Societal recommendations for anesthetic neuraxial procedures most commonly used a limit of  $80,000 \times 10^6/L$ .<sup>58</sup> However, the Scandinavian Society of Anaesthesiology recommends lower thresholds for anesthetic neuraxial procedures that are thought to be associated with a lower risk for anesthesia-related morbidity and mortality than the alternative, general anesthesia. Likewise, they recommend a lower threshold for single-shot spinal compared to epidural procedures.<sup>59</sup> The Association of Anaesthetists of Great Britain and Ireland (AAGBI) is the only society that specifically addresses obstetric patients and provides risk levels of spinal epidural hematoma at various platelet count thresholds for specific disease states such as preeclampsia, ITP, intrauterine fetal demise, and placental abruption (Supplemental Digital Content 2, Table 1, <http://links.lww.com/AA/D309>).<sup>60</sup>

### RECOMMENDATIONS FOR PHYSICIAN ANESTHESIOLOGISTS AND OTHER PRACTITIONERS

This consensus statement is not intended to set out a legal standard of care and does not replace medical care or the judgment of the responsible medical professional considering all the circumstances presented by

an individual patient. This statement is not intended to ensure a successful patient outcome in every situation and is not a guarantee of any specific outcome. This consensus statement is subject to periodic revision as additional data becomes available. In all cases, it is assumed that the obstetric patients with thrombocytopenia do not have additional contraindications to neuraxial anesthesia.

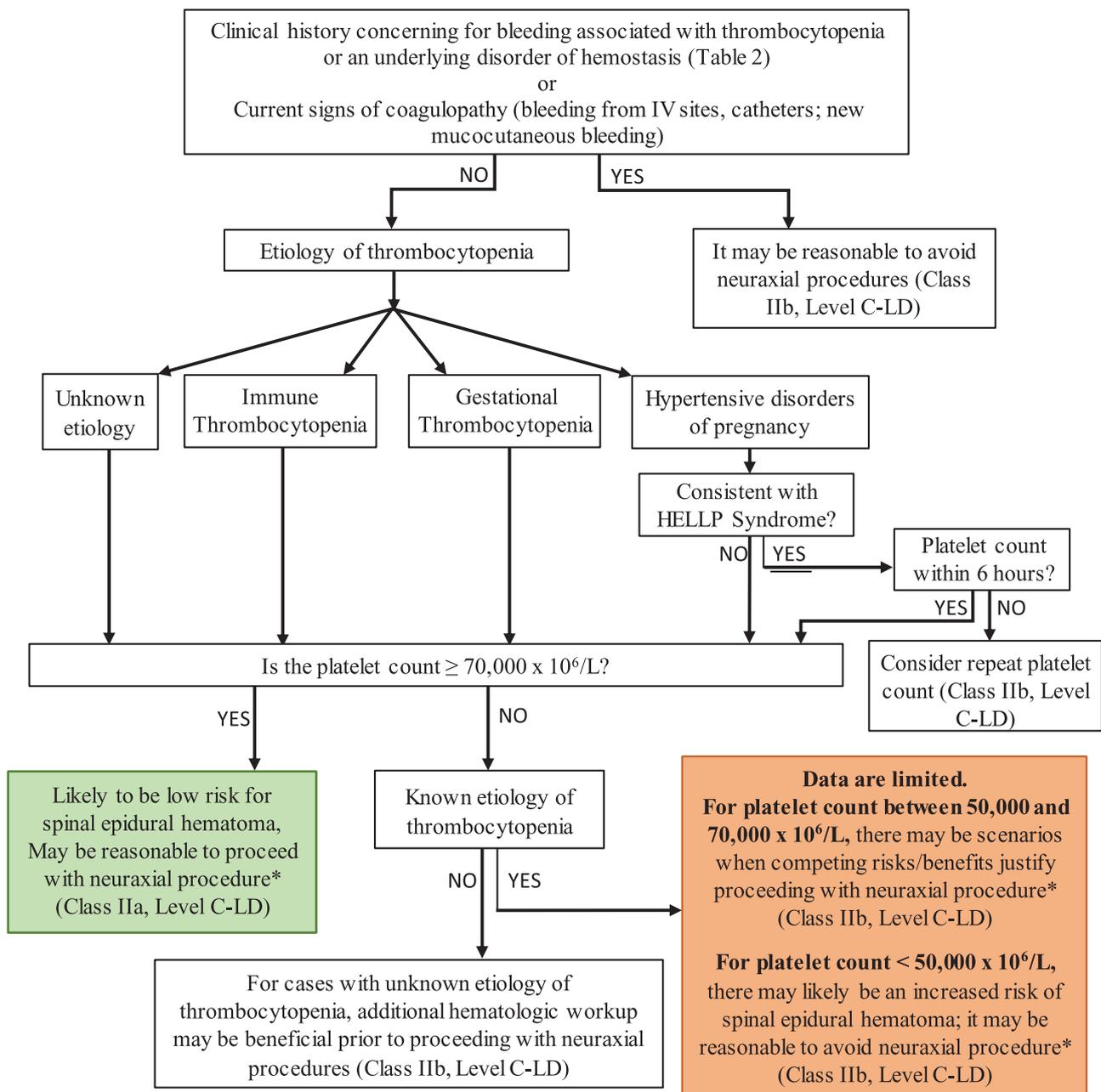
The decision of whether to proceed with a neuraxial procedure in an obstetric patient with thrombocytopenia occurs within a clinical context. Potentially relevant factors include but are not limited to comorbidities, obstetric risk factors, airway examination, available airway equipment, risk of general anesthesia, and patient preference. Invariably, concern for spinal epidural hematoma with a neuraxial procedure must be weighed against the consequences of withholding neuraxial analgesia and/or proceeding with general anesthesia. Each of these factors was considered during the modified Delphi process. Additionally, in some centers, expert hematologic consultation is available 24 hours a day, 7 days a week; at others, it is rarely or never available. In response, the recommendations were crafted to account for patient and practice setting variation. Finally, there were lengthy discussions of whether the risk of spinal epidural hematoma was lower in the setting of a spinal versus an epidural procedure because this distinction appears in some publications and international professional organizations' recommendations. This hypothesis is intuitively plausible, given the smaller gauge (25–29 g) and “pencil point” needle tip commonly used in obstetric practice, compared with epidural needles (17–18 g), larger (20–22 g) “cutting” needle tip used for lumbar punctures, and the lack of in situ catheter. However, the literature to support this notion in patients with thrombocytopenia is sparse. In the 2020 systematic review of spinal epidural hematomas in patients with thrombocytopenia, the largest number of hematomas occurred in severely thrombocytopenic oncology patients ( $<50,000 \times 10^6/L$ ) that received lumbar punctures, in part because relatively few obstetric and other patients received spinal or epidural anesthetics with that degree of thrombocytopenia.<sup>6</sup> The taskforce, with its representatives from SOAP, ASRA, ASH, ACOG, and SMFM, chose the threshold platelet count for neuraxial procedures of  $70,000 \times 10^6/L$  with the caveats described below based on the available data suggesting a low sample spinal epidural hematoma event rate at or above that platelet count, and the known hypercoagulability of pregnancy. The taskforce acknowledged, however, that (a) the CBC has an approximately  $\pm 3\%$  coefficient of variation, meaning these data and recommendations cannot be precise and (b) there are maternal comorbidities and competing risks that will impact clinical decision making.

For guiding the assessment of whether to proceed with neuraxial anesthesia in the pregnant patient, we have divided the thrombocytopenic obstetric population into 2 categories: (a) the patient with a known thrombocytopenia etiology and (b) the patient without a known thrombocytopenia etiology. For the purposes of this consensus statement, patients with a known diagnosis of ITP have had a workup by a hematologist before pregnancy. Patients with gestational thrombocytopenia will have had a normal platelet count before pregnancy or early pregnancy and had a decline during pregnancy to  $\geq 70,000 \times 10^6/L$ . Patients with hypertensive disorders of pregnancy have met diagnostic criteria. Patients with an unknown thrombocytopenia etiology may include a patient that presents during pregnancy with new thrombocytopenia compared to previous platelet counts, without a clear etiology, or one for whom no previous platelet counts are available for comparison. Neuraxial procedures are defined as the following: spinal, epidural, combined spinal epidural, dural puncture epidural, and epidural catheter removal procedures.

### **The Obstetric Patient With a Known Etiology of Thrombocytopenia by Prior Workup or Confirmed Diagnosis of Hypertensive Disorders of Pregnancy<sup>a</sup>**

1. Assess for history of bleeding associated with thrombocytopenia (Table 2) and confirm no visible signs of DIC such as bleeding from intravenous (IV) sites, catheters, wounds, or new mucocutaneous bleeding (Figure).
  - a. For confirmed diagnosis of gestational thrombocytopenia or ITP, or confirmed diagnosis of hypertensive disorders of pregnancy (eg, preeclampsia):
    - i. If concern for a history of bleeding associated with thrombocytopenia or DIC (as described above), then it may be reasonable to avoid neuraxial procedures or seek expert hematologic evaluation before proceeding with the neuraxial procedure (class IIb and level C-LD).
    - ii. If the platelet count is  $\geq 70,000 \times 10^6/L$ , then there is likely to be a low risk of spinal epidural hematoma and it is reasonable to proceed with a neuraxial procedure if clinically indicated (class IIa and level C-LD).
    - iii. If the platelet count is between  $50,000$  and  $70,000 \times 10^6/L$ , then there may be scenarios when competing risks/benefits justify proceeding with a neuraxial procedure (class IIb and level C-LD).

<sup>a</sup>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 (ie, spinal versus epidural anesthetic).



\*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).

This consensus statement is not intended to set out a legal standard of care and does not replace medical care or the judgement of the responsible medical professional considering all of the circumstances presented by an individual patient. This statement is not intended to ensure a successful patient outcome in every situation and is not a guarantee of any specific outcome.

**Figure.** Thrombocytopenia in obstetric patients: decision aid for when to proceed with a neuraxial procedure. HELLP indicates hemolysis, elevated liver enzymes, low platelet count; IV = intravenous; LD = limited data.

- iv. If the platelet count is  $<50,000 \times 10^6/L$ , then there may likely be an increased risk of spinal epidural hematoma compared to a platelet count  $\geq 70,000 \times 10^6/L$  and it may be reasonable to avoid neuraxial procedures (class IIb and level C-LD).

The optimal frequency of laboratory testing in a pregnant patient with preeclampsia before neuraxial procedure is unknown and is at the discretion of the provider. Published recommendations range from 6 to  $\geq 12$  hours,<sup>61,62</sup> and clinical practices vary even more.<sup>63</sup> Some retrospective evidence suggests that thrombocytopenia in patients with preeclampsia is rare, and that platelet count changes from  $>100,000 \times 10^6/L$  to  $<100,000 \times 10^6/L$  within the 72 hours before delivery are even rarer.<sup>64</sup> Patients with HELLP syndrome are the subgroup most likely to experience a rapid decline in platelet count, and, therefore, the taskforce confined its recommendations of frequency of platelet count testing to this subset of the population. Identifying patients with HELLP can be challenging because up to 15% of afflicted patients lack hypertension.<sup>62</sup> Laboratory values that define HELLP syndrome include the following:<sup>62</sup>

- lactate dehydrogenase (LDH)  $\geq 600$  IU/L,
- aspartate aminotransferase (AST) or alanine aminotransferase (ALT) elevated more than twice the upper limit of normal, and
- platelet count  $<100,000 \times 10^6/L$ .

Acknowledging that some patients with HELLP syndrome may particularly benefit from an early epidural or combined spinal-epidural (CSE) procedure before the platelet count drops precipitously, the expert panel agreed that it might be reasonable to verify the platelet count within 6 hours of the planned neuraxial procedure or catheter removal.

- a. If clinical scenario is consistent with HELLP syndrome, then it may be reasonable to verify platelet count within 6 hours of the planned neuraxial procedure (class IIb and level C-LD).

### The Obstetric Patient Without a Known Etiology of Thrombocytopenia<sup>a</sup>

Some obstetric patients present to the labor and delivery floor with newly recognized thrombocytopenia. This heterogeneous group of patients includes those that were known to be thrombocytopenic in the antepartum period (but may not have received a formal diagnosis), those with new thrombocytopenia, and

<sup>a</sup>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 (ie, spinal versus epidural anesthetic).

patients without prior platelet counts available for comparison. When assessing the appropriateness of neuraxial anesthesia in an obstetric patient with thrombocytopenia:

1. Assess patient for bleeding history and possible underlying disorder of hemostasis (Table 2) and confirm no visible signs of DIC such as bleeding from IV sites, catheters, wounds, or new mucocutaneous bleeding.
  - a. If concern for an underlying disorder of hemostasis or DIC (as described above), then it may be reasonable to avoid neuraxial procedures or seek expert hematologic consultation before proceeding with the neuraxial procedure (class IIb and level C-LD).
  - b. If platelet count is  $<70,000 \times 10^6/L$ , then additional hematologic workup may be beneficial before proceeding with the neuraxial procedure (class IIb and level C-EO).
  - c. If there is no concern for an underlying disorder of hemostasis or DIC and the platelet count is  $\geq 70,000 \times 10^6/L$ , then there is likely to be a low risk for spinal epidural hematoma and it is reasonable to proceed with neuraxial procedure if clinically indicated<sup>a</sup> (class IIa and level C-LD).

### Other Recommendations

1. Aspirin, neuraxial procedures, and thrombocytopenia.
  - a. The taskforce members concluded that there was insufficient evidence to make a recommendation about performing neuraxial procedures in obstetric patients with thrombocytopenia taking aspirin.
2. Other laboratory testing and thrombocytopenia before neuraxial procedure.
  - a. The taskforce members concluded that there was insufficient evidence to make a recommendation about the use of additional laboratory tests (eg, PT, aPTT, TEG, ROTEM, and PFA) to aid in decision making regarding the safety of neuraxial anesthesia in obstetric patients with thrombocytopenia.

### QUALITY ASSURANCE/QUALITY IMPROVEMENT

Improvements in the care of an obstetric patient with thrombocytopenia depend on optimal interdisciplinary communication, iterative systems that identify patients at risk, and a culture that promotes nonjudgmental debriefings of cases. In addition, large-scale acquisition of better outcome data is needed. Specific recommendations at the local, national, and international levels include

1. Interdisciplinary knowledge of the etiologies of thrombocytopenia in pregnancy, and the associated protocols related to neuraxial procedures.
2. Early consultation with anesthesiology and hematology experts during pregnancy in patients with thrombocytopenia to coordinate treatment plan and address patient expectations.
3. Institutional pathways to quickly identify patients with suspected spinal epidural hematoma and obtain urgent magnetic resonance imaging (MRI) and follow-up care.
4. Population-level data on complications of neuraxial anesthesia in patients with thrombocytopenia, such as a national or international registry to catalog neuraxial procedures in these patients (all sub-populations) and occurrences of spinal epidural hematomas.

### CONCLUSIONS

The best available evidence indicates that the risk of spinal epidural hematoma with a platelet count  $\geq 70,000 \times 10^6/L$  is likely to be very low in the obstetric patient over a range of thrombocytopenia diagnoses that include gestational thrombocytopenia, ITP, and hypertensive disorders of pregnancy. There may be clinical scenarios where decisions are made to proceed with a neuraxial anesthetic at lower platelet counts. Patients with HELLP syndrome likely require closer monitoring and a more recent platelet count before neuraxial procedures. Because there are substantial risks associated with withholding a neuraxial analgesic/anesthetic procedure in obstetric patients, every effort should be made to investigate the bleeding history and thrombocytopenia etiology before admission for delivery. Ultimately, the decision of whether or not to proceed with a neuraxial procedure in an obstetric patient with thrombocytopenia occurs in a clinical context with relevant factors that include maternal comorbidities and airway examination, obstetric risk factors, available airway equipment, type of neuraxial procedure, and patient preference. These combined factors inform clinical decision-making and risk-benefit discussions with patients with thrombocytopenia. This approach maximizes the ability to consider potential therapies and use shared decision making between obstetric patients with thrombocytopenia and their providers regarding the safety, benefits, and putative risks associated with neuraxial anesthesia. ■

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