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

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Abstract

Background—Thrombocytopenia has been considered a relative or even absolute contraindication to neuraxial techniques due to the risk of epidural hematoma. There is limited literature to estimate the risk of epidural hematoma in thrombocytopenic parturients. The authors reviewed a large perioperative database and performed a systematic review to further define the risk of epidural hematoma requiring surgical decompression in this population.

Methods—The authors performed a retrospective cohort study utilizing the Multicenter Perioperative Outcomes Group (MPOG) database to identify thrombocytopenic parturients who received a neuraxial technique and to estimate the risk of epidural hematoma. Patients were stratified by platelet count and those requiring surgical decompression were identified. A systematic review was performed and risk estimates were combined with those from the existing literature.

Results—573 parturients with a platelet count <100,000 mm⁻³ who received a neuraxial technique across 14 institutions were identified in the MPOG database, and a total of 1,524 parturients were identified after combining the data from the systematic review. No cases of epidural hematoma requiring surgical decompression were observed. The upper bound of the 95% confidence interval for the risk of epidural hematoma for a platelet count of 0–49,000 mm⁻³ is 11%, for 50,000–69,000 mm⁻³ is 3%, and for 70,000–100,000 mm⁻³ is 0.2%.

Conclusions—The number of thrombocytopenic parturients in the literature who received neuraxial techniques without complication has been significantly increased. The risk of epidural hematoma associated with neuraxial techniques in parturients at a platelet count $<70,000 \text{ mm}^{-3}$ remains poorly defined due to limited observations.

Introduction

Neuraxial analgesia and anesthesia remain the standard of care for management of the laboring parturient and cesarean delivery.^{1,2} Even with modern advances in airway management, the incidence of failed intubation in pregnant women during cesarean delivery is approximately 1:443 with maternal mortality occurring at a rate of one death per 90 failed intubations.³ Intubation failure, inadequate ventilation, and aspiration represent leading causes of anesthesia-associated obstetric morbidity.⁴ Therefore, neuraxial techniques, which afford an opportunity to avoid airway instrumentation, are advocated for labor (to allow for conversion from labor epidural analgesia to cesarean delivery anesthesia) and cesarean delivery.

Thrombocytopenia, depending on its severity, has long been considered a relative or even absolute contraindication to neuraxial techniques due to a potential increased risk of epidural hematoma, a rare but dreaded complication that can result in permanent neurologic injury.⁵ Although there is no consensus on the acceptable platelet count required to safely perform neuraxial techniques, recent literature suggests that lower thresholds may be safe in pregnant women compared with the general population. There is limited data suggesting that epidural hematomas in obstetric patients appear to be rare, possibly due to the physiologic hypercoagulability of pregnancy and the generally high compliance of the epidural space in young parturients.^{6–8} The American College of Obstetricians and Gynecologists (ACOG)

Thrombocytopenia in Pregnancy Practice Bulletin recently concluded that neuraxial techniques are acceptable in parturients with platelet counts greater than 80,000 mm⁻³.9

Some studies estimate the overall risk of epidural hematoma associated with neuraxial techniques in obstetric patients to be approximately 1:200,000.^{10,11} However, the estimation of the risk of epidural hematoma in thrombocytopenic parturients following neuraxial techniques is evolving. Goodier *et al.* and Bernstein *et al.* recently reported 173 and 254 thrombocytopenic parturients (platelet count less than 100,000 mm⁻³) from two institutions and one institution, respectively, who received neuraxial techniques without an incident of epidural hematoma requiring surgical decompression. Both studies combined their findings with well-known case series of thrombocytopenic parturients receiving neuraxial techniques and found the upper bound of the 95% confidence interval for the risk of epidural hematoma to be 0.6% and 0.4%, respectively.^{12,13} While these studies provide information regarding overall risk of epidural hematoma in thrombocytopenic pregnant women, no multicenter study to date has stratified the risk of this complication by platelet count. Multicenter studies with larger datasets are essential to the study of infrequent events because they offer not only a larger sample size, but also generalizability that spans different patient populations, practice environments, and providers.

The current study sought to further define the risk of epidural hematoma requiring surgical decompression stratified by platelet count following neuraxial techniques in thrombocytopenic parturients (<100,000 mm⁻³) using the Multicenter Preoperative Outcomes Group (MPOG) database. We also sought to perform a systematic review of the literature to combine our data with previous studies reporting neuraxial techniques in thrombocytopenic pregnant women.

Materials and Methods

Approval from the University of Michigan (Ann Arbor, Michigan, USA) Institutional Review Board was obtained for this retrospective observational study. Each contributing organization's Institutional Review Board also approved aggregation of a Health Insurance Portability and Accountability Act limited data set into the MPOG centralized database. No patient care interventions were involved in this study so signed patient consent was waived and all patient identifiers were destroyed following data collection. In addition, Oregon Health & Science University (Portland, Oregon, USA) obtained an additional institutional review board approval for manual review of the source electronic health record for a specific patient requiring additional data collection per protocol. The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines were reviewed and followed in the conduct and reporting of this study.¹⁴ The protocol was presented and registered at the MPOG publications committee on September 14, 2015 and accepted with revisions on October 19, 2015.

The MPOG database and its data entry process have been described in detail previously.^{15,16} MPOG was formed in 2008 as a consortium of medical centers that routinely extracts the anesthetic intraoperative electronic health record data from each member institution into a

common database for research purposes. Data are compiled and rigorously validated to enable perioperative outcome comparisons across centers.

The MPOG database was queried for all obstetric patients age 18-55 with a platelet count <100,000 mm⁻³ within 72 hours prior to receiving a neuraxial technique – including epidural, spinal, and combined spinal-epidural analgesia/anesthesia from January 2004 through September 2015. A combination of administrative billing codes and free text query for relevant phrases including 'labor', 'epidural', 'c-section', 'cesarean', and 'caesarean' was used to identify possible obstetric neuraxial procedures. The complete list of query terms is found in Appendix II. The flowchart for patient selection is presented in Figure 1. Patients who had an underlying coagulopathic diagnosis (von Willebrand disease, platelet dysfunction, factor XIII deficiency, factor VII deficiency, Evan's syndrome, hemophilia carrier, history of abnormal bleeding, pharmacologically induced, May-Hegglin anomaly, platelet storage pool deficiency) or were taking an antiplatelet medication were excluded. Patient characteristics including age, ASA class, emergent nature of surgery, body mass index (BMI), coexisting conditions predisposing to thrombocytopenia (gestational thrombocytopenia, preeclampsia, idiopathic thrombocytopenic purpura, and HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome), and anesthetic technique were identified and recorded.

Thrombocytopenic obstetric patients receiving neuraxial techniques were stratified into predefined categories based on the pre-placement platelet count. The platelet ranges were defined as $0 - 49,000 \text{ mm}^{-3}$, $50,000 - 69,000 \text{ mm}^{-3}$, and $70,000 - 99,000 \text{ mm}^{-3}$. Patients who underwent surgical evacuation of an epidural hematoma within 6 weeks of receiving a neuraxial technique, regardless of platelet count, were identified by administrative billing codes. For centers not reporting administrative billing codes, all operative episodes not typically associated with obstetric care (D&C for retained placenta, tubal ligation) within 6 weeks of receiving a neuraxial technique were manually reviewed to identify decompressive laminectomies. For operative episodes identified in the database suggestive of decompressive laminectomy, individual medical charts were manually reviewed in detail to confirm the performance of this surgery.

In order to combine our risk estimates with those from the existing literature, we conducted a systematic review of studies reporting 10 or more thrombocytopenic parturients who received neuraxial techniques. The systematic review was undertaken in order to increase the power of our study to define the risk of this rare event. PubMed and Embase.com searches were performed on June 9, 2016 to capture English language, human studies dating to the inception of PubMed and Embase that detail neuraxial techniques in pregnant patients with thrombocytopenia. Both searches consisted of controlled subject headings (Medical Subject Headings in PubMed; EMTREE in Embase) and a set of title or abstract keywords, which included synonyms and spelling variations. Sentinel articles were used to harvest terms and test the effectiveness of the searches. We used Web of Science to search the references and forward citations of the included studies. Conference abstracts and papers, letters, and editorials were included in the Embase search. The searches retrieved 749 unique citations after duplicates were removed in Endnote X6 (Thomson Reuters, New York, NY, USA). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines

were reviewed and followed when performing the systematic review.¹⁷ The complete search strategies are available in Appendix III. After the search was completed, two authors (LL and MB) reviewed each article for inclusion. Criteria for inclusion were as follows: studies reporting neuraxial techniques in thrombocytopenic parturients, description of whether or not epidural hematomas occurred, and platelet count stratification. Studies (or portions of studies) were excluded for transfusion of platelets prior to neuraxial technique and if parturients with normal platelet counts became thrombocytopenic after receiving a neuraxial technique. If clarification of data presented was needed, authors were emailed for further information and that data were included and cited as personal communication. Once final articles were selected, data were extracted by one author (LL) and validated by another (MB).

Statistical Analysis

The 95% confidence intervals for the incidence of epidural hematoma of each platelet range were reported using the "rule of 3" – a statistical method to estimate the upper bound of the 95% confidence interval for zero-numerator problems. The "rule of 3" states that for trials in which no events have occurred, the upper bound of the 95% confidence interval can be estimated by 3/n.¹⁸ All analyses were performed using SPSS 21.0 software (SPSS Inc., Chicago, IL, USA).

Results

In the MPOG database, we identified 84,471 obstetric patients across 19 academic medical centers and private hospitals who received a neuraxial technique with platelet counts measured within 72 hours prior to placement. Of these, there were 573 patients from 14 institutions with platelet counts <100,000 mm⁻³ (0.7%) included for analysis.

The characteristics of the thrombocytopenic parturients who received a neuraxial technique are described in Table 1. The number of anesthetic techniques performed and the etiologies of thrombocytopenia stratified by platelet count are illustrated in Table 2.

Automated review of post-neuraxial operative records identified one patient who underwent laminectomy within 6 weeks of the neuraxial procedure. The patient's platelet count was 205,000 mm⁻³ at the time of labor epidural placement, and she developed symptoms of lateral thigh pain, medial knee numbness, and weakness with hip flexion and knee extension following vaginal delivery. She underwent laminectomy for a suspected epidural abscess 14 days after epidural placement, however no abscess or hematoma was identified. A prolapsed L3-L4 disc was thought to be the source of her neurologic symptoms and the patient made a complete neurologic recovery. No cases of epidural hematoma resulting in decompressive surgery within 6 weeks of follow-up were identified among any patients, regardless of platelet count.

The data obtained from MPOG are outlined in Table 3. For those patients with platelet counts of 70,000 – 99,000 mm⁻³ (n = 522) the upper bound of the 95% confidence interval was 0.6%, for counts of 50,000 – 69,000 mm⁻³ (n = 36) the upper bound of the 95% confidence interval was 8%, and for platelet counts of 0 – 49,000 mm⁻³ (n = 15) the upper

bound of the 95% confidence interval was 20%. The distribution of thrombocytopenic parturients from the MPOG database that received a neuraxial technique is illustrated as a histogram in Figure 2. The time differences between obtaining the platelet count and performing a neuraxial technique in thrombocytopenic parturients from the MPOG database are displayed in Supplemental Digital Content I. The distribution based on platelet count for these time differences is displayed in Supplemental Digital Content II.

For the systematic review, 14 studies were identified that met inclusion criteria. The study selection process is presented in Figure 3. Details of the included studies are presented in Table 4.^{6,12,13,19–29} Reported platelet count ranges from several studies did not discretely fall within the platelet count ranges of $50,000 - 69,000 \text{ mm}^{-3}$ and $70,000 - 100,000 \text{ mm}^{-3}$ used in the analysis of the MPOG cases; these were not included in the risk analysis for these ranges but were included in the overall reported number of neuraxial procedures performed in thrombocytopenic parturients. None of the centers involved in these previous studies contributed data to MPOG, resulting in no patient overlap. The platelet count ranges were selected after reviewing the literature and recognizing that multiple studies, including the largest study identified in our systematic review, reported data using a platelet count of 70,000 mm⁻³ as a cutoff.²² After combining data from previous case series with the data from MPOG, 84% (n = 1,286) had platelet counts of $70,000 - 100,000 \text{ mm}^{-3}$ with the upper bound of the 95% confidence interval calculated as 0.2%; 6% (n = 89) had platelet counts of $50.000 - 69.000 \text{ mm}^{-3}$ with the upper bound of the 95% confidence interval calculated as 3%; 2% (n = 27) had platelet counts of $0 - 49,000 \text{ mm}^{-3}$ with the upper bound of the 95% confidence interval calculated as 11%. These results are summarized in Table 5.

Discussion

We present the largest and most generalizable published series of thrombocytopenic parturients undergoing neuraxial techniques: 573 patients across 14 academic medical centers and private hospitals. After the MPOG data were combined with data from the systematic review, we identified 1,524 neuraxial techniques performed in thrombocytopenic parturients with platelet count 100,000 mm⁻³. No cases of epidural hematomas requiring surgical decompression were identified in either the MPOG database or in previously published studies. Combined with data from studies identified in the systematic review, the upper bound of the 95% confidence interval for the risk of epidural hematoma for a platelet count of $0 - 49,000 \text{ mm}^{-3}$ is 11%, for a platelet count of 50,000 – 69,000 mm⁻³ is 3%, and for a platelet count of 70,000 – 100,000 mm⁻³ is 0.2%.

We have advanced our understanding of epidural hematoma requiring surgical decompression by performing a generalizable multicenter study and systematic review that more than doubles the number of thrombocytopenic parturients who received a neuraxial technique without complication reported by Bernstein *et al.* (n=1,524 vs. n=755). The increased sample size also enabled risk estimates by stratified platelet ranges. Performing a comprehensive systematic review, which expanded upon the literature reviews performed by Goodier *et al.* or Bernstein *et al.*, was an important process to definitively identify the published data regarding total numbers of neuraxial anesthetics performed in thrombocytopenic patients. Additionally, while Bernstein *et al.* and Goodier *et al.* reported

data from only one institution and two institutions respectively, our multicenter study that reported data from 14 diverse institutions increases by approximately 50% the number of neuraxial placements in thrombocytopenia obstetric patients reported in the literature. Because the objective standard of measurement for platelet count and diagnosis of an epidural hematoma have remained the same, the data obtained through MPOG and the systematic review are exchangeable and generalizable over time and between institutions.

Performing neuraxial techniques in obstetric patients has a number of advantages, including avoiding airway instrumentation, providing effective analgesia/anesthesia while minimizing maternal and neonatal sedation, allowing for neuraxial morphine to provide postoperative analgesia following cesarean delivery, and allowing the patient to be present for the birth of her child. The practitioner must weigh these benefits against the risk of epidural hematoma, which continues to be a challenging assessment to make in thrombocytopenic parturients as the literature remains limited. Although performing neuraxial techniques offers many benefits, 2% of thrombocytopenic parturients receiving neuraxial techniques in the MPOG analysis were converted to general anesthesia suggesting that practitioners should counsel patients that neuraxial techniques reduce but do not eliminate the risk of requiring a general anesthetic. This study increases the overall number of thrombocytopenic obstetric patients in the available literature who received neuraxial techniques without complication. The results of this study support the assertion that the risk of epidural hematoma from neuraxial anesthetics in a parturient with a platelet count greater than 70,000 mm^{-3} is exceptionally low (less than 0.2%). However, the exact risk of epidural hematoma associated with neuraxial techniques at a platelet count $<70,000 \text{ mm}^{-3}$ remains uncertain with an upper bound of 3% for counts of $50,000 - 69,000 \text{ mm}^{-3}$ and 11% for counts of $0 - 49,000 \text{ mm}^{-3}$. This uncertainty must be considered by practitioners when making the difficult risk and benefit assessment of neuraxial placement in parturients with a platelet count of <70,000 mm^{-3} .

This study has a number of important strengths. First, after a thorough literature review, this MPOG cohort of thrombocytopenic parturients receiving neuraxial techniques is the largest reported to date, consisting of more than double the number of subjects as the largest previously reported case series. These data were derived from a multicenter database with almost 150,000 obstetric anesthetic records screened. In addition, this study contributes significantly to the number of thrombocytopenic parturients reported in the literature that have received neuraxial techniques without an epidural hematoma requiring surgical decompression.

The limitations of this study include that the high upper bounds reported here, particularly at platelet counts less than 70,000 mm⁻³, suggest that more data are needed. Several institutions maintain policies advising against neuraxial techniques below a specified platelet count. Inclusion of these centers may have resulted in a limited number of patients receiving neuraxial techniques with a platelet count less than 70,000 mm⁻³, leading to reduced power in detecting this rare event. We only assessed those that received a neuraxial technique in our analysis, as thrombocytopenic individuals that did not receive a neuraxial technique have an extremely low risk of epidural hematoma. Our methods only detected patients from the MPOG database and systematic review studies who reportedly underwent decompressive

laminectomies, therefore we did not identify epidural hematomas that were managed nonoperatively or at other institutions not included in MPOG. However, it is unlikely that the patients were transferred to another institution since most participating centers are major academic centers and clinical practices would warrant the center performing the neuraxial procedure also being the site of epidural hematoma evaluation and management. We were also unable to collect attempted neuraxial procedures that were aborted because of bleeding or difficult placement. Also, the etiology of thrombocytopenia was not specified in the anesthetic record for 416 of 573 MPOG patients. Future studies that report the etiology of thrombocytopenia or serial platelet counts may improve our understanding of the risk of epidural hematoma for various disease states.

The results of our study have increased the precision of epidural hematoma risk estimates for thrombocytopenic obstetric patients receiving neuraxial techniques and may help improve clinical decision-making. Despite our contributions, published outcome data regarding thrombocytopenic obstetric patients receiving neuraxial techniques remains sparse. Further reporting of large cohorts of thrombocytopenic pregnant women receiving neuraxial techniques can help to better define the risk of epidural hematoma, especially in those patients with a platelet count of less than 70,000 mm⁻³.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

- Jones L, Othman M, Dowswell T, Alfirevic Z, Gates S, Newburn M, Jordan S, Lavender T, Neilson JP. Pain management for women in labour: an overview of systematic reviews. Cochrane Database Syst Rev. 2012:Cd009234. [PubMed: 22419342]
- Chestnut DH. Anesthesia and maternal mortality. Anesthesiology. 1997; 86:273–6. [PubMed: 9054244]
- Kinsella SM, Winton AL, Mushambi MC, Ramaswamy K, Swales H, Quinn AC, Popat M. Failed tracheal intubation during obstetric general anaesthesia: a literature review. Int J Obstet Anesth. 2015; 24:356–74. [PubMed: 26303751]
- 4. Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, Harper A, Hulbert D, Lucas S, McClure J, Millward-Sadler H, Neilson J, Nelson-Piercy C, Norman J, O'Herlihy C, Oates M,

Shakespeare J, de Swiet M, Williamson C, Beale V, Knight M, Lennox C, Miller A, Parmar D, Rogers J, Springett A. Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006–2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. BJOG. 2011; 118(Suppl 1):1–203.

- Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990–1999. Anesthesiology. 2004; 101:950–9. [PubMed: 15448529]
- Beilin Y, Zahn J, Comerford M. Safe epidural analgesia in thirty parturients with platelet counts between 69,000 and 98,000 mm(-3). Anesth Analg. 1997; 85:385–8. [PubMed: 9249118]
- Thornton P, Douglas J. Coagulation in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2010; 24:339–352. [PubMed: 20097136]
- Bateman BT, Mhyre JM, Ehrenfeld J, Kheterpal S, Abbey KR, Argalious M, Berman MF, Jacques PS, Levy W, Loeb RG, Paganelli W, Smith KW, Wethington KL, Wax D, Pace NL, Tremper K, Sandberg WS. The risk and outcomes of epidural hematomas after perioperative and obstetric epidural catheterization: a report from the Multicenter Perioperative Outcomes Group Research Consortium. Anesth Analg. 2013; 116:1380–5. [PubMed: 22504213]
- 9. American College of Obstetricians and Gynecologists. Thrombocytopenia in pregnancy. Practice Bulletin No. 166. Obstet Gynecol. 2016; 128:e43–53. [PubMed: 27548554]
- Ruppen W, Derry S, McQuay H, Moore RA. Incidence of epidural hematoma, infection, and neurologic injury in obstetric patients with epidural analgesia/anesthesia. Anesthesiology. 2006; 105:394–9. [PubMed: 16871074]
- Stafford-Smith M. Impaired haemostasis and regional anaesthesia. Can J Anaesth. 1996; 43:R129– R141. [PubMed: 8706215]
- Goodier CG, Lu JT, Hebbar L, Segal BS, Goetzl L. Neuraxial anesthesia in parturients with thrombocytopenia: a multisite retrospective cohort study. Anesth Analg. 2015; 121:988–991. [PubMed: 26378701]
- Bernstein J, Hua B, Kahana M, Shaparin N, Yu S, Davila-Velazquez J. Neuraxial Anesthesia in Parturients with Low Platelet Counts. Anesth Analg. 2016; 123:165–7. [PubMed: 27159067]
- 14. www.strobe-statement.org STROBE statement and website. Accessed December 7, 2016
- Freundlich RE, Kheterpal S. Perioperative effectiveness research using large databases. Best Pract Res Clin Anaesthesiol. 2011; 25:489–98. [PubMed: 22099915]
- Kheterpal S. Clinical research using an information system: the multicenter perioperative outcomes group. Anesthesiol Clin. 2011; 29:377–88. [PubMed: 21871400]
- Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analysis: The PRISMA Statement. PLoS Med. 2009; 6(7):e1000097.doi: 10.1371/journal.pmed1000097 [PubMed: 19621072]
- Hanley JA, Lippman-Hand A. If nothing goes wrong, is everything all right?: interpreting zero numerators. JAMA. 1983; 249:1743–1745. [PubMed: 6827763]
- Agaram R, Douglas M, Fan S. Safe regional anesthesia in ITP in pregnancy-A retrospective study. Anesthesiology. 2006; 104:B39.
- Beilin Y, Arnold I, Hossain S. Evaluation of the platelet function analyzer (PFA-100®) vs. the thromboelastogram (TEG) in the parturient. Int J Obstet Anesth. 2006; 15:7–12. [PubMed: 16256341]
- Campbell D, Sawatzky K, Yip R. Thromboelastographic evaluation of thrombocytopenic parturients. Anesthesiology. 1999; 90:A12.
- 22. Frenk V, Camann W, Shankar KB. Regional anesthesia in parturients with low platelet counts. Can J Anaesth. 2005; 52:114–114.
- Huang J, McKenna N, Babins N. Utility of thromboelastography during neuraxial blockade in the parturient with thrombocytopenia. AANA J. 2014; 82:127–130. [PubMed: 24902455]
- Palit S, Palit G, Vercauteren M, Jacquemyn Y. Regional anaesthesia for primary caesarean section in patients with preterm HELLP syndrome: a review of 102 cases. Clin Exp Obstet Gynecol. 2008; 36:230–234.
- 25. Shalev O, Anteby E. Epidural anesthesia can be safely performed in gestational thrombocytopenia of> 50.000/mu L. Blood. 1996; 88:62B.

- 26. Sibai BM, Taslimi MM, El-Nazer A, Amon E, Mabie BC, Ryan GM. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. Am J Obstet Gynecol. 1986; 155:501–509. [PubMed: 3529964]
- Tanaka M, Balki M, McLeod A, Carvalho JC. Regional anesthesia and non-preeclamptic thrombocytopenia: time to re-think the safe platelet count. Rev Bras Anestesiol. 2009; 59:142– 153. [PubMed: 19488526]
- 28. Vigil-De Gracia P, Silva S, Montufar C, Carrol I, De Los Rios S. Anesthesia in pregnant women with HELLP syndrome. Int J Gynaecol Obstet. 2001; 74:23–27. [PubMed: 11430937]
- Webert KE, Mittal R, Sigouin C, Heddle NM, Kelton JG. A retrospective 11-year analysis of obstetric patients with idiopathic thrombocytopenic purpura. Blood. 2003; 102:4306–4311. [PubMed: 12947011]

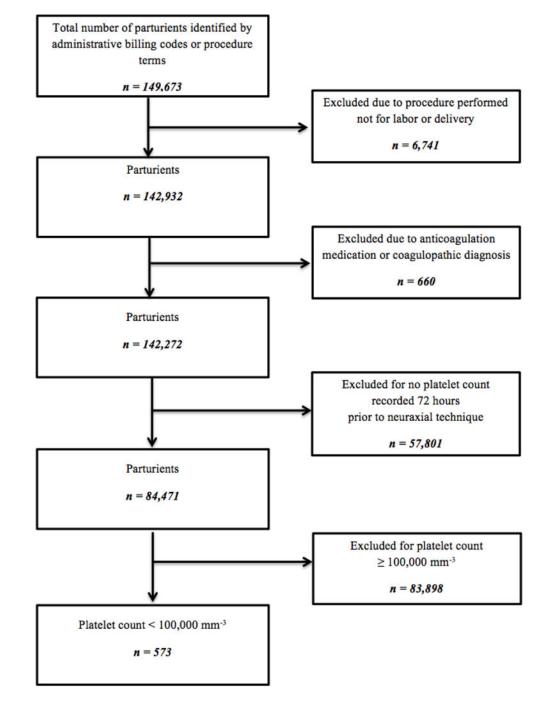
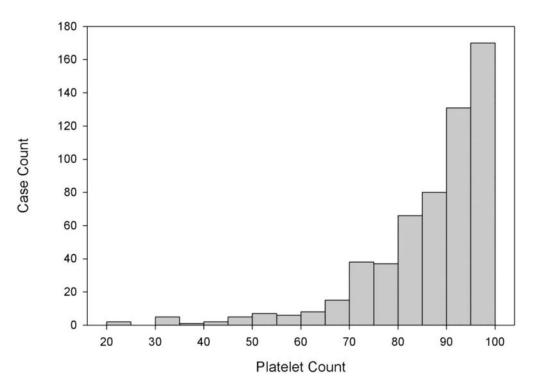


Figure 1.

Multicenter Perioperative Outcomes Group Patient Selection Flowchart of Thrombocytopenic Parturients Receiving Neuraxial Techniques





Distribution of Thrombocytopenic Parturients Receiving a Neuraxial Technique from the Multicenter Perioperative Outcomes Group Database

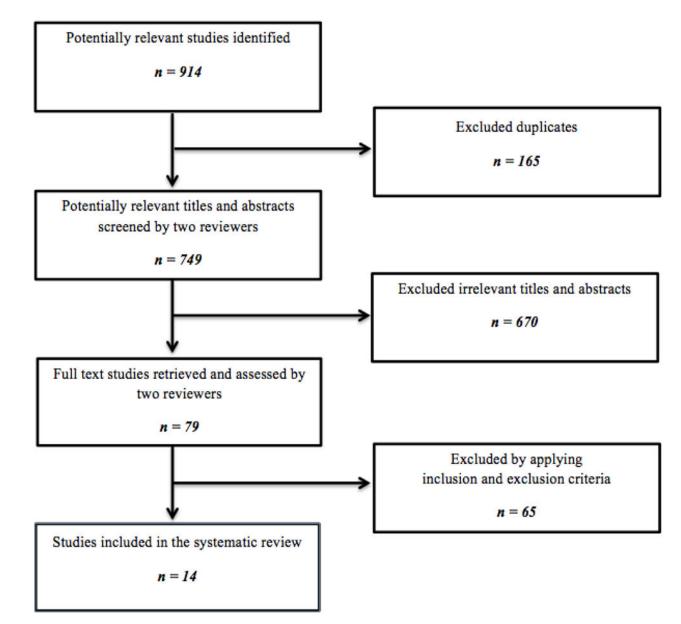


Figure 3. Systematic Review Case Series Selection Flowchart

Table 1

Characteristics of Thrombocytopenic Parturients Receiving a Neuraxial Technique Identified from the Multicenter Perioperative Outcomes Group Database

Characteristic	Mean ± Standard Deviation or n (%)
Patient Information	
n	573
Age	30 ± 6
ASA Physical Status Classification	
2	391 (68)
3	130 (23)
4	10 (2)
Emergent	75 (13)
Missing	42 (7)
BMI Classification (kg/m ²)	
Underweight (<18.5)	1 (0.2)
Normal (18.5–24.9)	47 (8)
Overweight (25.0–29.9)	129 (23)
Obese (>30.0)	169 (29)
Missing	227 (40)
Etiology of Thrombocytopenia	
HELLP syndrome	31 (5)
Preeclampsia	67 (12)
Idiopathic thrombocytopenic purpura	25 (4)
Gestational thrombocytopenia	34 (6)
Missing	416 (73)
Anesthetic Technique	
Epidural	327 (57)
Spinal	200 (35)
Combined spinal-epidural	46 (8)
Neuraxial techniques converted to general anesthesia	9 (2)

ASA - American Society of Anesthesiologists; BMI - Body Mass Index; HELLP - Hemolysis, elevated liver enzymes, low platelet count

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Table 2

Anesthetic Technique and Etiology of Thrombocytopenia by Platelet Range of Thrombocytopenic Parturients Receiving a Neuraxial Technique Identified from the Multicenter Perioperative Outcomes Group Database

Platelet Count (mm ⁻³)	u		Anestł	Anesthetic Technique		Etiolo	gy of T	Etiology of Thrombocytopenia	
		Epidural	Spinal	Combined Spinal-Epidural	HELLP Syndrome	Preeclampsia	ЧТI	Spinal Combined Spinal-Epidural HELLP Syndrome Preeclampsia ITP Gestational Thrombocytopenia Unspecified	Unspecified
0-49,000	15	10	5	0	5	2		0	7
50,000-69,000	36	19	15	2	5	7		1	22
70,000–100,000	522	298	180	44	21	58	23	33	387
Total	573	327	200	46	31	67	25	34	416
-	:								

HELLP - Hemolysis, elevated liver enzymes, low platelet count ITP - Idiopathic thrombocytopenic purpura

Table 3

Neuraxial Techniques in Thrombocytopenic Parturients Reported from the Multicenter Perioperative Outcomes Group Database

Platelet Range (mm ⁻³)	n (%)	Frequency of Epidural Hematoma Requiring Surgical Decompression	95% Confidence Interval For Risk of Epidural Hematoma
0-49,000	15 (3)	0	0 to 20%
50,000 - 69,000	36 (6)	0	0 to 8%
70,000 - 99,000	522 (91)	0	0 to 0.6%
Total	573 (100)	0	

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Table 4

Studies Identified by Systematic Review

Author, Year	Study summary	0-49,000 mm ⁻³ (n)	50-69,000 mm ⁻³ (n)	$70-100,000 \ \mathrm{mm}^{-3} \ \mathrm{(n)}$	$50{-}100,000 \ \mathrm{mm}^{-3} \left(\mathrm{n}\right)$	Epidural hematomas reported
Agaram, 2006 ¹⁹	Retrospective study of parturients with ITP	2	#	63	97	0
Beilin, 1997 ⁶	Retrospective study of thrombocytopenic parturients	0	#	24	30	0
Beilin, 2006 ²⁰	Prospective study in parturients to evaluate platelet function analyzer and thromboelastogram	0	2	11	13	0
Bernstein, 2016 ¹³ ¶	Retrospective study of thrombocytopenic parturients	1	9	247	253	0
Campbell, 1999 ²¹	Prospective study in thrombocytopenic parturients utilizing thromboelastography	0	9	6	12	0
Frenk, 2005 ²²	Retrospective study of thrombocytopenic parturients	0*	13	153	166	0
Goodier, 2015 ¹² ¶	Retrospective study of thrombocytopenic parturients	2	22	149	171	0
Huang, 2014 ²³	Prospective study in thrombocytopenic parturients utilizing thromboelastography	0	#	16	61	0
Palit, 2009 ²⁴	Retrospective study of parturients with HELLP syndrome undergoing primary cesarcan delivery	$1^{\dot{\tau}}$	#	#	11 /	0
Shalev, 1996 ²⁵	Prospective study in thrombocytopenic parturients with gestational thrombocytopenia	0	#	33	45	0
Sibai, 1986 ²⁶	Retrospective study of parturients with HELLP syndrome	0	#	#	16	0//
Tanaka, 2009 ²⁷	Retrospective study of thrombocytopenic parturients	0	4	43	47	0
Vigil-De Garcia, 2001 ²⁸	Retrospective study of parturients with HELLP syndrome	5#	#	#	28	0
Webert, 2003 ²⁹	Retrospective study of parturients with ITP	1^{S}	#	19	25	0
Total		12	53	764	939	0
ITP – idiopathic thrombocy	ITP – idiopathic thrombocytopenic purpura, HELLP – hemolysis, elevated liver enzymes, low platelet count	vated liver enzymes, low	/ platelet count			

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4 patients not included due to platelet transfusion prior to neuraxial technique

 $\dot{\tau}_{10}$ patients not included due to platelet transfusion prior to neuraxial technique

 \sharp patients not included due to platelet transfusion prior to neuraxial technique

 g One patient with platelets less than 50,000 mm⁻³ received platelet transfusion but it's unclear if they also received a neuraxial technique

n Although bleeding in the epidural space in a patient with a platelet count of 93,000 mm⁻³ was reported, it was further confirmed that the bleeding was actually blood in the epidural catheter and the patient had no actual epidural hematoma or neurologic injury (personal communication by email on July 30, 2016 with Baha Sibai, M.D.)

Stratification of data obtained by personal communication by email with Jeffrey Bernstein, M.D. (July 12, 2016) and with Christopher G. Goodier, M.D. (August 19, 2016)

#for $50,000-100,000 \text{ mm}^{-3} \text{ mm}^{-3}$ (n) and was not included in the risk analysis

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Table 5

Neuraxial Techniques in Thrombocytopenic Parturients Reported from Systematic Review Case Series Combined with Multicenter Perioperative Outcomes Group Data

		Systematic Review Data	ata		MPOG Data Combined with Systematic Review Data	atic Review Data
Platelet Range (mm ⁻³)	(%) u	Frequency of Epidural Hematoma Requiring Surgical Decompression	95% Confidence Interval For Risk of Epidural Hematoma	(%) u	Frequency of Epidural Hematoma Requiring Surgical Decompression	95% Confidence Interval For Risk of Epidural Hematoma
0 - 49,000	12 (1)	0	0 to 25%	27 (2)	0	0 to 11%
50,000 - 69,000	53 (6)	0	0 to 6%	(9) 68	0	0 to 3%
70,000 - 100,000	764 (80)	0	0 to 0.4%	1,286 (84)	0	0 to 0.2%
Total	951 (100)	0		1,524 (100)	0	

MPOG - Multicenter Perioperative Outcomes Group