Risk of Epidural Hematoma after Neuraxial Techniques in Thrombocytopenic Parturients

A Report from the Multicenter Perioperative Outcomes Group

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., Melissa E. Bauer, D.O., on behalf of the Multicenter Perioperative Outcomes Group Investigators*

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 using the Multicenter Perioperative Outcomes Group 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: A total of 573 parturients with a platelet count less than 100,000 mm^{-3} who received a neuraxial technique across 14 institutions were identified in the Multicenter Perioperative Outcomes Group 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% CI for the risk of epidural hematoma for a platelet count of 0 to 49,000 mm^{-3} is 11%, for 50,000 to 69,000 mm^{-3} is 3%, and for 70,000 to 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 less than 70,000 mm^{-3} remains poorly defined due to limited observations. **(Anesthesiology 2017; 126:1053-64)**

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

What We Already Know about This Topic

- Thrombocytopenia is considered a relative or even absolute contraindication to neuraxial techniques for labor analgesia due to potential risk of epidural hematoma
- There is no consensus on the acceptable platelet count required to safely perform neuraxial techniques, and no multicenter study to date has stratified the risk of epidural hematoma by platelet count

What This Article Tells Us That Is New

- The Multicenter Perioperative Outcomes Group database and a systematic literature review were combined to estimate the relationship between platelet count and the risk of epidural hematoma requiring surgical decompression after neuraxial techniques
- The upper bound of the 95% CI for epidural hematoma risk was 11% for a platelet count of 0 to 49,000 mm^{-3}, 3% for 50,000 to 69,000 mm^{-3}, and 0.2% for 70,000 to 100,000 mm^{-3}

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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 are 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 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 after neuraxial techniques is evolving. Goodier *et al.*[12] and Bernstein *et al.*[13] 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% CI for the risk of epidural hematoma to be 0.6% and 0.4%, respectively.[12,13] Although 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 data sets 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 after neuraxial techniques in thrombocytopenic parturients (less than 100,000 mm^{-3}) using the Multicenter Perioperative 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.

Submitted for publication October 11, 2016. Accepted for publication February 28, 2017. Department of Anesthesiology, University of Michigan Health System, Ann Arbor, Michigan (L.O.L., S.K., T.T.K., M.H., M.E.B.); Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts (B.T.B.); Department of Anesthesiology and Perioperative Medicine, Oregon Health & Science University, Portland, Oregon (M.F.A., K.W.H.); Taubman Health Sciences Library, University of Michigan, Ann Arbor, Michigan (M.M.); Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Medical University of South Carolina, Charleston, South Carolina (C.G.G.); and Department of Anesthesiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York (J.B.).

*Multicenter Perioperative Outcomes Group Investigators are listed in appendix 1.

Materials and Methods

Approval from the University of Michigan Institutional Review Board (Ann Arbor, Michigan) 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 after data collection. In addition, Oregon Health and Science University (Portland, Oregon) 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 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 to 55 yr with a platelet count less than 100,000 mm^{-3} within 72 h before 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 queries 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 2. 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, or platelet storage pool deficiency) or were taking an antiplatelet medication were excluded. Patient characteristics including age, American Society of Anesthesiologists class, emergent nature of surgery, body mass index, coexisting conditions predisposing to thrombocytopenia (gestational thrombocytopenia, preeclampsia, idiopathic thrombocytopenic purpura, and hemolysis, elevated liver enzymes, and low platelet count syndrome), and anesthetic technique were identified and recorded.

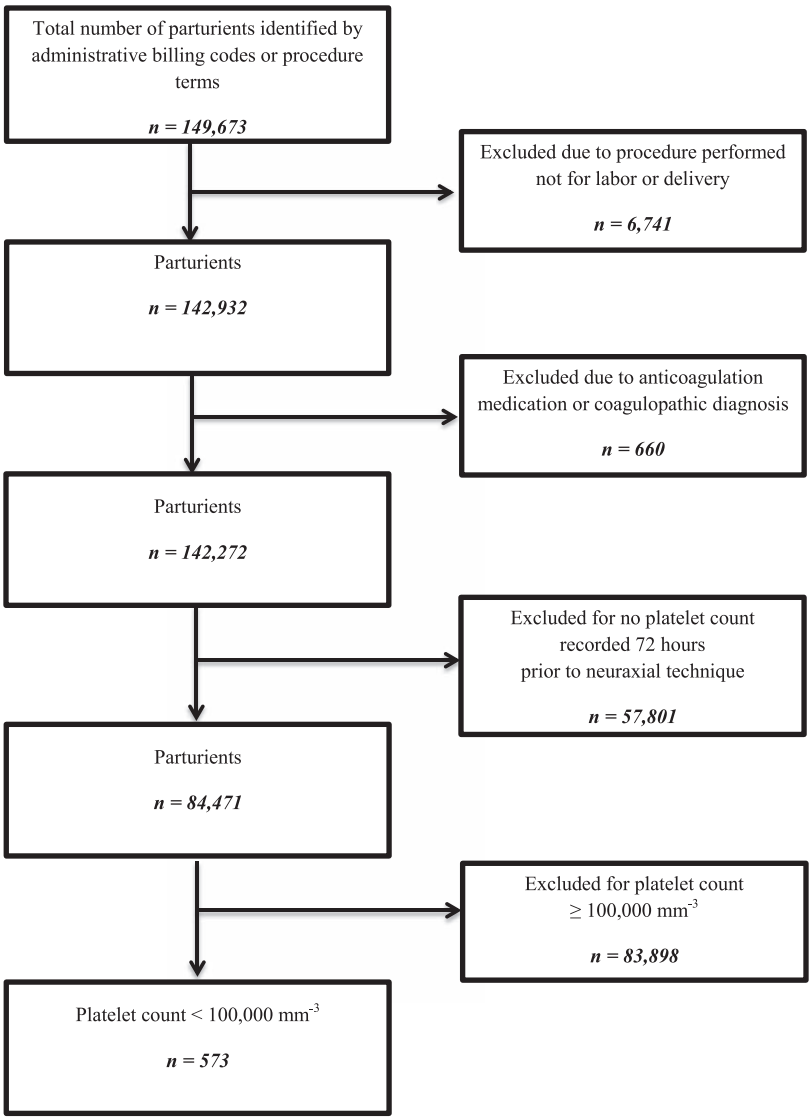

Fig. 1. Multicenter Perioperative Outcomes Group patient selection flowchart of thrombocytopenic parturients receiving neuraxial techniques.

Thrombocytopenic obstetric patients receiving neuraxial techniques were stratified into predefined categories based on the preplacement platelet count. The platelet ranges were defined as 0 to 49,000 mm^{-3}, 50,000 to 69,000 mm^{-3}, and 70,000 to 99,000 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 (dilation and curettage for retained placenta or 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.

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 to increase the power of our study to define the risk of this rare event. PubMed and EMBASE 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 key words, 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 articles, letters, and editorials were included in

the EMBASE search. The searches retrieved 749 unique citations after duplicates were removed in Endnote X6 (Thomson Reuters, USA). The Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines were reviewed and followed when performing the systematic review.[17] The complete search strategies are available in appendix 3. After the search was completed, two authors (L.O.L. and M.E.B.) reviewed each article for inclusion. Criteria for inclusion were as follows: (1) studies reporting neuraxial techniques in thrombocytopenic parturients; (2) description of whether epidural hematomas occurred; and (3) platelet count stratification. Studies (or portions of studies) were excluded for transfusion of platelets before 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 additional information, and that data were included and cited as personal communication. Once final articles were selected, data were extracted by one author (L.O.L.) and validated by another (M.E.B.).

Statistical Analysis

The 95% CIs 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% CI for zero-numerator problems. The rule of 3 states that, for trials in which no events have occurred, the upper bound of the 95% CI can be estimated by 3/n.[18] All of the analyses were performed using SPSS 21.0 software (SPSS Inc., 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 h before placement. Of these, there were 573 patients from 14 institutions with platelet counts less than 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 postneuraxial 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 after 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 to 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.

Table 1. Characteristics of Thrombocytopenic Parturients Receiving a Neuraxial Technique Identified from the Multicenter Perioperative Outcomes Group Database

Characteristic	Data, Mean ± SD or n (%)
Patient information	
N	573
Age, yr	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.

The data obtained from MPOG are outlined in table 3. For those patients with platelet counts of 70,000 to 99,000 mm^{-3} (n = 522), the upper bound of the 95% CI was 0.6%; for counts of 50,000 to 69,000 mm^{-3} (n = 36), the upper bound of the 95% CI was 8%; and for platelet counts of 0 to 49,000 mm^{-3} (n = 15), the upper bound of the 95% CI was 20%. The distribution of thrombocytopenic parturients from the MPOG database who 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 1 (http://links.lww.com/ALN/B417). The distribution based on platelet count for these time differences is displayed in Supplemental Digital Content 2 (http://links.lww.com/ALN/B418).

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 to 69,000 mm^{-3} and 70,000 to 100,000 mm^{-3} used in the analysis of the

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

		Anesthetic Technique			Etiology of Thrombocytopenia				
Platelet Count, mm^{-3}	n	Epidural	Spinal	Combined Spinal–Epidural	HELLP Syndrome	Preeclampsia	ITP	Gestational Thrombocytopenia	Unspecified
0–49,000	15	10	5	0	5	2	1	0	7
50,000–69,000	36	19	15	2	5	7	1	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% CI For Risk of Epidural Hematoma, %
0–49,000	15 (3)	0	0–20
50,000–69,000	36 (6)	0	0–8
70,000–99,000	522 (91)	0	0–0.6
Total	573 (100)	0	

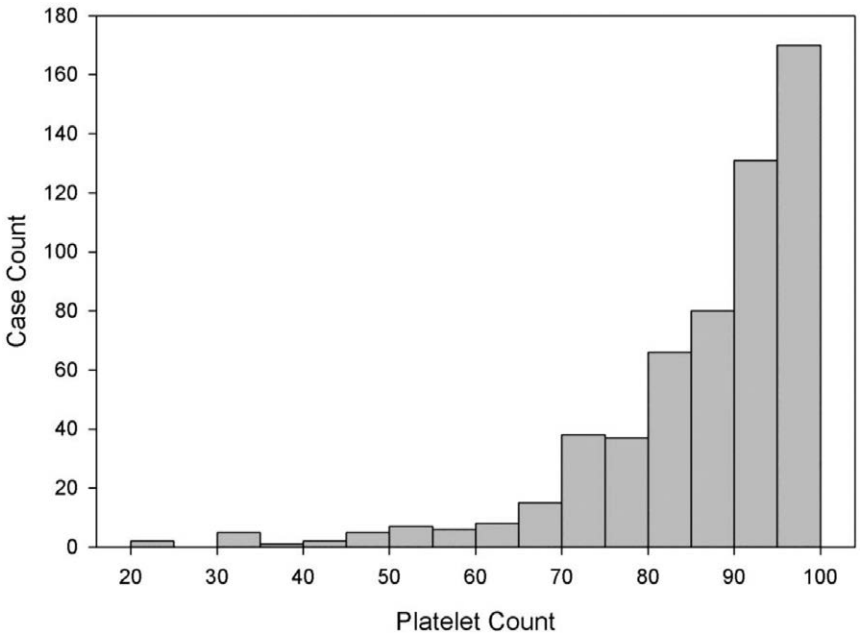

Fig. 2. Distribution of thrombocytopenic parturients receiving a neuraxial technique from the Multicenter Perioperative Outcomes Group database.

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 to 100,000 mm^{-3}, with the upper bound of the 95% CI calculated as 0.2%; 6% (n = 89) had platelet counts of 50,000 to 69,000 mm^{-3} with the upper bound of the 95% CI calculated as 3%; and 2% (n = 27) had platelet counts of 0 to 49,000 mm^{-3} with the upper bound of the 95% CI calculated as 11%. These results are summarized in table 5.

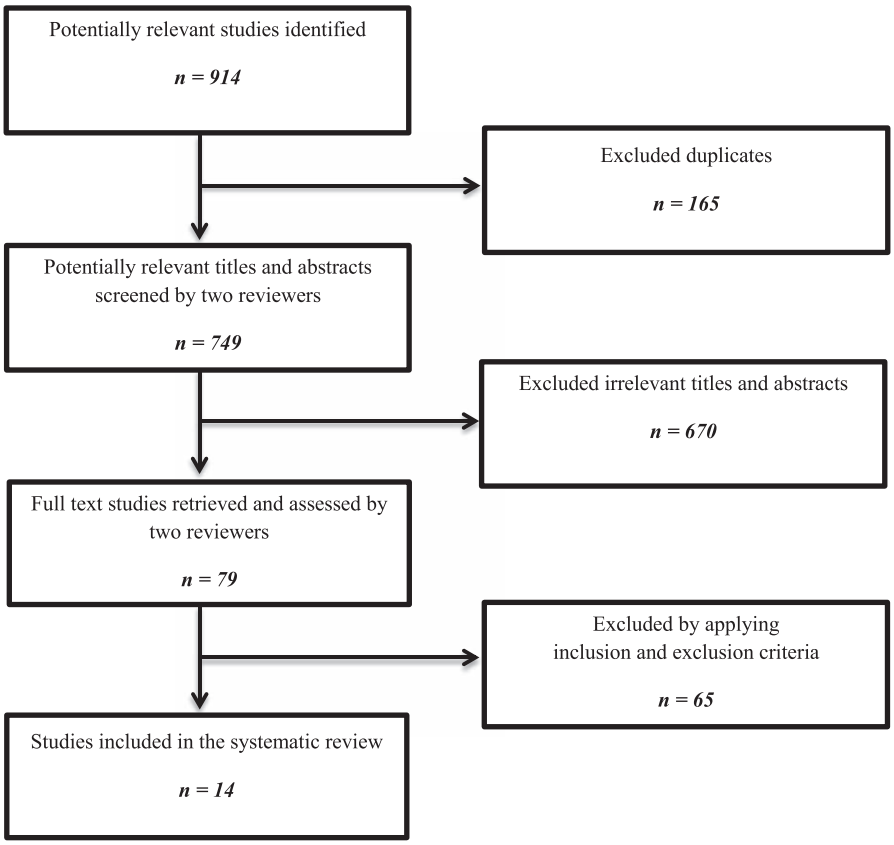

Fig. 3. Systematic review case series selection flowchart.

Discussion

We present the largest and most generalizable published series of thrombocytopenic parturients undergoing neuraxial techniques, including 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 at or less than 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% CI for the risk of epidural hematoma for a platelet count of 0 to 49,000 mm^{-3} is 11%, for a platelet count of 50,000 to 69,000 mm^{-3} is 3%, and for a platelet count of 70,000 to 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.*[13] (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 on the literature reviews performed by Goodier *et al.*[12] or Bernstein *et al.*,[13] was an important process to definitively identify the published data regarding total numbers of neuraxial anesthetics performed in thrombocytopenic patients. In addition, although Bernstein *et al.*[13] and Goodier *et al.*[12] 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 thrombocytopenic 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 after 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, because the literature remains limited. Although performing neuraxial techniques offers many benefits, 2% of thrombocytopenic parturients receiving neuraxial techniques in the MPOG analysis were converted

Table 4. Studies Identified by Systematic Review

Author, Year	Study Summary	0–49,000 mm^{-3}, n	50,000–69,000 mm^{-3}, n	70,000–100,000 mm^{-3}, n	50,000–100,000 mm^{-3}, n	Epidural Hematomas Reported
Agaram *et al.*, 2006[19]	Retrospective study of parturients with ITP	2	*	63	97	0
Beilin *et al.*, 1997[6]	Retrospective study of thrombocytopenic parturients	0	*	24	30	0
Beilin *et al.*, 2006[20]	Prospective study in parturients to evaluate platelet function analyzer and thromboelastogram	0	2	11	13	0
Bernstein *et al.*, 2016[13]†	Retrospective study of thrombocytopenic parturients	1	6	247	253	0
Campbell *et al.*, 1999[21]	Prospective study in thrombocytopenic parturients using thromboelastography	0	6	6	12	0
Frenk *et al.*, 2005[22]	Retrospective study of thrombocytopenic parturients	0‡	13	153	166	0
Goodier *et al.*, 2015[12]†	Retrospective study of thrombocytopenic parturients	2	22	149	171	0
Huang *et al.*, 2014[23]	Prospective study in thrombocytopenic parturients using thromboelastography	0	*	16	19	0
Palit *et al.*, 2009[24]	Retrospective study of parturients with HELLP syndrome undergoing primary cesarean delivery	1§	*	*	17§	0
Shalev and Anteby, 1996[25]	Prospective study in thrombocytopenic parturients with gestational thrombocytopenia	0	*	33	45	0
Sibai *et al.*, 1986[26]	Retrospective study of parturients with HELLP syndrome	0	*	*	16	0‖
Tanaka *et al.*, 2009[27]	Retrospective study of thrombocytopenic parturients	0	4	43	47	0
Vigil-De Gracia *et al.*, 2001[28]	Retrospective study of parturients with HELLP syndrome	5#	*	*	28	0
Webert *et al.*, 2003[29]	Retrospective study of parturients with ITP	1**	*	19	25	0
Total		12	53	764	939	0

*Stratification of platelet counts overlapped the ranges of 50,000 to 69,000 and 70,000 to 100,000 mm^{-3} and were not included in the stratification risk analysis by platelet count but are included in the total n for 50,000 to 100,000 mm^{-3}. †Stratification of data obtained by personal communication by email with Jeffrey Bernstein, M.D. (July 12, 2016), and Christopher G. Goodier, M.D. (August 19, 2016). ‡Four patients were not included due to platelet transfusion before neuraxial technique. §Ten patients were not included due to platelet transfusion before neuraxial technique. ‖Although bleeding in the epidural space in a patient with a platelet count of 93,000 mm^{-3} was reported, it was additionally 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.). #Seven patients were not included due to platelet transfusion before neuraxial technique. **One patient with platelets less than 50,000 mm^{-3} received platelet transfusion but it is unclear whether she also received a neuraxial technique.

HELLP = hemolysis, elevated liver enzymes, low platelet count; ITP = idiopathic thrombocytopenic purpura.

Table 5. Neuraxial Techniques in Thrombocytopenic Parturients Reported from Systematic Review Case Series Combined with Multicenter Perioperative Outcomes Group Data

	Systematic Review Data			MPOG Data Combined with Systematic Review Data		
Platelet Range, mm^{-3}	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.

to general anesthesia, suggesting that practitioners should counsel patients for whom 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 more 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 less than 70,000 mm^{-3} remains uncertain, with an upper bound of 3% for counts of 50,000 to 69,000 mm^{-3} and 11% for counts of 0 to 49,000 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 less than 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 who 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 who received a neuraxial technique in our analysis, because thrombocytopenic individuals who 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, because 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 remain sparse. Additional 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}.

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Competing Interests

The authors declare no competing interests.

Correspondence

Address correspondence to Dr. Lee: Department of Anesthesiology, 1H247 UH, SPC 5048, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109. lindenl@med.umich.edu.

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Appendix 1. Multicenter Perioperative Outcomes Group (MPOG) Investigators

The MPOG investigators for this study are as follows: Philip Lirk, M.D., Department of Anesthesiology, Academic Medical Center, Amsterdam, The Netherlands, Janet Wilczak, M.D., Beaumont Health, Dearborn, Michigan, Roy Soto, M.D., Beaumont Health, Royal Oak, Michigan, Simon Tom, M.D., Department of Anesthesiology, Perioperative Care, and Pain Medicine, New York University Langone Medical Center, New York, New York, Germaine Cuff, M.D., Department of Anesthesiology, Perioperative Care, and Pain Medicine, New York University Langone Medical Center, New York, New York, Daniel A. Biggs, M.D., Department of Anesthesiology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, Traci Coffman, M.D., St. Joseph Mercy, Ann Arbor, Michigan, Leif Saager, M.D., Department of Anesthesiology, University of Michigan Health System, Ann Arbor, Michigan, Warren J. Levy, M.D., Department of Anesthesiology, University of Pennsylvania, Philadelphia, Pennsylvania, Michael Godbold, M.D., Department of Anesthesiology, University of Tennessee Medical Center, Knoxville, Tennessee, Nathan L. Pace, M.D., M.Stat., Department of Anesthesiology, University of Utah, Salt Lake City, Utah, Kevin L. Wethington, M.D., Department of Anesthesiology, University of Utah, Salt Lake City, Utah, William C. Paganelli, M.D., Ph.D., Department of Anesthesiology, University of Vermont College of Medicine, Burlington, Vermont, Marcel E. Durieux, M.D., Ph.D., Department of Anesthesiology, University of Virginia, Charlottesville, Virginia, Karen B. Domino, M.D., M.P.H., Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington, Bala Nair, Ph.D., Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington, Jesse M. Ehrenfeld, M.D., M.P.H., Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee, Jonathan P. Wanderer, M.D., Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee, and Robert B. Schonberger, M.D., Department of Anesthesiology, Yale School of Medicine, New Haven, Connecticut.

Members of the MPOG publications committee are as follows: Joshua Berris, D.O., Beaumont Health, Farmington Hills, Michigan, Steven Lins, M.D., Bronson Healthcare, Battle Creek, Michigan, Peter Coles, M.D., Bronson Healthcare, Kalamazoo, Michigan, Kenneth C. Cummings, M.D., Anesthesiology Institute, Cleveland Clinic, Cleveland, Ohio, Kamal Maheshwari, M.D., M.P.H., Anesthesiology Institute, Cleveland Clinic, Cleveland, Ohio, Mitchell F. Berman, M.D., Department of Anesthesiology, Columbia University Medical Center, New York, New York, Christopher Wedeven, M.D., Holland Hospital, Holland, Michigan, John LaGorio, M.D., Mercy Health, Muskegon, Michigan, Peter M. Fleishut, M.D., Department of Anesthesiology, New York-Presbyterian Hospital, Weill Cornell Medicine, New York, New York, Terri A. Ellis II, M.D., St. Joseph Mercy Oakland, Pontiac, Michigan, Susan Molina, M.D., St. Mary Mercy Hospital, Livonia, Michigan, Curtis Carl, M.D., Sparrow Health System, Lansing, Michigan, Bassam Kadry, M.D., Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, California, Wilton A van Klei, M.D., Ph.D., Department of Anesthesiology, University Medical Center Utrecht, Utrecht, The Netherlands, Wietze Pasma, D.V.M., Department of Anesthesiology, University Medical Center Utrecht, Utrecht, The Netherlands, Leslie C. Jameson, M.D., Department of Anesthesiology, University of Colorado, Aurora, Colorado, Daniel L. Helsten, M.D., Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri, and Michael S. Avidan, M.B.B.Ch., Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri.

Appendix 2. Procedure Description Query Terms

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csxn
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deilvery
deivery
dekivery
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deleivery
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dewlivery
dfelivery
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eclampsia
elivery
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EXIT
failure to progress
fetal bradycardia
fetal distress
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labour
labpor
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lccs
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ltsc
nsvd
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pprom
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preeclampsia
pre-eclampsia
pre-eclampsia
preeclamsia
preterm
previa
primary section
prolapsed cord
prom
ptl
rcs
rc-s
repeat cs
repeat section
repeat w/ tubal
repeat with tubal
repet cs
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secondary cs
secondary section
-section
srom
stat cs
svd
teriary cs
tertiary cs
tertiary csx
tertiary section
tocolysis
tolac
urgent cs
vag del
vaginal birth
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Appendix 3. Systematic Review Search Methodology

- Conducted on June 9, 2016
- Endnote X6 for eliminating duplicates
- Excluded animal and non-English studies
- Searched Web of Science for bw/fw citations

Embase.com

'thrombocytopenia'/exp OR thrombocytopeni*:ab,ti OR thrombocytopaeni*:ab,ti OR thrombopeni*:ab,ti OR thrombopaeni*:ab,ti OR macrothrombocytopaeni*:ab,ti OR macrothrombocytopeni*:ab,ti OR ((platelet OR thrombocyt*) NEAR/2 deficienc*):ab,ti AND ('pregnancy'/exp OR 'pregnancy complication'/exp OR 'pregnant woman'/exp OR pregnan*:ab,ti OR obstetric*:ab,ti OR parturient*:ab,ti) AND ('anesthesia'/exp OR anaesthe*:ab,ti OR anesthe*:ab,ti) AND [english]/lim NOT ([animals]/lim NOT [humans]/lim)

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("thrombocytopenia"[mh] OR thrombocytopeni*[tiab] OR thrombopeni*[tiab] OR thrombocytopaeni*[tiab] OR thrombopaeni*[tiab] OR macrothrombocytopaeni*[tiab] OR macrothrombocytopeni*[tiab]) AND (pregnancy[mh] OR pregnan*[tiab] OR "pregnancy complications"[mh] OR obstetric*[tiab] OR parturient*[tiab]) AND ("anesthesia"[mh] OR "analgesia"[mh] OR anesthesia*[tiab] OR anaesthesia*[tiab] OR anestheti*[tiab] OR analgesia*[tiab]) AND english[la] NOT (animals[mh] NOT humans[mh])

ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

Tolling the Bell-cap-sic Bell Against Pain: A Belladonna, Capsaicin, and Aconite Plaster

After earning his medical degree from Harvard and serving in America's Civil War as an assistant surgeon in the Union Army, John Milton Grosvenor, M.D. (1839 to 1917), returned to Boston to garner fame as a respected physician and fortune from topical medications, such as his proprietary medicinal plasters. By 1897 he was advertising that each of his "Bell-cap-sic Plasters" contained the "same quantity of Belladonna [atropine] as in…the standard U. S. P. Belladonna Plaster, one half the quantity of aconite [a numbing neurotoxin] plaster, and the same amount…as in the standard Capsicum [capsaicin] plaster." While reddening the skin with his plaster's Capsicum, Grosvenor tried to avoid blurring his patients' vision. He did so by balancing the pupillary effects of his plaster's Belladonna (dilation) against those of Bell-cap-sic's Aconite (constriction). With its trademark Bell-cap-sic bell (enlarged, *upper right*), this advertising card (*lower left*) suggests that no home is complete without a puppy or without a Bell-cap-sic plaster, presumably in the medicine cabinet. After all, by "combining two anodynes and a rubefacient" [Capsicum], Grosvenor boasted that Bell-cap-sic was "without doubt the best medicinal plaster ever produced!" (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

George S. Bause, M.D., M.P.H., Honorary Curator and Laureate of the History of Anesthesia, Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.