PCRC Proposal Cover Sheet

Title of Study or Project:	The Risk of Epidural Hematoma After Neuraxial Anesthesia In Thrombocytopenic Obstetric Patients: A Report from the Multicenter Perioperative Outcomes Group Research Consortium
Primary Institution:	University of Michigan Health System
Principal Investigator:	Linden Lee MD
Co-Investigators:	Brian Bateman MD, Sachin Kheterpal MD, Thomas Klumpner MD, Michelle Housey MPH, Melissa E Bauer DO
Type of Study:	X Retrospective Observational ☐ Exploratory ☐ Prospective Randomized
IRB Number/Status:	IRB approval has been obtained for MPOG and informed consent will be waived. In patients found to require a decompressive laminectomy due to epidural hematoma, IRB approval will be obtained from each individual site prior to additional data collection.
Hypothesis:	Epidural hematoma following neuraxial anesthesia in thrombocytopenic parturients without a hematological diagnosis, and who are not taking anticoagulants or antiplatelet medications is a rare complication that increases in frequency with decreasing platelet count.
Number of Patients/Participants:	The MPOG database will be queried for all obstetric labor patients receiving neuraxial procedures, including epidural, spinal, and combined spinal-epidural anesthesia. Any patients on anticoagulants or antiplatelet agents, as well as those with hematological diagnoses will be excluded.
Power Analysis:	This is a retrospective study in which all obstetric labor patients in the MPOG database receiving neuraxial procedures will be included, except for those with hematological diagnoses and those on anticoagulant/antiplatelet medications.
Proposed statistical test/analysis:	Point estimates and 95% confidence intervals (CI) will be calculated based on observed counts for numerators (cases with hematomas) divided by denominators (cases receiving neuraxial anesthesia). Cases will then be stratified based on platelet count - categorized as 0 to 24 $x10^9$/L, 25 to 49 $x10^9$/L, 50 to 59 $x10^9$/L, 60 to 69 $x10^9$/L, 70 to 79 $x10^9$/L, 80 to 89 $x\ 10^9$/L, 90 to 99 $x\ 10^9$/L – to determine incidence of hematomas at various platelet levels. The incidence of epidural hematoma will also be determined for each different type of neuraxial technique – epidural, spinal, and combined spinal-epidural anesthesia. For manually- reviewed decompressive laminectomy cases, we will report the incidence of neurosurgical interventions and neurological outcomes as well as other circumstances surrounding each individual occurrence.
Resources (Brief summary of resources for data collection, personnel, financial):	The MPOG database will be queried for the specified Concept IDs. Statisticians will perform statistical analyses to determine the overall incidence of epidural hematoma and the incidence at various platelet levels. If a patient requires decompressive laminectomy, investigators at individual sites will obtain site-specific IRB approval and obtain more information about individual incidents

The Risk of Epidural Hematoma After Neuraxial Anesthesia in Thrombocytopenic Obstetric Patients: A Report from the Multicenter Perioperative Outcomes Group Research Consortium

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Introduction

The incidence of failed intubation in the obstetric population is approximately 1:443 with maternal mortality occurring at a rate of one death per 90 failed intubations. (1) Intubation failure, inadequate ventilation, and aspiration represent leading causes of anesthesia-associated obstetric morbidity. (2) Therefore, neuraxial techniques, which afford an opportunity to avoid airway instrumentation, are common in the anesthetic management of the parturient.

Thrombocytopenia has long been considered a contraindication to neuraxial anesthesia due to the increased risk of bleeding complications. Specifically, epidural hematoma is a rare but dreaded complication that can result in devastating permanent neurological injury. There is no consensus for an absolute platelet count below which neuraxial anesthesia is contraindicated. Bromage recommended that a neuraxial anesthetic be withheld if the platelet count is <100,000 mm^{-3}; however, a retrospective chart review performed by Beilin et al. reported safe epidural catheterization in thirty parturients with platelet counts between 69,000 and 98,000 mm^{-3}. (3, 4) It has been suggested that the low incidence of epidural hematoma in parturients may be due to the physiologic hypercoagulability of pregnancy. (5) Nonetheless, many practitioners have adopted the 100,000 mm^{-3} threshold, but great variation exists in practice.

Some studies estimate the overall risk of epidural hematoma associated with neuraxial anesthesia to be approximately 1:200,000. (6, 7) However, the estimation of this risk is evolving. An extensive review of case series and case reports of thrombocytopenic patients (platelet count less than 100,000 mm^{-3}) receiving epidural or spinal anesthesia found no evidence of epidural hematoma in the 345 parturients that were reviewed. (8) Bateman et al. investigated the frequency of epidural hematomas after epidural catheterization in obstetric and non-obstetric patients in a retrospective review of eleven centers participating in the Multicenter Perioperative Outcomes Group (MPOG). (9) Seven of 62,450 non-obstetric patients undergoing epidural catheterization developed epidural hematoma requiring decompressive laminectomy, whereas none of 79,837 obstetric patients undergoing epidural catheterization developed an epidural hematoma. These data demonstrate that the risk of epidural hematoma after neuraxial anesthesia in obstetric patients may be significantly lower than in non-obstetric patients. While these studies provide substantial information regarding overall risk of epidural hematoma in obstetric patients, we are aware of no multicenter studies with stratification of this complication by platelet count and neuraxial technique.

Our primary aim is to determine the incidence of epidural hematoma following neuraxial anesthesia in thrombocytopenic parturients (<100,000 mm^{-3}) without a concomitant hematological diagnosis and who are not taking anticoagulants or antiplatelet medications. Our secondary aims include assessing the incidence of epidural hematoma following neuraxial anesthesia in parturients stratified by platelet count, and reporting neurosurgical interventions in parturients with epidural hematoma following neuraxial anesthesia. The incidence of epidural hematoma will also be determined for each type of neuraxial technique – epidural, spinal, and combined spinal-epidural anesthesia. We hypothesize that epidural hematoma following

neuraxial anesthesia in thrombocytopenic parturients without a hematological diagnosis, and who are not taking anticoagulants or antiplatelet medications is a rare complication that increases in frequency with decreasing platelet count. The results of this study will yield a more accurate assessment of the risks of epidural hematoma associated with neuraxial anesthesia in the obstetric population. If an increased incidence of epidural hematoma is not observed in thrombocytopenic parturients, the benefits of receiving neuraxial anesthesia may potentially be extended to those who previously would not have been considered candidates.

Methods

For this study, we will collaborate with the Multicenter Perioperative Outcomes Group (MPOG), which is an international consortium of 47 medical centers combining large sets of observational electronic medical record data. By accessing the large collection of data assembled by MPOG, the risk of epidural hematoma stratified by platelet count may be more accurately determined. IRB approval has been obtained for MPOG and informed consent will be waived. The MPOG database will be queried for all obstetric labor patients age 18-55 receiving neuraxial procedures, including epidural, spinal, and combined spinal-epidural anesthesia (anesthesia CPT code 01961 and 01967) from January 2004 through September 2015. For facilities not currently contributing professional fee CPT codes, procedure descriptions will be screened for the phrases such as ‘labor’, ‘epidural’, ‘c-section’, ‘cesarean’, and ’caesarean’ to identify possible obstetric neuraxial techniques. A manual review of procedure descriptions will be used to exclude patients receiving non-labor neuraxial anesthesia. Information that will be collected from the database will include: most recent platelet count from the complete blood count within 72 hours prior to neuraxial anesthesia, any anticoagulant usage (aspirin, clopidogrel, heparin, enoxaparin,

dalteparin, fondaparinux, rivaroxaban, apixaban, edoxaban, warfarin, argatroban, bivalirudin, dabigatran, desirudin, lepirudin), and any hematological diagnosis. Any patients on anticoagulants or antiplatelet agents, as well as those with hematological diagnoses will be excluded. These cases will also be screened for patients who underwent decompressive laminectomy within 6 weeks of receiving neuraxial anesthesia. For centers not reporting professional fee CPT codes, we will screen all operative episodes not typically associated with obstetric care (D&C for retained placenta, tubal ligation, etc.) within 6 weeks of receiving neuraxial anesthesia to identify decompressive laminectomies. Only individual sites reporting decompressive laminectomies after neuraxial anesthesia will be required to obtain IRB approval. In patients found to require a decompressive laminectomy, additional data will be collected (see Case Report Form) including medications and associated diagnoses to ensure patients are appropriate for the study population. The patient will be identified by the individual site and data collection will be performed prior to transmitting the data to MPOG in a de-identified fashion. Institutions in which no decompressive laminectomy is performed due to epidural hematoma will not be required to obtain IRB approval for chart review.

Statistical Analysis

To determine the incidence of epidural hematoma associated with neuraxial anesthesia, all cases meeting inclusion criteria will be pooled across institutions. Point estimates and 95% confidence intervals (CI) will be calculated based on observed counts for numerators (cases with epidural hematomas) divided by denominators (cases receiving neuraxial anesthesia). Given the low likelihood of identifying cases of decompressive laminectomy, conservative methods for asserting 95% confidence interval of incidence will be employed using the R package ”binom” (3.2.1). Cases will then be stratified based on platelet count - categorized as 0 to 24 $x10^9$/L, 25 to

49 x10^9/L, 50 to 59 x10^9/L, 60 to 69 x10^9/L, 70 to 79 x10^9/L, 80 to 89 x 10^9/L, 90 to 99 x 10^9/L – to determine incidence of hematomas at various platelet levels. The incidence of epidural hematoma will also be determined for each different type of neuraxial technique – epidural, spinal, and combined spinal-epidural anesthesia. For manually-reviewed decompressive laminectomy cases, we will report the neurosurgical interventions performed as well as other circumstances surrounding each individual occurrence.

Limitations to be addressed in the discussion

Our study has several limitations. Several institutions maintain policies advising against neuraxial anesthesia below a specified platelet count. Inclusion of these centers will bias toward an overall lower incidence of epidural hematoma associated with neuraxial anesthesia.

Additionally, not all institutions participating in MPOG contribute professional fee CPT codes. Therefore, a screen of procedure descriptions is necessary to identify obstetric cases where a neuraxial technique was performed. This screening process may lead to omission of neuraxial procedures and inadvertent inclusion of non-neuraxial and/or non-obstetric procedures.

Our methods only detect patients who underwent decompressive laminectomies, therefore we do not identify epidural hematomas that were managed non-operatively. The MPOG dataset does not allow for the identification of patients discharged from one hospital and treated at another. Therefore, it is possible that patients could have been discharged with symptoms of epidural hematoma and treated at another hospital. We are also unable to collect attempted neuraxial procedures that were aborted because of bleeding or difficult placement. All of these limitations may lead to an underestimation of the risk of epidural hematoma.

Variables to be collected

Element	**Source**
MPOG case identifier	General_Case_Information.MPOG_Case_ID
MPOG patient identifier	General_Case_Information.MPOG_Patient_ID
MPOG institution identifier	General_Case_Information
Case Date	General_Case_Information.AIMS_Scheduled_DT
Scheduled procedure description from AIMS text	General_Case_Information.AIMS_Scheduled_Procedure_Text – see appendix for search terms
Actual procedure description from AIMS text	General_Case_Information.AIMS_Actual_Procedure_Text – see appendix for search terms
Primary Surgical Service	General_Case_Information. MPOG_Primary_Procedural_Service_Concept_ID
Primary Surgical Service	General_Case_Information. MPOG_Primary_Procedural_Service_Concept_Desc
Anesthesia CPT code	General_Case_Information. Charge_Capture_Primary_Anesthesia_Code – 01961, 1961, 01967, 1967, 00600 – 00700
Surgery CPT code	General_Case_Information. Charge_Capture_Primary_Surgery_Code – 63000 - 70000
ICD code	General_Case_Information.Charge_Capture_Primary_Diagnosis_Code – 286.xx, 287.0, 287.1, 287.31, 287.8, 287.9
ASA class	ASA_Class.ASA_Class
Emergent	ASA_Class.Emergent
Height in cm	Anthropometrics.MPOG_height_cm
Weight in kg	Anthropometrics.MPOG_weight_kg
BMI	Anthropometrics.Body_Mass_index
Age	Patient_Demographics.AIMS_Patient_Age_Years
Gender	Patient_Demographics.AIMS_Sex
Block_yn	Anesthesia_Technique.Block_yn
Epidural_yn	Anesthesia_Technique.Epidural_yn
General_yn	Anesthesia_Technique.General_yn
Spinal_yn	Anesthesia_Technique.Spinal_yn
POC – Coulter counter – Platelets	Laboratory or Testing Observations - 3445
Formal lab- Platelets	Laboratory or Testing Observations - 5004
Hematologic – Anticoagulation	Preoperative Observations - 70243
Hematologic – Bleeding Disorder	Preoperative Observations - 70064
General- Medications – Anticoagulation	Preoperative Observations - 70073
Epidural	Anesthetic Technique View – 2005
Neuraxial – spinal performed	Anesthetic Technique View – 50680
Neuraxial technique – Combined Spinal/Epidural technique note	Anesthetic Technique View – 50614

References

1. Kinsella SM, Winton AL, Mushambi MC, Ramaswamy K, Swales H, Quinn AC, Popat M. Failed tracheal intubation during obstetric general anesthesia: a literature review. International Journal of Obstetric Anesthesia (2015), http://dx.doi.org/10.1016/j.ijoa.2015.06.008

2. Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, et al. 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 Mar;118 Suppl 1:1-203.

3. Bromage PR. Neurologic complications of regional anesthesia in obstetrics. In: Shnider SM, Levinson G, editors. Anesthesia for obstetrics. 3rd ed: Williams & Wilkins; 1993. p. 443-4.

4. Beilin Y, Zahn J, Comerford M. Safe epidural analgesia in thirty parturients with platelet counts between 69,000 and 98,000 mm^{-3}. Anesthesia and analgesia 1997 Aug;85(2):385-8.

5. Thornton P, Douglas J. Coagulation in pregnancy. Best Practice & Research Clinical Obstetrics & Gynaecology 2010 Jun;24(3):339-52.

6. 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 Aug;105(2):394-9.

7. Stafford-Smith M. Impaired haemostasis and regional anaesthesia. Canadian journal of anaesthesia 1996 May;43(5 Pt 2):R129-41.

8. van Veen JJ, Nokes TJ, Makris M. The risk of spinal haematoma following neuraxial anaesthesia or lumbar puncture in thrombocytopenic individuals. Br J Haematol 2010 Jan;148(1):15-25.

9. Bateman BT, Mhyre JM, Ehrenfeld J, Kheterpal S, Abbey KR, Argalious M, et al. The risk and outcomes of epidural hematomas after perioperative and obstetric epidural catheterization: a report from the Multicenter Perioperative Outcomes Group Research Consortium. Anesthesia and analgesia 2013 Jun;116(6):1380-5.

Case report form

MPOG Case ID: _____

(1) Description of delivery:
Vaginal delivery _____ assisted vaginal delivery _____ cesarean delivery _____
Emergency surgery (as defined by ASA status) Yes ____ No ____
Duration of surgery _____hrs _____min (from incision to time out of OR)
EBL _____ml
Lowest intraop Hct _____%
Lowest intraop Platelets_____k
Highest intraop INR _____
Fibrinogen _____mg/dl
Units transfused _____#
Cell Saver transfused _____ml
Platelets transfused _____units
FFP transfused _____ml

(2) Description of neuraxial anesthesia placement:
Type of neuraxial anesthesia: epidural _____ spinal _____ CSE ____
Time of neuraxial anesthesia placement: _____ (0 to 24:00)
Needle gauge/type_____
Number of placement attempts_____
Approach: Midline _____, paramedian _____
Loss of resistance to: Air _____, Saline _____
Bloody placement: Yes ____, No ____ (blood dripping from needle at any time during placement procedure)
Initial intravascular placement: Yes ____, No ____
Level of placement (eg L2/3 T9/10, etc): _____
Length of catheter left in space (cm) _____
Place catheter was placed (operating room, labor and delivery room)_____

(3) Description of patient:
Patient age_____
ASA Status 1 ___ 2 ____ 3 ____ 4 ____ 5 ____ E Yes ___ No ___
Body mass index (kg / m2) _____
Type of antibiotic administered for surgical prophylaxis_____
Presence of comorbidity (check all that apply):
___ Insulin Dependent DM
___ Oral hypoglycemic DM
___ Gestational DM
___ Hypertension requiring chronic medication
___Preeclampsia
___Eclampsia
___HELLP syndrome
___Chronic renal disease, baseline creatinine_____

___Acute renal failure, peak creatinine_____
___Congenital coagulopathy, describe type_____

Preoperative antiplatelet/anticoagulation medications and dose (check and write dosing for all that apply, and the time stopped (day, hour) prior to surgery)

Plavix Dose_____ Time stopped, **days** before surgery:_____
Aspirin Dose_____ Time stopped, **days** before surgery:_____
Coumadin Dose_____ Time stopped, **days** before surgery:_____
Heparin (SQ) Dose _____ Time stopped, **hours** before surgery:_____
Heparin (IV) Dose_____ Time stopped, **hours** before surgery:_____
Lovenox Dose_____ Time stopped, **hours** before surgery:_____
Fragmin Dose_____ Time stopped, **hours** before surgery:_____
Argatroban Dose_____ Time stopped, **hours** before surgery:_____

Postoperative antiplatelet/anticoagulation medications and dose (check and write dosing for all that apply, and postoperative day resumed)

Plavix Dose_____POD resumed_____
Aspirin Dose_____POD resumed_____
Heparin (SQ) Dose_____ POD resumed_____
Heparin (IV) Dose_____ POD resumed_____
Lovenox Dose_____ POD resumed_____
Fragmin Dose_____ POD resumed_____
Argatroban Dose_____ POD resumed_____
Coumadin Dose_____ POD resumed_____

INR when: (1) catheter placed_____, (2) catheter removed_____
Partial thromboplastin time when: (1)catheter placed_____, (2)catheter removed_____
Platelet count when: (1) catheter placed_____, (2) catheter removed_____

Length of time catheter is left in place (hours) _____hrs.
History of spinal surgery including kyphoplasty/laminectomy, describe procedure: ____ _____, and level_____

(4) Description of lesion:
Date and time of first symptom: _____ /_____ /_____ (dd/mm/yy) _____(0 to 24:00)
Date and time of imaging study: _____ /_____ /_____ (dd/mm/yy) _____ (0 to 24:00)
Date and time of laminectomy incision: ____ /____ /____(dd/mm/yy)_____(0 to 24:00)
How did the lesion present (please note location, deficit, and laterality): _____
Symptoms (pain, weakness, etc.): _____
Neuro deficits: _____
Laterally: Rt._____, Lt. _____, Bilateral _____
Lesion: Epidural hematoma _____, Intrathecal hematoma _____, Abscess _____

Did lesion present before or after catheter removal: _____
Neurological outcome: Complete recovery ___, Major residual deficit ___, Mild residual deficit ____
Description of deficit: _____
_____

Please comment on any other details that may be pertinent to the case: _____
_____
_____
_____
_____

Appendix I: search list terms

% cle %
% cs %
% cs, %
% exit %
;abor
assisted second
c cection
c cesction
c esction
c sec
c- sec
c- section
c setion
c sxn
c. sec
c. section
c/ s
c/d
caaesarian
caecerean
caesaerian
caesearean
caeserian
caessarean
casearean
caserean
cearean
ceasarean
ceasarian
ceasearan
ceasearean
ceasearn
ceaserean
ceasrean
cecearean
c-ection
ces sect
cesaeran
cesaerean
cesaerian
cesaian
cesaran
cesarea
cesarea n
cesarean
cesareean
cesaren
cesarena
cesarian
cesarian section
cesariean
cesasrean
cesasrian
cesceran
cesearan
cesearean
cesearen
cesearian
ceseraen
ceseran
ceserean
ceserian
cessarian
cs
c-s
csbti
csbtl
csd
csec
c-sec
c-setion
cssab
cssalpin
cssection
csx
csxn
cxsn
de3livery
decels
deilvery
deivery
dekivery
del8ivery
deleivery
delevery
delievery
delilvery
delinery
deliuvery
deliveery
deliver
delivery
delivewry
delivey
deliveyr
deliviery
delivry
delivvery
dellivery
deloery
delvery
delviery
delviey
dewlivery
dfelivery
dleviery
dlivery
dlivry
eclampsia
elivery
esarea
esarean
esarian
EXIT
failure to progress
fetal bradycardia
fetal distress
hellp
i o l
inductino
induction
iol
iufd
iugr
l & d
l &d
l and d
l& d
l&d
l_d
l+d
labir
labot
labour
labpor
labro
lccs
lcts
lscs
ltcs
ltsc
nsvd
pih
pol
post dates
post-dates
pprom
preclampsia
preecl
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
rom
s/cection
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
vaginal del
vbac