Evaluating hemostatic thresholds for neuraxial anesthesia in adults with hemorrhagic disorders and tendencies: A scoping review

Wynn Peterson MD¹ | Brandon Tse BSc² | Rachel Martin MD³ | Michael Fralick MD, PhD, SM⁴ | Michelle Sholzberg MDCM, MSc⁵

¹Division of Medicine, University of Toronto, Toronto, ON, Canada
²Faculty of Medicine, University of Toronto, Toronto, ON, Canada
³Department of Anesthesia, St. Michael’s Hospital, Toronto, ON, Canada
⁴Sinai Health System and the Department of Medicine, University of Toronto, Toronto, ON, Canada
⁵Division of Hematology, Department of Medicine and Department of Laboratory Medicine and Pathobiology, St. Michael’s Hospital, Toronto, ON, Canada

Abstract

Neuraxial anesthesia can be complicated by spinal or epidural hematoma and may result in permanent neurologic injury. There is a paucity of literature characterizing this serious complication in patients with congenital and acquired hemorrhagic disorders or tendencies. The objective of this scoping review was to describe the hemostatic laboratory parameters where neuraxial anesthesia has been administered with and without spinal and epidural hematoma in patients with preexisting hemorrhagic disorders and tendencies, including immune thrombocytopenia, gestational thrombocytopenia, thrombocytopenia associated with hypertensive disorders of pregnancy, platelet function disorders, von Willebrand disease, coagulation factor deficiencies, and fibrinogen disorders. A systematic search of Ovid MEDLINE, CINAHL, Embase, Scopus, and Web of Science was performed. Two authors independently reviewed all titles, abstracts, and full texts to determine study eligibility and extract data. Qualitative synthesis of 91 studies revealed significant gaps in our understanding of the risk of spinal and epidural hematoma in patients with hemorrhagic disorders and tendencies, including few studies of males and in nonobstetric settings. Most reviewed articles were small, retrospective studies at high risk for potential bias. With such low-quality data, we were unable to provide any true estimates of the risk of spinal or epidural hematoma for these patients, nor could we attribute any specific hemostatic or laboratory values to increased risk of hematoma. There is a need both for larger and more rigorously designed and reported studies on this subject and for structured, comprehensive recommendations for safe administration and removal of neuraxial anesthesia in patients with hemorrhagic disorders and tendencies.
1 | INTRODUCTION

Neuraxial anesthetic techniques, including spinal, epidural, and combined spinal-epidural blocks, are commonly used for acute pain control in surgery and obstetrics. Neuraxial anesthetics may offer patients numerous benefits over general anesthetic, including decreased 30-day mortality, reduced length of stay, and lower risk of venous thromboembolism. They may also provide more effective pain control compared to intravenous patient-controlled analgesia.

In obstetrics, neuraxial techniques have long been the preferred method of analgesia for labor and delivery, reducing pain more effectively than other methods.

One serious complication of neuraxial anesthesia is spinal or epidural hematoma, which can lead to permanent neurologic injury, including paralysis, sensory loss, or autonomic dysfunction. According to one large retrospective review, the risk of spinal or epidural hematoma following neuraxial blockade is estimated at 2.14 per 100,000 (95% confidence interval, 0.44–6.25 per 100,000) in the population at large. In the general obstetric population, the risk of spinal or epidural hematoma is approximately 0.54 per 100,000. The risk of spinal or epidural hematoma is generally accepted to be higher in patients with bleeding diatheses compared to the general population; however, this conclusion is largely based on anecdotal data rather than empirical evidence.

There is extensive literature describing spinal and epidural hematoma after neuraxial anesthesia in patients receiving antithrombotic therapy; however, there is a paucity of literature characterizing this serious bleeding complication in patients with congenital or acquired hemorrhagic disorders/tendencies unrelated to medications. Without a robust body of literature, clinicians are often unable to determine which patients suffering from congenital and acquired hemorrhagic disorders/tendencies can safely receive neuraxial anesthetics.

A review by Choi and Brull described the frequency of hemorrhagic complications after neuraxial anesthesia in patients with immune thrombocytopenia (ITP), von Willebrand disease (VWD) and hemophilia. However, there are no systematic, scoping studies that describe the existing body of literature related to hemorrhagic complications from neuraxial anesthesia in patients with other, less common, hemorrhagic disorders or tendencies. The aim of this scoping review was to describe the hemostatic laboratory parameters where neuraxial anesthesia has been administered with and without spinal or epidural hematoma in patients with single preexisting hemorrhagic disorders/tendencies, including ITP, gestational thrombocytopenia, thrombocytopenia associated with hypertensive disorders of pregnancy, platelet function disorders, VWD, coagulation factor deficiencies, and fibrinogen disorders. While gestational thrombocytopenia does
not confer additional bleeding risk, placing neuraxial anesthesia for a patient with thrombocytopenia of any etiology can be a source of anxiety for patients and healthcare providers alike. Thus, we included gestational thrombocytopenia in this scoping review to help inform the clinical approach to patients affected by this condition.

Ultimately, our objective for this scoping review was to develop an evidence-based framework that may facilitate clinical decision making surrounding neuraxial anesthesia and to identify areas where additional evidence is urgently needed to best support clinical care.

2 | METHODS

This scoping review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines. The review’s protocol can be found here: https://osf.io/r7qaz/?view_only=fa1088e165cb43a59f1097f0119a56fd.

2.1 | Information sources and searches

A detailed search strategy was developed in collaboration with a medical librarian. Examples of keywords used in the search include “thrombocytopenia,” “coagulopathy,” “factor deficiency,” “bleeding time,” “clotting factor assays,” “neuraxial anesthesia,” “spinal anesthesia,” “epidural anesthesia,” and their derivatives. The full search strategy is available in Appendix S1. The search was performed in Ovid MEDLINE (1946 to July 10, 2019), CINAHL (inception to July 10, 2019), Embase (1947 to July 10, 2019), Scopus (inception to July 10, 2019), and Web of Science (inception to July 10, 2019). The search was limited to English-language studies only. There were no limits placed on date of publication in order to maximize the repository of data potentially included in the review. Gray literature identified by this search strategy was included. Reference lists of all publications included in full-text review were screened to identify additional sources for inclusion.

2.2 | Study selection

This scoping review included all types of studies, including case reports, case series, observational studies, interventional studies, systematic reviews, meta-analyses, scoping reviews, narrative reviews, guidelines, and editorials. Any individual study with results that had also been reported in a systematic review was excluded to prevent double counting of data.

Titles and abstracts were screened by two reviewers (WP and BT) independently, followed by full-text review. A third reviewer (MS) resolved conflicts through adjudication. Studies were included if patients with a known diagnosis of a single hemorrhagic disorder/tendency received either an epidural, spinal, or combined spinal-epidural anesthetic. In studies that reported hemorrhagic complications, consisting of either spinal or epidural hematoma, the diagnosis must have been confirmed on computed tomography or magnetic resonance imaging for inclusion in the review. Patients with an additional hemorrhagic disorder or other comorbidity predisposing to bleeding (eg, arteriovenous malformation) were excluded because these conditions can independently increase the risk of hematoma. Peripheral nerve blocks and lumbar punctures were also excluded due to their unique risk of complications and indications for use.

After completion of initial title and abstract review, the decision was made to exclude patients with coagulopathy secondary to liver or renal disease, as these patients were too heterogeneous to draw meaningful conclusions from. Thus, we included only patients with ITP, gestational thrombocytopenia, thrombocytopenia associated with hypertensive disorders of pregnancy, platelet function disorders (eg, Glanzmann thrombasthenia), VWD, factor VII deficiency, hemophilia A or B (or carriers), factor XI deficiency, factor XIII deficiency, and fibrinogen disorders.

2.3 | Data collection/charting process/data items

Data were collected using a prepiloted data collection form for each hemorrhagic disorder/tendency. Relevant study characteristics were extracted, including authors, title, publication details and type of study, and whether a full article was available or only an abstract. Available population demographics were collected for all studies, including number of neuraxial procedures, mean age, sex, and bleeding history. The type of surgery or procedure was noted along with relevant details of the neuraxial anesthetic technique and the outcome of the procedure (ie, hematoma or no hematoma).

For case reports and case series, reviewers extracted the last known hemostatic parameter before administration of neuraxial anesthesia, any relevant treatment administered before the anesthetic procedure, and the hemostatic parameter at the time of neuraxial catheter removal. For narrative reviews, systematic reviews, and observational studies, the minimum hemostatic parameter that was reported before an uncomplicated neuraxial anesthetic was recorded. If any study proposed a minimum hemostatic threshold for safe administration of neuraxial anesthesia or removal of the catheter (eg, a guideline statement), this was also recorded. For each included narrative review, data sources with which the reviews generated their recommendations were extracted. Additionally, reviewers were able to clarify any specific details of extracted data in a “notes” section if desired.

2.4 | Synthesis of results

Qualitative synthesis was used to summarize the existing cases, reviews, observational and interventional studies for each hemorrhagic disorder/tendency and report the hemostatic thresholds proposed by guidelines, reviews, and expert opinion papers. Certain
study features were recorded as indicators of potential risk of bias. For review articles, we recorded the proportion that were systematic reviews compared to narrative reviews. Among systematic reviews/meta-analyses, we also noted the proportion analyzing prospective studies. For nonreview studies (ie, observational studies) we identified the presence or absence of three key aspects: prospective design, well-defined population, and measurement of association between the laboratory parameter and risk of hematoma.

3 | RESULTS

We identified 1418 abstracts for review, of which 91 met the criteria for inclusion (Figure 1). Relevant characteristics of these studies are summarized in Table 1. We reviewed 23 case reports/case series, 27 cohort studies, 5 surveys, and 36 review articles. No randomized controlled trials or meta-analyses were identified. Twenty-three percent of articles we reviewed were available only as abstracts. Full results of data extraction can be found in Appendix S2.

Among the studies that reported on neuraxial anesthesia administration in patients with thrombocytopenia, many did not differentiate between disorders. For example, 25 studies did not differentiate between ITP, gestational thrombocytopenia, and hypertensive disorders of pregnancy. In these cases, data were categorized under “thrombocytopenia not otherwise specified.”

Results are described in detail below according to hemorrhagic disorder/tendency.

3.1 | Immune thrombocytopenia

Nine studies relating to patients with ITP and neuraxial anesthesia were found and are presented in Table 2.

Our search yielded two systematic reviews and seven narrative reviews. There were three articles included in the analysis of both systematic reviews, so data were carefully scrutinized to avoid duplicate reporting. One systematic review included data from guidelines and from patients not meeting our inclusion criteria. These data were not extracted and are not reported below.

Within the systematic reviews, one neuraxial procedure was successfully completed at a platelet count < 10 × 10⁹/L, which was reported in both articles. One additional procedure was performed
at a platelet count between $10 \times 10^9/L$ and $20 \times 10^9/L$. The most commonly proposed platelet count threshold for administration of neuraxial anesthesia in patients with immune thrombocytopenia was $50 \times 10^9/L$, with a range of other proposed thresholds from $70 \times 10^9/L$ to $75 \times 10^9/L$. One narrative review stated that neuraxial anesthesia is generally contraindicated in patients with ITP but did not cite evidence to support this claim. Only one review suggested a threshold for the removal of a neuraxial catheter—a minimum platelet count of $60 \times 10^9/L$—which was taken directly from the recommendations of a previous study. Most narrative reviews developed their recommendations based on observational studies, review articles, or expert opinion. There was only one source article that was cited in the recommendations of more than one narrative review.

3.2 | Gestational thrombocytopenia

We extracted data from three studies of women with gestational thrombocytopenia. A single retrospective cohort study summarized 20 neuraxial procedures—all epidurals—performed at platelet counts as low as $71 \times 10^9/L$. None resulted in hemorrhagic complications.

Of two narrative reviews, one suggested that neuraxial anesthesia is safe for patients with ITP and gestational thrombocytopenia if the platelet count is $>50 \times 10^9/L$ and "stable." The other review article stated that neuraxial anesthesia may be performed in patients with gestational thrombocytopenia "if coagulation tests are normal." Both of these recommendations were based on expert opinion. It is important to highlight that gestational thrombocytopenia is generally considered to be a physiologic condition where, by definition, platelet counts do not fall below $50 \times 10^9/L$ and there is no increased bleeding risk or abnormal coagulation status. Thus, the recommendations made by these narrative reviews do not reflect the underlying physiologic nature of the disorder, and their merit in guiding management in this setting is unclear.

No studies recommended a minimum threshold for neuraxial catheter removal.

3.3 | Thrombocytopenia associated with hypertensive disorders of pregnancy

We extracted data from 29 studies of patients with hypertensive disorders of pregnancy, including 12 with preeclampsia,20,26-26 2 with eclampsia,37,38 and 9 with HELLP syndrome (hemolysis,
TABLE 2 Studies with data relevant to use of neuraxial anesthesia in immune thrombocytopenia

| Study | Study design | Type of procedure | Type of neuraxial anesthesia | Sample size, No. | Minimum platelet count reported before administration of neuraxial anesthetic (×10^9/L) | Before removal of neuraxial anesthetic | Minimum safe platelet count threshold proposed (×10^9/L) | Before removal of neuraxial anesthetic |
|-------|--------------|-------------------|------------------------------|------------------|----------------------------------------|--------------------------------------|-----------------------------------------|--------------------------------------|
| American College of Obstetricians and Gynecologists (2019) | Narrative review | Obstetric | Epidural | N/A | N/A | N/A | 70 | N/A |
| Bailey et al (2019) | Systematic review | Obstetric | Unspecified | 366 | 2 | N/A | N/A | N/A |
| Choi & Brull (2009) | Systematic review | Obstetric | Unspecified | 323 | 2 | N/A | N/A | 60 |
| Chow et al (2011) | Narrative review | Obstetric | Unspecified | N/A | N/A | N/A | N/A | Remove as soon as possible |
| Harrop-Griffiths et al (2013) | Narrative review | Obstetric | Unspecified | N/A | N/A | N/A | 50 | N/A |
| Moen & Irestedt (2009) | Narrative review | Obstetric | Unspecified | N/A | N/A | N/A | N/A | Usually contraindicated |
| Myers & Truelove (2011) | Narrative review | Obstetric | Unspecified | N/A | N/A | N/A | 75 | N/A |
| Ozelo et al (2018) | Narrative review | Obstetric | Unspecified | N/A | N/A | N/A | 50 | N/A |
| Pavord (2016) | Narrative review | Obstetric | Unspecified | N/A | N/A | N/A | 50 | N/A |

N/A, not applicable.

3.4 | Thrombocytopenia not otherwise specified

Twenty-five studies reported laboratory thresholds for administration of neuraxial anesthesia in patients with low platelets, but did not specify the underlying etiology of thrombocytopenia. Among these studies, 15 were narrative reviews, 6 were systematic reviews, and 4 were descriptive case reports. The most commonly proposed minimum platelet count for neuraxial anesthesia was 80 × 10^9/L (range, 50-100 × 10^9/L). Among 15 narrative reviews, 26% recommended removal of the neuraxial catheter only if "coagulation status" was normal. Also, 25% of articles made recommendations based on observational data. There was limited overlap in the articles used to generate these recommendations; only three articles cited more than 10 studies. Although the majority of authors did not differentiate between spinal and epidural anesthetics, some patients were supported with platelet transfusions. In this study, all patients with platelet counts <50 × 10^9/L were not given neuraxial anesthesia. However, two studies described women during labor and delivery who received neuraxial anesthesia with platelet counts of >100 × 10^9/L. Two studies reported on multiple hypertensive disorders of pregnancy, but did not differentiate between them.
A total of 1192 neuraxial procedures were described within 12 retrospective cohort studies, 23,24,66-75 1 prospective cohort study,65 and 1 case series.54 There were 68 epidural anesthetics24,54,66 and 2 spinal anesthetics.75 The types of the remaining procedures were not specified. One study analyzed 13 case reports of spinal or epidural hematoma occurring in patients with thrombocytopenia (Table 3); seven of these patients had platelet counts <80 × 10^9/L; however, the author did not report precise platelet counts at the time of bleeding for any case.11 Neuraxial procedures in the other studies were performed uneventfully at platelet counts ranging from 2 × 10^9/L62 to 92 × 10^9/L.23 One study reported a platelet count of 36 × 10^9/L at the time of neuraxial catheter removal.23

Table 3: Summary of hematomas

| Study                  | Study design     | Type of procedure | Type of neuraxial anesthesia | Sample size, N | Hematomas, No. | Platelet count at time of block (×10^9/L) |
|-----------------------|------------------|-------------------|-------------------------------|----------------|----------------|------------------------------------------|
| Lagerkranzer (2017)   | Narrative review | Nonobstetrics     | Unspecified                   | 166            | 13             | <150 (n = 6), <80 (n = 7)                |
| Yuen et al (1999)     | Case report      | Obstetrics        | Epidural                      | 1              | 1              | 71                                       |
| Koyama et al (2010)   | Case report      | Obstetrics        | Spinal                        | 1              | 1              | 91                                       |
| Sibai et al (1986)    | Retrospective cohort | Obstetrics  | Epidural                      | 16             | 1              | 93                                       |

3.5 | Platelet function disorders

We extracted data from five studies of patients with platelet function disorders, including Bernard-Soulier syndrome,76,77 Glanzmann thrombasthenia,76,77 gray platelet syndrome,78 and other unspecified disorders.79,80 Of the five studies, there were three case reports/case series78-80 that described a total of four neuraxial anesthetic procedures, including one spinal anesthetic,78 two combined spinal-epidural anesthetics,80 and one that was of unspecified type.79 No epidural or spinal hematomas were reported. Only one study reported a hemostatic laboratory parameter tested before administration of neuraxial anesthesia. In this study, a woman with gray platelet syndrome uneventfully received a spinal anesthetic with a platelet count of 112 × 10^9/L.78 Among the two narrative reviews identified, one paper warned that neuraxial anesthesia is contraindicated in platelet function disorders,76 and the other study advised that neuraxial anesthesia should only be considered in mild platelet function disorders where benefit outweighs bleeding risk.77 Both recommendations were based on expert opinion.

3.6 | Von Willebrand disease

We identified 19 studies relating to neuraxial anesthesia in patients with VWD,13,17,18,63,64,77,79,81-92 Of the 19 studies, 5 described patients with type 1 VWD,81,83,84,86,90 and 2 described patients with type 2 VWD,82,85 while the remainder did not specify the subtype. Studies are summarized in Table 4.

Six case reports/case series,81-86 one prospective cohort study,90 and three retrospective cohort studies79,91,92 were reviewed, which described 134 neuraxial anesthetic procedures without any reported spinal or epidural hematoma. Fifteen epidural procedures,82-84,92, two spinal anesthetics,83,86 and one combined spinal-epidural81 were reviewed. The remaining 116 procedures were performed in studies reporting a mixture of both spinal and epidural anesthetics. All but one neuraxial procedure was performed in the obstetric population.83 Patients in some studies received treatment with desmopressin or VWF/factor VIII concentrates before administration of neuraxial anesthesia; however, important details were missing from each. Authors either did not specify which patients received treatment81-92 or they did not publish a replacement target.82,83,85,86 Overall, neuraxial anesthesia was performed at VWF levels ranging from 10 IU/dL13 to 198 IU/dL83 and factor VIII levels ranging from 38 IU/dL13 to 249 IU/dL84 without bleeding complications. Only one study reported VWF and factor VIII levels at time of neuraxial catheter removal: 136 IU/dL and 100 IU/dL, respectively.83

Among eight narrative reviews,17,18,63,64,77,87-89 and one systematic review,13 five studies recommended a VWF and factor VIII threshold of 50 IU/dL for placement of neuraxial anesthetics.18,63,77,82,89 Three studies stated that neuraxial anesthesia was appropriate if VWF and factor VIII levels were “normalized.”17,64,87 One study suggested that these procedures are contraindicated regardless of VWF and factor...
### TABLE 4  Studies with data relevant to use of neuraxial anesthesia in von Willebrand disease

| Study                     | Design           | Type of procedure | Type of neuraxial anesthesia | Sample size, No. | Type | Before administration of neuraxial anesthetic | Before removal of neuraxial anesthetic |
|---------------------------|------------------|-------------------|-------------------------------|------------------|------|---------------------------------------------|---------------------------------------|
| Amorde et al (2011)       | Case report      | Obstetric         | Epidural                      | 1                | 2    | N/A                                         | N/A                                   |
| Breivik et al (2018)      | Narrative review | Surgery           | Unspecified                   | N/A              | All  | N/A                                         | N/A                                   |
| Cata et al (2009)         | Case report      | Obstetric         | Spinal                        | 1                | 2    | N/A                                         | N/A                                   |
| Chi et al (2009)          | Retrospective cohort | Obstetric     | Unspecified                   | 12               | 1; 2 | Type 1 41; Type 2 72                        | N/A                                   |
| Choi & Brull (2009)       | Systematic review | Obstetric         | Unspecified                   | 74               | All  | 10                                          | N/A                                   |
| Chow et al (2011)         | Narrative review | Obstetric         | Unspecified                   | N/A              | All  | N/A                                         | N/A                                   |
| Demers et al (2018)       | Narrative review | Obstetric         | Combined spinal-epidural      | N/A              | 1    | N/A                                         | N/A                                   |
| Hara et al (2009)         | Case report      | Surgery           | Epidural                      | 1                | 1    | 198                                         | 136                                   |
| Kailash & Wilkerson (2009)| Case report      | Obstetric         | Epidural                      | 1                | 1    | 99                                          | N/A                                   |
| Katz & Beilin (2015)      | Narrative review | Obstetric         | Unspecified                   | N/A              | All  | N/A                                         | N/A                                   |
| Kazi et al (2018)         | Case report      | Obstetric         | Spinal                        | 1                | Unspecified | 64                                      | N/A                                   |
| Lipe et al (2011)         | Narrative review | Obstetric         | Unspecified                   | N/A              | All  | N/A                                         | N/A                                   |
| Malina et al. (2015)      | Retrospective cohort | Obstetric     | Unspecified                   | 22               | All  | N/A                                         | N/A                                   |
| Moen & Iresedt (2008)     | Narrative review | Obstetric         | Unspecified                   | N/A              | All  | N/A                                         | N/A                                   |
| Pavord et al (2017)       | Narrative review | Obstetric         | Unspecified                   | N/A              | All  | N/A                                         | N/A                                   |
| Schuitemaker Requena et al (2010) | Case report | Obstetric         | Combined spinal-epidural      | 1                | 1    | 88                                          | N/A                                   |
| Sood et al (2010)         | Prospective cohort | Obstetric         | Unspecified                   | 8                | 1    | 128                                         | N/A                                   |
| Thornton & Douglas (2010) | Narrative review | Obstetric         | Unspecified                   | N/A              | All  | N/A                                         | N/A                                   |
| Yousuf et al (2017)       | Retrospective cohort | Obstetric     | Epidural                      | 12               | All  | N/A                                         | N/A                                   |

N/A, not applicable; VWF, von Willebrand factor.

VIII levels, without providing rationale for this recommendation. Recommendations were made with data from observational studies, review articles, or were generated from expert opinion. One observational study was cited in the recommendations of two review articles.

### 3.7 Factor VII deficiency

Four studies of patients with factor VII deficiency were identified, all of which described obstetric patients receiving neuraxial analgesia for labor and delivery. One case report and two small retrospective cohort studies described nine neuraxial procedures, not specifying between spinal and epidural anesthetics. There were no reports of spinal or epidural hematoma. No studies reported the factor VII level before administration of neuraxial anesthesia or at the time of catheter removal.

In the single narrative review identified, neuraxial anesthesia was recommended only in mild to moderate factor VII deficiency when “adequate” factor replacement therapy has been provided. Authors did not specify what factor VII level would constitute adequate replacement. These conclusions were made on the basis of expert opinion.

### 3.8 Hemophilia A (including carriers)

We extracted data from 11 studies related to hemophilia A and neuraxial anesthesia, which are summarized in Table 5. These studies included three case reports/case series.
TABLE 4

| Study Design                        | Type of anesthesia | Type 1 | Type 2 | Type 3 |
|-------------------------------------|--------------------|--------|--------|--------|
| Yousuf et al. (2017)                | Narrative review   | Obstetric | N/A    | N/A    |
| Sood et al. (2010)                  | Obsteic             | N/A    | N/A    | N/A    |
| Schuitemaker Requena                |                    | N/A    | N/A    | N/A    |
| Pavord et al. (2017)                |                    | N/A    | N/A    | N/A    |
| Moen & Iresedt                      |                    | N/A    | N/A    | N/A    |
| Malina et al. (2015)                |                    | N/A    | N/A    | N/A    |
| Lipe et al. (2011)                  |                    | N/A    | N/A    | N/A    |
| Kazi et al. (2018)                  |                    | N/A    | N/A    | N/A    |
| Katz & Beilin (2015)                |                    | N/A    | N/A    | N/A    |
| Hara et al. (2009)                  |                    | N/A    | N/A    | N/A    |
| Demers et al. (2018)                |                    | N/A    | N/A    | N/A    |
| Chow et al. (2011)                  |                    | N/A    | N/A    | N/A    |
| Choi & Brull (2009)                 |                    | N/A    | N/A    | N/A    |
| Chi et al. (2009)                   |                    | N/A    | N/A    | N/A    |
| Cata et al. (2009)                  |                    | N/A    | N/A    | N/A    |
| Amorde et al. (2011)                |                    | N/A    | N/A    | N/A    |

Minimum factor VIII level reported without spinal/epidural hematoma (IU/dL)

| Before administration of neuraxial anesthetic | Before removal of neuraxial anesthetic | Minimum safe VWF threshold proposed (IU/dL) | Minimum safe factor VIII threshold proposed (IU/dL) |
|-----------------------------------------------|---------------------------------------|---------------------------------------------|--------------------------------------------------|
| N/A                                           | N/A                                   | 50                                          | 50                                               |
| N/A                                           | N/A                                   | Usually contraindicated                      | N/A                                              |
| N/A                                           | N/A                                   | N/A                                         | N/A                                              |
| Type 1 95; Type 2 225                         | N/A                                   | N/A                                         | N/A                                              |
| 38                                            | N/A                                   | 50                                          | Remove as soon as possible                       |
| N/A                                           | N/A                                   | "Normal" value                              | If coagulation is "normal"                       |
| N/A                                           | N/A                                   | 165                                         | 50                                               |
| N/A                                           | N/A                                   | 249                                         | Remove immediately                              |
| N/A                                           | N/A                                   | 79                                          | N/A                                              |
| N/A                                           | N/A                                   | 50                                          | N/A                                              |
| N/A                                           | N/A                                   | N/A                                         | N/A                                              |
| N/A                                           | N/A                                   | "Normal" value                              | N/A                                              |
| N/A                                           | N/A                                   | 176                                         | 50                                               |
| N/A                                           | N/A                                   | 134                                         | N/A                                              |
| N/A                                           | N/A                                   | N/A                                         | N/A                                              |

and two retrospective cohort studies. In total, 10 neuraxial anesthetic procedures were described in patients with hemophilia A, and the remaining 12 procedures were performed for hemophilia A carriers during labor/delivery. A systematic review analyzed an additional 54 neuraxial procedures in patients with hemophilia A or B, which were performed for a variety of indications. These authors did not specify how many patients with hemophilia A received neuraxial anesthesia. In total, there were two epidural anesthetics and one spinal anesthetic. The remaining procedures did not specify between spinal or epidural techniques. No epidural or spinal hematomas were reported.

Few studies published factor VIII values before neuraxial anesthesia administration. One case report described uneventful spinal anesthesia for a hemophilia A carrier with a factor VIII level of 76 IU/dL. Another retrospective chart review reported successful neuraxial procedures in 10 female carriers of hemophilia A, the lowest factor level at which anesthesia was placed being 78 IU/dL. Neuraxial procedures were supported by factor VIII replacement in four studies, however, only one repeated a factor VIII level after replacement and before neuraxial anesthesia. Only published a factor VIII replacement target; however, the author of this case report did not repeat a factor VIII level after replacement, and it was not clear if their target value of >50 IU/dL was reached. Epidural catheters were removed either as soon as possible after use or when factor levels were >50 IU/dL.

Five narrative reviews and one systematic review were located. The proposed minimum factor VIII value for insertion of a neuraxial anesthetic was 50 IU/dL in all reviews except one, which suggested that neuraxial blockade was generally...
### TABLE 5  Studies with data relevant to use of neuraxial anesthesia in hemophilia A

| Study                  | Study design     | Type of procedure | Type of neuraxial anesthesia | Sample size, No. | Minimum factor VIII level reported without spinal/epidural hematoma (IU/dL) | Minimum safe factor VIII threshold proposed (IU/dL) |
|------------------------|------------------|-------------------|------------------------------|------------------|-----------------------------------------------------------------------------|-----------------------------------------------------|
| Breivik et al (2018)   | Narrative review | Surgery           | Unspecified                  | N/A              | N/A                                                                         | N/A                                                                 |
| Chi et al (2009)       | Retrospective cohort | Obstetric       | Unspecified                  | 10               | 78                                                                          | N/A                                                                 |
| Choi & Brull (2009)    | Systematic review | Obstetric & surgery | Unspecified                  | 54               | >50                                                                         | 50                                                                 |
| Chow et al (2011)      | Narrative review | Obstetric         | Epidural                     | N/A              | N/A                                                                         | N/A                                                                 |
| Eason & Wight (2009)   | Case report      | Obstetrics        | Spinal                       | 1                | 76                                                                          | N/A                                                                 |
| Finzer & Lawrence (2016)| Case report     | Surgery           | Epidural                     | 1                | 182                                                                         | N/A                                                                 |
| Katz & Beilin (2015)   | Narrative review | Obstetric         | Unspecified                  | N/A              | N/A                                                                         | 50                                                                 |
| Lacalle et al (2015)   | Retrospective cohort | Surgery        | Unspecified                  | 9                | N/A                                                                         | N/A                                                                 |
| Pavord et al (2017)    | Narrative review | Obstetric         | Unspecified                  | N/A              | N/A                                                                         | 50                                                                 |
| Skatvold (2012)        | Case report      | Obstetric         | Epidural                     | 1                | N/A                                                                         | N/A                                                                 |
| Thornton & Douglas (2010)| Narrative review | Obstetric       | Unspecified                  | N/A              | N/A                                                                         | N/A                                                                 |

N/A, not applicable.
contraindicated in patients with hemophilia A irrespective of factor VIII activity level. No evidence was provided to support this recommendation. Three reviews commented on thresholds for removal of epidural catheters, two recommended a factor VIII level of >50 IU/dL,73-75 and one stated that “normal” factor VIII levels were required.64 Recommendations were made on the basis of observational data,18,63,64,69 review articles,21,64 or expert opinion.18,21,63,64,88 There were no duplicate citations.

3.9 Hemophilia B (including carriers)

Eight studies of hemophilia B and neuraxial anesthesia were reviewed.12,18,63,64,77,98,99,101 Two retrospective cohort studies described six neuraxial procedures in individuals with hemophilia B and carriers in both obstetric and nonobstetric settings.79,98 Neither study specified the type of neuraxial anesthesia administered. A systematic review described an additional 54 neuraxial procedures, which were performed on patients with either hemophilia A or B but did not specify how many patients with hemophilia B received neuraxial anesthesia.13 Only one study published a factor IX level before a neuraxial procedure, reporting a hemophilia B carrier with a factor IX value of 37 IU/dL before obstetric analgesia.79 Patients in three studies received factor IX replacement13,79,98; however, none of the studies published factor IX levels before or after replacement, nor did they provide target values for replacement. No epidural or spinal hematomas were reported.

Among five narrative reviews18,63,64,77,88 and one systematic review,13 the almost universally proposed minimum safe factor IX threshold for placement of neuraxial anesthesia was 50 IU/dL. The only study that did not suggest this threshold advised that neuraxial anesthesia was generally contraindicated in this patient population irrespective of factor IX activity level.88 The authors of this review did not provide any evidence upon which their recommendations were based. Recommendations for catheter removal and the sources of data used were the same as stated above for patients with hemophilia A.

3.10 Factor XI deficiency

Eleven studies relating to neuraxial anesthesia in patients with factor XI deficiency were identified,18,64,77,99,102,103,104 including four case reports/case series99-102 and four retrospective cohort studies,79,94,103,104 In total, 66 neuraxial procedures were performed, all in women for labor analgesia. There were four combined spinal-epidurals99,100 and one spinal procedure.101 The type of neuraxial analgesia was not specified for the remaining procedures. Some women received hemostatic treatment before neuraxial blockade including recombinant factor Xia,79,99 fresh frozen plasma,101,102,104 or tranexamic acid.79,100 Reported data were not comprehensive, as numerous authors did not describe exactly which patients received hemostatic treatment,99,102 and one study100 did not publish factor XI levels after replacement with recombinant factor Xia. Only O’Connor et al99 precisely described pre- and posttreatment factor XI levels, though they did not specify their replacement goal. Overall, neuraxial analgesia was placed at factor XI levels ranging from 5 IU/dL102 to 74 IU/dL.79 No factor XI values were reported at the time of catheter removal. There were no epidural or spinal hematomas.

Of three narrative reviews,18,64,77 two provided recommendations regarding administration of neuraxial anesthesia in this population.64,77 Both stated that bleeding history was the most important factor to consider when deciding to administer neuraxial anesthesia in women with factor XI deficiency. Both reviews advised that any patient with factor XI deficiency and history of excessive bleeding should not receive neuraxial anesthesia. These recommendations were formulated from observational data,64,77 and expert opinion.77 Two studies were cited more than once.64,77

3.11 Fibrinogen disorders

A total of three studies that described neuraxial anesthesia in patients with fibrinogen disorders were reviewed.63,77,105 A single case report described a woman with hypofibrinogenemia (pregnancy fibrinogen antigen 0.40 g/L) who received uneventful epidural analgesia for labor and delivery.105 However, this report did not provide quantitative or qualitative fibrinogen values at the time of neuraxial administration or removal.

Both of the narrative reviews that were analyzed stated that neuraxial anesthesia should be avoided unless adequate fibrinogen replacement has been confirmed, though neither review provided hemostatic levels that would denote “adequate” replacement.63,77 There was no discussion of neuraxial catheter removal in either study. One review made recommendations based on data from another review article63 and the other’s recommendations were based on expert opinion.77

3.12 Factor XIII deficiency

We identified two narrative reviews63,77 on the topic of factor XIII deficiency in obstetric analgesia. One paper stated that neuraxial anesthesia is contraindicated in factor XIII deficiency, a recommendation based on expert opinion.63 According to the authors of the second study, neuraxial anesthesia should be avoided in patients with severe deficiencies but may be safe if factor XIII levels are adequately replaced.77 However, these authors did not specify which factor XIII values would constitute “severe deficiency” or “adequate replacement.” These recommendations were based on expert opinion. No comments were provided regarding removal of neuraxial anesthesia.
3.13 | Potential risk of bias

We analyzed 36 review articles, among which only 5% were systematic reviews. Among the two systematic reviews, only one was a review of prospective studies. Of the 55 nonreview studies, 5% featured a prospective design, 31% had a well-defined population, and 7% included an analysis of association between the laboratory parameter and risk of hematoma.

4 | DISCUSSION

We reviewed 91 studies describing 2047 neuraxial procedures performed on patients with a variety of common and uncommon hemorrhagic disorders and tendencies. Spinal and epidural hematomas were rarely reported, as only 16 cases were described overall (Table 3). Case reports detailed spinal or epidural hematomas in three women with hypertensive disorders of pregnancy and platelet counts between 71 × 10^9/L and 93 × 10^9/L. Lagerkranser summarized all reports of spinal and epidural hematomas secondary to neuraxial anesthesia from 1994 to 2015. This study described a multitude of personal and procedural factors that increased risk for complications of neuraxial blockade, including 13 cases of local hematoma associated with thrombocytopenia. Six of these cases occurred in patients with platelet counts <150 × 10^9/L, and seven hematomas developed in patients with platelet counts <80 × 10^9/L. However, in this review, we described many uneventful neuraxial procedures performed for individuals with thrombocytopenia at much lower platelet counts. This discrepancy suggests that other, undescribed variables may have contributed to the increased risk of spinal and epidural hematoma in these individuals. These risk factors may include spinal disorders, renal insufficiency, anticoagulant use, and procedural factors, including multiple attempts or use of larger-sized needles. It is also important to consider how the etiology of thrombocytopenia might modify the risk of local hematoma. For example, platelet function is typically thought to be preserved in immune thrombocytopenia but not in platelet function disorders, which may also be associated with a similar degree of thrombocytopenia but an elevated bleeding risk. Finally, risk of local hematoma is also likely moderated by the type of neuraxial anesthesia administered, with epidural anesthesia considered at higher risk for bleeding than spinal anesthesia.

Our study had some important limitations. First, our search strategy was not peer reviewed. Additionally, most studies we reviewed lacked clarity in how authors differentiated related hemorrhagic disorders; thus, data were often challenging to extract into the appropriate category. Diminishing the quality of our data further was the fact that many review papers we analyzed included studies...
that were also included individually within our scoping review. Every effort was made to exclude conclusions that were made on the basis of data already presented separately in the scoping review; however, some duplication may still have occurred. Finally, as a large proportion of our data were published in the form of case reports, case series, or very small observational studies, these data are vulnerable to publication bias. This may have skewed our results toward extreme cases and may not accurately reflect hematologic laboratory thresholds that are used more commonly in clinical practice.

As our data revealed, there are many significant gaps in our understanding of the risk of spinal and epidural hematoma in individuals with single preexisting hemorrhagic disorders and tendencies (Table 6). These gaps may be divided into four large categories: population gaps, data gaps, evidence quality gaps, and treatment uncertainties.

The majority of studies we reviewed examined neuraxial anesthesia in obstetric populations, resulting in very limited data from men and from women in nonobstetric settings. Since pregnancy induces significant physiologic pro-hemostatic changes, any conclusions developed with data from the obstetric population has limited validity in other settings, such as nonpregnant patients, and should be interpreted with caution.

All of the hemorrhagic disorders/tendencies we examined had gaps in their respective bodies of literature. These gaps were either due to a significant paucity of studies overall or gaps in data presented by individual studies. Thrombocytopenias, including ITP, gestational thrombocytopenia, and thrombocytopenia associated with hypertensive disorders of pregnancy, were the most well-characterized disorders in our review, likely due to the fact that they are among the most prevalent hemorrhagic disorders and tendencies in the general population. The remaining hemorrhagic disorders/tendencies were less robustly described. Gaps in individual studies were often significant, including failure to publish important laboratory values before and after hemostatic replacement and/or before administration of neuraxial anesthesia. Target values for hemostatic replacement were also rarely described. Furthermore, authors often failed to accurately report which patients in a cohort received hemostatic replacement or neuraxial anesthesia. Such significant gaps in presented data introduced a high risk of bias into any conclusions that could be developed from this scoping review.

Evidence quality gaps notably included the overwhelming lack of large prospective studies and systematic reviews of prospective studies. The majority of the articles we reviewed were at high risk for bias, as only a small number featured our indicators for low risk of bias. While there was a higher proportion of observational studies that featured well-described populations, few studies included analysis of the association between hematologic laboratory parameters and risk of hematoma. This high risk of potential bias suggests lower-quality evidence within the body of literature we reviewed and reduced the quality of our potential conclusions.

Finally, treatment uncertainties reflected the universal lack of high-quality guidelines found in our scoping review. Where guidelines were available, concordance among the entire body of reviewed literature was often low and recommendations were rarely evidence based. Furthermore, guidance statements were often vague and recommended that neuraxial anesthesia is safe if replacement is “adequate” or coagulation status is “normal.” Many other guideline statements advised neuraxial anesthesia if the benefits outweighed the risks. These statements leave too much to the discretion of the anesthetic provider and do not add further value over clinical judgment.

With such low-quality data, we found that we were unable to provide any true estimates of the risk of neuraxial anesthesia for individuals with preexisting hemorrhagic disorders/tendencies. Similarly, it was not possible to attribute any specific hemostatic or laboratory values to increased risk of spinal or epidural hematoma based on the small number of hematomas we reviewed. At minimum, data from prospective or high-quality retrospective studies would be required to appreciate the potential for increased hemorrhagic complications of neuraxial anesthesia in individuals with preexisting hemorrhagic disorders and tendencies.

5 | CONCLUSION

In conclusion, this scoping review summarized the scant data describing the use of neuraxial anesthesia in patients with single preexisting hemorrhagic disorders and tendencies. We highlighted areas of particularly limited evidence in male populations and non-obstetric settings. There is a glaring need for larger and more rigorously designed and reported prospective studies on this subject. In particular, there is an urgent need for structured, comprehensive recommendations for safe administration and removal of neuraxial anesthesia for individuals with common and uncommon hemorrhagic disorders and tendencies. Until a more robust and rigorous body of literature can be developed, these recommendations must be based on expert consensus.

ACKNOWLEDGMENTS
The authors thank David Lightfoot, Information Specialist at the Health Sciences Library at St. Michael’s Hospital, Toronto, Canada, for assisting with the literature search.

RELATIONSHIP DISCLOSURE
WP, BT, RM, and MF declare no conflicts of interest. MS reports personal fees from Amgen, personal fees from Novartis, outside the submitted work.

AUTHOR CONTRIBUTIONS
WP and MS conceived the article. WP, MF, and MS designed the study. WP and BT screened titles, abstracts, and articles and extracted data. WP performed data analysis and wrote the initial
draft of the article. BT, RM, MF, and MS contributed to critical revision. All authors were responsible for the final approval of the article.

**REFERENCES**

1. Kreppel D, Antoniadis G, Seeling W. Spinal hematoma: a literature survey with meta-analysis of 613 patients. Neurosurg Rev. 2003;26:1-49.

2. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. BMJ. 2000;321(7275):1493.

3. Metmtsoyd S, Sun X, Chiu YL, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. Anesthesiology. 2013;118:1046-1058.

4. Wu CLC, Richman SR, Rowlingson JM, et al. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. Anesthesiology. 2005;103:1079-1088.

5. Liu EHC, Sia ATH. Rates of caesarean section and instrumental vaginal delivery in nulliparous women after low concentration epidural infusions or opioid analgesia: systematic review. BMJ. 2004;328(7453):1410.

6. Li S-L, Wang D-X, Ma D. Epidural hematoma after neuraxial blockade: a retrospective report from China. Anesth Analg. 2010;111:1322-1324.

7. Ruppen WDS, McQuay H, Moore RA. Incidence of epidural hematoma, infection, and neurologic injury in obstetric patients with epidural analgesia/analgesia. Anesthesiology. 2006;105:394-399.

8. Dunkley SM, Russell SJ, Rowell JA, et al. A consensus statement on the management of pregnancy and delivery in women who are carriers of or have bleeding disorders. Med J Australia. 2009;191:460-463.

9. Leffert LR, Dubois HM, Butwick AJ, Carvalho B, Houle TT, Landau R. Neuraxial anesthesia in obstetric patients receiving thromboprophylaxis with unfractionated or low-molecular-weight heparin: a systematic review of spinal epidural hematoma. Anesth Analg. 2017;125:223-231.

10. Vandermeulen EP, Aken HV, Vermylen J. Anticoagulants and spinal epidural anesthesia. Anesth Analg. 1994;79:1165-1177.

11. Lagerkranse M. Neuraxial blocks and spinal haematoma: review of 166 case reports published 1994-2015. Part 1: Demographics and risk-factors. Scand J Pain. 2017;15:118-129.

12. Bos EMEH, de Queueri M, Vandertop WP, Kalkman GJ, Hollmann MW, Lirk P. Haematoma and abscess after neuraxial anaesthesia: a review of 647 cases. British J Anaesth. 2018;120:693-704.

13. Choi S, Brull R. Neuraxial techniques in obstetric and non-obstetric patients with common bleeding diatheses. Anesth Analg. 2009;109:648-660.

14. Tricco AC, Lillie E, Zarin W, et al. Prisma extension for scoping reviews (PRISMA-Scr): checklist and explanation. Ann Intern Med. 2018;169:467-473.

15. American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 207: Thrombocytopenia in pregnancy. Obstetrics Gynecol. 2019;133:e181-e193.

16. Bailey LJ, Shehata N, De France B, Carvalho JCA, Malinowski AK. Obstetric neuraxial anesthesia at low platelet counts in the context of immune thrombocytopenia: a systematic review and meta-analysis. Canadian J Anesth. 2019;66(11):1396-1414.

17. Moen V, Irestedt L. Neurological complications following central neuraxial blockades in obstetrics. Curr Opin Anaesthesiol. 2008;21:275-280.

18. Chow L, Farber MK, Camann WR. Anaesthesia in the pregnant patient with hematologic disorders. Hematol Oncol Clin N Am. 2011;25:425-443.

19. Myers B, Truelove E. Diagnosis and management of thrombocytopenia in pregnancy. Fetal Mater Med Rev. 2011;22:144-167.

20. Harrop-Griffiths W, Cook T, Gill H, et al. Regional anaesthesia and patients with abnormalities of coagulation: the Association of Anaesthetists of Great Britain & Ireland The Obstetric Anaesthetists’ Association Regional Anaesthesia UK. Anaesthesia. 2013;68:966-972.

21. Pavord S. Immune thrombocytopenia in pregnancy. Hematology. 2016:21:10.

22. Ozelo MC, Colella MP, de Paula EV, do Nascimento ACKV, Villaca PR, Bernardo WM. Guideline on immune thrombocytopenia in adults: Associacao brasileira de hemotologia, hemoterapia e terapia celular. Project guidelines: Associacao medica brasileira - 2018. Hematol Transfus Cell Ther. 2018;2018(40):50-74.

23. Frenk VCV, Shankar KB. Regional anesthesia in parturients with low platelet counts. Can J Anaesth. 2005;52:114.

24. Bellin Y, Zahn J, Comerford M. Safe epidural analgesia in thirty parturients with platelet counts between 69,000 and 98,000 mm<sup>3</sup>. Anesth Analg. 1997:85:385-388.

25. Ciobanu AMCS, Campob A, Peltecu G, Panaitescu AM. Thrombocytopenia in pregnancy. Maedica (Bucur). 2016;11:55-60.

26. Voulgaropoulos DS, Palmer CM. Coagulation studies in the pre-eclamptic parturient: a survey. J Clin Anesth. 1993;5:99-104.

27. Gatt SP. Clinical management of established pre-eclampsia and gestational hypertension: an anesthetist’s perspective. Bailliere’s Best Pract Res Clin Obstet Gynaecol. 1999;13:95-105.

28. Botfield C, Howell P. The use of spinal anaesthesia in severe pre-eclampsia. Fetal Mater Med Rev. 2001;12:67-79.

29. Mandal NG, Surapaneni S. Regional anaesthesia in pre-eclampsia: advantages and disadvantages. Drugs. 2004;64:223-236.

30. Gogarten W. Preeclampsia and anaesthesia. Curr Opin Anaesthesiol. 2009;22:347-351.

31. Turner JA. Diagnosis and management of pre-eclampsia: an update. Int J Womens Health. 2010;2:327-337.

32. Henke VG, Bateman BT, Leffert LR. Spinal anaesthesia in severe preeclampsia. Anesth Analg. 2013;117:686-693.

33. Bajwa SJS, Kulshrestha A, Bajwa SK. Labour analgesia in pre-eclampsia: the current perspectives. Anaesth Pain Intens Care. 2014;18:419-423.

34. Devroe S. Preeclampsia and the anesthetist. Reg Anesth Pain Med. 2016;41:e11-e13.

35. Peer P, Bhatia K. Pre-eclampsia and the anesthetist. Anaesth Intensive Care Med. 2016;17:331-336.

36. Schindler MGS, Isert P, Morgan D, Cheung A. Thrombocytopenia and platelet functional defects in pre-eclampsia: implications for regional anaesthesia. Anaesthesia Intensive Care. 1990;18:169-174.

37. Nafiu OO, Salama R, Elebge EO. Anaesthetic dilemma: spinal anaesthesia in an eclamptic patient with mild thrombocytopenia and an “impossible” airway. Int J Obstet Anesth. 2004;13:110-113.

38. Yuen TSKJ, Tan IK. Spinal haematoma following epidural anaesthesia in a patient with eclampsia. Anaesthesia. 1999;54:350-354.

39. Ezri T, Abouleish E, Lee C, Evron S. Intracranial subdural hematoma following dural puncture in a parturient with HELLP syndrome. [hematome sous-dural intracranien post-ponction duree chez une parturiente atteinte du syndrome HELLP]. Canadian J Anesth. 2002;49:820-823.

40. Crosby E. Obstetrical anaesthesia for patients with the syndrome of haemolysis, elevated liver enzymes and low platelets. Canadian J Anesth. 1991;38:227-233.
85. Cata JP, Hanna A, Tetzlaff JE, Bishai A, Barsoum S. Spinal anesthesia for a cesarean delivery in a woman with type-2m von Willebrand disease: case report and mini-review. *Int J Obstet Anesth.* 2009;18:276-279.

86. Kazi S, Malinowski AK, Whitehead C, et al. Successful management of pregnancy with severe von Willebrand disease in a Jehovah's Witness with recombinant von Willebrand factor. *Blood.* 2018;129(suppl 1):5077.

87. Demers C, Derzko C, David M, Douglas JN. 163-gynaecological and obstetric management of women with inherited bleeding disorders. *J Obstetrics Gynaecol Canada.* 2018;40:e91-e103.

88. Breivik H, Norum H, Fenger-Eriksen C, Alahuhta S, Vigfusson G, Thomas O, et al. Reducing risk of spinal haematoma from spinal and epidural pain procedures. *Scand J Pain.* 2018;18:129-150.

89. Lipe BC, Dumas MA, Ornstein DL. Von Willebrand disease in pregnancy. *Hematol Oncol Clin N Am.* 2011;25:335-358.

90. Sood SL, James AH, Bolgiano D, et al. Pregnancy in type 1 von Willebrand disease: a prospective study of VWF levels and risk factors for bleeding. *Blood.* 2010;116(21):1410.

91. Malina M, Abdul-Kadir R, Pollard D, Siebert M, Halimeh S. Severe von Willebrand disease (VWD) in pregnancy and childbirth: a case series. *Thromb Res.* 2015;135:583.

92. Yousuf S, Cohen AJ, Eris E, Astsaturov A. A single institutional study on pregnancy outcomes in patients with von Willebrand disease. *Blood.* 2017:130:1086.

93. O’Rourke N, Lee C, Kodali BS, Harnett M. Thromboelastographic monitoring of the efficacy of recombinant factor VIIa administration in a parturient with factor VII deficiency [3]. *Canadian J Anesth.* 2006;53:528-529.

94. Luzi ATL, Quinty F, Iacobelli S, Winer A. Maternal rare bleeding disorders: a case series in a tertiary care maternity department. *Int J Obstetric Anesth.* 2017;31:550.

95. Skatvold S. Placement of labor epidural in hemophilia A carrier. *Int Student J Nurse Anesth.* 2012;11:15-8.

96. Finzer B, Lawrence J. Thoracic epidural analgesia in patient with hemophilia a for video-assisted thoracoscopic surgery (VATS) lobectomy. *Reg Anesth Pain Med.* 2016:41.

97. Eason S, Wight W. Caesarean section in a patient with mediastinal B-cell lymphoma and haemophilia a. *Int J Obstetric Anesth.* 2009;18:551.

98. Lacalle L, Espinosa N, Segura A, Calvo JM, Fernandez N, Delgado P. Surgical management of elective surgery in patients with mild haemophilia from a single institution. *Haematologica.* 2015;100:670-671.

99. O’Connor M, Graham B, Turner DP, Ward S. Use of thromboelastography in a patient with haemophilia C undergoing caesarean section with regional anaesthesia. *Reg Anesth Pain Med.* 2012;37:E308.

100. Setty S, Reddell A, England A, Gomez K, Kadir R. The role of recombinant factor VIIa for obstetric block in women with severe factor XI deficiency. Case report. *Rev Bras Anesthesiol.* 2010;60:176-180.

101. Modolo NSP, De Azevedo VLF, Santos PSS, Rosa ML, Corvino DR, Castro Alves LJS. Anesthetic strategy for cesarean section in a patient with factor XI deficiency. *Rev Bras Anesthesiol.* 2011;61:906-909.

102. Singh A, Harnett MJ, Connors JM, Camann WR. Factor XI deficiency and obstetrical anesthesia. *Anesth Analg.* 2009;108:1882-1885.

103. Kadir RA, Lee CA, Sabin CA, Pollard D, Economides DL. Pregnancy in women with von Willebrand’s disease or factor XI deficiency. *BJOG.* 1998;105:314-321.

104. Reuveni A, Orbach-Zinger S, Eidelman LA, Ginosar Y, Isocvich A. Peripartum anesthetic management of patients with factor XI deficiency. *J Perinat Med.* 2014;42:295-300.

105. Eden-Green B, Fleming I. Case presentation: individualised decision-making based on thromboelastography in a patient with inherited hypofibrinogenaeia. *Reg Anesth Pain Med.* 2017;42:e194.

SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Peterson W, Tse B, Martin R, Fralick M, Sholzberg M. Evaluating hemostatic thresholds for neuraxial anesthesia in adults with hemorrhagic disorders and tendencies: A scoping review. *Res Pract Thromb Haemost.* 2021;5:e12491. [https://doi.org/10.1002/rth2.12491](https://doi.org/10.1002/rth2.12491)