"Safe" Cutoff for Platelet Count Prior to Interlaminar Epidural Access

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Myth: An absolute platelet count exists above which it is safe to proceed with interlaminar epidural access.

Fact: An evidence-based absolute "safe" platelet count value does not exist. The decision to proceed in the setting of thrombocytopenia should be based on patient-specific factors and overall bleeding risk.

Thrombocytopenia is classified as a platelet count below the lower limit of normal (i.e., <150,000/microL [150 x 109/L] for adults). The safety of epidural access procedures in thrombocytopenic patients is unclear due to the potential for increased risk of epidural hematoma and permanent neurologic injury. There is a paucity of interventional pain literature to guide clinical decision-making including identification of thrombocytopenic patients prior to procedures. Data can be cautiously extrapolated from other thrombocytopenic populations, including parturients undergoing labor neuraxial anesthesia [1-3] and oncologic patients undergoing lumbar punctures [4]. Ultimately, absolute platelet count does not necessarily correlate with platelet function, and consultation or additional testing may be indicated to evaluate function. It also stands to reason that needle size (gauge) may affect risk with interlaminar epidural access, but limited data is available to provide insight on the relative risks of specific needle sizes. Additional caution may be warranted with spinal cord stimulation lead placement in patients with thrombocytopenia due to the larger needle size for interlaminar access and maneuvering of leads within the epidural space.

Data on "safe" platelet values for epidural access procedures are most robust in the obstetric anesthesia literature. It is important to be cognizant, however, that the etiologies of thrombocytopenia and baseline population characteristics are markedly distinct between parturients and outpatient pain patients. A mixed retrospective observational and systematic review study from the Multicenter Perioperative Outcomes Group (MPOG) database was conducted by Lee *et al.* to estimate the risk of epidural hematoma in parturients with platelet counts < 100,000 who underwent a neuraxial procedure including epidural, spinal, and combined spinal-epidural analgesia/anesthesia [1]. Patients who had an underlying coagulopathy or who were taking an antiplatelet medication were excluded. A total of 573 patients were identified and combined with data from a systematic review of existing literature for a total of 1,524 patients. Of these, 53 patients had platelet counts between 50,000 and 69,000, and 12 patients had a platelet count between 0 and 49,000. No cases of epidural hematomas requiring surgical decompression were identified.

In both the obstetric and oncologic literature, upper bounds of statistical confidence of a zero proportion are calculated with the "Rule of 3" due to a lack of identified events [7]. The "Rule of 3" states that if a specified event did not occur in a sample with n subjects, then the interval from 0 to 3/n is a 95% confidence interval for the rate of occurrences in the population. The Lee *et al.* study calculated a 95% confidence interval (CI) upper bound for risk of a clinically significant epidural hematoma of 11% for platelet counts between 0-49,000, 3% for 50,000 to 69,000, and 0.2% for 70,000 to 100,000. As the majority of cases evaluated had platelet counts >70,000, the calculated CI is most robust at this level. The data are less clearly defined for counts <70,000 given the limited population evaluated. The authors' methods only identified patients who reportedly underwent decompressive laminectomies due to epidural hematomas; and, therefore, were unable to identify epidural hematomas that were non-operatively managed.

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These data built on prior smaller cohort studies in comparable patient populations that yielded similar upper bounds of statistical confidence [5,6]. A multicenter retrospective cohort study of 173 parturients with thrombocytopenia (< 100,000) was conducted by Goodier *et al.*, and the data were then aggregated with 326 cases from previous studies for a final sample of 499. The estimated upper 95% CI for probability of spinal-epidural hematoma was 0.6%. A subsequent single center retrospective study was conducted by Bernstein *et al.* of 256 parturients with platelet counts <100,000. This was combined with 173 patients from the Goodier *et al.* study and the 326 prior published cases for a calculated upper 95% CI of 0.4%. Meaningful analysis was not possible for platelet counts < 50,000 given the very small number of patients.

Further data on "safe" platelet values for neuraxial techniques are available in the oncologic population undergoing lumbar punctures. Again, extrapolation to a general pain population is applied cautiously. A systematic review of the MEDLINE database was conducted by Ho *et al.* in which eight case series were identified where a total of 13,975 lumbar punctures were performed with varying degrees of thrombocytopenia. Despite a number of "bloody taps", no cases of clinically apparent spinal hematoma were reported. Thus, Ho *et al.* calculated an upper CI limit of 0.17% based on 1,747 patients who underwent lumbar punctures with a platelet count range between 51-100K (×109/L).

In contrast to the obstetric and oncologic literature, which used the "Rule of 3" due to lack of identified events, a systematic review published in 2020 identified 33 reported cases of spinal epidural hematoma from an aggregated 7,509 thrombocytopenic patients (less than 100,000 × 106/L) who underwent lumbar neuraxial procedures [3]. The authors searched multiple databases for patients who received a neuraxial procedure with platelet count less than 100,000 × 106 /L. Neuraxial procedures included lumbar puncture, spinal or epidural or combined spinal-epidural (CSE) analgesia/anesthesia, and epidural catheter removal. Of the 33 cases identified, 25/33 (75.8%) were lumbar punctures; 6/33 (18.2%) spinal analgesia/anesthesia; 1/33 (3%) an epidural; and 1/33 (3%) an epidural catheter removal. Within the platelet count ranges of 1,000–25,000; 26,000–50,000; 51,000–75,000; and 76,000–99,000, there were 14, 6, 9, and 4 spinal epidural hematomas, respectively. The authors identified an inflection point and narrow CIs near a platelet count of 75,000 or above. Between a platelet count of 75,000–99,999, the estimated event rate was 0.097% [95% CI: 0.002% - 0.19%)]. On the basis of this review, the Society for Obstetric Anesthesia and Perinatology released a consensus statement suggesting that if the platelet count is ≥70,000 × 106/L, there is likely to be a low risk of spinal epidural hematoma (class IIa and level C-LD) [8]. This guidance applies to obstetric patients with thrombocytopenia secondary to gestational thrombocytopenia, immune thrombocytopenia (ITP), and hypertensive disorders of pregnancy in the absence of other risk factors. It is important to again acknowledge that the etiology of thrombocytopenia in parturients is physiologically distinct from outpatient pain patients.

Literature is also limited with respect to the utility of platelet transfusions for thrombocytopenia prior to neuraxial interventions such as lumbar punctures or epidural anesthesia. A 2018 Cochrane review identified only three retrospective cohort studies that contained participants who did and did not receive platelet transfusions prior to lumbar punctures; only two of which reported outcomes separately for participants who did and did not receive platelet transfusion [9]. Both studies had methodological limitations including retrospective design, small sample size, and non-standardized reporting of results. No evidence was found on which to base an assessment of the appropriate platelet transfusion threshold before insertion of a lumbar puncture needle or epidural catheter.

The utility of platelet transfusions for thrombocytopenia has also been called into question in the interventional radiology literature [10]. A 2017 retrospective cohort study identified 2,060 patients with thrombocytopenia (≤100 x 109/L) undergoing invasive image-guided interventions with 203 patients receiving preprocedural platelet transfusion. No significant difference was observed in bleeding complications in terms of postprocedural red blood cell transfusion requirements. Incidence of epidural hematoma was not specifically evaluated in this study and may not have been captured if transfusion was not necessary.

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Conclusions and Recommendations

- Coagulation and the coagulation cascade are complex processes, and a multitude of factors and organ systems may affect bleeding risk outside of platelet counts alone.
  - It is important to consider patients' medical histories to ensure appropriateness prior to recommending an epidural access procedure.
- The decision to proceed with interlaminar epidural access in a patient with thrombocytopenia should be based on consideration of risks and benefits including patient-specific factors, procedural factors, and overall bleeding risk.
  - Consultation with a hematologist may be beneficial to guide work-up and pre-procedural management of thrombocytopenia.
- Limited evidence is available to guide the safety of interlaminar epidural access with thrombocytopenia in terms of an absolute platelet count cutoff.
  - Data cautiously extrapolated from alternative patient populations suggest that interlaminar epidural access with platelet counts of at least 70,000 are associated with low risk of epidural hematoma in the absence of coagulopathy and drugs that are capable of inducing platelet dysfunction.
- There is no current evidence that preprocedural transfusion of platelets reduces the risk of epidural hematoma in patients with thrombocytopenia. Routine use is not indicated.

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